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# APEC 17<sup>th</sup> ISTWG Special Seminar on Emerging Infections in Asia Pacific: Proceedings, Monday, August 16, 1999, Seattle, Washington, USA

Ann Marie Kimball and Tiffany G. Harris Editors

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#### U.S. DEPARTMENT OF COMMERCE Technology Administration

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# APEC 17<sup>th</sup> ISTWG Special Seminar on Emerging Infections in Asia

## **Pacific: Proceedings**

Monday, August 16, 1999 Seattle, Washington, USA

Ann Marie Kimball, MD, MPH Tiffany G. Harris Editors

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#### Introduction

#### Ann Marie Kimball, MD, MPH

Associate Professor, University of Washington and Project Director, APEC Emerging Infections Network, United States

Clifford Meyer, MPA

Communications Manager for the APEC Emerging Infections Network, U.S. Delegate to the Past Six Meetings of the APEC Industrial Science and Technology Working Group

Even as financial ills linger for many of the Asia-Pacific Economic Cooperation (APEC) member economies, a recent Seattle meeting of the trade group focused squarely on that other kind of health: human.

The meeting, held in August as part of the APEC Industrial Science and Technology Working Group's semi-annual gathering, brought together some of the Asia-Pacific region's best experts on infectious diseases and outbreak control. By the next day, health officials from Australia, Canada, Japan, South Korea, Malaysia, the United States, and other economies began working on a new plan for increasing the exchange of information and pooling of resources.

Why should APEC concern itself with health issues? APEC's goal of free and open trade between the 21 economies has an irrefutable tie to outbreaks of infectious diseases, which can close borders to the flow of goods and travelers in a matter of hours or days. Just prior to the founding of APEC community in 1989, the global AIDS pandemic reawakened the world to its continued vulnerability to the emergence and transmission of new infectious diseases. Since then, outbreaks have continued to demonstrate the Asia-Pacific region's vulnerability. Hong Kong's experience with "bird flu" in 1997 left six people dead and led to destruction of more

than a million chickens. Increased media presence and interest in epidemics also brought additional public attention to the issue.

Presentations ranged from the issues related to government efforts at controlling recent Nipah virus outbreaks in Malaysia to the potential of global childhood immunization programs being funded by the Gates Foundation. Ultimately, the meetings resulted in a new initiative, led by the United States, to evaluate the capacities of the APEC economies to collaborate further on infectious disease prevention, surveillance, and research.

#### An Overview of the Nipah Virus Encephalitis Outbreak in Malaysia,

#### September 1998 to May 1999

#### Mohamad Taha Arif, MBBS, DPH, AM\*

Disease Control Division, Ministry of Health, Malaysia and the Study Groups

#### Abstract

From September 1998 to May 1999, 265 cases of viral encephalitis with 105 deaths were reported to the Ministry of Health, Malaysia. Of the cases, 194 were serologically confirmed as being caused by the Nipah virus. The infection was transmitted through contact with live pigs. One million infected pigs were culled to contain the outbreak.

Over a 35-week period from the 29 September1998 to 31 May 1999, 265 cases of viral encephalitis were reported to the Ministry of Health, Malaysia. The cluster of cases occurred at four localities and started in the Kinta District of Perak on 29 September. The cases spread 200-km southward to the Sikamat and Bukit Pelandok areas with the movement of infected pigs. The last case, with an onset on 27 May 1999, was reported at Sungai Buloh Selangor. There were 105 fatalities due to the outbreak with a case fatality rate of 39%. Those who were discharged are now being seen for follow-up seven times a year to study the pathophysiology of the disease and to follow-up the clinical progression.

<sup>&</sup>lt;sup>\*</sup> Correspondence: Dr. Mohamad Taha Arif, MBBS, DPH, AM, Director of Disease Control, 2<sup>nd</sup> Floor, Block E, Offices Complex, Jalan Dungun, Damansara Heights, 50490 Kuala Lumpur, Malaysia

The cases typically presented with fever, headache, altered sensorium, myalgia, drowsiness, and other signs and symptoms indicating involvement of the brain and brain stem. The incubation period of the illness was between 15 to 20 days. The disease involved pig farmers and those who had direct contact with infected live pigs. They were mostly young adult Chinese males. Consequently, the public health measures taken were to restrict movement of pigs and to cull pigs at the infected farms. About one million pigs were culled. Farmers were evacuated from infected areas and infected farms were quarantined. A public announcement about the outbreak was made and extensive health education was carried out to advise high-risk groups on self-protection when dealing with pigs. The most effective means of protection is the use of protective clothing and improved personal hygiene. A 24-hour disease control operating room was established at the Ministry of Health that included representation from other ministries. A series of epidemiological studies were conducted to elicit the mode of transmission and risk factors related to human and animal transmission.

A new virus, now named Nipah virus, was discovered at the University of Malaya in March 1999 and on the 18 March was confirmed by CDC Atlanta as *Paramyxovirus*, an enveloped RNA virus, which is closely associated with the Hendra virus that was first isolated in Australia in 1994. With the development of the capture ELISA test using Hendra antigen serology, tests for IgM and IgG were made possible to confirm infection. Subsequently, 194 of the cases were classified as positive for the test. Laboratory diagnosis using serum neutralization test and PCR, and isolation of virus and vaccine development should be carried out in a biosecurity level four laboratory, which Malaysia does not have. There are only two such labs in the area, one in Japan and one in Australia.

Evidence of infection was also seen in dogs, cats, and horses. Flying foxes are suspected to be a natural reservoir. Active surveillance for infected pig farms is continuing. In addition, further research on the natural reservoir and the natural history of the virus and the mechanism and risk factors for infection is being conducted.

