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U.S. DEPARTMENT OF COMMERCE / National Bureau of Standards

Implant Retrieval: Material and Biological Analysis

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Implant Retrieval: Material and Biological Analysis

Proceedings of a Conference
Held at the National Bureau of Standards,
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Foreword

Four years ago a symposium on retrieval and analysis of implants was held at the National Bureau of Standards. That symposium dealt exclusively with orthopaedic implants and was designed to bring together manufacturers, orthopaedic surgeons, engineers and others interested in understanding and improving the performance of orthopaedic implants. This second symposium was developed with the same basic purpose but has been broadened in scope to include cardiovascular as well as orthopaedic implants. It is envisaged that the experiences of the one clinical specialty can be translated to the other. The program of this symposium deals mainly with the experience that has been gained in understanding the performance of implants by studying devices that have been removed from patients. However, basic concepts and testing methods have also been included. Their importance cannot be overstressed in improving our understanding of host-implant interactions. The basic issue to be addressed is still: "this is what happens, so let's try to understand how and why." The benefits to be derived from the evaluation of the performance of retrieved implants were succinctly stated by Dr. Victor Frankel five years ago and they are still true today: "The more reliable implant appliances can be made, the greater security and safety the patient will experience." Only through the study of retrieved implants will it be possible to obtain the critical information that will make devices more reliable.

Allan Weinstein
Donald Gibbons
Stanley Brown
William Ruff

September 1980

Preface

This publication contains the proceedings of a Conference on Implant Retrieval: Material and Biological Analysis held at the National Bureau of Standards, Gaithersburg, Maryland, on May 1 and 2, 1980. It also contains a summary of a workshop held the following day in Washington, DC on the subject of Implant Retrieval Programs in current use. The conference and the workshop were sponsored by seven Federal agencies and groups: The National Bureau of Standards; The Food and Drug Administration; the National Institute for Arthritis, Metabolism and Digestive Diseases; the National Heart, Lung and Blood Institute; the Veterans Administration; the National Institute for Handicapped Research; and the American Society for Testing and Materials. The meeting was designed to bring together scientists and engineers, manufacturers, Federal Government representatives and others concerned over the proper design and application of orthopaedic and cardiovascular implants. The objective of the meeting was to review the state-of-the-art in material and biological analysis associated with implant retrieval. Topics considered at the meeting included practices for obtaining and evaluating data concerning implant retrieval as well as discussions of advances in material and biological science relevant to implant retrieval.

The Conference was organized by a steering committee consisting of A. Weinstein, Tulane University, Conference Chairman; J. Black, University of Pennsylvania; P. Brown, ASTM; S. Brown, University of California-Davis; R. Cohen, National Consumer League; A. Fraker, NBS; D. Gibbons, Case Western Reserve University; S. Gordon, NIAMDD; P. Laing, ASTM-F4; B. Morrissey, NBS; V. Nickel, VA; F. Pitlick, NHLBI; W. Ruff, NBS; R. Stromberg, FDA; J. Traub, NIHR. The Committee also acknowledges the very capable assistance of the Conference arrangements staff at NBS, in particular Joanne Lorden and Kathy Stang for their help in carrying out this meeting, as well as substantial contributions of typing and editing work on the part of Joan Marshall and the NML text editing staff.

Abstract

This book contains the proceedings of a conference on implant retrieval and analysis as well as a report on a workshop concerned with implant retrieval systems. Twenty-six invited papers that were presented at the conference are included. Four subject areas are specifically addressed: bulk phenomena, release phenomena, interface phenomena, and information utilization. Implants of both orthopaedic type and cardiovascular type were considered at the conference. Data on the failure modes of implants were presented. Specific consideration of biocompatability problems was included. Several operating data/information systems were described in detail. Recommendations were made in the workshop concerned with uniformity and standardization of information systems dealing with implant retrieval data.

Key words: Analysis; biological; cardiovascular; implants; metals; orthopaedic; polymers; retrieval.

Disclaimer

Certain trade names and company products are identified in order to adequately specify the experimental procedure. In no case does such identification imply recommendation or endorsement by the National Bureau of Standards, nor does it imply that the products are necessarily the best available for the purpose. Views expressed by the various authors are their own and do not necessarily represent those of the National Bureau of Standards.

WELCOME

I am pleased to have this opportunity to welcome all of you to the National Bureau of Standards and to this Conference on Implant Retrieval: Material and Biological Analysis. As many of you may recall, NBS also acted as host for the first Conference on Implant Retrieval about four years ago. It is particularly pleasing to have that opportunity again and to be able to learn of the growth and developments in this important field.

This Conference is sponsored by a number of Federal agencies and organizations. In addition to NBS these include the Bureau of Medical Devices of the FDA, the Veterans Administration, the National Institute of Handicapped Research, the National Heart, Lung and Blood Institute, the National Institute of Arthritis, Metabolism and Digestive Diseases and the American Society for Testing and Materials. The potential importance of the work to be presented here can be demonstrated in part through the recognition by these sponsoring groups of the need for this conference. The Federal Government investment in health-related activities is of course very large. All of the agencies sponsoring this Conference are involved in important aspects of those activities. The findings reported here along with the conclusions you will reach will become an important input to the plans and activities of these agencies and to the entire effort directed toward safe and effective synthetic implants.

I would like to briefly mention some of the involvements that NBS has in its program concerning synthetic implants. Our contributions basically involve measurement methods, standards, and needed data on materials used in implant devices. This information will become the central basis for improved performance and reliability of implant devices. It will be used by implant manufacturers and surgeons, and will benefit the public in many ways. It is our understanding that the lack of comprehensive and acceptable standards for implants is one of the most significant barriers to progress in this field. This is the area where contributions from NBS may form a particularly useful response to the overall need.

The subject for these next two days will be implant retrieval analysis. We all hope to hear of new techniques and new information that have resulted from recent research efforts and studies of retrieved devices. Clearly a unique opportunity is presented by modern techniques of implant retrieval. Fundamentally this involves the ability to learn of the performance and durability of implant devices in actual service. This information can be one of the most significant inputs to the further development of safe and effective implants.

I am pleased that NBS has been instrumental in gathering together the experts in physical and medical science that are involved in this conference. We have always regarded this field of endeavor as a high scientific challenge with even higher rewards in terms of human needs. You have my best wishes for a very successful Conference.

John D. Hoffman
Director
National Measurements Laboratory
National Bureau of Standards

WELCOME

I would like to welcome you to this Conference on Implant Retrieval. We are pleased to be able to join other Federal health agencies and the National Bureau of Standards in co-sponsoring this meeting. Many of the regulatory decisions that we at the FDA must make require sound technical information. This is true, whether we are considering a new product for approval, developing a standard, or attempting to determine if a device on the market is unsafe.

Medical devices can, of course, be tested in laboratories. Nevertheless, the correlation between such examinations--no matter how well one may try to simulate *in vivo* conditions--to their performance in the body is often poor and always suspect. This meeting, at which a variety of personal expertise and experiences will be oriented toward an understanding of the problems associated with the use of devices in humans, is of critical importance to our Bureau. Development of consensus regarding the methods by which data are obtained would be important to us as well as the entire field. In other words, we need the types of information that are included in this program, in both the cardiovascular and orthopedic areas, in order to carry out our mission more effectively. I hope that all of you enjoy this meeting.

Victor Zafra
Acting Director
Bureau of Medical Devices
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CONTENTS

BULK PHENOMENA

THE IN-VIVO PERFORMANCE OF POLYETHYLENE COMPONENTS OF TOTAL JOINT REPLACEMENTS

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The polyethylene components of retrieved total joint replacements are investigated with the scanning electron microscope to assess the degree and causes of wear and other deterioration in vivo. The highly variable performance of the implants, ranging from no observable wear to disintegration of the articular surface, can be associated in some cases with the presence of particles of acrylic cement or bone abrading the articular surface. Severe wear in the absence of such abrasives may originate with the structure of the polyethylene itself, and may be caused by molecular weight degradation during processing: in such cases the primary damage loci are fusion defects in the molded or extruded material.

1. Introduction

The magnitude of the problem posed by the wear of ultrahigh molecular weight polyethylene (UHMWPE), a material used in total joint replacements, has yet to be fully defined. In small volumes, wear debris can be eliminated from the body via the lymph system. In larger amounts, however, particles of UHMWPE wear debris are known to cause giant cell foreign body reactions with a tendency toward scar tissue formation in the articular capsule.[1,2][1] Scar tissue formation can severely reduce joint mobility, which may result in the removal of the prosthesis; or a strong resporptive reaction in the bone may loosen the prosthesis.[1,2]

[1]Figures in brackets indicate the literature references at the end of this paper.

Recent studies [3,4,5,6] both in vivo and in vitro, have demonstrated extreme variability in the wear of total joint prostheses. Variability is generally the greatest problem encountered when analyzing clinically failed prostheses since the physiological forces on joints are different for each patient depending on prosthesis design, patient physiognomy and activity. However, variability in the wear behavior of UHMWPE was also observed for identical conditions in in vitro simulations of prostheses of similar design produced by different manufacturers.[7]

It is commonly believed that a three-body wear mechanism, involving particles of the relatively harder polymethylmethacrylate (PMMA) cement used to fix the prosthesis in the bone, is responsible for the catastrophic wear often observed on the polyethylene articular surface. Three-body abrasion is a problem primarily in knee prostheses. While three-body abrasion is known to occur in hip prostheses, the geometry of the knee is more conducive to entrapping acrylic particles between the articulating surfaces. While three-body wear is a major mode of failure, [1] recent studies have suggested alternate mechanisms which do not involve abrasive schemes yet which can account for the severe wear often observed in failed prostheses.[6,8,9]

As of this date, we have examined 35 total knee prostheses and 15 total hip prostheses, all clinical retrievals, with the scanning electron microscope. While such analysis cannot be, and is not intended to be, exhaustive, it does provide useful insight into the mechanisms responsible for catastrophic material wear and failure of UHMWPE used in total joint replacements.

2. Materials

Fifteen total hip and 35 total knee prostheses were obtained from the Orthopaedics Associates Group of the Robert Breck Brigham Hospital in Boston. The summary of the clinical information for the prostheses is presented in tables 1 and 2. The UHMWPE articulating surfaces were examined using Scanning Electron Microscopy.

3. A Note on Fabrication Techniques Used in Total Joint Prostheses

The UHMWPE components of total joint prostheses are manufactured by low temperature compression molding or extrusion of the powdered polymer. The prostheses can be molded to the final shape or they can be machined from a roughly-shaped block of polymer. This processing strategy is necessary due to the high melt viscosity of UHMWPE. Also, it is commonly thought that such processing minimized thermal and mechanical degradation of the polymer. It has been found, however, that the high melt viscosity of the polymer prevents total consolidation of the UHMWPE powder. Fusion defects which appear as voids have been observed.

Previous scanning electron microscope studies have revealed that the roughly-cylindrical polyethylene powder granules consist of aggregates of smaller spherical particles. These aggregates are held together by virtue of a network of tie chains or fibrils. When the polymer is molded at temperatures low enough to avoid concomitant degradation of these fibrils and of the molecular weight, the particles do not fuse completely.

Table 1. Clinically Failed Hip Prostheses

Prosthesis Number	Design	Time in Service	Patient Age	Patient Sex	Reason for Removal
1	Aufranc - Turner	5 years	-	M	loosening
2	Aufranc - Turner	2 years	-	F	loosening
3	Aufranc - Turner	23 months	-	M	loosening
4	Aufranc - Turner	---	36	F	recurrent dislocation
5	Charnley-Mueller	8 years	-	F	loosening & infection
6	Aufranc - Turner	---	-	F	loosening
7	Charnley-Mueller	5 years	49	F	loosening (both comp.)
8	Aufranc - Turner	26 months	-	F	loosening
9	Aufranc - Turner	5 years	-	M	loosening
10	Aufranc - Turner	20 months	-	F	loosening
11	Aufranc - Turner	unknown	-	F	recurrent dislocation

Table 1. (Cont'd)

Prosthesis Number	Design	Time in Service	Patient Age	Patient Sex	Reason for Removal
12	Aufranc - Turner	23 months	-	M	loosening
13	Charnely-Mueller	8 years	-	F	loosening and infection
14	Charnley (modified)	5 years	-	F	loosening
15	Aufranc - Turner	---	-	F	loosening

Table 2. Clinically Failed Knee Prostheses

Prosthesis Number	Design	Time in Service	Patient Age	Patient Sex	Reason for Removal
1	Geomedic (right)	5 years	71	M	loosening of both components
2	Total Condylar (left)	1.5 years	63	M	limitation of joint mobility and pain
3	Total Condylar (fem) Duo Patella (tib) (left)	8 months	75	M	Varus Deformity, secondary ligamentous laxity
4	Duo Patella (right)	---	85	F	loosening
5	Geomedic (left)	3 years	68	M	pain and swelling
6	Unicondylar (left, medial)	3.5 years	62	F	pain and instability
7	Duocondylar (left)	6 years	57	F	patello-femoral pain
8	Unicondylar (left, medial)	2.5 years	73	F	lateral subluxation
9	Duocondylar (right)	3 years	69	M	loosening of medial component
10	Duo Patella (right)	1 year	68	M	ligamentous laxity and instability
11	Savastano (medial)	4 years	58	F	no loosening
12	Geomedic	26 months	69	F	loose tibial comp.

Table 2. (Cont'd.)

Prosthesis Number	Design	Time in Service	Patient Age	Patient Sex	Reason for Removal
13	Duo Patella	15 months	68	M	slight loosening of femoral comp.
14	Geometric	---	--	-	-----
15	Hinge	---	--	-	-----
16	Duo Patella	10.5 months	65	F	loosening of medial tib. comp.
17	Duo Patella	17 months	60	F	loose tibial comp.
18	Duo Patella	---	--	-	-----
19	Geomedic	3 years	64	F	loose medial tib. piece
20	Geometric	26 months	--	F	loosening
21	Geometric	36 months	--	F	loosening
22	Geometric	11 months	--	F	lateral dislocation
23	Geometric	26 months	--	F	patello-femoral joint degeneration

Table 2. (Cont'd)

Prosthesis Number	Design	Time in Service	Patient Age	Patient Sex	Reason for Removal
24	Duo Patella	8 months	--	F	posterior dislocation
25	Duo Patella	17 months	--	F	loosening
26	Duo Patella	15 months	--	M	failure due to valgus deformity
27	Duocondylar	7.5 months	--	F	posterior dislocation
28	Duocondylar	11 months	--	F	patello-femoral joint degeneration
29	Duocondylar	11 months	--	F	loosening; cement loose in joint
30	Duocondylar	unknown	--	-	loosening
31	Savastano (medial)	52 months	--	F	lateral compartment deterioration, no loosening
32	Savastano	10 months	--	F	pain, range of motion
33	Marmor	11 months	--	M	lateral dislocation
34	Unicondylar	4 months	--	F	posterior dislocation
35	Stabilocondylar	2.5 months	--	F	failure due to valgus deformity

This produces a fusion defect as shown in figure 1.

4. Acrylic Cement and Abrasion

Scanning electron microscopy (SEM) examination of clinically-failed total joint prostheses has revealed the presence of acrylic cement on the UHMWPE articular surfaces. Particles becoming trapped between the articulating surfaces are ground into the surface and become embedded. The embedded particles can be identified in various ways. Most conclusively, X-ray fluorescence may indicate the presence of barium sulfate inclusions which appear as white spots in the acrylic matrix. Fracture planes within acrylic particles are also characteristic. In addition, cement particles are usually found in an abraded region since acrylic is significantly harder than polyethylene. A typical particle of cement embedded in the polyethylene surface is shown in figure 2. The cement particle was identified using energy dispersive X-ray fluorescence analysis. The presence of barium in an analyzed area yields characteristic fluorescence peaks as shown in figure 3. A magnified view of the particle, figure 4, shows the presence of white spots within the cement particle. These are the barium sulfate inclusions in the acrylic.

In certain cases, particles embedded in the surface appear to be acrylic cement yet X-ray fluorescence yields the absence of a barium peak. One such example appears in figure 5. This is a close-up of the particle of cement. The spherical cavities apparently were left when incompletely-cured acrylic powder pulled out of the matrix. The questionable identity of this particle is confirmed by the clear fracture planes shown in the general view of the particle, shown in figure 6. The identity is again confirmed by the presence of abrasion in the material surrounding the particle.

Acrylic cement is not the only abrasive influence found in joint replacements. In isolated cases particles of bone have been known to contribute to three-body abrasion. Such a particle is shown in figure 7, identified by strong calcium peaks in the EDAX spectrum.

Two-body abrasion is also observed to occur in joint prostheses, as asperities or defects in the femoral components of hip and knee prostheses gouge and scrape material from the softer polyethylene surface. This results in minor dimensional change of the polyethylene and generation of particulate wear debris. However, given the current state-of-the-art of surface finishing of the metal components, this process generally ceases as the polyethylene surface smooths out and a transfer film builds up on the metal surface.

5. The Formation of Craters in UHMWPE Components of Total Joint Replacements

When it is present at the articulating surface, debris is certainly responsible for at least some of the observed abrasion. Cement particles also are involved in the formation of craters. After a particle of cement becomes embedded in the articular surface, local stresses begin to break up and disintegrate the brittle cement. Figure 8 shows the appearance of a particle in this stage of its lifetime. When the acrylic particle is completely disintegrated and removed from the surface, a crater is left

behind. The resulting crater, as shown in figure 9, is typically flat-bottomed and surrounded by abrasion.

Cement particles are not the only agency involved in crater production, however. Craters also seem to form by a mechanism which is unrelated to the presence of acrylic. The mechanism involves the presence of incompletely-fused UHMWPE powder granules at the articular surface. Such defects seem to be formed during the low-temperature compression molding or extrusion operations.

Most prostheses in use presently are manufactured by the machining of a block of UHMWPE which was compression-molded or extruded from powdered UHMWPE. The migration of polymer chains to form fibrils between the powder granules is responsible for the cohesion of the powder in the solid. Fibrils bridging the gap between granules are shown in figure 10. The migration is often impeded by the high melt viscosity of the polymer and it is often observed that incomplete knitting of the powder granules occurs. A typically incompletely-fused particle is shown in figure 11. The outline of the particle is clearly visible. In addition to incompletely-fused granules, fusion defects which are observed as voids, have also been detected. These can elevate local stress levels by acting as stress concentrators. The tie chains, which maintain the mechanical integrity of the material, can fatigue and fracture when exposed to these cyclical stresses. As a consequence, the powder particles may be removed from the surface as debris. The fusion defects, therefore, act to nucleate a process which can cause the release of debris within a local area. This mechanism can result in the formation of cracks and craters. An example of a typical crater so formed is shown in figure 12. The floor of the crater is dimpled. These indentations were left by the spherical particles as they were released from the surface.

6. The Influence of Molecular Weight on Wear

The nature of the fatigue and failure mechanism indicates that several factors may influence the catastrophic nonabrasive wear observed in the study of clinically failed prostheses. These same factors will also effect the length and number of intergranular fibrils. These fibrils probably represent the highest molecular weight fraction in the polymer. Any degradation in molecular weight will also degrade the fibrils which in turn reduces the wear resistance of the polymer.

It appears that the presence of a lower molecular weight fraction at the surface may contribute significantly to the observed clinical wear. Figure 13 is a scanning electron micrograph of the surface of polyethylene worn *in vitro* which has a molecular weight of 500,000.[9] Figure 14 shows the articulating surface of a knee prosthesis which was produced from UHMWPE (molecular weight = 2×10^6 to 6×10^6). The severe deformation in both surfaces is so strikingly similar that it suggests the presence of a low molecular weight fraction on the articular surface of the polyethylene component of the prosthesis. Such deformation was observed in several cases of clinically failed prostheses. This fraction may have been formed by degradation during processing through thermal, mechanical or chemical agencies.

7. Conclusions and Recommendations

Scanning electron microscopic studies of the articulating surfaces of the polyethylene components of 15 total hip and 35 total knee prostheses revealed that catastrophic wear was caused both by the presence of acrylic cement particles between the surfaces and by the fatigue and fracture of molecular tie chains which maintain the mechanical integrity of the polymer. The fatigue and failure of the tie chains is accelerated by fusion defects in the material and is responsible for the formation of craters and cracks which have been observed on severely worn clinically failed prostheses. While the fusion defects seem to result from the high melt viscosity and the low temperatures required to mold the UHMWPE, they are at present virtually impossible to avoid.

Severe deformation observed in clinical failures suggests the presence of a low molecular weight fraction at the articulating surface. It is assumed that this fraction was formed by the degradation of UHMWPE, possibly during forming operations. The degradation of the molecular weight of the polymer at the surface may be difficult to avoid using present methods of manufacture.

The clinically failed prostheses used in this study were well preserved, however dried serum on the surfaces often presented problems. Serum can coat the prosthesis making microscopic wear studies difficult. Dried serum which adheres to the prosthesis is extremely difficult to remove using conventional solvents (e.g., isopropyl alcohol, acetone or alkyli) and cleaning apparatus (e.g., ultrasonic cleaning). While the greatest success in removing the serum was with acetone, this presents a problem since it is also a solvent for acrylic cement. Consequently, prostheses which are cleaned with acetone will not be expected to have acrylic particles embedded in the surface. This problem would be alleviated if clinical failures which are to be analyzed in wear studies were cleaned in saline or alkaline solutions immediately after surgical removal.

We wish to acknowledge several sources of support for this work: the Howmedica Corporation, via a grant-in-aid to M.I.T.; the National Institutes of Health via Biomedical Research Support Grant NIH-5-507-RR07047-13; and the Hughes Scholarship which supported W. R. Cimino during part of this research.

The gracious cooperation of the Orthopaedics Associates Group at the Robert Breck Brigham Hospital in Boston, MA in providing the failed implants is acknowledged, with gratitude and the hope that our labors will ultimately lessen the availability of such material.

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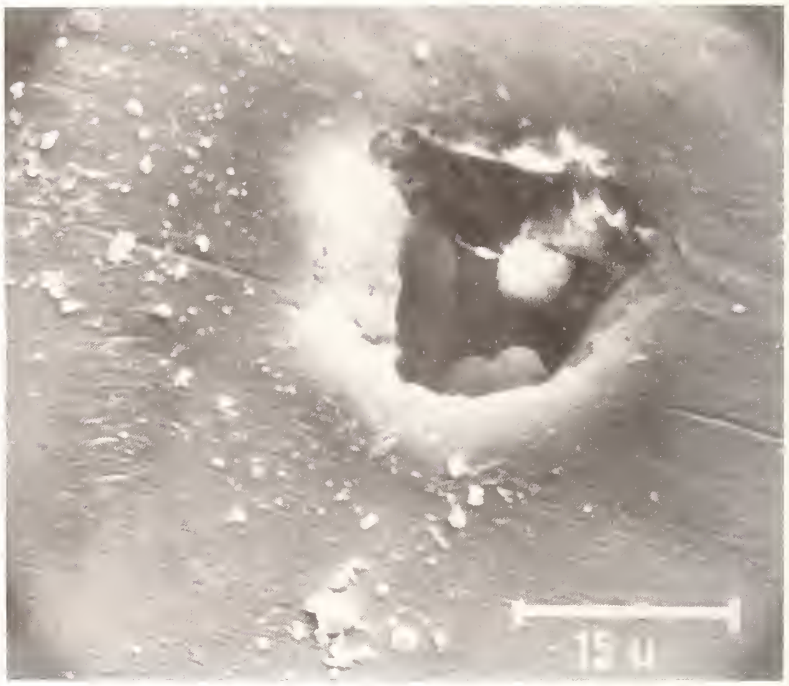

Figure 1. A typical fusion defect in the molded surface of a total joint replacement component made of ultrahigh molecular weight polyethylene (UHMWPE).

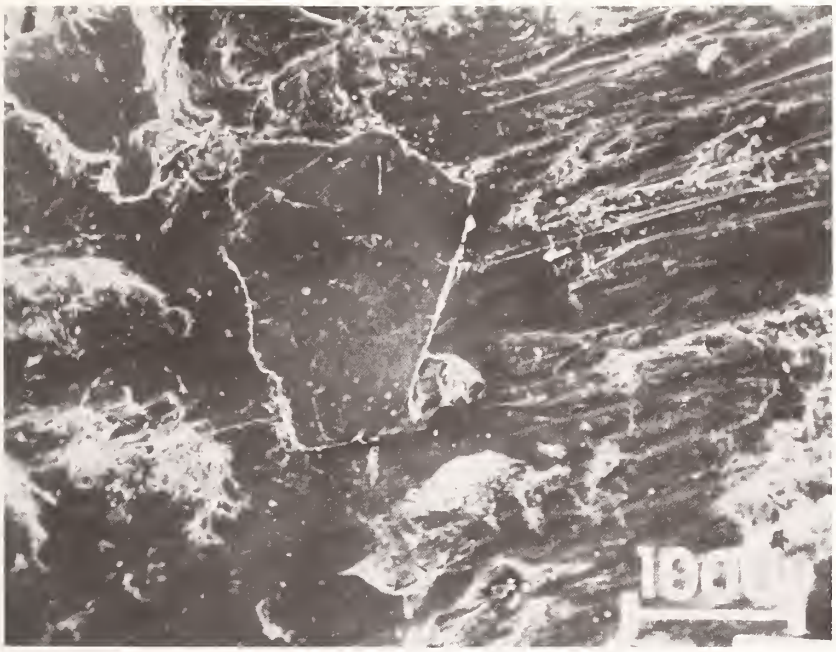

Figure 2. An acrylic cement particle embedded in the UHMWPE articular surface of a total knee prosthesis.

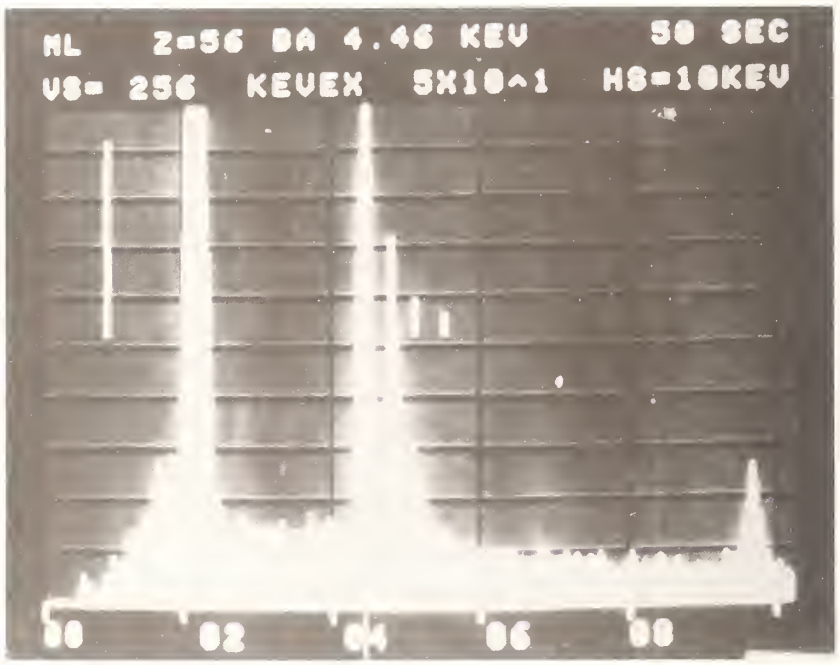

Figure 3. The EDAX spectrum for the inclusion shown in figure 3. Peaks for barium, gold (used to coat the specimen) and sulfur are all in evidence.

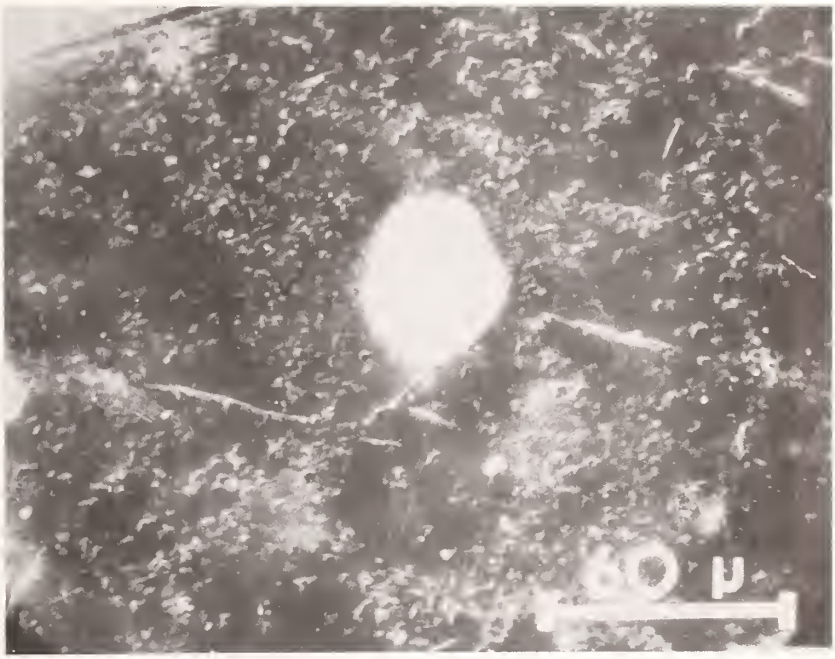

Figure 4. A barium sulfate inclusion in the acrylic cement particle shown in figure 2.

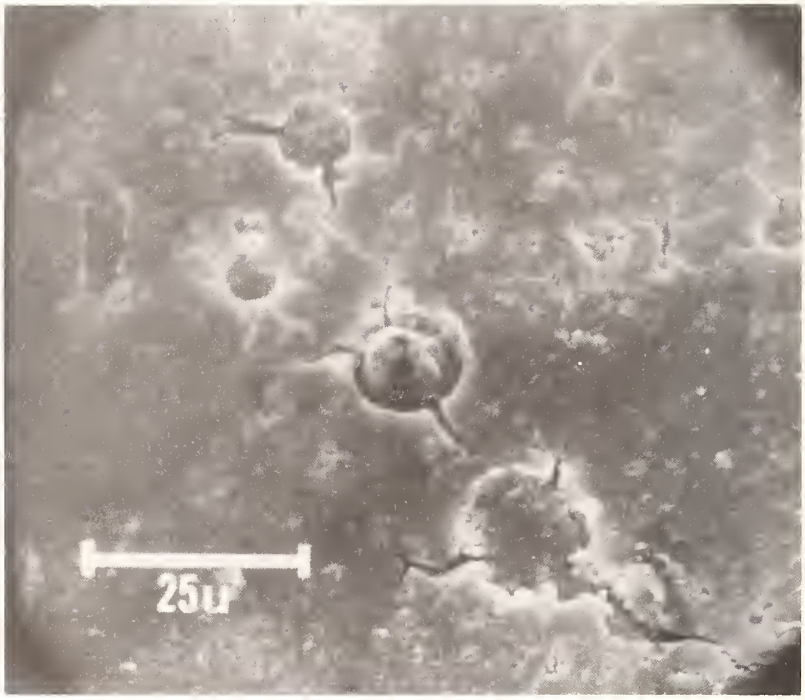

Figure 5. High magnification view of an acrylic cement particle, showing pullout of acrylic globules due to incomplete curing.

Figure 6. Lower magnification view of the same particle as in figure 5, showing fracture planes characteristic of embedded acrylic, and heavily abraded UHMWPE surrounding the particle.

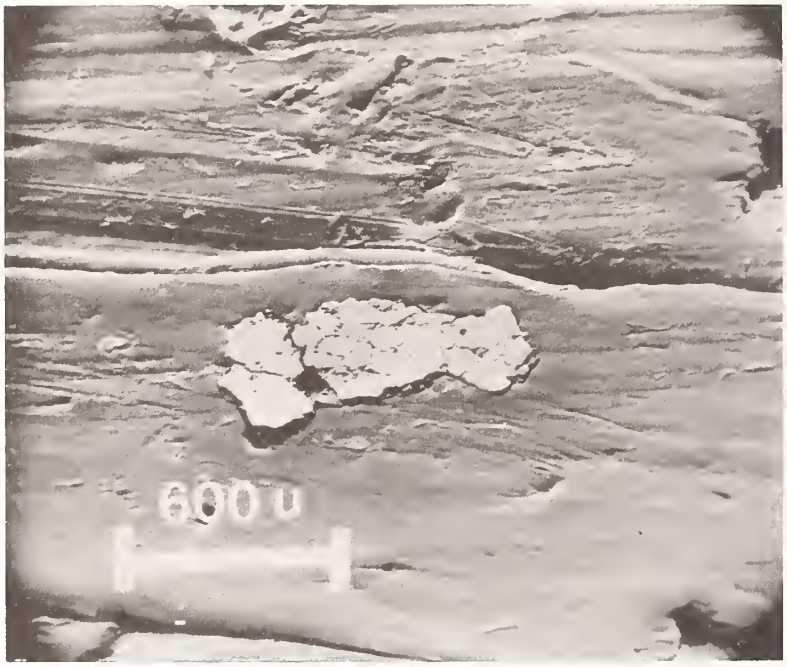

Figure 7. Bone fragments found embedded in the surface of an UHMWPE tibial component of a total knee prosthesis.

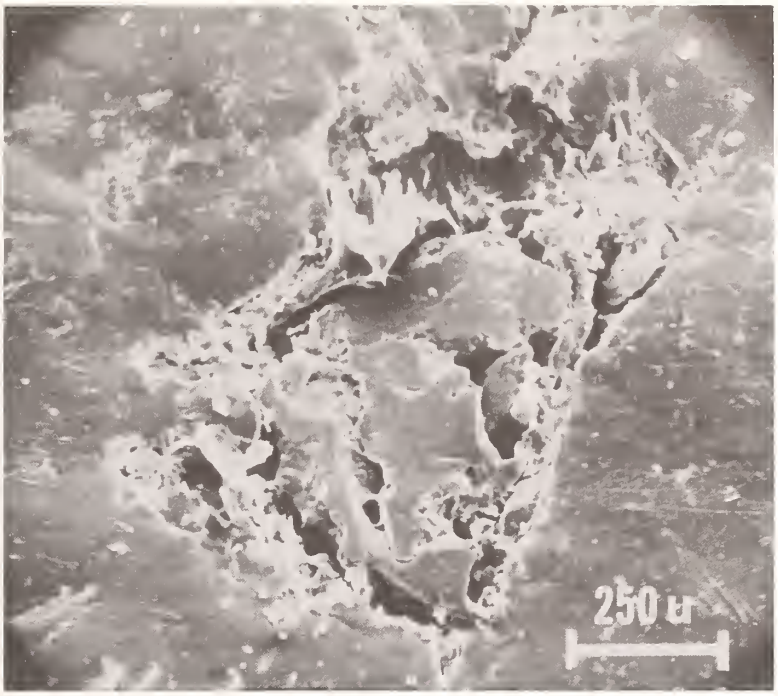

Figure 8. An embedded acrylic cement particle in the act of breaking up.

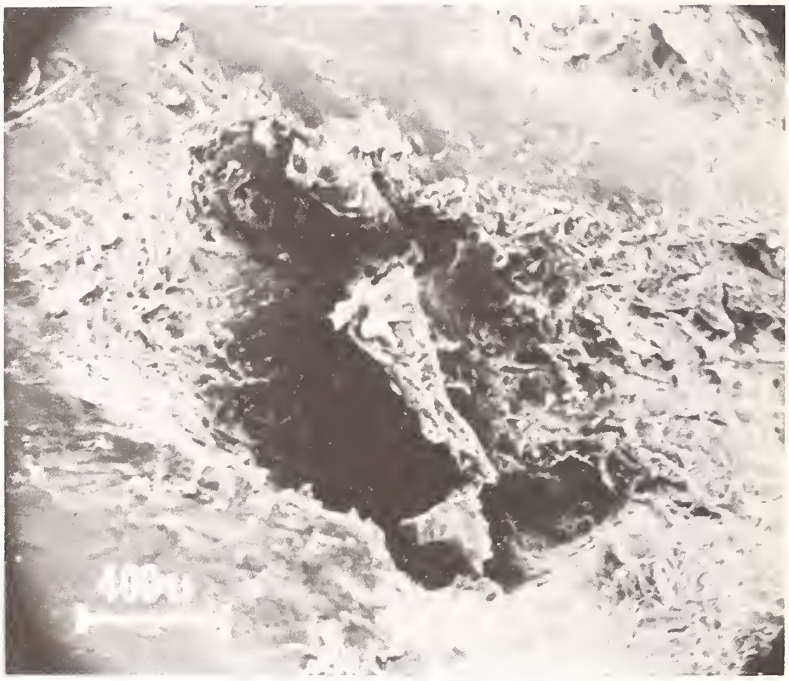

Figure 9. A crater left by a departed acrylic particle, afer break up.

Figures 6, 8 and 9 constitute sequential pictures of the history of an embedded acrylic particle.

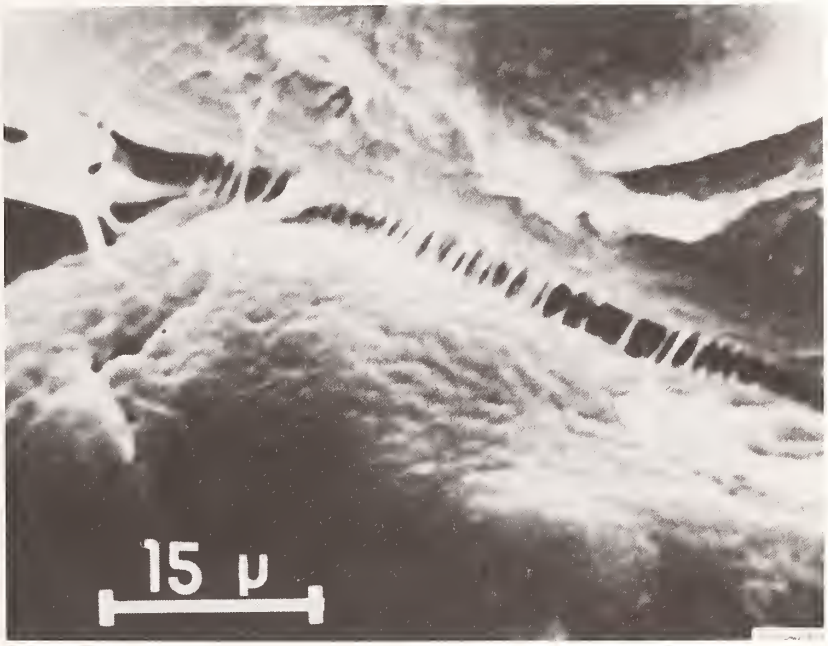

Figure 10. Fibrils bridging two granules at a fusion defect in the UHMWPE component of a total joint replacement.

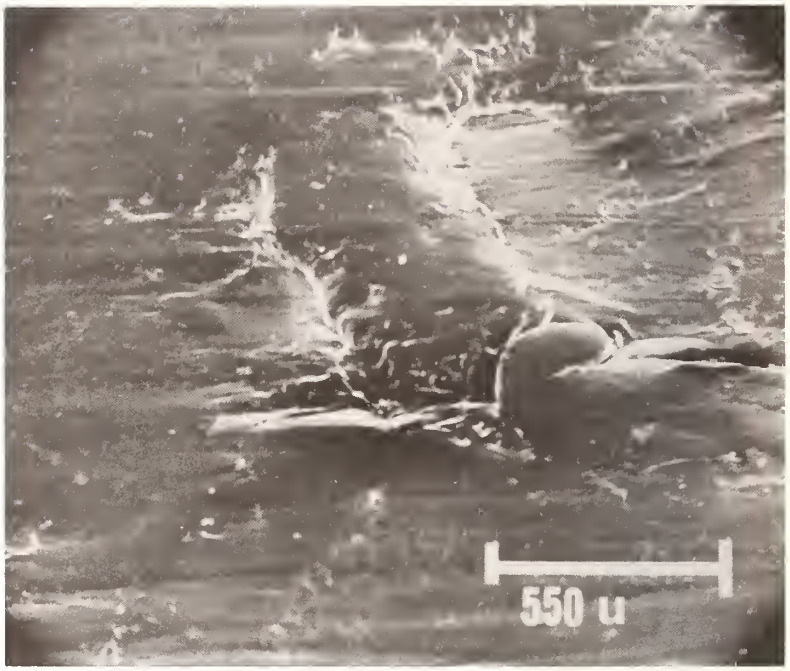

Figure 11. An incompletely-fused UHMWPE granule, exposed at the articular surface.

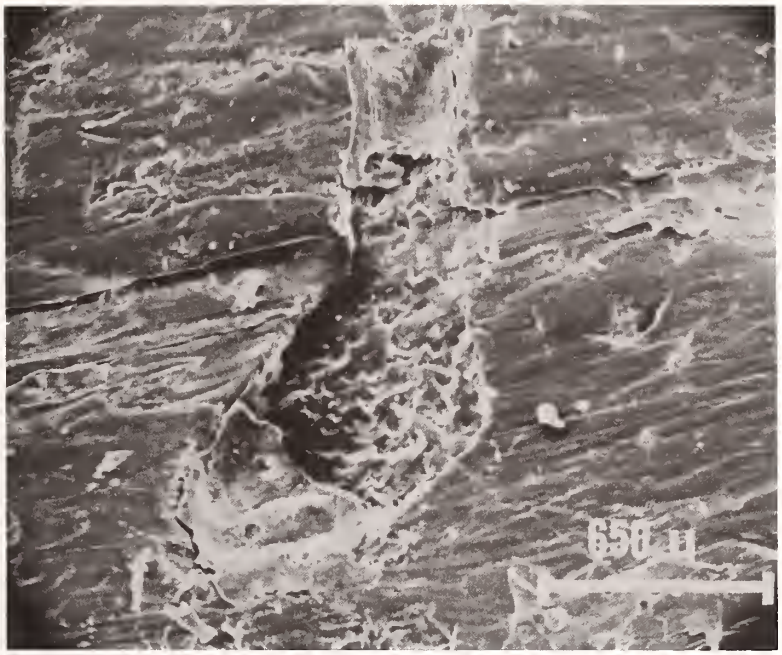

Figure 12. An incompletely-fused UHMWPE granule delaminating from the articular surface. This process generates craters even in the absence of acrylic cement debris.

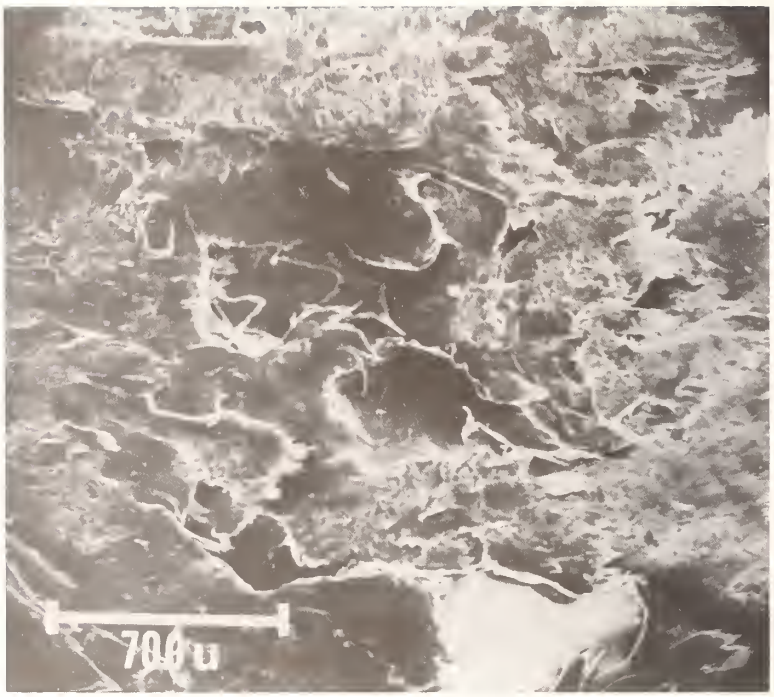

Figure 13. Surface of a polyethylene sample tested *in vitro* under simulated total knee replacement conditions.[9] The average molecular weight was 5×10^5.

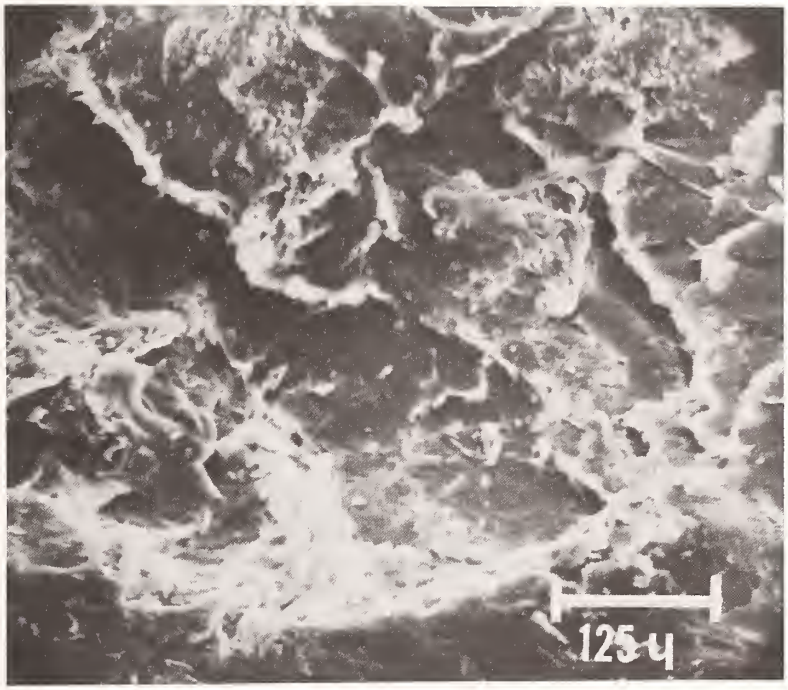

Figure 14. Surface of a tibial component (clinical) produced from UHMWPE (average molecular weight 2-6 x 10^6). The similarity to figure 13 suggests that the molecular weight at the articular surface may have been degraded.

Discussion

Question (S. Barenberg, University of Michigan): What direct and/or indirect evidence do you have that the bridging fibers are the high molecular weight portion?

Answer: To the best of my knowledge there is no evidence, only opinions, and these are controversial. On the one hand, the "high molecular weight" school of thought maintains that the fibrils are indeed tie molecule agglomerations; on the other, the "low molecular weight" school maintains that the fibrils are the result of turbulence in the reactor. As I have stated elsewhere, critical experiments to resolve this question remain to be done.

A BIOLOGICAL AND STRUCTURAL EVALUATION OF RETRIEVED DACRON ARTERIAL PROSTHESES

R. Guidoin[a], M. King[b], P. Blais[c], M. Marois[d], C. Gosselin[e], P. Roy, R. Courbier, M. David, H.P. Noël.

Pioneered in the 1950's, reconstructive procedures involving the implantation of synthetic blood conduits have become relatively common since the early 1970's. However, long term success is largely dependent on patient selection and surgical techniques as well as the design, the dimensions and the material chosen to repair the nature conduit. Polyethylene terephthalate(Dacron) tissue ingrowth fabric devices have accounted for the larger portion of commercial devices and are currently implanted in a rapidly broadening spectrum of patients, many of whom could potentially outlive the service lifetime of some of the newer prostheses. "In-vitro" observations and studies on explanted prostheses suggest that herefore unrecognized textile design and material biodeterioration considerations may have impact on long term prognostics of success. In this work, the results of an ongoing prosthesis recovery program encompassing more than 120 devices collected at autopsies and reoperations are discussed. The evaluation protocol addresses healing, textile geometry, product identification, dimensional stability of the fabric, morphological changes of the yarns and fibres, mechanical properties and chemical changes in the material with "in-vivo" residency time. The significance and the limitations of data derived from cardiovascular device recovery programs are also discussed.

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f) See Table 1 for affiliation of other authors.

1. Introduction

From more than ten materials used clinically since 1954, polyethylene terephthalate (Dacron^{R}) has proven to be most desirable among different porous fabric prostheses for cardiovascular replacement (1-4). One style of device is currently available in more than twelve commercial variations (5). Superposed on the differences in design are the variations in porosity, weave style, fibre structure and fabric weight.

Over the last 20 years, emerging technology from the textile industry has been adapted to medical fabrics and has enabled the routine production of low cost and relatively effective arterial prostheses for the replacement of many types of blood vessels (6). With the growing success of these prostheses as permanent arterial substitutes, research efforts to refine surgical technics and develop new and improved products have intensified.

Although a wide range of cardiovascular repair products have been investigated and implanted in humans, a wholly satisfactory device of universal applicability has not yet been found. This may, in fact, be an utopian goal. Instead, specialized classes of products and technics, each with specific merits and disadvantages, have emerged (3). Currently, there are activities which aim at formulating standards for such products; this suggests that the sector has reached maturity. Some properties such as thickness, permeability to water (porosity), bursting strength, and elongation are addressed in proposed standards for vascular prostheses currently under development in the United Kingdom, Australia and the U.S.A. (7-9). Yet comparatively little is know of the mechanism of "healing", the biodeterioration rate "in-vivo" and the impact of common pharmacologic regimes for the management of related or concurrent clinical problems and other factors which determine the clinical figures-of-merit for this class of devices. The thickness and the nature of the ingrowth tissue, the displacements and stresses due to limb movement as well as cyclic tension and compression associated with pulsatile blood flow have implications with respect ot the useful lifetime of the prostheses "in-vivo" (10). Premature mechanical failure, wear and deterioration of mechanical properties with extended post-implantation lifetimes are also becoming more important considerations in view of the better prognosis fo many implanted patients due to improved surgical techniques.

As a consequence, the use of Dacron fabric grafts in cardiovascular surgery has become more clinically acceptable and more widespread over the last decade. The introduction of superior and more easily implanted devices has made the surgery very common (1, 2). Late trends in the development of these prostheses have led to major reductions in the fabric weight and tenacity in order to facilitate tissue ingrowth within the fabric interstices (11). In 1976, several surgical centres in the U.S.A. reported clinical difficulties with lightweight and other thin-

wall versions of these prostheses (12-16). Post operative dilation, false aneurisms, suture line disruption and interstitial bleeding were reported to occur shortly after the installation of the devices. Similar anecdotes involving thin-walled prostheses had also appeared earlier (17-19) but had not attracted attention. As a result, use of "ultra-lightweight" prostheses was discontinued in the U.S. in spite of the fact that the nature of the difficulty was not unequivocally established. Of greater concern is the possibility that other synthetic prostheses may be equally vulnerable over the long term because of insufficiently large safety factors in the mechanical properties or excessive reactivity of the constituent fibres towards the biological environment.

Some of these questions cannot be dealt with without the evaluation of a reasonable number of devices which have been in clinical use; although, well controlled experimental evaluation of implants on animal models are indispensable, they do not simulate the realities of the operating theatre or the condition of the average patient at the time of surgery.

They have been relatively few implant recovery programs for cardiovascular prostheses. Although the literature has a considerable core of "ad hoc" recovery of devices (10, 12-32) incidental to interesting case histories, the overall aspect of explantation and analysis technology for this class of clinical material is more anecdotal than systematic. Instead, the emphasis has been placed on patient history follow-up with minimal involvement in the pathology of the devices. Recent examples include the work of Reichle and others where the discussion is related to cardiovascular repair technics but do not address the issue of failure analysis at the level of the prostheses or its materials (33-40). It was the aim of this study to extend the present grasp of "in-vivo" failure processes in fabric devices. This is needed in order to rationally plan the necessary improvements to this class of implants and to identify and correct possible deficiencies in the currently prevailing surgical implantation technics.

This laboratory, heavily invested in the evaluation of cardiovascular repair materials, has collected explanted vascular prostheses of various classes from human patients for nearly four years. To date, more than 300 such devices have been analyzed and cataloged as part of an ongoing program. Here, the results of work carried out on more than 120 Dacron devices of comparable properties, collected from 10 surgical centres, are presented with a summary of the case histories; autopsies and re-operations provided the major volume of clinical material to this study.

2. Materials and Methods

2.1 Clinical Material - Sources

Explanted prostheses were obtained at autopsy, reoperation or limb amputation. Specimen size largely dictated the conditions under which the analyses could be conducted. The retrieval program spans several years and involved several centres from July 1975 to March 1979. It was made possible through the collaboration of many surgeons in Canada and in France. Table 1 lists the principal participating centres and their surgeons.

TABLE 1

Country	Surgeon	Hospital or Centre	City
Canada	Camille Gosselin Claude Rouleau Jean-François Girard	Hopital St. François d'Assise	Québec
	Paul Roy Jacques Côté	Hopital de l'Enfant Jesus	Québec
	John Awad	Centre Hospitalier de L'Université Laval	Québec
	Henry-Paul Nöel Robert Côté	Hopital du St. Sacrement	Québec
France	Robert Courbier Jean-Marie Jausseran	Hopital St. Joseph	Marseille
	Michel David	Hopital du Bocage	Dijon
	Jacques Descôtes E. Chignier	Hopital Edouard Herriot	Lyon
	Roger Bénichoux	CHU	Nancy
	Francis Godard	Clinique St. Joseph	Caen
	Gabriel Camelot	CHU	Besançon

Participating surgeons and centres in the retrieval program.

Since April 1979, several additional centres joined the retrieval program from The Québec City area, Winnipeg, Montréal (Canada), and Bordeaux, La Rochelle and Metz (France). These data will be discussed in a subsequent work.

Grafts obtained at autopsy were explanted by local pathologists. Autopsies were performed within a few hours after death. Grafts obtained at reoperation were collected during the surgery with little delay.

Explanted Dacron specimens included more than 200 grafts recovered at autopsy, amputation or replacement reoperation and represented "in-vivo" residency times ranging from a few hours to nearly eleven years. The collected prostheses included a typical assortment of tissue-ingrowth cardiovascular textile products routinely used. Analysis of the first 120 grafts are reported here.

Unused grafts were commercial products indentical to those sold for human implantation. Their origin is given in Table 2. Manufacturers included: Meadox Medicals Inc., Oakland, N.J., U.S.A.; United States Catheter and Instrument Co., (U.S.C.I.), Billerica, Mass., U.S.A.; Goalski Laboratories Inc., Philadelphia, Pa, U.S.A.

2.2 Specimen preparation and method of analysis

In the event of death, the following procedures were followed: autopsy is performed by the local pathologist within a few hours of death after the family consent is obtained. The synthetic graft is opened longitudinally and photographed. Post-mortem blood deposits are eliminated by gentle rinsing with heparinized saline. The graft is then divided into several specimens. Small samples (1 x 1 cm) are taken from different representative areas and identified. For example, for aorto-femoral bifurcations, specimens are taken in the proximal anastomosis, in the middle of the body of the graft, at the bifurcation itself, in the middle of both limbs and at both distal anastomoses. These specimens are also divided into two sub-groups. The first one is fixed in Bouin's solution (formaldehyde and picric acid) for twenty-four hours and thin sections (5 microns) are cut and stained following routine pathological procedures. At the beginning, only hematoxylin safran were used to differentiate fibrin from collagen. Later, other staining techniques were added to identify other components of the tissue - polymer composite sample. The second sub-group is fixed in a phosphate-buffered solution of 2% glutaraldehyde for up to one week, followed by an overnight post-fixation using osmium tetroxide. The specimens are then washed in distilled water. Drying is performed by immersion in a graded series of ethanol-water solution terminating with absolute ethanol. The specimens are then transferred to amyl acetate prior to the final drying by critical point drying using CO_2 as the transfer medium. The specimens are finally mounted on SEM sample holders and coated with about 100nm of gold-palladium in a sputter device for viewing in a Cambridge S600 Scanning electron microscope at 10 or 15 kilovolts. More detailed pathological analysis procedures using light microscopy and SEM are presented elsewhere (41).

TABLE 2. FABRIC CONSTRUCTION OF COMMERCIAL PROSTHESES AS SUPPLIED

NAME	TYPE	CONSTRUCTION	STITCH COUNT[a] Wales/cm	STITCH COUNT[a] Courses/cm	STITCH DENSITY[b] cm^{-2}	THICKNESS[c] mm	FABRIC WEIGHT g/m^2	FABRIC DENSITY kg/m^3
Woven Cooley	Taffeta	1/1 plain weave	60	33	-	0.24	175	0.73
Woven De Bakey	Taffeta	1/1 plain weave	56	34	-	0.25	165	0.65
De Bakey Standard	Weft Knit	Single jersey	22	31	680	0.46	200	0.44
Ultra-light Weight (ULW)	Weft knit	Single jersey	32	42	1,340	0.30	130	0.43
Milliknit	Weft knit	Reverse single jersey	26	35	910	0.33	140	0.42
Microknit	Weft knit	Reverse single jersey	39	43	1,680	0.18	103	0.57
Weaveknit	Warp knit	Reverse 2-bar locknit	26	33	860	0.34	165	0.48
Cooley Double Velour Graft	Warp knit	2-bar locknit	20	28	560	0.64	280	0.43
Vasculour D	Weft knit	Single jersey	20	26	520	0.55	195	0.35
Microvel	Warp pile knit	Half tricot base inlaid pile yarns	22	32	700	0.89	200	0.23
Sauvage Guideline	Weft knit	Reverse single jersey	23	29	670	0.58	220	0.38

a) Measured by ASTM methods D1376 or D1910 as appropriate
b) Calculated from wales / cm x courses/cm
c) Measured by ASTM method D1777

Grafts collected at reoperation are generally in a poorer condition since they are often collected incidental to emergency surgery where the patient is the primary concern. Normally, the useful size of the graft is reduced. Such specimens are prepared in a way identical to that of grafts collected at autopsy. When the size of sample is sufficient, the remaining portions are assigned to mechanical and chemical evaluation. Specimen size largely dictates the conditions under which the analyses can be conducted.

In such cases the remaining parts of the grafts must be stripped of tissue prior to analysis. Tissue removal is achieved according to the method of Hartigan (42): grafts are boiled in a 5% sodium carbonate solution, then immersed in commercial bleach and exhaustively washed with distilled water and air dried. This treatment was shown not to be deleterious to the Dacron fabrics; new prostheses treated with this procedure are not significantly different with respect to the properties of interest.

Virgin specimens were used as supplied for analysis and microscope examination.

2.3 Analysis of Physical Properties

2.3.1 General Consideration

During "in-vivo" use, prostheses can suffer changes in dimension and in shape. These are lateral dilation, loss of crimping and/or longitudinal growth. The mechanical properties can also change concurrently. The aim of the analysis is to estimate these parameters separately and to compare those of used prostheses to reference samples of the product as supplied.

In some rare cases, prostheses cannot be unequivocally cross-matched to reference samples and their identity is uncertain. In other cases remaining fabric samples are too small or severely damaged. Such specimens are not assessed for mechanical properties.

Microscopy techniques can also be used as coarse methods for the assessment of deterioration in mechanical properties. This approach is based on flexing, stretching, or chemically etching used fabrics or fibres and comparing their behaviour with virgin reference material. Such techniques reveal the depth ot which chemical attack has taken place or the physical changes which have occurred in the polymer (fiber) structure of filaments. These techniques were developed in the latter phase of the program and will be reported elsewhere.

In order to understand the behaviour of the fabric under "in-vivo" use, it is necessary to have some insight of prosthesis fabrication technology. This aspect is covered under Appendix A.

Chemical analyses are generally laborious and a very limited number of samples can be dealt with. In the present study, only samples with exceptional experimental significance are subjected to chemical analysis and molecular weight measurements.

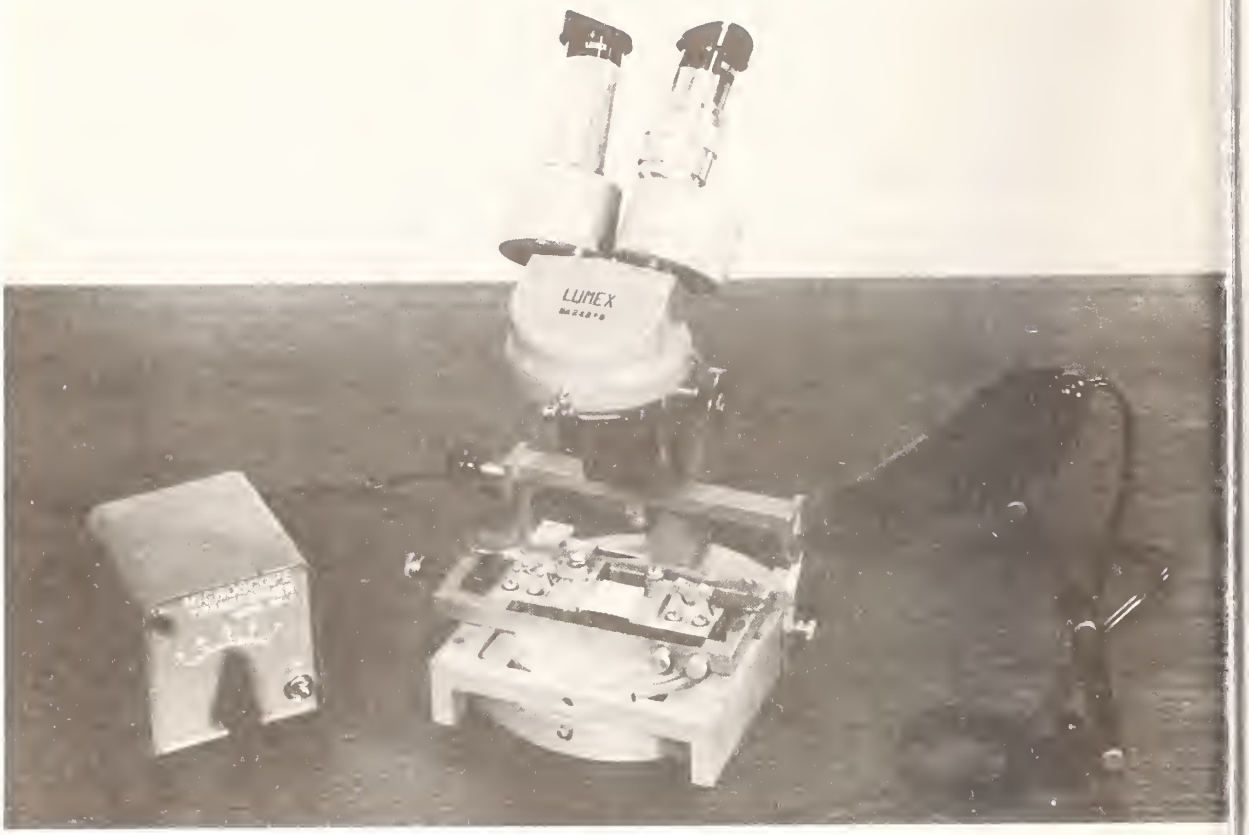


Figure 1 : Pick Counter measuring crimp of explanted prosthesis in reflected light.

2.3.2 Measurement of Crimp Retention

The fabric specimen were mounted in a relaxed state on a specially made Crimp Tester. This device is shown in Figure 1. It is able to measure the length of the specimen to the nearest 0.2mm while extending it sufficiently to remove all the crimp. The end point is readily determined by ensuring that the fabric appears flat when viewed from above in reflected light through an optical microscope. The amount of crimp in the specimen is calculated from the difference between the extended and relaxed length and is expressed as a percentage of the original relaxed length.

2.3.3 Liquid Permeability

The measurement of liquid permeability (porosity) is carried out according to techniques described by Buxton and Cooley (43, 44). It gives an index of the intersticial leakage rate of the fabric prior to surgical preclotting. It also has a relative index of fabric "openness". There, it only has meaning for clean fabrics without tissue.

It was originally believed by us to be a useful measurement of "in-vivo" fabric "growth" since changes in fibre geometry, fibre dimension and fabric density affect the apparent porosity and the flow rate of liquid through the network. In this work, however, its used is limited to characterizing the prostheses according to established methodologies.

2.4 Bursting Strength

The measurement of bursting strength was carried out with a Mullen Burst Tester (Mullen Model AH; B.F. Perkins and Sons Inc., Holyoke, Mass. U.S.A.) fitted with a modified specimen holder suitable for a small circular (1 cm^2) sample of fabric (Figure 2). This instrument requires the use of pressure equilizing membranes for porous samples and is used widely in the textile, paper and rubber industries. It amounts to a coarse biaxial tensile tensile test method which reflects the coherence or the tenacity of films, webs and fabrics which cannot be realistically assessed by uniaxial tensile tests. In all measurements, identical compliant (latex rubber) pressure equalizing membranes of 0.014" were used (Triaxial Ty14-WF 11090; Rubber Sleeves Inc.; 95 Montpellier St., Montréal, Canada). Appropriate corrections were applied to compensate for the membrane contribution. All fabric samples were preconditioned at 23° and at relative humidity of 65% for 24 hours prior to testing. Samples were flattened prior to insertion in the specimen holder in order to make the crimps disappear, but stretching was avoided. Expansion and bursting of a graft is shown in Figure 3.

2.5 Stitch Density

This measurement is performed with the specimen mounted in the extended state with its crimp removed by the Crimp Tester, the number of stitches are counted in the warp and weft directions. A row of stitches in the warp direction is called a wale, while a row of stitches in the weft direction is called a course. When sufficient fabric is available, determinations are made along 3 cm lengths in both directions with the aid of an optical microscope in transmitted light. The stitch density is the wales/cm multiplied by the courses/cm. The difference between the stitch density of the graft and the explaned graft represents the permanent deformation experienced by the fabric during implantation due to distortion of the knitted loops and stretching of the yarns (Figure 4).

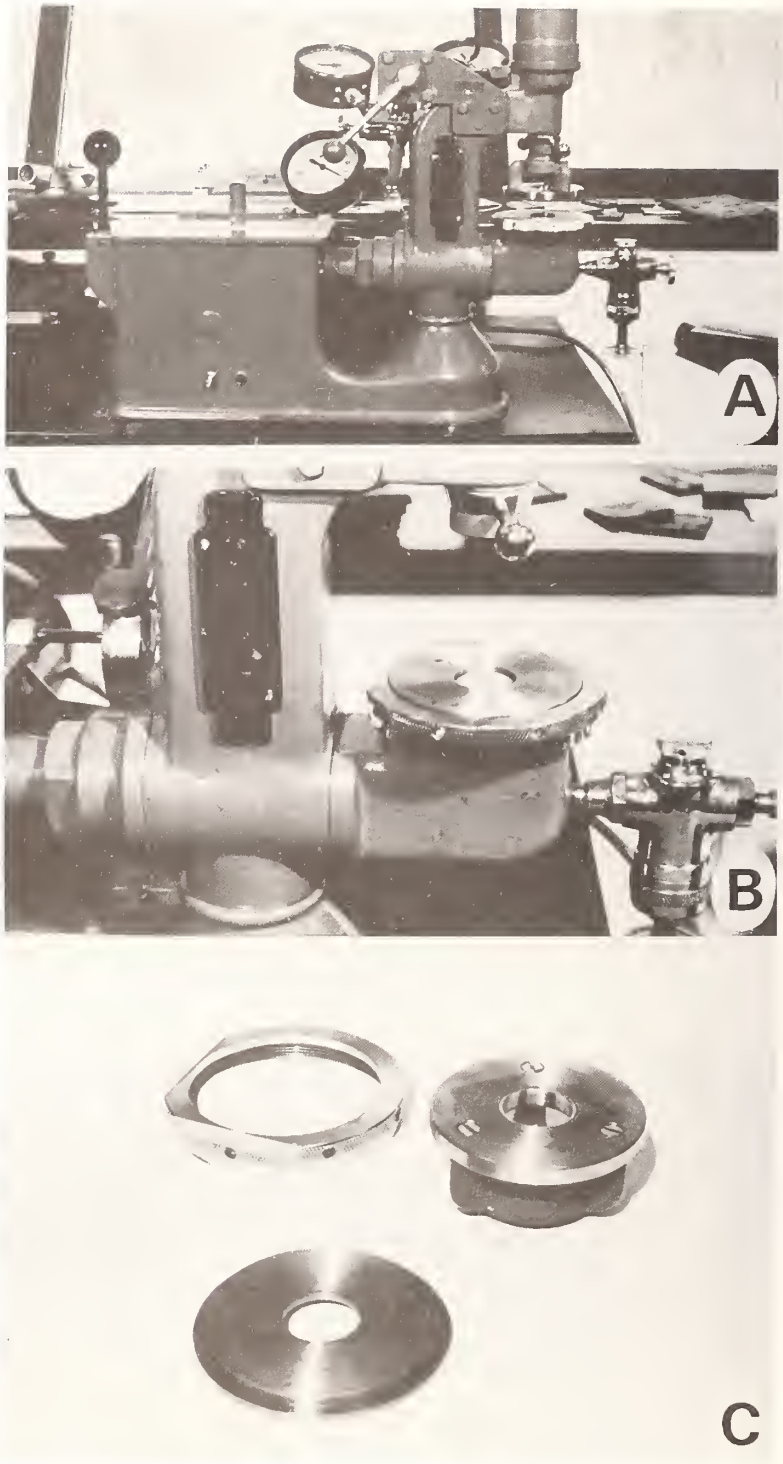


Figure 2 : Mullen Burst Tester fitted with a modified specimen holder suitable for small circular (1 cm^2) sample of fabric.

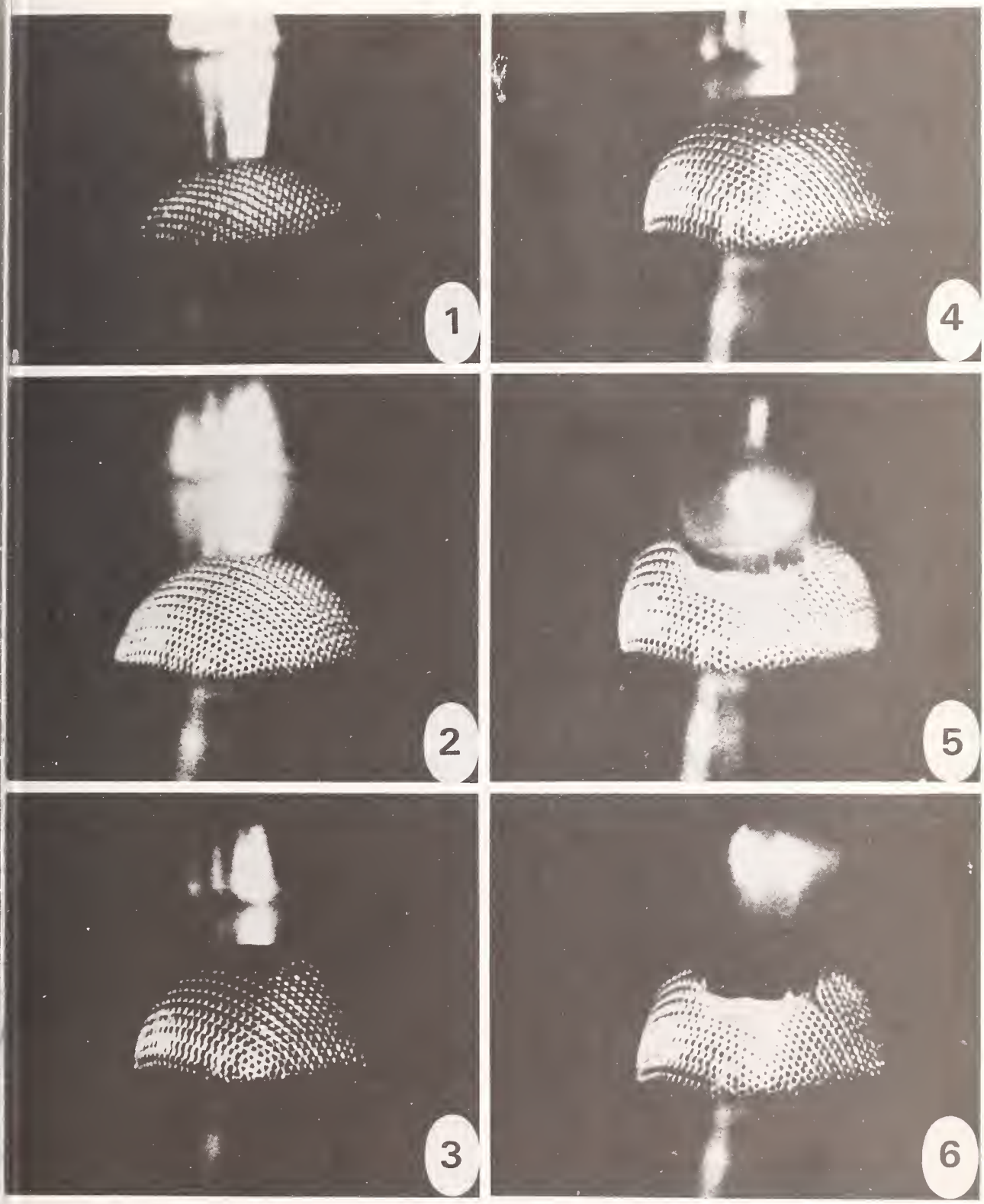


Figure 3 : Expansion and bursting of the graft.

Figure 4 : Measuring the number of courses per centimeter of an explanted prosthesis with the pick counter in transmitted light.

2.3.6 Scanning Electron Microscopy of Fabrics

SEM study of samples was carried out with the aid of a Jeol JSM 35C instrument after coating with carbon (50 nm). A coating with gold-palladium (100nm) by evaporation was added for conductance improvement. A silver paste was added on each corner of the graft to provide electrical continuity with the specimen mount. The microscope was fitted with a backscattered electron detector of enhanced sensitivity and reduced noise. Attempts to obtain satisfactory images with conventional secondary electron collector led to charging. This problem is common in many synthetic textile products and is severe in polyethylene terephthalate systems.

2.3.7 Filament Diameter

Filament diameters are measured on individual yarns which are removed from the cleaned prostheses. The diameter of 20 filaments selected at random from each yarn is measured using an optical microscope at 400 times magnification with a micrometer eyepiece. The eyepiece scale is calibrated against a stage micrometer and the average diameter of the filaments is calculated for each prosthesis. Any significant difference betweeen the average diameters of the unused and the explanted filaments represents either longitudinal stretching, lateral swelling, dissolution, abrasion of wear during "in-vivo" residency of the prosthesis.

2.3.8 Chemical Analysis

In the case of prostheses showing visible damages with the unaided eye, the mode and the cause of the damage is investigated. This is supplemented by chemical analysis using mass spectrometry and infrared spectrophotometry. Mass spectrometry is used to determine the amount and the type of volatile materials which can be removed at 205-295°C. The ratio of peaks associated with volatiles molecular weight corresponding to oligomeric species with two benzene nuclei is compared to the peaks associated with fragments containing a single benzene nucleus; this measurement allows an estimate of the ratio of very low weight oligomers to dimeric species. For extensively degraded samples, the quantity of oligomers containing a single benzene nucleus is expected to be larger. This technique still has to be refined and quantified and will be the object of subsequent papers.

The infrared absorption of the polyester fabric has been measured using conventional transmission infrared spectrophotometry, attenuated total reflection infrared spectrometry (ART) and Fourrier Transform infrared spectrophotometry. The two former techniques did not of immediate

TABLE 3. CHARACTERISTICS AND PROPERTIES OF PROSTHESES AS SUPPLIED

NAME	CRIMP			MECHANICAL PROPERTIES		
	TYPE	FREQUENCY (cm^{-1})	DEPTH (mm)	BURSTING STRENGTH (kg/cm^2)	PERMEABILITY TO WATER ($ml/min/cm^2$)	ELONGATION LONGITUDINAL STRENGTH (%)
Woven Cooley	Helical	10.7	0.73	50	120	83
Woven De Bakey	Helical	7.7	0.75	50	350	30
De Bakey Std.	Helical	7.5	1.37	30.9	2,530	160
De Bakey Ultra-light-weight	Helical	10.5	0.64	14.7	2,650	115
Milliknit	Helical	24.8	0.99	19.3	5,300	475
Microknit	Helical	22.1	0.91	15.2	3,340	490
Weavenit	Helical	14.7	1.07	15.3	2,920	275
Cooley Double Velour Graft	Circular	4.8	1.44	11.8	1,660	95
Vasculour "D"	Circular	10.4	1.43	17.6	2,250	255
Microvel	Circular	6.5	1.45	11.2	2,400	160
Sauv. Guideline	Circular	9.0	1.79	17.3	3,420	285

usefulness and were abandoned early in the work. On the other hand, Fourrier Transform spectrophotometry can be used to measure subtle variations in the carboxy and hydroxyl end-group concentration in new and explanted samples by comparing the absorption corresponding to 3,290 cm^{-1} and 3,535 cm^{-1} respectively. These techniques are described by Clark and Mickie (45).

The molecular weight of new and recovered prostheses material is measured according to standard ASTM textile techniques (46, 47). This measurement is possible only in instances where substantial amounts of material are available. For this purpose, specimens are weighed, dissolved in O-chlorophenol and serial dilutions are taken to generate viscometric data at 25°C, according to conventional procedures.

Viscosity average molecular weight ($\overline{Mv}$) can be calculated from the intrinsic viscosity (η) according the following equation from the literature (48).

$$\overline{Mv} = \left[\frac{(\eta) \times 10^4}{1.9}\right]^{.81}$$

3. Results

3.1 General Considerations

Specimen collected during this program numbered in excess of 300 including biological and PTFE grafts. However, analysis of 120 Dacron grafts have been totally completed at the time of writing. Medical histories were also available for almost all donor patients. The most detailed examples came from reoperation cases. On the other hand, the best specimens of prostheses originated from autopsies of patients who died for a reason unrelated to the prosthesis.

Reference prostheses were available for most of the collected samples and were characterized and cross-matched to explanted devices; only very few could not be identified. The physical characteristics of unused reference textiles are listed under Table 2 and 3. This list includes only devides which were encountered in the recovery program; it represents approximately 50% of the devices which have been marketed over the last decade.

Table 4 is a compilation of devices received in a state such that meaningfull physical properties measurements could be carried-out; it includes less than 50 devices to date, the majority of which are in the aorto-femoral bifurcation configuration. This is expected as this

Table 4.01

SUMMARY OF CLINICAL MATERIAL USED IN MECHANICAL PROPERTIES MEASUREMENT

PROSTHESIS TYPE	CODE	SOURCE *	IMPLANTATION RATIONALE	CAUSE OF DEATH OR REOPERATION	IN-VIVO RESIDENCY MONTHS	IMPLANTATION SITE	SPECIMEN STATUS**
Cooley Double Velour	B21	R	stenosis	aorto-enteric fistula	20	aorto-femoral (bilateral)	CD
Microvel	B30	A	aneurism	intestinal necrosis and thrombosis (arterial)	5	aorto-femoral (bilateral)	CD
ULW	B31	A	stenosis	infarct	65	aorto-femoral (bilateral)	CD
Sauvage Guide-line	B33	A	stenosis	respiratory insuffi-ciency	0.5	aorto-femoral (bilateral)	CD
Microvel	B34	A	gangrene (foot)	lung cancer	3	aorto-femoral (bilateral)	CD
Weavenit	B36	A	stenosis	axphyxia	35	aorto-femoral (bilateral)	CD
Weavenit	B37	A	aneurism	cardiac insufficiency	44	aorto-femoral (bilateral)	CD
Microvel	B39	A	aneurism	cardiac insufficiency	0.5	aorto-femoral (bilateral)	CD
Weavenit	B41	A	iliac thrombosis	infarct	44	aorto-femoral (bilateral)	CD
Microvel	B42	A	aneurism	respiratory failure; kidney damage	1	aorto-femoral (bilateral)	CD

* Source: A: autopsy; R: reoperation
** Specimen status: CD: complete device; S: segment; F: fragment

SUMMARY OF CLINICAL MATERIAL USED IN MECHANICAL PROPERTIES MEASUREMENT

SUMMARY OF CLINICAL MATERIAL USED IN MECHANICAL PROPERTIES MEASUREMENT

PROSTHESIS TYPE	CODE	SOURCE *	IMPLANTATION RATIONALE	CAUSE OF DEATH OR REOPERATION	IN-VIVO RESIDENCY MONTHS	IMPLANTATION SITE	SPECIMEN STATUS**
Microvel	B43	A	stenosis	infarct	.04	aorto-femoral (bilateral)	CD
Cooley Double Velour	B44	R	stenosis	infection	26	aorto-femoral (bilateral)	damaged device
Knitted de Bakey	B46	A	stenosis	cancer	107	aorto-femoral (bilateral)	CD
Weavenit	B47	A	stenosis	post-operatively to a nephrectomy	39	aorto-femoral (bilateral)	CD
Knitted de Bakey	B52	R	stenosis	infection	82	aorto-femoral (bilateral)	CD
Microvel	B53	R	stenosis	degradation of distal vascular bed	1	aorto-femoral (bilateral)	F
Cooley Knitted	B55	R	stenosis	infection and thrombosis	48	aorto-femoral (bilateral)	F
Microvel	B56	A	necrosis (foot)	pulmonary failure	0.7	aorto-femoral (bilateral)	CD
Weavenit	B57	A	stenosis	pulmonary failure	57	aorto-femoral (bilateral	CD
Microvel	B58	A	aneurism	artheriosclerosis and terminal complications	2	aorto-femoral (bilateral)	CD

* Source: A: autopsy; R: reoperation
** Specimen status: CD: complete device; S: segment; F: fragment

Table 4.03

SUMMARY OF CLINICAL MATERIAL USED IN MECHANICAL PROPERTIES MEASUREMENT

PROSTHESIS TYPE	CODE	SOURCE *	IMPLANTATION RATIONALE	CAUSE OF DEATH OR REOPERATION	IN-VIVO RESIDENCY MONTHS	IMPLANTATION SITE	SPECIMEN STATUS**
Microvel	B60	A	stenosis	vascular insufficiency and brain damage	0.6	aorto-femoral (bilateral)	CD
Knitted de Bakey	B61	A	aneurism	infarct	98	aorto-femoral (bilateral)	CD
Weavenit	B62	A	stenosis	infarct	43	aorto-femoral (bilateral)	CD
Woven de Bakey	B66	A	ruptured aneurism	infarct	1.5	aorto-femoral (bilateral)	CD
Weavenit	B68	A	stenosis	infarct, brain damage	38	aorto-femoral (bilateral)	CD
Knitted de Bakey	B69	R	stenosis	false aneurism	115	aorto-femoral (bilateral)	S
Microvel	B70	R	stenosis	hyperplasia at anasto-moses	15	aorto-femoral (bilateral)	S
Knitted de Bakey	B73	R	stenosis	thrombosis of one limb of the prosthesis	97	aorto-femoral (bilateral	F
Weavenit	B74	A	aneurism	infarct	0.1	aorto-femoral (bilateral)	CD
Knitted de Bakey	B75	R	claudication and thrombosis	false aneurism	72	aorto-femoral (bilateral)	F

* Source: A: autopsy; R: reoperation
** Specimen status: CD: complete device; S: segment; F: fragment

SUMMARY OF CLINICAL MATERIAL USED IN MECHANICAL PROPERTIES MEASUREMENT

SUMMARY OF CLINICAL MATERIAL USED IN MECHANICAL PROPERTIES MEASUREMENT

PROSTHESIS TYPE	CODE	SOURCE *	IMPLANTATION RATIONALE	CAUSE OF DEATH OR REOPERATION	IN-VIVO RESIDENCY MONTHS	IMPLANTATION SITE	SPECIMEN STATUS**
ULW	B77	A	claudication and necrosis	infarct	77	aorto-femoral (bilateral)	CD
Weavenit	B78	A	aneurism	infarct	40	aorto-femoral (bilateral)	CD
Knitted de Bakey	B79	R	stenosis	false aneurism	84	aorto-femoral (bilateral)	F
Weavenit	B80	R	stenosis	false aneurism	74	aorto-femoral (bilateral)	F
ULW	B82	R	vascular lesions	thrombosis of device	72	aorto-femoral (bilateral)	F
Microvel	M08	R	stenosis	thrombosis of device	0.5	femoro-femoral	CD
Vasculour D	M015	A	necrosis (foot)	uterine cancer	59	axillo-femoral	CD
Knitted Cooley	M016	R	stenosis	thrombosis of device	8	femoro-femoral	CD
Microvel	M18	R	stenosis	hyperplasia at anastomoses	18	femoro-femoral	F
Knitted de Bakey	M022	R	stenosis	sterile reaction to device	23	sub-clavian	F
ULW	M023	R	stenosis	false aneurism	36	aorto-iliac	F
Microvel	FP18	R	stenosis	thrombosis of device	3	femoro-popliteal	S

* Source: A: autopsy; R: reoperation
** Specimen status: CD: complete device; S: segment; F: fragment

Table 4.05

SUMMARY OF CLINICAL MATERIAL USED IN MECHANICAL PROPERTIES MEASUREMENT

PROSTHESIS TYPE	CODE	SOURCE *	IMPLANTATION RATIONALE	CAUSE OF DEATH OR REOPERATION	IN-VIVO RESIDENCY MONTHS	IMPLANTATION SITE	SPECIMEN STATUS**
Microknit	FP23	R	stenosis	thrombosis of device	6	femoro-popliteal	S
Microvel	F24	R	stenosis	thrombosis	6	femoro-popliteal	S
Microvel	F25	R	stenosis	thrombosis	9	femoro-popliteal	F
Weavenit	F26	R	stenosis	severe dilation of device	84	femoro-popliteal	S

* Source: A: autopsy; R: reoperation
** Specimen status: CD: complete device; S: segment; F: fragment

junction is the most common site of reconstruction in peripheral vascular surgery. This table also includes other date of clinical relevance such as the indication for implantation, durantion if implantation (residency time), cause of death and site of implantation.

Patient-related information is presented in Tables 5.01-5.08 (reoperations and first surgery) and in Tables 6.01-6.07 (autopsies). These summarize the age at which patients received their first device, the type of device(s) implanted, the implantation site, the useful life of the device "in-vivo" before death or a second surgery, the indications for surgery of the cause of death, the aim of the subsequent surgery, and the total number of device collected during specific phases of the program. Such data were obtained from medical records and will be the object of a separate publication. For the present need, the following points are of value: the average of age of implantation candidates is dropping rapidly and patients are, on average, several years younger than a decade ago. More velour and lightweight devices are now implanted; occlusive diseases affect the larger segment of implanted patients while the resection of aneurisms is a much less frequent indication of surgery; bilateral aorto-femoral replacement is the most common procedure; almost a third of implanted patients require additional surgery in the same field within 2 years of the first implantation; some patients may undergo as many as 4 related operations; although, thrombus formation and degradation of the distal vascular bed are the most common problems, device-related problems such as dilation, false aneurism and stenosis are common; more patients fitted with velour devices are reoperated upon; the primary cause of death is not prosthesis-related.

3.2 Reoperations (Figures 5.01-5.08)

Prostheses collected incidental to reoperations were seldom of good quality; most had suffered some damages during excision. A limited number provided fragments which were suitable for mechanical properties; these are listed in Table 4. Unlike devices collected at autopsies, many prostheses issuing from reoperations were involved in problems intrinsic to the site of surgery, the distal vascular bed or the device itself. Occlusive thrombosis was very common.

Dominant contributing factors to reoperation include the natural progression of degenerative diseases such as atherosclerosis which gradually increases the peripheral impedence of the circulatory system. The probability of thrombosis is increased by any drop in arterial pressure (flow velocity reduction), such phenomena can occur during an infarct or during surgery; it is even present when the threshold blood flow velocity is approached. Parallel pharmacological therapy may also contribute to reducing or enhancing these effects by modifying blood

Table 5.01

REOPERATIONS : IMPLANTATION SITE; (FIRST SURGERY)

IMPLANT SITE	PROSTHESIS TYPE			TOTAL
	WOVEN	KNITTED	VELOURS	
Aorto-Femoral - (Bilateral)	1	30	9	40
Aorto-Femoral (with 1 Fem. Popliteal)			2	2
Femoro-Popliteal	1	10	5	16
Axillo-Femoral			1	1
Others (Upper extremities)		1		1
TOTAL	2	41	17	60

Table 5.02

AGE OF PATIENT AT SURGERY *

TYPE OF PROSTHESES	MEN			WOMEN			TOTAL PATIENTS	AVERAGE AGE	RANGE
	NUMBER	AVERAGE	RANGE	NUMBER	AVERAGE	RANGE			
Woven	2	73	68-78	-	-	-	2	73.0	68-78
Knitted	35	55.5	28-73	6	57	41-67	41	55.7	28-73
Velours	15	53	42-67	2	53.5	53-54	17	53.1	42.67
TOTAL	52	55.8	28-78	8	56.1	41-67	60	55.8	28-78

* First surgery

Table 5.03

TYPE OF PROSTHESES

(FIRST PROSTHESIS IMPLANTED)

PROSTHESIS TYPE	BRAND	PATIENT		TOTAL
		MALE	FEMALE	
Woven	Woven de Bakey	2		2
Knitted	Weavenit	11	4	15
	Knitted Cooley	4	1	5
	Microknit Golaski	1	-	1
	Knitted de Bakey	11	-	11
	ULW	4	-	4
	Unidentified	4	1	5
Velours	Microvel	12	1	13
	Vasculour D	2	-	2
	Cooley Double Velour	1	1	2
TOTAL PATIENTS		52	8	60

Table 5.04

RATIONALE FOR FIRST SURGERY

	DEVICE IMPLANTED			TOTAL
	WOVEN	KNITTED	VELOUR	
Aneurism (elective surgery)	0	4	1	5
Occlusive Disease	2	37	16	55
TOTAL	2	41	17	60

Table 5.05

REOPERATIONS

PATIENT STATUS	SPECIMEN COLLECTED
First Reoperation	53
Second Reoperation	16
Third Reoperation	4
Fourth Reoperation	4
TOTAL REOPERATIONS*	77
TOTAL PATIENTS*	60

* Some patients provided two or more prostheses to the recovery program.

Table 5.06

NUMBER OF CASES AND INDICATION FOR REOPERATION

	POST OPERATIVE		1 to 6 MONTHS		6 to 24 MONTHS			MORE THAN 24 MONTHS			
Patient status*	1	2	1	2	1	2	3	1	2	3	4
Thrombus	5	3	1	3	6	2		4			
Degradation of vascular bed	1		4	1	3	1		8	1		
Prosthesis Dilation								1			
False aneurism					2	1		5	2		
Infection					3	1		0	3	1	1
Aorta-enteric fistulae									1	1	1
Hemorrhage					2			1			1
Stenosis					3		1	1	1	1	1

* Number of related surgical acts in the area

Table 5.07

REOPERATIONS

	POST OPERATIVE		1 to 6 MONTHS		6 to 24 MONTHS			MORE THAN 24 MONTHS			
Patient status*	1	2	1	2	1	2	2	1	2	3	4
Thrombectomy	3	3	2	1	3	1	1	5			
Replacement of prosthesis	2				15	3	1	16	6	3	
Addition of supplemental prosthesis	1		3	1	5	3		4	2	1	3
Amputation			1	1	1	1					

* Number of related surgical acts in the area

Table 5.08

FABRIC CLASS OF PROSTHESES AND ELAPSED TIME COLLECTION

(REOPERATION)

	IN-VIVO RESIDENCTY TIME (MONTHS)				TOTAL PROSTHESES *
	Post-(or in tra)operative	1 to 6 months	6 to 24 months	more than 24 months	
Woven	0	0	1	1	2
Knitted	4	4	12	31	51
Velours	5	5	11	6	27

* Includes devices issuing from reoperations.

** Samples of 2 kinds of grafts were occasionnally collected at reoperation.

coagulation properties, local blood hemodynamics or altering blood pressure. Many patients showed recurrence of the original underlying cause which led to the first implantation. Reoperation does not necessarily precipitate replacement of the prosthesis. Successful thrombectomy could obviate the need for excision and reanastomosis of a new device. However, any interruption in blood flow or a "reworking" of the area greatly increased the prospects for replacement. Occasionally, closely supervised patients gave evidence of dilation or stenosis of the prosthesis and replacement of the device was elected. Some patients underwent as many as four successive replacements of prosthesis, several of which found their way into the recovery program. Occasionally a patient from this pool also provided a supplemental prosthesis at autopsy upon death.

False aneurism adjacent or contiguous to the anastomotic site were also cited as indications for replacement of the prosthesis or supplemental surgery on adjacent areas. It is not uncommon to encounter situations where reoperations aimed at thrombectomy or resection of aneurism adjacent to a prosthesis did not require removal of the original prosthesis. False aneurisms are common after more than six months postoperative; there were ten cases. The development of the condition appears to take place over a protracted period of time and was generally known for sometime before the planned surgery. Such prostheses sometimes exhibited ruptured fibers or ruptured sutures as well as other local mechanical damages to the anastomoses area. Arteries with friable walls and inadequate mechanical properties do not securely anchor sutures and increase the risks of hemorrhage. Such arteries were occasionally encountered.

Stenosis of the adjacent parts of the affected arterial network or of the prosthesis itself accounted for eight cases of reoperation leading to removal and replacement of the device. Fibrous hyperplasia was a primary factor in the development of stenosis and was more commonly encountered with double velour grafts and other devices with thick, large surface area fabrics. In the case of double velours, spectacular collagen ingrowth on the external wall was found. Such devices had highly organized and thick thrombotic deposits on the lumen wall; microvasculature (capillaries) were sometimes encountered within this mass. The full clinical implications of the inordinately thick wall are not known. Nevertheless prostheses which show such features generally develop problems leading to replacement of the device. Fabric stretching was observed in recovered samples. However, this was rarely evident before surgery or at the time of explantation. Clinically obvious and objectionable dilation in a prosthesis is cited only once as a cause for prosthesis replacement. In this instance, a two-fold increase in diameter of the device was noted over a distance of approximately 4 cm. Fiber damage was present in that area and appeared to be a consequence as opposed to a cause of the observed dilation. There was little evidence of healing and fibrin deposits were present. The problem was further compounded by a mild bacterial colonization.

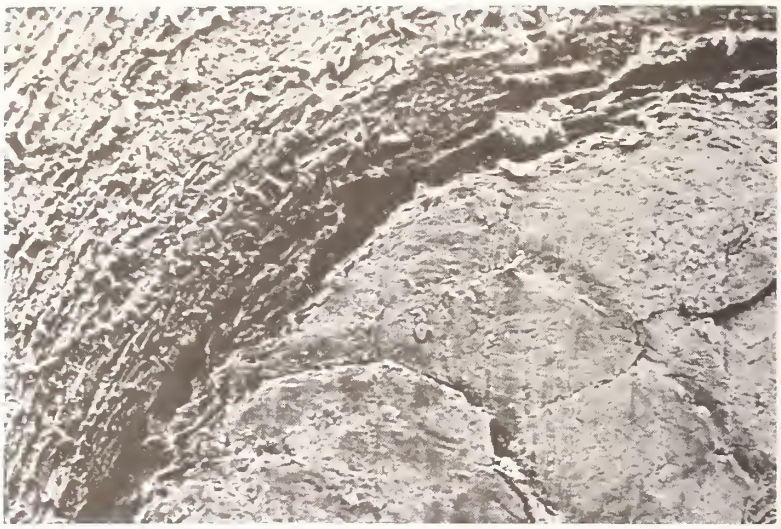


Figure 5.01 : Femoro-popliteal graft (FP08); SEM cross-section; 52 years old patient; Milliknit 49 months in situ. Section transverse to flow directio upper left hand segment shows dense organized concentric deposits and lower ri hand corner shows disorganized occlusive thrombus in the lumen of the prosthes (x80).

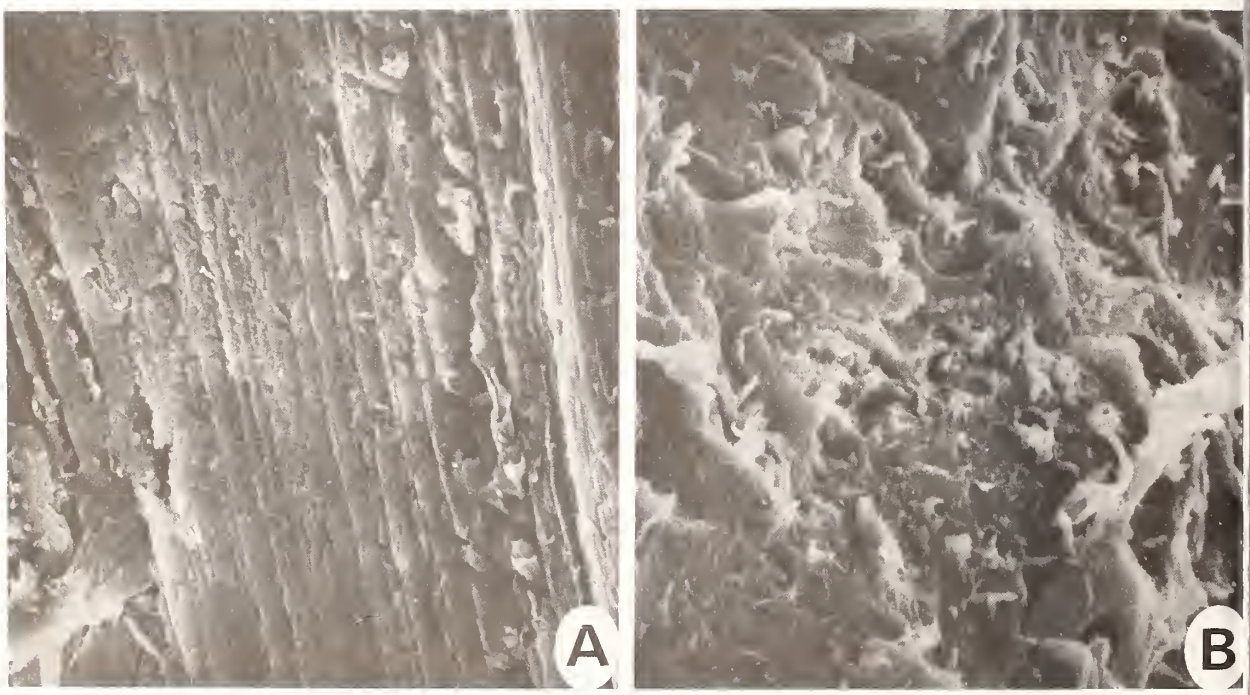


Figure 5.02 : Aorto femoral bifurcated graft (B04) implanted in a 65 years old female for 28 months; graft of unknown origin; similar phenomenon to figure 5.01 at higher magnification: A(x500) layers adjacent to the prosthesis wall, B(x500) lumen of the prosthesis.

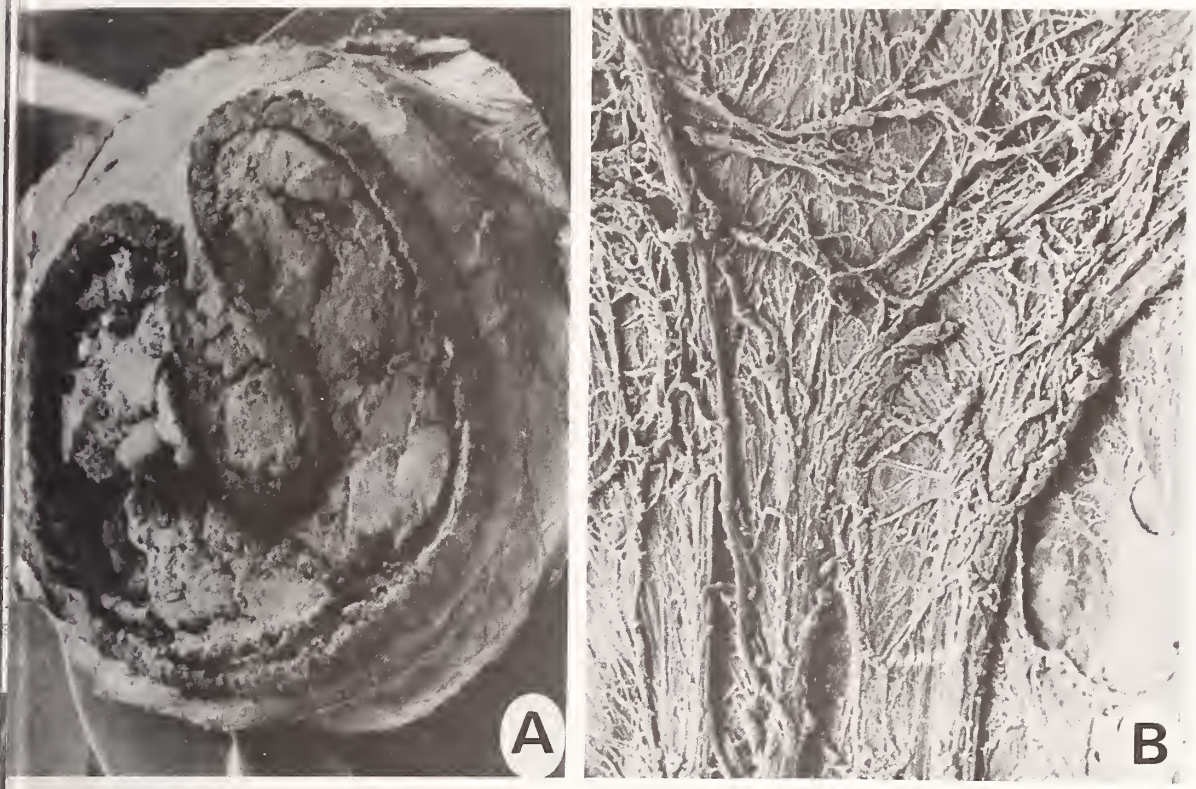


Figure 5.03 : Femoropopliteal graft, 14 months in situ (FP15) totally thrombosed in the distal segment (A:x30) and well healed proximally, SEM surface area shows an orderly layer of compacted fibrin (B:x150).

Figure 5.04 : B79; poorly healed internal surface of a prosthesis after 7 years in situ (standard knitted de Bakey). The patient was reoperated upon because of a false aneurism.

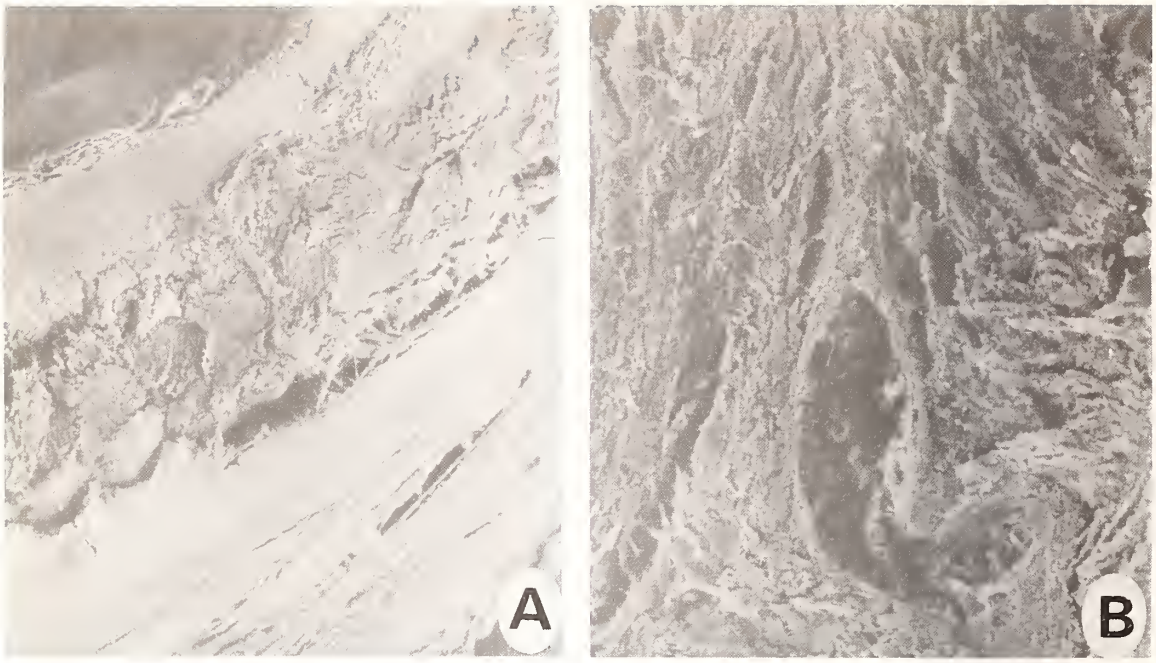


Figure 5.05 : Microvel aorto-femoral bifurcation (B05) implanted in a 54 years old male for one year; the patient was reoperated upon because of stenosis at both anastomoses. Note thick capsule with amorphous neointima and dense concentric layers of collagen surrounding the graft in Figure A (x60); Figure B is a higher magnification of Figure A showing the structure of capillaries in the internal capsule wall (x1200).

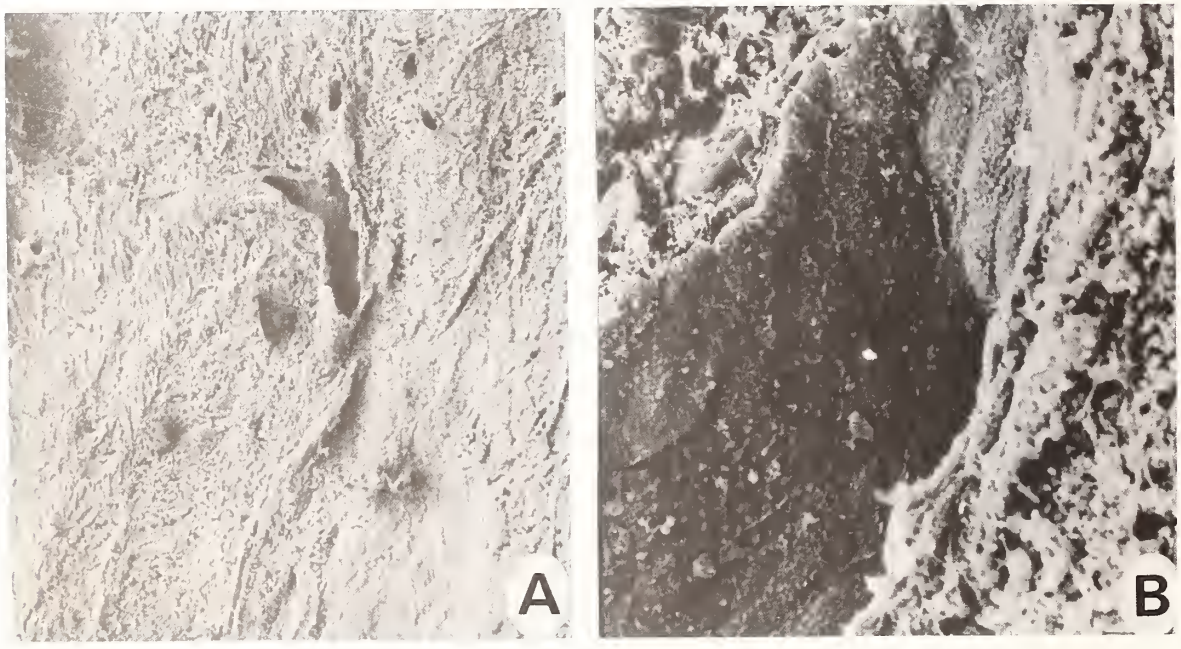


Figure 5.06 : Lightweight knitted graft of unknown origin implanted as a femoro-popliteal by-pass in a 54 years old male (alcoholic) for 28 months; note the presence of capillaries in the internal capsule (A: x 150; B: x 1200)

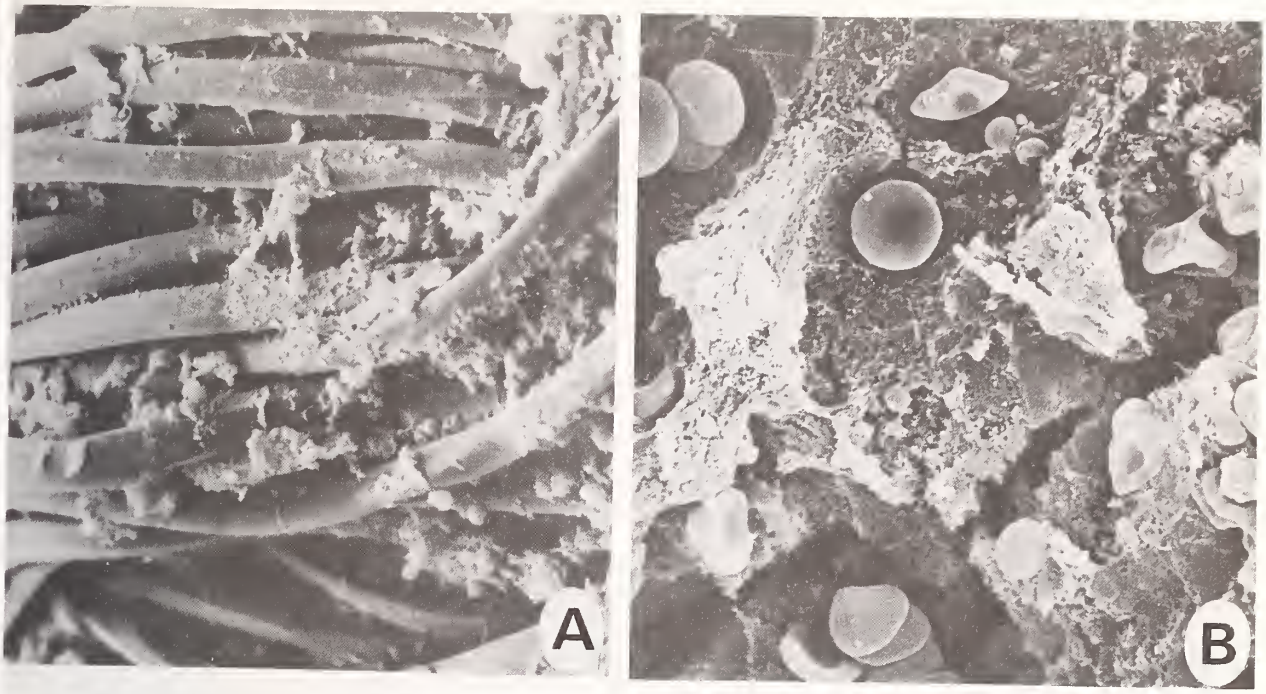


Figure 5.07 : B52, aorto-femoral bifurcation implanted in a 56 years old male; 4th reoperation with incipient thrombosis and gangrene; uncharacterized infection associated with absence of healing (A:x600; B:x2500).

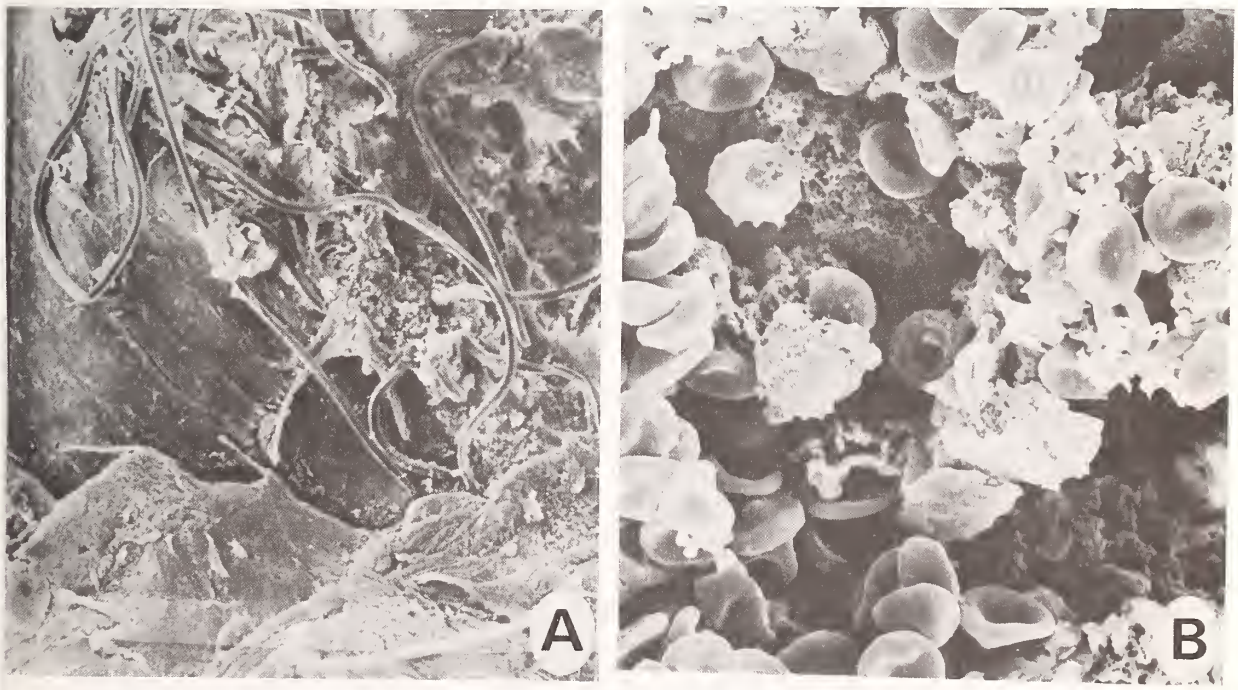


Figure 5.08 : FP13, staphyloccocus aureus invasion after 6 months in situ (Microvel); infection sites coincide with protruding fibers, bare areas and zones of poor healing (A:150; B:x4000).

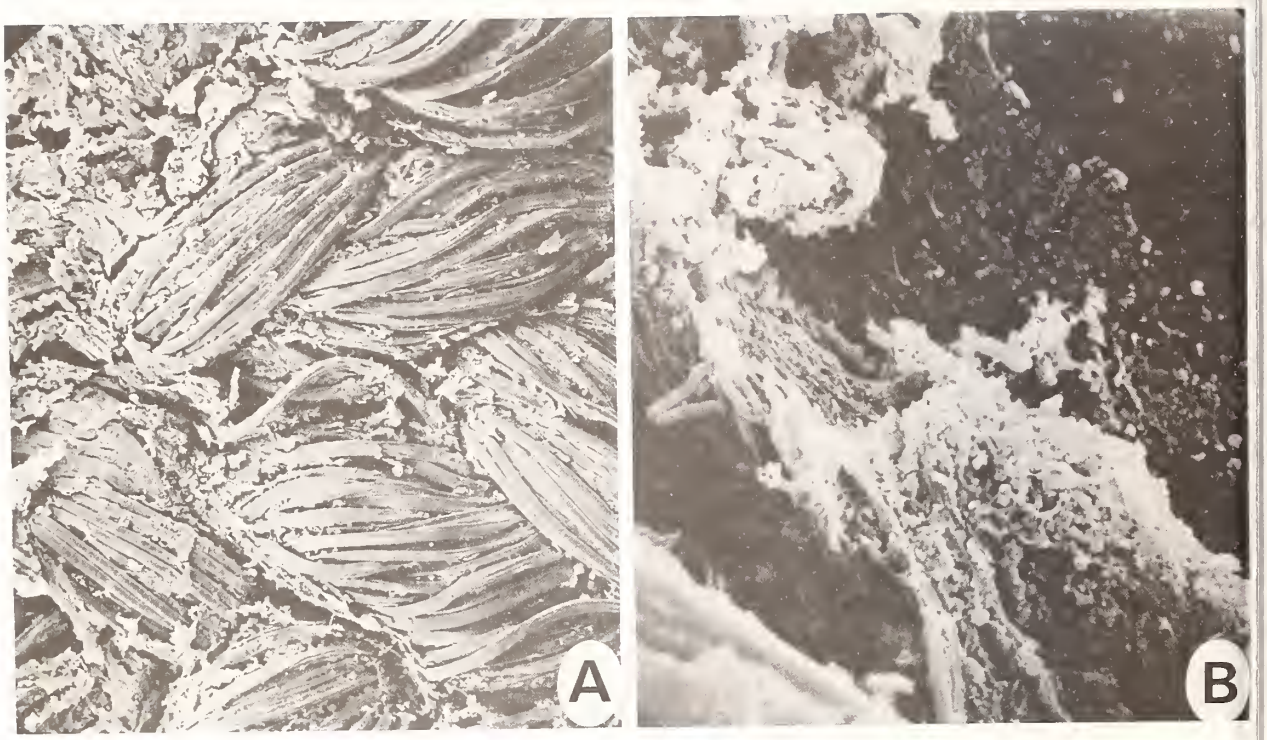


Figure 5.09 : B44, device collected at the 4th reoperation for aorto enteric fistula (Cooley Double Velour). Note the total absence of neointima and the presence of bacterial activity in the area of the fistula (A: x 200; B: x 5000).

Infection sites were found on some prostheses. Common causes are: inadequate surface wound healing and pre-existing infections. The problem is exacerbated by multiple reoperations. Staphiloccocus aureus was the most commonly encountered bacterial pathogen although other organisms were occasionally found. It was noted that infected areas were generally devoid of coherent neoendothelium. Although it is possible that the infection pre-existed and forbade the development of a lumen lining, it is equally possible that a healthy lining formed first and was then invaded by bacteria and destroyed by them. Although bacterial activity would not be expected to damage polyester fibers, it may still cause interstitial hemorrhage by eroding the deposit which ensures the integrity of the capsule.

The recovery program received three prosthesis from patients with aorto enteric fistulae. This included one Weavenit, one Cooley Double Velour and one Microvel. Two of these patients died soon after the second surgery. The noteworthy observation on such prostheses is that healing and development of a neoendothelium does not take place on the part which was in contact with the duedenum wall. The direct contact between the duodenum and the fabric prosthesis promotes erosion of the prosthesis lining in the lumen.

3.3 Prostheses Collected at Autopsy (Figures 6.01-6.06)

Samples originating from autopsies were generally in good condition and included segments of the vascular tissue. This class of retrieved specimen contained the largest number of "ideal" explants which provided insight on the morphology and the thickness of the neointima on the lumen wall and the degree of external tissue encapsulation. Newly deposited luminal surface linings (pseudo-neointima) were overwhelmingly acellular; endothelial-like cells suggestive of systematic endothelialization beyond the anastomotic site were absent. Perhaps extensive endothelialization of the luminal surface is not necessary for long term patency of cardiovascular grafts; also adhering microthrombi and minor embolic structures were not uncommon and are perhaps normal for most patients. Packed fibrin, collagen and fibroblasts seem sufficient to prevent leakage and contain the blood elements. Very thick linings of blood products are not necessary to prevent interstitial blood leakage through the fabric; a thin layer is sufficient. For patients affected by systemic diseases, such as diabetes, it was not uncommon to find large areas of prostheses which were totally devoid of any deposits. Such diseases may account for the considerable variations in the extent of healing found on autopsy samples. The healing sequence of a prosthesis consists of a rapid deposition of low density fibrin which adheres loosely to the prosthesis. The second phase of the process consists of a reorganization of this fibrin mat to constitute a much denser and more hydrophobic luminal surface. Complete healing with the development of pseudo-endothelial cells over the fibrin mat does not take place extensively on the lumen. At best, only small islands of surface cellular activity is evident even after many years post-implantation.

Thrombosis was one of the more frequent complications. Evidence of infection and hemorrhage were seldom encountered. The degree of fiber and fabric integrity in most explanted prostheses was surprisingly good. Nevertheless, prostheses with isolated areas of damaged fibers could be found in many samples. The pattern of fabric damage was occasionally suggestive of a vascular clamp or by abrasion by an other surgical instrument, which may have taken place during the surgical procedure.

For most autopsies, it was possible to remove a portion of the pannus which included the interface with the artery as well as the suture. For prostheses which had functioned for long periods of time the anastomotic area was well healed and appeared continuous with prosthesis. Irregularities at that site generally lead to early problems due to unfavorable haemodynamics and thrombosis becomes a more probable event.

Grafts exhibiting poor healing and incompletely covered luminal surfaces were typical of those where patients had a diabetic history. Fibrin deposits, in such cases, appeared irregular, sparse, and formed rough luminal surfaces; distal embolization at or near the anastomosis site was common. Much of the lumen surface remained uncoated but the interstitial spaces between the fibres seemed adequately sealed to prevent blood leakage. Patches of uncoated yearns were readily found for most prosthesis originating from patients who had been in a poor state of health in the latter part of their life.

Sterile inflammatory reactions are not common in fabric cardiovascular implants. Nevertheless, one case was cited where such a reaction led to the mandatory replacement of a device. A Knitted de Bakey, implanted at the sub-clavian position in a 71 years-old patient, developed this condition after 23 months and had to be replaced. It was tentatively concluded that the patient developed an "allergy" to the polyester material. Other than evidence of poor healing, the prosthesis was unremarkable. Blood cultures for this patient proved negative and no bacterial development was noted by scanning electron microscopy; bacterial invasion therefore does not appear to have been a factor.

Interstitial hemorrhages, in particular those near the anastomosis, were encountered and were sometimes related to the distention of prosthesis fibers and other fabric deformation phenomena. These led to local interstitial leakage of blood; ruptured prosthesis fibers were not found. Healing was relatively poor on such samples.

TABLE 6.01

SUMMARY OF PROSTHESES

OBTAINED AT AUTOPSIES

PROSTHESIS TYPES		MALE	FEMALE	TOTAL
Woven	Woven de Bakey	1	0	1
	Unidentified	1	0	1
				2
Knitted	Weavenit	17	0	17
	ULW	4	0	4
	Knitted de Bakey	4	0	4
	Milliknit Golaski	1	0	1
	Unidentified	1	0	1
				27
Velours	Microvel	9	4	13
	Vasculour D	0	1	1
	Sauvage Guideline	1	0	1
				15
TOTAL		39	5	44

TABLE 6.02

AVERAGE OF PATIENTS AT FIRST IMPLANTATION

(AUTOPSY CASES)

		AGE AT IMPLANTATION (MALE)	AGE AT IMPLANTATION (FEMALE)	AVERAGE AGE
Knitted	Weavenit	58.625	-	58.625
	ULW	60.33	66	61.75
	Knitted de Bakey	59.25	-	59.25
Velours	Microvel	63.667	63.33	63.58

Excludes patients with traumatic and congenital indications for surgery.

TABLE 6.03

FUNCTIONAL LIFETIME OF PROSTHESIS

AS A FUNCTION OF AGE*

AGE	POST-OPERATIVE	1 - 6 MONTHS	6 - 24 MONTHS	24 MONTHS & ABOVE	TOTAL
30 - 40	1	-	-	-	1
40 - 50	1	-	2	-	3
50 - 60	3	2	2	8	15
60 - 70	5	3	2	8	18
70 - 80	3	2	-	2	7
TOTAL	13	7	6	18	44

* Age at implantation.

TABLE 6.04

FUNCTIONAL LIFE OF PROSTHESES

WITH TYPE OF PROSTHESIS

(AUTOPSY CASES)

TYPE OF PROSTHESIS		POST-OP	1 - 6 MONTHS	6 - 24 MONTHS	MORE THAN 24 MONTHS	TOTAL
Woven	Woven de Bakey	-	1	-	-	1
	Unidentified	-	-	1	-	1
Knitted	Weavenit	4	0	5	8	17
	ULW	-	-	-	4	4
	Knitted de Bakey	-	-	-	4	4
	Milliknit Golaski	1	-	-	-	1
	Unidentified	-	-	-	1	1
Velours	Microvel	7	6	-	0	13
	Vasculour D	-	-	-	1	1
	Sauvage Guideline	1	-	-	-	1
TOTAL		13	7	6	18	44

For aorto-femoral bifurcations, uncoated fibres are almost always encountered in or near the bifurcation zone. The bifurcation zone appeared as a site of difficulty. It does not form a defined pseudo-intima and most prostheses showed exposed yarns in that area, no matter how long they had been implanted. It is noted that the bifurcation is normally larger than the original artery which it replaces and that the haemodynamics are not ideal; it is an area of turbulence. Recovered samples confirmed this suspected inadequacy in current device designs.

TABLE 6.05

INDICATIONS FOR IMPLANTATION

	WOVEN	KNITTED	VELOURS	TOTAL
Aneurism	1 *	7 *	6 *	14
Claudication		21 *	7 *	28
Coarctation of the aorta	1			1
Congenital malformation			1	1
TOTAL	2	28	14	44

* Includes 5 ruptured aneurisms cases

The following anecdotal observations are worthy of mention in connection with the autopsy data. Neoendothelization with endothelial-like cell development was noted in only four cases. In all instances it was confined to small patches on or near the anastomosis or on isolated areas not far from the anastomotic site: an aorto-femoral Weavenit after 17 months of implantation in a elective patient (48 years-old, abdominal aorta aneurism, iliac stenosis), a well healed Weavenit bifurcation implanted for 50 months in a 55 years-old patient treated for claudication; a Knitted de Bakey implanted for 98 months after resection of an abdominal aneurism in a 64 years-old patient and a Knitted de Bakey implanted for 84 months in two femoro-popliteal positions to bypass bilateral blockage in a 58 years-old candidate. In summary, there are relatively few points in common for all these patients other than the observation that they were somewhat younger and free of additional degenerative disease such as diabetes. Three Microvel prostheses (figure 6.06) implanted by the same surgeon and collected after two months, showed radically different healing characteristics; the first, B16, was the best in spite of the fact that it originated from a high risk patient (75 years-old, emergency surgery for a ruptured aneurism, post-operative kidney failure). All traces of healing were absent from a second prosthesis, B25, which originated from an elective patient (71 years old, diabetic). This same patient had an uneventfull post-operative recovery. The third device, B58, was also from an elective patient (59 years old, aneurism of the aorta). This device exhibited only a thin coat of fibrin with a smooth surface but without densification or organ-

TABLE 6.06

CAUSE OF DEATH OF PATIENTS

(AUTOPSY CASES)

CAUSES	POST OP.	1 - 6 MONTHS	6 - 24 MONTHS	MORE THAN 24 MONTHS	TOTAL
Infarct	3	1	1	10	15
Post operative shock	2	-	-	1	3
Kidney failure	2	2 (1)	-	(1)	4
Respiratory failure	3 (2)	1 (1)	1 (1)	2	7
Intestinal necrosis	1	1	-	-	2
Cancer	-	1	1	3	5
Artheriosclerosis	-	1	2 (1)	(3)	3
Hemorrhage	2	-	1	-	3
Infection	-	-	-	1	1
Others	-	-	-	1	1
TOTAL	13	7	6	18	44

1 main cause

(1) associated cause

TABLE 6.07

IMPLANTATION SITE OF PROSTHESES COLLECTED AT AUTOPSIES

Site	Woven	Knitted	Velours	Total
Aorto-femoral (bilateral)	1	24[a]	12	37
Ilio-femoral	-	1	-	1
Femoro-popliteal	-	1[b]	1[c]	2
Coarctation of the aorta	1	-	-	1
Femoro femoral	-	1	-	1
Axillo-femoral and fémoro-fémoral	-	-	1	1
Abdominal	-	-	1	1
Total	2	28	14	44

(a) First surgery for unilateral by-pass followed by a replacement with a bilateral by-pass on a second surgical attempt.

(b) Bilateral

(c) Unilateral

ization; his death was primarily the end result of generalized atherosclerosis with terminal complications. Thus of all candidates, the one who appeared a poor risk prior to surgery and during post-operative recovery showed the best healing characteristics thus illustrating the impact of a patient's general state of health and the key role of associated degenerative diseases on healing processes.

Although no death can be attributed directly to failure of a prosthesis, the risk can be demonstrated for one patient. The patient who provided prosthesis M015 (Vasculour D), was exposed to a hemorrhagic risk since many of the fibres of that device were broken at several sites. Also, the external capsule to this prosthesis was particularly thin and contained no elastin fibers, smooth muscle or connective tissue of any king. M015 could be thus regarded as an incipient case of prosthesis rupture.

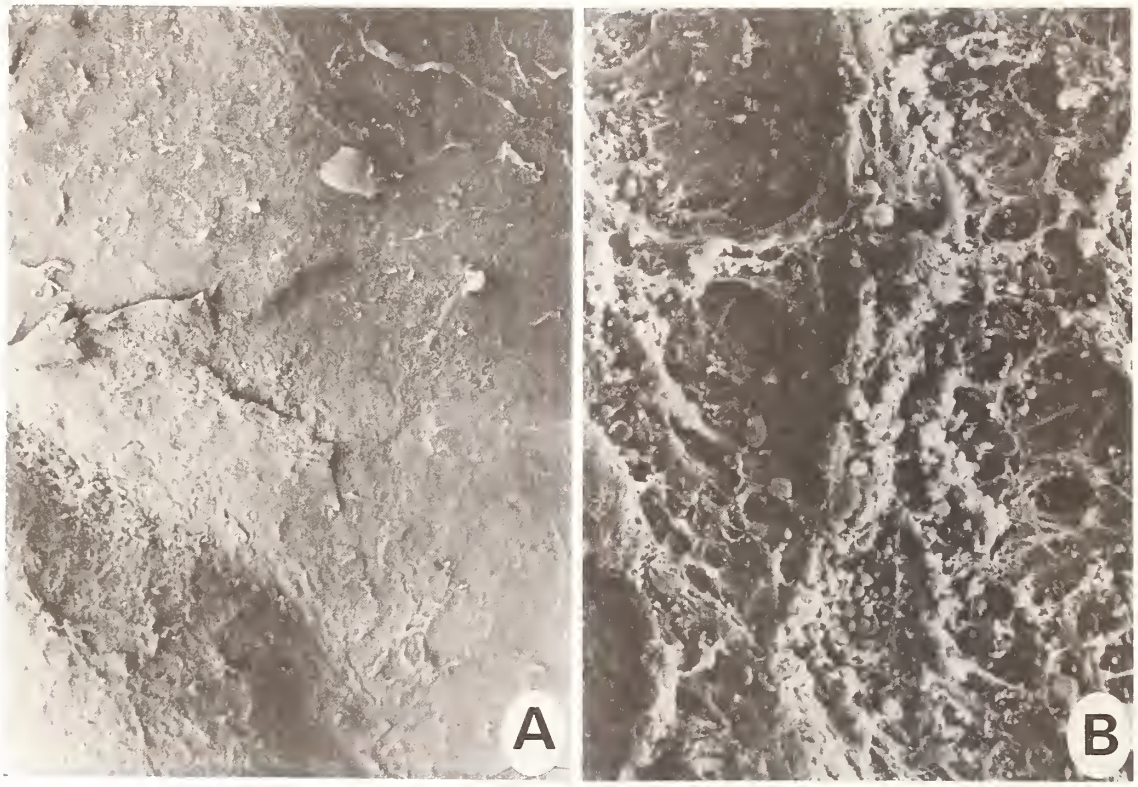


Figure 6.01 : Flow surface of a prosthesis after 6 weeks in-situ in a 67 years old poor risk patient (ruptured aneurism resection); note dense network of fibrin and smooth surface. (Woven de Bakey, B66)

Several patients had prostheses with insecure anastomoses due to: disturbances in the suture line, tissue or prosthesis fabric tears or hyperplasic tissue proliferation in the area.

Noteworthy examples of these effects are presented in Figures 6.01 to 6.07, with appropriate comments in the figure captions.

3.4 Fabric Properties

Prostheses which had sufficient amounts of fabric were evaluated with respect to fabric properties. The results of these measurements are shown in Table 7 and are presented graphically in Figure 7. Crimp, stitch density and burst strength were all found to decay with "in-vivo" residency (duration of implantation). Only the filament diameter showed and initial increase; however, a decrease eventually took place over a period of about 2-3 years of implantation.

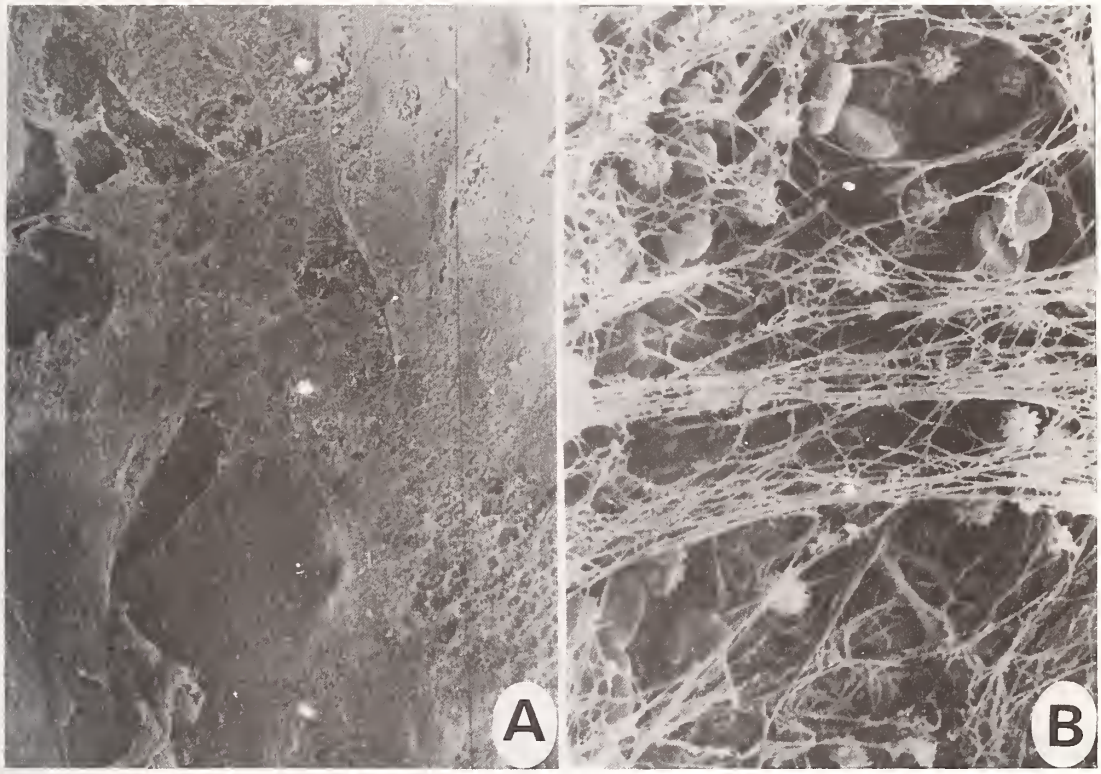


Figure 6.02 : Surface of a prosthesis after 3 days in-situ in a 53 years old patient (elective aneurism resection); note mesh of fibrin with entrapped cells (Weavenit, B74).

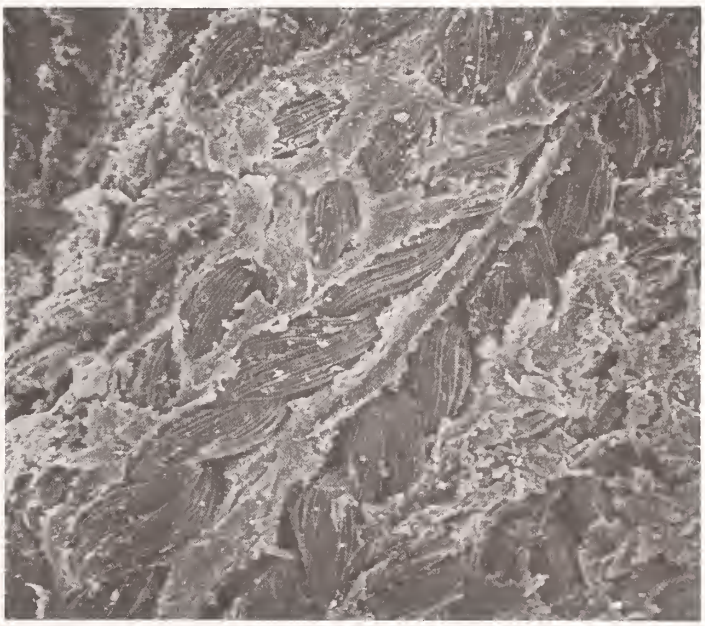


Figure 6.03 : Flow surface of a prosthesis after 9 days in a 72 years old diabetic; note bare fibres and pore filling debris. Such prostheses in spite of their thin coating do not leak blood. (Weavenit, B1)

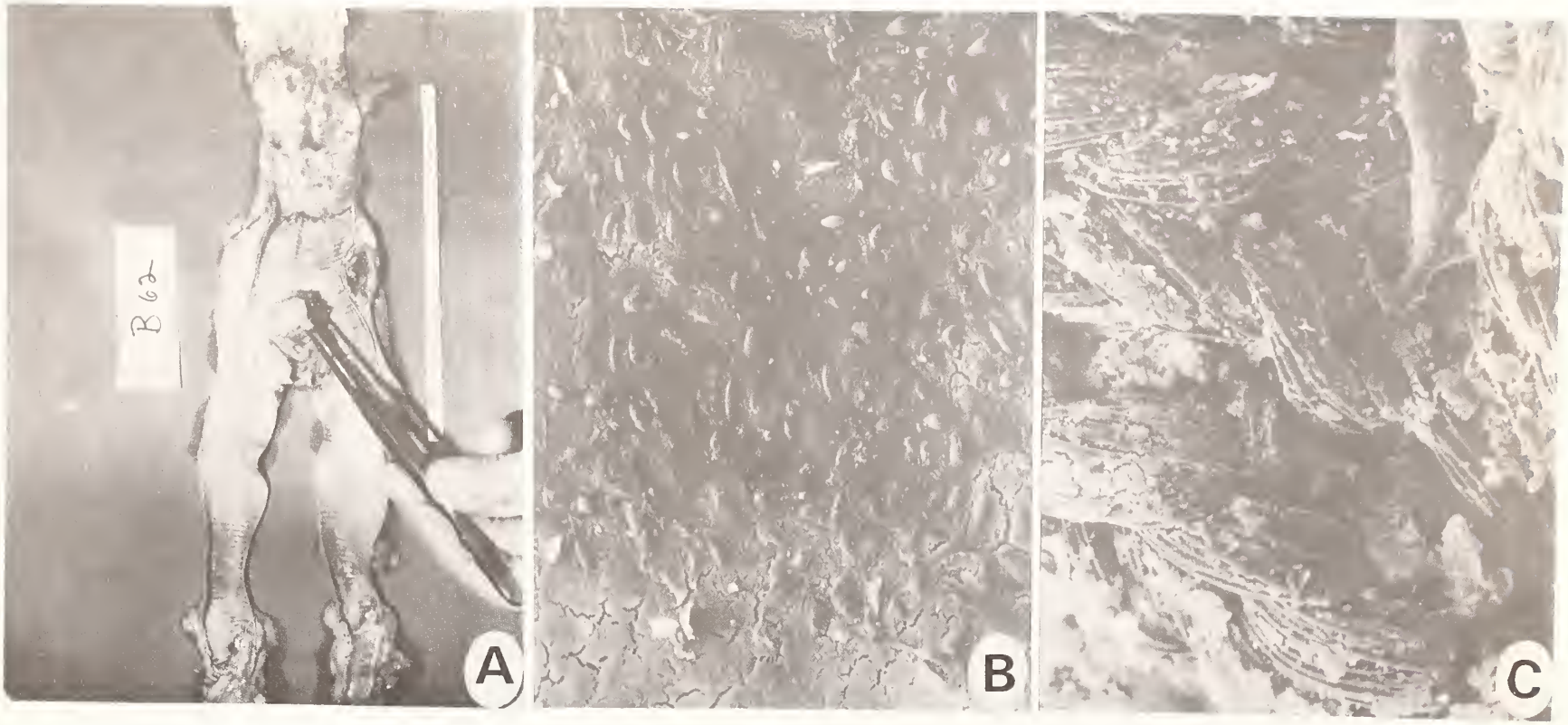


Figure 6.04 : Flow surface of an aorto-femoral bifurcation prosthesis in-situ for 43 months in a 55 years old (Weavenit, B62)
A: General macroscopic view
B: Higher magnification showing endothelial-like cells near the anastomoses (x 100)
C: High magnification showing bare fabric near the bifurcation shelf (x 100)

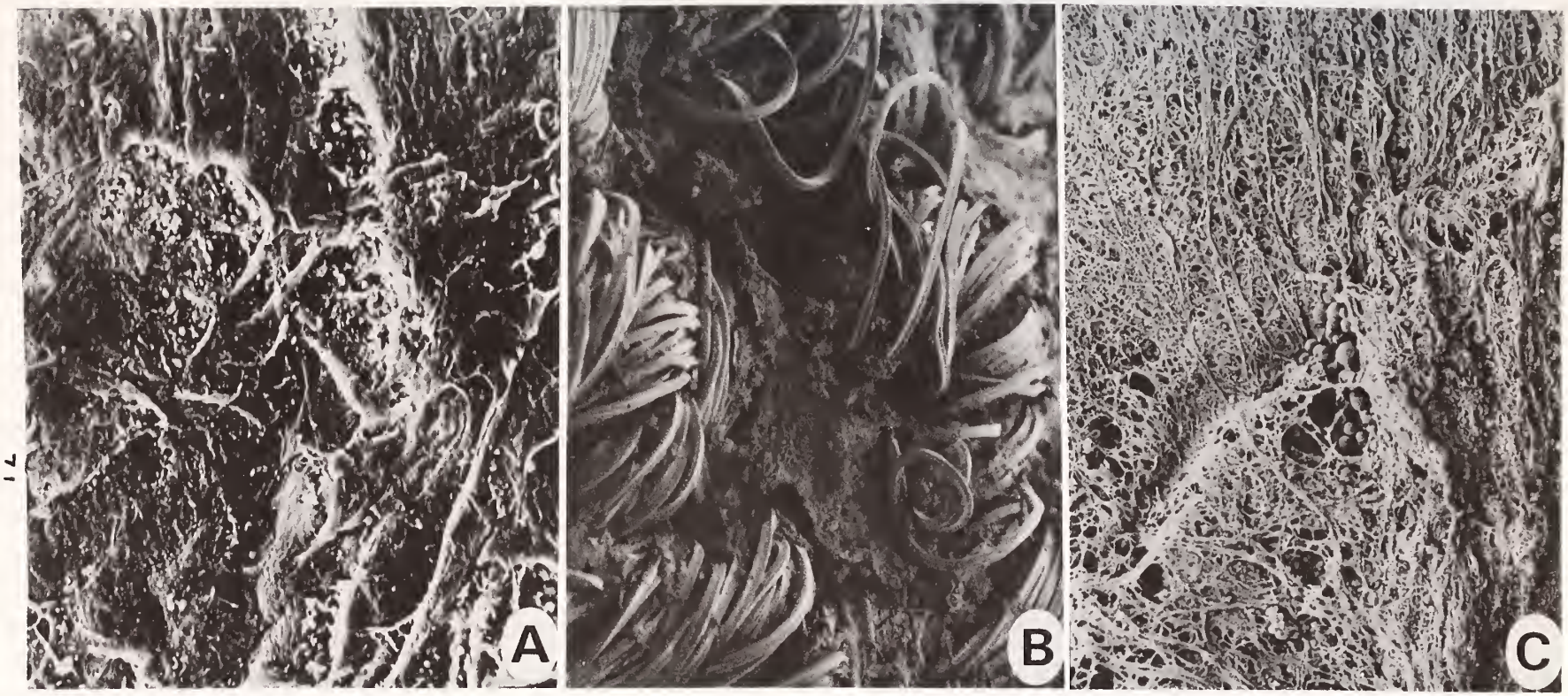


Figure 6.05 : Flow surface of three Microvel bifurcation grafts implanted by the same surgeon (after 2 months):
A: 75 years old male (B16) operated upon because of ruptured aneurism and dead because of an irreversible renal insufficiency (x 200)
B: 71 years old male (B25) operated upon because of artheriosclerosis and dead because of an infarct. (x 100)
C: 59 years old male (B58) operated upon because of elective aneurism and dead because of pneumonia. (x 200)

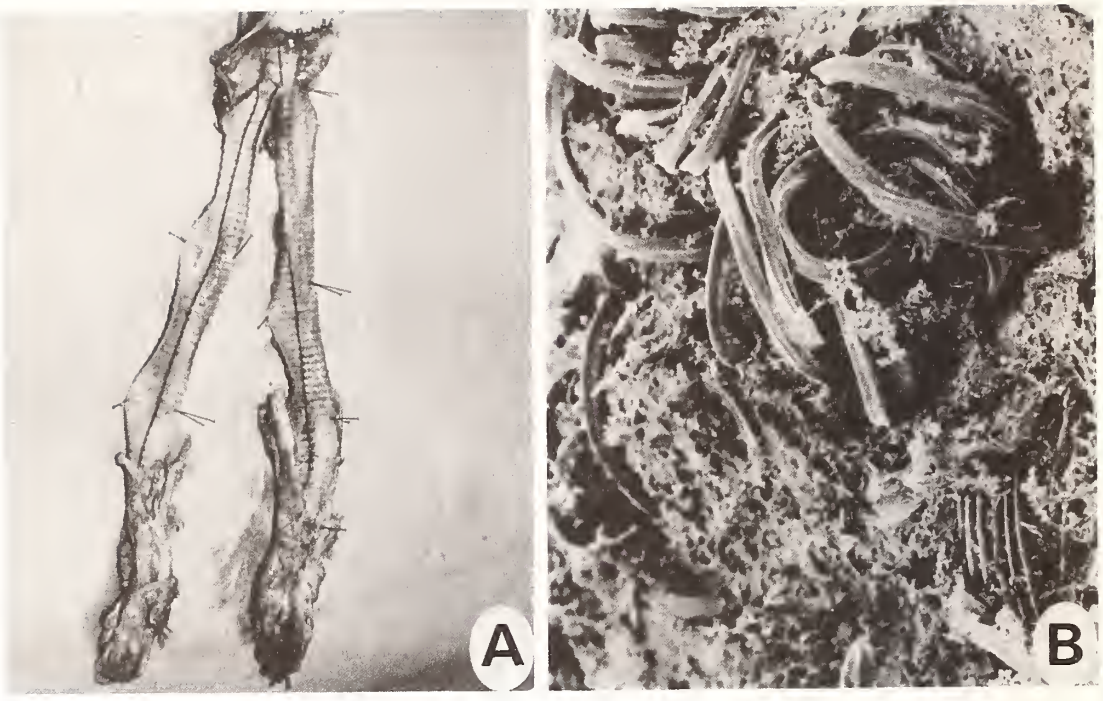


Figure 6.06 : Flow surface of a velour bifurcation (Microvel B56) in-situ for 3 weeks in a 69 years old patient;
A: General view
B: Detail of surface of A, note irregular covering with wall thrombi and protruding trilobal fibres (x 200)

3.5 Polymer Properties

The results of preliminary chemical analyses for the assessment of chemical deterioration which were carried-out on fibres are presented in the discussion.

3.6 Fibre Damage

A number of samples showed areas of macroscopic damage. Others gave evidence of damage only at higher magnification under scanning electron microscopy. Examples of damage, distorsion and deterioration are shown in Figure 8. These separate into three classes: fabrication damage, handling trauma and physico-chemical deterioration. Violent extension and breakage of fibres yield characteristically thinned and "fibrillated" structures whereas physico-chemical deterioration is more likely the cause of fibres with longitudinal cracks or splits and transverse crevices which do not extend across the fibre. Porous surfaces and sharply broken fibres are other expressions of physico-chemical deterioration. These types of damage are never found on new prostheses as supplied.

Fibres with regularly spaced features such as flats, depressions, protuberances and other details suggestive of compressive deformation are the characteristics of harsh shrinkage, compaction and crimping processes and are found on new prostheses as well as on explanted ones.

Type of graft	Reference Code	Duration of implantation	Bursting strength	FABRIC COUNT			Crimp	Filament Diameter
				stitches	stitches	stitch density		
		months	kg/cm^2	Wales/cm	Courses/cm	stitches cm^2	%	um ± 0.3
Woven de Bakey	As supplied (9mm diam)	0	50	50.4	32.7	1650	16	12.5
	B 66	1.2	43.9	50.9	32.9	1670		12.8
Knitted de Bakey Standard	As supplied (8mm diam)	0	30.9	21.3	30.4	648	350	12.6
	MO22	23						
	B 75	72		17.5	26.0	455		13.2
	B 52	82	32.9	15.7	20.7	325	60	12.8
	B 79	84		15.5	22.8	353	20	12.7
	B 73	97						
	B 61	98	34.1	17.9	26.4	473	62	13.3
	B 46	107	28.7	17.3	24.2	419	37	13.5
	B 69	115						

Table 7.02: FABRIC PROPERTIES OF EXPLANTED GRAFTS

Type of graft	Reference Code	Duration of implantation	Bursting strength	FABRIC COUNT			Crimp	Filament Diameter
				stitches	stitches	stitch density		
		months	kg/cm^2	Wales/cm	Courses/cm	stitches cm^2	%	um ± 0.3
ULW	As supplied (7mm diam)	0	14.7	22.4	27.3	612	120	13.6
	MO23	36						
	B 31	65	18.9					
	B 82	72						
	B 77	77	17.6	18.6	24.0	446	56	12.5
Microknit	As supplied (8mm diam)	0	15.2	37.2	39.8	1480	310	11.1
	FP 23	29		33.7	35.0	1180		12.9
Weavenit	As supplied (8mm diam)	0	15.3	25.6	33.6	860	125	13.6
	B 74	0.1	14.4	23.8	32.9	738	93	13.8
	B 36	35	14.6					
	B 68	38	15.5	12.0	31.1	684	46	13.3
	B 47	39	14.6	20.5	32.0	656	34	14.9
	B 78	40	12.5	23.1	30.6	707	29	14.2

Type of graft	Reference Code	Duration of implantation	Bursting strength	FABRIC COUNT			Crimp	Filament Diameter
				stitches	stitches	stitch density		
		months	kg/cm^2	Wales/cm	Courses/cm	stitches cm^2	%	um ± 0.3
Weavenit	B 62	43	17.2	22.1	34.9	771	45	13.3
	B 37	44	13.9					
	B 41	44	12.5	24.2	28.6	692	22	13.9
	B 57	57		23.9	31.6	755	45	13.3
	B 80	74		21.0	35.5	746		14.0
	FP 26	84	13.4	21.2	32.2	683	30	14.1
Knitted Cooley	As supplied (8mm diam)	0	27.7	20.3	27.9	466	110	16.2
	MO 16	8	23.2	18.7	28.1	525	44	16.5
	B 55	48	23.4	18.9	27.6	522	33	15.7
Microvel	As supplied (8mm diam)	0	11.2	21.7	32.3	701	145	12.5*
	B 43	0.05	11.2	19.0	28.1	535	18	
	B 37	0.1	10.9					
	B 60	0.3	10.3	16.5	29.9	493	19	

* Circular fibres

Table 7.04: FABRIC PROPERTIES OF EXPLANTED GRAFTS

Type of graft	Reference Code	Duration of implantation	Bursting strength	FABRIC COUNT			Crimp	Filament Diameter
				stitches	stitches	stitch density		
		months	kg/cm^2	Wales/cm	Courses/cm	stitches cm^2	%	um ± 0.3
Microvel	MO 8	0.5	10.6					
	B 39	0.5	10.7					
	B 56	0.7	9.6	16.9	26.8	453	16	
	B 42	1	11.0					
	B 53	1						
	B 58	2	9.4	17.1	29.3	493	19	
	FP 18	3	10.1	16.7	24.7	412	20	
	B 34	3	10.9					
	B 30	5	10.1					
	FP 24	6		18.8	31.0	583	22	
	FP 25	9		18.2	31.3	570	10	
	B 70	15						
	MO 18	18	10.3					
Cooley Double Velours	As supplied (7mm diam)	0	11.8	19.6	27.2	528	38	13.6*
	B 21	20	10.3	17.4	15.8	449	22	18.1*
	B 44	26						

* Circular fibre

Type of graft	Reference Code	Duration of implantation	Bursting strength	FABRIC COUNT			Crimp	Filament Diameter
				stitches	stitches	stitch density		
		months	kg/cm^2	Wales/cm	Courses/cm	stitches cm^2	%	um ± 0.3
Vasculour D	As supplied (8mm diam)	0	17.6	20.2	25.6	517	260	13.8
	MO 23	36		17.8	21.0	374	38	13.8
	MO 15	59	10.1	18.5	22.4	414	22	12.9
Sauvage Guideline	As supplied (8mm diam)	0	17.3	23	29	670	220	13.2
	B 33	0.5	18.9					

Figure 7.01

LOSS IN STITCH DENSITY WITH DURATION OF IMPLANTATION

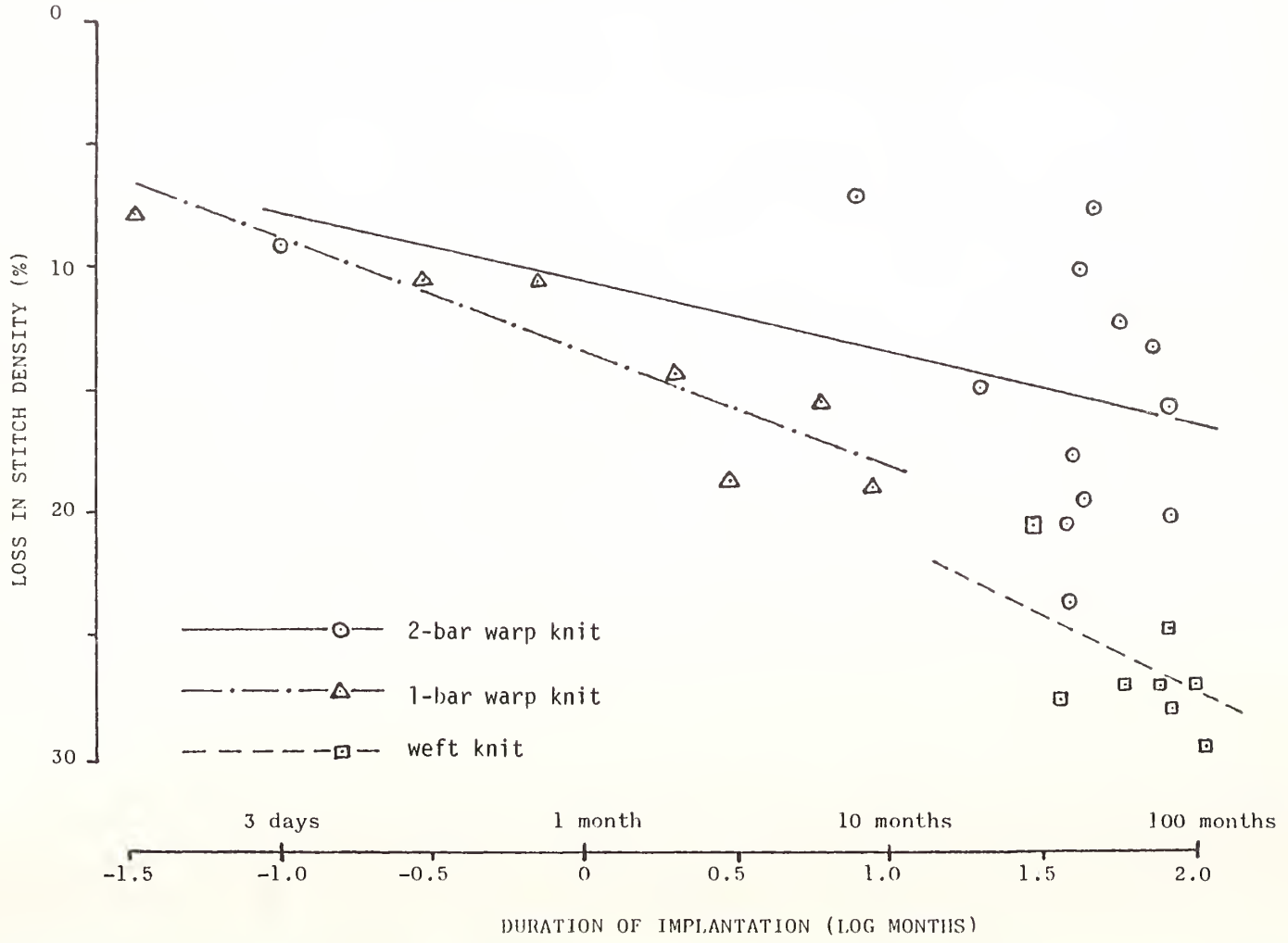


Figure 7.01A

Figure 7.01A

LOSS IN STITCH DENSITY WITH DURATION OF IMPLANTATION

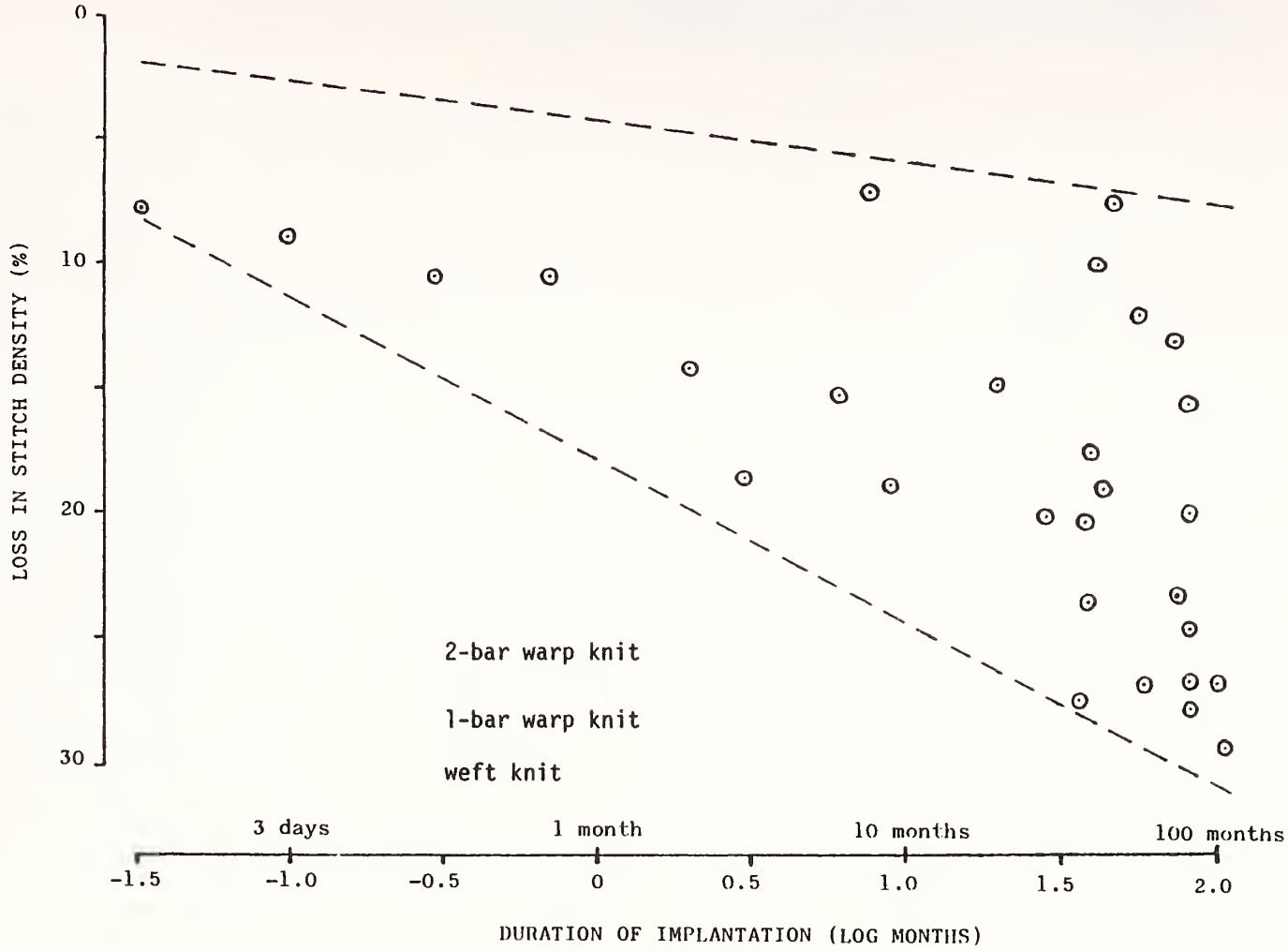


Figure 7.02

LOSS IN CRIMP WITH DURATION OF IMPLANTATION

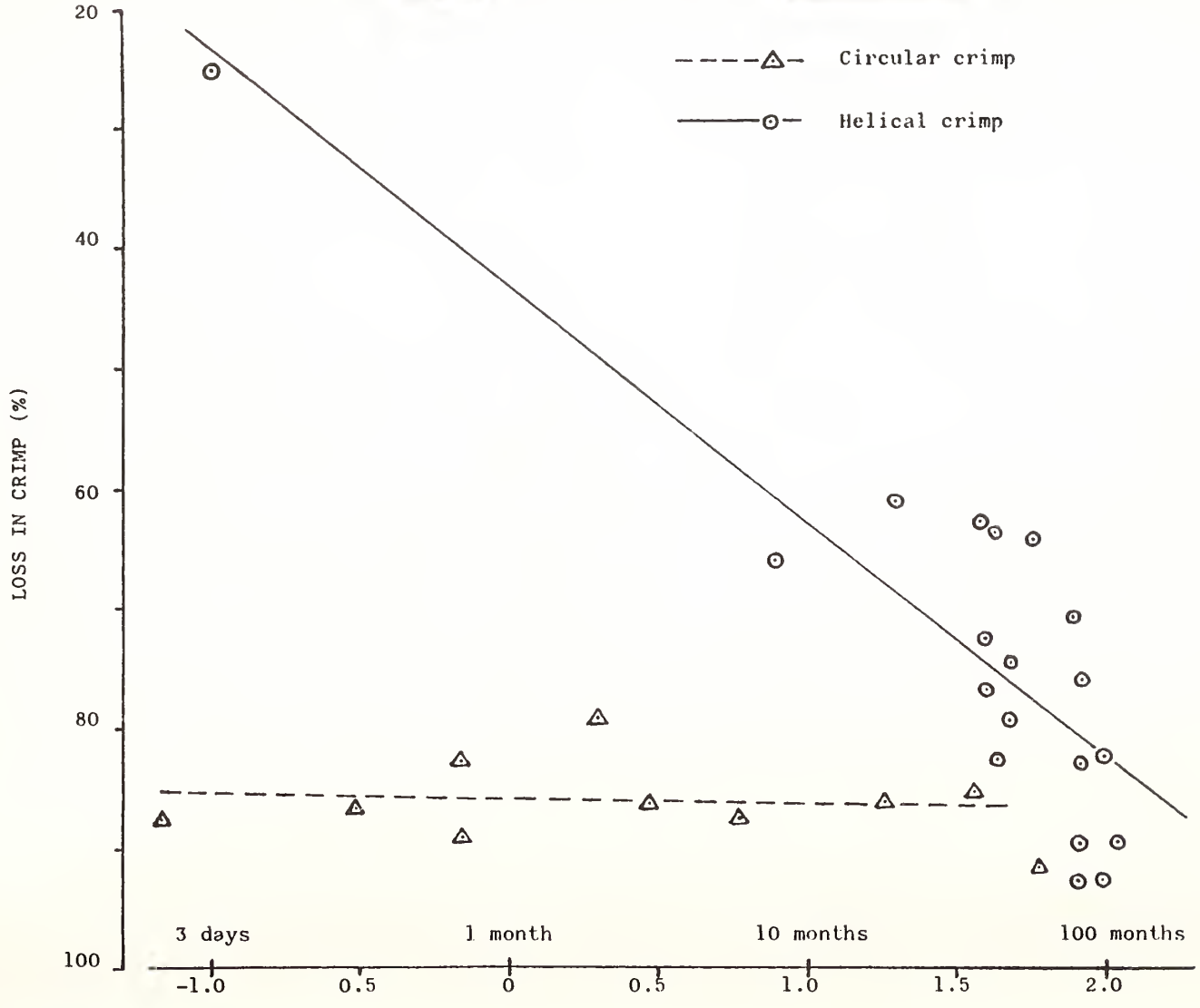


Figure 7.03

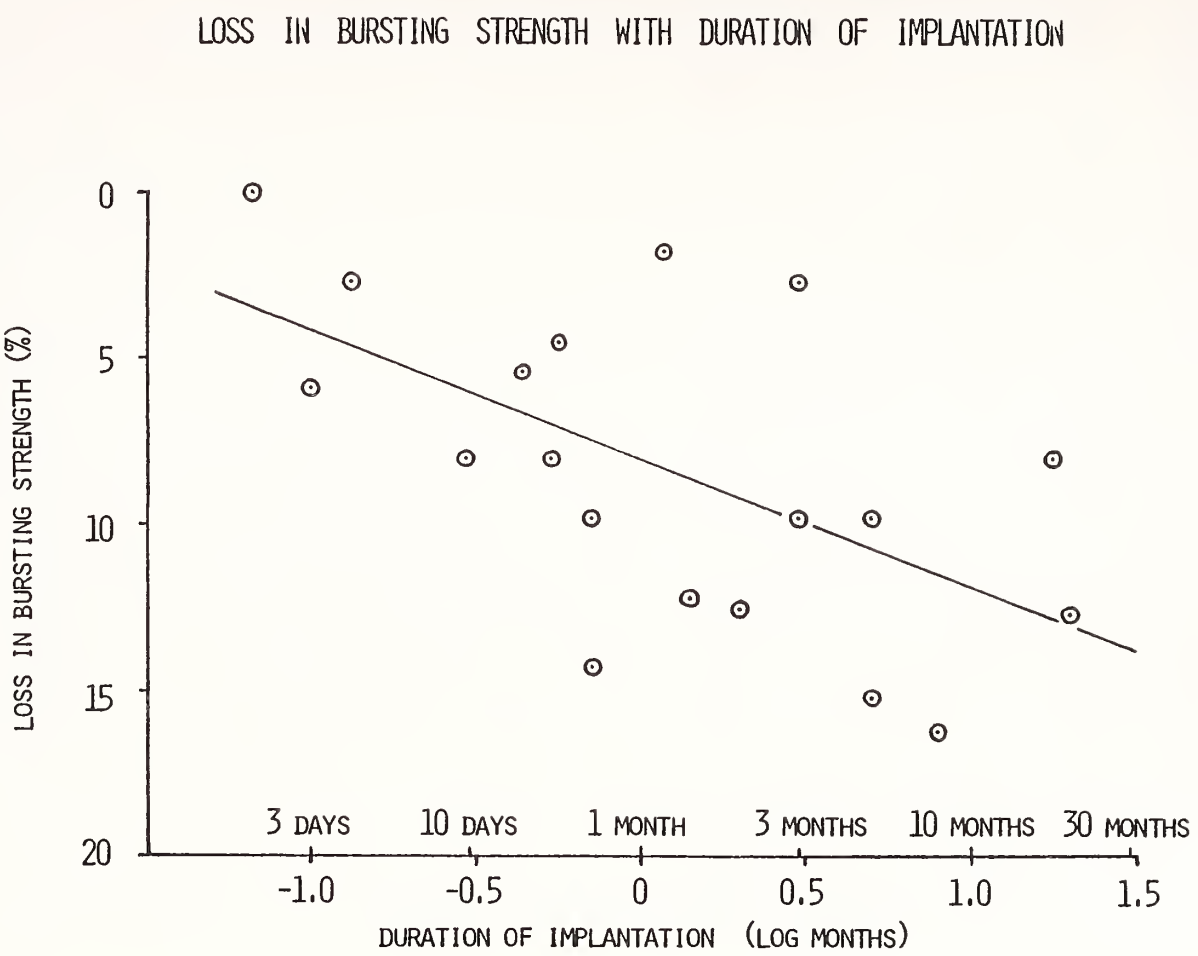

LOSS IN BURSTING STRENGTH WITH DURATION OF IMPLANTATION
LOSS IN BURSTING STRENGTH (%)
0
5
10
15
20
3 DAYS
10 DAYS
1 MONTH
3 MONTHS
10 MONTHS
30 MONTHS
-1.0
-0.5
0
0.5
1.0
1.5
DURATION OF IMPLANTATION (LOG MONTHS)

Figure 7.04

CHANGE IN FILAMENT DIAMETER WITH DURATION OF IMPLANTATION

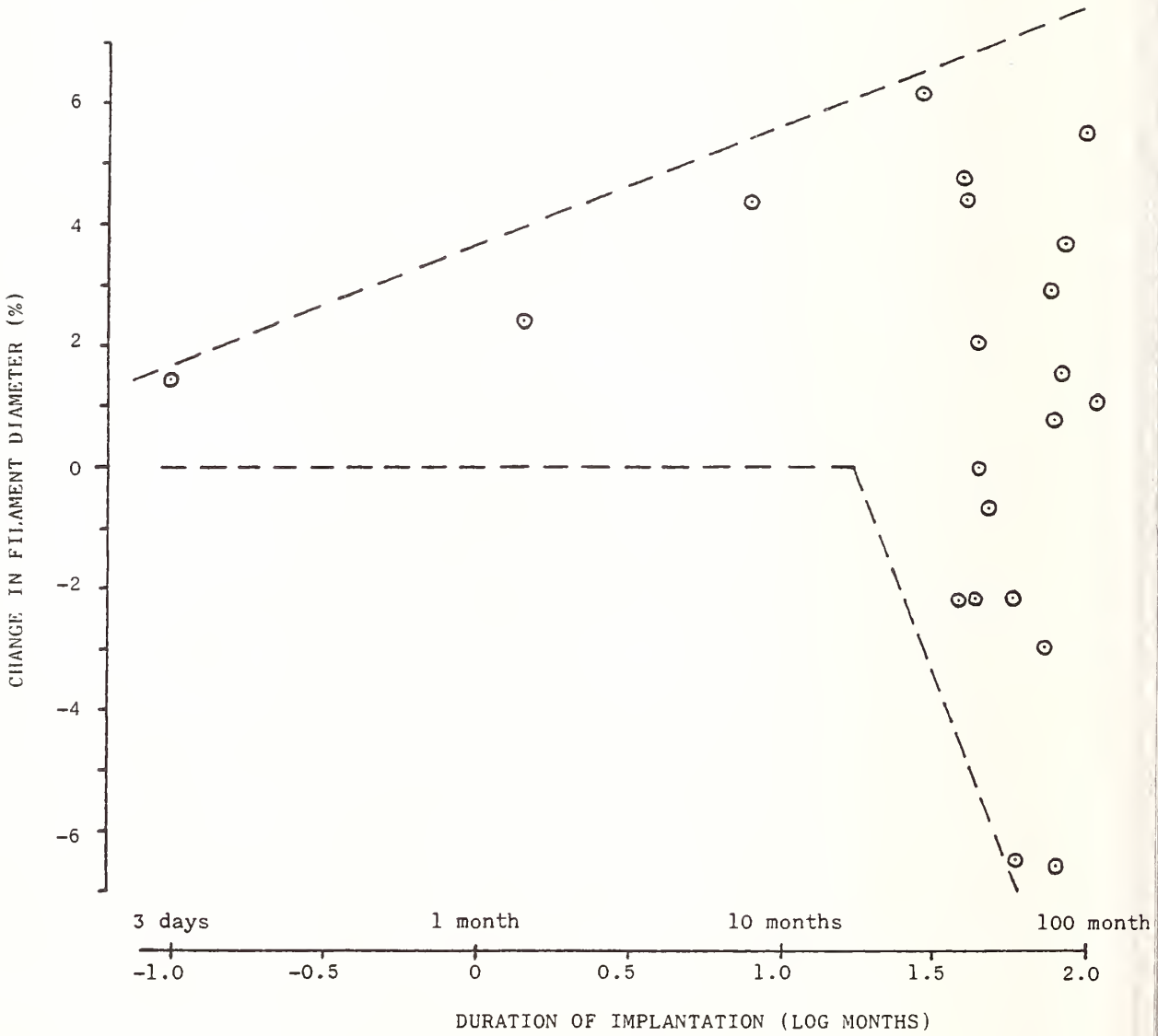


Figure 7.04A

CHANGE IN FILAMENT DIAMETER WITH DURATION OF IMPLANTATION

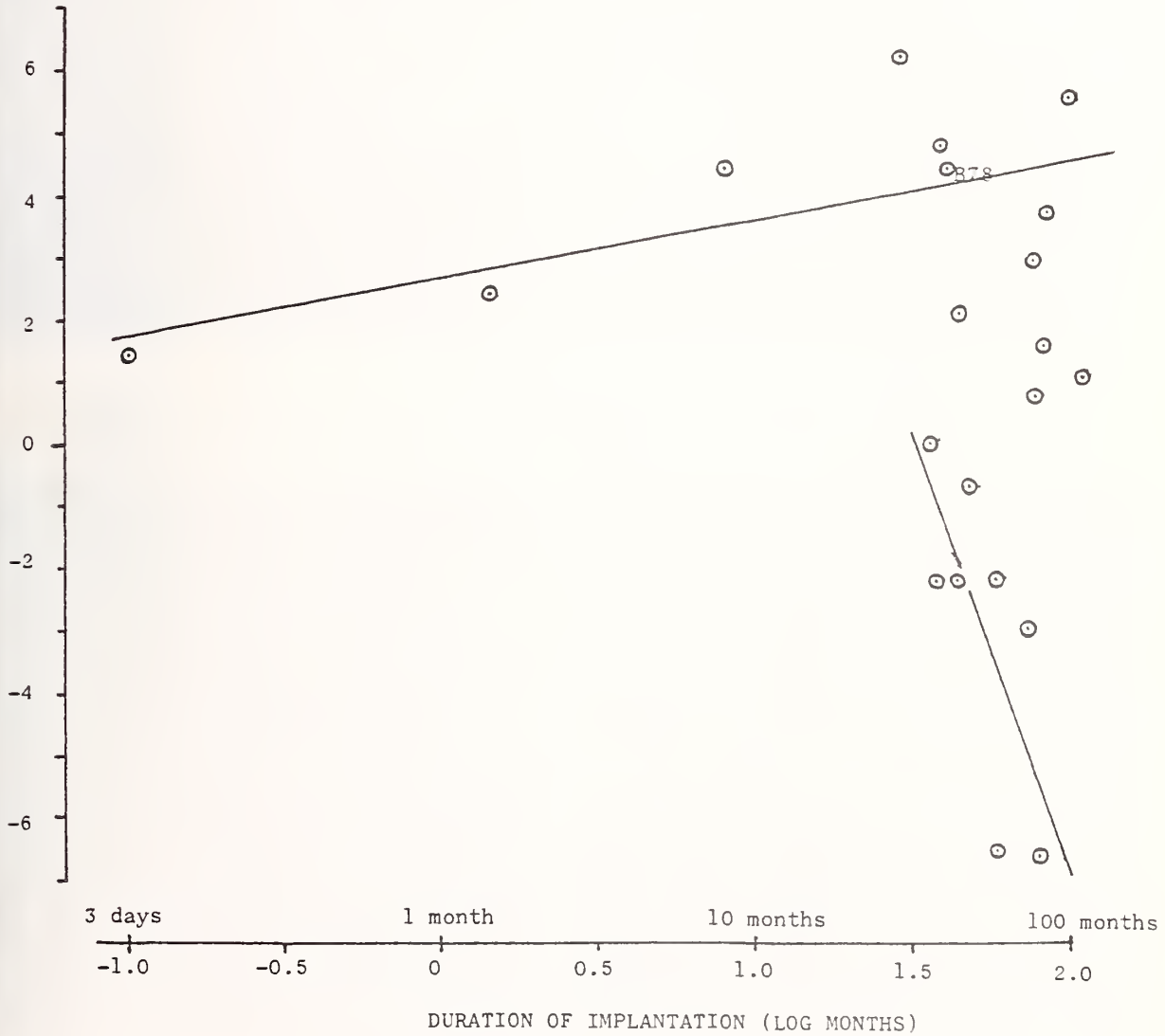
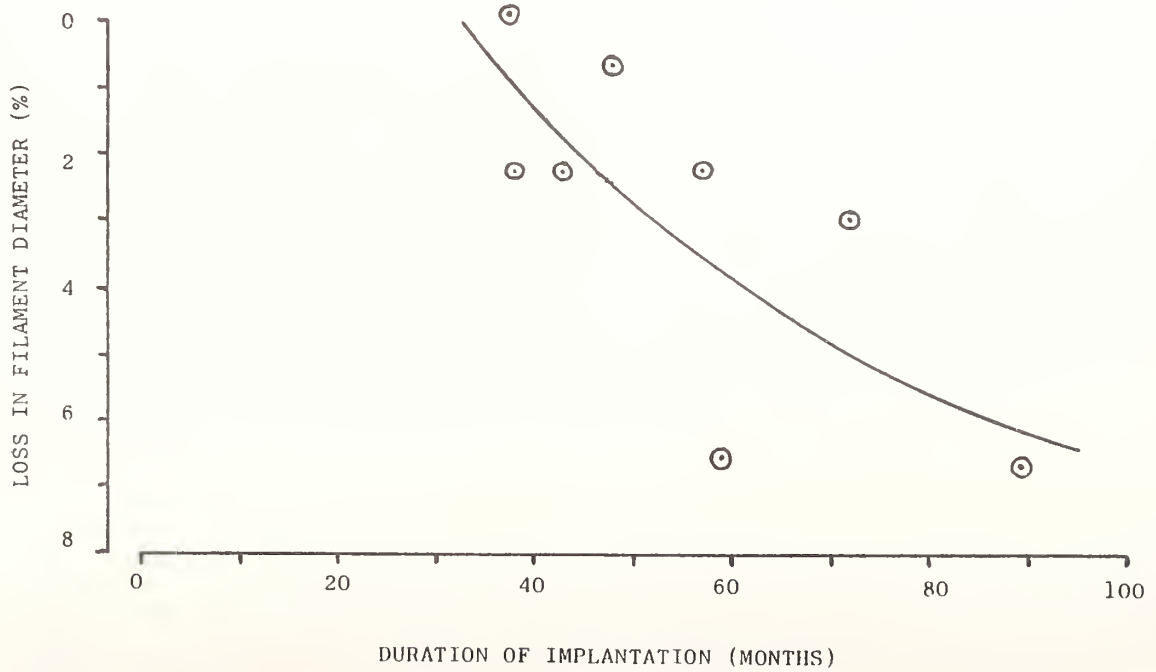


Figure 7.05

LOSS IN FILAMENT DIAMETER WITH DURATION OF IMPLANTATION



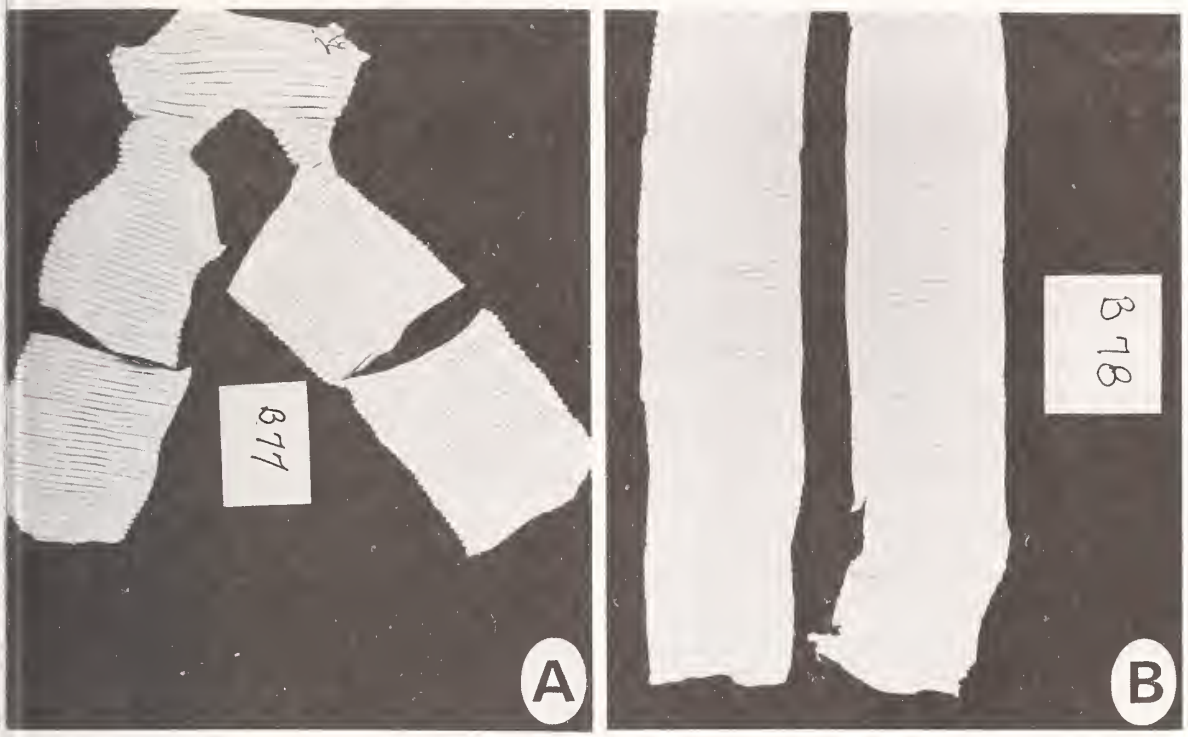


Figure 8.01 : View of prostheses explanted after 77 months (A: Ultralight-weight), and 40 months (B: Weavenit).

