Conference Session Summaries[1]

Healthcare Settings as Amplifiers of Infectious Disease[2]

Global outbreaks of severe acute respiratory distress syndrome (SARS) in 2003 demonstrated the potential of healthcare facilities to serve as amplifiers of a new communicable disease. However, healthcare settings can also be amplifiers of multidrug-resistant bacteria and bloodborne viruses.

In the public health and healthcare delivery systems, amplifying forces include weaknesses in communication, coordination, early detection and control of emerging diseases, and oversight of healthcare services. Among healthcare personnel, weaknesses include gaps in infection control knowledge and practice.

SARS was spread globally by relatively few people and amplified by super-spreading events that occurred primarily in healthcare settings. Healthcare personnel were disproportionately affected, accounting for up to 57% of cases in some countries. The combination of increasing infectivity in the later stages of SARS, performance of the aerosol-generating procedures (bronchoscopy, intubation), and clustering of SARS patients further enhanced transmission of the SARS-associated coronavirus.

Systems for early detection and isolation of persons with suspected SARS and public quarantine effectively reduced transmission. Conversely, absence of control measures at initial points of patient encounter, particularly in hospital emergency departments, rendered hospitals particularly vulnerable to SARS transmission.

Unsafe injection and blood donation practices have contributed to the global spread of bloodborne viral diseases. Worldwide, unsafe injections alone are estimated to cause 21,000 cases of hepatitis B, 2,000 cases of hepatitis C, and 260 cases of HIV each year. Countries with limited resources are at a disproportionate risk for adverse injection-related outcomes. While lack of sterile supplies is important, unnecessary injections and poor understanding of infection control principles and practices also contribute to the spread of bloodborne viruses. These last two factors are not unique to the developing world. Four recent outbreaks of hepatitis B and C viruses in patients in ambulatory care facilities in the United States are a reminder that unsafe injections can occur in any healthcare setting. In these outbreaks, a lack of administrative oversight and poor understanding of infection control practices contributed to the contamination of multidose vials or the reuse of injection equipment and transmission of hepatitis B or hepatitis C virus to numerous patients.

In contrast to SARS and bloodborne viruses, the rise and amplification of multidrug-resistant organisms in healthcare settings have been gradual and subtle. These organisms limit treatment options, increase transmission risks for vulnerable patient populations, increase illness and death, prolong the hospital stay, and add to healthcare costs. The rise of these organisms has been most dramatic in U.S. intensive care units, where 50% of *Staphylococcus aureus* isolates are resistant to methicillin (MRSA) and 25% of enterococcal isolates are resistant to vancomycin. Cases of vancomycin-intermediate *S. aureus* and three recent cases of vancomycin-resistant *S. aureus*, both in outpatient settings, attest to the potential for amplification of these organisms in healthcare settings. Gram-negative organisms resistant to extended-spectrum β-lactamases present similar concerns and have been associated with numerous outbreaks in healthcare facilities.

The problem of multidrug-resistant organisms is multifaceted. While colonized and infected patients constitute the major reservoir for dissemination of these organisms, inappropriate use or overuse of antimicrobial agents contributes to acquiring and expressing resistance genes. Healthcare settings become breeding grounds of additional resistance and distribution centers for amplification of multidrug-resistant organisms to other healthcare settings and the community.

The notion that our healthcare settings contribute to the amplification of infectious disease contradicts our expectations. Usually, healthcare systems work well, and quality healthcare is delivered safely and efficiently. Nonetheless,

[1]Authors are the session moderators; first author for each session is the rapporteur. Actual presenters of sessions are listed in footnotes. More session summaries are available at http://www.cdc.gov/ncidod/EID/vol10 no11/iceid.htm.

[2]Presenters: Mark Loeb, McMaster University; Yvan Hutin, World Health Organization; and Larry Strausbaugh, Portland Veterans Administration Medical Center.

there are gaps in infrastructure, knowledge, and practice that can open the door to disease outbreaks.