The outbreak has damaged the pig farming industry because of the substantial economic loss that occurred from the culling of over one million pigs. This loss is estimated to be at approximately US\$100 million. In addition, Singapore has banned the importation of Malaysian pigs since March 1999. There were also economic losses due to the cost of evacuating people from affected areas. The outbreak has also caused a change in the direction of the future of the pig farming industry.

#### **Further Reading**

- Centers for Disease Control and Prevention. 1999 Apr 30. Update: outbreak of Nipah virus Malaysia and Singapore, 1999. *Morb Mortal Wkly Rep* 48: 335-7.
- Chua K. B., K. J. Goh, K. T. Wong, A. Kamarulzaman, P. S. Tan, T. G. Ksiazek, S. R. Zaki, G. Paul, S. K. Lam, C. T. Tan. 1999 Oct 9. Fatal encephalitis due to Nipah virus among pig-farmers in Malaysia. *Lancet* 354: 1257-9.
- M. N. Mohd. Nor, C. H. Gan, B. L. Ong. 1999 Aug. Nipah virus infection of pigs in peninsular Malaysia. Report submitted to the OIE Chapter of Scientific and Technical Review, 8 Aug 1999. Available online: http://agrolink.moa.my/jph/dvs/nipah/oie990808.html.
- Paton N. I., Y. S. Leo, S. R. Zaki, A. P. Auchus, K. E. Lee, A. E. Ling, S. K. Chew, B. Ang, P.
  E. Rollin, T. Umapathi, I. Sng, C. C. Lee, E. Lim, T. G. Ksiazek. 1999 Oct 9. Outbreak of Nipah-virus infection among abattoir workers in Singapore. *Lancet* 354: 1253-6.

#### Influenza Surveillance in Hong Kong

Mak Kwok Hang, MB, BS, MScPH, FHKCCM, FHKAM\*

## Specialist in Community Medicine, Department of Health, Hong Kong Special Administrative Region, China

Hong Kong has been designated as a WHO Influenza Surveillance Centre for more than three decades. The existing surveillance system consists of sentinel surveillance of influenzalike illnesses involving 92-sentinel sites and laboratory surveillance of specimens collected from hospitals, sentinel points, and outbreak investigations. Government facilities and practitioners in private practice are invited to take part in the surveillance and the government renders support to private labs for surveillance. Communities are provided with intense health education and treatment guidelines. In addition, case definitions are distributed to doctors in the private sector. There is rapid dissemination of surveillance results back to participating sentinel sites.

The surveillance system has been time tested. Hong Kong succeeded in the identifying of the new H3N2 strain in the pandemic of Hong Kong flu in 1968 and in the isolation of two new avian flu viruses from humans (H5N1 virus in 1997 and H9N2 virus in 1999). Such discoveries fully illustrate the importance of influenza surveillance.

Following the identification of the first human case of H5N1 in August 1997, 17 more cases appeared in late 1997. A total of six cases died. The outbreak was brought to an end after slaughtering 1.5 million chickens and other poultry. Poultry exports were suspended voluntarily.

<sup>&</sup>lt;sup>\*</sup> Correspondence: Dr KH Mak, Consultant Community Medicine, Department of Health, 21/F, Wu Chung House, 213, Queen's Road East, Wan Chai, Hong Kong, Fax: (852)-2836-0071

The outbreak resulted in many economic, trade, and political issues. The farmers wanted compensation for the loss of the culled poultry. Chickens are brought into Hong Kong from Mainland China, pointing to the importance of China continuing to conduct surveillance of chicken sources.

This outbreak reconfirmed the need to maintain vigilance in influenza surveillance and the need to establish central slaughtering of the poultry. It also calls for continual efforts and endeavors in international collaboration and surveillance involving specialists and experts from different disciplines and specialties.

#### **Further Reading**

- Anonymous. 1999 Apr 9. Avian strain of influenza A virus isolated from humans in Hong Kong. *Commun Dis Rep CDR Wkly* 9: 131, 134.
- Mounts A. W., H. Kwong, H. S. Izurieta, Y. Ho, T. Au, M. Lee, C. Buxton Bridges, S. W.
  Williams, K. H. Mak, J. M. Katz, W. W. Thompson, N. J. Cox, K. Fukuda. 1999 Aug.
  Case-control study of risk factors for avian influenza A (H5N1) disease, Hong Kong, 1997. J Infect Dis 180: 505-8.
- Peiris M., K. Y. Yuen, C. W. Leung, K. H. Chan, P. L. Ip, R. W. Lai, W. K. Orr, K. F. Shortridge. 1999 Sep 11. Human infection with influenza H9N2. *Lancet* 354: 916-7.
- Snacken R., A. P. Kendal, L. R. Haaheim, J. M. Wood. 1999 Mar-Apr. The next influenza pandemic: lessons from Hong Kong, 1997. *Emerg Infect Dis* 5: 195-203.
- Yuen K. Y., P. K. Chan, M. Peiris, D. N. Tsang, T. L. Que, K. F. Shortridge, P. T. Cheung, W.
  K. To, E. T. Ho, R. Sung, A. F. Cheng. 1998 Feb 14. Clinical features and rapid viral diagnosis of human disease associated with avian influenza A H5N1 virus. *Lancet* 351: 467-71.

# Enterohemorrhagic Escherichia coli (EHEC) Infections and the Government's Responses

#### in Japan

Ken Osaka, MD, MPH\*, Hiroshi Takahashi, MD, PhD, and Sakae Inouye, MD, PhD Infectious Disease Surveillance Center

Haruo Watanabe, MD, PhD

Department of Bacteriology, National Institute of Infectious Diseases, Tokyo, Japan.