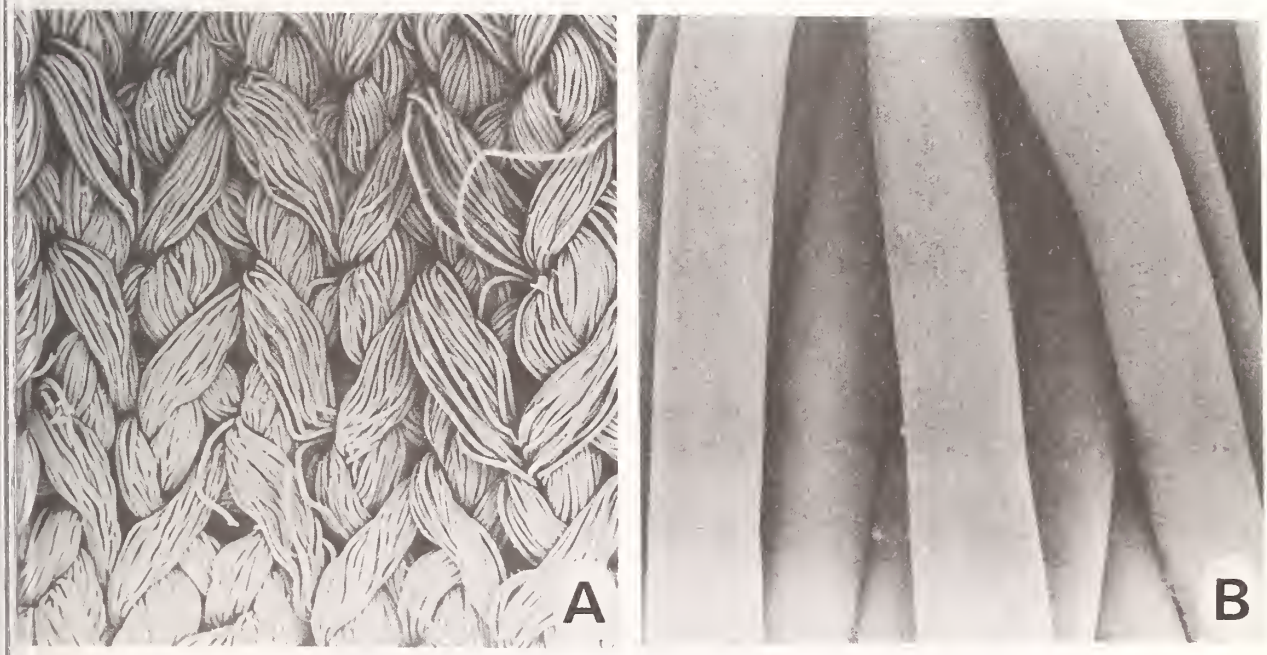


Figure 8.02 : (B47) A. External view of Weavenit prosthesis after 39 months showing isolated filament failure and some variation in the loop length of individual filaments. B. Circular cross-section filaments showing smooth and undamaged surfaces.

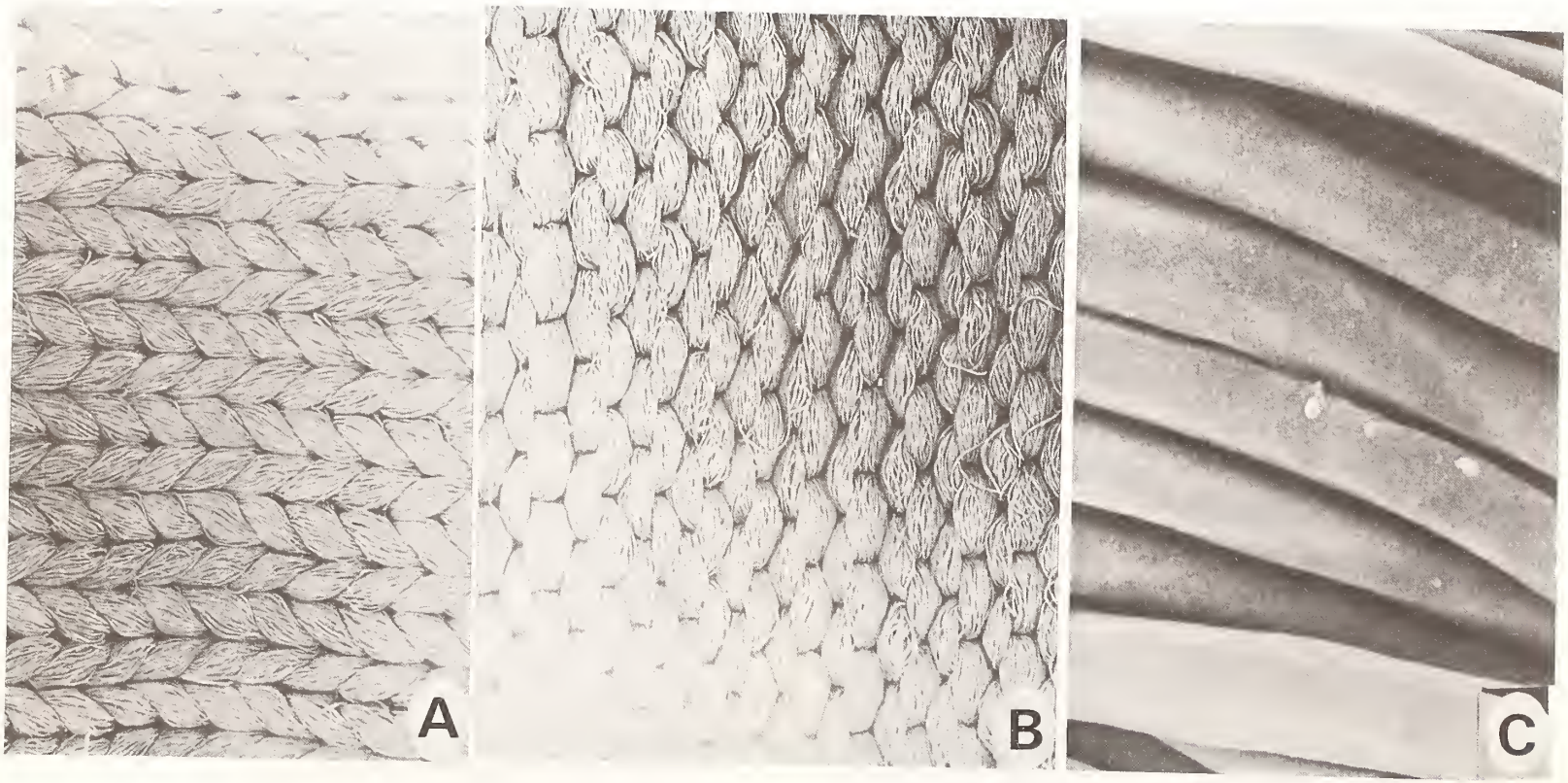


Figure 8.03 : (B46) A. External view of Standard Knitted Debakey prosthesis explanted after 107 months. B. Internal view of Standard Knitted DeBakey prosthesis after 107 months showing some disruption of the filament order within the yarns. C. Filaments flattened incidental to prosthesis fabrication have smooth and undamaged appearance.

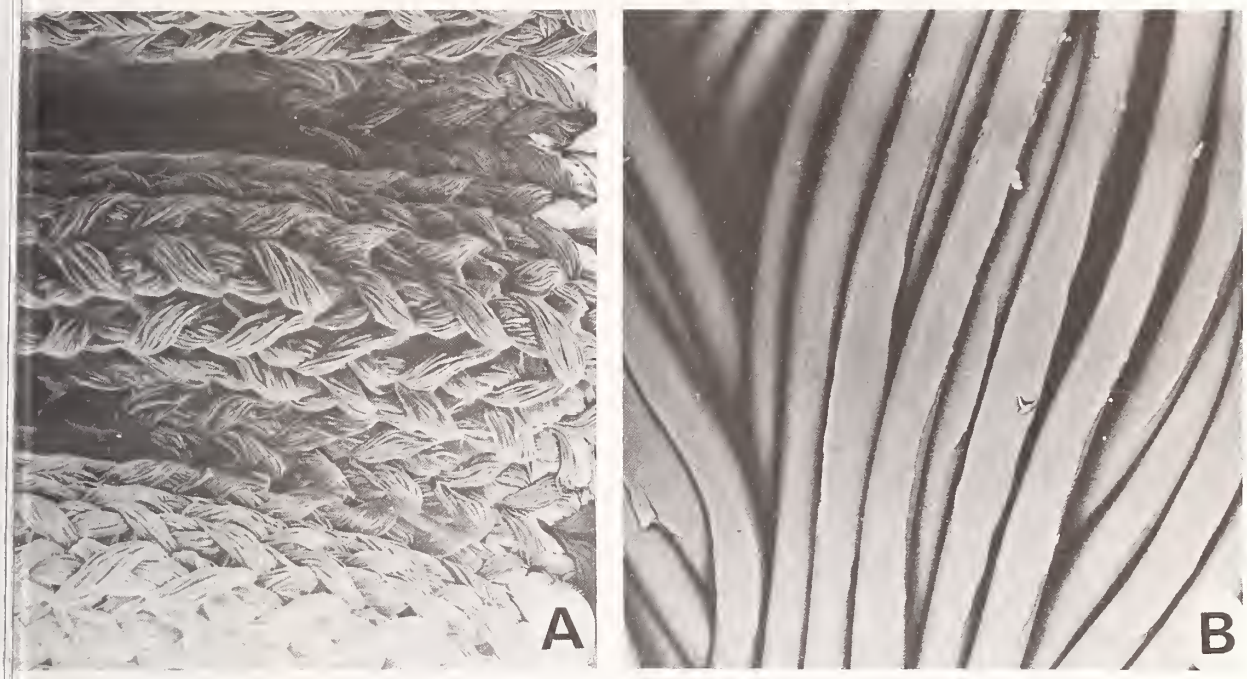


Figure 8.04 : (B55) A. External view of Knitted Cooley prosthesis explanted after 48 months. B. Internal lumen side view of filaments at the crest of a crimp showing flattened surfaces probably caused by contact of the mandrel during crimping.

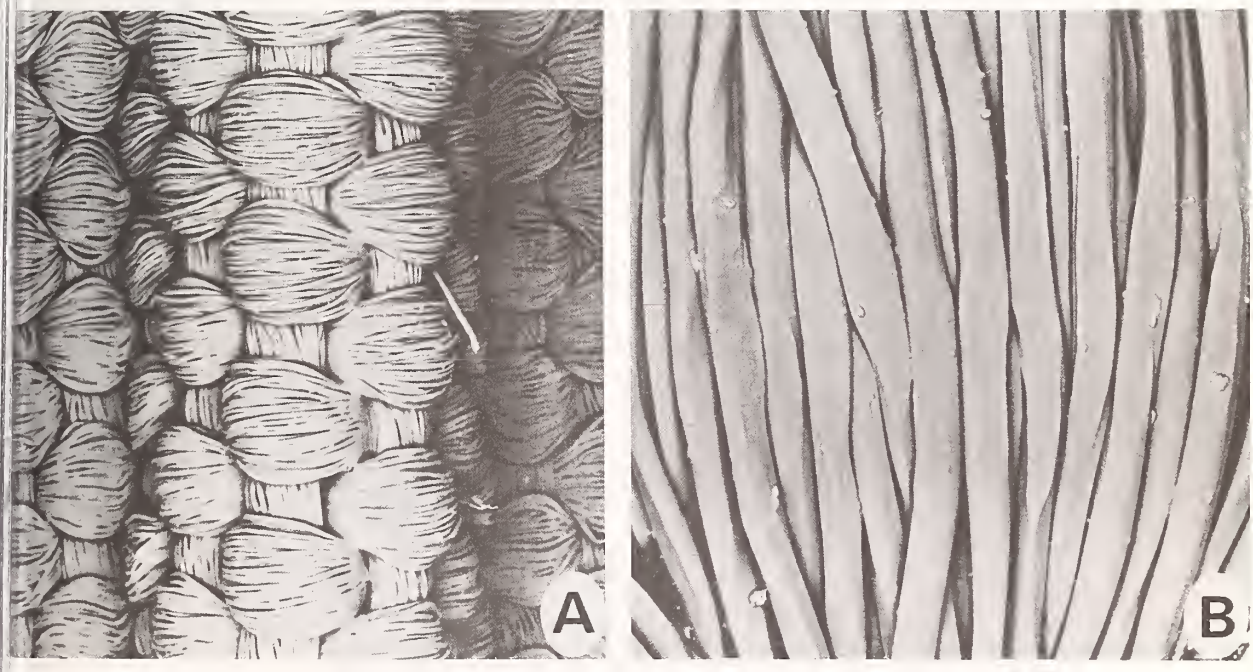


Figure 8.05 : (B66) A. External view of Woven De Bakey prosthesis after explantation at 6 weeks. B. Internal view of filaments at the crest of a crimp showing flattened surfaces probably caused by the contact of the mandrel during crimping.

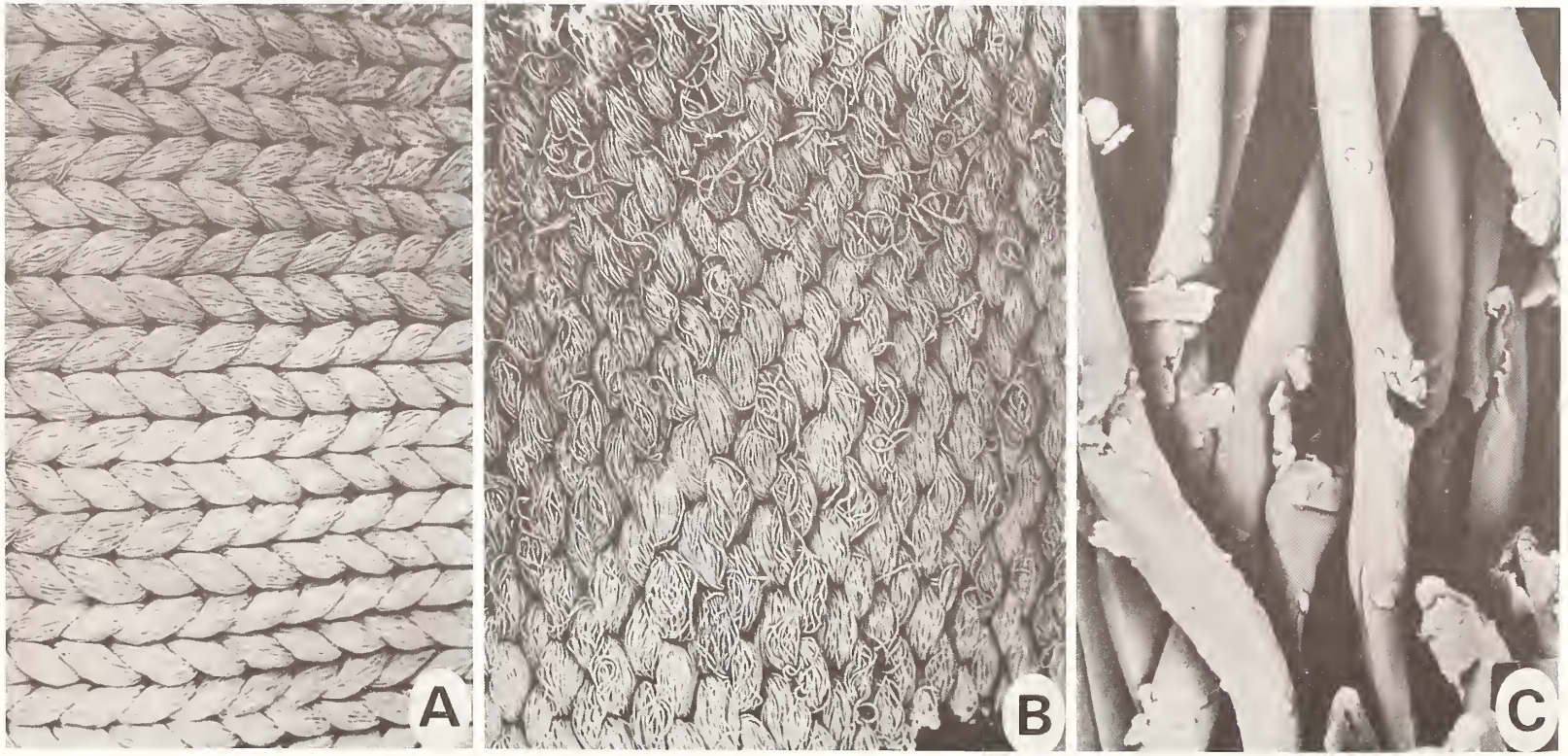


Figure 3.06 : (B61) A. External view of Standard Knitted De Bakey prosthesis explanted after 98 months. B. Internal view of Standard Knitted De Bakey prosthesis after 98 months showing ruptured filaments. C. Damaged filaments showing transverse cleavages, probably caused by vascular clamps at the time of surgery.

Figure 8.07 : (B73) Internal view of Standard Knitted De Bakey prosthesis after 97 months showing yarns ravelled from a damaged area.

Figure 8.08 : (B74) Internal view of a Weavenit prosthesis with undamaged fabric structure and preserved crip after 3 days in-vivo.

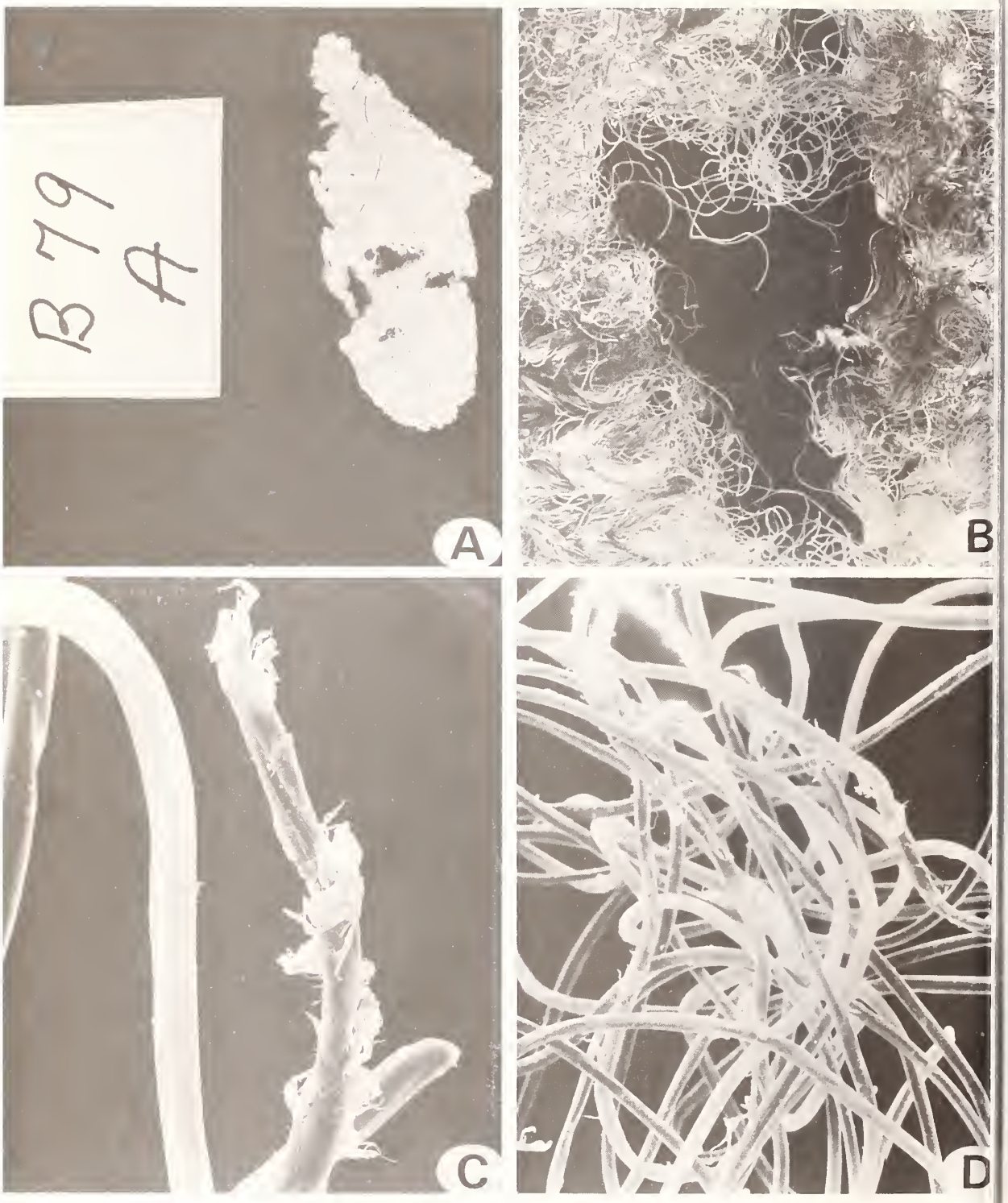


Figure 3.09 : (B79) A. External view of a damaged Standard Knitted De Bakey prosthesis in the area of the false aneurism showing fractured filaments and ravelled yarns explanted after 84 months. B. Ravelled filaments showing smooth and damaged areas. C. Fractured filament containing many micro-fibrils and exhibiting extensive fibrillation, probably due to mechanical fatigue.

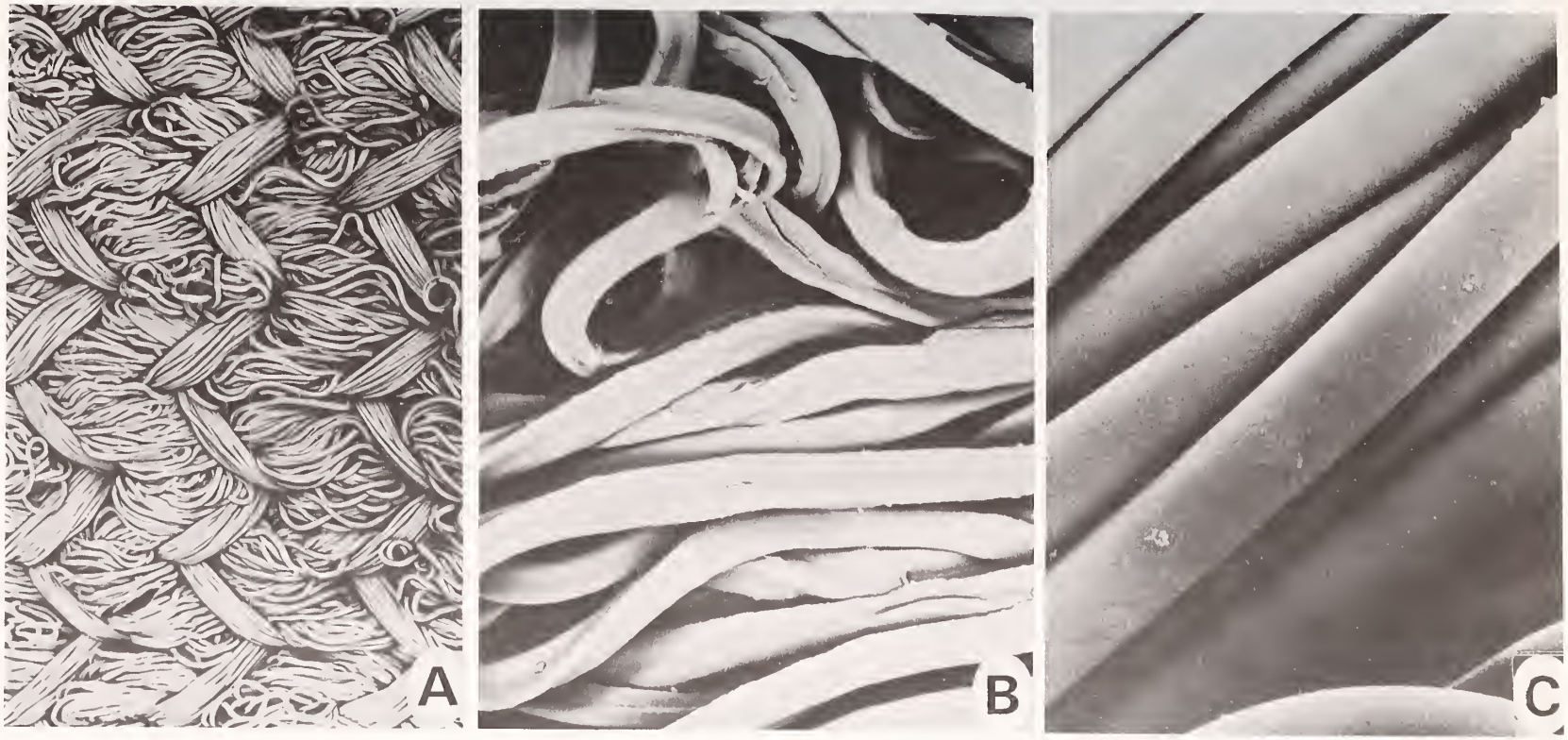


Figure 8.10 : (FP18) A. Internal view of Microvel prosthesis that thrombosed after 3 months implantation. B. Cracks in velour (fill) trilobal cross-section filaments showing axial splitting under bending stresses. C. Circular cross-section filaments in base mesh of fabric have smooth and undamaged appearance

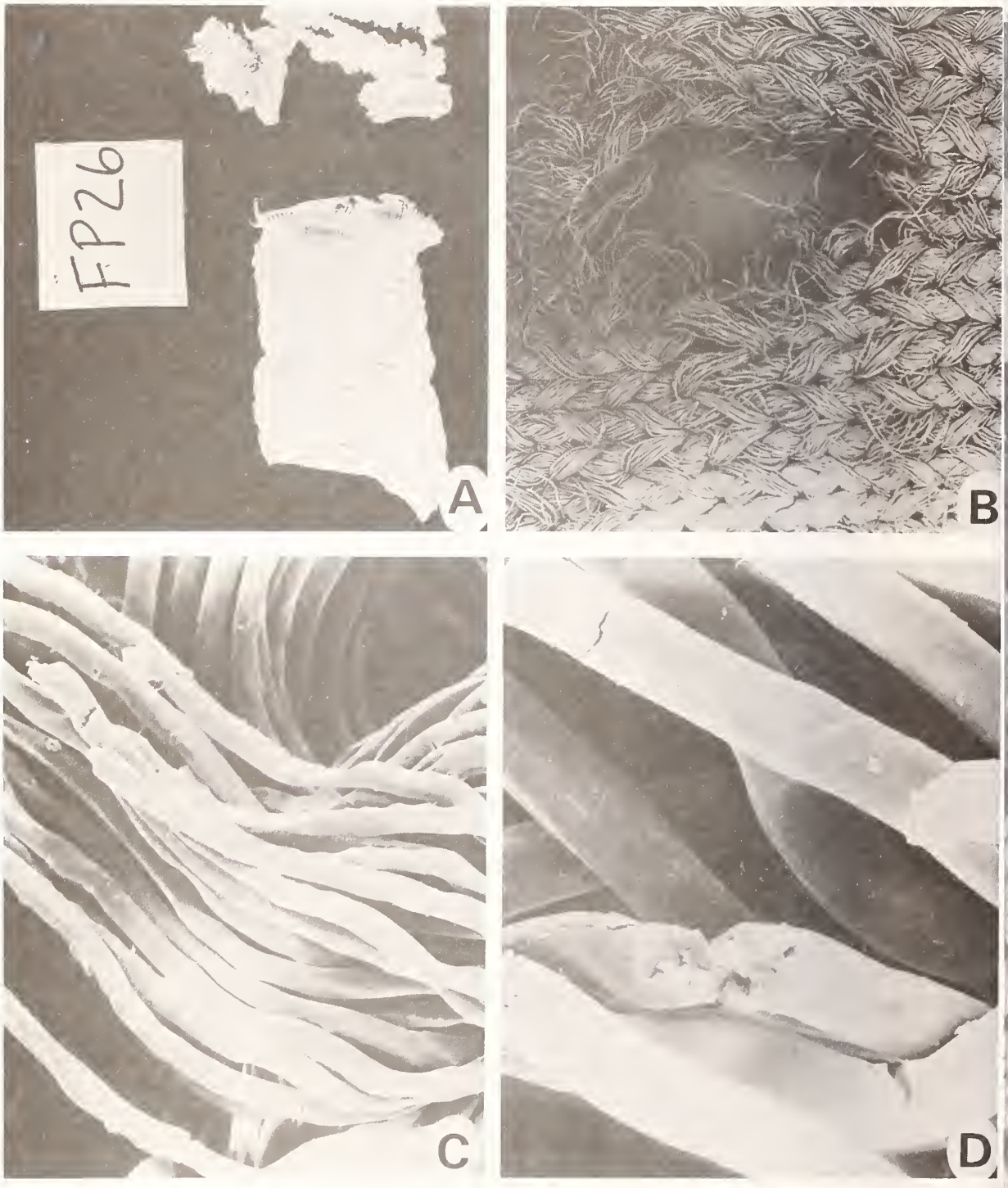


Figure 3.11 : (FP26) A. View of damaged Weavenit prosthesis after 84 months B. Yarn failure. C. Non-circular filaments deformed pressure from adjacent yarns during prosthesis manufacture. D. Transverse cracks and fracture surfaces of embrittled filaments.

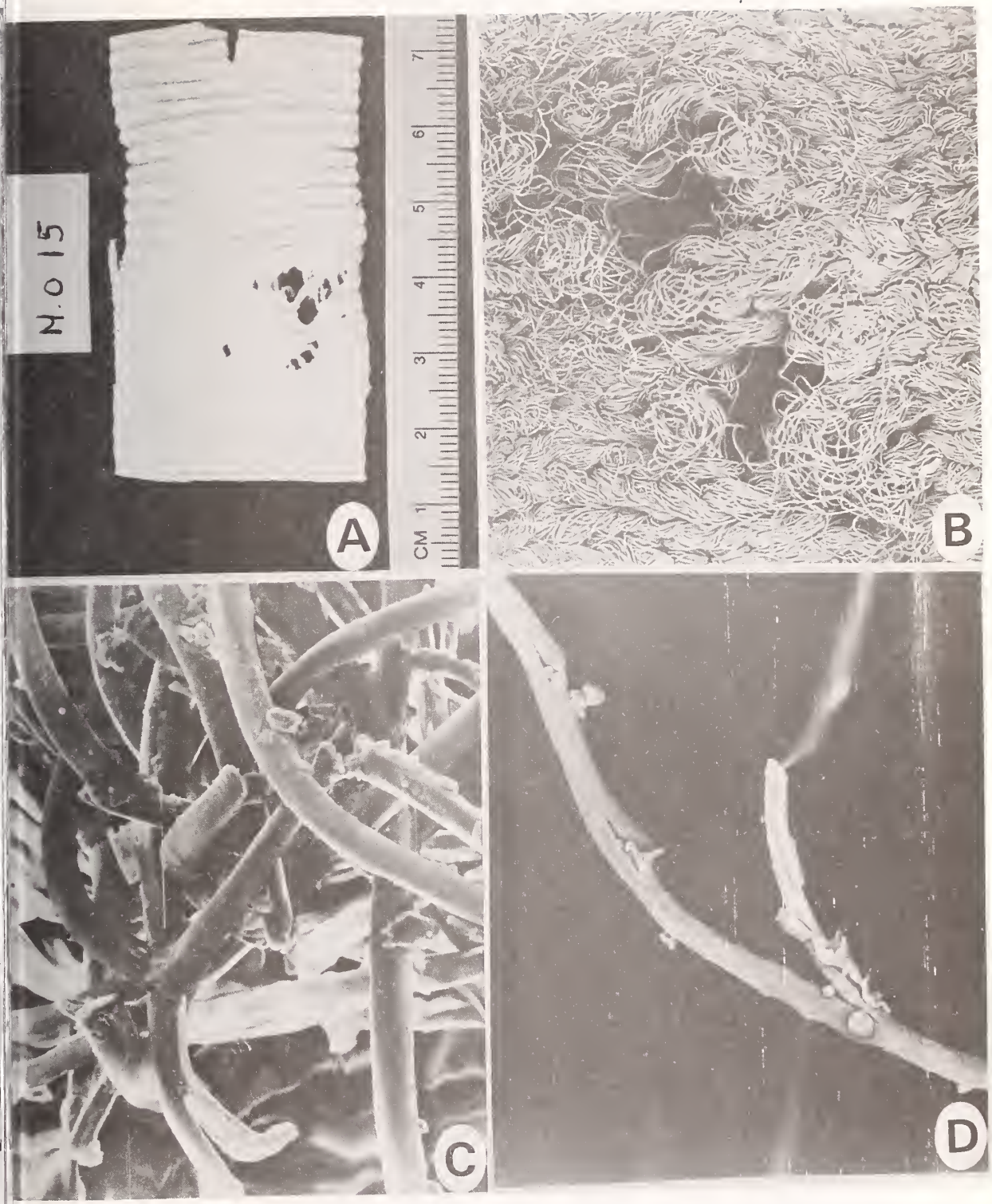


Figure 8.12 : (MO15) A. View of damaged De Bakey Vasculourprosthesis after 59 months in-vivo. B. Yarn failure. C. Failed filaments showing fracture surfaces. D. Cracks in filament showing axial splitting.

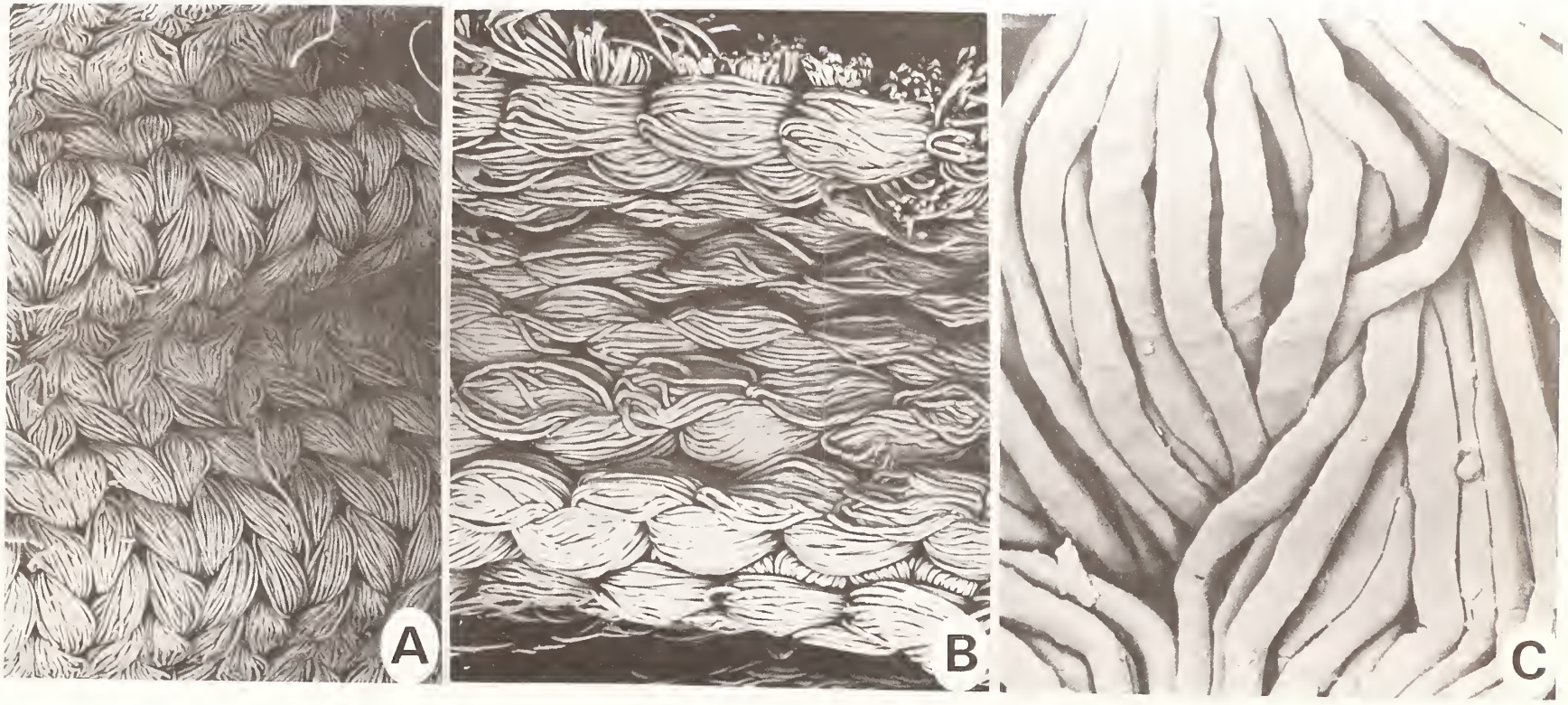


Figure 3.13 : (MO22) A. External view of Ultralightweight prosthesis after 23 months in-vivo. B. Internal view of Ultralightweight prosthesis after 23 months. C. Non-circular cross-section filaments deformed by high pressure contact of adjacent yarns during prosthesis manufacture and showing incipient cracks under bending stresses.

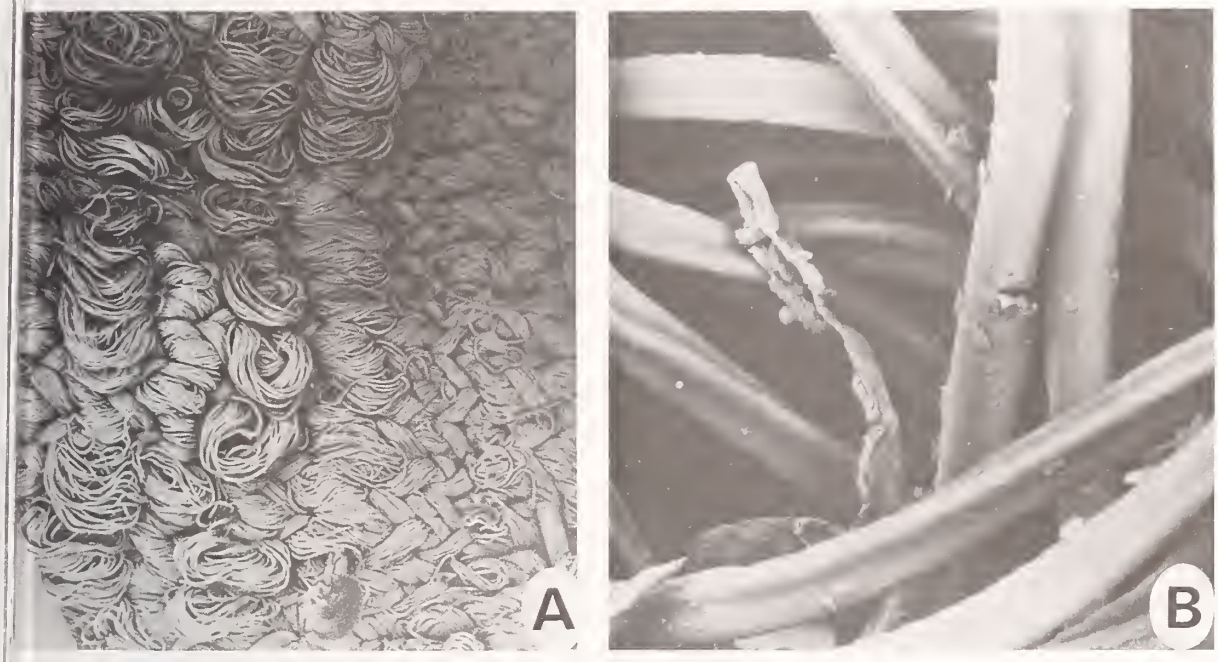


Figure 8.14 : (M018) A. External view of Microvel prosthesis after 17 months in-vivo. B. Velour trilobal cross-section filament with isolated transverse cracks.

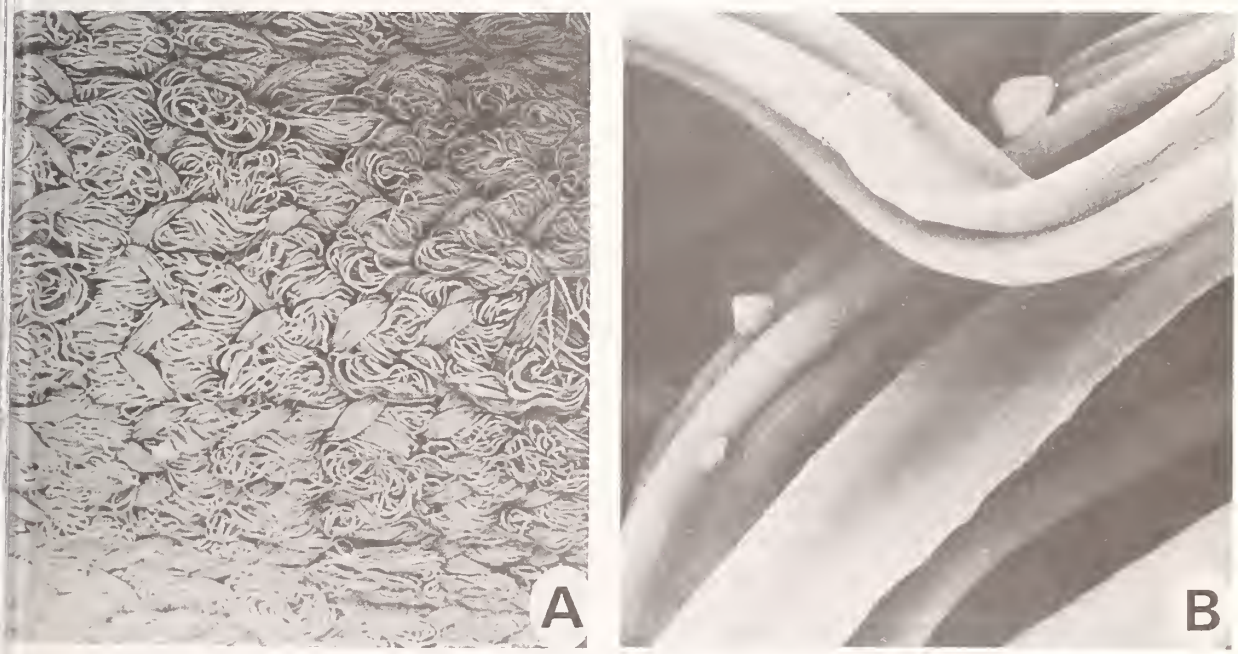


Figure 8.15 : (B43) A. External view of Microvel prosthesis after 2 days implantation yarns. B. Velour trilobal cross-section filaments showing axial cracking on the surface and between the lobes.

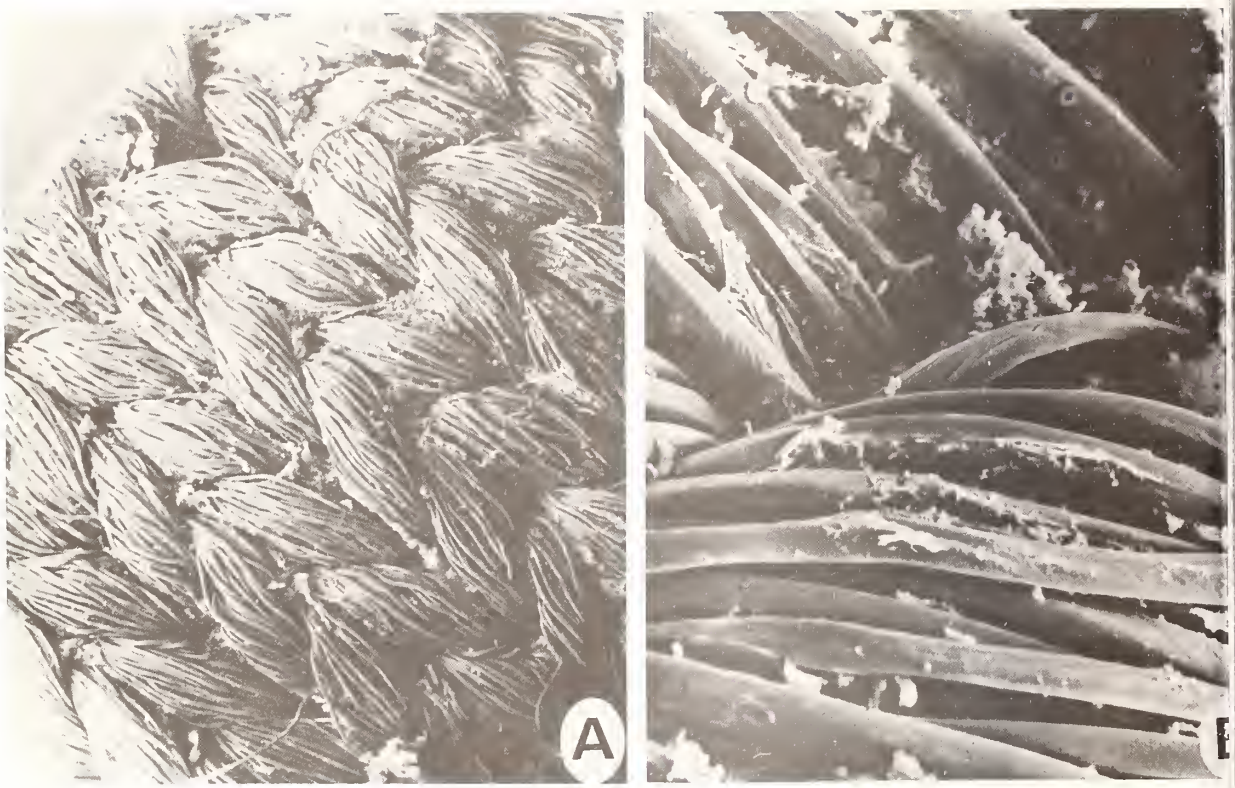


Figure 8.16 : (B75) A. External view of a Standard Knitted De Bakey prosthe explanted after 72 months (inadequately cleaned). B. Filaments with adherin tissue (residual) showing axial splitting.

4. Discussion

4.1 General Consideration

Cardiovascular reconstructive techniques which make use of fabrics have progressed from the stage of surgical curiosities in the 1950's to common management strategies in the 1970's. Implantable fabrics have also changed and are still evolving. The rationale for the evolutionary trends, however is not clear. At present, the life expectancy of patients bearing implants is increasing since younger candidates are being accepted; elective operations take place earlier on the basis that prognostics of success diminish rapidly with age and disease progression. Concurrently, the original concerns regarding the longevity of the implants "in-vivo" has largely vanished from the list of preoccupations of the surgical team. In effect, the new generations of prostheses are now taken for granted by many clinicians who view this class of products as a "stock" surgical supply unlikely to undergo further major developments. In response, more recent develpments on these prostheses have centered on production considerations in the absence of clearly identifyable guiding criteria from the clinical sector. New products released on the market are often re-issues of older styles of devices superficially modified to accept different commercial yarns or more elegant production technologies.

Once the gross anatomic configuration or the geometry of the needed replacement device is established, it becomes very difficult to choose one device over another on the basis of conventionally accepted performance criteria. Product literature reflects this dilemma.

This condition has prevailed over the last decade. However the pool of implanted patients has increased enormously since 1970. Pre - 1970 devices are therefore more rarely recovered, not only because most of these patients died before the start of one recovery program but also because their relatively small numbers were overwhelmed by post - 1970 implantations. Considering that there were "fashion" cycles in the populairty of certain devices, then the recovery distribution must also reflect the degree of local commercial success and the fashions which indirectly controlled the total number of devices of each king implanted at different surgical centres.

In summary, the background against which thus recovery program was carried-out can be seen in the following way. Devices reported to be clinically superior (or equivalent) were made by many manufacturers in a wide range of different configurations and fabric styles, sold and implanted in different patients by different surgeons under different conditions. Some of these patients subsequently returned to the general population pool, but never reappeared into the health care delivery system. Over a period of time which varied from a few month to a decade, other patients, for one reason or another, suffered recurring circulatory difficulties. Some died suddenly outside of health care facilities and the clinical performance of the implanted device or the value of the replacement did not become known to the original surgeon. In other instances, circumstances forced the patients to re-enter the health care system where they were reoperated upon or else died of unrelated causes. This last group constitutes the primary pool from which explanted cardiovascular prostheses originate.

In establishing the value of a recovery program and drawing conclusions from its statistics, it should be remembered that this pool was not a normal population of patients; it was one tilted towards the less healthy and less successful surgical candidates. There is, therefore, an apparent mismatch between the real device performance and that perceived through an implant recovery program. In the present case, there are other elements which further affect the result. For example, many patients had degenerative diseases which brought on the condition. Re-operation candidates tended to be "habitual"; patients with two marginally successful attempts at reconstructive surgery had more chances of being reoperated upon than the ones who had a single successful surgery and had been discharged from the hospital.

Experimental implantation of devices in animal models under closely controlled conditions is essential in the evaluation of cardiovascular implants. However, it is not sufficient; it does not accurately simulate the conditions which will be met when such devices are used on humans in large numbers. The first genuine insight on the clinical performance of an implant in the field inevitably comes from the first

few recovered devices. Broad-based recovery programs, on the other hand, provide knowledge regarding the long-term performance, the possible contraindications and the ultimate lifetime of the implant "in-vivo" as well as the limitations of the prevailing surgical technics and the impact of other common parallel disease management procedure. They are also invaluable in directing evolutionary development of these devices. Recovery programs need not recover only failed devices in order to forecast the ultimate lifetime of an implant. With current techniques of "forensic" chemistry, pathology and other disciplines, it is possible to ascertain the presence of subtle damages which have no clinical significance at the time of explantation but can eventually culminate in explicit failure at a later date. Collected devices and their attached tissue, the sutures and adhering thrombi are also good diagnostics with respect to the compatibility of the device with the host organism under clinical conditions. Complications related to parallel or complementary pharmacotherapeutic treatments can sometimes be forecast by the examination of explants; the presence of sorbed pharmaceuticals, bacterial and fungal invasion can often be detected. This is particularly important in the cardiovascular sector where the average patient is in the later quarter of his life and a variety of related or concurrent health problems may be treated simultaneously and may assist or jeopardize the function of the implant.

The general state of health of the patient is perhaps the most important factor in cardiovascular reconstructive surgery involving textile products since the living organism must provide the complementary part of the prosthetic system through healing. A device recovery program does not always give reliable information on the state of health of the patient; case histories are needed to provide the etiologic context in which such prostheses may be evaluated. From Table 4, it is readily seen that most implantation candidates who provided explants had major health difficulties at the time of implantation. Possible exceptions included elective patients where aneurisms were the primary indications for surgery. Also the causes of death (from autopsy specimens) suggested parallel development of other major health problems. Yet examination of Tables 5A and 5B confirms that most patients were of a relatively advances age and were affected with occlusive diseases.

The life expectancy of properly treated, implanted patients with peripheral occlusive arterial diseases, not too uncomplicated by other cardiovascular problems, is not significantly different from that of a healthy population of comparable age distribution (34, 38, 39); surgical techniques which aim to correct or by-pass defective or occluded areas have merit primarily because, when successful, they can do much to the patient's enjoyment of life. Their comfort is increased and their mobility is retained. Unfortunately, the underlying causes which led to the first surgery generally remain and further surgical acts may be needed at a later date. The implantation of a prosthesis into or near an area of blockage in order to irrigate the distal vascular bed does not, by itself, arrest the progression of a degenerative disease: arteriosclerosis continues to increase. This is evident from Table 5.07 which indicates that thrombus formation and degradation of the distal vascular bed are amongst the primary cause of reoperations for patients with occlusive diseases.

Tables 5 and 6 illustrate that over the last five years, three devices dominated the sector and accounted for more than two thirds of the products recovered; velours alone accounted for nearly a third. Yet on considering tables 5.02 and 6.04, it seems that most of all velours were recovered within two years of implantation where as almost 70% of knits were carried for more than three years "in-vivo" before re-operation or death. This, "a priori", suggests that the present popularity of velours is not fully justified on the basis of their long term performance and that older styles of devices are at least as safe and effective.

Functional cardiovascular fabric prostheses are composites of synthetic fibres and soft tissue at the moment of explantation. Their performance assessment and their failure analysis are correspondingly more difficult to carry out. "Healing" of the fabric and development of pannus at the anastomoses are therefore crucial to the performance of the implant "in-vivo".

Observations carried out on animal models and on recovered human implants to compare the healing rate of fabric prostheses confirmed that the healing process is identical for all Dacron prostheses; it depends primarily on the reorganization of the initial thrombotic matrix which deposits on and within the fabric. Velour textiles appear to provide a better encapsulation at a faster rate since a thicker lumen wall deposit forms. However, the velour fibres are not fully incorporated in the neoendothelium and remain exposed to the flow of blood, in particular near the anastomoses. The initial appearance of pseudo-endothelial cells occurs within two to three weeks post-operative; these are concentrated in the anastomotic area and develop along a continuous front with the endothelium of the aorta and occasionally appear within the folds of the crimps and in shielded or stagnant areas. However, their clinical value is still debatable as they occupy only a minute fraction of the total luminal wall area even after long "in-vivo" residency. During healing, the intrinsic thrombogenicity of the surface of the endothelializing prostheses diminishes rapidly and finally stabilizes after two months post-operative. Porosity as measured by permeability, a factor which is given considerable importance in the literature (2, 11, 43), does not seem to be a determining factor in the healing process, at least in the range and types of porosities which are represented by current commercial products.

A living organism fitted with a fabric prosthesis constitutes a new system which behaves in a satisfactory fashion if the disturbance cause by the prosthesis can still be accomodated by natural adaptation of the organism. This is strongly dependent on the general state of health of the organism, even when considering only hemostasis blood coagulation characteristics and connective tissue metabolism, factors which have severe impact on the behavior of fabric cardiovascular devices. Adaptation is dependent on the general health and vitality of the organism. In a patient, this is a difficult factor to define in which the medical history of the patient, this genetic heritage and etiologic factors specific to the site of the surgery contribute. Very large individual

healing rate differences can be found within a population. Such factors affect endothelialization and healing of the anastomoses. In turn, these same factors can indirectly affect other performance determining characteristics. Proper healing and endothelilization of the prosthesis coincide with the return of normal platelet survival time and reduces the consumption of fibrinogen. Well-healed anastomoses and endothelialized prostheses are no longer macroscopically porous and are thus less exposed to bacterial invasion and growth.

Made up entirely of fibrin, collagen and fibroblasts, the primary function of the internal capsula is to control the thrombogenecity of the lumen wall. This is sufficient for a successful prosthesis. Complete cellular neoendothelialization may contribute little to improve the situation. Massive proliferative growth of perivascular collagen on the exterior of the prosthesis appears as a net disadvantage; it constraints the flexible prosthesis into an unstable matrix of tissue which has a tendency to grow and eventually stenose the prosthesis or the adjacent vessels.

The following sequence of events holds true for the healing of grafts in healthy animal models; immediately following exposure to blood flow, the surface of the prosthesis becomes covered with blood proteins, platelets, red cells and some fibrin. After about two days, this culminates in a relatively thick layer of disorganized fibrin entrapping red blood cells and other blood elements. Cells resembling fibroblasts or transitional form T cells appear between two and eight weeks post-operative and the fibrin layer becomes dense and well organized; other blood debris may act as cementing matrix. Some local cellular activity at the lumen wall becomes visible between two to eight weeks and may culminate into a thin layer of pseudoendothelial cells on the anastomoses after several months. Finally, the healing process reaches a plateau with the development of a patchy covering of thick, dense endothelium, with occasional clusters of cells at the surface. Such complete healing is rarely observed in prostheses explanted from human patients. Such an effect may be expected in young and healthy patients implanted as consequence of traumatic damage. Such patients, however, form a negligible minority of implantation candidates amongst a pool of much older individuals with various stages of degenerative or occlusive diseases; their healing rates are slow and it is unrealistic to expect the development of autogenous tissue in sufficient quantities and of adequate mechanical properties to act as adequate blood vessels. Explanted devices examined to date generally had very thin deposits of fibrin and other materials of little cohesive strength. Even velours with their propensity for depositing thick linings with occasional microvasculature channels (capillaries) rarely locked stable, coherent linings over much of the prosthesis area.

Some patients yielded devices almost devoid of surface lining after considerable "in-vivo" residency periods; this was typical of diabetic candidates. Contrary to previous beliefs, it now appears that the fabric device is not just a scaffold or a model on which deposited blood elements and other macromolecular substances can deposit and around which connective tissues grow; the fabric does not become redundant when the graft reaches maturity. It is still needed to consolidate the weak neoendothelium. In addition, it may be called upon to protect it from the crushing and deforming forces generated by the developing perivascular tissue in velours. Finally, this weak neoendothelium appears more vulnerable to bacterial attack than normal vascular tissues.

Although some mechanical properties of the fabric, design features of the prostheses and the geometry are secondary factors in healing, they may nevertheless play a decisive role in the long term prognostics of the patient. In the case of bifurcations, the junction of the legs to the body is inevitably a poorly healed point for currently made devices. This fork remains a nearly bare fabric, uncovered by endothelium, and remains thrombogenic for the duration of the prosthesis lifetime. Alterations in blood flow in that region may therefore present a major risk for the patient, particularly with highly thrombogenic velours. Although recent improvements in the haemodynamics of this area have taken place, there is room for improvement, as turbulence and stagnation are undesirable factors. Yet there are severe technological limitations to improving the geometry of that area with classical techniques of textile engineering; not only is the combination of a seamless branch points and crimping difficult to achieve but it is also very unfavorable to laminar flow and may preclude endothelialization. The ratio of cross sectional areas between the trunk and the tributaries is also of relevance. This issue has been addressed by other authors (5) but wholly satisfactory solutions have yet to be found.

A related issue is that of the mismatch between the prosthesis cross-section and that of the blood vessel to which it is anastomosed. A prosthesis, when pressurized, has a slightly larger diameter than the artery. The result is a conduit with a larger blood volume per unit length than the artery and a correspondingly lower blood velocity. Given the higher thrombogenecity of the prosthesis as a whole, in particular if it has areas of bare fabric, thrombosis is therefore more probable as the thrombotic threshold velocity is reached sooner in the bifurcation area and at the anastomoses.

The growth of stenosing perivascular tissue may also be stimulated by a prosthesis with a weak, compliant fabric structure which expands during the systole and contracts during the diastole. Sustained and cyclic tension on collagen-forming tissues is known, empirically, to stimulate growth of the tissue capsule and may further accelerate the onset of stenosis.

In summary, the importance of the fabric component of prosthesis in retaining the strength and the shape of the composite blood conduit appears to have been neglected during the last decade.

4.2 Fabric Properties

All prostheses were found to lose stitch density. That is, the fabric mesh opened-up gradually during "in-vivo" residency. The implications of this phenomenon is at the effective amount of material per unit area which held the prosthesis together diminished during use. Therefore, even if physical and chemical degradation of the fibres did not take place, the strength of the prosthesis could still diminish with time.

A time-dependent diminishing stitch density suggests that the fabric, initially compressed during fabrication, can somehow relax after implantation. As a consequence, the fabric structure inevitably suffers some form of irreversible dilation upon pressurization in the presence of lubricants and plasticizing liquids such as may be found in blood. Alternately, the fabric can expand due to a distortion in shape and increase in tension transfered to local portions of the knitted network; some fibres loops can tighten more in some areas than in others and thus allow dilation.

The rate of loss of stitch density depends on the type of fabric construction and is not limited to medical textiles; it also takes place in consumer and industrial fabrics. Empirically, knitted fabrics such as the "two-bar warp knit" are more stable than the weft-knit devices. Prostheses do not loose stitch density at the same rate; some fabrics are more stable. Fabric structures differ in the amount of "free or loose" filaments which can tighten under pressure or tension. Cyclic tension and pressurization facilitate and accelerate the process.

In addition, inherently unstable fabrics exhibit stitch density loss and dilation in non-linear fashions. Some knitted configurations show extremely rapid initial fabric relaxation with measurable reduction in stitch density and distortion almost from the moment of blood pressurization. This explains the findings of other authors who demonstrated some knit configurations are particularly prone to dilation when pressurized during surgery (35).

Prostheses were also found to lose the crimp geometry with time "in-vivo". Crimp is not lost in the same way for all types of fabric geometry. For example, very tight fabric structures with little interstitial space between yarns and minimal excess interloop filaments length retain crimp more readily unless there is a loss in the crease or "set" of individual fibres and yarn. On the other hand, more open fabrics allow rotation and displacement of fibres and rearrangement in the fabric which culminate in loss of (macroscopic) crimp. However, the individual fibres can still retain the "set". A very rapid loss of macroscopic crimp in a fabric where individual fibres retain their "set" suggests an unsuitable fabric construction.

Loss of crimp follows a similar pattern to the stitch density reduction and exhibits extremely rapid changes upon implantation for the circular crimp devices. This implies that the loss of crimp in such devices may be primarily due to rearrangement of fibre geometry as opposed to actual fibre fatigue and loss of "set". The helical crimp prostheses examined were more crimp stable than circular crimp devices. The rate of loss of crimp in helical crimp devices was much less severe initially and was gradual. The causes for the difference may not be intrinsic to the geometry of crimping; they may simply reflect the different fabric styles or processes which are used to achieve crimping. However, this hypothesis cannot be tested since the same fabric geometry is not available in both crimping style. Different crimping techniques are found in the literature; "a priori", these could have a large influence (for example, hot pressurization against a suitably shaped external mandrel or spiral winding of a thread with heat setting in a longitudinally compressed state). Neverthe-

less, it is apparent that different prostheses can have dramatically different degrees of crimp stability. The loss of crimp in a prostheses, as well as some currently available, do not have crimps, such devices appear more subject to stenosis, suture disruption kinking and other forms of haemodynamically unfavourable geometries, in particular at points where there is substantial movement of flexing. For the need of the moment, it is perhaps sufficient to say that a rapid loss of crimp, may it be clinically important or not from the geometric or haemodynamic point of view, is nevertheless a diagnostic of an unstable prosthesis fabric configuration and may forecast the occurence of more objectionable events at a later date.

During this recovery program, random samplings of fibres were examined by scanning electron microscopy. Prostheses showing evidence of macorscopic damages received particular attention and various forms of damage were encountered. Such damages separated into several categories and by analogy with textile fibres subjected to controlled mechanical abuse, it was possible to assign a probable cause of damage. Thus, chemical deterioration with large losses in molecular weight produced porous fibre surfaces, cracking and fibre cleavage perpendicular to the fibre axis. Surface deterioration led to fibres with shallow crack on the surface upon bending. Mechanically pulled or distended fibres fibrillated and cracked longitudinally and frequently "necked" to smaller diameters prior to failure. They also left dangling microfibres near the break site.

Certain patterns of fibre damage indicate that surgical handling may be the primary factor in failure or local damage. For example, the application of unprotected vascular clamps can cause rupture of fibres and perforation of prostheses. Yet in the prostheses examined where the pattern of damage was suggestive of clamps, the morphology of the broken fibre was not suggestive of mechanical abuse. Instead, it was concluded that the clamp may have predisposed the fibres to an accelerated rate of deterioration by modifying the physical structure (residual strain, cold working, kinking). The damage may therefore not have been evident at the moment of the surgery. Over the subsequent "in-vivo" residency period, deterioration preferentially took place in these areas of enhanced chemical reactivity and culminated in rupture of fibres and perforation of the wall. In summary, the long-range impact of mechanical abuse during fabrication, crimpingm sterilization and surgical handling of such prostheses have not been fully assessed. Retrieval shows that these are not negligible factors; they appear of considerable importance as they may control the ultimate lifetime and the reliability index of prostheses "in-vivo".

The measurement of diameter and cross-section of filaments from explanted prostheses confirmed that the polyester used in prostheses sell measurably during the first 30 months of implantation. This swelling is gradual and reaches a peak of about 5-6%. It may be associated with the absorption of water or other blood components with a specific affinity for the polyester. It may also be an indication of molecular weight break-

down with the insertion of hydroxy and carboxy groups into the surface layers of the fibre. Observations on prostheses with long "in-vivo" residency confirmed that fibres can also suffer a reduction in diameter with time. These observations are, at firts, contradictory. However, a possible interpretation is that fibres first swell, then degrade. Finally, the molecular weight becomes so low that the surface material dissolves or becomes or mechanically detached from the fibre core thus causing a decrease in diameter. Two discrete effects can be recognized: fibres recovered from prosthesis with relatively short implantation times, increase in diameter are noted during the first 30 months while those with long residency time show a gradual decrease in diameter which begins after 30-50 months. Mechanical stretching of the weakened filaments can also cause a diameter reduction.

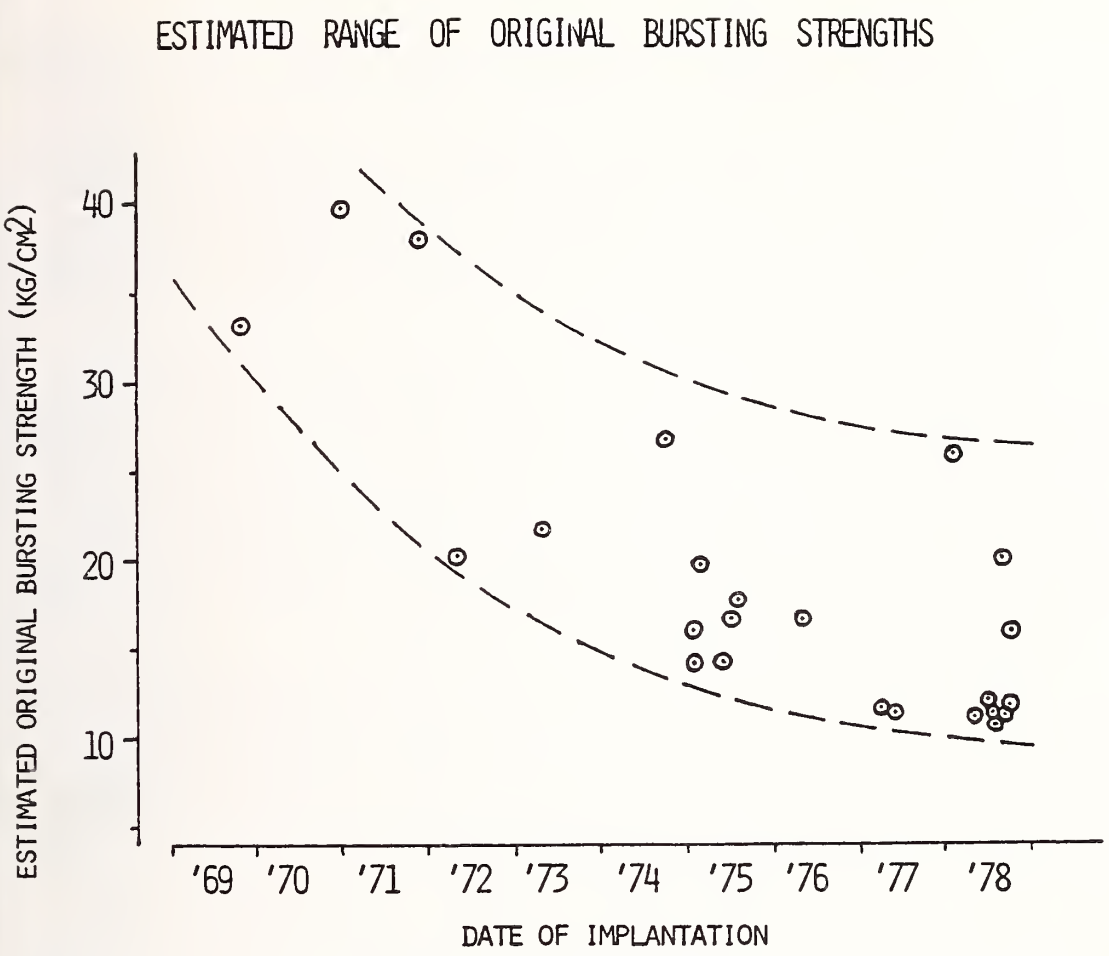
In summary, the polyester fibres used in existing prostheses are affected by the biological environment and the changes are suggestive of multiple concurrent degradative processes with considerable short-term and long-term impact on the over-all mechanical properties. Material is lost from prostheses. This may ultimately enhance the risks in long-term implantation candidates. Perhaps reformulation of improvements in the polyester fibre, the spinning technology, the heat treatment and/or the crimping procedures could lead to improvements in the chemical resistance of existing fibres and the prostheses that are made from them. Conventional transmission infrared spectroscopy is not adequately sensitive to establish the presence of chemical degradation in textile samples such as those used here. Conventional attenuated total reflection infrared spectroscopy ATR also yielded equivocal results. However, Fourier Transform infrared spectroscopy confirmed the presence of an excess of hydroxy and carboxy functions in yarns which had been "in-vivo" for more than 20 months when compared to the unused reference products. By analogy with environmental deterioration of polyesters, it is tentatively concluded that hydrolysis takes place. Mass spectometry of thermally decomposed yarn also suggested the presence of a larger quantity of very low molecular weight fragments and a generally lower molecular weight measurements in samples which had been implanted for several years.

Further work in these areas is necessary to establish the mechanism of "in-vivo" degradation and the factors which contribute to it.

Bursting strength, as measured by the method chosen here, is an insensitive parameter to detect subtle changes in mechanical properties. Considerable scatter in data is noted. However, regression analysis of the date showed a strong downward change in bursting strength with "in-vivo" residency time. This change amounted to about 10-15% after 2-3 years post-implantation, when all recovered prostheses were included.

Prostheses consisting of smaller diameter fibres generally showed a larger drop in bursting strengths with time of residency. This is an expected result because the large surface area of the fine fibres gives rise to a more rapid (volume) deterioration.

Figure 9



Of greater concern, however, is the actual bursting strength of the prostheses at the moment of fabrication. These date are shown in Figure 9, where the extrapolated original bursting strength of prostheses are plotted against chronologic year of implantation. A severe decrease in average reserve strength of prostheses is evident and reflects the introduction and increasing popularity of the current velours and light-weight knits which can have as little as one fifth of the bursting strength of earlier devices. In combination with the observable decay in mechanical properties with implantation residency and the vulnerability of low burst strength devices to intro-operative surgical damages, the low initial burst strength devices appear less than ideal for patients with long expected residual lifetimes.

5. Conclusions

5.1 Clinical and Technological Aspects

The pathology of recovered human cardiovascular implants constitutes a key element in any device evaluation program. However, total reliance on anecdotal observations is not justified. Ethical considerations in surgery tend to bias the patient selection process towards the poorer implantation candidates. In addition, the haphazard recovery of implanted materials embodies many uncontrollable variables which complicate the assessment of the implant's performance. Early data derived from recovery programs tend to originate preferentially from implanted patients who suffer further complications leading to premature death or repeated cardiovascular surgery. Early data can therefore be deceptive as they frequently originate from sedentary, debilitated patients. This may constitute an insufficiently stringent test on novel technology. Conversely, it may also accentuate negative aspects in the implant performance. However, when used devices are recovered in sufficient numbers, these programs establish the clinical limits of that technology and of its therapeutic value. They can also point the way to possible improvements.

The present work, even in its partly completed state, confirms that even after more than two decades of clinical use, polyester textile prostheses are incompletely understood with respect to their "modus operandi" in humans and that their performance in average diseased patients is not analogous to that in healthy animals. It also confirmed that healing characteristics are not significantly different between the various devices which have appeared on the market overt the last fifteen years, except for the velours. This latter group encourages the development of excessive perivascular tissue and develops unnecessarily thick lumen linings which has a repercussion on the service lifetime "in-vivo"; hyperplasia, stenosis and adhesion to adjacent tissue are more common. Sterile inflammatory reactions are also found and empirically, their average "in-vivo" residency time, before the onset of difficulties, seems shorter than woven or knitted products.

Anecdotal evidence of other short-comings in various products was also found and confirms isolated reports already present in the literature. These include dilation, loss of crimp, loss of mechanical properties, exceptional susceptibility to damage, embrittlement for lightweight knits and velours (10, 12-20) and sterile inflammatory reactions for high-surface area velours (26, 50).

Noteworthy is the observation that the ultralightweight graft, singled out for criticism because of its tendency to dilate soon after being placed into service, has a bursting strength slightly under 15kg/cm^2 and that Table 2 shows five other types of prostheses with bursting strength hear or below this value. Although strict correlation between early post-operative dilation and bursting strength is not demonstrated, it seems unwise to assume a large safety factor in the mechanical strength and dimensional stability of prostheses which present low values for this parameter. For these reasons, pre-operative manipulations and intra-

operative techniques may be more critical than for earlier devices of stronger gauge. Additional work to fully assess the clinical risks in the light of current surgical techniques will have to take into account the limitations of the textile technology. Low fabric weight and high porosity which benefit biocompatibility may be mutually exclusive with large mechanical safety factors which are often strategic assets in certain clinical circumstances. This is made even more important by the observation that polyester fabric measurably with "in-vivo" residency time.

It is presently necessary to establish design criteria for the forthcoming generation of cardiovascular prostheses. There is increasing evidence that the current family of devices do not share the same characteristics of dimensional stability, biocompatibility with adjacent tissue, resistance to mechanical significant biodeterioration and surgical convenience as those used a decade ago. Yet quantification of the long-term clinical value of individual devices is difficult since there appears to be an insufficient number of "ex-vivo" test parameters available. The burst test is a very coarse measurement which integrates many interrelated fabric design features into a single relatively insensitive number; it is therefore not wholly satisfactory. Although efforts have been devoted to the establishment of "ex-vivo" design and performance criteria for textile cardiovascular products (2, 11, 46, 47, 51, 53), it is becoming apparent that these parameters do not adequately predict the clinical merit and the service lifetime of the implants. Therefore the rational choice of prostheses for a given clinical situation remains difficult in spite of more than twenty-five years of implantation experience.

Bursting strength of devices as a function of "in-vivo" residence time indicate that there is measurable decay in the mechanical properties. However, there is no basis, at this time, to fear early catastrophic mechanical failure of these implants under normal physiology conditions since they all exceed the bursting strength of average vascular tissue. However, catastrophic rupture of the prosthesis "in-vivo" is not necessary for a clinical failure. Deformation leading to interstitial bleeding or longitudinal tearing at the suture points is sufficient. The tenacity of such fabrics and their resistance to fatigue is much worse under cyclic pulsations and natural stresses caused by movement of the patient. An inherently weak device with brittle fibres is also more vulnerable to handling damage; local fibre scission, stretching and abrasions caused by contact with surgical instruments and by cutting, suturing and occluding procedures incidental to anastomosis accelerate the deterioration process. Futhermore, these polyester fabrics suffer a significant loss of tensile strength "in-vivo" over a period of several years, this corresponds to a decrease of about 4-7% annually. In addition, some constituent filaments have been shown to "craze", split and cleave under "in-vivo" conditions. On the basis of "ex-vivo" testing, the process is further accelerated when fibres are under small sustained tension. Thus the newer generations of thin lightweight grafts are potentially more vulnerable to trauma, dimensional instability and embrittlement than the older devices.

At present, the newer prostheses are finding increased popularity while the older, more robust ones, are falling into disuse. In turn, an increasingly large segment of cardiovascular surgery patients with widely varying prognoses are receiving fabric devices which may yet prove less durable than anticipated. While congenital and traumatic cardiovascular defects in relatively young patients are now more frequently repaired with fabric products which ideally should last several decades, there are also many cases where concerns about long term durability are perhaps academic. At present, most of the new lightweight prostheses appear satisfactory for the less stringent applications involving large size blood vessels at unstressed locations.

As for fabrics such as velours which have a tendency to hyperplasia and stenosis because of a stimulating influence on proliferative perivascular tissue growth, a more basic question of loss of patency must be addresses in addition to the issue of marginal mechanical strength inherent to the fabric construction. One may wonder however whether the new prostheses have sufficiently large safety factors and biocompatibility for all situation, regardless of patients' estimated residual lifetime and their degree of activity. Specific questions which remain to be answered include the following. Should some versions of these devices be contraindicated in surgery for certain patient classes (i.e. congenital defect repairs and traumatic damage in the young)? Should there be more stringent and meaningful "ex-vivo" criteria of performance on general purpose device? Are they the best products which contemporary biomedical and textile technology can provide?

Eventually, recovery programs such as are described here will provide answers.

5.2 On Retrieval Programs

An interdisciplinary, multicenter implant retrieval program can become an education for all participants. In this particular case, it demonstrated that removed prostheses and associated tissue can contain as much information as conventional pathology specimen. Although the analysis of these complex systems appeared at first more difficult than conventional pathology, it is now evident that this was primarily due to inadequate collective knowledge in all of the disciplines which make-up cardiovascular fabric technology.

Most surgeons participating in this program originally believed in the immunity of polyester to the biological environment and to conventional surgical handling. Non-clinical workers in the research team were under the impression that implantation of prostheses follow the same ideal protocol and follow-up which take place in experimental surgery with animal models. Clinicians and non-clinicians believed that materials and procedures associated with cardiovascular prosthesis fabrication were specific to that sector. It is now recognized that

this is not so and that such products, no matter how refined, still have much in common with consumer textiles. Perhaps the most useful result derived from the recovery program is that it has underlined the realities of industrial production, of practical surgery and of materials limitations.

Retrieval programs take a long time to become established, absorb considerable amounts of resources and manpower and require long term commitments. More often, they start as small, "ad hoc" "hobby" collections of failed devices given by colleagues in the same department. This takes relatively little energy; conversely the information derived is proportionnally smaller. The broadening of such implant collection into significant retrieval and analysis programs inevitably require multicenter participation of several surgical groups. In addition, it requires the cooperation of several pathology departments as well as access to medical records. In the case of fabric cardiovascular devices, there is the problem of prosthesis identification. It is only recently that manufacturers have begun to "label" prostheses directly with thermosol inks. Presumably this will simplify identification in a few cases. However prostheses are occasionally trimmed prior to surgery and there are strong possibilities that the identification code is removed, discarded or obliterated during the preparation of the device or its explantation. Therefore, unequivocal identification of devices must be within the capability of the research group. This is not as difficult as it appears at first sight. However, it requires an in-depth knowledge of textile practices and fiber identification techniques. It also requires an up-to-date and complete retrospective bank of reference samples since it is not uncommon for manufacturers to alter the production technology of a given product after its introduction. Therefore, a certain degree of vigilance over the commercial sector is necessary and timely purchase of new products must be done. Furthermore, the introduction of new devices is often synchronized with the phasing out of older products which have lost popularity. Therefore, old samples can be extremely valuable as such devices often reappear during recovery programs and may present cross-matching difficulties if references are no longer manufactured. Some surgeons have the habit of saving and filing the leftover prosthesis trimmings directly in the patient records. The value of this procedure is obvious as it gives a precise reference on the textile as it was at the time of implantation. Without this remnant, the material analyses are always subject to uncertainties; prosthesis with long production lifetime are not always made from the same materials by the same procedures, even if the fabric geometry is not changed. Manufacturers depend on large fibre spinners for their yarns and thus are at the mercy of the market and the goodwill of the primary supplier when they deplete their first batch of yarn.

It is sometimes possible to estimate the original properties of a series of prostheses which were implanted at various times in the past. For this purpose, the properties of devices implanted for different times and originating from comparable families of products, can be extrapolated

to the moment of implantation. This is possible for burst tests and molecular weight determinations which lend themselves to extrapolation if enough different explanted samples are available. In summary, the identification and characterization of textiles forms a key element in recovery programs of this nature. This is in contrast with the simplicity of identification in implants for total hip replacement of cardiac pacemakers; such devices have been engraved with serial numbers and commercial information almost from the moment of their introduction. At any rate, their characteristics and appearance are so unique that misidentification is precluded. For fabrics, this demands more labor and may require sophisticated microscopy and chemical analysis equipment.

Over the last five years, a number of manufacturers have introduced patient reference cards for a number of implants. Pioneered for cardiac pacemakers, this feature is slowly spreading to other sectors. Such implant-patient cross reference file cards are enormously valuable during any type of implant retrieval; it is unfortunate that only a minority of surgical centers make use of these cards. The filing of special information is very difficult and there is considerable resistance to the introduction of any more "redtape" to the normal protocols. Perhaps a simplification of the card and or electronic data filing or processing techniques could be of some help in order to minimize the clerical load on the surgical staff.

The fabric device is only one part of the prosthetic system. The anastomoses, the ingrow tissue and the pathology of the patient at the site of the operation, as well as the case history may have an equal, if not superior information content. Much could be done to improve the recording, collection and processing of information of this nature. However, it is also labor intensive and is often clinically impractical. The significance of some surgical details may also be unrecognized at the time of the surgery. Therefore, recovery programs must still depend, to a certain degree, on "forensic" sciences in order to extract certain pathological information which are not available, recorded or obvious from the explanted samples, or which have been partly obliterated during the explantation step by a pathologist unfamiliar with all the peculiarities of the device which he excised; good liaison with pathology department yields valuable returns in any implant recovery program.

Since ingrowth tissue and pannus form integral parts of functional prostheses, it is necessary to develop histo-pathologic techniques for the preservation of the biologic component which are not deleterious to the synthetic fibres. This problem may not be unique to cardiovascular prostheses. This was done to some extent in this laboratory and the technics are still being refined; it seems that it is always possible to extract more information by the introduction of a new procedure. The question is one of optimum returns for the invested labor. Tissue staining methodologies were developed in house for this class of samples. Originally, it was decided to differentiate only collagen from fibrin in

the soft tissue; it now appears important to locate and identify other soft tissue components. For example, identification and the quantification of bacteria, elastin, smooth muscle, lipids, inorganics, the location and severity of inflammatory reactions, the classification and properties of pseudo-endothelial cells and their genesis are now interesting. Small implant recovery programs expose their staff to only a limited range of phenomena of relevance. Thus as the recovery program becomes larger, collective experience and insight builds up rapidly, efficiency increases and success breeds more success. It is now apparent that protein analysis, high pressure liquid chromatography, x-ray diffraction, electron probe microanalysis and neutron activation analysis will become mandatory in order to elucidate some of the more subtle yet important aspects of prosthesis biodegradation, tissue interaction, the impact of common drugs and other features which are now know to be essential in order to further improve the clinical value of these devices. Such work however inevitably depends on the spontaneous and frequently unremunerated participation of groups of workers in areas far removed from pathology, surgery and textile physics.

Finally, the complexity of case histories which involve cardiovascular replacement surgery, in combination with the multiplicity of participating centers and the large number of potentially recoverable devices which contain important information make it imperative to develop standardized formats of data collection and storage. The existence of unrelated embryonic recovery programs in different locations, the sharing of clinical and pathological information and the statistical analysis of results from national and international programs will soon become imperative in order to extract the maximum information from collected cardiovascular implants. The further development of mathematical and statistical analysis techniques also appears worthwhile at this juncture. It would appear that some form of standardized electronic data processing techniques where sample records are encoded in an internationally accepted fashion would have much to offer in order to facilitate the retrieval of clinical and technical informations. Finally, it must be emphasized that information or experimental details which seemed unimportant yesterday, all of a sudden acquire importance in the light of new knowledge. For these reasons, the cataloguing and the preservation of samples according to standardized techniques would be most beneficial, as it would allow retrospective investigations for missed information.

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APPENDIX A

PROSTHESIS PROPERTIES AND FABRICATION TECHNOLOGY

1. Yarn

Current polyethylene terephthalate (PET) vascular prostheses consist of continuous multifilament yarns. Each yarn is composed of 20-100 fine filaments which measure between 10-20 um in diameter. The number of filaments per yarn is called the "filament count" and the width of the filaments is called the "filament diameter". The filament diameter is controlled by the size of the holes in the spineret, the degree of filament stretching as well as lateral shrinkage that takes place during subsequent drawing, texturizing, compacting, crimping and cleaning stages. A great variety of yarns can be produced by combining identical or separately spun filaments.

The total size or "coarseness" of a yarn is measured in terms of its linear density (weight per unit length). It can be seen from table 2 and 3 that the woven and the early knitted prostheses (Cooley, De Bakey Standard, Milliknit) are constructed of heavier yarns; they have bursting strengths above 19 kg/cm^2. Recent designs of lightweight prostheses have used finer yarns in order to provide more flexible, more porous and more easily sutured grafts. However, finer yarns, and particularly fine filaments entail a higher surface area of material and are more susceptible to damage from chemical treatments and handling as well as from biodegration after implantation. Consequently the values for the linear density of yarns may not be reduced without a penalty in strength. There is a relationship between prosthesis diameter and linear density value for a given fabric configuration which ensures that the bursting strength of the resulting prosthesis is in excess of 12 kg/cm^2. This value corresponds to a proposed minimum requirement in the Draft British Standard and aims to provide an adequate safety factor for long term implantation (7).

The first generation of densely woven and knitted grafts were originally critized because of poor adhesion between the fabric and the neointima. This disadvantage could be circumvented by using "texturized" multi-filament yarns instead of "flat", non-texturized yarns. Texturizing involves heat setting the flat yarn in deformed states so that the individual filaments are not densely packed.

Such yarns may show evidence of random or periodic local damage or other filament characteristics which reflect the severety of the treatment (flattened surfaces, cross section and diameter irregularities, sharp kinks and dents); texturizing processes may be applied to separate filaments which are subsequently assembled or to preassembled yarns. Both processes generate yarns with increased bulk and more open structures. The methods used include forcing filaments or yarns, into a hot compartment to induce random kinks (stuffing box), shock cooling, crimping, twisting, heating or stretching periodically, kinking with hot loosely meshed gear wheels and asymmetrically heating the fibres on hot bars. Such processes generally enhance the reactivity of the filaments and, on

average, reduce the tenacity of the yarns. With the increased volume occupancy and stretch of texturized yarns, thicker and more porous grafts can be fabricated. Stiffness can also be reduced and surgical handling characteristics may be improved by texturizing. Because of the increased exposed surface area of filament, blood interaction and thrombogenicity of the yarn is enhanced thus facilitating pre-clotting. On the other hand texturizing reduces dimensional stability.

Most prostheses have used yarns consisting of filaments with circular cross sections. However, some recent prostheses use yarns with trilobal cross-section filaments. Such yarns have optical, mechanical and tactile properties which differ subtly from conventional ones. They scatter more light for a given opacifier (filler) concentration and can be textured more easily. The reasons for their inclusion in medical fabrics is not clear at present although it has been suggested that trilobal filaments increase the porosity and facilitate the clotting process; superior adhesion and more efficient entrapment of blood components are claimed (49). Trilobal filaments exhibit fatigue damage under in vitro and in vivo conditions and their larger surface area, the filament may be more susceptible to physico-chemical and biochemical deterioration.

2. The Fabric

All commercial PET devices currently in use are woven or knitted as seamless cylinders and may subsequently be processed to give circular or helical crimped tubes. Thermal and chemical treatments may be used to achieve crimping. Prostheses fall under three classes. These are the woven, the knitted and the "velour" fabric configurations. However, in effect, there are only two types of fabric construction, the woven and the knitted; the latter class comprises the velour as a variant.

Early experimental and commercial vascular prostheses were woven; some made use of stock consumer or industrial fabrics. Later versions had custom-woven textiles. Yarns production however, is a high capital cost operation. Therefore custom-made yarns are seldom used; instead suitable stock consumer or industrial yarns are selected and given supplemental treatments.

Woven fabrics consist of two sets of yarns, called the warp and the weft, which are interlaced at right angles to each other. This is the type of construction found in the Woven de Bakey and Cooley Grafts. The warp yarn lie alternately over and under each of the weft yarns. Consequently this fabric is designated a 1/1 plain weave and is called a "taffeta". This is the strongest construction; it has the best dimensional stability, the highest fabric density and the lowest permeability to water. These and other characteristics, such as thickness and fabric weight (mass per unit area) are controlled by the size (linear density) and number of yarns interlaced together. The number of yarns per centimeter called wales/cm and courses/cm in table 2 gives the fabric count in each direction. Woven prostheses are less prone to kink and collapse than knits. However, the construction has poor compliance, limited elongation, limited water permeability and a tendency to fray. These properties confer notoriously difficult

handling characteristics. The limited degree of compliance to longitudinal deformation can lead to high stresses at the anastomoses and eventual failure of the suture or anchoring natural tissue for devices implanted in the "stretched" state. Fraying must be guarded against. Woven prostheses are particularly suited to emergency surgical situations, for example in the resection of aortic aneurysms, where large grafts are needed.

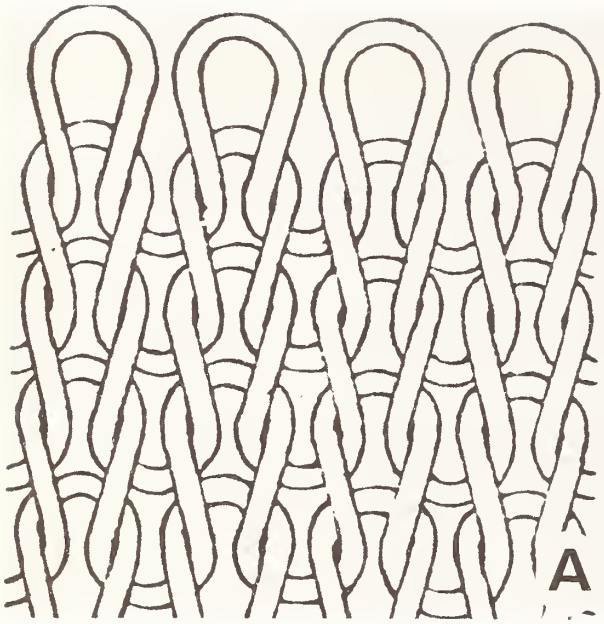
Knitted constructions were introduced with the aim of circumventing the problems of traditional weaves. Knitted constructions contain sets of yarns which are interlooped around each other instead of being interlaced. The compliance behaviour of knitted fabrics depends on the direction in which the yarns are interlooped. If the yarns lie predominantly in the lengthwise direction then the fabric is a "warp knit", whereas if they lie in the transverse direction, it is a "weft knit". Figures A and B illustrate the difference in construction between a single "jersey weft knit" and a "2-bar locknit warp knit" when viewed from the frontal plane.

All commercial knitted grafts have either "regular" or "reverse" constructions. The advantage of the reverse jersey knit over the normal orientation is that the wales on the inside of the fabric cause less turbulence in the blood flow. The black yarns are included in the diagrams for clarity.

Figures C and D show the external and internal views respectively of a De Bakey^{R} Standard weft knit graft with single jersey construction. Figures E and F show external and internal views, respectively of a warp knitted Cooley Graft with reverse "2-bar locknit" stitch. A significant difference between these two types of knit is that weft knit fabrics unravel, whereas warp knits do not.

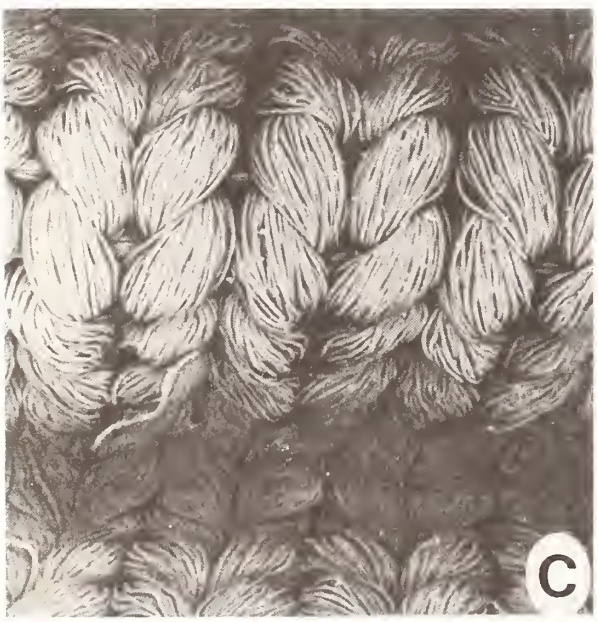
Knitted fabrics have much more open constructions than wovens. This is illustrated by the water permeability values of table 3. Table 3 shows values of permeability to water for knitted grafts in the range of 2,300 to 5,300 ml min^{-2} cm^{-2}. These values were obtained in our laboratories using an applied pressure of 120 mm of Hg according to the test method described by Buxton & Cooley (43). Water permeability values ranging from 2,000 to 5,000 ml min^{-1} cm^{-2} are believed to be an optimum figure (2). The more porous knitted grafts require elaborate preclotting prior to implantation; thus the fabric walls are rendered impervious by the accumulation of blood debris (2).

The increased stretch of knits provides better pulsatile compliance and mechanical compatibility with the host vessels. A disadvantage is the lack of dimensional stability; when exposed to cyclic stresses, as experienced in the arterial system, such structure do not behave perfectly elastically and tend to fatigue or "grow" over a period of time. This has been confirmed in-vivo on recovered prostheses. Growth or dilation takes place with concurrent loss in stitch density and the concentration of bending stresses on the loops. This implies a decay in the tenacity of the fabric even in the absence of chemical deterioration.



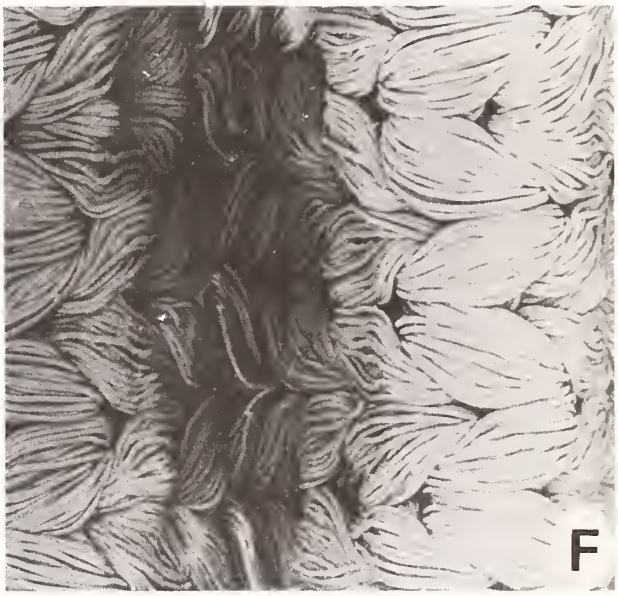
A: Single-bar jersey weft knit

B: Two-bar "locknit" warp knit



C: External surface of a de Bakey standard weft knit prosthesis

D: Internal surface of a de Bakey standa knit prosthesis



xternal surface of a warp-kitted Cooley
rosthesis with reverse two-bar locknit

F: Internal surface of a warp-knitted Cooley prosthesis with reverse two-bar locknit.

So-called lightweight constructions were attempts at further improving compliance and surgical handling characteristics as well as healing properties by further reducing fabric density and thickness. Recent clinical experience suggest that such devices have inadequate stability and mechanical strength for most applications (12-19) and that healing is not significantly better than other constructions. Catastrophic rupture is not necessary for failure. Dilation, fabric growth and deformation leading to interstitial bleeding, suture line disruption or stretching at the suture anchoring sites are sufficient. Light weight devices appear more vulnerable to deformation and stretching resulting from cyclic blood pulsations.

All commercial velour grafts have knitted constructions; they are a late evolutionary variant of the knitted prosthesis. Except for Microvel, they are all knitted from the same type of jersey weft knit or "2 bar bocknit" (warp knit) described previously. They differ from the earlier knits by a much thicker fabric construction, a greater porosity, a low fabric density and/or lower stitch density (table 2). The "velour characteristic" is incorporated by the use of a finer and lower linear density texturized yarn (Cooley Double Velour, Microvel), a lower stitch density (vasculour D), napping the fabric with wire brushes to give a raised, disorderly pile and/or laying an additional set of texturized yarns under low tension so that they form a looped pile above the base fabric (Microvel).

Velours aimed at improved adhesion of the initial thrombus layer and the neointima to the lumen wall and minimum hemorrhagic blood loss during and after the surgery. With a rougher and more porous surface internally and externally, neointimal and perigraft tissue is expected to grow more extensively into the device. The graft acts as a porous trellis which provides an improved hypothrombogenic surface, accelerates preclotting by trapping fibrin and retains the cellular blood constituents within the fabric so as to promote interstitial growth of a fibrin matrix.

It is generally believed that the porosity of a fabric, as measured by permeability to water, reflect potential for tissue adhesion. This is misleading because the permeability to water is a property that depends more on the porosity of the non-velour component of the fabric. It is on the size and shape of the interstitial and interfilamentary pores in the flow controlling layer of the fabric and the surface tension of the material with reference to water which dominate. Tissue adhesion, on the other hand, is controlled principally by the porosity near the fabric's surface. It may be preferable to measure the internal lumen wall surface porosity in terms of an "internal velour index" which measures the total amount of "cilia" or accessible yarn extending into the lumen.

Since velour grafts have highly porous constructions with little substance, their bursting strengths are not related to fabric thickness, but are influenced primarily by the linear density of their yarns and filaments in the base component of the fabric. The "fill" or velour component contributes little to the tenacity or the stability.

Microvel's low burst strength is also a consequence of its unique construction. It is the only graft where the base fabric is knitted with a half-tricot stitch with only one set of yarns. Two sets are used in the locknit construction of all other warp knit grafts. Microvel^{R} does contain a second set of yarns but they are used exlusively to form the loose looped pile and are therefore unable to contribute to strength and dimensional stability.

3. Compaction and Shrinkage

On removal from the knitting machine, the water permeability of the knitted and velour fabric is too high. Shrinkage of the knitted construction is necessary to bring the fabric porosity within acceptable limits. This can be accomplished by chemical or thermal treatments.

The Chemical process consists of an immersion in swelling agents (e.g. methylene chloride) and acid solvents (e.g. trichloroacetic acid). The thermal process uses dry heat or a heat transfer medium at 120 - 155°C. In either case, the molecular structure of the PET is given such mobility that the filaments can experience considerable diameter increase and longitudinal shrinkage thus reversing the structural changes incorporated during the drawing of fibres and yarns. So forceful is the swelling that individual filaments in a multifilament yarn bundle are often crowded against each other while soft and develop periodic flattened surfaces at the contact points.

These macroscopic changes are visible evidence of major alterations in the macrolecular order. Thus compaction processes are accompanied by significant changes in molecular orientation, crystallinity and surface chemistry of the PET fibres.

4. Crimping

Concurrently or subsequently to compaction, most grafts are crimped to radially stiffen the structure and increase the potential elongation. This feature inhibits collapse, stenosis, wrinkling and kinking after implantation. This can be done by winding a thread spirally around the graft after fitting it on a mandrel and heating it after compressing the fabric tube from both ends. This produces a helical crimp. Such methods, however, are not suitable for velours and high bulk texturized yarn since the thread pressure will permanently flatten the pile. An alternative crimping method using internal steam pressure in a mold is preferred for velour grafts; the technique can produce circular as well as helical crimps. The depth and frequency periodicy of the crimps in a prosthesis (table 3) therefore depend either on the pitch of thread windings or on the form and shape of the steam pressure mold.

It has been suggested that the helically crimped grafts have better blood flow characteristics than the grafts with circular crimps. A priori, a differences between flow characteristics of circularly crimped and helically crimped devices of the same periodicity would be, at best, marginal. Instead, the depth of the crimp in relation to the average lumen diameter, the crimp frequency and the shape of the crest on the crimp overshadow helicity or circularity insofar as the haemorheological characteristics of the devices are concerned.

The crimped configuration increases the longitudinal and radial compliance of a graft. The presence of crimps provides a longitudinal and volume compliance which are believed to facilitate maintenance of patency of the graft, reduce the stresses and likelihood of stricture and thrombosis at the anastomosis line and buffer the local blood pressure pulse (water hammer effect) that results from an unmatched graft/arterial compliance. However, the compliance and flexibility of crimped grafts are severely limited when the graft becomes extensively encapsulated with new perivascular collagenous tissue; external velours and double velours are known to develop abundant external perivascular tissue.

The processes through which the prosthesis and its intermediates must pass are not unlike those which lead to consumer products; the melting, compounding, handling, spinning, weaving, knitting, crimping and shrinking introduce contamination which cannot be tolerated on the finished product and must be removed prior to packaging and sterilization.

5. Final Cleaning

Proprietary cleaning techniques for prostheses issue from conventional textile cleaning technology. They include hydrocarbon washes, mechanical or ultrasonic agitation, countercurrent or continuous solvent refluxing, caustic scouring, chemical bleaching and other harsh treatments. Such treatments therefore have impact on the physical properties and the surface chemistry of the device.

In many cases, yarns intended for wearing apparel or industrial textiles must also be used for medical applications for lack of suitable alternatives. Occasionally, such yarns are already contaminated to a level where they are difficult to process without jeopardizing the knitting machinery; they must therefore be pre-cleaned on arrival. These treatments may impose further penalties on the performance of the finished product.

It is occasionally claimed that "medical grades" of yarn are used for some prostheses. The only significant difference between the PET used in vascular prostheses and that used in regular apparel, furnishing and industrial applications is that the "medical grade" appears to have received an extra scour and bleach treatments to remove surface impurities. Inevitably, the internal impurities and additives remain. Thus, traces of initiators, oligomers, anti-oxidants, stabilizers, delusterant and pigment particles will be found in the yarns even after several years in-vivo.

Porous vascular prostheses must be free of pathogens. It is noted that, if infected at implantation, prostheses and their neointima have poor antibiotic accessibility and control of infection is difficult. Therefore implants must be freed of micro-organisms by post-manufacturing sterilization. This must destroy both bacteria and spores and may be achieved by the use of dry heat, moist heat, gamma irradiation or chemical agents according to established practices. Such treatments are often deleterious to PET fibres and the changes which

occur in the material and the fabric must therefore be taken into account.

6. Sterilization

Today, almost all prostheses are sold pre-sterilized in porous envelopes or other similar packaging systems suitable for autoclaving or gas sterilization. Some prostheses are claimed to be resterilizable by steam according to traditional hospital practices. Other manufacturers advise against resterilization under any circumstances.

Heat sterilization is most common. In dry heat sterilization, pathogens are thermally oxidized at temperatures between 160° and 190°. Moist heat sterilization is effective atlower temperatures (120-140°C) but the presence of superheated water vapor is a potential plasticizer for certain PET formulations. Predictably, such treatments can oxidize the surface of PET and cause other physical and chemical damages to the fibre.

Some hospitals resterilize whole grafts or portions of grafts left over from previous surgeries. Multiple sterilization cycles in steam cause some grafts to lose mechanical compliance and make them more difficult to handle. Experiments in this laboratory do not support the contention that repeated steam sterilization causes significant changes in the gross permeability to water and in the bursting strength of grafts. However, such thermal treatments, in combination with liquid or reactive gas plasticization may sufficiently alter the surface morphology and chemistry of the fibres to affect in vivo biocompatibility or accelerate biodeterioration.

Amongst chemical sterilization processes, only ethylene oxide is now used for prostheses; the reactive gas is normally diluted with other gases such as Freons, carbon dioxide and water vapour. Ethylene oxide can polymerize to oligomeric polyethylene glycols and remain sorbed in the PET and act as a plasticizer or else change the surface properties of fibres so as to influence the pre-coagulation step.

At present, it appears that only minimal physico-chemical changes occur in spun and drawn yarns and in some of the woven devices as a consequence of sterilization. This is not necessarily the case for knitted prostheses after compaction, crimping and finishing. Work in our laboratories suggest that changes occur to the chemistry and microstructure of compacted and crimped yarns when exposed to ethylene oxide sterilization conditions.

Gamma radiation sterilization is becoming more popular. However, conventionally accepted dosage for sterilization near 2-3 mrad and is harsh on polyester molecules; it can cause chain scission, cross-linking, oxidation and other undesirable chemical changes. One manufacturer uses this sterilization process. It is not unequivocally established that cardiovascular fabric devices can sustain this treatment without changes in properties.

In summary, polyester devices, once believed unaffected by sterilization treatment, are emerging as subtly vulnerable systems. Their in-vivo performance and durability are controlled by many factors, some of which are integral parts of the sterilization treatment. Even too mild sterilization processes which have no obvious chemical repercussions on the chemistry of the fibre, there are still many unanswered questions regarding changes in the physics of the textiles.

Discussion

Question (R. Leininger, Battelle-Columbus Laboratories): Your presentation indicates that there is a change in burst strength of cardiovascular prostheses with in vivo residency time but the correlation coefficient of the data is not stated. Can the statistics of measured burst strength be quantitied or defined more precisely?

Answer: The nature of our recovery program is such that a remnant of prosthesis of the same type and batch as that was originally implanted in the patient is seldom available. Therefore, it is necessary to depend on average properties of prostheses fabricated when the original device was implanted. However, even that is not always available. Also, our samples are not numerous. For these reasons, strict mathematical correlation is difficult if not impossible for many types of early devices. It is noteworthy that a severe decrease in burst strength is noted for some families of devices whereas others such as the Standard Knitted DeDakey appear to be as tenacious after 10 years in vivo residency as the products which are commercially produced today.

Question (R. Leininger, Battelle-Columbus Laboratories): Are there plans to do further fiber characterization work such as tenacity, molecular weight and molecular weight distribution of the polyester in the fibre?

Answer: This type of study has been considered and some portions of it are currently in progress. However, there are severe difficulties in conducting polymer characterization work on such small samples which are contaminated by absorbed and adhering biological products.

Question (S. Bruck, Stephen Bruck Associates, Inc.): The biological performance, as opposed to physical performance of grafts is influenced amongst others by the post-surgical anticoagulation regime of the patient. Since there is no data presented on this factor, could you please comment on anticoagulation in these patients?

Answer: Such information is occasionally included in patient records. However, more often, it is omitted along with many other elements which, in retrospect, appear very important in establishing the performance of prostheses in individual patients. More detailed medical and surgical records are necessary for any comprehensive study on implant performance; these at present are not available except in rare cases.

Question (S. Bruck, Stephen Bruck Associates, Inc.): There is need for appropriate statistical analysis of performance data. Although there is data presented on approximately 150 arterial grafts, there

were some of different construction and from different manufacturers. There may not have been enough samples in various categories to reach definite conclusion. Please comment?

Answer: In order to carry out comprehensive retrospective studies on the prosthesis' performance, many thousands of protheses would be needed. However, for reasons which are outlined in the paper, collection of samples in a pathological study is dictated by factors over which there is no control. In fact, we should be grateful to have had that many prostheses collected in conditions such that they could be studied. Ultimately, there will be sufficient autopsy and recovery data to make the statistical analysis on graft properties more meaningful. Until that time, however, the results presented in this paper can only be regarded as qualitative. Nevertheless, trends towards reduction in burst strength with in vivo residency are clearly shown.

Question (James Anderson, Case-Western Reserve University): Porous vascular grafts in animals have been shown to undergo complete endothelialization of the blood contact surface. However, this has not been seen in human vascular grafts. Have you evaluated the degree of endothelialization in your retrieved grafts? If there is not complete endothelial coverage, is it possible to explain? Could the endothelial layer, which is extremely fragile, be lost in the specimen work-up procedure or is the luminal surface not completely endothelialized?

Answer: Endothelialization of tissue ingrowth devices is still controversial and has been so for approximately 10 years in the clinical and scientific literature. Studies on healthy animals carried-out in our laboratories confirm there is some endothelialization on the luminal surface in particular near the anastomoses. This occurs more readily in some classes of prostheses in certain experimental animals. Chemical fixation treatment do not destroy the morphology. Such structures readily service the specimen work-up techniques and can be clearly seen even at low magnification in some cases. However, it is noteworthy that endothelialization with cellular development appears to proceed with great difficult even in healthy animals. In the case of recovered prostheses used in humans, cellular endothelialization is virtually absent or at best sparse. Perhaps this reflects simply the age and the overall vitality of the patient. This point is discussed further in the paper.

Question (Walter L. Scott, Food and Drug Administration): From the data presented, the number of samples examined at each point in time appears to be low. Therefore, the exact geometric location of each sample could be an important variable when comparing prosthesisartery morphology. Has this consideration been taken into account in sample selection?

Answer: These factors have been taken into consideration when possible. Details of explanation sites and even parts of sample are often lost

between the operating room and the pathological laboratory. However, the work is continuing and the protocol of collection is being refined. Such considerations are now being taken more closely into consideration for currently collected prostheses.

Question (U. M. Gross, Free University, Berlin, Germany): You use the statements "healing" and "no healing" to describe the state of the imolantation bed and the luminal surface of the Dacron arterial prostheses. Please elaborate on the meaning of this terminology?

Answer: "Healing" in this context implies a healthy and well irrigated tissue capsule of uniform and reasonable thickness throughout the length of the prosthesis. This generally consists of new tissue approximately 100 microns in thickness. Morphologically, this translates as a smooth, glistening interior wall which has little obvious porosity even when seen under high magnification. Absence of "healing", on the other hand, implies the lack of an internal capsule or the existence of a porous, disorganized mass of fibrin and/or blood components even after several months. This situation normally correlates with patients afflicted by several concurrent diseases such as diabetes and/or atheroselerosis. Such prostheses also have greater probabilities of showing irregular thrombotic structures on the lumen and will generally show many totally exposed Dacron fibers and sutures.

Clinical, histo-morphological and material related observations on removed alumina-ceramic hip joint components.

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1. Introduction

Every new biomaterial has to stand its test of time in clinical practice after a period of extensive experimental testing. In the case of high density alumina ceramic 5 years of clinical experience as a bearing surface for artificial hip joints have recently been completed in Western Germany. During this clinical test period some 3.000 hip endoprostheses with Al_2O_3/Al_2O_3 ceramic bearing surfaces for socket and ball have been implanted. Besides considerable success reports (GRISS et al., 1977; MITTELMEIER et al., 1980) material specific complications appeared (Fig. 1). This paper deals with investigations of now 15 cases of removed endoprostheses with bearing surfaces of high density, high purity alumina ceramic.

The report will be subdivided into the following sectors of investigation.

- Clinical observations
- Histo-morphological results from the tissue surrounding alumina hip endoprostheses
- Complete or partial fractures of alumina ceramic components with special reference to the self-locking taper for ball fixation to the metallic stem.
- Wear behaviour of the ceramic bearing surfaces.

2. Clinical results

The one of us (P.G.) has recently reviewed his own 129 cases of Al_2O_3/Al_2O_3 ceramic endoprostheses implanted since 1974. An overall clinical success rate of 84.2 p.c. (Fig. 2) is contrasted by 15.8 p.c. of fair and poor results, the latter being caused by mainly individual clinical reasons not directly related to the material and prosthesis design. Most of the patients are very satisfied with the endoprosthesis function.

Two prostheses had to be reoperated for cemented stem loosening, 7 patients sustained a ceramic ball fracture in the body requiring reintervention (Fig. 3 and 4). Loosening of a non-cemented screw-socket (GRISS et al., 1976; 1977) was not observed in this series. This part of the ceramic hip prosthesis concept therefore proved to be very satisfactory in clinical practice.

3. Histo-morphological observations.

Human material for histo-morphological examination was obtained from 15 reinterventions in ceramic on ceramic hip joint replacements. The prostheses were in function between 2 weeks and 3 years. Both, joints with a macroscopically visible high wear rate and those with minimal visible wear of the retrieved ceramic parts could be investigated. The size of most of the ceramic wear particles (crystals) stored in the neocapsular tissue around Al_2O_3/Al_2O_3 ceramic hips was below 2µm. However, some large grains "pulled out" in toto from the

articulating surface were in the range of up to 20 µm. All small particles were stored intracellularly within histiocytes or accumulated superficially in a layer of amorphous fibrin-collagen separating the underlying scar tissue from the joint surface. Macrophages overloaded with phagocytized ceramic wear material tend to form clusters or islands within the scar tissue (Fig. 5a). In deeper layers they concentrate around small blood vessels (Fig. 5b). This indicates transport of the wear material in macrophages via perivascular lymphatic vessels to local lymph nods. Observations in experimental animals support this view (GRISS et al., 1973; 1974; HARMS and MÄUSLE, 1980). Within crystal accumulations only a small number of round cells are scattered in between. More pronounced inflammatory cell reactions are seen in areas where ceramic and metal wear (from the naked metal taper articulating to the ceramic socket after ball fracture) are deposited together. In cases of stem loosening foreign body giant cells may be seen storing PMMA particles freed from the cement cuff by fretting of the metallic stem against the cement. In conclusion the morphologic reaction to ceramic wear debris in the human body is well in line with the experimentally established good tissue compatibility of particulate Al_2O_3 ceramic material.

4. Ceramic ball / socket fractures in vivo.

Fig. 1 collected the ball / socket fractures reported in the literature since 1974 in Western Germany. This includes components of 3 different designs and manufacturers (Fa. Feldmühle, Friedrichsfeld, Rosenthal). Fig. 3a/b shows typical X-ray examples of ball fractures. Fig. 4 is a collection of ball fragments removed from the body at re-intervention after ball fracture in vivo. To explain these ball fractures a number of hypotheses have been developed. From a clinical point of view extremely high strains occuring during a "short term" subluxation of the joint and the following hard rebounding into the normal position, a non ideal fitting of the male and female taper, "inborn" frozen strains within the ball created during its production, cement or bone fragments caught between taper and ball during insertion or even only a blood coated taper may produce extremely high stresses at the ball metal interface during accidentally high loading and cause ball fracture.

A too vigorous blow with a mallet onto the ball during its fixation to the metal stem at insertion can as well produce "frozen" stresses in the ball itself. A wet "slippery" cone during fixation of the ball causes unfavourable friction-conditions in the ball / self-locking cone system and creates a "frozen" stress condition in the system.

In cases of socket fractures besides design dependant reasons (large ceramic neck) an unfavourable steep position of the socket may induce a levering of the ball over the sockets rim. This levering may occur during routine movements of the leg and produce local stress concentration in the socket and the ball thus creating local implant damage and fracture of ball and/or socket in vivo.

Impaired strength of the high quality, high density, high purity Al_2O_3 ceramic may be another reason for ceramic component failure in vivo. The strength of this material depends among other characteristics on grain size and grain homogeneity. Coarse grains as seen in some removed cases can reduce the local strength and initiate a material fracture.

In laboratory investigations HINTERBERGER and UNGETHUEM (1978) have produced ceramic ball fractures under static loading conditions by means of the test equipment shown in Fig. 6. At an average constant load of 40.000 N (min. 19.000 N, max. 56.000 N) fractures of ceramic balls (diameter 26 - 32 mm, 3 manufacturers) occured. In dynamic tests several metal stems with ceramic balls have been tested in "physiological position" without corresponding socket (Fig. 7). No ball fractures were observed using this test assembly under sinus load of 5.000 $\pm$ 4.000 N.

5. Wear phenomena in ceramic hip joints.

As substantiated by WILLERT et al. (1976; 1978) basically every wear particle of a given material for artificial joint replacement may have a detrimental effect on long term function. The amount of wear per unit of time and the morphology - in other words form and size - of the wear particles are considered to be a decisive criterion in the functional failure of the artificial joint system. One of the main causes fully recognized only recently is the overflow of wear particles within the joint space. This results in overstressing of the body's capacities to deal with this debris, that means to store and to eliminate it. Granulation tissue, bone resorption and loosening of the implant are common features in this process of particle "incorporation and elimination".

We have observed one singular case of extreme wear of a ceramic ball in a correctly implanted endoprosthesis (Fig. 8). This component had to be removed 3 years after implantation for stem loosening. The maximum loss of material in the center of the load transmitting area amounts of about 0.9 mm. The worn area comprises approximately 650 mm^2, representing almost two third of the available ball surface. A scanning electron microscopic surface analysis of this ball (Fig. 9) demonstrates massive destruction of the surface.

Picture E in Fig. 9 on bottom left documents the frequently observed phenomenon of grain excavation which is probably the initial phase of the whole destruction process. The arrow in E points to a crack in the material which may be recognized as a starting point for a future grain excavation mechanism. It has to be emphasized again that in this case correct socket orientation and slight valgus position of the prosthetic stem as well as two and a half years of good function could not contribute to explain this wear phenomenon. Studying the cases in total all showed areas of wear in a more or less impressive amount. Therefore, besides mere defective surgical technique (subluxation) further individual not yet fully defined factors are involved in the process of wear in ceramic total joint replacement.

Essentially the same manifestations of destruction occur both in sockets and balls. In the cases investigated the destroyed surface area of the socket is always smaller than that of the corresponding ball. Fig. 10 shows the worn out sections of surface area as an informative example; Fig. 11 shows the clinical aspect of the removed implant.

6. Proposed mechanism of alumina ceramic wear in vivo.

Instead of discussing the cases in more extensive detail (they almost exclusively show the same basic wear phenomena) the authors present their hypothesis of wear mechanism in Al_2O_3/Al_2O_3 ceramic hip endoprostheses in vivo (Fig. 12). The starting point in surface destruction of alumina on alumina gliding partners is in our opinion always a grain excavation. Fig. 13 represents such a grain excavation in the ball surface of object F / 10 shown in Fig. 11. Following our hypothesis such a sharp edged hard particle is caught between both gliding surfaces moving one against the other under load. This causes the crystal to change position and consequently create further damage to the areas being passed through the gliding way. This may create further grain loosening and thus sustain a snow ball effect (Fig. 14). As a consequence an avalanch-like acceleration of further grain excavations and finally the destruction of the whole bearing surface can result. Fig. 15 compares a polished surface above with a worn out surface below to support our observations and interpretations more drastically.

In summing up these observations it can be stated that material quality, design and implant finish as well as adequate surgical technique are the challenging factors for minimizing wear of Al_2O_3/Al_2O_3 ceramic hip components (Fig.16). Newer developments are aimed at further reducing the average grain size of the material, improving density, surface roughness, matching of socket and

ball (sphericity) as well as the technique of the self-locking taper or other anchoring techniques between ceramic balls and metal components. Presently running and future experiments however have to prove the efficiency and relevance of these new developments for clinical practice.

7. Summary

All of the stated possible causes for component fractures and/or surface wear do not generally occur isolated from one another but exist quite simultaneously, whereby they can reciprocally influence each other adversely. Concerning the virtual connection between the component loosening factors and the observed wear we can only record that the tissue reaction onto wear-particles as it is shown in section 3 may be supported by the increase of the friction-moment between ball and socket which is remarkable in case of destroyed surfaces. We have by clear mind not made a statistical evaluation and classification of individual cases because the total picture is still too inconsistent.

In conclusion we would like to confirm the following: Based on the total number of implanted hip endoprostheses with ceramic-ceramic bearing surfaces, the number of failures we have experienced appears to be minimal. After an implantation period of now 5 years in Western Germany we consider it premature to calculate a general percentage failure rate at

this time especially because reliable complete figures are not available for either of the implanted or removed designs. Despite the constant manufacturer's claims alumina ceramic has proved to be not absolutely free of wear or the danger of component fracture. Therefore alumina ceramic components deserve further critical observation.

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Mechanical failures of Al_2O_3-ceramic hip implants

Author	Ball / socket	unclassified	total
MITTELMEIER WEIGERT BRINKMANN DOERRE 1980	5 / 3	2	10
SALZER 1977 KNAHR 1980	8 / 0	Ø	8
GRISS 1978 RÜTT 1980	10 / 0	Ø	10

Fig. 1: Comparative listing of mechanical failures reported in the literature of 3 different designs and manufacturers.

Alumina / Alumina Ceramic Metal Hip Prostheses :

Clinical hip evaluation, Merle d'Aubigne , score Feb. 80:

N = 129 hips

	excellent 18 - 17	good 16 - 15	moderate 14 - 13	fair - poor 12
praeop.	Ø	1 = 0,7 %	14 = 10,8 %	114 = 88,3 %
postop.	72 = 55,8 %	29 = 22,4 %	8 = 6 %	20 = 15,8 %
%	84,2 %			15,8 %

Fig. 2: Statistical analysis of 5 years clinical success rate in Al_2O_3/Al_2O_3 ceramic hip endoprostheses (Orthop. Klinik Lindenhof).

Fig. 3: a) X-rays of Alumina/Alumina hip endoprostheses after ball fracture (two different designs and manufacturers).

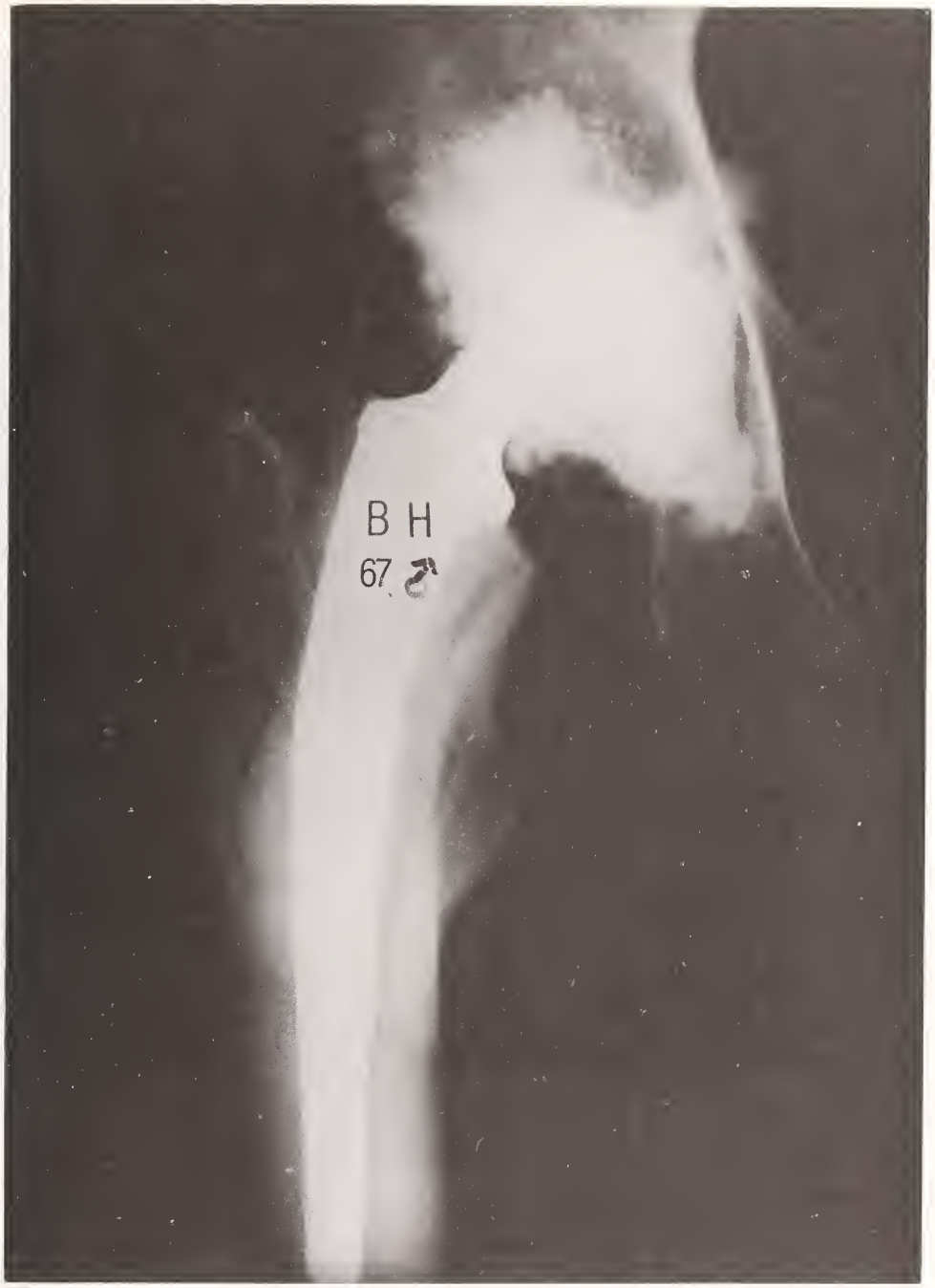

Fig. 3: b) X-rays of Alumina/Alumina hip endoprostheses after ball fracture (two different designs and manufacturers).

Fig. 4: Macroscopic appearance of broken parts of a 26 mm ceramic ball.

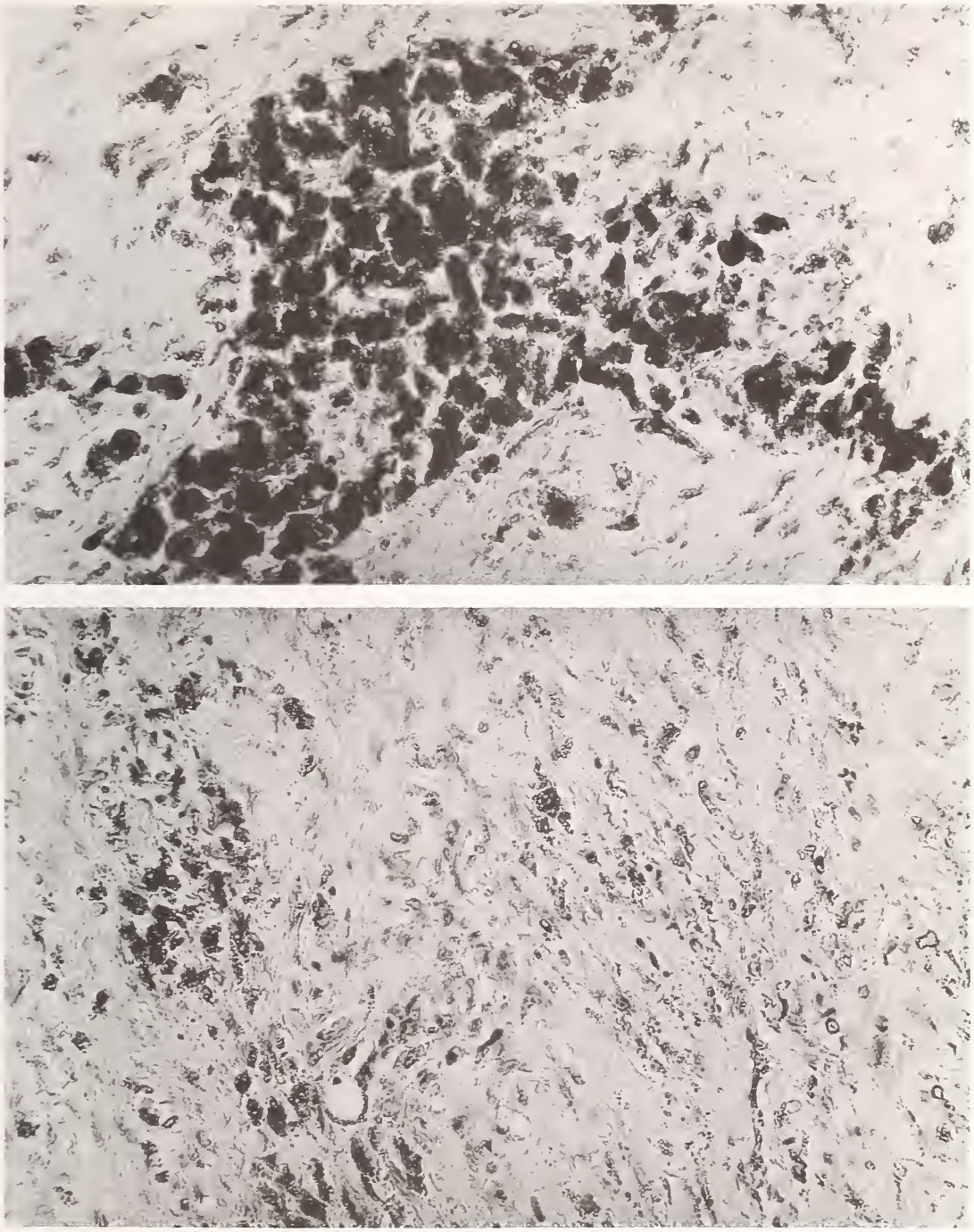

Fig. 5: a/b: Histo-morphologic picture of ceramic wear deposits in human periarticular scar tissue.

a) Cluster of macrophages loaded with phagocytized Al_2O_3 ceramic wear particles.

b) Peri-vascular concentration of macrophages with Al_2O_3 wear particles. Note only minimal round cell reaction!

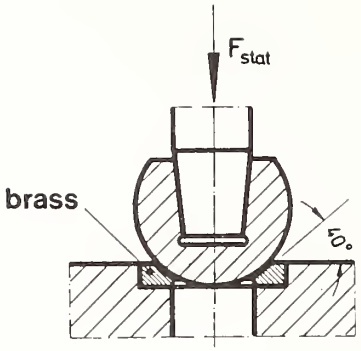

Fig. 6: Line drawing of equipment for static cone test (after HINTERBERGER and UNGETHÜM).

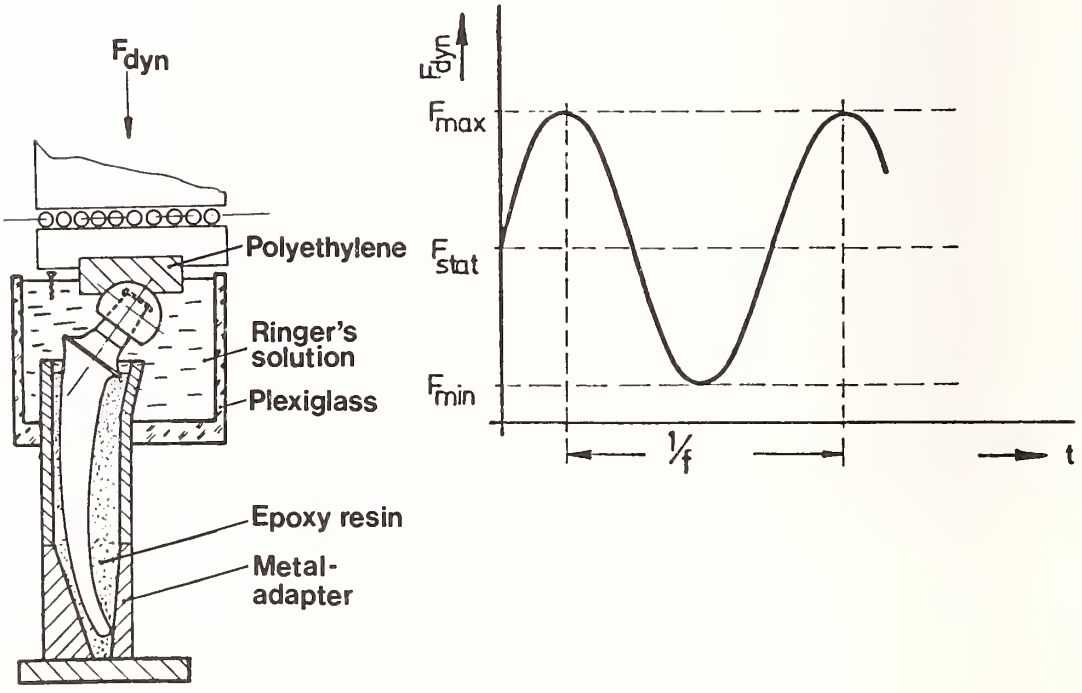

Fig. 7: Line drawing of equipment for dynamic cone testing.

Fig. 8: Removed Al_2O_3-ceramic hip joint prosthesis (implantation period 3 years).

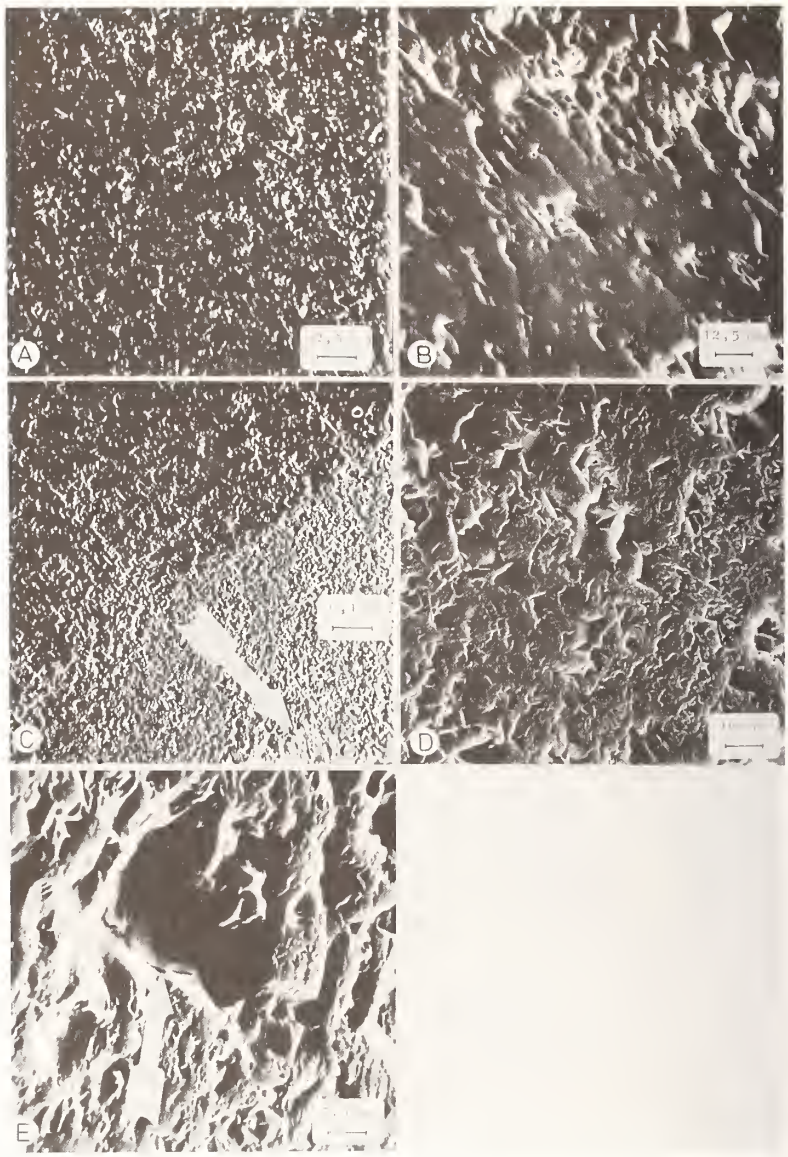

Fig. 9: SEM analysis of the ball surface in Fig. 8.

A undamaged surface

B same area as in A magnified 800 x

C Boarder zone between damaged and undamaged area. Arrow indicates area of very high surface roughness.

D Damaged surface area (grain excavation with average 10 - 15 µm diameter).

E Grain excavation hole, higher magnification.

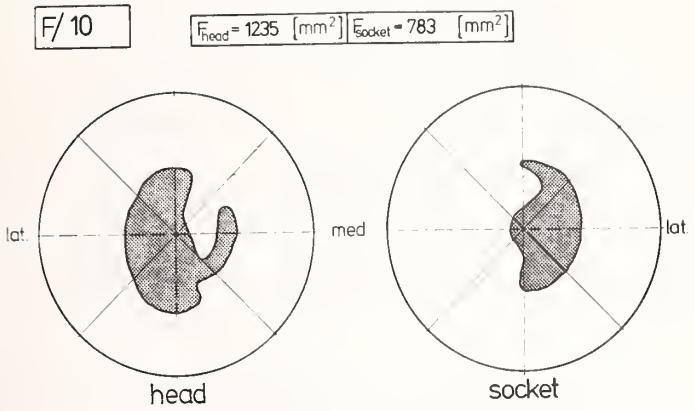

Fig. 10: Destroyed surface area of removed object Fig. 11.

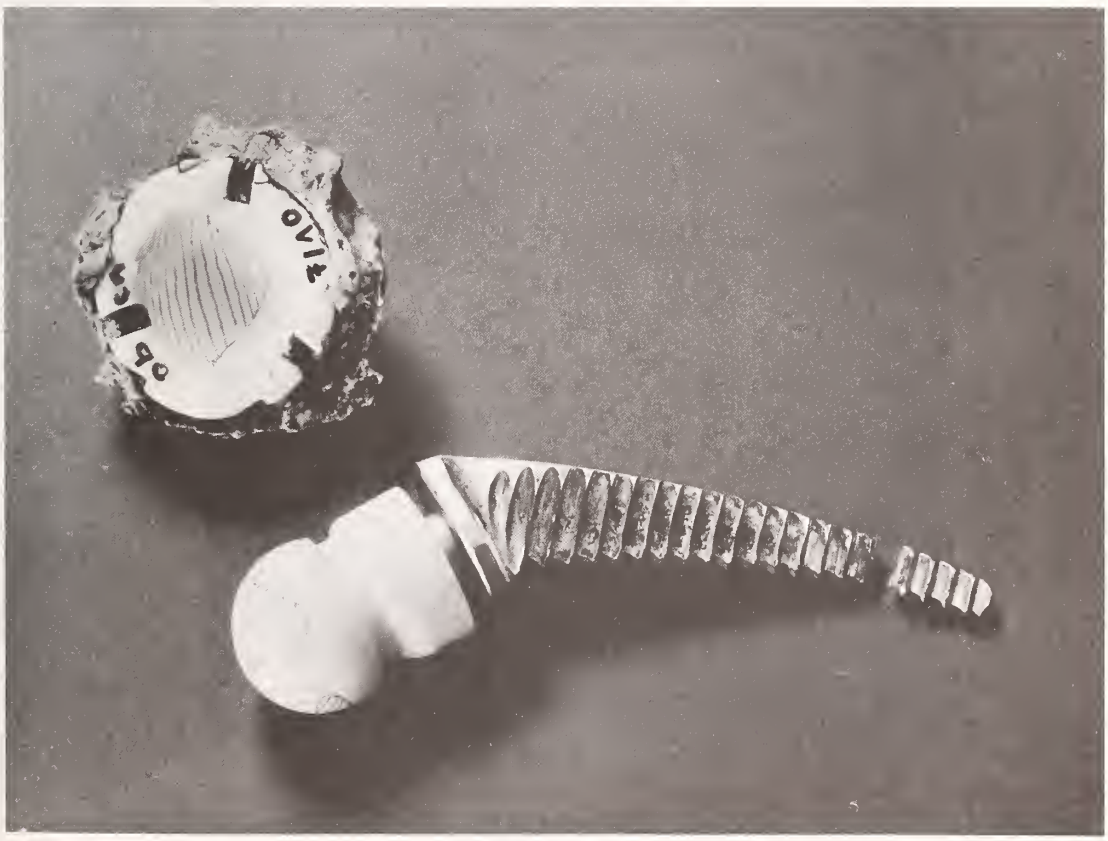

Fig. 11: Removed implant F/10

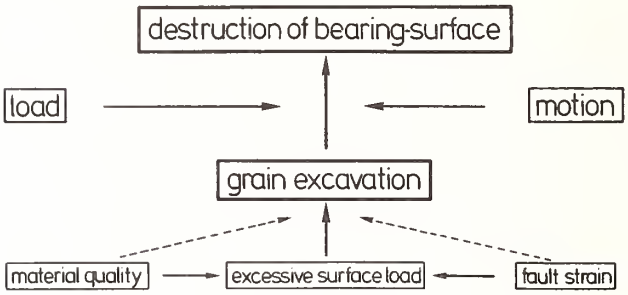

Fig. 12: Schematic representation of proposed destruction mechanism.

Fig. 13: Grain Excavation in the ball-surface of the removed object shown in Fig. 11 (magn. 6300 x).

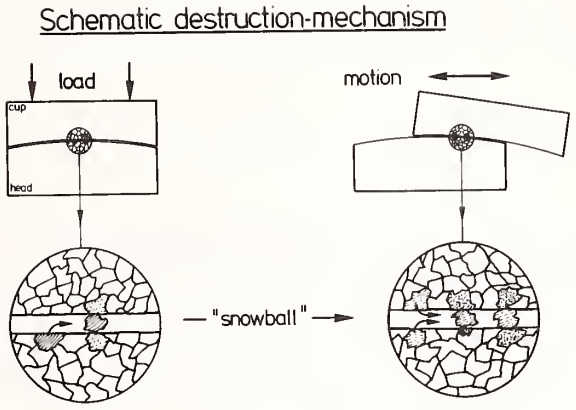

Fig. 14: Destruction-mechanism of Al_2O_3 bearing surfaces in hip joints.

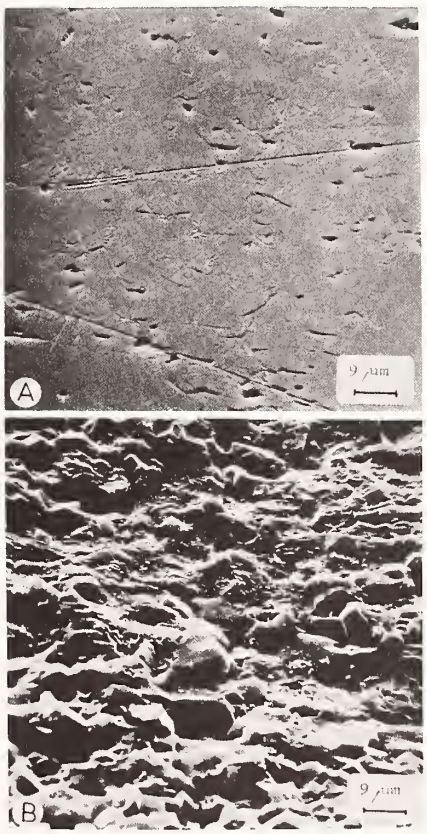

Fig. 15: Comparison of "as delivered" surface (above) with worn surface (below).

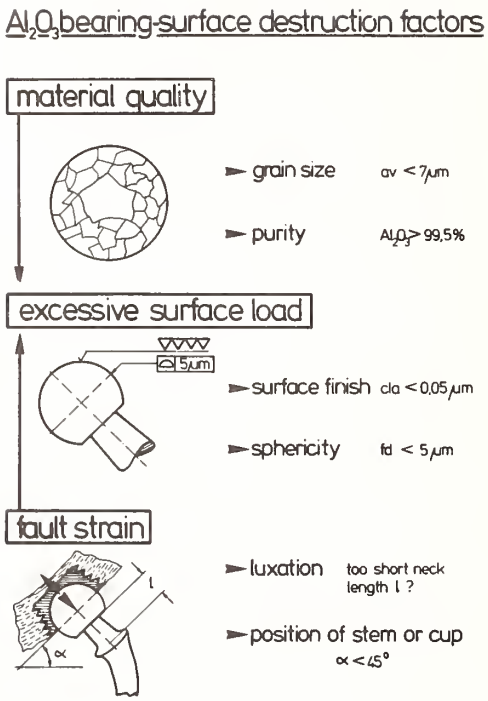

Fig. 16: Possible destruction-factors of Al_2O_3 on Al_2O_3 surfaces.

MICROSCOPIC ANALYSIS OF RETRIEVED POLYMETHYLMETHACRYLATE (PMMA) BONE CEMENT

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Metallographicaly prepared sections from retrieved bone cement were examined with reflected light microscopy. Gross plastic deformation was observed in the femoral collar region and interdigitating bone regions. Deformation strain lines are also observed frequently associated with cracks in the cement. Plastic deformation of the bone cement under physiological stress states can therefore account for femoral component loosening. Cracks are also observed radiating from the corners of the medial edge of the femoral stem. The bone-trabeculae interface was observed to be closely adapted with no fibrous capsule interposed. The surface morphology of the cement with bone was demonstrated to range from smooth to porous. These data correlate well with previous scanning electron microscopic evidence. Bone debris from the surgical procedure was also observed. Abrasive wear of the bone cement at the prosthesis interface was observed which can account for the small PMMA particles observed in the tissues of the joint capsule.

Introduction

The successful implementation of an in situ polymerizing polymethylmethacrylate (PMMA) cement by Charnley [1] for the stabilization of the components in total hip replacement (THR) caused a dramatic increase in the total number of joint prostheses implanted in both Europe and the USA [2]. The objective of the cement was to uniformly distribute the transfer of stress from the femoral component to the surrounding bone and thus avoid bone resorbtion in regions which were unloaded, due to lack of direct contact with the prosthesis. Until that time bone resorbtion had usually produced disasterous loosening of the femoral component and thus severely compromised the clinical efficacy of joint replacement.

Although the use of the PMMA cement for fixation of the components has made total joint replacement an acceptable surgical procedure, a significant number of the joint components become loose with time. The loosening mainfests itself clinically as pain and may subsequently lead to fracture of the femoral stem, either of which require surgical revision. A number of explanations for the loosening of the components of the prostheses, particularly of the femoral component of total hip replacements,

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have been suggested. Mechanical failure of the PMMA cement, as a result of the stresses applied during walking and other normal activities has been implicated. Excessive wear debris, produced at the acetabular-femoral head articulating interface, has also been suggested as being responsible for local bone resorption [3].

Many factors which influence the mechanical and physical properties of bone cement have been investigated in vitro. The cement [4] consists of spherical particles of PMMA, or a copolymer with ~2% styrene, powder produced by suspension polymerization. The powder also contains a catalyst, benzoyl peroxide. The bone cement is prepared by mixing the powder with a liquid which consists primarily of the monomer, methylmethacrylate (MMA), together with an accelerator, N,N-dimethyl-p-toluidene, and an inhibitor, typically hydroquinone. After mixing the liquid MMA swells and starts to dissolve the PMMA powder, however polymerization of the MMA is also initiated and the mixture increases in viscosity and eventually becomes a hard solid as total polymerization is achieved. The final product is a two phase material consisting of the original spherical particles of the powder embedded in a martix of in situ polymerized MMA. The matrix may contain either $BaSO_4$ or ZrO_2 powder (~10%) to make the final cement radiopaque. The mechanical properties and heat evolved during the exothermic polymerization reaction have been shown to depend upon the ratio of liquid to powder [5], presence and amount of $BaSO_4$ or ZrO_2 [6,7,8] and amount of catalyst [8]. The effect of the mixing rate, which influences the volume percentage and size of air voids incorporated in the cement, has also been demonstrated to affect the mechanical properties [9,10].

This study was undertaken to analyze the PMMA bone cement recovered at surgical revision or autopsy and evaluate evidence for mechanical deterioration of the cement. Polished and etched sections were prepared from the retrieved PMMA bone cement [11,12]. This method allows the visualization of deformation and cracks in the cement as well as the structure, including void content. A previous study of retrieved bone cement [13] examined the surface with Scanning Electron Microscopy (SEM) with the object of correlating the surface morphology with the surrounding tissue. As a result of this study the authors speculated that the irregular surface, in which the individual spheres of powder were observed to be in an apparently "porous" array, could initiate cracks.

Materials and Methods

The series of retrieved bone cement samples which we analyzed were obtained from 9 cases of THR, 8 obtained at surgical revision and one at autopsy. This analysis is part of the Implant Retrieval and Analysis program of the Department of Pathology at CWRU. Table 1 summarizes the pertinent data from these cases. The time of implantation ranges from

Origin of Bone Cement Samples

Sample	Implantation Period	Specimen obtained at	Patient Age	Sex	Activity	Comments
A	6y	Surgical revision	29	M	active	-
B	3y 8m	Surgical revision	53	M	active	-
C	4y 6m	Surgical revision	62	M	active	stem loose in cement
D	4y	Surgical revision	40	M	very active	stem fractured
E	4y 6m	Surgical revision	60	M	active	from acetabular cup
F	4y 2m	Autopsy	54	F	limited	-
G	5y 4m	Surgical revision	83	M	active	-
H	1y 3m	Surgical revision	51	M	limited	fell on hip 4m. p.o.
J	2y 6m	Surgical revision	51	F	limited	loose at cement/ bone interface

15 months to 5 years and 4 months* and the cement was either Simplex-P** or Zimmer.***

The sections for examination were selected from regions which were anticipated to provide potentially significant information e.g. the medial and lateral collar region, medial and lateral borders of the stem (proximal and distal), regions exhibiting cement interdigitation with bone, acetabular cup, areas showing defects, such as voids, folds and debris visible by eye or under 20x power with a binocular dissecting microscope.

The sections were cut from the specimens by hand with a jewelers saw. They were secured in a metallurgical mounting ring with Hysol epoxy cement and polished by a standard metallographic technique to a 0.03μm finish. After polishing the specimens were etched with nitric acid fumes for periods of from 2-5 min [14]. The metallographic specimens were then examined with reflected light by a Zeiss Universal Microscope using Nomarski differential interference - contrast optics.

Results

a) Deformation: Figures 1-3 illustrate examples of gross deformation of the bone cement. The spherical powder phase is highly deformed and the cross sections are no longer circular but tend to be elliptical with major: minor axis ratios ranging up to 5:1. The deformed regions also exhibit a high density of deformation strain lines indicating regions of concentrated flow in both the powder and matrix phases. The regions of gross deformation were located

i) at the bone-PMMA interface, beneath the collar of the femoral component, in the medial, mediolateral region, Fig. 4(a),

ii) regions of PMMA which had penetrated into and were surrounded by the bone bed, Fig. 4(b),

iii) occasionally at the prosthesis-PMMA interface, the medial border, at the junction between collar and stem, Fig. 4(a).

*We wish to greatfully acknowledge the three specimens included in this series received from Dr. C.O. Townley (Port Huron, Michigan), the remaining specimens were received from Drs. C. Herndon and V. Goldberg of the Department of Orthopaedics, CWRU.

**Howmedica Inc., Medical Division, Rutherford, N.J.
***Zimmer USA, Warsaw, Indiana

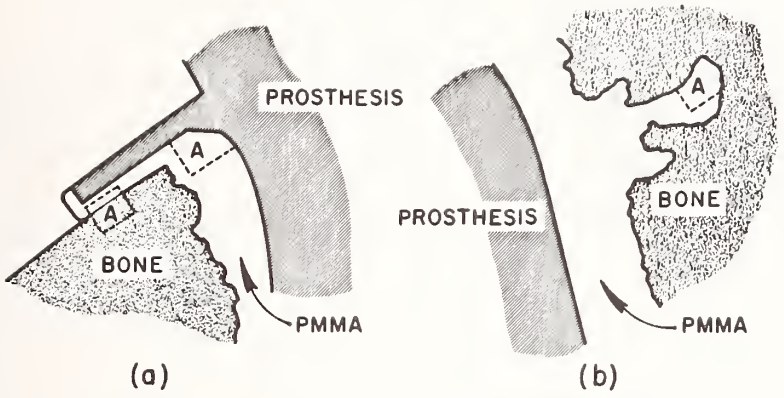

Figure 4. Areas of observed gross deformation, A
a) collar region
b) interdigitating cement-bone

Figure 5 illustrates an example of deformation strain lines. These regions of plastic deformation may also be associated with cracks, Fig. 6. The regions where deformation strain lines are frequently observed are the same as those described in i) and ii) for gross plastic deformation. They are, however, quite frequently observed in regions which exhibit no gross deformation.

Figures 7-9 illustrate examples of crack propagation in the bone cement. The cracks are most frequently associated with the intersection of the medial and lateral faces of the stem. The general appearance of the cracks, which are ascribed to failure of the bone cement - in vivo, is quite different to those produced in the cement during removal of the cement at surgical revision, Fig. 10. Cracks are also observed in bone cement which interdigitates with the bone bed.

b) Wear: Abrasive wear of the bone cement at the prosthesis interface, whenever present, is readily visible on sections. Figures 11 and 12 show the interface of the cement with the proximal medial surface of the femoral stem; the originally spherical powder phase exhibits flat abraded facets produced by the relative motion between cement and femoral stem. Figure 13 illustrates a typical example of the cement-prosthesis interface where no relative motion occurred.

c) Cement-Bone interface: Figures 14-16 illustrate the range of morphologies observed at the surface of the cement. The morphology ranges from a relatively smooth surface, no interdigitation with the bone bed where the spherical powder phase rarely protrudes above the surface (Fig. 15) to a highly porous surface with some spherical powder particles barely attached to the body of the cement by slender filaments of matrix phase.

Figures 17 and 18 show examples of the close adaptation of bone trabeculae to the cement surface. This adaptation may occur with viable bone

trabeculae either completely surrounded by cement (Fig. 17) or contiguous with a smooth surface of cement (Fig. 18).

d) Cement Morphology: Figure 19 (a) and (b) illustrate the structure of Simplex-P and Zimmer bone cement respectively; these sections were from cement mixed and polymerized in air in vitro at an ambient temperature of 23°C. The Zimmer cement contains non spherical particles of powder, typical of comminuted PMMA. Figures 20 and 21 illustrate examples of bone debris incorporated into the cement; the bone chips appear to be nonviable.

Discussion

Figures 1-3 clearly demonstrate that in vivo there are locations where the bone cement is subjected to a predominantly compressive stress and that the cement is capable of substantial plastic defromation. Presumably the plastic deformation occurs slowly and may be characterized as creep deformation. The creep rate of bone cement at 24°C and subjected to compressive stresses 62.0 N/mm^2 (9,000 psi) has been measured [8] and shown to be markedly increased by the plasticizing effect of water; Ringers solution was used to simulate the biological environment. The lower stress range for significant creep rates at 37°C in an aqueous environment has, to the best of our knowledge, not been determined. It is, therefore, not possible to estimate the probable stress to which the regions illustrated were subjected.

The observation of gross plastic deformation correlated with those of Willert et al. [13] who demonstrated with SEM, the presence of highly deformed spheres at the surface of retrieved cement. However, they speculated that the deformation occurred at the time of insertion, when the spherical particles were softened by swelling of the MMA monomer. We consider that this explanation is not consistent with the observations we have presented. At the time of insertion the matrix is still viscous and in order to produce the observed degree of deformation the matrix would be extruded from between the particles in order to produce sphere-sphere contacts. This is not observed, the matrix phase still separates the powder phase particles. In addition the presence of deformation strain lines in both phases strongly suggests that the deformation occurred in the fully polymerized state.

The deformation strain lines (Fig. 6) suggest that creep deformation of both phases may also occur under a predominantly shear stress state. These strain lines propogate through both the spheres and matrix indicating no major difference between the mechanical properties of either phase. This is not unexpected since the powder is produced by suspension polymerization rather than thermal polymerization under pressure, used in the mechanically stronger commercial PMMA (Lucite®). The deformation strain lines may provide a nucleus for the initiation of a crack (Fig. 6) however, with the data available we are not able to substantiate such a relationship.

The abrasion of the bone cement at the interface with a loose prosthesis

is of interest since the abraided debris presents a significant source for the very small particles of PMMA which can be observed in the tissues of the joint capsule [3]. Because the comminuted debris is restrained at the cement/prosthesis interface it can accelerate the abrasive wear process and induce highly non-uniform wear, with crater formations, which is observed at the cement-prosthesis interface, particularly in the proximal region near the collar.

The close adaptation of viable bone trabeculae to the bone cement has been unambiguously demonstrated at both smooth surfaces (Fig. 18) and interdigitating surfaces (Fig. 17). This is of considerable improtance in understanding the mechanical aspects of fixation. Charnley [15] had demonstrated that thermal necrosis occurred in the tissue adjacent to the polymerizing cement and that fibrous tissue was then formed at the interface. The data presented by our examination of retrieved cement, many months after surgery, show that either viable bone can be maintained at the initial interface or that stress transfer to the bone is sufficient to induce new bone formation which grows into the intersticies of the cement or up to a smooth surface. Growth up to a smooth surface strongly supports the later hypothesis, since it is unlikely that a smooth trabecular bone surface would exist at the reamed surface produced at surgery to receive the implant and cement.

Analysis of retrieved bone cement using standard reflected light metallographic techniques has provided a useful method for exploring the mechanical behavior of PMMA bone cement, which has been subjected to the stress states experienced in humans with partial or total joint replacements. The technique has demonstrated that considerable plastic deformation, by creep, can occur in the cement under certain physiological loading conditions. These data suggest that these stresses may cause sufficient plastic deformation to the cement so that the stem becomes loose within the cement bed; a situation frequently confirmed by clinical observation at revision of the prosthesis. The direct interaction of plastically deforming cement with the bone bed is also of significance in that it represents another contribution to the factors influencing the bone remodeling and/or resorbtion.

The authors wish to acknowledge that this investigation was carried out as part of The Implant Retrieval and Analysis Program of the Department of Pathology, CWRU.

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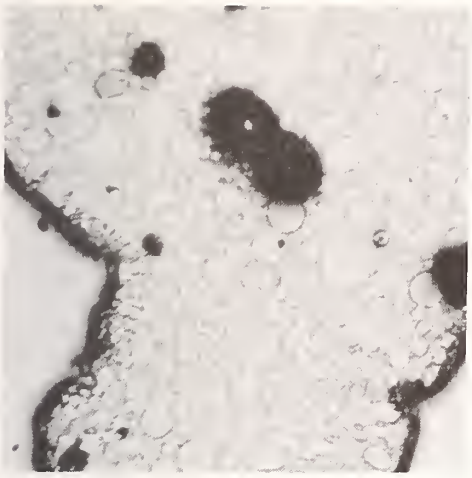
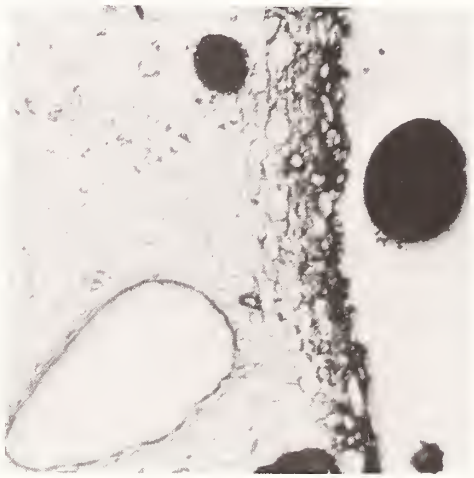


Figure 1, Cement-Bone Interface: Sample D-medial collar region x 75

Figure 2, Cement-Bone Interface: Sample F - proximal medial region x 75



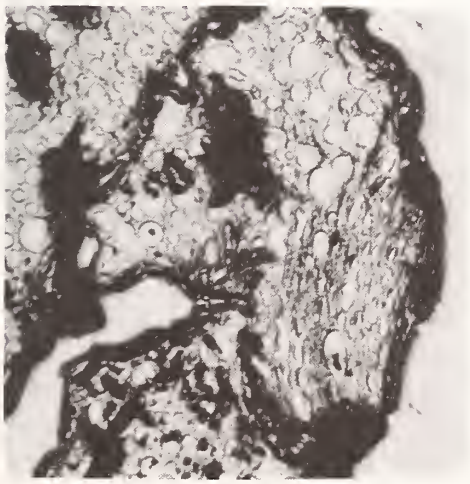


Figure 3, Cement-Bone Interface: Sample E - superior lateral region of acetabular cup x 75

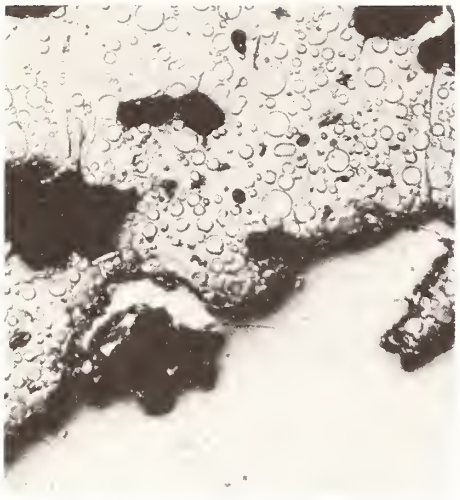
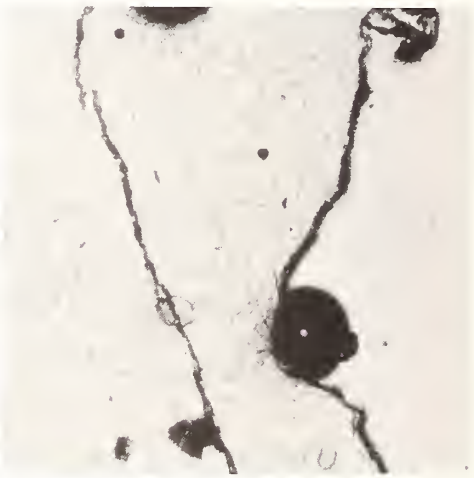


Figure 5, Cement-Bone Interface: Sample F - proximal medial region x 75

Figure 6, Cement-Bone Interface: Sample D - medial collar region x 75



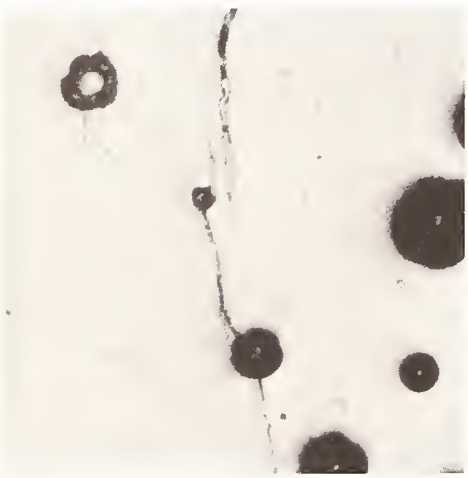


Figure 7, Cement-Prosthesis Interface: proximal stem region, transverse section.

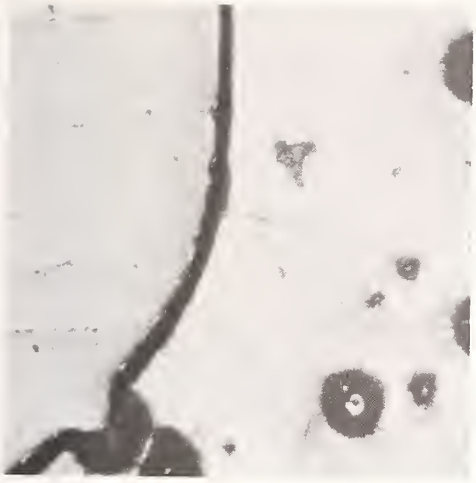
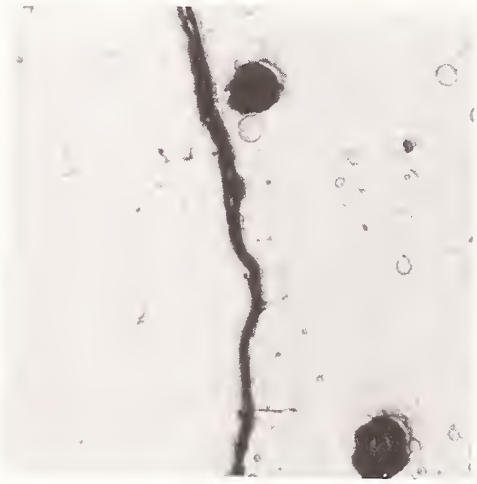


Figure 8, Cement-Prosthesis Interface: Sample D - proximal medial stem region x 75

Figure 9, Cement-Prosthesis Interface: Sample J - proximal medial stem region x 75



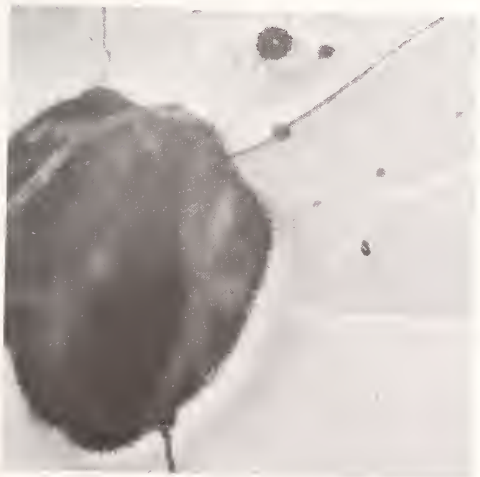


Figure 10, Cement-Prosthesis Interface: Sample C - cracks produced during removal x 75

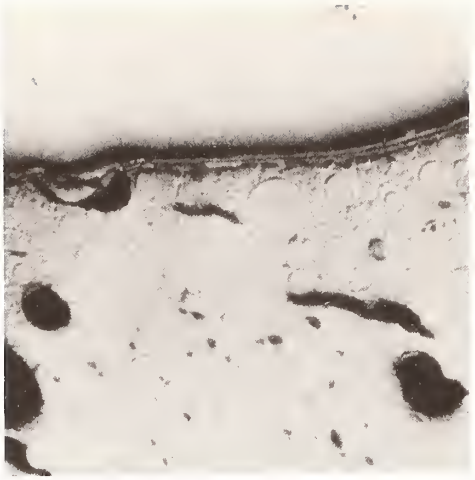


Figure 11, Cement-Prosthesis Interface: Sample B - wear in medial collar region x 100

Figure 12, Cement-Prosthesis Interface: Sample J - wear and cracks proximal medial stem region x 75

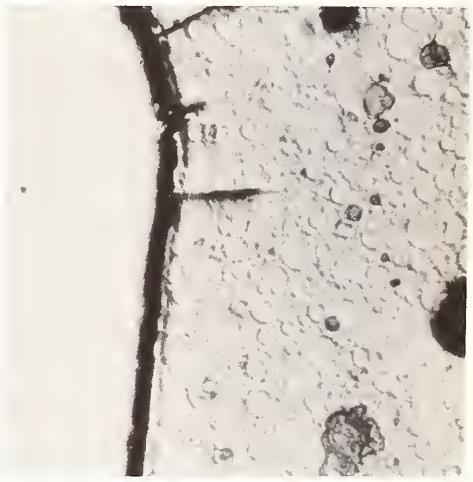


Figure 13, Cement-Prosthesis Interface: Sample A - "normal" interface x 75

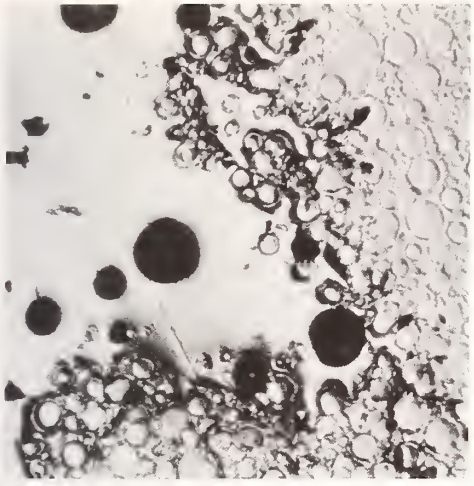
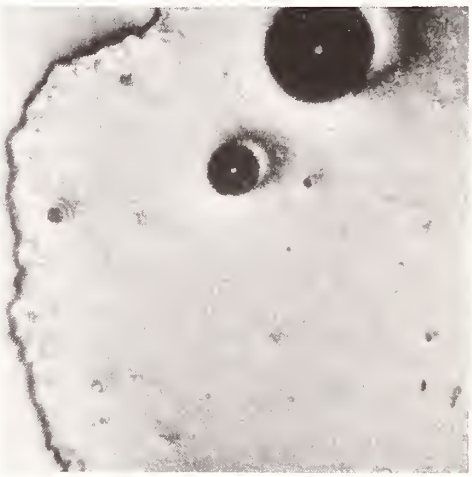


Figure 14, Cement-Bone Interface: Sample H - distal medial region x 75

Figure 15, Cement-Bone Interface: Sample D - proximal region x 75



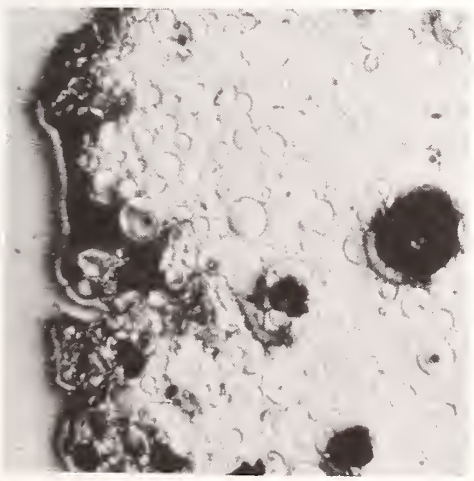


Figure 16, Cement-Bone Interface: Sample H - central lateral region x 75

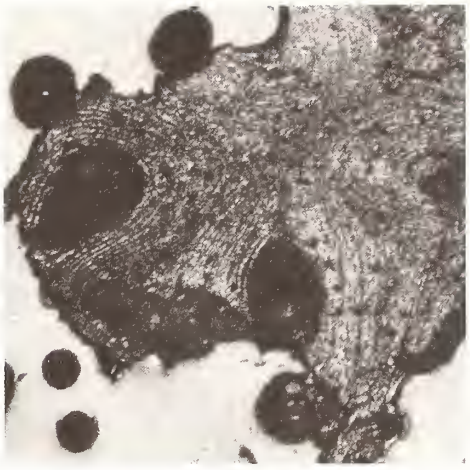


Figure 17, Cement-Bone Interface: Sample D - central lateral region x 75

Figure 18, Cement-Bone Interface: Sample F - proximal lateral region adaptation to trabeculae x 75

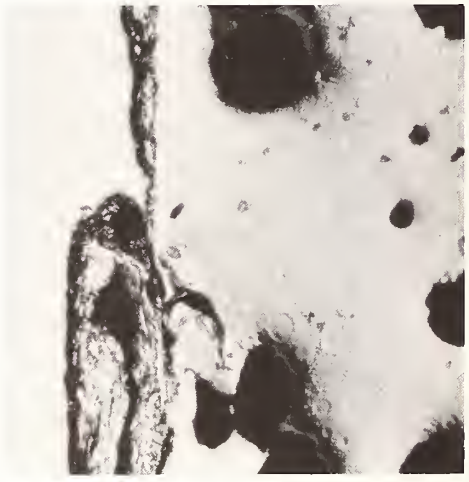
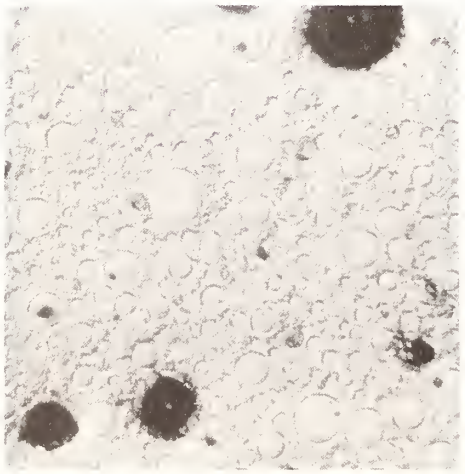


Figure 19, Bone Cement: (a) Simplex-P <u>in vitro</u> polymerized x 75



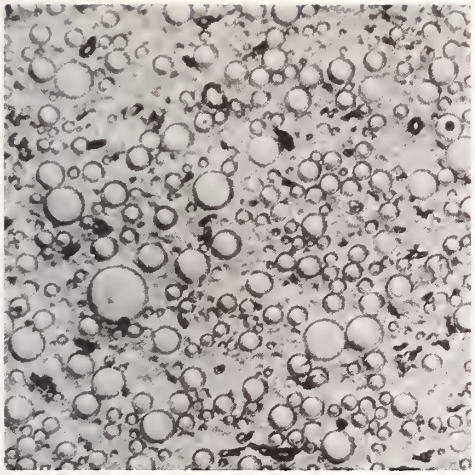
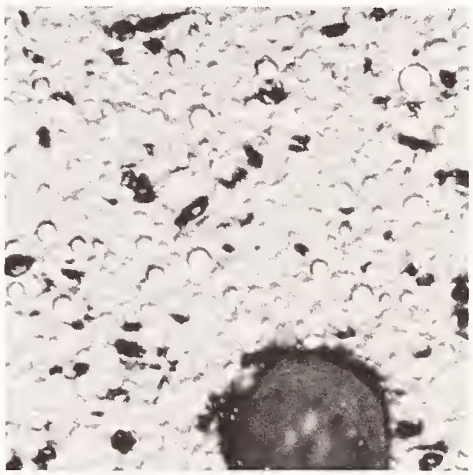


Figure 19, Bone Cement: (b) Zimmer *in vitro* polymerized x 75

Figure 20, Bone Cement: Sample F - bone debris x 75



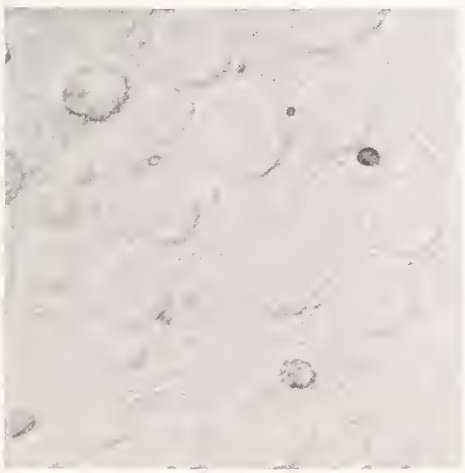


Figure 21, Bone Cement: Sample J - bone debris x 275

Discussion

Question (Anthony K. Hedley, University of California at Los Angeles): I would like to address the comments about the intimate contact between cement and bone. Have you any histology to show that there are no cellular elements at the interface? Where did the cement come from with respect to the prosthesis and what was the implantation period? What was the mode of failure which lead to the retrieval? What was the size of the trabeculae present? How do you know the bone was viable? We believe that there is always a cellular response at the interface which may only be a single cell thick. Under conditions of prosthetic instability metaplasia and bone resorption may occur with formation of the fibrous capsule. A bone to be viable within acrylic nutrients must reach the deepest parts. If the trabeculae are small (less than 100μ), the blood supply is peripheral so capillaries must exist at the interface. With larger trabeculae (more than 100μ), the blood vessels are contained inside the trabeculum, much like an haversian canal, so a more intimate contact between bone and cement is feasible. Thus, there are several factors involved in attaining close contact between bone and cement and I would welcome your observations with respect to these.

Answer: In the series examined so far and reported in the paper, we have no histopathology data because the retrieval protocol did not include formalin fixation. With the resolution available on specimens prepared for reflected light microscopy it is not possible to resolve details within less than $\sim$ 10μ of the interface. It is possible in principle therefore to have a single cell layer between the cement and bone. We have observed "viable" bone trabeculae in specimens retrieved after 4 years and 4 years 6 months. The samples originated from the central and proximal, lateral regions. The size of trabeculae ranged from 600 to 300 nm and contained more than one haversian system. The failure mode in one case was loosening in the cement and the other was an autopsy case. The only case where the bone was unambiguously surrounded by cement the haversian structure is readily observed (fig. 17). However, in other cases trabeculae were observed at or near a surface where indeed one might anticipate that the nutrient artery supply is superficial. Because of the retrieval protocol we do not have standard histopathology evidence of viability; future retrieval will include recovery in formalin.

We have data from a series of implant experiments in canine femora which demonstrates that a rough or textured surface, such as occurs at an interdigitated PMMA surface, does allow direct apposition between a foreign implant surface and bone, with no cellular or fibrous capsule interposed. It thus appears that the stress pattern at an interface can markedly influence the nature and morphology of the cellular response.

Question (Darrel W. Haynes, University of Arkansas Medical Sciences): Can you be sure, using reflected light microscopy or transmitted light, that the osteocytes are viable and are not just encapsulated or entombed thus not enabling cell lysis to occur? Could the differences in sphere sizes be due to the possible differing polymerization rates due to the warm bone and a cooler metal stem? Charnley has stated that thin cement fails. Did you look at thin cement? What in your opinion is the minimum and optimum cement thickness?

Answer: With the data presently available, we cannot categorically establish that the bone is viable. However, in regions where we have observed nonviable bone debris, there is a significant loss of lamellar detail.

The spheres are prepolymerized PMMA, it is only the matrix which is polymerized in situ. There exists of course a range of diameters for the spherical powder particles in the unmixed state.

We do not have sufficient data to answer the question of optimal cement thickness. We would anticipate that it would vary with position along the stem, since the interface stresses vary with location.

Question (Vimal Desai, Johns Hopkins University): In your study, did you take any bone cement samples from the lateral side of an artificial hip which experiences lesser load as compared to the medial side? Did the samples from the lateral side show a lesser degree of gross deformation?

Answer: We have examined samples from all positions, proximal, distal, lateral and medical, etc. As indicated in figure 4, samples where gross deformation was observed originated from the proximal-medial aspect.

Question (D. C. Richardson, Food and Drug Administration): In the series of retrievals you have had the opportunity to examine, a) were clinical parameters such as the time delay between mixing and the means of cement insertion (finger pressure, syringe injection) retrieved as well, and if so, b) do your optical microscopic observations confirm published reports that good initial filling of the extremely reamed-out medullary cavity with low-viscosity "dough" at moderate-to-high injection pressures insures better interdigitation into bone than the older Charnley-recommended technique?

Answer: The study was retrospective and so no data was available regarding the elapsed time between mixing and insertion. In all samples retrieved so far the cement was manually inserted. However, in all cases the degree of interdigitation of the PMMA with bone varied widely in any single case. Typically, all retrieved samples had regions of good interdigitation as well as areas which were completely smooth.

Question (Pei Sung, Food and Drug Administration): The failure of bone cement caused either by brittle fracture or plastic deformation is probably very sensitive to the polymerization induced stress (internal microstress), shrinkage and porosity generated from the mixing procedures. I wonder is there any nontoxic, ionic polymerized, zero shrinkage (during curing) bone cement available? Is anyone performing research in this area yet?

Answer (D. F. Gibbons): To the best of my knowledge no cement, such as you describe, exists at the present time. I believe that a few groups are attempting to develop a more effective "cement", including Dr. D. C. Smith, who played an important role in the early development of the PMMA cement with Dr. Charnley.

Question (I. C. Clarke, University of Southern California, Los Angeles): You referred to viable bone in DIRECT contact with cement. Other detailed histological studies (e.g. Hedley, HIP Society, San Francisco, 1979) have described live bone always separated by a fibrous membrane from the acrylic cement. In other words, if the bone is dead, there can be no reaction to the cement; if it is viable, a membrane forms. Your data appears to contradict this argument and raises questions about when is bone dead and how careful was the preparation protocol? (i.e., preservation of soft tissue interfaces?)

Answer: As I indicated in my response to Dr. Hedley, the data on retrieved bone cement cannot rule out the presence of a single cell layer; certainly no fibrous capsule is observable with the resolution available. However, the surface roughness or "texture" caused by interdigitation with bone, is known in other systems, to allow direct apposition between a foreign surface and viable bone.

PROSTHETIC HEART VALVES: WHAT HAVE WE LEARNED FROM OUR CLINICAL PATHOLOGIC EXPERIENCE

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Some of our clinical and pathologic observations, and in vitro hemodynamic experiences with the Björk-Shiley, Starr-Edwards (ball valves), Smeloff-Cutter, St. Jude, Kay-Shiley and tissue bio-prostheses are discussed. It is quite clear that at present there is no ideal prosthetic heart valve. The major problems that affect the mechanical valves are thromboembolism and tissue overgrowth, while the porcine valves are affected by structural degradation and poor hemodynamic performance in the small sizes.

The observed problems of thrombus formation, tissue overgrowth, red-cell destruction and damage to the endothelial lining of vessel walls adjacent to the valve prosthesis are directly related to the hemodynamics of the respective prostheses. It is our experience that all prosthetic heart valves that are presently commercially available are liable to thrombus formation and tissue overgrowth. Therefore, correlative studies such as described in this article should be conducted with all heart valve prostheses. Detailed pathologic studies on approximately 150 to 200 recovered prosthetic heart valves of different types are presently in progress.

1. Introduction

Heart valve prostheses have been used successfully since 1960. As stated by Roberts [1] the decade of 1960 will probably be remembered most

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[1] Figures in brackets indicate the literature references at the end of this paper.

in the annals of cardiology as the decade during which cardiac-valve replacement became a successful reality. Of the nearly 50 or more different cardiac valves introduced over the past 20 years, many have been discarded due to their lack of success, and of those remaining several modifications have been made or are being made. In addition, the next few years will see the introduction of new designs of cardiac valves. The most commonly used basic types of prosthetic valves at present are: (a) the caged ball, (b) tilting or pivoting disc, (c) tissue bioprostheses, and (d) caged-disc valves. At present over 90,000 prosthetic valves of different designs are used annually throughout the world.

Even after 20 years of clinical and pathologic experience the problems associated with heart valve prostheses have not been totally eliminated. The most serious problems associated with them are: (a) thrombus formation, (b) red-cell destruction, (c) damage to the endothelial lining of the vessel wall adjacent to the valve, (d) excessive tissue overgrowth, (e) valve failure due to material fatigue and/or chemical change, (f) tearing of sewing sutures [1-10]. The current status of prosthetic heart valves has been recently reviewed in some excellent articles and books [1,5,6,7]. Problems (a)-(d) are directly related to the hemodynamics associated with the various heart valves. The other problems are indirectly related to the hemodynamics.

In vitro physical and hemodynamic characteristics of prosthetic heart valves strongly influence their initial use. They are eventually, however, judged clinically by the frequency and severity of the complications they engender. Ideally, a prosthetic cardiac valve should not be degraded by its biological environment nor cause any adverse effects on surrounding tissues or blood.

(1) It should ideally have a durability equaling or exceeding the normal life expectancy of the patient.
(2) The valve design should be such that it produces minimal restriction (and therefore pressure drop) to forward flow for the tissue annulus area that it occupies.
(3) Its size and shape should be such that it does not interfere with the normal function of the surrounding tissues.
(4) It should be made as radiographically visible as possible without significantly compromising its function or durability, or without making it thrombogenic.
(5) It should not be so loud that it distracts the patient; yet ideally its opening and closing sounds should be distinctive enough to allow detection of significant alterations.
(6) The physical and hemodynamic characteristics of the prosthesis should be such that it produces minimal damage to red blood cells, platelets and the surrounding tissues. It should not create large regions of flow stagnation or separation which cause thrombus formation and/or excess tissue overgrowth on the valve super-structure.