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Transformation of the Developing World: Socioeconomic Matrix[1]

Economic disparity affects the health of persons around the world, and various societal, environmental, and economic factors influence the emergence of infectious diseases. Similarly, emerging infectious diseases have a social and economic impact, including diminished economic productivity, increased expenditures on public heath, deferred external investment and development, and reduced travel and retail sales.

The thriving consumer demand for exotic and rare animals as “tonic” food in China, especially in the southern regions, raises concern for the risk for animal-human cross-infections through contact with live and recently slaughtered animals. The increased demand for civet cat, suspected as the source of severe acute respiratory syndrome, is one such example. The demand for tonic food has risen with improving economic conditions in post-1978 China and is a form of conspicuous consumption that expresses economic and social distinction and prestige. A Chinese medical paradigm based on “humors” inherent in the concept of tonic food, combined with the well-understood cultural symbolism of distinction and prestige associated with conspicuous consumption, has lent weight to the demand for rare and exotic animals perceived to be “pure,” “safe,” and “virile.” Since this rising demand is not likely to be suppressible, regulated production of these animals is needed to make them safe.

Additional contemporary issues in China include the effect of migration and urbanization on the spread of sexually transmitted diseases. The forces driving this effect can be divided into three overlapping categories: the dismantling of the organizational and spatial structures that helped keep order in China's cities during the Maoist era (from 1949 to 1978); a dramatic increase in the overall fluidity of urban societies in China (accompanied by the erosion of traditional moral and behavioral boundaries); and a new set of cultural values that has encouraged more urban Chinese to think of themselves as actors with individual agency. These overlapping forces, which are geographic, socioeconomic, and cultural, are interwoven with and thoroughly implicated in the emergence of new behavior and lifestyles that have put a growing number of Chinese at risk for infectious diseases.

More broadly, climate can also affect public health and emerging infectious diseases. Factors affecting emergence can also be examined in an eco-epidemiologic framework that can often drive epidemics. Examples include the effects of rains and flooding on vector-borne and diarrheal diseases and the effect of heat and fires on respiratory infections.

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Emerging Issues for the Public Health Laboratory[2]

U.S. public health laboratories face challenges from within and outside the system, including emergence of new pathogens, introduction of new testing methods, new security requirements, shortages of well-qualified personnel, and collaboration with new partners.

The public health system depends on hospital and commercial laboratories as major sources of reliable epidemiologic information. Thus, the current crisis in these laboratories is of great concern. The pressures come from the need to address emerging infectious diseases, detect antimicrobial resistance, and recognize potential agents of bioterrorism while updating procedures, practices, and facilities to meet new biosafety, biosecurity, confidentiality,

[1]Presenters: Christopher Smith, University of New York; Gerry Keusch, National Institutes of Health; Paul Epstein, Harvard University Medical School; and Josephine Smart, University of Calgary.

[2]Presenters: Roberta Carey, Centers for Disease Control and Prevention; Reynolds Salerno, Sandia National Laboratories; Bruce Budowle, Federal Bureau of Investigation; and Nancy Warren, Pennsylvania Department of Health.

and other regulations. Laboratories face a rising demand for services from an aging population at increasing risk for infectious diseases.

Clinical laboratories are receiving diminished revenues and facing increased productivity demands that result from downsizing, consolidation, and mergers. There is a shortage of qualified personnel, resulting from loss of senior staff because of retirement and difficulties in recruiting and retaining younger microbiologists. A solution to this crisis will require higher starting salaries, better tuition reimbursement, increased provision of distance learning for current staff, and increased test automation.

Bioscience laboratories are potential sources of threatening pathogens and toxins. Control of these materials is essential, but how this is achieved must be carefully considered and implemented. Potential threat agents can often be acquired from nonbioscience sources. Moreover, the nature of these materials makes their diversion difficult to prevent, and because many biological materials and technologies have dual uses, illegitimate activities can be very difficult to detect. Although many security experts believe that the most credible threat comes from persons with legitimate access to bioscience facilities, security at such facilities has largely been focused on protection against outside adversaries. Such facilities cannot be protected unless their staff understand and accept the need for security measures.