#### Abstract

Japan experienced a large-scale outbreak of EHEC O157:H7 infection in Sakai, Osaka, which affected more than 6,000 children and resulted in three deaths in 1996. After the outbreak, various efforts have been made to control the disease from spreading nationwide. These include introducing HACCP, improving national surveillance systems, and strengthening the capacity of outbreak response.

In July 1996, Japan experienced a large-scale EHEC outbreak in Sakai City, Osaka, which was related to a public school lunch program. The outbreak affected more than 6,000 children and resulted in three deaths due to hemolytic uremic syndrome (HUS) (Watanabe et al. 1996, Izumiya et al. 1997). After the investigation, the Ministry of Health concluded that hydroponic radish sprouts served as part of the school lunch program were implicated as the source of the outbreak (Michino 1996). This tragic incident became a wake-up call for the need

<sup>&</sup>lt;sup>\*</sup> Correspondence: Ken Osaka MD, MPH, Infectious Disease Surveillance Center, National Institute of Infectious Diseases, Toyama 1-23-1, Shinjuku-ku, Tokyo 162-8640, Japan; fax: 81-3-5285-1129; e-mail: kosaka@nih.go.jp

for increased awareness of infectious diseases and lead to a variety of countermeasures against the disease. In the following year, two EHEC outbreaks occurred in other prefectures in which hydroponic radish sprouts were also implicated and the DNA fingerprinting pattern of the isolated bacteria from these two outbreaks was identical to that of the isolates from the Sakai outbreak of the previous year. The sprout seeds were found to have been imported from the United States and PCR-amplified DNA fragments of verotoxin was identified in the implicated seeds, although the bacterium was not successfully isolated.

As Japanese consumers avoided radish sprouts, their annual production dropped to 12,800 tons in 1996, which was approximately 40% of the previous year's level. Japanese sprout manufacturers refrained from importing the seeds from the United States and, as a result, the trading volume decreased remarkably from \$3.9 million in 1995 to \$2.2 million in 1996 to \$1.4 million in 1997 (A. M. Kimball, personnel communication).

Thereafter, many investigations have been conducted and the results reveal that the EHEC bacteria, which originates from infected cow feces has widely spread to fruits, vegetables, marine products, and domestic flies. For example, salmon roe (*Ikura*) products processed at a company in Hokkaido were confirmed as the causative foods in diffuse EHEC outbreaks that occurred at *sushi* bars throughout the country in 1998 (Terajma 1999). However, transmission routes of EHEC still remain unclear in most of these outbreaks.

Much effort has been made to tackle this disease, and, as a result, no large-scale outbreaks as serious as that in Sakai have occurred again to date. Annual symptomatic cases remarkably decreased from 17,877 in 1996 to 1,576 in 1997 to 1,455 in 1998. However, the reported number of EHEC isolations has not decreased (2,793 in 1996, 1,782 in 1997, and 2,021 in 1998) (Figure 1).

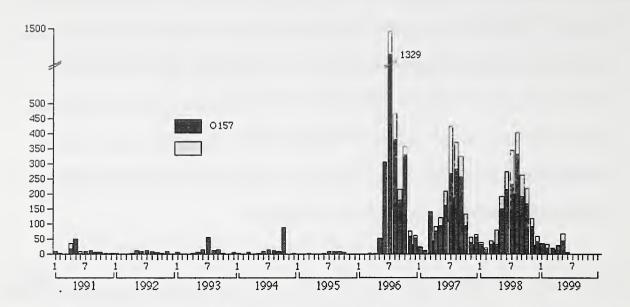


Figure 1. Number of EHEC isolates reported from the Prefectural Public Health Institutes in Japan, January 1991 through June 1999.

The Ministry of Health decided to include EHEC infection in the list of nationally notifiable diseases in August 1996, a month after the Sakai outbreak. The Ministry of Agriculture and the Ministry of Health organized a task force to update the radish sprouts production manual. HACCP (Hazard Analysis Critical Control Point) methods were actively introduced, and feedback of sampling examination was made mandatory in the new manual. The Ministry of Education also distributed a special notification to the Board of Education of all Prefectural Governments to enforce sanitary protocol for school lunch programs.

The National Institute of Infectious Diseases (NIID) was encouraged to disseminate new techniques to detect EHEC, such as pulsed-field gel electrophoresis (PFGE) and random amplification of polymorphic DNA (RAPD), to PHIs. The Ministry approved several commercial diagnostic kits for EHEC. These new techniques contributed to the detection of various serotypes of EHEC in addition to O157:H7.

The disease surveillance systems have also been strengthened. The government revised the 100-year-old Infectious Diseases Control Law and the new law came into effect in April 1999. Reportable infectious diseases are categorized into four groups according to the impact on public health and the severity of the disease. EHEC was in the category III reportable disease under the new law (NIID 1998). An electronic reporting system was developed and it has been in service. Prompt feedback of the surveillance results has been promoted through an Internet web-site and both the weekly and monthly reports, "Infectious Diseases Weekly Report (IDWR)" and "Infectious Agent Surveillance Report (IASR)", are regularly posted (http://idsc.nih.go.jp/index.html). Geographical distribution maps presenting the trends of EHEC outbreaks and revealing high-risk areas, using a geographical information system (GIS), are included in the reports (Figure 2).

A two-year on-the-job field epidemiology-training program (FETP) started at the Infectious Disease Surveillance Center (IDSC) in collaboration with CDC (USA) in September 1999. Five physicians from the health departments of the local Department of Health and the Universities enrolled in the program in 1999. These medical epidemiologists are expected to participate in EHEC and other outbreak investigations.