Hellums and his co-workers [11,12] and Hung et al. [13] have studied the effects of shear stress on blood cell damage, while Fry [14,15] has studied the effects of shear stress on the vascular endothelium. Damage to platelets has been produced in a cylindrical viscometer at shear stresses as low as 100-500 dynes/cm^2 with ~100 second exposure times. Damage to

normal red blood cells can occur at 1500 dynes/cm^2, yet sickle cells can be lysed at shear stresses of 500 dynes/cm^2. Fry has conducted two studies of the effects of wall shear stresses on canine aortic walls with variable exposure time. He found that endothelial cells on the vessel wall could be damaged at wall shear stresses of about 400 dynes/cm^2 and could be eroded off the vessel wall at shear stresses of about 950 dynes/cm^2. Blackshear [16,17] and Mohandas, et al. [18] have suggested that red blood cells which adhere to a damaged vessel wall or the super-structure of the valve (such as the cloth fabric) could be damaged at shear stresses as low as 10-100 dynes/cm^2.

2. Experimental Methodology

During the past 15-20 years one of the authors (E.C.H.) has had the opportunity to follow hundreds of valve patients and also to study approximately 100-200 recovered heart valve prostheses of different designs. In this paper we will discuss briefly some of these clinical and pathologic experiences with the Björk-Shiley, Starr-Edwards (ball valves), Kay-Shiley, Smeloff-Cutter, St. Jude and tissue bio-prostheses.

In addition, we have studied the in vitro hydrodynamics of these valves. Such studies included the measurements of pressure drop, velocity and shear stress, and the opening and closing motion of the valve. Velocity and shear stress measurements were made using laser-Doppler anemometry. Detailed descriptions of the experimental apparatus and techniques have been previously published [19-22]. We will also attempt to correlate the in vitro hydrodynamic results with some of the clinical pathologic observations made on recovered heart valve prostheses.

3. Results & Discussion

3.1. Björk-Shiley aortic prosthesis

The Björk-Shiley tilting disc aortic prosthesis has been in clinical use since January 1969. Approximately 95,000 of the standard (flat disc) prostheses have been implanted in the aortic position. The prosthesis has undergone various modifications in design and materials since its initial use. The original Björk-Shiley aortic valve had a Delrin disc. The Delrin disc, however, caused auto-claving and handling problems during surgery. Therefore, since the spring of 1971 the disc has been made out of pyrolytic carbon manufactured by General Atomic Company, San Diego. Over the past few years it has been observed that thrombus formation on the aortic face of the disc could lead to impaired or abolished mobility of the tilting disc. Unfortunately, it was not possible to monitor the disc movement by radiographic techniques. In order to overcome this drawback valves manufactured after September 1975, have a radio opaque Tantalum hoop incorporated in the aortic well of the disc.

In our clinical use of the Björk-Shiley aortic prosthesis we have found that its major advantages are (1) low pressure drop, (2) low level of hemolysis, (3) low profile and (4) structural durability. The majority of patients achieve significant functional improvement after replacement of their aortic valves with this prosthesis.

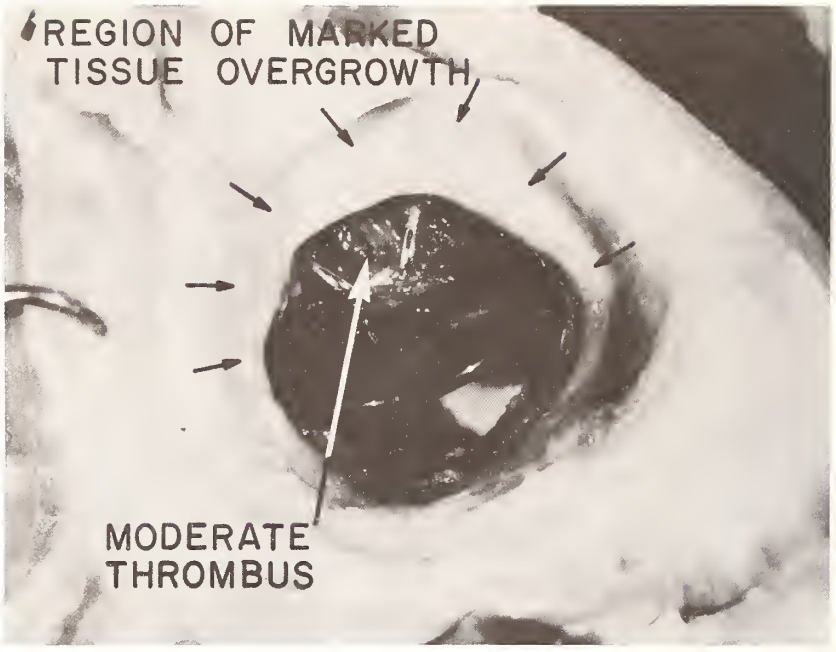

Figure 1. Recovered Björk-Shiley aortic valve. Moderate thrombus formation on aortic face of disc and marked tissue overgrowth along the perimeter of the valve adjacent to the minor outflow region.

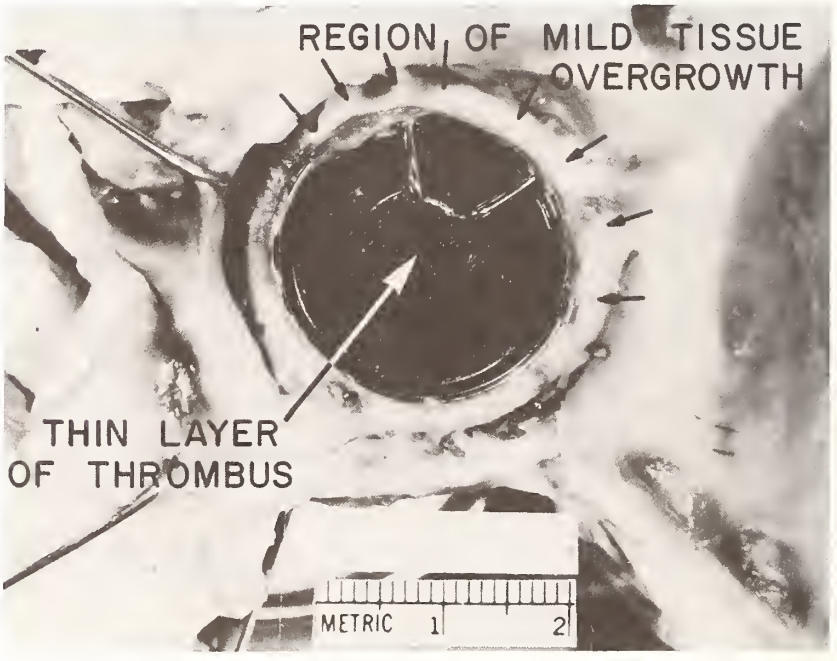

Figure 2. Recovered Björk-Shiley aortic valve. Thin layer of thrombus on aortic face of disc and mild tissue overgrowth along the perimeter of the valve adjacent to the minor outflow region.

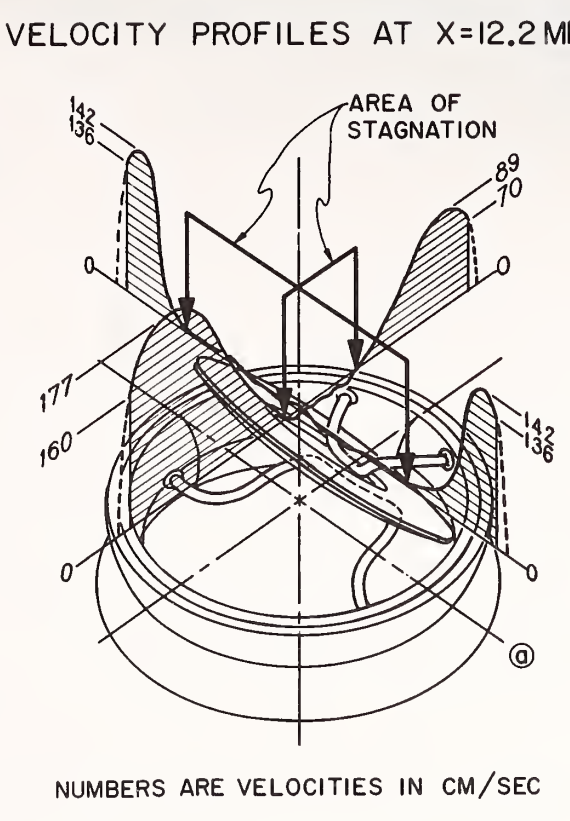

Figure 3. Velocity profiles immediately downstream of the fully open Björk-Shiley aortic valve at a steady flowrate of 25 ℓ/min.

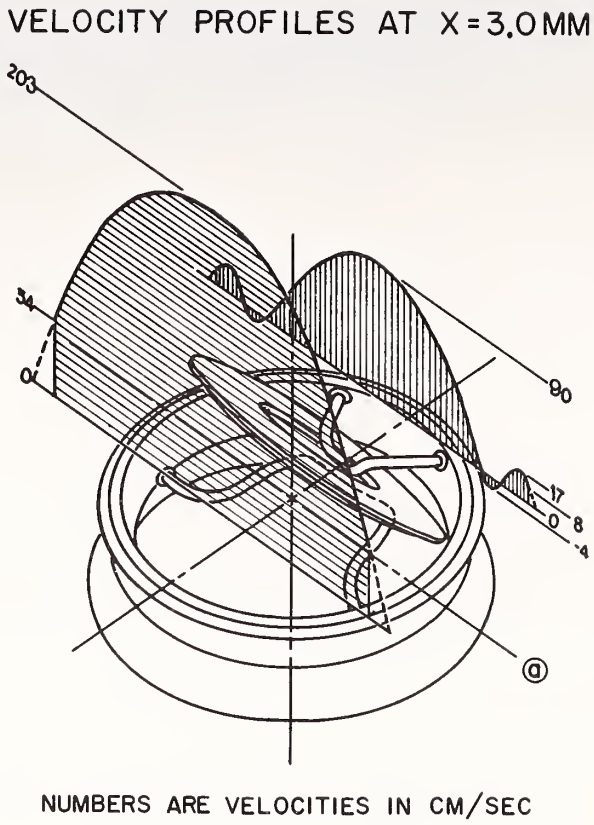

Figure 4. Velocity profiles in the major and minor outflow regions of the Björk-Shiley valve at a steady flowrate of 25 ℓ/min.

Unfortunatley, we have also observed thrombus formation and tissue overgrowth in ten aortic prostheses recovered six months or longer after implantation as shown in figures 1 and 2. Such thrombus formation and tissue overgrowth have also been observed by others [23-26].

These pathologic findings may be attributed to the flow characteristics of the prosthesis. The open disc of the valve separates the flow into two unequal regions. Varying degrees of thrombus formation were observed in the minor outflow region, including the depression in the aortic face of the disc and the metal strut bridging this area. Tissue overgrowth was noted along the perimeter of the prosthesis adjacent to the minor outflow region. That overgrowth further reduced the available cross section for flow in this already constrained area. In vitro measurements with a laser-Doppler anemometer identified a zone of stagnation about 20 mm wide near the aortic face of the disc (fig. 3) of a size #27 Björk-Shiley valve. The average velocities in the major and minor outflow regions were around 100 and 25 cm/sec, respectively, and the corresponding peak-shear stresses were approximately 700 and 150 dynes/cm^2 (fig. 4). There is reason, then, to attribute the thrombus formation and tissue overgrowth to the stagnation zone and the low shear in the minor outflow region [23].

Figure 5 shows the upstream aspect of a Björk-Shiley aortic valve. The valve had been implanted 23 months earlier. This case demonstrates accumulation of thrombus between the upstream hinge and the base ring of the prosthesis. A portion of the native aortic valve not removed at the time of surgery probably produced flow stagnation and encouraged thrombus formation. Figure 6 shows another consequence of undebrided tissue on a Björk-Shiley tilting disc aortic valve. In this case the tissue impeded the complete opening of the tilting disc.

In the hope of reducing the pathologic conditions of thrombus formation on the aortic face of the disc and tissue overgrowth along the sewing ring adjacent to minor outflow region, the new convexo-concave Björk-Shiley prosthesis was developed. In vitro velocity measurements made with a laser-Doppler anemometer in the immediate downstream vicinity of the convexo-concave Björk-Shiley aortic valve indicate that the design changes have decreased the size of the stagnation zone and have increased flow and shear in the minor outflow region. We conclude that the problems of thrombus formation and tissue overgrowth may be reduced in the new convexo-concave Björk-Shiley aortic valve.

3.2 Starr-Edwards ball valve prostheses

The Starr-Edwards 1260 valves are closed caged silastic ball valves. They are comprised of a polished Stellite alloy 21 cage with a combination of Teflon and polypropylene cloth sewing ring. The cloth on the sewing ring extends to the orifice, leaving no exposed metal on the in-flow face of the valve. The ball is made of silicone rubber and contains 2 percent-by-weight barium sulfate for radiopacity. The radiopacity aids visualization of the ball motion on cinefluoroscopy. The 1260 model was first made generally available in July 1969 as a modification of the model 1200 aortic prosthesis. Approximately 30,000 have been implanted in the aortic position. It has an excellent record of durability.

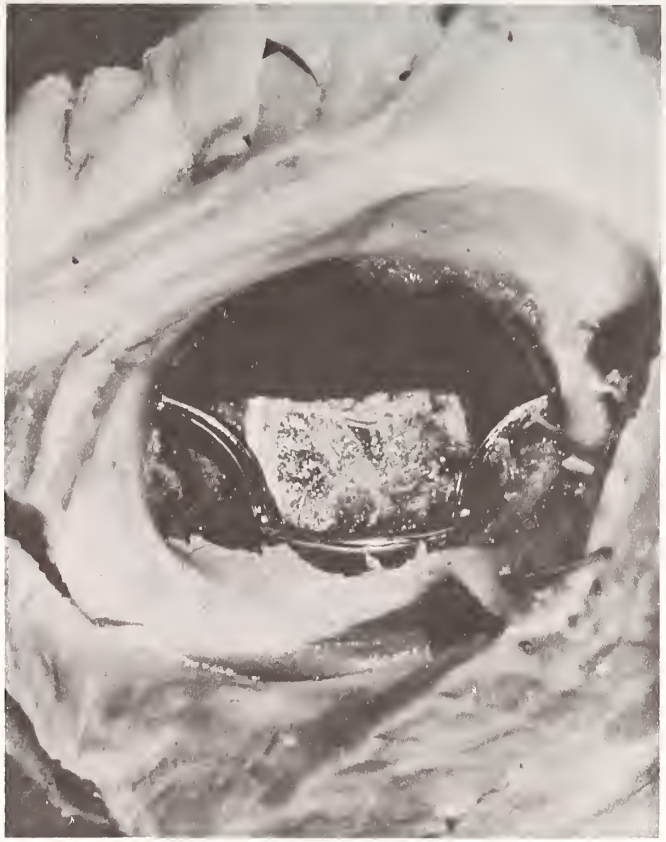

Figure 5. Upstream aspect of a Björk-Shiely aortic valve showing accumulation of thrombus between upstream hinge and the base ring of the valve.

Figure 6. Undebrided tissue preventing the complete opening of a Björk-Shiley aortic valve.

The Starr-Edwards Model 2320 closed caged ball valve prosthesis is comprised of a Stellite alloy 21 cage with completely cloth covered struts and a composite orifice consisting of metal and cloth to form the poppet seating surface. The metallic stops project through the knitted orifice at regular intervals. The cloth covering which is made of Teflon and polypropylene is intended to promote tissue invasion and encapsulation of the valve cage and its orifice. The ball is hollow and made of Stellite alloy 21. It has potentially greater resistance to biodegradation as compared with silicone rubber. This model has been on the market since 1968.

The Starr-Edwards 2400 closed caged ball valve is known as a composite track valve prosthesis. It is comprised of a partially cloth covered Stellite alloy 21 and a hollow poppet made of the same material. The cage legs are covered with a porous knit polypropylene cloth except for an exposed metal track on the inner aspect which protects the strut cloth and metal stops which protrude through the cloth at regular intervals and protect the orifice cloth from poppet impact. All other surfaces which do not come into contact with the poppet are completely cloth covered.

Examinations were made at the USC - Los Angeles County Medical Center of 15 Starr-Edwards aortic ball valve prostheses recovered during autopsy and/or surgery. Thrombus formation and tissue overgrowth were observed at various locations on the recovered as illustrated schematically by figure 7. Figures 8-11 show examples of some of the recovered ball valves. Varying amounts of thrombus formation were observed predominantly at the base of the struts and the apex of the cage, while varying degrees of tissue overgrowth were predominantly observed on the aortic side of the sewing ring and on the struts of the cloth covered valves. In some cases the thrombus had grown along the struts, probably starting either at the apex or the base of the struts. In addition, examination of the vessel walls immediately downstream of the valve sewing rings indicated varying degrees of endothelial damage and fibrous tissue proliferation in some of the specimens. Detailed pathologic studies on the recovered valves are in progress at the present time.

Clinical and pathologic studies on recovered Starr-Edwards aortic ball valves by other investigators have also identified: (a) thrombus formation on the apex of the cage, at the base of the three struts and occasionally along the struts, (b) tissue overgrowth on the aortic side of the sewing ring and on the struts of the cloth covered models, (c) endothelial damage and tissue proliferation of the proximal ascending aorta, and (d) increased hemolysis with the cloth covered strut models [1,3,4,27-31].

Clinical experience with the cloth covered Starr-Edwards aortic ball valves indicated an increase in hemolysis as opposed to the non-cloth covered valves. There was also excess tissue overgrowth along the cloth covered struts. This seriously affected the motion of the poppet (ball). Another frequent problem with the cloth covered valves was deterioration of the cloth on the struts (probably due to ball impact) as shown in figure 11. This figure shows a 2320 Starr-Edwards aortic prosthesis which had to be removed due to severe mechanical hemolytic anemia.

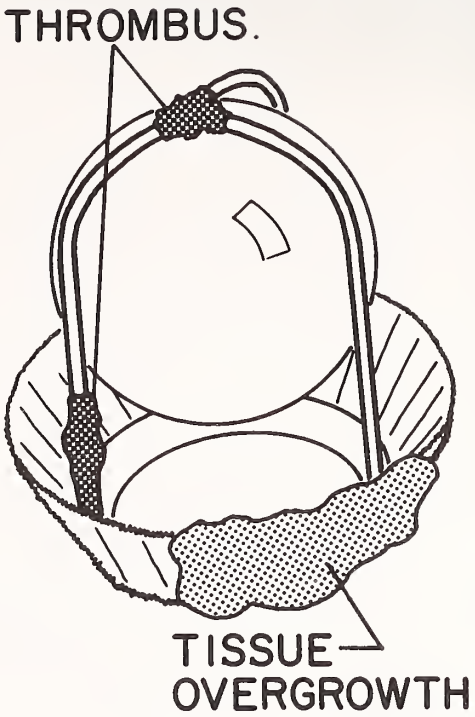

Figure 7. Schematic example pattern of thrombus formation and tissue overgrowth on Starr-Edwards (S-E) aortic ball valves.

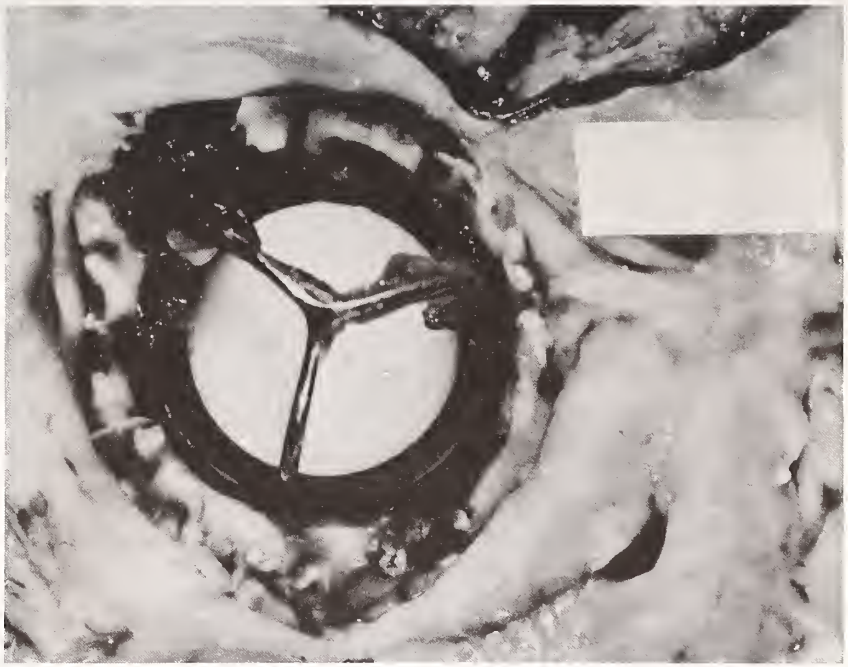

Figure 8. Recovered S-E aortic valve. Thrombus formation on apex of cage and at the base of the struts; fibrotic tissue overgrowth also on base of two struts.

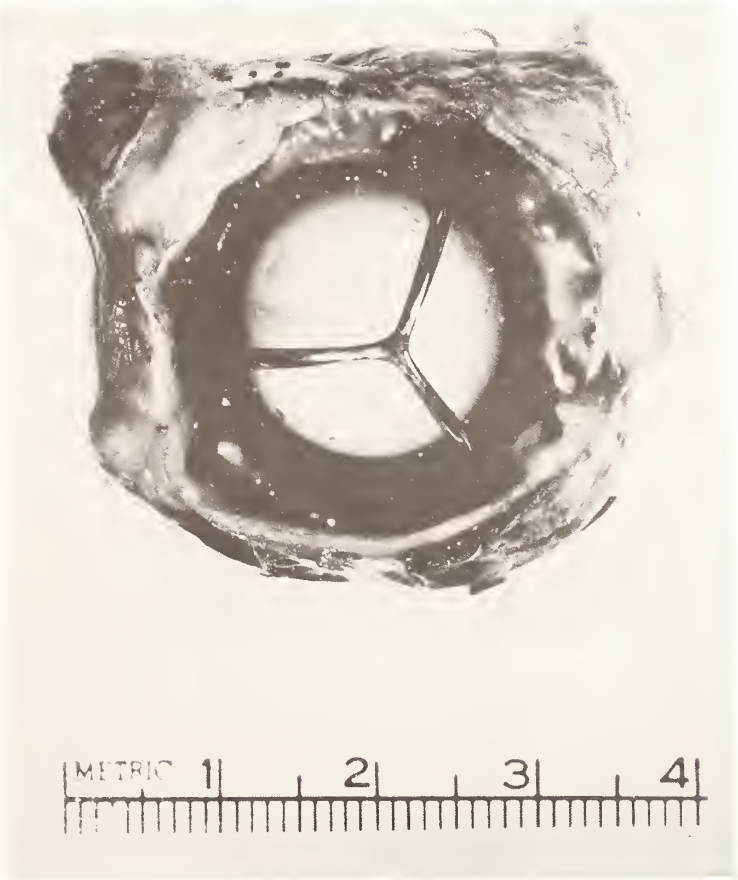

Figure 9. Recovered S-E 1260 aortic valve. Thrombus formation at the base of the three struts and tissue overgrowth on aortic side of sewing ring.

Figure 10. Recovered S-E 2320 aortic valve. Thrombus formation on apex of cage; tissue overgrowth on aortic side of sewing ring and along the base of the struts.

Figure 11. Recovered S-E 2320 aortic valve shows destruction of cloth covering on the metal struts. Valve caused severe hemolysis.

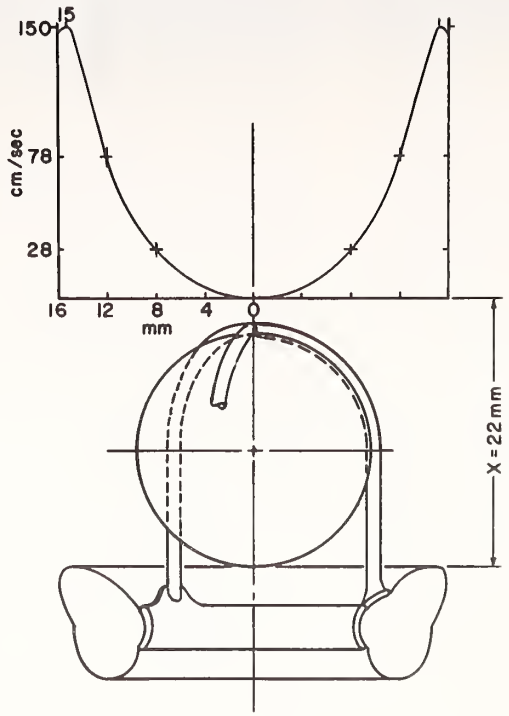

Figure 12. Schematic of velocity profiles immediately downstream of S-E 1260-12A valve at a steady flow rate of 25 ℓ/min.

Our in vitro studies on a 1260-12A valve (sewing ring: 27 mm), indicate that the Starr-Edwards ball valves have major fluid dynamic drawbacks [32] such as: (a) relatively large pressure drop (17.3 to 31.0 mm Hg at a flow rate of 417 cm^3/sec), (b) hydrodynamically unstable poppet, (c) regions of flow separation at the base of each of the three struts, (d) region of flow stagnation at the apex of the cage (∿7 to 15 mm in diameter) (see fig. 12), (e) large wall-shear stresses (∿500-2000 dynes/cm^2) and bulk turbulent shear stresses (on the order of 100-5000 dynes/cm^2) in the immediate downstream vicinity of the valve, and (f) large shear stresses adjacent to the poppet surface and struts (on the order of 10^2 - 10^3 dynes/cm^2).

The observed stagnation zone could encourage thrombus formation on the apex of the cage, while the observed regions of flow separation could lead to thrombus formation and tissue overgrowth at the base and upwards along the struts. The observed wall shear could lead to damage of endothelial tissue in the proximal ascending aorta, to hemolysis, and to thrombus formation. In addition, the elevated shears adjacent to the struts and the surface of the poppet could lead to increased hemolysis with those Starr-Edwards ball valves having cloth covered struts.

3.3. Smeloff-Cutter ball valve

The Smeloff-Cutter prosthesis is a double-cage full orifice ball valve. It consists of a double open-ended cage which is machined as one unit from commercially pure titanium and a poppet made from solid silicone rubber. The suture ring is made of non-reactive Teflon and loops of heavy Dacron suture embedded inside the metal ring, with multiple knots for maximum security. This valve has been on the market since 1966 and has a proven record of durability. Approximately 20,000 valves have been implanted, mostly in the aortic position. The valve is presently being manufactured by Sutter-Biomedical, Inc. (San Diego, CA).

Our clinical experience with this valve has been very satisfactory [33]. Of a total of 46 patients followed over a period of 8 years, two patients had pulmonary embolism and only one had a case of bland systemic embolism. Fifteen of sixteen patients had mild hemolysis as evidenced by increased serum lactic dehydrogenase or decreased haptoglogin or presence of urinary hemosiderin. No ball variance or other types of material failure were detected in eight valves that were recovered at autopsy. Most of the recovered Smeloff-Cutter aortic valves showed no regions of thrombus formation and/or tissue overgrowth on the valve superstructure. A few (2 or 3) of the recovered valves showed small amounts of thrombus formation at the base of the aortic side of the struts as shown by figure 13. In addition, examination of the vessel walls immediately downstream of the valve sewing rings indicated varying degrees of endothelial damage and fibrous tissue proliferation in some of the specimens.

Our in vitro flow studies on a A5 Smeloff-Cutter valve (sewing ring: 26 mm) indicated that this peripheral flow valve creates relatively high wall shear stresses (∿ 1670 dynes/cm^2). As shown in figure 14 the velocities near the apex of the cage were negative and on the order of -10 to -20 cm/s. This may produce a mild "washing" effect and tend to prevent material adherin

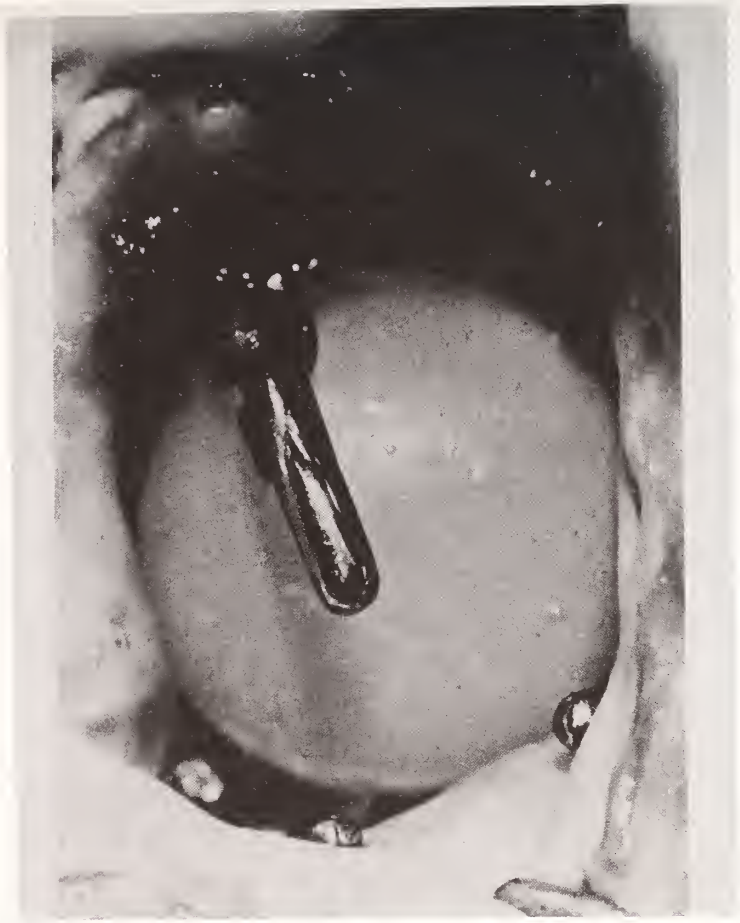

Figure 13. Recovered Smeloff-Cutter ball valve. Thrombus formation at the base of aortic side of the struts.

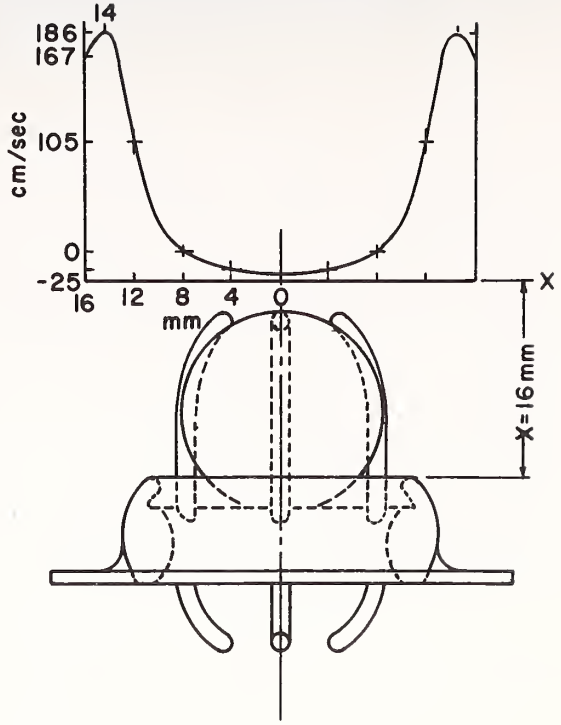

Figure 14. Velocity profiles immediately downstream of a Smeloff-Cutter A5 valve at a steady flow rate of 25 ℓ/min.

to the apex of the cage. A region of flow separation was observed near the base of the aortic side of the struts. Such a region of flow separation could lead to thrombus formation at the base of the aortic side of the struts as shown in figure 13.

3.4. St. Jude bi-leaflet valve

Since July 1976, St. Jude Medical Inc. has been testing a new bi-leaflet prosthetic valve made of pyrolytic carbon. At present this valve is undergoing clinical testing and evaluation at selected medical centers throughout the world. As of April 1980, approximately 3000 implants have been made in the aortic, mitral and/or tricuspid positions.

Velocity measurements [34] made in the immediate downstream vicinity of a #27 St. Jude valve show that the flow field that emerges from the valve is centralized (see fig. 15). The velocity measurements also indicated that there was a region of flow separation adjacent to the vessel wall and immediately downstream from the sewing ring as can be seen in figure 16. Such a region of flow separation could lead to tissue overgrowth along the aortic side of the sewing ring. The wall shear stress (500 dynes/cm^2) and pressure drops across the St. Jude valve were lower than other valves tested.

Our clinical experience with the St. Jude valve indicates that post-operatively this valve creates relatively low pressure drops and the patients seem to achieve significant functional improvement after surgery. The mechanical durability of the St. Jude valve is not yet proven. One of the major clinical disadvantages of this valve is that the motion of the valve leaflets cannot be seen properly in cine-fluoroscopy. If viewed in the same projection during fluoroscopy the St. Jude valve is not properly visible until the leaflets are in the fully open position as shown in figure 16.

3.5. Tissue bio-prostheses

Tissue bioprostheses have been in clinical use since about 1968. However, it is only during the past five to seven years have they gained widespread use throughout the world. Their main advantage compared to the rigid prosthetic heart valves is that they have a lower incidence of thromboembolic complications [6,35].

At the present time the Hancock, Carpentier-Edwards and Angell-Shiley porcine valves, and the Ionescu-Shiley calf pericardial valve are the most widely used tissue heart valve prostheses. As of January 1980 approximately 50,000 Hancock valves and 25,000 Carpentier-Edwards valves had been implanted throughtout the world. Numbers for the other two valves are not available.

Our clinical experience with the tissue valves is that they have a lower incidence of thromboembolic complications as compared to mechanical prostheses. Of a group of 34 recipients of single Hancock mitral valves the incidence of atrial thromboembolic events was 7.0/1000 patient months. Death due to thromboembolism occurred in one patient. Considering the multiple factors involved in production of thrombi, it is unlikely that the

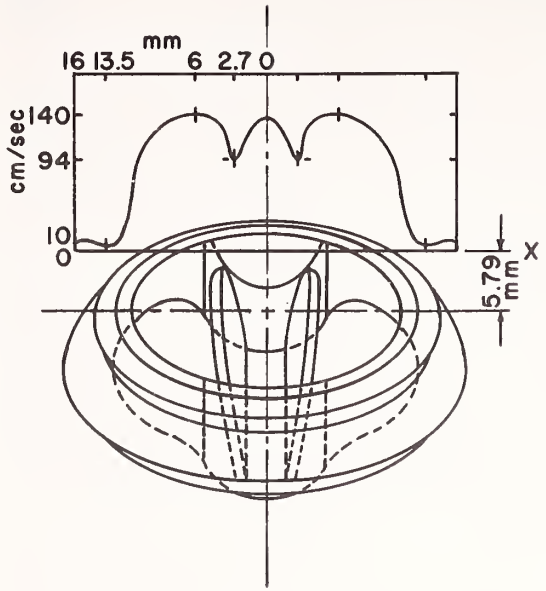

Figure 15. Velocity profiles immediately downstream of a #27 St. Jude aortic valve at a steady flow rate of 25 ℓ/min.

Figure 16. The fully open discs of the St. Jude valve as seen by cine-fluorscopy.

placement of any prosthetic valve (even tissue valves), especially in the mitral position, will allow a patient to be totally free of the complications of thromboembolism.

The tissue bio-prostheses in general do unfortunately have the following clinical disadvantages: (a) relatively large pressure drops compared to some of the rigid prostheses, especially in the smaller sizes, (b) jet-like flow through the valve leaflets, (c) poor opening and closing characteristics, (d) material fatigue or wear of the valve leaflets, and (e) valve leaflets are subject to changes that affect the natural valves, namely, lipid deposition and calcification. Figures 17-20 show examples of recovered porcine tissue valves. Figures 17 and 18 show a Hancock porcine aortic prosthesis (sewing ring: 24 mm) which had been implanted approximately 6 months earlier. Figure 18 is the downstream aspect of the prosthesis trans-illuminated by back lighting. The valve demonstrates heavy calcification. There was near complete immobilization of two of the cusps. The valve has a 79 mm Hg pressure drop at a steady flow rate of 20 ℓ/min. Figures 19 and 20 show a Hancock porcine mitral (27 mm) and an aortic (19 mm) valve which had been implanted approximately 2 years ago and were recovered during surgery. As shown in figure 19 the mitral valve has large tear in one of the leaflets. There was also calcification and prolapse of the leaflets. The aortic porcine valve did not exhibit any obvious stiffening of the valve leaflets. It, however, exhibited a pressure drop of about 60 mm Hg at steady flow rate of 10 ℓ/min. During cardiac catheterization a mean systolic pressure drop of 55 mm Hg was observed across this valve. The foregoing example illustrates quite clearly the fact, that in the smaller sizes the porcine tissue valves are indeed stenotic. Figure 20 illustrates the phenomena of "creep" in the valve stents. The above clinical pathologic problems have also been observed by other investigators [8,9,36].

Even though the above examples discussed pertian to the Hancock prosthesis it is felt similar problems will be observed with the other types of bioprostheses especially porcine valves. Detailed pathologic studies on the recovered bioprostheses are presently in progress. Our experience indicates that of the tissue valves in current clinical use the Ionescu-Shiley pericardial valves is hemodynamically the best.

3.6. Kay-Shiley disc valve

The Kay-Shiley prosthesis has been in clinical use since 1967. It has been used exclusively in the mitral and tricuspid positions. It is a low profile valve. It has a Delrin disc poppet, bare Stellite 21 struts and a Teflon cloth sewing ring.

Our clinical experience with this valve stems from the study of 82 Kay-Shiley mitral valve recipients [37]. Of a group of 63 patients followed in the clinic the incidence of arterial thromboembolic events was 10.3/1000 patient months. Death due to thromboebolism occurred in seven of the 63 patients. Figures 21 and 22 show examples of recovered Kay-Shiley valves. Of the 20 Kay-Shiley valves examined at autopsy eleven had thrombus formation and/or tissue overgrowth on the valve superstructure. The thrombus formation mainly occurred at the base of the valve struts as shown in figure 21. Tissue overgrowth occurred along the ventricular side of the sewing ring. The thrombus formation and tissue overgrowth in some instances prevented the disc from seating properly and thereby causing the

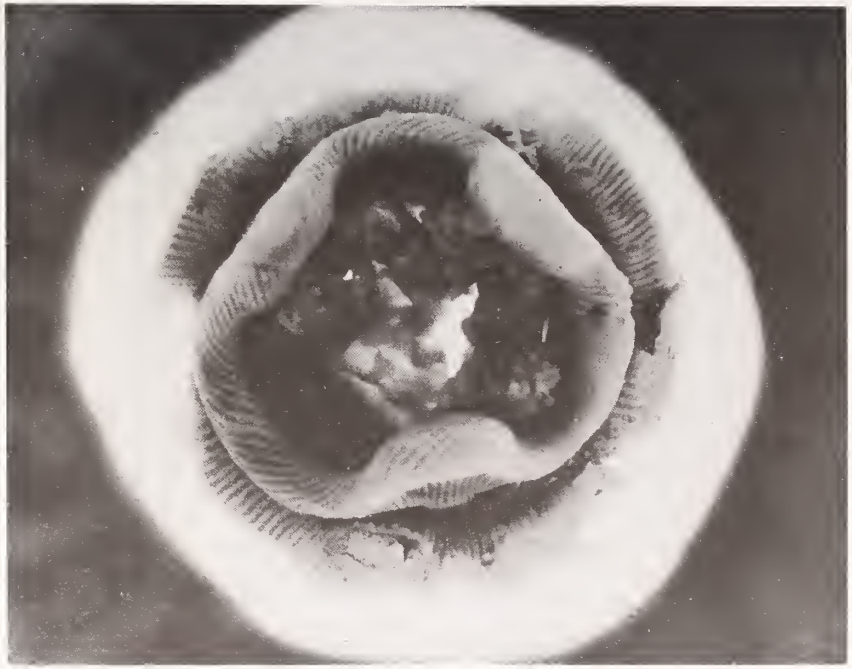

Figure 17 & 18. Recovered Hancock porcine aortic prosthesis. Downstream aspect of valve is shown demonstrating severe calcification of the leaflets. Figure 18 shows the valve transilluminated by backlighting.

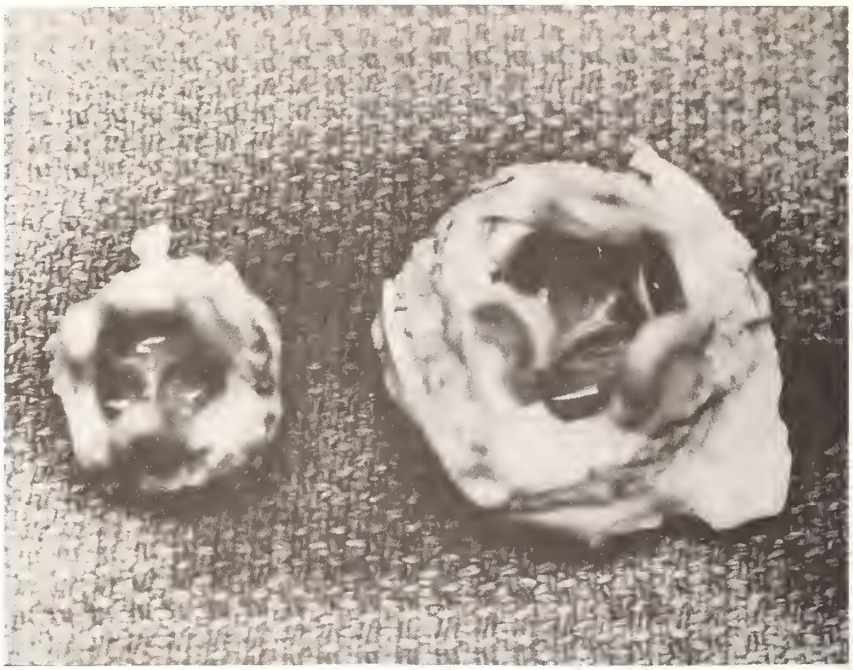

Figure 19. Recovered Hancock porcine aortic (left) and mitral (right) valves. The mitral valve has large tear in one of the leaflets. Calcification was also observed.

Figure 20. Same two recovered valves. This figure shows the phenomena of "creep" (drooping inwards) of the stents of the mitral valve.

Figure 21. Recovered Kay-Shiley mitral valve. Thrombus formation at the base of the struts.

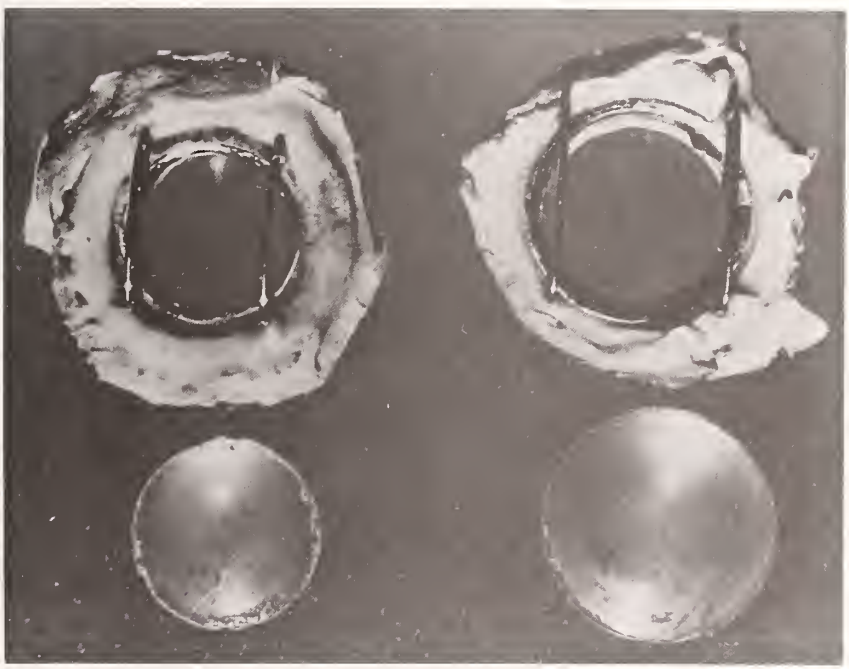

Figure 22. Recovered Kay-Shiley mitral valves. Thrombus formation at the base of the struts and tissue overgrowth along sewing ring prevented proper motion of the discs. Figure also shows clearly grooving and notching of the discs.

valve to leak during ventricular systole. The thrombus formation and/or tissue overgrowth could be attributed to flow separation at the base of the struts.

Another problem observed with this valve was the grooving and notching of the Delrin disc as shown in figure 22. The grooving and notching of the disc was due to the prevention of proper disc motion because of thrombus and/or tissue overgrowth on the valve superstructure. Proper disc motion includes movement up and down the cage during the cardiac cycle as well as rotation.

4. General Comments and Conclusions

An important aspect to the clinical evaluation of valve prostheses is to determine how effectively the valve prostheses utilize the available space in the aortic or mitral root. The space occupied by the valve in the root can be estimated by knowing the mounting or sewing ring diameter. However, because the primary orifice area of the valve is further obstructed by the valve occluder or leaflets and the hinge or strut mechanisms, an effective valve orifice area must be estimated. The method for estimating the effective orifice area described by Aaslid [38] was used in our *in vitro* studies where peak volume flow and peak flow gradients were known. The effective area indicies of the valves we studied were then calculated by the following formula:

$$EOA = \frac{0.32 \quad PF}{\sqrt{\Delta p}}$$

where 0.32 is a constant determined by the units used and the density of blood

EOA = effective orifice area
PF = peak volume flow (ℓ/min)
Δp = peak flow pressure drop (mm Hg)

The effective area index as suggested by the pressure drop data showed that the St. Jude valve allows the most forward flow for the space it occupies. The other valves in descending order are: Björk-Shiley, Ionescu-Shiley, Smeloff-Cutter, Starr-Edwards (ball valves), and Carpentier-Edwards and Hancock porcine valves.

A further important clinical consideration is a comparison of valve profile heights as they relate to mounting diameters as shown in figure 23. The ball valves tend to have the greatest profile height while the St. Jude valve has the lowest. There is a good deal of variation in profile height between the smallest and the larger valves of each valve type. The size and shape of a prosthetic heart valve should be such that it does *not* interfere with the normal function of the surrounding tissues. Pathology specimens shown in figure 24 suggest very strongly why all valve prostheses should and must have radiographically visible components. More advanced cases of poppet variance and partial obstruction to motion can be

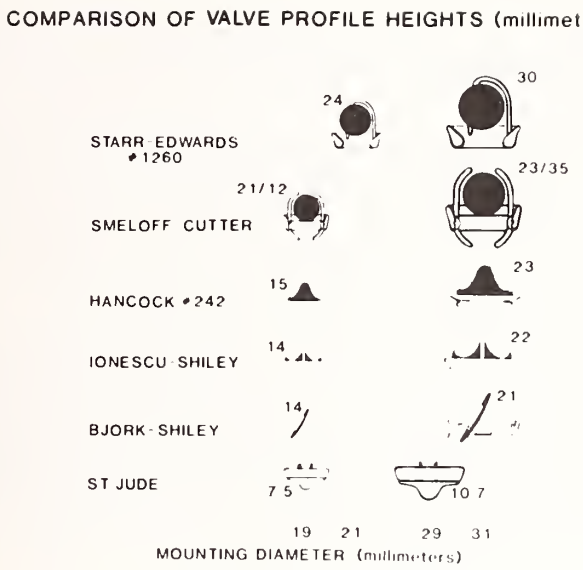

Figure 23. Comparison of profile heights of different valve types.

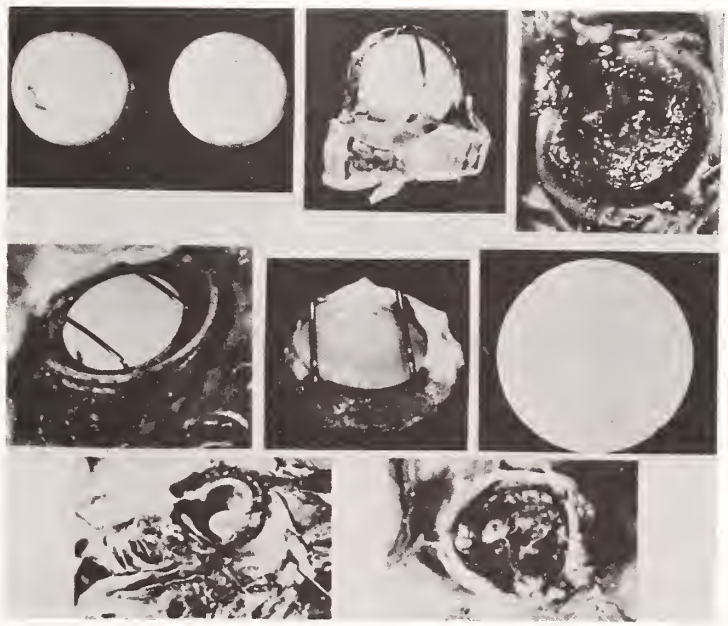

Figure 24. Pathology specimens of various types of recovered valves indicating the need for radiographically visible heart valves.

determined fluorscopically if the poppet is opaque. In the case of tilting disc valves it is important to be able to assess both the opening and closing angle of the disc. It is also important to have a visible base ring in all valve types in order to assist in diagnosing valve dehiscence. Not only is it important to evaluate proper opening and closing of disc valves but it is advantageous to know if they are able to rotate. The Björk-Shiley valve can be readily seen radiographically. A tantallum loop has been implanted in the disc to assist in calculation of its opening and closing angle. The model 1260 Starr-Edwards ball valve can also be readily seen radiographically. Two-percent-by-weight barium sulfate in the silastic poppet allows an examiner to determine the completeness of both the opening and closing of the valve. The silastic poppet of the Smeloff-Cutter valve contains no barium and its motion can not be easily visualized fluoroscopically. The titanium stent of the Ionescu-Shiley valve and the stellite metal ring of the Hancock valve allow ready visualizaiton of the base ring motion flouroscopically. The leaflet motion, however, can not be visualized. As stated previously if viewed in the same projection during fluoroscopy the St. Jude valve can not be properly seen until the leaflets are in the open position.

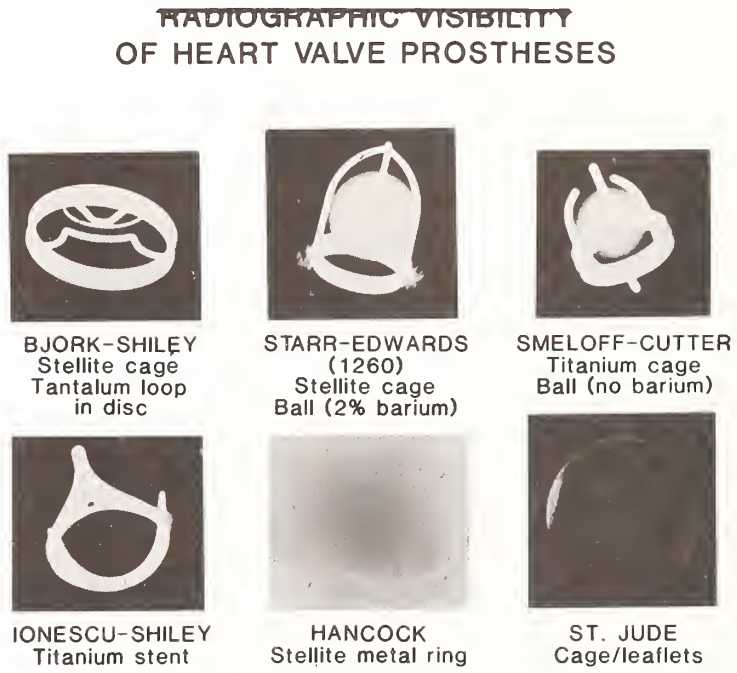

Figure 25. Radiographic visibility of various types of heart valve prostheses.

Everything else being equal the patient would prefer a quiet valve. The bioprostheses are clearly the "quietest" valves while valves made of pyrolytic carbon and hard durable metals are the loudest.

Some of the clinical, pathological, physical and hemodynamic characteristics of prosthetic heart valves which influence their use have been considered. Our experience is that all valve types are liable to thrombus

formation and tissue overgrowth. The "ideal" prosthetic heart valve has yet to be developed. Accelerated fatigue testing and clinical experience indicate that the Starr-Edwards 1260, Smeloff-Cutter and Björk-Shiley valves are the most durable. The St. Jude valve produced the least restriction to forward flow for the mounting area it occupied. It also had the smallest profile height. X-ray visibility of the Björk-Shiley and Starr-Edwards ball valves was the best. The tissue bioprostheses were the quitest and probably the least thrombogenic of the valves studied.

5. Acknowledgment

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EXAMINATION OF ORTHOPAEDIC IMPLANT FAILURES

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A study of 110 removed metal prostheses and internal fixation devices was conducted over a 26 year period. The case histories accompanying each implant allowed the correlation of the metallurgical analyses with possible causes of failure. Statistical tables provide information regarding classifications of the implants by cause for removal, anatomical location, type of implant, fabrication method and alloy, fracture mode and location for various implants, and general patient information relative to the implants. The required metallurgical analysis (designed to comply with all ASTM specifications), consisting of non-destructive testing, semi-destructive testing, and in certain cases mechanical tests, is briefly described. The characteristics of different fracture modes, such as due to mechanical fatigue and fatigue corrosion, are discussed and illustrated by photomicrographs, and the origins of the failures presented when possible. The difference between stress corrosion and fatigue corrosion is also explained. The study utilizing metallurgical analysis, patient histories, and the physiological aspects surrounding the events prior to and after failure, indicates correlations between implant fractures and lack of bony union, fatigue forces, design deficiencies, surgical implantation techniques, and improper use of the implants. Experience in metallurgy and its application to the implant and its environment required for acceptable and proper retrieval analysis is emphasized.

1. Introduction

The 110 fractured metal prostheses and fixation devices included in this study were chosen from more than 500 submitted for analysis over the last 26 years. The implants selected were accompanied by sufficient patient medical information to make it feasible to correlate the conclusions of the metallurgical analyses with other conditions possibly causing or contributing to the failures. Tabulations of statistical information derived from these case histories and specific examples of failures are presented.

In the context of this article "failure" is defined to mean that the implant did not accomplish its intended function and/or actually fractured, and had to be retrieved.

The implants examined were manufactured by nine competitive companies, both U.S. and foreign. Their distributors, several hospitals, numerous doctors, and legal firms also became involved when litigation resulted from the failure of an implant.

During the period 1954-59 establishing development and testing procedures in the laboratories of implant manufacturers, investigating heat treatment methods for improving implant properties, and determining specifications for materials and fabricating techniques were the most significant problems to be solved. Since then, due greatly to the impact of the American Society for Testing Materials F-4 Committee for Medical and Surgical Materials and Devices, formed in 1962, the effort has concentrated on the evaluation of failures (1).[1]

The failed implants were subjected to appropriate metallurgical tests such as chemical analysis, light and electron microscopy, mechanical testing and other procedures depending on the nature of the problem. All testing conformed to applicable ASTM F-4 Committee specifications.

2. Procedures

The first phase of testing is non-destructive, and after visual and macroscopic inspection, may involve light and electron microscopy, radiography, fluorescent penetrant examination and energy dispersive x-ray analysis. After the non-destructive phase has been completed, semi-destructive testing including chemical analysis, determination of grain size, inclusion content, and hardness and other metallurgical properties is conducted. Then, depending on the sample size, mechanical tests such as tensile or deflection tests may be performed. (See section 4. Metallurgical analysis.)

[1]Figures in () at the end of a sentence indicate the literature references at the end of this article.

3. Statistical Summaries

The following information presented in tabular form was compiled from written statements, hospital records, manufacturing information, and various other documents, and is limited to information extracted from case histories in file.

Table I is a general classification of the investigations performed on 110 implants retrieved from patients, and divided into three categories of reported causes.

TABLE I

Classification by Reported Cause for Removal

Reported Cause	No. of Implants[a]
Fractured implant	105
Suspicion of tissue reaction	2
Bending without fracture	3
TOTAL	110

[a]Selection of implants for metallurgical analysis required that pre-op and post-op data was available for inclusion in the evaluation.

Table II indicates the general classification, by anatomical location, and reveals that the majority of the failed implants in this group were removed from femoral head, neck and shaft areas.

TABLE II

Classification of Removed Implants by Anatomical Location

General Location	No. of Implants
Femoral head and neck	80
Femoral shaft and condyle	23
Tibial	4
Humeral	1
Mandibular	2
TOTAL	110

Table III presents a more detailed classification of the implants by general type, and the sub-type under each group. Again, the majority of investigations relate to the hip and femoral area.

TABLE III

Classification of Examined Implants by General Type

Type		Totals
Intertrochanteric Nail/Plate Combinations		
One piece	19	
Two piece	11	
Sliding nail	9	
		39
Hip Prostheses		
Proximal femoral prosthesis	3	
Total hip-femoral component	23	
		26
Intramedullary Nails		
Solid cross-section	13	
Cloverleaf type	4	
		17
Fixation Pins	7	7
Bone Screws	5	5
Bone Plates		
Slotted	4	
Standard	6	
Compression type	6	
		16
TOTAL		110

Table IV summarizes the implants by fabrication method and alloy type. Most of the devices are in the stainless steel category which, in all probability, correlates with the number of stainless steel implants in current use and being marketed. The larger number of failed stainless steel implants should not be interpreted to mean that stainless steel is more prone to failure than other materials.

TABLE IV

Classification of Implants by Fabrication Method and Alloy Type

Type		No. of Implants Examined	
Stainless Steel (ASTM F-55, 56, 138, 139)[a]			
	Forged	30	
	Wrought	59	
	Cast	8	97
Cobalt Base Alloy (ASTM F-75)			
	Cast	11	11
Titanium (ASTM F-67)			
	Wrought	2	2
TOTAL			110

[a]ASTM specifications apply only to wrought and forged classes of stainless steel.

Table V concerns the distribution, by location, of the fractures of nail/plate intertrochanteric combinations. It is apparent that the majority of the failures occur at the first hole of the plate. The second portion of Table V correlates the fracture mode with the percentage of occurrence and shows the other phenomena associated with the fracture mode (2,3,4,5). Of particular interest is the predominance of mechanical fatigue compared to fatigue corrosion, and the high incidence of crevice/fretting corrosion.

TABLE V

Location of Implant Fracture Mode Identification
(By per cent approximation)

Intertrochanteric Nail/plate Combination				
Location of Metal Fracture	Per cent			
	Nail	Junction	1st Screw Hole	2nd Screw Hole
One piece	20	25	45	10
Two piece	10	20	55	15
Sliding nail	25	5	60	10
Failure Mode[a]				
Mechanical fatigue[b]	56			
Fatigue corrosion	40			
Bending	4			

[a]Crevice and/or fretting corrosion of bone screw holes detected in 75% of the implants examined.

[b]The cross section penetrated by the fatigue crack is larger in the fatigue corrosion mode than mechanical fatigue.

Table VI presents the distribution, by location of fractures in femoral hip prostheses, and the percentage of fracture modes and related phenomena. It is evident that the majority of failures involving femoral hip prostheses occur approximately 2 in. (5 cm) from the distal tip, and that the largest number of these fractures are created by mechanical fatigue, predominantly in a torsional fatigue mode. Based not only on these case histories, but also evidence presented by other investigators, there is a correlation between the stress concentration zone created by the anatomical stresses applied to the femur and the fracture point of the hip prosthesis (6,7,8,9). Also there is a definite contribution by the support, or non-support, of any polymeric material used to secure the stem in the femur. It is interesting to note that beyond 3 in. (7.6 cm), there is evidence that all fractures are associated with inherent metallurgical defects or weld repairs of the casting.

TABLE VI

Location of Implant Fracture and Identification of Fracture Mode for Hip Prosthesis

Implant Fracture Location Location (Approx.) of Fracture Zone from Distal Stem Tip	Per cent
1 in. (2.5 cm)	4
2 in. (5.0 cm)	66
2½ in. (6.4 cm)	8
3 in. (7.6 cm)	6
3½ in. (8.9 cm)	16[a]
Fracture Mode[b]	
Mechanical fatigue	87
Corrosion fatigue	13[c]

[a]Fracture associated with weld repair or serious casting defects.

[b]Fracture origin predominately at the lateral surface and with a bending-torsional vector.

[c]Limited to stainless steel.

Table VII relates to the distribution of the fractures and the fracture modes for intramedullary nails. Of particular interest is the location of the majority of the fractures at the one-third quadrant from the proximal tip of the intramedullary nail. Also, mechanical fatigue predominates with some correlation to bending prior to failure. It was noted, generally, that the fatigue corrosion cracking progressed through a larger area of the implant prior to the final failure than did mechanical fatigue cracking. It is not surprising that such a correlation exists since there is definite evidence relating to corrosion assisted fatigue fractures and their selected paths of fracture progression. Also, generally, the fatigue stresses required to initiate and propagate the fatigue corrosion cracking are at a lower level, thus causing the critical length of the crack to be longer prior to catastrophic failure (10).

TABLE VII

Location of Implant Fracture and Identification of Fracture Mode for Intramedullary Nails

Implant Fracture Location (Approx. zone)	Per cent
1/3 length from proximal tip	75
1/2 length from proximal tip	17
At threads or broach area	8
Fracture Mode[a]	
Mechanical fatigue	45
Fatigue corrosion[b]	55

[a]Approximately 17% of fractured nails possessed detectable bending prior to fracture.

[b]Limited to stainless steel.

Studies by other investigators have revealed that trauma at the bone fracture may be accompanied by a lowering of the pH in the area as well as the possibility of oxygen starvation (11). It is shown by the tables that fatique corrosion fractures are limited, according to the study, to the stainless steel alloys.

Table VIII, which shows the distribution of bone plate fractures and the fracture mode, indicates that 95% of the failures occurred at the first screw hole or slot from the center of the plate, and that the fracture modes were mechanical fatigue and fatigue corrosion. It is logical to conclude that the high stress point would be at the first stress concentration from the center since the bone plates are normally placed with their center portion over the bone fracture. Further evaluation indicated that the lack of bony union, or early weight bearing, is directly related to bone plate fractures, as indicated in subsequent tables.

TABLE VIII

Location of Implant Fracture and Identification of Fracture Mode for Bone Plate

Implant Fracture Location	Per cent
1st screw hole or slot from center of plate	95
2nd screw hole or slot from center of plate	5
Fracture Mode	
Mechanical fatigue	40
Fatigue corrosion[a]	60

[a]Limited to stainless steel.

Tables IX and X are related to the correlation of patient information based on case histories.

Table IX simply shows the percentage of male and female patients and their age distribution, based on the relatively small sampling.

TABLE IX

General Patient Information Relating to Removed Surgical Implants

Sex and Age Distribution	Per cent
Male	37
Female	63
Age	
8 - 44 years	5
45 - 65 years	40
66 - 86 years	55

Table X is a classification of the implant type and the average length of time the devices were in service. Of probably the most significance is the evidence of non-union of the bone related to the various categories. As can be seen, failed intramedullary nails have, almost always, a relation to non-union. Bone plates and intertrochanteric nail plates also have a predominance of non-union case histories.

TABLE X

General Patient Information Relating to Removed Implants
(By insertion-to-removal-time and evidence of non-union of bone)

Implant Type	Time in Months[a]		Evidence of Non-union
	Range	Average	Per cent
Intertrochanteric nail/plate	2 - 11	6½	60
Bone plates	6 - 11	9	75
Intramedullary nails	6 - 19	11	92
Femoral hip prostheses	19 - 36	28	—

[a]Based on time of operation to time of implant removal.

Table XI presents additional patient history information regarding the non-union of bones and implant failures.

TABLE XI

Patient History Related to Evidence of Non-Union and Implant Fracture

History with Non-union Evidence	Per cent
No unusual case history	56
Report of falls or accidents prior to implant fracture	19
Early weight bearing	14
Miscellaneous	11

4. Metallurgical analysis

The metallurgical examination and analysis of failed implants, as briefly described in section 2, consists of non-destructive testing followed by semi-destructive testing and then, if the sample allows, by mechanical tests. (The tests are carefully designed to comply with all ASTM specifications.)

Visual and macroscopic examination, that is inspection of the fractured surface at magnifications of less than approximately 50X, reveals a considerable amount of information to a trained metallurgist. Of course, some information has been effaced by the abrasion and peening which occurred during and after the fracture of the implant, and as a result of its surgical removal.

An example of the information that can be retrieved from visual and macroscopic examination is illustrated by figure 1. This is a photomacrograph of the fractured surface of a cobalt base (F-75) total hip femoral component. Note that the origin of the fatigue failure can be traced by the macro-fatigue striation lines, and is illustrated by the arrow. This evaluation also indicated that probably torsional components were involved in the fatigue loading.

Non-destructive tests such as fluorescent penetrant examination and radiography are common methods of quality control for surgical implant products. In fact, a vast majority of the metal surgical implant manufacturers have achieved 100% non-destructive testing by using one or both of these methods. Further, specifications have been promulgated by the ASTM F-4 Committee relating specifically to the procedures for both fluorescent penetrant and radiographic examinations of surgical implants (1).

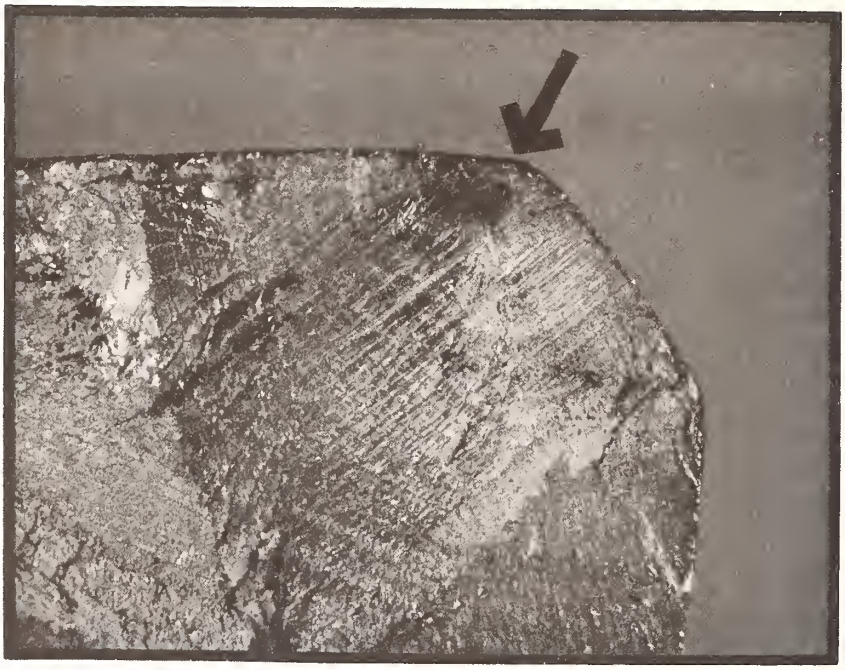

Figure 1. Photomacrograph (15X) of fatigue origin on the femoral stem portion of total hip prosthesis (ASTM F-75). The macro-fatigue striation emanates from the portion indicated by the arrow.

In retrieval analysis, it is advisable to apply non-destructive testing to determine if there are any defects, voids, cracks, etc., adjacent to or near the zone of failure. Many times these areas of defects are sub-surface and/or cannot be detected by visual and macroscopic examination. Fluorescent penetrant inspection becomes very valuable in revealing cracks adjacent to fatigue failures in plates, pins, and nails, since these implants usually have a high luster and cracks cannot easily be viewed by visual or macroscopic examination.

The scanning electron microscope (SEM) is basically employed to determine the mode of fracture, its origin, its continuity, and any evidence of inherent or service defects. For example, high magnification photomicrographs with the SEM show the differences between various fracture modes such as a typical mechanical fatigue fracture (illustrated by figure 2 which represents a mechanical fatigue fracture of a bone plate), a fatigue corrosion progression (which is shown by figure 3), a fatigue failure assisted by corrosion through the plate portion of an intramedullary nail, and a ductile overload failure (illustrated by figure 4) of a bone screw.

Figure 2. Scanning electron microscope photomicrograph (2100X) illustrating mechanical fatigue failure of a stainless steel (ASTM F-55) bone plate.

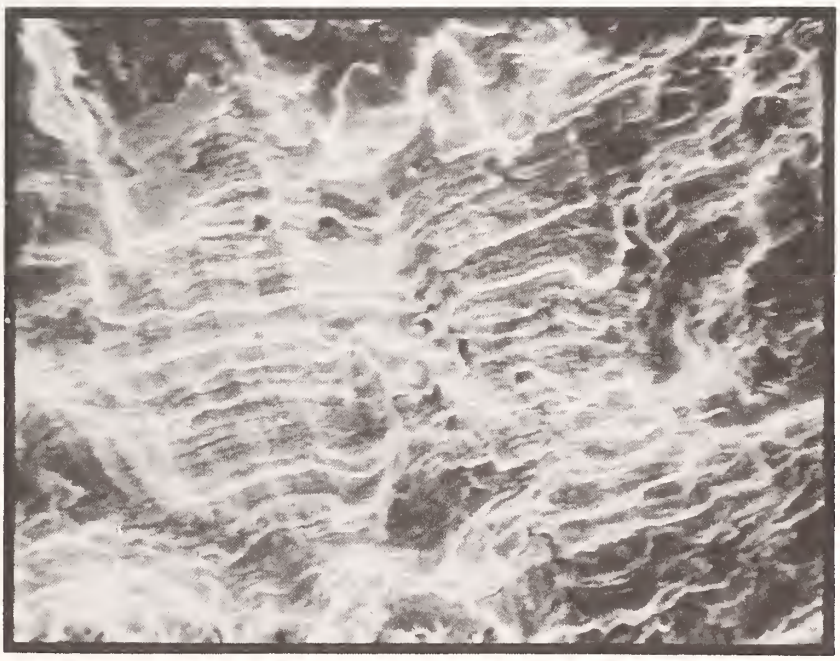

Figure 3. Scanning electron microscope photomicrograph (2500X) illustrating a fatigue corrosion fracture through a stainless steel (ASTM F-55) intramedullary nail.

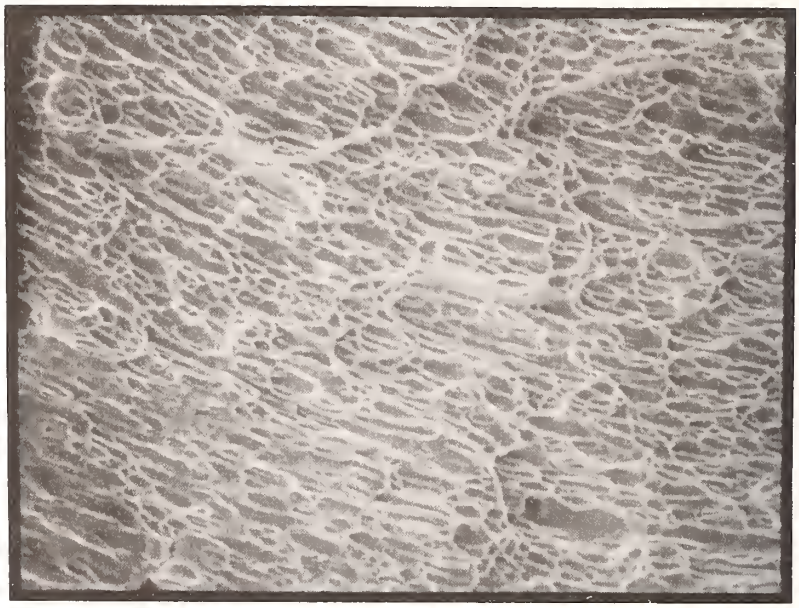

Figure 4. Scanning electron microscope photomicrograph (500X) illustrating a ductile overload fracture of a stainless steel (ASTM F-138) bone screw.

When warranted, and dependent upon the amount of material available, chemical analyses should be performed using ASTM Methods and used for comparison with ASTM Specifications for Surgical Implant Materials.

In many cases, when inadequate sample is available for identifying the materials by other tests (such as with small bone screws), the use of energy dispersion x-ray analysis is valuable. This technique, or other similar techniques, is also valuable in identifying corrosion residue or unusual surface characteristics.

Metallographic analysis requires the removal of a cross section of material and preparation of the surface for study with a metallographic microscope (metallograph). This type of examination reveals information concerning the fabrication, heat treatment (if any), fracture progression, associated cracking and a general history of the material. Metallography is also a quantitative tool used to determine grain size, ferrite content, presence of carbides and other characteristics of the samples (as required by many ASTM F-4 Standards). A skilled metallographer can also perform a qualitative evaluation of the material and its type by his examination.

Examples of some of the information that can be retrieved through metallographic examination are illustrated in figures 5 and 6. Figure 5 shows a fatigue corrosion crack emanating from a thread notch. The progression, of a transgranular nature, and the emanation from an initiating corrosion pit lead the experienced metallographer to the identification of the mechanism as fatigue corrosion. Figure 6 shows a series of fatigue corrosion cracks which are located immediately adjacent to and parallel to the primary fatigue failure. In cases where a broad zone of stress concentration is involved in the fatigue loading, it is common for a group of fatigue corrosion cracks to form.

Figure 5. Photomicrograph (100X) of a metallographic cross section through a stainless steel (ASTM F-138) bone screw. The transgranular fatigue corrosion crack progression emanates from the thread root and a corrosion pit. (Etchant: 10% Ammonium Persulfate Electrolytic)

Figure 6. Photomicrograph (250X) illustrating an unetched metallographic cross section adjacent to a bone plate fracture of stainless steel (ASTM F-138) with a group of fatigue corrosion cracks adjacent to the primary fracture.

The identification of fatigue corrosion in stainless steel is made from the microscopic crack geometry, and the way it progresses through the grain structure. Many times stress corrosion and fatigue corrosion cracking of stainless steel surgical implants are confused, in that some aspects of the crack progression are similar. However, on the basis of the investigations performed, a literature search, and the reports of other authoritative investigators, it is apparent that stress corrosion cracking, in the true sense, cannot occur in stainless steel implants (12,13,14,15,16,17,18). One of the factors is the temperature dependence necessary to create the stress corrosion cracking process in a saline solution. Also fracture mechanics studies have shown that fatigue corrosion cracking may proceed in both intergranular and transgranular progressions similar to that of stress corrosion cracking. (Lacking the specific background, and not having studied surgical implants in their environment, some investigators mistakenly identify a fatigue corrosion crack as stress corrosion in stainless steel.)

5. Conclusions

The retrieval analysis of failed surgical orthopaedic implants employs metallurgical analysis which applies scientific methods of testing and evaluation to the failure, but the patient background, history, and when possible, the physiological conditions surrounding the events prior to and after the failure must also be utilized.

This paper not only presents some of the procedures of metallurgical analysis used in failure examination, but also a statistical analysis of the information pertinent to the fractured implants. The 26 year long study of approximately 500 fractured orthopaedic implants, of which 110 failures accompanied by patient information are considered in this paper, suggests that only a relatively small number of implants fracture as a result of inherent or metallurgical defects.

Most implants, other than prostheses, are not designed to be weight-bearing for any extended period of time. They are intended primarily to keep the fracture reduced and allow the bone to form a callous, and subsequently a strong union.

As a prime example of the retrieval analysis concept of failure analysis, experience has shown that the fracture of bone plates or intramedullary nails are almost always related to the lack of a bony union of the femur. However, an investigator without this knowledge would tend to blame the design or material of the implant for failure to resist the fatigue forces when, in fact, unusual fatigue forces were applied to the implant due to the non-united bone.

This paper also attempts to point out that experience, not only in metallurgy is required, but the application of this knowledge to the implant environment and the parameters affecting implant failures is necessary to reach valid conclusions. Unfortunately, many metallurgists assume the attitude that "if the implant failed, it therefore was defective," which is not in accordance with acceptable and proper retrieval analysis.

Further, knowledge of the various fracture mechanisms is essential when human body environments are involved. A common error of inexperienced investigators is to identify fatigue corrosion fractures of stainless steels as stress corrosion. It has been proved, not only by this investigator, but by many others, that stress corrosion cracking does not occur within the parameters (particularly temperature), acting on surgical orthopaedic implants.

The ultimate function of the metallurgical failure analysis of implants is to focus on needed improvements, whether they exist in manufacturing methods, design, or surgical techniques. The analysis of failed surgical implants should not be relegated to only areas of product liability investigations and malpractice litigation, but be used to improve implants with the sole purpose of helping the patient.

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Discussion

Question (D. F. Williams, University of Liverpool, U.K.): Could you explain how you differentiate between fatigue and corrosion fatigue mechanisms?

Have you performed any control experiments in which stainless steel specimens have been tested under fatigue conditions in air and then in a saline environment to determine the difference in morphology or the fracture surfaces in these two modes?

Assuming you can differentiate between the two, can you explain why some samples of stainless steel should be susceptible to corrosion fatigue rather than fatigue, whereas others suffer fatigue only.

Answer: The difference between the mechanism of fatigue or fatigue corrosion of stainless steel surgical implants has been determined not only be our personal examination but by research of other investigators concerning this subject.

We, that is Taussig Associates, Inc., have not performed any controlled experiments in our laboratory personally; however, we have performed examination of stainless steel specimens which have been subjected to fatigue conditions in other laboratories (primarily manufacturers). The analysis concerns not only fatigue fracture in air but also in such solutions as Ringers and similar saline solutions known to be comparable to body fluids *in situ*.

The SEM examination of the fracture mechanisms, based on fracture analysis of actual implants fractured *in vivo* and the samples supplied from controlled conditions have led to a differentiation of the fracture pattern as follows:

Mechanical Fatigue:

Mechanical fatigue of stainless steel surgical implants is characterized by a continuous striation pattern passing primarily in a transgranular manner. The photomicrograph in our paper is typical of mechanical fatigue. The effects of inclusions, grain boundary materials and changes in hardness many times can be detected in the striation pattern.

The evaluation of fatigue in ASTM F-75 castings does present a problem in that only macro-striations are normally detectable by laboratory techniques. We have not been able to substantiate micro-striations by SEM techniques in F-75 material--this has been confirmed by Dr. Donald Cox of Failure Analysis, Inc., Los Angeles, California in his doctoral dissertation of 1977.

Fatigue Corrosion:

Fatigue corrosion exhibits a different fractographic appearance than mechanical fatigue as found in surgical implants. The two (2) photomicrographs in this paper are typical of the differences.

Fatigue corrosion is more difficult to identify since the striation pattern is somewhat masked by the corrosion reactions--additionally, the fracture can progress by both intergranular and transgranular paths. Another factor that may confuse investigators is the appearance of slip planes in stainless steel which can be mistaken for fatigue striations. The photomicrograph shown in this paper illustrates the fatigue striations progressing normal to the crystallographic pattern of the stainless steel--this is the type of fatigue corrosion evidence that we look for in our SEM examination.

Also, we have noted a separate artifact which is common to fatigue corrosion fractures--that is the presence of secondary cracks sometimes appearing as branch cracking--this should not be confused with stress corrosion cracking.

We cannot answer, with authority, as to why some implants fracture by mechanical fatigue and others by fatigue corrosion. It is our current opinion that those appliances such as intramedullary nails, bone plates and intertrochanteric implants are subject to failure in conjunction with and caused by the lack of a bony union. When the bone does not unite, it is our opinion that a concentrated area of trauma and subsequent corrosion potential is created thus increasing the factor of corrosion in the fracture mechanism. It may be possible that only the stage I fracture is created by mechanical fatigue while the state II fracture progresses by fatigue aided by corrosion.

Question (D. F. Gibbons, Case Western Reserve University): The observation that chemical analysis of trace elements, particularly nitrogen concentrations which are high, in 316 LVM stainless steel could well account for cases of corrosion fatigue. The stability of the austenitic transformation, allowing "galvanic" type corrosion to occur within the crack!

Answer: We believe that some of the trace elements may have an effect on the initiation or retardation of corrosion fatigue. We do not normally analyze the stainless steel implants for % nitrogen; however, based on the metallurgy of stabilization, it would follow that nitrogen could certainly affect the mechanism of corrosion fatigue.

We are planning to address this subject in the future based on a review of previous findings and future analyses of fractured stainless steel implants.

We do, routinely, analyze the stainless steel composition for % copper. We intend to review our records to determine if there may be any relation between % copper and the occurrence of mechanical fatigue and/or fatigue corrosion.

Question (P. Sung, Food and Drug Administration): You mentioned that 316 stainless steel will not go through the stress corrosion process during fracture. Your detailed explanation with experimental confirmation of your claims would be of interest.

Answer: This paper does present our opinion concerning the temperature dependence of stress corrosion and its relation to the fracture process of stainless steel implants. We have included some pertinent references which substantiate this finding--we hope in time, to publish a supplementary paper specifically related to stress corrosion verses fatigue fracture of stainless steel implants.

Aside from the references shown in this paper, we can provide many additional references concerning the mechanism of stainless steel cracking and the dependency not only on temperature and concentration of solution, Ph and oxygen content. Only recently have investigators concerned themselves with temperature dependence. Most investigators used boiling $MgCl_2$ solutions as their test criteria--this criteria does not relate to conditions found *in vivo*.

Question (R. Wilkinson, Strathclyde, U.K.): Did you measure the concentration of the elements or the implant components? If you did, how many failed to meet specification?

Answer: If we have permission to perform semi-destructive testing, we do routinely analyze the components for chemical composition.

Of the stainless steel implants analyzed, all manufactured within the last 10 years have fallen within the composition requirements of F55, F56, F138, or F139.

Cobalt-chromium cast alloys for ASTM F75 have had some deviation in compliance to ASTM composition requirements and are usually manufactured in Switzerland--their specifications have slight variances from ASTM.

Therefore, we find no trend nor any significant findings of elemental analysis beyond specifications of the applicable surgical implants.

Question (Allan Weinstein, Tulane University): Have you tried to correlate the chemical composition as regards the percentage of the minor constituents with the propensity towards corrosion-fatigue vs. mechanical fatigue.

Answer: Our answer to Dr. Donald F. Gibbons of Case Western Reserve University essentially addresses itself to Dr. Weinstein's suggestion.

We do intend in future investigations to attempt a correlation between the trace elements and fatigue corrosion and/or mechanical fatigue.

Question (Kirk J. Bundy, Johns Hopkins University): Did you examine fracture surfaces with energy dispersive analysis in order to differentiate between mechanical fatigue and corrosion fatigue?

Answer: We have examined the fractured surfaces of surgical implants by Energy Dispersion X-ray Analysis (EDX). Our findings did not show or indicate a differentiation between those fractures which were classified as mechanical fatigue or fatigue corrosion.

We doubt that we would ever find a correlation since most samples when received in our laboratory have been cleaned in some manner; however, there may be some symptomatic residue which is on the surface that has been cleaned by some pathologist or some intermediary.

A STUDY OF INCLUSIONS IN STAINLESS STEEL IMPLANTS AND THEIR EFFECT ON CORROSION

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A study of stainless steel implants nominally conforming to BS 3531 has been undertaken. Corroded areas have been examined using the SEM and inclusions visible in the corroded areas identified using energy dispersive X-ray analysis. Inclusions present in a polished section of the component were also identified and measured to produce inclusion ratings which were then compared with the estimated corrosion. Some components were analysed using wavelength dispersive X-ray analysis and 5 screws were found deficient in nickel. Screws having low nickel were then compared with the others. The interrelationships of the different inclusions and relationships with corrosion are discussed and the case for more stringent metallurgical control considered.

1. Introduction

Inclusions are non-metallic particles embedded in a metal matrix which may affect both chemical and mechanical properties[1,2] In steels, they arise from a number of different sources and these will be considered in turn. Modern steel making reduces the carbon content of steels using oxygen which must be removed in its turn. This is accomplished by the use of deoxidants, commonly aluminium and silicon, but elements such as titanium and vanadium have been used [3]. The kinetics of deoxidation are extremely complex [4,5] and the details are not well understood.

After the original addition of aluminium to the melt the aluminium and oxygen react to form Al_2O_3 which then floats to the surface. To produce a clean steel it is necessary to produce melt conditions which will facilitate this 'float off'. A low concentration of aluminium and oxygen remains dissolved in the melt but cannot remain in solution after solidification. As the temperature falls and solidification begins, a supersaturation of aluminium and oxygen builds up ahead of the solidification front and a number of small inclusions are produced [5]. The concentration falls and then builds up again as solidification proceeds, leading to an inhomogeneous distribution of small nuclei [6].

If silicon is used as well as aluminium the situation becomes even more complex since SiO_2, Al_2O_3or various silicates can be produced

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depending on the way the two elements are added. The oxygen content of steel is said to be more uniform if silicon is used [4]. Complex oxides may also be produced involving deoxidants and components of the melt [7]. Components of the melt such as manganese and chromium are strong oxide formers and if conditions are right, simple and complex oxides of these metals may be formed. This reduces the quantities of these materials in solid solution but not necessarily the total amount in the melt.

Inclusions from deoxidation are almost impossible to eliminate in a single stage process. Thus various forms of re-melting have been developed in an effort to reduce impurities. The most common are Vacuum Arc Remelting (VAR) and Electro-Slag Refining (ESR). VAR seems more effective for oxides and ESR for sulphides [8]. When considering effects of inclusions it is therefore necessary to consider effects due to the different types of inclusions.

Other sources of inclusions are the refractories lining a steel-making plant, chemical reactions of impurities in the raw materials and pre-formed inclusions from scrap if the temperature of the melt was too low to bring them into solid solution. More careful selection of raw materials will obviously reduce inclusions due to impurities but will lead to increased costs. Improved refractories and better control of pouring and casting procedures will reduce refractory wear.

1.1 Formation of complex inclusions

As has already been indicated, the kinetics of inclusion formation are complex. In the melt, nucleation, growth and inhibition must be considered as well as 'float off'. In the solid state nucleation, diffusion and growth are important. Homogeneous nucleation requires a degree of supersaturation, at least on a local scale, and even then may be delayed in static conditions [4]. In commercial steel making there are normally adequate nuclei for heterogeneous nucleation in the melt [4], but homogeneous may be necessary in the solid state.

Heterogeneous nucleation may lead to the growth of 'onion' like inclusions where layers of materials deposit around a central core. Deposition of distinct crystals of one phase on crystals of a second phase is also observed [7]. Aggregation of inclusions may also be important as this affects 'float off' [5]. But if solidification has occurred retaining the inclusion within the ingot then different spots of an apparently single inclusion may contain very different elements.

In solid solution diffusion plays a dominant role in the kinetics of growth. Because of greater ease of nucleation and increased diffusion rates many inclusions nucleate at grain boundaries. The most notorious of these in stainless steels is probably chromium carbide which leads to intergranular corrosion by chromium depletion of the adjacent grain [9].

1.2 Inclusions and mechanical properties

Inclusions may affect mechanical properties. Because inclusions are discontinuities they affect dislocation and grain boundary migration and

may act as sites for crack initiation. This last effect is most important in fatigue strength [1,10]. The likelihood of crack initiation depends on the stress field around the inclusion which depends on its size, the difference in modulus between inclusion and matrix, the shape of the inclusion in relation to the applied stress, and the strength of the interfacial bond. In general, large, hard inclusions with sharp edges are the most damaging [11]. Examination of ductile fractures often reveals inclusions at the base of the 'dimples' showing that failure has initiated at the relatively weak interface [1]. Grain boundary inclusions may also be implicated in some cases of intergranular fracture although this is often due to precipitation of a second phase[12]. The subject will not be pursued further in this paper but reviews may be found in ISI Special Report 134.

1.3 Inclusions and corrosion

Inclusions may affect the corrosion resistance of metals because of local galvanic cells set up between the inclusion and its matrix [2]. Poor interfacial bonding may lead to the production of crevices, possibly forming concentration cells [13] or matrix depletion of a particular component may affect protective oxide formation [14].

Residual elements in the matrix may also affect corrosion resistance and these effects may be complex, for example low concentrations of copper increase the resistance of stainless steels except in the presence of molybdenum when it is reduced [9]. It should be borne in mind that in quenched steels residual elements may be found in greater than equilibrium concentrations because of the kinetics of nucleation.

Most studies have concentrated on particular inclusions e.g. Al_2O_3 under a condition relevant to industrial needs or on looking at oxides, sulphides, nitrides and carbides as classes [6]. The latter studies have tended to use the optical microscope where identification of the metallic component is often not possible. Laboratory studies tend to use special small melts where conditions have been adjusted to affect the concentration of a particular class of inclusions [15].

2. Method

Stainless steel implants removed in the course of surgery were collected from two Glasgow hospitals. Where possible, swabs were obtained and the implants themselves cultured. A sample form was provided for the theatre staff to complete (fig. 1); if information was missing, where possible the patient was traced and the missing information obtained from medical records. Staff were also requested to mark the proximal end of bone plates with a loop of thread.

After culture and sterilisation, the implants were thoroughly washed and dried then stored in labelled polythene bags. Hardness of all components was measured using a Vickers Pyramid Diamond Indentor. Screw heads were removed and mounted for examination in the SEM. The remainder of each screw was mounted for metallographic examination.

Corrosion was assessed using a scale developed for this study[16,17]

A series of standard SEM micrographs of corroded areas was assembled representing minimal to severe corrosion (fig. 2). These were ranked, choosing photographs which represented as linear a scale of metal loss as possible. A corrosion rating was then obtained by estimating the area of corrosion corresponding to a particular grade and using the equation

$$CORR = \sum_{1}^{n} A_1G_1 + \ . \ . \ . \ + A_nG_n$$

where A = area in μm and G = grade. The numbers were felt to be extremely large and so for final analysis all the earlier ratings were divided by 10 yielding the final equation

$$CORR = 0.1 \sum_{1}^{n} A_1G_1 + \ . \ . \ . \ + A_nG_n$$

Polished, unetched sections were carefully mounted for SEM examination with the top face parallel to the stub. The plastic mount was painted with either colloidal carbon or colloidal silver to reduce charging. Inclusions were identified using energy dispersive X-ray microanalysis and the area of the inclusion estimated. An inclusion rating, consisting of the area occluded by inclusions of a given type in a specimen area of 0.5 mm sq, was produced for each section examined. Attempts were made to analyse the matrix but the simultaneous presence of molybdenum and sulphur led to unreliable results. A few samples were mounted for examination in an electron probe microanalyser at Edinburgh which used wavelength dispersion. This is slower but has better discrimination. A wavelength dispersive system is being commissioned at Strathclyde and this aspect of the work will be extended shortly.

Inclusions in the corroded areas of the screw heads were identified using the energy dispersive system. Attention was confined to screws in this study except for measuring the hardness difference between screw and plate.

The partly commissioned wavelength dispersive unit was used to examine inclusions on the polished sections in order to detect the low atomic number elements. The energy dispersive system identified the metallic elements although if carbon was sought it was necessary to use 12 KV to excite the metallic elements while 6 KV gave better detection of carbon. Approximate peak to background ratios were determined although these should be interpreted with caution because the system was not fully calibrated.

Results were analysed using the SPSS statistical package on an IBM 2980 computer.

3. Results

3.1 Bacteriology

Three implants from the series were found to be infected although not all the implants could be cultured. One case produced pathogenic organisms (staph. aureus) and two organisms often considered non-pathogenic (diptheroid; 2 types of strep. viridans and 2 types of staph. epidermidus). In addition 4 cases of infection were reported in the case notes (coagulase +ve staph and diptheroids; staph aureus; E-coli and unspecified) where swabs were not provided nor the implant placed in sterile jars.

3.2 Comparison of screws having low nickel content

Table 1 shows the means of different variables for the two groups. Despite the low numbers certain statistically significant differences are apparent. Because this work is in an early stage significances as low as 0.10 will be considered and further investigations made. The first difference is in corrosion where the low nickel group showed increased corrosion although the variance is high. However, the time of implantation was longer for this group. Inclusions found in the two groups are also different, titanium, mixed metal-aluminium containing, and silicon inclusions all being higher in the low nickel group. Aluminium inclusions (presumed Al_2O_3) were not found in the low nickel group at all although the absence is not statistically significant. None of the other variables showed significant differences, including the amounts of other alloying elements.

Table 1. Comparison of screws with low and normal nickel contents

		Corr	Time	*Ti Inc	*Al cont Inc	*Si Inc
Low Ni	No.	5	3	5	5	5
	Mean	389	68	152	213	63
	St. dev.	548	55	292	299	83
Normal Ni	No.	31	26	28	28	27
	Mean	144	27	2	67	15
	St. dev.	203	26	4	87	45
Significance		0.10	0.05	0.02	0.05	0.10

* Ti Inc - titanium inclusion rating. Al cont Inc - rating for all aluminium containing inclusions. Si Inc - silicon inclusion rating.

3.3 Comparison of corroded screws containing chromium inclusions in the corroded areas with corroded screws without corrosion associated chromium inclusions

Table 2 shows there were no significant differences in either the estimated corrosion or the time of implantation. Inclusions present in the polished sections showed no significant differences, the high Ti rating in the chromium present group was caused by one very 'dirty' screw containing massive amounts of titanium. However the amounts of alloying elements did differ significantly. Measured chromium was less, possibly reflecting loss of chromium to the inclusions which then floated off, although chromium containing inclusions in the area analysed would have contributed to the chromium signal.

Nickel was lower in the chromium present group, the significance is not clear since the quantities present should be adequate to stabilise the austenitic phase. The higher value for manganese may reflect the tendency for chromium inclusions to also contain manganese, possibly as a spinel type mixed oxide. A chromium inclusion rating was not considered since it proved extremely difficult to separate chromium and manganese except in the case of manganese sulphide.

Table 2. Comparison of corroded screws having chromium inclusions present in corrosion with those having no such inclusions

		Corr	Time	Ti Inc	%Ni	%Mn	%Cr
Cr Inc present	No.	22	21	10	8	8	8
	Mean	119	49	68	10.8	1.9	17.8
	St.dev.	286	42	212	0.9	0.2	0.3
No Cr Inc present	No.	57	49	25	24	24	24
	Mean	104	33	6	12.2	1.7	18.2
	St.dev.	183	27	18	1.5	0.16	0.4
Significance		NS	NS	NS	0.025	0.01	0.02

3.4 Comparison of corroded screws having aluminium containing inclusions in the corroded areas with corroded screws without corrosion associated aluminium inclusions

Table 3 shows that there were no significant differences in either corrosion or time of implantation. A significant difference in screw and plate hardness difference was detected but this was felt to be random chance since their values for hardness of the two sets of screws were similar. The only other significant difference was in titanium inclusions where those screws with the aluminium inclusions did not contain much titanium, this may reflect deoxidation practice since both elements have been used as deoxidisers.

Table 3. Comparison of corroded screws having aluminium inclusions present in corrosion with those without such inclusions

		Corr	Time	VH diff	Ti Inc*
Al Inc present	No	68	61	65	30
	Mean	96	36	42	5
	St.dev.	170	31	64	17
No Al Inc present	No	11	9	8	5
	Mean	182	50	108	136
	St.dev	398	41	40	299
Significance		NS	NS	0.01	0.05

3.5 Other types of inclusions

No significant differences were found for subjects produced by considering silicon, manganese sulphide, sulphur, calcium and aluminium without other metals in the same way.

3.6 Relationship of inclusions in the corroded areas to those in polished sections

No attempt was made to quantitate inclusions present in corroded areas but merely to report their presence and relative abundance. The first and striking difference was that aluminium, presumed to be Al_2O_3 was frequently detected in corroded areas but relatively rarely in polished sections. Also Al/Si combinations were found in corroded areas but hardly ever in polished sections without other elements e.g. Al/Si/Ti or even more complex agglomerated.

The other striking difference was in the presence of obviously incidental inclusions (those whose presence was due to contamination rather than deliberate additions). Silver, copper, mercury, tin, zinc and gold have all been found. Very few have been found in polished sections. This may be due to sampling but in the case of silver a number of silver inclusions are usually detected within the corrosion if one is found. Silver has been found on a number of occasions in corrosion but only once in a polished section. Because of the relative rarity more screws will have to be studied before the effects of these inclusions can be assessed.

3.7 Oxygen content of inclusions

As expected the aluminium inclusions produce relatively high oxygen peaks. Inclusions containing chromium and manganese also show reasonably high oxygen peaks indicating that the chromium in these steels

is probably participating in oxide rather than carbide formation. As expected, sulphur containing inclusions rarely revealed significant oxygen concentrations unless in a mixed inclusion with a strong oxide former such as aluminium. Silicon inclusions have variable oxygen concentrations, most of them on the low side, indicating that the SiO_2 range of minerals is relatively rare.

3.8 Carbon content of inclusions

As expected, the carbon content of inclusions containing oxide formers is usually low. Four chromium containing inclusions with significant amounts of carbon have been found; two inclusions in each of two screws. Only 10 screws have been studied in this way, seven of which contained chromium bearing inclusions. Even in the two screws with chromium and carbon containing inclusions there were more inclusions containing low to negligible amounts of carbon than containing significant amounts.

Only 3 silicon inclusions were studied all of which contained measurable amounts of carbon (lower than the chromium but higher than most aluminium and sulphur ones). One inclusion containing aluminium had a very high carbon peak which was puzzling. In certain areas a 'dark stain' with diffuse edges appeared. The metallic signal was indistinguishable from that of the matrix but the carbon content was relatively high. This has been observed on 10 occasions, the explanation is not clear but this may represent a carbon rich second phase. Further studies are planned.

4. Discussion

4.1 Nickel content

Although the numbers are low, nickel was found to be out of specification in over 10% of components (6/43, 5 of which were screws). All other constituents analysed (carbon was not measured) were within specification. The low nickel components tended to have higher corrosion. The duration of implantation was longer but in a multivariate regression analysis time could not be shown to have any significant correlation with corrosion [16, 17] .

Chromium and aluminium containing inclusions all showed higher ratings in the low nickel group but in the larger series they were not shown to have any significant effect on corrosion resistance. Poor control of the melt may be indicated by the simultaneous occurrence of low nickel and high inclusion ratings.

In the absence of other evidence the nickel content should be more carefully controlled, both because of its austenite stabilising effect and also because of its possible effect on corrosion resistance. Further investigations are planned, first to establish the incidence of failure to meet specification on a larger sample and then to establish any effect on corrosion resistance.

4.2 Instrumental problems in the analysis of inclusions

Inclusions may be analysed either in situ or extracted from the matrix. Both conditions have their advantages but in this study only in situ analysis was undertaken because removal from the matrix is essentially a destructive process and the amount of material from a screw available for analysis is relatively small and destructive testing was avoided. Composition analysis is difficult in situ because of matrix contributions to the signal. With small inclusions, even using the spot mode, X-rays are generated outside the inclusion. The volume of excitation can be reduced by reducing the voltage and spot size but both may reduce the signal. Reducing the voltage from 25 KV to 12 KV has little effect on the lower atomic number elements e.g. Al, but reduces the signal and broadens the peaks for elements such as chromium and manganese. Reducing the voltage is required for very low atomic number elements such as oxygen and carbon but sacrifice at the higher AN end of the spectrum is then necessary. Reducing the spot size reduces the number of exciting electrons which worsens the signal to noise ratio.

True quantitation is only possible for flat (or at least geometrically defined) surfaces and so only inclusions in polished sections could be analysed quantitatively. Polishing however cuts through the complex structure of many inclusions [7] and creates its own problems in interpretation. This cutting may explain the greater number of multi-element inclusions in polished sections. An inclusion such as that in fig. 3, embedded in matrix, may only produce recognisable signals from its outer component while a polished section may allow all the components to be excited.

A restriction on this type of study is the time taken to acquire the information. Energy dispersive analysis is relatively fast and an inclusion assessment takes about 30 min/sample. Wavelength dispersion is much slower, particularly if the crystal settings have to be changed. The present analysis was done by analysing for oxygen and then going back and analysing the same specimens for carbon on different days.

Wavelength dispersion does not cope well with alloys where molybdenum and sulphur co-exist. Confidence in the results obtained was insufficient to allow definite statements on conformity with BS3531 to be made. The results obtained with a borrowed instrument indicate that such studies should be pursued despite the longer times involved.

4.3 The role of chromium

Austenitic stainless steels owe their corrosion resistance to an adherent oxide film in which chromium plays a major part [18]. If chromium is bound in inclusions it is not available to form the oxide film even though chemical analysis would include bound chromium in the total chromium content. Carbides are more significant than oxides because many oxides form while the steel is still molten, allowing a homogeneous distribution of free chromium while carbides form in the solid state and precipitation tends to occur at grain boundaries and leads to depletion in the surrounding grain.

The formation of chromium oxides is governed by deoxidation practice [5] and can be reduced but probably not eliminated. It would seem that lower manganese and higher nickel concentrations might help.

4.4 Implications of the results

Results from this study seem to indicate that improvements in corrosion resistance of stainless steel could be obtained by better metallurgical control. This would obviously increase the cost of the implant. This increase could only be justified on economic grounds if it could be demonstrated that such a reduction in corrosion or associated improvement in mechanical reliability would lead to less morbidity and a lower rate of medically necessary removal. The cost of the implant is a relatively small proportion of the total cost of the initial treatment, the cost of failure is also high and so a relatively large percentage increase in the cost of the implant might still be cost effective. Possibilities of producing small to medium sized special melts of steel should be explored and the increased costs calculated.

This study could not have been undertaken without the provision of implants by Glasgow Royal Infirmary and Gartnavel General Hospital Orthopaedic Departments. A grant from the SRC towards purchase of the SEM and research studentships from SRC and MRC are gratefully acknowledged. Special thanks are due to Mrs. R. Cuthbert for her patience and help in the preparation of the manuscript.

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Fig. 1 Form supplied to theatre staff for use with retrieved implants

Age and Name of Patient

Patient Hospital Number

Date of Implantation Date of Removal

Antibiotics used: Yes/No. If yes, time administered

Quantity and make

Reason for removal:

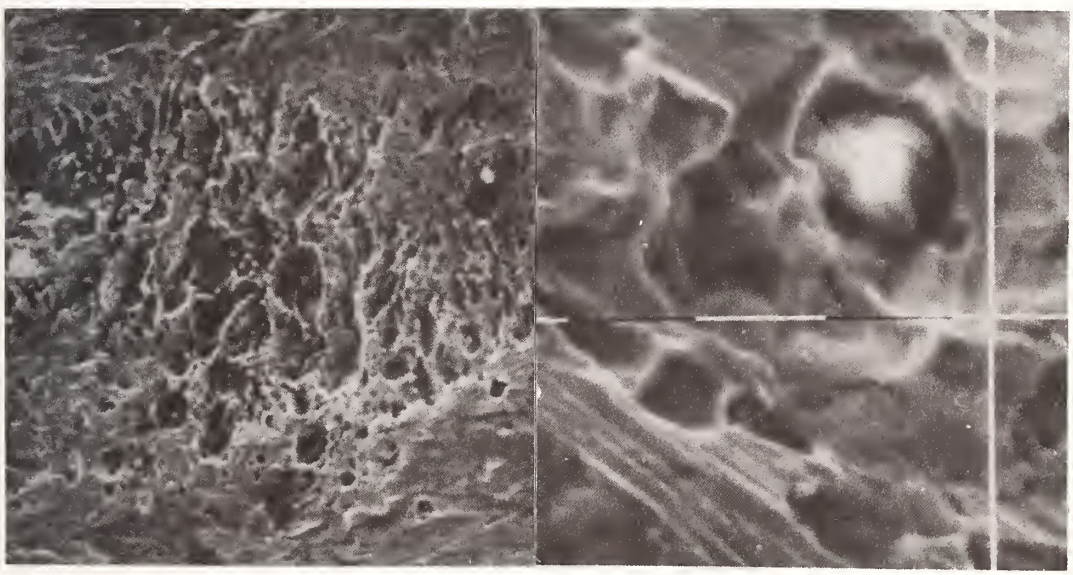

Figure 2. An example of a grade 7 corroded area.

Figure 3. Inclusion in matrix.

RELEASE PHENOMENA

TISSUE RESPONSE TO WEAR DEBRIS IN ARTIFICIAL JOINTS

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Macroscopic and microscopic examinations of the tissue from the joint capsule and the bone / cement - border of revised artificial joints are carried out. The tissue response to wear products of the biomaterials (CoCrMo - cast alloy, stainless steel - AISI 316 L, Polyester, Polyethylene, silicone rubber and bone cement on acrylate base) is described and its connection with implant loosening is demonstrated. The particles are characterised and some clinical measurements of the wear rate of polyethylene are reported.

Looking at the state of art in artificial joint replacement one can say that within the last ten years important improvements have been made on the technical aspect, for example in the design of implants, the quality and combination of biomaterials, the implantation technique and so on. /1/*

On the other hand, the biological aspect has not changed very much, and we must admit, that we still do not know very much about it and that there are still more questions than answers.

The living tissue responds to the material, the artificial joints are made of, as to a foreign body. This reaction is modified by the type of the implant, the type of the material, as well as by the size and the shape of the 'foreign bodies'. Basically, however, the pattern of the tissue reaction is always the same.

The subject of this paper is the interaction between wear particles of biomaterials used for artificial joints and the surrounding tissue.

1. Material and Methods

*Figures in brackets indicate the literature references at the end of this paper.

The results I am going to present were obtained by investigating tissue specimen, taken at reoperations from the capsule surrounding the moving parts of the artificial joints and from the bone in which the implant had been anchored (in the majority of cases by means of bone cement) (table 1.).
Up to now we studied and collected data on 552 tissue samples. The majority of them came from revisions of hip endoprostheses (73.5%) others from second operations of knee-, elbow-, wrist- and fingerjoint endoprostheses of different types.

Table 1. Origin of the Tissue Samples studied in the time period January, 1970 - December,1979

O R I G I N		N U M B E R
Capsule		236
Bone/Cement border		154
not specified	44	
of the pelvis	54	
of the leg	56	
Bone		59
not specified	21	
of the pelvis	9	
of the leg	29	
Debris of tissue		23
Fibrous tissue, not specified		63
Patella		8
Interposition		4
Fistula		2
Zone of Osteolysis		2
Lymphnode		1
total number of tissue samples		552

The materials included metals, polymers, ceramic and X-ray contrast medium of the bone cement.
The metals were CoCrMo-cast alloy, FeNiCrMo steel (AISI 316L) and CoNiCrMo-forged alloy.
The CoNiCrMo-forged alloy is now used only for the anchoring parts of the prostheses; in some types of joints also the moving parts had been made out of CoNiCrMo-forged alloy, but in those cases the articular surfaces were especially chromium plated.
The polymer materials were Teflon (Tetrafluorethylene), Ultra High Molecular Weight Polyethylene (RCH 1000 type), Polyester (polyethyleneterephthalate, Hosta-

dur KVP - 4022/AP4), Polyacetal (polyoxymethylene, homopolymer, Ertacetal) and Silicone Rubber. As bone cement on the basis of Methylmethacrylate mainly PALACOS, seldom CMW-Bone Cement, was used. The contrast medium of PALACOS is Zirconiumdioxide (ZrO_2), the contrast medium of CMW-Bone Cement is Bariumsulphate ($BaSO_4$).

The ceramic material was High Density Aluminium Oxide.

The materials of the articulating surfaces were used in different combinations, as metal to metal, metal to polymer, ceramic to ceramic and ceramic to polymer coupling.

The causes, which made a surgical revision of the artificial joint necessary were loosening, evtl. with fracture of the implants, paraarticular calcifications, complications due to malposition or technical errors during implantation as well as complaints of the patient without any visible fault in the function of the prosthesis.

Cases with deep infection were excluded from this study.

The tissue material subjected to investigation consequently originated chiefly from joint replacement failures that means it represents a negative selection. Such cases, however, are most suitable to illustrate the whole range of problems connected with tissue reactions to wear particles.

Immediately after excision from the patients' bodies, the pieces of tissue were fixed in neutral formalin and representative samples were selected for analysis and histology. The analytical methods used were spectral analysis, atomic absorption spectrophotometry and electron microprobe analysis /2/. For histological examination, serial sections prepared from paraffin embedded tissue material were used; where necessary, decalcified material and frozen sections were also employed. The preparations were studied by light microscopy, polarized-light microscopy and - after special preparation - by scanning electron microscopy as well.

2. Results

The presentation of our findings is subdivided into a synoptic description of the processes taking

place in the tissue and a special discussion of the tissue reactions associated with the respective implant materials used. The identification of particles of the different materials by microscopic and analytic investigations we described in detail elsewhere /3/.

2.1 Tissue Reactions in General

After an endoprosthesis has been implanted, a new capsule of connective tissue is formed in the wound cavity around the artificial joint. This replaces the original capsule, if it has been excised. The new capsule resembles a normal synovium. However the architecture of the tissue is rather rough and sometimes it is hard to identify the different layers, expecially if regenerative processes are combined with reactions to foreign bodies /4,5,6/.

These foreign bodies consist of particles produced by wear either from the moving surfaces of the joint, from the bone cement within the implant bed or from broken prosthetic parts. Like every other material even polymer plastics, metal and ceramic materials especially selected for articulating joint surfaces are subjected to abrasion. The worn off particles, which accumulate in the joint cavity are incorporated into the capsule mainly by direct phagocytosis.

The continuous production of wear particles necessitates a constant supply of cells capable of phagocytosis. Thus a foreign body granulation tissue is formed within the capsule. Depending on the worn off foreign material it may consist almost entirely of histiocytes or it may contain predominantly multinucleated giant cells. Small particles are usually stored by mononuclear histiocytes, whereas foreign body giant cells accumulate around bigger particles.

All of these cells may agglomerate and form nodules which tend to become necrotic in the center.Also superficial layers of the capsule can become necrotic. When the necroses are rejected into the joint cavity, they accumulate there as caseous, paste like masses, intermingled with foreign body particles. This joint content permanently irritates the capsular tissue and promotes further organization, which leads to the production of even more granulation tissue.

Another feature of the foreign body granulation tissue is its tendency towards fibrosis and scar formation. In this process more and more collagen fibres are differentiated. The capsule is growing thicker and the cells are perished with increasing fibrosis .

Lymphocytic and plasmacellular infiltrations may occur even without bacterial inflammation. This may be a

sign of a humoral defense process or of a hypersensitivity to the incorporated material respectively.

The capsular tissue is able to transport the phagocytized particles away and to eliminate them. This transprt is accomplished through the lymphatic system via perivascular lymph spaces.

It seems to be proved, that a certain amount of wear particles can be eliminated in this way by the capsular tissue. This mechanism can establish an equilibrium between the abrasion, phagocytosis and elimination of wear particles. This equilibrium has to be looked upon as the optimum state as long as wear cannot be avoided totally (fig. 1).

An increasing release of wear particles induces an increased formation of foreign body granulation tissue. But the bigger the granulomas, the greater is their tendency to become necrotic. The necroses, accumulating in the joint cavity, cover most of the inner surface of the capsule. Such a capsule is no longer able to eliminate wear products. At this point, the foreign body reaction in the surrounding of the artificial joint decompensates (fig. 2). Now, in addition to the joint capsule, other tissues become involved in the phagocytosis, storage and transport of wear debris. These tissues are

-the connective tissue at the interface between bone and implant,
-the bone marrow.

With a development of a typical foreign body granulation tissue in the neighbourhood of bone, bony trabeculae are subjected to resorption too. This results in a loss of bony anchors, required for the fixation of the implant (i.e. the bone cement) and loosening of the implant develops.

2.2 Tissue Reactions in Relation to Different Materials

2.2.3 Metal

The amount of metallic wear particles, stored in the adjacent tissue varied from case to case and there was also a great variation with the different types of endoprostheses. 83% of visible particles measure less or equal 1.13μm^2. Fig. 3 shows the size distribution of metal wear particles measured by television image analysis of unstained histological sections.

The smallest amount and the smallest sizes of me-

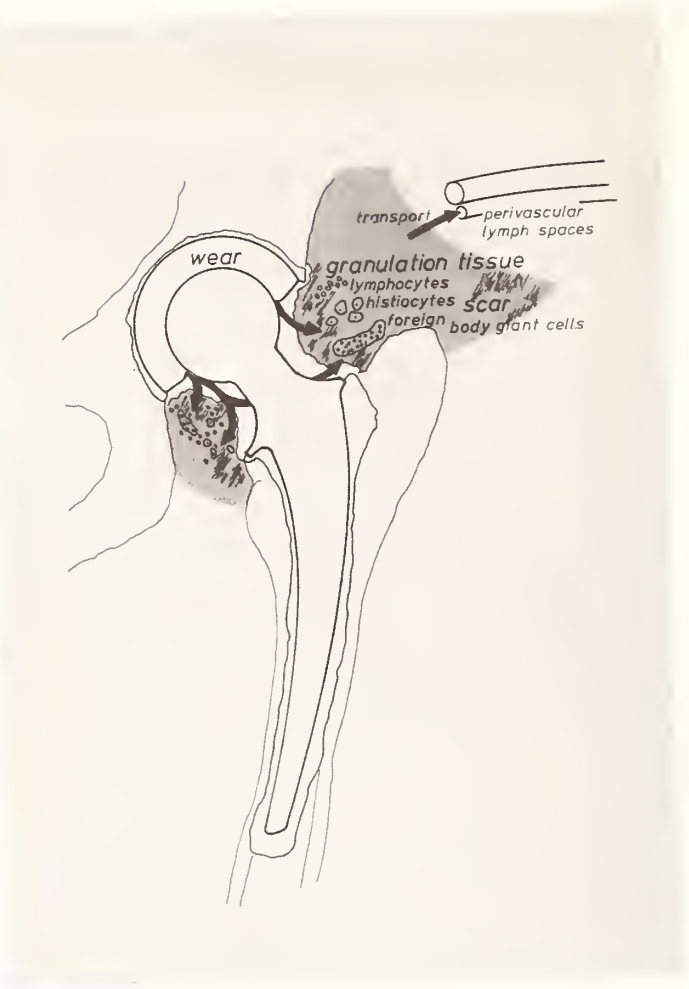


Figure 1. Equilibrium between the abrasion, phagocytosis and elimination of wear particles.

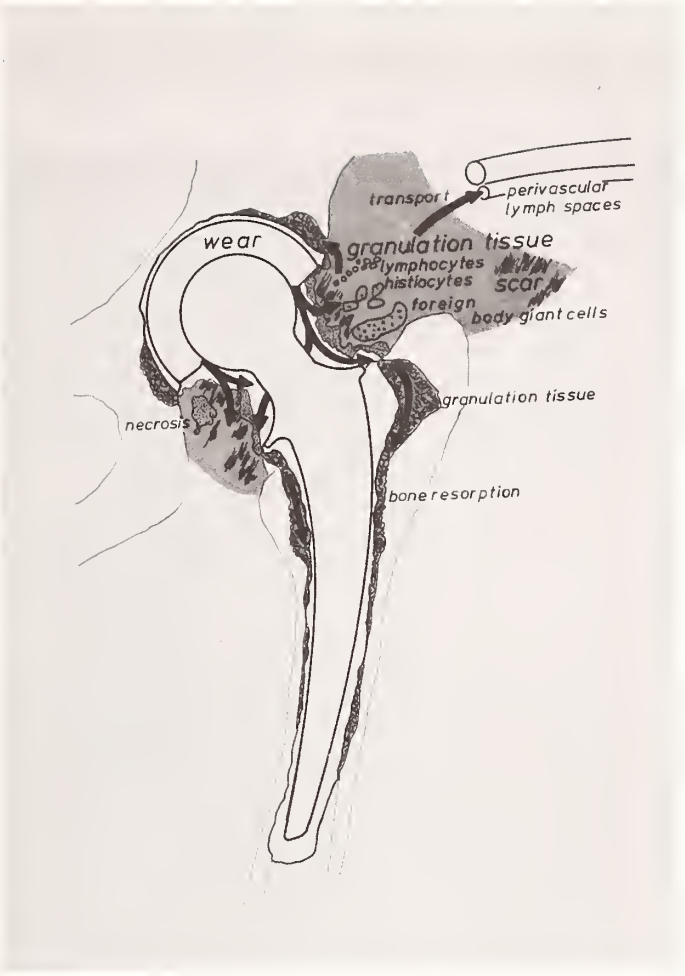


Figure 2. Decompensation of the foreign body reaction. The bone / cement - border of the femur as well as of the acetabulum is involved in the storage of wear particles.

tallic wear particles were detected when the artificial joint consisted of a metal and a polyethylene component, and the prosthetic parts had been intact. The tiny particles were phagocytozed by histiocytes as well as by foreign body giant cells, together with plastic and PMMA-debris. One cannot see that the tiny metal particles do any har to these cells.

Greater amount of metallic wear products and bigger sizes of particles we sometimes found in the surrounding of joints with plastic and metal components when they were in function for a longer period of time (more than 6 years), or when the femoral stem had become loose and was broken. Furthermore around metal to metal joints, like the McKee-Farrar-type, greater amount of metallic wear products could be seen. The particles were stored mainly in histiocytes. In those cases the newly formed joint capsule showed a stronger tendency towards fibrosis and necrosis.

Excessive amounts of metallic wear debris were produced by hinged, all metal knee- and elbow-prostheses. In those types also the size of the particles was considerably larger.
In these cases, macroscopically the capsular tissue had a more or less intense black colour, in particular at the inner layer facing the joint cavity. The metallic particles mainly were to be found in histiocytes whose cytoplasm often was completely packed with black particles. The phagocytes were mostly arranged perivascularly in strings or foci, so that they appeared to form granulomas. A strongly marked lymphoplasmacellular infiltration was sometimes notable without any evidence of bacterial infection. The tissue shows a strong tendency to form collagenous fibres, i.e. fibrosis and scar formation. On the other hand we found together with an above the average amount of metallic wear a considerable tendency of the capsular tissue to become necrotic. Then, in the joint cavity masses of fibrin and necrotic debris were found, aggregated on the inner surface of the capsule. They also contained large amount of black, metallic particles. This indicates a decompensation of the foreign body reaction in the joint capsule. The tissue at the interface between bone and cement-implant as well as the RHS of the bone marrow had already become involved in the storage of metallic wear particles. This could be recognized macroscopically by the black colouring of the tissue. By help of the microscope, a foreign body granulation tissue with phagocytes containing the metal particles and with resorption of the adjacent bone trabeculae could also be seen at the bone / cement - interface and in the marrow spaces. Clinically most of these endoprostheses had been loose (fig. 4). A comparative survey is given

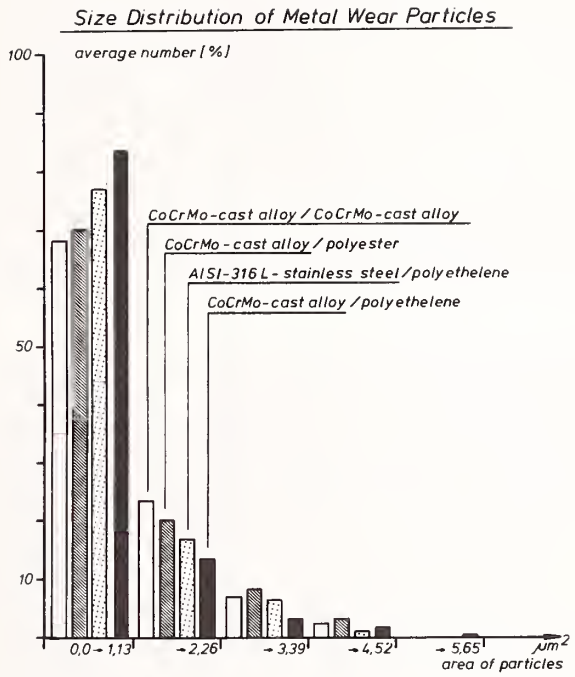
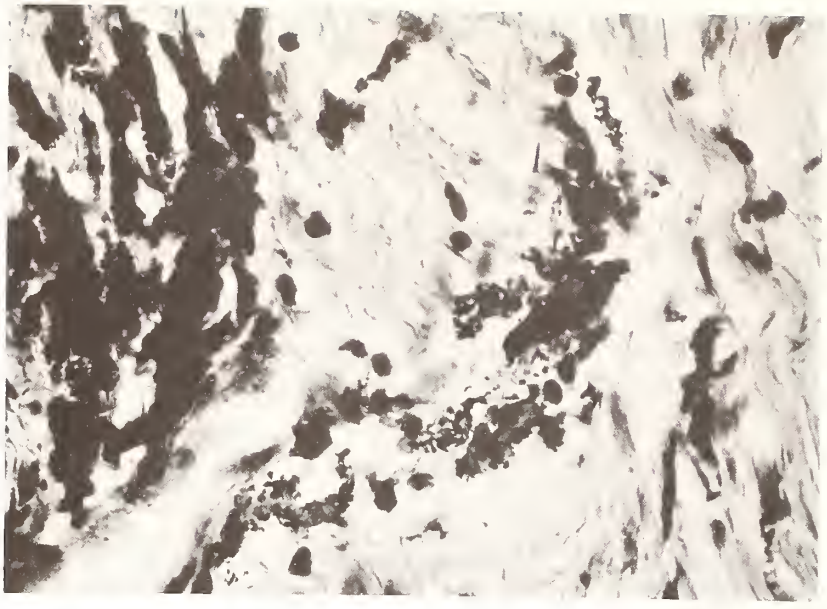


Figure 3. Size distribution of metal wear particles stored in tissue surrounding total hip replacements of different material combination. The average number (%) of particles measured to ly in a certain range of size is given. Metal-on-metal total endoprostheses produced the most, metal-on-polymer less amount of metallic wear. The material combination CoCrMo-cast alloy on Polyethylene proved to cause the least metallic wear.



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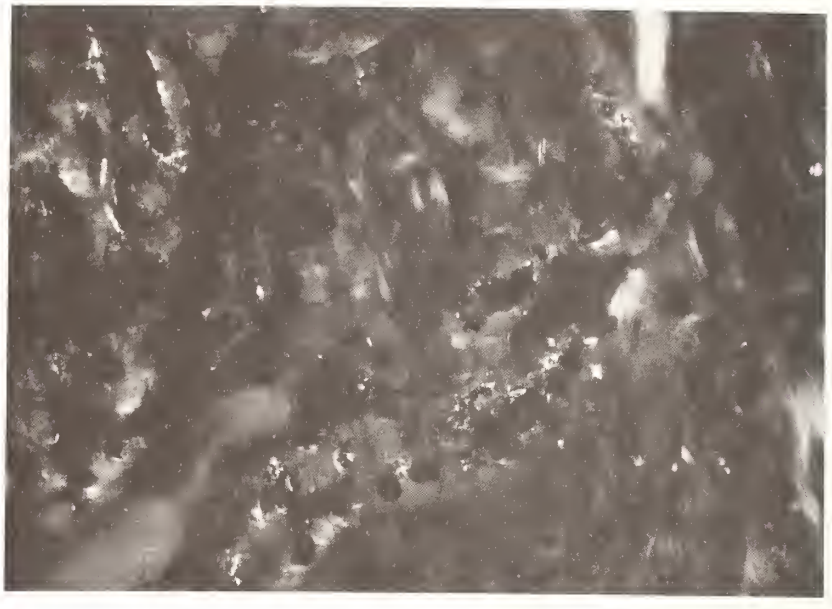


b)

Figure 4. Microphotographs, 800 magnification, a) bright light, b) polarized light show a tissue section, stained H&E, of capsular tissue surrounding a total elbow-joint replacement after two years of function, material combination: metal on metal. Diffraction of the polarized light on orientated particle borders causes changes of the rotatoinal plane of polarisation. Thus the particles produce bright light effects.

in table 2.

2.2.4 Polymer Materials

2.2.4.1 Teflon (Tetrafluorethylene) and Fluorosint (Tetrafluorethylene filled with mica)

Acetabular cups made out of Teflon or Fluorosint were subjected to a high rate of wear. The metallic head of the femoral component shifted on an average of 2.5mm pa. into the cup, producing an enormous amount of wear particles in a wide range of size. They caused a foreign body reaction in the joint capsule which was characterized by formation of large granulomas, containing numerous giant cells and a strong tendency to necrosis. That means the foreign body reaction of the capsule decompensated soon. In the joint cavity masses of caseous, necrotic tissue debris accumulated, containing the wear particles. The tissue at the cement / bone - interface always had become involved in the response to the wear products, forming a foreign body granulation tissue which caused resorption of the adjacent bone. The osteolysis markedly occured at the calcar femoris and in the depth of the acetabulum. Loosening or fracture of the prosthetic components most often led to a failure of the artificial joint.

Since Teflon and Fluorosint are no longer used as materials for artificial joints we will not go into further details.

2.2.4.2 Polyester (Polyethyleneterephthalate)

In artificial joints, having a metal component for the femoral head and a polyester socket, the production of wear debris resembles in somewhat those hip replacements with metal and polyethylene combination, showing an increased rate of abrasion. In other words: the polyester sockets were subjected to a greater amount of wear than polyethylene sockets. In some instances the polyester sockets broke after some years of function.

In artificial hip joints with trunnion bearing, where the ball was made out of polyester and the femoral stem and the socket out of metal, an excessive amount of wear occured with the polyester. The polymer was abraded mainly at the bore of the cylinder of the ball. The size of the abraded particles ranged from 0.5 up to 20 µm (seldom up to 100 µm) in diameter. 34 % of the visable particles ranged from 1.1 up to 2.2 μm^2. Figure

5 shows size distribution of polymer wear particles measured by means of television image analysis. In such cases the joint capsule was considerably increased in thickness and consisted, expecially in the inner layers, of a granulation tissue in which mono- and binuclear histiocytes of epitheloid appearance predominated, whereas multinucleated foreign body giant cells were less frequent. The small and medium sized polyester particles were stored in the plasm of the histiocytes while larger polyester particles were either surrounded by giant cells or were situated extracellularly in the tissue (fig. 6). The foreign body granulation tissue formed large nodules with necroses in the center and a palisade-like arrangement of cells as well as lympho-plasmacellular infiltration in the periphery. Together with the appearance of giant cells the picture resembled tuberculosis. The tendency to necrosis was highly pronounced in these capsules. The capsular tissue furthermore showed a strong tendency to fibrosis and hyalinisation and consequently to scar formation. Decompensation of the foreign body reaction was indicated by the accumulation of large amounts of pasty masses (histologically recognizable as fibrin and necrotic tissue) in the joint cavity, covering the inner surface of the capsule and filling deep crypts between course capsular villi. The necrotic masses are intermingled with polyester particles similar to those incorporated in the capsule. In all of these cases a typical foreign body reaction additionally developed at the bone - cement - interface and within the marrow spaces of the adjacent spongious bone (see comparative survey given in table 2). Again, here the bone trabeculae were resorbed and the prosthetic implants loosened. The loosening clinically occured on average after a relatively short period of 3 to 4 years of function of the joints in the human body.

2.2.4.3 Polyacetal (Polyoxymethylene, homopolymer)

The changes of the histological response to the implant evoced by wear particles released from polyacetal resemble very much those observed with polyester.

2.2.4.4 Polyethylene

(Ultra-High-Molecular-Weight Polyethylene)

In artificial hip joints we found that the material combination of polyethylene (socket) and CoCrMo-cast alloy or chromium-plated CoNiCrMo-forged alloy (femoral head) showed the smallest rate of wear. In the surroun-

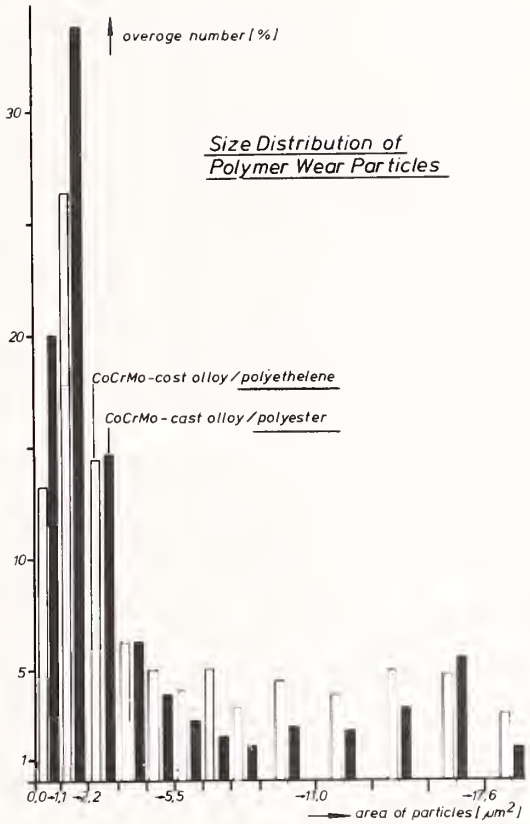
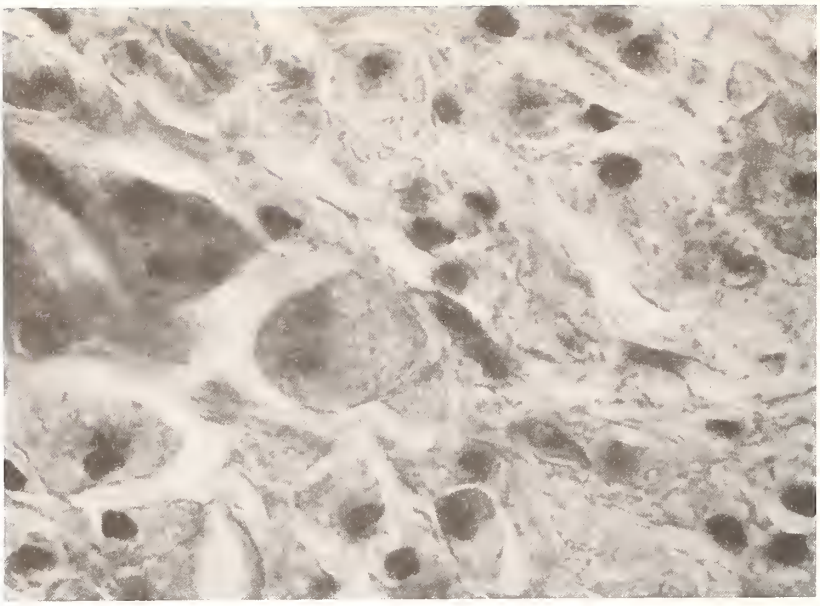


Figure 5. Size distribution of polymer wear particles gained by television image analysis of tissue sections surrounding total hip replacements. The average number (%) of particles measured to ly in a certain range of size is given. The polyester particles are on average twice as much stored in the tissue as polyethylene particles.



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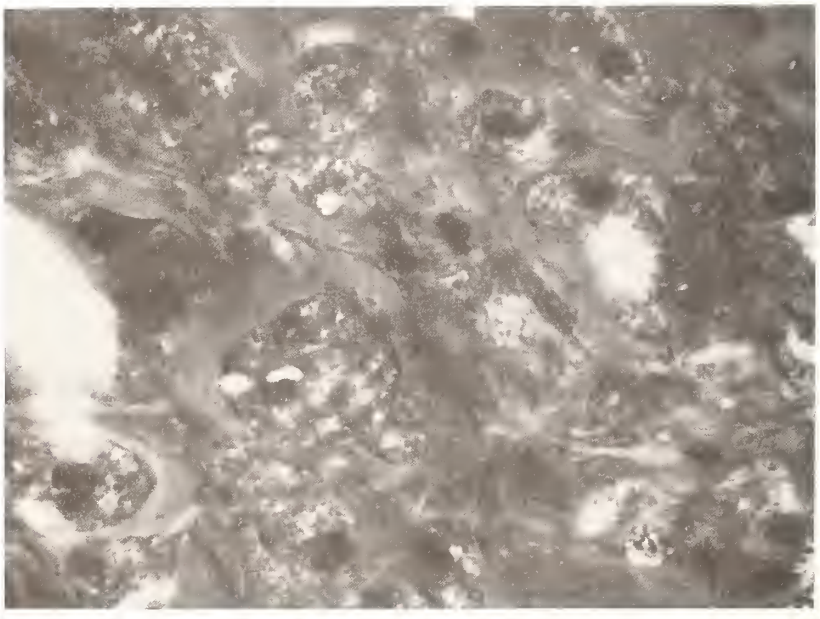


b)

Figure 6. Microphotograph of tissue section, stained H&E, of capsular tissue surrounding a Weber-Huggler total hip replacement after three years of function, material combination: CoCrMo-cast alloy on Polyester. a) bright light, b) polarized light, note double diffraction of the polymer particles.

PROSTHETIC MATERIAL	STORAGE OF PARTICLES: HISTIOCYTES	STORAGE OF PARTICLES: FOREIGN BODY GIANT CELLS	GRANULOMAS	NECROSIS	FIBROSIS	LYMPHOPLASMACELLULAR INFILTRATION	DECOMPENSATION	TOTAL AMOUNT OF WEAR PARTICLES
METAL	+++	+	+	++	++	+++	+	+ or ++
TEFLON/ FLUOROSINT	+++	+++	++++	++++	+++	++	+	++++
POLYESTER	+++	+	++++	++++	+++	++	+	++++
UHMW-POLYETHYLENE	+	++	+	+	++	(+)	+	++
SILICONE RUBBER	+	++	++	+	+++	(+)	+	+++
BONE CEMENT	++	+++	++	(+)	+	(+)	+	+++
AL_2O_3-CERAMIC	++	+	+	?	+	?	+	++

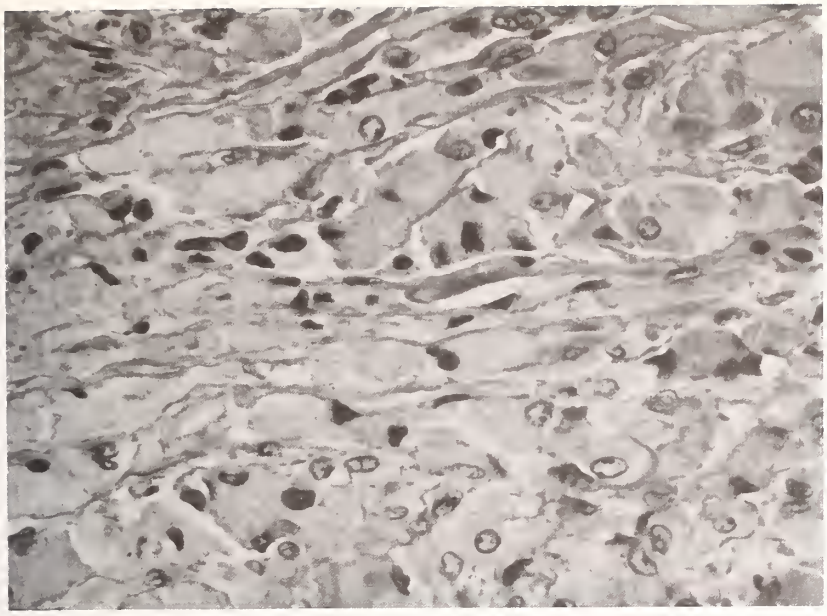
(+) very small + slight ++ moderate +++ much ++++abundant

Table 2.

ding tissues of these joints only very few polyethylene particles were to be seen, mainly situated in the vicinity of vessels, where they apparently were transported away via the perivascular lymph spaces (fig. 7). Here, obviously an equilibrium had been established between the release of wear particles and the tissue reaction, and had been maintained even after a long lasting function period of the endoprostheses. Their size ranged from 0.5 to 50 µm in diameter, some even up to 100 µm. Most of the polyethylene particles were found to be in the same range of size as those from polyester when measured by television analysis (fig. 5). But in the range of 4.4 up to 15.6 μm^2 greater amounts polyethylene particles were found.

The wear of the polyethylene sockets in dependance of time can be determind by measuring the X-ray-pictures of the hip prosthesis, taken during the follow-up period. Using the method of SCHEIER and SANDEL /7/ we measured the wear of polyethylene sockets of 254 hip prostheses with an implantation period of 6 to 96 months. The measuring method based on the determination of the position of the prosthetic head in the socket. If wear occurs at the articular surface of the cup, the head migrates in the direction of abrasion which lies in the main bearing area of the joint. The metal wire marker of the polyethylene socket runs equatorially around the socket and appears on radiographs as an ellipse. The displacement of the head can be estimated by measuring the distances 1. between the margin of the head and the vertices of the ellipse and 2. between the center of the head and the main axis of the ellipse. During the first year after operation the shift of the head was about 0.3 mm on average but decreased in the following years to an average value of 0.14 mm per year / 8,9,10 / (fig. 8). Most of the measured hip prostheses clinically showed good functional results and a normal weight bearing of the artificial joints was possible. There were no hints of imminent failures of the endoprosthesis, neither signs of loosening nor other complaints (except some typical pain when starting to walk).

Basing on these results it can be considered that the capsular tissue is able to incorporate and transport continuously wear particles, originating from the articular surface of a polyethylene socket with a rate of wear of 0.1 mm per year. This amount of wear can be taken as a limit for the ability of the tissue to cope with wear particles and maintain the postulated "equilibrium".



a)

b)

Figure 7. Microphotograph of tissue section, stained H&E, of capsular tissue surrounding a Müller total hip prosthesis after four years of function, material combination: CoCrMo-cast alloy on UHMW Polyethylene, 400 magnification, a) bright light, b) polarized light. Particles are visible by means of their birefringence.

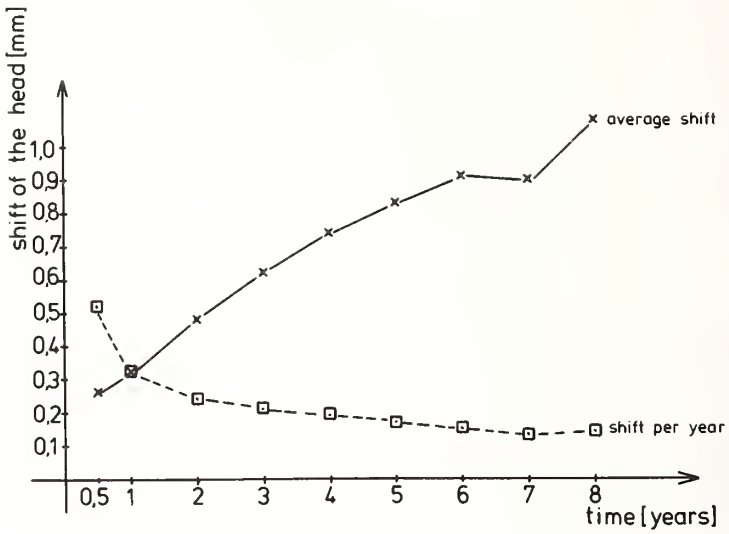


Figure 8. Evaluation of the shift of the prosthetic head into the hip socket measured from radiographs. The hip prostheses were of the Müller type with a metal stem and head (CoCrMo-cast resp. CoNiCrMo-forged alloy) and a polyethylene socket. The average values of the shift and the yearly rate of shift are shown in dependance of the time period after operation.

An increase of the amount of wear particles of polyethylene can occur if unfavourable conditions exist in addition to the functional stress of the joints. For example high abrasion of polymer material can be caused by

- scratches at the highly polished joint surface of the metallic head,
- bone fragments being entrapped between the artucular surfaces,
- a design of the prosthesis not corresponding to the material' s properties.

This was true, for example, when polyethylene had been used as material for the ball of a total hip endoprosthesis. An enormous abrasion of the polyethylene took place at the convex surface of the ball which finally caused loosening of the prosthetic parts (11).

Extremely worn-out polyethylene sockets can cause wedging of the metal head and, because of an overstress of the cement anchors, loosening of the implants can be induced.

In cases with a relatively high wear of polyethylene, a massive storage of polyethylene particles could be found in the capsular tissue, often in connection with small amounts of metallic debris. The smaller polyethylene particles are stored in histiocytes,the larger ones in multinucleated giant cells. If histiocytes and giant cells accumulate, they form a foreign body granulation tissue,which is typical for the storage of polyethylene wear debris. Furthermore there is a more or less strongly marked formation of collagenous fibres, resulting in fibrosis and scar formation. On the other hand, the capsular tissue shows little tendency to hyalinization and necrosis. Lymphoplasmacellular infiltrates, if at all , were observed on a very small amount only (see table 2).

Under circumstances of a higher wear rate we found even in joints with polyethylene bearings a decompensation of the foreign body reaction. Then, the tissue at the cement / bone - interface also showed the development of a foreign body granulation tissue which contained polyethylene wear products, and which initiated bone resorption, finally leading to loosening of the implants. Thus, in principle, loosening due to excessive wear even can occur with polyethylene bearings.

2.2.4.5 Polymethylmethacrylate Bone Cement and Contrast Medium ZrO_2 and $BaSO_4$

Deposits of Polymethylmethacrylate (PMMA) and

contrast medium could always be found in the tissue of the implant-bed and in the joint capsule.

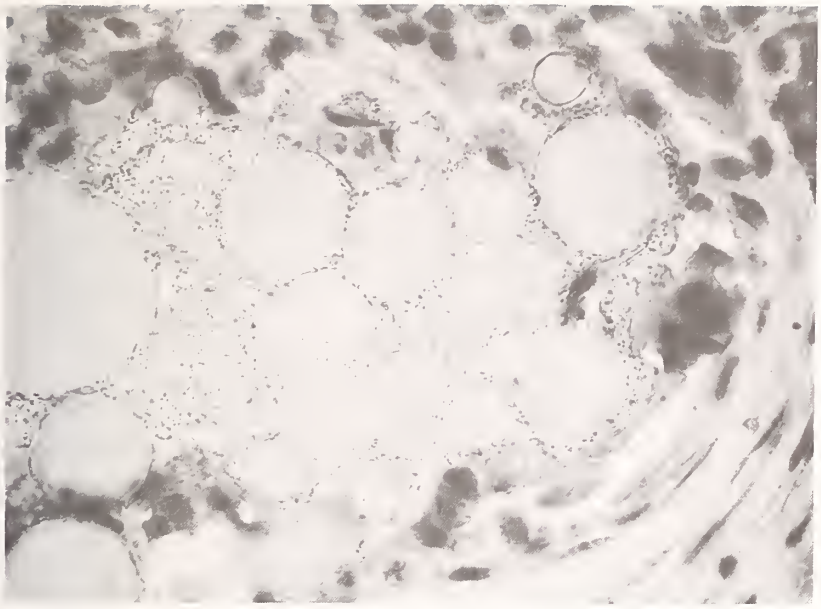
PMMA is soluble in conventional solvents used in histology-preparations. Consequently it is dissolved in histological sections prepared from paraffin-embedded tissue material. On the other hand, in frozen sections polymethylmethacrylate remains preserved without any changes. It stains red-orange with SUDAN III (fig. 9).

The contrast medium (ZrO_2 or $BaSO_4$) which is usually added to the bone cement is not soluble in conventional solvents. It therefore remains in place even after paraffin-embedding and can therefore be used as a tracer to detect or to prove inclusions of bone cement particles in the tissue.

Within fragments of bone cement the contrast medium shows the same distribution as in the cured bone cement mass : The particles lie between the pearls. In the neighbourhood of smaller PMMA-inclusions often the particles of contrast medium can be found in histicytes as well as in giant cells. Sometimes the foreign body granulation tissue contains relatively large amount of particles of the contrast medium.From this finding one might conclude that bigger bone cement fragments had been disintegrated by cellular activity so that the particles of the contrast medium could become liberated an phagocytosed by the cells.

Larger Polymethylmethacrylate particles (up to 1 and 2 mm) were surrounded by numerous foreign body giant cells. Frequently, a cell-containing notwork could be seen extending between the beads of the polymer. Medium sized and small fragments (only few µm) are completely incorporated in the plasm of multinucleated foreign body giant cells. The very small, dust-like PMMA-particles were stored in mononuclear histiocytes; the plasm of these cells became granular and foamy. The PMMA-containing cells accumulated and formed granulomas (compare with table 2).

Depending on whether large or small particles preponderate, foreign body giant cells or histocytes dominate the histological picture. When only a few acrylate inclusions are present, they are distributed irregularly within the capsular tissue and are mostly enveloped by foreign body giant cells. The tendency to fibrosis of the tissue containing PMMA-particles is weak, especially in areas abounding with giant cells. Necroses and hyalinization were observed sometimes; lymphoplasmacellular infiltrates were rare. Frequently PMMA particles were observed in the peri-



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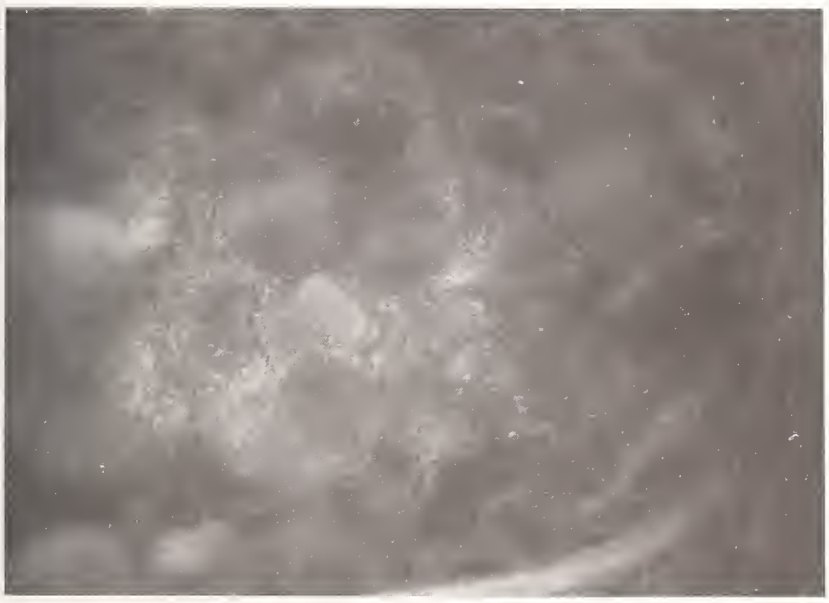

b)

Figure 9. Microphotograph of frozen tissue section, stained Sudan III, of the bone - cement border from a Müller total hip replacement after five months of function, material combination: CoCrMo-cast alloy on Polyethylene. 560 magnification, a)bright light, b) polarized light. Note that non dissolved PMMA-beads show little if any double diffraction.

vascular lymph spaces, even in a great distance from the inner surface of the capsule. This finding suggests that a transport of bone cement fragments too via the perivascular lymph spaces occours.

Like the other biomaterials, also particles of the PMMA-bone cement can cause a loosening of the implants due to the development of a foreign body reaction at the bone / cement - interface. The only difference is that the particles of PMMA originate not at the joint surfaces but directly at the bone / cement - interface. This occurs if the bone cement cuff breaks or if single pearls or clusters thereof are abraded or broken out of the surface of the cement implant, for example due to micromovements during weight bearing. These fragments are incorporated or surrounded by histiocytes and foreign body giant cells, which again are forming a granulation tissue capable to resorb the bone from the inside (fig. 10).

2.2.4.6 Silicone Rubber

This material is used for implants which are called 'interpositional arthroplasties' in finger-, wrist- and elbow joints. These implants are not firmly anchored to the bone but become fixed by an encapsulation process due to the formation of a functionally adapted fibrous capsule /12/. Under movement of the joint, a shifting and rubbing of the implant against the bone can occour which sometimes causes a considerable abrasion of silicone rubber particles (size of a wide range: 1 - 50 - 100 µm) from the surface of the implant. These particles are phagocytosed by the surrounding tissue, which is the abovementioned fibrous capsule (see table 2). The tissue develops a foreign body reaction with the appearance of foreign body giant cells and histiocytes which incorporate the silicone particles and form granulomas of considerable dimensions (fig. 11). Not only in the fibrous capsule but also in the marrow spaces of the adjacent bone this foreign body granulation tissue occurs and gives rise to bone resorption, resulting in a more or less pronounced osteolysis /13/.

2.2.5 Ceramic

In contrast to the initial hope, the combination of ceramic material in artificial joints will not produce a substantial amount of wear particles, one had to learn in the meantime that even the highly wear

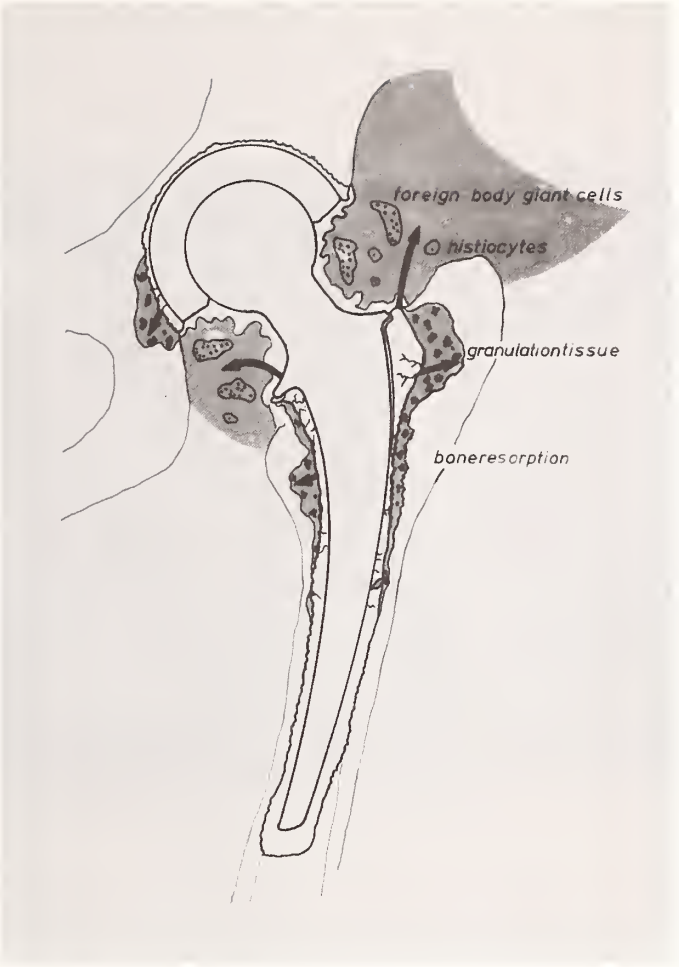

Figure 10. Formation of a foreign body granulation tissue and bone resorption induced by scattered bone cement.

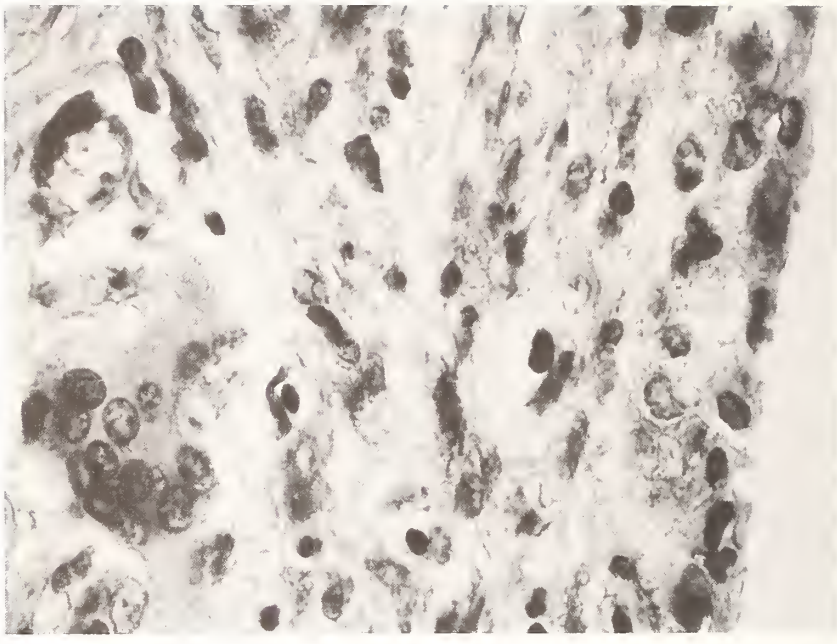

Figure 11. Tissue sample, stained H&E, surrounding a Swanson hand interponent, completely made out of silicone rubber after 1.75 years of function. Abraded particles are hardly visible in normal transmitted light. Stored in foreign body giant cells and histiocytes as well as extracellularly the round and oval particles show a slight dark-lined border. Microphotograph, 800 magnification, normal transmitted light.

resistant High Density Aluminum Oxide Ceramic (14) is subjected to abrasion (15) (fig. 12). The ceramic particles released from the articluar surfaces were incorporated in phagocytes of a foreign body granulation tissue which appeared in the joint capsule as well as at the bone / cement - interface (comperative table 2).

3. Discussion and Conclusions

Investigating the biological response to wear debris in total joint replacement we came to the following conclusions:

- the presence of a foreign body reaction in the surrounding of an implant at all indicates, that constituants of the implant's material are released into the tissue.
- The intensity of the foreign body reaction and the amount of particles incorporated in the tissue can be taken as measure for the materials'wear resistance under use in the human body.
- The biocompatibility of implant materials can be estimated from the character of the foreign body reaction.
- Judging the effects which biomaterials may have on the living tissue one should keep in mind that tissue necroses can appear not only as a result of toxicity but also as a consequence of excessive proliferation of a foreign body granulation tissue.

- The occurence of lymphocytes and plasma cells in the tissue in connection with a foreign body reaction does not necessarily indicate a bacterial inflammation.

  It might be supposed that these infiltrates have something to do with a hypersensitive response. Besides an accumulation of lymphocytes and plasmacells especially adjacent to metallic wear debris, we did not find any changes which could be designated as characteristic for an allergic reaction to materials of the implants. Thus we could not confirm the statement of EVANS et al. /16/ or Jones et al. /17/ that loosening of the implants can be a result of tissue changes due to metall allergy.

- A certain amount of wear particles even of bigger sizes can be eliminated by the capsule tissue. This mechanism allows to achieve an equilibrium between abrasion, phagocytosis and elimination of wear particles. This equilibrium we have to look upon as optimal as long as it is not possible to avoid wear totally.

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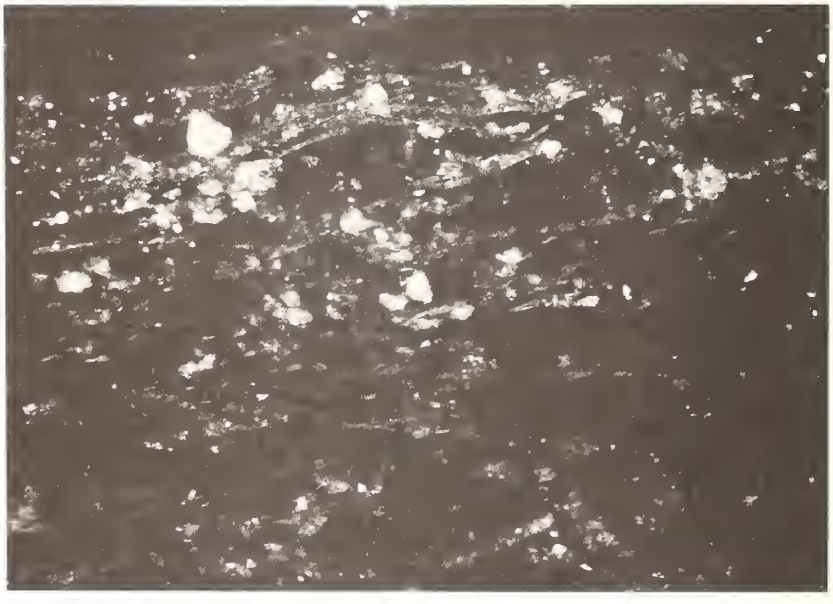

b)

Figure 12. Microphotograph of ceramic particles out of capsular tissue of an all-ceramic total joint replacement, 320 magnification, a)normal bright light, b) polarized light. Birefringence of particles depending on their orientation to the optical axis.

The release of excessive amounts of wear particles causes a decompensation of the foreign body reaction in the joint capsule recognizable by the incidence of large areas of necroses in the foreign body granulation tissue. These necroses impede the phagocytic activity of the capsular tissue. Then in addition to the capsule, the tissue of the bone / implant-interface becomes involved into the foreign body reaction, resulting in the formation of a foreign body reaction, resulting in the formation of a foreign body granulation tissue, resorption of the adjacent bone and finally loosening of the implant. The relationship between excessive wear, bone resorption of the implant bed and loosening of the implant has been proved now for 7 different materials. The connecting link of these phenomena is the foreign body reaction to wear products. For this mechanism the chemical structures of the implant materials seem to be much less important than the amount of wear products.

- If larger amounts of tissue necroses accumulate within the joint cavity, they can interfere with the lubrication of the articulating surfaces.

- The tendency to thickening and fibrosis of the joint capsule can result in an increasing loss of mobility of the artificial joint. This is most important in particular for the finger joints /13/.

- For the moment, we found, that the material combination of polyethylene with metal still seems to be the best, because it showed the smallest quantity of wear and the slightest foreign body reaction of the surrounding tissues.

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MATERIALS DEGENERATION CAUSING LATE FAILURE OF MECHANICAL HEART VALVE PROSTHESES: PROBLEMS AND PROMISE

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Materials degradation with resultant clinically significant valvular dysfunction has been an important late complication of cardiac valvular replacement with mechanical prostheses. Major mechanisms of failure are primarily related to either lipid absorption by silicone elastomers or abrasive wear of polymers. In a review of the necropsies of 99 patients dying late after cardiac valvular replacement, we encountered two cases of fatal valve deterioration, one involving each of the above failure modes. We examined by scanning electron microscopy and analytical surface profilometry seven contemporary heart valve prostheses recovered from this series, all of which had no clinical or pathological evidence of degeneration/dysfunction, and all of which contained pyrolytic carbon components and had been in-situ for 30 months or longer. Results of this analysis suggest that progressive deterioration by abrasive wear of pyrolytic carbon heart valves will not be a significant problem.

1. Introduction

Prosthetic valve malfunction resulting from materials degeneration has been an important late complication after cardiac valvular replacement. Reoperation with replacement of the prosthetic valve for degeneration/dysfunction was required in 2.5% of 891 patients undergoing valve replacement from 1962 to 1977 in one study [1][2] and 1.5% of 799 in another [2]. Mortality for reoperation has been high --- 36% and 42% in the above studies. In a necropsy study of patients having a variety of

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mechanical prostheses, prosthetic valve deterioration was the cause of death in 19% of 134 patients dying more than 60 days after valve replacement [3]. The significance of dysfunction among specific prosthetic valve designs varied widely.

In this report we examine the problem of mechanical prosthetic valve dysfunction due to materials degeneration from three approaches. First, we review the various modes of failure that have been identified for the wide variety of mechanical heart valve prostheses in past and current use. Secondly, we examine fatal valve degeneration among 99 patients dying late (up to ten years) after receiving prosthetic heart valves. Lastly, we summarize our analysis of abrasive wear in eight pyrolytic carbon-containing heart valve prostheses recovered from patients who died or required reoperation, seven of these after implantation times of greater than two-and-a-half years.

2. The Problem: Materials Degeneration and Valve Durability

The silicone ball occluder in early models of the Starr-Edwards[3] and Smeloff-Cutter caged ball prostheses was subject to lipid infiltration and subsequent swelling, distortion, grooving, cracking, embolization of poppet material or abnormal movement of the poppet due to sticking [5,6]. This phenomenon, known a ball variance, often led to acute valvular malfunction and death. In one large series, 16 of 25 (64%) of deaths of patients who survived more than two years (average 43 months) after aortic valve replacement with caged ball prostheses were caused by ball variance [7]. Mitral ball variance (fig. 1) has been less common than aortic, suggesting that hemodynamic factors play a role [7,8]. For valves produced since 1964, changes in the fabrication of the silicone elastomer have almost eliminated ball variance as a problem. However, there have been occasional reports of severe poppet wear in some cloth-covered silicone ball containing valve prostheses that were implanted during 1971-74 [9]. The mechanism of this complication is abrasive wear and is not related to lipid infiltration. Use of a hollow ball fabricated from metal (chromium-cobalt alloy) has now virtually eliminated post-implantation changes in the poppets of caged ball valvular prostheses.

Cloth-covered caged ball valves with silicone and metal poppets do suffer problems related to cloth wear (fig. 2) and attendant hemolysis [9-11]. Although the exact incidence is not known, evidence of cloth wear in areas of abrasion by the metal poppet was seen in 10 patients reoperated for prosthesis-related complications in one study [10], and in another series, 5 of 204 (2.5%) patients with cloth-covered metal ball Starr-Edwards prostheses were reoperated for consequences of cloth wear [11]. Symptomatic embolism of the cloth covering the cage struts has been reported as a secondary problem. A recently introduced modification of the cloth-covered ball valve prosthesis incorporating a metal track is designed to eliminate direct contact of the metal ball with the cloth-covered cage [10], but the long term fate of this prosthesis is not yet certain.

Wear of the caged disk valves has been a significant problem and

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[3]Descriptions of the specific prosthetic cardiac valve designs discussed are available [4].

abnormalities in the disks of a variety of caged disk valves have been reported [12,13]. Abrasion in this design may be concentrated at critical points. When extensive material loss occurs disk motion may become irregular. Although it is intended that the disk rotate over time and abrasive action be distributed symmetrically around its circumference, this is not always the case, and notching as well as severe decrease in diameter of the disk may occur. In designs which have a plastic disk and plastic-coated metallic struts, the struts may also be a localized site of wear, to the extent that underlying metal may be exposed (fig. 3).

The functional results of disk wear include partial tilting of the disk in a fixed position that may lead to acute valvular dysfunction with mixed obstructive and regurgitant components, chronic valvular regurgitation accelerating cardiac decompensation, hemolytic anemia and systemic embolization of valve material. In one series in which thirteen Beall valves (Teflon disk and strut coating) implanted for periods greater than 29 months were recovered and analyzed, twelve valves had notching of the disk and focally complete denudation of the plastic coating on the struts, always worse on the dependent struts [13]. Nine of these 12 patients (75%) had hemolysis with anemia. Excessive mechanical destruction of the formed elements of blood (particularly red blood cells) may lead to iron deposits in the kidneys, with potential clinical significance (fig. 4a). A consequence of the degeneration of the materials of construction of such prostheses is the systemic embolization of plastic fragments. In such cases, polymeric fragments are often seen in the small arteries of the heart (fig. 4b) and other organs with a surrounding foreign body giant cell inflammatory reaction.

Tilting disk valves in general have had a good record with regard to durability. The design of both the Bjork-Shiley and Lillehei-Kaster valve prostheses allows for disk rotation and minimal stress, so that progressive mechanical failure is unlikely [3,14,15]. The design of the Wada-Cutter valve, on the other hand, does not allow for disk rotation and thus localized wear and its consequences may occur [16].

Trileaflet polymeric aortic valve prostheses, exemplified by the Hufnagel prosthesis, showed severe fatigue degeneration and were discontinued [17].

The long term durability of the glutaraldehyde-stabilized porcine heterograft remains uncertain, despite favorable clinical experience of over six years [18,19]. Recent evidence indicates that degeneration with dysfunction is a common late occurrence; a particularly high incidence of calcification of the valve leaflets is seen in children receiving this prosthesis [20].

3. Fatal Valve Malfunction Due to Degeneration

From April, 1962, to June, 1979, 99 patients died and underwent necropsy at The Methodist Hospital of Houston, Texas, 30 days to ten years after cardiac valvular replacement. From analysis of pertinent clinical and pathological data, the causes of death in these patients could be grouped into three categories: (1) residual or associated cardiovascular defects or complications of operation; (2) prosthesis-associated complica-

tions; and (3) conditions unrelated to the cardiovascular problem (fig. 5)[4]. The prosthesis-associated complications, which were responsible for 40% of late deaths were thromboembolic catastrophies (including thrombotic occlusion, systemic thromboembolism and antocoagulation-related hemorrhage) in 24%, prosthetic valvular infection in 14% and materials degeneration with dysfunction in 2%. The lattermost two cases are of major interest in this paper.

In one of the two cases of fatal dysfunction, a 44 year old woman had undergone aortic and mitral valve replacement for rheumatic heart disease in 1964. The mitral prosthesis was a Starr-Edwards caged ball valve with a silicone occluder and the aortic was a Smeloff-Cutter ball valve with a silicone poppet. Nine years later she died of congestive heart failure. The aortic valve poppet was markedly discolored, swollen and virtually immobile in the cage (fig. 6a). The poppet of the mitral prosthesis was slightly discolored but there was no apparent distortion of shape or function. In the other case, a 48 year old man with rheumatic mitral valve disease received a DeBakey mitral prosthesis with a Teflon disk in 1969 and died sixty-nine months later of congestive heart failure caused by prosthesis incompetence. The disk occluder was markedly notched and reduced in size (fig. 6b). A striking finding in this case was the presence of intense foreign body giant cell reaction to fragments of plastic in the heart and kidneys.

4. Valves without Malfunction

In an effort to assess the significance of abrasive wear occurring on components of mechanical heart valve prostheses utilizing pyrolytic carbon components, we recovered 9 prostheses for detailed analysis (table 1). Eight were from the necropsy series described above and one was recovered from a patient requiring reoperation for a minute thrombus occluding valve motion. Eight of these valves had carbon occluders or both carbon occluders and cages; seven of the eight valves had duration in-situ of greater than thirty months. A Teflon Beall disk valve implanted for thirty-four days and a DeBakey disk valve with a carbon disk implanted for forty-four days served for comparison to the valves of longer function. No clinically significant wear was apparent on any of these prostheses.

After retrieval, the valves were carefully cut so that that the occluders could be removed and sent for analytical surface profilometry and the cage struts oriented and prepared for scanning electron microscope examination. A detailed description of this study will be reported in a separate communication.

A cage strut from a Teflon Beall valve implanted for thirty-four days is compared with that from a pyrolytic carbon Beall valve implanted for four years in figure 7. More abrasive wear occurred on the Teflon cage strut than on the carbon cage strut, even though the latter had been in service more than ten times as long as the former. Little difference in

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[4]For the purposes of this report we consider late separation of the valve prosthesis from the tissue annulus (dehiscence) to be a complication of the operation rather than a complication of the prosthesis per se.

wear was seen among the four vertical components of the struts of each of the carbon valves examined; in contrast, there was a large difference in the degree of wear among the four Teflon struts, as previously reported after longer periods of function [4].

The DeBakey caged ball valves with carbon occluders and titanium cage struts had noticeable wear on the struts (fig. 8), but this was not of clinical significance. This contrasts with the report of extensive titanium abrasion in an unusual case where proper excursion of the ball of this aortic prosthesis was prevented by anatomical constraints [21]. The markings on the titanium cage struts of a DeBakey carbon disk valve after only forty-four days of implantation (fig. 9) are somewhat similar to those of the carbon Beall valve after considerably longer duration of implantation (fig. 7).

Representative traces obtained by surface profilometry[5] of the carbon disks from a Beall valve, a Cooley-Cutter valve, a Bjork-Shiley valve and a Lillehei-Kaster valve are shown in figure 10. The traces were selected from those areas of the disk known to have contact with the cages. The only disk having any localized abnormality was from a Lillehei-Kaster prosthesis in which a circumferential groove of minimal depth ($<0.5\mu$) was noted, as reported by Lillehei [15].

5. Concluding Comments

Materials degeneration of prosthetic heart valves with dysfunction, either fatal or significant enough to require reoperation, has been an important late complication of heart valve replacement. There is evidence from both clinical and pathological studies that this complication is decreasing with improvements in prosthesis design and materials.

Despite the significant advantage offered by tissue prostheses not requiring chronic anticoagulation of the patient, tissue prostheses have not been shown to have reliable lifetimes exceeding those of currently available mechanical prostheses. Therefore, further consideration and development of mechanical heart valve prostheses is critical.

Traditionally, analysis of implanted medical devices in general has concentrated on those devices that failed in service. Little attention has been paid to those serving the patient well until death or removal for reasons other than device malfunction. The present study is additional verification that detailed analysis of functional prostheses removed from patients after long durations of implantation may yield worthwhile data regarding the insidious development of complications. As an increasing fraction of patients with prostheses die of causes other than complications of their devices, such studies will continue to be an important source of information not obtainable in-vitro or in pre-clinical animal investigations.

Pyrolytic carbon is a material that has found wide application in cardiovascular prostheses, especially prosthetic heart valves [22]. It is

[5]Analytical surface profilometry was done by Dr. H.S. Shim of CarboMedics, Inc., San Diego, CA.

well to keep in mind, however, that although pyrolytic carbon is extremely strong and abrasion resistant, under certain conditions the material has brittle characteristics which render it sensitive to cracks and notches, particularly those induced during pre-implantation manipulation. Rare reports of catastrophic failure of carbon valve components have appeared [23,24]. Nevertheless, the use of pyrolytic carbon as an occluder and strut material for mechanical heart valve prostheses appears to have eliminated abrasive wear as a long term complication of cardiac valvular replacement.

The authors wish to thank the American Lung Association for partial support of this study through a Clinical Training Fellowship awarded to one of us (FJS).

Table 1

Valves Examined, Sites and Implantation Times

Prosthesis type	Site[a]	Duration in-situ
DeBakey (PYC[b] disk)	M	44 days
Lillehei-Kaster (PYC disk)	T	30 mos
Beall (PYC disk)	M	32 mos
DeBakey (PYC ball)	A	48 mos
Beall (PYC disk)	M	48 mos
Cooley (PYC disk)	M	48 mos
Bjork (PYC disk)	A	60 mos
DeBakey (PYC ball)	A	85 mos
Beall (Teflon disk)	M	34 days

[a] T=tricuspid valve, M=mitral valve, A=aortic valve

[b] PYC=pyrolytic carbon

Figure 1. Ball variance in a Starr-Edwards mitral valve prosthesis. The silicone ball occluder is markedly swollen and fixed in position.

Figure 2. Cloth wear in a Braunwald-Cutter cloth-covered aortic prosthesis with a silicone ball occluder.

Figure 3. Beall mitral prosthesis with a Teflon disk and Teflon-coated cage struts. Notching of the disk and complete focal denudation of the Teflon coating exposing the underlying metal of one of the struts is apparent.

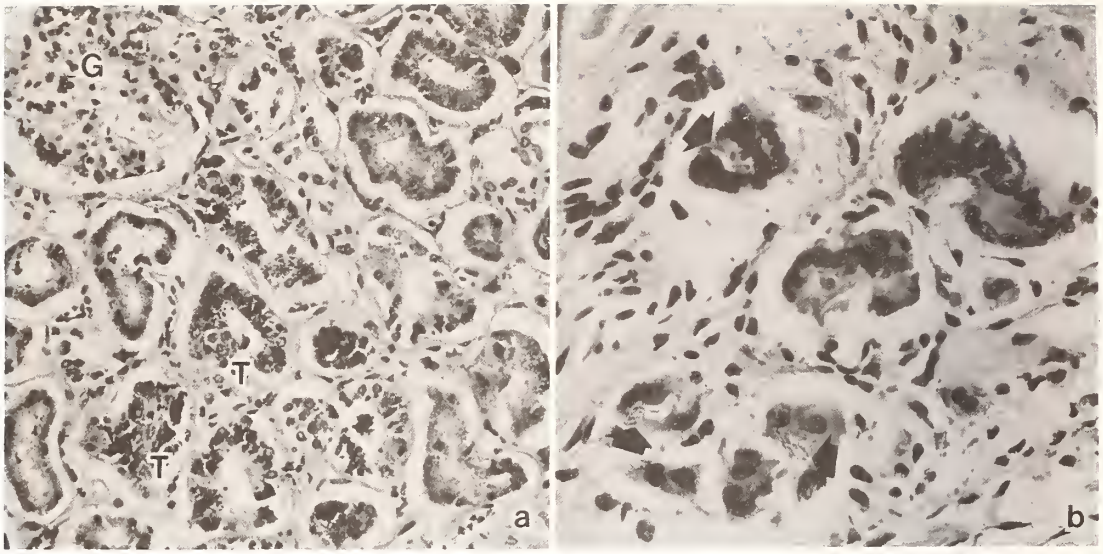

Figure 4. Distant effects of prosthetic cardiac valve degeneration. a) Renal hemosiderosis. Large deposits of granular iron-containing material are seen in the epithelial cells of the renal tubules (T) of a patient with extensive valve-related hemolysis. There is a glomerulus at upper left (190X). b) Multiorgan plastic embolization. Large foci of foreign body reaction are seen in the heart of this patient with a deteriorating prosthesis. Fragments of valve material eliciting this inflammatory response are marked by arrows (300X).

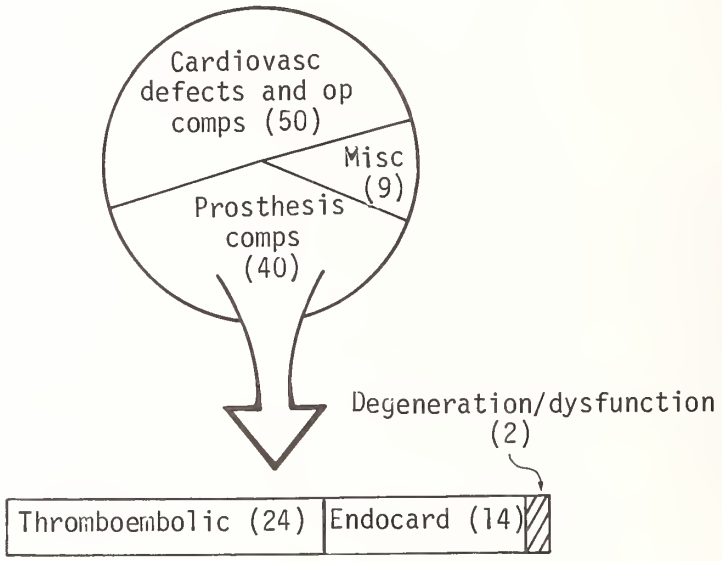

Figure 5. Causes of death in 99 patients dying late after cardiac valvular replacement. Forty patients (40%) died of prosthesis-associated complications, including thromboembolic catastrophies (24 patients), prosthetic valve endocarditis (14 patients) and degeneration of materials with dysfunction (2 patients).

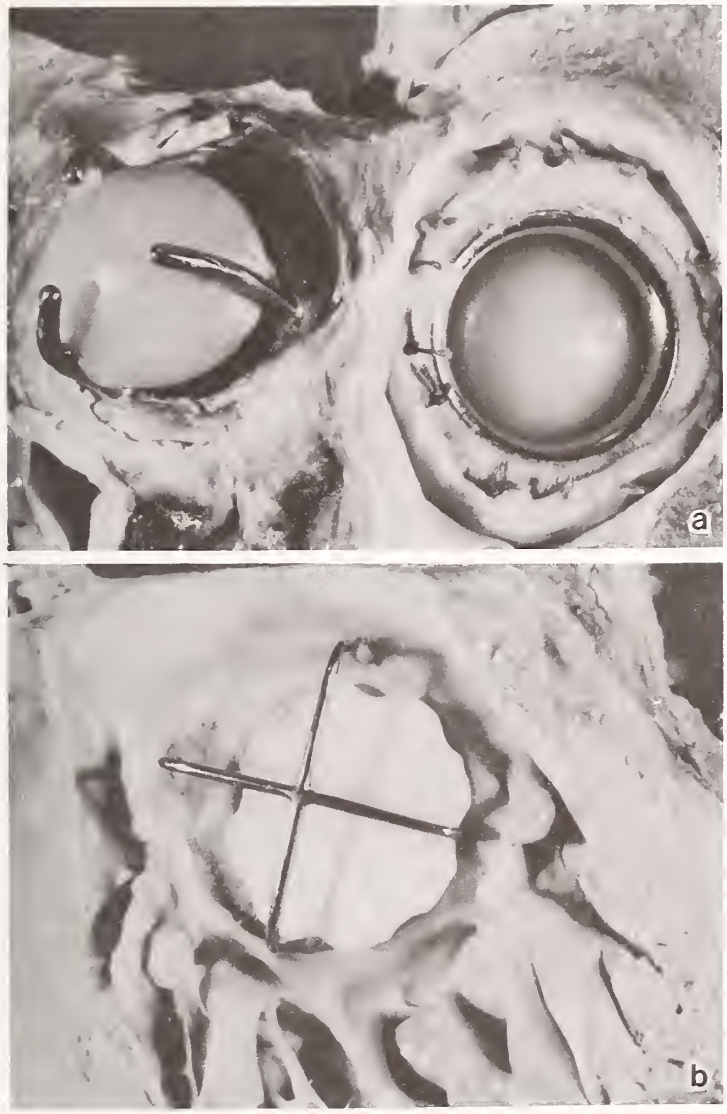

Figure 6. Fatal valve degeneration with dysfunction. a) Smeloff-Cutter aortic prosthesis (left) with ball variance after 9 years. This patient also had a mitral Starr-Edwards (right) which had a slightly discolored ball but normal function. b) DeBakey mitral disk prosthesis after 69 months. The disk is severely notched leading to incompetent valve function and congestive heart failure.

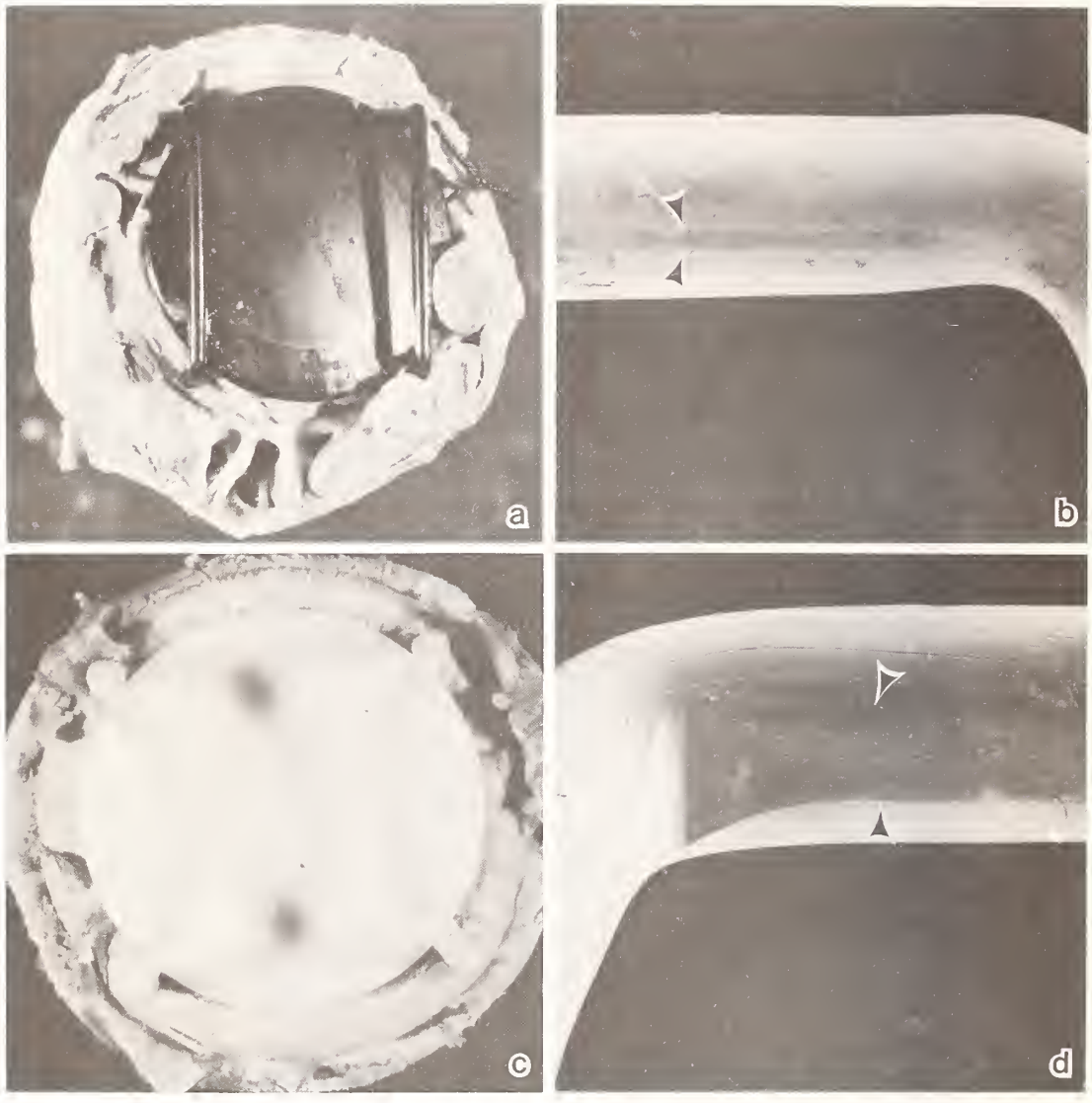

Figure 7. Comparison of strut wear on carbon and Teflon Beall valves. a) Beall carbon valve, gross photograph. b) Scanning electron micrograph of wear on cage strut from valve shown in (a) indicating thin superficial abrasion after 48 months service (9X). c) Teflon Beall valve, gross photograph. d) Scanning electron micrograph of strut of valve shown in (c). The wear mark at the site of disk/cage contact is evident. In each micrograph, the wear marks are deliniated by arrows.