Globalization of food distribution and human travel is rapidly growing. More than 15 million Japanese, which is approximately 13% of Japan's citizens, went abroad in 1998. Fiftynine percent of Japanese calorie intake depends upon imported food. Under such circumstances, international exchange of information on foodborne illness is becoming more urgent. In addition, international investigation teams from multiple countries should be formed when outbreaks cross the boundary.



Figure 2: Geographical Distribution of Symptomatic Cases of *E. coli* O157:H7 per 100,000 in Japan, 1998.

#### References

- Izumiya H., J. Terajima, A. Wada, Y. Inagaki, K. I. Itoh, K. Tamura, and H. Watanabe. 1997. Molecular typing of enterohemorrhagic *Escherichia coli* O157:H7 isolates in Japan by using pulsed-field gel electrophoresis. *J Clin Microbiol* 35: 1675–80.
- Michino H., Araki K., Minami S., Takaya S., Sakai N, Miyazaki M., Ono A., and Yanagawa H.
  Massive Outbreak of Escherichia coli O157:H7 Infection in Schoolchildren of Sakai City,
  Japan, Associated with Consumption of White Radish Sprouts. Am J Epidemiol
  1999;150:787-96
- National Institute of Infectious Diseases and Infectious Diseases Control Division, Ministry of
   Health and Welfare of Japan. 1998. Enterohemorrhagic Escherichia coli infection, 1996
   April 1998. Infectious Agents Surveillance Report 19: 122–123.
- National Institute of Infectious Diseases and Infectious Diseases Control Division, Ministry of Health and Welfare of Japan. 1998. The National Epidemiological Surveillance of Infectious Diseases in compliance with the enforcement of the new Infectious Diseases Control Law. *Infectious Agents Surveillance Report* 19: 122–123.
- Terajma J., H. Izumiya, S. Iyoda, K. Tamura, and H. Watanabe.1999. Detection of a multiprefectural *E. coli* O157:H7 outbreak caused by contaminated Ikura-sushi ingestion. *Jpn. J. Infect. Diseases* 52: 51–52.
- Watanabe H., A. Wada, Y. Inagaki, K. Itoh, K. Tamura. 1996. Outbreaks of enterohaemorrhagic *Escherichia coli* O157:H7 infection by two different genotype strains in Japan, 1996. *Lancet* 348: 831–2.

#### **Further Reading**

- Fukushima H., T. Hashizume, Y. Morita, J. Tanaka, K. Azuma, Y. Mizumoto, M. Kaneno, M. Matsuura, K. Konma K., Kitani T. 1999 Apr. Clinical experiences in Sakai City Hospital during the massive outbreak of enterohemorrhagic *Escherichia coli* O157 infections in Sakai City, 1996. *Pediatr Int* 41: 213-7.
- Michino H., K. Araki, S. Minami, S. Takaya, N. Sakai, M. Miyazaki, A. Ono, H. Yanagawa. 1999 Oct 15. Massive outbreak of *Escherichia coli* O157:H7 infection in schoolchildren in Sakai City, Japan, associated with consumption of white radish sprouts. *Am J Epidemiol* 150: 787-96.
- Takeda Y. 1997. Enterohaemorrhagic Escherichia coli. World Health Stat Q 50: 1-2, 74-80.
- Watanabe Y., K. Ozasa, J. H. Mermin, P. M. Griffin, K. Masuda, S. Imashuku, T. Sawada. 1999
   May-Jun. Factory outbreak of Escherichia coli O157:H7 infection in Japan. *Emerg Infect Dis* 5: 424-8.

#### Surveillance of antibiotic resistance in Neisseria gonorrhoeae in the

#### WHO Western Pacific Region

#### John Tapsall, MBBS, FRCPA, MD\*

WHO Western Pacific Region Collaborating Centre for STD and HIV, Australia

#### Abstract

Antibiotic resistant strains of *Neisseria gonorrhoeae* hamper effective treatment of gonorrhea in the WHO Western Pacific Region. A program of surveillance of gonococcal susceptibility to antibiotics, GASP, continued in the region in 1998. A high proportion of isolates in many participating countries was resistant to quinolones and penicillins, continuing trends observed by this program since 1992. Resistance to the later generation cephalosporins and to spectinomycin was absent or infrequent. Options for effective treatment of gonorrhea in the region have been severely compromised by antibiotic resistance.

Globally gonorrhea remains a major disease, but about half the total estimate of 60 million cases per year occur in the WHO Western Pacific (WP) and South East Asian (SEA) regions. One essential element for control of gonorrhea is the provision of effective antibiotic treatment. Appropriate therapy also reduces morbidity associated with gonorrhea. The amplification of HIV transmission, which occurs in the presence of gonorrhea, can also be

<sup>&</sup>lt;sup>\*</sup> Correspondence: John Tapsall, MBBS, FRCPA, MD, The Prince of Wales Hospital, Randwick, Sydney, New South Wales, Australia 2031; fax + 61 2 9398 4275; e-mail: j.tapsall@unsw.edu.au

ameliorated with correct treatment (Cohen 1998). Thus, there are a number of important reasons why gonococcal disease should be properly treated.

The gonococcus has a well-developed capacity to become resistant to antibiotics. Historically much of this resistance has appeared first in the WP and SEA regions. There is however a strong correlation between likely outcome of antibiotic therapy and the *in vitro* susceptibility of gonococci. This means that if the susceptibility of prevalent gonococci to antibiotics is determined systematically using an epidemiological approach, a timely and reliable guide to the choice of suitable standard treatment regimens can be provided in a country or region. The WHO WP Gonococcal Antimicrobial Surveillance Programme (WPR GASP) functions at a regional level and has monitored the antibiotic susceptibility of gonococci isolated in the WPR since 1992.

Sixteen WPR countries contributed data on about 10,000 isolates in 1998. Resistance to the penicillin group remained widespread. The highest rates of penicillin resistance were reported by Korea (90%), the Philippines (82%), Vietnam (76%), Mongolia (70%), China-Hong Kong (69%), China (62%), and Singapore (59%). Resistance to the quinolone antibiotics (QRNG) continued to increase in a number of centers and was maintained in others as a high proportion of the isolates examined in 1998. Quinolone resistance in gonococci is incremental and due to different but additive chromosomal changes. This means that levels of resistance in QRNG, as determined by MICs, show a sequential change. It is therefore relevant to monitor both low (MIC of ciprofloxacin = 0.06 to 0.5 mg/L) and high level (MIC of ciprofloxacin  $\geq 1$  mg/L) resistance to quinolone antibiotics. Quinolone resistance was assessed in thirteen countries in 1998 and QRNG were found in 11, the exceptions being Fiji and the Solomon Islands. More than 90% of the isolates in China and China-Hong Kong were QRNG and about

half in each setting possessed high level resistance. The Philippines (63%) had a high proportion of high level QRNG, continuing a pattern observed for some time. Korea (62%) and Japan (52%) again reported a high percentage of QRNG, mostly in the category of lower level QRNG. Other centers such as Vietnam, Papua New Guinea, and Singapore had a lower proportion of mixed low and high level QRNG. In other countries, including Australia and New Zealand, QRNG are most often represented by imported strains, but with some endemic transmission also occurring. The data from the WPR show that more countries recorded the presence of QRNG, the proportion of QRNG in these countries has increased, and the MICs in those QRNG present were higher.

Although some increase in MICs to ceftriaxone was again noted, all isolates remained sensitive to the third generation cephalosporin ceftriaxone. Spectinomycin resistance is rarely encountered in the WPR and only in sporadic cases. Tetracyclines, although not a recommended treatment for gonorrhea, are still widely used in the WPR and a special form of high level resistance to tetracyclines (TRNG) exists. TRNG have been clustered in certain countries in the WPR, notably Singapore and Malaysia, for some time. Centers with a high rate of TRNG in 1998 were Singapore (80%), the Solomon Islands (75%), and Vietnam (36%). Six other centers had TRNG rates of less than 10% and in Japan and Korea no TRNG were detected. Other agents such as chloramphenicol or gentamicin are sometimes used in the WPR mainly because of cost considerations. Data on the resistance patterns to these antibiotics are scanty.

The changes observed in the 1998 susceptibility patterns of gonococci found in the region are incremental. However, there was an increase on top of an already high and worrying level of resistance. The observations confirm the limited options for treatment in the WPR of a disease with high incidence. Withdrawal of an antibiotic should occur when resistance levels reach 5%,

but the treatment options then available are often in a cost bracket that makes their use difficult even when they are a "recommended" treatment. However, substitution of cheaper, but less efficacious agents is, in the longer term, more expensive and counter productive.

Acknowledgments: The following members of the WHO WPR GASP supplied data in 1998: Members of the Australian gonococcal surveillance programme; Ye Shunzhang and Su Xiaohong China; M. Shah, Fiji; K. M. Kam, Hong Kong; Toshiro Kuroki, and M. Tanaka, Japan; K. Lee and Y. Chong, Korea; Erdenechimeg Lkhamsuren, Mongolia; B. Garin, New Caledonia; M. Brett and M. Brokenshire, New Zealand; Tony Lupiwa, Papua New Guinea; C.C. Carlos, Philippines; A.E. Ling, Singapore; A. Darcy, Solomon Islands; Ane Tone Ika, Tonga; H. Wamle, Vanuatu; Le Thi Phuong, Vietnam.

#### References

- Cohen M. S. 1998. Sexually transmitted diseases enhance HIV transmission: no longer a hypothesis. *Lancet* 351[suppl III]: 5–7.
- WHO Western Pacific Region Gonococcal Surveillance Programme. 1997. Surveillance of antibiotic susceptibility of *Neisseria gonorrhoeae* in the WHO Western Pacific Region 1992–4. *Genitourin Med* 73: 355–361.

#### **Further Reading**

- Gerbase A. C., J. T. Rowley, D. H. L. Heymann, S. F. B. Berkley, P. Piot. 1998. Global prevalence and incidence estimates of selected curable STDs. Sex Transm Inf 74[suppl 1]: S12–S16.
- Ison C. A., J. A. Dillon, J. W. Tapsall. 1998. The epidemiology of global antibiotic resistance among Neisseria gonorrhoeae and Haemophilus ducreyi. Lancet 351(Suppl III): 8-11. (Published erratum appears in Lancet 1998 Oct 17; 352(9136): 1316.)
- Tapsall J. W. 1995. Surveillance of antibiotic resistance in *Neisseria gonorrhoeae* and implications for the therapy of gonorrhoea. *Int J STD AIDS* 6: 233-236.
- Tapsall J. W., E. A. Limnios, T. R. Shultz. 1998 Sep. Continuing evolution of the pattern of quinolone resistance in *Neisseria gonorrhoeae* isolated in Sydney, Australia. *Sex Transm Dis* 25: 415-7.
- WHO Western Pacific Gonococcal Antimicrobial Surveillance Programme-WHO WPR GASP.
   1998 Dec 24. Resistance in gonococci isolated in the WHO Western Pacific Region to various antimicrobials used in the treatment of gonorrhoea, 1997. *Commun Dis Intell* 22: 288-91.