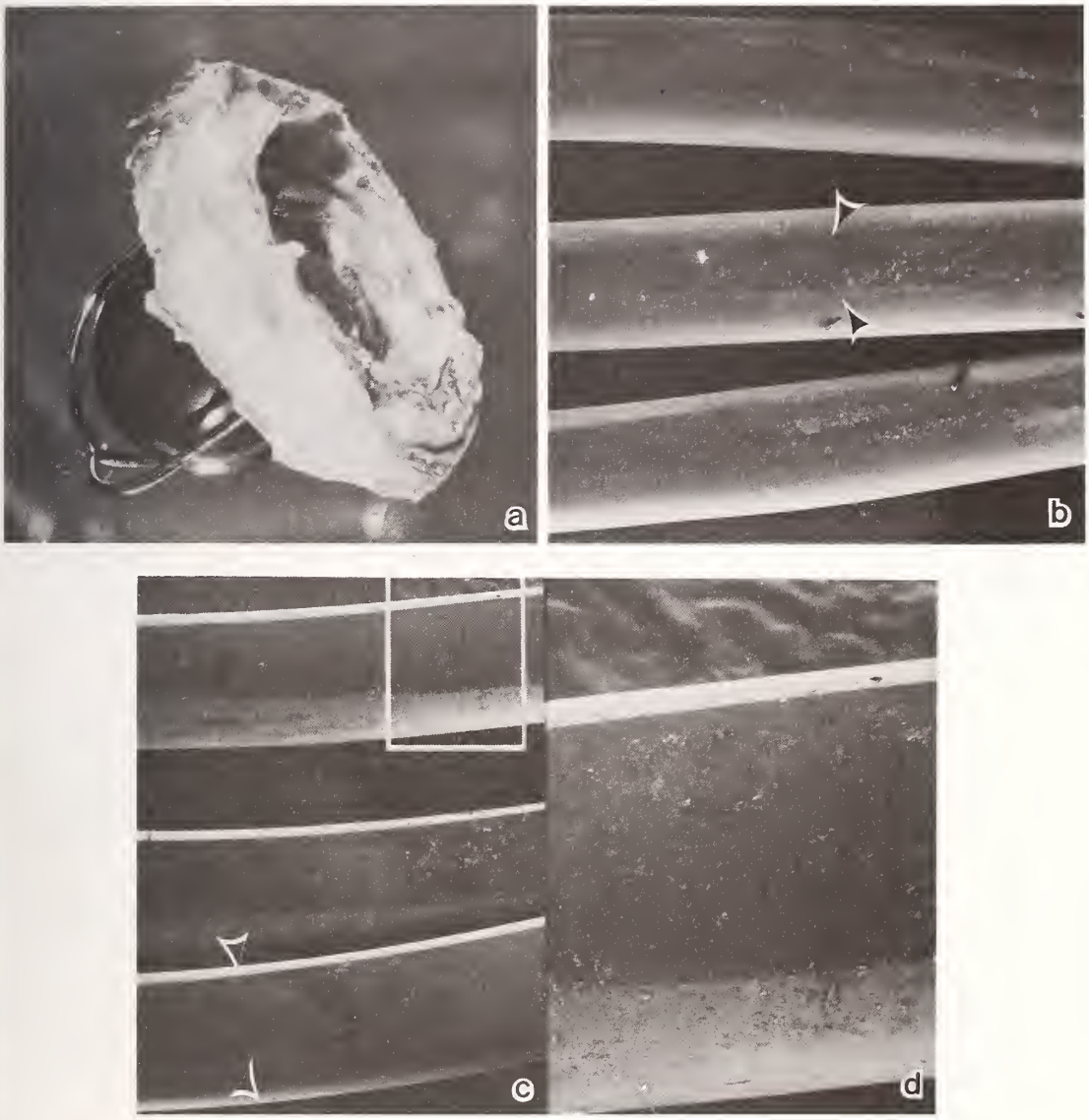

Figure 8. DeBakey ball valve. a) Implant of 7 years duration, gross photograph. b) Scanning electron micrograph of wear on metallic cage struts by pyrolytic carbon ball of valve similar to that shown in (a), implanted for 48 months (11X). c) Scanning electron micrograph of strut wear on valve shown in (a) (11X). d) Higher magnification of area within box in (c) (33X). In both (b) and (c) the wear marks on the struts are emphasized by arrowheads.

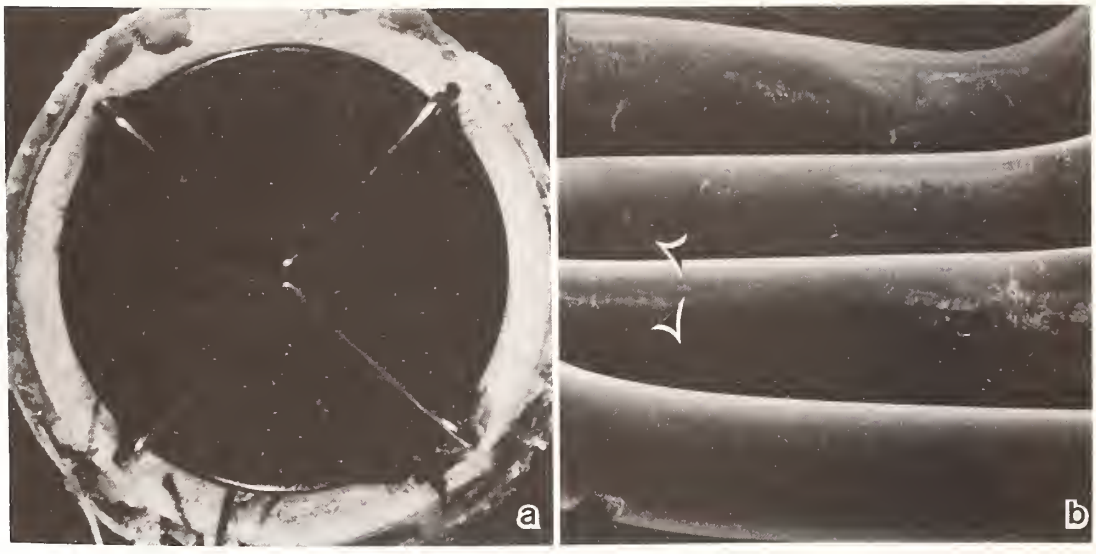

Figure 9. DeBakey carbon disk valve implanted for 44 days. a) Gross photograph. b) Scanning electron micrograph of wear on cage struts by pyrolytic carbon disk of valve shown in (a). A superficial area of wear is marked by arrowheads (11X).

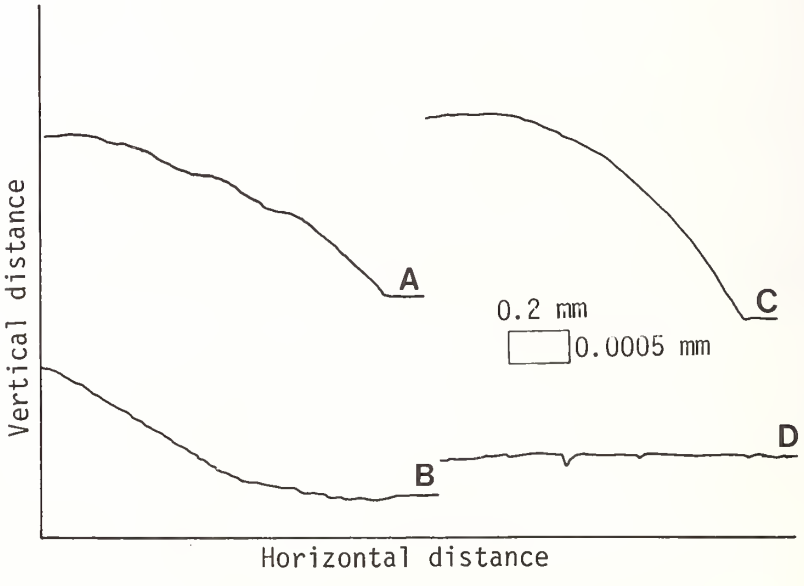

Figure 10. Surface profile analyses of pyrolytic carbon occluders after long durations of implantation, taken over critical wear areas. a) Beall mitral disk, 32 months. b) Cooley mitral disk, 48 months. c) Bjork-Shiley aortic disk, 60 months. d) Lillehei-Kaster tricuspid disk, 30 months.

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PROSTHETIC VALVE WEAR PRODUCTS--EMBOLIZATION AND SYSTEMIC PRESENTATION

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An uncommon but potentially catastrophic mode of prosthetic heart valve failure is related to the inadequate durability of the materials used in the construction of the heart valve. The inadequate durability of these materials results in wear of the disc or ball occluders, the polymeric fabric covering the seat and struts and the metallic frame. This paper presents some of the common modes of wear of prosthetic heart valves with an emphasis on the embolization and systemic presentation of wear products. In particular, the identification in organs of ball occluder fragments from the Braunwald-Cutter aortic prosthesis will be presented.

1. Introduction

Since the advent of surgical replacement of diseased cardiac valves by prostheses and prosthetic materials in the early 1950's, the clinical success of these devices has been modulated by the incidence of serious complications. These serious complications include thromboembolism, infective prosthetic valve endocarditis, prosthetic structural dysfunction, suture dehiscence, hemolysis, hemolytic anemia and sudden death. [1,2,3][1]. Excluding those causes of prosthetic valve failure related to surgical judgement and procedure, the majority of failures of prosthetic heart valves are related to their respective design and structural characteristics. For example, caged-ball or disc valves are all obstructive to varying degrees. This obstruction to flow may lead to turbulence and stasis and predispose to thrombus formation and thromboembolism. Thrombogenicity is primarily related to the materials used in the constuction of the blood contacting components of the valve. It is not the purpose of this paper to discuss those modes and mechanisms of failure related to inappropriate blood/materials interactions or design, but rather, to discuss those failures which result due to inadequate durability of the materials used in the construction of the respective prosthetic valves. Moreover, this discussion will be limited to the systemic findings in selected surgical pathology and autopsy pathology cases from the Implant Retrieval and Evaluation Program at Case Western Reserve University.

It must be emphasized that prosthetic valve failures resulting from

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[1]Figures in brackets indicate the literature references at the end of this paper.

inadequate durability of the component materials range from common to uncommon to rare, depending on the specific type of valve and the respective materials under consideration. Thus, this review will deal with the principal failure modes with little emphasis being placed on the incidence of specific types of failure modes as they relate to each type of valve. The reasons for this approach are that the real numbers of such cases are small and that many cases are probably not documented through surgical or autopsy follow-up.

In general, the cause of prosthetic valve failure due to durability problems can be related to one or more of the valve components. These components are the disc or ball occluder, the polymeric fabric covering the seat (and in some cases, the struts) and the metallic frame, including the seat and struts. Over the past two decades, numerous combinations of metallic and polymeric materials have been used in the construction of prosthetic valves. These materials are listed in table I for the sewing ring (fabric covering the valve seat), the cage or cage and strut, and the occluder or poppet.

Table I. Materials Used in the Construction of Prosthetic Heart Valves.

Sewing Ring	Occluder/Poppet	Cage/Strut
Dacron	Silicone Rubber	Dacron over Titanium
Teflon	Polytetrafluoroethylene	Dacron over Stellite 21
Polypropylene	Polyethylene	Teflon over Stellite 21
	Delrin	Teflon over Titanium Alloy
	Pyrolytic Carbon	Polypropylene over Stellite 21
	Stellite 21	Titanium Alloy
	Titanium or Alloy	Stellite 21
		Pyrolytic Carbon (Coated)
		Dacron over Delrin (Stent)
		Teflon over Elgiloy (Stent)
		Polypropylene (Stent)

Wear and embolization of wear products from prosthetic heart valves may involve any combination of the valve components; the disc or ball occluder, the valve seat or fabric covering the seat and the struts. Embolization of valve fragments may occur following catastrophic failure via a fracture mechanism and in some cases this has been preceded by wear.

Ball or disc occluder variance is the most commonly found example of wear phenomenon in prosthetic heart valves. The first case of this problem was reported by Krosnick and Ablaza in 1965 [4,5]. In these cases, wear and ball variance occurred in a Starr-Edwards model 1000 aortic valve to the point where the silicone poppet embolized and caused the death of the patient. In addition to wear, the use of the Starr-Edwards Model 1000 valve identified another mechanism by which the

silicone ball could develop ball variance with the end result being ball fragmentation, embolization of the fragments and the death of the patient due to acute aortic insufficiency. This mechanism involves physical chemical changes brought about by the inappropriate interaction between the blood and the silastic ball, and results in the loss of the structural integrity of the ball occluder by fatty infiltration, swelling, lobulation and cracking or fissuring [6,7,8,9]. Starr has estimated that this phenomenon occurred in approximately 75% of the patients receiving the Starr-Edwards model 1000 valve between 1962 and 1964. [10]. These results led to the improved design and development of the models 1200 and 1260 series of valves with a change in the fabrication techniques for the silastic ball. The incidence of swelling, fatty infiltration, lobulation and cracking or fissuring has been markedly reduced, but the problem of silastic ball wear remains a problem. For this reason, the Braunwald-Cutter aortic prosthesis has been removed from clinical use [11,12,13]. The problem of poppet wear and embolization of wear fragments in the Braunwald-Cutter aortic prosthesis will be presented in detail in the discussion.

Disc wear has been observed in those valves which employ a plastic occluder: Beall-Surgitool models 103 and 104 (Teflon), Bjork-Shiley (Delrin) and Kay-Shiley (silicone rubber) [14,15,16,17,18,19]. Edge wear of the disc is commonly seen with the Beall-Surgitool models 103 and 104 and this clinical observation has lead to the use of a Pyrolitic carbon coated disc. The disc material has also been changed for the Bjork-Shiley and Kay-Shiley valves.

Disc variance due to edge wear may lead to subluxation of the disc with the disc being cocked between the struts and the valve seat. Edge wear may also limit rotation of the disc and exacerbate erosion and wear. This wear occurs on both the disc edge and the Dacron fabric covering the valve seat, and fiber embolization may result if the fabric wear is severe. Clark and coworkers have correlated the disc variance as measured radiologically by the disc-cage ratio with hemolysis and coagulation deficits in patients with Beall-Surgitool model 103 and 104 valves [20]. Anemia, marked elevations of LDH and large urinary iron losses are important clinical indicators of disc variance in these valves.

Strut wear may be observed in valves where there is a mismatch in the hardness properties of the occluder material and the strut material. This has been seen in the Bjork-Shiley, DeBakey-Surgitool and Cooley-Cutter valves, and the latter two examples result from the hard carbon occluder eroding the soft titanium struts [18,21,22,23]. This may result in strut fracture. Wear is also commonly seen on the Teflon coated struts of the Beall-Surgitool models 103 and 104 valves. In general, embolic wear particles are too fine to be identified in the peripheral organs in cases of strut wear.

The success of an implant retrieval and evaluation program hinges upon the correct identification of the type of prosthesis, device or biomaterial under consideration. In regard to prosthetic heart valves, the type of valve must be known since different valves have different failure modes. Indeed, various models within the same group of valves

may have different design and structural characteristics which can lead to different modes of failure. The identification of the valve type and model has been facilitated by the manufacturers by providing patients with implant identification cards. If the identification card is not available, the investigator may make use of the original operative report in identifying the prosthetic valve. If neither of these means of identification are available, the investigator may turn to several reports which are available in the literature and permit the identification of the specific type of prosthetic valve based on their respective structural characteristics.

In 1975, Silver and coworkers published "A Key to Identifying Heart Valve Prostheses" [24]. They have provided schemes for identifying the various types of caged-ball and disc valves based on the structural characteristics of the cage and struts. Chun and Nelson have published on the radiologic features of prosthetic heart valves. [25]. Morse and Steiner have provided an atlas which provides for each type of valve, the photographic and radiological appearance, the physical characteristics and materials used, size range and available dimensions, and orifice area [26]. Finally, the definitive work by Lefrak and Starr provides information on the clinical performance of each type of valve in addition to an excellent review of the literature [1].

2. Results and discussion

2.1. Sewing ring fabric wear

Tearing, fraying and deterioration of the fabric covering the sewing ring (valve seat) may occur due to the trauma of the occluder disc or ball striking the valve seat. This phenomenon has been observed for nearly all valves which employ a cloth covering of the valve seat and has been seen most commonly in the Beall-Surgitool mitral valve. Fabric covered prosthetic heart valves were developed to reduce the incidence of postoperative thromboembolic complications. Braunwald and her associates carried out studies which showed that the rate of thromboemboli formation could be reduced by a neointima which formed over and was adherent to the fabric over the inflow surface of the valve. This concept coupled with an appreciation of the wear phenomenon lead Starr and his associates to design the Starr-Edwards Model 2310 valve, which made use of the fabric orifice covering with metal studs on which the Stellite 21 ball occluder could seat. Accelerated test studies have shown that even this design may be susceptible to fabric wear [27].

An example of sewing ring fabric wear is shown in figures 1 and 2. This Beall-Surgitool 104 mitral valve had been implanted for 6.5 years and was surgically replaced following the clinical diagnosis of valve malfunction. It can be seen that the Dacron covering over the valve seat has worn away, causing the fabric to extend into the inflow tract and reduce the inflow surface area. In this case, the inflow surface area has been reduced by ca 35%. This reduction in inflow tract surface area can lead to a compromise in the patient's hemodynamics and increased turbulence and blood trauma. This extent of sewing ring fabric wear is usually accompanied by disc variance and strut wear.

Figure 1. Ventricular view of a Beall model 104 mitral valve with marked sewing ring fabric wear. Implanted for 6.5 years, note exposed metallic frame.

Figure 2. Atrial view of a Beall model 104 mitral valve with marked sewing ring fabric wear. Implanted for 6.5 years, note loss of neointima from frayed fabric in the inflow tract.

2.2. Fabric embolization

The diagnosis of fabric embolization from worn prosthetic heart valves is rare. This phenomenon is occult and with the Beall-Surgitool

104 valve it is associated with disc variance. The clinical diagnosis of disc variance (valve malfunction) is usually made and appropriate surgical measures taken to replace the valve. These circumstances obviously do not permit microscopic examination of the organs and obviously, the diagnosis of prosthetic valve embolization cannot be made. Thus, this diagnosis can only be made in autopsy cases which have a worn valve or which have had surgical replacement of a worn valve. The exception to the preceding discussion may be the diagnosis of wear particle embolization from Braunwald-Cutter prosthetic heart•valves and this will be presented in the following discussion.

This case involved a 54-year-old white female with a long history of rheumatic heart disease. At 50 years of age, she underwent an aortic valvulotomy and mitral valve replacement with a Beall-Surgitool 104 valve. Four years following these procedures, the diagnosis of valve malfunction was made on the basis of increasing congestive heart failure and hemolytic anemia, and she underwent a valve replacement procedure. Two days postoperatively she expired following pulmonary arrest. The pertinent autopsy findings relative to this discussion were the presence of numerous foreign body giant cells in the arterial walls of blood vessels in the brain and heart.

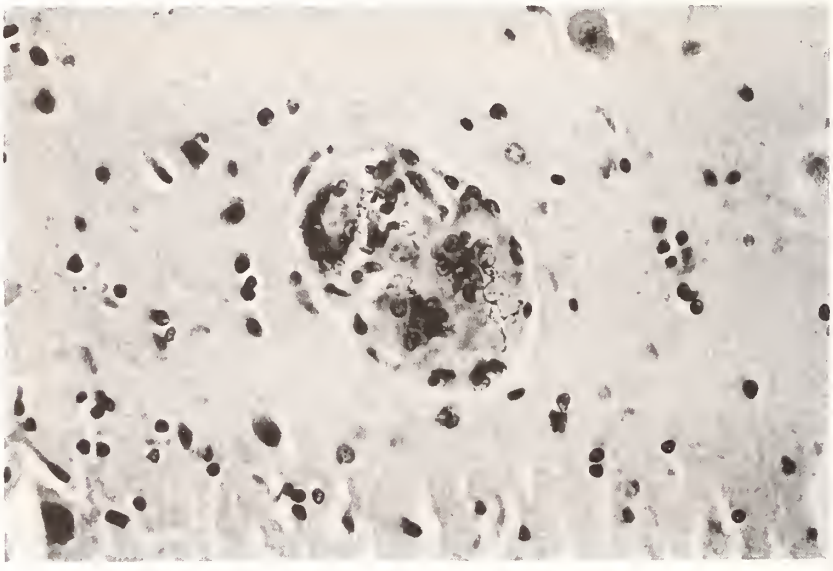

Figure 3. Cerebral cortex with foreign body giant cells containing birefringent fibers (original 200X). Beall model 104 mitral valve implanted for 4 years.

Microscopic examination of routine sections of the cerebral cortex, figure 3, the basal ganglia, figure 4, and the cerebellum, figures 5 and 6, revealed numerous foreign body giant cells. Polarized light examination showed birefringent fibers present in the cytoplasm of the multinucleated giant cells. These are consistent with fiber emboli from the worn Dacron fabric of the sewing ring. The presence of anoxic neurons adjacent to the perivascular foreign body giant cells in the basal gang-

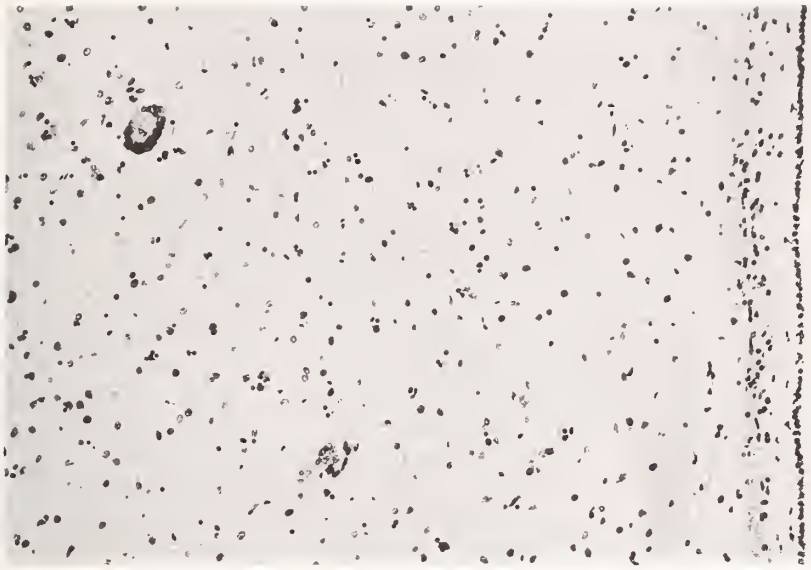

Figure 4. Basal ganglia with foreign body giant cells containing birefringent fibers (original 120X). Beall model 104 mitral valve implanted for 4 years.

lia (fig. 4) are suggestive of ischemia. In the cerebellum (figs. 5 and 6), neurons show eosinophilic nuclei suggestive of early microinfarction by the cellular reaction to the fiber emboli. Older microinfarcts would show more tissue damage with astrocytic proliferation and activated microglia. As these features are not seen, the microinfarcts may be early (days) or only partial, leading to the observed ischemic changes.

Fiber embolization leading to vasculitis has also been observed in patients who have undergone intracardiac operations or cardiac catheterization. While fiber embolization is more commonly seen in small vessels, this process may involve larger vessels with associated morbidity and mortality. Dimmick et al. have observed this phenomenon in two cases, one involving the death of a patient and the second requiring amputation of an extremity. [28]. They described the presence of fibers within a thrombus which had occluded a major pulmonary artery resulting in pulmonary infarction. This patient subsequently died shortly after a corrective procedure for tetralogy of Fallot. Their other case involved the cannulation of the radial artery in a patient undergoing an intracardiac operative procedure. This patient subsequently developed gangrenous necrosis of the hand requiring amputation. Fibers were observed in the thrombus which had occluded the radial artery leading to ischemia of the extremity and subsequent gangrenous necrosis.

2.3. Disc occluder variance

As previously described in the introduction, disc variance usually arises due to the use of a relatively soft material such as Teflon for the disc. Edge wear can be autoaccelerating as the rotational motion of the disc is inhibited. Edge wear as well as focal grooving of the disc

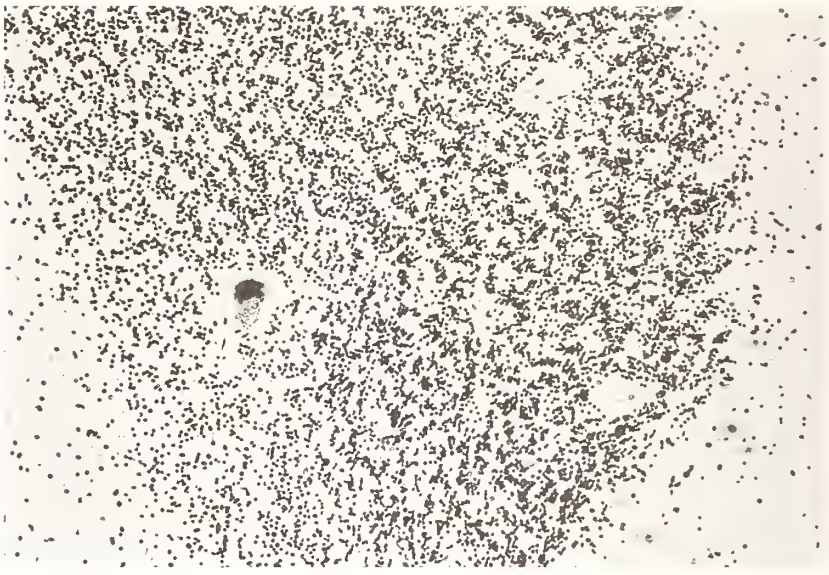

Figure 5. Cerebellum with foreign body giant cells containing birefringent fibers (original 120X). Beall model 104 mitral valve implanted for 4 years.

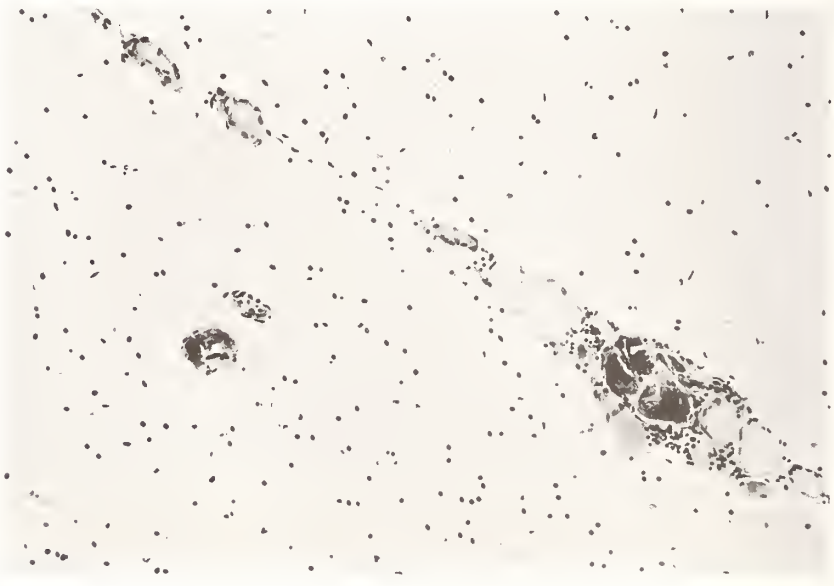

Figure 6. Cerebellum with foreign body giant cells containing birefringent fibers (original 120X). Beall model 104 mitral valve implanted for 4 years.

can also increase the wear and deterioration of the sewing ring fabric. An example of extensive variance is shown in figure 7. This Beall-Surgitool mitral valve had been implanted 6.5 years previously and at the time of reoperation, the patient had developed a severe chronic

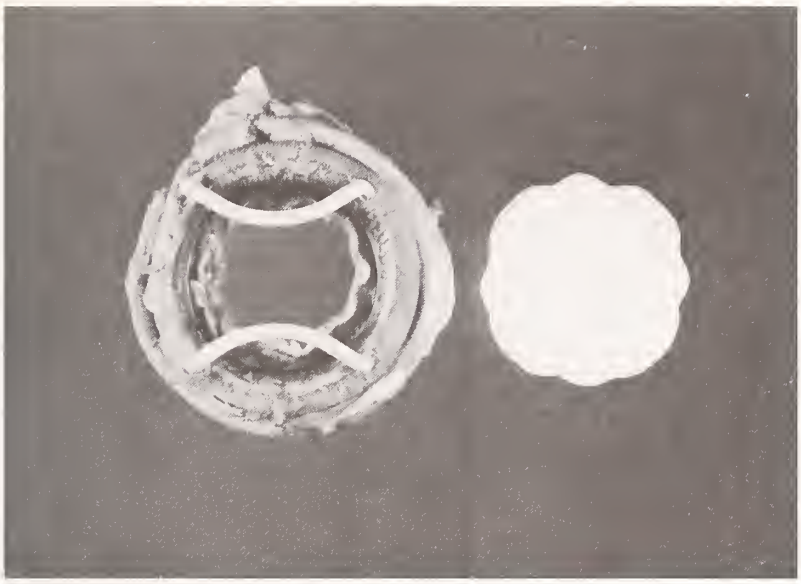

Figure 7. Beall model 104 mitral valve implanted for 6.5 years. Note marked disc variance with grooving and the exposure of the metallic frame.

anemia. The disc/cage ratio for this valve is approximately 0.89 indicating moderately severe wear [20].

2.4. Ball occluder variance

While ball occluder variance due to wear has been noted for all types of prosthetic valves, this phenomenon has led to disastrous results with the Braunwald-Cutter aortic prosthesis [12,13]. This valve makes use of a Dacron fabric over the struts to promote neointima formation. Unfortunately, cloth fragmentation due to the trauma of the ball impacting on the cloth-covered struts occurs first. Fragmentation of the cloth on the struts causes the cloth to slide down the struts where it can disturb the normal seating of the ball. In addition, the ball then continues to impact on the bare metal struts, increasing the wear rate on the silicone rubber ball. The loss of fabric from the struts increases the distance from the struts and thus the potential for ball embolization. Figure 8 shows a typical example of a Braunwald-Cutter aortic valve with ball variance and cloth fragmentation from the struts. This valve had been implanted for 6.5 years and when removed at surgical replacement, the ball could slide easily between the struts. Note the marked variance of the ball leading to "flat" portions on the surface of the ball occluder. Wear particles from these valves, either in the form of silicone rubber and/or silicon dioxide, embolize to various organs, in particular the liver, where a characteristic foreign body granuloma results. This will be discussed in the following section.

2.5. Embolization of ball occluder wear products

At the present time, our implant retrieval and evaluation program

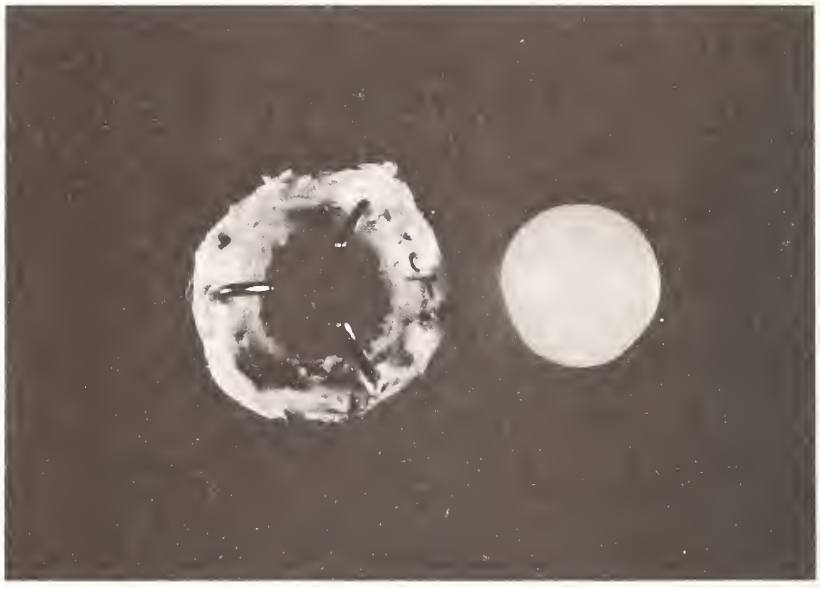

Figure 8. Braunwald-Cutter aortic valve implanted for 6.5 years. Note "flat" portions over the surface of the ball occluder.

has identified three cases in which occluder embolization has occurred from Braunwald-Cutter aortic valves. The following case report is a brief description of one of these cases and, in general, describes the events leading to the patients' demise and the autopsy findings in cases involving Braunwald-Cutter occluder embolization.

A 59-year-old white female had previously received a Braunwald-Cutter prosthetic valve of the aortic type for severe aortic insufficiency. She was admitted for her last hospital admission following a two-week period of urinary frequency, pyuria, dysuria and hemoglobinuria. Her hematocrit had dropped five points over this two-week period and was 27. On physical examination, her blood pressure was 130/65 with a pulse of 68. There was a grade 5/6 holosystolic murmur over the entire precordium. Workup procedures were instituted, however, two days following her admission she was found on her bed breathing but unresponsive. Ten minutes prior to this she had been observed in the halls of the ward walking and alert. Her pulse was 50 but no measurement of the blood pressure could be obtained. In a few seconds the pulse was lost and cardiac resuscitative measures failed and the patient died.

At autopsy, it was readily observed that the silicone occluder ball from her Braunwald-Cutter aortic valve prosthesis had embolized and was found lodged in the abdominal aorta at the level of the renal arteries. The occluder ball was grossly intact and there were no fracture lines or cracks over the surface; it was smooth and without missing fragments. The struts of the valve prosthesis were bare, exposing the metallic struts and the dacron fabric had been partially pushed to the base of the struts. The liver, spleen, kidneys and lungs showed acute and chronic passive congestion and edema. Microscopic examination of the

liver and spleen showed occasional periportal foreign body giant cells containing a foreign material which was not birefringent and could not be stained with hematoxylin and eosin, PAS or trichrome stains.

In recent years, there have been several reports describing the erosion and subsequent embolization of ball occluders from caged-ball cardiac valve prostheses. Associated with these findings has been the presence of foreign body giant cells in the liver, spleen and kidneys [29]. It has been suggested that the foreign particles within these giant cells are fragments of the occluder ball and that the wide dissemination in several organs represents the systemic embolization of wear particles. We have made use of KEVEX X-ray dispersion analysis to identify the particles within the foreign body giant cells as containing silicon and thus provide the first direct identification of the material within these foreign body giant cells.

In the three cases, the metallic struts of the cage were exposed to varying degrees and the occluder balls were absent from the cages. In the two complete autospy cases, the occluder balls were found in the abdominal aorta. In both cases, they were spherical and could easily slide between the struts of the valve cage. No grooving, cracking or other macroscopic signs of variance in the occluder balls were seen. Histologic examination of the liver, spleen and kidneys in these two cases revealed the characteristic perivascular foreign body granulomas; and within the liver foreign body giant cells were present in the periportal areas with variable degrees of inflammation and fibrosis (figures 9 and 10). The foreign material within these foreign body giant cells consisted of refractile irregular clumps which were not birefringent and could not be stained with hematoxylin and eosin, PAS or trichrome stains.

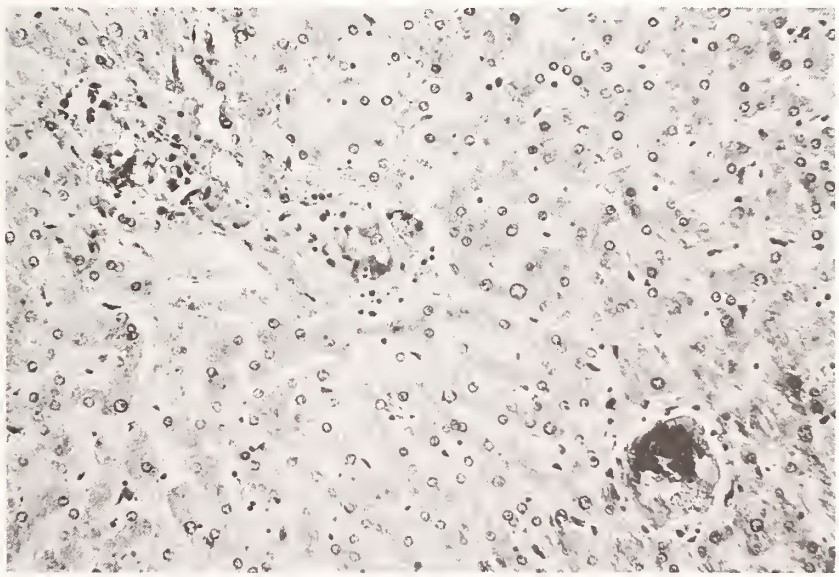

Figure 9. Periportal foreign body giant cells in the liver; Braunwald-Cutter aortic valve implanted for 3 years (original 200X).

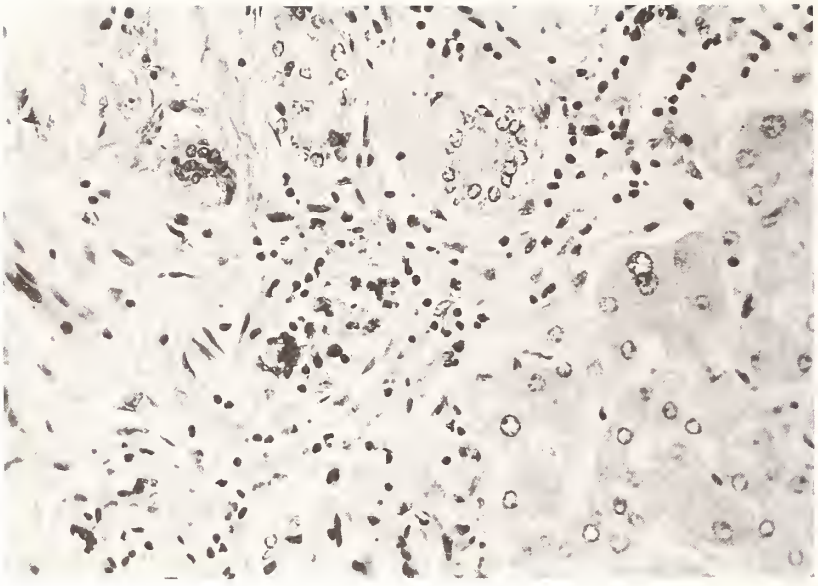

Figure 10. Periportal foreign body giant cells in the liver; Braunwald-Cutter aortic valve implanted for 3 years (original 320X).

Infrared spectral analysis and atomic absorption spectrophotometry have been previously used to identify silicon-containing materials in tissues. Unfortunately, neither of these techniques allows a direct appreciation of the cellular-material interaction. For this reason, we turned to the use of KEVEX X-ray dispersion analysis coupled with scanning transmission electron microscopy using a JEOL 100-B instrument with 100 kV accelerating voltage. Appropriate stained and unstained 50 nm thin sections were prepared in our electron microscopy laboratory and mounted on copper grids. Simultaneous characterization using scanning transmission electron microscopy and KEVEX X-ray dispersion analysis was carried out. Figure 11 shows the general type of inclusion (white arrow) which was analyzed and Figure 12 is a photograph of the KEVEX video display showing the presence of the $K\alpha$ and $K\beta$ peaks of silicon.

3. Conclusion

With the increasing effort directed toward the development of non-thrombogenic materials for cardiovascular applications and the continued improvement in surgical techniques, it is anticipated that the long term durability of materials used in valve prostheses will play an increasing role in determining the life-time of the respective valve prostheses. If the modes and mechanisms of valve failure due to durability problems are to be recognized, evaluated and used as a basis for future design of valve prostheses, it is important that retrieval and evaluation programs be developed in which the participating individuals not only have a knowledge of the clinical aspects of valve prostheses, but also a knowledge of the physiological and biomaterials aspects of valve prostheses.

Figure 11. Scanning transmission electron micrograph of a typical inclusion in the foreign body giant cells in the liver. Braunwald-Cutter aortic valve implanted for 3 years.

In closing, we would like to make one further statement regarding the retrieval and evaluation of valve prostheses. While the Braunwald-Cutter aortic prosthesis is no longer in clinical use today, having been removed from the market in 1974; there are patients who still have this prosthesis and are at risk for the problems presented in the preceding discussion. The problem of long-term durability cannot necessarily be judged from animal studies and accelerated in vitro tests. Therefore, implant retrieval and evaluation programs are necessary if we are to appropriately determine the clinical efficacy of prostheses, implants and other devices.

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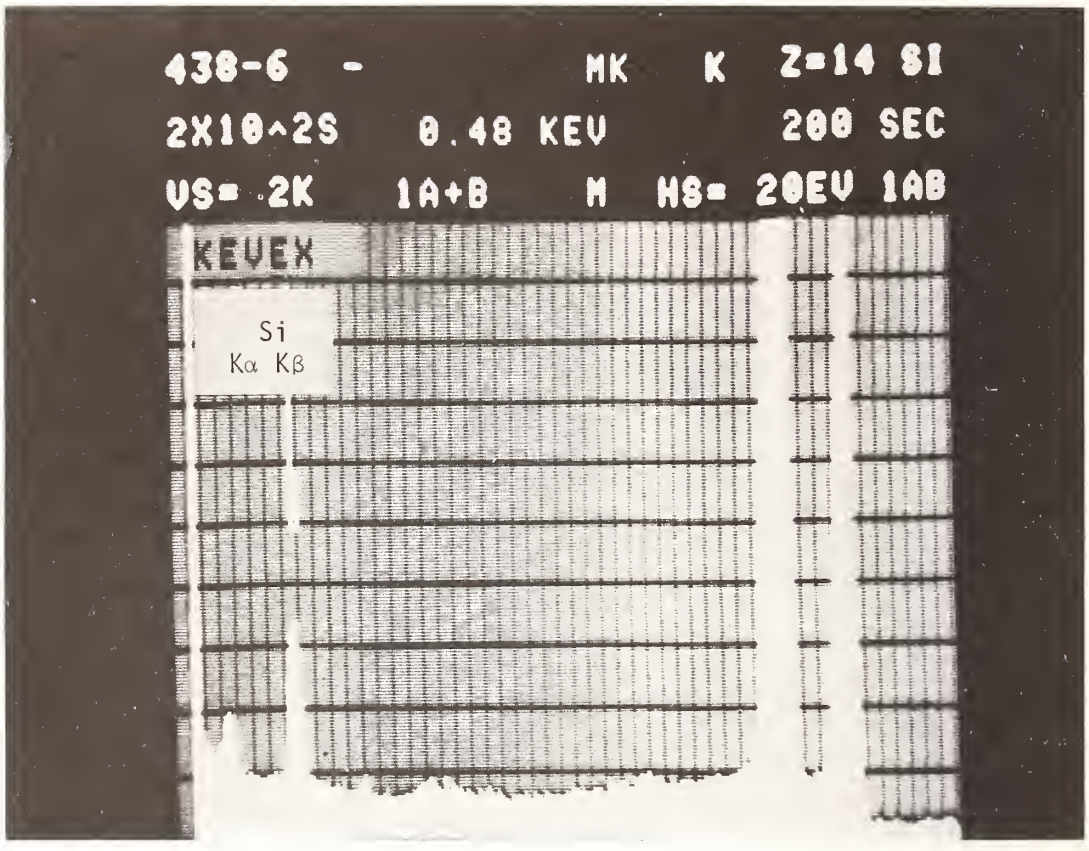

Figure 12. KEVEX video display with Kα and Kβ peaks of silicon from the inclusion pictured in figure 11.

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METAL ALLERGY AND METALLURGY

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Metal allergy reactions result from sensitization of T-lymphocytes to metal ion-protein complexes. In the case of reactions to implants it is presumed that the metal ions as corrosion products complex with local tissue proteins. An in vitro test for metal sensitivity is described in which lymphocytes are challenged with metal chlorides in the presence of plasma proteins. The test can differentiate between patients with no sensitivity to nickel, cobalt, or chromium, sensitivity to one or more of the metals, and patients with allergic reactions to implants. The test results performed on 164 patients at the time of implant removal show that 37% of the patients in this group were reacting to their implants. The results of implant analysis and the blood test results are presented for cobalt-chrome hip hemiarthroplasties, stainless steel plates, and stainless steel nail-plates. Specific cases are presented in which metallographic and SEM analysis of the implants are used to demonstrate correlations between implant degradation and the immune response.

1. Introduction

When an implant made of surgical grade stainless steel or cobalt-chromium alloy is placed in tissue, the implant surface will quickly passivate due to the self passivating nature of these alloys. However, as has been shown by Laing et al. [1][1], there will be a release of some alloy constituents into the surrounding tissues, even when the passive metal is in an unstressed condition as with a cylinder in the muscle of an animal. In more challenging situations, such as orthopaedic implants, the release of metal ions into the tissue is accelerated due to mechanisms of fretting and crevice corrosion. As has been published previously by others, and is presented in other papers in this volume, the tissue levels of implant constituents can reach disturbingly high levels.

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[1]Figures in brackets indicate the literature references at the end of this paper.

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In reviewing the literature, one finds occasional references to adverse tissue reactions to metallic implants, which are attributed to metal sensitivity to corrosion products. Barranco and Soloman [2] reported a case of an eczematous dermatitis reaction to a stainless steel screw in a patient with sensitivity to nickel. McKenzie et al. [3] reported a case of urticaria after insertion of a cobalt-chromium Smith-Peterson nail. While there have been other reports concerning fracture fixation devices, the most convincing literature has been in the area of tissue reactions to metal-metal total joint prostheses, which have shown a positive correlation between pain and prosthesis loosening and metal sensitivity [4, 5, 6]. For more complete discussions of the literature, the reader is referred to recent publications by the authors [7, 8]. The objectives of this report are to discuss the effects of metal ions on the human immune system, and to look at the relationships between implant degradation and the development of immune reactions in the form of metal sensitivity.

2. Immunology and Metal Sensitivity

In the ionic state, metallic implant corrosion products, although foreign to the body's immune system, are too small to be recognized by the immune system. However, when complexed with protein carriers, the metals can stimulate an immune response. Thus, metal ions are haptens which, when complexed with protein carriers, are immunogenic. From an orthopaedic implant viewpoint, the haptens of importance are nickel, cobalt, and chromium.

There are two branches of the immune system which must be discussed if one is to understand the possible immune reactions to metallic implants [9]. Both branches stem from lymphocytes which are made in bone marrow and differentiate in other organs. Lymphocytes are the memory cells of the immune system, in that they carry binding sites on their cell membranes which allow the cells to recognize that "which is not self." The B-lymphocyte will, when stimulated, undergo blastogenesis and produce plasma cells. These plasma cells will produce and release antibody against the specific antigen that stimulated the B-lymphocyte. The T-lymphocyte, when stimulated, will undergo blastogenesis to produce more T-lymphocytes, all of which will release a number of soluble substances known as lymphokines. There are also B-cell T-cell interactions which are beyond the scope of this presentation. Concerning allergic or hypersensitivity reactions, it is the B-cell reaction that causes allergy to dust and pollen. The T-cell is responsible for what is known as delayed or cell-mediated immunity, and it is the T-cell reaction that is of primary importance in a discussion of metal sensitivity reactions.

T-lymphocytes are capable of becoming sensitized to metal-protein complexes. The sensitivity can be acquired by repeated exposure to metals or metal salts on the skin, by metal salts injected in muscle, and presumably by repeated exposure to corrosion products. Once sensitized, the T-cells will react whenever they are challenged

by (exposed to) the metal ion-protein complex to which they are sensitive. The reaction in vitro results in the production of a number of substances known as lymphokines, which can be used for sensitivity testing, and which are responsible for the symptoms associated with in vivo hypersensitivity reactions.

The classic test for metal sensitivity is the skin test [10]. The method involves placing a salt of the metal in question on the patient's skin and observing the skin reaction 24 and 48 hours later. If the patient's T-cells are sensitive, they will react to the complexes formed between the metal ions and the skin proteins. There are a number of concerns about using skin testing for metal sensitivity in orthopaedic patients. First the reaction is only to skin protein complexes which may be antigenically different from deep tissue-metal ion complexes. Second, the method only tests for T-cell mediated reactions and does not determine if there is any B-cell dependent sensitivity. But perhaps most importantly, the method of skin testing is the same as the method of sensitivity induction. A patient (or animal) can be made sensitive by repeated skin testing [11]. Thus we feel that skin testing may not be sensitive nor safe enough to be used routinely in implant sensitivity studies. There are, however, in vitro tests for metal sensitivity.

When T-lymphocytes from a patient's blood sample are challenged with metal-protein complexes in vitro, they will respond by releasing lymphokines. The two that are most commonly used for in vitro testing of cell-mediated immunity are blastogenic factor and migration inhibition factor. The assay for blastogenic factor involves the use of radioactive labels and takes five to seven days. The assays for migration inhibition are faster, easier, and less expensive. While doing both in our laboratory studies, we have selected and modified the migration inhibition test [12] for our clinical study of implants and metal allergy [7, 8, 13].

When incubated in agarose in vitro, leukocytes such as polymorphonuclear leukocytes and macrophages will migrate in an ameboid fashion. This migration is inhibited by migration inhibition factor released by T-lymphocytes. There are probably two factors, one which inhibits macrophages (MIF) and one which inhibits the monocytes and polymorphonuclear leukocytes in peripheral blood (LIF). For the purposes of this paper we will simply refer to LIF. It is important in these in vitro studies to test for normal T-cell function as a control. We use phytohemagglutinin (PHA) to test for normal T-cell function. Normal T-cells should produce LIF when stimulated with PHA, and the response to the metal salts in question can be compared. To provide a source of protein for metal salt complexing, we incubate the metal salts with plasma and then the cells. As a normal migration control, we incubate the cells in plasma alone. Thus, there are three test conditions: serum for migration control, PHA for T-cell function, no migration control, and incubation with the metal salt(s) in question.

We have found in the clinical and animal studies that there are three results from the test [7, 13, 14]. A patient with no sensitivity will show normal cell migration with serum, no migration with PHA, and normal migration in the presence of the metal salts. A patient with metal sensitivity will show normal migration in serum, no migration with PHA, and no migration in the presence of the specific metal salt to which the T-cells are sensitive. The third condition is that of no cell migration in any of the test conditions. Patients in this third condition are referred to as "nonmigrators."

The condition of no cell migration has only been observed with blood samples taken from patients bearing metallic implants. In all cases where blood samples have been obtained after implant removal, the test has shown normal cell migration in serum and a specific sensitivity to one or more of the metals tested (nickel, cobalt, and chromium). We interpret this no migration condition to mean that the T-cells have been stimulated *in vivo* by metal ion corrosion products released by the implant. In animal studies, we have shown this condition to be associated with very severe tissue reactions at metal implant sites [14]. Thus, we consider the condition of no migration to be diagnostic for the presence of allergic reaction.

The problem of diagnosis of a metal sensitivity reaction to an implant is probably one of the most critical clinical issues. If the reaction results in a skin rash, then sensitivity is suspected. However, if the symptoms are pain, swelling, or loosening of the implant, there are many more probable causes, with infection being the most probable. In cases of contact dermatitis reactions to watches or jewelry, the diagnosis is comparatively easy: there is a rash under the metal item; one cannot see rashes around implants. Thus, we consider the diagnostic nature of the condition of no migration to be important and have been studying these patients in some detail. While the immunological details of the nonmigrators are not the subject of this presentation, it is worthwhile discussing them briefly.

The observation of the existence of the condition of nonmigration in some of our patients with metallic implants raised a number of fundamental questions. Theoretically the situation where there was no migration in the cell control would indicate an invalid test. However, this nonmigration occurred only in patients who were currently bearing metallic implants. In addition, tests set up at the same time or using the same reagents showed excellent migration in the control wells. Furthermore, within a few weeks of removal of the implant, the nonmigrators returned to the situation of good migration in the control well. Thus, the error did not seem to be with the test method. The question then focused on what was wrong with the patient cells. Cell viability studies were done using the method of exclusion of trypan blue according to the protocol described by GIBCO (Grand Island, NY) with their reagent. Cell viability was similar with migrators and nonmigrators with viability of 90% or greater.

The next question was what was the capacity for lymphocyte function. In order to assay for this, we chose to test for the production of blastogenic factor using PHA (Difco) as the stimulating lectin. The data on the human patients and on rabbits indicated that the lymphocytes of the nonmigrators were fully capable of responding to PHA. The data is insufficient at this time and thus has not been analyzed to determine if there is a small but definite difference in the degree of division in the unstimulated control cultures between migrators and nonmigrators or during the progression to the situation of nonmigration. However, the conclusion can be drawn that the lymphocytes do respond to PHA.

The next question was what about the function of the ameboid polys and monocytes which are the nonmigrators in this situation. It is evident that these cells are incapable of responding to chemotactic factor: either to C5a generated by zymosan and serum or to n-formyl peptides from bacteria. We are currently evaluating the binding and cleaving of the peptide which seems impaired and phagocytosis and killing of bacteria which do not seem impaired in the nonmigrator cells [15]. Thus, at the moment we feel that the defect resides on the ameboid leukocytes. It is possible that the lymphocyte has produced a factor which is bound to and inhibiting these cells. Attempts to cleave it off with trypsin and neuraminidase have been unsuccessful to date.

Another question would be whether or not there is a factor in the serum of nonmigrators which would inhibit migration. Serum from nonmigrators was concentrated 5x, diluted in increments to 1/100, and was used undiluted. There was no evident inhibition of migration of normal cells.

Similarly, the buffy coat leukocytes from nonmigrators were mixed at the starting concentration for the test and at dilutions of 1/2, 1/5, and 1/10 with normal migrating cells. There was no inhibition of normal migration.

Thus, at this time we have not found a factor that is soluble or a factor on cells that inhibits other cells. We also have not been successful in turning nonmigrating cells into migrating cells *in vitro*. This conversion requires the removal of the metallic implant from the patient or animal *in vivo* and then a recovery period of a few weeks for normal migration to be evident in the *in vitro* test.

The effect of the situation of nonmigration on various immune functions and nonspecific defense mechanisms remains an important aspect of this study and is under active investigation.

On the other side of the tissue-implant interaction leading to metal sensitivity and sensitivity reactions is the role of the implant and mechanisms of implant degradation leading to release of sensitizing ion haptens. To this end we are examining all implants

retrieved from patients whose blood has been tested for LIF. The objectives are to determine if there is any correlation between the immune response and the macro- and microscopic appearance of the implants; i.e., is there anything about the implant that suggests accelerated rates of corrosion that would result in elevated levels of alloy constituents in the tissues?

3. Methods

The patients presented in this study were all admitted to the Orthopaedic Service at Mary Hitchcock Memorial Hospital for surgical removal of a metallic appliance. The reasons for removal were primarily pain, implant revision, or routine removal after fracture healing. The blood samples and implants were contributed with informed consent. Pertinent clinical information was gathered using ASTM F-561 [16].

3.1. LIF test

To perform the LIF test, 10 cc of venous blood was withdrawn into a heparinized vacutainer and allowed to settle. After the red cells had settled, the white cell buffy coat on the top of the tube was removed and the cells washed, centrifuged, and resuspended in 100 µl of saline. The lymphocytes in the buffy coat were then subjected to five test conditions by pipetting 20 µl of the resuspended cells into each of five test tubes which contained 10 µl of the patient's plasma and 10 µl of the test solution. The test solutions were saline for normal cell migration control, PHA for T-cell function control, 0.2% $NiCl_2$ for nickel sensitivity testing, 0.2% $CoCl_2$ for cobalt sensitivity, and 0.2% $CrCl_3$ for chromium sensitivity. The tubes were then incubated at 37°C for thirty minutes to allow the metal ions to complex with the serum proteins and challenge the lymphocytes.

The migration of leukocytes was determined using 60 x 15 mm petri dishes containing 5 ml of a mixture of agarose and Click's growth medium [17]. Two sets of five 3 mm diameter holes were punched out of the medium, and 10 µl of the test solutions placed in duplicate in the wells. The plates were then incubated overnight at 37°C in 5% CO_2 (in a candle jar). The cells were then fixed with methanol, the agarose dried and stained with methylene blue or Giemsa, and examined for migration with a microscope. The distance the cells had migrated from the edge of the well was determined for each of the five test conditions. If the cell migration in the presence of a metal salt was less than 50% of the cell control, then the patient was said to be sensitive to that metal. There should be no migration with PHA.

3.2. Implant analysis

The method of implant analysis depended to some extent on the type of implant and the alloy used for manufacture. In all cases the implants were first examined with a dissecting microscope for evidence of surface damage in the form of wear, burnishing, or corrosion as per ASTM F-561 [16]. Interactions between screw heads and plates were described using the forms and contact area code described in this volume in the paper by Simpson et al. [18]. Implants were then sectioned with a carbide cutoff wheel with water cooling and the sections embedded for metallographic examination using standard techniques. After sanding to 600 grit, and polishing to 0.05 μ alumina, samples were examined for evidence of gas porosity. They were then electro-etched to reveal inclusions and microstructure and described using ASTM E-45 and ASTM E-112 [19, 20]. Stainless steel was etched for 20 seconds in 50% HNO_3 at 1.5 volts; cobalt alloy was etched for 2 seconds in 2% HCl at 3.5 volts. Rockwell hardness of cobalt alloy implants was determined using ASTM E-18 [21] and converted according to ASTM E-140 [22].

4. Results

The results of LIF testing of 164 patients at the time of implant removal are shown in table 1. The data are subdivided according to implant type and implant material. In the first column, the total number of patients with a given implant type is shown; the numbers in the "#" columns are the number of patients with implants of the particular alloy. The results of the LIF test are listed as "GOOD" meaning good cell migration with no metal sensitivity, "SENS" meaning sensitivity to one or more metals, and "NOM" meaning no migration in any of the test conditions.

NUMBER FOR EACH	COBALT-CHROME				STAINLESS STEEL			
TYPE OF DEVICE	#	GOOD	SENS	NOM	#	GOOD	SENS	NOM
45 SCREWS	29	10	5	14	16	4	5	7
20 HEMI-HIPS	19	7	2	10	1	1	-	-
17 PLATES	4	-	2	2	13	8	1	4
24 NAIL PLATES	11	2	4	5	17	7	2	4
20 I.M. RODS	3	-	3	-	17	4	9	4
9 STAPLES	7	2	2	3	2	2	-	-
29 PINS; WIRE	-	-	-	-	29	8	13	8
164 TOTAL	73	21	18	34	91	34	30	27
		29%	24%	47%		37%	33%	30%

Table 1. Breakdown of patients according to LIF test results, implant type, and implant alloy.

The patients in this group include those whose implants were removed as part of routine postoperative care, as in tibular-fibular screws and fracture plates, as well as those who presented with symptoms such as pain or skin rash, and thus removal was not routine in the strict sense of the word. The time of implantation ranged from 6 weeks to 16 years. Thus, it is difficult to draw many specific conclusions from this table.

Taking the 164 patients as a group, we find 55 (34%) with no sensitivity, 48 (29%) with a sensitivity, and 61 (37%) nonmigrators. In comparison, blood tests performed on 159 patients at the time of implantation (some of whom had previously had implants) revealed 72% with no sensitivity and 28% with sensitivity to one or more metals, with sensitivity to nickel (19%) being the most common.

In looking at table 1, one must be careful about drawing any conclusions about the differences between the two alloys, because of the wide range of implant type and duration. One group within the table that is relatively comparable is the bone screw group. These 45 patients had single or multiple screws which were removed routinely or because of pain. The incidence of allergic reactions as evidenced by no cell migration was 48% for cobalt-chrome, 43% for steel, and 47% overall. It is doubtful if this difference is statistically significant. As for differences in symptoms, there were several patients with cobalt screws presenting with skin reactions, while no patients with steel screws had obvious reactions. Complaints of pain were reported with both materials. At the time of this writing, there can be no statements concerning differences between the alloys used for screws. Unfortunately, our metallurgical analysis has not revealed any correlation either.

Because of the variation of implants, we do not feel detailed further analysis of table 1 is appropriate. However, detailed analyses of implants are appropriate, and there are some findings of interest in the analyses of specific implant groups. To look at correlations between implants and the immune response, we will discuss three implant groups: cast cobalt-chromium hemi hip arthroplasties, stainless steel fracture plates, and stainless steel nail-plates.

4.1. Hemi hip arthroplasties

Table 1 lists 19 patients with cobalt-chrome hemi hip arthroplasties. Of these, 14 were of the Moore or Thompson variety and were available for metallurgical analysis. Being large, weight-bearing devices with significant surface areas with direct bone-metal contact, it is not surprising that this class of implant had the highest incidence of allergic reactions (53% when another nonmigrator whose implant was lost is included). Because of the bone-metal contact in the stem and collar area, both microstructure and hardness were considered important material properties for corrosion and wear resistance. Similarly, the stems were examined for evidence of wear

and burnishing. The results of implant analysis, LIF testing, and the pertinent clinical findings are listed in table 2.

HEMI HIPS

#	YRS	RHA	VOID	G.B.	BURN	LIF	CLINICAL
1	1	67	0	O-C	0	GOOD	PAIN, INF
2	1.8	66	0	O-C	2	GOOD	PAIN, INF, MIG
3	3	66	0	0	4	GOOD	PAIN
4	5	63	2	O-C	6	GOOD	LATE INF
5	5	67	0	O-C	6	GOOD	PAIN
6	0.7	62*	>3	I	1	SENS	PAIN
7	3.7	60*	>3	C	2	SENS	INF, PMMA
8	0.5	60*	2.5	C	1	NOM	PAIN, MIG!
9	3	59*	>3	I	2	NOM	PAIN
10	4	65	0	0	6	NOM	PAIN, MIG!
11	4.7	62*	1.5	I	6	NOM	PAIN, MIG!, ASTHMA
12	5	60*	2.5	C	5	NOM	PAIN, LOOSE
13	11	66	0	0	7	NOM	PAIN, MIG
14	16	65	0	O-C	5	NOM	PAIN, ASTHMA

Table 2. Patients with hemi hip, Moore or Thompson implant prostheses.

G.B. = grain boundaries
O = indistinct
C = clean
I = precipitates or inclusions

RHA = Rockwell hardness A

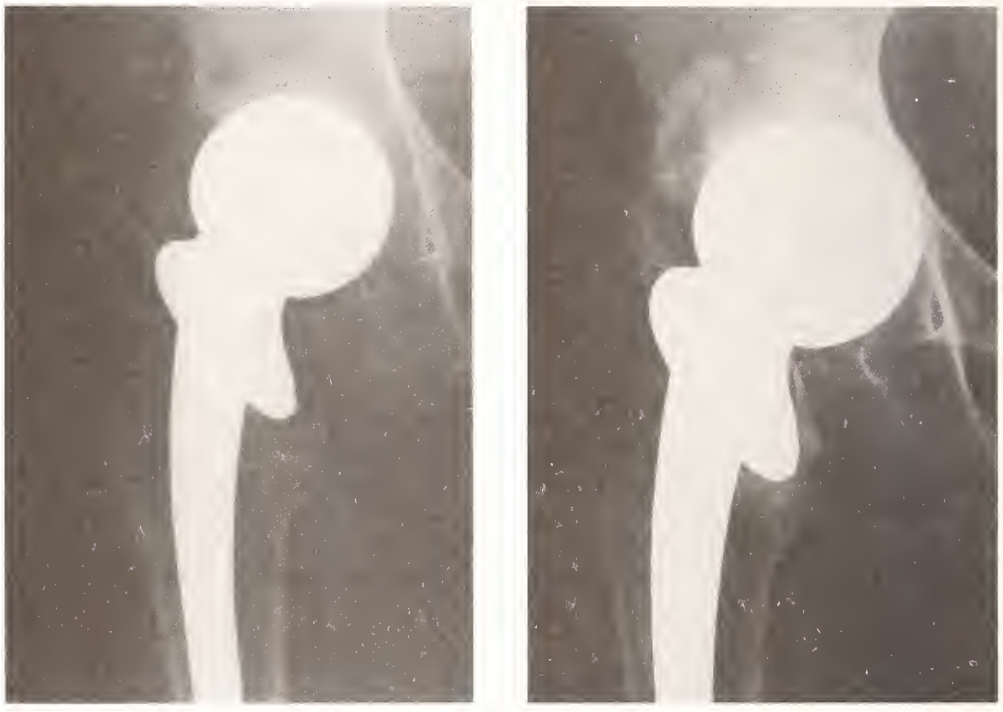
*means below ASTM F-75 specifications

In looking at the clinical symptoms listed, one sees that virtually all the patients complained of pain, whereas roentgenographic evidence of implant migration in the absence of infection was only seen in the no cell migration group. Three patients had severe implant migration as indicated by the exclamation mark "!". The two patients with asthma are discussed subsequently.

The implants were examined grossly for signs of wear and burnishing of the collar and stems, and graded on an arbitrary scale. Table 2 would suggest that burnishing had a stronger correlation with time than with the immune response. Sections were cut from the stem portion of the implants and hardness determined using the Rockwell A scale. ASTM F-75 Standard Specification for Cast Cobalt-Chromium-Molybdenum Alloy for Surgical Implant Applications [23] specifies that the hardness shall be Rockwell C 25 to 34, which when converted by ASTM E-140 [22] gives a Rockwell A range of 63 to 67. Those implants which were below specifications for hardness are indicated with an asterisk "*". It can be seen in the table that the hardness of the implants in the good migrator group were all within specifications, that the implants in the patients with sensitivity were below specifications, and four of the five implants from patients with no cell migration and implantation times of five or fewer years were below specifications. The two long-term (11 and 16 year) implantation times were implants within specifications. From this we can begin to draw a conclusion that hardness correlates with the LIF test.

Sections were also cut from the stems and embedded for metallographic examination of void content and grain boundary prominence. ASTM chart E-45 was used to attach a number to the void content. It

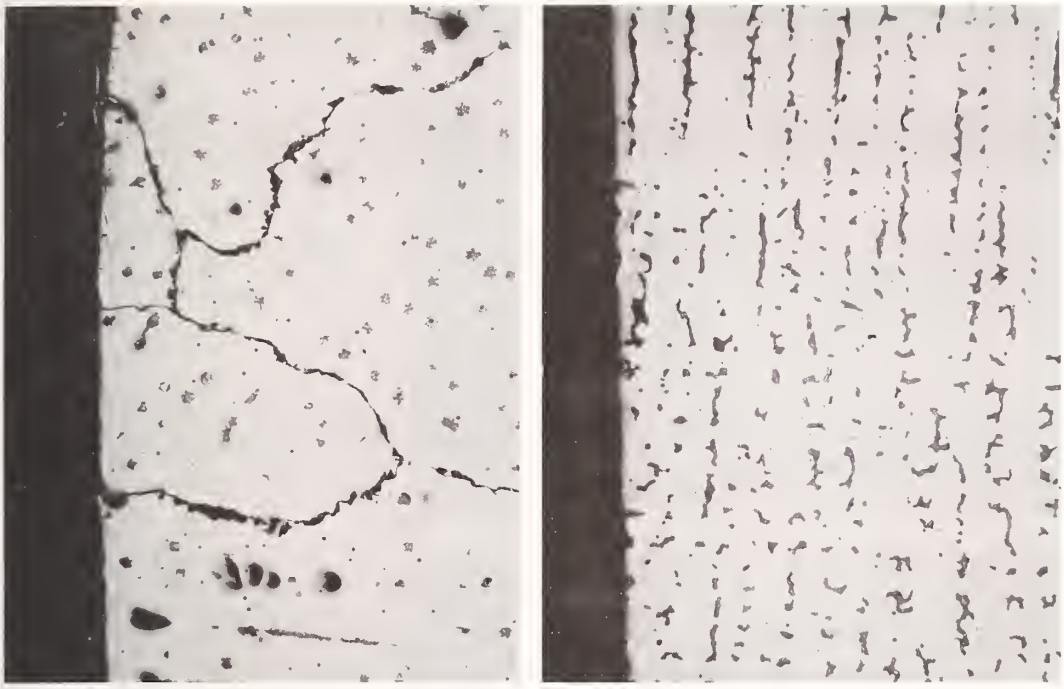
can be seen that void content has the same correlation as hardness, which is not surprising. Grain boundaries "G.B." were rated as being indistinct "O", distinct but clean "C", or containing precipitates of non-metallic inclusions or eutectoid blocky carbides "I". Here we see a weak correlation between grain boundary structure and LIF results. The significance of grain boundaries and the objectives of the investigation are seen in the following comparison [13].



(a) (b)

Figure 1
Roentgenographs of patient #11 in table 2 at the time of implantation (a) and 4 years later (b), demonstrating migration of the prosthesis down the femoral canal and into the acetabulum.

The roentgenographs in figure 1 demonstrate a significant amount of migration of the Thompson prosthesis both down the femoral canal and into the acetabulum during the four years between films. After about two years implantation, the patient began to complain of pain and symptoms of respiratory asthma. Patient #14 in table 2 also developed symptoms of pain and asthma, but in this case the symptoms developed 14 years after implantation of the Moore prosthesis. In this second case, there was no roentgenographic evidence of migration or loosening. Thus, the question is posed: why was the time course so different in these two cases?



(a) (b)

Figure 2
Comparative metallographic sections of hemi hip patients #11 (a) and #14 (b), with outer surface of implants on left sides of the figures. Original magnification x100.

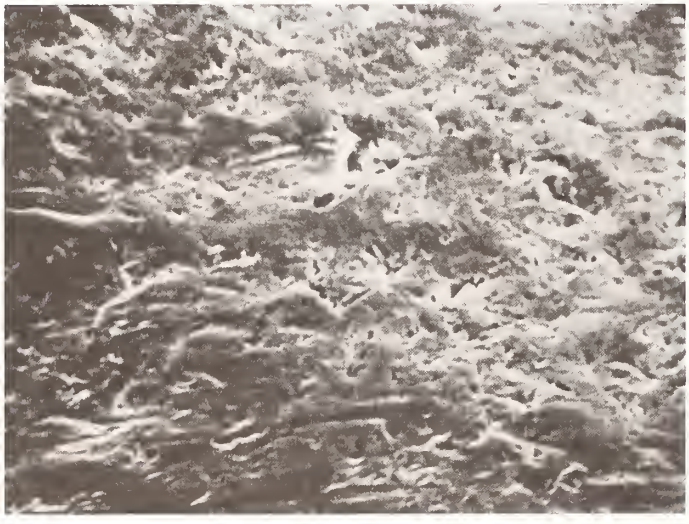
The transverse metallographic sections of figure 2 were taken to reveal the microstructure and grain boundary pattern of the stems of the prostheses of these two patients. The section in figure 2a reveals a significant amount of grain boundary inclusions and voids due to gas porosity. In contrast, the grain boundary in figure 2b is free of precipitates, and the microstructure is that of interdendritic carbides. The differences in these identically etched sections suggested that there might be a difference in the response of the actual prosthesis stem surfaces in the corrosive in vivo environments.

The scanning electron microscope photographs in figure 3 are of the actual outer surfaces of the stems of patient #11 (a) and patient #14 (b). Both pictures were taken at the same magnification. Figure 3a reveals a severely pitted surface with some deep cracks or slots which are suggestive of corrosive attack of intersecting grain boundaries. Figure 3b reveals a rough surface typical of a cast implant, with slight evidence of corrosive attack. It must be remembered that the corrosion attack seen in figure 3a was after 4.7 years in vivo, while that in figure 3b was after 16 years in vivo.

Figure 3
Scanning electron photomicrographs of prosthesis stems.

(a) hemi hip patient #11

original magnification x680



(b) hemi hip patient #14

original magnification x680

The hypothesis is that the grain boundary sensitization of the first case resulted in more rapid implant attack and tissue exposure to alloy constituents, and thus the development of a metal sensitivity reaction in two years, whereas the cleaner metal of the second case resulted in greater implant stability in vivo.

Another interesting finding in these two cases is that both patients complained of asthma, with onset of symptoms coincident with the onset of pain. After implant removal and replacement with cemented THR prostheses, both patients were relieved of their asthma, and LIF tests in both cases showed normal cell migration with sensitivity to cobalt and chromium in the first case, and to cobalt, nickel, and chromium in the second case.

4.2. Steel plates for fracture fixation

Thirteen patients tested for LIF production were admitted for removal of stainless steel fracture fixation plates. The plates from these patients were analyzed using the contact area code and plate analysis form described by Simpson et al. in another paper in this volume [18]. The results of the analysis and review of pertinent clinical findings are summarized in table 3. It will be noted that most of the plates were 4- or 5-hole plates used for forearm fractures.

STEEL PLATES

#	YRS	PLATE	SCREW PLATE CORR. AVERAGE	TOTAL	LIF	CLINICAL
1	0.6	4H	0/0	0/0	GOOD	ROUTINE
2	0.6	8H	0/0	1/1	GOOD	PAIN (SHOULDER)
3	1	5H	1/1	2/2	GOOD	ROUTINE
4	1.2	5H, 4H	1.7/1, 1.7/1.7	7/4, 7/7	GOOD	ROUTINE
5	1.2	4H	1/1	2/5	GOOD	ROUTINE
6	2.7	4H, 4H	1/0, 1/0	4/1, 4/1	GOOD	PAIN
7	3	5H	1/1.3	7/8	GOOD	INF
8	6	4H	1.7/2	7/8	GOOD	PAIN
9	0.7	10H	3.7/3.1	34/31	SENS	PLATE FX
10	0.5	7H	1/1	10/9	NOM	RASH, SCREW LOOSE
11	1.2	4H	0	2/0	NOM	PAIN
12	1.5	4H	3/2	11/8	NOM	ROUTINE
13	2	4H	3.2/3	13/12	NOM	ROUTINE, MILD PAIN

Table 3. Summary of implant analysis and clinical findings of patients with stainless steel plates.

Corrosion ratings are given as "plate/screw."

In looking at table 3, one can see that the average ratings for corrosion of the plates and screws from the patients with no metal sensitivity were all very low. In contrast the sensitive patient and two of the nonmigrators had average corrosion values higher than the first group. The table also shows that the total corrosion is higher in the sensitive and nonmigrator groups than in the first. While the numbers in this study are too low to draw definitive conclusions, there is a suggestion of correlation between corrosion and the development of metal sensitivity.

One of the patients, #10, who at first glance appears to be a glitch in the data, is in fact a very interesting case, and points to the question of what is more important, total corrosion or local corrosion. This patient had a 7-hole plate on the tibia, which was removed at 6 months, primarily because the proximal most screw came loose. The average corrosion was 1/1, which is very low, yet the total was 10/9. Two of the distal plate/screw contact areas showed significant attack, especially in position d2. Position d2 showed three 2/1/6 (medium size/minimal depth/corrosion) contact areas on the plate, similar contact areas on the screw head, and a rainbow pattern indicative of corrosion products on the upper plate surface. The patient also presented with an itchy rash on his shin over this screw position. The plate and screw d2 from this patient were examined with the scanning electron microscope and examined metallographically.

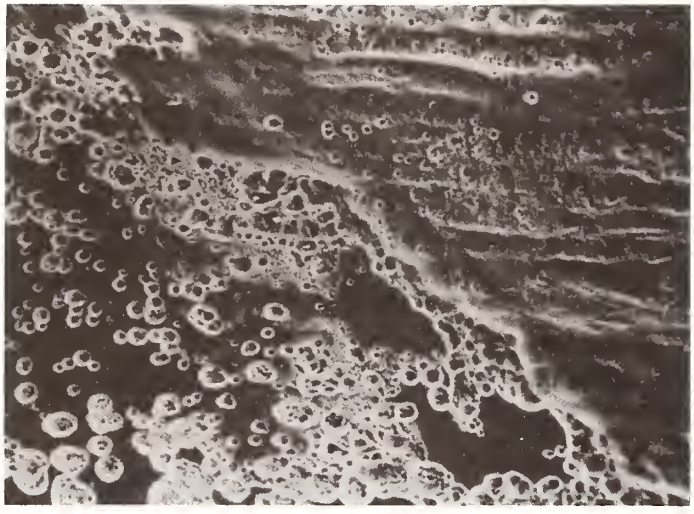


Figure 4
SEM photograph of contact area on plate position d2 from patient #10 in plate study. Contact area is in upper right, with edge running diagonally. Pitting is outside of primary contact area.

original magnification x500

Figure 4 is a SEM photograph of the contact area on the plate in position d2. The plate contact shows a parallel line pattern in the upper right portion of the figure, while significant pitting is seen outside of the primary contacting area in the lower left of the figure. The parallel line pattern in this round hole plate contact area is suggestive of the cold rolling cold work pattern of this class of metal. This and other SEM pictures of this plate hole and position d4 showed significant corrosive attack.

At low power the corresponding contact area of the screw d2 showed a superficial attack with a crack-like structure in the middle. The SEM photograph of figure 5a shows that the crack was a result of corrosive attack, possibly by crevice corrosion. Surrounding the crack was a region with superficial pitting. Elsewhere in the middle of the contact area, a structure similar to that seen in metallographic etching of a cold worked steel was seen, as shown in figure 5b. Near the edge of this screw contact area, figure 5c, the metal showed crystallographic pitting suggestive of low pH corrosive attack.

The significant amount of corrosive attack and hence metal removal from the contact area in position d2 correlated with the allergic skin reaction seen over this screw, and is consistent with the nonmigration status of this patient in the LIF test. However, this seems like a significant amount of corrosion for only 5 months *in vivo*. Thus, the question of metal quality was raised.

Longitudinal and transverse metallographic sections of the plate and screw d2 are shown in figure 6. The four sections were etched and photographed under identical conditions. So as not to over-etch the transverse section of the screw, the other sections are somewhat under-etched. Both plate and screw show a comparatively clean, fine-grained structure, with elongated grains in the longitudinal sections.

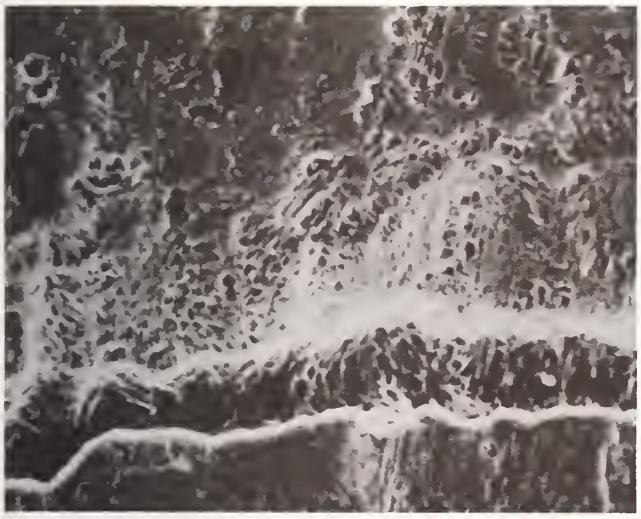
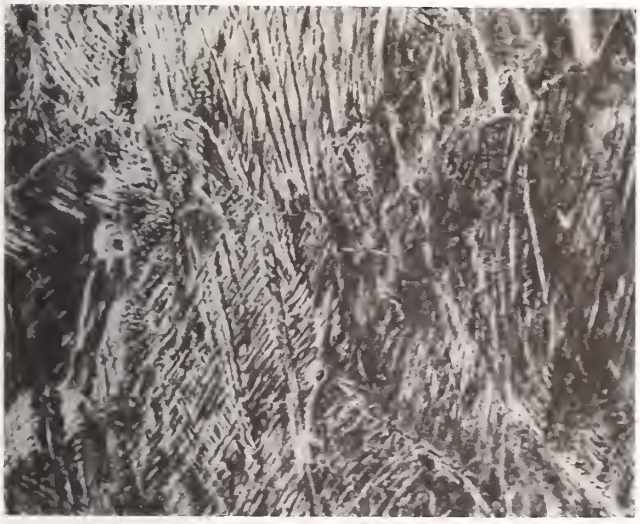


Figure 5
SEM examination of screw d2 from plate patient #10.

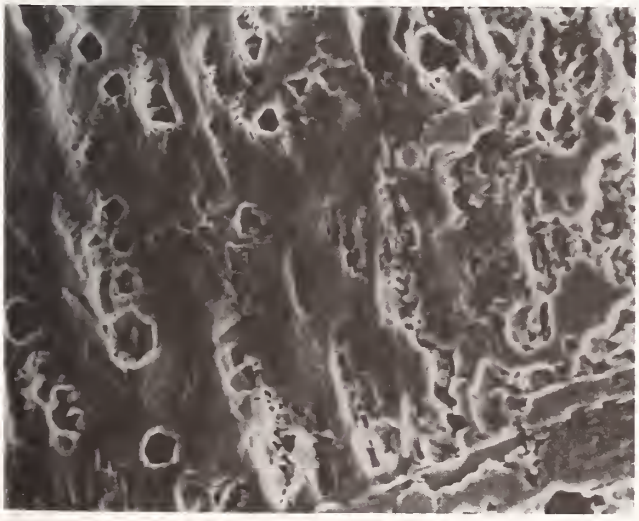
(a) crack and corrosion near center of contact area

original magnification x1200



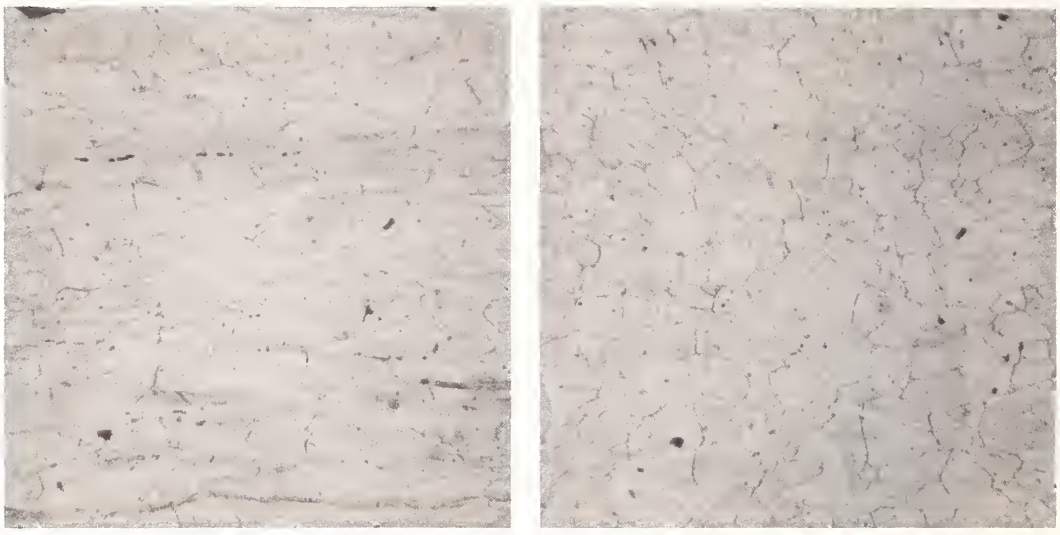
(b) corrosion revealing cold work microstructure from middle of contact area

original magnification x600

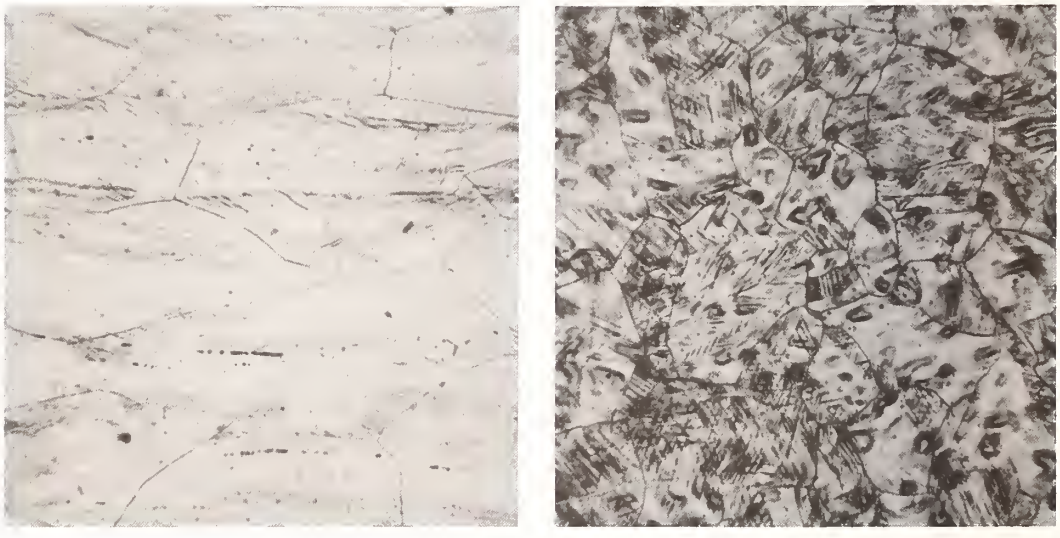


(c) crystallographic corrosion pitting near edge of contact area

original magnification x1200



(a) Plate (b)



(c) Screw (d)

Figure 6
Metallographic sections of plate (a, b) and screw d2 (c, d) from patient #10 in the plate study. Figures on the left (a, c) are longitudinal sections; figures on the right (b, d) are transverse sections. Original magnifications x320.

The longitudinal sections, especially that of the screw, show a stringy sort of cold working pattern related to cold working during rolling. It is hypothesized that this cold forming structure corresponds to the parallel line pattern seen in the plate contact area of figure 4. Aside from these observations, the metallographic examination did not reveal anything unusual about the metal used for manufacture of this plate and screw.

4.3. Stainless steel nail plates

Thirteen patients in the LIF and implant removal study were admitted for removal of nail plates or angle blade plates. The implants were analyzed using the same contact area code [18] and a variation of the analysis form as depicted in figure 7. The plate holes were numbered as though all were distal, and the contact area code was used to describe the plate/screw interaction and the interaction between the various components of the nails, bolts, and sleeves.

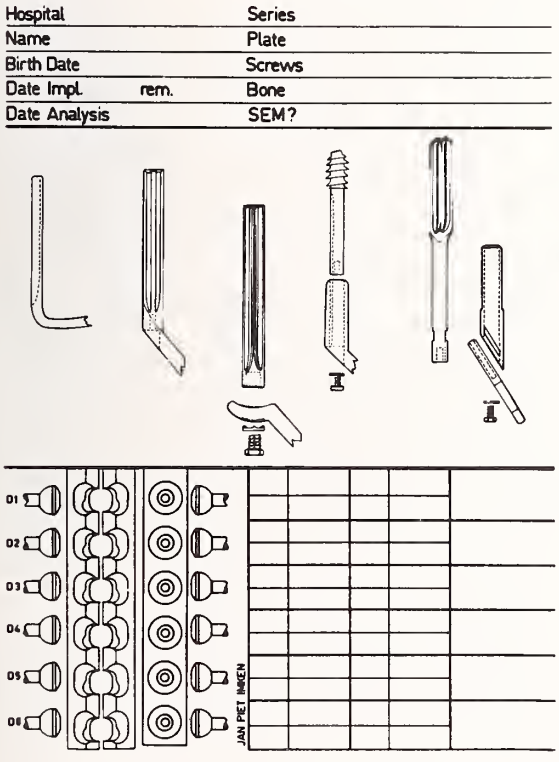


Figure 7
Form used for recording results of implant analysis of nail plates.

The implants, implantation times and the results of implant analysis, LIF testing, and patient history review are listed in table 4. The description of corrosion lists the screw positions where plate/screw interaction was seen and where interaction of the bolt

and washer was observed. The most striking observation one can make about this table is the wide variation of implants used. There is some suggestion of more significant corrosion in the sensitive and nonmigrator patients, although the correlation is not strong.

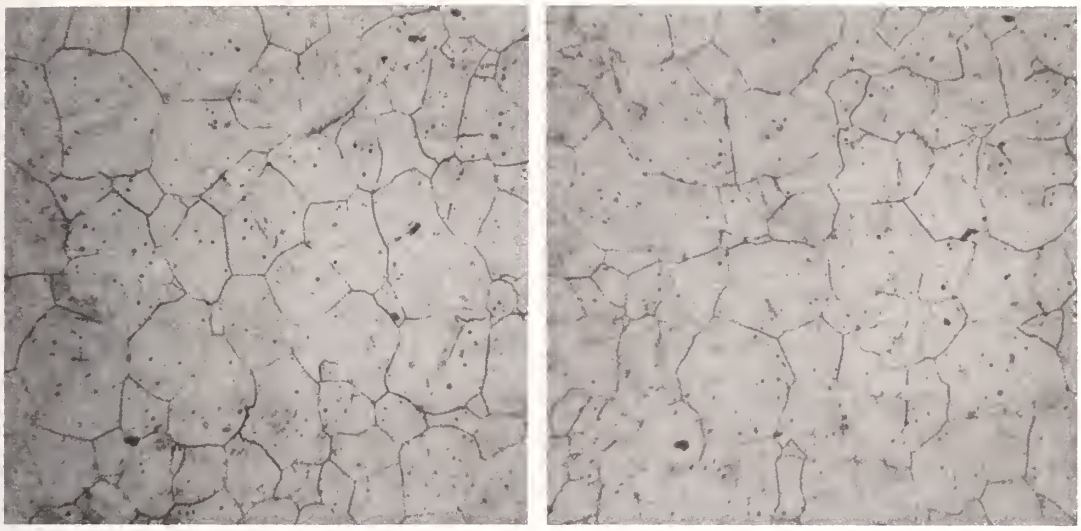
STEEL NAIL PLATES

#	IMPL	YRS	CORROSION	LIF	CLINICAL
1	M	2 MO	MIN	GOOD	THR
2	J4	2 MO	D2 (2/1/6)	GOOD	BAD POSITION
3	C3	5 MO	MIN	GOOD	MIG
4	J5	9 MO	D2, D5 (2/2/6)	GOOD	ROUTINE
5	M	10 MO	D2 (2/2/6)	GOOD	AVASC. N. THR
6	M	2	NAIL-SLEEVE	GOOD	PAIN, N.U.
7	M	9	MIN C.W. N=S	GOOD	THR
8	SP+M	1	WASH, D1, D5 (3/3/6)	SENS	PAIN
9	SP+M		D2, D5, D6 (2/2/6)	SENS	
10	C3	5 MO	D2 (3/1/6), N-S (3/2)	NOM	INF. AVASC. N.
11	2 A5	11 MO	D5 (3/1/3)	NOM	ROUTINE
		5 MO	D4 (3/2/6, 7)		
12	E	1.2	BURNISHING	NOM	NONU.
13	2 SP+T	9	WASH, D1 (3/2/6)	NOM	PAIN BURSA
		12	D1 (2/1/6)	NOM	PAIN, BOLT MIG

Table 4. Steel nail plate study.

M = Massie nail
J4 = Jewett with 4 screws
C = compression screw
SP+M = Smith-Peterson + McLaughlin
SP+T = + Thornton plate
A = angle blade plate
E = Elliot blade plate

If we are to hypothesize that time and corrosion will lead to elevated tissue levels of alloy constituents and thus the possibility of metal sensitivity, one might ask why the patient #7, with a multi-component Massie nail had no sensitivity after 9 years implantation. In examination of the implant, there was virtually no evidence of degradation between plate and screws, nor between nail and sleeve. It is proposed that one reason for the lack of nail-sleeve interaction is that, unlike most similar implants, there were no microstructural differences between the nail and sleeve. As is shown in figure 8, the grain size and degree of cold working of these two identically etched and photographed sections was virtually the same. While hardness testing would be a better method for differentiating degrees of cold work, the issue here is electrochemical differences which might lead to galvanic corrosion. The response of these two sections to the electrochemical etch was the same, and thus their response to the corrosive in vivo milieu could be expected to be the same. In contrast, most sliding nail-plate implants show a significant difference in cold working. Such was the case in the implant from patient #6, which showed large areas of superficial corrosive attack in nail-sleeve contact areas.



(a) (b)

Figure 8
Metallographic sections of identically etched and photographed sections of the nail (a) and sleeve (b) of the Massie nail-plate implant from patient #7 in table 4.

5. Discussion

In considering the clinical significance and the role of implant corrosion in metal sensitivity reactions to metallic implants, we must bear in mind that there is a very significant patient variable in this subject: genetics. Some patients have or can develop metal allergy while others will not. Most people can go through life wearing jewelry and stainless steel watch bands with impunity, while others will develop contact dermatitis. It has been reported that the incidence of metal allergy in the "normal" population is 13% for nickel, and 7.8% for chromium [24]. Thus, our studies looking at correlations between the results of implant analysis and LIF testing are skewed by patient genetics.

Another issue to be raised is the sensitivity and specificity of the LIF test. It is well known that some of these metallic elements are toxic, and thus their presence in the LIF cell culture could have a toxic effect on the leukocytes rather than a stimulatory effect on the T-lymphocytes. We have conficence that toxic effects are minimal since most patients show good migration in the presence of the metals in the concentrations used. However, the issue still remains as to differences in individual patient sensitivities to the toxicity of the metals. Since T-cells will only respond to metal ion haptens complexed with proteins, the immunogenicity of the specific protein complex may play a role in the

sensitivity and specificity of the test results. We have been critical of the skin test since only skin proteins are involved, and yet use plasma rather than tissue proteins in the test. Nevertheless, the plasma proteins are certainly available at the implant site for hapten binding. Another disadvantage of the skin test is that it does not assay for sensitivities involving T-cell, B-cell and antibody interactions, as does LIF test. However, these interactions may result in the LIF test being too sensitive.

In looking at the LIF test results for specific implant types, one sees a surprising number of nonmigrators in the bone screw group. While these are comparatively small implants, they are in a mechanically stressed situation, with direct bone-metal abrasion possible, and the implants themselves tend to have surface defects such as small casting defects or machine tool chatter marks. In comparison, the much larger intramedullary rods tend to be much smoother and more highly polished. One interesting patient with a Lottes tibial nail was a nonmigrator until the rod failed in fatigue. Some months later he had good migration with a nickel sensitivity. Analysis of the retrieved rod revealed significant burnishing of the distal stem of the rod. Presumably the burnishing was occurring prior to failure, and after failure and re-casting of the leg, the bone-metal abrasion was reduced to the point where presence of the otherwise polished rod was no longer producing tissue levels sufficient to stimulate an immune response.

This hypothesis of wear between bone and metal being a causative factor in metal sensitivity reactions has been applied in the discussion of hemi hip arthroplasties in section 4.1. One of the difficulties of the implant analysis was determining how much metal had been worn off the stems. The burnishing code numbers in table 2 were more an estimation of the area of burnishing than of the depth of the worn area. Thus, the numbers do not truly reflect the amount of metal lost. On the other hand, the hardness of a metal is related to its wear resistance. Table 2 shows a good correlation between soft metals and patients developing early complications associated with metal sensitivity. The process of wear would also lead to fretting accelerated corrosion [25], and set up a crevice corrosion environment. This mechanism is also proposed for the severe attack seen in screw and plate d2 of patient #10 in the plate study.

With this discussion of bone-metal wear, it is of interest to observe that the treatment for the hemi hip patients, and some of the hip-nail plate patients was total hip arthroplasty with cemented femoral components. These devices have been well tolerated, presumably by isolation of the metal component with PMMA bone cement and articulation with UHMWPE acetabular cups. The polished prosthesis neck seems to be sufficiently passive to avoid immune reactions. However, some patients have had allergic complications when stainless steel wire (bone-metal contact) was used for reattachment of a trochanteric osteotomy [8].

As for the two patients with asthma, prior to implant removal both were well controlled with medication, and both discontinued using medication after prosthesis removal and total hip replacement. Whether the implant allergies actually caused the asthma is still a subject for debate at our institution. Asthma is a complex clinical syndrome with many endogenous and exogenous causes. It may have been coincidence in these two cases. However, these patients were among the few in our and other studies with allergy to chromium, and asthma is known to occur in chromium workers.

6. Conclusions

It can be concluded from this study of 164 patients at the time of implant removal that metal sensitivity reactions can be a cause of patient morbidity associated with metallic implants. However, sensitivity is probably not a major cause of complications; e.g., all the hip arthroplasties hurt. In reviewing a patient's symptoms, sensitivity should be considered. If the patient is reacting to the device, the symptoms probably will not improve, and if appropriate, removal of the device should be considered.

Cases have been presented where evidence of implant degradation due to wear and corrosion do correlate with the immune response. The study is still too limited in size to make any definitive conclusion concerning specific alloys or implant types. It does suggest that implants subjected to situations conducive to wear and fretting corrosion are likely to stimulate an immune response. The question of whether implants can cause metal sensitivity and sensitivity reactions is the subject of an ongoing prospective study in which sensitivity testing is performed prior to and during the implantation period and at the time of removal. The retrieved implants are also analyzed. We believe that such prospective studies are essential for the development of a better understanding of the relationships between metal implants, metallurgy and metal allergy. We do not recommend skin testing for such prospective studies.

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TECHNIQUES FOR THE EXAMINATION OF TISSUES IN IMPLANT RETRIEVAL ANALYSIS

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A detailed examination of the tissue response to implanted high purity metals has been undertaken. The methods used include conventional histology, enzyme histochemistry, transmission and scanning electron microscopy, EDAX analysis and elemental analysis by flame and flameless atomic absorption spectrophotometry and polarography. Details of these techniques are given in this paper with a summary of some of the results obtained in experiments and the applicability of the methods to the examination of tissue samples taken at implant retrieval.

1. Introduction

It has long been recognised that the greatest value in implant retrieval analysis is obtained when the examination involves the biopsy (or autopsy) tissue samples and clinical data in addition to the materials of the device. A full understanding of the reasons for failure, or conversely of the conditions predisposing to success, can only be achieved when all the factors are considered. This point was emphasised in earlier work from our laboratory. [1,2][1] The significance of metallic corrosion, for example, can only be assessed by an examination of the tissues adjacent to the implant and with reference to the clinical observations leading to implant removal.

In most of the reports of the tissue examination subsequent to implant removal, reference is only made to haematoxylin and eosin stained sections of tissue, studied by light microscopy. Whilst giving a reasonable amount of information, and being quite adequate in many circumstances, such an examination cannot always determine the extent or significance of the implant-tissue interaction and it may be desirable to use other methods.

[1]Figures in brackets indicate the literature references at the end of this paper.

In view of this situation, attempts have been made to utilise a variety of microscopical and analytical techniques in the assessment of the biological response to orthopaedic implants and these are discussed in this paper. It must be recognised that there are other aspects of the biological response that are not included here, such as the immunological and microbiological aspects, their ommission being due solely to the constraints of the present experimental programme, without any reflection on their importance.

Because of the difficulties involved with standardising data from retrieval specimens, and the absence of controls, the experimental work described has been carried out with animal models, with a view to gaining a greater understanding of the fundamental aspects of biocompatibility and to developing techniques for later use in a programme of device retrieval.

2. Animal Model

All of the experimental work has been performed with black and white hooded Lister rats of the Liverpool strain. These are usually three months old at the time of operation. Two types of experiment are relevant to the present discussion. In the first, metallic discs are implanted intramuscularly, bilaterally in the paravertebral muscles, where they are retained for varying periods of time. After sacrifice the tissues and discs are prepared for examination by one of the methods described below. In the second type of experiment the distribution of metal ions in the animal tissues is determined following the intramuscular or intraperitoneal implantation of powders. In this case, one of several types of analytical method may be used on the dissected tissues. The methods described are those found to be most suitable in our laboratory, although naturally there are alternatives which other workers may prefer.

3. Materials

Since this programme of work is primarily aimed at providing a better understanding of the biocompatibility of metals, only pure metals have been used. It is difficult enough evaluating the tissue response to one metal without introducing the complexities of alloy systems, where there may be three, four or even more elements of significant concentration, each being released at a different rate and each with a different potential for cytotoxic behaviour. Nevertheless, the techniques used, which are the main concern of this paper, are equally applicable to pure metals or alloys.

The metals used in the study include nickel, cobalt, copper, aluminium, titanium and lead. Table 1 indicates the purity of each metal. The implanted discs were 5mm in diameter and the powders were of 20 mesh particle size.

Table 1 Pure Metals Used[1]

	Disc	Powder
Nickel	99.999%	99.995%
Cobalt	99.998%	99.995%
Copper	99.999%	99.999%
Aluminium	99.998%	99.98%
Lead	99.999%	-
Titanium	99.8%	99.8%

4. Microscopical Technique

Conventional histological methods involving either paraffin wax embedded or frozen blocks stained by haematoxylin and eosin give a considerable amount of information about the morphology of the tissue. For example, detailed studies of the fibrous tissue capsule around the implanted discs of the pure metals have been undertaken using frozen section techniques, representative areas being shown in figure 1 (a-e). These techniques are standard and need no further comment here. They may, however, be supplemented by other techniques to give more detail about the effects in the tissue.

4.1 Histochemical methods

The response of tissue to the implantation of a foreign body usually involves a considerable cellular infiltration. These cells will be continuously synthesising and releasing enzymes for specific functions, associated with, for example, phagocytosis. Each type of cell has associated with it a variety of lysosomal enzymes such that the presence of enzymes in tissue is indicative of the types of cell that are present and, more importantly, the quantity of the enzyme reflects cellular activity and, by implication, the extent of the effect of the foreign body on the tissue. Salthouse [3-5] was the first to demonstrate the relationship between lysosomal enzyme activity in the tissue with the toxicity of implants, in this case plastics and has refined the techniques to allow a quantitative analysis of the response [6]. The techniques presented here are those used in our laboratory for the study of the soft tissue response to metals.

The principle of the technique is that if enzymes in tissue are presented with their own specific substrate, a reaction will take place, yielding a well defined product which may be possible to detect. Often this primary reaction product is invisible and so it is coupled with another substrate that is insoluble but visible. Thus, the tissue is stained according to the enzymes which are present.

[1] Metals Research Ltd., Cambridge, U.K.

The coupling substrate used varies with different enzymes, diazonium salts being used for phosphatases and tetrazolium salts for dehydrogenases for example. It is important to note that pH control is very critical in this process.

It is also important that controls are performed, since substrates deteriorate and may give false negatives. A positive control should always be included which will confirm the activity of the chemicals used whilst negative controls, produced for example by deliberate omission of the substrate from the incubation medium or inclusion of specific enzyme inhibitors, should indicate that any positive results obtained with test samples are not artefact and exclude non-specific background staining.

For this work, frozen sections are necessary and rapid freezing is essential to avoid ice crystal artefacts. Isopentane suspended in liquid nitrogen is suitable and the tissue sample is placed in the liquid while held between two metal discs to give faster heat conduction. Approximately 7μm thick sections are prepared at -15^{0} C in a cryostat and placed on glass coverslips.

The following is a brief outline of the methods used for selected enzymes.

4.1.1. Phosphatases

The hydrolysis of organic phosphate esters provides the basis for the reactions. After reaction with the enzyme, the alcoholic residue of the substrate is allowed to react with a diazonium salt to give a highly coloured insoluble azo dye.

(1) Alkaline phosphatase. The substrate used here is naphthol AS-Bl phosphate which is hydrolysed by the enzyme producing an insoluble naphthol derivative. This is reacted with a diazonium salt such as fast red TR, which yields an insoluble azo dye at a final pH of 9.0.

(2) Acid phophatase. A substituted napthol is also used here to yield an insoluble naphthol derivative, which is reacted with hexazonium pararasaniline at a pH of 4.7 to 5.0. An example is given in figure 2a.

4.1.2. Dehydrogenases

The coupling substrates used for dehydrogenases are tetrazolium salts which are water soluble and almost colourless and accept H^{+} released from the substrate after reaction with the enzyme, giving an insoluble highly coloured deposit of a formazan compound.

(1) Succinate dehydrogenase. The substrate is sodium succinate and the coupling substance a monotetrazolium salt (MTT). Formazan is then chelated with Co^{2+} ions to give a coloured insoluble granular deposit. The pH is 7.0.

(2) Lactate dehydrogenase. The technique is essentially the same but uses sodium lactate as the substrate. In addition, NAD is required as a hydrogen acceptor before the tetrazolium salt can be converted into a formazan compound (Fig. 2b).

4.1.3. Leucine aminopeptidase

The substrate is l-leucyl-4-methoxy-β-naphthylamine, which is split by the enzyme. A diazonium salt, fast blue B is used to react with this yielding an insoluble azo dye which can in turn be treated with $CuSO_4$ when the copper ions form a chelate with the azo dye. An example of a section stained in this way is seen in figure 2c.

4.2. Electron Microscopy

The electron microscope, with all its analytical facilities, provides a very useful tool for the analysis of biological tissue. Scanning electron microscopy (SEM), transmission electron microscopy (TEM) and Energy Dispersive X-ray Analysis (EDAX) have all been used.

4.2.1. Scanning electron microscopy

Critical point drying is used in the preparation of specimens for scanning electron microscopy. This involves the following sequence of solutions.

50%	ethanol/water	10 mins
70%	ethanol/water	10 mins
90%	ethanol/water	10 mins
95%	ethanol/water	10 mins
100%	ethanol/water	15 mins
3:1	ethanol/acetone	15 mins
1:1	ethanol/acetone	15 mins
1:3	ethanol/acetone	15 mins
100%	acetone	2 x 20 min changes

The tissue previously fixed in formal saline, is placed in mesh baskets and covered with acetone, which is then flushed with CO_2 until the acetone layer is removed. It is left for 1 hour in liquid CO_2 before the CO_2 is sublimed off, which should occur at 38^0 C. The specimens are mounted on aluminium stubs and coated in the normal way prior to examination in the microscope.[1]

Interesting observations have been made on the tissue adherent to implanted metal surfaces using this technique, some examples being shown in figure 3.

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[1] Jeol JSM-3SC

4.2.2. Transmission electron microscopy

Transmission electron microscopy[1] is carried out on specimens prepared in the following way.

Fixation:	1 1/2 hours in glutaraldehyde (cacodylate buffered at 6.25%).
	1 1/2 hours in cacodylate buffer (with changes.
	1 1/2 hours in osmium 1% (2% in water diluted to 1% in cacodylate buffer).
Wash:	Cacodylate buffer, pH 7.4.
Dehydrate:	10 mins 70% methanol
	30 mins 90% methanol
	2 hours 100% methanol, with changes
Embedding:	15 mins propylene oxide
	overnight 50/50 araldite[2]/propylene oxide at 60° C.
	Transfer to araldite containing accelerator, with 2-3 changes before final embedding in gelatine capsule.

4.2.3. EDAX

The same method may be used for the preparation of specimens for EDAX investigations, although it may be preferable to use a non-aqueous process to avoid any problem of leaching of metal ions. In this case, the procedure is as follows:

12 hours in glycol
24 hours in Cellusolve
48 hours in 50/50 Cellusolve/Spurr resin.

24 hours in 100% Spurr resin. The specimens are preferably mounted on aluminium grids rather than copper to prevent masting.

5. Analytical Methods

When examining the tissue adjacent to metallic implants, it is desirable to determine the concentration and if possible, the distribution of metal in that tissue. It would also considerably increase our knowledge of the effects of metallic prostheses on patients if samples of organs could be taken at post mortem examination for analysis. There are several methods available for this analysis, two of the more important, atomic absorption spectrophotometry (AAS) and polarography being discussed in this paper.

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[1] JEOL, JEM 100c X
[2] Ciba-Geigy

5.1. Ashing techniques

The traditional method of preparing biological tissue for elemental analysis involves digestion in acid. The method used in our laboratory is as follows. The sample is weighed, dried at 110° C and reweighed. Approximately 0.25 cm^3 of a solution comprising 1 part conc. HNO_3 and 3 parts H_2SO_4 is added per 100mg wet weight. This is heated until it becomes clear, with no further brown fumes evolved, or until no further clarification occurs. Heating is carried out at 80° C in polypropylene vessels. The product is usually a brown liquid, fully miscible with water and quite suitable for AAS. However, it is not entirely successful with fatty tissue, which tends not to dissolve, and bone which may give a precipitate of calcium sulphate.

This technique has the advantage that many samples can be processed at the same time. If complete digestion can be achieved and the solution is clear, then all metals and anions are accessible to any of the analytical techniques. With solutions that do not clear, complexing agents may be present leading to interference with ion-selective electrodes, polarography and other methods. The main disadvantage of the technique is that the concentrated acids used can be a source of contamination, especially for the lighter elements such as aluminium, and ultimately controls the sensitivity. All solutions are made up in conc. H_2SO_4 which makes dilution difficult and implies all standards have to be in H_2SO_4 as well. In flameless AAS the signal tends to be very noisy.

An alternative technique is now used exclusively in our laboratory since it is less susceptible to contamination. This involves subjecting the sample to a low temperature discharge in an instrument referred to as a Plasma Asher.[1] The sample is weighed, dried in vacuo and reweighed. Dry samples, contained in glass or quartz vessels are placed in the chamber of the instrument which is then operated for about 18 hours with an oxygen flow rate of 2-3 cm^3 min^{-1}, at a pressure of 1 torr and 100 watts power. For most materials, the sample should be stirred to disturb the upper layer of ash which would otherwise obstruct the access of the plasma to the sample. After ashing the sample is dissolved in diluted HCl at, for example, 0.1 cm^3 0.5M per 100 mg wet weight. The technique is slow since a limited number of samples can be ashed at any one time and there is a possibility of contamination from the glass vessels, although this has not been detected so far. Hydrochloric acid is the purest of acids and hence gives rise to considerably less contamination than the acids used in wet digestion. The solutions are dilute and so no problems occur with standards or dilutions.

[1] Plasmaprep 100: Nanotech (Thin Films) Ltd., Manchester.

5.2. Atomic Absorption Spectrophotometry (AAS)

This technique is based on the absorption of light by atoms of the element to be analysed. A lamp specific to the element in question is used (i.e. giving radiation of a specific wavelength) and noise can be reduced by chopping this with a continuous source (e.g. D_2) which envelops the chosen wavelength, typically to $\pm$ 0.2nm.

There are two basic types of AAS, the difference lying with the method of atomisation of the sample and the sensitivity. With flame AAS[1] a solution containing the element is sprayed into a flame, either acetylene-air or acetylene-nitrous oxide, where it atomises. The nitrous oxide flame gives a higher temperature and hence a higher atomisation rate. With flameless AAS[2] a small volume of the sample is injected into a graphite tube. Here automatic temperature programming will dry the sample, volatilise unwanted material, especially organic substances, and then vaporise the sample. The atomisation temperature may be as high as 3000^0 C. An inert gas is used as a blanket to prevent oxidation of the tube. This may be nitrogen, but for metals which form stable nitrides, such as aluminium or titanium, argon is preferable.

It is necessary in all cases to prepare a series of standard solutions covering the expected sample concentration. Each is analysed to prepare a calibration curve. Since the atomisation process is very fast with the flameless AAS, only single values can be obtained so that replication of injections is essential.

Generally the flameless AAS is more sensitive than the flame AAS, their use being optimum in the ranges 5-500 p.p.b. and 0.5-100 p.p.m. respectively. The flame AAS technique is fast (10 sec per sample) and precise as sample spraying is not under operator control, but has limited sensitivity and requires relatively large volumes (71.5 cm^3). Flameless AAS is slower (2 mins per injection) and its accuracy is controlled by the precision of injection. However, it is 100 to 1000 times more sensitive and there is less risk of interference because of the ashing stage and the high temperature attained.

5.3. Polarography

This technique involves conversion of the metal from an ionic form to a lower oxidation state, which may be the metal itself. The rate of this reaction is a function of the standard electrode potential, the diffusion coefficients for the reactants and products and the concentration of the reactants and products. The rate is measured as the electrical current that flows and by the use of standards this can be converted to a concentration of the metal.

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[1] SP 192 Pye Unicam Ltd.
[2] SP 9-01 Digital Flameless Atomiser, Pye Unicam Ltd.

The apparatus required is a reproducible anode at which the reactions may occur, a current carrying cathode, a reference electrode, an accurate scanning potentiometer and a very sensitive ammeter suitable for currents less than 0.02μA.[1]

There are several different varieties of polarographic technique available which primarily reflect electrical refinements to eliminate background contributions to the current and to avoid electrochemical effects which reduce the sensitivity. The conditions of pH, redox potential and chelating species must be selected to separate the metal of interest from others that may be present.

Anode stripping voltammetry is one variation of polarography that can increase the sensitivity by almost 1000-fold, giving a detection limit in the region of 0.01 p.p.b. If the metal forms an amalgam with mercury and is reducible at a mercury electrode, then it may be concentrated by electrolysis into the mercury drop. On scanning the potential in a positive direction the metal is oxidised, giving a large current peak. The technique is restricted to a few metals, chiefly lead, cadmium, thallium, copper, zinc and antimony, although other metals can be included by use of various esoteric refinements.

One problem with polarographic techniques is the sensitivity to contamination due to either chelating or surface active species, which places a greater emphasis on the digestion procedures.

5.4. Comparison of Polarography and AAS

Table 2 illustrates the technique most suitable for a range of metals and the sensitivity that can normally be achieved.

Table 2 Analytical methods

Metal	Technique	Sensitivity
Aluminium, Al	AAS (flameless)	0.2 ppb
Cobalt, Co	AAS (flameless)	0.5 ppb
Chromium, Cr	AAS (flameless)	1.0 ppb
Copper, Cu	Polarography	0.01 ppb
Iron, Fe	AAS (flame)	0.2 ppm
Molybdenum, Mo	AAS (flameless)	0.3 ppm
Nickel, Ni	AAS (flameless)	1.0 ppb
Titanium, Ti	Polarography	1.0 ppb
Vanadium, V	Polarography	2.0 ppb
Tungsten, Tu	Polarography	2.0 ppb

[1] PAR 174A: Brookdeal Electronics Ltd.

An example of the results obtained with these techniques is shown in Table 3, which compares the cobalt levels in various tissues and organs of rats which were maintained either on a standard diet or a diet supplemented with a ten-fold increase in cobalt content, or were implanted with cobalt powder, either intraperitoneally or intramuscularly. Analyses were performed by flameless AAS.

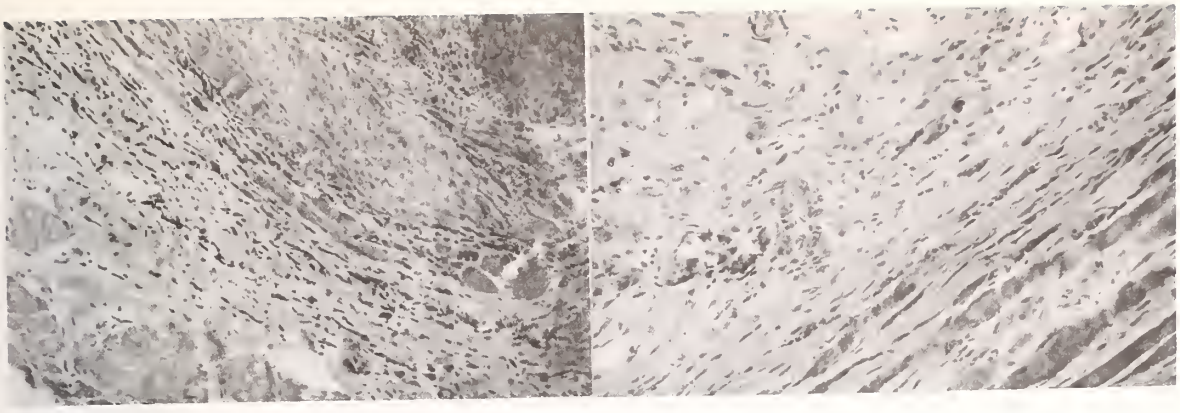
Table 3 Cobalt Levels in Rats (ppm)

Tissue	Control	Cobalt Supplemented Diet	10 wk I.M.	10 wk I.P.	26 wk I.M.	26 wk I.P.
Adrenals	0.23	0.51	1.28	5.68	1.10	0.18
Kidney	0.44	1.86	42.0	30.9	6.74	3.07
Liver	0.25	1.16	5.28	25.4	0.86	1.02
Blood	0.11	0.11	0.94	0.71	0.26	0.50
Heart	0.18	0.60	1.7	2.50	3.23	2.62
Brain	0.21	0.32	0.28	0.33	-	-
Spleen	0.18	0.53	1.48	1.11	0.21	0.17
Muscle	0.16	0.60	0.06	1.05	0.28	0.14
Implant Site	-	-	1.8×10^5	8×10^3	2.24	2.5×10^3
Peritoneal Wall	-	0.10	3.24	-	1.34	1.96
Bone	-	0.81	0.17	1.13	-	-

It can clearly be seen from these results that there is a significant increase in the level of cobalt in the kidneys at 10 weeks but this level is reduced by 26 weeks. Most tissues have slightly raised cobalt levels following implantation.

6. Discussion

The techniques reported in this paper are those which have been found to be the most suitable in our laboratory for tissue examination. Although representing a personal preference in many cases, where quite adequate alternatives exist (with enzyme histochemistry, for example), in other cases they represent what are considered ideal conditions after extensive investigations of the alternative methods (for example, with the digestion of tissues). These techniques have been fully utilised in the animal experiments discussed and should be readily applicable to any tissue samples obtained at implant retrieval. Detailed results of the specific experiments mentioned are to be reported elsewhere.



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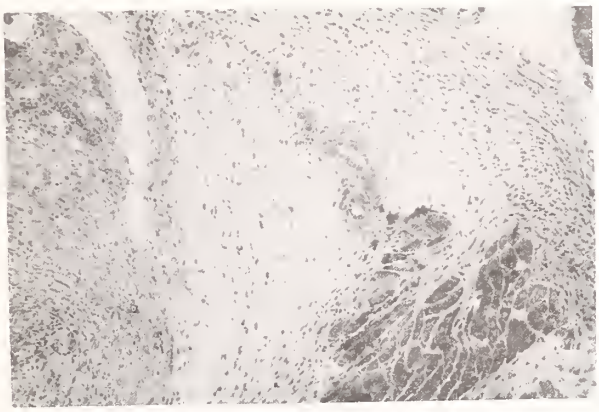
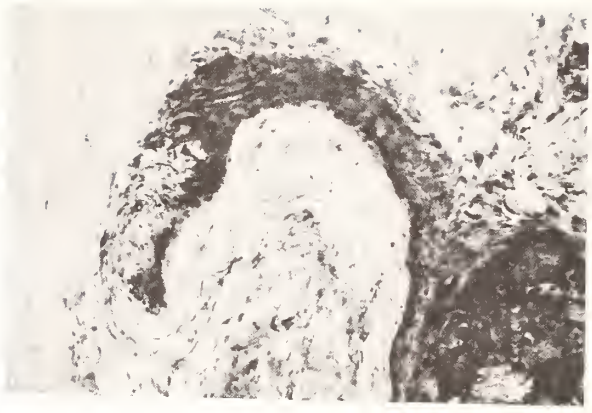


c

d e

Figure 1 Haematoxylin and eosin stained sections of tissue adjacent to pure metals, implanted intramuscularly.
a) Ni x 100; b) Co x 150;
c) Cu x 50;
d) Al x 50; e) Pb x 50



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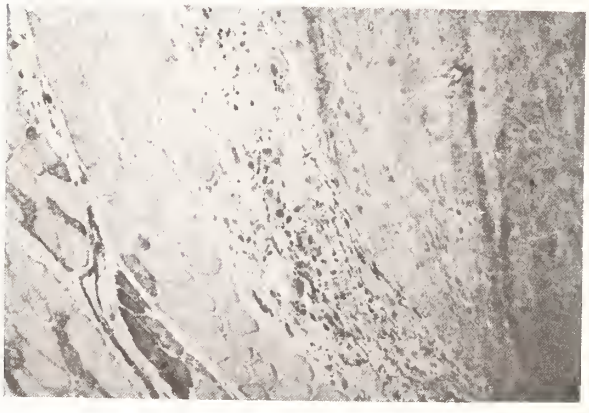

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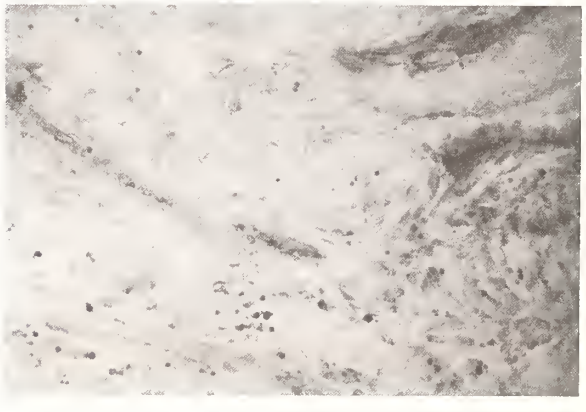

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Figure 2 Enzyme activity in tissue adjacent to intramuscular implants of pure metals.
a) Acid phosphatase, aluminium implant x 50.
b) Lactate dehydrogenase, nickel implant x 50.
c) Leucine aminopeptidase, nickel implant x 150.

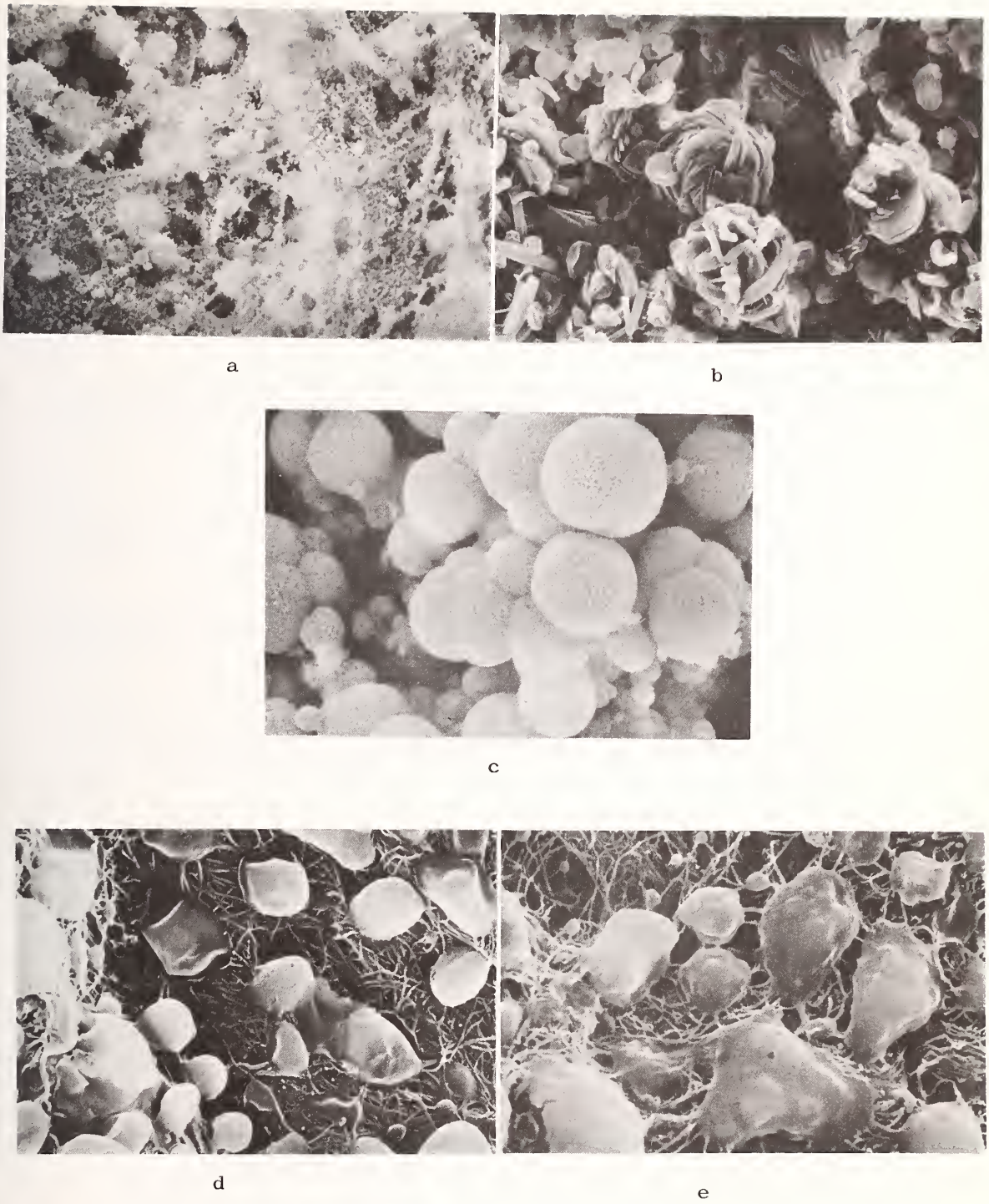

Figure 3 Scanning electron micrographs of metal surfaces and adherent tissue after intramuscular implantation.
a) Ni x 600; b) Co x 750;
c) Cu x 550;
d) Al x 5000; e) Pb x 5000.

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INTERFACE PHENOMENA

RETRIEVAL ANALYSIS OF CALCIFIC DEGENERATION OF PROSTHETIC TISSUE VALVES: THE ROLE OF VITAMIN K-DEPENDENT PROCESSES AND OTHER REGULATORY MECHANISMS

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Calcification of glutaraldehyde preserved porcine xenograft valves represents a major clinical problem affecting the use of these prostheses. Currently, there is no satisfactory explanation for this pathologic process. The present work explores the inter-relationships of both clinical parameters and biochemical changes in the affected valve tissue. The results of the present study show that the prosthesis failure in our patient population was always associated with calcification, and this complication was noted to occur only in those patients under 15 years of age at the time of valve replacement. Amino acid analysis of calcified leaflet tissue revealed the presence of high levels of proteins containing the vitamin K-dependent, Ca++ binding amino acid, gamma-carboxyglutamic acid (Gla), in mineralized specimens, with no Gla present in non-calcified valve tissue. In addition, the Ca++ binding amino acid O-phosphoserine was detected in relatively greater amounts in the mineralized specimens, compared to control. Calcified xenografts also demonstrated a relative reduction in collagen content (as evidenced by hydroxyproline analysis). The implications that vitamin K-antagonism could be of benefit in treating or preventing prosthesis calcification is discussed.

1. Introduction

Calcification of glutaraldehyde preserved porcine xenograft valves has emerged as a major problem affecting these prostheses. Precise data on the incidence of this complication is not as yet available, but work to date suggests that the problem is more frequent in children [1,2][1] and that increased mineralization occurs with time [1,2,3]. Clinically, calcific degeneration of the xenograft valves can produce either valvar stenosis or regurgitation depending upon the presence of mineral associated tears in the leaflets [1,2,3]. Pathologic studies of xenograft mineralization reveal dystrophic calcium deposits to be present either as superficial nodules, or associated with the collagen fibrils in the valve stroma [3,4].

[1]Figures in brackets indicate the literature references at end of this paper.

The pathogenesis of porcine xenograft valve calcification is poorly understood. However, recent work has indicated that proteins containing the vitamin K-dependent Ca++ binding amino acid, gammacarboxyglutamic acid (Gla) occur in a wide variety of pathologic calcifications including calcified atherosclerotic plaque and calcified cardiac valves [5,6,7]. Gla was first discovered by Stenflo to occur in the Ca++ binding sites of the prothrombin molecule [8]. Subsequent work demonstrated that Gla synthesis occurs in the vitamin K-dependent coagulation factors as a vitamin K-dependent, post-translational enzymatic carboxylation [9] of specific glutamic acid residues. In fact, warfarin therapy (fig. 1) results in inhibition of Gla synthesis, with loss of Ca++ binding and anticoagulation [9].

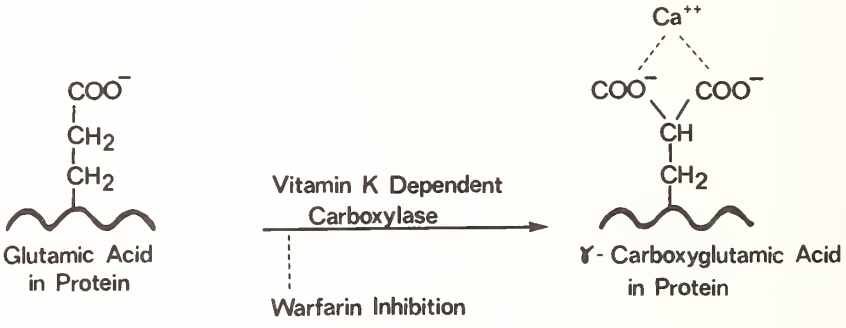

Figure 1. Post-translational Gla synthesis

In 1975 Hauschka, Lian and Gallop demonstrated the presence of a unique Gla containing protein in normal bone, which they named osteocalcin [10]. Following this, Lian and her colleagues demonstrated Gla containing proteins to be present in pathologic calcifications including calcium containing renal stones [5,6], calcified skin deposits occurring in dermatomyositis and scleroderma [5], and calcified atherosclerotic plaque [5]. Following this, Levy, Lian and Gallop [11] isolated and have partially characterized a unique Gla containing protein from atherosclerotic plaque which they have named atherocalcin. In addition, Levy, Zenker and Lian [7] have recently demonstrated the presence of Gla containing proteins in calcified aortic valves including several cases of porcine xenograft calcification.

In the present paper, we will present further evidence linking vitamin K-dependent processes involving proteins containing Gla to

porcine xenograft valve mineralization. In addition, data will be presented indicating that relative diminution of collagen content is also associated with xenograft calcification, and that phosphoproteins containing the Ca++ binding amino acid, O-phosphoserine also occur at high levels in porcine xenograft valvar calcification.

2. Methods

2.1 Clinical Material

Stent-mounted porcine xenograft valves were retrieved at cardiac surgery for prosthesis failure. In addition, clinical and physiologic data on all patients with this type of prosthesis were compiled to compare those patients with valve failure to those with xenografts still in place.

The xenograft specimens obtained at surgery were subjected to a brief pathological exam and then frozen at -20°C. Control tissue analyzed consisted of porcine aortic valves obtained fresh at slaughter and commercially prepared glutaraldehyde preserved porcine aortic valves. In addition, human aortic valve tissue obtained at surgery for aortic stenosis was also examined, as was tissue from a non-preserved, calcified aortic valve homograft. Control human aortic valve tissue was obtained at autopsy.

2.2 Biochemical analyses

Individual valve leaflets were rinsed with normal saline to remove adherent blood and thrombus; the leaflets were then freeze dried. Lyophillized tissue specimens were ground to a coarse powder over liquid nitrogen. 2N KOH hydrolysis (which circumvents decarboxylation of Gla to glutamic acid) of the powder aliquots was carried out at 110°C for 24 hours for the detection of Gla as previously published [12]. The presence of Gla was confirmed by 6 N HCl decarboxylation of the apparent Gla peak, with resultant formation of glutamic acid. 6 N HCl hydrolysis of separate powder aliquots was performed at 110°C for 24 hours for total amino acid analysis (using a Beckman Spinco 121M amino acid analyzer), and for calcium content by atomic absorption spectroscopy (using a Perkin Elmer Model 603). Tissue protein content was computed from total amino acid content. O-phosphoserine amino acid analysis was performed and calculated as previously described for bone extracts [13]. The lower limit of sensitivity for amino acid analysis in our laboratory is 10 picomoles with ninhydrin peak variation (in triplicate) of less than 2% [12].

3. Results

3.1 Clinical aspects

At our institution, porcine xenograft failure was always associated with valvar mineralization. As presented in Table I, a marked age effect was noted with all cases of calcific valve failure occurring in patients receiving prostheses before the age of 15 years (8 of 14 cases). Of the 11 patients over the age of 15 at

prothesis insertion, none have calcified xenografts (follow up range 21 to 50 months). Clinical data presented in table I indicate that valve size in general was more than adequate and probably not a factor in valve calcification. Furthermore, valve mineralization resulted in valvar stenosis or regurgitation, regardless of valve size or age.

Table I

Calcific Xenograft Failure - Clinical Parameters

Case No.	Age at Implant (y)	Body Surface Area (m^2)	Valve Size (mm)	Site	Duration in Place (mos)	Diagnosis at Retrieval
1	3 7/12	.6	23	Mitral (Mi)	22	regurgitation
2	6 3/12	.6	27	Mi	42	stenosis
3	10 7/12	1.0	31	Mi	36	regurgitation
4	10 8/12	1.0	27	Mi	34	stenosis
5	10 9/12	0.9	27	Mi	34	regurgitation
6	12 4/12	1.1	29	Mi	49	regurgitation
7	14 3/12	1.4	25	Aortic	32	stenosis
8	14 6/12	1.2	29	Mi	64	stenosis

Complete analysis of our clinical data also indicated that the sex of the patients was not a determinant of valve failure, and that those patients without valvar mineralization at the time of the study had valves in the same size range as patients with calcific valvar degeneration.

3.2 Biochemical aspects

Gla was present in all calcified porcine xenografts suitable for analysis (N=6) and was not present in fresh porcine aortic valves and in nonimplanted glutaraldehyde preserved porcine aortic valves (table II and figure 2). As Figure 2 indicates, Gla content appears to be related to valvar calcium, and the relative amounts of protein bound Gla present were comparable to those found in calcific aortic stenosis and in a case of aortic valve homograft calcification. No Gla was detectable in normal human aortic valves, or in noncalcified valve tissue from patients with congenital aortic stenosis.

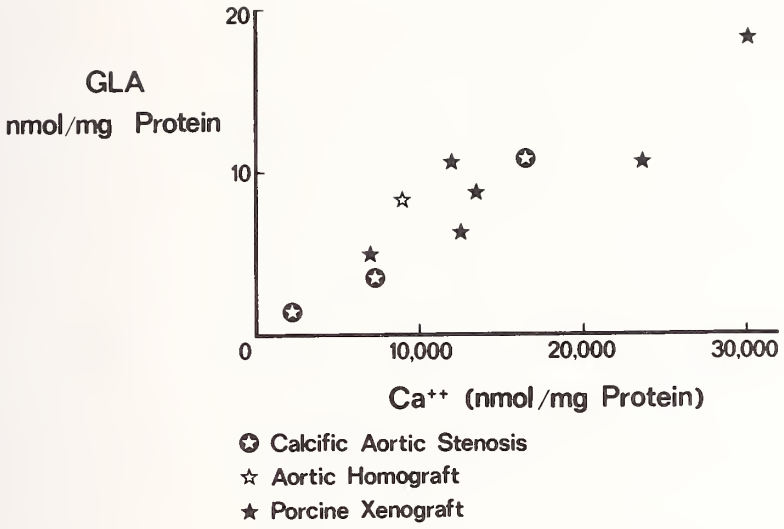

Figure 2 . Aortic valve Gla and Ca++ content

Amino acid analysis for hydroxyproline (Hyp) as well as specialized O-phosphoserine (P-Ser) determinations are also presented in table II. As evidenced by the hydroxyproline level [14], calcified glutaraldehyde preserved porcine xenograft valves exhibited markedly lower relative collagen content than does either the fresh prosthetic material or human valves. Furthermore, high levels of O-phosphoserine also occurred in the calcifed xenografts at levels comparable to those found in calcified human aortic stenosis leaflets.

Table II

Comparative Amino Acid Analysis and Calcium Content in Human and Porcine-Xenograft Valves

Tissue Diagnosis	No. of Valves	Ca++(NM/mg Protein)	Gla(NM/mg Protein)	P-Ser(res/ 1000aa)*	Hyp(res/ 1000aa)
Fresh Porcine Aortic Valve	1	146	0.0	-	94
Nonimplanted Xenograft	2	108-133	0.0	.35-.60	94-99
Normal Human Aortic Valve	2	36-164	0.0	.40-.59	44-92
Calcific Aortic Stenosis	4	2080-16197	2.0-10.6	3.9-5.9	42-88
Calcified Aortic Valve Homograft	1	9180	8.3	4.2	66
Calcified Porcine Xenograft	6	7527-30441	4.3-18.3	4.0-9.3	14.1-36.7

* res/1000aa = residues/ 1000 amino acids

4. Discussion

The results of the present study indicate that proteins containing the vitamin K-dependent calcium binding amino acid, Gla, occur at high levels in the pathologic calcifications associated with porcine xenograft valve failure. The role of vitamin K-dependent processes in mineralization, both normal and pathologic, is currently being elucidated. In bone, a unique Gla containing protein, known as osteocalcin, has been discovered [10]. The function of osteocalcin is not as yet clear, but work to date suggests that this protein serves as a regulator of normal mineralization [15,16]. Osteocalcin biosynthesis in bone has been shown to occur *in situ* as a vitamin K-dependent process [15]. Warfarin anticoagulant therapy has been shown in experimental animals to result in suppression of Gla synthesis in osteocalcin with resulting associated diminished bone density[16]. Levy,Lian,and Gallop have recently isolated a new Gla containing protein called atherocalcin from calcified human atherosclerotic plaque [11]. Partial characterization of atherocalcin indicates that it has a molecular weight of about 80,000,and an amino acid composition and charge distinctly different from other known Gla containing proteins of human origin. Furthermore, increased levels of Gla and hence

atherocalcin occurred in atherosclerotic lesions of increasing severity [11]; these results suggest that atherocalcin may play a role in the pathologic progression of atherosclerotic lesions. It may be that atherocalcin or related proteins occur in the mineralizing xenografts and work is in progress to establish the functional role of Gla containing proteins in this type of cardiovacular calcification.

The clinical observation that age at implantation is a crucial determinant of subsequent xenograft mineralization may be interrelated to a number of developmental considerations concerning normal vitamin K metabolism and other endocrinologic factors. Gundberg et al [17] have shown that Gla metabolism as evidenced by urinary Gla excretion is markedly elevated in younger children and decreases with age to adult levels by age 14 to 16 years. This observation together with the present data suggests that younger children may be more prone to the induction of vitamin K-dependent pathologic mineralization since their vitamin K metabolism is normally occurring at a higher level. Furthermore, serum phosphorus is also significantly higher in younger children and decreases steadily to adult levels by about age 15 years [18]. It may be that there is some increased mineral deposition secondary to the higher phosphate in the younger children, making them more prone to precipitate mineral at nucleating sites. Work is now in progress to evaluate possible age dependent effects in those patients at risk for porcine xenograft calcification.

The presence of proteins containing O-phosphoserine in the calcified xenograft leaflets and the associated observation of diminished collagen content are of importance with respect to considerations of both valve mineralization, and ultimate durability. O-phosphoserine occurs in phosphoproteins of dentin and bone, and has been thought to occur at nucleating sites of hydroxyappatite deposition [13]. O-phosphoserine may serve a similar function in xenograft mineralization. In fact, the levels of O-phosphoserine found in the calcified valves reported in the present work are comparable to what one finds in bone [13], and suggest that mineral deposition occurring in cardiac valves takes place as an ordered process with some important similarities to bone mineralization. Unlike bone, however, relative amounts of collagen in the mineralizing xenograft valves are diminished compared to normal porcine aortic leaflets. This biochemical observation agrees well with the ultrastructural observations of Ferrans et al [4] of marked disruption of collagen fibrils with time, occurring in glutaraldehyde preserved porcine xenograft valves. These findings, plus the present data, suggest that associated with valvar calcium depositions, there may be significant deterioration in the tensile strength of the xenograft due to collagen degradation.

In conclusion, the present study has provided evidence that the mineralization of glutaraldehyde preserved porcine xenograft valves occurs in association with the deposition of vitamin K-dependent, calcium binding proteins in the valve leaflets. We have also demonstrated the associated presence of protein bound O-phosphoserine, which may serve as a nucleating site. Finally, there is also associated

a marked diminution of valvar collagen in the mineralizing leaflets, indicating a probable deterioration in strength due to reduction of this principle structural protein of valves. Furthermore, there is an overriding age effect,with calcific valve failure occurring only in recipients younger than 15 years, suggesting an age dependent endocrine interaction.It may be that Gla protein synthesis is a crucial regulator for the entire pathologic process, and that the use of vitamin K-antagonists such as warfarin or related drugs,either in valve preparation or therapeutically,could be of benefit.

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PROSTHESIS - RELATED INFECTIONS

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Thirty-one patients with prosthesis related infections have been identified. Seventeen patients treated for hydrocephalus with ventriculojugular, ventriculoatrial and ventriculoperitoneal shunts exhibited bronchopneumonia and/or evidence of septic emboli. An additional fourteen patients had evidence of direct infection of prostheses. In the latter group, histological examinations in conjunction with positive bacterial or fungal cultures was superior to either technique alone in confirming an infectious process. The causative organisms were similar to those reported in other series on device-related infection, and are similar to those seen in immunosuppressed patients.

1. Introduction

The significance of infections of indwelling devices, and the peculiarities associated with them, were demonstrated convincingly approximately 25 years ago by Elek and Conen (10) in their studies of Staphylococcal infections of sutures. Numerous reports document the role of catheters on the development of bacterial disease, with more recent studies considering their influence on the development of fungal disease (14). The majority of studies relate to temporarily implanted vascular catheters. The present study deals with retrieved implants designed to be permanent and is part of The Implant Retrieval and Analysis Program of The Institute of Pathology and Case Western Reserve University.

2. Materials and Methods

The problem of prosthesis related infections has been divided into two categories: (1) infections of target organs associated with devices and (2) direct infections of the prostheses. The first category of infection was approached by a retrospective analysis of polyethylene ventriculojugular, ventriculoatrial, and ventriculoperitoneal shunts used in the treatment of hydrocephalus.

The autopsy records of University Hospitals of Cleveland, Ohio from 1954 to the present were reviewed, and 28 patients with ventricular shunts of all types were recovered. The histopathology of the central nervous system findings in the same group of patients has been the subject of a separate report (19).

Additional prospective analyses were carried out on implants removed at surgery or autopsy beginning circa 1976. In both groups of patients, prosthesis-related infections were defined as present when (1) the tentative clinical diagnosis of prosthesis-related infection was made (e.g. prosthetic valve endocarditis) and was verified by a positive bacterial or fungal culture or (2) there were classical signs of infection (e.g. fever) in the absence of positive bacterial or fungal cultures.

Histopathology was carried out using routine sectioning, preparation and staining, with additional standard special stains used to detect bacteria, fungi or parasites.

3. Results

3.1. Ventriculojugular, Ventriculoatrial and Ventriculoperitoneal Shunts

The single greatest problem with ventriculojugular and ventriculoatrial shunts is continued thrombosis and thromboembolism with subsequent pulmonary infarction, pulmonary hypertension (6) and cor pulmonale. Bronchopneumonia secondary to septic thromboemboli is an additional complicating factor. Seventeen of 28 patients with a ventriculojugular, ventriculoatrial, or ventriculoperitoneal shunt had bronchopneumonia (Table 1). Of the 15 with pneumonia and a ventriculojugular or ventriculoatrial shunt, two had cor pulmonale (Cases 11 and 17). Of the entire group of 17 patients with bronchopneumonia five had an associated ventriculitis, implying that the pulmonary infectious complications of ventriculojugular, ventriculoatrial and ventriculoperitoneal shunts are independent of those of the central nervous system. In only one case, Case 3, was there simultaneously obtained positive cultures made premortem on cerebrospinal fluid and blood.

Case	Time in Situ Months	Type of Shunt	Causative Organism
1	½	V-J (1)	* (2)
2	1	V-J	*
3	1½	V-P	E. coli
4	1½	V-J	Nocardia Asteroides
5	2	V-J	E. coli and candida sp.
6	2½	V-J	S. aureus, B-Hemolytic strep
7	3½	V-J	*
8	4½	V-J	Proteus Mirabilis
9	7	V-J	Proteus Mirabilis
10	14	V-J	*
11	17	V-J	*
12	24	V-J	*
13	29	V-J	Micro coccus sp.
14	39	V-P	*
15	43	V-J	E. coli
16	48	V-J	*
17	72	V-J	S. aureus

(1) V-J = Ventriculojugular, V-P = Ventriculoperitoneal
(2) * = No growth or mixed growth

Table 1. Pulmonary Infections Secondary to Ventricular Shunts

In eight of 17 patients there were either no positive cultures postmortem or there was a mixed growth of organisms. Failure to obtain a positive culture postmortem is most frequently the result of premortem therapy with antibiotics. Such therapy may either eradicate the causative organism or prevent its growth postmortem. Mixed growths have been attributed to the overgrowth of the normal gut flora.

In the remaining nine patients where either one or two organisms grew in large numbers postmortem, four had their ventricular shunts in place because of hydrocephalus secondary to a malignant process (Cases 4, 5,6,8). Since treatment of their malignancies included immunosuppressive agents, it is unclear whether the shunt or the therapy predisposed to infections by such unusual pathogens as Nocardia asteroides. In the remaining five patients, (Cases 3,9,13,15,17) pneumonia was secondary to the less frequently encountered lung pathogens such as Staphylococcus aureus, Proteus mirabilis, E. coli as well as micrococcus sp., usually a nonpathogen.

3.2. Direct prosthesis infection

Definitive, positive bacteriological cultures were obtained in seven of 14 patients whose prostheses were removed since 1976 (Table 2). Twelve of the 14 had a definitive diagnosis of an infectious process when histological examination was coupled with isolates recovered on culture (Table 2).

3.3 Histopathology of infections

The histopathology within the lungs reflected the pneumonia superimposed on recurrent thromboembolism in all patients with ventriculojugular shunts. Vegetations were present at the site of the fibrous capsule, where the shunt entered the jugular vein or right atrium (figure 1a)*. In several cases, septic embolization obviously had occurred, as indicated by multiple, peripheral, pleural based abscesses (figure 1b) and necrotizing bronchopneumonic foci (figure 1c). While septic emboli could not be illustrated definitively in every case, the finding of pneumonia with pulmonary emboli and/or vegetations was uniformly observed in all patients with ventriculojugular shunts.

The bronchopneumonia secondary to Nocardia asteroides was unique, in as much as the organism is a fungus-like bacterium with a filamentous structure (figure 1d).

The histopathological changes observed in cases of direct infection of prosthesis were of greater variability. In vascular prostheses the causative bacterial organisms were in the lumens (figure 2a) and formed septic thrombi (figure 2b). Fungal infections of vascular devices, on the other hand, were located near the anastomoses with the natural blood vessels, and tended to be on the adventitial surface rather than the luminal surface.

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* All figures appear at the end of the text.

Table 2 - Direct Prosthesis Infections

Case	Type of Graft	Time in Situ	Organisms Isolated	Organisms by Histology
18	Vascular, Expanded PTFE	7 Days	Mixed GM+ (1)	Isolated budding yeast
19	Vascular, Expanded PTFE	11 Days	* (2)	GM+ Cocci (3)
20	Total Hip Replacement	2 Mos.	E.Coli (5)	(4)
21	Total Hip Replacement	1 Yr.	*	Aspergillus species
22	Total Knee Replacement	2 Yrs.	*	*
23	V-P Shunt	2 Yrs.	*	*
24	Total Hip Replacement	4 Yrs.	E. Coli (5)	(4)
25	Prosthetic heart valve, aortic	4 Yrs.	Micrococcus sp. (6)	GM+ Cocci
26	Vascular, dacron	6 Yrs.	*	Budding yeast
27	Prosthetic Heart valve, aortic	9 Yrs.	S.Aureus (7)	*
28	Prosthetic Heart valve, mitral	10 Yrs.	S.Epidermidis (7)	*
29	Vascular, Expanded PTFE	-	Streptococcus Salivarius(7)	GM+ Cocci
30	Vascular, dacron	-	*	Budding yeast
31	Vascular, dacron	-	*	Bacteria in Thrombus

(1) Culture from swab of adventitial tissue
(2) * = No growth
(3) GM+ = Positive on Gram stain
(4) No sections submitted
(5) Culture from hip aspirate
(6) Culture from valve vegetation
(7) Blood culture

In the two cases of orthopedic appliance infections where tissue sections were submitted, only 1 case of fungal infection demonstrated an organism (figures 2c and 2d). The presence of mycelial forms with septate hyphae, with no apparent yeast forms, strongly implicates Aspergillus species as the infecting agent.

The histopathology seen in the cases of prosthetic heart valves was similar to that seen with infected ventriculojugular or ventriculoatrial shunts. Friable microscopic vegetations consisted of disorganized necrotic material, fibrin and occasional organisms.

4. Discussion

Although the numbers of patients with prosthesis-related or direct prosthetic infections are small, the findings are of significance with regard to the nature of the infecting organism and the detection of infection. The frequent isolation of opportunistic organisms, such as Aspergillus, Nocardia, Micrococcus, and S. epidermidis suggests an underlying altered immune response in these individuals. The observed organisms, as well as Proteus mirabilis may also be expected in patients that are severely immunocompromised (29).

Fungal infections, for example, have been observed in dialysis patients (18), and in patients who are leukopenic secondary to immunosuppressive therapy. None of these patients, however, were leukopenic, (White blood cell count less than 5000 cells per cubic millimeter), and only four were on immunosuppressive therapy, thereby excluding an a priori deficiency of immunocompetent cells. It is postulated that the prosthesis, possibly through the induction of the fibrous capsule that is ubiquitous in soft tissue interactions, leads to a "localized immunosuppression" at the site of implantation. The absence of macrophages in the peri-prosthetic inflammatory infiltrate suggests suppression of this population. The absence of macrophages further suggests that suppression of this cell population may partially account for the bacteriological findings.

Infections of prostheses have been divided into "early" and "late" stages. The exact definition of early and late has been related to the nature of the prosthesis. Early infections of prosthetic heart valves are those occurring within three months of replacement, late infections are those occurring beyond three months (9). Most (70%) infections of ventriculoatrial, ventriculojugular and ventriculoperitoneal shunts were apparent within two months (24) while a large fraction of orthopedic prostheses infections occurred within the first year (11). Other clinical studies have indicated that the types of organisms responsible are related temporally to the time of prosthesis placement. In all types of prostheses, Staphylococcus aureus or S. epidermidis were the organisms most commonly encountered in early infections. Late infections of prosthetic heart valves were caused by streptococcal species, staphylococcal organisms, and less frequently by other gram negative bacteria and fungal organisms (2,9). The incidence of streptococcal infection reflects the condition seen in the endocarditis of natural tissue heart valves. Staphylococcus

aureus was also the most frequent cause of early infection of prosthetic hips and of ventricular shunts (24) while late infections of prosthetic hips and ventricular shunts involved gram negative bacteria, anaerobes and aerobes of low virulence. Anaerobic bacteria present a major technical problem of isolation. To date, anaerobic infection has been rare, (possibly reflecting the technical difficulties!) and in prosthetic hip replacements has included gram positive organisms (15) in contrast to the usual clinical anaerobic infection (27).

The early infections correspond to the early phase of wound healing. The difference in organisms causing late infections implies a difference in innate reactivity of the material (12) or in a conditioning of the protein coat adherent to devices placed within the blood stream and soft tissues (4,22). Such conditioning has been implicated in experimental studies of bacterial adherence to various solid substrates (8,26) and in experimental vascular graft infections where the "protein coat" forms the neointima (23).

In the present study the organisms responsible for infection did not fit easily into the prescribed pattern of "early" or "late" infections. It is unclear why this occurred, but may reflect a sampling bias or may be the result of too few cases.

In addition to temporal considerations, there appears to be at least two mechanisms of prosthesis infection. The first mechanism is the direct ingress of the organisms onto the prosthesis at the time of surgery. The direct introduction of organisms has been used to explain early endocarditis caused by Staphylococcal species (9,11) and late "delayed" infections of prosthetic hip replacements (11). Direct invasion would appear to be the mechanism of Aspergillus sp. infection in Case 21 (25). A second route of importance, especially in orthopedic appliances, is the hematogenous spread of organisms from another site. Staphylococcus aureus infection of decubitus ulcers in Case 17 preceded the septic pulmonary infarcts. Similarly in Cases 20 and 24 an E. coli urinary tract infection preceded E. coli infection of the total hip replacement. Hematogenously carried organisms have been responsible for infections caused by S. epidermidis (3), and for infections of orthopedic devices by Mycobacterium fortuitum (7), M. tuberculosis (17), among others (1,16).

Affirmation of direct prosthesis infection by bacteriological means was encumbered by the manner in which the prosthesis was infected. Routine swabs of the periprosthetic regions and/or wound sites were made. However, as evidenced by the infections of the expanded polytetrafluoroethylene grafts, the process began on the luminal surface. Although the bacteria were observed "percolating" through the pores, apparently none made it to the adventitial surface where the culture was taken. Similarly, small colonies of yeast at the junction of the prosthesis and natural vessel would be unlikely isolates of a random swab of the periprosthetic area.

Further complicating the assessment of infection was the paucity of clinical signs and symptoms. Fever was present only in five of 14 patients with direct prosthesis infection. Two of these, Cases 20 and 24, had urinary tract infections prior to the onset of prosthesis infections and in two others, Cases 22 and 23, no positive cultures were made. Leukocytosis (more than 10,000 cells mm^3) was present in less than half of the patients with direct prosthesis infection. In several cases, the erythrocyte sedimentation rate (ESR) was measured, and was elevated above the range of normal in all cases where it was recorded. The ESR is a useful indicator of acute inflammation, reflecting the levels of fibrinogen as an acute phase reactant. The ESR is subject to many variables, and in future studies, quantitative levels of C-reactive protein (4) may provide better clues regarding prosthesis-related infections.

In summary, infections of prosthetic devices cause disease by direct infection, leading to failure of the device, and in the case of intravascular devices, to dissemination of the organisms throughout the body. The infections in the present study are similar to previous reports in as much as usually avirulent or low virulence organisms were responsible. Studies on the effect of material on bacterial growth and bacterial inhibiting properties of cells and serum are indicated and have apparently begun (20). An associated problem of isolation and confirmation of infection may require new culture techniques and new ancillary tests (13,28).

Acknowledgments

The author would like to acknowledge first the continued interactions with Dr. Donald F. Gibbons, Director of the Implant Retrieval Service at Case Western Reserve University, Institute of Pathology and second, useful conversations and the critical review of the manuscript by Dr. Joseph F. Tomashefski, Jr.

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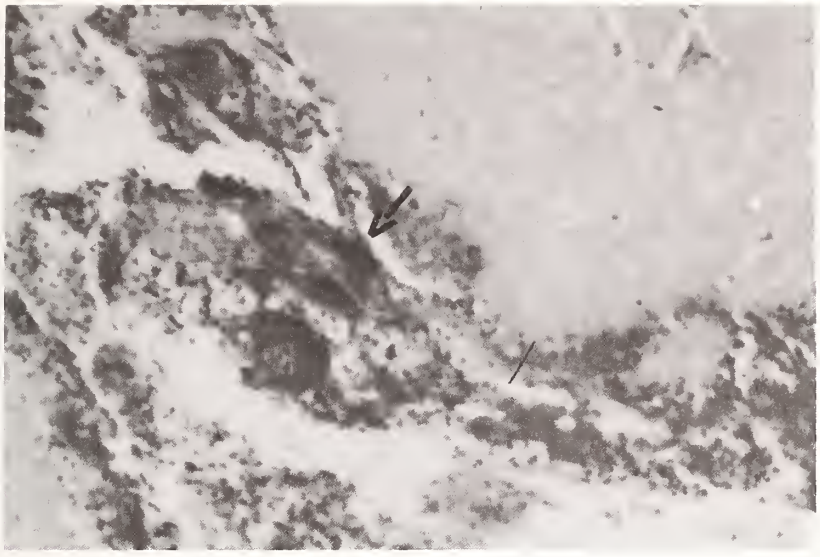

Figure 1a. Pulmonary infections complications of ventricular shunts. Micrococcal vegetation on fibrous capsule surrounding jugular portion of V-J shunt. H&E, 100X.

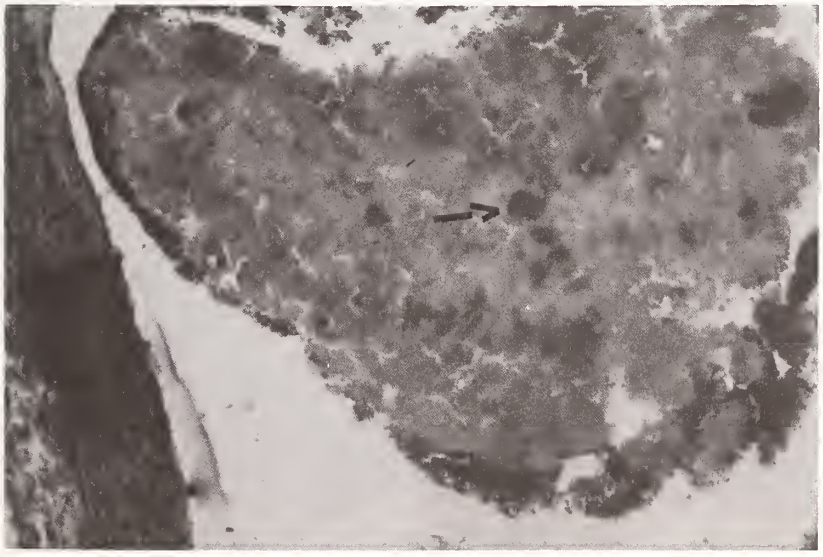

Figure 1b. Pulmonary infections complications of ventricular shunts. Septic embolus secondary to S. aureus, 40X.

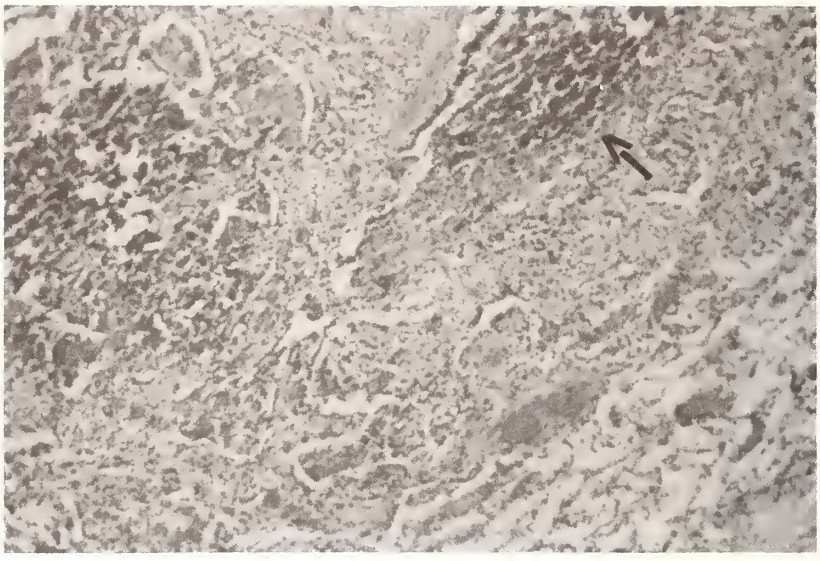

Figure 1c. Pulmonary infections complications of ventricular shunts. Necrotizing bronchopneumonia, H&E, 40X.

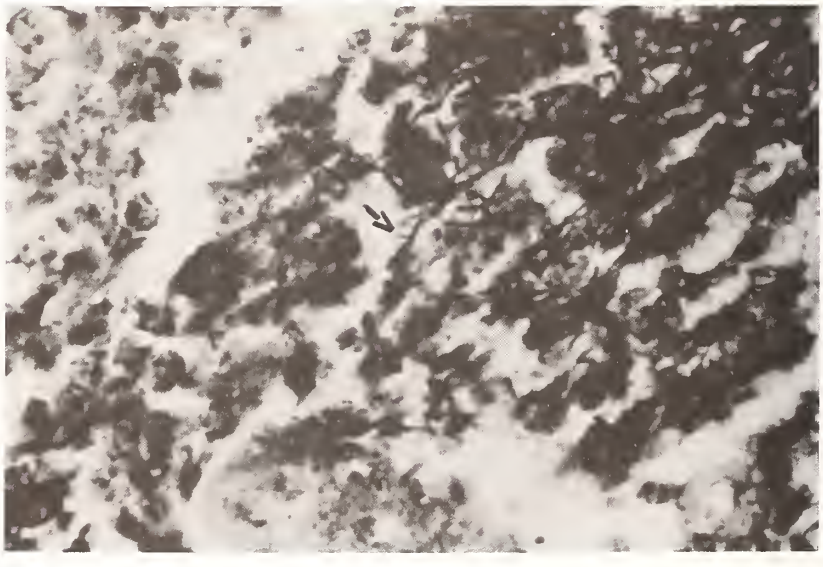

Figure 1d. Pulmonary infections complications of ventricular shunts. Nocardia asteroides pneumonia, GMS, 400X.

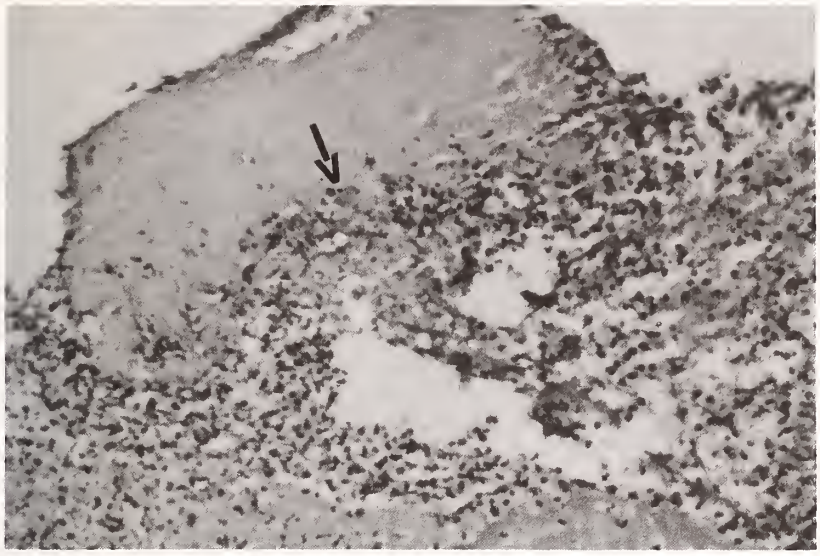

Figure 2a. Direct prosthesis infections.
Septic thrombus, H&E, 40X.

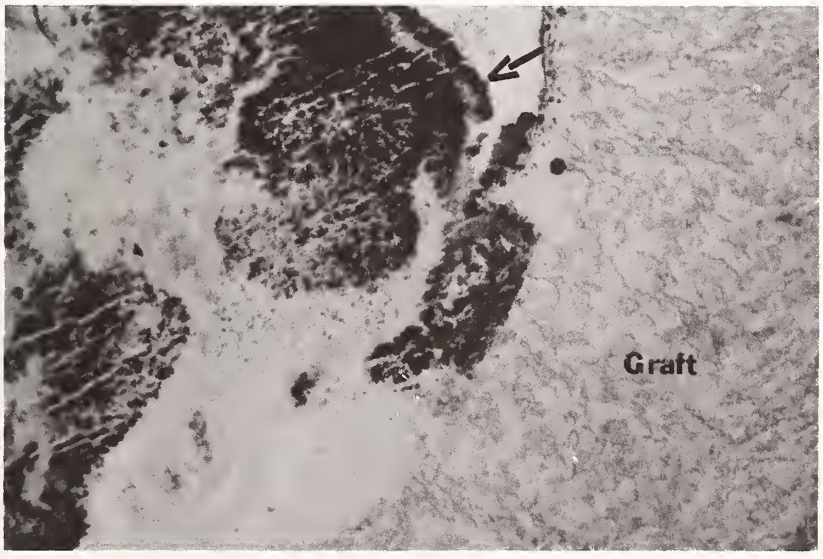

Figure 2b. Direct prosthesis infections.
Septic thrombus of expanded PTFE, B&B, 100X.

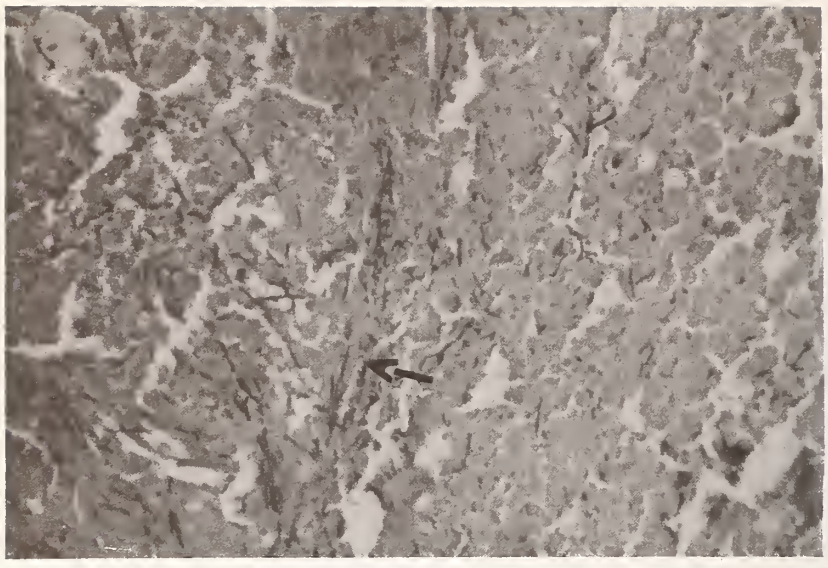

Figure 2c. Direct prosthesis infections.
Aspergillus species in necrotic tissue adjacent to prosthetic hip replacement, GMS, 40X.

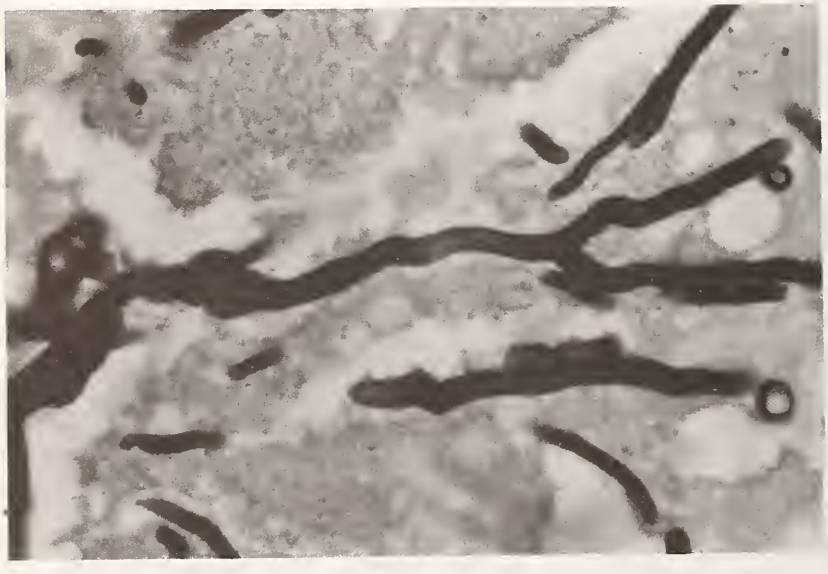

Figure 2d. Direct prosthesis infections.
Aspergillus species in necrotic tissue adjacent to prosthetic hip replacement, GMS, 400X.

STUDY OF 208 EXPLANTED BIOPROSTHESIS: DISTRIBUTION OF DYSFUNCTION PATTERNS AND ASSESSMENT OF DURABILITY AT 10 YEARS OF USE

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As the HANCOCK* bioprosthesis completed 10 years of clinical use as a human valvular substitute, specific dysfunction patterns have become evident in a very small percentage of the xenografts. Simultaneously, the durability or longevity of this porcine derived material extending over this period has been questioned. Studies at this laboratory have addressed both phenomena: dysfunction and durability of these bioprostheses. An explanted valve retrieval program has been ongoing at HANCOCK Laboratories Inc. for the past eight years and the observations and studies generated are the subject of this paper. A total of 208 explanted valves are analyzed and reported. The distribution of the modes of dysfunction show they may be due mainly to: 1) two distinct forms of mineralization, 2) unhealed prosthetic valvular endocarditis, 3) early uncomplicated thrombosis, and other minor reasons. A statistical breakdown for each occurrence is given. Physical and biochemical studies on excised valves returned in non-fixative solutions give clues as to the nature of interstitium material reported elsewhere to be products of valve material degeneration. Together the findings indicate that the HANCOCK* bioprosthesis demonstrates conservation of intrinsic pre-implant characteristics for up to 100 months in vivo, and a longer projected prosthetic durability in the absence of extrinsic factors.

1. Introduction

Over the past decade, continuous research and development and the support of a unique technology at HANCOCK Laboratories Inc., has resulted in a clinically proven widely accepted bioprosthesis, the HANCOCK* Stabilized Glutaraldehyde Process porcine aortic heart valve mounted on a flexible stent [1] [1]. Clinical acceptance is evidenced by the nearly exponential increase of its use as a human valvular substitute and the long term clinical experience at numerous institutions throughout the world where it has become the valve of choice. Estimates at present (fig. 1), conservative as they may be, set the number of these valves used in replacement at well over 60,000.

1. Figures in brackets indicate the literature references at the end of this paper.

*TRADEMARK

This estimate is presented only to provide context and perspective while examining the explanted valve population reviewed in this report.

Three types of prostheses: aortic valves, atrioventricular valves and valved conduits (figs. 2A, B, C) have been used, though the process is chemically the same in all cases and starts from the same material: the porcine aortic valve.

It must be realized that while a large number of implant-patient years and impressive actuarial outlook [2,3,4,5,6,7,8,9,10,11], for patient survival are important in determining the benefits of a tissue bioprosthesis, the surgeon, cardiologist and patient need and deserve to be made aware of the individual outlook or predictability with respect to implant duration and possible dysfunction. Thus, this report presents information obtained from the Clinical Valve Explant Retrieval Program conducted in this laboratory since 1974. It is felt that clinical users of this bioprosthesis will derive important information concerning the efficacy and predictability of the valve, especially with regard to its dysfunction and durability.

2. The Explanted Valve Retrieval Protocol

When released from the manufacturing laboratory, the clinical grade valve possesses characteristics designed towards proper functionality and durability in its intended position. Care is taken during the Stabilized Glutaraldehyde Process to preserve collagenous components as well as the elastic lamina which forms the blood contact interphase, as it is believed that this preservation results in the reported low thrombogenic potential of this bioprosthesis.

2.1 The explanted bioprosthesis

The explanted bioprosthesis represents an invaluable source of research material. Only through an objective comparison is the explanted valve with characteristics present before implant which are documented photographically through the manufacturing process, coupled with patient parameters received from implanting and retrieving centers can valuable information be derived. Patient history includes 1) reason for initial valvular replacement, 2) intra- and postoperative course, 3) reason for extirpation and 4) patient age, sex, valve position, physiological profile, etc. Additionally, a complete analysis of the explanted bioprosthesis will include physical, biochemical, structural and ultrastructural and microbiological observations in this laboratory. The information thus obtained may be used to begin assessment of the possible causes of dysfunction as well as of the projected durability or longevity of this bioprosthesis.

To date about 300 explanted bioprostheses have been received at HANCOCK Laboratories. While this does not represent the entire pop-

ulation of explanted HANCOCK valves, discussions with various major centers throughout the world suggest that this represents a substantial fraction of the total explanted valve population.

2.2 Methods

Explanted valves are received in two types of sterile solutions. The majority of valves implanted for less than five years may be returned in 10% buffered formalin or any other buffered fixative. Those valves having implant duration longer than five years are preferably received in cold, sterile saline or balanced electrolyte (5-15°C) sealed container packed in ice (not frozen). The latter are not exposed to fixative since some of our studies require that the valve be in as close a condition as it was in the physiological environment, and that it arrives within 18 hours from the time of excision. Valves in fixative may be mailed. This protocol is also used for valves explanted from animal studies (canine MVR).

When the valve is received in the laboratory, it is assigned a study number for identification, and a file is opened for each individual bioprosthesis.

If it arrived in saline, it is routed immediately through the Microbiological Laboratory where seals and solution are carefully studied to determine if contamination or infection is present. In some instances its hydrodynamic characteristics are determined in the Flow Testing Laboratory. All explants proceed through the Histopathology and Electron Microscopy Laboratories. The Chemistry Laboratory will qualify and quantify the nature and concentration of the shipping solution. Routing of the valve is illustrated in figure 3.

Following gross anatomical description of valve and components, as well as gross photography of both inflow and outflow aspects of the valve, the pathologist indicates the plane and morphological location of sections for study in the map in figure 4, indicated by the gross morphology. Sections are stained by various techniques always including hematoxylin-eosin (HE), von Kossa (vK) Gramm (G) and Acid-Fast (AF) stains. In many instances, tissue may be processed for transmission electron microscopy.

Complete light microscopic description of each section is obtained and light micrographs of representative sections are included in the bioprosthesis file.

The explanted bioprosthesis file is considered complete only when all observations and descriptions are gathered and a final report is generated. This report may be used to provide periodic information to those centers retrieving the valves.

3. Results

The entire explanted valve population, intitally consisting of 180 valves and later updated to 208 valves was categorized principally by etiology of the dysfunction involved necessitating extirpation. This analysis made use of the patient's medical and surgical history and all observations on the bioprosthesis as outlined above.

A summary of the number of these bioprostheses by position and implant duration is shown in figure 5. Each vertical bar represents the number of valves retrieved within the interval, i.e. the first bar represents valves retrieved from a few hours after operation up to the end of the first twelve months, etc.

This figure indicates that nearly 40% of all valves in the study were removed within one year of implant time. The first three categories will indicate that most of these bioprostheses were removed for truly non-dysfunctional or non-valve related reasons.

3.1 Non-valvular related removal

Thirty five of 180 (19.4%) explants were removed for reasons not directly related to valve dysfunction. Chief reasons for this category were: patient death not due to valve dysfunction, outgrown by the patient of non growing valve as happens with youngsters, missizing, degenerative aortic roots, perivalvular leaks, and disease other than valvular disease, i.e. carcinoma, death, etc. In nearly all cases, valve characteristics were almost identical to preimplant specimens. Figure 6 A shows the time course of removal category, and figure 6 B shows a gross photograph of a 92 month (7 years, 8 months) explant excised because of a degenerative aortic root. Examination showed this valve was well conserved in all aspects.

3.2 Unknown etiology

In this category are grouped valves which were removed and sent to our laboratory with no more data than implant and explant dates. No obvious defects were noticed and all these bioprostheses had characteristics similar to preimplant valves and could not be assigned to any other category. The time course of retrieval is illustrated in figure 7 A and an example of this type valve received within the heart sent to us is shown in figure 7 B.

3.3 Endocarditis

Seventeen percent of the explanted population (31/180) were removed at the time the patient was experiencing acute, subacute or chronic infective endocarditis without healing. In some instances there was involvement of the bioprostheses. Figure 8 A shows the chronology

of removal and figure 8 B is a photograph of a valve removed at 6 months because of this occurrence.

3.4 Mineralization

One major alteration in the functional morphology of the porcine heterograft is associated with mineralization or calcification. Of the explants reported here, 83 valves (46%) were removed at some stage of mineralization. Careful analysis of all these explants indicates that functionally significant calcification occurs as a result of various phenomena categorized by two rather distinct patterns of salt deposition.

3.4.1 Extrinsic mineralization

This form of calcification appears to be usually associated with a previous episode of infective bacterial or thrombotic endocarditis. This pattern represents 23% (42/180) of the entire explanted valve population discussed here. For this population, the time course of removal is illustrated in figure 9 A. No distinction can be made by sex, age, or position of valve implantation and the frequency of this occurrence.

Leaflet surfaces are commonly filled with dense mineralized verrucous deposits (fig. 9 B) which can often be peeled off, leaving underneath a leaflet which, in crossection, appears histologically and architecturally intact (fig. 9 C), the fibrinous material on the surface showing positive von Kossa (black) material indicative of calcific deposits.

3.4.2 Intrinsic mineralization

We have observed a totally distinct form of mineralization which, by its mode of occurrence, we have termed "intrinsic mineralization" or fibrocalcification. Intrinsic mineralization is characterized by calcific deposits WITHIN the valvular or leaflet structures. Of the total calcific population, one-half appears to occur in this manner representing 23% (41) of the total explants studied. The time frame of extirpation is shown in figure 10.A. This form of calcific deposition exhibits differences in rate of occurrence related to the age of the recipient. In children at-risk, (patients under 20 years of age) if it happens, it will do so early. For adults at-risk, there is no specific chronology, but it seems that in those prone to calcify the bioprosthesis in this manner, the occurrence may be related to length of implantation; the probability thus, being higher the longer the implant duration. However, no all patients, children or adults, will calcify the porcine heterograft.

Figure 10 B illustrates the typical picture of this occurrence in its intermediate stages. Subsurface nodules are evident which resulted from the idiopathic calcification of the fibrous collagenous bundles near the attachment of the leaflet to the aortic wall. With time, this calcification may proceed from initial nidi to disruption of leaflet collagenous tissue, though the surfaces may not be initially affected (figs. 10 C, D, E).

3.5 Thrombus

A significant benefit of the HANCOCK* bioprosthesis is its low thrombogenic potential, the management of the majority of patients without long term anticoagulation or embolic penalty. Valves removed because of thrombotic episodes represent 4.5% (8) of the explanted valve population in this report and their removal chronology is given in figure 11 A. None of these demonstrated obvious etiology in terms of alterations to histological architecture or leaflet surface appearance at both LM or EM levels. Figure 11 B shows a histological section of a leaflet on whose surface a massive thrombus can be observed.

3.6 Primary tissue dysfunction

This phenomenon, tears of unknown etiology, represents less than 2% of the explanted valve population (fig. 12 A). Valves in this category typically have one or more leaflet tears or punctures which, at present, appear to show no correlation with implant duration or any other cause. With the exception of this fact, the bioprostheses present excellent histological architecture and grossly normal appearance (fig. 12 B). Light microscopy (fig. 12 C) at and near the tear site presents well defined tissue discontinuities with total absence of degeneration of surrounding collagenous tissue. Iatrogenic tears were excluded on the basis of surgical notes; tears secondary to calcification or bacterial activity were likewise excluded.

4. Summary

The data described above is summarized in figure 13. Late update from 180 to 208 explanted valves indicates that there are no drastic changes in the distribution of dysfunction patterns found for the bioprostheses retrieved and accumulated in this laboratory. Table I illustrates the results obtained after the addition of 28 explants.

5. Durability of the HANCOCK* Bioprosthesis

The long term success of glutaraldehyde process porcine aortic valves utilized for human valvular replacement depends upon various

extrinsic and intrinsic factors. The former, as described above, are primarily associated with phenomena related to cardiac function, sepsis, healing, and metabolic conditions. The latter are closely associated with conservation of the underlying constituents as a consequence of preservation by processes and resistance to continued deleterious host-graft interactions.

In the native condition, the functionally significant anatomic regions of the various valvular structures are composed primarily of collagen in association with non-fibrous components consisting mainly of mucopolysaccharides and glycoproteins. The HANCOCK process, eliminates the majority of non-fibrous components along with much of the cellular constituents. Except for the aortic wall and some regions of the inflow aspect, which exhibit a rather significant elastic component, the resulting bioprosthesis is mainly composed of collagen.

Collagen is one of the few biological entities whose molecular structure both explains and is reflected by its observable ultrastructure. Maintenance of the fiber structure, either by turnover, repair or inherent stability most certainly is requisite for biologic or functional competency, and continued conservation of the fiber configuration would also seem logical exigencies for in vivo prosthetic function

Recently studies have investigated the fate of glutaraldehyde processed collagen in vivo [28]. Moreover, the studies were concerned with durability of tissue prostheses as a function of collagen fiber degeneration. The authors indicate that shortly after prosthetic implantations in humans, valvular collagen begins to undergo morphologic degradative alterations. They further indicate that these changes relate to durability and, therefore, potentiate prosthetic dysfunction. That is, the ultimate fate of tissue prostheses must be intimately associated with the rate and chronology of these events.

Their conclusions are partially dependent on the appearance shortly after implantation (as early as 28 days) of a granular electron dense material associated with collagen fibers and permeating the interstitium. This phenomenon is interpreted as representing the onset and, with time, continued collagen disintegration. A blurring or focal loss of the characteristic crossbanding pattern of collagen was also noted accompanying or preceding fiber disruption.

Should these precipitous changes occur, degradation of glutaraldehyde fixed collagen must certainly be related to the efficacy of the tanning process. The exact mechanism of glutaraldehyde preservation has not yet been elucidated, but it is reasonable to assume that ultrastructural conservation is dependent upon "mechanical" crosslinking by single or polymerized glutaraldehyde molecules. Thus, the loss or preservation would be reflected in the results from various physiochemical studies designed to evaluate their failure or diminution.

5.1 Studies on long-term implants

The preservation of the tissue components of HANCOCK valves implanted for extended periods of time has been the subject of continuous study by this laboratory since the early stages of success of this bioprosthesis. Analysis of these components by various physical, biochemical and microscopical means is used to partially asses the durability and to begin projection of the longevity of this bioprosthesis.