### Global Childhood Immunization for the 21<sup>st</sup> Century

James E. Maynard, MD, PhD\*

# Senior Vice President and Medical Director, PATH and Technical Director, Bill and Melinda Gates Children's Vaccine Program, United States

#### Rationale for the Bill and Melinda Gates Children's Vaccine Program

The International Declaration of the Rights of the Child states, "Every child has the right to the timely receipt of the needed life saving vaccines without regard to their socioeconomic status or country." Since 1991, there have been decreases in routine immunization coverage in many of the poorest countries. The rich are getting richer and the poor poorer. New vaccines have been developed and are routinely being used in developed countries, but not in developing countries. Newer vaccines are biotech inventions and therefore cost more and are encumbered by trade agreements. The vaccines are available, yet millions of children continue to die.

#### **Guiding Principles**

The Program will work with global partners to upgrade and improve routine immunization aimed at the poorest countries. Primary responsibility for guiding the implementation of these efforts rests with WHO and UNICEF through the Expanded Program on Immunization (EPI). Our Program will work to strengthen the role of those institutions in promoting and sustaining routine immunization, which is the bedrock of EPI.

<sup>&</sup>lt;sup>\*</sup> Correspondence: James E. Maynard, MD, PhD, PATH Seattle and Headquarters, 4 Nickerson Street, Seattle, WA 98109-1699 USA

The primary obstacle in improved global childhood immunizations is financial, not technical. Until we solve the problem of financing sustainable immunization delivery services to include newer lifesaving vaccines for all children who need them, global equity will not be achieved.

#### Issues of Concern with Purchasing and Distribution of Vaccines

The first problem is that early corporate profit taking by vaccine producers in richer countries delays the introduction of vaccines to poorer nations until the cost of vaccine development is recovered. Secondly, immunization is and must remain a public sector responsibility. Cost recovery systems, which require individual families to pay for vaccines for their children, may act to deprive children of needed vaccination because of inability to pay. This kind of access system denies equity and should not be applied to vaccines. Health care reform that decentralizes responsibility for vaccine procurement may result in adverse effects such as increased vaccine prices and reduced vaccine quality. This kind of decentralization must be avoided.

#### Advocacy

Advocacy is a key ingredient. It must contain the essential elements of vision and strategy, and be clear and unambiguous. All agencies involved in immunization efforts must have the same vision and priorities. Middle level commitment is not enough. Heads of international agencies must take up the fight.

#### Financing

Adequate immunization financing is the key element to global equity of access. Rich nations must recognize and reassure a continuous assistance to poor nations in order to achieve immunization equity.

#### Activities

To date, cooperative agreements have been made with WHO, UNICEF, and other organizations that provide support for Hepatitis B and Hib vaccine introduction activities and support for participation in a new global initiative. Ongoing activities include country assessments, advocacy, and financing. The Program also has been recently successful in securing a \$750 million commitment from the Bill and Melinda Gates Foundation for the establishment of the Global Fund for Children's Vaccines.

## Further Reading

Bill and Melinda Gates Children's Vaccine Program website:

http://www.path.org/childvac/index.htm.

Ferber D. 1998 Dec 11. Pediatric vaccines. Gates launches \$100 million initiative. *Science* 282: 1971.

#### International Networking – Addressing the Challenge of Emerging Infections

Ann Marie Kimball, MD, MPH\*

Associate Professor, University of Washington and Project Director, APEC Emerging Infections Network, United States

International networking has become a burgeoning area of endeavor with the increased availability of electronic communications. Networks related to "Health" as a domain have been set up globally, regionally, nationally, and among a variety of interest groups. While there is no comprehensive catalogue of such networks, at least three have been operating in the Asia Pacific region with some consistency over the past five years in the areas of prevention and control of infectious diseases. They are ProMED-mail, which offers a disease alert service; SEA-AIDS, which offers an unmoderated list that discusses issues of HIV/AIDS prevention and control in Southeast Asia; and EINET, which focuses on emerging infections. This presentation will describe and compare and contrast two disease alert networks active in Asia Pacific: ProMEDmail and EINET. We will further contrast EINET with its counterpart in the European Union, which is known as "EuroSurveillance."

ProMED-mail (Program for Monitoring Emerging Diseases) is a worldwide system of electronic mail communications that has joined scientists interested in new or reemergent infectious diseases. ProMED-mail works via electronic mail and has become a prototype for other such moderated lists. ProMED-mail breaks into the users' email irregularly, depending on the timing of information provided to the moderator for distribution to the list. Information

<sup>&</sup>lt;sup>\*</sup> Correspondence: Ann Marie Kimball, MD, MPH, School of Public Health and Community Medicine, University of Washington, Box 357660, Seattle, WA 98195-7660

sources are diverse, and the "strings" of conversation about a given topic are carried forward a variable amount of time. ProMED-mail has also established a web site and an archival service for its participants. Its service is free and financed by grant support. ProMED-mail 's user group is diverse, as are those who contribute information to it. Participants include scientists, students, public health officials, news organizations, and reporters. Access is open and all information is available to all users.

The APEC EINET (Emerging Infections Network) was established in 1996. The original vision for this effort was a surveillance and monitoring network. However, experience in the first three years of activity has resulted in the current network, which is actually a disease alert and information network rather than a true surveillance network. EINET is similar to ProMED-mail in a number of aspects: it is a "free" service, financed by public funds and available to users without cost and its usership is diverse and includes scientists, public health workers, and others with an interest in its content. It differs from ProMED-mail in that it is a regional network that focuses on membership from within the Asia Pacific Economic Cooperation; it addresses emerging infections that are of importance to trade and travel within the geographic region of the Asia Pacific; it is moderated and regular in the provision of information; and its sources of information are largely from outside its usership, although information from the network users is also used.

The telecommunications technology that is used in these two networks is similar, and relies heavily on connectivity over telephone lines and hubs of information processing at internet servers. Both networks include a website. The website developments of these networks are not the same, and viewing the websites provides additional insight into the unique nature of each effort. The ProMED-mail site includes an attempt to catalogue and map resources for prevention

and control of infectious diseases by region. (Figure) This effort remains in an early stage of development. The EINET site included a password-protected site for viewing recent multidrug resistant tuberculosis surveillance data, however, the quality and timeliness of data from the



Figure 1. ProMED-mail Inventory of Asia Resources for Combating Infectious Diseases.

member economies was not adequate to sustain this site. Now the focus of the EINET site includes distance-learning materials for teaching emerging infections, and these materials are updated regularly. In addition, the EINET site links to other companion sites relevant to the Industrial Science and Technology Working Group of APEC.

Just as the APEC EINET activity seeks to bring timely information about outbreaks and new information on prevention to its users in the APEC trading community, the EuroSurveillance Network serves the European Union (EU) trading community. However, these two efforts reflect the organizational differences in their user groups. The EU network benefits from the government-to-government treaty basis of that organization, and has through the Maastricht Treaty extended that legal mandate to the area of infectious disease surveillance. In contrast, the APEC group exists largely through consensus building rather than formal treaties among its partner economies. As a consequence, there is no treaty or legal basis for EINET to carry out disease surveillance, although it is a formal project of the APEC working ISTWG group. Secondly, the formality of user access to the EuroSurveillance network depends upon gatekeepers at each member nation who broker the acceptance of information to be shared and the access of those who share it. This contrasts sharply to the informal and open access of EINET. Lastly, orchestration across laboratories for development of protocols for pathogen isolation, identification, and description has been facilitated through the government-togovernment cooperation of the EU. This level of cooperation is not in place within APEC. Thus the laboratory-based surveillance of Salmonella (SALM-NET), which has successfully identified trade-related outbreaks, such as S. agoni and others, is not in place within APEC. (Table)

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Outbreak	# of Cases	Countries with Cases
<i>E. coli/</i> HUS	12	Denmark, England & Wales, Finland, Sweden
S. anatum	24	Eire, England & Wales, France, Scotland
S. agona	2000+	Canada, England & Wales, Israel, USA
S. dublin	30+	France, Switzerland
S. stanley	100+	Finland, USA
S. tosamanga	28	Eire, England & Wales, France, Germany, Sweden, Switzerland
Shigella sonnei	100+	England & Wales, Germany, Norway, Scotland, Sweden

Table. International Outbreaks Recognized and Investigated by SALM-NET.

These three networks are only three among literally hundreds of health related networks, which are in place or in the process of using electronic communications. These networks provide some illustration of the utility and flexibility electronic communications provide in disease alert and information sharing across international boundaries. Over time, these applications will continue to evolve. Thus, efforts to track and understand the utility, limits, and generalizability of these networking experiences will eventually provide insight into new directions and some guidelines for new developments in the field.

# **Further Reading**

APEC Emerging Infections Network URL: http://www.apec.org/infectious/

EuroSurveillance URL: http://www.ceses.org/eurosurv/eurosurv.htm

- Kimball A. M., C. A. Horwitch, P. W. O'Carroll, S. Arjoso, C. Kunanusont, Y. S. Lin, C. M. Meyer, L. E. Schubert, P. L. Dunham. 1999 Aug. The Asian Pacific Economic Cooperation Emerging Infections Network. Am J Prev Med. 17: 156-8.
- Kimball A. M., C. A. Horwitch, P. W. O'Carroll, S. Arjoso, C. Kunanusont, Y. S. Lin, C. Meyer,
  L. Schubert, P. Dunham. 1998 July-September. The APEC Emerging Infections
  Network: prospects for comprehensive information sharing on emerging infections within the Asia Pacific Economic Cooperation. *Emerg Infect Dis* 4: 472.
  ProMED-mail URL: http://www.promedmail.org:8080/promed/promed.folder.home

SEA-AIDS URL: http://www.hivnet.ch:8000/asia/sea-aids/

#### Food Safety and PulseNet

John Kobayashi, MD, MPH\*

Senior Epidemiologist, Communicable Disease Epidemiology Section, WA State Department of Health

For many years, Washington State has been a leader in surveillance and investigation of foodborne disease outbreaks. In 1993, the Washington State Department of Health identified the source of America's largest foodborne *E. coli* O157:H7 epidemic (Bell et al. 1994). While we identified the outbreak source within five days of our first notification, and were able to confiscate over 60 percent of the contaminated meat (over 250,000 hamburger patties), over 600 people became ill.

Since 1993, we have obtained funds from the US Centers for Disease Control and Prevention to perform DNA fingerprinting of *E. coli* O157:H7 and other bacteria through the PulseNet System (Gautom 1997). This allows us to look at *E. coli* at a much finer level, suggesting links that might be otherwise unrecognizable. While DNA fingerprinting existed in 1993, it was only available months after the outbreak. Since then, it has become a routine part of *E. coli* O157:H7 surveillance. Since 1996, these fingerprints have been stored in computers and sent electronically to the CDC and other state health departments. We have expanded this technique to other pathogens such as *Salmonella* and *Legionella*. These improvements have made it possible to investigate outbreaks sooner, quicker, and when they are smaller.