5.1.1 Histological comparisons

Careful observations of diverse areas of valvular tissues obtained from explants ranging from 2 years to 5 years, 10 months, compared to preimplant specimens showed that no difference in morphology is observable at the light microscopic level. Figures 14 A and B are photographs of a valve implanted for 5 years, 10 months from inflow and outflow aspects. The sections in figure 14 C represent regions of the valve known to be under continuous physiological stress. No significant alterations were noted at gross histological levels when these tissues were compared with tissue from preimplant valves.

5.1.2 Shrinkage temperature

Shrinkage temperature has been shown to reflect the degree of collagen crosslinking by aldehydes [27]. The shrinkage temperatures of explanted valves returned in cold sterile saline and having no contact with any fixative solution, were determined. Figure 15 shows the distribution of temperatures observed and the best fit curve obtained from these results. More data is being incorporated to extend this line to encompass valves retrieved up to nine years implantation time.

5.1.3 Disruption, enzyme and electron microscopy studies

Tissue for the various studies was obtained from three Hancock porcine heterograft valve prostheses (three patients) explanted at reoperation for valvular replacement. Implant duration for the three prostheses was 34, 92, and 100 months. The 92 month implant was replaced because of a degenerative aortic root; the other two valves were explanted because of intrinsic prosthetic mineralization. The explants were received in cold saline and had not been exposed to any form of fixation subsequent to explantation. Pieces of tissues (1 mm x 1 mm) were removed from the valve leaflets, rinsed in saline, and either in 2.5% .1 M cacodylate buffered glutaraldehyde (untreated controls) or retained for enzyme and disruption studies.

5.1.3.1

Pieces of leaflet tissue were incubated with continuous shaking

in 5 ml of a 4 M guanidine HCl solution adjusted to pH 7.5 with Tris base. Similarly treated unfixed and glutaraldehyde processed unimplanted leaflet tissues served as controls.

5.1.3.2 Enzyme studies

Up to four pieces of tissue were incubated for 24 hours at 25°C with constant orbital shaking in a 50 mM Tris buffered (pH 7.5) trypsin solution containing 10 mM $CaCl_2$. Pieces of explant tissue were also incubated in the buffer $CaCl_2$ solution without enzyme. When collagenase was used the concentration of enzyme was 1 mg/ml in the same buffer system containing 0.004% $CaCl_2$.

5.1.3.3 Electron microscopy

After incubation the pieces of tissue were rinsed (x3) for 10 minutes in .1 M cacodylate buffer (pH 7.4) and transferred to cold (3°C) 0.1 M cacodylate buffered (pH 7.4) 2.0% glutaraldehyde for 24 hours. After fixation the samples were postfixed with cold 1% OsO_4 in 0.1 M cacodylate buffer (pH 7.4), dehydrated in 2, 2-Dimethoxypropane and embedded in Maraglas. Half-micron and ultrathin sections were cut with an LKB Ultratome IV, stained with uranyl acetate and lead citrate, and examined with a Philips EM 400 electron microscope.

5.2.1 Ultrastructural morphology of explanted valvular heterografts

Comparison of collagen from leaflets of the explanted valves (fig. 16 A) with that from comparable regions of the unimplanted controls (fig. 16 B) revealed (1) a variable loss of contrast or blurring of the collagen fiber crossbanding pattern, (2) electron dense granular material associated with the collagen fiber surface, and (3) an accumulation of similar material in the interfiber spaces. Close examination of individual fibers showed associated granular and filamentous material which appeared to be attached to the fiber surface and possibly within the fiber intermolecular interstices (fig. 16 C).

5.2.2 Effects of guanidine HCl on leaflet ultrastructure

Fresh, unfixed porcine aortic leaflet tissue exposed to 4 M guanidine HCl showed collagen fiber alterations ranging from fiber "unwinding" to almost complete disruption into microfibrillar components (fig. 17 A). Glutaraldehyde processed unimplanted tissue appeared resistant to dissociative treatment and showed no significant ultrastructural changes (fig. 17 B). Collagen from the explanted valves (figs. 18 & 19) also exhibited no morphologically significant changes when compared to either the unimplanted or untreated controls. It should also be noted that guanidine HCl treatment did not appear to have a significant effect on the presence or appearance of the granular

material in the explanted samples.

5.2.3 Effects of trypsin on leaflet ultrastructure

Exposure to trypsin (fig. 20) resulted in rather striking changes in the explanted tissue when compared to the untreated controls. The most apparent effect was a significant decrease of the amount of material associated with both the fibers and the interfiber regions. The paucity of the granular material was accompanied by a more distinct fiber surface and crossbanding pattern resulting in an overall collagen ultrastructural profile comparable to unimplanted controls.

6. Discussion

The results obtained from these analyses suggest that distinction should be made when areas of critical importance to the long term functionality of tissue prostheses are reviewed. Specifically, the dysfunction patterns of the bioprosthesis should be viewed separate from a seemingly distinct issue, that of its durability and longevity. However, that the former may in some way be contributory in some instances to the latter may not be excluded.

6.1 Dysfunction

As pointed out earlier, the majority of factors related to dysfunction of tissue bioprostheses appear to be extrinsic in nature. These factors seem to be primarily associated with phenomena related to cardiac function, sepsis and healing, and metabolic conditions.

While the population described perhaps represents only a fraction of all valves explanted to date, it is substantial in that no other group has reported numbers comparable to these. Also the distribution of dysfunction patterns appear to be plausible, and communications with numerous users of the HANCOCK* bioprosthesis reflect agreement with our findings.

Non valvular problems (18.2%) active infective and bioprosthesis endocarditis (17.3%) as causes for removal account for nearly half of the dysfunction patterns reported in the explant population. Both are extrinsic factors to the dysfunction of the bioprosthesis. Magilligan et al [12] in relating their experience with the Hancock valve concluded that: 1) it is as resistant to infection when inserted in the face of active infective endocarditis as are rigid prostheses; 2) is resistant to early post operative bacteremias; and 3) it is easier to sterilize than rigid prosthesis as well as being more durable than other tissue valves in the face of prosthetic valve endocarditis. The review of the Stanford group experience by Rossiter and associates [13] concluded that heterograft aortic endocarditis was more easily cured by medical treatment than a mechanical valve endocarditis, if treated before annular abscesses

occurred. They also showed agreement with Magilligan in regards to the advantages of medical over surgical treatment of the condition. However, failure of medical therapy must be identified without delay and reoperation undertaken promptly to avoid excessive operative mortality.

A survey of the experience of various authors with endocarditis and porcine valves [14] reveals that with nearly 5000 valves, in a comparable number of patients, the percentage of cases was substantially less than 1%.

Forty six percent of the dysfunctions observed in this explanted valve population was secondary to calcification. Reports on this type of valve related complication have been uncommon [15,16,17,18,19].

While generally calcification of the valve is considered overall as a single process, the data in this report points to a dual phenomenon characterized by rather different patterns of initiation and proliferation.

The sequence of events in extrinsic mineralization (23%) bears similarity to those occurring in human valvular endocarditis, where extensive fibrinous and cellular deposits occur. These deposits are associated with previously infected regions of the valve as a consequence of host mechanisms. The susceptibility to salt deposition demonstrated by these deposits is, in our estimation, most likely associated with specific molecular conformations of organized or unorganized fibrin. The probable sequence of events is illustrated in figure 21, where it is seen that as mineralization progresses, leaflet function is compromised. Eventually the erosive effects of salt deposits may result in leaflet fraying and tearing.

This form of mineralization does not seem to occur as a result of any intrinsic or inherent characteristics of tissue valvular prostheses, nor does it show to occur with preferential dependency for age or sex of the valve recipient.

Another 23% of the explanted population was observed to occur by a totally different pattern we have termed intrinsic mineralization and which other authors [17,18,19] have referred to as idiopathic, or fibrocalcification. This form of calcification by contrast, rare as it must be considered, appears to occur with a chronology dependent on the age though not on the sex of the valve recipient. The chronology as well as the age dependency is shown in figure 10 A. For this analysis, patients under the age of 20 years are grouped separately from the remaining adult patients.

Thus, it can be deduced that when this form of mineralization occurs in children, it does so early after implantation of the bioprosthesis. We have observed this as early as six months and as late as six years. I report on a similar bioprosthesis to the Hancock valve, described its occurrence within 19 days of implantation [23]. In adults, there is no apparent chronology associated with its occurrence.

Only specific individuals, adults and children are at risk, and the factors which increase this risk are still poorly understood.

For adults with a propensity for calcification, a time relation is suggested, the probability of occurrence may increase with duration of implant.

Some factors which have been considered influential in precipitating the onset of calcification are associated with metabolic and electrolyte disturbances [6,18,19] such as may be found in patients under chronic hemodyalysis [6,31], sickle cell disease [15] elevated alkaline phosphatase levels, secondary hyperparathyroidism and increased calcium turnover. Levy and associates [20,21] have explored the possible role of a newly found calcium binding amino acid, γ-carboxyglutamic acid in valvar and tissue prostheses calcification. Their results suggest a possible relationship of vitamin K-dependent processes to the pathogenesis of these diseases.

An extension of their results can be envisioned in the possibility of correlating excretion levels of this amino acid and heterograft status in patients at risk of fibrocalcification.

One possible mechanism for the salt deposition within valvular structures is illustrated in figure 22. The intraleaflet regions affected seem to exhibit host protein infiltration as a consequence of voids produced by process variables which remove porcine proteins and mucopolysaccharides. This may be a desirable interaction as these viscous fluids may provide internal lubricity necessary to decrease shear stresses provided to the valve by the human hemodynamic environment. In certain patients extensive protein inundation of the interfiber spaces may promote salt deposition with progressive leaflet stiffening, and as there is crystalline growth, cusp tears. dehiscence, and total leaflet disruption as the final outcome.

However, it must be emphasized that the fibrocalcification process becomes a chronic process and an intrinsically calcified valve may continue to function for extended periods of time, gives ample warning of malfunction and in most cases allows elective rather than emergency surgery [22,23].

Seemingly this form of calcification is generic to all glutaraldehyde fixed tissue valves. It suggests there are heterograft sites which, in the presence of certain factors, may elicit the initiation of fibrocalcific deposits. This clearly introduces the possibility that additional treatments to block the potential nidi may help to delay or arrest the processes in the implanted valve.

In our experience, intrinsic calcification is an uncommon event. Our current estimate puts it in the neighborhood of 0.5% of all implanted valves. Certainly this is comparable to reports in the literature which show numbers in the same order; Cohn[6]: 0.3%; Lamberti [15]: less than 1%; Oyer[7]: 0.45%, showing in children 50% rate and Thandroyen

[23]: less than 1%, encompassing experience of these authors with over 3000 patients.

Numerous reports attest to the advantages of the HANCOCK* bioprosthesis over its mechanical counterparts with regards to its low thrombogenic potential [3,4,5,6,7,24,25] Hetzer and associates 24 have identified patient related factors associated with increased risk of thromboembolism after mitral valve replacement with this bioprosthesis and described specific anticoagulant regimens for patient subgroups with various thrombogenic factors. Cevese [4] in a series of 629 xenografts reports a total incidence of embolization for the entire group of patients as 2.3%. Oyer et al [7] reports over-all rates in 1118 patients at risk ranging from 1.7% to 2.6% with a maximum follow up of 7.3 years. Thus, the 4.3% rate we find in the population of explanted valves does not seem inordinately large.

Exposure to antibiotics during the rinsing sequence has been thought to be related to subsequent thrombosis due to electrochemical potential changes of the valve surface induced by these drugs (fig. 23).

Cohn [25] has described thromboembolic phenomena in patients with chronic valvular heart disease resulting from decreased cardiac output as a consequence of myocardial dysfunction, increased atrial chamber size, supraventricular arrythmias, and obstruction of flow. Thus, he concludes, any condition leading to decreased blood flow across the valve orifice, stagnation, or obstruction of blood flow may predispose to thromboemboli.

Patients with chronic atrial fibrillation, or decreased myocardial performance, following mitral replacement specially, are predisposed to thromboembolic episodes whether or not a tissue valve is inserted. It is interesting to note that a survey of 19 major cardiovascular centers [25] showed a wide variation in anticoagulation regimens for patients receiving tissue heart valves. It has become general practive to require long-term anticoagulation on patients showing poor hemodynamic performance, and for all patients in the perioperative period for 6 to 12 weeks.

Tears of unknown etiology, often referred to as primary tissue dysfunction represents about 2% of the explanted valve population [26]. Explanation for the causes of this dysfuntion at this time can only be speculative. Natural variations in porcine collagen may exist from animal to animal, differences which could result in potentially less durable areas. The possibility of leaflet trauma during retrograde catheterization, discussed with various users of this bioprosthesis leaves open a possibility for the initiation of events which could lead to eventual leaflet tears.

To date there has been no pattern to this occurrence, nor has the frequency increased in proportion to the explanted or implanted valve population [6].

In summary, the dysfunction patterns of this bioprosthesis, as assessed by examination of the explanted valve population accumulated in this laboratory and in relation to the total implant population, indicate that a small percentage of the xenografts are at risk of calcification and thromboembolic complications. Similarly, a fraction of the population may necessitate removal in the face of active infective endocarditis without healing or prosthetic valvular endocarditis.

6.2 Durability

No other tissue heterograft enjoys, at the present time, a decade long clinical experience. This fact affords the HANCOCK* bioprosthesis a unique opportunity to evaluate critical post implantation follow-up beyond five years. The explanted valve program has afforded the opportunity to evaluate bioprosthesis structural condition after extended *in vivo* functional periods of time.

As was stated above, the long term success of these bioprostheses depend on various extrinsic as well as intrinsic factors. Their durability, in the absence of all extrinsic factors, described in the section of dysfunction, depends solely on the durability of the underlying network of collagen constituting most of the functional aspects of the valves.

The shrinkage temperature of explanted valves indicated that valvular tissue maintained a relatively unaltered degree of collagen crosslinking after seven years of implantation. Histological observations did not reflect tissue degeneration in the absence of the extrinsic factors mentioned. However, electron microscopical examination of leaflets from clinically explanted prosthetic heart valve heterografts revealed post implant changes characterized by apparent collagen fiber alterations concommitant with the accumulation of a fine granular material. The latter appeared to coat the fibers and reside within the interfiber and valvular spaces previously occupied by nonfibrous protein-carbohydrate complexes eliminated during heterograft processing. The studies by Ferrans *et al* [28] indicate that the initial appearance and subsequent accumulation of the material occur as a result of progressive collagen disruption, and if the granulation does represent collagen degradative products it would seem reasonable to assume that the material originates as a consequence of fixation deterioration, host mediated enzymatic action, or a combination of both.

The first purpose of the study was to determine whether the glutaraldehyde crosslinks induced during initial fixation of the prostheses were conserved.

The mode of action of guanidinium dissociation appears to be based on the ability of the denaturant to disrupt or break hydrogen bonds with the loss of bonding resulting in the progressive disaggregation of collagen fiber into microfibrillar components [29]. The almost total disruption of the fresh unfixed valvular collagen (fig. 17A) indicates that

covalent lysyl-derived crosslinks only partially stabilize the fiber structure. The rather remarkable resistance of the unimplanted glutaraldehyde treated collagen to denaturation (fig. 17B) shows that the glutaraldehyde derived crosslinks significantly increase fiber stability. The results obtained with the explanted tissue, which also exhibited a comparable resistance, demonstrate that the aldehyde crosslinks are apparently conserved after implantation (figs. 18, 19, 20).

In a study examining the consequences of experimentally induced corneal immune injury Mohos and Wagner [30] have described the progressive dissolution of collagen fibers as a result of the injection of proteolytic and hydrolytic enzymes into intact, healthy rabbit cornea. Among the enzymes utilized trypsin was shown to be an effective proteolytic agent against collagen resulting in a superficial peeling of the fiber followed by a more complete dissolution into fragmented microfibrils. These changes were reported after only 2 hours of exposure of the tissue to enzyme. In the present study the effects of trypsin on unfixed and fixed unimplanted tissue were not examined but the resistance of explanted prosthetic collagen to 24 hours of enzyme exposure (fig. 20) further supports the stabilizing effect of the glutaraldehyde crosslinks as well as a conservation of that effect after extended prosthetic implantation. Studies designed to examine the effects of other proteolytic enzymes with both specific and general bond affinities are presently being performed.

The second purpose of the present study was to attempt to determine to what extent, if any, the post implant granular material observed coating collagen fibers and accumulating within interfiber spaces represents the consequences of fiber degradative alterations. It would seem reasonable to assume that if prosthetic collagen degradation does occur the granular material could be wholly collagenous in origin or consist of a combination of collagen and host material. In their studies concerning corneal immune injury Mohos and Wagner concluded that in the case of an immunological response associated with collagenous tissue the resulting fibrinoid was composed of an immune precipitate with entrapped fragmented collagen. Since glutaraldehyde processed prostheses do not appear to elicit any significant localized cell mediated immune response it seems doubtful that this would be the mechanism by which the material forms. Circulating immunologically derived components could, with time, infiltrate the prosthesis and possible contribute to the observed phenomenon but it would seem unlikely that an immune component in the absence of any localized cellular response could account for a significant breakdown of the collagen.

Even though the previously discussed findings indicate that prosthetic collagen fixation is conserved the possibility exists that over an extended time period there is, in the absence of any host mediated mechanism, a slow yet progressive fiber degradation with the resulting products accumulating as collagen fragments or as a complex involving host components. Such a mechanism or any involving a significant contribution of the prosthetic collagen to the formation of the material would be expected though to result in irreversible fiber ultrastructural

alterations. That treatment of explanted tissues with trypsin results in the elimination of the granular material, and the apparent "restoration" of the preimplant collagen ultrastructural profile, strongly supports the hypothesis that prosthetic collagen is not a significant component of the material. For example, even though close examination of the explanted collagen fibers reveals what appears to be focal disruption (fig. 19) fibers from the same region after enzyme exposure appear comparable to those of preimplant tissue (fig. 20). Alternatively the granular material could be wholly host in origin. We have observed that within days after prosthetic implant an electron dense granular material accumulates in association with the remaining basement membrane components at the leaflet surfaces and with the more superficial fiber bundles. The electron microscopic appearance of this material is virtually undistinguishable from that observed after extended implant time and appears to almost certainly result from the infiltration of host material. While the present study is primarily concerned with the collagenous component it should be noted that the trypsin exposure also results in the removal of the basement membrane associated material leaving behind an intact basement membrane with an electron lucent background. The generally accepted specificity of trypsin toward peptide bonds involving the carboxyl groups of lysine and arginine may have significance with regard to identity of the material especially since the latter is characteristic of fibrinogen. Studies concerned with the isolation and characterization of the material are suggested with special emphasis on amino acid profiles.

In summary, the results of this study indicate that the glutaraldehyde crosslinks induced at initial fixation of the prosthetic tissues are conserved and apparently effectual after extended prosthetic implant duration. The absence of a significant amount of the post implant granular material and the restoration of the collagen ultrastructural profile comparable to that of preimplant tissues as a result of enzyme exposure strongly suggests a noncollagenous host origin of the material. Together these findings offer evidence that glutaraldehyde processed valvular prostheses may not be subject to progressive intrinsic deterioration.

7. Comment

A population of HANCOCK* bioprostheses retrieved for various reasons after extended implantation, and their modes of dysfunction have been analyzed. The results we believe will be of interest to the medical community in evaluating the performance of this valve in terms of functionality and longevity. We believe that the durability of any tissue bioprosthesis can only be realized through extensive clinical evaluation and thorough examination of retrieved specimens.

Acknowledgments

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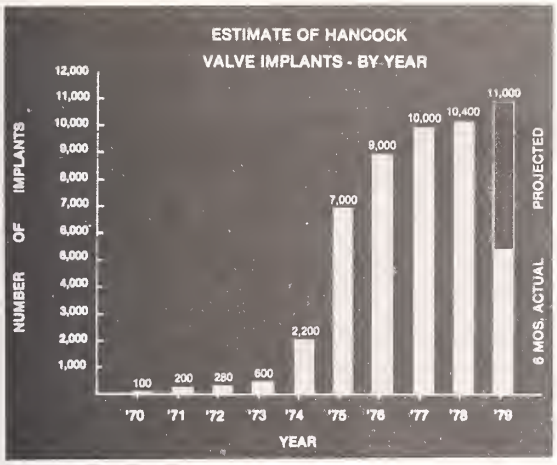


Figure 1. Estimate of Hancock valves implanted by year.

-Figure 2. Hancock bioprostheses. (A) A-V Model 342 inflow aspect. (B) A-V Model 342 outflow aspect. (C) Valved conduit

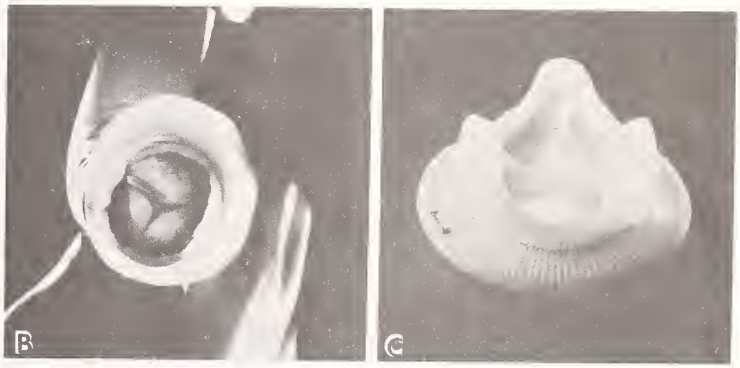
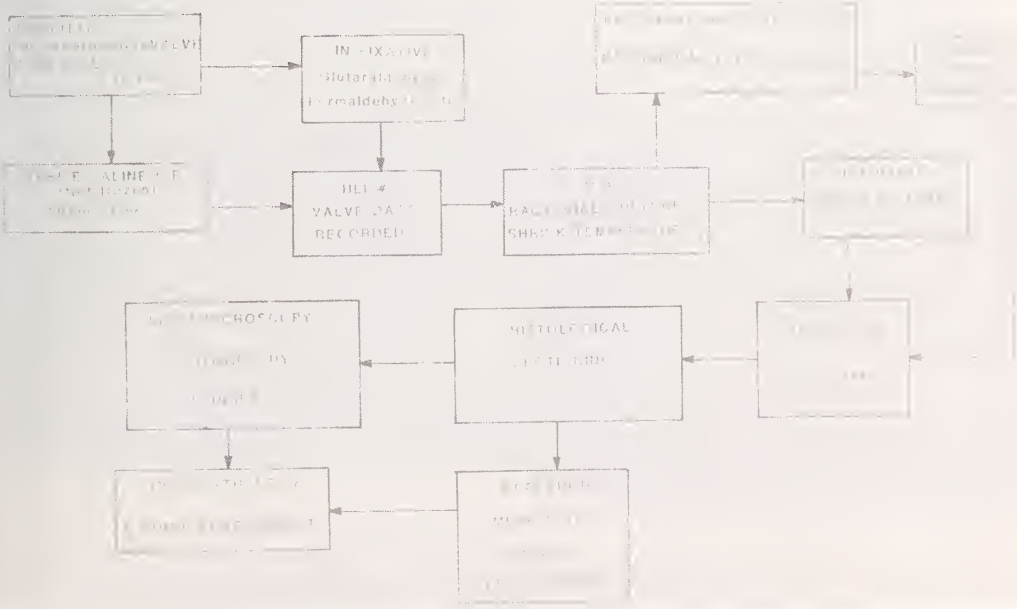


Figure 3.



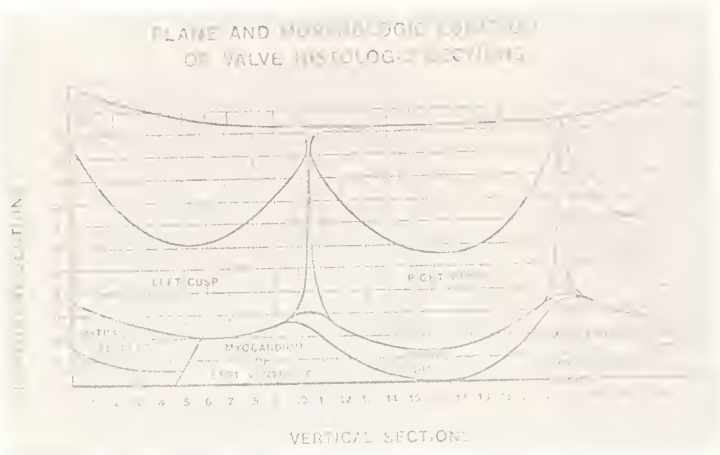


Figure 4. Map of plane and morphologic location of valve histologic sections.

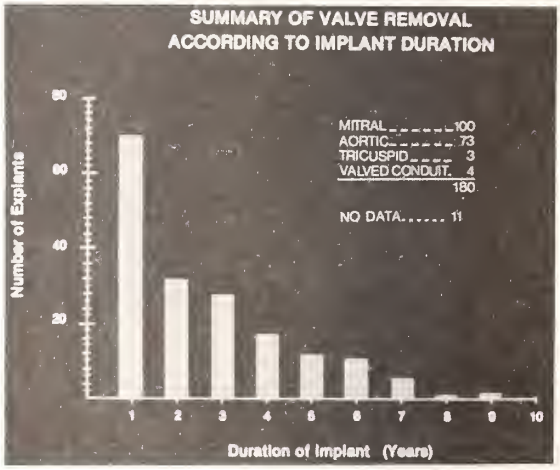


Figure 5. Summary of valves retrieved by position and implant duration.

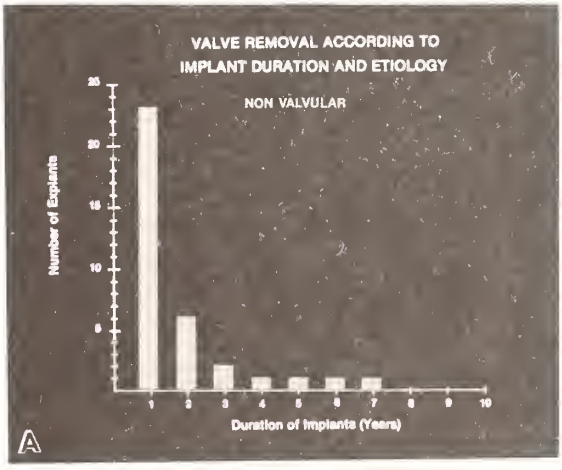
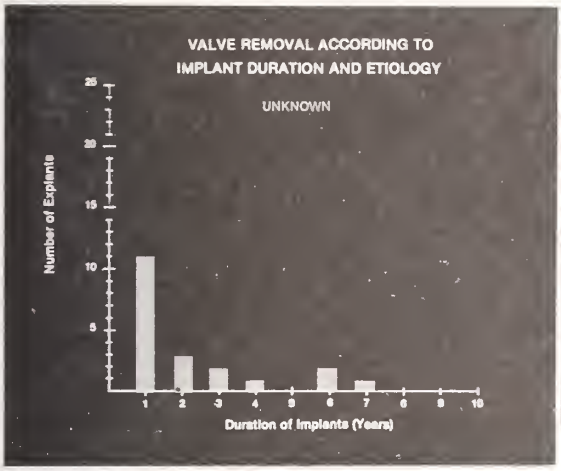


Figure 6.A. Non valvular reason for retrieval.
B. Outflow aspect of 92 month implant removed because of patient degenerative aortic root disease. Valve showed well conserved tissue at gross and microscopic levels.



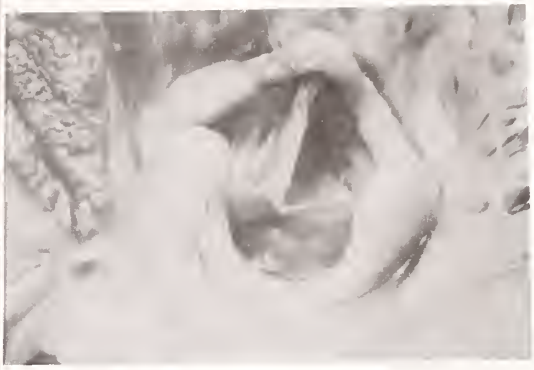


Figure 7. A. Time course of valve retrieval for unknown reasons.

B. Valve <u>in situ</u>, removed for unknown reasons.

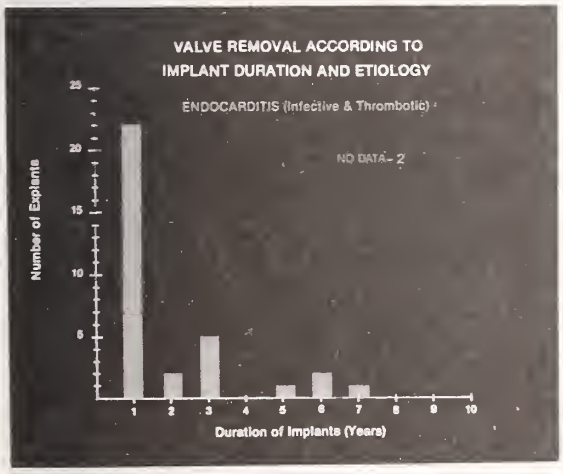
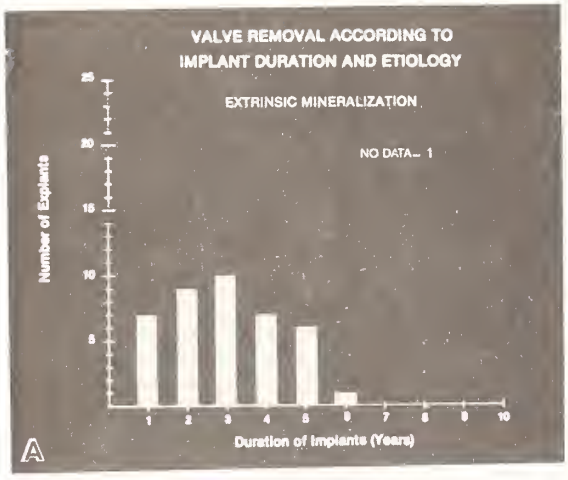


Figure 8. A. Chronology of retrieval in the face of active infective endocarditis or bioprosthetic endocarditis.

B. Valve removed at 6 months because of unhealed infective endocarditis. Histological sections revealed abundant aggregates of coccal organisms.



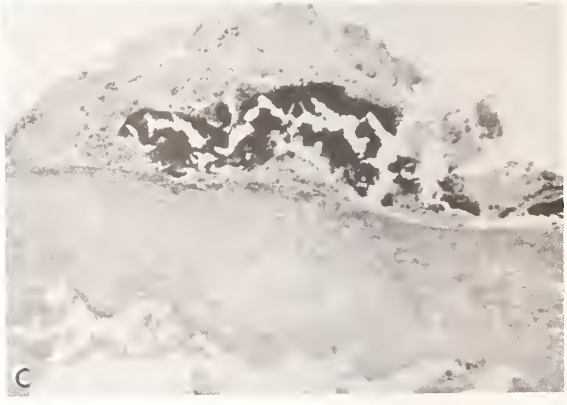


Figure 9.A. Extrinsic mineralization as reason for valve removal. B. Gross photograph of extrinsically calcified valve. Note mineralized verrucous deposits along commissural edges of valve leaflet. The remaining tissue is smooth and glistening. C. Fibrin accumulated on surface of valve demonstrates positive von Kossa (black) material indicative of calcific deposit. The architecture of the leaflet is well conserved.

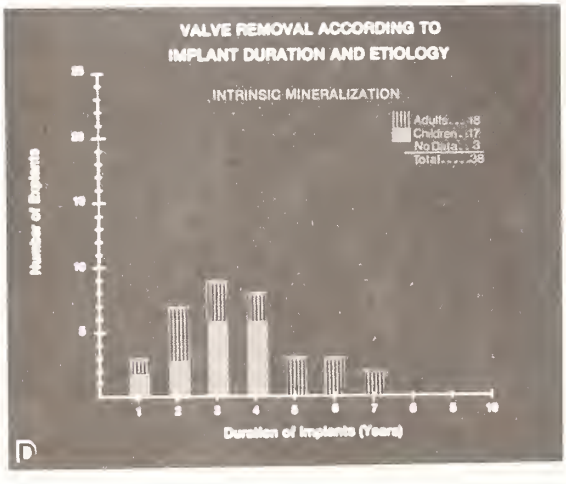
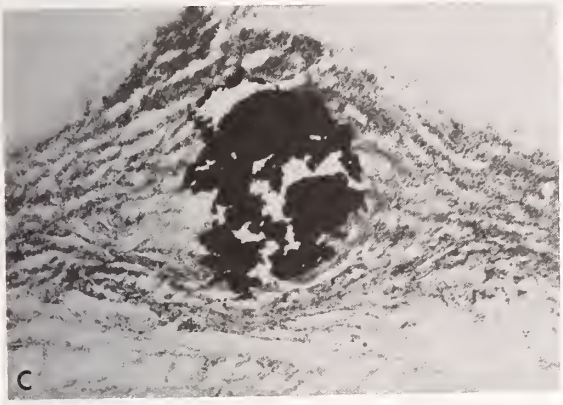


Figure 10.A. Removal due to INTRINSIC mineralization of valves. Distribution between children and adults demonstrate different chronology. B. Pictorial gross review of calcified "strut" and calcific nodules under surface.



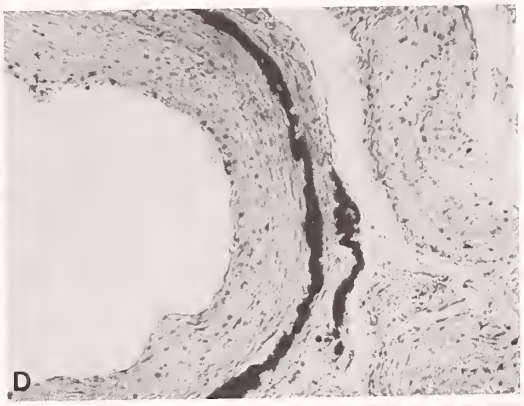
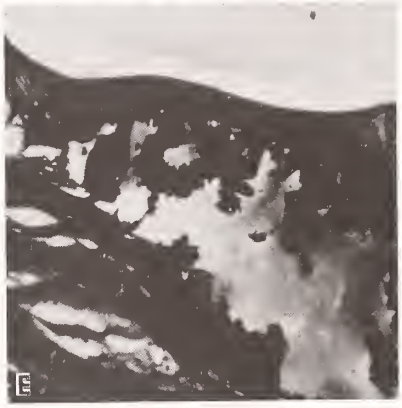
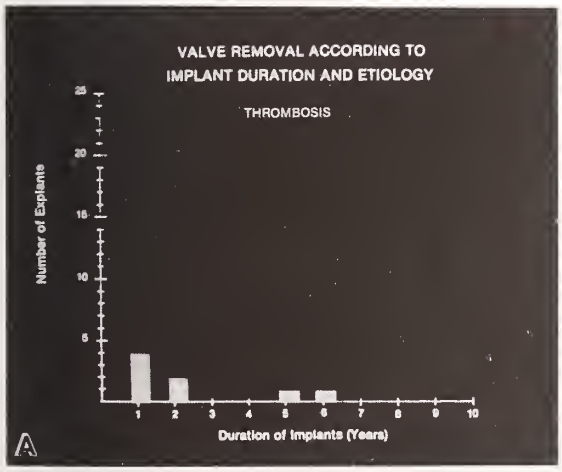


Figure 10.C. Crossection normal to the direction of collagenous bundle showing von Kossa positive material.
D. Intrinsic mineralization of collagenous bundles.
E. Subsurface mineralization of leaflet fibrosa. Notice that leaflet surface is not yet affected.





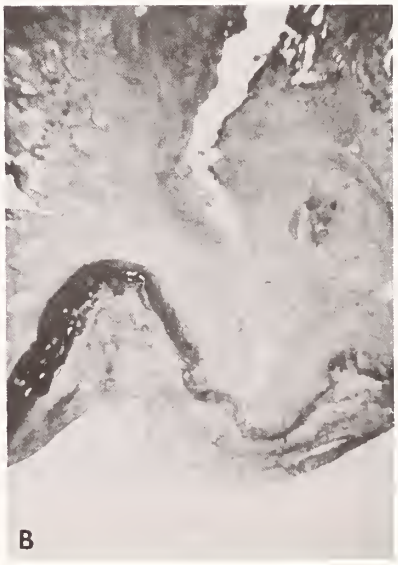


Figure 11.A. Idiopathic thrombosis requiring retrieval.
B. Histological section of well-conserved leaflet demonstrating massive thrombotic desposition.

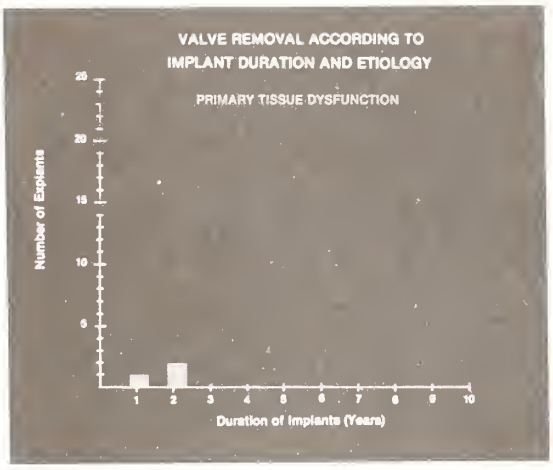


Figure 12. Tears of unknown etiology.
B. Gross view of the phenomenon.
C. Histological sections of leaflet at site of rupture. Notice good conservation of collagenous material throughout leaflet.

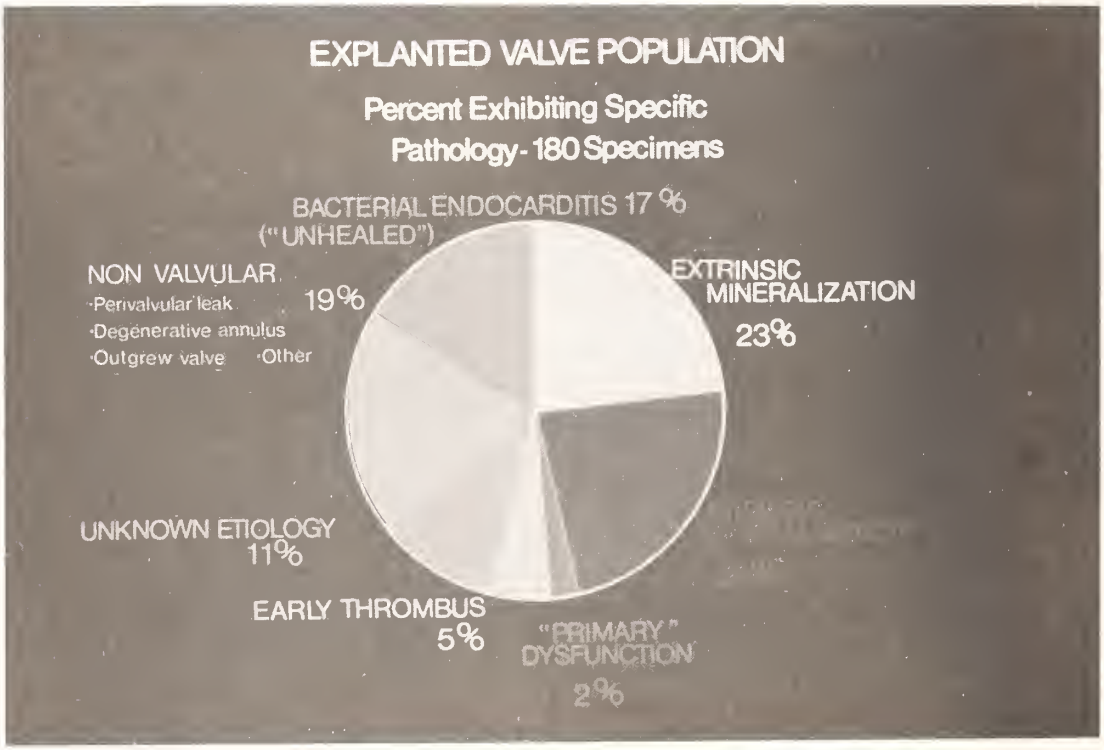


Figure 13. Summary of dysfunction (180 valves).

Table I

DYSFUNCTION

208 Excised HANCOCK Valves

	Non Valvular	Endocarditis	Mineralization Extrinsic	Mineralization Intrinsic	Leaflet Failure	Thrombus	Unknown
Number	38	36	47	51	5	9	22
%	18.2	17.3	22.6	24.5	2.4	4.3	10.6

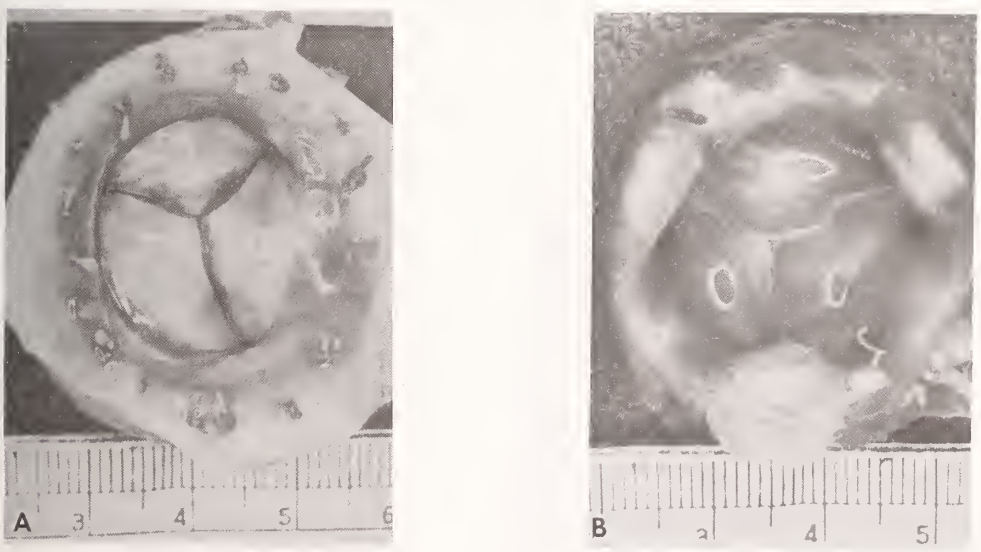


Figure 14. A and B. Inflow (A) and outflow (B) aspects of valve explanted 5 years 10 months (70 mos.). Exhuberant host fibrotic ingrowth into the sewing ring stops at points of leaflet flexure.

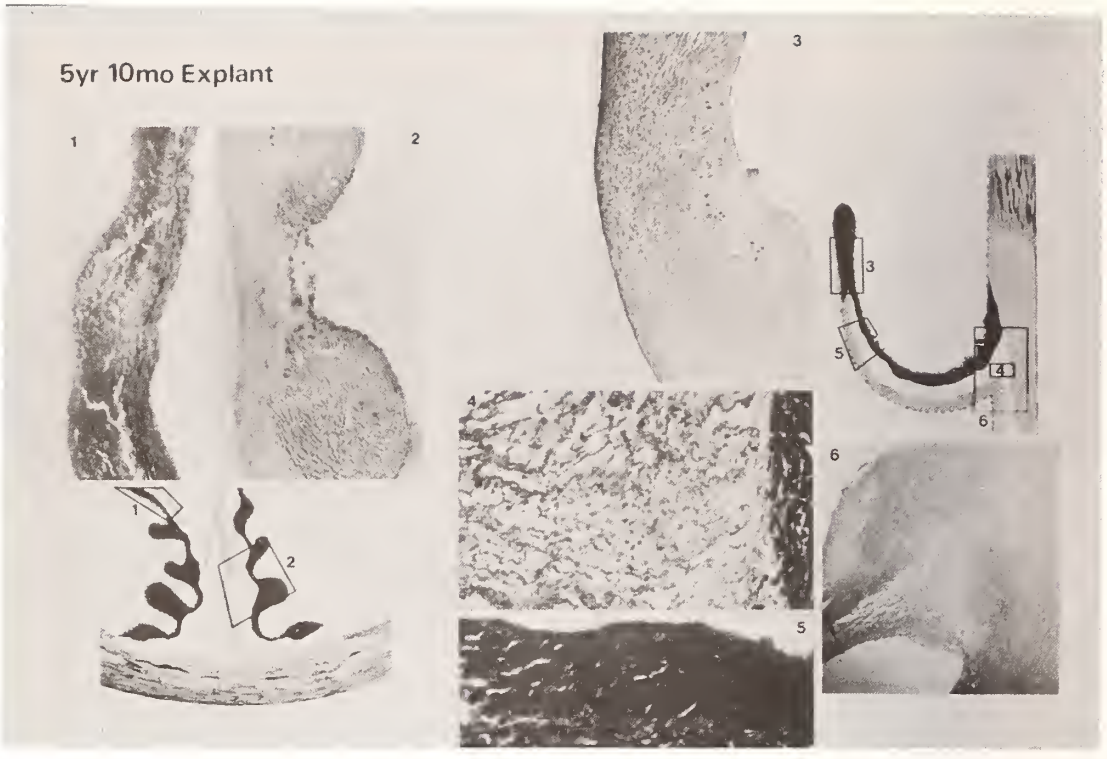


Figure 14 C. Cusp elastica showing elastin fibers. 2. Shows good conservation of collagenous bundles. 3. Near node of Arantius, point of high stress. 4 and 6. Ground substance from the elastic triangle which serves as an infinitely rolling hinge. 5. Cusp material. All comparable to preimplant tissue.

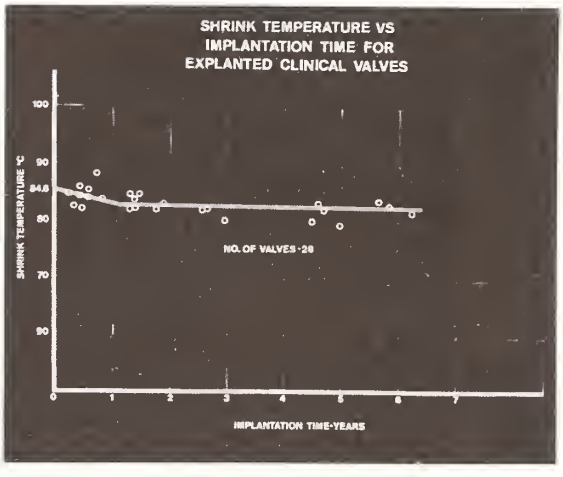


Figure 15. Shrinkage temp of valves retrieved in cold saline. After the initial drop of less than a degree, there are no changes in this temperature. This figure at present extends over 7½ years.

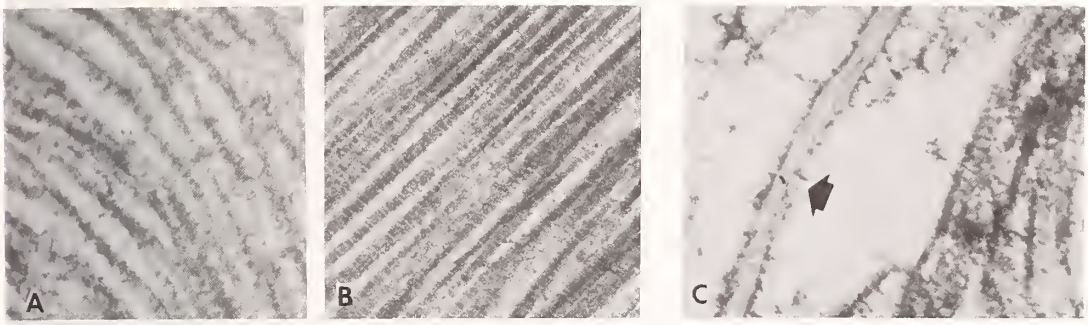


Figure 16 A. Ultrastructural view of collagen from leaflet of valve explanted at 92 months. Notice blurring of collagen fiber crossbanding and ubiquotous adherent material. B. Ultrastructure of preimplant collagen. C. Adherence of granular material to single elastin fiber (arrow). All X47,000

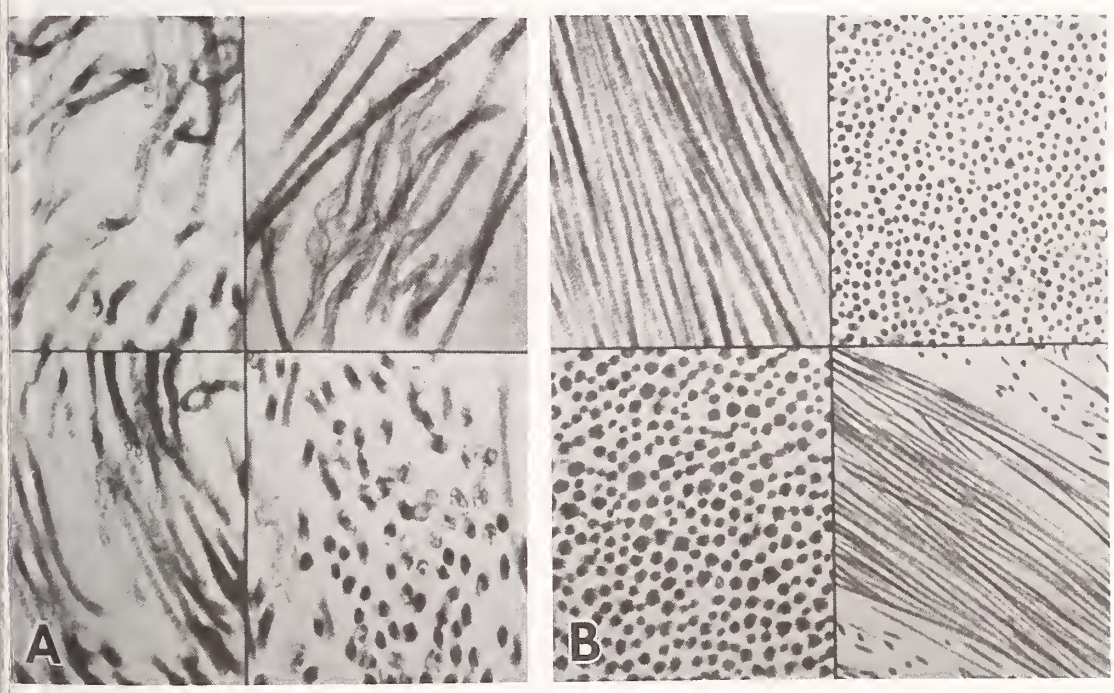


Figure 17 A & B. Effect of 4 M guanidine hydrochloride on unfixed and glutaraldehyde processed porcine valvular collagen. A. Unfixed collagen from various regions of leaflet. The dissociating effect is seen in both longitudinal and transverse aspects of fibers. Uncoiling or unwinding is evidenced after exposure of tissue to the agent. B. Glutaraldehyde fixed, unimplanted collagen. Stabilization of collagenic structure by glutaraldehyde crosslinks evidenced under the same condition as A. Crossbanding is sharp, fiber integrity conserved (X225,000).

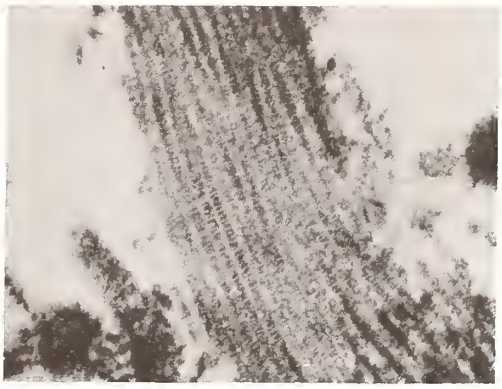


Figure 18. Ultrastructural section of collagen fibers from leaflet of 92 month explant treated with 4 M guanidine hydrochloride. Notice the blurring of typical periodic pattern and granular material everywhere. (X47,000)

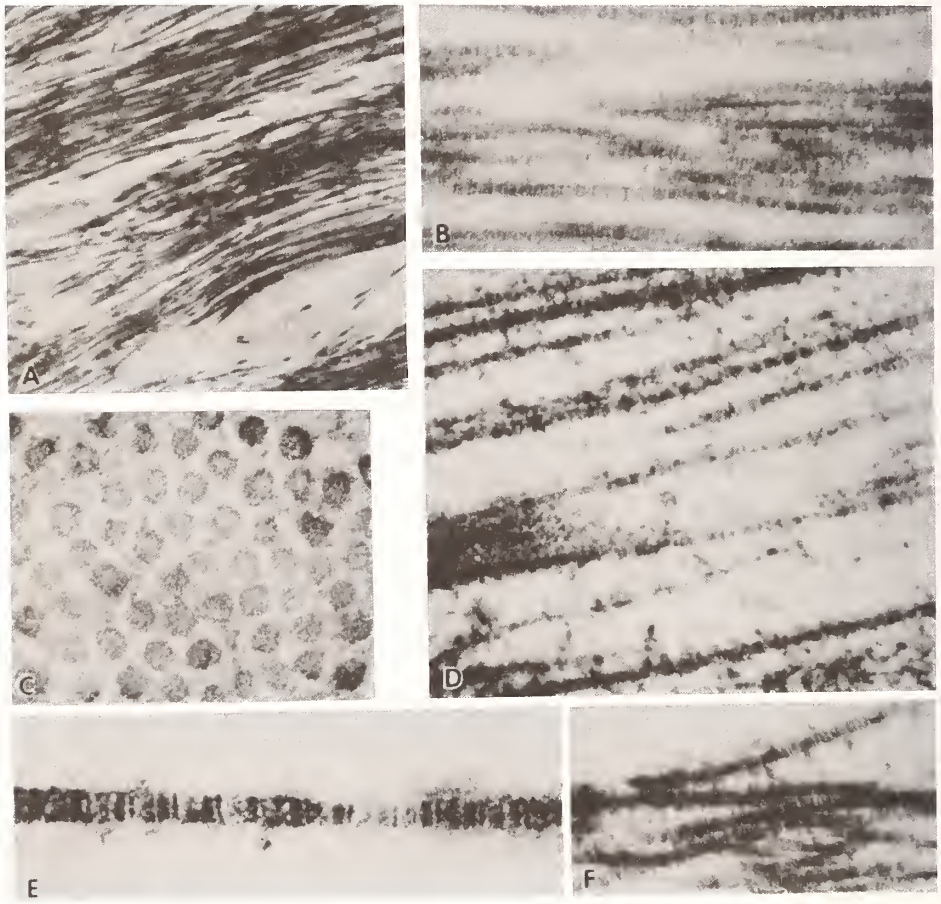


Figure 19. Electron micrographs of clinically explanted Hancock valves. A. After 100 months of implantation. Interstitium of the individual fibers, bundles of the fibrosa are occupied by electron dense material (X9,000). B.& C. (X175,000) Higher magnification of longitdunal (C) and transverse sectioned collagen show the fine granular nature of the electron dense material in A. D. (92mos. X225,000), E (34 mos. X225,000) and F (34,000 X71,000) show the intimate association of the material with the individual fibers.

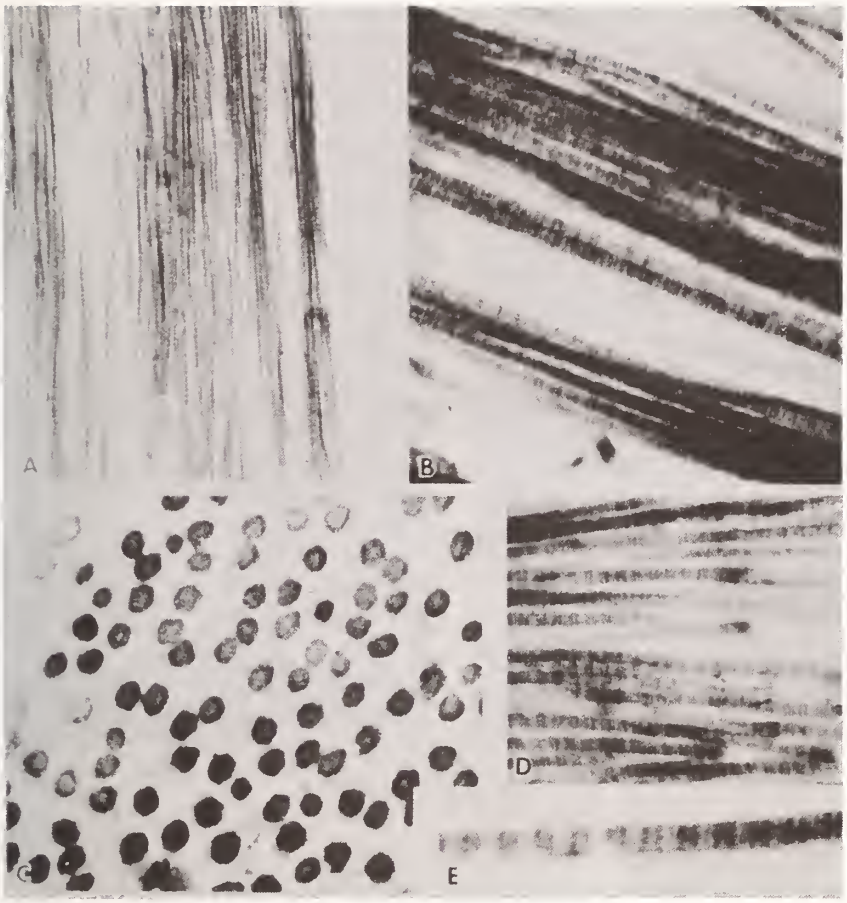


Figure 20. Electron micrographs of explanted Hancock valves after exposure to trypsin. A. 34 month explant illustrating the restoration of the lucent interstitium (X25,000). B, C and D. Higher magnification of 34, 92 and 100 month valves respectively showing the absence of electron dense granules and collagen ultrastructure comparable to unimplanted tissue (B X91,000, C X145,000, D X91,000, E X225,000).

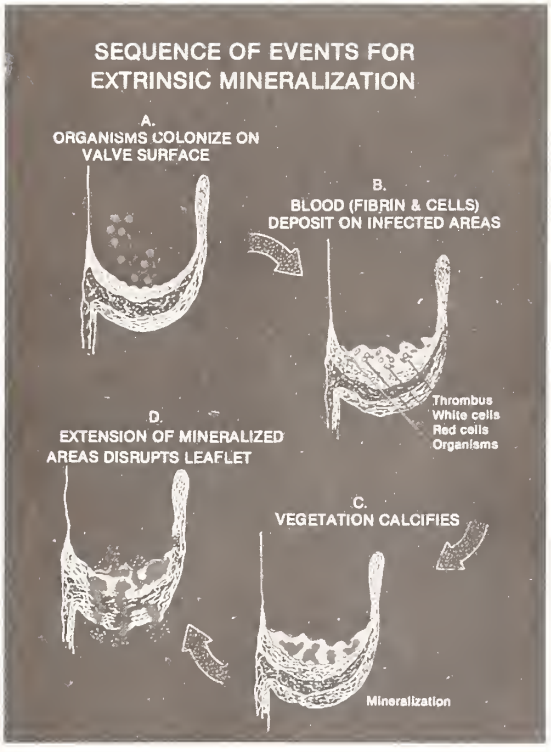


Figure 21. Probable sequence of events in extrinsic mineralization.

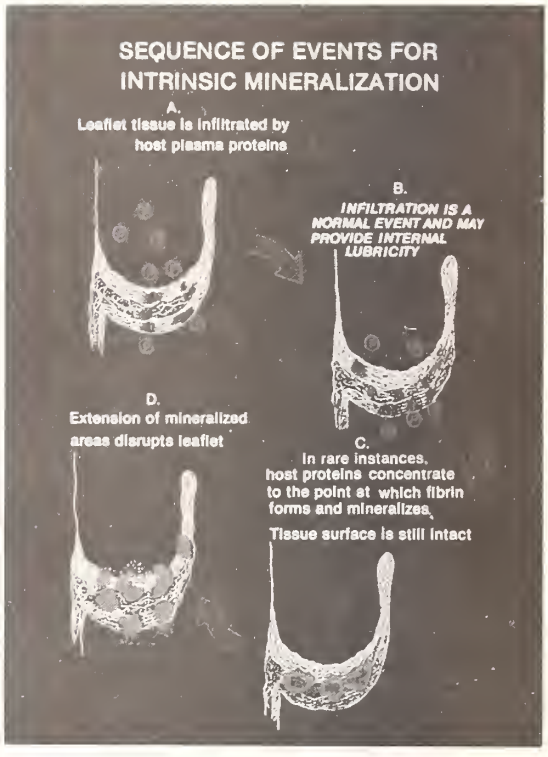


Figure 22. One possible mechanism leading to bioprosthetic mineralization.

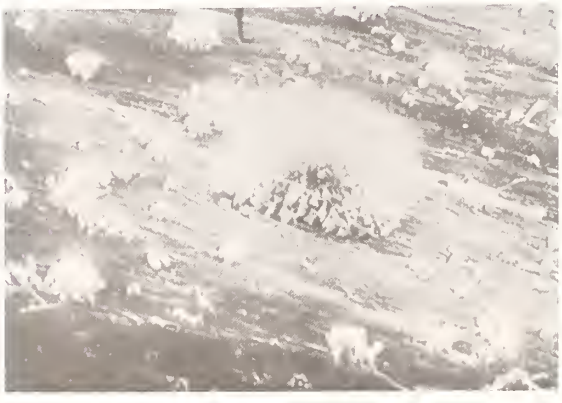


Figure 23. Scanning electron micrograph of the surface of a bioprosthesis which was rinsed in antibiotic solution. Notice massive thrombocyte deposition. (X5,000)

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RETRIEVED FRACTURE PLATES: IMPLANT AND TISSUE ANALYSIS

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A study was undertaken by AO/ASIF to investigate the suitability of different materials for bone plates for osteosynthesis. A total of 80 plates were retrieved together with clinical data, histologic data, and chemical analysis. The materials used were stainless steel 316 LVM, commercially pure titanium, titanium (Ti-6Al-4V) alloy, and a cobalt-chrome-nickel-tungsten-iron alloy as AO/ASIF compression plates and screws. The protocols used and the results of these first 80 cases are presented. The histologic analysis revealed the greatest differences occurring in the accumulation of lymphocytes, macrophages, and giant cells which were greatest with the cobalt alloy. The quantity of debris in the tissue was greatest with titanium. The chemical analysis revealed a wide scattering of values and the results are discussed. The examination of plates and screws revealed that stainless steel suffers fretting corrosion and that the amount of metal loss is less on the cobalt alloy, titanium, and the titanium alloy although significant corrosion was observed at the plate screw contact area for the cobalt alloy.

1. Introduction

The bulk of osteosynthesis implants in use today are stainless steel, implant grade 316 LVM. This alloy has often been criticized for its susceptibility to crevice and pitting corrosion [1, 2][1]. Cobalt base alloys and titanium and its alloys have been considered

[1]Figures in brackets indicate the literature references at the end of this paper.

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as suitable alternatives. However, these materials must not impair fracture healing or initiate an adverse host response. An AO/ASIF (Arbeitsgemeinschaft für Osteosynthesefragen/Association for the Study of Internal Fixation) study was undertaken to investigate the effects of different materials on fracture healing in patients. Clinical data was collected and the plates and screws retrieved for analysis along with a tissue sample taken at removal for histology and chemical analysis. The protocol is presented here as an example of how reliable and usable data from this type of multi-institutional study can be obtained for analysis of the suitability of implant material in fracture fixation. The results of this limited study are presented and indicate the trends in clinical acceptability and tissue reaction observed with the different implant types.

2. Methods: Collection of Material

2.1. Implants

Plates of 316 LVM stainless steel (ASTM F-138) [3], cobalt alloy (Co-Ni-Cr-Mo-W-Fe) (ASTM F-563) [4], titanium (ASTM F-67) [5], and titanium alloy (Ti-6Al-4V) (ASTM F-136) [6] were distributed for implantation. The materials were used in the following plate/screw combinations: stainless steel/stainless steel, titanium/titanium, titanium alloy/titanium alloy, titanium/titanium alloy, titanium/stainless steel, cobalt alloy/cobalt alloy. There were no cobalt alloy cancellous bone screws available; when required, stainless steel screws were substituted.

2.2. Patient selection

Three hospitals: Spital Davos, Kreuzspital Chur, and Kantonspital Basel, Switzerland, provided the material analyzed in this study. Patients who presented with fractures suitable for plating with the size plate distributed in this study received the test plate. The study was limited to fractures of the lower limb.

2.3. Plate removal

Plates were usually removed as part of the routine care of the patient. The duration of the implantation is considered in the evaluation of this study.

2.4. Clinical data

At the time of removal of the plate, the clinical form (fig. 1) was completed. This is a slightly modified translation of the original AO/ASIF form. This included questions on symptoms and evaluation of the general appearance of the tissue. The numerical data on the clinical performance of the test plate was allocated as indicated on the form. Higher values are regarded as less acceptable responses.

AO/ASIF PLATE REMOVAL

Pat. No.	Name	First Name
Bone	Address	Weight
Date Implanted		Date of Birth
Date Removed		Phone
Surgeon	Hospital	
Plate	Screws	

Clinical Results at Metal Removal

Pain in fracture area	0 - no	1 - seldom	2 - yes
Weather sensitivity	0 - no	1 - seldom	2 - yes
Swelling tendency	0 - no	1 - seldom	2 - always
Inflammation, redness	0 - no	1 - yes, when _____	
Infection	0 - no	1 - superficial	2 - deep
Function of limb	normal	lightly impaired	heavily impaired
Range of motion in the two adjacent joints	normal	_____ degree of flexion	contraction

---

Fracture healing: roentgenographic

0 - primary 1 - light callus 2 - heavy callus 3 - delayed

4 - pseudoarthrosis 5 - infection

Other complications _____

Local findings at metal removal:

Scar: 0 - inconspicuous 1 - distinct 2 - red 3 - eczematous

Tissue over plate: 0 - soft 1 - thickened 2 - bony

Coloration: 0 - none 1(+), 2(++); color: white, gray, brown, black

Tissue contacting plate: 0 - intimate 1 - cavity 2 - serum

Collar around screw head: 0 - connective 1 - bony 1/2 - combination

Plate bed: 0 - vascularized 1 - avascular 1/2 - combination

Biopsy of plate capsule: proximal distal

Others: _____

Figure 1

2.5 Tissue sample

At explantation, the tissue over the plate and the first two screws at the proximal end (unless otherwise indicated) was obtained for chemical and histological analysis. The protocol was that depicted in figure 2. The proximal ends were tagged with sutures. The tissue was split longitudinally down the middle. Both pieces were placed on a small piece of plastic and held in place with rubber bands to prevent curling of the tissue. One piece was placed in absolute alcohol for chemical analysis. The second half was placed in formalin for embedding, sectioning, and staining for histological analysis.

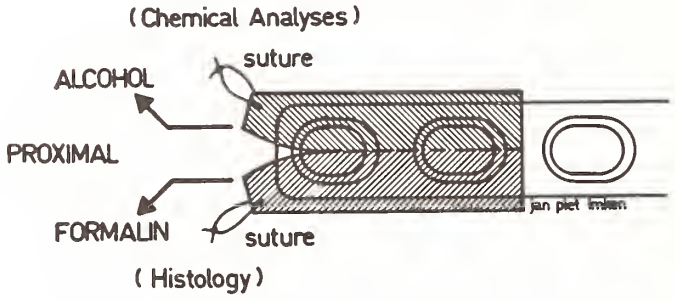


Figure 2
Procedure for tissue sampling for histology and chemical analysis.

3. Methods of Analysis

3.1. Histology

The tissue was embedded in poly (methyl methacrylate) [7] and positioned so that the sectioning plane was normal to the fracture plate, thus revealing contact and overlying tissue. The tissue was sectioned with a Zeiss Cutall to obtain 5 μ sections, and the sections were stained with hematoxylin and eosin, or with Giemsa.

The slides were examined by a single observer without knowledge of the plate material. A grading scale of 0 to 5 was used. The tissue was examined for the presence of bone, muscle, and connective tissue. The majority of the tissue samples were composed of connective tissue (fig. 3). The tissue was also examined for the presence of lymphocytes. A grade of 1 was given when occasional scattered lymphocytes were seen. A grade of 2 indicated a cluster of lymphocytes or many scattered lymphocytes. A grade of 3 indicated

more than one cluster or a cluster and extensive scattering of lymphocytes. Figure 4 depicts a cluster of lymphocytes with some scattered lymphocytes and some perivascular cuffing. A grade of 4 indicated several clusters of lymphocytes with lymphocytes scattered in the tissue. A grade of 5 indicated extensive lymphocyte accumulation with many large clusters and lymphocytes throughout the tissue.

The tissue was also examined for the presence of macrophages and giant cells. These cells were generally found in association with lymphocyte accumulations. A grade of 1 indicated a few macrophages or giant cells in the clusters of lymphocytes or scattered in the tissue. The grade increased with increasing numbers of these cells in the lymphocytic nodules or associated with debris or with perivascular cuffing. A grade of 5 indicated that there were large accumulations of macrophages or giant cells in the lymphocytic nodules and in the tissue. Figure 5 shows extensive accumulation of macrophages in a necrotic center of a lymphocytic nodule, and figures 6 and 7 depict giant cells and macrophages in a nodule.

The accumulation of debris was scored in two separate ways. One involved a scan of the tissue section at low power, and the deposition of debris in the tissue was scored. A few areas of debris were scored as a grade of 1 with the grade increasing through 5 when massive accumulations were seen in several areas (fig. 8, 9). Then the tissue was examined at a higher power to disclose the amount of debris that was actually engulfed by cells. Again, a few cells with debris were scored as 1 with many cells having engulfed debris being scored as 5. Figure 10 shows debris in cells with no other cellular reaction.

The tissue was also examined for the presence of blood vessels. A grade of 1 indicated the presence of some capillaries. A grade of 2 indicated a rich capillary bed. The grade increased to a score of 5 which indicated the presence of capillaries and arterioles and venules. Figure 11 shows a section classified as 5 for blood vessels.

The final examination was a rough score of the thickness of the capsule. A score of 1 indicated a small thread of tissue. A score of 2 indicated a section that filled 1/3 to 1/2 the field with a 1x objective (4x magnification). A score of 3 indicated a section that filled 1/2 to 3/4 of the field. A score of 4 indicated a section that was just within the field, and a score of 5 indicated a tissue section that more than filled the field with the 1x objective.

3.2. Chemical analysis

The size of the tissue samples received was variable, and the sampling technique did not allow an evaluation of the total metal in the tissue. It was thus decided to further divide the tissue in an attempt to find the range of metal concentration in the various areas of the tissue above the plates.

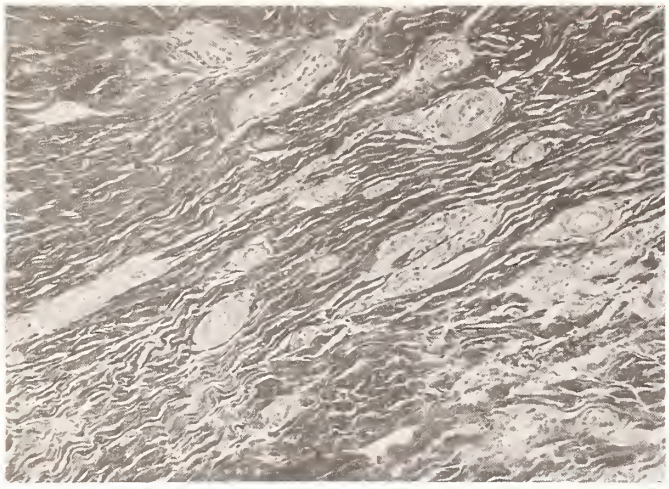


Figure 3
Typical connective tissue observed in sections.

Figure 4
Cluster of lymphocytes and lymphocytes scattered with some perivascular cuffing.

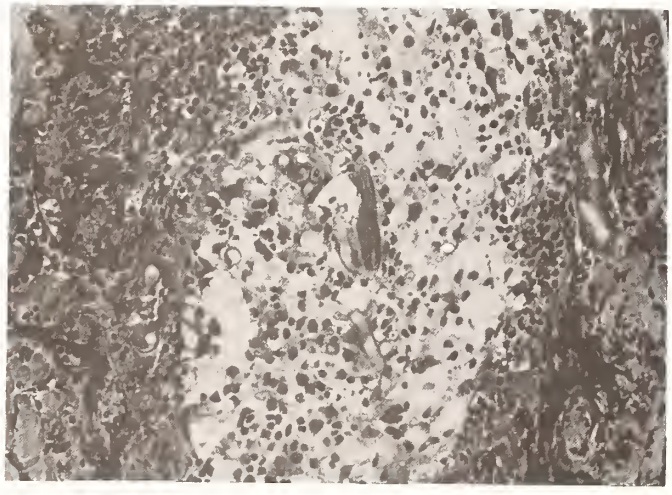


Figure 5
Macrophages in center of lymphocytic nodule.

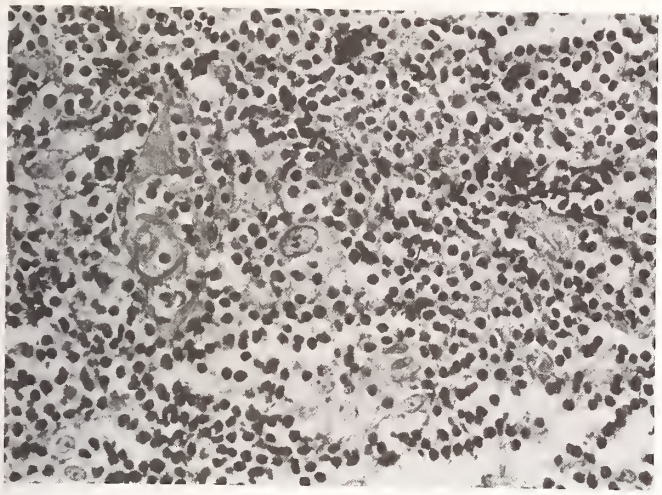


Figure 6
Giant cells and macrophages in a nodule.

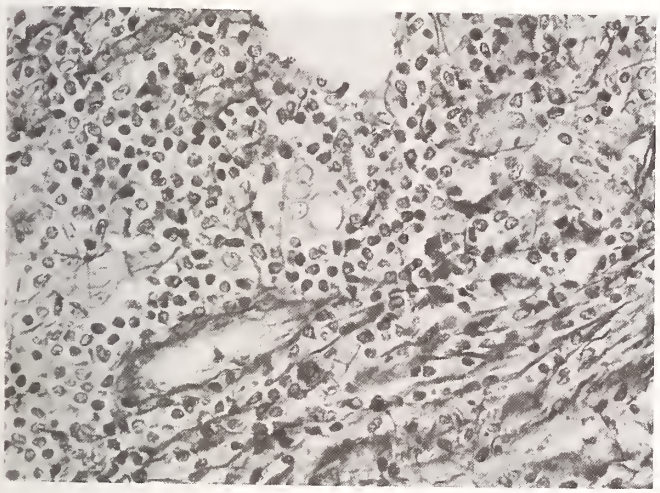


Figure 7
Lymphocytic nodule with giant cells and macrophages.

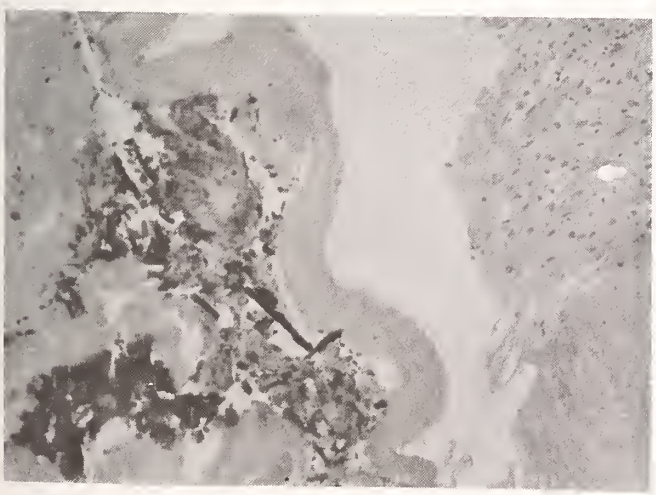


Figure 8
Grade 5 deposition of debris with no cellular reaction.

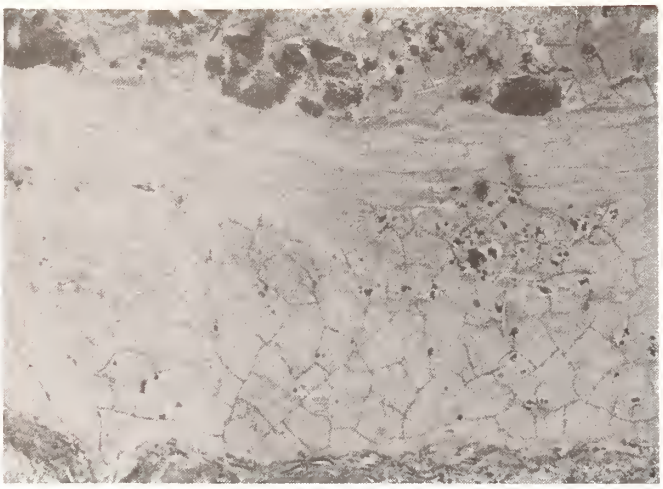


Figure 9
Grade 5 deposition of debris with cellular reaction and necrosis.

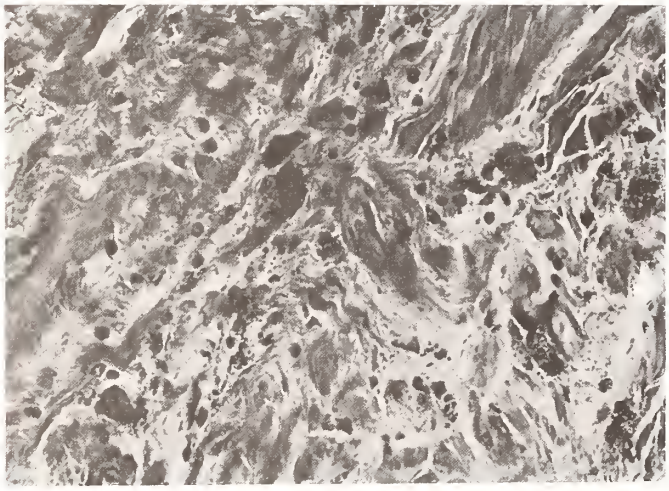


Figure 10
Debris engulfed by cells.

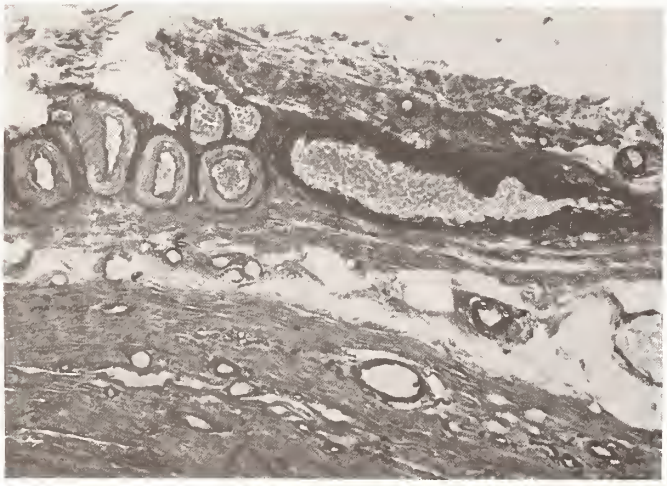


Figure 11
Grade 5 blood and lymphatic vessels.

The tissue was subdivided into different portions on the basis of discoloration intensity, or if the tissue was of a uniform color, the tissue from the immediate vicinity of the screw holes was separated from the remainder and analyzed separately. The discoloration normally coincided with the screw hole impression. The tissue sample was dried overnight at 70°C, allowed to cool for 1 hour exposed to the atmosphere, and weighed, and then in 1 hour heating and cooling cycles until the weight was constant. The samples were then dissolved in spectroscopic grade mineral acids using the following procedure.

A few drops of concentrated nitric acid - the smallest volume sufficient to cover the tissue - were added and the test tube immersed in boiling water. If after 1 hour the specimens had not dissolved completely, one or two drops of concentrated hydrochloric acid were added. Any residues still present after a further hour could normally be dissolved by a very small amount of concentrated sulfuric acid. A blank solution - without tissue but containing the same quantities of mineral acids - was prepared along with the test sample.

The dissolved samples were diluted to 3 ml with double distilled water and analyzed by flame atomic absorption spectroscopy. The elements analyzed were selected on the basis of the implant the patient had received.

i) stainless steel implants - Cr, Ni
ii) stainless steel with titanium - Cr, Ti, Ni
iii) titanium implants - Cr, Ti
iv) syntacoben implants - Cr, Co, Ni

The results were expressed as micrograms of element per gram of dried tissue (μg/g). In addition the color of the tissue and the detection limit for each sample were recorded.

3.3. Implant analysis

The retrieved implants were examined for fretting and corrosion damage which took place while in the body. It was necessary to quantify the degree of damage suffered by each screw or plate hole in order to differentiate between the materials. The form used is shown in figure 12 and will be described in detail here.

The contact damage evaluation method presented here was developed for compression hole plates as this study consists exclusively of this type of straight bone plate. The evaluation form, however, can be used for round hole plates and has been suitably adapted for other types of plates, e.g., compression hip screw plate, angle blade plate, etc. (See paper by Brown and Merritt in this proceedings [8].) The compression hole and its corresponding screw normally have two distinct contact areas, and the method for producing a numerical value for degree of damage used in this study is most suited to this type of plate hole.

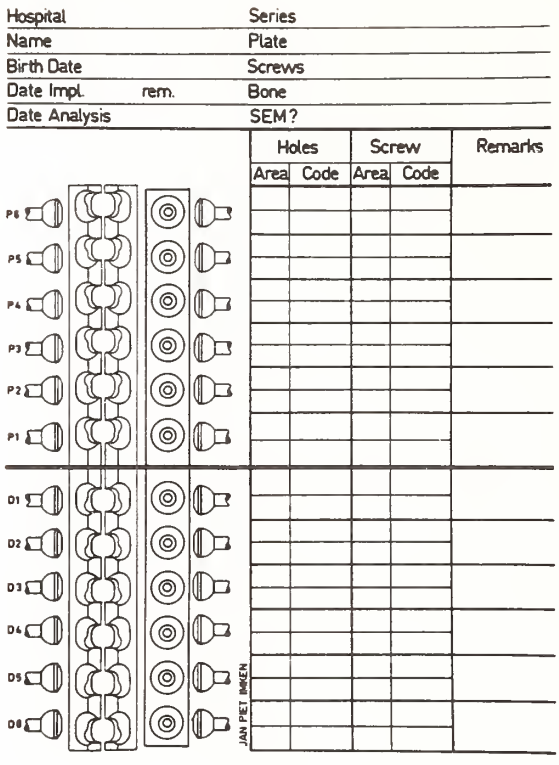


Figure 12
Recovered implant examination form.

The plate hole or screw was examined under a low power binocular microscope at 8-16x magnification. Both the area and the depth of each of the two contact areas for each screw head or plate hole were evaluated using the following scheme:

Size		Depth	
0	no contact	0	minimal
1	small	1	superficial
2	medium	2	significant
3	large	3	severe

The degree of damage was then obtained by summing the two size numbers and the two depth numbers for each screw head or plate hole and subtracting 3 (i.e., degree of damage = [size + depth] - 3).

This gave a damage scale of 0 negligible to 9 severe. If only one contact area was found, that is, size and degree for one of the two expected contact areas were zero, then the two remaining numbers

were summed and 1-1/2 subtracted. Such holes or screws were then identifiable by their fractional damage number.

Occasionally on one side of the screw two separate areas were seen, one on the head and one on the shaft, just under the head. These were always on one "side" of the screw, and the areas were "totalled" to make a size for this side of the screws. The size, shape, and position of the contact areas were also sketched on the implant evaluation form.

In this scheme for implant analysis, the damage to the screw or plate from implantation or removal was excluded. It was easy to identify on the plates when the inside of the plate hole had been drilled or tapped and when there was damage to the screw head from tightening or removing the screw. Unfortunately the damage to the plate hole on tightening and removal of the screw coincides with the contact site during the implantation period, and it was less easy to separate out this artifact on the plate hole.

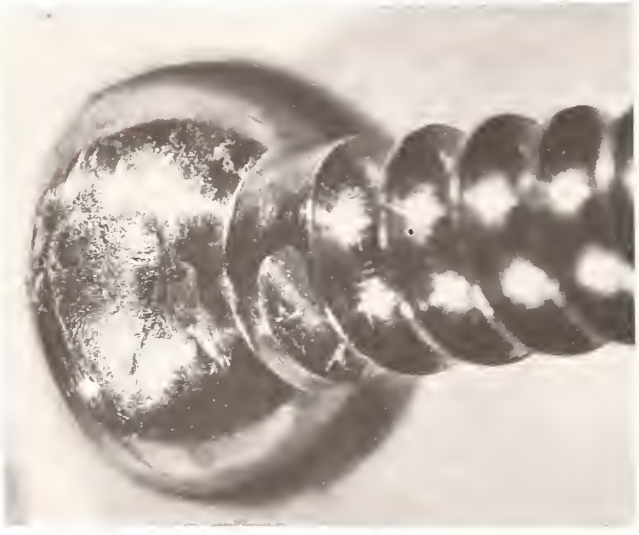
In addition to the degree of damage, it is also possible to classify the type of damage observed under the binocular microscope. To date, we have identified nine surface morphologies, and these are given classification numbers which are not implied to be in order of severity.

1. Plastic deformation - burrs of material or brows ploughed into the material.
2. Burnished - bright featureless contact area in the case of stainless steel or the cobalt-chrome-nickel alloy, matt but smooth for titanium.
3. Rough - the contact area is rough. This is common on titanium, and for the other two alloys when corrosion features were not positively identified (fig. 13a).
4. Parallel lines - the contact area shows parallel linear features.
5. Cracks, crevices - the contact area appears to have a crack in the surface although when this is further investigated on the SEM (fig. 14), it is a deep long corroded region, or the edge of the contact area is corroded in depth, a crevice.
6. Corrosion - the area appears corroded (fig. 13b, c).
7. Needle pitting - small holes in the surface indicating pitting in depth.
8. Gross pitting - large pits in the contact area (fig. 15).
9. Rainbow - a rainbow pattern may be present on the polished unattacked surface next to a corroded area.

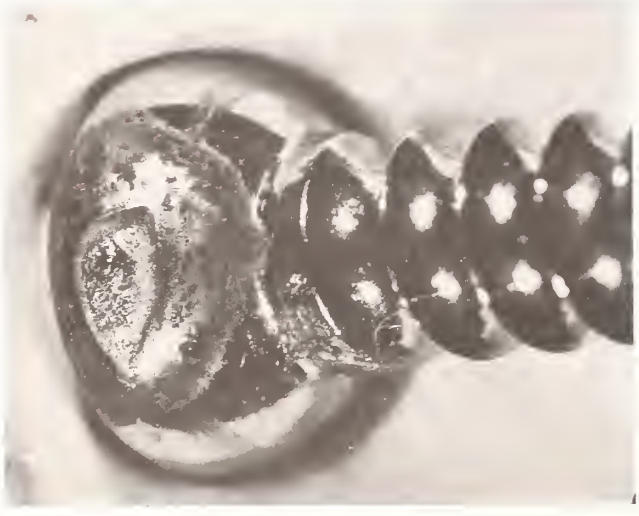
These numbers are entered into the implant evaluation form. It is common for a contact area to exhibit more than one of these features. The reader is referred to the completed implant form shown in figure 16.

Figure 13

a. Contact area on a titanium screw, size 2, degree 2, nature 3.



b. Contact area on a cobalt alloy screw, size 3, degree 2, nature 6.



c. Contact area on a stainless steel screw, size 2, degree 3, nature 5, 6.

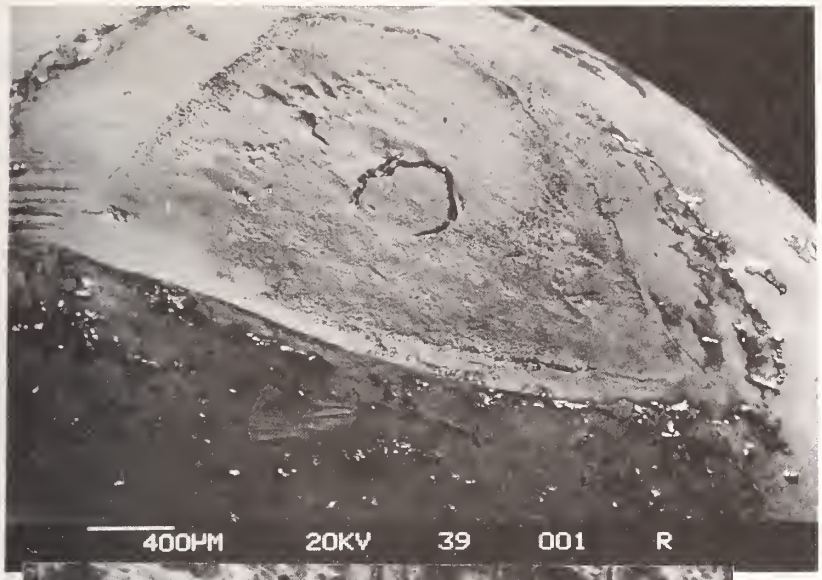


Figure 14
Scanning electron micrograph of a contact area containing a feature which appears to be a semi-circular crack under the binocular microscope.

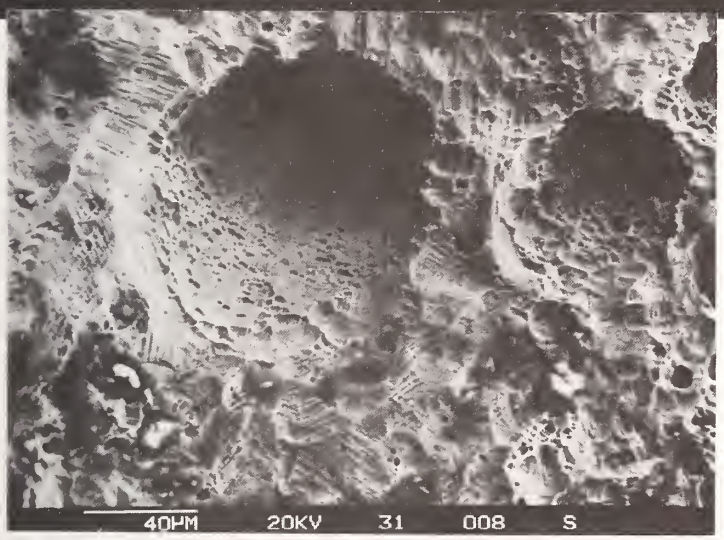


Figure 15
Scanning electron micrograph of deep pits on a stainless steel screw. These are easily identified under the binocular microscope as large black holes.

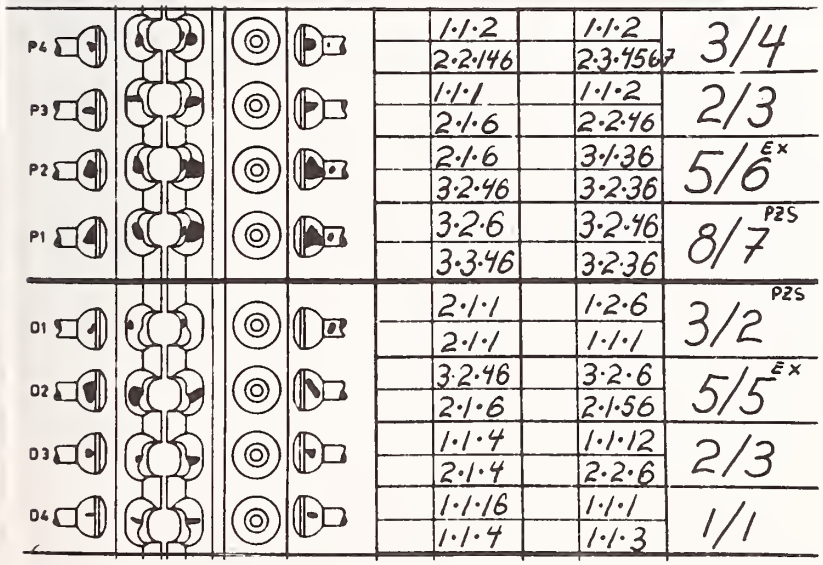


Figure 16
An example of a completed implant analysis form.

4. Results

The numbers of cases for each metal and the average implantation times are listed in table 1. The titanium alloy cases were grouped with the commercially pure titanium as insufficient numbers were available to make a separate analysis for these two alloys. First impressions are, however, that there is no large difference between titanium and its alloy; the alloy is randomly distributed in the group. It is anticipated that as more cases are added to the study we will be able to treat titanium and its alloy separately. In the series there are only four femurs, one each in the steel and cobalt alloy groups and two in the titanium steel group.

Table 1. The number of cases and implantation times are listed for the different materials.

Plate	Screws	Cases	Average Implantation Time (Months)
Steel	Steel	16	18.0
Co alloy	Co alloy	25	18.0
Titanium Ti alloy	Titanium Ti alloy	16	15.0
Titanium	Steel	23	15.9
TOTAL		80	16.9

4.1. Clinical performance

The values recorded for the clinical observations were averaged for the series of 80 and for each of the plate/screw combinations. These are recorded in table 2. It becomes evident throughout this study that the series is too small to attach statistical significance to more than a few observations. However, the trends observed are worth presenting and discussing. There was no pain or swelling reported by patients with the titanium plates, whereas with the other groups the pain reported was similar. Those patients with steel plates had the greatest amount of swelling recorded. When the values for these three clinical symptoms were combined, those patients with titanium plates had a much lower incidence of symptoms. There was more scar formation with the use of cobalt alloy plates. There was more tissue discoloration reported with steel and the cobalt alloy. These plate removals were for the most part routine removals, and the general clinical progression was similar and satisfactory for the four groups with good healing of the fractures.

Table 2. Clinical observations.

	Pain	Weather Sens.	Swelling	3 Values Combined	Inf.	Heal.	Scar.	Cap.	Color
Range	0-2	0-2	0-2	0-6	0-2	0-5	0-3	0-2	0-2
16 steel	.43	.43	.64	1.5	.07	.75	.15	.88	1
25 cobalt alloy	.42	.58	.45	1.45	.08	.43	.42	.78	.93
16 Ti	0	.29	0	0.29	0	.3	.14	.5	.6
23 Ti/S	.43	.7	.19	1.32	0	.58	.07	.7	.7
80 series	.35	.54	.32	1.21	.04	.52	.20	.72	.81

4.2. Histologic analysis

The histologic analysis was treated in a similar manner with the values for each category averaged for the series and for the different types of implants. The data for connective tissue, bone, and muscle was about the same for the groups. The tissue was predominantly a connective tissue with occasionally some bone and muscle. The types of connective tissue have not been subclassified at this time. The data for the remaining histologic evaluations are recorded in Table 3. The biggest difference is seen in the values recorded for lymphocytes. The tissue from patients with cobalt alloy plates had a statistically significant elevation of lymphocytes. When the gradings for lymphocytes, macrophages, and giant cells were added together the cobalt alloy tissue was still significantly higher. Titanium and titanium with steel screws had the lowest combined scores. The tissues in general were quite rich in vascular and lymphatic supply with titanium having the highest score. The presence of debris in tissue and in cells was also highest for titanium. These high values for debris associated with titanium plates with titanium screws are not quite statistically significant compared to the others. Finally, the estimated thickness of the tissue averaged about the same for all four groups.

Table 3. Average values of the histologic grading

Plate	Lymphs	Macro-phage	Giant Cell	3 Values Combined	Blood + Lymph Vessels	Debris in Tissue	Debris in Cells	Thick.
Steel	1.9	1.15	0.54	3.36	2.23	1	1.08	2.08
Cobalt Alloy	2.82	1.3	0.3	4.29	2.5	0.73	0.73	2.78
Titanium	1.36	0.35	0.21	1.92	3.64	1.4	2.14	2.0
Ti/Steel	1.25	0.5	0.04	1.78	2.67	1.1	0.89	2.6
Series	1.8	0.82	0.24	2.84	2.73	1.04	1.1	2.4

4.3. Chemical analysis

The other piece of tissue was analyzed for the presence of metal and the data on these chemical analyses are presented in Table 4. In all groups there were some tissue samples with no detectable metal and thus the minimum in all groups is zero. The maximum values found and the average values for each group are presented in Table 4. The range is thus zero to the maximum. The highest values for nickel were recorded with stainless steel plates; the highest values for cobalt were found with the cobalt alloy plates; the highest values for chromium were found with the steel plates; the highest values for titanium were found with the titanium plates. There is no statistical significance in the data. The data on chemical analysis needs to be considered carefully and discussed in relation to other findings.

Table 4. Chemical analysis of tissue over the plates (μg/gm tissue)

Plate	Nickel Ave	Nickel (Max)	Cobalt Ave	Cobalt (Max)	Chromium Ave	Chromium (Max)	Titanium Ave	Titanium (Max)
Steel	157	(910)	ND*		1595	(10464)	ND*	
Co alloy	85	(786)	371	(2510)	806	(10219)	ND*	
Titanium	ND*		ND*		14.5	(150)	1308	(9960)
Ti/steel	99	(640)	ND*		1129	(9727)	66	(255)

*ND = not done

4.4. Implant analysis

The examination of the recovered implant produced a degree of damage number for each platehole and screw head. The degree of damage scale runs from 0-9, and the histograms in figures 17-19 show the distribution of these scores. Figure 17 compares steel screws and plates and cobalt alloy screws and plates. Figure 18 shows the distribution for titanium alloy plates and screws compared with steel plates and screws. Figure 19 shows the distribution for steel screws and plates and steel screws on titanium plates. For the purposes of constructing these histograms, the values containing 1/2 points were rounded down.

The mean value of the degree of damage is the value in the top right of the figures and is also presented in table 5 with the number of entries for that combination.

Since stainless steel is the most common construction material for orthopaedic bone plates, it was taken as the reference material against which the cobalt alloy and titanium were compared.

Figure 17 shows the distribution of the degree of damage for the cobalt against that for steel. The mean value and the histogram both indicate that the cobalt alloy suffered less material loss. The χ^2 test showed the two distributions to be significantly different, as

were all three of the distributions presented (fig. 17-19). Qualitatively the cobalt alloy showed severe metal loss with a score of 5-9 in 17% of all entries compared with steel which had 39% in this range.

Table 5. Degree of damage on plate hole and screws.

Plate/Screw	Plates + Screws Counted	Screws Only Counted	Ave. Degree of Damage	No. of Entries
Series	X		3.1	1246
Steel/Steel	X		4.1	252
Co alloy/Co alloy	X		2.5	387
Titanium/Titanium	X		2.6	229
Steel/Steel		X	3.9	124
Titanium/Steel		X	3.4	184

The picture is similar for steel compared with titanium and its alloy which had only 15% in the 5-9 range and a lower average. However, the implantation time was on average shorter, at 15 months compared with 18 months for steel.

The average degree of damage on the cobalt alloy and titanium were about equal, 2.5 and 2.6 respectively, although there was one possibly important difference. Very severe damage (7-9) was found on only one plate hole for titanium but on 6% of the cobalt alloy plate holes and screws. The cause of this will be discussed later.

The performance of steel screws against titanium plates in comparison to steel screws against steel plates seems to support the conclusion of Rüedi [9] that the behavior of steel is not modified by the presence of titanium. The average degree of damage on steel screws is improved slightly from 3.9 to 3.4 when used on titanium plates, although the improvement in the heavy damage range is slight (fig. 19).

Figure 20 is another way of presenting the implant examination data. The degree of damage was first averaged for each patient, i.e., total degree of damage on holes plus screws divided by the number of holes and screws. The mean and standard deviation for each metal combination was calculated and the range indicated in figure 20 is one standard deviation either side of the mean. Steel screws with steel plates have the most severe metal loss. As expected, the steel screw, titanium plate combination falls midway between all steel and all titanium, again suggesting that the damage to either is independent of the presence of the other. The cobalt alloy and titanium had virtually the same mean, but the range of values for the cobalt alloy was greater.

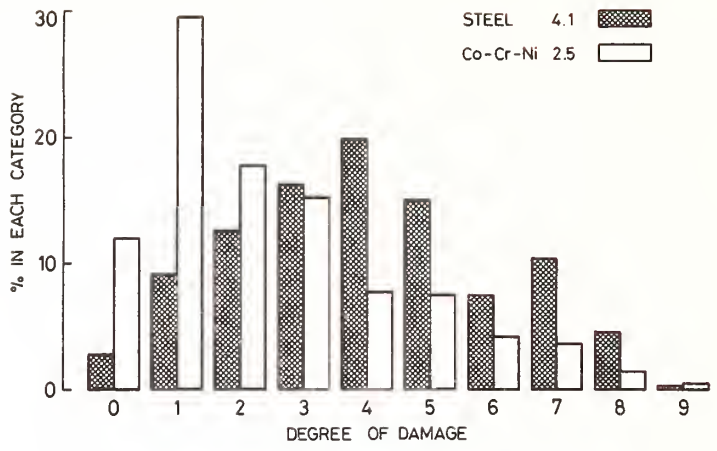


Figure 17
Distribution of degree of damage for stainless steel holes and screws compared with cobalt alloy holes and screws.

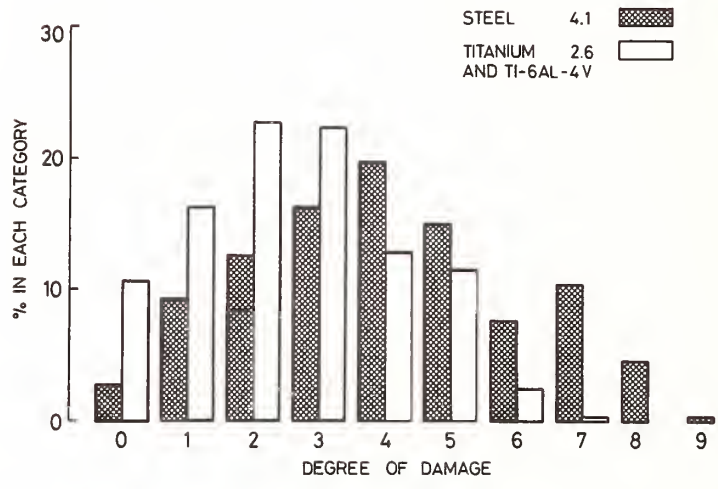


Figure 18
Distribution of degree of damage for stainless steel holes and screws compared with titanium and titanium alloy holes and screws.

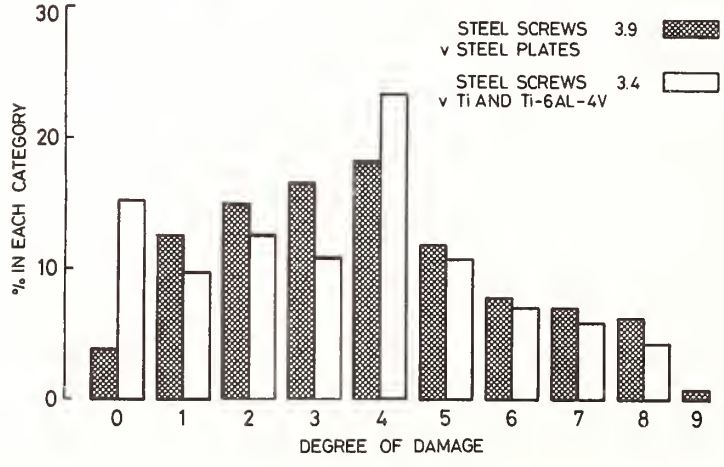


Figure 19
Distribution of degree of damage for stainless steel screws on stainless steel plates compared to stainless steel screws on titanium plates.

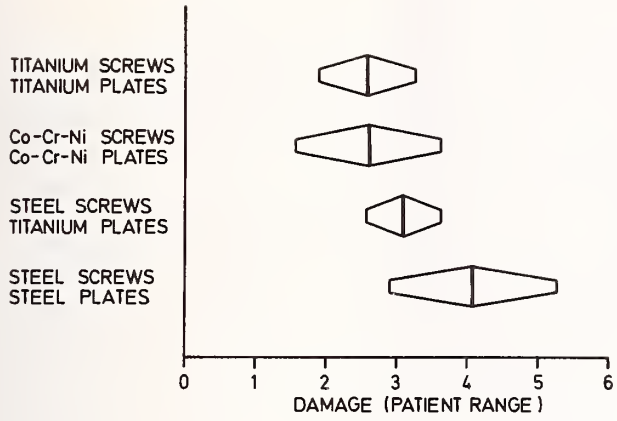


Figure 20
Damage (patient range) for the four metal groups.

As mentioned in the methods section, damage to the plate and screws caused by insertion or removal was, if possible, excluded from the degree of damage number. Thus the metal loss graded occurred while in the patient. The low power light microscope observations gave the following picture concerning the nature of the attack.

Corrosion was commonly observed at the contact area between steel and steel and on the steel screws in contact with titanium. This corrosion was in many cases severe and was the reason for the higher degree of damage scores for steel, as corrosion produces deep damage areas and thus large damage scores. The mechanism has been reported to be fretting induced crevice corrosion [10].

The cobalt alloy also corroded, although a lower proportion of screws and plate holes were corroded. Burnishing, probably produced by micromovement between the two components, was more common. This accounts for the high proportion of 0 and 1 scores (fig. 17) for this metal.

Titanium and titanium alloy screws and holes had almost exclusively 2's and 3's in the damage nature code. The contact surface was either a dull matt gray and smooth or a dark gray and rough.

Examples of these contact areas were also looked at under the scanning electron microscope. The figures 15, 21, and 22 are SEM pictures of contact areas of steel (fig. 15), cobalt alloy (fig. 21), and titanium (fig. 22a and 22b). Corrosion of the steel and cobalt alloys was confirmed by the presence of typical corrosion surface morphologies. The rough surface on titanium is shown to have no depth. This accounts for the lack of high degree of damage ratings, and metal loss appears to be via a gall and tear mechanism.

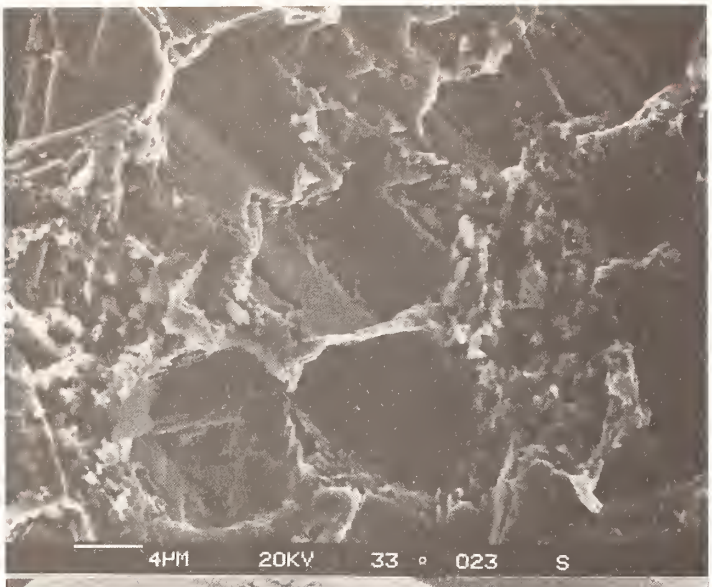


Figure 21
Crystallographic corrosion pattern on a cobalt alloy screw head.

Scanning electron micrograph.

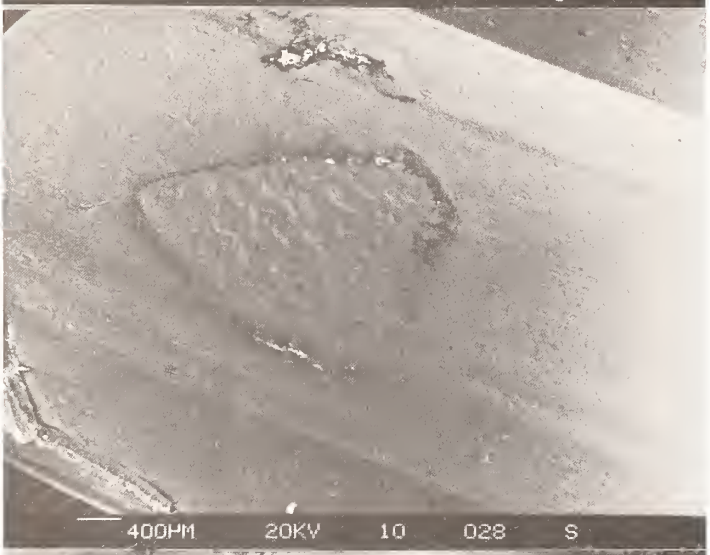
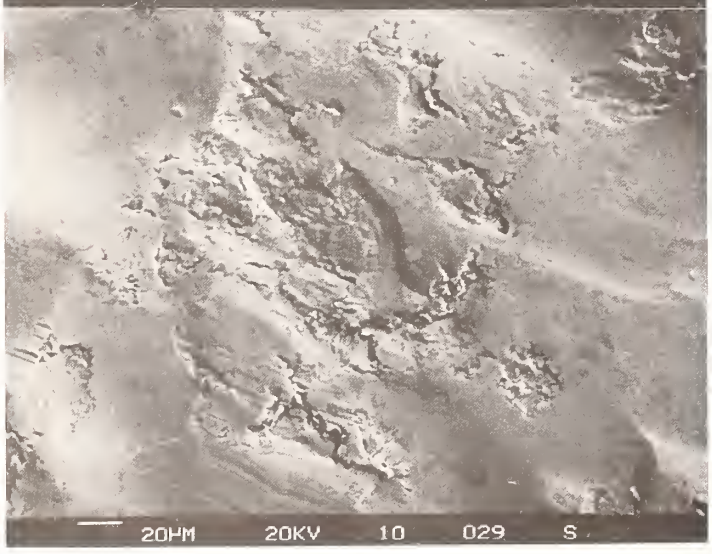


Figure 22

a. Contact area of figure 13a as a scanning electron micrograph. The contact damage has no depth.



b. Detail of figure 22a. Metal loss from titanium by a gall and tear mechanism.

4.5. Cross correlations

The data was subjected to correlation analysis and the r coefficient determined, and the 95% level taken to indicate a correlation. It must be pointed out again that the series is small, and statistical differences are generally not found. However, there were some correlations of special interest.

It might be expected that time is one of the important factors involved. The length of time the implant was in place should correlate with the amount of corrosion of plate and screw. The findings on these 80 patients do not support this hypothesis. Similarly, the amount of metal in the tissue should be affected by time, and this data does not support this hypothesis. Similarly, we saw no correlation between time and debris. However, when one compares time with the lymphocyte accumulation there is a negative correlation for the series, steel plates, cobalt alloy plates, and titanium plates with steel screws. There is no correlation between time and lymphocyte accumulation with titanium plates.

In the histologic analysis, it is of interest that the debris in the tissue and the debris in the cells shows a strong correlation with steel plates, cobalt alloy plates, and titanium plates with steel screws. The correlation between debris in the tissue and debris in the cells was not found with titanium plates and titanium screws.

When combined histology (lymphocytes, macrophages, and giant cells) was compared with corrosion values for the respective pair (values for damage to plate holes and screws under the position of the tissue biopsy), a strong correlation was observed with only the cobalt alloy plates. When the lymphocytes were considered alone, there was no correlation.

When chemical analysis was correlated with various other factors, the only strong correlation found was the concentration of titanium in the tissue and damage to the respective pair of plate holes and screws.

5. Discussion

In this paper a scheme for the evaluation of bone plates and screws for osteosynthesis has been presented. The object of this particular study was to investigate the differences between four different alloys.

It is not easy to demonstrate an advantage over a material (stainless steel) which has proven satisfactory in millions of cases and causes truly material related problems only in a very small percentage of them. Most important is clinical success, but this is very difficult to define. What is acceptable to one surgeon or patient may not be to another. Thus, it could be impossible and would certainly require a very large number of cases to prove an

improvement on an already good success rate due to the material change alone, solely on the basis of the success rate.

In this study it was hoped that this problem could be overcome by demonstrating that certain disadvantageous phenomena were on balance less severe for a particular material or materials. For instance, a reduction of pain or swelling during treatment; a reduction in the amount of material released to the host by corrosion or fretting; and a minimal histologic response could all be regarded as desirable improvements.

It is important to collect the maximum amount of data on each case in this type of study. The methods described here were designed to ensure this. Much of the type of data used in this study have previously been purely qualitative evaluations and thus not amenable to statistical methods. A grading scheme was established for each section, which although somewhat arbitrary, provided usable information. The histologic and degree of damage data were each generated by a single observer, whereas the clinical data stemmed from three different hospitals and many individuals. The biases and inaccuracies introduced by these evaluation methods are, by the nature of the data, undoubtedly large.

The implant examination part of this study will be considered first. The authors feel that the method outlined in this paper proved to be a satisfactory method for investigating the metal loss from the bone plates and screws used in this study. The data demonstrated that the metal loss is greatest from stainless steel and that the volume of metal released to the host can be reduced by substituting titanium or cobalt alloy. However, this is certainly insufficient evidence to come to the conclusion that this substitution should be recommended. The corrosion or wear products from titanium or the cobalt alloy could elicit less favorable healing or tissue responses compared to the steel. There is to date insufficient data to support or refute these possibilities.

A discussion of the method used for chemical analysis is necessary. When the study was planned, this was thought to be a useful input. However, it has become clear that there are some difficulties when interpreting these results. The method used - acid digestion of the removed tissue for atomic absorption spectroscopy - does not differentiate between solid particle contamination of the tissue and metal bound to tissue from metal ions released by corrosion. The solid particles are the problem. These may be the result of fretting, or they could be generated during implantation by mechanical action on the screw-plate interface when tightening down the screw (fig. 23). A further source is that some screws are inserted at such an angle that the bone tap or drill goes through the side of the plate hole. The large particles produced by the latter mechanism in particular, if included in the tissue analyzed, could produce misleadingly high metal concentrations. An illustration of this point is provided by the titanium group where chromium was found

in three cases of the 16 in the group. This presumably comes from the instruments used to insert or remove the implants. The authors doubt if these measurements will produce any useful information and are of the opinion that this total metal content analysis could well be of minor value and that an analysis method which separates solid wear particles from metal ions would be of more value.

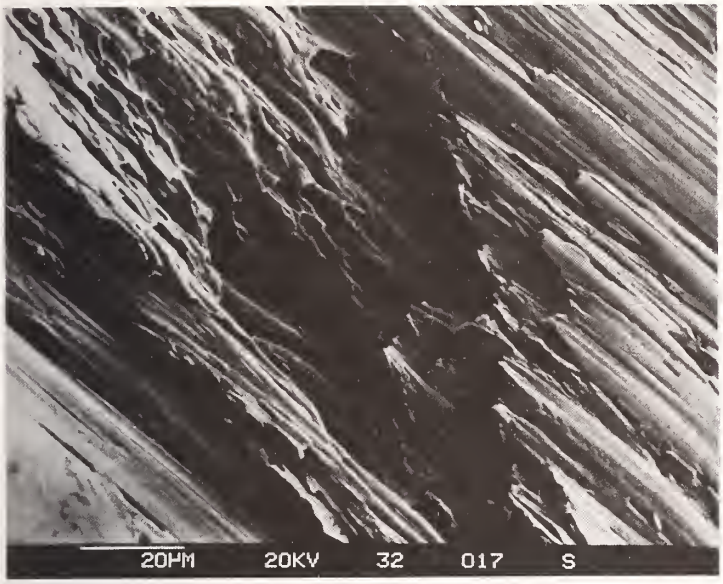


Figure 23
Scratch and tear marks on a stainless steel screw caused by tightening of screw. This is a possible source of solid metal debris.

The histologic analysis also raises a number of questions. The tissue type was similar in all groups. The tissue is mostly connective tissue, and the description of how much bone or muscle was present is not contributory. The connective tissue was not subdivided as to loose connective tissue, dense connective tissue, and the amount of adipose tissue found. This might possibly turn up some differences.

The biggest variations were found in the accumulation of lymphocytes, macrophages, and giant cells. The method of analysis is quite crude; however, detailed analysis including cell counting seems unwarranted. The tissue samples were not of the same size and, therefore, the cells should be counted per unit area. However, the lymphocytes tend to cluster, and the clusters might be missed in setting up grids for unit area measurements. Rough determination of number and size of clusters as well as scattered lymphocytes in the tissue sample seems less time consuming and, although crude, probably more accurate. A ratio of size of nucleus to cytoplasm as reported by Riede et al. [11] seems unwarranted because of the normal variability in nucleus to cytoplasm ratio of these cell types.

The correlation of lymphocyte accumulation with other factors was disappointing. There was a negative correlation with time; that is, the plates removed early had higher quantities of lymphocytes. However, the implant times cluster around the mean, but should this trend be confirmed, then the question whether or not they were removed early for subtle reasons not reflected in the clinical report forms must be addressed.

Of special interest is the strong correlation between the combined score of lymphocytes, macrophages, and giant cells with the degree of damage of the respective pair (plate and screws under the biopsy) for the cobalt alloy.

The question of metal sensitivity must be considered when a histologic reaction of this type is observed. The issue of metal sensitivity in relation to implant analysis is discussed in detail in another paper in this volume [8], and the reader is referred there for the details. It is the hypothesis that it is the damage to the implant in the tissue that will lead to metal ion release and that the metal ions may complex with proteins and stimulate a sensitivity reaction in some patients. A few of the patients in this series with the cobalt alloy plate were tested for LIF production [8]. There was one patient who was a nonmigrator (sensitive and reacting to the implant) who had a large accumulation of lymphocytes, macrophages, and giant cells. However, one patient with large accumulations of these cells did not have any sensitivity on testing. This series is too small to draw conclusions, but this may be an example that some patients develop sensitivities and others do not regardless of the metal ion concentration and the accumulation of these cells to remove the ion-protein complex.

There was also no correlation of debris in the tissue with the chemical analysis and corrosion. However, the debris ratings did produce one interesting correlation. The highest grading values for debris were found in the tissue from the patients with titanium plates. When the debris in the tissue was correlated with the grading scores for the debris in the cells, there was strong correlation with all groups except titanium. It was noted on the histology sections that some had large deposits of debris as in figure 10 with no cellular reaction. This was a feature of titanium plates. The debris produced by the other plate-screw combinations was being engulfed by cells and stimulating a cellular reaction. The only correlation between debris in the tissue and corrosion of the respective pair was found for the titanium group.

There were many histology sections suggestive of very bad tissue reactions with large areas of lymphocytes, macrophages, giant cells, inflammation, and slight necrosis. When the type of implant was checked against these specimens, all four groups were represented. Once again, more cases are required to identify a trend.

The ultimate test of an implant is its clinical acceptance. Thus, the clinical data in this type of study requires the care, understanding and enthusiasm of the physician. It is important to remind the physician, especially the intern and the resident, that decisions on compatibility of implants require careful attention to detail in completing a clinical evaluation from.

6. Summary

In this paper, a protocol for the evaluation of metal osteosynthesis plates has been presented along with a scheme for analyzing tissue responses and obtaining clinical data. The number of cases at present available for analysis does not permit any definite conclusions as to the advantages of one of the alloys tested over another. It is hoped that with the addition of more cases this will be possible. We recommend that the type of protocol we have described here be used so that comparisons can be made between different studies.

We would like to thank the entire AO/ASIF for undertaking this study with special thanks to Drs. Allgöwer, Matter, Perren, and Ruedi for their diligence in collecting the clinical data and supplying the plates and tissues used in this paper. The histology group at the Swiss Research Institute, Davos, especially Katie Reusser, are thanked for their beautiful work and superb records. We are grateful to Fredy Schmidli in Walderburg for performing the chemical analysis and finding one or two metal turnings in the tissue samples. Thanks go to Carrie Green, Dartmouth Medical School, for the computer analysis of this data.

This work was supported in part by the Educational Foundation of America and USPHS AMAI 20271.

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Discussion

Question (D. F. Williams, University of Liverpool, U.K.): Could it be made clear exactly what you are saying about titanium deposits in the tissue?

Are you saying that the presence of titanium in the tissue is solely due to mechanical damage?

Answer: In our opinion the bulk of the material we saw in the tissue samples is due to fretting i.e., mechanical wear due to micromovements between the bone plate and the screw head.

Question (William Ruff, National Bureau of Standards): Was there evidence for fatigue cracks in the specimens and if so, were there differences between the materials?

It would seem that the differences in the number density of surface cracks among materials might have a role in overall response differences.

Answer: There were no fatigue cracks observed during the macroscopic examination of the plates.

The use of the word cracks in the examination code is perhaps misleading. These features (fig. 14 in text) all turned out to be long narrow corrosion pits on examination in the scanning electron microscope. Furthermore, they were normally in the center of the contact area and not, as would be expected for a fatigue crack, at the top edge of the hole.

Question (Anthony K. Hedley, University of California at Los Angeles): The authors have shown very beautifully how titanium produces a much lesser reaction than steel and cobalt chrome alloy. Their phagocyte count is significantly less in local tissues with titanium than the latter two metals, yet there is more debris seen in the tissues with titanium. I am wondering if this is related to a diminished transport of the ions which therefore must accumulate rather than to the suggestion that to the suggestion that titanium produces more debris than the other metals described.

I would be interested to know if the authors have been able to show decreased or suppressed migration and phagocytosis by histocytes with titanium. This could have important clinical implications when infection or metal sensitivity are considered.

Answer: It seems from the data so far that titanium suffers less total metal loss from the implants than stainless steel and a similar amount compared to the cobalt alloy. In the authors' opinion the metal loss from titanium is mechanical by fretting but from the other

two materials a larger percentage of the loss is electrochemical. The first mechanism produces metal particles the second metal ions in solution. In the case of corrosion the metal ions are available for further reactions and may well bind to proteins etc. and trigger various biological responses.

On the other hand this route is not available to titanium, as the titanium debris is a purely mechanical product.

Our observation is that the titanium debris was not phagocytized to such a large extent as debris from the other materials, but whether this is due to a suppression of migration and phagocytosis or that these responses were just not triggered by the products from titanium is a question this study cannot answer.

Question (L. M. Taussig, Taussig Associates, Inc.): Can you clarify any data relating to the reasons for explantation (i.e., fracture, infection, routine removal).

Answer: In all but one of the cases (pseudoarthrosis) bony union of the fracture was achieved. There were no broken plates, but three screws failed on removal.

Infection was reported in three cases and although this may have resulted in removal earlier than normal; bone healing in these cases was also satisfactory.

Implant removal is recommended AO/ASIF practice and thus the majority of implants received came from routine removals.

Comment (L. M. Taussig, Taussig Associates, Inc.): On Dr. Ruff's question on the relation between implant fracture and bone screw corrosion reaction.

We at Taussig Associates have found no correlation between the incidence and position of bone plate corrosion and fatigue fracture of the plate.

Corrosion, Materials Characteristics and Local Tissue Reaction Associated with Osteosynthesis Devices

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Abstract

A series of 112 internal fixation devices, comprising 75 bone plates and 37 hip nails, have been retrieved and subjected to mechanical bend tests. In addition, the severity of any corrosion of these devices was measured, together with their metallurgical condition.

Further, in seven cases, the reaction of the tissue adjacent to the removed implant was examined and graded upon an arbitrary scale. Results from these tests are presented and discussed.

1. Introduction

The use of metallic implants to achieve internal fixation in the treatment of bone fractures is standard orthopaedic practice and for many year surgeons have achieved excellent results using such devices. A number of well-documented cases have been reported, however, in which an implant causing pain may be associated with an excessive degree of corrosion (1)[3]. Similarly, it is important that these devices have sufficient mechanical strength so that they do not fracture in service, and many cases of such an occurrence may be found in the literature (2-7).

The present study is concerned with the relationship between the material characteristics of internal fixation devices, the extent of

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[1]Department of Orthopaedic Surgery, Tulane University Medical School

[2]Biomaterials Laboratory, Tulane University School of Engineering

[3]Figures in parentheses indicate the literature references at the end of this paper.

any corrosion associated with them, the local tissue reaction observed around these implants, and their clinical performance.

2. Corrosion of surgical implants

A number of authors have reported the apparent incidence of corrosion in fracture fixation devices (1-12). It is important to recognize, however, that many of these studies were concerned only with the examination of those implants which had either mechanically failed in service, or were removed for clinical cause and consequently are not representative of the population of internal fixation devices as a whole. In addition, two of the earlier studies of retrieved implants, namely that by Scales et al. in 1959 (8) and again by the same authors in 1961 (9), were concerned with examining the relative corrosion resistance "in vivo" of different stainless steels. Since this point is no longer contentious and a standard of ASTM F 139 stainless steel has been agreed upon, these particular results will be excluded from further discussion.

Once these distinctions have been made, the number of studies which may be used to indicate the extent of corrosion in surgical implants becomes limited. Between 1967 and 1972, Meachim and Williams (1) collected a total of 190 orthopaedic implants which were then subjected to a number of metallurgical tests, including a close examination for evidence of any corrosion. Of the 190 implants, 119 were made of stainless steel, 49 of titanium, and 9 of Co-Cr alloy. Of the stainless steel implants, a total of 64 (54%) exhibited corrosion to some degree. Of the titanium implants, corrosion was not found to have occurred in any of the devices.

Weinstein et al. (10) have reported upon the incidence of corrosion in a total of 133 retrieved prostheses and internal fixation devices, collected as part of an earlier implant retrieval program. Of particular importance is the finding that corrosion was limited almost exclusively to the stainless steel devices compared to those manufactured from Co-Cr alloy. Ninety-six percent (96%) of the multi-component stainless steel devices exhibited interfacial corrosion, whereas in none of the single component stainless steel devices could any evidence of corrosion be observed. By comparison, corrosion was identified in 5.7% of the Co-Cr alloy implants.

In a similar implant retrieval study, Weinstein et al. (11) studied the incidence of corrosion in a total of 17 multi-component stainless steel implants, principally bone plates and hip nails. In all of the 17 implants, corrosion was observed at the interface between screw and plate. No relationship could be derived, however, between the severity of corrosion and the length of implantation time. This latter feature contradicts a finding of Colangelo and Green (12) who reported that both the incidence and severity of corrosion increased with time in situ for their series of stainless steel implants examined. However, Colangelo and Green found that 91% of the multi-component stainless steel devices exhibited some extent of corrosion compared to only 10% of the single component implants.

In summary, it is apparent that of the metallic biomaterials in use today for the manufacture of internal fixation devices, a very much higher incidence of corrosion may be expected from those made from stainless steel than from either Co-Cr alloy or titanium. Such a conclusion is consistent with the "in vitro" corrosion measurements conducted upon these alloys. In addition, the previous implant retrieval studies have demonstrated that in those stainless steel devices in which more than one component is present, typically bone plates, the incidence of interfacial corrosion may approach one hundred per cent of the cases.

3. Tissue reactions associated with internal fixation devices

As important as it is to understand the reaction of surgical implants to the body environment, it is equally clear that the reaction of the body to the degradation products of those implants must be appreciated. It is generally agreed that when present in bulk form, the primary alloys used provoke a minimal response aside from the formation of a fibrous membrane which serves to encapsulate the implant. In this case, a steady state condition may be envisaged between the rate of general dissolution of the alloy and the ability of the host environment to respond to the dissolution products.

The situation becomes more complicated, however, when either localized corrosion, wear, or a conjoint process occurs. In these cases, the quantity of dissolution products increases by orders of magnitude and the severity of the tissue reaction changes. The exact nature of the reactions differs according to the implant alloy involved and therefore will be considered separately.

3.1. Co-Cr alloy

As mentioned in the previous section, Co-Cr alloy exhibits good corrosion resistance, even within crevices around screw holes. This alloy, however, was used for many years in McKee-Farrar hip prostheses, having metal upon metal bearing surfaces, and most metal knee joints. In such cases, large numbers of wear particles were produced and the effect that these have upon adjacent tissue has been reported by Winter (14) and Willert and Semlitsch (15). These authors agree that the particles within the tissues in which the various constituents of the Co-Cr alloy may be identified are phagocytosed by macrophages. Evans et al. (16) have shown that those patients who had received an all-metal Co-Cr alloy total hip prosthesis were more sensitive to cobalt, chromium, and nickel than those who had received a metal-plastic joint. They concluded that the release of metal ions from the large quantities of wear particles generated by these prostheses may produce changes in the local blood supply and thereby lead to necrosis of bone and soft tissue. It should be emphasized that these reactions have only been observed for all-metal prostheses where the quantity of metal release is significantly greater than that found around internal fixation devices.

3.2. Stainless steel

Due to the lower corrosion resistance of 316 type stainless steel compared to either the Ti-6Al-4V or Co-Cr alloys, the problems of tissue reactions are inevitably more severe. This situation is further aggravated by the large number of stainless steel devices inserted for the internal fixation of fractures each year.

Meachim (17) has reported upon the examination of 120 tissue samples removed during surgery from areas adjacent to orthopaedic implants. It was found that the release of corrosion products was capable of causing a number of reactions in the surrounding tissue, ranging from the formation of a fibrous membrane when only mild corrosion occurred to the appearance of what were labelled "microplates." These latter particles, having a very similar appearance to haemosiderin were believed, however, to be extracellular in origin. Meachim and Williams (1) have reported that in four out of fifteen cases examined, where the removal of an implant was necessitated due to pain in its locality, severe corrosion of an internal fixation plate was accompanied by the presence of these microplates in the surrounding tissue.

Winter (14) in a similar type of study has categorized the types of foreign material found within tissue adjacent to stainless steel implants in the following manner:
Type I deposit: opaque, small irregular shaped particles, 0.3mm-0.1μm.
Type II deposit: large, platy, sometimes green particles, 5.0mm-0.1μm.
Type III deposit: yellow brown granules, mainly spherical, 3mm-0.1μm.

The Type I deposit was found to consist of small fragments of stainless steel and was more associated with the wear of stainless steel than with its corrosion. Type II and Type III particles were frequently found together. In a later report Winter (15) demonstrated that the Type II deposit consisted of a compound rich in chromium, iron and phosphorous. It was also observed that the Type II deposit was associated with tissue which was either acellular collagen or necrotic.

The Type III deposit would appear to correspond to the "microplates" reported by Meachim (17) in that close similarity to haemosiderin was noted. Winter performed selected area electron diffraction upon these Type III deposits and found the presence of the iron oxides αFe_2O_3 and γFe_2O_3 together with the hydrated iron oxide $\alpha Fe_2O_3 \cdot H_2O$ (geolite) and $\gamma Fe_2O_3 \cdot H_2O$ (lepidocrocite). As to whether this indicates that the Type III deposits are haemosiderin produced as a result of excessive ferrous iron in the body or whether they are a simple corrosion product remains uncertain. It would be expected, however, that if the latter were the case, then the simultaneous presence of chromium oxide, Cr_2O_3, would have been detected. The reaction of these particles to the tissue was found to be minimal when present in small quantities. Where contamination was heavy, however, a similar reaction to the Type II deposit was observed.

3.3. Titanium

Since, as mentioned previously, titanium and its major alloy Ti-6Al-4V, exhibits an extremely low incidence of crevice corrosion in vivo, the only alternative mechanism of titanium release is by uniform corrosion. Meachim and Williams (1) used neutron activation analysis to measure the titanium concentration in tissue adjacent to 19 titanium implants. They found that the concentrations varied from patient to patient, with no apparent influence of the duration of implantation. In three of the 19 cases, titanium concentrations of greater than 2000 ppm were measured compared to an average of 22 ppm around a control series of Co-Cr alloy implants.

Two types of particulate material were observed in the histological sections: Type "A" giving a positive Perls' stain and having the appearance of normal haemosiderin, and Type "B" which gave a negative Perls' stain. These latter particles were found in regions of reactive fibrosis and often within the cytoplasm of fibrocytes, perivascular cells and macrophages. Meachim and Williams concluded that the release of titanium from the implant was likely, though not proven to have necessitated the removal of the implant in five cases.

4. Correlation and conclusion

The insertion of an implant into the human body starts a series of reactions which may or may not influence the success of the procedure. Two of these reactions have been discussed here, namely, corrosion and the severity of any associated tissue reaction.

With regard to the extent of corrosion, it is clear that a certain degree of interfacial corrosion must be expected from multi-component stainless steel devices. It remains to be investigated, however, to what extent this corrosion is significant in determining the clinical success of these implants. The extent of this corrosion is sufficient to induce a variety of reactions ranging from a minimal encapsulation of the device by fibrous tissue to necrosis of adjacent tissue. In such cases the extent of the tissue reaction would appear to be related to the extent of the corrosion though this point is by no means certain since other variables such as patient sensitivity may influence the result.

The Co-Cr alloy implants would appear to exhibit interfacial corrosion at a very much lower rate than equivalent stainless steel devices. It is difficult, however, to determine what tissue reaction this provokes since the use of this alloy in internal fixation devices is restricted. Certainly, the presence of large wear particles of this alloy does induce a severe tissue response, but it is extremely unlikely that such a situation would ever occur around an internal fixation device.

Of the three alloys used for the manufacture of bone plates, titanium and its major alloy Ti-6Al-4V, possess the best corrosion resistance. Of greater concern is the observation of extremely high levels of titanium in the tissue surrounding titanium implants.

5. Methods of procedure

5.1. Retrieval of implants

A total of 112 internal fixation devices, 75 bone plates and 37 hip devices, obtained from the Moore Clinic in South Carolina, the V.A. hospitals in San Francisco and New Orleans, and the Children's Hospital in New Orleans, were studied. Of the bone plates, one was fabricated from Ti, one from a Co-Cr alloy and the remainder from stainless steel. Of the hip nails, 32 were fabricated from stainless steel and 5 from Co-Cr alloys.

Upon receipt, all of the implants were thoroughly cleaned with Alconox[4] and warm water. When necessary a soft brush was used to remove adherent tissue and blood. The implants were then photographed to provide a permanent record.

5.2. Tissue examination

During operation for the removal of five of the bone plates and two of the hip devices, the tissue adjacent to the plate was removed as a continuous strip and identified with respect to the anatomical orientation of the plate for transverse sectioning at the screw holes. These were embedded in parafin, sectioned to a thickness of 6 μm and stained with either H&E, Gomoris Trichrome, Perls' Iron, or Bathophenanthroline Iron. Representative sections corresponding to each screw hole, stained with each stain, were then examined and the reaction to any corrosion products graded on the following scale:

0: thin fibrous membrane containing lipid cells
1: thin acellular fibrous membrane
2: mild chronic inflammatory response
3: moderate chronic inflammatory response without giant cells
4: heavy chronic inflammatory response with giant cells and a few granulomas
5: severe inflammatory response with giant cells, granulomas and necrosis.

5.3. Metallurgical examination

Each of the implants was examined for evidence of any mechanical damage, wear, burnishing marks, surface flaws and deformation of the device. This information was recorded upon a standard report form as recommended in ASTM F561 - Recovery of Implant Engineering Examination. In addition to the above, the extent of corrosion was graded using a scale of 0-5 in the following manner:

0: no surface degradation visible at 60X magnification
1: very mild surface degradation visible at 60X magnification
2: mild surface degradation easily visible at 60X magnification
3: moderate surface degradation visible without magnification
4: heavy degradation visible without magnification
5: very severe surface degradation.

The implants were further tested to determine their mechanical properties. This involved both Rockwell hardness measurements and the

4: Alconox Inc., N.Y., N.Y. 10003

determination of their bend strengths. For the bone plates, four-point bend tests were conducted as per ASTM F 382. In order to follow this standard, however, only plates longer than 5 inches could be tested. The bend strengths reported are defined as the bending moment required to produce a permanent defleciton of 0.005 inches.

The bend strengths for the hip devices were measured using the ASTM F 38 standard method. In this test, the load is applied axially to the nail portion with the plate portion being held against a vertical support. The bend strength is agian defined as the bending moment required to produce a permanent deflection of 0.005 inches with the bending moment being calculated as the product of the perpendicular distance between the point of loading and the lateral edge of the device.

Following mechanical testing, transverse and longitudinal sections were cut from both bone plates and screws to enable metallographic examination. This involed a measurement of both inclusion content and grain size. A further section of the device was cut and used for the determination of chemical composition by either emission or atomic absorption spectroscopy.

6. Results

6.1. Mechanical testing

The results from the four point bend tests conducted upon the bone plates are presented in figure 1 as a function of their respective hardness value. A good correlation is obtained and it is noticeable that small changes in material hardness are accompanied by large differences in bend strengths. In figures 2 and 3, equivalent plots have been made for the hip nail devices. Here the results have been separated into two catagories, namely standard Jewetts and T-Beams, since the cross sections at the nail-plate junctions of these devices varied considerably. The apparently poor correlation between bend strength and hardness will be discussed later.

6.2. Corrosion examination

The corrosion examination revealed that, although none of the Co-Cr or titanium devices exhibited any evidence of any corrosion, 100% of both the stainless steel bone plates and hip nails were found to have corroded. This corrosion was concentrated almost entirely at the screw-plate interface, with the incidence of gross corrosion being negligible.

The severity of the corrosion for the stainless steel devices was graded on a scale of 0-5. A mean corrosion index of 1.35 was measured for both bone plates and hip nails. This compared to a mean corrosion index of 1.22 for the corresponding screws, figures 4 and 5.

When the corrosion indices for the different plates, averaged over all of the screw holes, were compared to the hardness of the individual devices, it was apparent that no correlation could be obtained, figure 6, This would indicate that increased cold work of the alloy, manifested in an increased hardness value, does not render the material more susceptible to interfacial corrosion.

The severity of corrosion was further compared to the length of implantation time for the various devices, and the results are displayed in figure 7. It is clear that, from this data, the extent of corrosion for fracture fixation devices is independent of the duration of implantation. This serves to illustrate well the peculiar nature of surgical implant corrosion compared to those environments encountered by normal corrosion-resistant materials, It was found, however, that those implants attached to weight bearing limbs exhibited a significantly higher average corrosion index (1,48) than those attached to the upper skeleton (0,98) ($P < 0,05$)

6.3. Appearance of corrosion

In conjunction with the grading scheme mentioned above, the appearance of the corroded areas was examined using scanning electron microscopy, One of the problems with such an investigation, however, is that the corrosion surfaces may be disturbed or damaged during the removal of the screws. Such damage is difficult to distinguish from both that caused by insertion of the screw and by possible movement during service. It was found, however, that by carefully following the scratches present within the plate countersink, the cause of the scratch could generally be determined. Representative photomicrographs of each corrosion grade are shown in figure 8, (a-f).

When the corrosion of a screw or plate hole was graded less than three, the appearance of the corrosion surfaces was that of small areas of pitting. Most noticeable, however, was the nature of the corrosion graded greater than three. In these cases, a large amount of grain boundary attack was apparent so that individual grains were released. A clear example of this is shown in figure 9 where both the longitudinal and transverse removal of grains is visible for a plate hole graded five. In other plates, the extent of preferential attack was such that selected corrosion within the grains was apparent, figure 10. This mechanism contrasted with that observed upon the screw chamfers where the coalescence of individual pits into cracks was visible, figure 11. In both screws and plate countersinks, however, the location of the corrosion corresponded to the area of surface damage caused by insertion of the screws.

6.4. Metallurgical examination

The metallographic examination of the microstructures revealed that almost all of the devices possessed grain sizes on the ASTM scale of between 5 and 8. Occasionally, however, specimens having an extremely large grain size were encountered. The inclusion content of all of the specimens was D1.5 Thin or less.

6.5. Influence of composition

The influence of composition upon the severity of corrosion for the fixation devices was analyzed for all of the elements as specified by ASTM F 139 and, in addition, for copper and the chromium and nickel equivalent elements. It was found that, apart from one element, the severity of corrosion was clearly independent of composition. For this one element, however, namely copper, a possible correlation could be observed, figure 12,

Obviously, the final actual corrosion of a surgical implant is dependent upon a number of factors, many independent of material characteristics. Consequently, an examination of the influence of corrosion is limited in its applicability for any given case. With sufficient numbers, however, the other factors should be averaged and a pattern emerge. Such is believed to be the case with the influence of this element.

6.6. Results of tissue examination

Gross examination of tissue directly adjacent to bone plates revealed a smooth, glistening "pseudomembrane" of fibrous tissue. This surface was interrupted by the screw holes which had tissue growing into the crevices and screwheads. Small pieces of tissue in the crevices were occasionally lost in dissection but usually almost all of the tissue could be preserved. Tissue next to some but not all of the screw holes had obvious discoloration.

Microscopic examination of each slide stained with H&G was performed to grade the tissue reaction. Examples of tissue sections representative of each grade are shown in figure 13. It could be seen that the tissue reaction was quite localized in most of the sections. The morphology of the section indicated that the tissue reaction was most severe at the screw-plate junctions. It was in these areas that tissue reaction grading was performed. At other areas of the plate, the tissue reaction was uniformly 0 or 1 grade.

In areas of severe (grades 4,5) tissue reaction, macrophages and multinucleate giant cells with intracellular blue-staining particulate material were common. In addition, haemosiderin-like material was also observed more frequently as the tissue reaction became more severe. Overall, the tissue reaction to the implants was mild. The mean tissue grade was 2.0, corresponding to mild chronic inflammatory response on the average.

Sections stained with Perl's stain generally demonstrated an increase in the amount of positive material that paralleled the severity of tissue reaction. Perl's stain is commonly used for staining iron (Fe) but has the disadvantage of false positries because it contains iron. Tissue detail with this stain was not as good but appeared to show Perl's positive material both intracellularly and extracellularly. Large deposits of the material around severe tissue reaction specimens stained Perl's positive.

Bathophenanthrolene (BPA) staining is specific for ferrous iron. Sections stained with BPA were most positive in areas where Perl's stain was most positive. BPA staining demonstrated small amounts of intracellular iron in macrophages in areas of severe tissue reaction. Addition of Thioglycolic acid to the BPA staining converted all ferric iron to ferrous. This revealed particles which were BPA positive, particles which stained green-blue, and opaque particles which did not stain. This suggests that from kinetic limitations, not all ferric iron was converted to ferrous and possibly metallic particles were present because of failure to stain.

6.7. Comparison of tissue and corrosion examinations

The comparison of the tissue reaction around each screw hole with the associated corrosion for that hole revealed a positive correlation, whereby the greater the corrosion in each hole the more severe the extent of the tissue reaction, figure 14. When a linear regression analysis was performed upon this data, a correlation coefficient of 0.41 was obtained, indicating that the degree of scatter of the results was too high to allow for any definitive conclusions. It must be remembered, however, that both tissue and corrosion indices were based on subjective decisions and therefore liable to considerable error. Even so, in certain individual cases, it was possible to obtain a correlation of the type shown in figure 15.

7. Discussion

7.1. Mechanical properties

The ASTM recommended tests used in the present research are designed to measure the mechanical properties of either bone plates or hip nails in such a way that the loading conditions approximate those occurring in vivo. Therefore, the results from these tests are indicative of the relative strengths which may be expected from the different devices when implanted.

The present examination has revealed that a large variation in mechanical properties may occur for both hip nails and bone plates, with only small differences being apparent in Rockwell hardness values. That this was so may be attributed to the interrelationship between hardness value, extent of plastic deformation or cold work and the true yield strength of the material. In particular, with austenitic stainless steels, the increase in hardness that is the result of cold work does not occur at the same rate as the increase in yield strength. Consequently in the present investigation and within the range of hardnesses measured, the small variations in hardness reflect large differences in the degree of cold work of the sample and therefore also of yield strength, which for a given geometry device is the property measured with the test method.

A less satisfactory correlation was apparent between bend strength and material hardness for the hip nail devices than for the bone plates. One of the major reasons for this is the difficulty involved in measuring a hardness value for the hip device in a location representative

of the area of maximum stress. For the bone plates the extent of cold work was uniform along the length of the plate, and therefore suitable hardness measurements could be made. For the hip nail devices, the extent of cold work varied with location and so the hardness values did not necessarily reflect the mechanical properties, measured with the strength test.

This large variation in mechanical properties for apparently similar devices, is disturbing from a clinical standpoint. These fracture fixation implants, and particularly the hip nail devices, are subjected to large loads even in the non-weight bearing condition, and it has been shown here that a two-fold difference in bend strength may occur for apparently similar devices. Therefore, devices may be utilized for essentially identical clinical situations, and yet perform very differently, i.e. undergo unwanted plastic deformation. Since a simple hardness test may be unreliable in determining the strength of any given implant, data from mechanical tests should be available to the physician to aid in making a choice of implant.

7.2. Corrosion examination

The results from the present investigation concur closely with those from previous examination in that while no corrosion was observed for the Co-Cr or Ti-alloy implants, interfacial corrosion was found to have occurred in 100% of the stainless steel devices.

The similar severity of corrosion observed for both plate countersinks and screw chamfers is interesting in view of their different hardnesses. According to Cigada et al. (13), the crevice corrosion resistance of 316L stainless steel is decreased with increasing degree of cold work. It would be expected, therefore, that the average corrosion index for the screws would be greater than that for the countersinks. That this was not so indicates that crevice corrosion above was not the sole mechanism by which the materials degraded. A competing mechanism of crevice and fretting corrosion may be envisaged whereby the softer plates corroded more by fretting while the harder screws degraded more by crevice corrosion. This postulation is supported by the fact that those devices implanted in weight bearing limbs exhibited a higher corrosion index than those in non-weight bearing locations. Furthermore, the average corrosion index of the plates was found to be independent of hardness.

The S.E.M. photomicrographs of the areas of corrosion support the theory of different mechanisms of corrosion operating upon the screw and plate. Upon the screw chamfer, attack occurred initially by pitting and progressed by the coalescence of these pits into cracks. Upon the plate countersinks, the mechanism resulted in intergranular attack and the subsequent loss of grains of metal. This would have required the adjacent tissue to accept a significantly larger volume of metallic debris than would be predicted on the basis of corrosion above. It should be emphasized that this phenomenon of intergranular attack on the countersink was observed in a number of plates, none of which exhibited any microscopic evidence of sensitization. Cigada et al. (13)

have proposed that the anisotropy of corrosion observed within plate countersinks may be related to the microstructure of the alloy and in particular to the shape of the inclusions. In the present investigation, however, no evidence to support this contention was observed. Rather the appearance of corrosion may be considered a function of the propensity of the material towards intergranular corrosion. The factors governing this intergranular attack are currently being investigated.

The possible influence of copper concentration upon the corrosion behavior of stainless steel is interesting, especially since this element is not governed by present ASTM specifications. Even though the presence of a relationship between corrosion and copper concentration is far from certain, it would be advisable for further research upon this matter to be conducted.

Conclusions

1) Hardness measurements have been shown to be a poor indicator of the strength characteristics of internal fixation devices. Therefore, it is recommended that the strength be reported for a particular device.

2) While the number of devices examined which were manufactured from materials other than stainless steel were small no evidence of interfacial corrosion was observed, whereas 100% of the stainless steel devices exhibited interfacial corrosion.

3) The corrosion between screws and plates has been found to be a conjoint crevice-fretting mechanism. Furthermore, the austenitic stainless steel is subject to intergranular attack in the non-sensitized condition resulting in large amounts of particulate material being released to the surrounding tissues.

Acknowledgements

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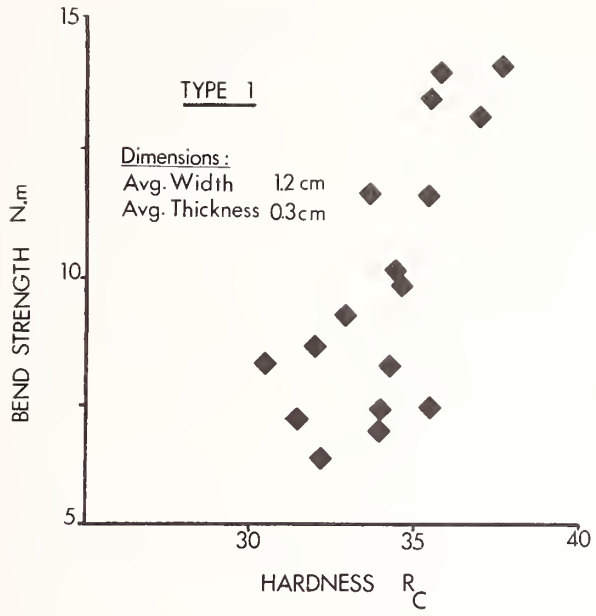


Figure 1. Variation in bend strength with Rockwell hardness for Cr-Ni-Mo stainless steel bone plates.

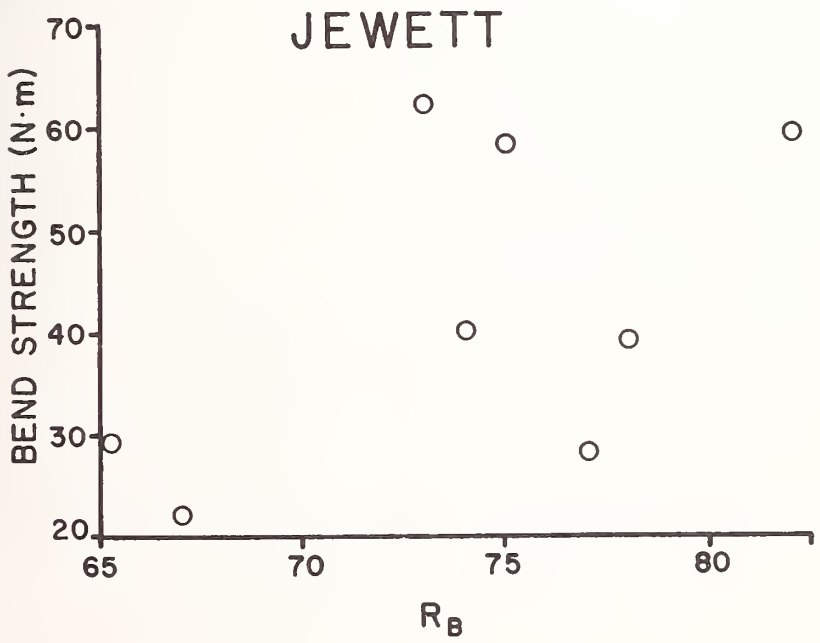


Figure 2. Variation in bend strength with Rockwell hardness for Cr-Ni-Mo stainless steel Jewett hip nails.

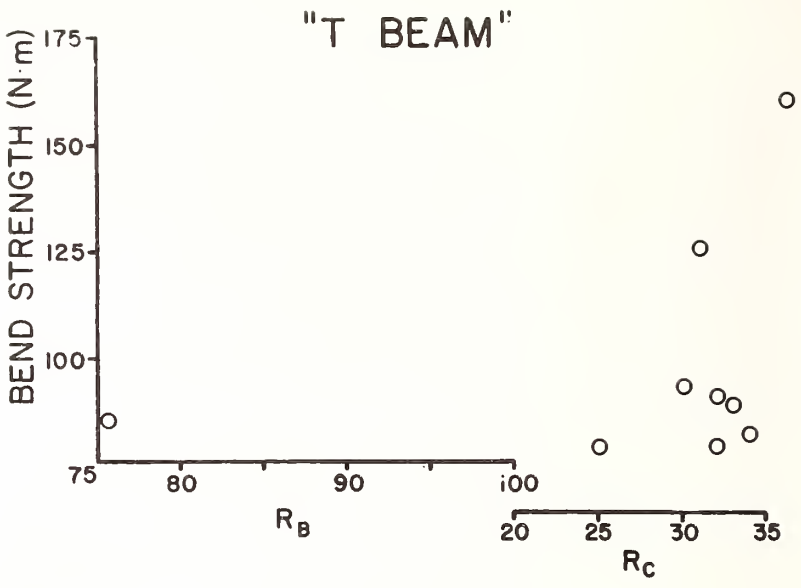


Figure 3. Variation in bend strength with Rockwell hardness for Cr-Ni-Mo stainless steel "T-beam" sliding hip nails.

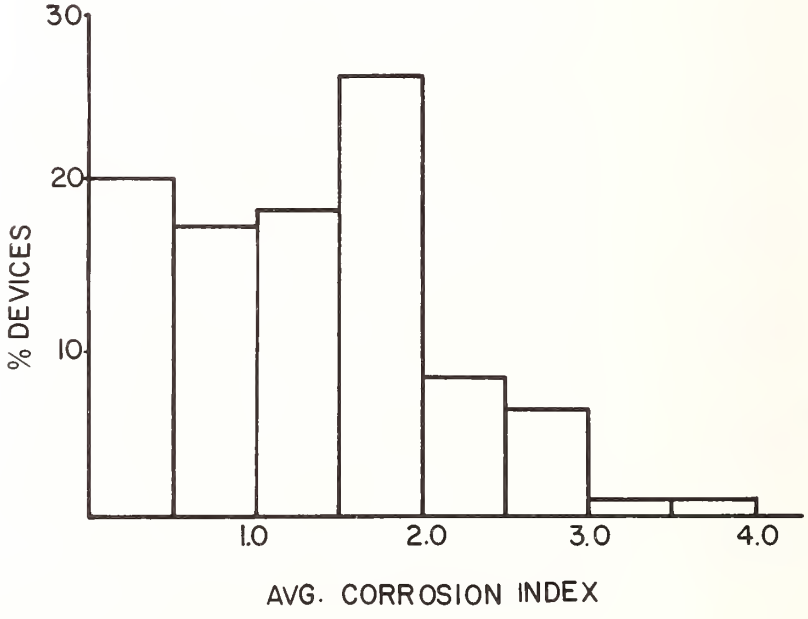


Figure 4. Histogram showing the range of average corrosion indices for both bone plates and hip nails.

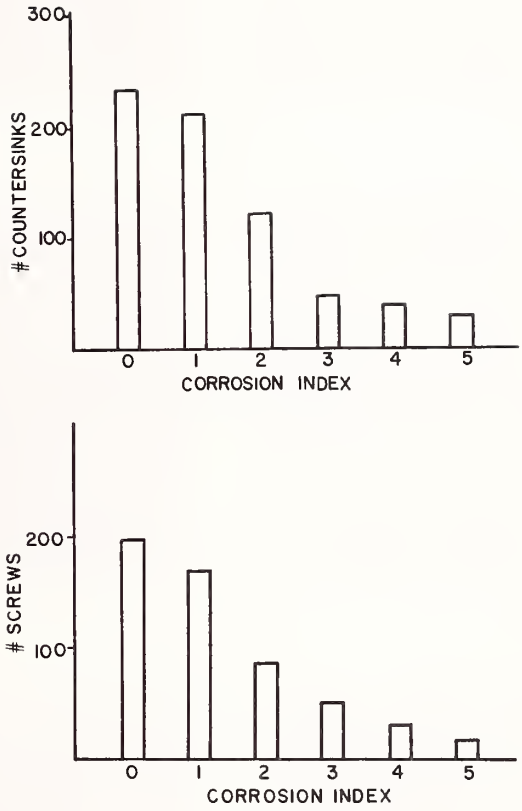


Figure 5. Histograms showing the range of corrosion indices measured for both the countersinks and screw chamfers.

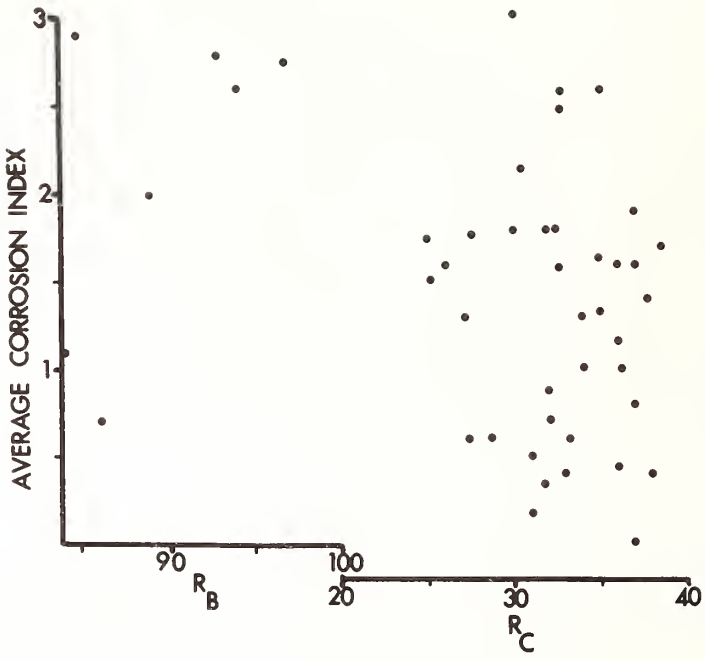


Figure 6. Average corrosion index of the fracture fixation devices as a function of their Rockwell hardness.

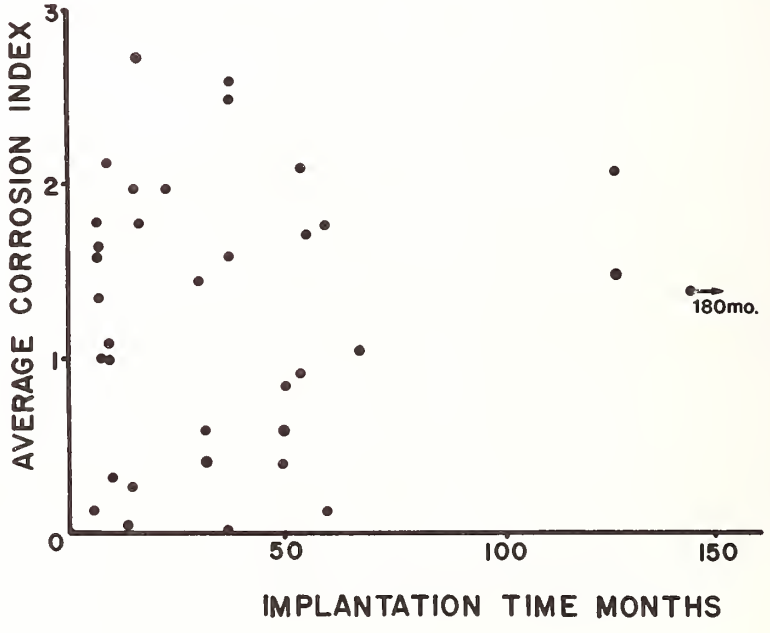
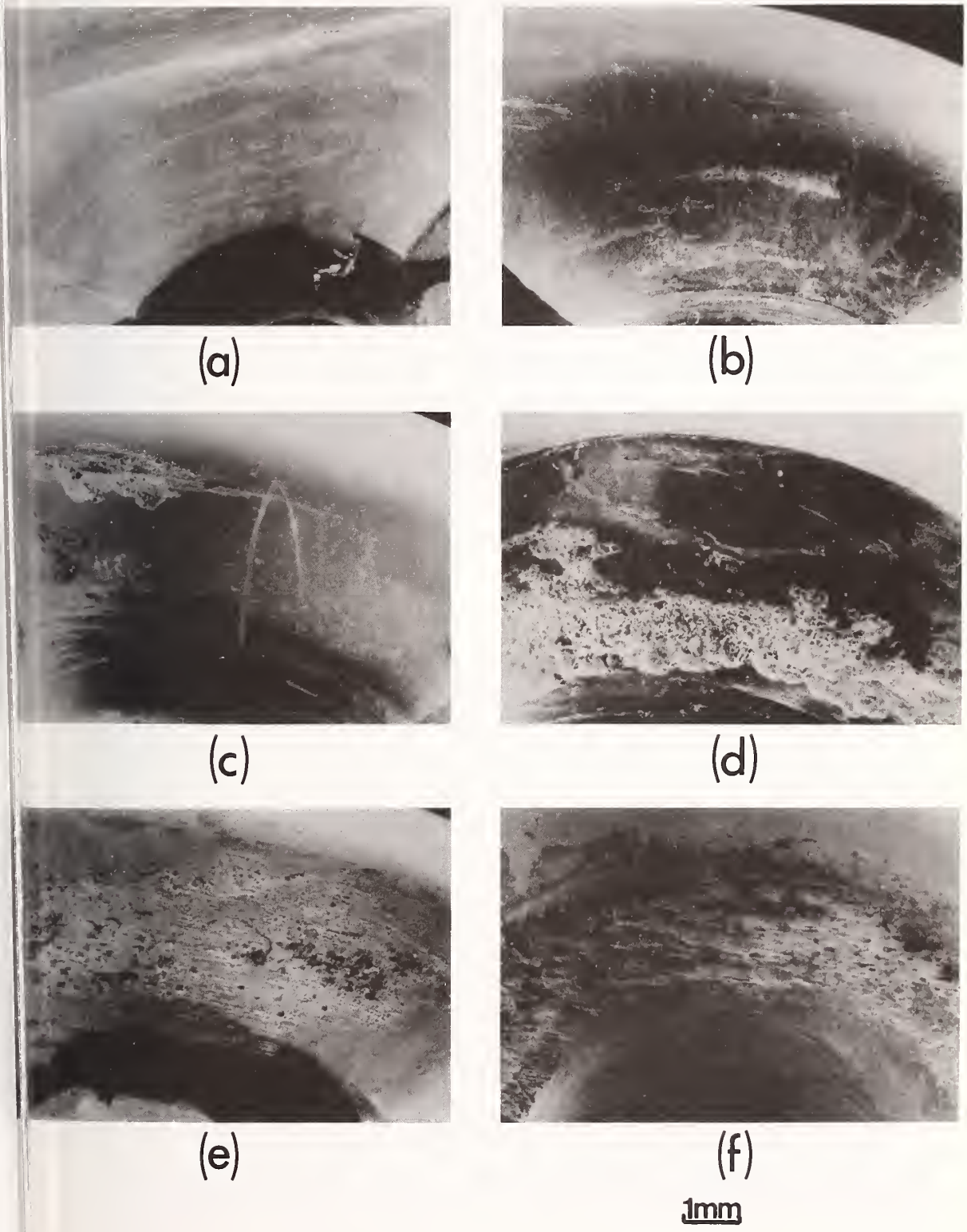


Figure 7. Average corrosion index of the fracture fixation devices as a function of their time in-situ.



re 8. Representative S.E.M. photomicrographs of the different grades of interfacial corrosion. (a) = 0, (b) = 1, (c) = 2, (d) = 3, (e) = 4, (f) = 5

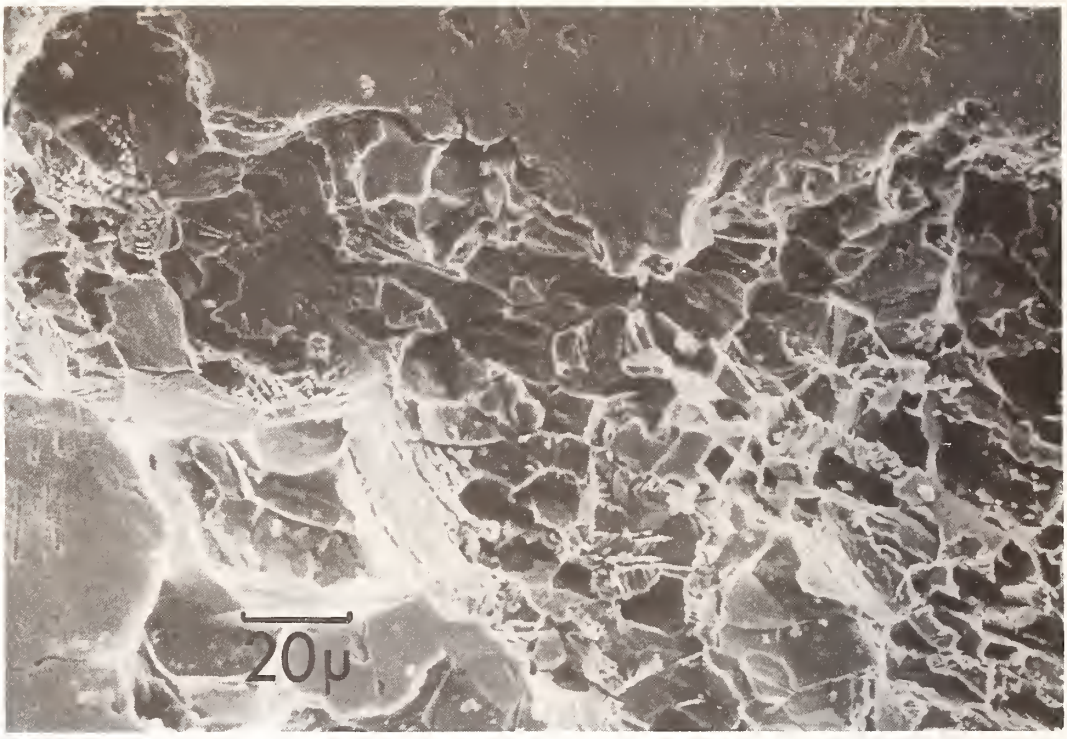


Figure 9. S.E.M. photomicrograph of a plate countersink showing intergranular corrosion.

Figure 10. S.E.M. photomicrograph of a screw chamfer showing pitting.

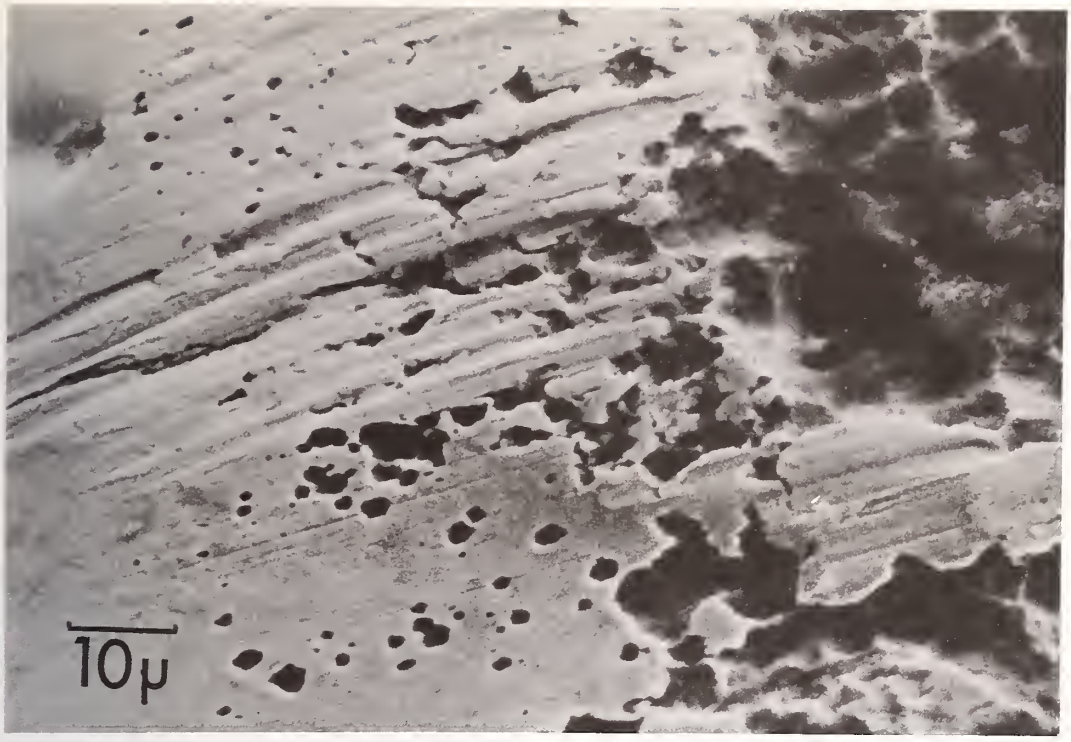


Figure 11. S.E.M. photomicrograph of a plate countersink showing selective corrosion within the grains.

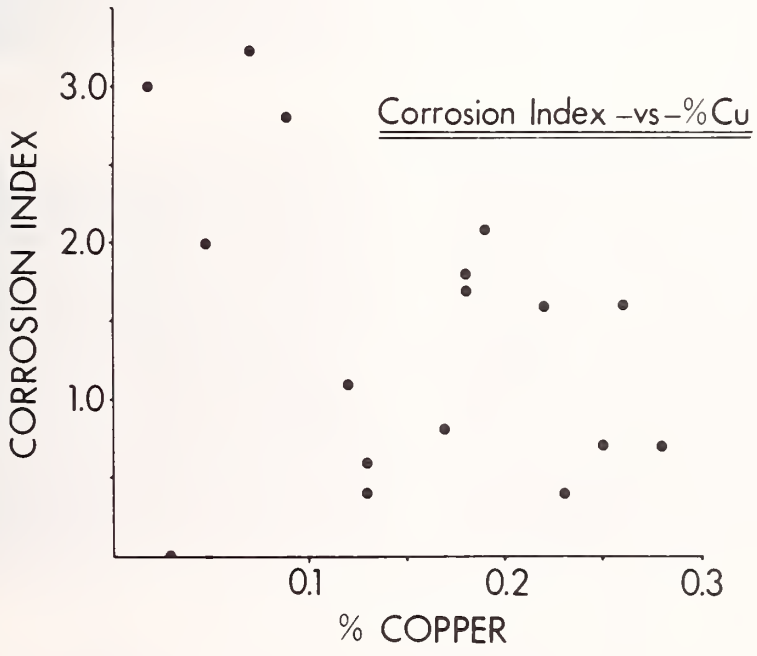


Figure 12. Average corrosion index of the fracture fixation devices as a function of their copper content.

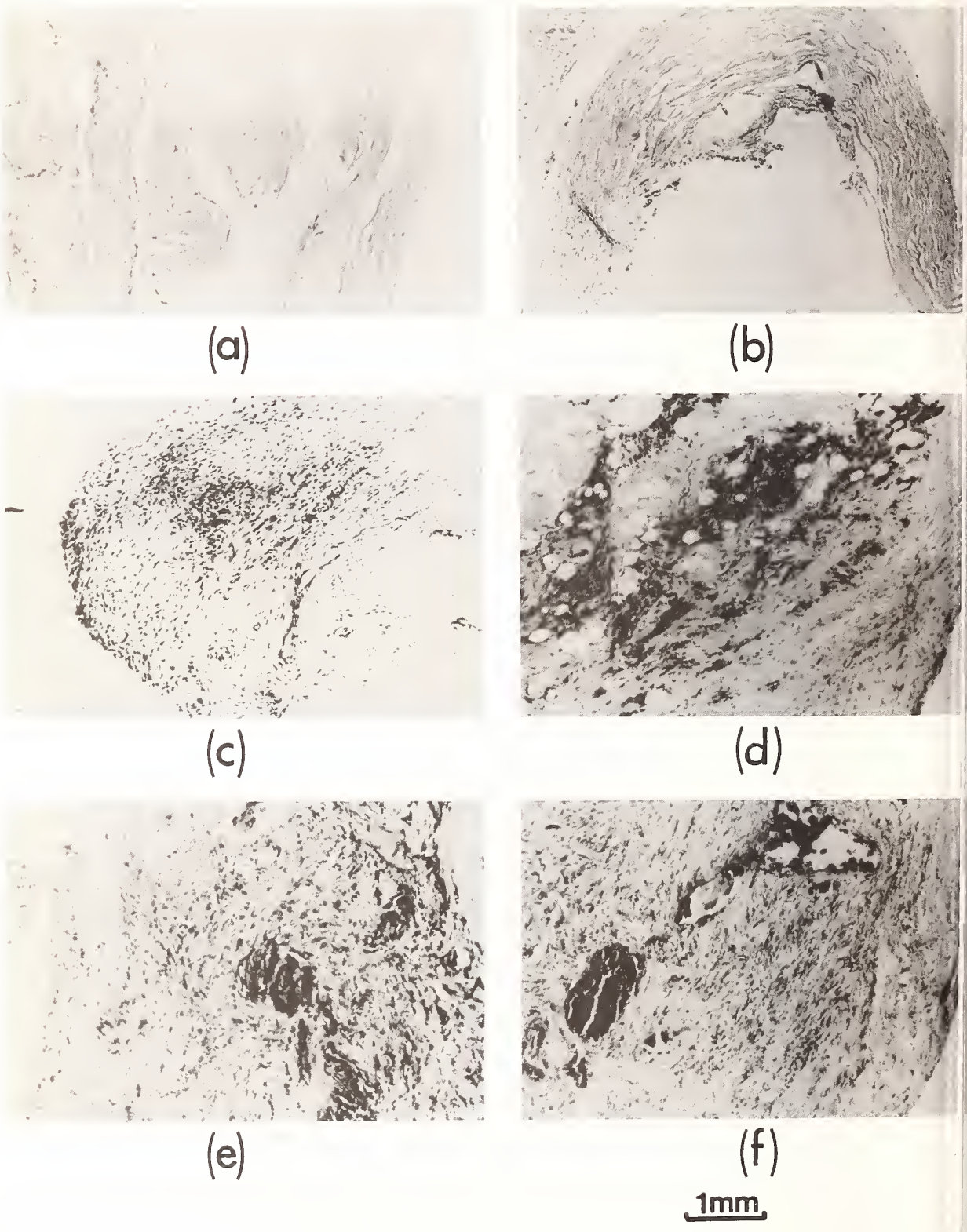


Figure 13. Representative photomicrographs of the different grades of tissue reaction. (a) = 0, (b) = 1, (c) = 2, (d) = 3, (e) = 4, (f) = 5

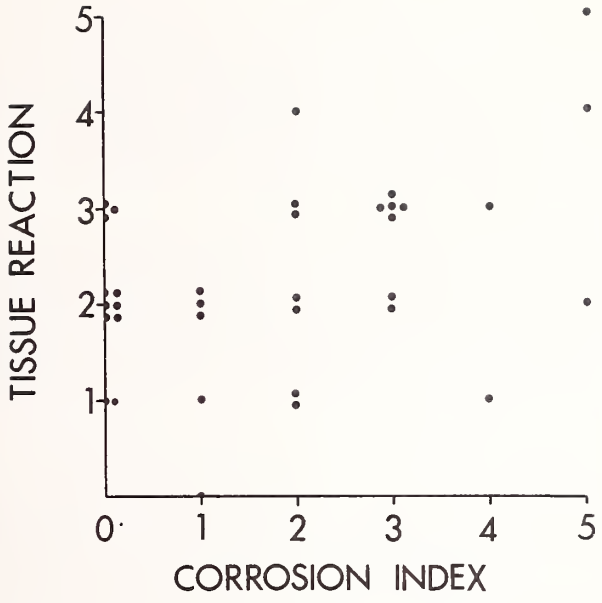


Figure 14. Tissue reaction at individual screw holes as a function of the associated corrosion index of that hole.

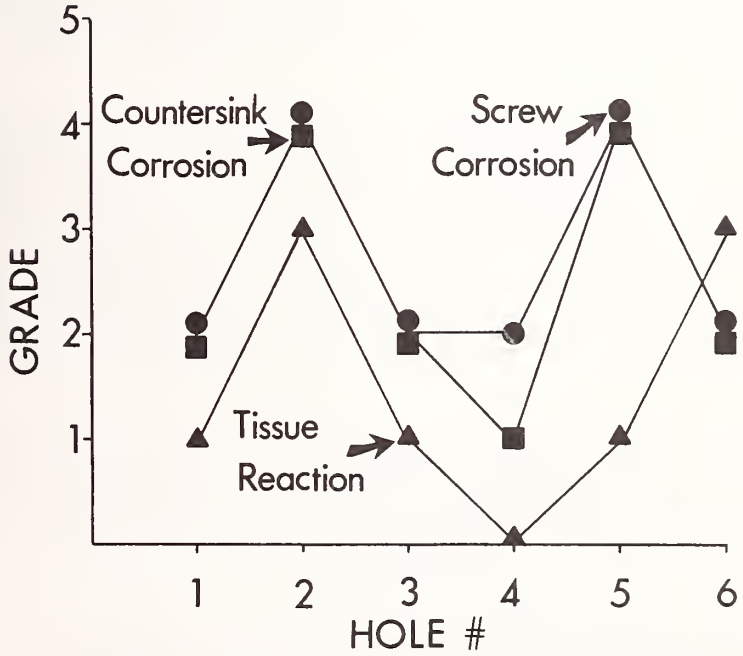


Figure 15. Comparison of tissue reaction at individual screw holes with the associated countersink and screw corrosion index along the length of a bone plate.

Discussion

Question (D. F. Williams, University of Liverpool, U.K.): A few examples of intergranular corrosion were shown. Could you say whether this was a frequent finding and if so, could you comment on how this correlates with the observation that none of the stainless steel specimens were outside chemical specification?

Answer: Our S.E.M. study revealed that intergranular corrosion was common whenever the corrosion index was within the range 3-5 according to our corrosion scheme mentioned in the text. In this respect it would appear to be an extension of the general crevice corrosion observed in all of the plates and therefore, it is not altogether surprising that it occurred for plates within the chemical specifications.

Question (D. C. Richardson, Food and Drug Administration): In the retrievals acquired after you began the prospective phase of your program: 1) were any of the patients tested at removal for metal sensitization, and, if so, 2) was there any semiquantitative correlation between the "index of tissue reaction" and the demonstration of immune sensitivity/sensitization?

Answer: Unfortunately, our patients were not tested for metal sensitization.

Question (unidentified): Did you find evidence for fretting damage and/or debris particles associated with the surfaces and tissue specimens studied? If so, did any correlation exist with alloy chemistry or type?

Answer: Conclusive evidence to demonstrate fretting damage could only be obtained by examination under the S.E.M. Even then it was frequently difficult to differentiate between areas of fretting and the damage caused by removal of the screw. We did see areas of fretting particularly upon the plates as opposed to the screws, but could not identify debris from this within the tissue samples. To date, we have not examined sufficient numbers of plates to show any correlation between fretting damage and alloy chemistry or type of device.

Question (Anthony K. Kidlet, University of California at Los Angeles): Did you see more corrosion with D.C.P. plates than with standard plates, and if so do you think this has important clinical application in terms of plate strength, and the degree of local tissue response to the implant?

Answer: Corrosion occurred almost exclusively at screw-plate junctions. Tissue response correlated with corrosion in that it was more marked at screw holes. There was a significant difference in corrosion

between lower extremity plates and uppper extremity plates, suggesting that motion from weight bearing might be important. Because of the manner in which D.C.P. plates are applied (i.e., compression with only one or two screws), we would expect no difference between D.C.P. and standard plates. We feel the degree of corrosion is unlikely to contribute to catastrophic failure before fracture union except in poorly-executed lower extremity fracture fixation.

Question (S. Leray, INSERM): Is it possible to relate the high release of metallic material and subsequent tissue reaction due to friction between screw and plate to the skin redness observed by Brown and Merritt at corresponding sites, (paper given on May 1 on metal allergy)? i.e., distinguish cell mediated reaction from local tissue damage and inflammation early.

Answer: Our seven prospective plate removals demonstrated no significant skin change. Only three of these plates were removed because of clinical symptoms.

THE EVALUATION OF EXPLANTED UMBILICAL VEIN GRAFTS

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The evaluation of retrieved vascular graft samples is critical if the clinical function of a vascular prosthesis is to be adequately understood. During the past five years, 36 explanted human umbilical vein grafts* have been evaluated after implant periods ranging from 1 minute to 42 months. The testing program included CST, ATR, SEM, EDAX, histopathology, TEM, and compliance studies. Critical surface tensions were stable and remained at the pre-implant value of about 25 dynes/cm for periods up to 42 months. Some lipid was identified within the graft using IR analysis, however, results indicate that this phenomena is primarily patient-related rather than graft-related. No calcification of any graft samples has been noted to date. The blood-contact surface of patent grafts is covered with protein, moreover, no neo-intimal proliferation has been seen within the graft material. Histological and TEM evaluations have demonstrated that the primary changes seen in a patent graft are: 1) a compaction of the graft, and 2) a decrease in cellularity with implant time. In general the graft has many characteristics similar to the ASV and excellent clinical results have been seen thus far.

I. Introduction

The evaluation of explanted graft materials has received relatively little attention in the past considering the large number of grafts that have been implanted since the early 1950's. Reports which exist in the literature include evaluation of explanted autogenous veins [1,2,3], Dacron^{R} grafts [4,5], and bovine carotid artery grafts [6]; but information is limited on recent vintage vascular grafts such as PTFE and the umbilical vein prosthesis. With the exception of the autogenous saphenous vein (ASV), the history of the biological-based vascular graft has not been impressive. The ASV is the "gold standard" in small vessel replacement; however, as can be seen from the work of Szilagyi [1] and DeWeese [3], this "gold standard" is not without its morbidity and failure.

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*Biograft®, Meadox Medicals, Inc., Oakland, New Jersey

Before an evaluation of explanted graft materials can be undertaken, careful consideration must be given to the objectives of the explant study. In many cases, grafts are explanted in the surgical environment with little thought as to the information sought and what preparation procedures must be utilized to best preserve the sample for future evaluation. For example, if a graft is to be evaluated for scanning electron microscopy, care must be taken to use the proper fixative to insure the highest quality scans; but, when a fixative is utilized, limited mechanical studies can be conducted because of resultant tissue fixation. In any study great care must be taken to define the testing program prior to explantation if a maximum amount of information is to be obtained from a small segment of graft material.

A complicating factor which can limit the information gained from an explanted sample is the mode of "graft failure". Some of these failures may, in fact, not be related to the graft; however, documentation of this point is not common. Typically, modes of "graft failure" reported in the literature include infection [7,8], aneurysmal dilatation [9,10], and thrombosis [11,12], but little data has been published on patent explanted human grafts or graft segments because of the complications associated with their retrieval. Further, if these explanted grafts are retrieved surgically, they rarely make their way to the manufacturer for evaluation because of several reasons, key among them are: 1) medical, legal implications, 2) complexities associated with proper graft retrieval, and 3) lack of interest in the subject.

In this paper I will focus on an explant program specifically developed for clinical evaluation of the human umbilical vein graft manufactured by Meadox Medicals, Inc., which goes under the tradename, Biograft®. This graft is constructed from human umbilical cords which are preserved in glutaraldehyde, stripped of the umbilical arteries and most adventitia, sterilized, and then stored in a pure 50% ethanol solution. A detailed description of this human umbilical cord graft is not presented in this paper as other references exist on the subject [13,14].

2. Methods

Our experience in the vascular graft field has shown that the first hurdle which must be overcome in any graft retrieval program is the acquisition of the samples. In our study the majority of the umbilical vein grafts were obtained from Drs. Herbert Dardik, Irving Dardik, and I. Ibrahim of Englewood Hospital. In addition, some graft samples were obtained from Dr. William Abbott at Massachusetts General Hospital. Attempts were made to obtain samples from other clinical centers, but, these attempts were universally unsuccessful.

Figure 1 illustrates the testing program which was used on preimplant and explanted Biografts®. This program consisted of surface

analyses, biochemical assays, physical tests, and morphological studies. The surface studies, conducted by Dr. Robert Baier at Calspan Corporation, included attenuated total reflection and critical surface tension. These tests have been described in detail elsewhere [15] and will not be repeated in this paper.

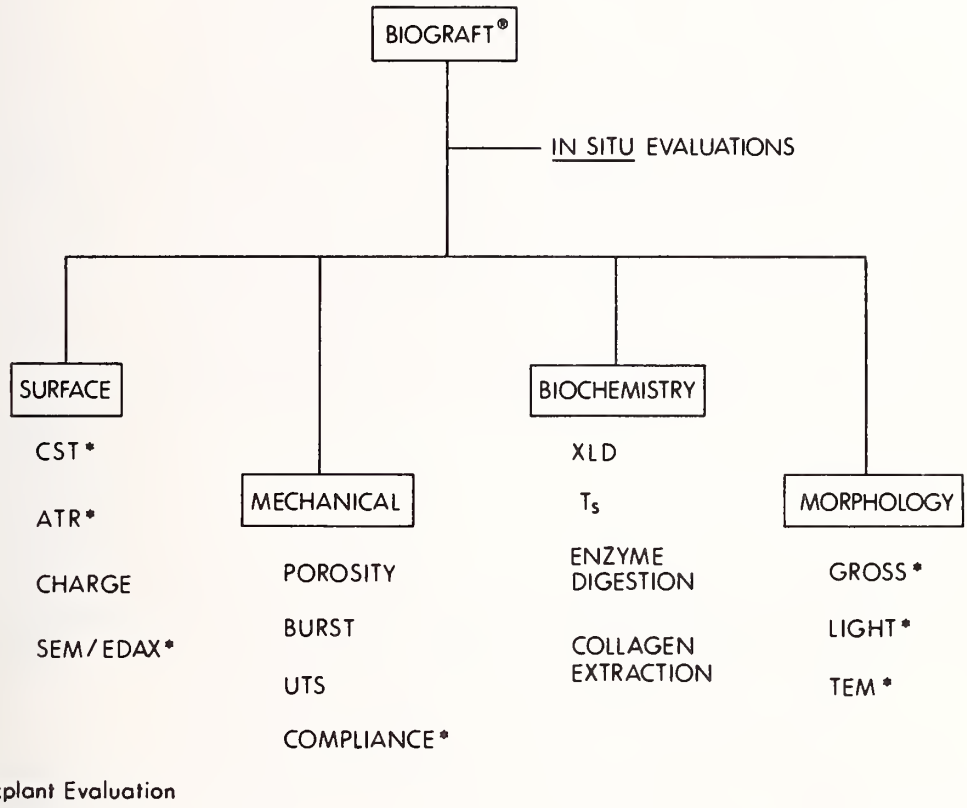


Figure 1. Description of the testing program.

Mechanical testing focused on graft characteristics which are believed to affect in vivo graft function. These tests included compliance testing, porosity, burst strength, and ultimate tensile strength. These tests coupled with biochemical assays such as cross-link density, shrink temperature, enzyme digestibility, and soluble collagen extraction studies yielded an excellent understanding of graft strength and tanning efficiency, respectively.

Histological and transmission electron examination of these samples were done by Drs. Michael Meenaghan and Joseph Natiella at the State University at Buffalo, New York; whereas, the SEM work was completed at Calspan by Dr. Robert Baier.

3. Results

Thus far, a total of 36 human explant samples have been received and evaluated with implant times ranging from 1 minute to 42 months. It is impossible to review all the information in this paper, so key points will be presented to illustrate the changes observed in the umbilical vein graft with time. Comparison will be made when applicable to pre-implant data.

3.1 SEM

Figure 2A is a typical pre-implant scanning electron picture (150X) showing the general architecture of the human umbilical cord vein graft. For the most part the surface is relatively smooth, but, as can be seen in this figure, some minor imperfections might occur as a result of processing. The corrugated appearance of the lumen, visible at 2000X, is a result of the internal elastic lamina which remains intact and is located below the subendothelial layer. With time the surface of the graft becomes smooth as a result of a uniform coating of protein. Figure 2B is the same graft 3½ years later, demonstrating a typical surface appearance. This surface is primarily protein with an occasional blood cell noted on the lumen. In the case of a thrombosed prosthesis, the surface is covered by a fiber network with entrapped cells. The early blood contact events were documented with human samples taken 1-10 minutes after blood contact. Figure 3A is a sample taken 4 minutes after blood contact. Figure 3B represents the same graft 6 months after implantation. In this case the coverage of protein is not yet complete and the folds associated with the internal elastic lamina can be clearly identified. In this sample some fibrin-like strands are also present after 6 months.

3.2 CST

In order to evaluate the relative biocompatibility of the graft surface, CST was chosen as the routine testing parameter. In contrast to some biocompatibility tests, this analysis can be conducted on explanted grafts as well as pre-implanted controls. Figure 4 represents a typical surface tension plot taken from a 3½ year old explanted specimen. The CST value falls into the reported biocompatibility range of 20-30 dynes/cm even after an extended implant period. The effect of implant period on CST is shown in figure 5. On patent graft samples the CST remains about 25 dynes/cm up to 42 months post-operatively. CST's typically could not be obtained on thrombosed grafts because total removal of the thrombus was impossible and measurements could not be made on the surface without interference from the remaining clot.

150X (20kv)

Figure 2A. (Pre-implant).

100μ

2B. (3½ years explant).

Figure 3A.

3B. (6-month explant).

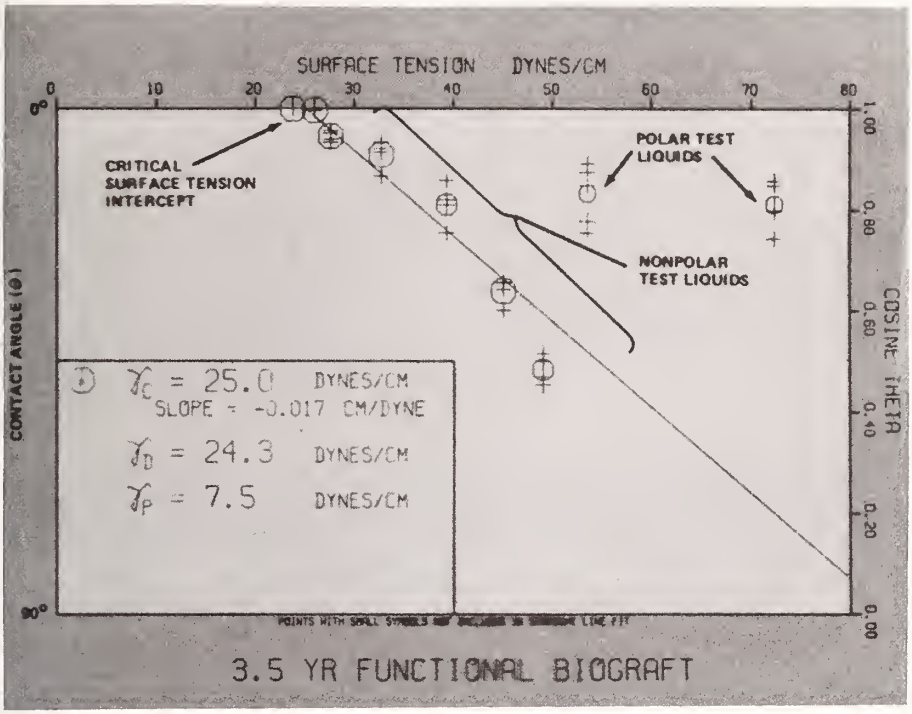


Figure 4. Contact angle data plot revealing the critical surface tension of an implanted, stabilized human umbilical cord vein's blood flow surface to have remained in the "biocompatible" range for more than 3 years.

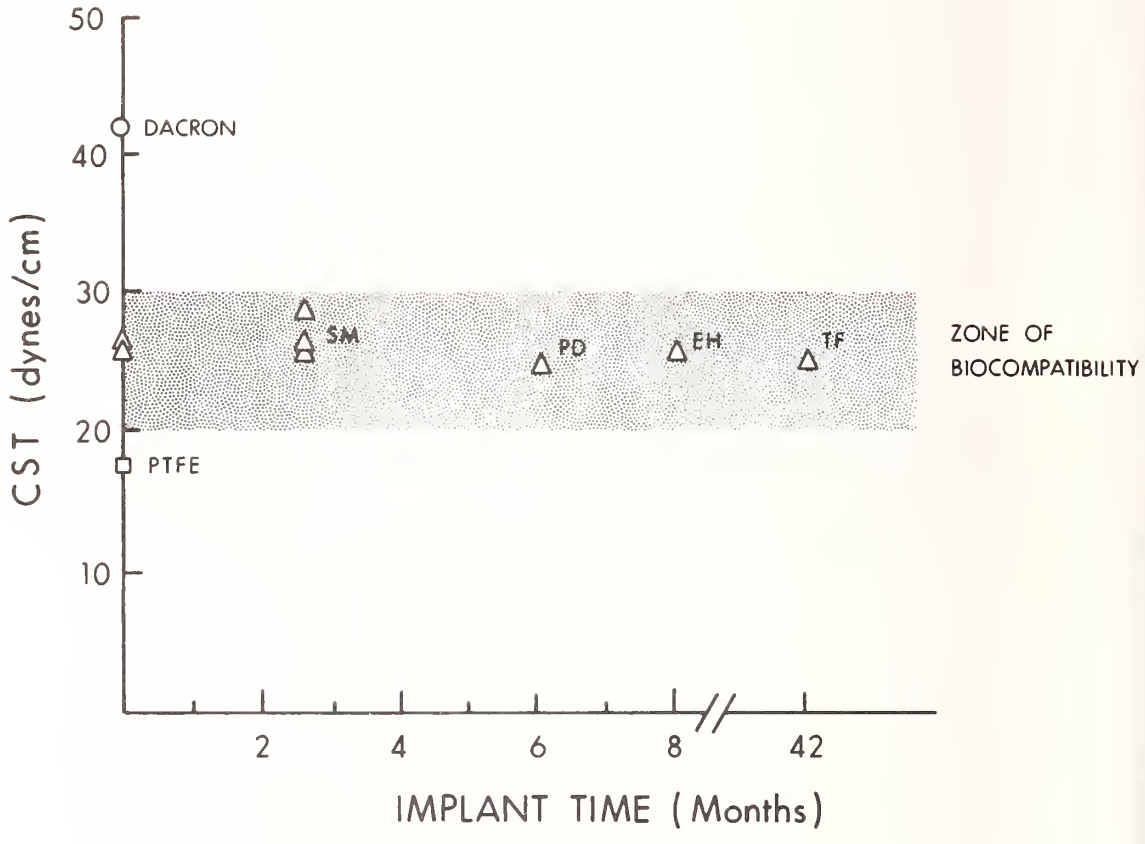


Figure 5. CST value after various periods of implantation.

3.3 ATR

The control infrared spectrum is shown in figure 6A demonstrating strong protein bands and weak or absent hydrocarbon peaks. In contrast, some explanted grafts have lipid peaks as demonstrated in the 3½ year sample shown in figure 6B. The presence of this lipoidal material appears not to affect the CST which in this graft was 25 dynes/cm. It should be stressed that even with some lipoidal material within the graft, calcification has not been identified in any explanted samples. The lipid level within the graft appears to be more patient- and hemodynamic-related than graft- or implant time-related. This point is demonstrated in figures 7A and 7B which represent the infrared spectra for two explanted grafts, 8 months and 34 months, respectively. The quantity of lipid in the 8-month sample is significantly higher than that seen in the 34-month sample, even though the explant period differs by a factor of 4.

3.4 Compliance

The work of Abbott [16], has demonstrated that a relationship exists between early thrombosis and graft compliance. In fact, Edwards [17] suggests that late graft failures of the autogenous saphenous vein may be compliance-related. Figure 8 is a plot of compliance versus pressure for the control human umbilical cord vein and several explanted samples of the graft ranging in implant period from 1 week to 36 months. A reduction in compliance is seen with this graft, which we believe is primarily due to fibrous encapsulation of the Dacron mesh material. For comparison, compliance values for PTFE, ASV, and Dacron at a pressure of 105mm are also shown on this plot.

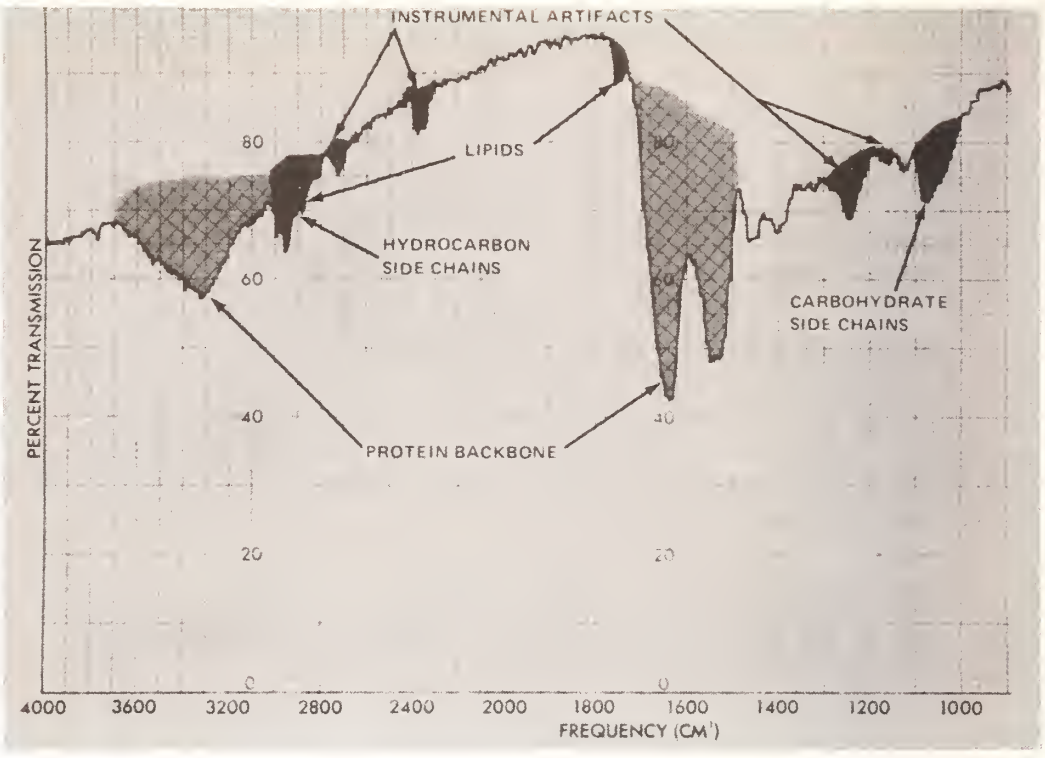


Figure 6A. Typical internal reflection infrared spectra characterizing the pre-implant blood flow surfaces of stabilized human umbilical cord veins as prepared for arterial grafting.

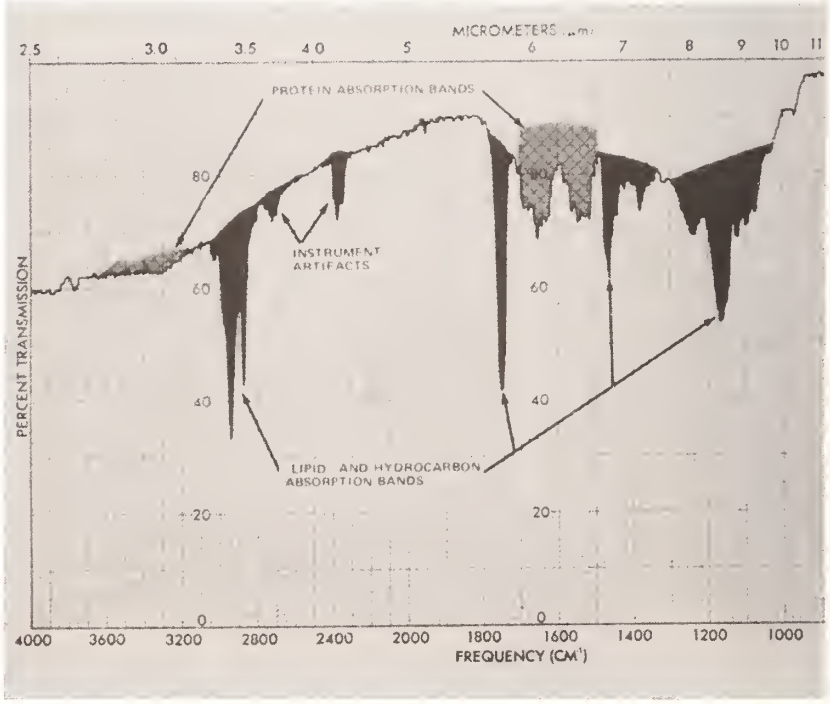


Figure 6B. Internal reflection infrared spectrum characterizing the blood flow surface of an implanted, stabilized human umbilical cord vein as harvested patent following 3½ years service as a human arterial graft.

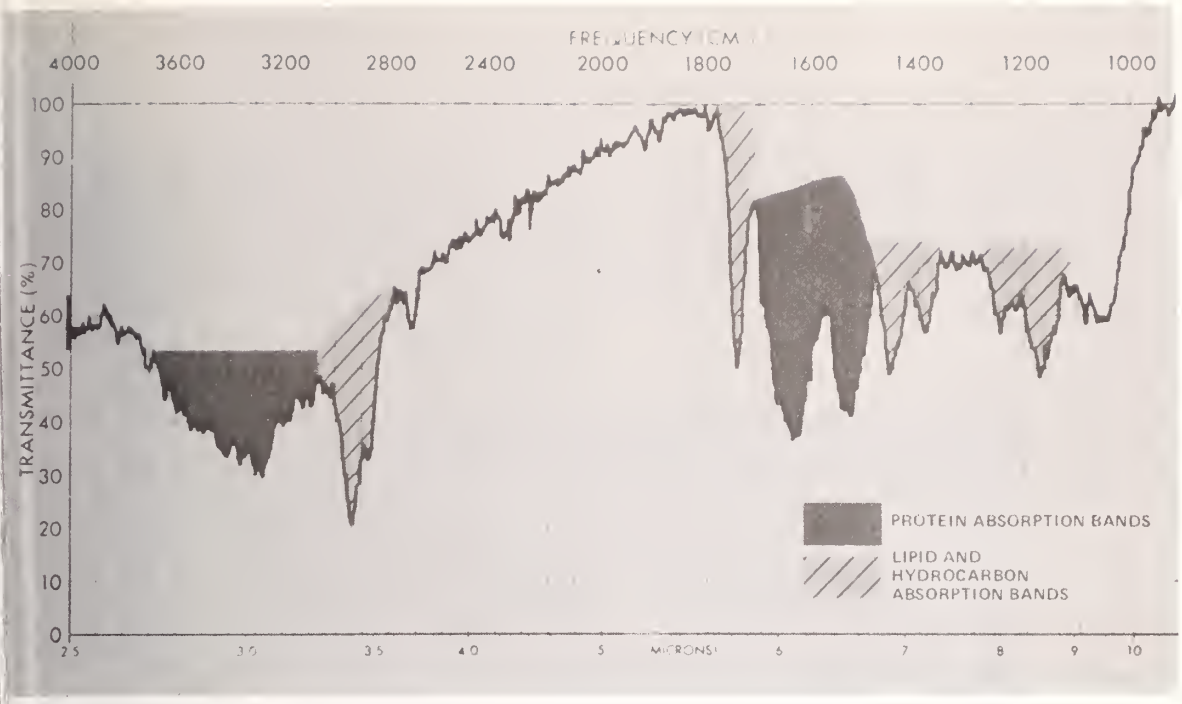


Figure 7A. Internal reflection infrared spectrum of the blood flow surface of a stabilized human umbilical cord vein harvested patent after 8-months implantation as a human arterial prosthesis.

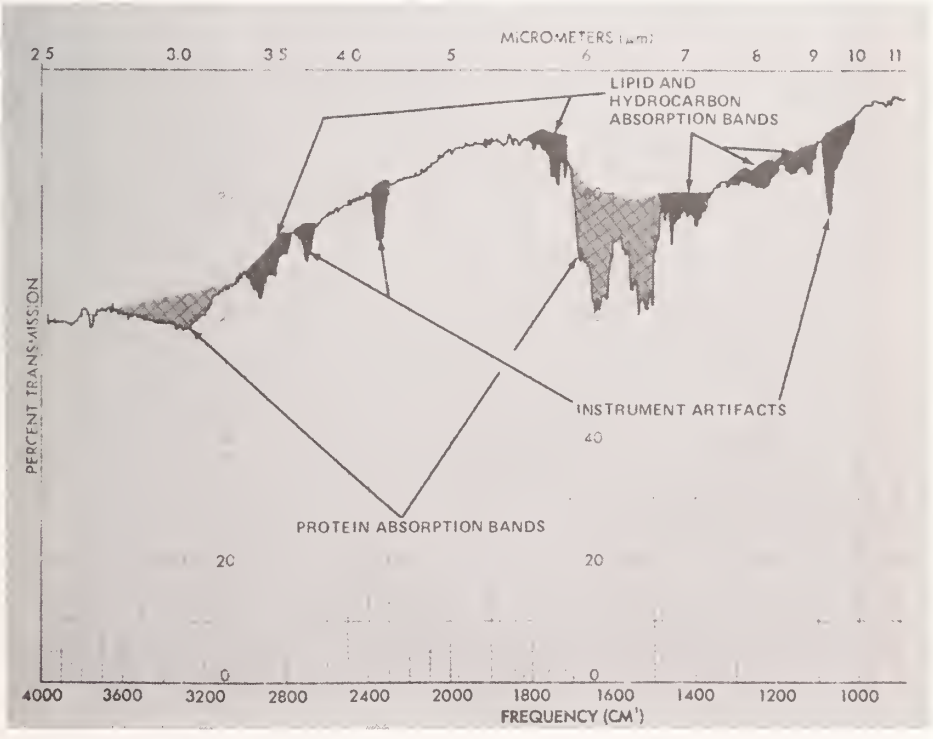


Figure 7B. Internal reflection infrared spectrum characterizing the blood flow surface of a stabilized human umbilical cord vein harvested after 34-months service as a prosthetic arterial graft.

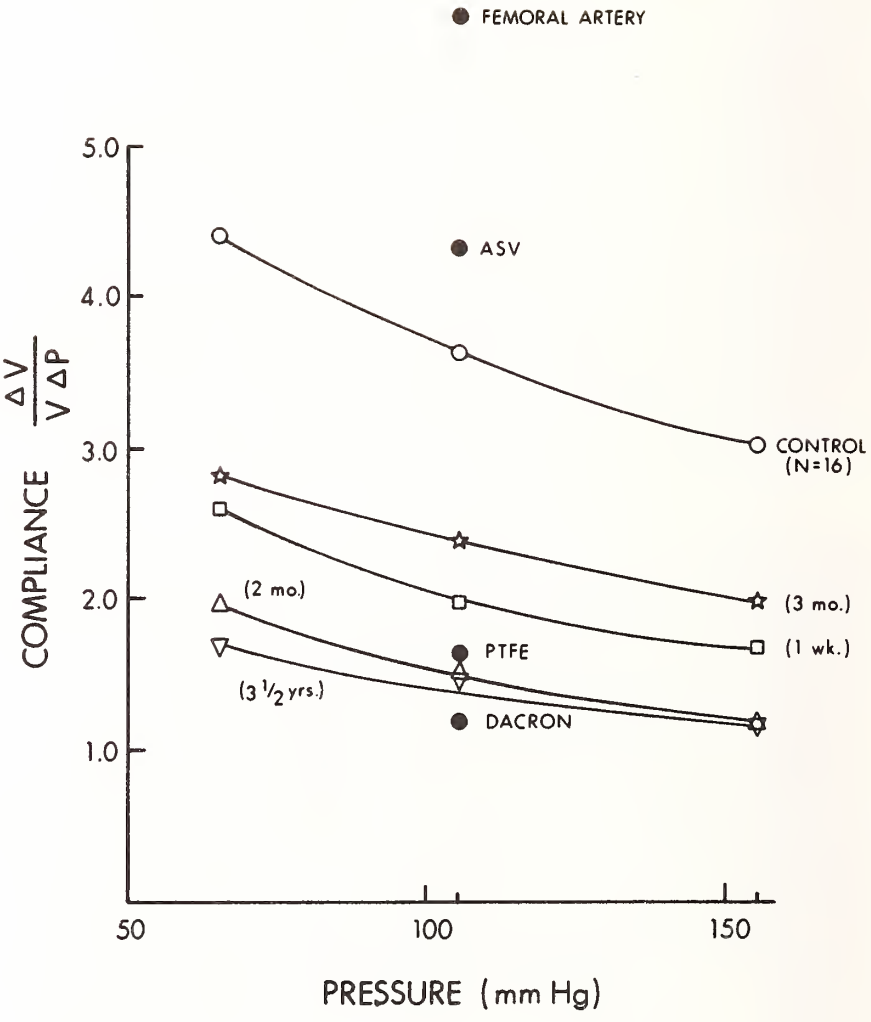


Figure 8. Compliance versus pressure for a series of explant umbilical vein grafts along with other graft materials.

3.5 Morphology

Morphological studies of explanted Biografts® included procedures ranging from gross evaluation to transmission and scanning electron microscopy. Typical histological changes seen in a patent graft are demonstrated by a comparison of figures 9 and 10 which represent a pre-implant and 8-month explant samples, respectively. Shortly after implantation the graft becomes compacted due to the hydrodynamic forces imposed upon the graft material.

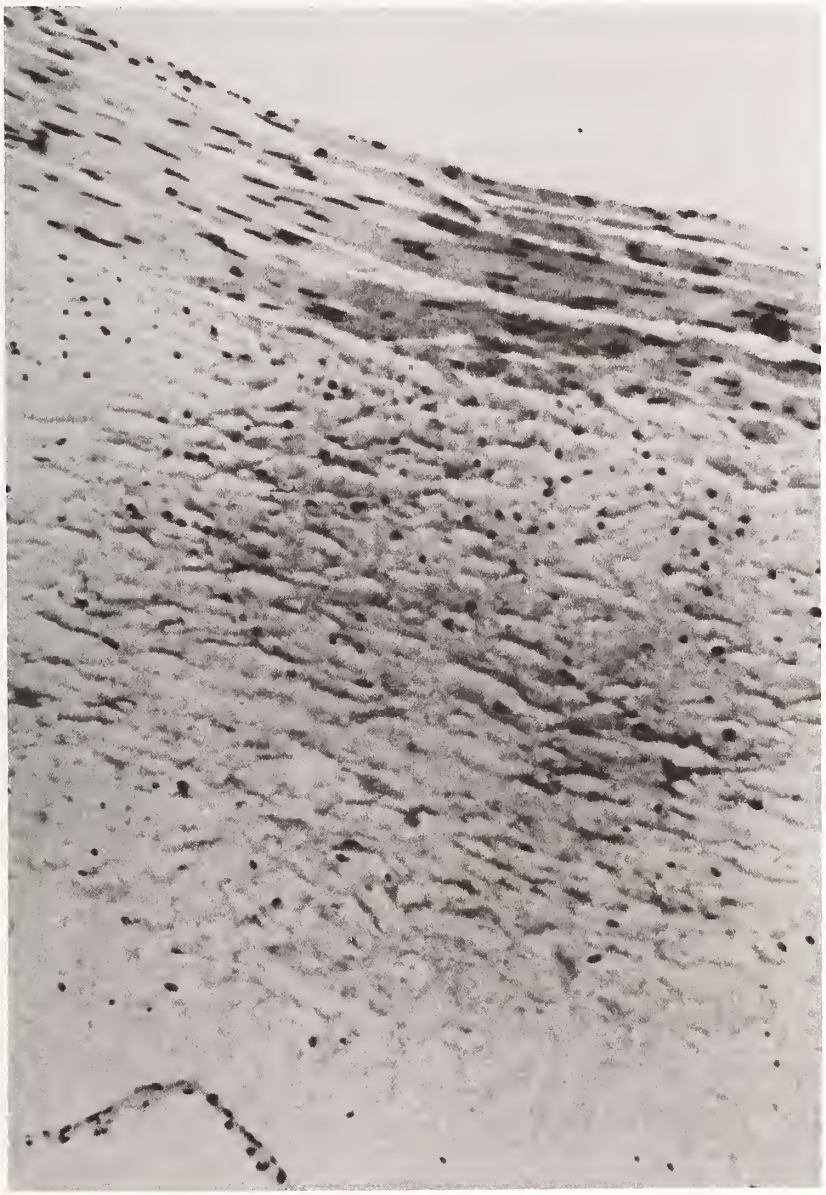


Figure 9. Histological section of pre-implant sample demonstrating the intact media and adventitia.

Figure 10. 8-month explanted sample demonstrating graft compaction and mild reaction around the mesh.

As time progresses, the cellularity of the graft decreases leaving the 42-month sample almost acellular (figure 11). Initially, the reaction to the Dacron mesh is relatively mild and, as can be seen in the 42-month sample, this reaction decreases with time (D). The compressed media is represented by the arrows and still can be distinguished from the connective tissue zone.

At the EM level the internal elastic lamina remains intact as does the external elastic lamina surrounding the smooth muscle cells.

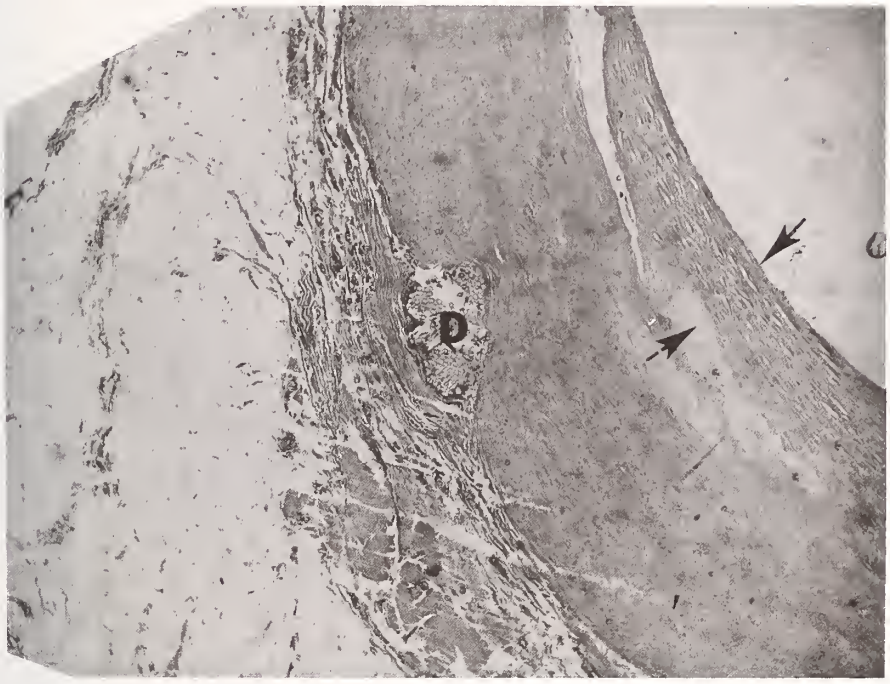


Figure 11. 3½ year explanted sample showing mesh material (D) and the compressed media (arrows).

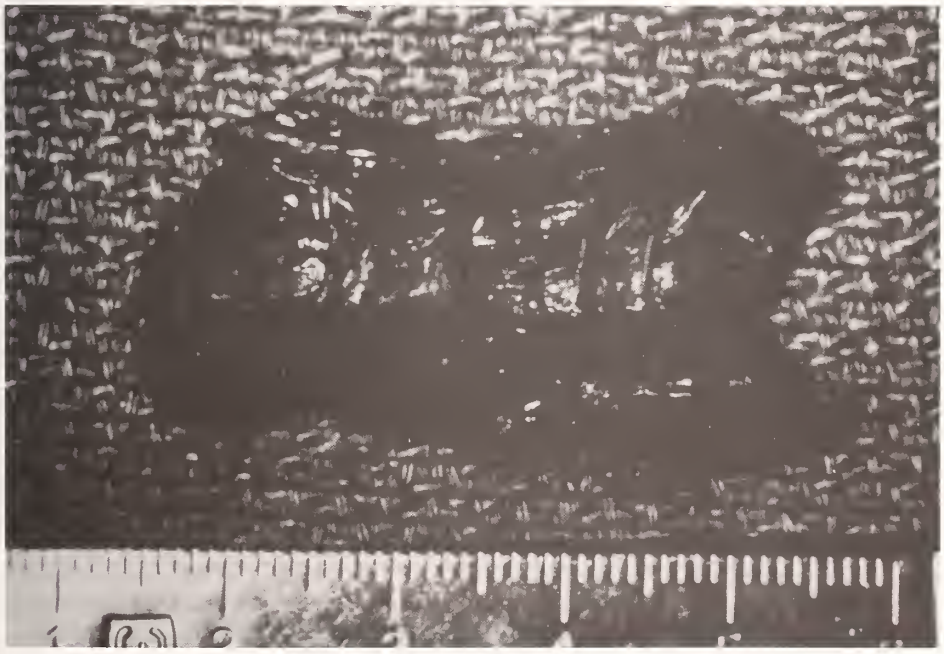
4. Discussion

Acquisition and evaluation of explanted devices has been, and still remains, one of the most difficult problems in the device industry. Most devices are explanted with minimal regard to future evaluation; and, in general, relatively little information is reported in the literature considering the large number of devices being implanted throughout the world. Biocompatibility of graft materials has been evaluated using various techniques ranging from protein absorption studies through animal implantation. In our case the CST was used as an indicator of biocompatibility even though the importance of this parameter has been at issue for many years within the biomaterials field. Dr. Baier has long been a proponent of this concept and its general use has recently become more widespread. Natural blood vessels have a CST ranging from 20-30 dynes/cm which is similar to that of the unprocessed and processed umbilical vein graft. The maintenance of this parameter even in the absence of the endothelial cells has yielded excellent results in the clinic and is currently being used as a routine QA parameter. Patent

grafts which have been explanted as a result of non-graft-related patient death or as a result of graft revision for progressive disease, have yielded CST values around 25 dynes/cm. This has been the case even when lipid has been identified within the graft wall. Explanted graft samples, up to 42 months post-operative, have CST within the biological (biocompatible) range. However, it should be noted that we have no definitive evidence at this time indicating that a CST value outside this range would be an indicator of an unacceptable implant.

Using infrared analysis, explanted grafts typically have strong peaks at $1650cm^{-1}$ and $1550cm^{-1}$ showing proteinaceous deposition on the surface. With some patients IR peaks may also be found at $1750cm^{-1}$ and $2950cm^{-1}$ indicating the presence of lipoidal material within the graft. The age of the sample does not appear to relate to the presence or quantity of the lipid within the graft. Our data suggests that the patient and his blood chemistry are more important in the lipid intake phenomena than the biochemical nature of the human umbilical vein graft. No calcification has been seen in any graft sample to date as evaluated by IR or EDAX. Up to 3½ years post-operative morphological changes which have been identified within the graft are minimal. At gross dissection the lumenal surface of most patent grafts retains its glistening appearance with minimal alteration of the blood interface as can be seen in the 33-month specimen in figure 10A. In a few cases some changes have been seen at gross evaluation. Figure 10B shows a gross specimen obtained at 12 months post-operative where circumferential rings appear to be present on the surface. This sample was functional at the time of explant and the significance of the change is yet undefined. At this time we have no explanation for this change, but it may be a result of lengthening of the graft <u>in situ</u> or excessive graft length at implantation.

Figure 10A. (33-month sample)



10B. (12-month sample)

Gross Specimens

At the light microscopy level the patent graft retains its basic structure with implant periods up to 3½ years. The major changes seen at the light level appear to be a compaction or reduction in wall thickness shortly after implantation due to hydrodynamic stresses, a mild foreign body reaction around the Dacron supportive mesh material, and a reduction in cellularity with time. No neo-intimal hyperplasia has been seen on any graft sample so the internal caliber of the graft maintains its initial pre-implant value. In some sections the internal elastic lamina becomes more visable at the light microscopy level as a result of lipid uptake within this structure. The internal elastic lamina appears to act as a barrier to lipid infiltration into the body of the graft; but, in a few TEM sections some lipid droplets have been seen within the body of the graft.

As the graft ages in situ, some cellular debris and cellular degeneration of the smooth muscle cell is seen at the EM level, however, the external basal lamina around the smooth muscle cells remains intact. The internal elastic lamina which separates the subendothelial zone from the media remains intact, at least up to 42 months, and the general morphological structure of the tanned umbilical vein graft remains intact.

The surface of the Biograft® after processing is similar in many respects to the de-endothelialized surface of the ASV. After delivery the endothelial cells coating the lumen of the vein graft slough from the surface and only a few endothelial cells remain on the graft after processing. The subendothelial layer between the lumen and the internal elastic lamina remains intact and becomes the "biocompatible" blood-contact surface.

A growing amount of data is being published with respect to the relationship between graft compliance and patency. As was shown in figure 8, the pre-implant compliance of the Biograft is similar to that of the ASV and significantly higher than either the Dacron or PTFE graft. With time the compliance of the graft decreases, and this reduction appears to be independent of implant time. We believe that compliance changes are, in part, due to encapsulation of the Dacron mesh surrounding the graft. It is not known, at this time, whether the ultimate patency rate is or is not dependent upon changes in compliance, however, future data may elucidate this point.

5. Conclusions

In general, the human umbilical vein graft has many characteristics similar to the ASV including CST, infrared spectrum, electronegativity, compliance, and morphology. These factors may not in themselves be controlling, but together they characterize a graft material which has yielded impressive clinical results in difficult salvage and pheripheral vascular cases. Data reported in this study were obtained at graft revision, bypass extension, and graft failure; and as a result of this explant evaluation, some general conclusions can be drawn concerning this graft.

1. The subendothelial surface of the Biograft® becomes covered with a smooth proteinaceous layer which does not thicken or reduce the graft's internal diameter with time.

2. The critical surface tension for patent grafts remain constant up to 42 months post-operative at a value of approximately 25 dynes/cm even with the presence of some lipid material within the graft.

3. Lipid accumulation in the graft wall appears to be patient- not graft-related.

4. No calcification of the Biograft® has been seen using any analytical test to date.

5. Compliance of the pre-implant Biograft® is near the ASV, however, reduction of compliance has been demonstrated after implantation.

6. Histologically, a graft becomes more compact as a result of hydrodynamic pressures and loses cellularity with time. The foreign body reaction associated with the Dacron mesh material becomes less pronounced as the implantation period increases.

Questions still remain with respect to the ten-year prognosis for this prosthetic graft, and these, unfortunately, can only be answered after extended implant periods. Thus far, results are impressive, and clinical acceptance of this prosthesis is increasing all over the world.

6. Acknowledgments

The author would like to thank and acknowledge the efforts of all members of the Biograft® retrieval and evaluation team. In particular, special thanks to Drs. Herbert Dardik, Irving Dardik, and I. Ibrahim of Englewood Hospital, Englewood, New Jersey, whose close clinical collaboration and graft retrieval efforts made successful completion of this program possible. Thanks also to Drs. Michael Meenaghan and Joseph Natiella for their detailed TEM and histological evaluations. Special thanks also to Dr. Robert Baier, Ms. Ann Meyer, Charles Ackers, Vito DePalma, and Dennis Goupil for their efforts on surface characterization of the umbilical vein graft, and to Drs. William Abbott, Joseph Megerman, and Gil L'Italien for compliance evaluation of pre-implant and post-implant Biograft® samples. Personal thanks to Debra Creighton for her efforts in typing this manuscript.

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WEAR OF POLYMERIC PROSTHESIS - CLINICAL REALITY, RETRIEVED IMPLANTS AND LABORATORY PREDICTIONS

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Up to 17 years clinical experience with polymeric components of hip prostheses has shown that (a) polyethylene femoral balls have poor wear resistance, and (b) with one exception the major series have generally had no reoperations due to wear or fracture problems in polyethylene acetabulae. Average wear rates expected in up to 10 years use may vary from a low of 40 um/year to a high of 200 um/year, (c) there are at least 5 published reports, each describing between 2 and 6 cases of documented gross wear or fracture of retrieved polyethylene acetabulae, (d) the effect of acrylic cement on polyethylene wear rates is unclear and (e) Delrin has also been used apparently successfully for 10 years in the Christiansen total hip.

Up to 9 years followup with tibio-femoral joints has not yet shown any wear revision problems. Retrieved polyethylene components feature more extensive disruption and deformation than in hips. Knee simulator studies indicated that contact stresses, volumetric and linear wear rates in various designs could vary by x270, x20 and x110, respectively. Patello-femoral results on implant performance are not yet available. Simulator studies of various patellar designs showed that volumetric and linear wear rates could vary x20 and x210 times, respectively. The clinical implications of these data may be worthy of concern. Concern was expressed that (a) the relatively large numbers of annual rates of implant exchanges seen nationwide in this country did not appear reflected in the collections of the current implant retrieval programs and (b) the public dissemination of the retrieved implant data seldom seemed effective.

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1. Introduction

One of our interests in current implant retrieval programs involves the study of wear and plastic deformation observed in polymeric components of various joint-replacements [17,35] (2). This provides a basis for realistic interpretation of problems encountered in-vivo with regard to material selection, implant design and patient usage, i.e. clinical reality. It also provides the essential feedback into experimental design and test protocols for laboratory wear tests and prosthesis-design programs.

The stainless steel and polyethylene materials combination first used in the total hip joint [8] has now been accepted as a very adequate wear combination with up to 14 years followup in some cases [10,21,29]. However, there is now an active search for better alternatives to polyethylene for three reasons. One is that the increasing incidence of such procedures in younger patients has placed considerable demands on the implants due to higher patient activity levels and and longer life expectancies [2,6,18]. Second, the conditions experienced by joint replacements other than the hip are generally much more severe. In particular, the tibial and patellar components of knee-joint replacements are at a considerable disadvantage compared to the acetabulum of the hip joint. Thirdly, certain designs of prostheses, such as surface replacements of the hip, are limited to very thin component wall thicknesses due to space constraints [15]

The objectives of this paper are therefore to review:

1. published clinical observations of wear assessments in various retrieved implants but mainly the hip and knee joints.

2. the role of laboratory wear studies in selection of suitable biomaterials.

3. the wear data gathered from the implant retrieval programs of the University of California at Los Angeles (UCLA) and University of Southern California (USC).

Current state of the art is focused on metal/plastic combinations of total joint replacements. Therefore the specific focus of this paper is on the deformation, creep and wear behavior of the polymeric components.

(2) Numbers in brackets indicate the literature references at the end of this paper.

2. Polyethylene Hip Prostheses

2.1. Clinical reality

The majority of data on wear and creep phenomena from implants comes from the hip joint and then, in rapidly descending order, the knee and ankle joints.

The adverse effects of any polymer, even polyethylene, bearing against cartilage or bone in a hemiarthroplasty situation have been well documented over the last two decades [20,24,26,40,67]. The rapid erosion of the polymer and the severe granulomatous tissue reaction (Fig. 1) to the debris with concomittant loosening of the implant results in disaster.

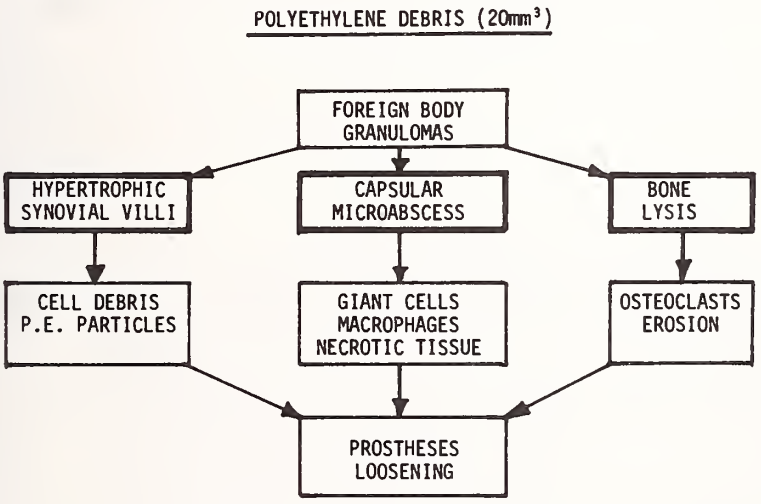


Figure 1: Foreign body granulomas formed as a reaction to the joint debris can effect synovium, capsule and bone. Note that "of the three materials used in artificial joints, high density polyethylene produced the most reaction" [61].

Wear occurs to a much lesser extent in total joint replacements. However, it is not clear which factors control the efficacy of debris removal from the joint. As Dr. Willert has emphasized in this conference, it is the volume of polymer which is retained in the joint that affects the severity of local tissue reactions. Therefore the volume of wear particles produced and their size distribution (for each material and implant design) may together determine the

debris retention rates and severity of the tissue reaction.

Wear of polyethylene acetabulae in total hip joint prostheses does not appear to be a significant clinical problem to date. Muller [41] reported that the wear plus creep seen after 8 to 10 years usage in his revision procedures was less than 1 mm. In his hands, wear did not therefore "seem to be a major problem for 15 to 20 years." Likewise, Leinbach in his series of 2000 hip implantations and experience in replacing 150 other prostheses has never seen more than 1 mm of creep plus wear [34]. In the Mayo Clinic series with up to 11 years followup and more than 10,000 patients, there have been no reoperations due to wear problems [19].

Griffith et al. [29] studied x-ray evidence of 491 Charnley hips with 7 to 9 years followup (average 8.3 years). Of these, 64% appeared to have worn less than 60 um per year. This apparent "wear" included plastic deformation of the socket as well as wear. Experimental studies by Buchholz and Strickle [5] showed that the plastic deformation in 20 mm diameter hip joints could vary from 280 to 380 um depending on the contact stress (8 to 15 N/mm2). In the clinical setting, this would imply an actual wear rate as low as 40 um/year. Thus, when the creep component was corrected for, 10 years of cup use would represent only 0.4 mm or less wear.

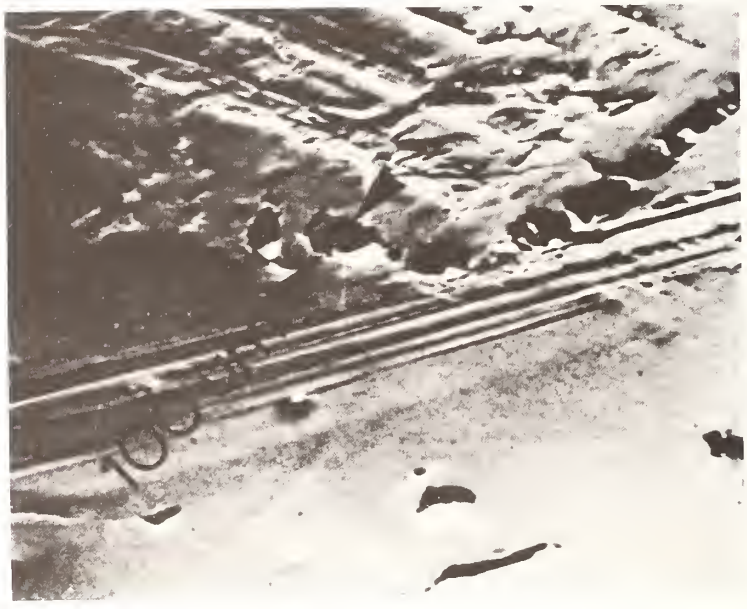


Figure 2: Highly polished wear areas in dome of acetabular cup (19 months implantation; original SEM magnification x48).

Figure 3: Disrupted areas of polyethylene surface in acetabulum (SEM magnification x330).

This finding of insignificant cup wear was confirmed by Beckenbaugh et al. [3] in their radiographic study of 333 Charnley procedures with 4 to 8 years followup. However, in this and the study by Clarke et al. [16], concern was expressed about the errors possible in radiographic measurements of such small quantities.

The highest range of radiographic migration reported in 4% of the cases by Griffith et al. [29] averaged 240 um/year, representing perhaps 210 um actual wear/year. Thus, in 10 years or more, wear of 2 mm would have taken place in these cups.

2.2. Retrieval experience

In our combined USC/UCLA retrieval experience, we have a group of approximately 30 retrieved polyethylene sockets with 6 months to 8 years followup. There were no examples of gross wear. The majority of the sockets varied from highly polished minimal wear appearance (Fig. 2) to moderate surface disruption (Fig. 3) due to impregnation with acrylic particles [17].

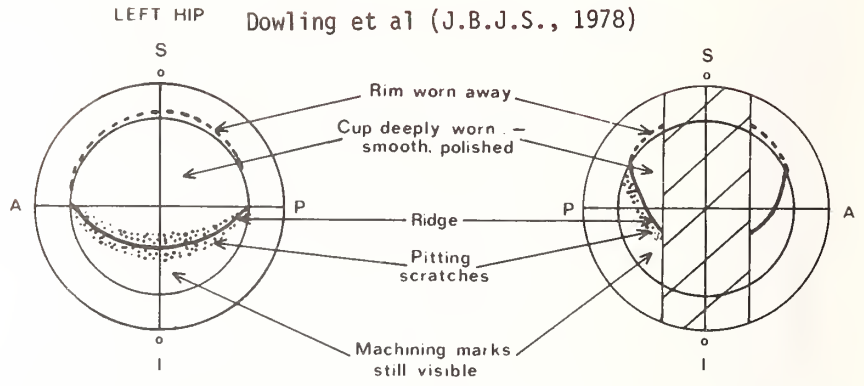


Figure 4: Details of worn areas in Charnley sockets [21].

The cup appearances (Fig. 4) were essentially similar to those reported elsewhere [21,47,48]. Therefore at this time we have made no effort to quantify the actual wear plus creep phenomena present. At this time we have no information as to whether wear debris per se resulted or was involved in these cases of implant loosening.

Semlitsch [55] has described a Muller hip socket with 5 mm wear present after 7 years use. However, the femoral ball had a large scratch on the surface which probably accounted for this severe wear. Amstutz ([1]) removed an acetabular component which had worn through from the reverse direction. The cup was loose in the acrylic mantle and had become severely abraded by the bone and remaining acrylic sheath such that at revision surgery, a large hole was visible all the way through the polyethylene.

Studies reporting major problems with wear or fracture of the polyethylene acetabulae have fortunately appeared only rarely to date (Table 1). Rose et al. [47] reported that "the wear rate can vary dramatically for essentially identical prostheses but from different manufacturers." However, this paper did not identify which of the prostheses were at fault or quantify the wear described.

Bonvallet and Dautry [4] reported severe wear and bone erosion in 6 out of a series of 34 Charnley hips with less than 6 years followup. One had fractured into 5 fragments. Rutt [50] reported 3 fractured polyethyelene sockets (2 traumatic) of the Charnley-Muller type at 4 to 6 years followup. Salvati et al. [51] reported two referred cases

where 2 Muller-type sockets had fractured into several pieces through the remaining 1 mm wall thickness at the location of the superior deep groove. Followup times were 4 1/2 and 6 1/2 years (fig. 5).

NO. OF CASES	F.U. YEARS	ACETABULAR PROBLEM		TOTAL	NO. IN SERIES
		WEAR	FRACTURE (+ WEAR)		
Bonvallet [4]	< 6	5	1	6	34
Rutt [50]	< 6		3	3	1095
Salvati [51]	< 7		2	2	R*
Greenwald [28]	2		2	2	R*
Lazansky [33]	< 7	2	1	3	1000
				16	

* Referred Cases

Table 1: Summary of studies reporting gross wear or wear plus fracture of polyethylene hip sockets.

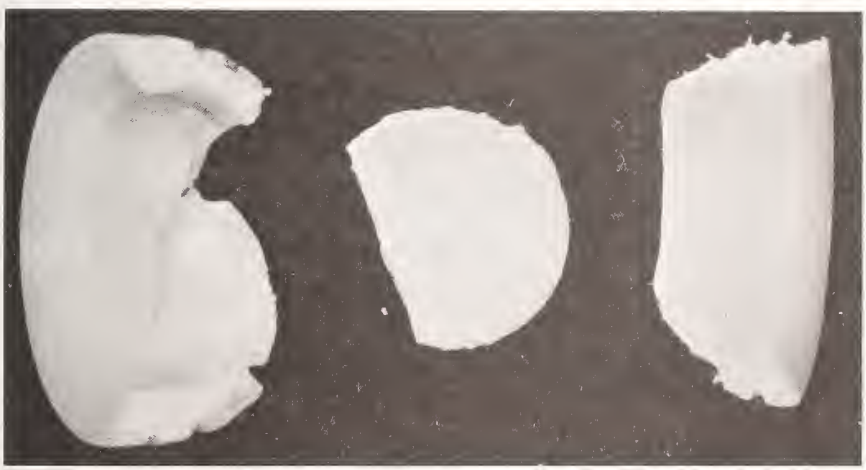


Figure 5: Worn and fractured polyethylene acetabulum described by Salvati etal. [51].

Greenwald [28] has two fractured Muller-type sockets, one of which was in three fragments after only 2 years of use. Lazansky [33] has revised 3 sockets where there was excessive wear present (Table 2). Revell et al. [44] described a salvaged Charnley prosthesis which had excessive wear present after only 2 years use. There was also considerable bone loss attributed to the effects of the debris.

1000 Cases in Series, (Charnley-THR)
200 Cases > 5 Years
32 Cases: Wear 1mm at > 5 Years

3 WEAR REVISIONS

AGE	CAUSE OF REOP.	F.U. YEARS	NOTES
44F	X-ray Wear	7 (Bilateral)	Almost Worn Out
66M	X-ray Wear	> 5	Almost Worn Out
52M	Stem Fx/Acetabular Wear	> 5	Severe Wear

Table 2: Summary of wear data recorded by Lazansky [33] in Charnley sockets.

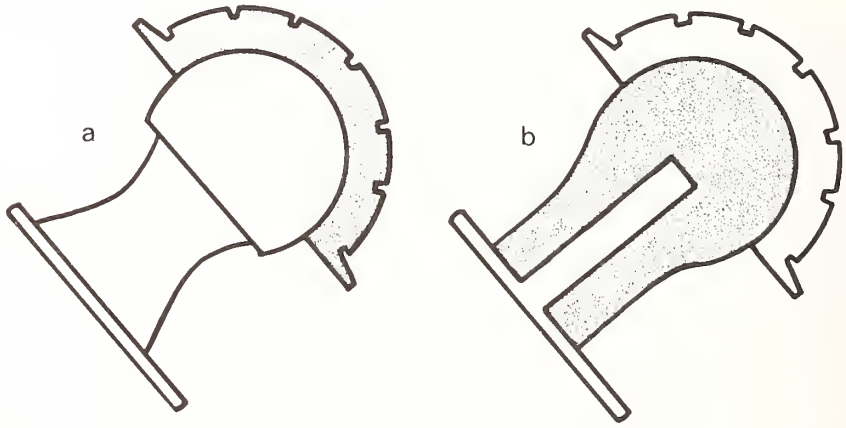


Figure 6: Polyethylene and other materials (a, concave) have been used for either the acetabulum (a, concave component) or the femoral ball (b, convex component). Experimental and clinical studies [44] indicate that convex polyethylene surfaces exhibit severe wear.

2.3. Reversed polyethylene geometries

The geometry of the polyethylene plastic component also appears to have a significant effect on its wear resistance (Fig. 6). Laboratory tests have shown that there is "significantly more polyethylene wear from a polyethylene ball/metal socket than from a polyethylene socket/metal ball configuration" [44]. The authors' clinical results with 16 polyethylene femoral components in a surface replacement hip design confirmed that large quantities of polyethylene debris were released with this configuration. The average increase in wear rates was a factor of 6 as derived in simulator tests using the reversed polyethylene configuration in ankle prostheses [41]. This brings up the question of the convex polyethylene patellar designs which will be discussed in section 5.

3. Other Polymeric Hip Prostheses

3.1. Polyester (Polyethylene Terephthalate) hip components

Polyester has been used in acetabular cups as well as the femoral balls of trunnion type of prostheses (Table 3). Scheier and Sandel [52] compared 56 polyethylene and 43 polyester acetabulae in a clinical radiographic wear study. They concluded that the average polyethylene wear (migration) was "somewhat slighter" than the polyester. They did not comment on any clinical, radiographic, reoperation or histological findings.

MATERIAL	FEMORAL	ACETABULAR	RESULT
Polyester		●	Similar PE (1976)?
Polyester (AP4)	●		Abandoned (1976)
PTFE		●	Abandoned (1963)
PTFE + MICA		●	Abandoned (1972)
Polyacetal (CO-P)	●		Abandoned (1974)
Polyacetal (HoP-Delrin)	●	●	In Use (72-80)*
Polyethylene	●		Abandoned (1974)
Polyethylene		●	In use (63-80)*

Table 3: Historical summary of polymeric material and design choices in the hip joint (PE: polyethylene).

Polyester (AP4) was used with a special radiochemical surface treatment [53] in the ball on a trunnion type of hip prosthesis [64]. However, the accumulating polyester debris seen after 3-4 years use had a deleterious effect on the

joint tissues and resulted in a foreign body reaction, bone resorption and loosening [65]. This difference between polyester wear rates in the femoral ball or acetabular cup may reflect a sensitivity to geometrical factors as described by Revell et al. [44].

3.2. Polytetrafluoroethylene (Fluon, P.T.F.E.) components

The initial Charnley design incorporated P.T.F.E. acetabulae. 300 of these had to be removed due to the granulomatous tissue reaction to the extensive erosion products of P.T.F.E. [7,9]. A P.T.F.E. socket reinforced with mica particles (Fluorosint) was also used clinically for 3 years and then abandoned due to similar aggressive foreign body reactions [54].

3.3. Polyoxymethylene Polyacetal hip components

The plastic copolymer "Ertacetal" reported by Semlitsch [54] was initially tried for the ball of the Weber-Huggler trunnion type of hip prosthesis. However, this material underwent biodegradation and "shrinkage" within 6 to 24 months of implantation and was abandoned [50,54].

The homopolymer polyacetal "Delrin" has been used as the trunnion collar and acetabulum in the Christiansen hip system [13]. Clinical experience over 10 years with approximately 7,000 cases has provided satisfactory results [14]. As yet, there have been no detailed publications on clinical or radiographic results of this procedure.

3.4. Laboratory wear studies

There is no universal agreement as to the clinical significance of the various wear screening programs using simplified specimen geometries [23,49]. Charnley has argued over the years that there is absolutely no correlation between clinical and experimental wear rates, citing his experiences with polyethylene and polytetrafluoroethylene as examples [10]. Despite these reservations, the UCLA wear screening program [36,38] has ranked a variety of polymers, many of them with known clinical behavior (Table 4). These data verified that polyethylene was the polymeric material of optimal wear resistance. The polymers known to perform poorly in joint replacements such as nylon, polyester and polytetrafluoroethylene ranked x530, x860 and x1600, respectively, above polyethylene. Delrin ranked at x47 and above. However this material has apparently been very successful in the Christiansen hip designs [14,23].

Joint-simulator studies have little better to offer in

the way of consistent data. So much so that Dumbleton [22] remarked "It is my view that simulators are useful but that they have been improperly used" and Swanson [57] concluded in his review that "no significant feature of current practice has been based on results obtained in simulators."

It is generally believed that the volumetric wear rate of hip prostheses does not vary with joint diameter whereas the linear wear rate does [66]. However,

MATERIAL		COEFFICIENT OF FRICTION	WEAR RATE RATIO POLYMER/UHMWPE
Extruded UHMWPE		.04-.08	1.0
Moulded UHMWPE		.05-.10	0.9
Carbon Fiber-Reinforced UHMWPE		.05-.13	1.6
Celcon	Polyacetals	.13-.22	40
Delrin 150	Polyacetals	.15-.23	60
Delrin 500	Polyacetals	.17-.22	47
Polybutylene		.10-.50	107
Polypropylene		.18-.25	132
Ekonol-TFE Copolymer		.13-.22	500
Nylon 6/6		.11-.16	530
Ryton R4 (PPSt glass fiber)		.25-.28	700
Ryton BR07 (PPSt graphite fiber)		.30-.33	830
Polyester AP-4		.25-.40	850
PTFE (Teflon)		.08-.12	1600
Hytrel		.25-.50	28,000
Urethane (Conap RN 2000)		.06-.08	Disintegrated

Table 4: Relative ranking of polymers in the UCLA wear screening program.

AUTHOR		THEORETICAL	LABORATORY	IDEAL BALL DIAMETER (MM)
CHARNLEY	1969	✓ (PTFE)		< 25
GALANTE	1973	✓		< 25
WEIGHTMAN	1973		✓	22 ≡ 32
GOLD	1974		✓	> 28
BUCHOLZ	1975		✓	> 38

Table 5: Published theoretical and experimental predictions on ball diameter versus wear.

when the relevant studies discussing volumetric wear are compared (Table 5), there are two theoretical studies indicating that the small-ball diameters are optimal, one experimental study which says it makes no difference and two which suggest that it is the larger diameter balls which are optimal.

4. Polyethylene Tibial Components

4.1. Clinical results

Polyethylene and carbon-fiber reinforced polyethylene appear to be the only two polymers currently used in knee joint replacements. Publications to date deal only with the polyethylene type and generally relate to complications of tibial component loosening. In the Mayo Clinic's series with a 9 years experience of approximately 3000 polycentric and geometricknees, no components have had to be removed because of wear problems [19]. With 1 to 5 years followup of 461 total condylars, the Hospital for Special Surgery also reported "no evidence of polyethylene wear or distortion" [31].

4.2. Retrieved tibial components

A number of reports have described deformation and surface damage on removed polyethylene tibial components. However, a prosthesis which has failed and requires revision may reflect a multitude of problems including malpositioning and impingement against either bone projections, osteophytes or acrylophytes. Subluxation/dislocation, loosening, acrylic fragmentation and impaction may have occurred as well as actual wear. The question then becomes what represented ac-

tual "normal" wear and what was surface disruption of the polyethylene created by the environment of the failing knee? For example, Shoji et al. [56] described polyethylene damage on four polycentric total knees. Three apparently failed due to malpositioning and one due to impingement of the bony tibial spine on the femoral component. In the latter case, there was no loosening and "no abnormal wear." The three other cases had "wear" areas with less than 1 to as much as 5.3 mm penetration.

Reckling et al. [43] reported an ex-vivo study of one geometric knee which was particularly interesting because it had not failed at the time of the patient's death. With 8 months use, the polyethylene components had considerable damage due to impingement against both femoral bone and acrylic cement.

Walker and Hsieh [62] examined 15 knee prostheses removed after 7 to 42 months. The surfaces of the non-conforming condylar prostheses (e.g. Marmor, DuoCondylar) appeared relatively smooth but did contain many small pits (less that 0.5 mm wide) as well as cracks perpendicular to the sliding direction. The authors indicated that these surface defects were probably the result of fatigue pitting [60,62] In contrast, the conforming tibial components contained

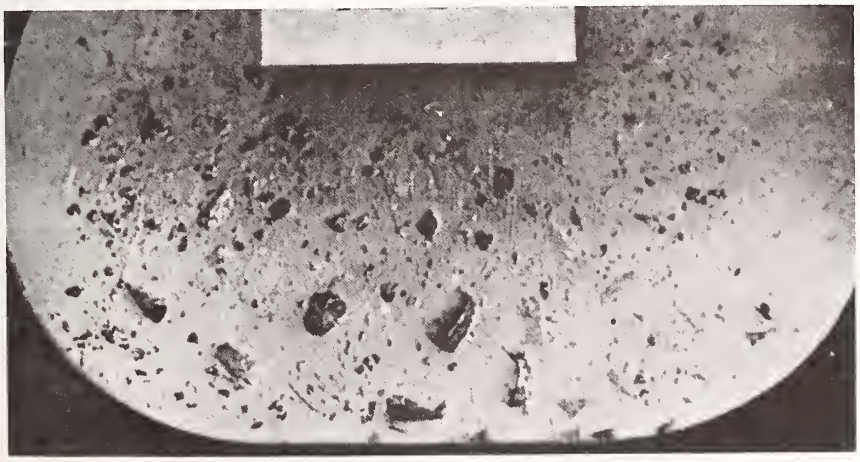


Figure 7: Pitting on ICLH tibial component after 7 months use (both components were found to be loose [60].

Figure 8: UCI knee component removed after 3 years use.

numerous scores and wide pits up to 4 mm wide and 0.5 mm deep (Fig. 7). The authors demonstrated that three-body abrasion from entrapped cement particles was the likely cause of these larger defects.

Figure 9: Fracture of a small ICLH polyethylene tibial component, history unknown [66].

Our USC/UCLA retrieval experience with approximately 40 condylar units was similar to that reported previously [17,47,62]. The tibial components of knees generally featured much more evidence of deformation, impaction and abrasion by acrylic (and bone) and other surface defects than did the hips (Fig. 8). So far, none of the studies of retrieved knee joints have been able to provide any quantitative assessment of the relative wear magnitudes seen either with respect to prosthesis design or whether acrylic cement ingress had occurred.

As in the polyethylene acetabulae, cracking and fracture of polyethylene tibial components have also occurred. Weightman et al. [66] reported one case of gross brittle fracture of an ICLH tibial component and another with two large cracks appearing in the same region (Fig. 9). The authors concluded that "polyethylene is susceptible to degradative fatigue in the human body and that when subjected to cyclic bending ... gross fracture can occur."

4.3. Laboratory wear studies

At present the only laboratory wear study of tibial-femoral prostheses appears to be that by Treharne et al. [45,58] and Young et al. [70]. Their simulator data on tests of 5 condylar knees were extremely provoking (Table 6). These data indicated that the volumetric wear rates (indicative of extent of debris formation) for the 5 prostheses varied by a factor of x20, depending on geometrical design and magnitude of the contact area. The linear wear rates (indicative of wear-out problems) varied

TYPE	* DYNAMIC CONTACT AREA Amm^2	DYNAMIC AREA RATIO	TOTAL AREA mm^2	% of TOTAL AREA	† WEAR RATE $mm^3/10^6$ cycles	VOLUMETRIC WEAR RATIO	‡ LINEAR WEAR RATE $um/10^6$ cycles
RMC	1385	8.8	3220	43	1.58	1.0	1.1
T-Condylar	283	1.8	2834	10	3.69	2.3	13
UCI	278	1.8	3481	8	32.41	20.5	117
Townley	263	1.7	2926	9	13.74	8.7	52
Anameric	158	1.0	2633	6	13.83	8.8	88

* area ewept by condylee in 60° flexion arc

† aseumed polyethylene deneity = $0.935 mg/mm^2$

‡ volumetric wear rate divided by area A

Table 6: Summary of experimental wear tests on total knee replacements illustrating contact area and other geometrical effects [45,68].

TYPE	NOMINAL CONTACT STRESS N/mm^2 (P.S.1)	RATIO
Charnley Hip	5.2 (750)	1
ICLH	0.01 (14.5)	0.02
Geometric	0.9 (130)	0.17
Duocondylar	11.6 (1700)	2.3
Marmor	26.9 (3900)	5.2
PE yield stress	14-21 (2-3000)	3.4

Table 7: Comparison of predicted Hertzian contact stresses for 4 designs of total knee replacements [60].

by a factor of x110 for the same reasons. These were calculated assuming that the wear occurred uniformly across the dynamic contact area. Further confirmation of the tremendous variation in knee design contact stresses comes from the study by Trent and Walker [60]. They calculated that the peak contact stresses for 4 types of condylar knees (Table 7) varied by as much as x269.

5. Polyethylene Patellar Components

The results on patellar resurfacing implants do not appear to be in yet, apart from the results of hemiarthroplasty procedures performed with polyethylene patellae [24].

TYPE	* DYNAMIC CONTACT AREA $A(mm^2)$	AREA RATIO	VOLUMETRIC WEAR RATE $mm^3/10^6$ cycles	VOLUME WEAR RATIO	LINEAR WEAR $um/10^6$ cycles	LINEAR WEAR RATIO
RMC	840	8.6	6.1	1.0	7.3	1.0
Townley	172	1.8	82	13	476	65
T-Condylar	113	1.2	131	21	1160	159
Universal	104	1.1	160	26	1538	211
RMC - F.T.	98	1.0	136	22	1388	190

* area swept by condyles in 80^o flexion arc

volumetric wear rate divided by area A

Table 8: Summary of experimental wear tests on patellar components of total knee replacements [46].

Treharne [46] has performed laboratory simulator stu-

dies on 5 designs of patello-femoral prostheses (Table 8). Their data showed that the volumetric and linear wear rates of the various designs varied by factors of x22 and x211, respectively.

6. Polymeric Ankle Components

6.1. Retrieved implants

Groth et al. [30] reported on bilateral ankle autopsy specimens, one with polyethylene (15 months implantation) and one with carbon-fiber reinforced polyethylene (CPE, 12 months implantation). The polyethylene unit was extensively worn (Fig. 9) and featured wrinkles perpendicular to the wear direction as well as "tiny cracks and pits." There was much less wear of the contralateral CPE ankle prosthesis (Fig. 10). Removed tissues featured minimal amounts of carbon fibers (20 to 100 um) and carbon debris (5 to 8 um). Tissue reaction appeared minimal.

Figure 10: Polyethylene tibial component of Oregon ankle removed after 15 months. Extensive scoring was noted [30] due to wear as well as surface defects inflicted on the talar unit during insertion.

6.2. Simulator wear studies

The simulated wear study of the ICLH ankle design by Kempson et al. [32] predicted that less than 0.3 mm linear wear would occur after 10 years use. The tibial and talar components were polyethylene and stainless steel, respectively. Reversing this configuration increased the wear rates by a factor of 6 on average [44].

Figure 11: Carbon-fiber reinforced tibial component of Oregon ankle removed after 12 months [30] in the same patient as the component shown in Figure 10.

7. Discussion and Conclusions

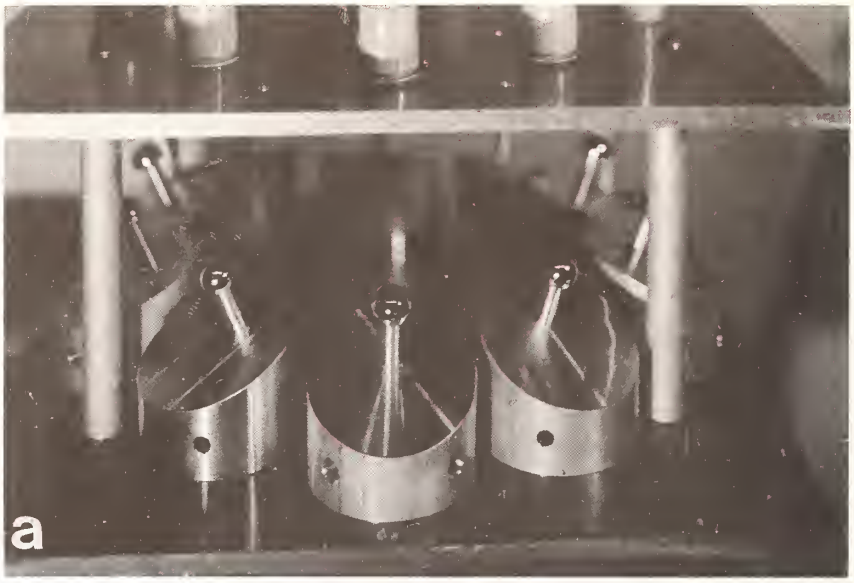
Overall clinical results with 7 to 14 years experience of hip prostheses illustrates that wear of the polyethylene acetabulae has not been a problem. Radiographic estimation of average wear rates vary from less than 0.04 mm/year to perhaps a high of 0.2 mm/year. However, despite this, there are at least 5 disquieting reports of gross wear and even fracture of the polyethylene sockets. The explanation of these phenomena or understanding of their future clinical significance is today uncertain.

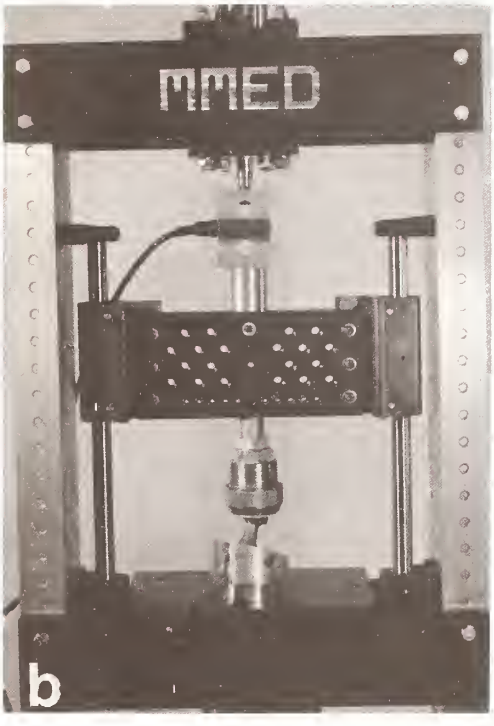
It has been suggested that the acrylic particles may contribute the severest form of damage to the polyethylene joint surfaces [17,48,62]. Certainly the visual effects are very dramatic. However, the few attempts at quantitative verification of such proposed "accelerated" wear rates by acrylic contamination are conflicting. Ankle simulation studies by Revell et al. [44] indicated that "the damaged polyethylene wore at its usual rate." In contrast, McKellop et al. [38] measured a 36 fold increase in wear due to acrylic particles trapped between the surfaces of their friction and wear specimens. However, this could in part reflect the differences between the stainless steel [32] and titanium-6Al-4V [38] alloys tested. Therefore it is uncertain whether the ingress of acrylic particles could account for the gross problems described above. Bonvallet and Dautry [4] and Rose et al. [47] implicated manufacturing variability on the abnormal and inconsistant wear results of the polyethylene.

In the tibio-femoral prostheses, up to 9 years experience apparently has not resulted in any significant wear problems requiring revision. What is not clear is whether any tissue reaction to wear debris accelerated or was indeed even totally responsible for these clinically loose prostheses. There have been many tibial components removed due to gross loosening and these generally featured much more extensive deformation and abrasion than was seen in the hip [44]. It is likely that, with time and improved fixation concepts, the knees will provide considerable additional problems with polyethylene deformation, wear and fracture. The contact stresses calculated for various designs has been shown to vary by as much as x270 [60]. In addition, simulated knee studies of various prostheses have predicted linear wear rates varying by as much as x120 [45,69]. Therefore, in the much more severe environment of the knee joint, it is anticipated that polyethylene deformation and wear will be considerably worse than that encountered in the hip to date. Revell et al. [44] suggested that the annual production of 57 cu. mm. of polyethylene debris, as seen in the hip, was a tolerable level. Some of the patellar resurfacing components clearly exceed that level (Table 8).

Polyethylene patellar replacements are at a peculiar disadvantage because of the high loads imposed, their limited contact areas and convex geometries. The clinical results are not in yet for the patello-femoral prostheses. However, one laboratory simulator study predicted very high wear rates indeed for four types of patellar resurfacings [46]. It is therefore likely that patellar wear will compound the problems of the knee joint replacements.

The issue of wear of convex or concave polyethylene





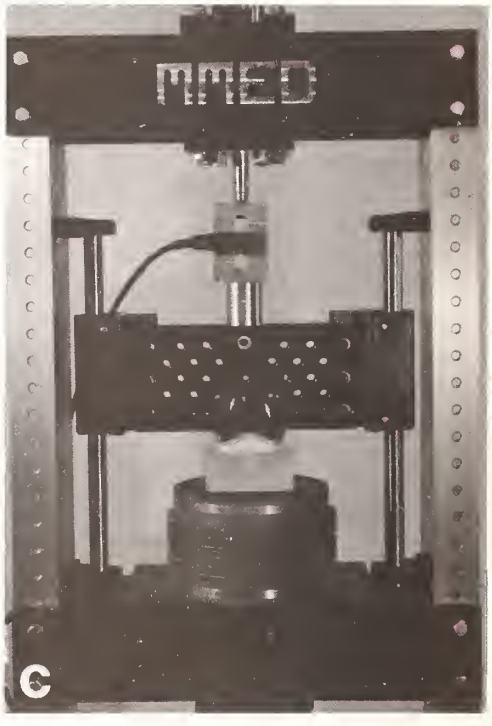


Figure 12: USCATS (Universal Scientific Computerized Anatomical Test System) test equipment installed in Orthopedic Hospital.

a) close-up view of 10-channels of hip joint wear simulator with dynamic loading capabilities controlled by USCATS computers.

b) one of 5 USCATS/MMED universal load frames programmed to test STH total hip prosthesis.

c) load frames can be adapted to many test configurations, in this case a condylar knee prosthesis.

components has not been satisfactorily resolved. One study suggested that the wear can increase 6 times for convex polyethylene ankle prostheses and has clinical evidence of wear problems from convex polyethylene femoral prostheses [44]. However, the Christiansen hip prostheses has been using this geometry with Delrin in thousands of cases with satisfactory results [14,23]. Other joint replacements such as the shoulder, elbow and ankle are also being designed with convex polyethylene components. Is there a conflict between design and material selections?

One of the problems of wear and deformation analyses of retrieved implants is that it is a case of a too few, too late. The numbers of procedures performed per year may number 100,000 for hips and 80,000 for knees [42]. Yet only a relative handful of the 8 to 20% revision rates find their way for analysis. In addition, the implants may have failed for a variety of biological and/or mechanical reasons which too many times can only be guessed at. Even then it is difficult to both retrieve sufficient clinical and radiographic data and quantify any changes detected. Lacking these data and with the need to provide a predictive service to orthopaedics rather than a retrospective or historical outlook, the Orthopaedic Biomechanics Laboratory of Orthopaedic Hospital is planning a series of experimental tests of actual hip and knee prostheses. The experimental USCATS facility incorporates computerized test-frames similar to that described by Young et al. (68,69]. The USCATS nomogram depicts the concept of a Universal Scientific Computerised Anatomical Test System. This system includes a ten channel hip simulator (Fig. 12) and 5 individual units (Fig.13) which can be programmed to simulate the load and motion behavior of any selected joint. Thus 15 channels of wear simulation capabilities are available for testing of "off-the -shelf" prostheses as received from the manufacturer. With this capability it is hoped to resolve some of the questions concerning design and material selection for various types of implants.

Acknowledgments

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Discussion

Question (B. W. Sauer, University of Mississippi): I would first like to complement Dr. Clark for an excellent presentation. His presentation has clearly demonstrated the problems associated with the analysis of retrieved implants. Contradictory data can be easily generated when all factors influencing the implant are not considered during its analysis. Factors such as patient age, weight and activity level; surgical technique, including complications and errors; adequate identification of the materials used in the implant etc. must be taken into account before meaningful comparisons can be made between implant designs or materials.

Answer: Dr. Sauer's comments highlight for me the difference between a meaningful implant-retrieval program and wasted effort. It is all too easy to gather a hardware collection of 19 of this, 5 of that and 1 of everything else. However, assessing the clinical relevance of these removed and/or falied implants is a different story. The reality is that the clinical data is the hardest to collect and is frequently incomplete as well as being the most difficult to quantitatively assess. Dramatizing only a little for example, the life expectancy for any unilateral prosthesis in an arthritic hip of a 40 year old male farmer in Iowa is completely different from that of a 40 year old lady from New York with two bad rheumatoid hips and other joint involvement. In addition, the surgeon's technique may play more of a role than the implant hardware he uses. Insertion of a large stem with poor cement packing may result in failure by loosening. Insertion of a smaller stem with a thick integral layer of cement may eventually result in some proximal loosening followed by stem fracture. Once again the patient, surgeon and implant are inextricably related and must be carefully reviewed as a system.

In conclusion, while we consider implant-retrieval program a potentially valuable source of data and are extending our USC retrieval system, we are also exploring the use of detailed clinical and radiographic analyses of large clinical series as well as extending the role of bench testing of the associated implants.

Question (H. Willert, University of Goettingen, W. Germany): Mr. Clark said no knee implant had been removed because of wear. My questions are: 1) were there implants removed because of loosening, and 2) if this was true, have you encountered, that loosening also can occur as a result of excessive wear?

Answer: Excluding infection, implant loosening is accepted as the major cause of joint-replacement failure as described in many clinical publications and various implant-retrieval programs. However, there has generally been little or no histopathological analysis work done on the interface tissues to determine conclusively whether wear

debris and the associated foreign body response was either wholly or partially responsible.

It is, therefore, impossible to answer Dr. Willert's major question directly. However, to answer it indirectly, the wear debris/tissue reaction phenomena would appear a very powerful mechanism in causing the implants to fail. Charnley's experience with 300 hip implants failing due to Teflonomas, the severe granulatomous reaction to excess PTFE debris [7], is a powerful remainder. Similar problems have also been encountered more recently with other polymers (Table). Even polyethylene debris can produce exactly the same result 20,24,26,40].

Revell et al. [44] correlated the design features of ankle, knee, and hip prostheses with regard to polyethylene debris in the tissues and their clinical rates of loosening. They found that "bone resorption and bone death were most commonly associated with the presence of abundant polyethylene particles in macrophases and giant cells. Such a cellular reaction, often seen with accompanying fibrosis, were seen in the articular soft tissues and also invading the bone of the implant bed". Their conclusion was that such polyethylene debris formation can result in implant loosening. They also noted that the amount of polyethylene debris and severity of cellular reaction were greater in relation to the tibial component of knee protheses". Faced with this evidence, I believe that Dr. Willert's concern about wear debris and tissue reactions is well justified.

INFORMATION UTILIZATION

Considerations Concerning International Standards for Accumulating and Reporting of Implant Experience with Cardiac Pacemakers

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Introduction

Implantable cardiac pacemakers have been in use for nearly two decades. Initially implanted to treat Stokes-Adams attacks, pacemakers are now indicated for a wide variety of defects of the conduction system of the heart. Recently control of tachyarrhythmias has become an area of investigation. With expanding indications, the number of implanted pacemakers has grown to several hundred thousand worldwide.

Technology has changed considerably over these decades. Discrete circuits in epoxy have given way to hybrid circuits hermetically sealed in metal cans. Mercury-zinc cells have been superceded by those based on lithium resulting in longer-lived pacemakers. The early pacemakers simply supplied an electrical stimulus to the heart. Sensing of cardiac activity became the next step. Now pacemaker parameters can be adjusted non-invasively for diagnostic purposes and to address the changing needs of the patient.

The large number of pacemakers in widespread use and a rapidly changing technology are at once the causitive and limiting factors in pacemaker standards work. Pacemaker standards work began in the Association for the Advancement of Medical Instrumentation (AAMI). After

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[1]Secretary, Joint Working Group ISO TC150/SC2/WG2, IEC SC 62D WG6

[2]Chairman, Joint Working Group ISO TC150/SC2/WG2, IEC SC 62D WG6

developing a draft standard under contract to the FDA, [1] [3] international standards work was started with participation from both the International Organization for Standardization (ISO) and the International Electrotechnical Commission (IEC) in a joint working group.

The working group is made up of clinicians, clinical engineers, manufacturers and government officials from several countries. From its inception the working group has emphasized writing standards which have clinical relevance and benefits. Accordingly, meetings are arranged to afford opportunities for clinician involvement. Care is also taken so that innovation may proceed unhampered.

A draft on pacemaker labeling and test methods is presently in preparation for final ballot. [2] The current working group project is a standard for manufacturers' reports of implant performance of pulse generators. [3] A pacemaker is defined as a combination of a pulse generator and a lead. [2] As the pulse generator is the element which most frequently needs replacement, this is the focus of current work.

The following discussion attempts to summarize basic considerations and current status of work on implant experience reporting.

1. Working group objectives

By implant performance we mean the experience with pacemakers implanted in patients. Because pacemaker patients are, for the most part, living lives typical of their age groups, they are active and mobile. Characterizing implant experience with pacemakers has the same uncertainty as characterizing any aspect of health of a large population.

Characterizing implant experience with pacemakers can be historical and of little value if pursued for its own sake. It was necessary to define the clinical value and the practical reasons for such reporting. The working group determined that the principal reason for reporting implant performance is to aid in managing pacemaker patients. A secondary objective is to provide information of use to the clinician in selecting a model for implant.

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[3] Figures in brackets indicate the literature references at the end of this paper.

These decisions have important implications for what aspects of implant experience are of interest and how experience is presented in reports.

2. Reports of value in patient management

For a report to be of value in the management of an individual patient it must say something relevant about his pulse generator. This requires a discriminating view of experience with pacemakers of the same model. Recent experience with pulse generators of the same manufacturing group or period is most relevant.

A clinician often has patients under his care with pulse generators from a number of manufacturing groups as well as manufacturers. With current reports which discriminate by manufacturing groups, he can take an equally discriminating view of patient management. Based on experience with the related manufacturing group, one patient may require close follow-up, possibly replacement of his pulse generator. Another patient with a pulse generator from a different manufacturing group may require less attention based on reports of implant experience with that group.

Clinical decisions to replace an implanted pulse generator or to leave it implanted both entail risk. Hence, the value of pertinent implant experience information.

Implant performance reporting in the past has effectively averaged experience over a given model and over time. This is roughly analogous to the weatherman giving you the average daily temperature, humidity and precipitation over the last three years in your region of the country. What you need is a report on local conditions today. In an emergency your welfare may depend on such a discriminating report. The same is true of the pacemaker patient.

3. Reports of cumulative implant performance

Among other pulse generator performance characteristics the working group has determined that the overview of a model is of value at the time of selecting a pulse generator for implant. Cumulative performance is viewed as showing an overall track record of a given model. However, the draft standard asks that care be taken to warn the clinician that such reports tend to obscure differences in recent experience of each manufacturing group of the model.

4. Issues currently under discussion

Incomplete information

Several factors including patient mobility cause a significant number of pulse generators to have little or no follow-up reported to the manufacturer after implant. Thus, at any point in time the manufacturer's implant experience information is incomplete. Even with periodic follow-up, pulse generator function cannot be concretely verified beyond the last follow-up event. Clinical centers, even those with large studies, only cover a small percentage of the pacemakers in use. These reports have value as indicators of overall model experience. However, insufficient numbers exist in these studies to show variation by manufacturing period.

The concepts of active and passive systems have been advanced to help in considering the problem of incomplete information. The passive system (i.e. available data) relies on assumptions about the data which is missing. An active system (i.e. close follow-up) based on a random sample of devices may provide information upon which to characterize some aspects of the population of implanted pulse generators.

Unreported mortality is one example. Recent pacemaker patient mortality rates have been reported in several published studies. [4-6] These studies show that an active follow-up system on a sample basis could give an accurate model for use with the passive system. Unreported explants is another area where the active system may provide a model of the population of implants. These approaches are undergoing careful analysis in the working group.

To further reduce the problem of incomplete data, better communication of experience is necessary from clinician to manufacturer so that he, in turn, can report on a thorough and timely basis. Clinician guidelines in this area will be included in future projects for the working group.

Failure

The present draft divides explants down into categories without using the term "failure". There are several reasons for this:

1. For a given patient, an out-of-specification device may not be a clinical problem and the clinician may elect to let it remain implanted. The same performance in another patient may require explant.

2. A patient may have unusual intracardiac signals which cannot be sensed properly by a pulse generator. Some consider this design failure.

3. A pulse generator which ceases to function due to normal battery exhaustion after providing the expected duration of a service can no more be considered a failure than a car which runs out of gas.

Characterization of explanted pulse generators is fundamental to any system of experience reporting and appropriately a subject of thorough discussion in the working group.

In summary, international standards for implant experience reporting for implantable pacemakers are on their way. The working group has the multidisciplinary experts necessary to write a challenging, yet practical standard. Several issues have been resolved but major ones remain.

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AN ANALYSIS OF 130 REMOVED TOTAL HIPS AND KNEES

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Retrieval analysis is an efficient means of monitoring and evaluating the problems associated with total joint replacements. In 5 years, 130 prostheses have been collected from 8 hospitals in the Chicago area, including 75 hips and 52 knees. All study data are summarized and coded for computer analysis.

Total hip replacements are being removed at a relatively constant rate with no evidence of an increase in removal with time. In contrast, the majority of total knee replacements collected were removed within 3 years of the original surgery. Fractured and cracked components appear to be almost always associated with loosening. Unlike most other TJR components which usually debond at the bone-cement interface, femoral stems, when loosened, generally debond at the cement-component interface. Such debonding may ultimately lead to gross component loosening.

1. Introduction

Total joint replacement has proven to be a highly successful procedure for the rehabilitation and restoration of persons crippled by severe arthritis. The results following total hip replacement are particularly dramatic with recent clinical series reporting good to excellent long-term ten year results of 91% for the patients followed.[1]

Total joint replacement (TJR) however, is not yet a perfected procedure, particularly for joints other than the hip. Prosthesis design and surgical procedures used to implant TJR's continue to evolve to meet perceived current or potential problems. Monitoring and evaluating the usefulness of these changes is difficult because of the lack of data on both frequency and types of TJR failure.

The most definitive means of obtaining such failure data is through large clinical series where all the patients of a physician or group of physicians are followed. Such series provide information on the actual performance of a prosthetic device and problems unique to a particular procedure become manifest. Although many clinical problems and their incidence can be determined through such a series, many patients and years are required to accumulate statistically significant

data, especially on the failed cases.

An alternative approach is to monitor and evaluate TJR performance by the retrieval and examination of removed TJR implants. The study of such retrievals, when coupled with surgical observations at the time of arthroplasty revision and the clinical history of the patients, can yield detailed information on the in vivo function of the implant and the conditions which led to its ultimate removal.

Retrieval studies cannot give absolute failure rates, since the patient population from which the sample is drawn is unknown, but TJR failure modes and their relative rate can be determined. Also, not all implants which may be classified as clinical failures come to removal so that retrieval studies do not monitor all failure modalities.

Nevertheless, retrieval analysis provides an efficient means of obtaining detailed information on the in vivo behavior of implants, particularly the failed implants which are of greatest interest, and is a good means of monitoring and evaluating the failure modes of TJR's in use.

This paper describes the TJR collection and analysis methods used at the Rehabilitation Engineering Program of Northwestern University; selected data on retrieved hips and knees is presented.

2. Materials

Over a period of six years, 130 prostheses were retrieved, including 75 hips and 52 knees; all were removed for clinical failure. The original participants of the study were six surgeons associated with the Northwestern University Medical School Hospitals. The study was then gradually expanded to encompass eight hospitals in the Metropolitan Chicago area with twenty-one contributing surgeons; no new contributors have been added since 1978. The surgeons agreed to contribute all removed components so, to our knowledge, all the TJR's removed by these physicians during their participation are included, although we have no way to verify compliance.

Of the 130 prostheses, 61 hips were of the metal femoral component and ultra-high molecular weight (UHMW) polyethylene acetabular component type. In addition, 44 knees were of the type where 1 or 2 metal femoral components articulate on 1 or 2 UHMW polyethylene tibial components. Results from a close examination of the data on these particular 61 hips and 44 knees are presented. The specific prosthesis types are given in table 1.

Of the 61 hips, 44 (72%) were originally implanted by the participating surgeon, 16 (26%) were referrals, mostly from the Chicago area, and one case was of uncertain origin. Of the 44 knees, 26 (59%) were originally implanted by the participating surgeon and 18 (41%) were referrals.

3. Methods

The study included (i) examination of patient medical records, (ii) analytical review of patient roentgenograms, (iii) observations at the time of revision surgery and (iv) postoperative examination of the removed components.

The data form used to code all of the acquired data is given in Appendix I. The form has been reviewed and updated on several occasions and currently conforms to American Society for Testing and Materials (ASTM) standard F-561-78 [2].

The medical history section of the data form is filled in by checking the patient's records and x-rays. The patient is interviewed to confirm and complete the medical history. When practical, a member of the engineering staff attends revision surgery to record all surgical findings; otherwise, the attending surgeon is interviewed.

The prosthetic components and all removed polymethylmethacrylate (PMMA) cement are gas sterilized as a precaution and then examined postoperatively in the laboratory. The postoperative study is normally limited to gross visual examination using a 70X dissecting microscope. The type and amount of prosthesis wear, the condition of the cement mantle about the prosthesis, and prosthesis damage through abnormal component-to-component contact or component-to-bone contact are among the factors which are of interest.

Although the microscopic, microstructural and metallurgical analyses called for by ASTM F-561-78 are not performed routinely, some or all of these detailed tests may be undertaken when compelling circumstances are present. For instance, if the patient history or the removed device suggests a manufacturing or design flaw may have contributed to device removal, then appropriate tests are performed to confirm or allay our suspicions. In other instances some of the retrieval specimens may be examined in detail as part of other laboratory projects.

Complete data collections was not always possible. Of the 130 study cases, 14(11%) have some missing items on the coding form. The items most frequently missing were the patient's exact height and weight, usually caused by a failure to complete the patient interview.

Photographic records taken of select X-rays, during revision surgery and of the removed prosthesis are filed. The components are labelled and stored after testing. Confidentiality of patients' and surgeons' names is strictly maintained.

Data from all medical records and analyses, summarized on the coding forms, are transferred to magnetic tape for storage and later computer analysis [3] using the university computer[1]. Through the use of RIQS [4], this system is capable of storing and sorting all the data for further study using SPSS [5], a package of computer programs

[1]CDC-6600, Control Data Corporation, Palo Alto, CA

specifically designed for statistical analysis. SPSS was developed so that various statistical tests, ranging from a simple correlation between two variables to an extensive non-linear multiple regression involving many variables, could be employed quickly with relatively little effort. A computer display terminal[2] in the laboratory permits on-line, interactive study of the stored data.

4. Results and Discussion

Several terms are used in discussing the results. The following is our definition of these terms:

Prosthesis Loosening: Although loosening has often been defined radiologically, for the purposes of this study, prosthesis loosening is a gross, clinical observation made at the time of revision surgery. A TJR prosthesis component was taken to be loose when, upon opening a joint, the attending surgeon could physically move the component with mild to moderate hand pressure. Such looseness could usually be both felt and seen with blood being expressed from between the prosthesis-cement of cement-bone interfaces.

Cause of Failure: After a careful review of the patient history and postoperative examination of the removed components, a final cause or factor leading to failure of the TJR is determined. As the observations and data used are somewhat imprecise, decisions on the cause of removal were made conservatively and very strong, persuasive evidence was required. Even under such strict conditions, a cause of TJR removal could be identified with confidence in about 70% of the cases, Table 3.

Iatrogenic: Severe malorientation of one or more of the prosthetic components or inadequate patient care leading to immediate, postoperative sepsis were among the factors included under the iatrogenically induced removals category for the cause of failure.

Trauma: Cases were listed in the trauma category of the cause of removals table when a specific major incident such as a fall could be identified as initiating the onset of symptoms which then continued until the time of arthroplasty revision.

Sepsis: Early sepsis was defined, for the purposes of this study, as infections occurring within the immediate 6 month postoperative time period following arthroplasty. All other infections were classed as late infections.

Idiopathic Loosening: There were a number of cases for which a clearly identifiable initiating factor leading to TJR removal was not apparent. These were listed as having been removed for pain only or as a result of idiopathic loosening, where pain is also implied. The category of idiopathic loosening was only used when one or more of the

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[2]Tektronix - 4010 Computer Display Terminal, Beaverton, OR

prosthetic components was observed to be loose at the time of surgery. There is a presumption in this definition. If it were shown that most TJR's which function preperly were, in fact, loose as defined here, then idiopathic loosening could no longer serve as a satisfactory classification since this condition would not necessarily be related to failure. These cases would then be more properly classed as having been removed for pain only.

Pain Only: If neither of the prosthesis components were grossly loose, the case was placed in the pain only category as the reason for removal. Some of the components in the pain only category were removed with very little effort so that suspicions of loosening lingered.

Other cases presented with very firmly fixed components; indeed, considerable effort was required to dislodge some.

The results presented are of two types. The first are those observations thought to be relevant to the clinician and relate to the expected performance of the implants. The second group is related more to information on basic processes and component design. The latter group of results are necessarily more speculative, and need to be continually checked and guided by the data. This speculation is justified on the basis of the potential importance of the results and on the lack of other means of obtaining such data.

4.1. Results Related to Prosthesis Performance

4.1.1. Cause of removal

The most frequent cause of total hip joint revision was idiopathic loosening of one or more of the prosthetic components, table 3. One third of all the removed hips were so classified. The other major causes of total hip removal were trauma (21%) and sepsis (15%). Iatrogenic factors were responsible for only 11% of the revisions.

By contrast, one third of the total knee revisions were performed for iatrogenically induced reasons. The other major reasons for total knee removal wereidiopathic loosening (30%) and trauma (11%).

The knee joint is an anatomically intricate joint, consisting of three separate articulations, multiple constaining ligaments and complex geometries. The relationships between multiple knee motions, rotation, antero-posterior sliding and flexion-extension, and knee joint structures are not yet fully understood. Accordingly, knee joint prosthesis design is a somewhat imprecise art with new designs and surgical procedures continually evolving. All these factors are reflected in the high incidence of technical problems leading to total knee revision.

4.1.2. Time between surgery and revision

The total time period, groups by years, for which the prostheses were implanted before removal is plotted in figure 1 for hips and knees. Both histograms seem to indicate a greater portion of the removals

occurred within 3 years after the original arthroplasty. However, some of the removals were prejudiced toward early failure from the very onset of the arthroplasty, namely those cases involving early sepsis or technical problems. If such cases are eliminated, the rate of total hip removal appears to be approximately constant or even slightly decreasing for at least 8 years. In particular, the data does not support the often expressed fear that the loosening rate may increase with time [9].

On the other hand, the incidence of total knee removal remains elevated for the initial 2 or 3 year postoperative time period even after the iatrogenic and early sepsis cases are removed. Thus, total knee patients may be at increased risk of joint failure during the short-to-intermediate postoperative time period. There were insufficient total knee cases retrieved after long-term use to be able to make any predictions on the long-term survival rates of knees, although no evidence of any upsurge of late (i.e. greater than 3 years) loosening was observed.

Total hip replacement has remained relatively unchanged with regard to overall design concept for the past decade and substantial numbers of patients have been reciving total hip arthroplasties at least since 1972 [6]. Thus, the rate of hip removal is probably not influenced by recent rapid changes in the total hip population. However, the number of patients receiving total knee replacement has been rising in recent years [6]. The lack of long-term total knee data is, in part, a reflection of the relatively few patients with total knee arthroplasties of long duration.

A second measure of TJR longevity is the time period that the arthroplasty functioned before the development of major symptoms, i.e., pain or joint dysfunction, after surgery. This time period, obtained during the patient interview, is, in some respects, a better measure of the successful operative time of the failed TJR's, figure 2. It is the time period that the patient would probably view as the time of successful rehabilitation.

The histograms again show that a very large number of the total knees that ultimately went on to revision had a relatively short symptom-free period even when the early sepsis and iatrogenic cases are eliminated. Indeed, twenty (46%) of the knee patients developed sysmtoms with 3 months and twenty-eight (64%) had symptoms within 1 year after the original arthroplasty. Twenty-six (93%) of these twenty-eight early symptom patients came to revision within 3 years.

The hip curve also shows a number of cases develop symptoms early within 2 years, though certainly not as rapidly as the knee patients. The data also seems to indicate a second group of patients may be developing symptoms 4-5 years postoperatively. Although the evidence is not strong and requires collaboration by further research, the implication of this finding is that perhaps evaluation of new prosthesis designs or procedures ought to be extended to 5 years.

4.1.3. Iatrogenic Cases

Although many of the removed prostheses demonstrated some evidence of technical implantation problems, a certain number had problems that obviously compromised the longevity or efficacy of the arthroplasty. Those cases where such factors significantly contributed to the eventual revision of the arthroplasty were classified in the iatrogenic category.

Fourteen knees and seven hips were revised as a result of problems which occurred at the time of surgery. Most of these problems (95%) were related to improper component implantation, either through inadequate bone preparation (e.g. skewed bone cuts), component malalignment or poor cementing techniques, table 4. None of these cases did well postoperatively.

Thirteen (93%) of the fourteen knees and five (71%) of the seven hips developed symptoms of joint pain or joint dysfunction (such as varus or valgus deformity, joint subluxation or dislocation or limited and restricted range of motion) within 1 year, table 5. In fact, eleven (79%) of these knees and two (29%) of the hips developed symptoms within 3 months following the original TJR arthroplasty and all came to revision within 3 years.

4.1.4. Trauma

In thirteen hip cases and five knee cases, the patient could identify a specific, major incident which precipitated the onset of major symptoms. As a group, these patients did very well postoperatively before the traumatic incident. Twelve (92%) of the hip patients and four (80%) of the knee patients were employed or fully active with minimal use of supports, table 6.

Four (80%) of the knee patients and eleven (85%) of the hip patients reported falling onto the joint which became symptomatic. Interestingly, two of the hip patients and four of the knee patients had other joint replacements which were not affected by the fall and remained asymptomatic. The two remaining trauma hip patients were pedestrians hit by automobiles. The last patient of the group reported straining her knee while lifting her mother out of a bathtub.

4.1.5. Previously revised cases

Six of the knees and twelve of the hip cases presented with a history of multiple surgical procedures, table 7. The arthroplasty had already been revised one or more times (9/12 hips and 6/6 knees), the rest had had other types of major joint surgery such as hemiprosthesis implantation. Of all these cases, four (67%) of the knees and seven (58%) of the hip patients developed new symptoms within 1 year postoperatively. Five (83%) of the knees and nine (75%) of the hips came to a second revision within 3 years.

Although a small number of these multiply-operated cases which eventually failed gave satisfactory long-term results (4-8 years), the majority failed in a relatively short period of time. Patients who

undergo multiple procedures on their joints appear to be at increased risk of early failure.

4.1.6. Fractured Components

Seven fractured femoral stems were recovered in this study, table 8. In six (86%) cases, the patients had a body weight greater then 75 kg (average wt = 86 kg). All seven patients were employed and very active. The average postoperative time period prior to fracture was 4 years (53 months) with a range of 2 to 8 years. The fractured components included 6 of 36 Charnley-Mullers and 1 of 4 Charnleys. None of the 19 Aufranc-Turner stems examined were fractured. As expected, all of the femoral stems were easily removed; none of the actabular cups were loosened.

In three other cases, the UHMW polyethylene acetabular cup was found to be cracked in the region of the weight-bearing dome of the cup, table 9. None of these cups actually fractured, i.e. split in half. All of these cracked cups were of the 32 mm inside diameter design and occurred in women weighing less than 75 kg. These patients were active and did not use any external supports. The average postoperative time period prior to fracture was 69 months with a range of 55 - 82 months.

Examination of the patient X-rays showed that the cement had cracked around each of the components and in one case, the pelvic wall of the acetabulum yielded so that part of the cup and cement protruded into the pelvic cavity. At revision surgery, the components were found to be freely loose from the cement; the acetabular cement was also broken and loosened from bone with a thick fibrous tissue interposed between bone and cement. Thus three of ten loose cups were cracked whereas, none of the 51 non-loose cups were cracked.

Four (14%) UHMW polyethylene tibial components out of twenty-eight Geomedic® type total knee replacements were found to be cracked or fractured through the anterior cross bar, table 10. In contrast to the total hip patients with cracked or fractured components, these patients were very elderly women (average age = 75 years) and were generally inactive; one patient was active with use of a single support. Also, three of the four patients weighed less than 75 kg. Two of the fractures occurred early, at 10 and 15 months, the other two occurred late, at 46 and 68 months postoperatively.

Examination of the X-rays in two cases showed the PMMA cement had cracked and loosened under only one of the tibial plateaux whereas a third case showed general cement disintegration under the entire tibial component. Roentgenograms of a fourth case were not available.

At revision surgery, three of the four tibial components were grossly loose with a fibrous tissue layer interposed between bone and cement. The fourth component was apparently firm but easily removed; a thick, fibrous tissue layer was reported interposed between bone and cement and X-rays showed a lucent line between bone and cement.

Thus three of seventeen loose components were fractured and one of twelve non-loose components was fractured, although there was a large amount of fibrous tissue around this component.

4.1.7. Sepsis

Seventeen (16%) of the 105 cases under consideration in this report were found, through positive culture, to be infected at the time of revision surgery although only twelve of these seventeen were suspected of being infected prior to revision, table 11.

Four (33%) hips and four (80%) knees were revised for early sepsis.

In most of the cases, the components were not found to be grossly loose at revision surgery; two acetabular cups, six femoral stems, one femoral knee component and three tibial knee components were loose.

Late infections occurred at variable postoperative time periods and had various etiologies. However, two knees and five hips previously had multiple surgical procedures and four other hips had a prior history of sepsis, so that, a majority (65%) of all the infected cases had a predisposition toward the development of sepsis. Only three cases presented with a history which indicated no increased risk toward joint sepsis.

4.1.8 Radiolucent lines

A commonly reported intermediate to long-term X-ray finding following TJR arthroplasty is the appearance of a radiolucent line demarcating and separating the radio-opaque bone and PMMA cement. This phenomenon was also observed in the current removal cases, but such a line was not always observed and no correlations could be obtained between the existence of this line and other study observations, table 12. All of the crosstabulations failed the chi-square test at the .05 level of significance.

In particular, not all the infected hips or knees were observed to have such lines. Not all the components found to be clinically loose displayed a radiolucent line on X-ray and conversely, not all the components with lines were grossly loose.

4.2. Results Related to TJR Science

4.2.1. Loosened interface and loosening etiology

The loosened interface varied with component. Since this observation may be important in understanding the etiology of the failure process, the nature of the failed interfaces were recorded. This was necessarily only approximate, since the condition *in vivo* could not be accurately assessed, even at revision surgery. Interface failure was classed as one of three: (i) bone-cement interface only, (ii) cement-component interface only, and (iii) at both interfaces.

A category was chosen if failure was predominantly of that type. Cement-component only failure was assumed if the component, primarily hip stems, came out freely, but all cement had to be forcibly removed. The results are shown in table 13.

A significant observation from this data is that all (31/31) loose total hip femoral components were loose at the cement-component interface. This finding is at odds to the data for the other three components which were loose more frequently at the bone-cement interface and less often at the cement-component interface. The most frequently observed failed interface might be expected to be the one which failed first. If failure occurred first at the bone-cement interface, which in turn led to cement-component interface failure, a significant number of bone-cement only interface cases should be seen.

The implication of this observation is that the hip stems are failing first at the cement-component interface and that this is the weak element in the system. This implication does not have direct data to support it; other processes are possible. However, it agrees with other studies [8] which show failure of this interface leads to high PMMA cement stresses, implying subsequent PMMA cement fracture and bone-cement interface failure. This observation also supports the need for more research on this interface regarding failure processes and prosthesis design.

Another observation from this data is that the metal femoral components of the knee rarely loosen and when they do or when a firmly fixed component is removed, the PMMA cement is firmly fixed to the component and there is not PMMA fracture. This implies that if the PMMA cement remains fixed to the metal, there will be no cement fracture.

The converse is observed with the UHMW polyethylene components, i.e., the acetabular cups and the knee tibial components. Although there were several cases where the cement-component interface only failed, the more frequent observation in these cases was failure at the bone-cement interface or both. In the cases where both interfaces loosened, sections or pieces of cement were sometimes found well adhered to the component or to bone. This implies cement fracture without total failure of the cement-component interface is possible. Thus, failure of the bone-cement interface or cement fracture is the more likely initial factor in the loosening process in these cases.

4.2.2. Wear

There were no components seen in which wear was a primary factor in failure, although wear was observed in many UHMW polyethylene components. Cups and knee tibial components will be discussed separately.

On gross examination, many of the acetabular cups showed evidence of smooth, 2-body wear between metal and plastic, but the amount or depth of wear was very difficult to measure. There were, in effect,

no significant dimensional changes and very little loss of material. The specimen with the greatest measurable amount of wear was the single Delrin cup collected where a reduction in wall thickness of approximately 2 mm was observed after 7½ years of active use.

There were, in addition, several acetabular cups with gross 3-body wear by cement particles. This demonstrates that inversion of the concave surface, by itself, will not prevent particle entrapment and 3-body wear. Another observation, possibly wear related, concerned the cracked cups. Of the three cracked cups, one was Delrin, so only two of the 60 UHMW polyethylene cups showed noticeable cracks. Also, all three cups were loose, suggesting prior loosening as the factor leading to the cracking; none of the 51 non-loose cups were cracked. However, the additional significant factor was that of the ten loose cups, three had been in place for greater than 4½ years. These were the three cracked cups. Thus, the cracked acetabular cups were those that were both loose and had been implanted a long time. No cracks were seen in the remaining seven loose cups which were implanted less than 3 years.

The implication of this data is that some time-dependant process is degrading the strength of the UHMW polyethylene, either wear or material property degradation. Even if occurring, it would pose a negligible problem for up to a 10 year period of use, but it may be of significance in the longer than 10 year period. The numbers to support this hypothesis are small, but it points out a potential problem which should be investigated.

With the knee tibial components, some visible smooth, 2-body wear has occurred with Marmor type components (less than 1 mm in depth) but no cracks have been apparent by gross examination. There is, very frequently, gross 3-body wear by entrapped PMMA cement particles, but this was usually associated with component loosening.

4.2.3. Stress Related Failure

A need for component design and comparison is a criterion of failure. Stress level is one obvious possibility, but material type and biological factors such as disease, etc., are also possibilities.

What factors influence component failure?

Since loosening of femoral stems and knee tibial components appears to be the major problem with hip and knee prostheses, a criterion for loosening is the highest priority. Since loosening implies failure of the interfaces or components, a stress criterion is most appealing.

Does the removal data support a stress criterion for loosening?

To determine this, correlations between loosening and high force variables will be sought. These variables are body weight, patient activity level, trauma and component impingement with edge loading.

For all components, there was no significant correlation between loosening and body weight or between loosening and activity level. All the crosstabulations in tables 14 and 15 failed the chi-square test at the .05 level of significance. However, there was a positive correlation between loosening and trauma and between loosening and component impingement.

With regard to trauma, four of five knees and twelve of thirteen hips that filed due to trauma had loosened components at revision surgery. Impingement of the femur with the anterior tibial lip of Geomedic® type tibial components was frequently observed. Such edge loading generates high bone-cement interface tilting stresses posteriorly, and could possible lead to component loosening.

There were twenty-eight Geomedic® type components. Fifteen of eighteen loose tibial components had evidence of anterior tibial lip impingement; two of the ten non-loose components had this impingement, table 16. The crosstabulations of table 16, passed the chi-square test at the .01 level of significance. These observations support the hypothesis that extraordinary, high stresses can cause loosening, but normal functional loads, even for the heavy or active patient, will not cause loosening. This data does not constitute conclusive support, but the hypothesis is supported by the data available.

Another observation that relates stress to failure is that fractured or cracked components are nearly always associated with loosening. Since broken components would imply relatively high stresses, this implies that loosening generates high stresses. This is expected intuitively and has been predicted from finite-element studies [7, 8].

5. Evaluation of the Northwestern University Joint Implant Retrieval Program

Our implant retrieval program has the inherent problems of a retrospective study and data collection from multiple institutions. Results of high statistical significance are difficult to obtain.

We initiated and have maintained our retrieval program on the basis that it appeared to provide useful information on implant failure. This was a presumption which eventually must be verified; sufficient data has now been collected and analyzed to decide on the actual value of such a program. The questions that must be asked are:

(i) What useful new information has come out of our retrieval program that wasn't already well known or available by some other means?

(ii) Of what use is the information; how will it alter practices or designs?

(iii) Is the cost worth the effort?

With regard to the first question, we feel the most significant results we have seen from our studies are as follows:

1) There is no evidence to support the hypothesis that the total hip loosening and removal rate will increase with implantation time up to 8 years, although there is a rise in the rate of total hip symptom development around 5 years. This suggests that 5 or 6 years might be a more appropriate time period for evaluation new hip designs or procedures. Later, very long-term failure rates are not yet known.

2) Falls and other trauma can cause prosthesis component loosening.

3) Fractured and cracked components are almost always associated with loosening.

4) A previously revised joint is more likely to be revised than an unrevised joint.

5) Radiolucent lines do not correlate well with loosening. Components with no lucent lines can be loose; components with thick lines may not be loose.

6) All loose femoral stems loosen at the cement-component interface. Many UHMW polyethylene components loosen at the bone-cement interface and are also often associated with fracturing of the PMMA cement. The removed polythylene components usually have cement still fixed to the component. In addition, metal femoral components of knee prostheses seldom loosen and almost always have no fractured cement. These observations support the hypothesis that stem loosening is frequently initiated by debonding at the cement-metal component interface and that tibial knee component loosening involves PMMA cement fracture and bone-cement interface failure.

7) High stress due to trauma and impingement is related to tibial component loosening.

8) There were no fractured Aufranc-Turner stems even though they comprised nineteen of the 61 hip cases. Six of 36 Charnley-Muller stems fractured.

This listing leads to the second question of how this information is now being used or will be used. Other investigators may find the information useful, but its use can best be illustrated by examples of how it has influenced our own practices.

First, the ongoing program has influenced our choice of research projects. Loosening of tibial components of knee prostheses is the major problem with knees; our study suggests many aspects of this problem are stress-related. We have instituted a comparative study of the stress distributions about several knee prosthesis designs.

Second, we have avoided being overly concerned with broken components and have concentrated more on prevention of loosening. Third, although not listed here, an observation on many of the loose femoral stems was frequent poor PMMA cement distribution around the stem and poor cement interdigitation with bone. We instituted a study of cementing techniques for delivering PMMA cement to the femoral canal. Clinical trials of the most appealing systems currently available are in progress. Fourth, we stopped work on a wear project because of its minor relative importance over the less than 10 year period. Finally, we have used detailed observations of the bone-cement interface to aid in a project on the biomechanics of this interface.

In addition to these specific instances of direct use of retrieval program results in specific projects and project selection, there have been some positive indirect benefits. The procedures of information collection and dissemination have established and maintained communication between surgeons in our area and our bioengineering team and has allowed the bioengineers direct access to implant patients. Such patient contact is frequently difficult to maintain for a basically engineering group. These contacts have given us a better understanding of the nature of patient and surgical problems

The work of analyzing the retrieval data has created an awareness on our part of the detailed questions and problems of joint implants, a sensitivity that probably would not exist to such a degree without our retrieval program.

We have concluded that these benefits are worth the time and funds required to maintain the program and we plan to continue it in the future. Whether this would be so for other centers must be decided on an individual basis, taking into account the needs and resources available.

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Table 1: Retreived Prostheses

NUMBER OF CASES:

hips -	75
knees -	52
other -	3
	130

PROSTHESIS TYPE:

HIPS		KNEES	
Aufranc-Turner	19	Duo-Patellar	5
Charnley	4	Geomedic	28
Charnley-Muller	36	Marmor	5
T-28	1	Polycentric	2
CAD	1	St. Georg Sled	2
	61	Total Condylar	1
		UCI	1
McKee-Farrar	7		44
Others	7		
	75	Others	8
			52

Table 2 : General Patient Data

105 cases

AGE:	Hips		Knees	
	Number	Percent	Number	Percent
less than 40	9	15%	0	
40 - 49	3	5%	2	5%
50 - 59	11	18%	5	11%
60 - 69	25	41%	24	55%
70 - 79	8	13%	11	25%
greater than 80	5	8%	2	5%
	61		44	

SEX:	hips	knees
males	26	11
females	35	33

WEIGHT:	Hips		Knees	
	Number	Percent	Number	Percent
normal	27	44%	16	36%
overweight	33	54%	25	57%
unknown	1	2%	3	7%
	61		44	
less than 75 kg	36	59%	25	57%
greater than 75 kg	25	41%	19	43%
	61		44	

DISEASE:	Hips		Knees	
	Number	Percent	Number	Percent
osteoarthritis	27	44%	29	66%
rheumatoid arthritis	7	11%	11	25%
traumatic arthritis	8	13%	4	9%
CDH	3	5%	0	
other	16	26%	0	
	61		44	

PRIOR REVISION:	Hips		Knees	
	Number	Percent	Number	Percent
yes	15	25%	8	18%
no	46	75%	36	82%
	61		44	

SYMPTOM DURATION:	Hips		Knees	
	Number	Percent	Number	Percent
less than 1 yr	48	79%	27	61%
1 - 2 yrs	11	18%	12	27%
greater than 2 yrs	2	3%	5	11%
	61		44	

Table 3: Patient Clinical Data

PRIMARY PREOPERATIVE INDICATION FOR REMOVAL OF TJR:

	Hips		Knees	
	Number	Percent	Number	Percent
loosening with pain	35	57%	20	45%
pain only	1	2%	12	27%
sepsis	8	13%	4	9%
dislocation/subluxation	9	15%	5	11%
bone fracture	1	2%	1	2%
prosthesis fracture	7	12%	1	2%
other	0		1	2%
	61		44	

REVISION PROCEDURE:

	Hips		Knees	
	Number	Percent	Number	Percent
replace component	34	56%	14	32%
new prosthesis	17	28%	21	48%
suction-irrigation	6	10%	3	7%
pseudo-arthrosis	3	5%	0	
arthrodesis	0		5	11%
other	1	2%	1	2%
	61		44	

SUMMARY REASON FOR TJR REMOVAL:

	Hips		Knees	
	Number	Percent	Number	Percent
iatrogenic	7	11%	14*	32%
sepsis-early	4	7%	2*	5%
sepsis-late	5	8%	1	2%
trauma	13	21%	5	11%
idiopathic loosening	20**	33%	13***	30%
prosthesis fracture	6**	10%	1***	2%
pain only	2	3%	3	7%
other	3	5%	5	11%
	61		44	

* 2 early sepsis listed as iatrogenic
** 1 prosthesis fracture listed under trauma
*** 3 prosthesis fractures listed under idiopathic loosening

Table 4: List of Iatrogenic Problems

Case	Joint	Technical Problem
1	knee	Malalignment of femoral component(flexed 30^{0}) Tibial component also malaligned.
2	knee	Malalignment - both components.
3	hip	Malalignment of femoral component (introverted).
4	hip	Malalignment of acetabular component.
5	hip	Malalignment of femoral component, stem perforated posterior-medial femoral cortex.
6	knee	Malalignment of tibial component.
7	knee	Too much cement superiorly, poor bone preparation inferiorly.
8	knee	Femoral component flexed, patellar impingement.
9	knee	Tibial component misplaced, set deep and tibial eminance is hitting in intra-condylar notch.
10	knee	Femoral component placed too far anteriorly.
11	hip	Acetabular malalignment.
12	knee	Femoral component malaligned.
13	knee	Bone Fx, tibial side-improper bone cuts.
14	knee	Bone in intra-condylar notch hitting femoral component.
15	hip	Malalignment of femoral component.
16	hip	Improper joint closure, allows subluxation.
17	knee	Femoral-excessive bone removed and excessive cement; Tibial-malalignment and excessive cement.
18	hip	Malalignment of both components.
19	knee	Excessive cement superiorly, impingement on tibial component and soft tissue.
20	knee	Malalignment of femoral component.
21	knee	Tibial component malalignment.

Table 5: Symptom - Free Period of TJR Iatrogenic Cases

Symptom - Free Period	Hips		Knees	
	Number	Percent	Number	Percent
less than 3 mo.	2	29%	11	79%
greater than 3 mo. but less than 1 yr.	3	43%	2	14%
greater than 1 yr.	2	29%	1	7%
	7		14	

Table 6 - Patient Activity, Trauma Cases

HIPS*	working/ active	active with support	inactive
before symptoms	10	2	0
after symptoms	2	6	5

KNEES	working/ active	active with support	inactive
before symptoms	4	0	1
after symptoms	2	0	3

* 1 case missing

Table 7: Time Period of TJR USE
Multiply-Operated Cases

Symptom - Free Period	Hips		Knees	
	Number	Percent	Number	Percent
less than 3 mo.	5	42%	3	50%
greater than 3 mo. but less than 1 yr.	2	17%	1	17%
greater than 1 yr.	5	42%	2	33%
	12		6	

Total TJR Implantation Time	Hips		Knees	
	Number	Percent	Number	Percent
less than 1 yr.	4	33%	3	50%
1 - 2 yrs	4	33%	0	-
2 - 3 yrs	1	8%	2	33%
3 - 4 yrs	1	8%	0	-
4 - 5 yrs	1	8%	1	17%
5 - 6 yrs	0	-	0	-
6 - 7 yrs	0	-	0	-
7 - 8 yrs	1	8%	0	-
	12		6	

Table 8: Summary of Data on Fractured Stems

7 cases

SEX: male - 5, female - 2

WEIGHT: less than 75 kg - 2
greater than 75 kg - 5

PROSTHESIS TYPE:

Charnley-Muller	6 of 36
Charnley	1 of 4
Aufranc-Turner	0 of 19

OTHER JOINTS WITH PROSTHESES:

none	5
contralateral joint	2
contralateral joint and others	0
others	0

PATIENT ACTIVITY:

	working/ active	active with support	inactive
before symptoms	7	0	0
after symptoms	0	5	2

SYMPTOM-FREE TIME PERIOD OF TJR USE:

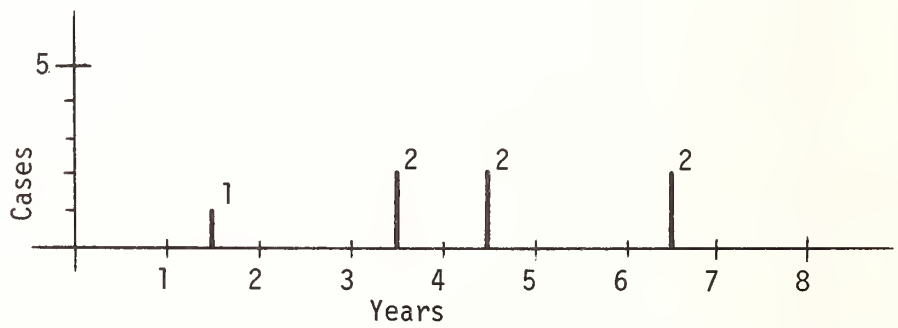


Table 9: Summary of Data on Cracked Cups

3 cases

SEX: male - 0, females - 3

WEIGHT: less than 75 kg - 3
greater than 75 kg - 0

PROSTHESIS TYPE:

Charnley-Muller	2 of 36
Aufranc-Turner	1 of 19
Charnley	0 of 4

OTHER JOINTS WITH PROSTHESES:

none	2
contralateral joint	1
contralateral joint and others	0
others	0

PATIENT ACTIVITY:

	working/ active	active with support	inactive
before symptoms	3	0	0
after symptoms	3	0	0

SYMPTOM-FREE TIME PERIOD OF TJR USE:

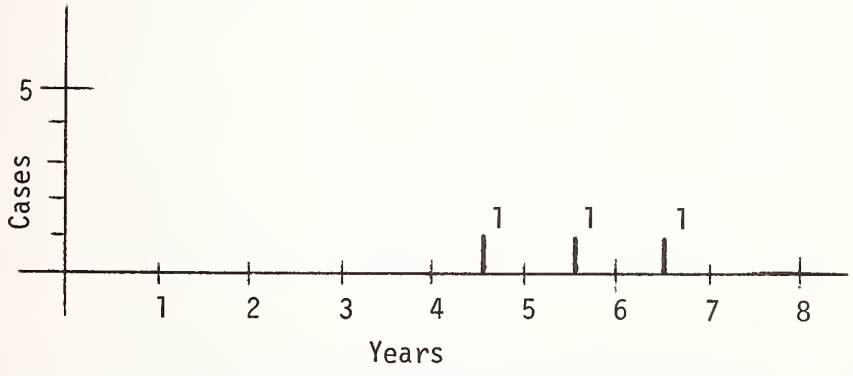


Table 10: Summary of Data on Broken Tibial Components

4 cases

SEX: male - 0, female - 4

WEIGHT: less than 75 kg - 3
greater than 75 kg - 1

PROSTHESIS TYPE: Geomedic 4 of 28
Others 0 of 16

OTHER JOINTS WITH PROSTHESES:

none	1
contralateral joint	1
contralateral joint and others	2
others	0

PATIENT ACTIVITY:

	working/ active	active with support	inactive
before symptoms	0	1	3
after symptoms	0	1	3

SYMPTOM-FREE TIME PERIOD OF TJR USE:

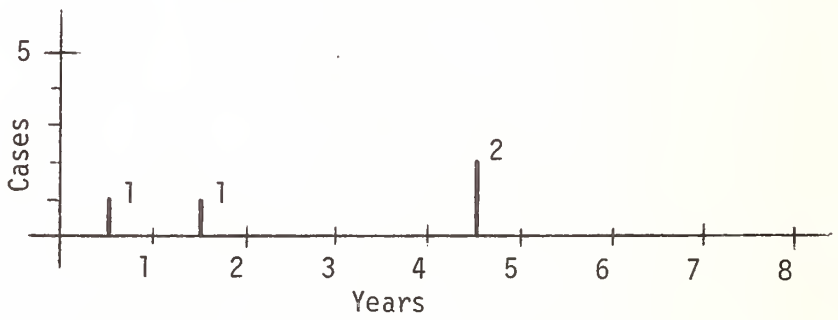


Table 11: Sepsis Cases, Summary Data
17 cases

PREOPERATIVE INDICATION FOR TJR REMOVAL:	Hips	Knees
loosening with pain	4	1
infection	8	4
	12	5

SYMPTOM-FREE TIME PERIOD OF TJR USE:	Hips	Knees
less than 3 mts	2	4
4 - 6 mts	2	0
7 - 12 mts	0	0
1 - 2 yrs	3	1
2 - 3 yrs	0	0
greater than 3 yrs	5	0
	12	5

LOOSENING:		
Hips	- acetabular component	2/12
	- femoral stem	6/12
Knees	- femoral component	1/5
	- tibial component	3/5

Table 12 : Radiolucent Lines and Loosening

Aseptic Hips:

Femoral Stem

	loose	not loose
line present	14	8
no line	17	10

$\chi^2 = .062$

Acetabular Cup

	loose	not loose
line present	6	28
no line	4	11

$\chi^2 = .114$

Aseptic Knees:

Femoral Component

	loose	not loose
line present	4	14
no line	1	20

$\chi^2 = 1.312$

Tibial Component

	loose	not loose
line present	20	10
no line	3	6

$\chi^2 = 1.951$

$\chi^2_{.95} = 3.84$

Table 13: Aseptic Loosened Interfaces

COMPONENT	LOOSENED INTERFACES			NOT LOOSE
	BONE-PMMA	PMMA-COMPONENT	BOTH	
HIP - FEMORAL	0	20	11	18
HIP - ACETABULAR	4	3	4	38
KNEE - FEMORAL	7	1	1	30
KNEE - TIBIAL	12	4	13	10

49 ASEPTIC HIPS
39 ASEPTIC KNEES

Table 14 : Prosthesis Loosening and Patient Weight

Aseptic Hips:

Femoral Stem

	loose	not loose
less than 75 kg.	12	13
more than 75 kg.	17	5

$\chi^2 = 3.095$

2 cases missing

Acetabular Cup

	loose	not loose
less than 75 kg.	8	17
more than 75 kg.	2	20

$\chi^2 = 2.427$

Aseptic Knees:

Femoral Component

	loose	not loose
less than 75 kg.	3	18
more than 75 kg.	2	13

$\chi^2 = .147$

1 case missing

Tibial Component

	loose	not loose
less than 75 kg.	11	10
more than 75 kg.	9	6

$\chi^2 = .025$

$\chi^2_{.95} = 3.84$

Table 15 : Prosthesis Loosening and Patient Activity

Aseptic Hips:

Femoral Stem

	loose	not loose
active	28	16
not active	3	2

$\chi^2 = .109$

Acetabular Cup

	loose	not loose
active	8	36
not active	2	3

$\chi^2 = .315$

Aseptic Knees:

Femoral Component

	loose	not loose
active	3	20
not active	2	14

$\chi^2 = .191$

Tibial Component

	loose	not loose
active	15	8
not active	8	8

$\chi^2 = .384$

$\chi^2_{.95} = 3.84$

Table 16 : Geomedic Tibial Component Loosening Through Anterior Lip Impingement

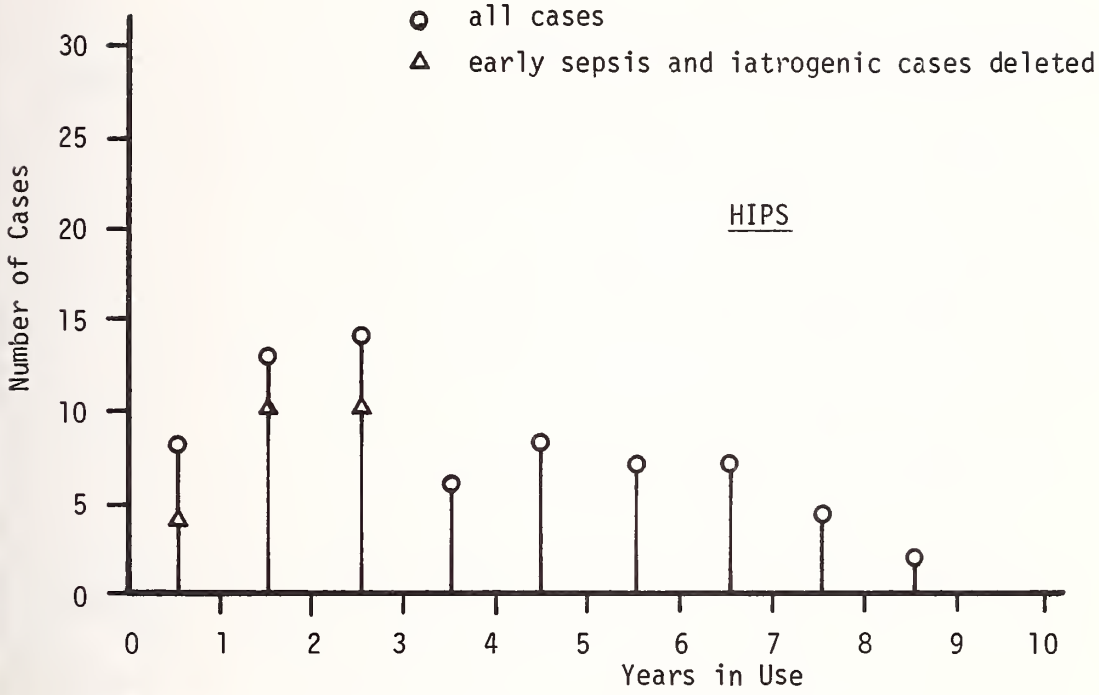
	loose	not loose
impingement on anterior tibial lip	15	2
no impingement on anterior tibial lip	3	8

$\chi^2 = 8.318$

$\chi^2_{.99} = 6.63$

FIGURE 1

TOTAL TJR IMPLANTATION TIME PERIOD



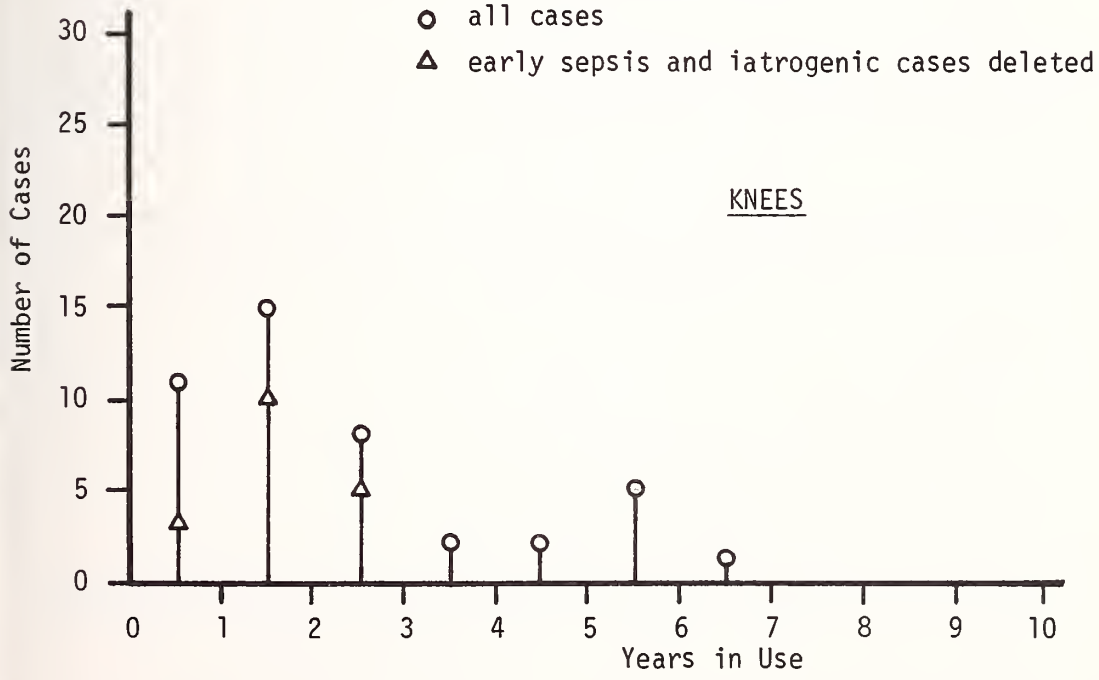
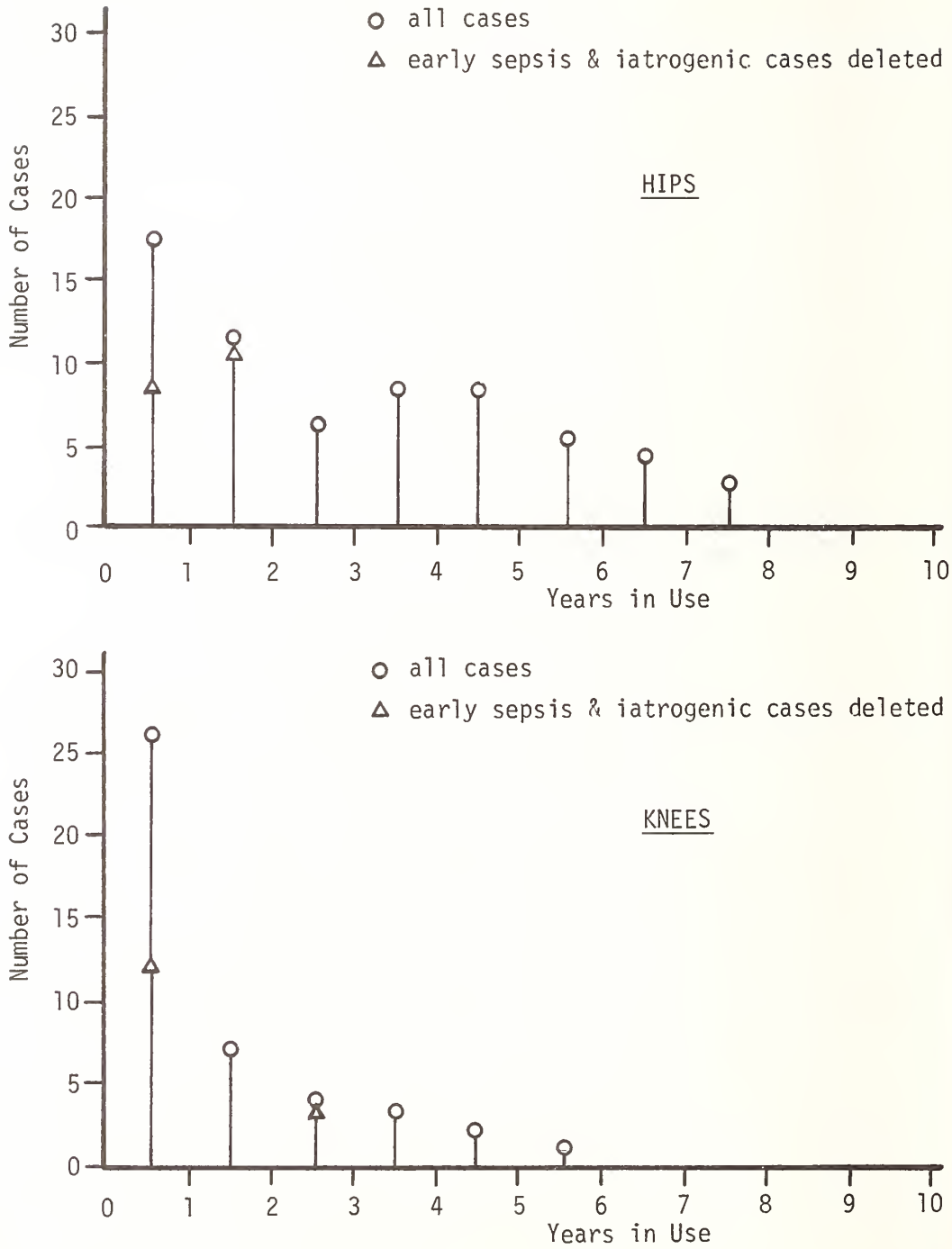


FIGURE 2

SYMPTOM - FREE TIME PERIOD OF TJR



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APPENDIX I

June 5, 1979
Rev. 6

NORTHWESTERN UNIVERSITY REHABILITATION ENGINEERING PROGRAM

REMOVED PROSTHESIS ANALYSIS
CLINICAL DATA

Recorder _____ Recording Date _____

Series No. _____

COLUMN	ITEM	
	GENERAL INFORMATION	
1-19	Patient Name __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __	
20-28	Social Security No. __ __ __ __ __ __ __ __ __	
29-31	Data Collection Center __ __ __ (use 3 letter abrev. of institution)	
32-34	Surgeon __ __ __	
35	Patient Source __	1) physian's own case 2) referral case
36-37	Age __ __	
38	Sex __	1) male 2) female
39-41	Shift Check 6 7 8	
42-44	Height __ __ __ (in cm) _____(in ft.-in.)	
45-47	Weight __ __ __ (in kg) _____(in lbs)	
48	Overweight Condition __	1) none 2) moderate 3) marked
	PRE-OPERATIVE ANALYSIS	
49	Joint Involved __	1) hip 2) knee 3) ankle 4) other
50	Side Involved __	1) right 2) left
51-56	Date of Original TJR* (mo.) (day) (yr.)	
57	Original Diagnosis leading to TJR __	1) osteoarthritis 2) rheumatoid arthritis 3) traumatic arthritis 4) sepsis 5) CDH 6) other (specify)_____

Manufacturer and Model of Prosthesis _____

* If day is not given, the first of the month will be assumed; if month is not given, January is assumed; if date is not known, set year to "99".

This code conforms to ASTM F-561-78.

Series No. _____

COLUMN	ITEM
58-63	FOR OFFICE USE ONLY Original Prosthesis Type __ __ __ __ __ __
64	Antibiotics at Previous TJR __ 1) yes 2) no 3)unknown
65	If YES, Reason __ 1) prophylactic 2) positive culture at surgery 3) history of sepsis 4) other _____ 5) no antibiotics 6) unknown
66	History of Foreign Body Reaction __ 1) yes 2) no 3)unknown
67	Arthroplasty previously revised __ 1) yes (specify)_____ 2) no
68	Other Joints with Prosthesis __ 1) none 2) contralateral joint only 3) contralateral joint and others 4) others
69-71	Length of Time Symptoms Have Persisted __ __ __ (months)
72-74	FOR OFFICE USE ONLY Length of Time TJR in Use Before Onset of Symptoms __ __ __ (months)
75	Blank
76-78	Shift Check 6 7 8
79-80	Card No. 7 A

O

1-9	Social Security No. __ __ __ __ __ __ __ __ __
10	Initial Factor Leading to Removal Symptoms __ 1) iatrogenic** 2) infection 3) trauma or fall 4) idiopathic 5) autopsy 6) other _____

** Iatrogenic problems include: poor component orientation, poor bony preparation, bone fracture, etc.

Series No. _____

COLUMN ITEM

11-12 Primary Pre-op Indication of Removal of TJ __ __

01) loosening with pain
02) loosening with minimal pain (prophylactic removal)
03) pain only
04) infection
05) dislocation/subluxation
06) bone fracture
07) autopsy
08) prosthesis fracture
09) restricted ROM
10) prominence of bursae
11) unsatisfactory position of implant
12) hyper-sensitivity reaction
13) other _____

13-14 Secondary Pre-op Indication for Removal of TJ __ __

01) loosening with pain
02) loosening with minimal pain (prophylactic removal)
03) pain only
04) infection
05) dislocation/subluxation
06) bone fracture
07) autopsy
08) prosthesis fracture
09) restricted ROM
10) prominence of bursae
11) unsatisfactory position of implant
12) hyper-sensitivity reaction
13) other _____
14) none

15-16 Contributory Conditions __ __

01) none
02) alcoholism
03) drug addiction
04) senility
05) neuromuscular disorder such as hx of polio, CVA, etc.
06) multiple previous procedures
07) other _____

Patient Activity

17 Prior to onset of symptoms __

18 After onset of symptoms __

1) active and working
2) active, uses no supports or one support intermittently
3) active, uses 1 support
4) active, uses 2 supports
5) inactive, uses 1 or 2 supports
6) inactive, wheelchair
7) inactive, confined to bed
8) other _____

Joint Range of Motion

19 Prior to onset of symptoms __

20 After onset of symptoms __

1) full ROM
2) functional ROM
3) restricted and limited ROM
4) joint contracture, limited ROM

Ability to Walk Up Stairs

21 Prior to onset of symptoms __

22 After onset of symptoms __

1) normally
2) slowly, alternating
3) one stair at a time
4) unable

Series No. _____

COLUMN ITEM

Ability to Stand from Sitting Position

23 Prior to onset of symptoms __

24 After onset of symptoms __

1) no arms required
2) arms required
3) other help required

Ability to Put On Shoes and Socks

25 Prior to onset of symptoms __

26 After onset of symptoms __

1) easily
2) with difficulty
3) socks only, cannot tie shoes
4) unable

27 Pain at Rest __ 1) yes 2) no

28 Pain with Weight-bearing __ 1) none 2) mild 3) moderate 4) severe

X-RAY FINDINGS

TJR on Current Pre-Op X-Ray

1^{o} 2^{o} 3^{o}

29-34 Proximal Component(s) __ __, __ __, __ __

35-40 Distal Component(s) __ __, __ __, __ __

01) loose
02) dislocated
03) component fracture or deformation
04) bone fracture
05) radiolucent line present
06) migration or settlement
07) malalignment
08) increased density(sclerosis, compaction)
09) penetration of implant through bone
10) other _____
11) normal
12) x-ray not available
00) no other factors

41-43 Shift Check 6 7 8

44 Heterotrophic Bone Formation __ 1) yes 2) no 3) x-ray not available

45 PMMA on X-Ray __

1) cement cracked
2) excessive cement seen in joint
3) normal
4) no cement
5) x-ray not available

PRESENT REVISION SURGERY

46-51 Date of Surgery* __ __ __
(mo.) (day) (yr.)

52-54 Length of Time TJR in Use __ __ __ (months)

Series No. _____

COLUMN	ITEM				
55	Revision Procedure __	1) replace component(s) 2) arthrodesis 3) new prosthesis (specify)_____ 4) suction-irrigation 5) Girdlestone (pseudarthrosis) 6) other (specify)_____			
	GENERAL APPEARANCE AT SURGERY				
56	Fibrous Membrane Between Bone & PMMA __	1) a little	2) a lot	3) no	
57	Excessive PMMA Around Components __	1) a little	2) a lot	3) no	
58	PMMA Fragment(s) in Joint & Synovium __	1) a little	2) a lot	3) no	
59	Proximal Component(s) Poorly Oriented __	1) a little	2) a lot	3) no	
60	Distal Component(s) Poorly Oriented __	1) a little	2) a lot	3) no	
61	Component(s) Dislocated __		1) yes	3) no	
62	Proximal Component(s) Fractured __		1) yes	3) no	
63	Distal Component(s) Fractured __		1) yes	3) no	
64	Soft Tissue Rubbing or Impingment by Prosthesis __		1) yes	3) no	
65	Bony Contact by Component(s) __		1) yes	3) no	
66	Sepsis __		1) yes	3) no	
67	Synovium Stained by Metallic Debris __		1) yes	3) no	
68	Joint Ligaments Intact __		1) yes	3) no	
69	Musculature Surrounding Joint Intact __		1) yes	3) no	
70	Foreign Body Reaction __		1) yes	3) no	
71	Abundance of Scar Tissue __		1) yes	3) no	
72	Abundance of Granulation Tissue __		1) yes	3) no	
73	Bursal Fluid __		1) yes	3) no	
74	Caseation __		1) yes	3) no	
75	Boney Reaction __		1) yes	3) no	
76-78	Shift Check 6 7 8				
79-80	Card No. 7 B				

Series No. _____

COLUMN	ITEM	Component #1	Component #2	
1-9	Social Security No. _ _ _ _ _ _ _ _ _			
	Degree of Loosening			
10-11	Proximal Component	__	__	1) freely loose, component easily removed 2) loose, component removed with little effort 3) loose, component removed with difficulty 4) firm, component removed without great effort 5) firm, component removed only with great effort 6) component not removed
12-13	Distal Component	__	__	
	Loosened Interface			
14-15	Proximal Component	__	__	1) bone/cement 2) cement/prosthesis 3) both of above 4) bone/prosthesis 5) not loosened but removed 6) component not removed
16-17	Distal Component	__	__	
	Cement Fractures			
18-19	Proximal Component	__	__	1) fresh from removal 2) old 3) both of above 4) no cement 5) none 6) component not removed
20-21	Distal Component	__	__	

TISSUE EXAMINATION

July 28, 1979
rev. 6

NORTHWESTERN UNIVERSITY REHABILITATION ENGINEERING PROGRAM

REMOVED PROSTHESIS STUDY
POST-REMOVAL ANALYSIS

Series No. _____

COLUMN	ITEM	Component #1	Component #2	
	PMMA, Amount Used			
22-23	Superior Component	__	__	1) excessive 2) insufficient 3) normal 4) no cement 5) component not removed 6) unknown
24-25	Inferior Component	__	__	
	Bony Interdigitation of PMMA			
26-27	Superior Component	__	__	1) good 2) moderate 3) poor 4) no cement 5) component not removed 6) unknown
28-29	Inferior Component	__	__	
	PMMA Distribution			
30-31	Superior Component	__	__	1) good even coverage 2) small part of prosthesis uncovered 3) large part of prosthesis uncovered 4) no cement 5) component not removed 6) unknown
32-33	Inferior Component	__	__	
	Prosthesis Articulating Surface Wea			
34-35	Superior Component	__	__	1) slight or none 2) shiny, smooth 2-body wear 3) dull, slightly rough 3-body wear 4) rough, abrasive 3-body wear 5) gross, pitting, gouging 3-body wear 6) component not removed 7) unknown
36-37	Inferior Component	__	__	
	Amount of Surface Wear			
38-39	Superior Component	__	__	1) none 2) slight 3) moderate 4) severe 5) component not removed 6) unknown
40-41	Inferior Component	__	__	
42-44	Shift Check 6 7 8			

Series No. _____

COLUMN ITEM

Component Damage

45 Abrasive Wear or Deformation of Either Component Due to Bony Contact or Impingement __ 1) yes 2) no

46 Abrasive Wear or Deformation of Either Component Due to PMMA Cementophyte Contact __ 1) yes 2) no

47 Abrasive Wear or Deformation of Either Component Due to Abnormal Opposing Component Contact __ 1) yes 2) no

Iatrogenic Problems

48 Superior Component __

49 Inferior Component __

1) excess bone removed or inadequate bone preparation
2) bone fracture
3) component malalignment
4) other (specify) _____
5) none
6) component not removed

50 Swab from Implant Site, Sterile __ 1) yes 2) no 3) unknown

51 If NO, Pathogen __

1) Staph. Aureus
2) Staph. Albus
3) Staph. Epidermidis
4) Pseudomonas Aeruginosa
5) Clostridium Perfringens
6) E. Coli
7) other
8) no sepsis

FINAL CONCLUSIONS

52-53 Cause of TJR Failure __ __

01) iatrogenic
02) sepsis - early
03) sepsis - late
04) trauma or fall
05) idiopathic loosening
06) autopsy
07) prosthesis fracture
08) pain only
09) other (specify) _____
10) unknown

MATERIAL PROPERTIES ANALYSIS

METALLIC COMPONENTS #1, #2

54-60 Dimensions of Implant (mm) #1 __ __ __ (length) x __ __ __ (width) x __ __ (thickness)

61-67 #2 __ __ __ (length) x __ __ __ (width) x __ __ (thickness)

Series No. _____

COLUMN	ITEM	#1	#2	
	Macroscopic Examination			
68-69	Wear or Burnishing	__	__	1) a little 2) a lot 3) no
70-71	Galling	__	__	1) a little 2) a lot 3) no
72-73	Scratching	__	__	1) a little 2) a lot 3) no
74-75	Change of Shape	__	__	1) a little 2) a lot 3) no
76-78	Shift Check 6 7 8			
79-80	Card No. 7 C			
1-9	Social Security No. __ __ __ __ __ __ __ __ __			
10-11	Mechanical Damage	__	__	1) a little 2) a lot 3) no
12-13	Macroporosity	__	__	1) a little 2) a lot 3) no
	Microscopic Examination			meets standard specifications
14-15	Inclusion Content (ASTM E-45)	__	__	1) yes 2) no
16-17	Grain Size (ASTM E-112)	__	__	1) yes 2) no
18-19	Grain Boundary Constituents	__	__	1) yes 2) no
20-21	Microporosity	__	__	1) yes 2) no

		#1	#2	
22-23	Corrosion	__	__	1) none 2) general corrosion 3) pitting corrosion 4) crevice corrosion 5) galvanic corrosion
24-25	Mechanical Failure	__	__	1) none 2) fatigue 3) torsion 4) impact 5) stress-corrosion 6) static overstress causing plastic deformation 7) corrosion fatigue 8) combination of above (identify _____) 9) other (specify _____)
26-27	Device Flaws	__	__	1) yes (type and origin _____) 2) no
28-33	Type of Material as Determined by Chemical Composition __ __ __ __ __ __			

Series No. _____

COLUMN	ITEM
	Mechanical Properties (samples should be taken from areas representative of the original material)
34-39	Sample Size (mm) __ __ (length) x __ __ (width) x __ __ (thickness)
40-42	Shift Check 6 7 8
43	Sample Orientation __ 1) parallel to principal load direction 2) perpendicular to principal load direction 3) diagonal to principal load direction
44	Hardness Test Method __ 1) Brinell 2) Rockwell B 3) Rockwell C 4) Vickers 5) Knoop 6) Scratch 7) Other
45-48	Hardness Number __ __ __ __
49-54	0.2% Offset Yield Stress (MPa) __ __ __ __ . __ __
55-60	Ultimate Tensile Strenght (MPa) __ __ __ __ . __ __
61-63	Per Cent Elongation __ __ . __
64-66	Per Cent Reduction in Area __ __ . __
	POLYMERIC COMPONENTS #1, #2
67-71	Blank
72-75	Series No. L __ - __ __ __
76-78	Shift Check 6 7 8
79-80	Card No. 7 D

Discussion

Question (I. Clarke, University of Southern California): 1) With reference to the DELRIN socket, Delrin has not been reported as used in the U.S.A. total joints. How did you ascertain that it was indeed 'Delrin' i.e., homopolymer polyacetal and not co-polymer, 'ERTACETAL'? Where did it originate? Was there any histological correlation with respect to wear debris?

2) With regard to the zero fracture incidence of Aufranc hips you received, could this be due to the fact that their mode of failures was from loosening as opposed to fracture?

Answer: Thank you for your interesting questions. I shall answer them in the order in which you asked them.

1) "Delrin" is the trade name used by DuPont for their form of polyformaldehyde resin. Polymerized formaldehyde is sometimes referred to as a polyacetal because of the repeating oxymethylene units ($-OCH_2-$) in the polymer structure.

Polyformaldehyde is an inherently unstable polymer and on heating, decomposes to the monomer. Polyacetals are stabilized by capping the hydroxyl end groups of the polymer chains or by introducing co-polymers which act as blocks for they polymer chains.

Even stabilized polyacetals will give off some formaldehyde when heated. This test was used to confirm that the actabular component collected was indeed a polyacetal. We took the component to be "Delrin" because there had been reports in the literature that this particular polymer had been used in Europe to manufacture acetabular components.

Unfortunately, our laboratory does not have the ability to perform infrared spectrum analysis on polymers so we have no way of determining whether the component is simply a polyformaldehyde resin or whether the polyacetal had been compounded with a co-polymer.

The word "Protosul" was etched onto the stem of the femoral component. The prosthesis was probably manufactured by Protek of Berne, Switzerland.

There was no histologic section made of tissue adjacent to the total hip implantation site and accordingly no attempts were made to look for wear debris embedded in the periarticular soft tissue.

The acetabular component had been in place and functioning for almost seven years. The articulating surface was smooth and shiny with no evidence of cement wear particles. There was no surface pitting, at least to visual inspection with a stereomicroscope.

The femoral component had worn into the polymer cup a distance of about 2 mm. It was difficult to tell if the loss of material was due to cold flow or wear but we took wear to be the primary surface phenomenon as the cup showed little evidence of having deformed in any way.

2) From our analysis, to date, there did not appear to be any difference in the failure mechanics between Aufranc-Turner hips and other hip stems. Essentially, all the stems seemed to debond at the cement-metal interface first and then go on to subside or drift into varus or severely loosen or fracture.

The Aufranc-Turner hips did not fracture. We have not determined the unique design feature of Aufranc-Turner hips that resists stem fracture.

Question (Vimal Desai, Johns Hopkins University): Did you look at the amount of bone resorption and could you form a correlation between the incidence of loosening and the incidence of bone resorption from your study?

Answer: First, let me restate our definition of loosening. For the purpose of this study, a prosthesis component was taken to be loose if it could be physically moved with mild to moderate hand pressure at the time of revision surgery. Often, such looseness could be both felt and seen with blood being expressed from between the bone-cement or cement-prosthesis interfaces.

Secondly, I am going to take your reference to bone resorption to mean radiographic evidence, specifically the development of a radiolucent line demarcating bone and radio-opaque PMMA cement.

Finally, for the purposes of illustration, I shall confine my remarks to the femoral hip stem only.

Using the radiographs taken just prior to TJR revision, we measured the maximum thickness of the lucent line around the prosthesis components. After correcting for any magnification of the radiograph figures, the results were recorded as "no line", "thin line" (less than 3 mm) or "thick line" (greater than 3 mm).

A cross tabulation between clinical loosening and the presence of a radiographic lucent line is attached in figure A. There is no apparent correlation between loosening and a lucent line.

In a recent article (J.B.J.S. 60-A: 306-313, 1978) Beckenbaugh and Ilstrup reviewed a number of their cases at the Mayo Clinic and attempted to characterize radiographic loosening of the femoral component using such variables as subsidence or varus drift (after Charnley). Attached is a cross-tabulation table, figure B, between

clinical loosening (our definition) and radiographic loosening (Mayo definition).

In this case, a very good correlation is obtained between clinical and radiographic loosening. What is surprising is that in some cases, femoral stems which had obviously shifted in position radiographically, were firmly fixed and difficult to remove at revision surgery.

Figure A

Crosstabulation Between Clinical Loosening and Radiological Lucent Line for Total Hip Femoral Stems

CLINICAL LOOSENING	RADIOLUCENT LINE: no line	thin line	thick line	
loose	10	14	10	34
not loose	3	7	9	19
	13	21	19	53

$\chi^2 = 2.08$

$p = 0.37$

Figure B

Crosstabulation between Clinical Loosening and Radiographical Loosening of Total Hip Femoral Stems

RADIOGRAPHIC LOOSENING	CLINICAL LOOSENING: loose	CLINICAL LOOSENING: not loose	
loose	28	6	34
not loose	4	13	17
	32	19	51

$\chi^2 = 16.78$

p is very small

THE METHOD OF IMPLANT RETRIEVAL ANALYSIS AT THE HOSPITAL FOR SPECIAL SURGERY

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An implant retrieval analysis program was established at The Hospital for Special Surgery in December, 1977, and since then over 1300 implants have been gathered and examined. The primary objective of the program is to identify problem areas in design and materials of implants with emphasis on total joint prostheses. All implants removed in the operating rooms at the Hospital and, in a few instances, at other institutions in the U.S.A. are included in the program. In addition, protocols have been established to retrieve whole joints (containing total joint implants) which have been removed en-bloc at autopsy or amputation. Examination of retrieved implants includes visual and light microscopy inspection, a review of the patient's radiographs and medical records, scanning electron microscopy of fracture and articulating surfaces, and metallurgical analysis where appropriate. Additional procedures, including examination of properties of bone and structure, are performed on the joints removed en-bloc. The biomechanical data obtained from the implant retrieval analyses are included in a data file of radiographic and medical history information for use in statistical analysis.

1. Introduction

Many orthopaedic surgical procedures include implantation of prosthetic devices. Often times these implants are removed routinely, such as in the case of many fracture fixation devices. Other prostheses, such as total joint replacements, are regarded as permanent and are removed only when a complication arises, such as infection and loosening or fracture of the prosthetic components. Regardless of the reason for removal, examination of these removed devices can provide information concerning their performance on both the material and structural levels.

An implant retrieval system has been operational in the Department of Biomechanics at the Hospital for Special Surgery since December, 1977. Over 1300 implants have been gathered. A significant

portion (more than 250) are total joint replacements obtained from revision or removal surgery. The emphasis of the retrieval program has been to analyze the components from these joint replacements, though all other fractured or severely damaged implants have also been examined. The objective of the analysis is to identify damage mechanisms and correlate them with design features and material properties.

2. Materials

All implants removed in the operating rooms at the Hospital for Special Surgery and, in a few instances, implants removed at other institutions in the U.S.A. are collected. Implants are currently collected at the rate of approximately 400 per year with about 100 of the 400 implants being total joint prostheses (table 1). At present,

Table 1. Revision and removal procedures at the Hospital for Special Surgery

	Revisions	Component Removals	Total
Total Hip Replacements			
1977	26	6	32
1978	25	11	36
1979	41	15	56
Total Knee Replacements			
1977	28	2	30
1978	29	2	31
1979	41	2	43

approximately 110 total knee joint prostheses and 120 total hip joint prostheses have been collected. There are also approximately 25 other total joints including total shoulder, wrist, finger, elbow and ankle implants.

In addition to the implants that are removed at surgery, there is also a growing collection of whole joints (containing total joint implants) which have been removed en-bloc at autopsy or at amputation. This represents a new program at the Hospital for Special Surgery having commenced in June, 1978. Four such specimens have been retrieved to the present time: a hip and two knee joints obtained from autopsies; and a knee joint obtained from an above-knee amputation necessitated by vascular disease in the foot.

3. Methods and Procedures

3.1 Procedures for obtaining removed implants

Implants that are removed at surgery are first forwarded to the Pathology Department where they are logged in the Pathology records. They are then sent directly to the Biomechanics Department where they are catalogued (including patient name and record number) and placed

individually in boxes to await inspection and/or storage. The removal, transportation and cataloging procedures are performed according to instructions from Biomechanics personnel to minimize any mishandling of the implants. Such mishandling could obliterate evidence of *in vivo* damage on the components or create artifactual damage which might be falsely interpreted as having occurred *in vivo*.

The procedure for acquiring joints removed en-bloc is somewhat different. Because of the large population of patients with rheumatic diseases at the Hospital for Special Surgery and because of the affiliation between the Hospital for Special Surgery and the New York Hospital, critically ill patients who have total joint replacements are identified by the medical staff of the Hospital for Special Surgery and autopsy permission is obtained. For amputation of limbs with total joint replacements, patient consent is obtained by the patient's surgeon at the Hospital for Special Surgery. Joints removed at autopsy or amputation are again catalogued in the Pathology Department records and a tissue specimen is obtained from the synovium of the joint at that time. This is done with a small, longitudinal straight-line incision in a region chosen so as not to measurably alter the joint kinematics. The remainder of the examination of the joint is performed in the Biomechanics Department, as described below.

3.2 Patient records and radiographs

For all removed implants, a complete set of patient medical records and radiographs are available. In most instances, a complete history of the joint implant can be obtained from the medical records. Missing information is obtained directly from the patient and/or the physician. Included in the records for each removed total joint is a summary review of the patient's status by the physician containing information pertinent to the condition of the patient before and after surgery and the surgeon's impression of the condition of the joint at surgery. Serial radiographs of the patient's joint are reviewed with the surgeon and a more detailed diagnosis for removing the implant is obtained. Whenever possible, a member of the Biomechanics Department is present in the operating room at the time of implant removal. Direct observations of the implant's condition are noted at this time, especially in cases where the implant has obviously undergone mechanical failure. These observations are then added to the patient's record file, a schematic of which is shown in figure 1.

3.3 Methods for examining retrieved implants

All removed implants are visually examined for evidence of mechanical damage and gross deformation and, in the case of the polyethylene components, discoloration due to absorption of body fluids. A detailed examination of the entire surface of each component is then performed using a stereo-optical light microscope at a magnification of ten times. Both the visual and light microscopy inspections are performed by two individuals (the light microscope has dual binocular tubes for viewing by two people simultaneously).

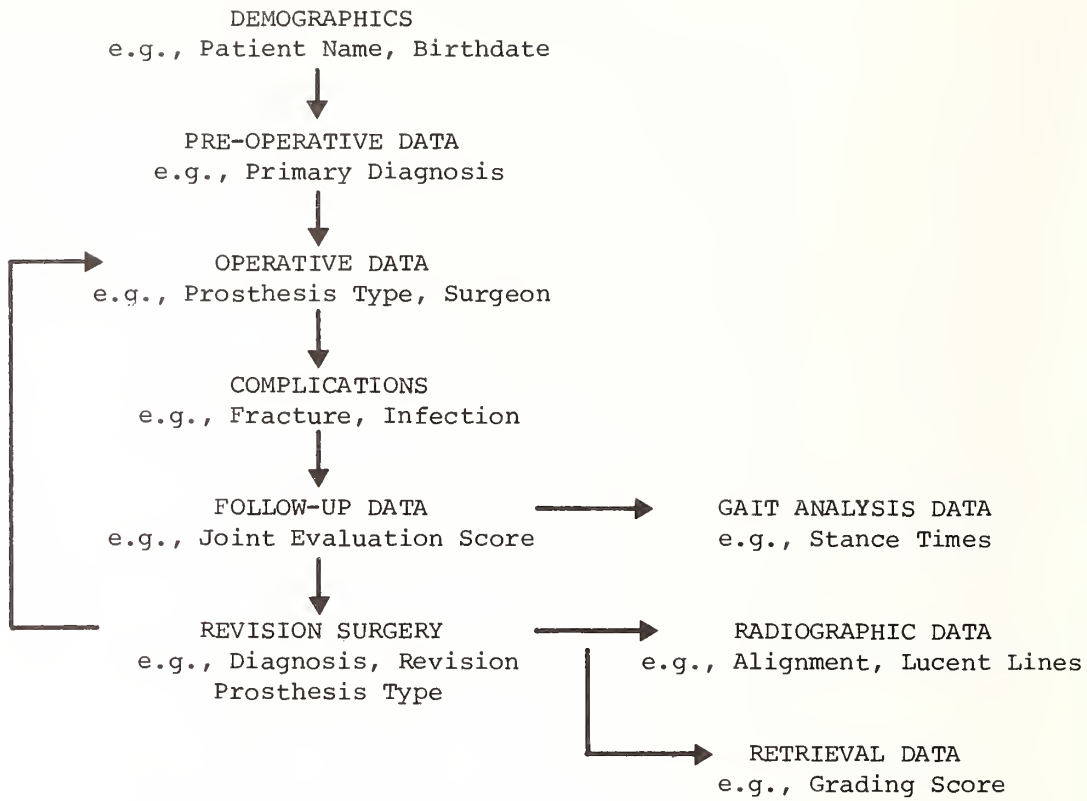

Figure 1. Schematic diagram of a patient's medical record file.

During light microscopy examination, each component is subjectively graded on the amount of mechanical damage present. Polyethylene components (e.g., acetabular cups from total hip replacements and tibial and patellar components from total knee replacements) are graded for embedded polymethylmethacrylate (PMMA) cement debris, pitting, wear tracks, burnishing, surface cracks and surface deformation. Metal components (e.g., femoral stems from total hip replacements and femoral components from total knee replacements) are graded for wear scratches, corrosion and fracture. Grading is done on both the severity of the damage and its distribution over the surface of the component.

Scanning electron microscopy is used to perform fractography on those components which have broken and to identify the characteristic features of the various wear processes. With fractography, an attempt is made to determine the fracture mechanism (e.g., fatigue), the crack initiation point and any pertinent features (e.g., porosity in cast metallic components) which contributed to the fracture.

3.4 Methods for examining joints removed en-bloc

The protocol for examining whole joints was developed using a hip joint recovered at autopsy [1][1]. The protocol includes range of motion measurements, mechanical testing of the bone tissue, and whole joint structures , estimation of debris in the surrounding synovium and standard retrieval analysis of the prosthetic components.

Care is taken to obtain whole joints directly from the operating room for amputation specimens and at autopsy for cadaver joints. Within one to two hours, the fresh joint is taken through a series of range of motion movements. Radiographs are taken of the joint in a neutral position and at the extremes of motion. The joint is then taken to the Pathology Department for cataloging and for the removal of a small synovial tissue specimen as previously described. Then the joint is returned to the Biomechanics Department where it is frozen and stored for the testing program.

The program begins with a dissection of the joint capsule. The dissection is recorded photographically and general features (such as the appearance of the soft tissues around the capsule) are noted. Samples of the synovium are examined histologically for a qualitative analysis of the type of debris present. This analysis is based on the size, shape and refractile quality (under polarized light) of the debris particles [2].

After dissection of the joint capsule, several other procedures are performed. The cortical bone from the metaphyseal region of the bones obtained with the joint is machined into standardized specimens and tested in uniaxial tension (or compression) following established methods [3,4]. These results can be compared to existing mechanical data for human bone of the same age taken from individuals without joint replacements [5].

The components themselves are mechanically tested while still in-situ. These tests provide knowledge of the in-vivo fixation strength of normal (i.e., not loosened or infected) total joint replacements. Such tests are generally carried out only until the initial failure of the bone-cement-prosthesis system is observed, so as not to disturb the underlying trabecular bone morphology. Initial failure is determined using acoustic emission, a non-destructive testing technique which records stress waves released from damage mechanisms within a material undergoing deformation. Acoustic emission has been shown to be a much more sensitive technique than, for example, attempting to measure changes in the load versus deformation behavior, when recording the intitiation of damage in a loaded structure. Experiments using acoustic emission on biological tissues have shown it to be a useful technique for

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[1] Figures in brackets indicate the literature references at the end of this paper.

investigating damage mechanisms in these materials [6,7]. One example of in-situ component testing is eccentric compressive loading of the medial plateau of total condylar tibial total knee components. Several patients with failures of total condylar knee replacements associated with cold flow of the tibial component have had revision surgery at the Hospital for Special Surgery. The wear patterns on the removed components revealed the eccentric loading. By in-situ mechanical testing of total condylar components which did not undergo mechanical failure (such as the one knee replacement recently obtained at autopsy) and correlation with finite element predictions [8], an understanding of the cause of the problem and possible design alterations to eliminate this type of failure can be found.

After testing, the components are removed and examined following the same procedures outlined above including visual and light microscopy inspection, subjective grading of articulating surfaces and scanning electron microscopy of wear surfaces. In some specimens the components are left in-situ and the entire specimen embedded in an epoxy resin and cross-sectioned. This procedure allows examination of the bone-cement and cement-prosthesis interfaces and stereological examination of the trabecular bone surrounding the implants for comparison with trabecular morphology in normal joints without prostheses.

4. Typical Results

Implant retrieval programs, such as the one described here, generate large amounts of information. Results are always changing as more devices are collected and added to ongoing studies. In this section, some typical findings from the retrieval program at the Hospital for Special Surgery are presented.

4.1 Fractured femoral components

Fracture of the femoral component in total hip replacement is one of the most noted forms of device failure [9-13]. At the present time, twenty-six fractured stems have been collected, twenty from the Hospital for Special Surgery and six from other cooperating institutions. The majority of the stems are of the Charnley design (10 out of 26) with the remainder being either Mueller (6 out of 26), T28 (5 out of 26), or Bechtol (5 out of 26) designs. Fourteen of the fractured stems (8 of the Charnley type and all of the Mueller type) are cobalt alloy and the remaining twelve are stainless steel.

The mechanism of fracture was fatigue in twenty-five of the stems. One stem, a cobalt alloy Charnley design, fractured catastrophically when the patient sustained a fall from a ladder. Examination of the fracture surface revealed no apparent previous fatigue damage.

In several cases, material defects and stress concentrations were found as the cause of fatigue crack initiation. The most prevalent

material defect was interdendritic porosity in stems cast from cobalt alloy. At least four of the fourteen cast cobalt alloy stems showed significant porosity in the region of crack initiation (fig. 2).

Figure 2. Scanning electron photomicrograph of the fracture surface of a Charnley stem cast from cobalt alloy showing dendritic structure at the crack initiation site. A 100 micron reference bar is included at the bottom. Time implanted was 74 months.

Two forms of stress concentration also lead to crack initiation. A stainless steel Charnley fractured in fatigue which initiated at a nick on the anterolateral corner of the stem cross-section. It was not possible to determine if the nick had been caused by a drill bit during reattachment of the greater trochanter or by subsequent migration and rubbing of the reattachment wire against the stem, though clearly one or both were responsible. Another form of stress concentration occurred in four of the five fractured T28 stems. All four stems fractured in fatigue and all had multiple cracks (always more than three) in addition to the crack causing failure (fig. 3). These cracks often initiated on the medial side of the stem. Their presence can be attributed to the trapezoidal cross-sectional shape, which causes higher stresses on the medial side than on the lateral side. When the stem is overstressed, the medial side yields first in compression, causing areas of residual strain which with continued cyclic loading can become tensile and act as a stress concentration. All four of the femoral components were the small stem size and all four were implanted in relatively active male patients weighing over 81.0 kilograms, so the potential for high stresses was present.

Figure 3. Multiple cracks emanating from the medial side of a fractured small stem T28 prosthesis made from stainless steel. Time implanted was 52 months.

4.2 Permanent deformation and fracture of polyethylene components

Reports of removed ultra-high molecular weight polyethylene components from total joint replacements have concentrated on the mechanisms of wear occurring on the articulating surface [14-16]. Another equally disturbing problem with many of these components is structural failure caused by gross or excessive permanent deformation and fracture. In the retrieval program at the Hospital for Special Surgery these failures have been noted in acetabular cups from total hip replacements, in tibial and patellar components from total knee replacements, and in the polyethylene inserts used in triaxial-type joint replacements in the upper limb.

As with the metallic femoral stems the fracture mechanism in the polyethylene components was primarily fatigue. Once again the initiation of the fatigue process often occurred at a stress concentration. For example, fracture in acetabular cups originated at the base of the circumferential grooves machined in the components to provide good fixation to cement [17]. The lack of adequate structural support from surrounding cement and cancellous bone was often associated with the fracture. For example, poor cancellous bone under the medial side of a Freeman-Swanson tibial component combined with the fact that the extreme medial and lateral edges of the component were supported on the cortical shell of the tibia lead to the fracture shown below in figure 4.

Figure 4. Freeman-Swanson type polyethylene tibial component showing partial fracture (arrow). Time implanted was 60 months.

Excessive permanent deformation leading to structural failure was also associated with poor cement and cancellous bone support in many instances. A stress fracture in the trabecular bone under the medial tibial plateau, for example, allowed gross deformation of a total condylar II tibial component (fig. 5) even though the peg remained well-fixed.

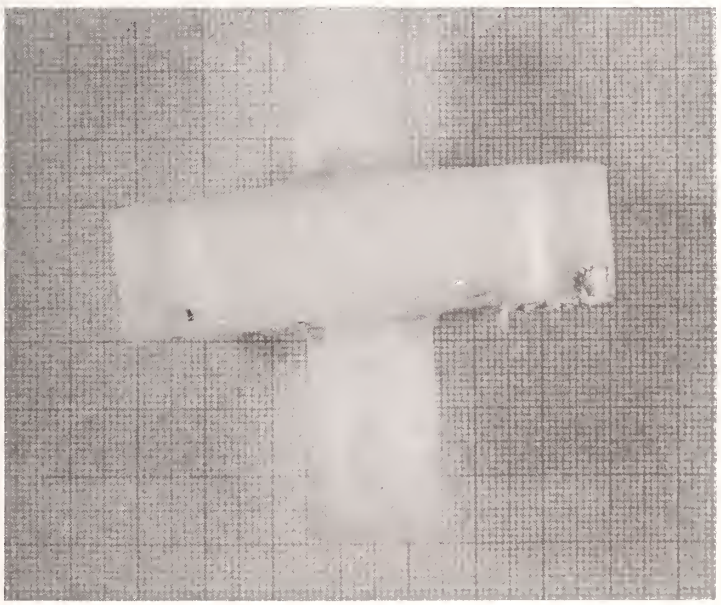

Figure 5. Total condylar II polyethylene tibial component with excessive deformation of the plateau relative to the peg. Time implanted was 25 months.

5. Discussion

An objective of most implant retrieval programs is to identify problem areas in prostheses and, therefore, indirectly suggest solutions. One area where this objective has been clearly met is in the mechanical performance of femoral components in total hip replacement. Material defects in fractured stems have been found by a number of investigators [10,11,18,19]. In an attempt to diminish the incidence of these defects, manufacturers have responded by introducing improved manufacturing techniques such as forging [20] and hot isostatic pressing [21]. These processes decrease the number of defects like interdendritic porosity and significantly improve the mechanical load carrying capability of the stems [22]. In the particular case of the retrieval program at the Hospital for Special Surgery, the high incidence of porosity in cast stems, along with results of static testing of cast stems [23], lead to a change in the total hip replacement systems used at the hospital.

The poor mechanical performance of polyethylene is a more recent discovery and has yet to be examined in any detail. Few reports of fractured polyethylene components have appeared in the literature [17,24] and permanent deformation is usually discussed as a combined mechanism with wear. Some solutions are available in the form of metal backing (such as the trays under plastic tibial components) and composite reinforcement with carbon fibers. Much less is known, however, about the stress fields in and around polyethylene joint replacement components when compared to the femoral stem, which has received considerable attention. As more stress analysis information becomes available to aid in interpreting the damage found on retrieved polyethylene components, more improvements, including changes in design and material, will hopefully result. This process has already begun for patellar [25] and tibial [8] components.

6. Conclusions

The retrieval program at the Hospital for Special Surgery has met its primary objective in that problem areas in design and materials for total joint prostheses have been identified. Two areas discussed here, namely, material defects in cast femoral stems and gross deformation in polyethylene components, were important considerations in the decision to change the commercial joint replacement systems stocked in the operating room and in the alteration of design criteria for custom and newly developed prostheses.

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Discussion

Question (Anthony K. Hedley, U.C.L.A.): The authors suggest that the disappearance or resorption of bone from under tibial components with central pegs is due to overloading of the cancellous bone leading to "bone failure". I would like to know what histological evidence he has for this supposition. Were healing microfractures seen in the supporting bone? Was the population present predominantly osteoblastic or osteoclastic?

The phenomenon of "stress relief" has been demonstrated in many situations where stress concentrating devices have been employed, such as fixation pegs, and I would like to ask why he does not accept that the changes he has seen are not due to resorption due to stress relief of the bone under the plateaus rather than overloading which in the in vivo situation is characterized by progressive hypertrophy, sclerosis and the presence of microfractures.

Answer: Dr. Hedley has raised a good point. At this time, we have no histological evidence of microfractures in the region of the tibial plateaus in those cases demonstrating gross deformation of the polyethylene plateau while the central peg remained well-fixed. We based our understanding of the problem on the following facts: 1) in general, these cases involved very heavy and relatively active (i.e., ambulating freely) patients; 2) often, the plateau which eventually crushed was loaded to a much greater degree as shown by radiographs which demonstrated the eccentric loading; and 3) while histological evidence of microfractures was not sought, radiographic evidence of a stress fracture in the plateau prior to failure was present in one of the cases.

Question (D. F. Williams, University of Liverpool, U.K.): Could you comment on whether chemical degradation has any role on the wear of the high density, ultra-high molecular weight polyethylene?

Answer: There is little doubt that the gross appearance (color and texture) of UHMW polyethylene changes during implantation for long periods of time as seen in our, as well as other researchers, collection of retrieved implants. This would lead one to suspect some form of chemical change, though we have not investigated what effect such changes would have on damage mechanisms in the polyethylene.

Question (Roy Hori, Northwestern University): Regarding your comments on polyethylene wear, how do you account for the many hip cups and knee components which were in use by active patients for a long time with very little wear. We have many such cases in our study and I suppose you might also, cases where the cause of removal did not involve loosening, e.g., sepsis.

Also in this regard, your study shows many ICLH prostheses with severe surface pitting. I believe the ICLH has one of the largest

contact areas of the currently available TKA's. If the ICLH has such high contact stress, do any of the other prostheses have any hope. By the way, we have several Marmors with little wear after several years of use.

Answer: We also have polyethylene components that show little wear or mechanical degradation, though we have not found these to be associated with one removal diagnosis versus another (e.g., sepsis versus loosening). Rather we have found the amount of wear to be related to patient weight and implantation time. For example, we have graded thirty-eight tibial components from retrieved total condylar knee replacements using the subjective grading system explained in our paper. We correlated the total damage grade with patient weight and the length of time the prosthesis was implanted and found significant ($P<.01$) positive correlations for both variables. The heavier the patient or the longer the patient used the prosthesis, the more damaged we found it to be upon removal. Of course, there are exceptions, in which little damage occurs even for heavy individuals and/or long implantation times. We have found, however, that in most of these cases, the patients were relatively inactive. Activity level, being a difficult parameter to obtain and quantify, was not included in our analysis.

The ICHL prostheses referred to in our paper and presentation were all implanted for long periods of time (at least five years), and this is one of the reasons they demonstrated such considerable damage. It is correct to consider the ICLH as having a large contact area at least in full extension. We have measured the contact areas and contact pressures of a number of contemporary knee designs and found the contact area of the ICLH to be one of the largest, though the area decreases sharply as the joint goes into flexion. The contact stresses, even for the ICLH, exceeded the compressive yield stress of UHMW polyethylene when the prosthesis was loaded to physiological loads at 0, 30, 60, and 90° of flexion. This does, in fact, present a bleak picture for polyethylene in long term implantation as an articulating surface.

An Interactive Computer System for Implant Data Retrieval/Analysis

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An interactive computer system for the storage, retrieval and analysis of clinical and material characterization data associated with orthopaedic implants is described. The system consists basically of four independent modules. The essence of the system centers on the cross-referencing capabilities which are unlimited. The system has been designed for use by non-computer trained personnel.

1. Introduction

The evaluation of retrieved orthopaedic implant devices can provide information about implant performance and potential health care benefits not available by any other method (1,2)[1]. The evaluation of clinical procedures and material characteristics can also provide criteria for establishing minimum performance levels for an implant device. To date, implant retrieval studies have been performed by many investigators using widely different experimental protocols (1-5). Attempts to compare the results of these investigations are frequently difficult if not impossible.