<sup>&</sup>lt;sup>\*</sup> Correspondence: John Kobayashi, MD, MPH, WA DOH, 1610 NE 150th St., MS: K17-9, Shoreline, WA USA 98155

In 1996, nationally distributed apple juice was identified as the outbreak source by using DNA fingerprinting and good epidemiology when only 10 cases occurred (Cody 1999). DNA fingerprinting also identified Washington residents involved in an *E. coli* O157:H7 outbreak in Alpine, Wyoming. A *Campylobacter jejuni* outbreak due to contaminated water in Canada was also identified through DNA fingerprinting when travelling Washington State residents became ill. In 1998, with only two *E. coli* O157:H7 cases, we identified the source of illness as a state fair, which was attended by over 1 million people. We are convinced that adequate cooking of hamburgers and sanitary measures prevented many other illnesses. Recently DNA fingerprinting was used in a multi-state *Salmonella* muenchen outbreak in which contaminated orange juice was the source of infection (Anonymous 1999).

In modern times, it seems that people, foods, and infectious agents are more mobile than ever before. Outbreaks can be widespread and scattered. The scenario for foodborne illness has shifted from the traditional "church dinner" or other event related outbreak to widespread, sometimes-simultaneous outbreaks. Food-production is now cheap and massive and food products are rapidly distributed. In epidemiology, we are continually reminded that we live in one world and that infectious diseases generally do not respect political boundaries. Techniques for investigating foodborne outbreaks need to match this changing scenario. We can compensate for this challenge by doing our work better and faster and by identifying problems at a smaller stage before they become big. New technologies like DNA fingerprinting and the Internet can help us do that, when used with old tools, such as the public health infrastructure, good field epidemiology, and teamwork across county, state, agency, national, and international lines.

## References

- Anonymous. 1999 Jul 16. Outbreak of *Salmonella* serotype Muenchen infections associated with unpasteurized orange juice United States and Canada, June 1999. *Morb Mortal Wkly Rep* 48: 582-5.
- Bell B. P., M. Goldoft, P. M. Griffin, M. A. Davis, D. C. Gordon, P. I. Tarr, C. A. Bartleson, J. H. Lewis, T. J. Barrett, J. G. Wells, R. Baron, J. Kobayashi. 1994 Nov 2. A multistate outbreak of *Escherichia coli* O157:H7–associated bloody diarrhea and hemolytic syndrome from hamburgers: the Washington State experience. *JAMA* 272: 1349.
- Cody S. H., M. K. Glynn, J. A. Farrar, K. L. Cairns, P. M. Griffin, J. Kobayashi, M. Fyfe, R. Hoffman, A. S. King, J. H. Lewis, B. Swaminathan, R. G. Bryant, D. J. Vugia. 1999 Feb
  2. An outbreak of *Escherichia coli* O157:H7 infection from unpasteurized commercial apple juice. *Ann Intern Med* 130: 202-209.
- Gautom R.K. 1997 Nov. Rapid pulsed-field gel electrophoresis protocol for typing of *Escherichia coli* O157:H7 and other gram-negative organisms in 1 day. *J Clin Microbiol* 35: 2977-80.

# **Further Reading**

- Proctor M. E., R. Brosch, J. W. Mellen, L. A. Garrett, C. W. Kaspar, J. B. Luchansky. 1995 Aug. Use of pulsed-field gel electrophoresis to link sporadic cases of invasive listeriosis with recalled chocolate milk. *Appl Environ Microbiol* 61: 3177-9.
- Thong K. L., S. Puthucheary, T. Pang. 1998 Jan-Mar. Outbreak of Salmonella enteritidis gastroenteritis: investigation by pulsed-field gel electrophoresis. Int J Infect Dis 2: 159-63.
- Threlfall E.J., L. R. Ward, M. D. Hampton, A. M. Ridley, B. Rowe, D. Roberts, R. J. Gilbert, P. Van Someren, P. G. Wall, P. Grimont. 1998 Oct. Molecular fingerprinting defines a strain of *Salmonella enterica* serotype Anatum responsible for an international outbreak associated with formula-dried milk. *Epidemiol Infect* 121: 289-93.
- Threlfall E.J., M. D. Hampton, L. R. Ward, I. R. Richardson, S. Lanser, T. Greener. 1999 Sep.
  Pulsed field gel electrophoresis identifies an outbreak of *Salmonella enterica* serotype
  Montevideo infection associated with a supermarket hot food outlet. *Commun Dis Public Health* 2: 207-9.
- Wegener H. C., D. L. Baggesen. 1996 Sep. Investigation of an outbreak of human salmonellosis caused by Salmonella enterica ssp. enterica serovar Infantis by use of pulsed field gel electrophoresis. Int J Food Microbiol 32: 125-31.

#### Summary

### Ann Marie Kimball, MD, MPH

Associate Professor, University of Washington and Project Director, APEC Emerging Infections Network, United States

The Seattle Special Seminar on Emerging Infections in Asia Pacific demonstrated three things. The first is that there is a strong interest among trade delegates in the subject of emerging infections, and a general appreciation of the pertinence of such infections to the activities of international trade and commerce. Secondly, the presentations of the speakers attest to the frequency with which new and emergent infections occur and are having an impact upon the economies of the region. Thirdly, the experience of coping with outbreak situations is a common one, and themes were repeated across the diverse scenarios presented which are important to understand as generalizations of this experience.

Themes that were emphasized by the speakers included the importance of information. Both access to timely information about new pathogens and sharing of information with concerned parties were emphasized. The difficulties of working across sectors and bureaucratic structures were frankly discussed and were repeated in each scenario. The need for technical excellence in diagnostics and investigation were emphasized, implying a need for additional investment in this area in the region. Although international assistance was uniformly acknowledged as important, the need to assure adequate and timely laboratory support "at home" was also brought forward. As we move into the new millenium, trade will continue to expand in our region. Trade represents an important avenue for advancing development and improving the quality of life for our peoples. However, the need to "trade safely" and the awareness of health investment as a necessary cost of doing business cannot be overstated.