A protocol for the retrieval and analysis of metallic orthopaedic implants used in humans has been developed by the American Society for Testing and Materials (ASTM) (5). The clinical data to be recorded and the material characterizations to be performed when an implant is retrieved are given in this protocol. The ASTM F 561 standard recommended forms for the recording of data with regard to the clinical experience and material examinations. The clinical data required includes a case history, roentgenogram review, tissue culture, and a histological evaluation of tissue adjacent to the implant. The material characteristics to be determined, utilizing standard ASTM testing practices, where applicable, includes chemical composition, macroscopic and microscopic examination and mechanical property determinations.

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[1] Figures in parentheses indicate the literature references at the end of this paper.

Once standard methods for examining and recording data on retrieved implants are followed, the results of independent investigators can be easily correlated in order to relate clinical performance with material characteristics. This information should lead to better implant performance through its use in updating material and device standards. The problem with such a system is the voluminous data bank involved and the need for easy access, sorting and cross-referencing of the data to provide meaningful results. Thus, this system is ideally suited for implementation on an interactive digital computer system. Once the data is adapted for computer manipulation, for example, actuarial statistical analysis can be performed to predict survival rates. Thus, the use of such a system as an early warning vehicle to improve health care should not be overlooked.

2. System description

The implant retrieval and analysis computer system described in this paper contains four independent program modules which were written in either the FORTRAN or COBOL computer languages. The system is currently being used in an interactive mode on a Digital Electronics Company (DEC) system 2060 digital computer. In this configuration all data is entered to the implant retrieval and analysis system from a keyboard and all input and output is displayed on a cathode ray tube (CRT) screen. A hard copy output on a line printer is also possible. All programs in the system are completely documented for an experience programmer or nonprogrammer user. Although the system is currently used in an interactive mode, it was also designed for use in a batch environment where all data input and cross referencing information is entered from data cards. The format for these cards and the use of the system in the batch environment is contained in the user documentation.

The implant retrieval and analysis system was written in standard computer languages and contains no computer installation dependent subsystems. It is, therefore, completely portable to other computer installations regardless of manufacturer or type of computer system used, as long as a FORTRAN and COBOL compiler are available. Since large quantities of retrieval data (greater than 1000 cases) may eventually be stored, all input data is placed onto magnetic tape for storage. It should be noted that most computer installations charge for permanently occupied disk storage space. However, if only smaller quantities of data are anticipated or in the period when massive amounts have not yet been accumulated, the user has the option to store data records on disk. Disk storage has the advantage of easier accessibility and faster response but is not economically practical for large quantities of data.

As noted above, the implant retrieval and analysis system contains four separate independent modules; one for initial clinical and material data entry, a cross referencing module to allow manipulation and statistical treatment of all data, a printing module to provide hard copy of any or all data, and an editing and updating module to allow entry of follow-up or missing data to a case that was previously entered. The use of these modules and their specific features will be described in the following sections.

3. Data input module

"ADDREC" is the implant retrieval and analysis module for the input of clinical history and material characterization data associated with each implant device. The input data required corresponds closely to that contained on ASTM F 561 standard forms (figures 1 and 2) for the retrieval and analysis of metallic orthopaedic implants. These forms are, however, to a certain degree applicable for both metallic and nonmetallic devices. Based upon these forms, a new set of forms were developed by the authors incorporating the recommended information, however, extending beyond this and revised to be more suitable for computer entry and analysis. The form was also made less ambiguous, providing for easier multicenter interaction. These forms are shown in figures 3 and 4. It should be noted that very specific data responses are requested in a manner which can be easily entered and stored in coded form on the computer.

The input module "ADDREC" was written entirely in the FORTRAN computer language and was designed for use by individuals with little or no computer experience. Continuous data checks are provided in the program to prevent erroneous data input and help files containing directional information are accessible during execution, if needed, to explain in detail the type of response expected. These features are illustrated in example 1. In the example, the program prompt asks the user to enter the diagnosis at insertion. Unsure of how to respond, the user enters a "?" and the program responds with additional descriptive information, as shown in example 1. The user then enters the letter "U" mistakenly. This is an incorrect entry since the possible range of responses is only the letters A through S. The program responds with the message "Invalid Data Entry" and repeats the question. The user then enters the letter "O", which is a valid entry and the program advances to the next question. Since an implant device may contain multiple components and a material characterization study may be conducted for each component, the "ADDREC" module is capable of accepting multiple material characterization forms for each clinical history form. An example of the use of "ADDREC" module for the entry of data for a two component total hip replacement is shown in example 2.

It should be observed in example 2 that question number 15 was not asked. Question 15, the bone the device was inserted or attached to, is only asked if the device is not a joint replacement. If the device is a joint replacement, this information plus the implant type, question 9, is sufficient for the computer system to know where the implant was placed.

It should also be observed in example 2 that each computer prompt was answered with a "?" to obtain further explanation of the expected response. Obviously, this would usually be unnessary since the retrieval data forms were designed based upon the computer system; however, the option is available if needed, for example if data for a case is being entered prospectively directly from a dictated operative report. Thus, data entry to the system is a simplified task easily

undertaken by a secretary or technician once the retrieval data forms have been completed.

Among the other useful features in the "ADDREC" module is the ability to review a clinical or material examination form before proceeding to the next form or case as demonstrated in example 3. Upon completion of each clinical or material form the computer prompt asks if you would like to review the data entered. A "yes" response presents a shorthand version of the data entered. A user may then choose to return to a particular question if a wrong entry has been made as illustrated in example 3. In the example, upon completion of a clinical form, the user requests a review of the data entered and notices an incorrect entry for functional level attained following surgery. The user returns to that question and enters the correct response. The user then requests another review of the data entered and being satisfied with the entry proceeds to the materials form. It should be observed that the use of the "?" response yielded additional user information.

If no data is available for a particular question at the time of data entry, the user may respond with simply a carriage return. The program then warns the user that no data was entered for the question and proceeds to the next question. The user can correct the entry if the carriage return was mistakenly used as described in the preceeding paragraph or can at a later date return to the case and enter the missing information with the "UPDATE" module described in a subsequent section.

4. Cross referencing module

"SELECT" is the implant retrieval and analysis module used for cross referencing the data entered into the module "ADDREC." "SELECT" was also written entirely in FORTRAN and is completely documented for the user. The "SELECT" module was designed for use by individuals with no computer experience and contains many computer prompts with additional help information available both before and during execution. Consistent with the "ADDREC" module a "?" response to any computer prompt will yield additional information concerning the range of user responses. A user may cross reference as few or as many variables at one time as he chooses. There are a total of 54 possible variables to cross reference. These span from single criteria, such as a hospital or particular device, to ranges in values of variables such as ranges of weights of patients or ranges of dates in-situ. To retrieve a particular patient's file, the user may use the patient's case number, name, or identification number. The case number is an installation supplied number and may be the only method of retrieving a specific file if the patient's name is not entered on the computer files and no identification number (Social Security Number or hospital number) was known for the case.

The use of the "SELECT" module is illustrated in example 4, which is a cross reference in which it was desired to obtain all cases on file for which the patients were 20-50 years old, weighing 150 to 200

lbs, who had hip replacements utilizing stainless steel for the stem component which had failed due to fatigue. In this session, the user first obtains a set of instructions and obtains a list of possible cross referencing variables by responding with a "?" to the computer prompt asking for which variables he would like to cross reference. The user enters the number associated with each variable that is to be cross referenced. The computer then prompts for the specific information for each of the variables that were chosen. Upon completion of the cross referencing information, the program searches its data banks for cases which satisfy the criteria chosen and responds with the number of cases searched (which are the total number of cases in the data bank) and the number of cases found satisfying the cross referencing criteria. The cases satisfying the cross referencing criteria are automatically written onto a new data file which can then be displayed on the CRT screen, printed on a line printer, or used for further statistical manipulation. These portions of the implant retrieval and analysis system are handled in the module "PRINT".

As noted above, the "SELECT" module can be used to retrieve a particular patient file by entry of patient case number, name or identification number. This feature is particularly useful for the surgeon for instant and efficient review of patients' files on followup since the system can be used for prospective studies with data initially entered at the time of surgery.

5. Print module

"PRINT" is the retrieval and analysis system module used to decode all data from its computer stored format and to prepare a printout of the case on a CRT terminal and/or a line printer. The "PRINT" mode was written entirely in the COBOL computer language, is well documented and exceedingly easy to use. A printout of the sample case entered with the "ADDREC" program is shown in example 5. Thus, the user has at his instant disposal any particular case in his data banks and the ability to generate printouts of all cases satisfying the cross referencing criteria as described in the "SELECT" module description above.

6. Editing and update module

The "UPDATE" module of the implant retrieval and analysis system was written to provide an efficient mechanism for updating or changing input data associated with a previously entered case. Since the retrieval and analysis system can be used for prospective as well as retrospective studies, clinical data and some data with regard to the implant (example: type, manufacturer) may often be entered before the device is actually retrieved. Upon retrieval of the implant device, material characterization forms are completed and this data along with any additions to the clinical data may be easily entered using the "UPDATE" module. The "UPDATE" module can also be used to add or change any information in a previously entered case which may have been incorrect or missing at the time of initial input. The use of the "UPDATE" module for this type entry is very similar to the method illustrated in example 3. The first entry to the "UPDATE" module is the patient

case number, name or identification number. The "UPDATE module then retrieves that case and displays the record to the user. Changes are then made in the record by transferring to the item number which needs data to be added or corrected. The user also has the option of entering a complete materials form for as many components as required. This latter type of usage is needed if the clinical data was entered prospectively and the device is subsequently retrieved and materials characterization forms completed. "UPDATE" supplies user prompts throughout the process and has additional help files which can be accessed by a "?" response to any prompt.

7. Summary

The implant retrieval and analysis computer system described in this paper provides a powerful tool for the analysis of orthopaedic implant performance. The system was designed to be extremely portable to other computer installations and extremely flexible in modular concept. No previous computer experience is required for the operation of the system and it was designed to simplify the interaction of multiple investigators interested in implant retrieval. In addition, memory space has been minimized through the storage of data in coded form on the computer; however, provisions have been made in the data storage for the addition of alternate input items at a later date as they are found to be necessary. These additional input items can be added without any disruption of existing data files and minimal programming changes.

The implant retrieval and analysis study by the Biomaterials Laboratory at Tulane University is ongoing and we expect to have over 500 cases entered to the system by the end of the year, and well over 1000 cases by the end of 1981. The system is being continuously updated and refined to provide more powerful features including statistical options and computer graphics as well as possible additions and modifications to the data entered.

Information regarding the acquisition of the implant retrieval and analysis system may be obtained from the authors.

8. Acknowledgements

The authors would like to acknowledge the support of the National Institute of Arthritis, Metabolism, and Digestive Diseases, National Institutes of Health and the Tulane University Computer Center.

Figure 1. ASTM F561 Case History Review Form

Recovery of Implant
Patient name_____ Case History Review Case Case # _____

1. Date Inserted _____ 2. Date Removed _____
3. Implant Type _____ 4. Patient Sex _____
5. Patient Date of Birth _____ 6. Patient Weight _____
7. Implant Location _____
8. Patient Activity or Occupation _____
9. History of foreign body sensitivity _____
10a. Diagnosis at Insertion _____
10b. Trauma--simple or comminuted; open or closed _____
10c. Contributory conditions (eg., alcoholism, senility) _____
11. Operation at Insertion _____
12. Antibiotics at insertion, if YES, answer the following:
    a) Reasons for antibiotics
        i) _____
        ii) _____
        iii) _____
    b) Type _____
    c) Dosage _____
    d) Duration _____
13. Functional level of the patient attained between insertion and removal
    ambulatory, ambulatory with aids, non ambulatory
    Comment on relevant physical activity or event for this treatment _____
    _____
14. Roetgenogram review (Indicate YES, NO, DOUBT, or NOT APPLICABLE)
    _____a) bony change in relation to implant
    _____b) absorption or rarefaction
    _____c) increased density (sclerosis - compaction)
    _____d) non-union
    _____e) bone fragments held apart
    _____f) migration of implant
    _____g) malalignment
    _____h) fracture of bone
    _____i) penetration of implant across joint space
    _____j) penetration of implant through bone
    _____k) other
    _____l) other
15. Reason(s) for removal (Indicate YES or NO - mark primary reason with an asterisk)

_____a) Routine	_____b) early infection (< 6 months)
_____c) Late infection (> 6 months)	_____d) breakage or deformation of implant
_____e) pain in the vicinity of implant	_____f) stiffness of joint in vicinity of implant
_____g) prominence of bursae	_____h) instability
_____i) unsatisfactory position of implant	_____j) non-union
_____k) allergic or hyper-sensitive reaction	_____l) reasons not known
_____m) other (specify)	

16. Findings at surgery (Indicate YES, NO, DOUBT, or NOT APPLICABLE)

_____a) pus	_____b) scar tissue
_____c) granulation tissue	_____d) foreign body (debris or stained tissue)
_____e) bursal fluid	_____f) implant easily removed
_____g) fractured grouting agent	_____h) caseation
_____i) boney reaction	

17. Swab from implant site (YES or NO)
    _____a) sterile, if NO, indicate type
18. Examination of tissue

Figure 2. ASTM F561 Metallurgical Review Form

Recovery of Implant
Metallurgical Examination Case #

(This report for component # _____ of _____ total components)
1. Implant Type
2. Number of comoonents
3. Macroscopic examination (YES, NO, DOUBT, or NOT APPLICABLE)

		Location	Estimate Degree
_____	a) wear or burnishing	_____	_____
_____	b) galling	_____	_____
_____	c) scratching	_____	_____
_____	d) change of shape	_____	_____
_____	e) mechanical damage	_____	_____
_____	f) macro porosity	_____	_____

4. Microscopic examination (Indicate location and orientation of sample)
   a) Inclusion content (ASTM E45)
   b) Grain size (ASTM E112)
   c) Grain boundary constituents
   d) Microporosity
   e) Other distinguishing features (ex. cast stainless steel-delta ferrite)
      i _____
      ii _____
      iii _____
5. Type of material (indicate method of determination)
   a) chemical composition
6. Corrosion (if YES, identify)
   a) general corrosion
   b) pitting corrosion
   c) crevice corrosion
   d) galvanic corrosion

_____ 7. Mechanical failure (if YES, identify mode)
   a) fatigue
   b) torsion
   c) impact
   d) stress-corrosion
   e) static-overstress beyond yield strength
   f) corrosion-fatigue
   g) combination of above (identify)
   h) other (specify)

_____ 8. Device flaws (if YES, identify type and origin)
   i _____
   ii _____
   iii _____

_____ 9. Mechanical properties (indicate N/A if not available). Samples should be taken from areas representative of the original material.
   a) sample size and orientation _____
   b) hardness (indicate type) _____
   c) .2% offset yield stress _____
   d) ultimate tensile strength _____
   e) % elongation in _____ in. _____
   f) reduction in area _____
   g) other ASTM recommended tests as applicable (ex. transverse bend tests). _____

_____ 10. Dimensions of implant

11. Conclusion _____

Figure 3. Clinical Case History Form
Implant Retrieval and Analysis
Biomaterials Laboratory

Clinical Case History

1. Case Number: _____

2. Patient's Name: _____

3. Patient's Social Security or Hospital I.D. No.: _____

4. Patient's Sex: _____

5. Patient's Normal Occupational Activity Level:
   - A: Extremely active
   - B: Moderately active (normal)
   - C: Slightly active
   - D: Sedentary
   - E: Other

6. Patient's Weight (lbs): _____

7. Patient's Birthdate (month, year): _____

8. Hospital:
   - A: Veterans Administration - New Orleans
   - B: Veterans Administration - San Francisco
   - C: Charity Hospital - New Orleans
   - D: Moore Clinic - South Carolina
   - E: Tulane Medical Center - New Orleans
   - F: Veterans Administration - Alexandria, La.
   - G: Veterans Administration - Jackson, Ms.
   - H-K: Others

9. Generic Implant Type:

A:	Ankle	H:	Plate
B:	Hip	I:	Hip nail plate
C:	Rod	J:	Staple
D:	Knee	K:	Shoulder
E:	Elbow	L:	Wrist
F:	Pin	M:	Finger
G:	Screw	N:	Others

Figure 3 continued

10. Date of Implantation (month, year): _____

11. Date of Removal (month, year): _____

12. Diagnosis(es) at Insertion:

A:	Unknown	K:	Malunion of fracture
B:	Primary osteoarthritis	L:	Tumor
C:	Secondary osteoarthritis	M:	Loosening of prosthesis
D:	Rheumatoid arthritis	N:	Malposition of prosthesis
E:	Dislocation of joint	O:	Trauma - simple - closed
F:	Asceptic necrosis	P:	Trauma - simple - open
G:	Pain	Q:	Trauma - comminuted - closed
H:	Pagets disease	R:	Trauma - comminuted - open
I:	Congenital deformity	S:	Other
J:	Pseudoarthrosis or non-union		

13. Was the implant inserted left, right or middle? _____

14. Was the implant a joint replacement? _____
If no, answer 15.

15. To which bone was the implant attached or inserted?

A:	Femur	E:	Radius
B:	Tibia	F:	Ulna
C:	Fibula	G:	Spine
D:	Humerous	H-J:	Others

16. Functional level attained after insertion:
(A-C, lower extremities; D-F, upper extremities)

A:	Ambulatory	D:	Functional
B:	Ambulatory with aids	E:	Functional with brace
C:	Not ambulatory	F:	Not functional

17. Reasons for removal:

A:	Routine	H:	Instability or loosening
B:	Early infection < 6 months	I:	Unsatisfactory implant position
C:	Late infection > 6 months	J:	Non-Union
D:	Breakage of implant	K:	Allergic or Hypersensitive reaction
E:	Pain related to implant	L:	Reason unknown
F:	Stiffness related to implant	M:	Other
G:	Prominence of bursae		

Figure 3 continued

18. Finding(s) at surgery:
    - A: Pus
    - B: Granulation
    - C: Foreign body (debris or stained tissue)
    - D: Bursal fluid
    - E: Implant easily removed
    - F: Fractured grouting agent
    - G: Boney reaction
    - H: Loose prosthesis
    - I-K: Others

19. Was a radiographic review performed? _____
    If yes, finding(s):
    - A: Bony change in relation to implant
    - B: Reabsorption or osteoporosis
    - C: Increased density (sclerosis - compaction)
    - D: Hip nail used alone has backed out
    - E: Bone fragments held apart
    - F: Migration of implant
    - G: Malalignment
    - H: Fracture of bone
    - I: Penetration of implant across joint space
    - J: Penetration of implant through bone
    - K: Loosening
    - L: Others

20. Was a swab performed? _____
    If yes, was the swab sterile? _____

21. Was an examination of the tissue performed? _____

22. Were antibiotics administered before or after insertion of the device? _____

Figure 4 Materials Examination Form
Implant Retrieval and Analysis
Biomaterials Laboratory

Materials Examination

Case Number: _____

Patient's Name: _____

Patient's I.D. No.: _____

Component ____ of ____

1. What is the specific implant component?

A:	Ankle distal	P:	Plate bone
B:	Ankle proximal	Q:	Plate Jewet
C:	Elbow humeral	R:	Plate Richards screw
D:	Elbow ulnar	S:	Plate sliding nail
E:	Hip acetabular	T:	Rod IM
F:	Hip femoral stem	U:	Rod spinal
G:	Hip femoral surface	V:	Screw cancellous
H.	Joint MCP	W:	Screw cortical
I:	Joint PIP	X:	Screw plate
J:	Knee femoral	Y:	Shoulder humeral
K:	Knee patellar	Z:	Shoulder other
L:	Knee tibial	+:	Staple
M:	Nail Richards screw	*:	Wrist
N:	Nail sliding nail	!:	Other 1
O:	Pin	$:	Other 2

2. Manufacturer of the implant:

A:	A-O	J:	3-M
B:	Biomet	K:	OEC
C:	Cintor	L:	Osteonics
D:	Cutter	M:	Richards
E:	DePuy	N:	U.S. Surgical
F:	Downs	O:	Wright-Dow Corning
G:	Howmedica	P:	Zimmer USA
H:	Hexcel	Q-T:	Other
I.	Medtec		

Figure 4 continued

3. Implant material?

A:	Stainless steel	E:	MP35N
B:	Co-Cr-Mo	F:	Silastic
C:	Titanium (Ti-6Al-4V)	G:	Aluminum Oxide
D:	Polyethylene (UHMWPE)	H-J:	Others

4. Was a macroscopic exam performed? _____
If yes, then scale for following is 0.0 - 4.0
0 = none 1 - mild 2 = moderate 3 = severe 4 = N.A.

A:	Wear _____	D:	Change in implant shape _____
B:	Galling _____	E:	Mechanical damage _____
C:	Burnishing _____	F:	Macro porosity _____

5. Was a microscopic examination performed? Y or N _____ If Y, then:

A: Inclusion content ASTM #45, i.e. DO.OT _____

B: Grain size ASTM E112, i.e. 4.5 _____

6. Was a corrosion examination performed? _____
If yes, scale is 0.0 - 5.0

A: Gross corrosion _____

B: Crevice corrosion _____

C: Galvanic corrosion _____

D: Fretting corrosion _____

7. Was there mechanical failure? _____
If yes, failure modes:

A:	Fatigue	E:	Overstress
B:	Torsion	F:	Corrosion-Fatigue
C:	Impact	G:	Other
D:	Stress-corrosion		

8. Was there a fabrication flaw? _____

9. Was there a mechanical property exam performed? _____
If yes:

A: Hardness, i.e. B31 _____

B: Offset yield strength (Psi) _____

C: Ultimate tensile strength (Psi) _____

D: % Elongation _____

E: Gauge length (in.) _____

F: Reduction in area _____

G: Bend strength (Psi) _____

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Example 1. Use of Help ("?") and Data Check Features

```
12.) ENTER DIAGNOSIS(S) AT INSERTION. SEPARATE WITH COMMAS.

      ?

         THE FOLLOWING IS A LIST OF POSSIBLE DIAGNOSES AT
         INSERTION:
         A:   UNKNOWN
         B:   PRIMARY OSTEOARTHRITIS
         C:   SECONDARY OSTEOARTHRITIS
         D:   RHEUMATOID ARHTRITIS
         E:   DISLOCATION OF JOINT
         F:   ASCEPTIC NECROSIS
         G:   PAIN
         H:   PAGETS DISEASE
         I:   CONGENITAL DEFORMITY
         J:   PSEUDOARTHROSIS OR NON-UNION
         K:   MALUNION OF FRACTURE
         L:   TUMOR
         M:   LOOSENING OF PROTHESIS
         N:   MALPOSITION OF PROTHESIS
         O:   TRAUMA-SIMPLE-CLOSED
         P:   TRAUMA-SIMPLE-OPEN
         Q:   TRAUMA-COMMINUTED-CLOSED
         R:   TRAUMA-COMMINUTED-OPEN
         S:   OTHER

12.) ENTER DIAGNOSIS(S) AT INSERTION. SEPARATE WITH COMMAS.

      U

     **  INVALID INPUT  **

12.) ENTER DIAGNOSIS(S) AT INSERTION. SEPARATE WITH COMMAS.

      O

13.) WAS THE IMPLANT INSERTED LEFT, RIGHT OR MIDDLE.

      TYPE  L  OR  R  OR  M  RESPECTIVELY .

      L

$
```

Example 2. Use of Input Module

```
@RUN ADDREC
 WOULD YOU LIKE INSTRUCTIONS? Y OR N

        Y

            'ADDREC.FOR' IS A PROGRAM DESIGNED TO ACCEPT CLINICAL AND
            MATERIALS CHARACTERIZATION DATA REGARDING ORTHOPAEDIC IMPLANT
            RETRIEVAL FROM STANDARD FORMS DEVELOPED BY THE BIOMATERIALS
            LABORATORY, TULANE UNIVERSITY. THE CLINICAL DATA, I.E. AGE,
            DATE OF REMOVAL, TYPE OF IMPLANT, ETC. IS STORED IN A DATA
            FILE CALLED 'PERSON.MST'. THE MATERIAL EXAMINATION DATA, I.E.
            CORROSION, FAILURE, ETC., IS STORED IN A DATA FILE CALLED
            'MATEXM.MST'. IT SHOULD BE NOTED THAT ALL DATA IS STORED IN
            CODED FORM FOR EFFICIENT COMPUTER USAGE AND MAY BE PRINTED OUT
            IN DECODED FORM WITH THE PROGRAM 'PRINT.CBL'.

                ONCE THE USER HAS THE STANDARD FORMS, HE MAY BEGIN
            INPUTTING THE DATA. SOME DATA HAS BEEN SIMPLIFIED SO THAT IT
            CAN BE ENTERED IN CODED FORM. FOR EXAMPLE, THE TYPE OF
            IMPLANTS HAVE BEEN CODED SO THAT AN 'A' REPRESENTS A HIP
            PROTHESIS OR A 'C' REPRESENTS A KNEE PROTHESIS. THIS IS DONE
            TO REDUCE COMPUTER STORAGE SPACE AND INPUT TIME.

                IF THE USER DOES NOT KNOW THE CODES FOR A SPECIFIC INPUT,
            HE CAN TYPE A '?' AND THE PROGRAM WILL DISPLAY EACH CODE AND
            IT'S REPRESENTATION.

                THERE ARE ALSO SOME OTHER SPECIAL DATA FEATURES. DATES
            ARE TO BE ENTERED AS THE MONTH AND YEAR. FOR EXAMPLE,
            DECEMBER 1939 SHOULD BE ENTERED AS 1239 . NOTE THAT THERE IS
            NO DECIMAL POINT AND LEAD ZEROS MUST BE INCLUDED. MULTIPLE
            ANSWER QUESTIONS DO NOT HAVE TO BE ENTERED IN ALPHABETICAL
            ORDER, BUT EACH RESPONSE MUST BE SEPARATED BY A COMMA WITHOUT
            ANY BLANK SPACES.

                AT ANY POINT AFTER A QUESTION HAS BEEN ASKED BY THE
            PROGRAM THE USER MAY TYPE 'BACK' OR 'HELP'. 'BACK' WILL ALLOW
            THE USER TO GO BACK OR AHEAD TO A PREVIOUS OR LATER QUESTION.
            THE DATA OF THE QUESTION IN WHICH THE USER TYPES BACK OR HELP
            IS ONLY AFFECTED WHEN THE USER CHANGES IT'S INFORMATION. IF
            THE USER DOES NOT KNOW THE NUMBER OF THE QUESTION HE WISHES TO
            RETURN TO, HE MAY TYPE A '?' AND THE PROGRAM WILL LIST THE
            QUESTIONS. TYPING 'HELP' WILL DISPLAY THIS MESSAGE.

                AT THE END OF EACH FORM, THE USER HAS THE OPTION OF
            REVIEWING THE DATA INPUT FROM THAT FORM. HE MAY THEN CHANGE
            ANY DATA BY TRANSFERRING TO THAT SPECIFIC QUESTION. THE
            PROGRAM WILL PROVIDE THE APPLICABLE PROMPTS.

                AT THE END OF THE CLINICAL DATA FORM THE USER WILL BE
            ASKED HOW MANY COMPONENTS THERE ARE IN THE RETRIEVED IMPLANT
            DEVICE. THIS REFERS TO THE NUMBER OF IMPLANT COMPONENTS THAT
            HAVE A MATERIAL EXAM- INATION FORM. THE PROGRAM WILL ACCEPT
            MATERIAL EXAMINATION DATA FOR EACH COMPONENT. THE PROGRAM
            WILL ALSO DISPLAY WHICH COMPONENT DATA YOU ARE ENTERING.
```

```
          UNDER NO CIRCUMSTANCES SHOULD ANY DATA  BE  ENTERED  WITH
        QUOTES.   YOU  MAY  END THIS PROGRAM ONLY AT THE COMPLETION OF
        THE LAST COMPONENT, OTHERWISE DATA MAY BE LOST.
          ****  END  OF   ADDREC.FOR HELP FILE ****

1.) ENTER CASE NUMBER.  (4-DIGIT INTEGER)

      ?

        THE CASE NUMBER IS A FOUR DIGIT INTEGER CODE AT THE TOP OF THE
        FORM.  PLEASE DO NOT PUT IN A DECIMAL POINT.

1.) ENTER CASE NUMBER.  (4-DIGIT INTEGER)

      1051

2.) ENTER PATIENTS NAME.

   LAST NAME FOLLOWED BY ONE BLANK AND THE FIRST INITIAL.

      ?

        PATIENTS NAME.  UP TO 12 LETTERS FOR LAST NAME FOLLOWED BY ONE
        SPACE  THEN  THE  INITIAL OF FIRST NAME I.E.  FOR ROBERT JONES
        TYPE IN JONES R

2.) ENTER PATIENTS NAME.

LAST NAME FOLLOWED BY ONE BLANK AND THE FIRST INITIAL.

      SMITHERS J

3.) ENTER PATIENT ID- .

      ?

        PATIENT ID NUMBER IS UP TO A NINE DIGIT LETTER  AND/OR  NUMBER
        RESPONSE  THAT  CORRESPONDS  TO  THE  PATIENTS  IDENTIFICATION
        NUMBER.
3.) ENTER PATIENT ID- .


      439806574

4.) ENTER PATIENTS SEX.  M  OR  F .

      ?

         M STANDS FOR MALE, F STANDS FOR FEMALE.
```

```
4.) ENTER PATIENTS SEX.  M  OR  F .

      M

5.) ENTER PATIENTS NORMAL OCCUPATIONAL ACTIVITY LEVEL.

      ?

         THE FOLLOWING IS A LIST OF POSSIBLE ACTIVITY LEVELS :
         A:   EXTREMELY ACTIVE
         B:   MODERATELY ACTIVE (NORMAL)
         C:   SLIGHTLY ACTIVE
         D:   SEDENTARY
         E:   OTHER

5.) ENTER PATIENTS NORMAL OCCUPATIONAL ACTIVITY LEVEL.

      B

6.) ENTER PATIENTS WEIGHT IN LBS (3-DIGIT INTEGER)

      ?

         ENTER WEIGHT IN LBS.  3 DIGIT INTEGER

         INCLUDE ZEROES BEFORE WEIGHT IF LESS THAN 100 LBS.

6.) ENTER PATIENTS WEIGHT IN LBS (3-DIGIT INTEGER)

      171

7.) ENTER PATIENTS BIRTH DATE. MONTH AND YEAR. 1259

      ?

        ENTER BIRTH DATE IN THE FOLLOWING FORMAT.  FOR DECEMBER  1945,
        TYPE IN 1245 .  NO DECIMAL PLEASE.  INCLUDE LEAD ZEROS.

7.) ENTER PATIENTS BIRTH DATE. MONTH AND YEAR. 1259

      0748

8.) ENTER THE HOSPITAL CODE.

      ?
```

```
          THE FOLLOWING IS A LIST OF CODES FOR HOSPITALS:
          A:   VETERANS ADMINISTRATION - NEW ORLEANS
          B:   VETERANS ADMINISTRATION - SAN FRANCISCO
          C:   CHARITY HOSPITAL - NEW ORLEANS
          D:   MOORE CLINIC - SOUTH CAROLINA
          E:   TULANE MEDICAL CENTER - NEW ORLEANS
          F:   VETERANS ADMINISTRATION - ALEXANDRIA, LA.
          G:   VETERANS ADMINISTRATION - JACKSON, MISS.
          H-K: OTHERS

8.) ENTER THE HOSPITAL CODE.

      E

9.) ENTER GENERIC IMPLANT TYPE.

      ?


          THE FOLLOWING IS A LIST OF GENERIC IMPLANT CODES:
          A:   ANKLE
          B:   HIP
          C:   ROD
          D:   KNEE
          E:   ELBOW
          F:   PIN
          G:   SCREW
          H:   PLATE
          I:   HIP NAIL PLATE
          J:   STAPLE
          K:   SHOULDER
          L:   WRIST
          M:   FINGER
          N:   OTHER

9.) ENTER GENERIC IMPLANT TYPE.

      B

10.) ENTER IMPLANTATION DATE.  MONTH AND YEAR. I.E. 0679

      ?


        ENTER IMPLANTION DATE IN THE  FOLLOWING  FORM.   FOR  DECEMBER
        1959, TYPE IN 1259 .  NO DECIMAL PLEASE.  INCLUDE LEAD ZEROS.
```

10.) ENTER IMPLANTATION DATE. MONTH AND YEAR. I.E. 0679

0179

11.) ENTER DATE OF REMOVAL. MONTH,YEAR. IE. 0667

?

ENTER DATE OF REMOVAL IN THE FOLLOWING FORMAT. FOR DECEMBER 1959, ENTER 1259 . NO DECIMAL PLEASE. INCLUDE LEAD ZEROS.

11.) ENTER DATE OF REMOVAL. MONTH,YEAR. IE. 0667

0280

12.) ENTER DIAGNOSIS(S) AT INSERTION. SEPARATE WITH COMMAS.

?

THE FOLLOWING IS A LIST OF POSSIBLE DIAGNOSES AT INSERTION:

A: UNKNOWN
B: PRIMARY OSTEOARTHRITIS
C: SECONDARY OSTEOARTHRITIS
D: RHEUMATOID ARHTRITIS
E: DISLOCATION OF JOINT
F: ASCEPTIC NECROSIS
G: PAIN
H: PAGETS DISEASE
I: CONGENITAL DEFORMITY
J: PSEUDOARTHROSIS OR NON-UNION
K: MALUNION OF FRACTURE
L: TUMOR
M: LOOSENING OF PROTHESIS
N: MALPOSITION OF PROTHESIS
O: TRAUMA-SIMPLE-CLOSED
P: TRAUMA-SIMPLE-OPEN
Q: TRAUMA-COMMINUTED-CLOSED
R: TRAUMA-COMMINUTED-OPEN
S: OTHER

12.) ENTER DIAGNOSIS(S) AT INSERTION. SEPARATE WITH COMMAS.

F,G

13.) WAS THE IMPLANT INSERTED LEFT, RIGHT OR MIDDLE.

TYPE L OR R OR M RESPECTIVELY .

?

ENTER REATIVE POSITION OF PROSTHESIS.
LEFT SIDE = L, RIGHT SIDE = R, MIDDLE = M

13.) WAS THE IMPLANT INSERTED LEFT, RIGHT OR MIDDLE.

TYPE L OR R OR M RESPECTIVELY .

L

14.) WAS THE IMPLANT A JOINT REPLACEMENT? Y OR N.

?

ENTER Y OR N ACCORDING TO WHETHER THE
PROSTHESIS WAS A JOINT REPLACEMENT.

14.) WAS THE IMPLANT A JOINT REPLACEMENT? Y OR N.

Y

16.) ENTER THE MAXIMUM FUNCTIONAL LEVEL ATTAINED

FOLLOWING IMPLANT INSERTION.

?

THE FOLLOWING ARE POSSIBLE FUNCTIONAL LEVELS:
(A-C:LOWER EXTREMITIES, D-F:UPPER EXTREMITIES)
A: AMBULATORY
B: AMBULATORY WITH AIDS
C: NOT AMBULATORY
D: FUNCTIONAL
E: FUNCTIONAL WITH BRACE
F: NOT FUNCTIONAL

16.) ENTER THE MAXIMUM FUNCTIONAL LEVEL ATTAINED
FOLLOWING IMPLANT INSERTION.

A

17.) ENTER REASON(S) FOR REMOVAL. SEPARATE BY COMMAS

?

THE FOLLOWING IS A LIST FOR REASONS OF REMOVAL:
A: ROUTINE
B: EARLY INFECTION < 6 MONTHS
C: LATE INFECTION > 6 MONTHS
D: BREAKAGE OF IMPLANT
E: PAIN RELATED TO IMPLANT
F: STIFFNESS RELATED TO IMPLANT
G: PROMINENCE OR BURSAE
H: INSTABILITY OR LOOSENING
I: UNSATISFACTORY IMPLANT POSITION
J: NON-UNION

```
          K:   ALLERGIC OR HYPERSENSITIVE REACTION
          L:   REASON UNKNOWN
          M:   OTHER

17.) ENTER REASON(S) FOR REMOVAL. SEPARATE BY COMMAS

       D,E

18.) ENTER FINDINGS AT SURGERY. SEPARATE BY COMMAS.

       ?


          THE FOLLOWING IS A LIST OF FINDINGS AT SURGERY:
          A:   PUS
          B:   GRANULATION
          C:   FOREIGN BODY (DEBRIS OR STAINED TISSUE)
          D:   BURSAL FLUID
          E:   IMPLANT EASILY REMOVED
          F:   FRACTURED GROUTING AGENT
          G:   BONEY REACTION
          H:   LOOSE PROSTHESIS
          I-K: OTHERS

18.) ENTER FINDINGS AT SURGERY. SEPARATE BY COMMAS.

       F

19.) WAS A RADIOGRAPHIC REVIEW PERFORMED? Y OR N.

       ?


          ENTER  Y  OR  N  AS TO WHETHER A RADIOGRAPHIC REVIEW WAS
         PERFORMED.
          THE FOLLOWING IS A LIST OF RADIOGRAPHIC OBSERVATIONS:
          A:   BONY CHANGE IN RELATION TO IMPLANT
          B:   RESORPTION OR OSTEOPOROSIS
          C:   INCREASED DENSITY (SCLEROSIS - COMPACTION)
          D:   HIP NAIL USED ALONE HAS BACKED OUT
          E:   BONE FRAGMENTS HELD APART
          F:   MIGRATION OF IMPLANT
          G:   MALALIGNMENT
          H:   FRACTURE OF BONE
          I:   PENETRATION OF IMPLANT ACROSS JOINT SPACE
          J:   PENETRATION OF IMPLANT THROUGH BONE
          K:   LOOSENING
          L-O: OTHERS

19.) WAS A RADIOGRAPHIC REVIEW PERFORMED? Y OR N.

       Y

ENTER REVIEW FINDING(S).  SEPARATE WITH COMMA.
```

```
       G

20.) WAS A SWAB PERFORMED? Y OR N.

       ?

         ENTER Y OR N AS TO WHETHER A SWAB  WAS  PERFORMED  IF  Y  THEN
         ANSWER  THE NEXT QUESTION EITHER Y OR N AS TO WHETHER THE SWAB
         WAS STERILE

20.) WAS A SWAB PERFORMED? Y OR N.

       Y

WAS THE SWAB STERILE? Y  OR  N

       Y

21.) WAS AN EXAMINATION OF THE TISSUE PERFORMED. Y  OR  N

       ?

          ENTER  Y  OR  N  AS TO WHETHER AN EXAMINATION OF THE TISSUE
            WAS PERFORMED.

21.) WAS AN EXAMINATION OF THE TISSUE PERFORMED. Y  OR  N

       N

22.) WERE ANTIBIOTICS ADMINISTERED BEFORE OR AFTER INSERTION OF DEVICE?

Y OR N

       ?

          ENTER  Y  OR  N  AS TO WHETHER ANTIBIOTICS WERE
          ADMINISTERED TO PATIENT BEFORE OR AFTER THE PROSTHESIS WAS
         INSERTED.
22.) WERE ANTIBIOTICS ADMINISTERED BEFORE OR AFTER INSERTION
  OF DEVICE? Y OR N

       Y

WOULD YOU CARE TO REVIEW THE RECORD? Y OR N.

       Y

         CASE NO. 1051, NAME SMITHERS J
         ID-NUMBER 439806574, SEX M
         WEIGHT 171, ACTIVITY LEVEL B
         BIRTH DATE 0748, HOSPITAL E, IMPLANT B
         IMPLANT DATE 0179, REMOVAL DATE 0280
         DIAGNOSIS FG                , POSITION L, JOINT? Y
         BONE TYPE  , FUNCTIONAL LEVEL A
```

```
         REASONS FOR REMOVAL DE           , FINDINGS AT SURGERY F

         RADIOGRAPHIC REVIEW? Y, RADIOGRAPHIC FINDINGS G
         SWAB? Y, STERILE SWAB? Y, TISSUE EXAM? N
         ANTIBIOTICS? Y
IS THERE SOME DATA YOU WISH TO CHANGE? Y OR N

       N

ENTER NUMBER OF COMPONENTS.

       2

ENTER THE DATA FOR COMPONENT   1

1.) ENTER THE SPECIFIC IMPLANT COMPONENT TYPE.

       ?

          THE FOLLOWING IS A LIST OF SPECIFIC IMPLANT CODES
          A:   ANKLE-DISTAL
          B:   ANKLE-PROXIMAL
          C:   ELBOW-HUMERAL
          D:   ELBOW-ULNAR
          E:   HIP-ACETABULAR
          F:   HIP-FEMORAL STEM
          G:   HIP-FEMORAL SURFACE
          H:   JOINT-MCP
          I:   JOINT-PIP
          J:   KNEE-FEMORAL
          K:   KNEE-PATELLAR
          L:   KNEE-TIBIAL
          M:   NAIL-RICHARDS SCREW
          N:   NAIL-SLIDING NAIL
          O:   PIN
          P:   PLATE-BONE
          Q:   PLATE-JEWET
          R:   PLATE-RICHARDS SCREW
          S:   PLATE-SLIDING NAIL
          T:   ROD-IM
          U:   ROD-SPINAL
          V:   SCREW-CANCELLOUS
          W:   SCREW-CORTICAL
          X:   SCREW-PLATE
          Y:   SHOULDER-HUMERAL
          Z:   SHOULDER-PROXIMAL
          +:   STAPLE
          *:   WRIST
          !:   OTHER 1
          $:   OTHER 2
```

(Example 2 cont.)

```
1.) ENTER THE SPECIFIC IMPLANT COMPONENT TYPE.

      F

2.) ENTER THE IMPLANTS MANUFACTURER.

      ?


         THE FOLLOWING IS A LIST OF MANUFACTURERS:
         A:   A-O
         B:   BIOMET
         C:   CINTOR
         D:   CUTTER
         E:   DEPUY
         F:   DOWNS
         G:   HOWMEDICA
         H:   HEXCEL
         I:   MEDITEC
         J:   3-M
         K:   OEC
         L:   OSTEONICS
         M:   RICHARDS
         N:   U.S. SURGICAL
         O:   WRIGHT-DOW CORNING
         P:   ZIMMER USA
         Q-T: OTHERS

2.) ENTER THE IMPLANTS MANUFACTURER.

      Q

3.) ENTER IMPLANT MATERIAL CODE.

      ?


         THE FOLLOWING IS A LIST OF MATERIAL TYPES:
         A:   STAINLESS STEEL
         B:   CO-CR-MO
         C:   TITANIUM TI-6AL-4V
         D:   POLYETHYLENE UHMWPE
         E:   MP35N
         F:   SILASTIC
         G:   ALUMINUM OXIDE
         H-J: OTHERS

3.) ENTER IMPLANT MATERIAL CODE.

      A

4.) WAS A MACROSCPIC EXAMINATION PERFORMED? Y OR N.

      ?
```

ENTER Y OR N AS TO WHETHER A MACROSCOPIC EXAMINATION WAS PERFORMED. IF YES, THEN THE SCALE FOR THE FOLLOWING QUESTIONS IS FROM 0.0 TO 4.0

4.) WAS A MACROSCPIC EXAMINATION PERFORMED? Y OR N.

Y

RATE THE WEAR.

0-NONE,1-MILD,2-MODERATE,3-SEVERE,4-N.A. I.E. 2.8

1.0

RATE THE GALLING.

0-NONE,1-MILD,2-MODERATE,3-SEVERE,4-N.A. I.E. 2.8

0.0

RATE THE BURNISHING.

0-NONE,1-MILD,2-MODERATE,3-SEVERE,4-N.A. I.E. 2.8

0.0

RATE THE CHANGE IN IMPLANT SHAPE.

0-NONE,1-MILD,2-MODERATE,3-SEVERE,4-N.A. I.E. 2.8

0.0

RATE THE MECHANICAL DAMAGE.

0-NONE,1-MILD,2-MODERATE,3-SEVERE,4-N.A. I.E. 2.8

1.0

RATE THE MACRO POROSITY.

0-NONE,1-MILD,2-MODERATE,3-SEVERE,4-N.A. I.E. 2.8

0.0

5.) WAS A MICROSCOPIC EXAMINATION PERFORMED? Y OR N.

?

ENTER Y OR N AS TO WHETHER A MICROSCOPIC EXAMINATION WAS PERFORMED. IF YES, THEN THE SCALES FOR THE FOLLOWING QUESTIONS ARE ON THE FORM.

```
 5.) WAS A MICROSCOPIC EXAMINATION PERFORMED? Y OR N.

       Y

 ENTER INCLUSION CONTENT ASTM E45. IE.  D1.0T

D2.5T

 ENTER GRAIN SIZE ASTM E112.  IE.   4.5

6.5

 6.) WAS THERE A CORROSION EXAMINATION PERFORMED. Y  OR  N

       ?


          ENTER Y OR  N  AS  TO  WHETHER  A  CORROSION  EXAMINATION  WAS
          PERFORMED.  INDEX SCALE:  0.0 TO 5.0

 6.) WAS THERE A CORROSION EXAMINATION PERFORMED. Y  OR  N

       Y

 ENTER GROSS CORROSION INDEX.  SCALE: 0.0-5.0

       0.0

 ENTER CREVICE CORROSION INDEX.  SCALE: 0.0-5.0

       1.5

 ENTER GALVANIC CORROSION INDEX.  SCALE: 0.0-5.0

       0.0

 ENTER FRETTING CORROSION INDEX.  SCALE: 0.0-5.0

       0.0

 7.) WAS THERE MECHANICAL FAILURE?  Y OR N.

       ?


          ENTER  Y  OR  N  AS TO WHETHER THERE WAS MECHANICAL FAILURE.
          THE FOLLOWING IS A LIST OF FAILURE MODES:

          A:   FATIGUE
          B:   TORSION
          C:   IMPACT
          D:   STRESS-CORROSION
          E:   OVERSTRESS
          F:   CORROSION-FATIGUE
          G:   OTHER
```

```
7.) WAS THERE MECHANICAL FAILURE?  Y OR N.

       Y

ENTER FAILURE MODE(S).  SEPARATE WITH COMMAS.

       A

8.) WAS THERE A FABRICATION FLAW? Y OR N

       ?

          ENTER  Y  OR  N  AS TO WHETHER THERE WAS A FABRICATION FLAW

8.) WAS THERE A FABRICATION FLAW? Y OR N

       N

9.) WAS A MECHANICAL PROPERTY EXAMINATION PERFORMED? Y  OR  N

       ?


         ENTER Y OR N AS TO WHETHER A MECHANICAL  PROPERTY  EXAMINATION
         WAS PERFORMED.  SCALE(S) FOR DATA ON FORM

9.) WAS A MECHANICAL PROPERTY EXAMINATION PERFORMED? Y  OR  N

       Y

ENTER HARDNESS.
3-CHARACTERS  I.E.  B31

       B90

ENTER OFFSET YIELD STRENGTH (UNITS PSI)
7-CHARACTERS  I.E.  70000.0

       75000.0

ENTER ULTIMATE TENSILE STRENGTH (UNITS PSI)
7-CHARACTERS  I.E.  180000.

       100000.

ENTER % ELONGATION.
5-CHARACTERS  I.E.  25.00

       8.000

ENTER GAUGE LENGTH (UNITS INCHES).
3-CHARACTERS  I.E.  1.3

       1.0
```

```
ENTER REDUCTION IN AREA.
5-CHARACTERS  I.E.  12.45

      20.00

ENTER BEND STRENGTH (UNITS PSI).
7-CHARACTERS  I.E.  70000.0

       **  NOTICE:  NO DATA WAS ENTERED !!!  **

WOULD YOU CARE TO REVIEW THE RECORD? Y OR N.

      Y


         CASE NUMBER 1051, COMPONENT NUMBER 1
         SPECIFIC IMPLANT TYPE F, MANUFACTURED Q
         MATERIAL A,MACRO EXAM ? Y, WEAR 1.0, GALLING 0.0
         BURNISHING 0.0, SHAPE CHANGE 0.0, MECH DAMAGE 1.0,  POROSITY
        0.0
         MICRO EXAM ? Y,INCLUSION CONTENT D2.5T
         GRAIN SIZE 6.5, CORROSION EXAM ? Y, GROSS INDEX 0.0
         CREVICE INDEX 1.5, GALVANIC INDEX 0.0, FRET INDEX 0.0
         MECH FAILURE ? Y, FAILURE MODES A
         FABRICATION FLAW ? N, FLAWS    , MECH PROPERTY EXAM ? Y
         HARDNESS B90, OFFSET YIELD STRENGTH 75000.0, TENSILE STRENGTH
        100000.
         % ELOGATION 8.000, GUAGE LENGTH 1.0, AREA REDUCTION 20.00
         BEND STRENGTH

IS THERE SOME DATA YOU WISH TO CHANGE? Y OR N

      N

ENTER THE DATA FOR COMPONENT   2

1.) ENTER THE SPECIFIC IMPLANT COMPONENT TYPE.

      E

2.) ENTER THE IMPLANTS MANUFACTURER.

      Q

3.) ENTER IMPLANT MATERIAL CODE.

      D

4.) WAS A MACROSCPIC EXAMINATION PERFORMED? Y OR N.

      N

5.) WAS A MICROSCOPIC EXAMINATION PERFORMED? Y OR N.

      N
```

```
6.) WAS THERE A CORROSION EXAMINATION PERFORMED. Y  OR  N

       N

7.) WAS THERE MECHANICAL FAILURE?  Y OR N.

       N

8.) WAS THERE A FABRICATION FLAW? Y OR N

       N

9.) WAS A MECHANICAL PROPERTY EXAMINATION PERFORMED? Y  OR  N

       N

WOULD YOU CARE TO REVIEW THE RECORD? Y OR N.

       Y


          CASE NUMBER 1051, COMPONENT NUMBER 2
          SPECIFIC IMPLANT TYPE E, MANUFACTURED Q
          MATERIAL D,MACRO EXAM ? N, WEAR     , GALLING
          BURNISHING     , SHAPE CHANGE     , MECH DAMAGE     ,  POROSITY

          MICRO EXAM ? N,INCLUSION CONTENT
          GRAIN SIZE     , CORROSION EXAM ? N, GROSS INDEX
          CREVICE INDEX     , GALVANIC INDEX     , FRET INDEX
          MECH FAILURE ? N, FAILURE MODES
          FABRICATION FLAW ? N, FLAWS    , MECH PROPERTY EXAM ? N
          HARDNESS     , OFFSET YIELD STRENGTH         , TENSILE STRENGTH

          % ELOGATION       , GUAGE LENGTH     , AREA REDUCTION
          BEND STRENGTH

IS THERE SOME DATA YOU WISH TO CHANGE? Y OR N

       N

DO YOU HAVE MORE CASES TO ENTER?  Y OR N

       N

STOP

END OF EXECUTION

$
```

Example 3. Use of Case Review and Correction Feature

```
22.) WERE ANTIBIOTICS ADMINISTERED BEFORE OR AFTER INSERTION OF

  DEVICE? Y OR N

       Y

WOULD YOU CARE TO REVIEW THE RECORD? Y OR N.

       Y

          CASE NO. 1055, NAME JONES J
          ID-NUMBER 145667812, SEX F
          WEIGHT 112, ACTIVITY LEVEL B
          BIRTH DATE 0148, HOSPITAL A, IMPLANT G
          IMPLANT DATE 0178, REMOVAL DATE 0678
          DIAGNOSIS A                , POSITION L, JOINT? N
          BONE TYPE A, FUNCTIONAL LEVEL A
          REASONS FOR REMOVAL A            , FINDINGS AT SURGERY

          RADIOGRAPHIC REVIEW? N, RADIOGRAPHIC FINDINGS
          SWAB? Y, STERILE SWAB? Y, TISSUE EXAM? N
          ANTIBIOTICS? Y

IS THERE SOME DATA YOU WISH TO CHANGE? Y OR N

       Y

WHICH QUESTION DO YOU WISH TO RETURN TO? INTEGER NO.

       ?

          THE FOLLOWING IS A LIST OF QUESTION NUMBERS.
          NOTE, YOU MAY RETURN ONLY TO A QUESTION ON THE FORM
          YOU ARE CURRENTLY WORKING ON.

          CLINICAL EXAMINATION FORM:
          1:   CASE NUMBER
          2:   NAME
          3:   ID-NUMBER
          4:   SEX
          5:   ACTIVITY LEVEL
          6:   WEIGHT
          7:   BIRTH DATE
          8:   HOSPITAL CODE
          9:   GENERIC IMPLANT CODE
          10:  IMPLANTTION DATE
          11:  REMOVAL DATE
          12:  DIAGNOSIS AT INSERTION
          13:  LEFT, RIGHT, MIDDLE POSITION
          14:  JOINT?
          15:  BONE IN WHICH INSERTED
          16:  FUNCTIONAL LEVEL ATTAINED
          17:  REASON(S) FOR REMOVAL
          18:  FINDINGS AT SURGERY
          19:  RADIOGRAPHIC REVIEW PERFORMED?
```

```
          20:  SWAB PERFORMED?
          21:  TISSUE EXAM PERFORMED?
          22:  ANTIBIOTICS?

          MATERIAL EXAMINATION FORM
          1:   SPECIFIC IMPLANT TYPE
          2:   MANUFACTURER
          3:   IMPLANT MATERIAL
          4:   MACROSCOPIC EXAM
          5:   MICROSCOPIC EXAM
          6:   CORROSION EXAM
          7:   MECHANICAL FAILURE
          8:   FABRICATION FLAW
          9:   MECHANICAL PROPERTY EXAM


WHICH QUESTION DO YOU WISH TO RETURN TO? INTEGER NO.

      16

16.) ENTER THE MAXIMUM FUNCTIONAL LEVEL ATTAINED

   FOLLOWING IMPLANT INSERTION.

      ?

          THE FOLLOWING ARE POSSIBLE FUNCTIONAL  LEVELS:
          (A-C:LOWER EXTREMITIES, D-F:UPPER EXTREMITIES)

          A:   AMBULATORY
          B:   AMBULATORY WITH AIDS
          C:   NOT AMBULATORY
          D:   FUNCTIONAL
          E:   FUNCTIONAL WITH BRACE
          F:   NOT FUNCTIONAL


16.) ENTER THE MAXIMUM FUNCTIONAL LEVEL ATTAINED

FOLLOWING IMPLANT INSERTION.

      B

WOULD YOU CARE TO REVIEW THE RECORD? Y OR N.

      Y

          CASE NO. 1055, NAME JONES J
          ID-NUMBER 145667812, SEX F
          WEIGHT 112, ACTIVITY LEVEL B
          BIRTH DATE 0148, HOSPITAL A, IMPLANT G
          IMPLANT DATE 0178, REMOVAL DATE 0678
          DIAGNOSIS A                , POSITION L, JOINT? N
          BONE TYPE A, FUNCTIONAL LEVEL B
          REASONS FOR REMOVAL A           , FINDINGS AT SURGERY
```

(Example 3 cont.)

```
          RADIOGRAPHIC REVIEW? N, RADIOGRAPHIC FINDINGS
          SWAB? Y, STERILE SWAB? Y, TISSUE EXAM? N
          ANTIBIOTICS? Y

 IS THERE SOME DATA YOU WISH TO CHANGE? Y OR N

        N

 ENTER NUMBER OF COMPONENTS.

        1

 ENTER THE DATA FOR COMPONENT    1

$
```

Example 4. Use of Cross Referencing Feature

```
@RUN SELECT

 WOULD YOU LIKE INSTRUCTIONS? Y OR N

       Y

          'SELECT.FOR' IS A PROGRAM DESIGNED TO CROSS REFERENCE DATA
          WHICH IS ASSOCIATED WITH EACH CLINICAL AND MATERIAL
          EXAMINATION RECORD.

               INPUT TO THE 'SELECT.FOR' PROGRAM STARTS WITH THE USER
          TYPING THE ITEMS TO BE CROSS REFERENCED.  TYPING A '?' AT THIS
          POINT WILL GIVE THE USER THE LIST OF POSSIBLE ITEMS THAT MAY
          BE SELECTED AND THE CORROSPONDING ITEM NUMBER.  THE USER THEN
          ENTERS FROM THE KEYBOARD EACH ITEM NUMBER TO BE CROSS
          REFERENCED SEPARATED BY COMMAS.

               THE PROGRAM THEN AUTOMATICALLY ASKS THE USER FOR SPECIFIC
          INFORMATION ON THE ITEMS HE HAS CHOSEN TO CROSS REFERENCE.
          BRIEF INSTRUCTIONS MAY BE OBTAINED FOR EACH PARTICULAR ITEM
          SELECTED BY TYPING A '?' WHEN ASKED FOR SPECIFIC INFORMATION.

               IF THE USER MAKES A MISTAKE WHILE INPUTING DATA ON AN
          ITEM FOR CROSS REFERENCE, THE RUBOUT KEY CAN BE USED FOR
          CORRECTIONS.  HOWEVER, SHOULD THE USER MAKE A MISTAKE ON AN
          ITEM AND PRESS THE CARRIAGE RETURN KEY THE ERROR CANNOT BE
          CORRECTED USING THE RUBOUT KEY.  THE USER MUST EXIT THE
          PROGRAM BY TYPING A 'CNTRL C' AND START THE CROSS REFERENCE
          PROCESS OVER.

               INPUT FILES FOR THE SELECT PROGRAM ARE PERSON.MST AND
          MATEXM.MST.  PERSON.MST IS THE MASTER FILE OF CLINICAL DATA
          AND MATEXM.MST IS THE MASTER FILE FOR THE MATERIAL EXAMINATION
          DATA.

               OUTPUT FROM SELECT.FOR CONSISTS OF THE FILE SELDAT.MST
          AND CONTAINS THE CLINICAL DATA OF EACH 'SELECTED' CASE
          FOLLOWED BY THAT CASE'S MATERIAL EXAMINATION DATA, THEN THE
          NEXT CLINICAL DATA ETC.  THIS FILE CAN THEN BE USED AS INPUT
          FOR THE PROGRAM 'PRINT.CBL'.


 WHAT ITEM(S) DO YOU WISH TO CROSS REFERENCE?
 IF MORE THAN ONE, SEPARATE WITH COMMAS.

       ?

          1:  CASE NUMBER (RANGE)
          2:  NAME
          3:  PATIENT ID
          4:  SEX
          5:  WEIGHT (RANGE)
          6:  ACTIVITY LEVEL
          7:  BIRTH DATE (RANGE)
          8:  HOSPITAL
```

(Example 4 cont.)

```
 9:  GENERIC IMPLANT CODE
10:  IMPLANTION DATE (RANGE)
11:  REMOVAL DATE (RANGE)
12:  LENGTH OF TIME IN PLACE (RANGE)
13:  DIAGNOSIS AT INSERTION
14:  LEFT,RIGHT,MIDDLE POSITION
15:  JOINT REPLACEMENT (Y,N)
16:  BONE IN WHICH INSERTED (ONLY IF QUESTION 15 IS NO)
17:  FUNCTIONAL LEVEL ATTAINED AFTER DEVICE INSERTION
18:  REASON(S) FOR REMOVAL
19:  FINDING(S) AT SURGERY
20:  RADIOGRAPHIC REVIEW PERFORMED(Y,N)
21:  RADIOGRAPHIC REVIEW FINDINGS
22:  SWAB PERFORMED(Y,N)
23:  SWAB STERILE(Y,N)
24:  TISSUE EXAMINATION (Y,N)
25:  ANIBIOTICS (Y,N)
26:  SPECIFIC IMPLANT COMPONENT TYPE
27:  MANUFACTURER OF IMPLANT
28:  IMPLANT MATERIAL
29:  MACROSCOPIC EXAMINATION PERFORMED (Y,N)
30:  RANGE OF WEAR
31:  RANGE OF GALLING
32:  RANGE OF BURNISHING
33:  RANGE OF CHANGE IN IMPLANT
34:  RANGE OF MECHANICAL DAMAGE
35:  RANGE OF MACRO POROSITY
36:  MICROSCOPIC EXAMINATION PERFORMED(Y,N)
37:  INCLUSION CONTENT
38:  GRAIN SIZE (RANGE)
39:  CORROSION EXAMINATION PERFORMED(Y,N)
40:  RANGE OF GROSS CORRSION
41:  RANGE OF CREVICE CORROSION
42:  RANGE OF GALVANIC CORROSION
43:  RANGE OF FRETTING CORROSION
44:  MECHANICAL FAILURE(Y,N)
45:  FAILURE MODES
46:  FABRICATION FLAW(Y,N)
47:  MECHANICAL PROPERTY EXAMINATION PERFORMED(Y,N)
48:  HARDNESS (RANGE)
49:  RANGE OF OFFSET YIELD STRENGTH
50:  RANGE OF ULTIMATE TENSILE STRENGTH
51:  RANGE OF PERCENT ELONGATION
52:  RANGE OF GAUGE LENGTH
53:  RANGE OF REDUCTION IN AREA
54:  RANGE OF BEND STRENGTH

WHAT ITEM(S) DO YOU WISH TO CROSS REFERENCE?
IF MORE THAN ONE, SEPARATE WITH COMMAS.


      5,7,9,28,45

ENTER RANGE OF PATIENT WEIGHTS TO CROSS REFERENCE.
I.E.  100,190
```

(Example 4 cont.)

```
       150,200

ENTER THE RANGE OF DATES FOR PATIENT BIRTH DATES.
IE.  BETWEEN DECEMBER 1932 AND MARCH 1980 YOU WOULD ENTER


       0130,0160

ENTER GENERIC IMPLANT CODE YOU WISH TO CROSS REFERENCE.

       ?

          THE FOLLOWING IS A LIST OF GENERIC IMPLANT TYPES:
          A:   ANKLE
          B:   HIP
          C:   ROD
          D:   KNEE
          E:   ELBOW
          F:   PIN
          G:   SCREW
          H:   PLATE
          I:   HIP NAIL PLATE
          J:   STAPLE
          K:   SHOULDER
          L:   WRIST
          M:   FINGER
          N:   OTHER

ENTER GENERIC IMPLANT CODE YOU WISH TO CROSS REFERENCE.

       B

ENTER MATERIAL YOU WISH TO CROSS REFERENCE.

       ?

          THE FOLLOWING IS A LIST OF MATERIAL TYPES:
          A:   STAINLESS STEEL
          B:   CO-CR-MO
          C:   TITANIUM  TI-6AL-4V
          D:   POLYETHYLENE UHMWPE
          E:   MP35N
          F:   SILASTIC
          G:   ALUMINUM OXIDE
          H-J: OTHERS

ENTER MATERIAL YOU WISH TO CROSS REFERENCE.

       A

ENTER FAILURE MODE(S). SEPARATE WITH COMMAS.
       ?
```

(Example 4 cont.)

```
          THE FOLLOWING IS A LIST OF FAILURE MODES:
          A:   FATIGUE
          B:   TORSION
          C:   IMPACT
          D:   STRESS-CORROSION
          E:   OVERSTRESS
          F:   CORROSION-FATIGUE
          G:   OTHER

 ENTER FAILURE MODE(S). SEPARATE WITH COMMAS.

        A


 NUMBER OF CASES READ:  111.
 NUMBER OF CASES SATISFYING
 CROSS REFERENCING CRITERIA :     1.


END OF EXECUTION
$
```

Example 5. Use of Print Module

```
@RUN PRINT

  WOULD YOU LIKE TO SEE OUTPUT ON THIS SCREEN, THE LINE

    PRINTER, BOTH, OR EXIT PROGRAM ?

  ENTER   SCREEN  ,  PRINTER  ,  BOTH  ,  EXIT

        SCREEN
 ********************************************************************

                    CASE NUMBER 1051

 ********************************************************************


      CLINICAL HISTORY

  PATIENT I.D. NUMBER : 439-80-6574
  PATIENTS NAME : SMITHERS J
  SEX: MALE          DATE OF BIRTH: 07-48
  PATIENT WEIGHT : 171 LBS.
  ACTIVITY LEVEL : MODERATELY ACTIVE (NORMAL)
  HOSPITAL : TULANE MEDICAL CENTER - NEW ORLEANS
  IMPLANT TYPE : HIP
  IMPLATATION DATE : 01-79      REMOVAL DATE : 02-80
  DIAGNOSIS AT INSERTION :
                             ASEPTIC  NECROSIS
```

(Example 5 cont.)

PAIN

IMPLANT POSITION : LEFT

THE IMPLANT WAS A JOINT REPLACEMENT.

FUNCTIONAL LEVEL ATTAINED : AMBULATORY

REASON(S) FOR REMOVAL :

BREAKAGE OF IMPLANT

PAIN RELATED TO IMPLANT

FINDINGS AT SURGERY :

FRACTURED GROUTING AGENT

A RADIOGRAPHIC REVIEW WAS PERFORMED.

RADIOGRAPHIC REVIEW FINDINGS :

MALALIGNMENT

A SWAB WAS PERFORMED.

THE SWAB WAS STERILE.

A TISSUE EXAMINATION WAS NOT PERFORMED.

ANTIBIOTICS WERE ADMINISTERED.

****

MATERIAL EXAMINATION DATA

CASE NUMBER : 1051 COMPONENT NUMBER : 1

IMPLANT TYPE : HIP-FEMORAL STEM

MANUFACTURER OF IMPLANT : OTHERS

IMPLANT MATERIAL : STAINLESS STEEL

A MACROSCOPIC EXAMINATION WAS PERFORMED.

SCALE : 0-NONE, 1-MILD, 2-MODERATE, 3-SEVERE, 4-N.A.

WEAR : 1.0

GALLING : 0.0

BURNISHING : 0.0

CHANGE IN SHAPE : 0.0

MECHANICAL DAMAGE : 1.0

MACRO POROSITY : 0.0

A MICROSCOPIC EXAMINATION WAS PERFORMED.

INCLUSION CONTENT ASTM E45 : D2.5T

GRAIN SIZE ASTM E112 : 6.5

A CORROSION EXAMINATION WAS PERFORMED.

GROSS CORROSION INDEX : 0.0

CREVICE CORROSION INDEX : 1.5

GALVANIC CORROSION INDEX : 0.0

FRETTING CORROSION INDEX : 0.0

THERE WAS MECHANICAL FAILURE. FAILURE MODES :

FATIGUE

THERE WAS NOT A FABRICATION FLAW.

A MECHANICAL PROPERTY EXAMINATION WAS PERFORMED.

HARDNESS : B90

OFFSET YIELD STRENGTH : 75000.0 PSI

ULTIMATE TENSILE STRENGTH : 100000. PSI

PERCENT ELONGATION : 8.000

GAUGE LENGTH : 1.0 INCHES

REDUCTION IN AREA : 20.00

BEND STRENGTH : PSI

****

(Example 5 cont.)

```
  MATERIAL EXAMINATION DATA


  CASE NUMBER : 1051      COMPONENT NUMBER : 2

  IMPLANT TYPE : HIP-ACETABULAR
  MANUFACTURER OF IMPLANT : OTHERS
  IMPLANT MATERIAL : POLYETHYLENE UHMWPE
  A MACROSCOPIC EXAMINATION WAS NOT PERFORMED.
  A MICROSCOPIC EXAMINATION WAS NOT PERFORMED.
  A CORROSION EXAMINATION WAS NOT PERFORMED.
  THERE WAS NO MECHANICAL FAILURE.
  THERE WAS NOT A FABRICATION FLAW.
  A MECHANICAL PROPERTY EXAMINATION WAS NOT PERFORMED.

  WOULD YOU LIKE TO SEE OUTPUT ON THIS SCREEN, THE LINE

  PRINTER, BOTH, OR EXIT PROGRAM ?

  ENTER   SCREEN  ,  PRINTER  ,  BOTH  ,  EXIT

        EXIT
EXIT
$
```

A DATA RETRIEVAL SYSTEM FOR IMPLANT FAILURES IN TOTAL JOINT REPLACEMENT SURGERY

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A prospective information system to measure arthritis surgery outcomes was developed cooperatively and over a period of years with the American Rheumatism Association Medical Information System and a national group of arthritis surgeons. The system called ASP (Arthritis Surgery Proforma) defines the essential minimum data for assessing surgical outcomes and is designed for use by multiple institutions in cooperative or independent studies.

To best implement the use of ASP, a Time-Oriented Record (TOR) is suggested. TOR allows for uniformity in data collection over time and uniformity among different investigators. The chart system itself can be modularized by sections such as history, physical exam, complications and x-ray findings. Data includes stratifying, intervention and outcome variables. A new diagnostic system was developed that is indexed by ICD code where it exists.

An advanced computer system in operation checks, stores, retrieves and analyzes data. This computer system known as TOD (Time-Oriented database) is nationally accessible through local phone lines via TELENET.

Stanford's experience with 584 total hip or knee replacements is briefly defined for the 21 patients requiring revision surgery for non septic loose or broken prostheses. This group of revision patients specifically includes only those patients whose failed prosthesis were initially put in at Stanford. Failed prostheses tended to occur in: 1) non rheumatoids; 2) men more than women; 3) heavier patients especially women; 4) accelerate with time since implantation and; 5) in younger patients. Complications were described by specific product or manufacturer and identified to specific surgeon.

1. Introduction

"Man's search is not so much for pleasure as it is a search for the relief of pain." Arthritis is both a painful and common condition. Surgical replacement of arthritic joints relieves this pain and restores function and as a result, it is no surprise to find that tens of thousands of these operations are performed annually. Although implant surgery is a recent explosive phenomenon of great success, there is a need for serious critical assessment in order to optimize this technology and prevent unnecessary failure. Shortcomings and delays in collection and analysis unnecessarily increase human suffering and expense. Of the several hundred available prosthetic designs for total hip or knee replacement which are equivalent, superior or deficient? Which materials and designs are least associated with loosening or breakage? What are the exact risks and reoperation rates for different catagories of patients?

The best way to understand risk in patients undergoing prosthetic replacement is to do so within the context of a population over time. It is not sufficient to examine patients or prostheses that have had problems without knowing something about the population from which they were sampled. What we need is an honest denominator. It is of great interest to know why a particular prosthesis failed. To make this information more relevant, we must know how similar prostheses fared in other patients. Aside from knowing the failure rate, one would like to know how the failure rate is influenced by patient factors such as age, physical activity, weight, disease, etc. Is the failure rate different among surgeons dealing with similar patients? What is the failure rate of the same design made by different manufacturers? Perhaps some prosthetic components will work well in certain circumstances but poorly in others.

Information about the results of total joint replacement may be derived from several approaches. These include anecdotal experience, randomized clinical trials at single or multiple cooperative institutional centers, retrospective analyses of patient courses, or a prospective recording of data in clinical care settings with pre-determined hypotheses. In the present discussion we have chosen to concentrate on the aspects of the last approach.

In ascertaining the effects of joint replacement in the arthritic a time-oriented approach has been selected to be applied ultimately in a multi-institutional cooperative venture. To understand this approach one needs to comprehend information acquisition in the clinical care setting.

The time-honored way of denoting aspects of a patient's disease process is the narrative progress note - a prose recording of items felt to possibly have import and justification for courses of action taken by the clinician in the patient's behalf. Retrieval of uniform or consistent observations from patient to patient by even one physician over time becomes difficult with conventional records. Anyone who has ever been involved in chart reviews for retrospective studies understands the limitations of the traditional chart. Similar limi-

tations are found when traditional charting techniques are used for prospective studies (1).

Structure has been imbued into the prose chart through the Problem-Oriented approach of Weed and others (2). While data about the patient's course are organized according to problems and indexed according to subjective complaints, objective physical and laboratory findings, clinical impressions, and management programs this approach is still based on the unstructured narrative format with all its limitations.

2. Time-Oriented Record (TOR)

The Time-Oriented Record (TOR) evolved from two considerations. First, a core set of observations could be used by different investigators; and second, these observations can be repeated uniformly through time. The chosen descriptors (i.e., elements, evaluations or facts) are, in fact, what has been termed the Arthritis Surgery Proforma (ASP). When this set of information is utilized over time, a patient's chart becomes a two dimensional array (Figure 1). A Time-Oriented Record can visually demonstrate changes in any one variable over time and also, readily allows one to look for associations between variables (Figure 2). The TOR concept serves: 1) the clinician as an outstanding method of charting for everyday patient care and; 2) the researcher by ensuring more reliable data collection and ease in computer tabulation.

Within the TOR database three types of descriptors have come to be recognized as necessary to bracket aspects of the disease process. These three non-exclusive variables are: 1) stratifying; 2) intervention and; 3) outcome. Stratifying variables are features which are known or suspected to be related to outcome. They include age, race, sex, weight and variables representing disease severity. Stratifying variables also include symptoms, physical exam measurements, e.g., range of motion, or laboratory tests. Intervention variables include those treatments which are applied to the patient during individual encounters. In particular, we are concerned with the type of prosthesis inserted and to some extent the type of medication given. Outcome can be defined by variables relating to discomfort, disability, drug toxicity, death, cost of treatment, or psychosocial perturbations (3). We are especially interested in the outcomes of prosthetic failure such as infection, loosening, breakage and the function and pain of a specific joint.

Items of the database should be defined and coded in an easily implementable fashion. In other words, the actual chart used by the physician or the patient should be tailored to the individual collecting the data. Many other important considerations have been identified for the successful implementation of the Time-Oriented Record. Research aspects and patient care aspects in chart design should be merged as much as possible. At least one person, preferably the organizer of any arthritis surgery program, should be dedicated to the

use of the format and be constantly surveying its application. Patient self-administered records for assessing historical and functional information can be more reliable than physician acquired information (5) and increase the efficiency of patient - physician contact. To improve the quality and accuracy of the data collected, multiple levels of informational cross-checking are useful. Patient self-administered records can be implemented by technical or lay help familiar with the intention and meaning of the forms. Physical therapists or nurses can perform and note many parts of the physical examination. In the university clinic, a resident can rapidly double-check the patient's and therapist's findings for accuracy. In turn, the house officer can be rechecked by an attending surgeon thereby resulting in a system of information collection in which two or three "experts" screen each piece of information. A pre-printed, color-coded, standardized form makes this system of re-checking convenient and easy. The few patients who do not enjoy filling out such questionnaires preoperatively quickly and aggressively gain interest in them postoperatively. A single charting system for any one program should be utilized. We have found a color-coded modular chart to be of great help. For example, one module may relate to history, another to physical exam, a third to the operation, and so forth.

3. Arthritis Surgery Proforma (ASP)

The historical development of the Arthritis Surgery Proforma (ASP) as well as its implementation and continuing evolution is of some interest. ASP is the outgrowth of many years of prospective planning and organization. In 1973, a national group of rheumatologists all of whom were experienced in data collection met and formed the American Rheumatism Association Medical Information System (ARAMIS). Their purpose was to create a national communication network for following patients with arthritis. In that same year, one of the authors (DJS) joined ARAMIS as an orthopedic surgeon with similar interests and the intent of developing an information system for patients undergoing arthritis surgery. ARAMIS itself has grown over the years to become a computer network of about ten nationally based institutions and one in Canada. The communications format utilized is under continuous development by a committee formed from approximately 30 institutions under the auspices of the American Rheumatism Association known as the Uniform Database in Rheumatic Disease Committee. The origins of ASP grew within this committee. ASP was presented and discussed at the semi-annual national meetings of the Committee. At the last national meeting in 1978, a subcommittee of rheumatologists joined with the author (DJS) to insure that ASP would contain the minimal information relevant to and required by rheumatologists. The suggestions were ratified by the general Committee and remain within ASP. In 1979, under the auspices of the Stanford Arthritis Center, a three day meeting was held with four nationally representative orthopedic groups. Those attending this meeting included Harlan C. Amstutz, M.D. from UCLA, Robert Fitzgerald, Jr., M.D. from the Mayo Clinic, Clement Sledge, M.D. from Robert Brigham Hospital, David J. Schurman, M.D. from Stanford and a data analyst from each of those institutions.

The year 1979 was an ideal time in the history of joint replacement surgery to achieve agreement on a prospective information system. It was the end of the first decade of joint replacement surgery in this country. The failures of other similar groups to reach agreement were instructive. Participants had a great deal of hands-on experience with exactly what was needed. And the group was able to benefit from the experience of our ARAMIS colleagues and leap-frog some of their difficulties.

With complete agreement from the four institutions, the Arthritis Surgery Proforma was born (Tables 1 & 2). The concept of ASP was that of a minimum core of questions that would be asked by all investigators participating in any prospective cooperative study. Unlike our rheumatologic colleagues who sought to completely define a total information system concerning every aspect of rheumatologic care, the Arthritis Surgery Proforma sought to define an essential minimum in assessing the outcomes of arthritis surgery and to include parameters of proven value only. It was a time ripe for such a meeting. From many previous years of experience, it became easier not harder for members to compromise on coding system. There were many pieces of information that all institutions had regularly collected. Some of these elements were maintained as part of the ongoing system. It was a surprise and delight to find many common elements dropped by unanimous consent because of their lack of proven value despite their previous ubiquity. Shortly after this meeting, arthritis surgeons from the following institutions either ratified or expressed serious interest in fully cooperating with this program: George Washington University, the University of Chicago, the University of California in San Francisco and the USC program.

While ASP is an essential set of questions for defining the progress and outcome of patients undergoing total joint replacement surgery, there is both the need and the latitude for incorporating additional questions and descriptors. ASP is a viable system and it is meant to improve with age. Collaborating scientists can use additional descriptors and are encouraged to do so. Some investigators may want to record large numbers of additional details about one or another specific areas of interest. ASP in no way discourages such additional data collection and analysis. On the contrary, the very concept of ASP seeks to make such special collections of information more significant by relating these findings to a critical standard reference of outcome variables (i.e., ASP). The use of a core data set does not prevent individualization within cooperating centers beyond the standard framework. By agreeing to collect the same items in the same manner, cooperating centers can emerge in multi-institution clinical trials without sacrificing independently pursued studies based on self-determined hypotheses. This fact underlies the concept of ASP, TOR and the computer system known as TOD (to be described below).

4. Computers and Databanks

There are three major prongs to ASP. The first is the data itself. The second is the use of a time-oriented record which allows for

easy collection of the data. The third is the computerization of this information. The use of the computer is optional to the value of ASP but the ability to analyse recorded data quickly and efficiently is a primary concern to any researcher. While no one computer software system is essential to ASP, we will describe the system which we have been using and which evolved with ASP over the past eight years. This computer system is available for use by any orthopedic institution or investigator in the country at cost. The system is accessible through telephones at local telephone rates via TELENET.

A databank is simply a group of Time-Oriented Records, i.e., a group of patients each with TOR records. The databank is, therefore, a three dimensional array of: 1) a set of patients; 2) each with their own file of information (elements), displayed over time (visits) as depicted graphically in Figure 3.

5. Time-Oriented Data (TOD)

A software computer system termed TOD (Time-Oriented Database) has been developed for the entry, storage and retrieval of information contained in the three-dimensional databank at the Stanford Center of Information Technology. TOD is a schema driven, positional databank system developed to insure accuracy of data entry and to maximize retrieval speed while minimizing retrieval cost. The schema is the map and compass which the investigator uses to drive the various TOD programs. The schema is a master flow chart or organization plan which directs entry, storage and retrieval programs to handle each piece of information according to the different needs of each type of databank. The schema defines, for each position in the databank, the name of each element (of the database), its units, data type, qualifiers and all characteristics needed for processing that element. This schema approach results, therefore, in only the actual element value being stored in the databank file. The position of the value within the databank cube determines its meaning.

6. TOD File Structures

TOD file structures consist of simple arrays which, given the nature of the software enviroment, permits the most cost efficient retrieval of data for statistical purposes.

There are two types of TOD schema elements: Headers and Parameters. Header elements are those defined once for each patient, such as name, date of birth, etc. Parameter elements are those items recorded at each encounter such that multiple values of the element exist for each patient. TOD is designed to study the changes in variables over time.

There are six principal files comprising a TOD databank. These files are: the Descriptor, Header Entry, Parameter Entry, Header Retrieval, Parameter Retrieval and Subset Library. Their interrelationships are diagrammed in Figure 4.

The Descriptor File is the machine-readable form of the schema. It is referenced by every TOD program and completely defines the specifics of each databank. Each element of the database is defined according to schema number, long and short names and computer-compatible coding termed element type. As indicated in Figure 5, additional aspects of element definition including units, compression factors (cell and scale factors), limit ranges and qualifiers are aspects of the Descriptor File definition of the database. The last attribute in Figure 5 - TRANSPOSED determines whether information for the specified element will also be stored in the appropriate retrieval files.

The Header Entry File contains one Header Record for each patient. Each Header Record is a character string consisting of a TOR number (computer assigned thereby keeping each patient unique), a counter of the total number of visits for the patient in the Parameter File, and pointers to the first and last visits in the Parameter File for the patient. The remainder of the Header Record consists of "n" spaces (where "n" is the number of Header elements specified in the schema) represented by "super dots". Information is pigeon-holed between dots as determined by the schema. The "super dots" are simply markers that the computer uses to locate information. The dots are adjacent when no information is stored and slide apart as information is added thus providing economy of storage space. The Header Entry File consists of an array of N such Header Records. The Header Record is graphically represented in Figure 6.

The Parameter Entry File contains one record for each patient visit. Each visit record is in the form of a floating point array consisting of "n" spaces where "n" is the number of parameter elements defined by the schema. The visit record also contains keys that contain the TOR number, visit number and pointers that allow chaining to the previous and subsequent visit records of the patient. The Parameter Entry File consists of an array of such visit records. The Visit Record is depicted in Figure 7.

Data are entered into the above two files from the patient care documents and subsequently used for checking, validating and listing individual patient courses.

The data contained in the Header and Parameter Entry Files are duplicated in two additional files termed Header and Parameter Retrieval Files. Data are organized by element within these two files thereby achieving quick and cost-efficient retrieval of information for statistical analysis. It is these two files coupled with the Subset Library File that make TOD a unique software system for medical research. All statistical retrieval programs reference these Retrieval Files. Parameter Retrieval File data are stored as integers in order to accelerate most of the I/O and statistical processing. The scale and cell factors of the Descriptor File contain specifications for placement of the decimal point, which is not inserted until the results of analysis are ready to be displayed to the user. A diagramatic

representation of a Retrieval File Record is given in Figure 8.

The Subset Library File contains records created by the Subsetting Programs. These programs allow the user to specify stratifying characteristics for grouping patients. Each member of the Subset Library consists of two records: one indicates (in machine-readable form) how the subset was defined; the other is a bit string equal to the number of patients in the databank, indicating which patients belong to the subset. The Subset Library is referenced by all retrieval programs to determine which patients to process.

All analytic programs as noted in Table 3 access the Retrieval Files in concert with a defined subset of the patient population as specified in the Subset Library File. Each program has code embedded within it for extracting the requisite data, employing the appropriate statistical tests and formatting the output to the specifics of the program utilized. The retrieval process is a one step on-line procedure with "turn-around" measured in seconds of specification.

Salient TOD characteristics are: 1) that each ingredient of the system is simple in itself; 2) that each program is independent of others and; 3) that file structures are rudimentary. The interaction of these elements produces a system which is complex yet flexible; fast but simple and inexpensive to use.

Because the TOD/Descriptor File determines the meaning of the positional data bank information, multi-center databanks can be stored as separate Header and Parameter Files with commonality defined by choosing to store similar data at identical positions in respective databanks. This creates the ability to combine data from individual databanks to increase the denominators for testing hypotheses or to compare the population within one data bank to that of another or to compare one sub-population to another within the same data bank. This is made possible by inter-institution agreement upon the elements of a structured database they will collect as a common core.

The collaboration and utilization of TOD on a national network scope currently exists in Rheumatology (ARAMIS), stroke and traumatic coma (NINCDS pilot) and in Arthritis Surgery Proforma. Aspects of the latter's implementation will serve as illustration of the national data bank network approach.

7. Stanford ASP Databank

At the time of this writing, the ASP databank at the Stanford Orthopedic program has TOR records on the TOD computer system for 380 patients who have undergone 584 total hip replacements (THR) or total knee replacements (TKR). This number includes 374 THR's in 252 patients and 210 TKR's in 139 patients. Twenty four percent of patients with THR had bilateral operations and 34% of TKR's were bilateral. Seventeen patients or 4.5% had at least one THR and one TKR of which only three patients had both bilateral THR and TKR. The types of THR's

are as follows: 120 Charnley-Mullers, 135 Aufranc-Turners, 63 Trapazoidal Twenty Eights, 24 long stem prostheses, 2 Harris and 14 others. Trochanteric osteotomy was performed in only nine operations. The types of TKR's included: 41 Geometrics, 71 Total Condylars, 27 Guepar hinges, 57 Zimmer offset hinges, 6 Condylar hinges, 5 Duopatellars and 3 others. The patella was resurfaced with a plastic button in 81 operations. The average followup for patients with THR's is 2.8 ($\pm$ 0.1 s.e.) years and 2.2 ($\pm$ 0.2 s.e.) years for TKR's.

The age at the time of the first THR was 60.2 ($\pm$ 1.0 s.e.) years ranging from 15 to 90 years. TKR patients' age was 63.2 ($\pm$ 1.1 s.e.) years ranging from 22 to 85 years. The difference in average age between THR and TKR patients was significant at the .05 level (T-test). Females comprised 56% of THR patients and 67% of TKR patients ($p < .05$). The mean weight of patients with THR's did not differ from those with TKR's and was 155 pounds. Men undergoing joint replacement averaged 172 pounds without significant difference between THR and TKR groups. The female weights averaged 143 pounds with THR females weighing 137.5 ($\pm$ 2.2) pounds and TKR females weighing 152.5 ($\pm$ 3.5) pounds ($p < .001$).

Primary diagnoses for THR patients were as follows (in percentages): osteoarthritis 50; osteonecrosis 17.2; polyinflammatory 12.5; dysplasia or protrusio 10.3; traumatic 7.3; post infectious 0.4; neuropathic 0.4; other 1.9. Secondary diagnoses included the following numbers of patients having revisions: 21 total joint replacement failures; 13 hemiarthroplasty failures and 2 failed arthrodeses.

Primary diagnoses of TKR patients included the following by percentage: osteoarthritis 50; polyarthritis 33.8; post traumatic 10.3; neuropathic 2.2; others 3.7. Secondary diagnosis included nine patients with failed TKR and one failed arthrodesis.

8. Loose or Broken Prostheses - Non Septic

Twenty one patients in the Stanford ASP data bank developed loose or broken prostheses after a Stanford total joint replacement. Two patients had loose prostheses immediately following an initial THR implant. One of these patients had had 12 previous failed hip operations including pinning and arthrodesis after sustaining a fracture. Her femoral stem was inadvertantly malpositioned in the femoral canal protruding through the foramen left by a previous hip nail. This was replaced with a long-stemmed femoral prosthesis after which she improved but continued pain being incapacitated by a stroke four years later. The other patient had rheumatoid arthritis with protrusio acetubulum. Postoperatively her acetabular cup was loose. The cup was replaced and she has been followed for six months with no pain and improved function.

Nineteen patients developed loose or broken prostheses after the initial post operative period. Let us look directly at total knee problems. Two Zimmer offset hinges of 52 broke at 2.6 and 3.2 years after insertion. One of 23 Guepar hinge knees broke at 2.4 years.

The followup of the non-broken hinge knees averages 2.9 years (s.d. 1.6). The two differently manufactured prostheses were almost alike. All breaks occurred at the ends of notches in the stems. Two of the 75 hinges loosened after 1.1 and 5.4 years. Both loosened after falls although the latter patient showed evidence of progressive signs of loosening before the fall.

Two of 28 patients with 34 Geomedic knees loosened after 2.5 and 4.5 years. The average followup of the non-loosened knees was 3.6 (s.d. 1.7) years. The first patient was a 200 pound woman with degenerative arthritis and the other was a 128 pound male with rheumatoid arthritis. Both underwent successful surgical revision.

The 11 remaining patients had loosened total hip replacements which required revision. One of these 11 patients also had a broken Charnley-Muller Howmedica femoral stem. The femoral component showed radiographic signs of loosening for 16 months prior to breakage with only occasional minimal symptoms. This 65 year old white male 174 pound osteoarthritic working physician fractured his prosthesis non-traumatically 4.2 years after insertion. The component was replaced with only a three month followup.

The 12 patients with loosened total hip replacement components had 13 involved joint failures. The one patient with bilateral loosened components had surgery for congenitally dislocated hip in 1973. The acetabulae were erroneously placed in the pseudo-acetabulae. Both cups subsequently loosened and were replaced at six months and 1.6 years. These replacements were also placed high in the pelvis and in turn reloosened. The patient appropriately sought treatment elsewhere.

Each of the 11 remaining patients had a problem with a single loosened femoral component (Tables 4 & 5). Three of these patients had their initial operation at our hospital for a loose total hip femoral prosthesis performed elsewhere. The first of these patients had an immediate postoperative failure after replacement. After four months he underwent his second Stanford replacement which also loosened. The patient went elsewhere thereafter for his fourth attempt and was lost to followup. The second patient successfully underwent replacement with a long stem prosthesis and was last seen two years post-replacement doing well. The third patient had a long stem femoral replacement and did well for two years. After seven months of progressive difficulty he underwent another revision for loosening and is now two months postoperative, and except for some phlebitis is doing well.

The remaining eight patients which eventually underwent replacement for loosening between 2.5 and 6.3 years after insertion with an average time of 4.6 years. The average total hip that did not loosen has been followed for only 2.9 ($\pm$ 0.1 s.e.) years with only 22.9% followed for 4.6 years or longer. Seven of these patients were replaced with Aufranc-Turner prostheses and one with a Charnley-Muller. None of the 62 T-28 prostheses loosened but these were only followed

for an average of 1.9 (± 0.2) years and all were performed by one surgeon who had no loosenings. This surgeon performed 19% of the hip operations. A second surgeon operated on 12 of the 13 joints which became loose on a delayed basis and one of the two which was initially loose. This surgeon's hip patients have been followed 3.1 (± 0.1 s.e.) years. He had performed 76.9% of the THR operations. A third surgeon performed only six hip replacements altogether of which one became initally loose and another had delayed loosening at 6.3 years.

The 11 patients with replaced loosened femoral components were studied for differences in a variety of factors as compared to 240 patients that had no loose or broken prostheses and underwent total hip replacement (Table 5). There were more men than women with loose components although for those without loosening it was the reverse. Weight was 15 pounds heavier for those that loosened although all of this discrepancy was in heavier women. No patient with a loose hip component weighed more than 200 pounds! Those with loosening were younger by about four years. Ability at walking prior to the first Stanford total hip was a bit better for the group which loosened as was upper extremity function. This is in part explained by the fact that all patients with loosened femoral components had a primary diagnosis of trauma, osteoarthritis or osteonecrosis and none had rheumatoid arthritis. In the non-loosened patients 11.5% had inflammatory polyarthritis.

There were 13 patients (with the same number of prostheses) who had a loose THR that had been performed elsewhere which we revised and which have not yet loosened. Their followup averaged only 2.6 (± 0.7 s.e.) years. Fewer of these patients which have not reloosened were male, 38%, as compared to our THR's that loosened, 73%. These 13 patients had an average age of 60.4 years and weighed 152.9 pounds and had an average operative time of 190 (± 15 s.e.) minutes. Thus those with successful resivions were older and lighter and more operative time was spent on their revision surgery.

This work was supported in part by NIH grant No. AM 21393 and NIH Grant No. AM 20610.

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(3) McShane, D.J., Harlow, A., Kraines, R.G. and Fries, J.F., TOD: A software system for the ARAMIS data bank. Computer 12, 34-41 (1979).

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(5) Liang, M.H., Schurman, D.J. and Fries, J.F., A patient administered questionnaire for arthritis assessment. Clin. Ortho. and Related Res. 13, 12-129 (March/April, 1978).

ARTHRITIS SURGERY PROFORMA
Table I

General Information

Patient Name
Medical Record Number
Date of Birth
Home Address
Handedness
Marital Status
Ethnic Origin
Date Disease or Difficulty Began

Medications: Current & Historical

Intra-articular steriods: Yes or No
  Specify joint(s) infected
  Number of injections
Non Narcotic Analgesics: Specify type & dose for each category (includes ASA & NSAI)
  Narcotics
  Corticosteriods
  Penicillamine
  Chrysotherapy
  Chemotherapy

Concurrent Disease (includes date onset)

Diabetes Millitus
Phlebitis
Pulmonary Embolism
Myocardial Infarction
Other Heart Disease: Specify
Alcohol: Amount & duration
Bone Infection: Specify
Joint Infection: Specify
Previous Joint Operations: Specify

Joint Involvement

Specify with each joint or anatomic area; yes, if definite involvement, very painful or disabling. Right & left specification for each peripheral joint. Code: 0, not involved & 1, involved.

Foot	Elbow
Knee	Shoulder
Hip	Neck
Hand	Back

Ambulation

Walking aids: Code 0 - None; 1 - One support parttime; 2 - One support fulltime; 3 - Two supports; 4 - Walker; 5 - Wheelchair; 6 - Bedridden.
Maximum distance able to walk at one time: Code 0 - One mile or more; 1 - 1/2 mile; 2 - 1/4 mile; 3 - Indoors around house; 4 - Unable.
Ability to climb stairs: Code 0 - No difficulty; 1 - Mild difficulty; 2 - Need handrail; 3 - Extreme difficulty; 4 - Unable.
Limp: Code 0 - None; 1 - Minimal; 2 - Mild; 3 - Moderate; 4 - Severe.

Activities

All activities coded as follows: 0 - No problem; 1 - Mild difficulty; 2 - Moderate difficulty; 3 - Severe difficulty; 4 - Unable.
  Put on socks (L & R)
  Arise from chair without using arms
  Use knife & fork
  Bathing & personal hygiene
  Drive car

Sports: Code in each category. Specify yes or no if any one within category is performed.
  Light sports: Golf, swim, bowl, garden
  Heavy sports: Jog, tennis, ski, skate

ARTHRITIS SURGERY PROFORMA
Table I (continued)

Joint Pain (for each operative joint)

Pain at rest
Pain with activity
Total pain sum: Sum of rest & activity pain. Code 0 - None; 1 - Minimal, i.e., occasional & slight; 2 - Mild, i.e., regular & slight, takes occasional analgesics; 3 - Moderate, i.e., frequent use of analgesics; 4 - Severe, i.e., regular use of analgesics.
Did operation help you? Code 0 - Much better; 1 - Little better; 2 - No change; 3 - Little worse; 4 - Much worse.
If operation did not help was it because: Code 0 - Problem not involving the joint operated on; 1 - Problem in other joint(s); 2 - Problem in the joint that was operated on.

Physical Exam

Height: Inches
Weight: Pounds
Apparent lower extremity difference. Code 0 - Equal; 1 - Right longer; 2 - Left longer.
Amount of apparent difference (in cm).
True lower extremity length (for R & L in cm).
Problems in non-operated joints: Code 0 - Normal; 1 - Involved & not impairing; 2 - Involved & impairing.

Physical Exam - Knee

Recorded separately for each knee.
All limits or motions recorded in degrees.
- Flexion
- Flexion arc
- Varus - valgus
- ML instability in extension;
- AP instability in 90° flexion; Code 0 - None; 1 - Minimal; 2 - Mild; 3 - Moderate; 4 - Severe
- Effusion: Code 0 - None; 1 - Some; 2 - Severe
- Patello femoral tenderness: Code 0 - None; 1 - Some; 2 - Severe
- Patella tracking: Code 0 - Normal; 1 - Subluxed; 2 - Dislocated
- Patella status: Code 0 - Present; 1 - Patellectomy

Physical Exam - Hip

Recorded separately for each hip.
All limits or motions measured in degrees.
- Flexion
- Flexion arc
- Adduction (in extension)
- Abduction (in extension)
- Abduction muscle power: Code 0 - Normal; 1 - Weak; 2 - Absent
- Trendelenburg: Code 0 - Normal; 1 - Equivocal; 2 - Positive.

ARTHRITIS SURGERY PROFORMA
Table I (continued)

Diagnosis

Diagnosis #1: Disease
Diagnosis #2: Previous surgery
Diagnosis #3: Additional

Operation

Name of Operation
Size of Prosthesis
Manufacturer of Prosthesis
Surgical approach

Complications

Pneumonia
Myocardial Infarction
Pulmonary Embolism
Cerebrovascular Accident
Nerve Palsey
Abnormal Wound Healing
Deep Infection
  Micro-organism
Clinically Loose Prosthesis
Prosthesis Breakage: Indicate proximal or distal component
Intra-operative Bone Fracture
Post-operative Bone Fracture
Trochanteric Non-Union: Code 1 - 1 cm; 2 - 1-2 cm; 3 - 2 cm
Dislocation
Subluxation
Hematoma: Code 1 - Not drained; 2 - Surgically drained; 3 - Spontaneous drainage; 4 - Other
Lost to Followup
Death

Radiographic Measurement of Cement-Bone Interface

For proximal & distal prosthesis each.
  Lucencies: Code 0 - None; 1 - incomplete; 2 - complete
  Lucency width: Code 0 - None; 1 - 1 mm; 2 - 1-2 mm; 3 - 2 mm
  Subsidence (in mm)
  Cement Fracture
  Calcar Resorbtion
  Osteolysis
  Cortical Hypertrophy

DIAGNOSIS
Table 2

ASP CODE		ICD CODE
901	POLYARTHRITIS OF UNKNOWN ETIOLOGY	714.9
901.1	Rheumatoid Arthritis	714.0
901.2	Juvenile Rheumatoid Arthritis	714.3
901.3	Ankylosing Spondylitis	720
901.4	Psoriatic Arthritis	696
901.5	Reiter's Syndrome	099.3
902	CONNECTIVE TISSUE DISORDERS	
902.1	Systemic Lupus Erthremotasis	710
902.2	Scleroderma	710.1
902.3	Polymyositis - Dermatomyositis	710.3
902.4	Mixed Connective Tissue Disease	734.91
903	OSTEOARTHRITIS	715
904	POST TRAUMATIC	
904.1	Closed Reduction only	
904.2	Open Reduction only	
904.3	Surgery Proximal	
904.31	Surgery Proximal & Reduction	
904.4	Surgery Distal	
904.41	Surgery Distal & Reduction	
904.5	Surgery Proximal & Distal	
904.51	Surgery Proximal; Distal & Reduction	
904.6	Unreduced Dislocation	
904.61	Unreduced Dislocation & Failed Surgery	
905	SEPTIC	711.9
905.1	Active Infection	
905.2	Previous Infection	
906	METABOLIC OR ENDOCRINE	
906.1	Gout	274
906.2	Gaucher's Disease	272.7
906.3	Paget's Disease	731
906.4	Hemaphilia	286
906.5	Chondrocalcinosis	275.4
907	TUMOR	
907.1	Primary Bone Tumor - benign	213.9
907.2	Primary Bone Tumor - malignant	170.9
907.3	Metastic Tumor	198.5
908	PRIMARY HIP DISEASE	
908.1	Congenital Dislocation	754.30
908.2	Subluxation	
908.3	Primary Protusio	

DIAGNOSIS
Table 2 (continued)

ASP CODE		ICD CODE
909	OSTEONECROSIS	733.4
909.1	Alcoholic	303.9
909.2	Corticosteriod Induced	962.0
909.3	Hemoglobinopathy	282.7
909.4	Legg Perthes	732.1
909.5	Post Traumatic	
909.6	Caissons	993.3
910	FAILED PRIOR SURGERY - Secondary Diagnosis	
910.1	Osteotomy - hip	77.3
910.2	Osteotomy - knee	77.3
910.3	Arthrodesis	81.20
910.4	Open Reduction	
910.5	Cup Arthroplasty	
910.6	Hemiarthroplasty	
910.7	Total Joint Replacement	
911	FRESH TRAUMA	
911.1	Proximal Fracture	
911.11	Proximal Fracture & Dislocation	
911.2	Distal Fracture	
911.21	Distal Fracture & Dislocation	
911.3	Proximal & Distal Fracture	
911.31	Proximal & Distal Fracture; Dislocation	
912	NEUROPATHIC (Charcot)	

Table 3

Analytic Programs for Accessing the Retrieval Files

PROFILE	-	Histographic Distribution
CRITTER	-	Diagnostic Criteria Counts
SCATTER	-	X-Y Graph of Variables
MULTREVU	-	Mean and Standard Error of Variable in Subsets
OUTCOME	-	Life Table Analysis of Variables
AUTOSET	-	Computer Assisted Consultation
LIST	-	List of Variables in Subset
TIMESCAT	-	X-Y Graph of Variable Over Time
SUBSET	-	Group Meeting Specified Criteria
MVV	-	Ranking Variables by Logistic Regression
STATPAC	-	Extraction Program to Pass Data to SPSS/SAS/BMDP
CONTING	-	Contingency Tables

TABLE 4

Revision of THR's for Loose Femoral Stems

Diagnosis	Revision* Time	Result	Followup*
Loose THR	0.4	Loose	1.3**
ON/Renal TX	2.3	Good	0.2 Died I.M.
Loose THR	2.7	Good	0.1
Loose THR	2.8	Good	2
ON/Trauma	3.7	Good	3
ON	4.1	Poor	0.6**
DJD	4.2	Fair	0.3
DJD	5.1	Fair	0.3
ON/Cup Arth	5.3	Good	2.1
DJD/Cup Arth	5.9	Good	1.0
DJD	6.3	Fair	0.3

* Years

** Sought treatment elsewhere and lost to followup.

TABLE 5

Patients with THR: Some Stratifying Variables

	Unit	All Patients with Loose Components	All Patients without Loose Components	Males Loose Components	Males Not Loose	Females Loose Components	Females Not Loose
Number		11	240	8	104	3	136
Males	Percent	73	43	100	100	0	0
Height	Inches	68.7 * (0.9)**	65.9 * (0.3)**	69.4 * (0.9)**	69.1 * (0.3)**	65.8 * (1.9)**	63.5 * (0.2)**
Weight	Pounds	167.3 (5.7)	151.9 (2.0)	170.0 (7.6)	171.4 (2.7)	156.8 (4.3)	136.9 (2.2)
Age	Sex	56.6 (3.4)	60.0 (1.0)	53.5 (3.7)	58.1 (1.6)	57.9 (3.8)	61.0 (1.6)
Pre op Max Walk	Code+	2.8 (0.4)	3.2 (0.1)	2.4 (0.4)	2.8 (0.1)	2.3 (0.9)	1.9 (0.1)
Upper Extremity	Index++	0.2 (0.1)	0.4 (0.0)	0.2 (0.1)	0.2 (0.0)	0.2 (0.2)	0.5 (0.1)
Operation Time	Minutes	176.0 (13.0)	165.0 (4.0)	182.0 (15.0)	165.0 (5.0)	158.0 (19.0)	165.0 (5.0)
Transfusion	Units	3.1 (0.6)	3.1 (0.1)	2.3 (0.7)	2.9 (0.2)	4.3 (0.8)	3.3 (0.2)
Post op Stay	Days	12.3 (1.1)	16.6 (0.6)	12.6 (1.6)	15.4 (0.6)	12.8 (1.3)	17.6 (1.0)

* Numbers represent the mean hereafter.

** Numbers in parentheses represent standard errors hereafter.

\+ Max walk code: 0 - unlimited distance; 1 - one mile; 2 - 1/2 mile; 3 - 1/4 mile; 4 - indoors.

++ The average of 12 upper extremities abilities where: 0 - Normal; 2 - unable.

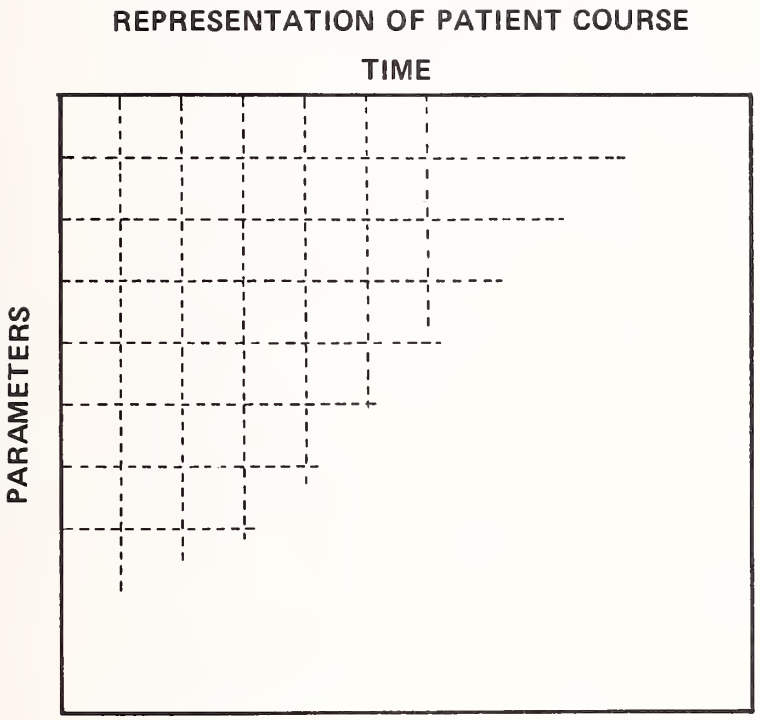


Figure 1

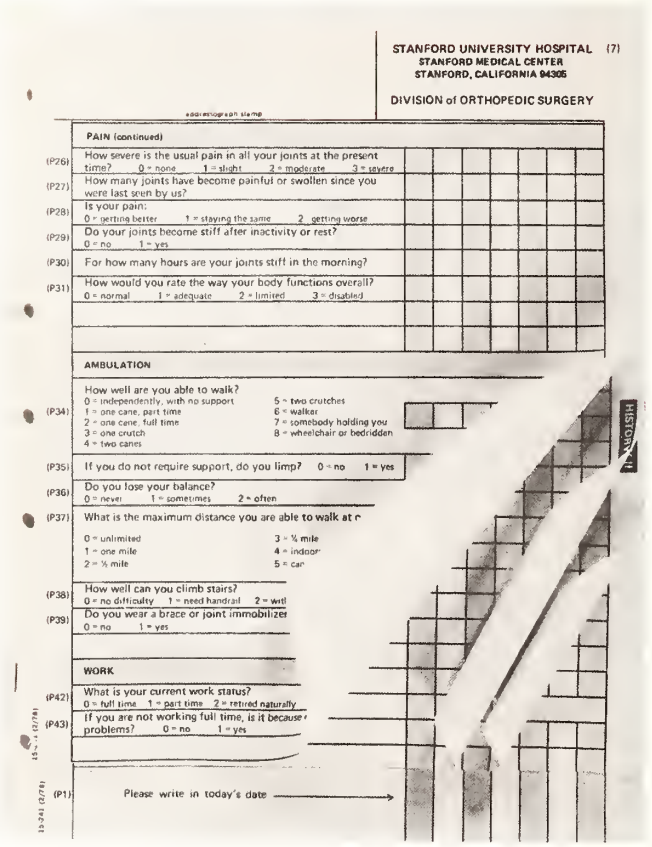
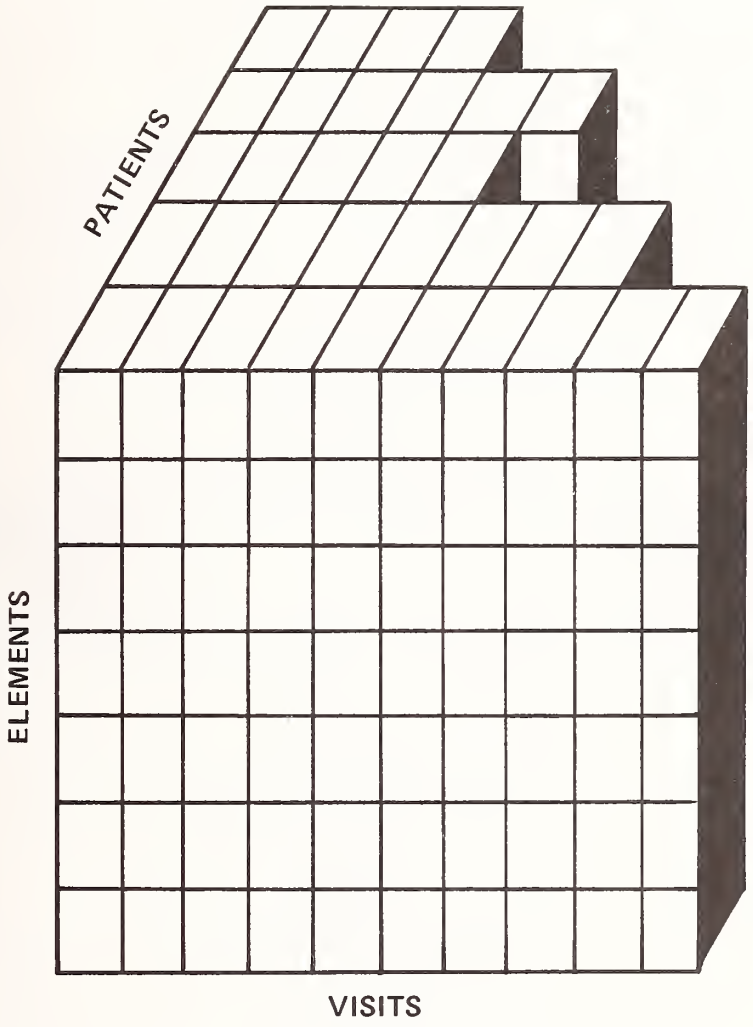


Figure 2

Example of Time-Oriented Record

In this format, the date is entered in the column opposite P1 and data for that visit entered on each page above it.



Graphic Representation of a Database

Figure 3

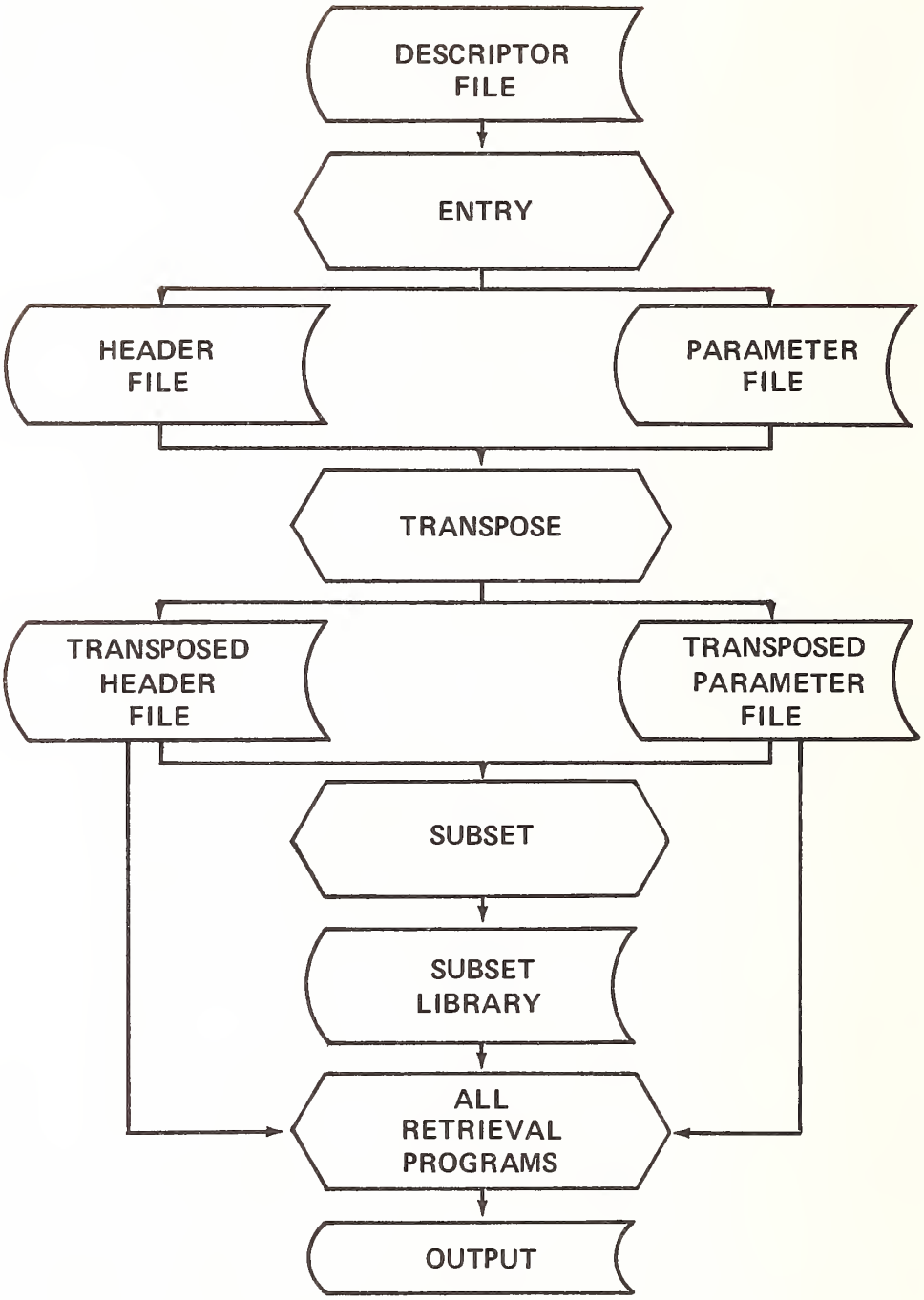
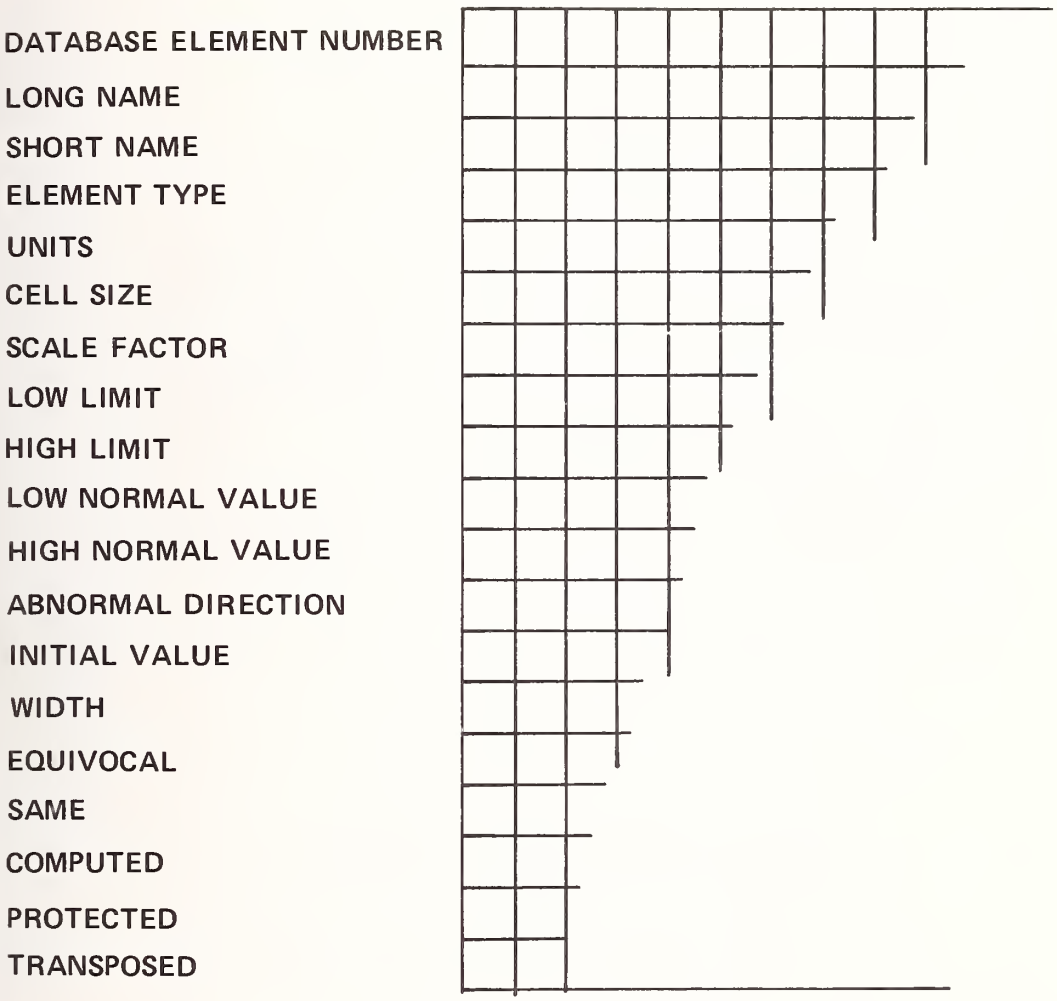


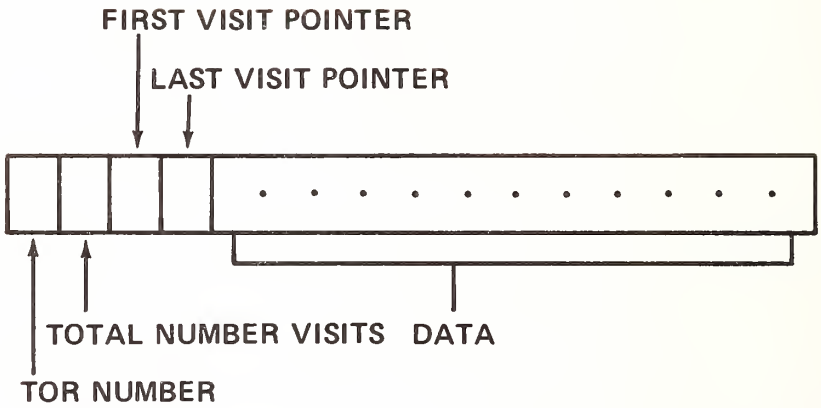
Figure 4

Schematic Relationship of the Principal Files



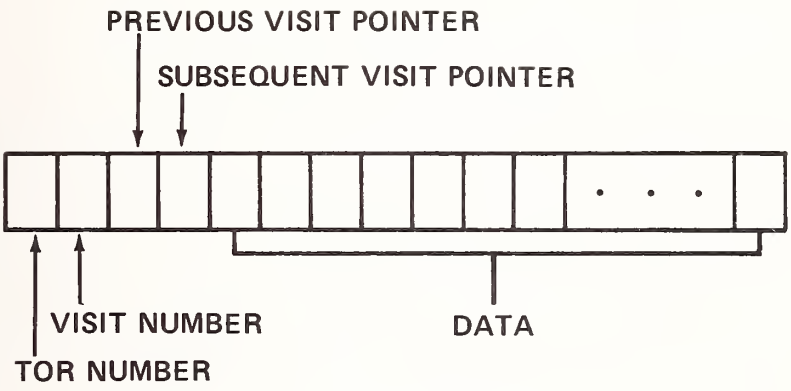
Graphic Representation of the Descriptor file

Figure 5



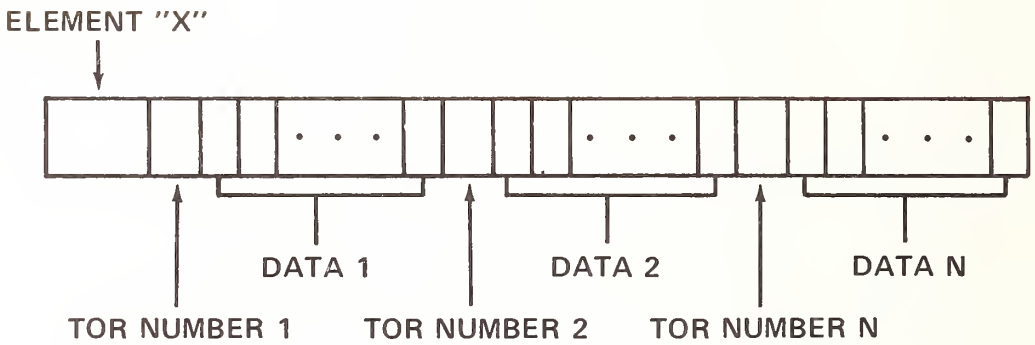
Graphic Representation of a Header Record

Figure 6



Graphic Representation of a Single Visit Number

Figure 7



Graphic Representation of a Retrieval File

Figure 8

PREDICTION OF FEMORAL COMPONENT PERFORMANCE THROUGH IMPLANT RETRIEVAL INFORMATION

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The use of standard actuarial methods for the analysis of total hip replacement performance is demonstrated by means of a study of the survival of total hip replacements in patients operated on at the Royal National Orthopaedic Hospital. Two types of Stanmore cobalt chrome molybdenum prostheses were considered : (1) metal-on-metal prostheses of various developmental designs inserted between 1963-72 (173) (2) metal-on-plastic prostheses of one design inserted between 1969-72 (248). The survival criterion was taken to be non-removal of the prosthesis and all cases not removed were regarded as survivors. The results indicate that for metal-on-metal prostheses the overall probability of survival was only 53% after 11 years and the average annual probability of removal irrespective of cause was 5.5%. As expected, for metal-on-plastic prostheses the results were considerably better, the figures being 88% after eight years and 1.5% respectively. For both prosthesis types the predominant failure mode was loosening and for this failure mode the annual rate of removal increased as the follow-up time increased, suggesting that loosening is a wearing-out process. Femoral component fracture occurred less frequently, but also appeared to be a wearing-out process. Finally, the advantages of the survival method as compared with conventional methods are discussed, and it is demonstrated how the analysis can be used to predict the probability of survival at sometime in the future.

1. Introduction

Follow-up studies of patients having total hip replacements appear regularly in the literature. Typically these studies are concerned with the causes of failure, the types of complications and the effects of various factors on the outcome. These factors may be surgical, clinical or pathological, or they may relate to the design or manufacture of the prosthesis. The outcome may be assessed in terms of function, movement and relief of pain. Usually these studies include statistics, but sometimes these statistics are not as meaningful as they might be, and can not readily be compared with statistics presented in other studies.

Thus for example, in determining the incidence of some failure mode or other only the overall incidence may be given i.e. the number of failures within a certain time period divided by the number in the study. But how is a two year follow-up to be compared with a four year follow-up? Moreover sometimes the study is concerned with a group of patients with varying follow-up periods, in which case the significance of the overall incidence becomes even less clear.

Fortunately actuarial methods exist for constructing life tables which enable both the annual and overall failure (or survival) rates to be determined as a function of time for a group of patients with varying follow-up periods. These methods are used in other branches of medical research, for example in studies concerning the survival of patients suffering from a particular disease. In these studies survival may be measured from a particular stage in the disease, or from the time when a particular operation took place. The end-point may be the death of the patient, or the reappearance of symptoms. Similar methods are used in engineering applications to study the reliability of components. Figure 1 shows the time dependence of the conditional failure rate for a typical engineering component. This curve, called the "bathtub" curve because of its shape, is composed of three distinct regions. It can be seen that a failure rate decreasing with time is characteristic of a running-in process, whereas one increasing with time is characteristic of a wearing-out process (1)[1].

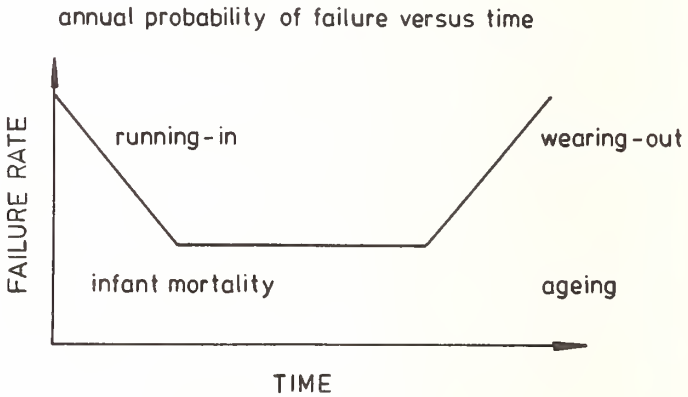


Figure 1. Bathtub curve

When considering total hip replacements it is the survival of the prosthesis <u>in situ</u> which matters and for the purposes of the present study the survival criterion was taken to be non-removal. Survival was measured from the date of insertion to the date of removal and a removal was considered to have occurred when all or part of the component was removed regardless of whether the component was subsequently reinserted. The chosen endpoint, namely removal, was perhaps not sufficiently severe, but it was relatively unambiguous and provided a conservative estimate of the chances of obtaining an unsatisfactory result. In principle any

[1]Figures in brackets indicate literature references at the end of this paper.

endpoint is possible and a more severe but subjective one such as the onset of pain could have been chosen instead.

Using these methods the survival of more than 400 total hip replacements inserted at the Royal National Orthopaedic Hospital over the period 1963-1972 was studied. The annual removal rate as well as the overall survival rate were determined as a function of time. Similarly the annual removal rate was determined for different failure modes, and the time dependence of removals due to loosening and fracture was determined. The behaviour of the earlier metal-on-metal (m/m) prostheses was compared with that of the more recent metal-on-plastic (m/p) ones. Finally the information obtained is used to assess the likelihood of any given total hip replacement being satisfactory at some time in the future.

2. Clinical and component details

Between April 1963 and August 1972, 173 total hip replacements using Stanmore metal-on-metal components were done. Sixty-one per cent of the operations were done by one surgeon, 29% by two others and the remaining 10% by a further ten. A pre-and postoperative antibiotic cover was given to all the patients and a local antibiotic powder, or irrigation was used at operation. In most cases the trochanter was detached in the method recommended by Charnley (2) although in a few cases the posterior approach was used, in which case the trochanter was not detached. All but one of the femoral components and all but 15 of the cups were inserted using acrylic bone cement.

Between June 1969 and April 1972, 248 total hip replacements using Stanmore metal-on-plastic components were done. Eighty-five per cent of the operations were done by four surgeons and the remaining 15% were done by a further five. The surgical and clinical details were similar to those for the former group, although in this group a larger percentage of the operations were done using the posterior approach. Table 1 summarises the insertion details for the two groups.

Table 1 : Insertion details

	metal-on-metal	metal-on-plastic
No. of insertions	173	248
Type of component	Mks 1-5	Mk 6
Insertion date	1963-1972	1969-1972

The metal-on-metal components were Marks 1-5 and articulated on metal cups of various designs. The metal-on-plastic components were all Mark 6's and articulated on a plastic cup of one design. All the components were manufactured by one manufacturer using air melt air cast cobalt chrome molybdenum alloy. Table 2 gives the number of insertions on a biennial basis. A previous publication gives additional information including the sex, age and weight of the patients, the design of the components, and the number of each mark (3).

Table 2 : Number of insertions on a biennial basis

Interval (Jan-Dec)	Number of m/m All marks	Number of m/p
1963-1964	3	-
1965-1966	17	-
1967-1968	103	-
1969-1970	35	73
1971-1972	15	175

3. Method

First, the length of the follow-up was determined for each patient. Since most of the patients in this study were being followed-up routinely at yearly intervals, their notes were reviewed. If for some reason the patient had not been seen recently, then a questionnaire was sent. Thus for each patient the length of the follow-up was determined either from the notes or from the questionnaire. In this study the final review was made in March 1979.

Next, the condition of the patient at the time of the last follow-up was determined. For each patient there were only two possible outcomes, namely removal or "withdrawal". "Withdrawals" consisted either of patients whose components had not been removed (i.e. they survived) or of patients who had died or who had been lost to the follow-up. Based on this assessment the required information was obtained from the notes or from the questionnaire.

Survivorship tables (modified life tables) were constructed using the method described in Armitage (4). The following is a brief account of the method:

(1) The time interval was chosen. In this case a one year interval was chosen since it gave a suitable number of intervals.
(2) The patients were classified according to the time interval during which their condition was last recorded. Thus a component removed after fifty months was classified as a removal within the interval four to five years. On the other hand a component which at the last follow-up was found to have survived after fifty months, or which was in a patient who died or was lost to the follow-up after fifty months was classified as a withdrawal within the same interval.
(3) The number of components surviving at the start of each interval was obtained by subtracting the number of removals plus the number of withdrawals from the number of survivors at the start of the previous interval.
(4) For any given interval the number of components at risk was obtained by subtracting half the number of withdrawals from the number at the start : it was assumed for convenience that the withdrawals survive half the interval.
(5) The probability of removal within any interval was obtained by dividing the number of removals by the number at risk.

(6) The probability of survival was obtained by subtracting the probability of removal from one.
(7) The percentage of survivors after any time period was obtained by successive multiplications of the probability of survival.
(8) The standard error due to sampling variation in the probability of removal was obtained using the usual formula.

4. Results

4.1. Removals irrespective of cause

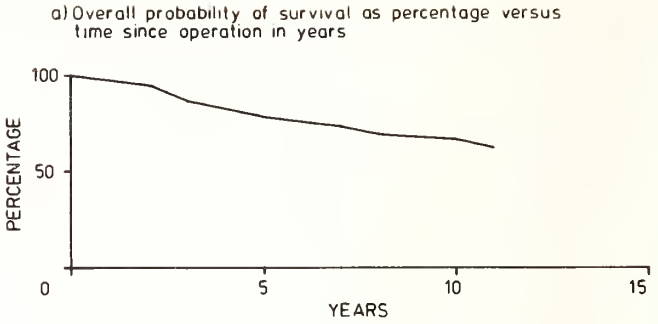
Tables 3 and 4 give the removal and withdrawal data on an annual basis for the two groups. From these data the survival tables were obtained using the above method. These tables are not given here, but are included in the articles cited previously (3).

Table 3 : Removals and withdrawals : metal-on-metal

Interval (years)	Removals	OK's	Deaths	Losses
0 - 1	3	-	2	8
1 - 2	5	-	1	4
2 - 3	12	-	1	3
3 - 4	9	3	3	2
4 - 5	8	5	5	2
5 - 6	3	6	3	2
6 - 7	3	10	1	1
7 - 8	5	17	3	1
8 - 9	2	11	-	-
9 - 10	1	12	1	-
10 - 11	1	3	1	-
11	2	7	1	-
Total	54	74	22	23

Table 4 : Removals and withdrawals : metal-on-plastic

Interval (years)	Removals	OK's	Deaths	Losses
0 - 1	4	-	4	19
1 - 2	-	-	3	2
2 - 3	1	-	-	4
3 - 4	2	1	1	4
4 - 5	4	18	2	5
5 - 6	2	42	2	-
6 - 7	1	82	2	-
7 - 8	1	39	2	-
8 - 9	-	1	-	-
Total	15	183	16	34



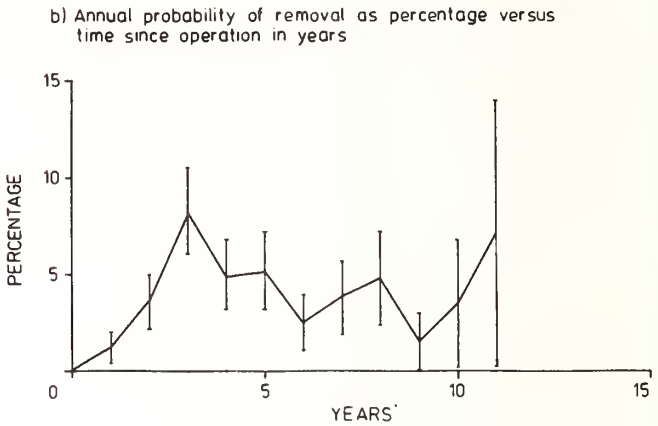
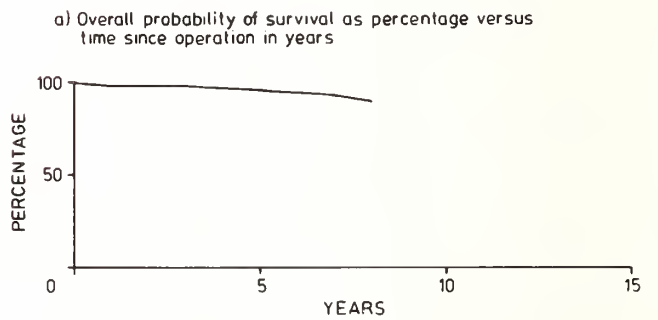


Figure 2. Survival of metal-on-metal total hip replacements



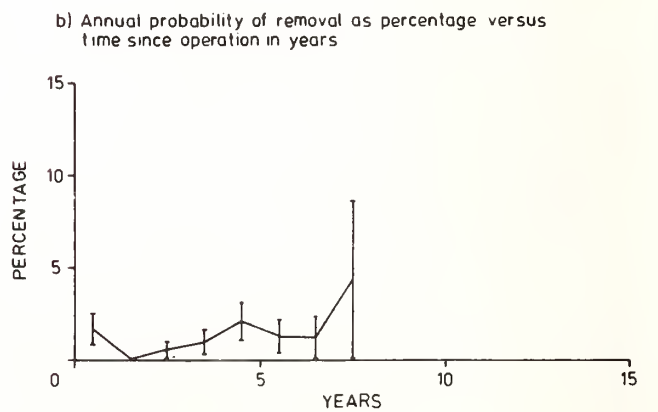


Figure 3. Survival of metal-on-plastic total hip replacements

From the tables, figures 2 and 3 were obtained which show the overall probability of survival and the annual probability of removal for the two prosthesis types. It can be seen that for metal-on-metal prostheses the overall probability of survival was 53% after eleven years, i.e. almost one in every two prostheses was removed within this period. The average annual probability of removal was 5.5%. For metal-on-plastic prostheses the figures were 88% after eight years and 1.5% respectively.

It can be seen from figures 2 and 3 that for both metal-on-metal and metal-on-plastic prostheses the annual failure rate was approximately constant (independent of time) and this observation was confirmed by more detailed statistical analysis. For the metal-on-metal case however the evidence for a constant failure rate was stronger if the first two post-operative years were omitted. Thus there was a suggestion that the failure rate increased over the first two years and then reached a constant values of 6% thereafter. There was also a suggestion that for both cases the failure rate increased after very long follow-up times as the consequence of a wearing-out process, but the evidence was insufficient to be sure about this.

4.2. Removal according to cause

Table 5 shows the cause of removals for both metal-on-metal and metal-on-plastic removals. It can be seen from the table that the majority of components were removed for looseness (78% for metal-on-metal and 60% for metal-on-plastic).

Table 5 : Cause of removals

Cause	Metal-on-metal number	Metal-on-plastic number
Loose	42	9
Dislocated	2	3
Infected	4	-
Broken	3	2
Other	3	1
Total	54	15

Because looseness was the predominant failure mode it was investigated in further detail (3). It was noted that for the metal-on-metal failures it was the cup which was loose in the majority of cases, presumably due both to the method of fixation and to high frictional torque, whereas for the metal-on-plastic failures it was the stem. The time-dependence of loosening was studied by constructing life tables as before. Figure 4 shows the behaviour of the annual failure rate, in this case using a two year time interval. There was a suggestion for both metal-on-metal and metal-on-plastic prostheses that the rate increased with time. This result is consistent with the view that loosening is related to the mechanical breakdown of interdigitations between acrylic cement and bone (5,6).

Annual probability of removal for loosening as percentage versus time since operation in years

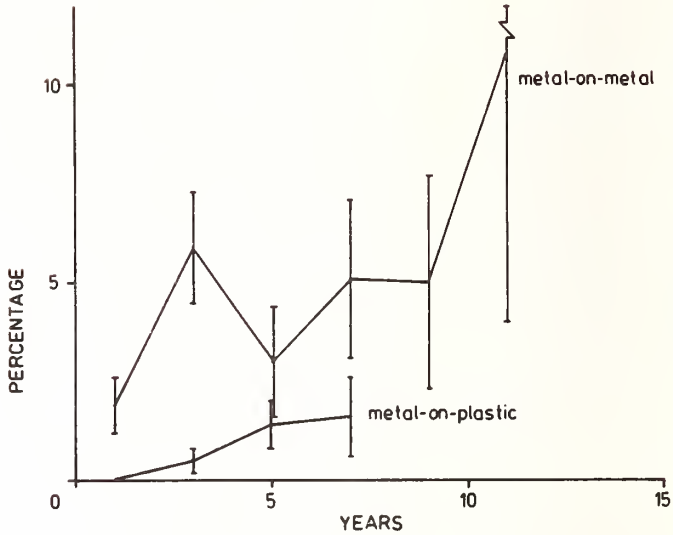


Figure 4.

Annual probability of femoral component fracture as a percentage versus time since operation in years.

metal-on-metal and metal-on-plastic combined.

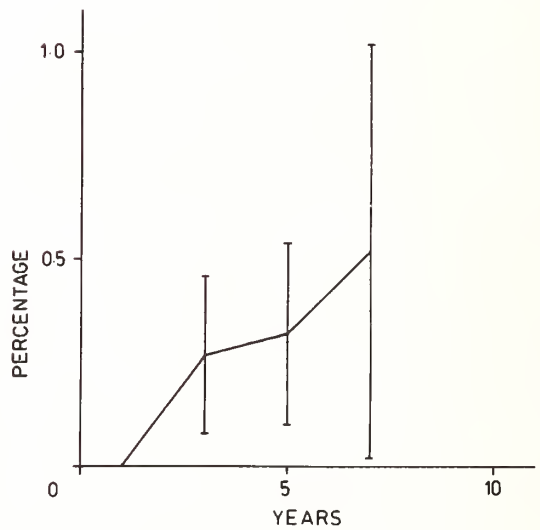


Figure 5.

As regards other failure modes little can be said on account of the relatively small numbers involved. It was evident, however, that removals due to dislocations and due to infections tended to occur early on. The time dependence of the fracture rate was determined as shown in figure 5 by combining the data for the two groups giving a total of five fractures. Although the data is too scanty to permit any firm conclusion to be drawn

the trend suggests a wearing-out process consistent with the view that the components fail by metal fatigue (7,8,9).

5. Discussion

To determine the validity of the chosen survival criterion, the patients were asked either at follow-up or by means of the questionnaire to give an assessment of their total hip replacement. For patients whose components had not been removed most were satisfied with their result, had little or no pain and were sufficiently active to cope with their daily needs. At least 90% of patients with metal-on-plastic joints fell into this category, and many were more active. On the other hand, for both types of joint there were a very few cases in which the component had not been removed even though there was considerable pain. These results, therefore, suggest that the survival criterion gave a reasonable but conservative estimate of the chances of having an unsatisfactory result.

As Armitage points out, two important assumptions underlie these life table calculations. First, it is assumed that the withdrawals are subject to the same probabilities of removal as the non-withdrawals. This is a reasonable assumption for withdrawals who are still in the study, but it may be a dangerous assumption for those who were lost to the follow-up, since failure to be followed-up for any reason may be related to the condition of the prosthesis. Secondly, the various values of the annual probability of removal are obtained from patients who entered the study at different points in time and it must be assumed that these probabilities remain reasonably constant over time.

In order to assess the magnitude of the error introduced by the first assumption the number of patients lost to the follow-up was determined. As shown in tables 3 and 4 there were 23 (13.3%) in the metal-on-metal study and 34 (13.7%) in the other. Because these percentages are small one can be reasonably sure that the resulting error is small. To verify this, one may calculate the worst possible probability of survival by assuming that all these losses resulted in removal, in which case the following values would be obtained : for metal-on-metal 45% instead of 53% and for metal-on-plastic 76% instead of 88%. These values demonstrate that the error is small and emphasise the need for as complete a follow-up as possible. To assess the error introduced by the second assumption it was noted that for both studies the majority of insertions fell within a four year period (see table 2). Since this is a relatively short time, and since the majority of the operations were done by only a few surgeons one can be reasonably sure that the resulting error is small. In addition, because the two types of prostheses were being inserted concurrently by the same surgeons one would expect that errors due to the second assumption would not invalidate a comparison.

It is interesting to compare the value of the overall probability of removal (one minus the overall probability of survival) obtained using survival methods with that which would have been obtained by conventional statistics. Using survival methods the values obtained were 47% for metal-on-metal after 11 years and 12% for metal-on-plastic after

eight years, whereas had the results been obtained simply by dividing the number of removals by the number of insertions the values would have been 31% and 6% respectively and had losses and deaths been deducted, 42% and 8%. Thus, it can be seen that conventional methods provide a more conservative and less accurate estimate than obtained by survival. This is true in all cases where there are losses and where the insertion dates vary.

To predict the survival probability at some future time, say after a twenty year period, the curves in figures 2 and 3 can be extrapolated. In this manner the median survival time can be obtained from the intercept at the 50% level:

metal-on-metal, median = 11.8 years

metal-on-plastic, median = 34.5 years

Alternatively, since the observed annual failure rate is approximately constant, and since a constant failure rate implies an exponential distribution of failure times, an exponential model can be used instead, i.e.

$$P = 1 - e^{-\lambda t}$$

where P is the overall probability of failure, t is the time after which the failure probability is to be predicted and λ is the value of the constant failure rate, determined from the data. For this model it is easy to show that the mean lifetime is $1/\lambda$, and the probability of survival after any time period can be obtained using the above formula. Thus, using the values of λ obtained previously, namely 5.5% and 1.5%, the following values were obtained for the probability of survival after twenty years:

metal-on-metal, probability = 33%

metal-on-plastic, probability = 74%

Both these methods of predicting future trends have the same disadvantage, namely they presuppose that past behaviour will be manifest in the future. Thus, neither method allows sufficiently for ageing or wearing-out processes and both fail to take into account the possibility that failures due to loosening and fracture may occur with even greater frequency after longer follow-up times. Consequently, although both methods demonstrate the type of predictions that can be made, these particular predictions must be treated with caution.

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naires. The work was supported by funds made available by the Department of Health and Social Security, contract number R/E1049/39 STS B5.

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LEGAL AND REGULATORY IMPLICATIONS OF IMPLANT RETRIEVAL AND ANALYSIS

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Implant retrieval and analysis can provide valuable input into the decisions made by our courts and regulatory agencies. The procedures used by these bodies in reaching their decisions, however, often place restraints on the ways in which the retrieval and analysis are performed in the first place. Implant retrieval and analysis is but one method by which risk reduction can be accomplished, i.e., the development and utilization of a clinical and/or device-related data base. The polling of experts and fault/failure analyses are viable, even preferable, alternatives to achieve expeditious risk reduction in certain situations. A threshold question which must be answered by any court or regulatory agency prior to a compensatory or regulatory decision is whether a device flaw (production or design) did indeed cause the failure or malfunction. Procedural modifications to liability trials and regulatory enforcement which respond to this threshold question are described, as are performance evaluation procedures which follow from the answer to this question. Laboratory fatigue data and results from litigated cases are introduced to indicate that risk reduction can expeditiously be accomplished through performance testing, and conformance to the performance standards can reduce or eliminate liability exposure.

1. Introduction

Implant retrieval and analysis has been and continues to be a valuable tool for reducing risks to patients, by pointing to modifications either in clinical practice or device design or manufacture. Surgeons,

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manufacturers, and the academic community have all been involved in both retrospective and prospective implant retrieval and analysis, which constitutes the principal voluntary private sector effort at reducing risks to patients. Our country has two additional pluralistic checks to ensure that patients are not subjected to unreasonable risks stemming from the use of implants: the courts and the Bureau of Medical Devices (BMD) of the Food and Drug Administration. The courts function primarily to compensate patients who have suffered damages resulting from past deficiencies in an implant or its utilization. The BMD, on the other hand, attempts to prevent future damages to patients by imposing various forms of regulation to reduce or eliminate risks.

A thorough failure analysis of a retrieved implant is the key to responsive medical device and/or malpractice litigation. In order to reach its conclusion, a court must not only explore the mechanism of failure but, more importantly the cause or source of failure. If the alleged device flaw is its inherent design, then statistical information concerning the performance of this device compared to alternate devices would be highly significant in showing that the present design is defective. If, on the other hand, the device is flawed in manufacture, i.e., it deviated from the manufacturer's specifications, then statistical information concerning the performance of an unflawed device is still useful in showing that an unflawed device would not have failed under the same service conditions. However, in either a design or a production defect case, it must be shown that the flaw caused the failure or malfunction. It is important to note that, unlike for most adverse reactions involving drugs, for example, detailed causal inferences can often be drawn from a careful examination of only one failed device and its related clinical information.

The same requirements for establishing causal links between device flaws and failures are essential for responsible regulation by the BMD. Unlike the courts, the effort of the BMD is seldom heavily focussed on the failure of a single implant. Its principal goal is to reduce unreasonable risks to implant recipients as a class. Hence the BMD is at the first level principally concerned with the incidence of failure(s). However, incidence-of-failure data must be supplemented with sufficient determinations of the sources or causes of failure before an appropriate regulatory intervention procedure can be developed and implemented.

The use of implant retrieval and analysis to develop and use a clinical and/or device-related data base for patient treatment is but one means by which risk reduction can be accomplished. These same data may be useful in developing a performance test to rank existing or new materials and/or devices. Various fault/failure analysis procedures are also often valuable to reduce risks, particularly at the design and development stages. Finally, polling of experts may also be used in certain situations to reduce risks especially where data are scarce and decisions must be made immediately.

After amplifying the material described above, specific recommendations for the use of implant retrieval and analysis in responsive litigation and regulation will be presented.

2. Risk Reduction Procedures

As mentioned in the Introduction, there are three principal types of procedures for risk reduction. These are based upon

1. Clinical and/or Device-Related Data Bases [1][2]
2. Fault/Failure Analysis Procedures [2]
3. Polling of Expert Opinion [3]

Polling of expert opinion is often the only resort if data are not currently available, and cannot be acquired in time to avoid a potentially hazardous situation which must be dealt with almost immediately. In a sense, juries are asked to evaluate or poll expert testimony in medical device and/or malpractice cases. Very often causation questions involved with device failure can be addressed only by seeking expert opinion, possibly assisted by modelling, analysis, and some simulative testing. Unambiguous usage data are typically not available to answer with certainty questions such as whether an unflawed device would not have failed under conditions similar to that causing failure in a flawed device. Since expert opinion is based so highly upon an individual's training and experience, it is the most difficult risk reduction procedure to ventilate for public scrutiny. In order to help evaluate expert testimony, ASTM Committee E-40 on Technical Aspects of Products Liability Litigation has developed E-620-77, "Standard Practice for Reporting Opinions of Technical Experts". Similar standard recommended practices for evaluation of technical data and examination and tests of items that are or may become involved in products liability litigation are expected to be issued shortly.

Fault/failure analysis procedures were developed and refined by the aerospace industry. These procedures are especially useful for evaluating the reliability of complex systems. These procedures are generally divided into two categories:

1. the functional fault/failure analysis (often referred to as the "top down" or "system" approach)

2. The hardware fault/failure analysis (often referred to as the "bottom up" or "hardware" approach)

The first approach is particularly useful during the design stages, where individual hardware items have not been specified. The second is especially useful in isolating and examining the consequences of the failure of individual hardware items. Both of these approaches

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[2]Figures in brackets indicate the literature references at the end of this paper.

are strengthened by the subsequent use of a criticality analysis, which focuses on the expected frequency of occurrence of particular failure modes as well as their effect on system performance.

Clinical and/or device-related data bases are most useful in evaluating the effectiveness of alternate treatment procedures for chronic or long term conditions. In fact, a period of years is typically required to generate a data base which is adequate for use in evaluating alternate treatment procedures, since data from a sufficiently defined subset of patients similar to the patient at hand must be available. Causal connections are most often inferred when using statistical data bases, and, as will be shown subsequently, such inferences may lead to inappropriate remedial measures. It should also be pointed out that the development and use of performance tests based on clinical and/or device-related data bases is an alternate means for risk reduction. These two alternate means to risk reduction are illustrated in figure 1.

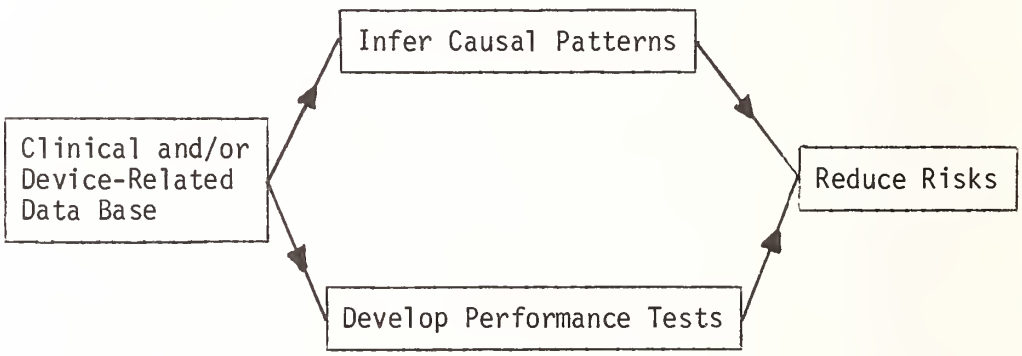

Figure 1. Paths by which data bases can be used to reduce risks to patients.

3. Current Status of Product Liability Litigation System

The apparent upsurge in the number of product liability cases filed annually during the last 15 years has been attributed both to an increase in consumer awareness and some fundamental changes in product liability law itself. The basis for recovery is now primarily based on the doctrine of strict liability, which examines the performance of the product itself, rather than negligence, which focuses on the behavior of the manufacturer. Strict liability has been enunciated in Section 402A of the Restatement (Second) of Torts (1965) as

(1) One who sells any product in a defective condition unreasonably dangerous to the user or consumer or to his property is subject to liability for physical harm thereby caused to the ultimate user or consumer, or to his property if

(a) the seller is engaged in the business of selling such a product, and

(b) it is expected to and does reach the user or consumer without substantial change in the condition in which it was sold.

(2) The rule stated in Subsection (1) applies although

(a) the seller has exercised all possible care in the preparation and sale of his product, and

(b) the user or consumer has not bought the produce from or entered into any contractural relation with the seller.

The application of Section 402A to production defect cases has produced no substantial difficulties. Its use in design defect cases has been much more troublesome, however, especially in those states which have removed the "unreasonably dangerous" criterion for defectiveness. This continuing uncertainty in the basic tort law is one of the factors cited by the Interagency Task Force on Product Liability [4] as contributing to the current "product liability crisis". The other two factors are

- questionable insurance rate making practices
- defective products themselves.

The last several years have witnessed the introduction of scores of state and federal product liability statutes directed at either insurance or tort reform. The plaintiff's bar has argued vehemently that what are reported as losses by insurance companies include not only payments to claimants, but reserves for known claims, and even reserves for claims incurred but not reported (IBNR). As has been pointed out earlier [5], however, these reserves are necessary in insuring a product, since, unlike automobile insurance which is paid annually, product liability insurance is paid only once in the year the product is manufactured, yet must be sufficient to pay for claims during the entire lifetime of the product. Representatives of the insurance industry have been trying to explain this accounting procedure in their arguments, yet lacked sufficient data to substantiate their position. These representatives point instead to the rapidly rising number of product liability cases (one source estimated one million annually) and the rapid rise in the size of awards as the primary reason for the "product liability crisis". This number, however, is at least an order of magnitude too high [5]. As the title of reference 5 suggests, this crisis is indeed a crisis of uncertainty, especially since no one can say with any degree of certainty whether specific insurance reform proposals will reduce rates or whether tort reform measures will weed out what are perceived as nonmeritorious cases.

Several insurance and tort reform bills have been passed in various states. Since no two of these bills are identical, substantial nonuniformity is being introduced in our country, creating enormous difficulties for those engaged in interstate commerce. The federal government has attempted to alleviate this nonuniformity by developing legislation of its own. The Risk Retention Act, H.R. 6152, was passed by the House on March 10, 1980. A companion bill, S.1789 is still pending in the Senate. Both these bills would allow, under the direction of the Department of Commerce, "risk retention" groups to be formed for the purpose of group purchase of product liability. The "Model Uniform Product Liability Act" [6] which was offered by the Commerce Department for voluntary use by the states, has, however, been introduced as H.R. 5976 in the House, where it is still pending.

The "model" law covers: basic standards of responsibility, unavoidable defects, relevance of the state of the art and of compliance with standards, requiring notice of possible claims, statutes of repose, alteration/modification by third parties, relevance of user's conduct, multiple defendants, the relationship of product liability and workers' compensation, responsibilities of sellers, sanctions against bringing frivolous claims and defenses, arbitration, expert witnesses, non-economic losses, the collateral source rule, and punitive damages.

4. Regulation by the Bureau of Medical Devices

With the enactment of the Medical Device Amendments of 1976, the FDA was empowered to regulate medical devices as well as drugs according to the level of risk which the device presents. The history of device regulation prior to 1976 has been reviewed elsewhere [7]. This regulation is accomplished by categorizing devices into one of three classes:

Class I. General Controls, which include regulations concerning good manufacturing practice and fraudulent mislabeling.

Class II. Performance Standards, which must be met to reduce device risks to an acceptable level.

Class III. Premarket Approval, for those devices for which performance standards cannot reduce device risks to an acceptable level.

The decision as to which class is appropriate is made by the Bureau of Medical Devices on the basis of recommendations from a classification panel, which reaches its decision on the basis of existing data and polling of expert opinion. To date, the Orthopedic Classification Panel has placed the vast majority of orthopedic implants into Class II, Performance Standards.

Recognizing the enormity of the task involved in developing such a large number of performance standards, the BMD published a proposed

"Voluntary Standards Policy for Medical Devices; Request for Comments" [8] on February 1, 1980. This procedure would have the FDA endorse voluntary standards which meet its "Criteria for Endorsement of Voluntary Standards." If an industry complies with such an endorsed standard, then the FDA might defer establishment of a mandatory standard.

Comments from the Pharmaceutical Manufacturers Association (PMA) [9] question whether this type of endorsement is indeed permissible under existing statutes. Their principal argument against such an endorsement is that this procedure essentially bypasses the detailed procedures for the promulgation of standards by the BMD, primarily because this endorsement fails to provide an opportunity for comment and does not provide for the creation of an administrative record. PMA urges that the BMD proceed instead with the promulgation of performance standards under their current mandate, possibly using existing voluntary standards as proposed performance standards.

The BMD has a continuing interest in clinical and/or device-related data bases in carrying out its regulatory mandates. As described in this volume, there are currently several such data bases being created. There is, however, substantial nonuniformity among these data bases. ASTM Committee F-4 on Medical and Surgical Materials and Devices has responded to this need for uniformity by promulgating F-561-78, "Standard Practice for Retrieval and Analysis of Metallic Surgical Implants." There was some suggestion that the ASTM might act to aggregate data based upon a compilation of these completed recommended practices. To date, however, not a single such recommended practice has been forwarded to the ASTM. Hence it is clear that these data bases will not emerge spontaneously, but must be developed by people or groups with a continuing self interest and need to use the data bases.

Since the development of these clinical and/or device-related data bases is at least partially funded from federal sources, the question of accessibility to the data base via the Freedom of Information Act (FOIA) naturally arises. The latest opinion on this point [10] is that, if data are requested and received by an agency, then these data become part of the agency's record and are discoverable under the FOIA. If, on the other hand, an agency has not requested or received such data, they are not compelled to ask the contractor for these data on the basis of an FOIA request. One wonders, however, whether requests for data will not now become routine with agencies, or whether the terms and cost of a contract will reflect who has access to these data bases.

5. Technical Causation: The Core Concern

The authors have previously urged [11] that medical device or combined medical device and malpractice litigation should focus on the issue of technical causation, i.e., establish the direct causal relationship between a flaw and a failure or malfunction. The initial concern for

combining medical device and malpractice litigation was that the two theories; one based on product performance, the other on a surgeon's behavior; were fundamentally incompatible. This concern turned out to be specious, however, in light of the fact that a surgeon and other medical personnel constitute a vital link between the device manufacturer and the patient. To ignore this link would not provide an adequate examination of the medical device in the environment of its actual use. It was thus concluded that it is imperative to include clinical descriptions and evaluations even in a case based solely on product liability, since the clinical performance might contribute to or solely cause the failure or malfunction of the medical device.

The entire seriated trial for a products liability case involving a medical device is shown diagramatically in figure 2. Both clinical and/or device-related technical causation answers are clearly admitted. If the technical causation question is answered affirmatively, then the injury causation question as to whether the malfunction caused the injury would be asked. If this question is answered affirmatively, the plaintiff would establish liability.

A causation-based record keeping system has also been proposed for use either by the BMD [7] or by a voluntary private-sector organization [12] to provide for responsive standardization and/or regulation. There appears to be some progress being made to aggregate the various private-sector clinical data bases to respond to this need. It is important, however, to recognize that causal patterns can often be determined more rapidly and accurately by focussing on failed devices in addition to clinical histories.

6. Recommendations for the Use of Implant Retrieval and Analysis in Responsive Litigation and Regulation

A structured causation-seeking approach such as is embodied in the seriated trial would enhance the quality of any liability or regulatory decision. Amassing frequency of failure data alone, even after drawing statistical inferences, can lead to inappropriate remedial actions. For example, it was shown in reference [13] that, while fretting corrosion was observed in the proximal screw-hole countersinks, this fretting corrosion often did not initiate the corrosion-fatigue failure. A causal inference would undoubtedly be drawn on a statistical basis as a result of the mere conjoint appearance of fretting and fatigue-crack initiation at the proximal screw-hole countersink. The natural tendency would be to try to alleviate fretting, but this would have no effect on those devices for which the fatigue fracture was not fretting initiated.

It is also apparent that laboratory performance tests, based on implant retrieval and analysis experience, are also useful tools for device improvement and lessening of the burden of litigation and regulation of the manufacturer as well. For example, the simulated corrosion-fatigue device performance test described in reference 13 was used to test Jewett nails of identical design fabricated from both 316L stainless steel and

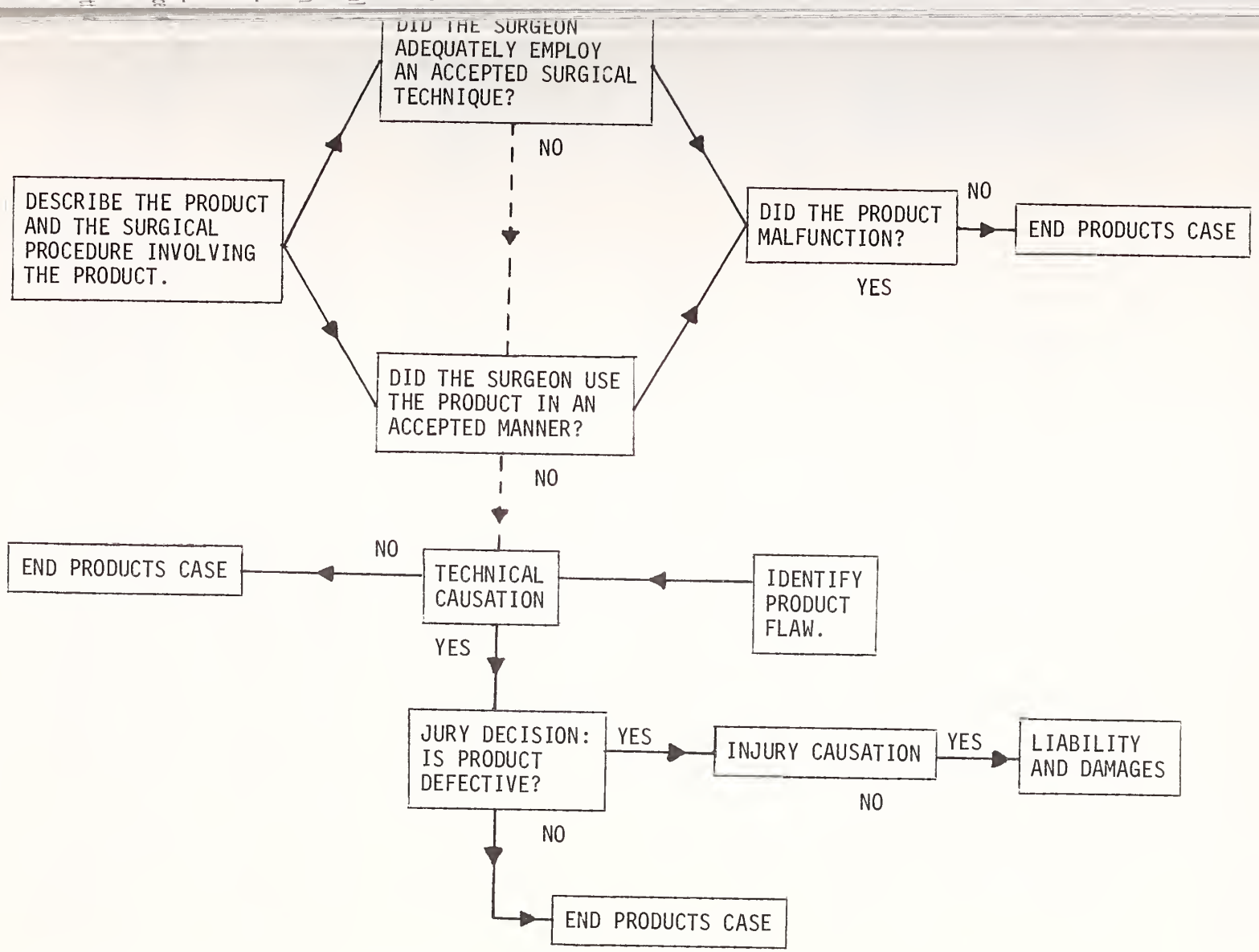

Figure 2. Seriated trial format proposed for products liability litigation involving a medical device.

Ti 6Al 4V. The results of these tests are shown in figure 3 in the form of cyclic load applied at the end of the nail versus number of cycles to failure [14].

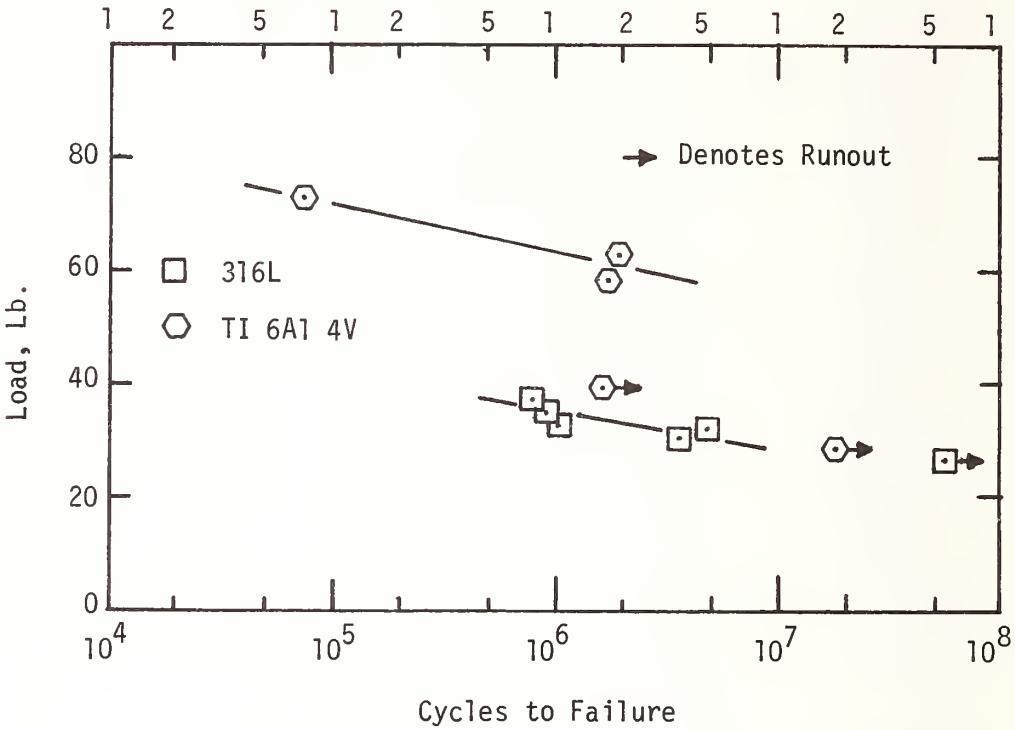

Figure 3. Load versus number of cycles to failure for 316L stainless steel and Ti 6Al 4V Jewett nails tested in Ringers solution.

The difference in performance of these devices is striking and certainly suggests that Ti 6Al 4V should be given serious attention as an implant material. Since loads applied to retrieved implants are virtually unknown, this superior performance of Ti 6Al 4V, if it translates into improved in vivo performance, would have taken years to observe from analyses of retrieved implants.

Whereas the authors recognize that this corrosion-fatigue performance test does not simulate every aspect of in vivo performance, it nevertheless appears to be a valuable initial step. Since the test is new and not widely proven, its adoption by the BMD as a performance standard is premature, if appropriate at all. However, its adoption as a regulatory guideline seems to make sense to us. In fact, many of the standards

already in existence would appear to be prime candidates for recognition as regulatory guidelines. It would appear to us that prudent manufacturers would adhere to these guidelines, and this procedure would circumvent the difficulties involved with the endorsement of standards or mandatory performance-standard development.

Even if such regulatory guidelines were universally utilized, the question still remains as to their persuasiveness in product liability litigation. One can get some insight into the relationship between product standards and litigation experience by examining what happened with children's flammable fabrics litigation after the 1953 Flammable Fabrics Act was amended [15]. The incidence of litigation based primarily on children's sleepwear began rising with the advent of strict liability, even though this sleepwear conformed to the then existing mandatory federal standard. After these standards were made more stringent in 1972 and 1975, the number of product liability claims dropped virtually to zero, as has the incidence of serious burns from conforming sleepwear. The lessons from this experience are quite simple:

- Courts will continue to attack standards, even mandatory federal standards, if these are shown to be societally unacceptable

- Any standard which reduces risks to users reduces the incidence of product liability litigation, regardless of the degree of blessing conferred upon the standard by the federal or any other government.

It is recognized that the potential for such a drastic risk reduction stemming from the use of implants is unlikely, largely because it is widely accepted that the vast majority of implant failures are clinical rather than device-caused. However, if a standard does nothing more than clarify the magnitude and nature of the clinical contribution to a device failure, the recognition of and response to this clinical information can reduce risks to patients as well.

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WORKSHOP ON IMPLANT RETRIEVAL PROGRAMS

Prologue

On Saturday morning, following the Implant Retrieval Conference, a small workshop was held to discuss implant retrieval. The attendees were all invited participants actively involved in implant retrieval and analysis programs. The objectives of the workshop were to air the current problems and protocols to see if we could begin to move toward a national system(s) for gathering, analyzing and pooling data. The morning was organized with two hours for simultaneous meetings of an orthopaedic group and a cardiovascular group. These two groups reconvened for a one hour final session. It is the proceedings of the joint session that are herein reported along with relevant appended material.

The orthopaedic section was chaired by Stanley Brown with the assistance of Steven Gordon. The cardiovascular section was chaired by Donald Gibbons with the assistance of Frances Pitlick. Without their thoughts and efforts, these workshop sessions would never have taken place so successfully.

Stanley A. Brown, Workshop Chairperson, May, 1980

Summary of Orthopaedic Group Proceedings

CHAIRPERSON BROWN: To begin and bring this session to order as a joint reporting session of the two groups, I would like to announce that the proceedings from this hour will be published in the Conference proceedings book. What I would like to do first is give you a brief summary of what we think came out of the orthopaedic group workshop and ask Don Gibbons to similarly report on the results of the cardiovascular group workshop. I would then like to discuss several subjects which I think are common areas of interest which we did not discuss in the orthopaedic workshop. They are problems of: 1) who is going to fill out necessary forms, 2) patient confidentiality, and 3) issues that pertain to the legal aspects of this particular problem. Being common problems, we did not pursue this discussion in the previous group session.

The orthopaedic group met, and started out by discussing the kinds of information that we want to gather in implant retrieval and analysis programs, the forms that can be used, and the methods of storing and handling this information. It was felt that, first of all, there have been several papers presented at the meeting that provided us with some starting points in terms of methods, protocols and forms. Secondly, the feeling was that we should look toward the next meeting of the ASTM committee F-4 on Medical and Surgical Materials and Devices for reconvening. The committee meets in Denver in the middle of this month, and we intend to have a second working session on this subject there.

The starting point for our discussion today was the problem of clinical information retrieval; what sort of information do we need to obtain concerning the patient, and concerning the clinical performance of the device. Secondly, we addressed materials issues, and thirdly, biological issues. One of the things that came out early in the discussion was that if we are to have effective forms for asking these questions, then sections of these forms should be prepared by the specialists of that particular area. The clinical forms should be written in the clinician's language; the materials form should be written in the language of the material scientist; the biologist or pathologist should be involved in the preparation of the questions concerning the histologic evaluations of performance.

Four documents for implant retrieval and patient analysis were presented during the Conference. They were the total hip system from Northwestern, the program from Tulane, the plate study from Dartmouth and the AO/ASIF, and the clinical protocol from Stanford. Two additional protocols were presented to the orthopaedic workshop: one for hip prostheses from Case Western, and one for knee prostheses from the Hospital for Special Surgery. Starting with these, I agreed to "cut-and-paste" all the sections that are in those forms now and combine them *en masse* according to the different ways of asking the same

question (e.g., the level of activity of the patient). Different people are asking these questions different ways. There may be a way of combining them so that we can all ask the question the same way, all provide the same kind of answers, and hence can produce a common data base that we can pass from institution to institution. Then, when we read someone's publication, we can all understand what they are saying.

This large core of data will hopefully be available for the coming F-4 meeting and will be included in the published proceedings of this workshop. Thus, as the first step, we will have all of these ways of asking questions down on paper, on record, and then we can begin to look at how we want to refine them so that we have a more concise document.

The group's feeling in terms of this large compendium was that there is a core set of data that we should all be gathering, which will be a subset of the entire document. The rest of the document will have types of data that are specific to the different types of studies that are being done. Some people are looking at one aspect; some people are looking at others. The implication is not that the entire form be filled out, but that the entire form will provide a standardized set of questions, a standardized way of gathering data; then we will simply extract those pieces of the data that we want for our own studies.

The reason for heading in this direction is to look toward the compilation of a national data pool. At the recommendation of Dr. Horowitz, we have been advised to contact Dr. David Lide at the National Bureau of Standards, concerning the National Standards Data Reference System which is an ongoing and funded system for generating national data pools in numerous other areas. It was the feeling of the group that if we can approach NBS and present a statement of need for compiling this data, then we might be able to get financial support and technical and organizational assistance. We also were told by a number of the industrial representatives that we should look to the industrial commercial sector for some financial assistance in these efforts as well. Concerning the technical details that we were able to address in the two-hour meeting, there were three papers presented yesterday and the day before specifically concerning the evaluation of corrosion at contact areas between bone plates and bone screws. Starting with this because I felt it was something we could actually come to terms with, the subsequent discussion generated the feeling that the concept of a two-part scheme where we evaluate the size of the contact area and the degree of attack of the contact area is one that we could work into a fairly common language. To address this, a number of us will try to develop a standard set of photographs, probably scanning electron micrographs, similar in concept to the ASTM grain size (E-112) and inclusion charts (E-45) which we can then all have and use to make comparisons during the microscope examinations of a particular contact area. Thus, we can then begin to quantify and

standardize our evaluations. The next step of how deep the corrosion attack is becomes more difficult. I think with the generation of the photographs, which probably will be ultimately turned into drawings so that they will reproduce better, will give us a starting point. This, I think, is one area where we can begin to move forward directly.

The next area which we looked at, and in many respects may be the more important one, concerned the evaluation of prostheses such as total hips, hemiarthroplasties, total knees, in terms of what we see as evidence of wear and degradation. There is a need to develop the same kind of standardized reference charts or reference codes to take these currently, very subjective, evaluations and try to make them objective and quantitative so that we can generate data and put them into a computer in common language.

I want to reemphasize that one of the most important aspects in which I think we have succeeded at our meeting is that of communication. This must be on an institutional level, on a national level, and ultimately on an international level. It must be between three groups: the surgeons, the biomaterial scientists and bio-engineers, and surgical pathologists. Fortunately, we had a surgical pathologist, Jim Anderson, with us today who described what can happen in an institution where the surgical pathology department is interested and involved. Jim has agreed to help further by way of communication and advertising so that perhaps we can begin to get more of this three-way effective communication.

Finally, there were twelve groups that expressed an interest in active participation in the development of these forms and moving further toward standardizing our evaluation of orthopaedic implants. These were the groups from Northwestern, Taussig Associates, Johns Hopkins, Hospital for Special Surgery, the University of Utah, Howmedica, Tulane University, Stanford, Zimmer U.S.A., the FDA, Case Western, NBS Materials Science Center, and my own group.

That concludes the summary from our group meeting. Are there any discussions from the floor concerning my report? Anything that the people who were in attendance feel I left out? The floor is open for discussion.

MR. WEISMAN (Howmedica): There was a reference made in the meeting to the fact that the information should also reflect the success rate in the use of the devices as well as some of the problems relating to what we have been discussing for the past several days. I think this is a very significant issue. In some way, the total user population has to be considered.

CHAIRPERSON BROWN: Agreed; we must not simply compare removed implants, but must, in fact, try to find out why they are removed and compare them with those that are currently performing well. We thus may find out why those that are doing well are doing well and why those that are explanted are being explanted. It is a good point.

Any further discussion? If not, then we will next hear from the second group that met this morning.

Cardiovascular Group

CO-CHAIRPERSON GIBBONS (Case Western Reserve University): I, together with Dr. Frances Pitlick (NHLBI-DBT) chaired the session on cardiovascular implants. The report which follows represents a summary of the deliberations of this session which consisted of a group of 22 biomedical scientists, surgeons and pathologists who were actively engaged in cardiovascular device retrieval.

After a preliminary discussion, the group divided into two subgroups; one addressing the problems associated with heart valve implant retrieval, and the other vascular graft retrieval. The specific objective of the discussion groups was to identify the types of data required for evaluation of implant performance and possible modes of failure; to discuss the availability of protocols for retrieval of natural or man-made heart valves and grafts from man and from research animals; and to make recommendations for future actions.

First, the stages of implant history were defined:

i) surgical implantation
ii) clinical followup
iii) explantation (at surgery or autopsy)
iv) analysis of retrieved implant, histopathology, engineering/materials

Stages (i) and (ii)

Both valve and graft subgroups unanimously emphasized that a registry of implanted grafts together with essential surgical and patient data was one of the most important and, at the same time, most difficult parameters to assemble. A data base regarding the number of implants per year was essential to establish an appropriate denominator for any effective study on performance. That these data are essential was amply illustrated by the presentations at the conference just concluded. The approach necessary to acquire such data is by no means obvious at this time.

SNOMED (Standard Nomenclature of Medicine) was identified as a computerized registry/data base which may serve as a model for data collection or which may facilitate this type of work. It was noted that SNOMED does not currently have the required vocabulary in the cardiovascular area, but it could be modified and expanded.

Stage (iii)

For implants retrieved at surgical revision, it was felt that an excellent rapport and working relationship is essential if usable data is to be retrieved. Thus, any retrieval program would, of necessity, have to be based on a number of small "regional" groups. The resultant

information could then be consolidated at a larger center, provided that a common data format is utilized by all the "region" groups. It was also suggested that there is a need for the development of an information sheet for surgeons listing the essential data required for the effective analysis of retrieved grafts and valves. This could also help the surgeons appreciate the requirements necessary for the analysis of material oriented parameters.

It was brought to the attention of the group that the Academy of Pathologists is attempting to create a data bank of all autopsies; this bank could serve as a basis for establishing incidence of death due to valve or graft failure.

It was agreed that retrieval of implants at all autopsies would be an important feature of a retrieval program. However, it was noted that, unless death is due to implant failure, the pathologist may have difficulty in identification of implant recipients during autopsy, unless the implant is in the chest or abdominal cavity. This naturally leads one to the conclusion that some easily identifiable "flag" must be placed on the outside jacket of the patients' records. It also suggests that autopsy pathologists should receive some minimal "education" in implants and the importance of the information to be gained by implant retrieval. Since the information to be gained may not directly benefit the patient in question, the surgeon and pathologist should understand the importance of cumulative data to further medical practice. The pathologist as well as the surgeon may not appreciate or recognize some of the constraints upon the engineer or biochemist with regard to evaluation techniques in their particular areas; a coordinated protocol should be capable of addressing this issue.

A draft report by Harrison et al., under contract to the FDA regarding heart valve retrieval and identification could serve as an initial basis for the development of valve data collection. The evaluation form will be appended to these proceedings. It has received minor revisions as a result of our discussions and could serve as a model way to collect data.

The Laval University/University of Manitoba protocols represent a basis for graft retrieval and identification. These should be supplemented by those used for specific graft types which have been developed in some of the manufacturers laboratories. Representatives of this later group indicated their willingness to contribute their protocols.

Stage (iv)

In certain respects the analysis stage probably represents one in which it will be easiest to develop a set of protocols. It was agreed that some uniformity of procedures was desirable and their development would appear to be feasible utilizing protocols already in use by several investigators. In a further discussion of protocols, it was noted that preparation or use of samples for one form of testing often precludes use of the sample for other types of testing. Thus, there is a

need for a triad system for analysis of specimens. Such a system would emphasize nondestructive testing by the pathologist, who is first to receive the specimen, and then the engineer. Destructive procedures would be undertaken by both types of investigators only after nondestructive testing had been completed or accommodated. The special needs of the biologically oriented investigator who wishes to study enzyme activities or cellular responses were also discussed.

The mechanism(s) to achieve the protocols described in the previous paragraphs were discussed at length. The graft retrieval subgroup discussed the desirability of "regional" retrieval and analysis centers. It was recognized that although many of the manufacturer's laboratories are experienced in this field it would not be appropriate for them to be used as a focus for "regional" centers. However, their contributions to a "noncommercial" center were acknowledged as being vital to the success of any program.

At least one multi-center ad hoc group of cardiovascular surgeons was identified as a group interested in establishing and participating in data registry of heart valve implants and the clinical progress of the recipients. The potential of voluntary organizations was also discussed. The potential of ASTM in serving as an agent in establishing a registry was also discussed. While there are ASTM groups addressing cardiovascular implants, the current emphasis of many of these groups is on materials design rather than performance standards. AAMI has been concerned primarily with performance standards. Many members of the group felt most comfortable with the proposal that a voluntary agency with broad interests (rather than specifically implant oriented), serve as the coordinator of the implant registry effort.

It was agreed that the NHLBI might well be an appropriate agency to sponsor a working group or a workshop for the development of graft and valve retrieval and analysis protocols. Dr. Watson of NHLBI pointed out that an interagency Technology Committee on Cardiovascular Biomedical Engineering existed which may well be helpful since information from the analysis of retrieved grafts and valves was of interest to both NHLBI and FDA-BMD.

It was emphasized by a number of participants that the financial cost of appropriate analysis of a retrieved implant is not insignificant. It was estimated that the current cost is about $600 an implant with the assumption that the specific equipment and personnel with the appropriate knowledge were already available.

The meeting concluded with the recommendations that a registry be established identifying the patients receiving implants and that their clinical course, explantation procedures, pathological and engineering analysis of the explanted valves and grafts be included in this registry. Finally, protocols for the analysis of explanted heart valves and grafts would be collected and collated with the objective that they serve as the basis for the development of common set of protocols to be used in the analysis of retrieved synthetic and tissue valves and grafts.

I think, at this point, I would like to ask whether members of either of the two subgroups would like to identify themselves and add anything that they feel we have missed in this summary?

Hearing no comments, I would like to close by saying that one thought that was expressed a number of times was that we are dealing with a specialized activity. It is not an activity to which any pathologist, polymer scientist, or material scientist can immediately contribute. It has to involve a commitment on their part to understand the specialized problems associated with implants. In addition, I would like to add that there are protocols available in the area of grafts which could be used to provide a basis for some more generalized protocol. So we do have in the graft area, as well as for valves, some basic ideas from which to try to develop a suitable beginning.

That, then, represents the end of our group's report.

CHAIRPERSON BROWN: Did you discuss any plans toward having these four graft protocols included in the proceedings of this workshop?

CO-CHAIRPERSON GIBBONS: No, not the details of the protocols. We had agreed, however, that at least we would include in the workshop the types of information each of these groups extracted. Probably the details of the protocols would be too cumbersome. Certainly there was an agreement, I think, of all of the graft group to have at least the listing of what they did evaluate.

DR. PITLICK (NHLBI): We didn't look at that specifically. Unless there is an objection, I don't think it would be a problem to include what types of information are available in the protocols that we have.

CHAIRPERSON BROWN: I think from my own point of view that one of the important things to try to accomplish from this workshop is to have material assimilated into one compendium so that we could look at different alternatives. Having seen the alternatives, we could then begin to either select the ones that make the most sense or simply dovetail them together to make a master list from which we can extract that set of observations and questions that are pertinent to the particular analysis under way. One reason that I am pushing this and would encourage rapid response is that the goal of the Conference committee is to have the proceedings available in four to six months. This means that we have a four week deadline to review the manuscripts from the previous two days; also that Don Gibbons and I are making a commitment to have the proceedings from this workshop edited by the same time.

I would strongly encourage and invite people to submit their documents to us as soon as they get home. If you are not going home for two weeks, call somebody in the office and have them send them to us so that they can be incorporated. Then we can really have a starting point upon which to build. Don, do you see any problem from your end as to getting that done?

CO-CHAIRPERSON GIBBONS: Just sleepless nights.

CHAIRPERSON BROWN: We are getting used to them. A point that has been brought up repeatedly is "what is good performance?". This is obviously the objective, as opposed to what are we seeing in our retrieval and analysis of removed implants, many of which are failures, and some of which are routine. It brings to mind a subject that we have tossed about from time to time on which I have not seen any progress (although I think Case Western University is making progress) and that is removal at autopsy. A lot of successful implants are going to the morticians. I wonder if anyone in the audience has had any experience or made any progress toward getting successful implants at autopsy so that they can be analyzed and we can learn from a good one?

DR. SCHOEN (University of Florida): I think the problem is a substantially different one in the orthopaedic and the cardiovascular areas and is perhaps somewhat different in the graft and the valve areas. I think the valves are probably the best example of the area that is included in every normal autopsy. Within that area, we are developing an understanding of what is good, as well as what is bad. The grafts are a little more difficult, but I don't think as difficult as the orthopaedic prostheses.

We have discussed one possibility. There needs to be some identification of a patient coming down to autopsy who has a prosthesis of any sort that is not included in the standard autopsy, basically the chest and the abdomen. I do not think we have made much progress in this. I am not sure exactly what is necessary to develop some sort of a flagging of a chart.

I think it is also necessary to understand the practical limitations of what is obtained in the way of clinical information when a patient comes down to autopsy. The autopsy generally has to be done in a period of a couple of hours after the patient's arrival and much of the clinical information is still on the floor or perhaps even in another hospital.

Nevertheless, there has to be some mechanism, I don't know what it is; perhaps it can't be done. But we ought to be thinking about some mechanism of identification.

DR. QUIJANO (Hancock Laboratories): Isn't it obvious to the pathologist at autopsy that there has been a median sternotomy in order to implant a valve? Then he will also get a sheet that says that there is a valve in this patient.

CHAIRPERSON BROWN: The same is true with orthopaedics. You can not put a plate on the tibia without leaving a scar.

DR. SCHOEN: But there are two aspects. One is that some of the most interesting patients are going to be the ones that had a valve implanted 15 years ago at another institution, and the reason that they are in the hospital is to have their colon cancer removed or something totally unrelated to the fact that the valve prosthesis is in there. The surgeon or the physician taking care of the patient at that time may simply not know.

Certainly a median sternotomy is obvious, and that incision is almost repeated in the standard autopsy. One needs a special permission to enter the extremities. And special procedures have to be developed. I guess some have been developed already, and I think that is one critical issue in developing the background of these patients that Sidney Weisman emphasized before. We want to know which patients have done well and have died in spite of their prosthesis rather than because of them.

DR. GIBBONS: May I amplify that thought from the point of view that if the patient has always been in a single institution, we have the idea of having a very visible flag on the front cover of the patient's record. The pathologist is not going to leaf through it, however, even if it is available in time. Of course, there will always be a subgroup of patients who received implants in another hospital and, therefore, it is a problem of educating the pathologists in each hospital to be aware of and to look out for these patients. I think it is the responsibility of the pathologists in each hospital. I see Dr. Anderson wants to amplify.

DR. ANDERSON (Case Western Reserve): Pat Parks, who is here, and I have done many autopsies, and we both can speak to the fact that, at least at our institution, a complete review of the record is necessary before one goes ahead with the autopsy. That, coupled with the scar, certainly gives us a clue as to what is there.

In regard to special procedures, at least in the state of Ohio, a complete autopsy is a complete autopsy. And we do not need special permission to look at the extremities. The only problem that we have is that if we somehow damage or disfigure portions of the body which are shown in the funeral home, we get into trouble with the funeral directors and morticians. But everything else, for the most part, is permissible at our institution.

DR. WESOLOW (Yale University): I have had an experimental program for 20 years on experimental grafts, and I have a specific interest in recovering human prostheses, both successful ones and unsuccessful ones. The unsuccessful ones are less of a problem. They come back to the surgeon, and being a surgeon, I deal with not only my own, but other unsuccessful ones.

The successful ones are more difficult. In past days, pathologists and others were not really interested in recovering these things. It

was a personal interest to be able to correlate the experimental data with the patient in terms of predictability and also with a view to improving prostheses.

Two mechanisms helped to make the system work. I had an experimental research lab and I cut my own sections. In order to enlist the aid of a pathologist at the institution, my histologic unit was officially a part of the department of pathology, administratively, although I ran the sections. This allowed me to be legally a pathologist and to gather specimens--which is one wrinkle.

The second, and much more successful mechanism, was direct enlistment of the patient and the family. At the time of implantation, I made it well known that I was interested in the prosthesis and that I would like to recover it. I would get calls from as far away as 100 or 200 miles: "My husband just died. Would you like the graft?" And I would get in an automobile, drive up and recover it. I have also gone into funeral parlors and all sorts of places in order to do this. I also got a reasonable collection of relatively normal vascular prostheses this way.

CHAIRPERSON BROWN: I think you have hit on one of the keys here; that the whole process of informed consent at the time of implantation should express a statement of interest in analysis and retrieval of implants so that we can look at the good ones as well as the bad ones.

DR. BLAIS (National Health and Welfare, Canada): One aspect which has been an undercurrent in much of the discussion and yet has been omitted is the question of blowing our own horn. On the average, the pathologists, the hospitals and the personnel peripheral to, and yet essential to any type of recovery program, are not fundamentally interested in what we are talking about. So it is the responsibility of each and every one of us to visit those who have potential value in the recovery process and to perhaps barter with them in other aspects, with intangibles like publications and things of this sort. In other words, there are two things to push for: (a) One is to make the average pathologist or forensic chemist working for a police laboratory or hospital interested from his own point of view in the implant and the implant pathology, and (b) to motivate him perhaps, not with money, but with other aspects which are barterable within our field of interest.

CHAIRPERSON BROWN: I would like to reinforce that statement and suggest we add an acknowledgment at the end of this workshop's proceedings, a very sincere and warm acknowledgment to all those O.R. supervisors, circulating and scrub nurses, and ward and clinical department secretaries who have made possible a large part of the implant retrieval and analysis that we have presented at this meeting. I hope that they will continue to remain our allies.

VOICE: Amen!

DR. WATSON (NHLBI): I wonder, Mr. Chairperson, is there any plan to present a four- or five-page summary of this workshop prior to the publication of proceedings? It might be useful in terms of the recommendations and general intent of the meeting. I know at NIH we would be interested in providing this to advisory groups and study sections. I think other groups might also be interested in a summary so that they could take it to their own institutions.

CO-CHAIRPERSON GIBBONS: May I answer from the cardiovascular group. It is my intention, with Dr. Pitlick, to attempt to do that and to circulate to those at the workshop beforehand early notes and drafts that we will then attempt to put together. It is our intention to try, and indeed, do that before actual publication.

CHAIRPERSON BROWN: I would certainly be willing and in favor of my doing the same for the orthopaedic workshop. But I am not sure if we can commit the committee to try to generate a summary from the two conference days that could be circulated ahead of time. I think our efforts are better directed toward getting the entire book out quickly.

DR. RUFF (National Bureau of Standards): We could certainly treat the proceedings of todays workshop as a somewhat separate entity and make it available to the Conference sponsors in advance of the book publication. Perhaps this would respond to the suggestion here.

CHAIRPERSON BROWN: One other question that I would like to put to the floor concerns the subject of patient confidentiality and patient identification. This discussion should then lead into whether there are any legal problems that will arise from storage of patient information.

MR. WEISMAN (Howmedica): I think that question was brought up at the Conference four years ago and discussed. I think it was agreed upon that there should be some sort of a hidden code for preserving the hospital information in a confidential manner. It was suggested that that information would remain within the institution, but there would be a reference number.

CHAIRPERSON BROWN: I think that was what was decided four years ago; but my question now is what is the current legal situation? Henry, do you have any comments?

DR. PIEHLER (Duke University): I think the way to start is to ask if anyone has ever had any problems of this nature.

DR. SCHURMAN (Stanford University): We have not had problems with it, but it is something that is of concern at our university since we have a national data bank center and like all institutions, we are governed by laws that I understand imperfectly. Nevertheless, there are regular steps and regulations for this. In order to collect information on patients beyond the ordinary charting, the patients are, at least at our institution, deemed to be part of an experiment.

Therefore, the protocol has to go through a Human Subjects Committee for approval, which our protocol has for many different studies. There are laws, or at least rules, that govern this. One is the guarantee of the protection of privacy of the patient. This is done when computers are involved by using secret codes that can only be accessed by the physician who is actually treating the patient. Whereas the data of a large group of patients can be available to numerous investigators, there are steps taken to guarantee that the identity of an individual within that group is not identified. That means an exclusion of clear identifying information. For example, you cannot pull out of our computer someones records on the basis of their age, sex, height, and weight. We allow our investigators to use only prearranged subsets. They can not define their own subsets.

I think there are Federal laws governing privacy. Someone in the room might know it.

CHAIRPERSON BROWN: In our institution, we are not allowed to put a patient's name in the computer. I think the way around this is simply to maintain a record of the patient's code number that you put into the computer and somewhere else, probably in the clinic. You keep the record that has the name attached to that number. Then someone else who uses the computer on a time-sharing system can not retrieve the patient's name.

CO-CHAIRPERSON GIBBONS: Obviously the point that Dr. Schurman has made is true for all of us. We have to go through a Human Involvement Committee. In our particular case, technically it involves the use of discarded tissue. In other words, it has to have gone officially through pathology. We are then allowed to use "discarded" tissue. And each of us has our own way of attempting to maintain confidentiality within our interpretation of the legal world. All of us try to achieve it by making sure that from the data that is published or generally made available, that no one could go back and say that had to be Patient X. This is really what you have to make sure of: that data can not possibly be then traced backwards.

MR. WEISMAN (Howmedica): There is another question that has to be addressed, and that is about the ownership of the prosthesis. Actually, the prosthesis belongs to the patient, and you have to be extremely careful not to do anything to that prosthesis unless you have permission from the patient or his heirs to handle that. I believe we ought to address that from the legal point of view of what the implications may be in gathering implements and how to handle them.

DR. PIEHLER (Duke University): There is some help in that from the ASTM Committee E-40 [Technical Aspects of Products Liability Litigation] which is, I believe, going to have a standard within this year on testing sequences. This standard has been six years in development, and it is very interesting as to the positions that different manufacturers take toward this very important issue.

Automobile manufacturers, for example, don't want anybody touching anything because typically the plaintiff always has the evidence first. Whereas, implant manufacturers want to "hack and hew" because typically they get it back from the doctors before the plaintiff or anybody else has it. Basically, the way the ASTM draft standard reads is that you should make every effort to inform all interested parties, particularly if the litigation is reasonably foreseeable. But it also says that under circumstances like the generation of information or like the situation where you might have a perishable item, that you may proceed with unilateral destructive testing if you take adequate steps to preserve the nature of the device and also leave enough for other people to repeat your tests as well as any other reasonable test that might be performed.

This document, I think, will be out very shortly. What weight it will have is another question, since it is entirely voluntary. But I think it addresses this issue. And one of the things that it recognizes is that there is value in doing unilateral destructive testing, but it also recognizes legitimate rights of other people to obtain their information.

CHAIRPERSON BROWN: I think part of the issue on patient ownership of the material goes back to the point that Dr. Wesolow was making earlier. That is, telling the patient at the time of implantation that this is interesting material that we would like to analyze at the time of removal or at the time of death.

One of the most beautiful studies I have ever heard was presented at the University of Ottawa (Conference on Internal Fixation of Fractures, May 10-12, 1979) by Mr. A. J. Partridge from Sussex, England who was working with the geriatric population. He has had hips and all kinds of other devices that he has implanted willed to him. As a result, he is generating a very nice series of analysis of the performance of his particular devices. It is by starting with the patient at the time of implantation that true performance data will be generated.

CO-CHAIRPERSON GIBBONS: May I say that we have a proposal for an extensive prosthesis retrieval and analysis program at Case Western Reserve University. An integral part of that is the surgeons who are involved in informing the patients prior to the implantation that we request them to be part of this analysis. So it does meet the kind of comments that Mr. Weisman just made as part of an overall protocol.

DR. SCHOEN (University of Florida): I think a point needs to be amended to this which creates a little difficulty. The person interacting with the patient prior to implantation is generally the surgeon or the physician. I think these people are concerned, perhaps rightfully so, that while they may indicate to a patient that a particular procedure does not have a 100 percent chance of success, there is some reluctance to indicate to the patient that there is a certain interest

in what is being done because it is of an experimental nature. I think this is a particularly touchy issue. It perhaps can be accomplished, but I think it is very delicate.

CHAIRPERSON BROWN: That is why I am saying we should state we have an interest, rather than saying we are performing an experiment, which, in fact, we are.

DR. WILKINSON (Strathclyde, U.K.): Could I bring up one point from a U.K. study in which the medical profession objected to retrieval data which might identify sources of excellence or lack of excellence between different hospitals or different surgeons. Perhaps this is something else that we ought to consider here today.

CHAIRPERSON BROWN: On that point, I think this meeting has been very refreshing compared to previous meetings at which we discussed the problems of doing implant retrieval and analysis. At this meeting we have heard the presentation of a large number of cases, examination of a large number of implants, and virtually no discussion of the problems of manufacturers being afraid that we are going to threaten one over the other, nor of surgeons being afraid that we are going to reveal that some may be better than others. This is obviously a critical issue to all, but it appears as though we are making some very comforting progress in this important area.

DR. HOROWITZ (Johns Hopkins University): On the cardiovascular protocols that you mentioned, I heard that we were going to bring those together for the publication, but I didn't hear you follow through and say that we were going to bring those to the coming ASTM meeting in Denver as we are with the orthopaedic protocols. Is it possible to have the cut-and-pasted version of that brought before the ASTM committee so that it could be worked on at that time also?

CO-CHAIRPERSON GIBBONS: Dr. Kaye, who is part of this group, is chairperson of the ASTM F-4 Cardiovascular Subcommittee and hopefully he will be there or will get it into the ASTM proceedings. Is that a fair statement, Dr. Kaye?

DR. KAYE (Mayo Clinic): That is correct.

CHAIRPERSON BROWN: Any further comments or discussion from the floor?

DR. BLAIS (National Health and Welfare, Canada): Maybe as an appropriate epilogue it can be said that part of the success that we have had up north is that for the first time ever a mixture of certain scientists applied and respected the constraints of the surgeons. There are many surgeons who participated within our program on the premise that we would protect them if the need arose. And we have held to our word up to now and will honor it further.

CHAIRPERSON BROWN: I would like to conclude the Workshop by expressing a note of thanks to you all. We were a little skeptical whether we would be able to accomplish anything in this session. Speaking from my own vantage point, I think we have, in fact, made much progress and have set a basis for getting things going in the near future. Ladies and gentlemen, the meeting is now adjourned.

Epilogue

As was stated during this Workshop, and was indicated by the success of the Conference as a whole, we all, physicians, material scientists, and pathologists, owe a tremendous amount of gratitude to the operating room teams for helping gather implants, and to the ward and department secretaries for helping gather the clinical information. Without their help, this meeting would have been very quiet; without their help we can not expect to make progress in the future. Thank you all!

Appendix A (attached) is a Compendium Code for Evaluation of Properties and Performance of Orthopaedic Patients and Implants. This document is the cut-and-paste product as described earlier. It was reviewed and revised by the Implant Retrieval Task Force of ASTM Committee F-4, at the May 1980 Denver meeting. The document is now a subject for the task forces' activities.

In the cardiovascular area, the following documents are appended to the workshop proceedings:

Appendix B: In 1979, Harrison et al., prepared a monograph for the FDA (Contract 01317) on "Identification and Evaluation of Explanted Heart Valve Prosthesis". The evaluation form in this monograph was reviewed by several members of the heart valve subgroup, including Drs. F. Schoen and P. J. Parks. Mr. E. Mueller has incorporated a number of their suggestions in a revised evaluation form check list.

Appendix C: The analysis protocols used by Gortex, Inc., USCI Surgical Products and Meadox.

In addition, comments on retrieval and analysis from their own experience by the Laval University, Quebec, Canada, group (Prof. M. Guidoin) can be found in the last section of their paper in the Conference proceedings.

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Appendix A

COMPENDIUM CODE FOR EVALUATION OF PROPERTIES AND PERFORMANCE OF ORTHOPAEDIC PATIENTS AND IMPLANTS

The attached document is a compilation of the questionnaires developed for implant retrieval and analysis and patient evaluation at the following centers: Stanford (Arthritis Surgery Proforma), Northwestern, Case Western Reserve, Hospital for Special Surgery, Tulane, Dartmouth, and the AO/ASIF. While some of the material in the compilation is also presented in the other papers included in this proceedings, it was felt that pooling of the ideas would make the subsequent development and adoption of a National Consensus document easier.

The objectives of the compendium development are to create an all inclusive list of line item questions with specific letter or number code answers in a form which is compatible with computer storage and analysis of data. The compendium will of necessity be a far more extensive list of items than that which would be used for a particular implant or patient analysis. Thus, the compendium is to serve as a master code list from which basic or core documents can be excerpted for the purposes of a particular study. If we can all reach an agreement as to the line item designation for each inquiry, then our respective computer data banks can be superimposed when pooling data.

The Compendium as presented here represents the efforts of one individual; it does not represent a group consensus. As a first step, this document has been divided into 16 sections, with each section subdivided into major and minor questions or items. For example, Section 1 is patient identification; the first items in section 1 are questions asked by all the centers, e.g., patient name, patient weight. The items with letter designations are more specific in nature, and do not necessarily apply to all centers, e.g., 1C patient home address, handedness, marital status, ethnic origin, and date of difficulty or disease onset. Thus, the numbered items represent a compendium core, while the lettered items represent additional inquiries. In some sections, especially in patient diagnosis and level of activity, there is significant redundancy between the numbered and lettered items. This is because different centers have slightly different ways of asking or answering some of the questions. Ultimately, it is anticipated that these redundancies will be resolved into unified questions and answer codes.

This document is being published herein to inform the reader about the current status of this effort. The document is also being submitted to a task force within the Implant Retrieval Section (F4.20.07) of the American Society for Testing and Materials (ASTM) committee F-4 on Medical and Surgical Materials and Devices, 1916 Race Street, Philadelphia, Pennsylvania 19103. The task force will modify the document and submit it to the consensus process of the Society. The result will be a Compendium code from which core documents can be extracted. (F-561 will probably remain as core document.) People interested in contributing to the development of the compendium code should contact ASTM.

1. PATIENT IDENTIFICATION

1.1 Case # _____ 1.2 Patient name _____
1.3 Patient S.S. or hospital I.D. # _____
1.4 Sex 1-male, 2-female
1.5 Weight _____
Overweight condition A-normal, B-moderate, C-marked
1.6 Height _____ 1.7 Date of Birth (Mo/Yr) _____
1.8 Hospital of implantation _____ (Use four-letter code.)
1.9 Hospital of removal _____
1.10 Date of implantation (Mo/Yr) _____
1.11 Date of removal _____
1.12 Joint involved A-hip, B-knee, C-ankle, D-finger, E-elbow, F-shoulder
1.13 Bone involved A-femur, B-tibia, C-fibula, D-humerus, E-radius, F-ulna, G-spine, H-J-others
1.14 Side involved A-right, B-left, C-middle

1A. Patient source A-physician's own case, B-referral case
Surgeon: _____ implantation; _____ removal

1B. Patient's normal occupational activity level
A-extremely active B-moderately active (normal)
C-slightly active D-sedentary E-other

1C. Home address _____

Handedness L R Marital status _____ Ethnic origin _____
Date disease or difficulty began _____

1D. Apparent lower extremity difference
0-equal, 1 right longer, 2 left longer
Amount of apparent difference _____ cm
True lower extremity length R_____ L_____ cm

1E. Problems in non-operative joints
0-normal, 1-involved and not impaired, 2-involved and impaired, 3-bilateral procedures

1F. Intra-articular steroids Yes, No; joints _____;
inject _____

1G. Non-narcotic analgesics _____ type, dose (include ASA and NSAI)
Narcotics _____ Chrysotherapy _____
Corticosteroids _____ Chemotherapy _____
Penicillamine _____

2. PATIENT DIAGNOSIS

2.1 Primary diagnosis, reason for implantation

A-unknown
B-primary osteoarthritis
C-secondary osteoarthritis
D-rheumatoid arthritis
E-dislocation of joint
F-aseptic necrosis
G-pain
H-Paget's disease
I-congenital deformity
J-pseudoarthrosis or non-union
K-malunion of fracture
L-tumor
M-loosening of prosthesis
N-malposition of prosthesis
O-trauma - simple - closed
P-trauma - simple - open
Q-trauma - comminuted - closed
R-trauma - comminuted - open
S-traumatic arthritis

2.1A. POLYARTHRITIS OF UNKNOWN ETIOLOGY
Rheumatoid arthritis
Juvenile rheumatoid arthritis
Ankylosing spondylitis
Psoriatic arthritis
Reiter's syndrome

CONNECTIVE TISSUE DISORDERS
Systemic lupus erythematosus
Scleroderma
Polymyositis - dermatomyositis
Mixed connective tissue disease

OSTEOARTHRITIS

POST TRAUMATIC
Closed reduction only
Open reduction only
Surgery proximal
Surgery proximal and reduction
Surgery distal
Surgery distal and reduction
Surgery proximal and distal
Surgery proximal, distal and reduction
Unreduced dislocation
Unreduced dislocation and failed surgery

FRESH TRAUMA
Proximal fracture
Proximal fracture and dislocation
Distal fracture
Distal fracture and dislocation
Proximal and distal fracture
Proximal and distal fracture; dislocation

NEUROPATHIC (Charcot)

SEPTIC
Active infection
Previous infection

METABOLIC OR ENDOCRINE
Gout
Goucher's disease
Paget's disease
Hemophilia
Chondrocalcinosis

TUMOR
Primary bone tumor - benign
Primary bone tumor - malignant
Metastatic tumor

PRIMARY HIP DISEASE
Congenital dislocation
Subluxation
Primary protusio

OSTEONECROSIS
Alcoholic
Corticosteroid induced
Hemoglobinopathy
Legg-Perthes
Post traumatic
Caissons

2.2 Other, concurrent diseases X-none

A-senility
B-chronic obstructive pulmonary disease
C-hypertension
D-diabetes mellitus
E-peptic ulcer disease
F-obesity
G-hyperthyroidism
H-coronary artery disease
I-congestive heart failure
J-cardiac arrhythmia
K-myocardial infarction
M-bone infection _____
N-joint infection _____
O-renal disease
P-thrombophlebitis
Q-peripheral vascular disease
R-alcoholism
S-neuromuscular disorder

2.3 History of foreign body reaction _____

2.4 History of metal sensitivity A-none, B-nickel, C-chrome, D-cobalt

2.5 Previous surgery A-ORIF, B-TJR, C-hemi-arthroplasty, X-none

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2.5A.
D-medial meniscectomy
E-lateral meniscectomy
F-joint debridement
G-removal of loose bodies
H-ligamentous reconstruction - med. collat.
I-ligamentous reconstruction - lat. collat.
J-lig. recon. - ant. cruciate
K-lig. recon. - post. cruciate
L-synovectomy
M-patellectomy
N-patellar shaving
O-drilling/shaving of femur
P-drilling/shaving of tibia
Q-osteotomy - high tibial
R-osteotomy - femoral
S-patellar realign. - proximal
T-patellar realign. - distal
U-Maquet procedure
V-Hauser procedure
W-arthroscopy

2.5B. FAILED PRIOR SURGERY - secondary diagnosis

Osteotomy - hip
Osteotomy - knee
Arthrodesis
Internal fixation
Cup arthroplasty
Hemiarthroplasty
Hip
Knee
Total joint replacement
Hip
Knee
Unicompartmental

2A. Physical exam HIP

_____ Flexion, _____ flexion arc, _____ adduction in extenstion,
_____ abduction in extension
_____ Abduction muscle power 0-normal, 1-weak, 2-absent
_____ Trendelenburg 0-normal, 1-equivocal, 2-positive

2B. Physical exam KNEE

a. Recorded separately for each knee.
All limits or motions recorded in degrees.

Flexion
Flexion arc
Varus - valgus
ML instability in extension
0-none, 1-minimal, 2-mild, 3-moderate, 4-severe
AP instability in 90° flexion
0-none, 1-minimal, 2-mild, 3-moderate, 4-severe

Effusion 0-none, 1-some, 2-severe
Patello femoral tenderness
0-none, 1-some, 2-severe
Patella tracking 0-normal, 1-subluxed, 2-dislocated
Patella status 0-present, 1-patellectomy

b. Pain walking (0-15)
Pain at rest (0-15)
Walk (0-12)
Stairs (0-5)
Transfer (0-5)
ROM (0-18)
Strength (0-10)

Flexion deformity (0-10)
Instability (0-10)
Cane (0-1)
Crutches (0-3)
Extension lag (0-5)
Valgus deformity (0-9)
Varus deformity (0-9)

Total Knee Score _____

2C. Joint range of motion
Prior to onset of symptoms _____
After onset of symptoms _____

1-full ROM
2-functional ROM
3-restricted and limited ROM
4-joint contracture, limited ROM

2D. Total pain sum: Sum of rest and activity pain
0-none; 1-minimal, i.e., occasional and slight; 2-mild, i.e., regular and slight, takes occasional analgesics; 3-moderate, i.e., frequent use of analgesics; 4-severe, i.e., regular use of analgesics

2E. Other joint involvement: yes if definite involvement, very painful or disabling. Right or Left 0-not involved, 1-involved
___ foot, ___ knee, ___ hip, ___ hand, ___ elbow, ___ shoulder, ___ neck, ___ back

3. SURGICAL IMPLANTATION PROCEDURE

3.1 Hospital _____ 3.2 Surgical team _____
_____

3.3 Anesthesia A-general, B-spinal
3.4 Incision time _____, close time _____
3.5 Tourniquet used Yes No, time _____
3.6 Blood replacement _____ # units
3.7 Surgical approach _____

3.8 Were antibiotics used? Yes No
3.9 Reason for antibiotics A-prophylactic, B-positive culture, C-history of sepsis, D-other _____
3.10 Antibiotic route A-intravenous, B-oral, C-intramuscular
3.11 Antibiotic used

A-keflin	F-erythromycin	K-carbenicillin
B-penicillin	G-cloxacillin	L-tetracycline
C-methicillin	H-dicloxacillin	M-cephazolithin
D-gentamycin	I-keflex	N-kefzol
E-cleocin (clindamycin)	J-ancef	

3.12 Anticoagulation A-aspirin, B-heparin mini-dose IM, C-dextran, D-heparin full dose IV, E-coumadin, X-none

3.13 Other concomitant procedures

A-quadricepsplasty	E-patellar realignment
B-valgus release	F-ligamentous release
C-perineal nerve dissection	G-posterior capsular release
D-patellectomy	H-debridement

3.14 Generic implant type

A-ankle	F-pin	K-shoulder
B-hip	G-screw	L-wrist
C-rod	H-plate	M-finger
D-knee	I-hip nail plate	N-others
E-elbow	J-staple	

4. POST OPERATIVE COMPLICATIONS

4.1 Pneumonia Yes No
4.2 Myocardial infarction Yes No
4.3 Pulmonary embolism Yes No
4.4 Cerebrovascular accident Yes No
4.5 Nerve palsy Yes No
4.6 Abnormal wound healing Yes No
4.7 Fracture Yes No
4.8 Arterial vascular problem Yes No
4.9 Sterile wound drainage Yes No
4.10 Trauma Yes No
4.11 Thrombophlebitis Yes No
4.12 Death Yes No

4.13 Infection A-none, B-superficial, C-deep
4.14 Infectious organism

A-Staph aureus
B-Staph epidermidis (albus)
C-Streptococcus
D-E. coli
E-Pseudomonas aeruginosa
F-Clostricium perfringens
G-Bacteroides
H-Enterobacter
I-Klebsiella
J-Diphtheroids
K-anaerobic
L-mixed

4A. Pain in fracture/implant area A-none, B-seldom, C-yes
Weather sensitivity A-none, B-seldom, C-yes
Swelling A-none, B-seldom, C-yes
Inflammation, redness A-none, B-yes, when _____

4B. Intra-operative bone fracture Yes No
Post operative bone fracture Yes No
Trochanteric nonunion 0-no, 1=1 cm, 2=1-2cm, 3=2 cm

4C. Hematoma 1-not drained, 2-surgically drained, 3-spontaneously drained

4D. Dislocation Yes No Subluxation Yes No

4E. Clinically loose prosthesis Yes No
Prosthesis breakage Yes No
Lost to follow up Yes No

5. FUNCTIONAL ACTIVITY

5.1 Functional level attained after insertion:
(A-C, lower extremities; D-F, upper extremities)

A-ambulatory
B-ambulatory with aids
C-not ambulatory
D-functional
E-functional with brace
F-not functional

Patient activity
Prior to onset of symptoms _____
After onset of symptoms _____

1-active and working
2-active, uses no supports or one support intermittently
3-active, uses one support
4-active, uses two supports
5-inactive, uses one or two supports
6-inactive, wheelchair
7-inactive, confined to bed
8-other _____

5.2 Ambulation

A. Walking aids 0-none, 1-one support part-time, 2-one support full-time, 3-two supports, 4-walker, 5-wheelchair, 6-bedridden
B. Maximum distance able to walk at one time 0-one mile or more, 1-one-half mile, 2-one-fourth mile, 3-indoors around house, 4-unable
C. Limp 0-none, 1-minimal, 2-mild, 3-moderate, 4-severe
D. Gait data
Velocity meter/min.
Gait cycle (sec.)
Cadence steps/min.
R-SLST (sec.)
L-SLST (sec.)
Initial double support
Terminal double support

5.3 Ability to walk up stairs
Prior to onset of symptoms _____
After onset of symptoms _____

1-normally
2-slowly, alternating
3-one stair at a time
4-unable

Ability to climb stairs 0-no difficulty, 1-mild difficulty, 2-need handrail, 3-extreme difficulty, 4-unable

5.4 Activities

A. Put on socks (L&R) _____
Arise from chair without using arms _____
Use knife and fork _____
Bathing and personal hygiene _____
Drive car

0-no problem
1-mild difficulty
2-moderate difficulty
3-severe difficulty
4-unable

B. Ability to stand from sitting position
Prior to onset of symptoms _____
After onset of symptoms _____

1-no arms required
2-arms required
3-other help required

C. Ability to put on shoes and socks
Prior to onset of symptoms _____
After onset of symptoms _____

1-easily
2-with difficulty
3-socks only, cannot tie shoes
4-unable

D. Light sports: golf swim, bowl, garden
Heavy sports: jog, tennis, ski, skate

Sports: Code in each category.
Specify yes or no if any one within category is performed.

5.5 Joint pain (for each operative joint)
Pain at rest
Pain with activity
Total pain sum: sum of rest and activity pain
0-none; 1-minimal, i.e., occasional and slight; 2-mild, i.e., regular and slight, takes occasional analgesics; 3-moderate, i.e., frequent use of analgesics; 4-severe, i.e., regular use of analgesics

5.6 Did operation help you?
0-much better, 1-little better, 2-no change, 3-little worse, 4-much worse

If operation did not help, was it because
0-problem not involving the joint operated on, 1-problem in other joint(s), 2-problem in the joint that was operated on

6. ROENTGENOGRAPHIC REVIEW

6.1 Bony change around implant A-calcar resorbtion, B-cortical hypertrophy, C-sclerosis or compaction, D-heterotrophic bone formation, E-osteolysis, F-cysts, G-osteoporosis, H-normal
6.2 Migration of implant, subsidence _____ mm
6.3 Implant deformity A-bent, B-rotated, C-tilted
6.4 Implant loosening Yes No
6.5 Prosthesis fracture Yes No
6.6 Bone fracture A-tibial plateau, B-femoral condyle, C-femoral shaft, D-tibial shaft, E-bone adjacent to implant

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6A. PMMA A-normal, B-cracked, C-excessive cement seen in joint, D-no cement seen
Lucent lines A-none, B-incomplete, C-complete
Lucency width _____ mm
Location A-proximal, B-medial, C-lateral, D-distal
Lucency progressive Yes No

6B. Subluxation A-posterior, B-anterior, C-medial, D-lateral, E-rotatory
Dislocation A-posterior, B-anterior, C-medial, D-lateral

6C. Fracture healing A-primary union, B-light callus, C-heavy callus, D-delayed union, E-pseudoarthrosis

6D. Penetration of implant across joint space Yes No
Penetration of implant through bone Yes No

6E. Scintimetry A-hot distal femur, B-hot proximal tibia, C-hot proximal femur, D-hot acetabulum, E-other hot spot

6F. Radiographic alignment
AP femur/tibia pre TKR (degrees)
(normal = 90°) AP prosthesis/tibia pre TKR (degrees)
(7° valgus normal = 83°) AP prosthesis/femur (degrees)
(no tilt normal = 90°) lat prosthesis/tibia (degrees)
(degrees of flexion) lat prosthesis/femur (degrees)
Overall alignment femur/tibia post TKR (degrees)

7. REASONS FOR IMPLANT REMOVAL

7.1 Primary indication for implant removal _____

7.2 Secondary indication for implant removal _____

A-routine
B-early infection <6 months
C-late infection >6 months
D-breakage of implant
E-pain related to implant
F-stiffness related to implant
G-prominence of bursae
H-instability or loosening
I-unsatisfactory implant position
J-non-union
K-allergic or hypersensitive reaction
L-loosening with pain
M-dislocation/subluxation
N-restricted range of motion
O-patellofemoral disease
P-autopsy
Q-reason unknown
R-other

7A. Contributory conditions

01-none
02-alcoholism
03-drug addiction
04-senility
05-neuromuscular disorder such as hx of polio, CVA, etc.
06-multiple previous procedures
07-other _____

7B. Initial factor leading to removal symptoms

1-iatrogenic**
2-infection
3-trauma or fall
4-idiopathic
5-autopsy
6-other _____

**Iatrogenic problems include: poor component orientation, poor bony preparation, bone fracture, etc.

7C. Results of allergy testing (LIF test)

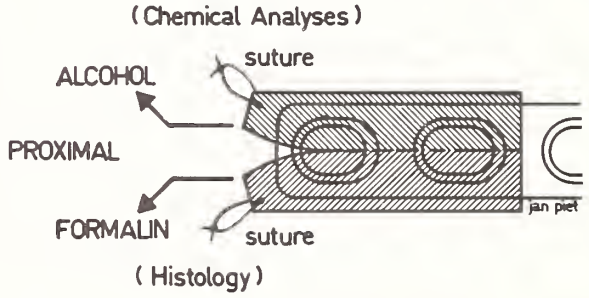
	No sensitivity 1	Ni 2	Co 3	Cr 4	No cell migration 5
A-pre-implantation					
B-follow-up					
C-implant removal					
D-follow-up					

8. FINDINGS AT SURGERY

8.1 General observations
- A-pus
- B-granulation tissue
- C-foreign body reaction
- D-tissue staining (debris)
- E-bursal fluid
- F-abundant scar tissue
- G-implant easily removed
- H-bony reaction
- I-loose prosthesis

8.2 Components removed
- A-prox fem
- B-acetabular
- C-dist fem
- D-tibial plateau
- E-patellar button
- E-patellar button
- F-other TJR
- G-internal fixation device
- H-some (not all) bone screws

8.3 Biopsy taken
- A-from over plate as in figure
- B-pseudo joint capsule
- C-fibrous tissue
- D-synovial fluid
- E-bone/cement interface



8A. Subsequent procedure A-fusion, B-new TJR, C-another int. fix., D-plaster

8B. Findings relative to fracture fixation plates
Scar 0-inconspicuous, 1-distinct, 2-red, 3-eczematous
Tissue over plate 0-soft, 1-thickened, 2-bony
Coloration 0-none, 1(+), 2(++); color: white, gray, brown, black
Tissue contacting plate 0-intimate, 1-cavity, 2-serum
Collar around screw head 0-connective, 1-bony, 1/2-combination
Plate bed 0-vascularized, 1-avascular, 1/2-combination
Biopsy of plate capsule proximal distal

8C. Findings relative to prostheses
Fibrous membrane between bone and PMMA 1-a little, 2-a lot, 3-no
Excessive PMMA around components 1-a little, 2-a lot, 3-no
PMMA fragment(s) in joint and synovium 1-a little, 2-a lot, 3-no
Proximal component(s) poorly oriented 1-a little, 2-a lot, 3-no
Distal component(s) poorly oriented 1-a little, 2-a lot, 3-no
Component(s) dislocated 1-yes, 3-no
Proximal component(s) fractured 1-yes, 3-no
Distal component(s) fractured 1-yes, 3-no
Soft tissue rubbing or impingement by prosthesis 1-yes, 3-no
Bony contact by component(s) 1-yes, 3-no
Joint ligaments intact 1-yes, 3-no
Musculature surrounding joint intact 1-yes, 3-no

8D. Degree of loosening

	Component #1	Component #2
Proximal component	___	___
Distal component	___	___

1-freely loose, component easily removed
2-loose, component removed with little effort
3-loose, component removed with difficulty
4-firm, component removed without great effort
5-firm, component removed only with great effort
6-component not removed

8E. Loosened interface

Proximal component	___	___
Distal component	___	___

1-bone/cement
2-cement/prosthesis
3-both of above
4-bone/prosthesis
5-not loosened but removed
6-component not removed

8F. Cement fractures

Proximal component	___	___
Distal component	___	___

1-fresh from removal
2-old
3-both of above
4-no cement
5-none
6-component not removed

9. HISTOPATHOLOGY

9.1 Fibrous tissue X-none, A-plate biopsy, B-prosthesis area
9.2 Thickness _____ mm
9.3 Inflammation Yes No
9.4 Cells PMN _____
9.5 Cells FBGC _____ 9.4 - 9.8, score scale 0 to 5
9.6 Cells macrophage _____
9.7 Cells lymphocytes _____
9.8 Cells plasma cells _____
9.9 Morphology A-granulation, B-capsular
9.10 Debris in cells X-none, A-PMMA, B-UHMWPE, C-metallic
9.11 Intercellular debris X-none, A-PMMA, B-UHMWPE, C-metallic

9.12 Pseudojoint capsule Yes No
9.13 Thickness _____ mm
9.14 Inflammation Yes No
9.15 Cells PMN _____
9.16 Cells FBGC _____
9.17 Cells macrophage _____ 9.15 - 9.19, score scale 0 to 5
9.18 Cells lymphocytes _____
9.19 Cells plasma cells _____
9.20 Morphology A-fibrous, B-granular, C-synovium
9.21 Debris in cells X-none, A-PMMA, B-UHMWPE, C-metallic
9.22 Intercellular debris X-none, A-PMMA, B-UHMWPE, C-metallic

9.23 Synovial fluid Yes No
9.24 Centrifuged _____ G's
9.25 Color _____
9.26 Debris X-none, A-PMMA, B-UHMWPE, C-metallic
9.27 Size range _____ to _____ micron
9.28 Cells A-few, B-moderate, C-many
9.29 Cell type _____

9.30 Bone/cement interface X-none, A-pelvic, B-prox fem, C-dist fem, D-tibia
9.31 Macro A-hemopoetic, B-white glistening

9.32 Bone Yes No
9.33 Location _____
9.34 Trabeculae A-organized, B-disorganized
9.35 Tissue A-osteoid, B-calcified
9.36 Marrow A-normal, B-abnormal

10. IMPLANT IDENTIFICATION

10.1 Implant classification A-prosthesis proximal, B-prosthesis distal, C-fixation device

10.2 Ankle A-Howmedica, B-Newton, C-Scholz, D-Oregon

10.3 Knee

A-TCP I
B-TCP II
C-TCP III
D-I/B
E-I/B P.S.
F-Unicondylar
G-Polycentric
H-Marmor
I-UCI
J-Duocondylar
K-Shiers
L-Duopatella
M-Gunston
N-Freeman-Swanson
O-Walldius
P-Guepar
Q-Spherocentric
R-MacIntosh
S-Geomedic
T-Stabilocondylar
U-McKeever
V-Geopatella
W-Custom design

10.4 Total hip

A-Charnley
B-Charnley-Muller
C-Muller
D-CAD
E-T-28
F-Series II
G-Anitomic
H-Bateman UPF
I-AuFranc-Turner
J-Weber
K-Bechtol
L-Christiansen
M-Giliberty
N-Tharies
O-Moore
P-Thompson
Q-Bipolar
R-Porous coat
S-Rough stem

10.5 Total hip stem/neck length _____/_____ A-std, B-short, C-long

10.6 THR head diameter _____ mm

10.7 Total shoulder A-Neer, B-Zimmer

10.8 Elbow A-Mayo, B-Tri-axial, C-Schlein, D-Coonrad

10.9 Wrist A-AMC, B

10.10 Finger A-MCP, B-PIP, C-Schultz

10.11 Plate type A-compression, B-self-compressing, C-semi tubular, D-"T", E-thin, F-uniform strength
Plate width A-std, B-wide

10.12 Plate number of holes _____/_____ screw diameter (4.5, 3.5, 2.7, 2.0)

10.13 Screws number _____, type _____ A-hex, B-philips, C-cruciate, D-single slot, E-cancellous, F-malleolar

10.14 Plate, nail plate

A-Smith-Peterson & Thornton
B-Smith-Peterson & McLaughlin
C-compression screw
D-angle blade plate
E-Jewet
F-sliding nail
G-Massie

10.15 Rods

A-Kuntscher
B-Rush
C-Hansen-Street
D-Schneider
E-Lottes
F-Steinmann
G-Kirschner
H-Enders
I-Smith-Peterson
J-Harrington

10.16 Staple _____

10.17 Wire _____

10.18 Implant manufacturer

A-Allo Pro
B-AO/ASIF
C-Cintor
D-Biomet
E-Cutter
F-DePuy
G-Downs
H-Howmedica
I-Hexcel
J-Medtec
K-3-M
L-OEC
M-Osteonics
N-Protec
O-Richards
P-U.S. Surgical
Q-Wright-Dow Corning
R-Zimmer USA
S-Zimmer GB
T-Custom

10.19 Implant material

A-Stainless steel wrought
B-Stainless steel forged
C-Stainless steel cast
D-Co-Cr-Mo (Prot-2) cast
E-Co-Cr-Mo (Prot-2) forged
F-Co-Cr-Mo (Prot-2) HIP
G-Micrograin
H-Co-Cr-Ni-W
I-Ti CP
J-Ti 6Al, 4V
K-Co-Ni-Cr-Mo (MP35N, Prot-10)
L-Co-Ni-Cr-Mo-W-Fe
M-Co-Ni-Cr-Mo/Co-Cr-Mo
N-Silastic
O-Al_2O_3
P-Polyester
Q-Acetal
R-C-UHMWPE
S-C-PTFE

11. NON-DESTRUCTIVE EVALUATION, METALLIC COMPONENTS

11.1 Was a macroscopic exam performed? Yes No
If yes, then scale for following is 0.0 - 4.0.
0-none, 1-mild, 2-moderate, 3-severe, 4-NA

A. Wear _____
B. Calling _____
C. Burnishing _____
D. Change in implant shape _____
E. Mechanical damage _____
F. Macro porosity _____

11.2 Was a corrosion examination performed? Yes No
If yes, scale is 0.0 - 5.0.

A. Gross corrosion _____
B. Crevice corrosion _____
C. Galvanic corrosion _____
D. Fretting corrosion _____

11.3 Was there mechanical failure? Yes No
If yes, failure modes:

A-fatigue
B-torsion
C-impact
D-stress-corrosion
E-overstress
F-corrosion-fatigue
G-other

Was there a fabrication flaw? Yes No

11A. Prosthesis articulating surface wear
A-slightly or none
B-shiny, smooth 2-body wear
C-dull, slightly rough 3-body wear
D-rough, abrasive 3-body
E-gross pitting, gouging 3-body
F-unknown

11B. Component damage
Abrasive wear or deformation due to bony contact or impingement.
Yes No
Abrasive wear or deformation due to PMMA cementophyte contact.
Yes No
Abrasive wear or deformation due to abnormal opposing component contact. Yes No

11C. Femoral stem burnishing (use chart A)
Burnishing, side of collar _____
Burnishing, under collar _____
Burnishing, proximal stem _____
Burnishing, distal stem _____
Burnishing, tip of stem _____

A-none
B-small superficial spots
C-large superficial or small deep
D-many superficial
E-large significant areas

11D. Bone plate corrosion _____ average, _____ total (use charts B, and C or D)

Size:	1-small	Nature:	1-plastic def
	2-medium		2-burnished
	3-large		3-rough
Depth:	1-minimal		4-parallel lines
	2-significant		5-cracks
	3-severe		6-corrosion
Corr = size + depth			7-needle pitting
			8-gross pitting
			9-rainbow

12. DESTRUCTIVE, METALLOGRAPHIC EXAMINATION

12.1 Metallographic sample orientation _____ (sketch location)

Relative to principal load	Relative to principal cold rolling
A-parallel	D-parallel
B-perpendicular	E-perpendicular
C-diagonal	F-diagonal

12.2 Void content (gas porosity) _____ (E-45 used for counting)
12.3 Inclusion content (E-45) _____/_____ A-meets spec., B-out of specs
12.4 Grain size (E-112) _____/_____ A-in specs, B-larger, C-smaller

---

12.5 Etch technique _____
12.6 Grain boundaries A-clean, B-precipitates, C-sensitized
12.7 Inclusion location A-intergranular, B-interdendritic, C-dispersed
12.8 Inclusion characteristics _____
12.9 Carbide distribution A-random, B-preferential orientation

HARDNESS TESTING

12.20 Macrohardness sample orientation _____ (code of 12.1)
12.21 Macrohardness _____/_____ Rockwell scale: A, B, or C

12.30 Microhardness sample orientation _____ (code of 12.1)
12.31 Microhardness _____/_____ A-Brinell, B-Vickers, C-Knoop, D-scratch

12.40 Mechanical testing performed Yes No
12.41 0.2% offset, yield stress _____ MPa
12.42 Ultimate tensile strength _____ MPa
12.43 Percent elongation _____%
12.44 Gauge length _____ cm
12.45 Reduction in area _____
12.46 Bend strength _____

13. PMMA EXAMINATION

13.1 PMMA sample A-acetabulum, B-prox fem, C-distal fem, D-prox tib, E-other

13.2 PMMA manufacturer A-Simplex, B-Zimmer

13.3 Amount of PMMA used

1-excessive
2-insufficient
3-normal
4-no cement
5-component not removed
6-unknown

13.4 Bony interdigitation of PMMA

1-good
2-moderate
3-poor
4-no cement
5-component not removed
6-unknown

13.5 PMMA distribution

1-good even coverage
2-small part of prosthesis uncovered
3-large part of prosthesis uncovered
4-no cement
5-component not removed
6-unknown

13A. PMMA macroscopic A-smooth, B-wrinkled, C-papillary (sketch)

13B. PMMA metallographic _____ % deformation (location _____)
Fracture(s) X-none, A-interparticle, B-intraparticle
_____ location
Porosity _____% _____ size range mm
Folds _____ location _____ comments _____
Bone/blood debris _____

13C. PMMA I.R. data _____
Other PMMA analysis _____

14. POLYMERIC ARTICULATING SURFACES

SUMMARY OF DAMAGE FROM USE (as derived from charts E or F)

14.1 Cement debris _____
14.2 Pitting _____
14.3 Scratches _____
14.4 Burnishing _____
14.5 Cracks _____
14.6 Wear _____
14.7 Creep _____
14.8 Discoloration _____
14.9 Iatrogenic from removal _____

1-none
2-slight
3-moderate
4-severe

14.10 Patellar eccentricity _____

14.11 Abrasive wear or deformity due to bony contact or impingement
Yes No
14.12 Abrasive wear or deformity due to PMMA cementophyte contact
Yes No
14.13 Abrasive wear or deformity due to abnormal opposing component contact Yes No

---

14A. Prosthesis articulating surface wear
A-slight or none
B-shiny, smooth 2-body wear
C-dull, slightly rough, 3-body
D-rough, abrasive 3-body
E-gross pitting, gouging 3-body
F-unknown

14B. Low M.W. 95°C xylene extraction _____ location, _____%

14C. Optical transmission _____ location, _____surface wear
Optical transmission depth of plastic deformation _____ mm
Optical transmission defects _____, type _____,
size _____ mm

14D. Thermal analysis type _____, location _____,
observation _____

14E. Spectroscopic analysis type _____, location _____,
observation _____

15. FINGER PROSTHESIS

15.1 Location A-MP, B-IP
15.2 Material, hinge A-silicone rubber, B-polyoefin, C-metal, D-other
15.3 Material, tang A-silicone, B-steel, C-Ti 6,4, D-other
15.4 Macroscopic A-fractured, B-wear/abrasion, C-discoloration
15.5 Location of 15.4 A-hinge, B-tang, C-other
15.6 Microscopic, hinge _____
15.7 Microscopic, tang(s) _____

16. FAILURE ANALYSIS

16.1 Mode of failure (confirm by SEM)
A-fatigue
B-torsion
C-impact
D-stress-corrosion
E-overstress
F-corrosion-fatigue
G-other

16.2 Fabrication flaw related
A-no
B-gas porosity
C-weld-filled defect
D-surface scratches
E-other surface defects

16.3 Related to implantation
A-no
B-surface scratches
C-surface deformation
D-screw-plate corrosion
E-stress concentration

16.4 Fluorescent penetrant studies A-no cracks, B-cracks

16.5 Radiography A-no defects, B-porosity, C-defects

RETRIEVED IMPLANT ANALYSIS - SUGGESTED SUMMARY WORKSHEET

Patient Data

Male /__/ Female /__/ Age _____ yrs.

Weight _____ lbs., _____ kg. Height _____ ft., _____ m.

Reason for implant _____

_____

_____

Reason for removal _____

_____

_____

Interval between insertion and removal _____ yrs. _____ mo.

Analysis of prosthesis completed /__/ not applicable /__/

Histopathology analysis completed /__/ not applicable /__/

Biomechanical analysis completed /__/ not applicable /__/

Summary diagnosis completed /__/

Final Conclusions

Cause of TJR failure

01-iatrogenic
02-sepsis - early
03-sepsis - late
04-trauma or fall
05-idiopathic loosening
06-autopsy
07-prosthesis fracture
08-pain only
09-other (specify) _____
10-unknown

CHART A: BURNISHING AND DAMAGE OF PROXIMAL FEMORAL PROSTHESES

Patient Name _____ # _____

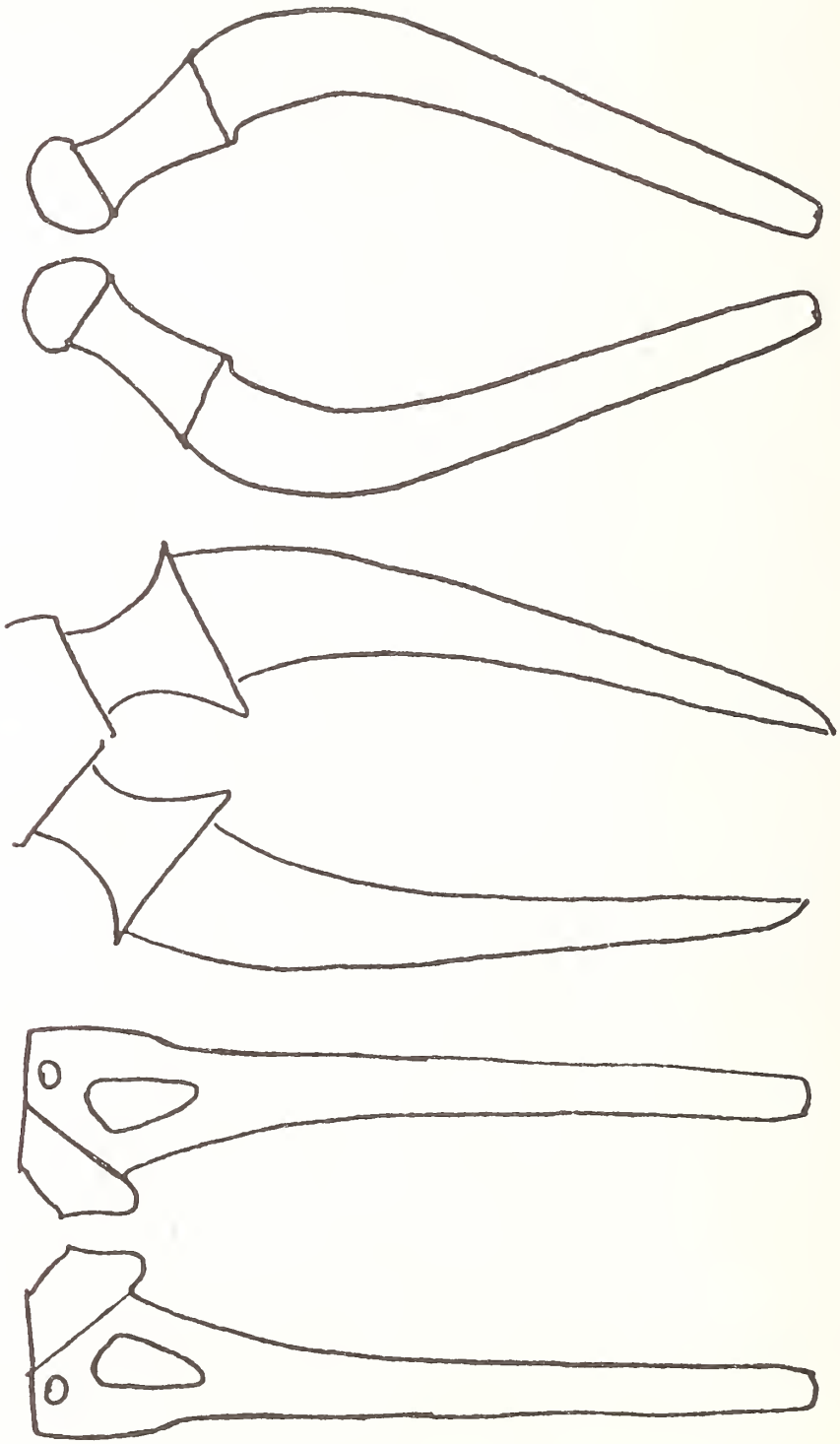


CHART B

PROTOTYPE

STANDARD REFERENCE CHART FOR DETERMINATION

OF DAMAGED AREA SIZE ON SCREW HEADS

FROM PLATE-SCREW CONTACT AND CORROSION

Size numbers and areas to be determined later

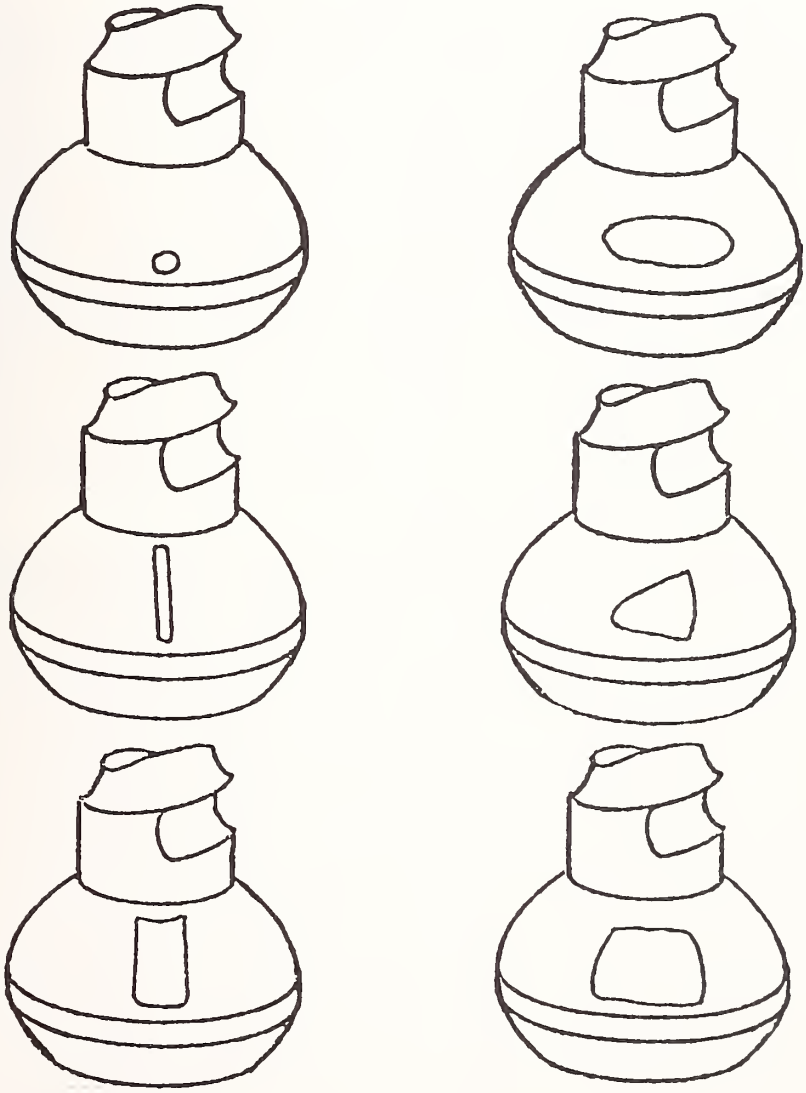
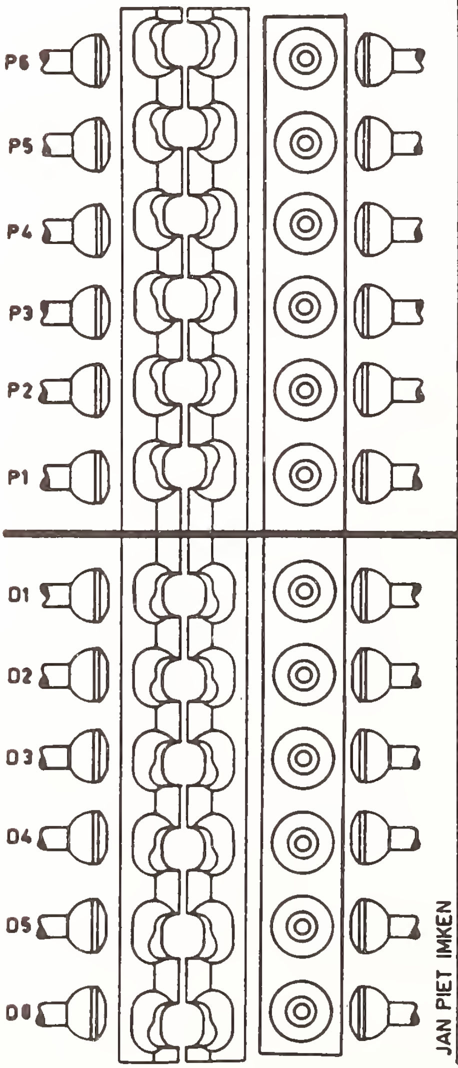


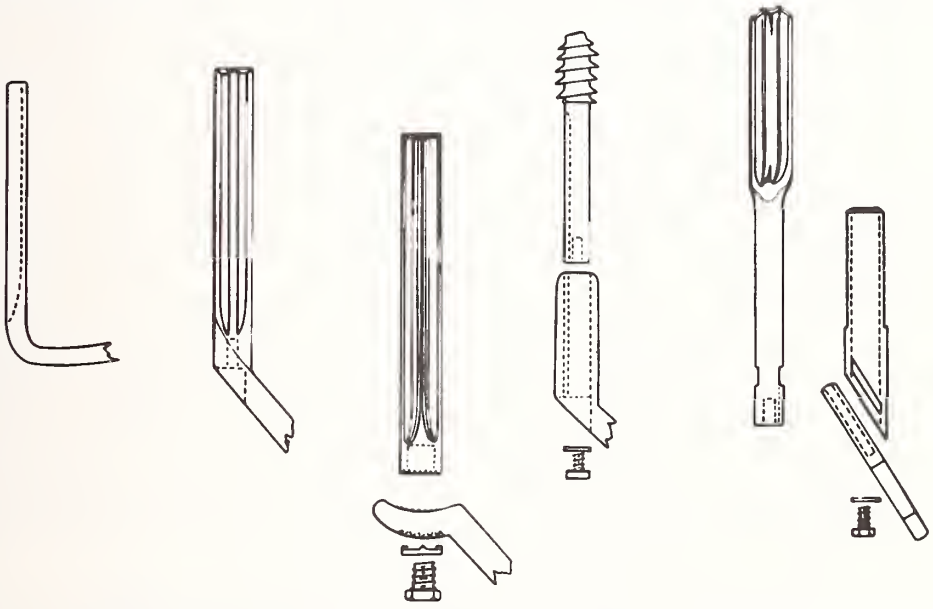
CHART C

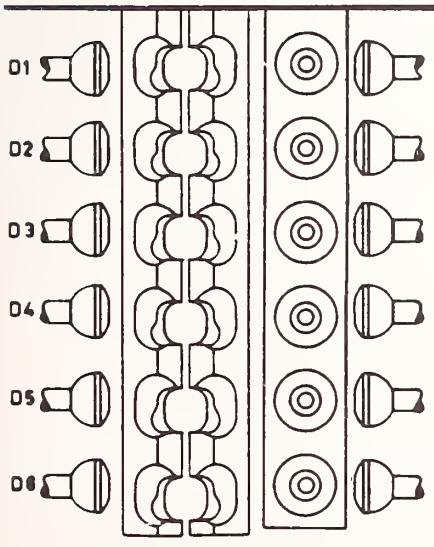
Hospital	Series
Name	Plate
Birth Date	Screws
Date Impl. rem.	Bone
Date Analysis	SEM?



Holes		Screw		Remarks
Area	Code	Area	Code	

Hospital	Series
Name	Plate
Birth Date	Screws
Date Impl. rem.	Bone
Date Analysis	SEM?





JAN PIET IMKEN

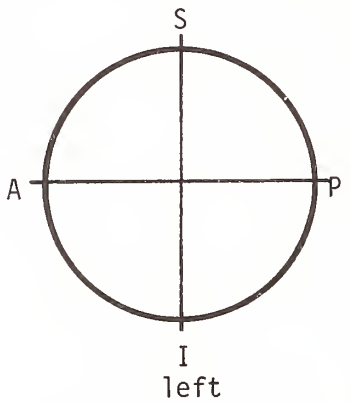
CHART E

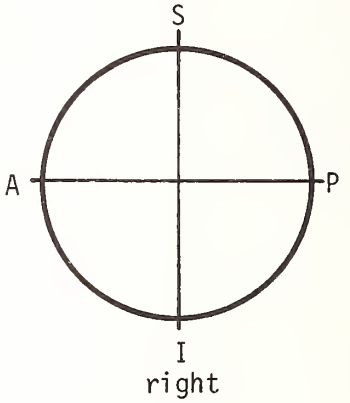
ACETABULAR COMPONENT MACROSCOPIC EXAMINATION

Right Left
Mfg _____, style _____

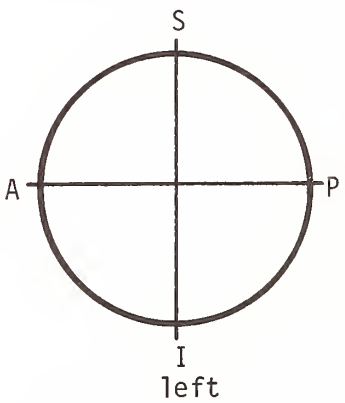
Patient name _____
Patient number _____

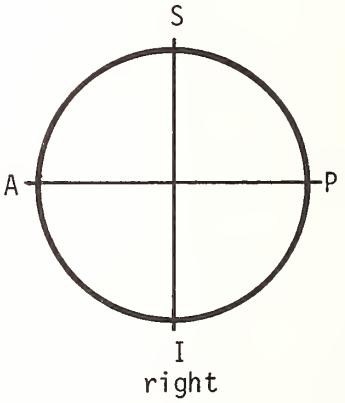
Iatrogenic damage at removal (mark locations on diagrams)





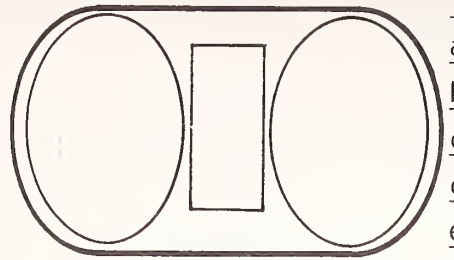
Surface markings

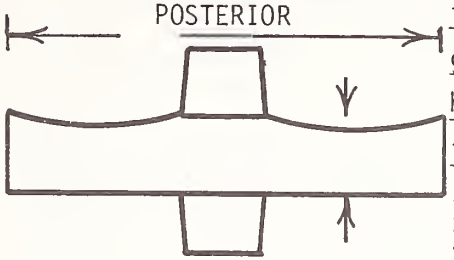




	S	I	A	P
a cement debris				
b pitting				
c scratches				
d burnishing				
e cracks				
f wear				
g creep				
h discoloration				
i iatrogenic				

A-none
B-slight
C-moderate
D-severe





	medial		central		lateral		patella			
	A	P	A	P	A	P	S	I	M	L
a cement debris										
b pitting										
c scratches										
d burnishing										
e cracks										
f wear										
g creep										
h discoloration										
i iatrogenic										

Intensity: 1-none, 2-slight, 3-moderate, 4-severe, X-area not available

CHART F

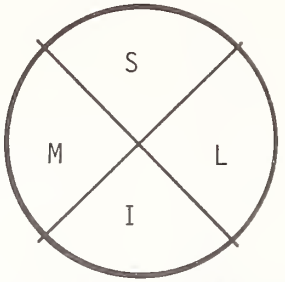
Patient _____

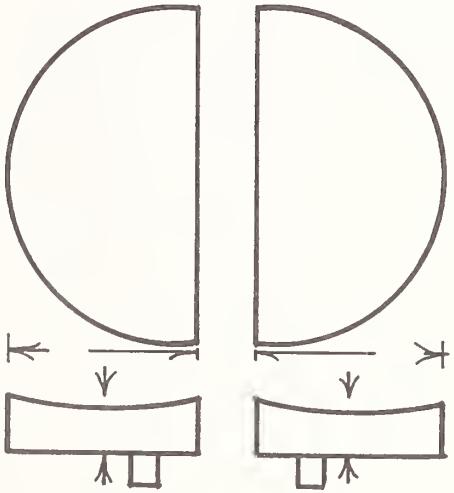
_____

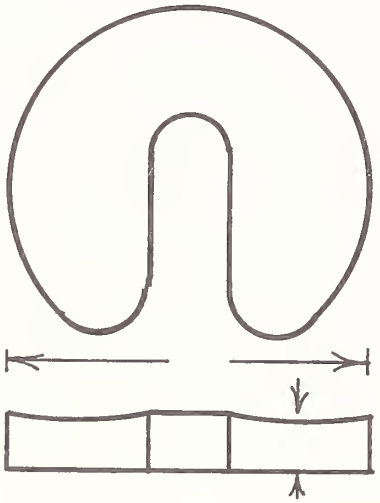
Eccentricity measurement

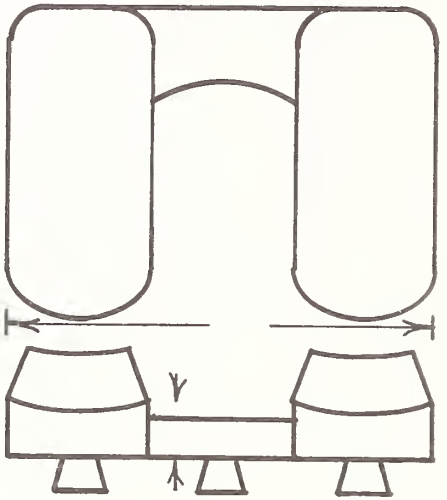
_____

PATELLA









Appendix B

IDENTIFICATION AND EVALUATION OF EXPLANTED HEART VALVE PROSTHESES

A Monograph

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California Institute of Technology

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Los Angeles
May 1979

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TABLE OF CONTENTS

IDENTIFICATION AND EVALUATION

OF EXPLANTED HEART VALVE PROSTHESES

INTRODUCTION

THIS MONOGRAPH CONSISTS OF TWO MAJOR PARTS:

Part 1: Information Materials, Tables, Charts, etc. for the identification of heart valve prostheses

Part 2: Evaluation Form (a write-in protocol) for explanted heart valve prostheses

BEFORE USING THIS MONOGRAPH, WE ASK THAT YOU PLEASE READ THE FOLLOWING:

1. Scan the monograph and identify the two portions indicated above.

2. Review both the identification flow diagrams and charts and the other informational materials in order to familiarize yourself with their content and use. This will facilitate reference to these portions at a later time.

3. The evaluation form itself (write-in protocol) is divided into six parts: I. Patient Information; II. Prosthesis Information; III. Specimen and Handling; IV. Prosthesis Examination; V. Gross Pathology; and VI. Summary Sheet. Throughout the form, informational paragraphs have been indicated by a black dot. Please read and understand these portions thoroughly.

4. While filling out the evaluation form (boxed sheets) either write in the appropriate response in the squares provided, or place a check mark or number, as appropriate. Please fill in all requested information as completely as possible.

5. The headings for aortic (A), mitral (M), and tricuspid (T) valves are provided in the event that the patient has more than one prosthesis. In these instances, please check the appropriate boxes as applicable to each valve. In all other cases, where the patient has only one prosthesis, place checkmarks in the boxes applicable to that valve only. (Example: If the patient being autopsied has a prosthetic aortic valve, all your checkmarks will be in the "A" column.)

6. Where you have been asked to draw or sketch findings in the evaluation form portion of the monograph, please approximate your drawing(s) as closely as possible to the objective data. Wherever necessary, use the transparent template attached to the back cover of this monograph to approximate size of occlusion, tissue overgrowth, etc.

7. Should you wish, please do not hesitate to write notes or remarks in the blank areas provided, or in margins.

EVALUATION FORM COMPLETED BY: (Please print)

Name: _____ M.D.

Title: _____

Address: _____

Phone Number: (Area code _____) _____

PART I

GLOSSARY OF HEART VALVE-RELATED TERMS

BASE RING.....The circular structure in the plane of the valve annulus which supports the cage in the case of mechanical prostheses, and which supports the stent in the case of bioprostheses.

BIOPROSTHESES..... Non mechanical prosthetic tissue heart valves which include homografts (human cadaver), heterografts (animal cadaver), and fascia lata valves (transplants from thigh tissue).

CAGE.....The portion of a mechanical prosthesis which, in conjunction with the base ring, restrains and limits the movement of the ball or disc. The cage is composed of struts which are joined to the base ring.

Single cage.....struts emerge on only one side of the base ring plane

Double cage.....struts emerge on both sides of the base ring plane

Open cage.....converging struts do not connect at the apex

Closed cage.....struts join at apex in a cruciform manner

CAGED-BALL VALVE....Hemodynamically, a central occluder type prosthesis in which a ball-shaped occluder (poppet), moves within the cage.

CAGED-DISC VALVE....Hemodynamically a central occluder (peripheral flow) type prosthesis in which a disc-shaped occluder (or poppet), moves within the cage.

CUSPS.....Leaflets of a bioprosthesis (or tissue valve) mounted on a stent.

DACRON.....Trade name by DuPont for a polyester fiber, e.g., Polyethyleneterephatalate, used as a sewing ring cloth.

DELRIN.....Trade name by DuPont for polyformaldehyde, a thermoplastic material based on acetal resin. This is used in the construction of prostheses occluders.

HETEROGRAFT.....A non-mechanical tissue valve made of animal cadaver and fascia lata valves (transplants from thigh tissue).

HOMOGRAFT..... A non-mechanical tissue valve made of human cadaver.

POLYPROPYLENE.....A thermoplastic material made from the polymerization of propylene. It is used as sewing ring material.

PRIMARY FLOW ORIFICE.....Space available for blood flow through open valve at the narrowest point of valve inlet.

PYROLITE CARBON.....A thick, structural carbon coating with unique combination of properties. It is biocompatible in the broadest sense; generally deposited on a graphite substrate such as a valve leaflet or occluder.

RIGID PROSTHESES....A classification of prosthetic heart valves which includes caged-ball, caged-disc and tilting-disc prostheses.

SECONDARY FLOW ORIFICE.....Minimum built-in area available for blood flow rather than those at the primary valve orifice.

SEWING RING..... A cuff-like cloth casing around the base ring that the surgeon uses to attach to the valve annulus.

SILASTIC..... Silicone rubber used as an occluder in caged-ball prostheses.

STELLITE..... A metal alloy that includes molybdenum, chromium and tungsten. This is used in the construction of struts and base ring of a valve.

STENT..... The structure which is attached at a right angle to the base ring of a bioprosthesis; the stent supports the valve leaflets.

STRUT..... The structure which projects vertically from the base ring to form a cage. They are made of bare metal, coated with cloth, plastic or pyrolytic carbon, or else are composite in nature.

TEFLON..... Trade name by DuPont for polytetralfluoroethylene fiber or cloth.

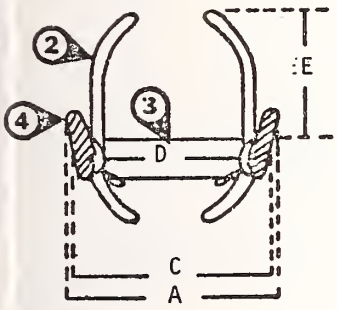
TILTING-DISC VALVE . Hemodynamically, a central flow type prosthesis in which the occluder (poppet) is a free-floating pivoting disc.

OCCLUDER OR POPPETT.....Moving ball or disc within the cage of a valve prosthesis which permits or stops the blood flow by opening or closing the valve orifice. In caged-ball and caged-disc valves, the poppet sits at the base in the closed position, and rests in the cage away from the valve orifice in the open position, thus allowing the blood to flow peripherally around the poppet. In tilting-disc valves, the disc tilts to a variable angle in the open position permitting blood to flow; in the closed position, the disc fits into the circumference of the inflow ring.

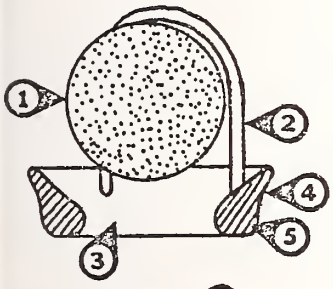
TITANIUM ..... A metal used in the construction of valve, struts, cages and stents.

GENERIC SCHEMA OF

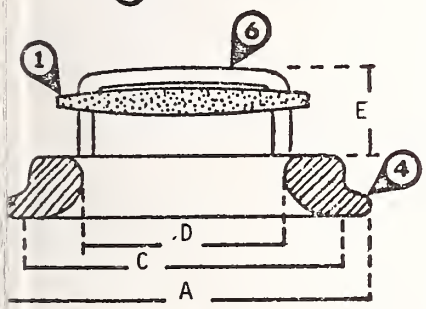
SOME MAJOR TYPES OF HEART VALVE PROSTHESES



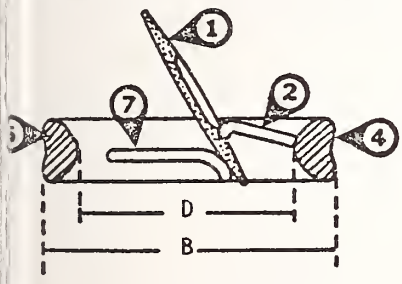
DOUBLE CAGED BALL



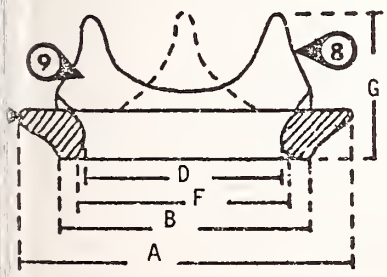
SINGLE CAGED BALL



CAGED DISC



TILTING DISC



BIOPROSTHESIS (TISSUE VALVE)

VALVE PARTS

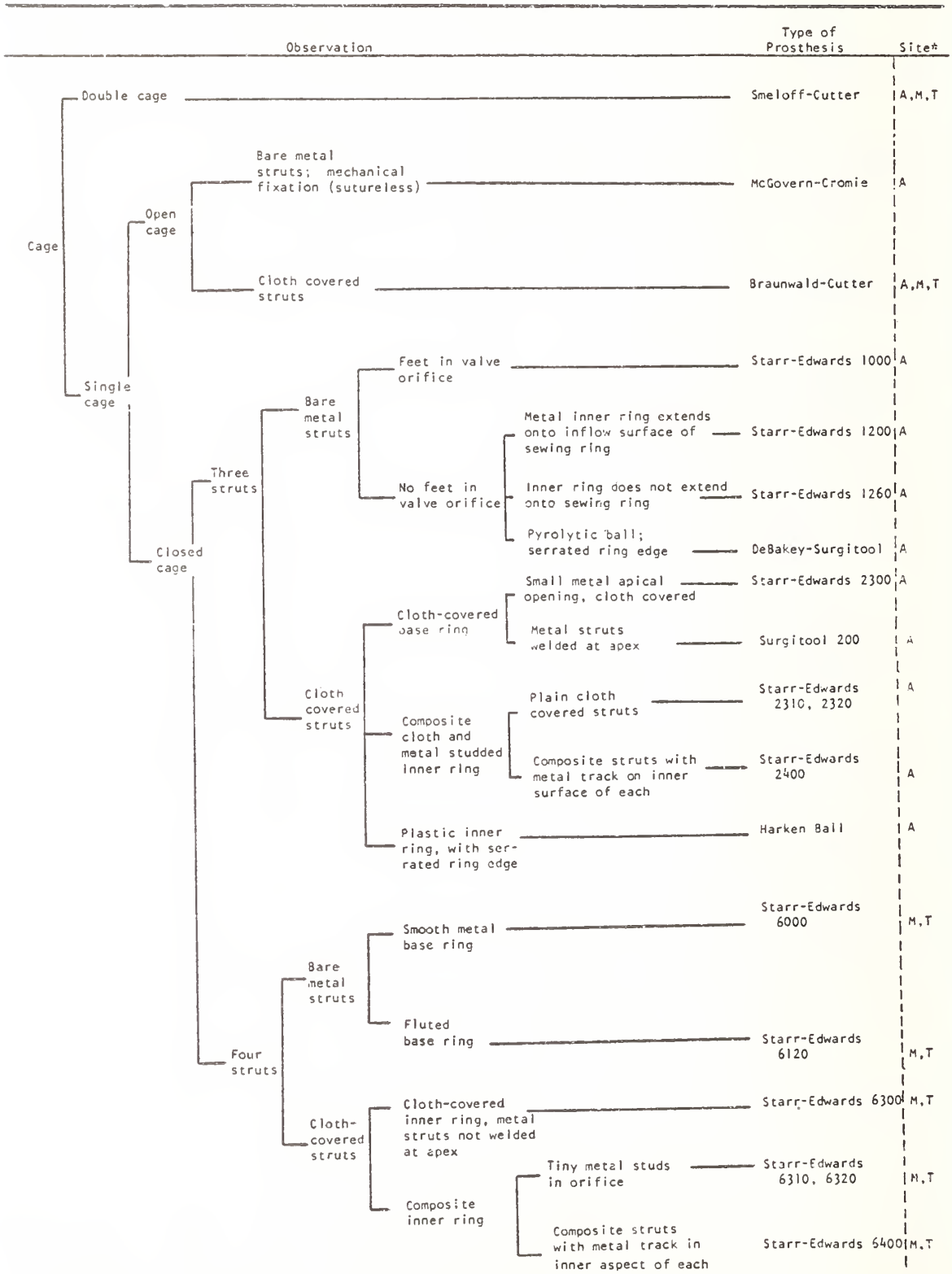
1. OCCLUDER
2. STRUT
3. VALVE ORIFICE
4. SEWING RING (cloth)
5. BASE RING (inside sewing ring)
6. HORIZONTAL BARS OR STRUTS
7. DISC STOPPER
8. STENT
9. TISSUE CUSP (or valve leaflet)

DIMENSIONS

A. OUTER DIAMETER
B. ANNULUS DIAMETER
C. MOUNTING DIAMETER
D. ORIFICE DIAMETER
E. STRUT PROJECTION
F. STENT INSIDE DIAMETER
G. HEIGHT

TABLE I

CAGED-BALL (High Profile) VALVES



* A = aortic; M = mitral; T = tricuspid

TABLE II

CAGED-DISC (Low Profile) VALVES

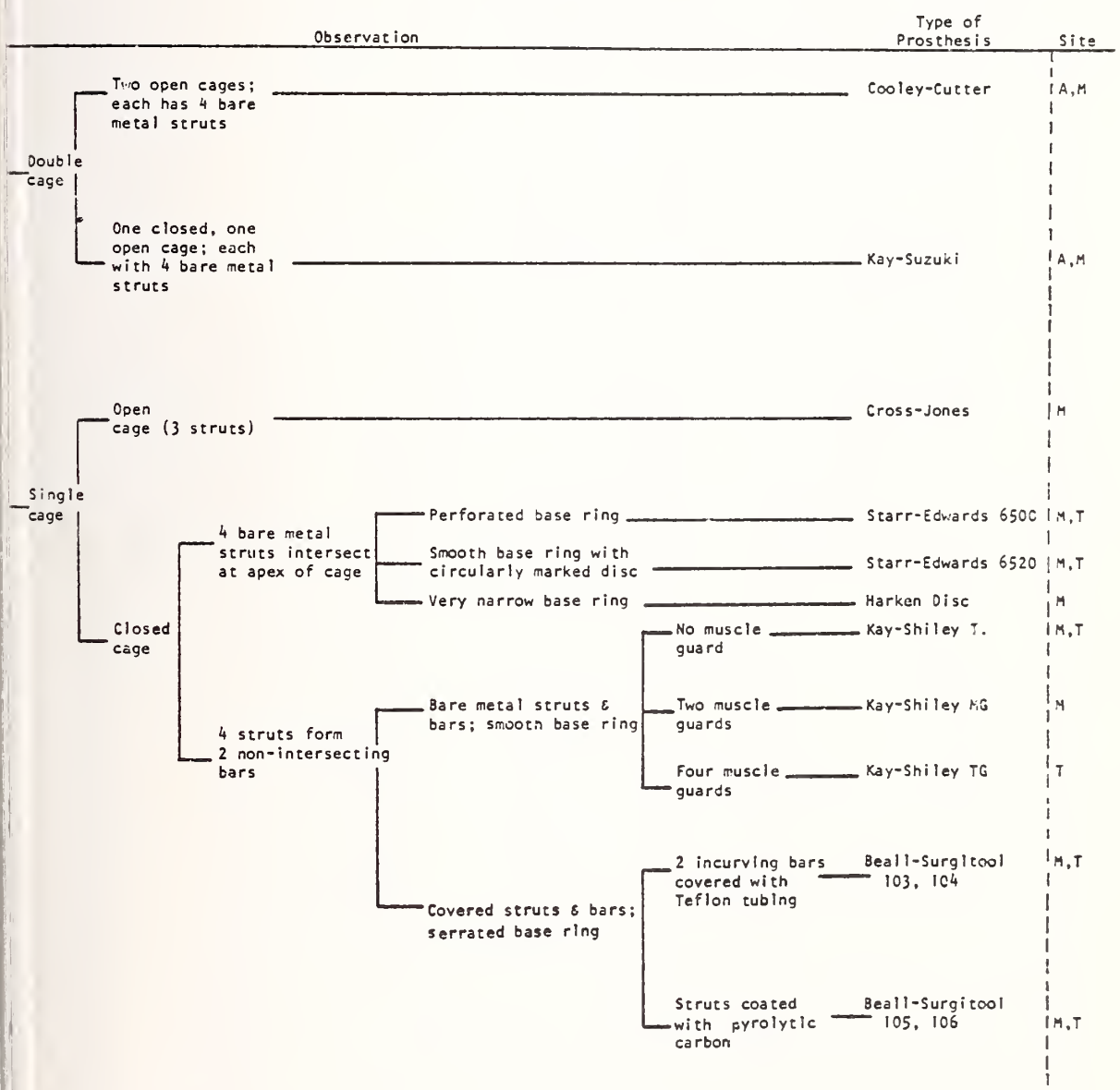


TABLE III

LOW PROFILE VALVES

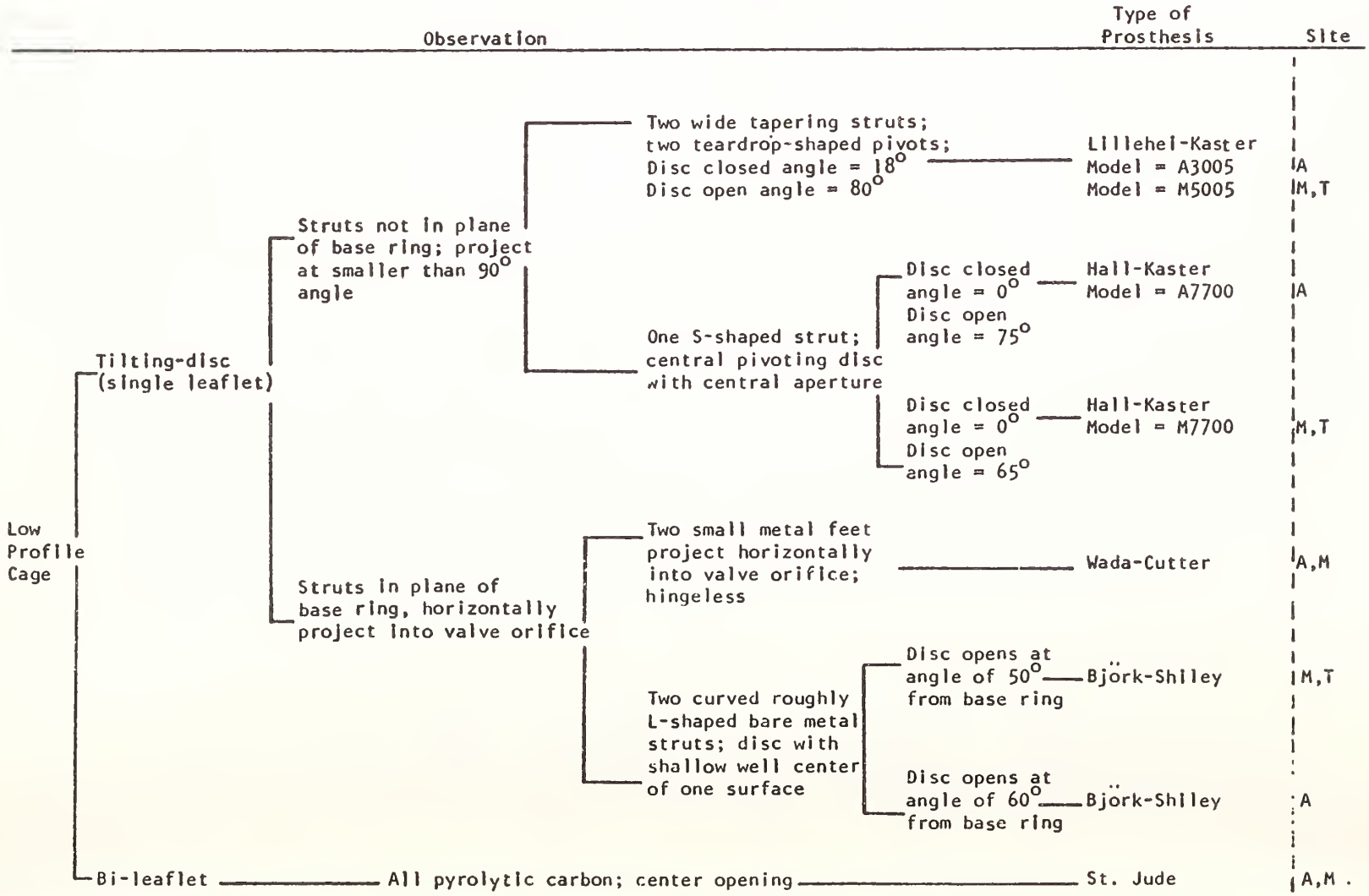
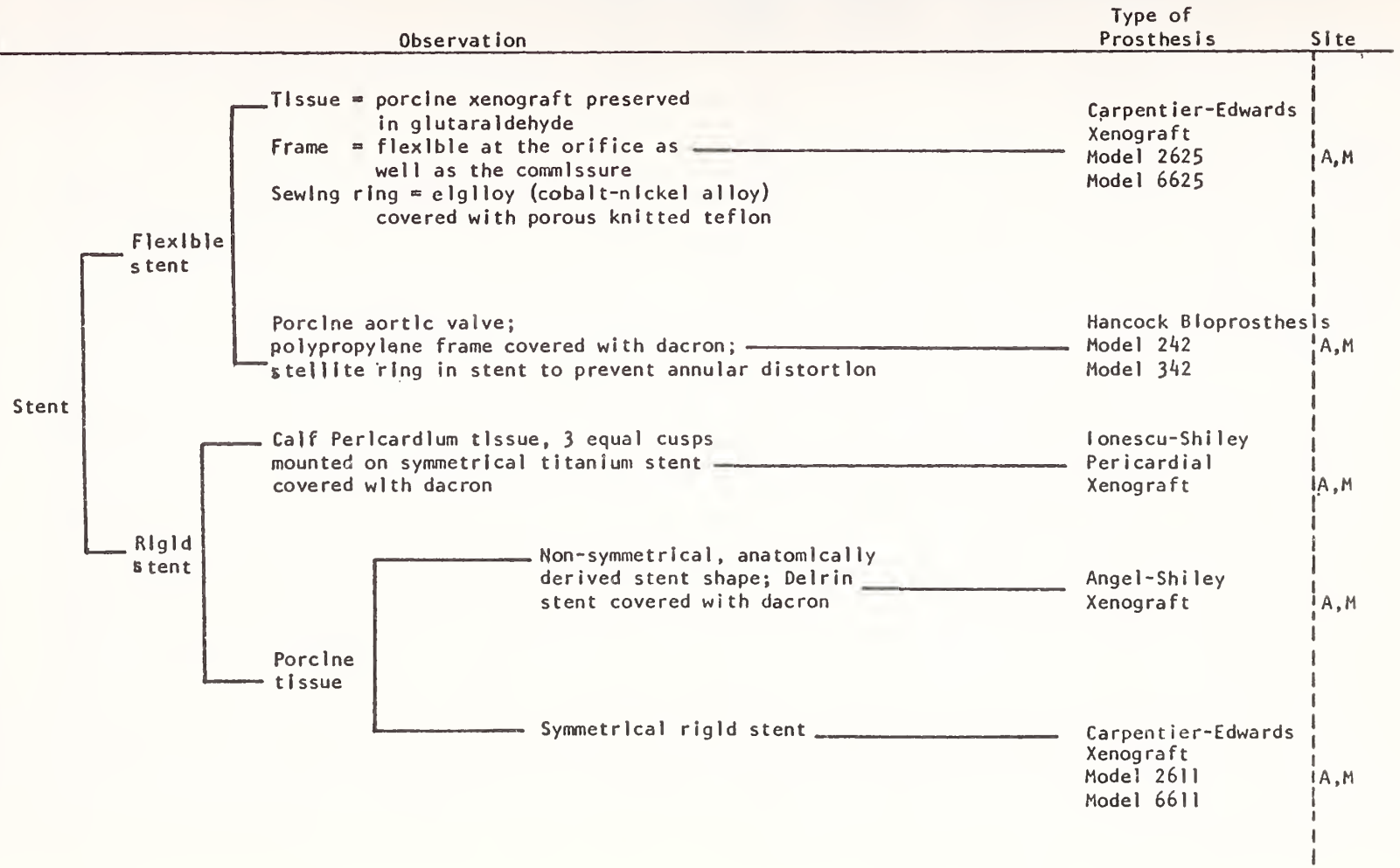


TABLE IV

BIOPROSTHESES (Tissue Valves)



Manufacturer	Prosthesis Name	Model No.	Dates Manufacture	Type/ Configuration	Site	No. Implanted	Occluder/ Poppet	Cages/Struts Design	Sewing Ring	SIZE DATA		
										Annulus DIA. (mm)	Orifice DIA. (mm)	Orifice AREA (mm^2)
Cutter Laboratories	Braunwald-Cutter		1968-1974	Caged-ball (open cage)	Aortic	Not Available	Silicone rubber ball	Dacron cloth over titanium	Polypropylene cloth	22-29	14.2-19.9	158-310
	Braunwald-Cutter		1968-present	Caged-ball (open cage)	Mitral; tricuspid	"	Silicone rubber ball	Dacron cloth over titanium	Polypropylene cloth	28-34	16.8-21.2	222-353
	Cooley-Cutter		1973-present	Caged-disc (open double cage)	Aortic	"	Pyrolite carbon disc	Bare titanium	Initially teflon, later double velour dacron cloth	20-28	13.1-22.0	135-380
	Cooley-Cutter		1971-present	Caged-disc (open double cage)	Mitral	"	Pyrolite carbon disc	Bare titanium	Initially teflon, later double velour dacron cloth	21-30	13.1-22.0	135-380
	Smeloff-Cutter		1966-present	Caged-ball (open double cage)	Aortic; mitral; tricuspid	"	Silicone rubber ball	Bare titanium	Teflon cloth	19.0-39.2 (aortic) 20.7-38.0 (mitral)	12.3-24.1 (aortic) 14-24.1 (mitral)	199-456 (aortic) 154-456 (mitral)
	Wada-Cutter		1967-1972	Tilting disc (hingeless)	Aortic; mitral	"	Polytetra-fluoro-ethylene disc	No cage; bare titanium fulcrum	Knit teflon cloth	23-29 (aortic) 24-34 (mitral)	14-20 (aortic) 14-24 (mitral)	150-307 (aortic) 150-445 (mitral)
Edwards Laboratories	Starr-Edwards	1000	1964-1966	Caged-ball	Aortic	10,000[a]	Silicone rubber ball	Bare stellite 21 metal struts	Knit teflon cloth	NOT AVAILABLE SINCE 1966		

Manufacturer	Prosthesis Name	Model No.	Dates Manufature	Type/ Configuration	Site	No. Implanted	Occluder/ Poppet	Cages/Struts Designs	Sewing Ring	SIZE DATA		
										Annulus DIA. (mm)	Orifice DIA. (mm)	Orifice AREA (mm^2)
Edwards Laboratories	Starr-Edwards	1200	1966-present	Caged-ball	Aortic	7,500[a]	Silicone rubber ball with 2% barium sulfate	Bare stellite-21 metal struts	Knit teflon and polypropylene cloth	16 & 18	11 & 12	90 & 119
	Starr-Edwards	1260	1968-present	Caged-ball	Aortic	27,500[a]	Silicone rubber ball with 2% barium sulfate	Bare stellite-21 metal struts	Knit teflon and polypropylene cloth	21 - 31	13 - 19	141-289
	Starr-Edwards	2300	1967-1968	Caged-ball (open cage)	Aortic	7,500[a]	Hollow stellite 21 ball	Dacron cloth-covered stellite-21 struts	Dacron cloth	19 - 31	12 - 19	120 - 293
										NOT AVAILABLE SINCE 1968		
	Starr-Edwards	2310	1968-1970	Caged-ball	Aortic	7,500[a]	Hollow stellite 21 ball	Teflon and polypropylene cloth-covered stellite 21 struts	Teflon and polypropylene knit	19 - 31	12 - 19	120-293
										NOT AVAILABLE SINCE 1970		
	Starr-Edwards	2320	1970-1976	Caged-ball	Aortic	14,000[a]	Hollow stellite 21 ball	Teflon and polypropylene cloth layers over stellite 21	Seamless teflon and polypropylene cloth	19 - 31	12 - 19	121-292
										NOT AVAILABLE SINCE 1976		
	Starr-Edwards	2400	1972-present	Caged-ball	Aortic	2,500[a]	Hollow stellite 21 ball	Stellite 21 struts covered with one layer polypropylene; bare metal track on inside of each strut	Porous teflon and polypropylene cloth	22 - 31	15 - 19	170-292
	Starr-Edwards	6000	1964-1965, (pre 6000 1960-1964)	Caged-ball	Mitral; tricuspid	12,000[a]	Silicone rubber ball	Bare stellite 21 metal struts	Teflon cloth	NOT AVAILABLE SINCE 1965		
	Starr-Edwards	6120	1966-present	Caged-ball	Mitral tricuspid	27,500[a]	Barium sulfate impregnated silicone rubber ball	Bare stellite 21 metal struts	Teflon and polypropylene cloth	20 - 34	13 - 22	127-366

(cont.)

[a] Number implanted through July 1, 1977

Manufacturer	Prosthesis Name	Model No.	Dates Manufacture	Type/ Configuration	Site	No. Implanted	Occluder/ Poppet	Cages/Struts Design	Sewing Ring	SIZE DATA		
										Annulus DIA. (mm)	Orifice DIA. (mm)	Orifice AREA(mm^2)
Edwards Laboratories	Starr-Edwards	6300	1967-1968	Caged-ball	Mitral; tricuspid	4,500[a]	Hollow stellite 21 ball	Dacron cloth-covered stellite 21 struts	Knit dacron	NOT AVAILABLE AFTER 1968		
	Starr-Edwards	6310	1968-1970	Caged-ball	Mitral; tricuspid	4,500[a]	Hollow stellite 21 ball	Teflon covered stellite 21	Knit teflon and polypropylene	23 - 32	15 - 21	170 - 330
										NOT AVAILABLE SINCE 1970		
	Starr-Edwards	6320	1970-1976	Caged-ball	Mitral; tricuspid	14,000[a]	Hollow stellite 21 ball	Cloth-covered stellite 21 struts polypropylene over teflon	Knit teflon and polypropylene	23 - 32	15 - 21	170 - 330
										NOT AVAILABLE SINCE 1976		
	Starr-Edwards	6400	1972-present	Caged-ball	Mitral; tricuspid	2,500[a]	Hollow stellite 21 ball	Polypropylene cloth over stellite 21 struts; metal track on inside of each strut	Knit teflon and polypropylene	28 - 32	18 - 21	250 - 330
	Starr-Edwards	6500	1968-1970	Caged-disc	Mitral; tricuspid	2,500[a]	Hollow stellite 21 disc	Bare stellite 21 struts	Knit teflon	NOT AVAILABLE SINCE 1970		
(cont.)	Starr-Edwards	6520	1970-present	Caged-disc	Mitral; tricuspid	3,600[a]	Ultra high molecular weight polyethylene disc	Bare stellite 21 struts; no exposed metal on inflow surface	Knit teflon & polypropylene	26 - 32	16 - 20	211 - 324
	Carpentier Edwards xenograft	2625	1975-present	Bioprosthesis	Aortic	10,000 (as of January 1979)	No poppet, porcine tissue	No cage; cobalt and nickel alloy (elgiloy) frame covered with teflon, flexible stent	Porous teflon cloth	19 - 31	17 - 28 (stent I.D.)	
	Carpentier Edwards xenograft	6625	1975-present	Bioprosthesis	Mitral	10,000 (as of January 1979)	No poppet, porcine tissue	The same as model 2625	Porous teflon	25 - 35	23 - 33 (stent I.D.)	

[a] Number implanted through July 1, 1977

Manufacturer	Prosthesis Name	Model No.	Dates Manufacture	Type/ Configuration	Site	No. Implanted	Occluder/ Poppet	Cages/Struts Design	Sewing Ring	SIZE DATA		
										Annulus DIA. (mm)	Orifice DIA. (mm)	Orifice AREA (mm^2)
Hancock Laboratories	Hancock bioprosthesis	242	1971-present	Bioprosthesis	Aortic	17,500	No poppet, porcine tissue	Polypropylene flexible stent	Dacron cloth	19 - 31	16.5-27.4 (Stent I.D)	
	Hancock bioprosthesis	342	1971-present	Bioprosthesis	Mitral; tricuspid	17,500	No poppet; porcine tissue	Polypropylene flexible stent	Dacron cloth	19 - 35	16.5-31.06 (Stent I.D.)	
Medical Incorporated	Lillehei Kaster	Series 300S	1970-present	Tilting disc	Aortic	Not available	Pyrolite carbon disc	No cage; annular bare titanium pivot housing	Dacron cloth	17.5 - 32	12 - 25	110 - 491
	Lillehei Kaster	Series 500S	1970-present	Tilting disc	Mitral	Not available	The same as series 300S		Aortic valve	17.5 - 35	12 - 25	110 - 491
Pemco Incorporated	Cross-Jones		Introduced in 1965, presently not manufactured	Caged-disc	Mitral	2,300	Silicone rubber disc with titanium reinforcing ring	Bare titanium struts, open at apex		NOT IN ACTIVE USE AT PRESENT TIME		
Shiley Laboratories	Angel-Shiley xenograft		1970-present	Bioprosthesis	Aortic; mitral; tricuspid	Not available	No poppet; porcine tissue	No cage; Delrin stent covered with dacron	Dacron cloth	23 - 34	19.5-28.3 (Stent I.D.)	296 - 630
	Björk-Shiley		1969-present	Tilting-disc	Aortic; mitral; tricuspid	125,000	Pyrolytic carbon or delrin disc	No cage; bare stellite pivot structure	Teflon cloth	17 - 31	12 - 24	111 - 460
	Ionescu-Shiley pericardial xenograft		1971-present	Bioprosthesis	Aortic; mitral; tricuspid	Not available	No poppet; calf pericardium tissue	No cage; titanium stent covered with dacron cloth	Dacron cloth	17 - 33	13.4-29.4	141 - 679
	Kay-Shiley	MG;T; & TG Series	1967-present 1969-present	Caged-disc	Mitral; tricuspid	Not available	Delrin disc	Bare stellite 21; MG and TG series have muscle guards	Teflon cloth	23 - 35	14 - 24	150 - 430

Manufacturer	Prosthesis Name	Model No.	Dates Manufactured	Type/ Configuration	Site	No. Implanted	Occluder/ Poppet	Cages/Struts Design	Sewing Ring	SIZE DATA		
										Annulus DIA. (mm)	Orifice DIA. (mm)	Orifice AREA (mm^2)
St. Jude Medical, Inc.	St. Jude		1976 - (In (in clinical trial phase)	Low profile bi-leaflet	Aortic, mitral	100[b]	All pyrolytic carbon leaflets	No cage, no struts all pyrolytic carbon base ring and orifice	Double velour dacron tubing	19 - 27 (aortic) 25 - 31 (mitral	14.7 - 22.3 (aortic) 20.4 - 26.0 (mitral	161 - 367 (aortic) 309 - 518 (mitral)
Surgitool Medical Engineering	Beall Surgitool	103 104	1967- present 1969- present	Caged-disc	Mitral	15,000 3,000	Teflon disc	Titanium covered with teflon tubing	Dacron velour	26.7-34.2	16.5-22.8	214 - 410
	Beall Surgitool	105 106	1972- present 1974- present	Caged-disc	Mitral	2,500 3,500	Pyrolite carbon disc	Pyrolite carbon coated	Dacron velour	28 - 35.5	16.5-24.1	214 - 457
	DeBakey-Surgitool	1, 2 & 3	1969- present	Caged-ball	Aortic	3,500	Hollow pyrolite carbon ball	Bare titanium	Dacron cloth	20.3-27.9	12.7-20.3	126 - 324
	Harken Ball		1969- present	Caged-ball	Aortic	700	Hollow titanium ball	Dacron cloth over titanium	Dacron cloth	20.5-29.1		150.5-320
	Harken Disc		1967- present	Caged-disc	Mitral	2,300	Silicone rubber disc	Bare titanium	Dacron cloth	27.9 - 33		237 - 296
	Magovern-Cromie		1963- present	Caged-ball (suturless)	Aortic	7,300	Silicone rubber ball	Bare titanium	Suturless; mechanical fixation	26.4-39.1	13.3-20.9	139 - 345
	Surgitool	200	1969- present	Caged-ball	Aortic	1,000	Hollow titanium ball	Teflon cloth over titanium	Dacron cloth	20.5-29.1		150.5-320.2
Valve Research	Kay-Suzuki		1964- ?	Caged-disc	Mitral	1,100	Silicone rubber disc	Bare metal				
Kastec Corporation	Hall-Kaster	A-7700 M-7700		Tilting / pivoting disc	Aortic; mitral	Not available	Pyrolite carbon disc	Pivoting in titanium housing	Knitted teflon cloth	21 - 29 (aortic) 23 - 31 (mitral)	16 - 24 (aortic) 18 - 24 (mitral)	201 - 452 (aortic) 254 - 452 (mitral)

[b] Number implanted experimentally between Oct. 77 and June 1978

PART II

EVALUATION FORM

I. PATIENT INFORMATION

NAME ☐☐☐☐☐☐☐☐☐☐☐☐ last ☐☐☐☐☐☐☐ first ☐ M.I.

ADDRESS ☐☐☐☐☐☐ number ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ street

☐☐☐☐☐☐☐☐☐☐☐☐☐☐ city ☐☐ state ☐☐☐☐☐ zip

HOSPITAL ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ name

☐☐☐☐☐☐ number ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ street

☐☐☐☐☐☐☐☐☐☐☐☐☐☐ city ☐☐ state ☐☐☐☐☐ zip

BIRTH DATE ☐☐ month ☐☐ day ☐☐ year AGE ☐☐ SEX ☐ M ☐ F

RACE ☐ CAUCASIAN ☐ ORIENTAL ☐ BLACK ☐ OTHER ☐ HISPANIC _____

HEIGHT ☐☐☐ cm. LENGTH ☐☐☐ cm. WEIGHT ☐☐☐ ☐ kg.

MARITAL STATUS ☐ SINGLE ☐ DIVORCED ☐ MARRIED ☐ WIDOW(ER) ☐ SEPARATED ☐ OTHER

PREVIOUS KNOWN CLINICAL EVENTS (Is patient known to have had...)

	ACUTE*	CHRONIC**	Rx***
CONGESTIVE HEART FAILURE	☐	☐	☐
MYOCARDIAL INFARCTION	☐	☐	☐
CEREBROVASCULAR ACCIDENT	☐	☐	☐
ENDOCARDITIS	☐	☐	☐
ATRIAL FIBRILLATION	☐	☐	☐
PULMONARY EMBOLUS	☐	☐	☐
PERIPHERAL EMBOLUS	☐	☐	☐
HEMOLYTIC ANEMIA	☐	☐	☐
CHOLELITHIASIS	☐	☐	☐
ANTICOAGULATION THERAPY	☐	☐	☐
OTHER (specify) _____	☐	☐	☐

* 1 month or shorter
** longer than one month
*** check if treated

	M	A	T
ORIGINAL VALVE FUNCTIONAL DESCRIPTION			
STENOSIS	☐	☐	☐
REGURGITATION	☐	☐	☐
NORMAL	☐	☐	☐

INDICATION FOR ORIGINAL VALVE REPLACEMENT	M	A	T
RHEUMATIC-TYPE DEFORMITY	☐	☐	☐
CALCIFIC AORTIC STENOSIS,3 CUPS	☐	☐	☐
CALCIFIC AORTIC STENOSIS, 2 CUPS	☐	☐	☐
AORTIC STENOSIS, OTHER	☐	☐	☐
ENDOCARDITIS			
ACTIVE	☐	☐	☐
HEALED	☐	☐	☐
CONGENITAL LESION	☐	☐	☐
OTHER, EXPLAIN			

_____

_____

_____

NYHA CLASSIFICATION (Just prior to surgical explantation or death)

☐ I ☐ II ☐ III ☐ IV

CARDIOPULMONARY RESUSCIATION PERFORMED? ☐ YES ☐ NO ☐ UNKNOWN

- THE RECIPIENT OF A CARDIAC VALVE PROSTHESIS MAY HAVE IN HIS POSESSION A CARDIAC VALVE IDENTIFICATION CARD WHICH LISTS:

  VALVE TYPE
  VALVE SIZE
  VALVE SERIAL NUMBER
  VALVE MANUFACTURER
  IMPLANT SITE
  IMPLANT DATE
  IMPLANTING SURGEON

- THE ABOVE INFORMATION MAY ALSO BE PRESENT IN THE PATIENT'S HOSPITAL PROGRESS CHART OR IN THE OPERATIVE NOTES

- IN THE EVENT THAT THE IDENTIFICATION CARD (OR THIS INFORMATION) CANNOT BE LOCATED, THE IDENTIFICATION KEY AND CHARTS PROVIDED IN THE FRONT PORTION OF THIS FORM SHOULD BE USED TO DETERMINE THE VALVE MANUFACTURER, MODEL, NAME, MODEL NUMBER, AND TYPE/CONFIGURATION

- IN MANY VALVES, THE SERIAL NUMBER IS FOUND UNDERNEATH THE FABRIC OF THE OUTER ASPECT OF THE BASE RING. - TO OBTAIN SERIAL NUMBER IN THIS MANNER SHOULD BE CONSIDERED A LAST RESORT. - BE SURE TO DOCUMENT ALL PERTINENT INFORMATION PRIOR TO THE REMOVAL OF THE FABRIC

- THROUGHOUT THIS FORM, "M" DENOTES MITRAL, "A" DENOTES AORTIC, AND "T" DENOTES TRICUSPID VALVES. AS THE INCIDENCE OF PULMONARY VALVE REPLACEMENT IS EXTREMELY RARE, NO PROVISIONS HAVE BEEN MADE TO ACCOMMODATE IT. IF, HOWEVER, YOU HAVE OCCASION TO EVALUATE AN EXPLANTED PULMONARY VALVE, PLEASE CHANGE ONE OF THE HEADINGS (e.g. M, A, or T) to "P" AND PROCEED AS FOR OTHER VALVES

VALVE IDENTIFICATION INFORMATION AVAILABLE ☐ YES ☐ NO

IMPLANT SITE ☐ MITRAL ☐ AORTIC ☐ TRICUSPID ☐ PULMONARY

MANUFACTURER

M	A	T		M	A	T	
☐	☐	☐	CUTTER LABORATORIES	☐	☐	☐	SAINT JUDE MEDICAL
☐	☐	☐	EDWARDS LABORATORIES	☐	☐	☐	SHILEY LABORATORIES
☐	☐	☐	HANCOCK LABORATORIES	☐	☐	☐	SURGITOOL
☐	☐	☐	KASTEC				
☐	☐	☐	OTHER (specify) _____				

II. PROSTHESIS INFORMATION

TYPE/CONFIGURATION OF VALVE

M	A	T	
☐	☐	☐	DOUBLE CAGED BALL
☐	☐	☐	SINGLE CAGED BALL
☐	☐	☐	CAGED DISC
☐	☐	☐	TILTING/PIVOTING DISC
☐	☐	☐	BIOPROSTHESIS (e.g. porcine valve)
☐	☐	☐	BI-LEAFLET, CENTRAL OPENING
☐	☐	☐	OTHER (specify) _____

MITRAL VALVE PROSTHESIS - IMPLANT INFORMATION

NAME OF PROSTHESIS ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

IMPLANT DATE ☐☐ month ☐☐ day ☐☐ year

DURATION ☐☐ month ☐☐ day ☐☐ year

EXPLANT DATE ☐☐ month ☐☐ day ☐☐ year

MODEL NUMBER ☐☐☐☐☐☐☐ SIZE ☐☐ ☐ mm.

SERIAL NUMBER ☐☐☐☐☐☐☐ SIZE NUMBER ☐☐ OR

IMPLANTING HOSPITAL ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ name

☐☐☐☐☐☐ number ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ street

☐☐☐☐☐☐☐☐☐☐ city ☐☐ state ☐☐☐☐☐ zip

IMPLANTING SURGEON(s) 1. ☐☐☐☐☐☐☐☐☐☐☐☐ last name ☐☐☐☐☐☐☐ first

2. ☐☐☐☐☐☐☐☐☐☐☐☐ last name ☐☐☐☐☐☐☐ first

(indicate surgeon(s)' position by placing appropriate number in box)

☐ attending staff ☐ thoracic resident ☐ other resident

☐ other (specify) _____

☐☐☐☐☐☐ number ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ street

☐☐☐☐☐☐☐☐☐☐ city ☐☐ state ☐☐☐☐☐ zip

AORTIC VALVE PROSTHESIS - IMPLANT INFORMATION

NAME OF PROSTHESIS

IMPLANT DATE month day year

EXPLANT DATE month day year

DURATION month day year

MODEL NUMBER

SIZE mm.

SERIAL NUMBER

SIZE NUMBER ..OR

IMPLANTING HOSPITAL name

number street

city state zip

IMPLANTING SURGEON(s) 1. last name first

2. last name first

(Indicate surgeon(s)' position by placing appropriate number in box)

attending staff thoracic resident other resident

other (specify) _____

number street

city state zip

TRICUSPID VALVE PROSTHESIS - IMPLANT INFORMATION

NAME OF PROSTHESIS

IMPLANT DATE month day year

EXPLANT DATE month day year

DURATION month day year

MODEL NUMBER [ ] SIZE [ ] mm.

...OR

SERIAL NUMBER [ ] SIZE NUMBER [ ]

IMPLANTING HOSPITAL [ ]
name

[ ] number [ ] street

[ ] city [ ] state [ ] zip

IMPLANTING SURGEON(s) 1. [ ] last name [ ] first

2. [ ] last name [ ] first

(indicate surgeon(s)' position by placing the appropriate number in box)

[ ] attending staff [ ] thoracic resident [ ] other resident

[ ] other (specify) ______________________

[ ] number [ ] street

[ ] city [ ] state [ ] zip

III. SPECIMEN AND HANDLING

1. SURGICAL PATHOLOGY...(Complete this section if specimen is a surgically explanted valve; if not, go to AUTOPSY section, p. 23)

SURGICAL EXPLANTATION DATE [ ] month [ ] day [ ] year

SURGICAL PATHOLOGY NUMBER [ ]

HOSPITAL [ ]
name

[ ] number [ ] street

[ ] city [ ] state [ ] zip

SPECIMEN HANDLING - ENTIRE SPECIMEN

(Indicate your handling sequency by numbering each step in your examination process in the order in which you performed them)

M	A	T	
☐	☐	☐	PHOTOGRAPHY
☐	☐	☐	COLD (SUB-FREEZING) STORAGE
☐	☐	☐	FIXATION
			☐ FORMALDEHYDE
			☐ GLUTERALDEHYDE
			☐ OTHER (specify) _____
☐	☐	☐	RADIOGRAPHY
☐	☐	☐	PHYSICAL MEASUREMENTS (also see gross pathology section)
☐	☐	☐	BLOOD CULTURE
☐	☐	☐	TISSUE CULTURE
☐	☐	☐	ELECTRON MICROSCOPY
			☐ SCANNING
			☐ TRANSMISSION
☐	☐	☐	TISSUE STAINS
			☐ H & E
			☐ P A S
			☐ P A S DIGESTED
			☐ TRICHROME
			☐ OIL RED "O"
			☐ OTHER (specify) _____
			☐ CONGO RED
			☐ MUCIN
			☐ ELASTIC TISSUE
			☐ P T A H

ADDITIONAL STUDIES PERFORMED ☐ YES ☐ NO

STUDY ☐☐☐☐☐☐☐☐ DATE ☐☐ month ☐☐ day ☐☐ year

2. AUTOPSY

DATE OF DEATH ☐☐ month ☐☐ day ☐☐ year

PLACE OF DEATH ☐☐☐☐☐☐ number ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ street

☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ city ☐☐ state ☐☐☐☐☐ zip

☐ HOSPITAL ☐ PUBLIC AREA

☐ HOME ☐ OFFICE

☐ OTHER (specify) _____

EXPLANTING SURGEON(s) 1. ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

2. ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

(Indicate surgeon(s)' position by placing appropriate number in box)

☐ attending staff ☐ thoracic resident ☐ other resident

☐ other (specify) _____

INDICATION FOR EXPLANTATION (more than one may be indicated; please number each in order of priority)

☐ RED CELL HEMOLYSIS
☐ PARAVALVAR LEAK
☐ MATERIALS FAILURE
☐ HIGH PRESSURE GRADIENT
☐ THROMBUS / TISSUE OVERGROWTH
☐ EMBOLISM
☐ INFECTIOUS ENDOCARDITIS
☐ OTHER (specify) _____

SURGICAL PATHOLOGIST(s) 1. ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

2. ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

(Indicate pathologist(s)' position by placing appropriate number in box)

☐ attending staff ☐ pathology resident ☐ other resident

☐ other (specify) _____

SPECIMEN DEFINITION

M	A	T	
☐	☐	☐	INTACT VALVE
☐	☐	☐	VALVE CAGE ONLY
☐	☐	☐	OCCLUDER (POPPET) ONLY
☐	☐	☐	VALVE WITH SURROUNDING TISSUE
☐	☐	☐	OTHER (specify) _____

DEATH WITNESSED ☐ YES ☐ NO

DEATH WITNESSED BY 1. ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

2. ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

(Indicate witness' relationship to patient by placing appropriate number in box)

☐ SPOUSE ☐ PARAMEDIC ☐ FRIEND ☐ CO-WORKER

☐ PHYSICIAN ☐ NURSE ☐ FAMILY MEMBER

☐ OTHER (specify) _____

AUTOPSY DATE ☐☐ ☐☐ ☐☐ AUTOPSY NUMBER ☐☐☐☐☐☐☐☐

month day year

PATHOLOGIST(s) 1. ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

2. ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

(Indicate pathologist(s) position by placing appropriate number in box)

☐ ATTENDING STAFF ☐ CORONER (OR STAFF) ☐ RESIDENT

☐ OTHER (specify) _____

CLINICAL IMPRESSION OF CAUSE OF DEATH

☐ PRIMARY CARDIAC DISEASE IMMEDIATE CAUSE OF DEATH

☐ CARDIAC DISEASE CONTIRIBUTING FACTOR BUT NOT PRIMARY CAUSE OF DEATH

☐ DEATH NOT RELATED TO CARDIAC DISEASE

SPECIMEN DEFINITION

M	A	T	
☐	☐	☐	HEART WITH VALVE IMPLANTED
☐	☐	☐	VALVE WITH SURROUNDING TISSUE
☐	☐	☐	INTACT VALVE ONLY
☐	☐	☐	OCCLUDER (POPPET) ONLY
☐	☐	☐	VALVE WITHOUT OCCLUDER
☐	☐	☐	OTHER (specify) _____

SPECIMEN HANDLING - ENTIRE SPECIMEN

M	A	T	
☐	☐	☐	PHOTOGRAPHY
☐	☐	☐	COLD (SUB-FREEZING) STORAGE
☐	☐	☐	FIXATION

- ☐ FORMALDEHYDE
- ☐ GLUTERALDEHYDE
- ☐ OTHER (specify) _____

☐	☐	☐	RADIOGRAPHY
☐	☐	☐	PHYSICAL MEASUREMENTS
☐	☐	☐	BLOOD CULTURES
☐	☐	☐	TISSUE CULTURES
☐	☐	☐	ELECTRON MICROSCOPY

- ☐ SCANNING
- ☐ TRANSMISSION

☐ ☐ ☐ TISSUE STAINS

- ☐ H & E
- ☐ P A S
- ☐ P A S DIGESTED
- ☐ TRICHROME
- ☐ OIL RED "O"
- ☐ OTHER (specify) _____
- ☐ CONGO RED
- ☐ MUCIN
- ☐ ELASTIC TISSUE
- ☐ P T A H

ADDITIONAL STUDIES PERFORMED ☐ YES ☐ NO

STUDY ☐☐☐☐☐☐☐☐☐☐☐☐ DATE ☐☐ month ☐☐ day ☐☐ year

IV. PROSTHESIS EXAMINATION

I. OCCLUDER / LEAFLETS / CUSPS

IS OCCLUDER/LEAFLET/CUSP MOTION RESTRICTED? ☐ YES ☐ NO

IF YES, DESCRIPTION OF RESTRICTED OCCLUDER/LEAFLET/CUSP MOTION

M	A	T	
☐	☐	☐	OCCLUDER/LEAFLET(s) IMMOBILIZED IN OPEN POSITION
☐	☐	☐	OCCLUDER/LEAFLET(s) IMMOBILIZED IN CLOSED POSITION
☐	☐	☐	OCCLUDER/LEAFLET(s) IMMOBILIZED IN INTERMEDIATE POSITION
☐	☐	☐	FULL CLOSURE POSSIBLE, FULL OPENING IMPEDED
☐	☐	☐	FULL OPENING POSSIBLE, FULL CLOSURE IMPEDED
☐	☐	☐	BOTH FULL OPENING AND FULL CLOSURE TOTALLY OR PARTIALLY IMPEDED

CAUSE OF RESTRICTED OCCLUDER/LEAFLET/CUSP MOTION (If cusps or leaflets, indicate number involved. You may check as many as applicable)

M	A	T		
☐	☐	☐	THROMBUS/TISSUE OVERGROWTH ON CAGE (rigid prostheses only)	
☐	☐	☐	THROMBUS/TISSUE OVERGROWTH IN PRIMARY FLOW ORIFICE	
☐	☐	☐	THROMBUS/TISSUE OVERGROWTH IN SECONDARY FLOW ORIFICE	
☐	☐	☐	THROMBUS/TISSUE OVERGROWTH ON OCCLUDER/LEAFLET(s)/CUSPS	
☐	☐	☐	POST SURGICAL UNDEBRIDED TISSUE	
			☐ UPSTREAM	☐ DOWNSTREAM
☐	☐	☐	MURAL THROMBUS	
			☐ UPSTREAM	☐ DOWNSTREAM
☐	☐	☐	CUSP CALCIFICATION	☐ NUMBER OF CUSP(s) INVOLVED
☐	☐	☐	CUSP VEGETATION	☐ NUMBER OF CUSP(s) INVOLVED
☐	☐	☐	CUSP FIBROSIS	☐ NUMBER OF CUSP(s) INVOLVED
☐	☐	☐	SUTURE MATERIAL PROJECTING INTO PRIMARY ORIFICE	
			☐ UPSTREAM	☐ DOWNSTREAM
☐	☐	☐	DEFORMATION OF CAGE	
☐	☐	☐	STRUT, STENT, AND/OR HINGE FRACTURE	
☐	☐	☐	RETRACTION/FRAYING OF CLOTH	
☐	☐	☐	VALVE ALIGNMENT PROBLEM	
☐	☐	☐	VALVE SIZING PROBLEM	
☐	☐	☐	MISSHAPEN OCCLUDER	
☐	☐	☐	THROMBUS/TISSUE OVERGROWTH INTERFERES WITH COMPLETE EXAMINATION	
			☐ TO NAKED EYE	☐ UNDER MICROSCOPE
			☐ WITH HAND LENS	☐ WITH ELECTRON MICROSCOPE
☐	☐	☐	OTHER (specify) _____	

IS THERE EVIDENCE OF OCCLUDER/LEAFLET/CUSP CHANGES? ☐ YES ☐ NO

IF YES, (you may check more than one)

M	A	T	
☐	☐	☐	SWELLING
☐	☐	☐	SHRINKAGE
☐	☐	☐	CUSP CALCIFICATION (bioprostheses only)
☐	☐	☐	CUSP FIBROSIS (bioprostheses only)
☐	☐	☐	DISTORTED SHAPE
☐	☐	☐	DISCOLORATION
☐	☐	☐	CRACKING
☐	☐	☐	PITTING (e.g. from corrosion)
☐	☐	☐	SUBSURFACE INCLUSIONS (transilluminate)
☐	☐	☐	GROOVING (of disc occluder only)
☐	☐	☐	NOTCHING (of disc occluder only)
☐	☐	☐	OTHER (specify) _____

ADHERENT MATERIALS (are there thrombi, vegetation, tissue, or other materials present on occluder, leaflets, and/or cage?)

OCCLUDER/POPPET (rigid prostheses)

M	A	T	
☐	☐	☐	FRIABLE THROMBUS
☐	☐	☐	NON-FRIABLE THROMBUS
☐	☐	☐	VERRUCUS VEGETATIONS
☐	☐	☐	TISSUE OVERGROWTH
☐	☐	☐	NOT FULLY EVALUATED
☐	☐	☐	OTHER (specify) _____

LEAFLETS/CUSPS (bi-leaflet and bioprostheses)

M	A	T	# CUSPS	
☐	☐	☐	☐	FRIABLE THROMBUS
☐	☐	☐	☐	NON-FRIABLE THROMBUS
☐	☐	☐	☐	VERRUCUS VEGETATIONS
☐	☐	☐	☐	TISSUE OVERGROWTH
☐	☐	☐	☐	NOT FULLY EVALUATED
☐	☐	☐	☐	OTHER (specify) _____

CAGE

M	A	T	
☐	☐	☐	FRIABLE THROMBUS
☐	☐	☐	NON-FRIABLE THROMBUS
☐	☐	☐	VERRUCUS VEGETATIONS
☐	☐	☐	TISSUE OVERGROWTH
☐	☐	☐	NOT FULLY EVALUATED
☐	☐	☐	OTHER (specify) _____

2. VALVE FRAMEWORK (struts, stent, hinges, and muscle guard ring)

M	A	T	
☐	☐	☐	FRACTURE
☐	☐	☐	SCRATCHING
☐	☐	☐	PITTING
☐	☐	☐	BENDING
☐	☐	☐	FRAYED/TORN CLOTH
☐	☐	☐	MISSING CLOTH
☐	☐	☐	RETRACTED CLOTH
☐	☐	☐	NOT FULLY EVALUATED
☐	☐	☐	OTHER (specify) _____

3. SUTURE / TISSUE INTERFACE

SUTURE LINE

M	A	T	
☐	☐	☐	INTACT
☐	☐	☐	ENDOCARDITIS
☐	☐	☐	BLIND SINUS PRESENT
☐	☐	☐	ANEURYSM PRESENT
☐	☐	☐	PARAVALVAR LEAK
☐	☐	☐	VEGETATIONS
☐	☐	☐	THROMBUS
☐	☐	☐	TISSUE OVERGROWTH
☐	☐	☐	CALCIFICATION
☐	☐	☐	OTHER (specify) _____

CALCIFICATION

METHOD OF SUTURE PLACEMENT (check as many as applicable)

M	A	T	
☐	☐	☐	INTERRUPTED
☐	☐	☐	UNINTERRUPTED
☐	☐	☐	MATTRESS
☐	☐	☐	PURSE-STRING
☐	☐	☐	OTHER (specify) _____

TYPE OF SUTURE MATERIAL (check as many as appropriate)

M	A	T		M	A	T	
☐	☐	☐	SILK	☐	☐	☐	TEVDEK
☐	☐	☐	WIRE	☐	☐	☐	DACRON
☐	☐	☐	MERSILENE	☐	☐	☐	NYLON
☐	☐	☐	PROLENE	☐	☐	☐	CHROMIC CATGUT
☐	☐	☐	DEXON	☐	☐	☐	PLAIN CATGUT
☐	☐	☐	VICRO	☐	☐	☐	COTTON
☐	☐	☐	OTHER (specify) _____				

4. BASE RING

INFLOW FACE (includes fabric covering)

M	A	T	
☐	☐	☐	FRACTURE
☐	☐	☐	SCRATCHING
☐	☐	☐	PITTING
☐	☐	☐	BENDING
☐	☐	☐	FRAYED/TORN CLOTH
☐	☐	☐	MISSING CLOTH
☐	☐	☐	RETRACTED CLOTH
☐	☐	☐	TISSUE INGROWTH
☐	☐	☐	OTHER (specify) _____

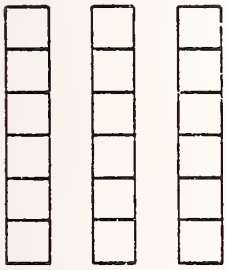
☐☐☐ % fabric area covered with adherent tissue

OUTFLOW FACE (includes fabric covering)

M	A	T	
☐	☐	☐	FRACTURE
☐	☐	☐	SCRATCHING
☐	☐	☐	PITTING
☐	☐	☐	BENDING
☐	☐	☐	FRAYED/TORN CLOTH
☐	☐	☐	MISSING CLOTH
☐	☐	☐	RETRACTED CLOTH
☐	☐	☐	TISSUE INGROWTH
☐	☐	☐	OTHER (specify) _____

☐☐☐ % fabric area covered with adherent tissue

DEHISCENCE (PARAVALVAR LEAK)

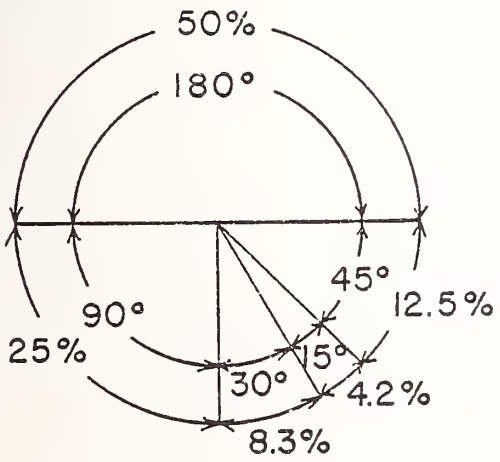


1 - 5 mm.
6 - 10 mm.
11 - 20 mm.
21 - 30 mm.
30 - 49 mm.
> 50 mm.

- NUMBER EACH DEHISCED AREA ON SKETCH BELOW: THEN, ACCORDING TO SIZE, PLACE THE NUMBER OF EACH DEHISCED AREA IN THE APPROPRIATE BOX ABOVE.

TOTAL PERCENT OF VALVE PERIMETER DEHISCENCE: ☐☐☐ %

KEY: (DIAMETER = 6 CM.)



SKETCH FINDINGS BELOW:

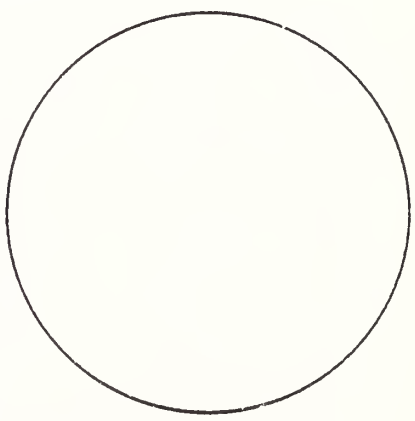
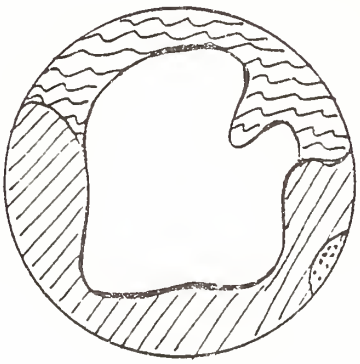


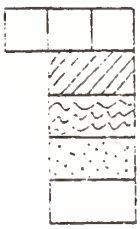
FIGURE 1

ESTIMATED REDUCTION IN PRIMARY FLOW ORIFICE AREA

- TO APPROXIMATE SIZE AND NATURE OF THE REDUCTION IN THE ORIFICE, USE THE TRANSPARENT TEMPLATE ATTACHED TO THE END OF THIS FORM. SKETCH YOUR FINDINGS ACCORDING TO THE KEY IN THE APPROPRIATE VALVE ORIFICE FIGURE.

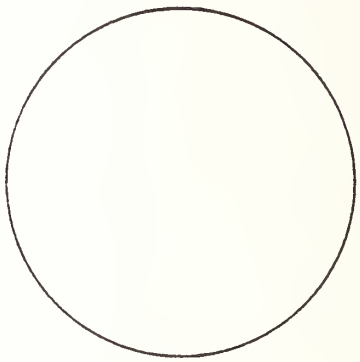
KEY





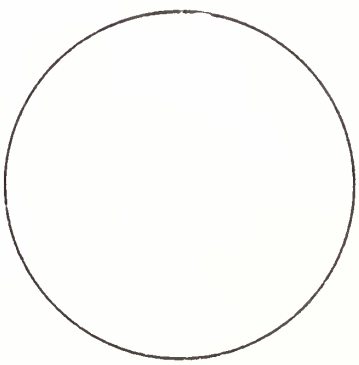
ESTIMATED TOTAL % REDUCTION
THROMBUS
TISSUE OVERGROWTH
VEGETATION
OTHER (specify) _____

AORTIC VALVE



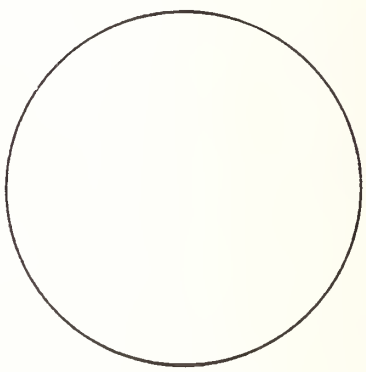
ESTIMATED TOTAL % REDUCTION

MITRAL VALVE



ESTIMATED TOTAL % REDUCTION

TRICUSPID VALVE

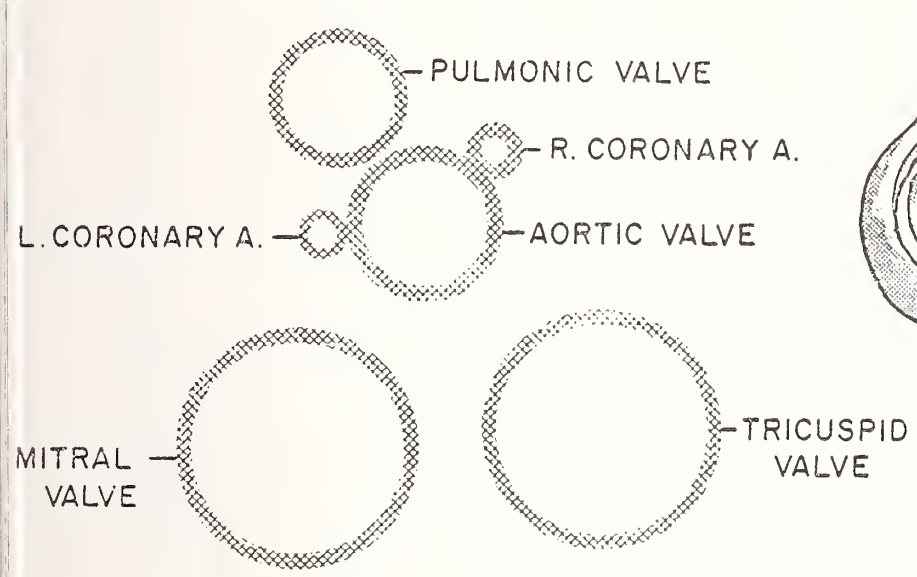


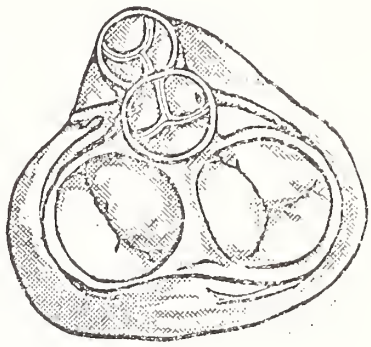
ESTIMATED TOTAL % REDUCTION

FIGURE 2

OSTHESIS ORIENTATION

IN THE FOLLOWING FIGURE, SKETCH THE APPROPRIATE ORIENTATION OF THE IMPLANTED PROSTHESIS (es). e. g., AN ARROW SHOULD POINT IN THE DIRECTION OF THE LARGE ORIFICE, OR STRUT OR STENT POSITIONS SHOULD BE DRAWN IN.





REFERENCE

FIGURE 3

GROSS PATHOLOGY - AUTOPSY ONLY

ART MEASUREMENTS

HEART WEIGHT	☐☐.☐	gm.
RIGHT VENTRICLE LENGTH (valve ring to internal apex)	☐☐.☐	cm.
RIGHT VENTRICLE THICKNESS (at midpoint of free wall)	☐☐.☐	cm.
VALVE RING CIRCUMFERENCE - TRICUSPID (natural valve)	☐☐.☐	cm.
VALVE RING CIRCUMFERENCE - PULMONIC (natural valve)	☐☐.☐	cm.
LEFT VENTRICLE LENGTH (valve ring to internal apex)	☐☐.☐	cm.
LEFT VENTRICLE THICKNESS (at midpoint of free wall)	☐☐.☐	cm.
VALVE RING CIRCUMFERENCE - MITRAL (natural valve)	☐☐.☐	cm.
VALVE RING CIRCUMFERENCE - AORTIC (natural valve)	☐☐.☐	cm.
AORTIC CIRCUMFERENCE (2cm. above prosthetic valve ring)	☐☐.☐	cm.
RIGHT CORONARY ARTERY OSTIUM (distance above prosthetic valve ring)	☐☐.☐	cm.
LEFT CORONARY ARTERY OSTIUM (distance above prosthetic valve ring)	☐☐.☐	cm.
OTHER (specify) _____	☐☐.☐	cm.
OTHER (specify) _____	☐☐.☐	cm.

TOPOGRAPHICAL SCHEMA OF THE HEART SHOWING THE CORONARY VESSELS

(Sketch below only pericardial, epicardial, and graft findings)

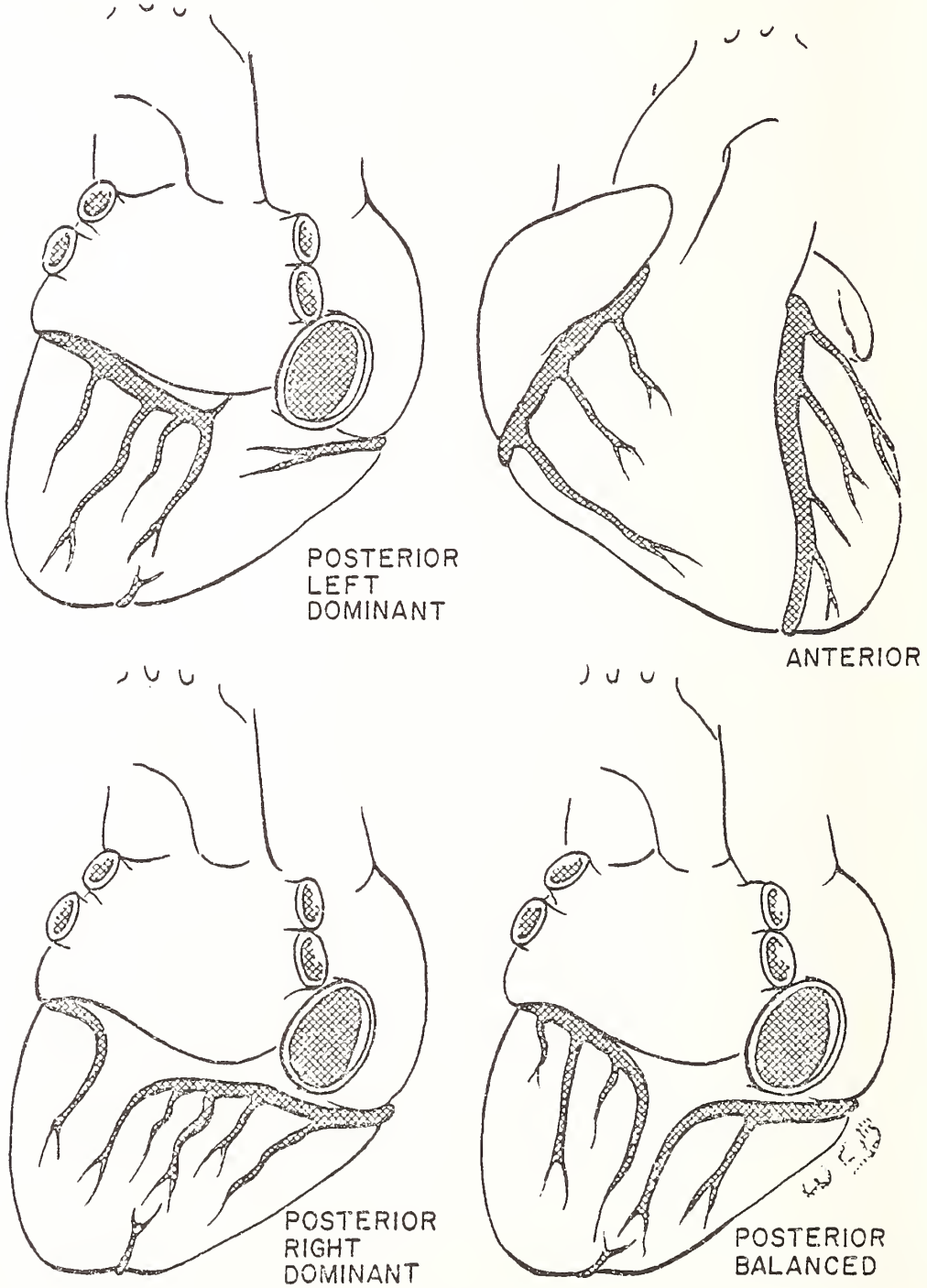


Figure 4

PERICARDIUM / EPICARDIUM AND PERICARDIAL SAC

- ☐ PERICARDITIS - CHRONIC
- ☐ PERICARDITIS - ACUTE
- ☐ ADHESIONS
  - ☐ EASILY LYSED
  - ☐ DENSE FIBROUS
- ☐ FLUID
  - ☐ HEMORRHAGIC ☐☐☐☐ cc.
  - ☐ CLEAR ☐☐☐☐ cc.
  - ☐ CLOUDY ☐☐☐☐ cc.
- ☐ PACING WIRES (show location on topographical sketch)
  - ☐ TEMPORARY
  - ☐ PERMANENT

● IN THE FOLLOWING SECTION, ABBREVIATIONS ARE USED FOR HEADINGS: R A denotes RIGHT ATRIUM; L A denotes LEFT ATRIUM; R V denotes RIGHT VENTRICLE; and L V denotes LEFT VENTRICLE. M, A, T, and P stand for MITRAL, AORTIC, TRICUSPID, AND PULMONIC AS PREVIOUSLY NOTED

CHAMBER SIZE

	RA	RV	LA	LV
APPEARS NORMAL	☐	☐	☐	☐
DILATED	☐	☐	☐	☐
REDUCED IN SIZE	☐	☐	☐	☐

ENDOCARDIUM (A)

1	FOCAL FIBROSIS/THICKENING	☐	☐	☐	☐
2	DIFFUSE FIBROSIS/THICKENING	☐	☐	☐	☐
3	MULTI-FOCAL FIBROSIS	☐	☐	☐	☐
4	FRIABLE THROMBUS	☐	☐	☐	☐
5	NON-FRIABLE THROMBUS	☐	☐	☐	☐
6	SEPTIC VEGETATION	☐	☐	☐	☐
7	BLAND VEGETATION	☐	☐	☐	☐
8	PACING WIRE(s)	☐	☐	☐	☐

VIEW OF CARDIAC FINDINGS

(Sketch or indicate below your intracardiac findings, coding each finding with the corresponding letter and number found in the text)

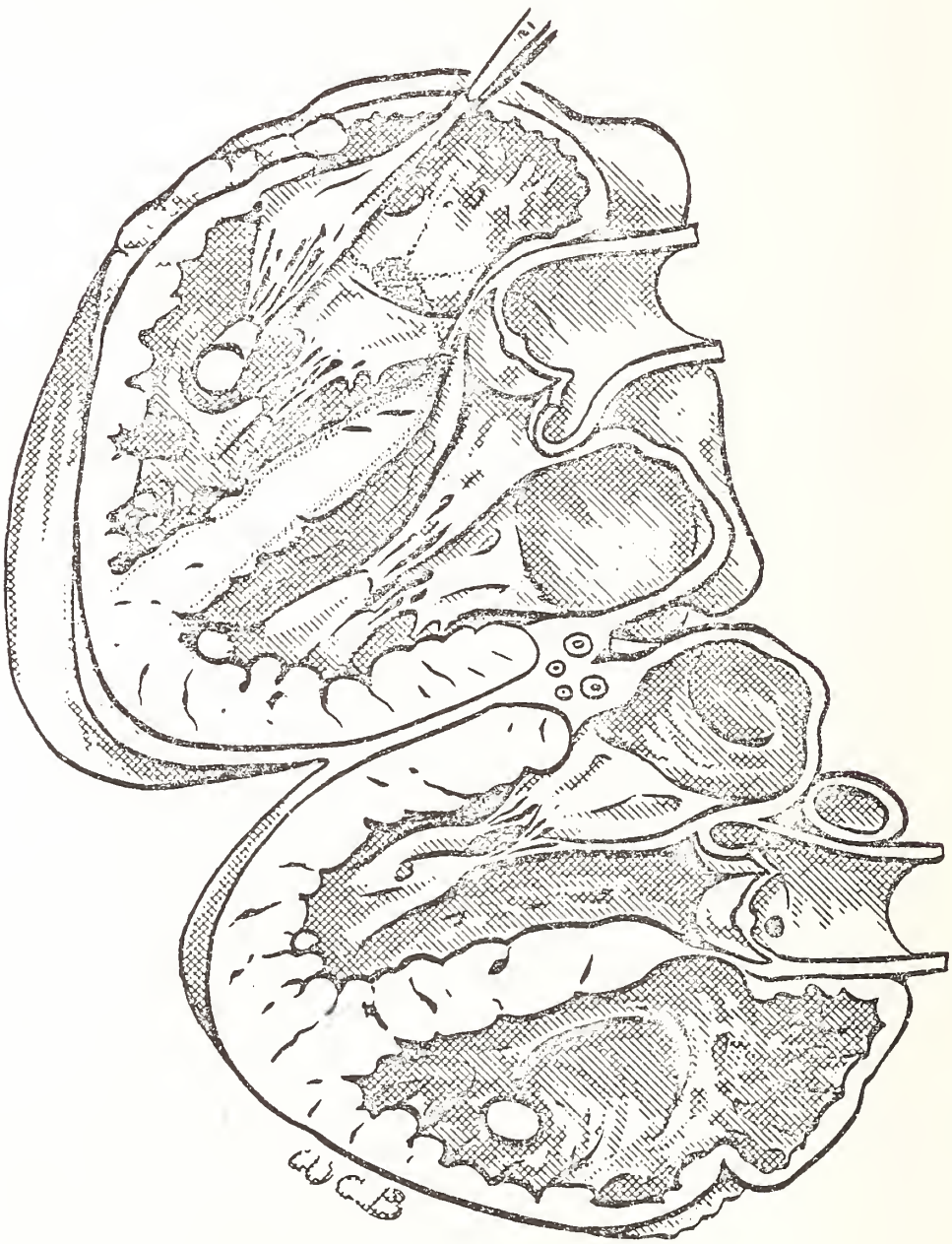


Figure 5

MYOCARDIUM (B)

	RA	RV	LA	LV
1 HYPERTROPHY/THICKENING	☐	☐	☐	☐
2 THINNING	☐	☐	☐	☐
3 FOCAL FIBROSIS	☐	☐	☐	☐
4 DIFFUSE FIBROSIS	☐	☐	☐	☐
5 MULTI-FOCAL FIBROSIS	☐	☐	☐	☐
6 FOCAL HEMORRHAGE	☐	☐	☐	☐
7 DIFFUSE HEMORRHAGE	☐	☐	☐	☐
8 MULTI-FOCAL HEMORRHAGE	☐	☐	☐	☐
9 ABSCESS	☐	☐	☐	☐
10 ACUTE INFARCTION	☐	☐	☐	☐
11 HEALING INFARCTION	☐	☐	☐	☐
12 HEALED INFARCTION	☐	☐	☐	☐
13 PERFORATION/RUPTURE	☐	☐	☐	☐
14 SUTURES	☐	☐	☐	☐

CHORDAE TENDINEAE (C)

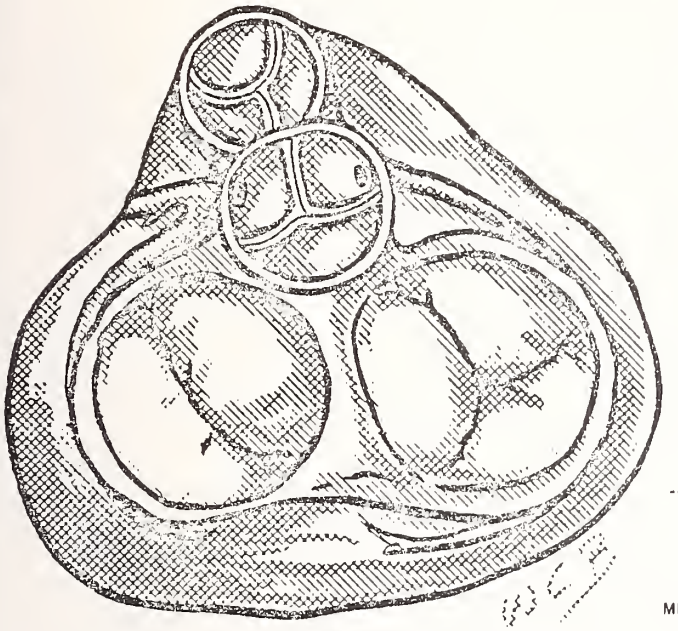
1 THICKENING	☐	☐
2 FUSION	☐	☐
3 SHORTENING	☐	☐
4 RUPTURE	☐	☐
5 VEGETATIONS	☐	☐
6 SURGICAL REMOVAL	☐	☐

PAPILLARY MUSCLES (D)

1 THICKENING	☐	☐
2 THINNING	☐	☐
3 FIBROSIS	☐	☐
4 HEMORRHAGE	☐	☐
5 INFARCTION	☐	☐
6 ABSCESS	☐	☐
7 RUPTURE	☐	☐
8 SURGICAL REMOVAL	☐	☐

FOR THE ABOVE INFORMATION, PLEASE SKETCH YOUR FINDINGS ON FIGURE 5 , FOUND ON PAGE 38. INDICATE YOUR FINDING BY THE LETTER AND THE NUMBER OF THE ABNORMALITY, AS CODED TO THE TERMS ABOVE.

NOTES OF SKETCHES (supplemental)



PLEASE SKETCH OR INDICATE FINDINGS, AS APPROPRIATE.

REFERENCE

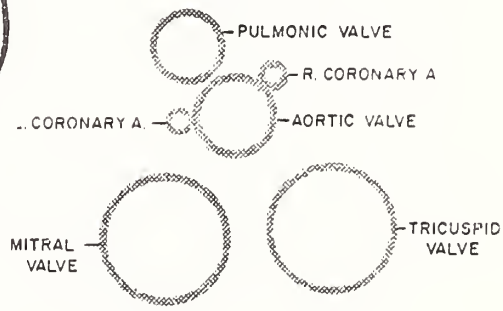


FIGURE 6

ATURAL VALVES (E)

	M	A	T	P
1 REPLACED BY PROSTHESIS	☐	☐	☐	☐
2 VALVE RING				
a DILITATION	☐	☐	☐	☐
b STENOSIS	☐	☐	☐	☐
c CALCIFICATION	☐	☐	☐	☐
d HEMORRHAGE	☐	☐	☐	☐
e ABSCESS	☐	☐	☐	☐
f PERFORATION	☐	☐	☐	☐
g SUTURES	☐	☐	☐	☐
OTHER (specify) _____				
3 VALVE CUSPS				
a THICKENING	☐	☐	☐	☐
b CALCIFICATION	☐	☐	☐	☐
c RETRACTION/ROLLING	☐	☐	☐	☐
d BLAND VEGETATIONS	☐	☐	☐	☐
e SEPTIC VEGETATIONS	☐	☐	☐	☐
f FUSION OF COMMISSURES	☐	☐	☐	☐
OTHER (specify) _____				

ASCENDING AORTA / SINUS OF VALSALVA (F)

		M	A	T	P
1	RUPTURED ANEURYSM				
2	UNRUPTURED ANEURYSM				
3	INFECTIONS / ENDOCARDITIS				
4	FATTY STREAKS				
5	COMPLICATED LESIONS				
6	CALCIFIED LESIONS				
7	EMBOLIC FRAGMENT				
	OTHER (specify)				

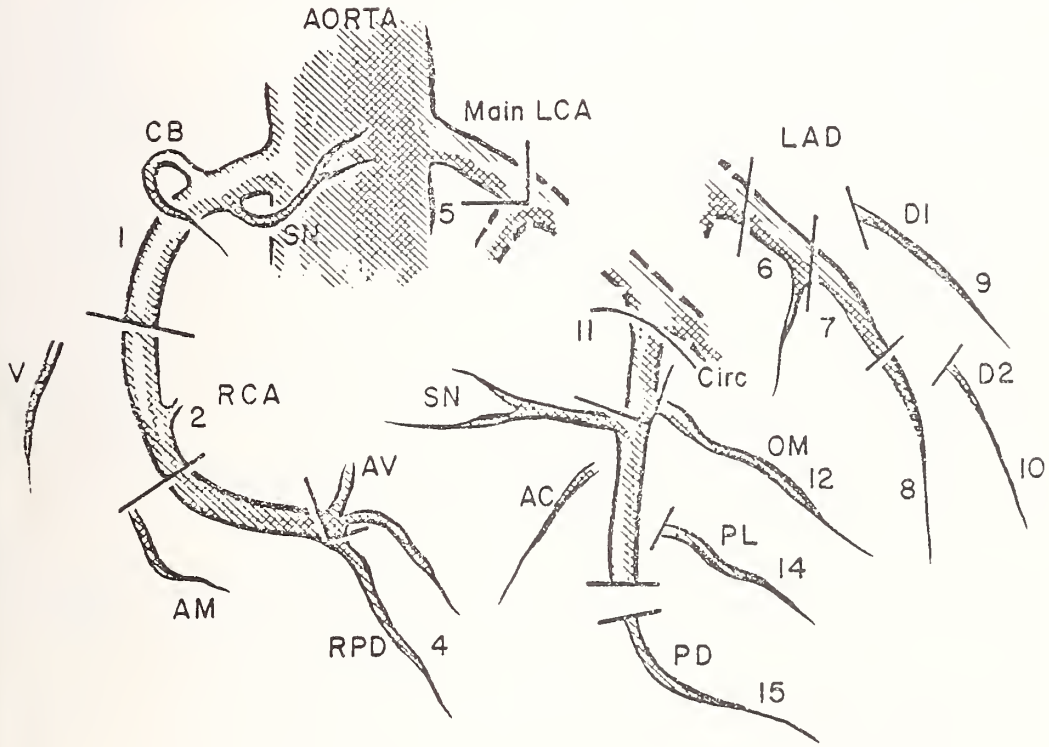
CORONARY ARTERIES AND BRANCHES

- IN THE FOLLOWING SECTION, THE COLUMN ABBREVIATIONS ARE AS FOLLOWS: T denotes THROMBUS, E F, EMBOLIC FRAGMENT; F S, FATTY STREAKS; F P, FIBROUS PLAQUES; COL, COMPLICATED LESIONS; CAL, CALCIFIED LESIONS; AND %RED, PERCENT REDUCTION IN CROSS-SECTIONAL AREA IN THE MOST SEVERE SECTION OF ARTERIAL NARROWING.

CORONARY BRANCH		T	EF	FS	FP	COL	CAL	%Red.
	Right coronary arteries							
1	PROXIMAL							
2	MID							
3	DISTAL							
4	POSTERIOR DESCENDING							
	Left coronary arteries							
5	MAIN							
6	PROXIMAL LEFT ANTERIOR DESCENDING							
7	MID LEFT ANTERIOR DESCENDING							
8	APICAL LEFT ANTERIOR DESCENDING							
9	FIRST DIAGONAL							
10	SECOND DIAGONAL							
11	PROXIMAL CIRCUMFLEX							
12	OBTUSE MARGINAL							
13	DISTAL CIRCUMFLEX							
14	POSTEROLATERAL							
15	POSTERIOR DESCENDING							

PLEASE MARK YOUR ABOVE FINDING ON THE SKETCH ON p. 42.

CORONARY ARTERIES AND BRANCHES



FROM AUSTEN et al
Circulation '78

Figure 7

ON THE SKETCH ABOVE, PLEASE INDICATE YOUR FINDINGS CORRESPONDING TO THE COLUMN ABBREVIATIONS ON p. 42. (EXAMPLE: EMBOLIC FRAGMENT OF PROXIMAL LAD SHOULD BE WRITTEN AS E F IN THE #6 AREA OF THE SKETCH).

BY-PASS GRAFT No. 1 (Indicate site of graft as G1 on coronary artery sketch or topographical sketch,

- ☐ FIBROUS INTIMAL PROLIFERATION
- ☐ MEDIAL FIBROSIS
- ☐ THROMBUS
- ☐ FATTY STREAKS
- ☐ FIBROUS PLAQUES
- ☐ COMPLICATED LESIONS
- ☐ CALCIFIED LESIONS
- ☐ REDUCTION IN DIAMETER ☐☐☐ % ESTIMATED REDUCTION
- ☐ OTHER (specify)

BY-PASS GRAFT No. 2 (Indicate site of graft as G2 on coronary artery sketch or topographical sketch

- ☐ FIBROUS INTIMAL PROLIFERATION
- ☐ MEDIAL FIBROSIS
- ☐ THROMBUS
- ☐ FATTY STREAKS
- ☐ FIBROUS PLAQUES
- ☐ COMPLICATED LESIONS
- ☐ CALCIFIED LESIONS
- ☐ REDUCTION IN DIAMETER ☐☐☐ % ESTIMATED REDUCTION
- ☐ OTHER (specify)

BY-PASS GRAFT No. 3 (Indicate site of graft as G3 on coronary artery sketch or topographical sketch

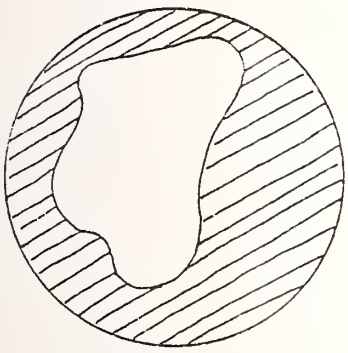
- ☐ FIBROUS INTIMAL PROLIFERATION
- ☐ MEDIAL FIBROSIS
- ☐ THROMBUS
- ☐ FATTY STREAKS
- ☐ FIBROUS PLAQUES
- ☐ COMPLICATED LESIONS
- ☐ CALCIFIED LESIONS
- ☐ REDUCTION IN DIAMETER ☐☐☐ % ESTIMATED REDUCTION
- ☐ OTHER (specify)

TIMATED NARROWING OF CORONARY ARTERIES

TO APPROXIMATE THE EXTENT AND PERCENTAGE OF NARROWING OF THE CORONARY ARTERIES, USE THE TRANSPARENT TEMPLATE ATTACHED TO THE END OF THIS FORM. SKETCH YOUR FINDINGS SIMILAR TO THE EXAMPLE SHOWN AND INDICATE THE ARTERY IN QUESTION.

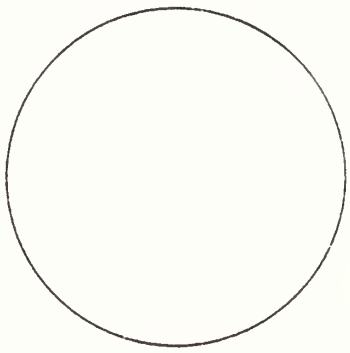
AMPLE

TERY _____



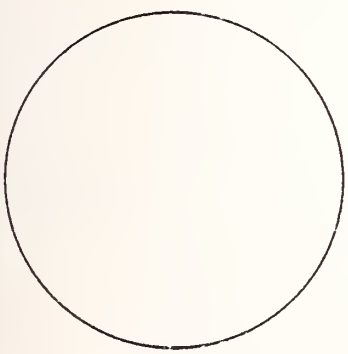
PERCENT OCCLUSION ☐☐☐ %

ARTERY _____



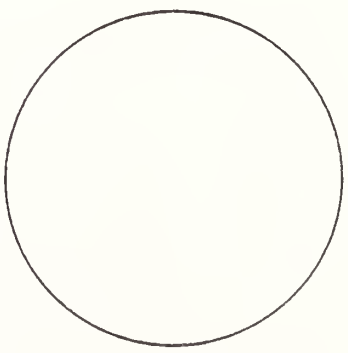
PERCENT OCCLUSION ☐☐☐ %

TERY _____



PERCENT OCCLUSION ☐☐☐ %

ARTERY _____



PERCENT OCCLUSION ☐☐☐ %

FIGURE 8

VI. HISTOPATHOLOGY

1. TISSUE OVERGROWTH ☐

2. VEGETATIONS ☐

3. REPRESENTATIVE SECTIONS ☐
(Interventricular septum as reference point)

   a. 12 o'clock ☐

   b. 3 o'clock ☐

   c. 6 o'clock ☐

   d. 9 o'clock ☐

4. OTHER, describe _____
_____
_____

VII. SUMMARY SHEET

Please summarize below your key findings according to the Systematized Nomenclature of Medicine (SNOMED).

ETIOLOGY

TOPOGRAPHIC FINDINGS

MORPHOLOGIC FINDINGS

DISEASE

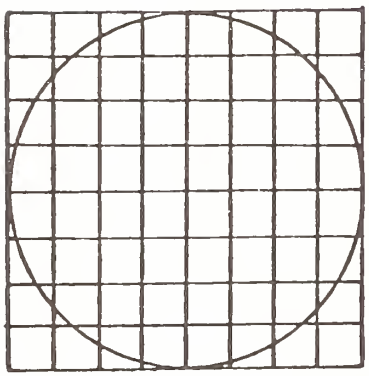
PROCEDURES

Signed _____ M.D.

Date _____

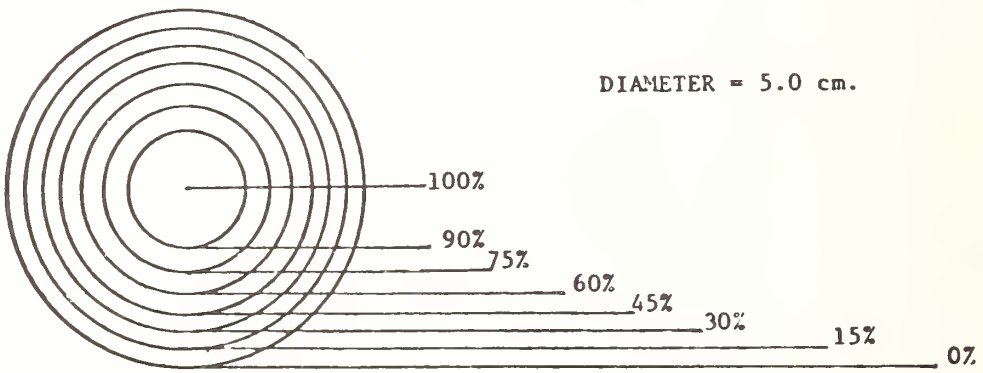
ORIFICE MEASUREMENT TEMPLATE

USE THIS TRANSPARENT TEMPLATE TO APPROXIMATE AND MARK THE OBSERVED REDUCTION IN PRIMARY FLOW ORIFICE AND REDUCTION (NARROWING) OR CORONARY ARTERIES. SKETCH YOUR FINDINGS ON 32 AND 44 OF THE EVALUATION FORM.



DIAMETER = 5.0 cm.

EACH SQUARE = 2% OF ORIFICE AREA



DIAMETER = 5.0 cm.

USE EITHER FIGURE (OR BOTH) TO APPROXIMATE ACTUAL SIZE

Evaluation Protocols*

This protocol was designed for the evaluation of retrieved, expanded teflon graft material, GORE-TEX^{R}.

Documentation

Every returned sample we receive is logged into the Histology Logbook. A histological log number is written on each specimen container received. The log number corresponds to the date the specimen arrived in Histology and the number of specimens logged in on that particular day. For example, the first specimen logged in on May 21, 1980, would receive the log number 5-2180-1. In addition to the histology log number, all the information sent with the specimen is recorded into the histology logbook. Any information needed which is not included with the specimen is requested with a thank you letter.

To identify each sample for the gross photographic documentation, a typed I.D. label with the histology log number, patient's name and surgeon's name is prepared.

The following equipment is used to photograph the returned samples:

1. Photo table with 4-BBA number 1 daylight bulbs and adjustable camera holder.
2. 35mm Canon AT-1 camera with Canon 100mm Macro lens.
3. Kodachrome KPA 40, Type A professional transparency film.
4. Dissecting tray, eye dropper, forceps, scissors, green sponge-cloths, mm ruler, latex gloves and safety glasses.

The specimens usually arrive in a fixative of either cacodylate buffer or 10% formalin. For protection, gloves and safety glasses are worn during photograph preparation. The specimen is removed from the container with forceps with care to avoid disrupting the gross appearance. To insure that the tissue does not dry and become damaged, it is periodically moistened with fixative.

*Provided by Ms. B. Boyce, W.L. Gore Associates Inc., 1505 N. Fourth St. Flagstaff, Arizona 86002

The moisture also highlights the specimen for a quality photograph. The specimen is placed on a green sponge-cloth in the dissecting tray. The I.D. label is placed directly below the sample and the ruler directly above the sample. A picture of the graft outer surface appearance is taken first. If possible, a transverse picture is taken to demonstrate the appearance of the lumen. The graft is then cut along its longitudinal axis and pinned open to expose the luminal surface. Each photograph is taken in duplicate, a slide for the analysis and one slide for the gross photograph notebook.

When a specimen is too small to photograph with the 35mm camera, a Nikon SM-10 Stereoscope with a Nikon M-35 FA 35mm camera is used. For lighting the subject, an MK 11 Fiber Optic light is used. This scope allows up to 40 power magnification, which is especially beneficial for small diameter grafts.

Gross Examination

a) All GORE-TEX graft specimens submitted to the Histology laboratory for evaluation are inspected grossly, following a standard method of examination. The length of the graft segment is measured and expressed in centimeters or millimeters. Host vessel attachment, if present, is noted and the respective proximal and distal host vessel segments are examined for evidence of intimal hyperplasia, pannus extension, suture line dehiscence, etc.

The graft outer surface is then considered, and tissue attachement, or lack thereof, is noted. When tissue is present, relative degree of attachment is determined with a needle probe inserted between the tissue and the graft outer surface. A subjective determination of tissue attachment is concluded from the force necessary to pull a portion of tissue away from the graft outer surface. Any evidence of hematoma is also noted.

The GORE-TEX graft assumes a tan or off-white appearance after days or weeks of implantation. Any wall discoloration, such as a red or dark-brown continuous or mottled appearance is recorded. A careful examination of the entire graft luminal surface is performed. If clot is present, clot consistency,

attachment, color and thickness is recorded. Near the anastomoses, the luminal surface is checked for evidence of pannus extension, and the suture line is examined for evidence of tissue overgrowth. If the appearance of the graft is consistent along its length, one representative longitudinal section is taken. If both anastomoses are present or if the luminal or outer surface matrices differ along the length of the graft, several longitudinal sections are taken. Transverse sections are taken if clot is present on the luminal surface to determine degree of occlusion of the lumen.

Also, transverse sections are taken of GORE-TEX grafts used as A-V fistulae for dialysis, if the graft presents with a pseudoaneurysm. With a transverse section, the pseudoaneurysm capsule can be visualized.

b) Occasionally grafts are returned with questions regarding the mechanical integrity of the graft material. In these instances, the graft sample is placed in a potassium dichromate solution** and all organic matter is digested from the specimen, 1/2-12 hrs. The sample is thoroughly rinsed in distilled water, dried, and submitted to our Quality Control department.

A destructive water entry pressure (WEP) test is performed on the sample. The test consists of subjecting the graft to a initial water entry pressure of 2 psi, then increasing the pressure .2 psi/minute until the graft leaks. A minimum WEP of 3.0 psi is required for confirmation of structural integrity. All findings are recorded and reported to the surgeon who submitted the sample.

Microscopic Examination

The sections taken at gross examination are processed for standard paraffin sections, using alcoholand toluene in the tissue processor.

**A sulphuric acid - potassium dichromate mixture used for cleaning laboratory glassware (e.g. Dichrol). The digestion is carried out at room temperature.

The GORE-TEX graft is cut with an American Optical "820" Spencer Microtome. The majority of grafts are cut at 6 microns thickness. Standard microtome knives are used. Disposable microtome blades are not recommended as they are not sharp enough to cut proper ribbons from specimens which contain graft material. A 7203 Thomas Fanz Microtome Knife Sharpener is utilized and is one of the most important reasons for obtaining good tissue slides. The blades must be sharpened frequently to keep them at the peak of perfection for high performance. The blades are also honed on a leather strop for final fine finish.

The following routine stains are used for the sections:

H & E
Milligan's Trichrome
Ledrum's Acid Picro-Mallory Fibrin

Occasionally we are asked to do special stains. These consist mainly of Dahl's Calcium, Brown & Brenn Bacteria, Verhoeff's Elastin, & Hall's Bilirubin. These are requested either by the party who sends us the specimen or by our laboratory technician upon gross examination of the specimen. We use these particular stains because they are the best we have found to use with our graft material. The sections are examined in a routine manner, progressing from host vessel characteristics (if the host vessel is present), the suture line, graft outer surface, interstitial space (wall) to the luminal surface.

The host vessel examination includes looking for evidence of hemorrhaging or hematoma formation in the adventitia, medial calcification, intimal hyperplasia near the suture line, presence or absence of the endothelium and assessment of the relative health of the vessel. The suture line is examined for possible clot formation, pannus extension or endothelial cell overgrowth. Tissue necrosis around suture material is also assessed.

Examination of the graft outer surface includes determination of the degree of tissue attachment, and penetration of tissue through the reinforcing material and into the graft wall. Both H & E and Trichrome stained sections are examined. Any cellular response is noted. If indicated by the appearance of the tissue, the Brown and Brenn bacterial stain or Dahl's calcium stain are performed on sections to check for sepsis or calcification.

Graft wall contents are investigated using sections stained with H & E, Trichrome, Fibrin and when applicable, bacterial, calcium and bilirubin stains. The graft wall is specifically examined for fibroblastic infiltration, collagen production, infiltration of blood elements, bacterial colonization, and uniformity of wall filling.

A microscopic examination of the luminal surface is performed to assess deposition of blood elements, including fibrin, erythrocytes and neutrophilic leukocytes, or tissue extension from the host vessels. Attachment of luminal surface matrices is assessed by noting degree of matrix penetration into the graft interstitial spaces. If clot is present, a relative assessment of the age of the clot is performed based on clot constituents. Clusters of erythrocytes and leukocytes represent post-removal or post-mortem clot, while laminated fibrin is indicative of pre-mortem deposition. Measurements of any luminal surface matrix are recorded as is degree of surface covered by the matrix. Sections stained with the usual stains (H & E, Trichrome and Fibrin) are examined. If pannus extensions are present, a section stained with Verhoeff's Elastin stain is examined for presence of elastic tissue.

Histological observations are summarized, and the analysis and summary are recorded on a standard form (see attached).

When scanning electron microscopy is performed on sections of a returned graft sample, light microscopy observations are correlated with scanning electron microscopy observations in a combined summary.

Scanning Electron Microscopy

A representative sample of each specimen analysed is examined by SEM. The specimens are cut, placed in a divided process basket, and immersed in a Wheaton dish of cacodylate buffer and refrigerated for 24 hours.

The specimens are then washed with a continuous flow of distilled water for 3-4 hours, to remove the cacodylate buffer solution.

The specimens are then dehydrated by sequentially immersing in 50%, 70%, 80%, 95%, and 100% ethanol solutions. This is followed by immersion in a 50% ethanol/50% amyl acetate solution and then by immersion in 100% amyl acetate. The specimen is then dried for examination in the SEM with a CO_2 critical point dryer. For fatty specimens immersion in chloroform is included prior to critical point drying.

For examination of transverse sections the specimen may be freeze-fractured in liquid nitrogen after critical point drying. Specimens are examined using an Amray 1000A scanning electron microscope employing a tungsten filament. The entire flow surface of the sample is scanned using double display CRT's with a one to four magnification ratio. The usual magnifications are 200X and 800X, or 500X and 2000X. The host vessel is scanned to determine the composition of material and/or tissue on the flow surface. The host vessel endothelial layer is often sloughed during specimen implantation or removal, and scanning electron microscopy can sometimes determine the areas of regeneration of this layer. The degree of confluence of the endothelial cells is noted as well as the areas of extension over the suture line onto the graft luminal surface. Other material or tissue composition of the graft flow surface is noted. Any areas of exposed graft luminal surface are scanned to determine if any material, cells or tissue appear to be penetrating the interstices. The specimen is changed to an approximate 90 degree orientation to the beam to determine the thickness of the material and/or tissue on the flow surface.

Any abnormalities of the specimen such as bacteria or artifacts due to specimen preparation, are also noted. The wall interstices are not routinely scanned. The graft structure usually shows a smeared appearance when sectioned with a cutting instrument. Freeze fracturing, which prevents structural smearing, is not usually performed due to the large number of specimens processed.

A low magnification (approximately 6x-20x) micrograph is taken to show the overall view of the sample and to indicate the sites of the higher magnification micrographs. These higher magnification micrographs are usually taken between 500 X and 2000X, as this is the magnification range that appears to best demonstrate the cell tissue and/or material type. Polaroid type 52 film is used for all micrographs. The micrographs are treated with Blair spray fix, workable matte fixative (Blair Art Products, Inc., Memphis, Tenn.) rather than the Polaroid jelly. The jelly is messy, caustic, reflects light which interferes with the observation of the micrograph and takes a long time to dry. To date, micrographs up to 2 1/2 years old and treated with Blair spray fix reveal no discoloration or other abnormalities. A duplicate set of 35mm slides are taken of each micrograph, one set for our files and one set for the surgeon. A combined summary of scanning electron microscope and light microscope observations is included with the completed analyses.

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№

RETURNED CLINICAL SAMPLE EVALUATION

Gore No. _____ Date: _____

SAMPLE IDENTIFICATION:

LOT No._____ SERIAL No._____ I. D. _____

RETURNED FROM:

SAMPLE HISTORY

PATIENT IDENTIFICATION:

AGE OF PATIENT:_____ SEX: _____ IMPLANT DATE: _____

REMOVAL DATE: _____ IMPLANT DURATION: _____

SITE: _____

REASON FOR IMPLANTATION:

PATIENT CONDITION AFTER IMPLANTATION:

REASON FOR REMOVAL:

PATIENT CONDITION AFTER GRAFT REMOVAL:

ETURNED CLINICAL SAMPLE EVALUATION

ROSS SAMPLE OBSERVATIONS:

Nº

RETURNED CLINICAL SAMPLE EVALUATION

HISTOLOGICAL OBSERVATIONS:

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RETURNED SAMPLE EVALUATION

ore No. _____ Animal I.D. _____ GORE-TEX® Type: _____

ETURNED FROM:

AMPLE HISTORY:

ROSS SAMPLE OBSERVATIONS:

STOLOGICAL OBSERVATIONS:

ATE: _____ 773 SIGNED: _____

Testing Procedure*

This protocol was designed for the mechanical evaluation of weft knit graft material in the form of small samples, which precludes fabric testing.

After receipt of the retrieved graft (not fixed in formalin) the graft is cleaned by the following procedure:

Materials:

Terg-A-Zyme^{R} - 7.5 g/liter water.

Cleaning Procedure:

1) The explanted grafts are handled using plastic gloves.
2) Fill beaker with distilled water, drop in spin bar and place beaker on hotplate. Start bar spinning slowly and turn heat on low. Optimum temperature is 120^{o}F (50^{o}C).
3) Weigh the appropriate amount of Terg-A-Zyme into disposable weighing tin and pour it into the spinning water.
4) When Terg-A-Zyme has dissolved put graft into solution.
5) Change Terg-A-Zyme solution every 2 hours until water is clean and tissue is soft. Rinse graft when changing solutions, rubbing graft between fingers under running water.
6) When tissue has become soft hold graft under running water and carefully strip tissue away from graft by using tweezers. Put tissue in plastic bag for disposal. When graft is clean rinse thoroughly to remove any Terg-A-Zyme.

Evaluation:

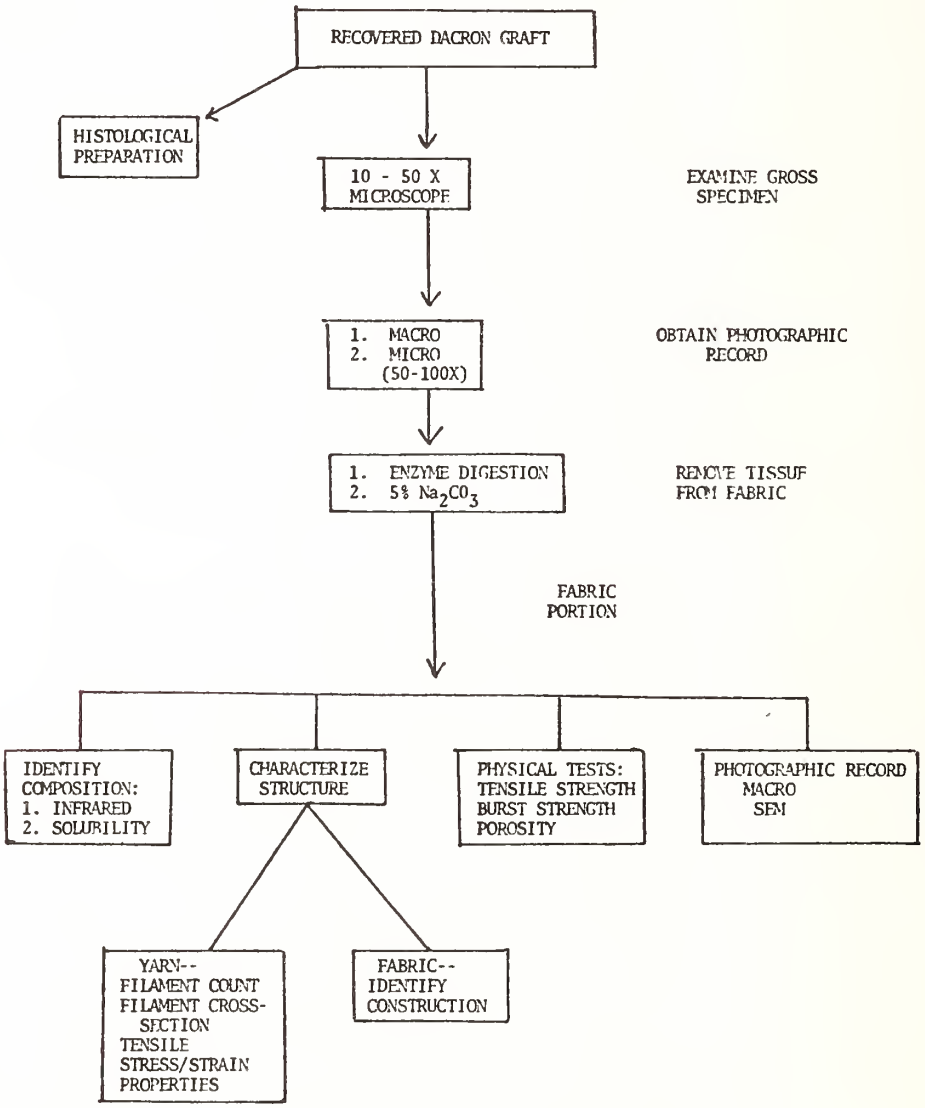
The identity of the graft is checked by visual examination and a filament count of the yarns. Stitch density was measured by counting the number of stitches in each direction using a 1 cm eye piece micrometer. If the sample was a complete cylinder, the diameter was measured and the

*Provided by Ms. K. Botzko, USCI Surgical Products, Box M, Billerica, MA. 01821

total number of stitches around the circumference counted. Individual yarns were unravelled from the graft and were used for tensile tests. The tests were performed on a Tineus Olsen tensile tester using air grips with a 5 cm spacing at 50mm/min crosshead speed.

Dacron Graft Evaluation Protocol*

The following flow diagram illustrates the evaluation program used for the evaluation of retrieved Dacron grafts. The specific tests which are conducted on any graft are based upon the reason for the return of the graft as well as the size and condition of the sample when received by Meadox.



*Provided by Dr. S. Weinberg, Director of Research, Meadox Medicals, 103 Bauer Dr., P.O. Box 530, Oakland, New Jersey 07436

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☐ Document describes a computer program; SF-185, FIPS Software Summary, is attached.

ABSTRACT (A 200-word or less factual summary of most significant information. If document includes a significant bibliography or literature survey, mention it here)

This book contains the proceedings of a conference on implant retrieval and alysis as well as a report on a workshop concerned with implant retrieval systems. enty-six invited papers that were presented at the conference are included. Four bject areas are specifically addressed: bulk phenomena, release phenomena, inter- ce phenomena, and information utilization. Implants of both orthopaedic type and rdiovascular type were considered at the conference. Data on the failure modes of plants were presented. Specific consideration of biocompatability problems was cluded. Several operating data/information systems were described in detail. Rec- mendations were made in the workshop concerned with uniformity and standardization information systems dealing with implant retrieval data.

KEY WORDS (Six to twelve entries; alphabetical order; capitalize only proper names; and separate key words by semicolons)

Analysis; biological; cardiovascular; implants; metals; orthopaedic; polymers; retrieval.

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