To adequately protect collections of virulent biologic agents, those responsible for the design of biosecurity systems must understand biologic materials and research and have the active involvement of laboratory scientists. Since risk will always exist and every asset cannot be protected against every threat, distinguishing between acceptable and unacceptable risks is imperative. Facilities should conduct an agent-based, security-risk assessment to ensure that protection of their assets is proportional to the risk for theft or sabotage of those assets.

The list of potential human health, animal, and agricultural threat agents is extensive. Areas at risk include not only public health and well-being, but economic well-being, public trust, consumer confidence, and the national infrastructure.

Forensic science involves applying scientific procedures to the investigation of both criminal and civil legal matters. The principal questions that microbial forensics sets out to answer are the following: What is the agent? Was the event intentional? Was the pathogen engineered? Where did the pathogen come from? and Who committed the crime? The manner in which forensic evidence is generated is critical if it is to be admissible in court. To assist law enforcement, the Scientific Working Group for Microbial Genetics and Forensics has been established. This group has identified research needs for methods to identify and type threat agents. It has established quality management guidelines for laboratories, with the goal of promoting development of forensic methods that are rigorous and scientifically valid.

Recent reports from the Institute of Medicine (1) and others recognize that the public health laboratory system has many components. The challenge presented by emerging and reemerging infectious diseases, whether these be old microbes with new scenarios (e.g., *Bacillus anthracis*), new microbes (e.g., severe acute respiratory syndrome), or old microbes with new resistance patterns (e.g., multidrug-resistant *Mycobacterium tuberculosis*), requires greater coordination between public health, clinical, and commercial microbiology laboratories. Each segment produces unique, yet overlapping, data essential to the nation's health. Essential to good coordination is communication, which can be enhanced by joint participation in meetings, collaborative studies, training opportunities, cross-cutting committees, and service on regional or national advisory boards.

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Mathematical Modeling and Public Policy: Responding to Health Crises[1]

Mathematical models have long been used to study complex biologic processes, such as the spread of infectious diseases through populations, but health policymakers have only recently begun using models to design optimal strategies for controlling outbreaks or to evaluate and possibly improve programs for preventing them. In this session, three examples of such models were examined.

[1]Presenters: Marc Bonten, Utrecht University Medical Center; Mark Woolhouse, University of Edinburgh; and Ellis McKenzie, National Institutes of Health.

Antibiotic Resistance in Hospital Settings

Patient dependency characterizes the epidemiology of disease transmission within multiple small wards with rapid patient turnover. Other variables affecting the epidemiology of resistance are the use of antimicrobial agents, introduction of colonized patients, and efficacy of infection-control measures. A Markov chain model originally made for vector-borne diseases was used to elucidate the relative importance of different routes within intensive care units.

Managing Foot-and-Mouth Disease Epidemics

State-of-the-art modeling approaches were used in Britain during the outbreak of 2001 to address such questions as: Were planned control policies sufficient to bring the epidemic under control? What was the optimal intensity of preemptive culling? Would a logistically feasible vaccination program be a more effective control option? This "real-time" use of models, although of help in devising an effective control strategy, also proved controversial.

Developing Smallpox Models as Policy Tools

Although models of infectious diseases have influenced public policy, that process and its results could be improved by regular, direct contact and communication between modelers, policy advisors, and other infectious-disease experts. At the U.S. Department of Health and Human Services, the Secretary's Council on Public Health Preparedness is sponsoring initiatives using various modeling approaches to assess biodefense strategies.

Common themes in this session were: 1) involving substantive experts, thereby ensuring that conceptual frameworks underlying the mathematics are faithful to current understanding of complex natural phenomena, 2) including all possible interventions, which could then be evaluated alone or in various combinations, and 3) identifying inadequacies in available information, for augmentation through further research.

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Public Health Workforce Development[1]

Until the early 1990s, most of Uganda's public health workforce obtained master's degrees from abroad. The responsibility for health training institutions has been shifting between the Ministry of Health and the Ministry of Education, although it is currently under the Ministry of Health, also the main employer of public health workers. The Ugandan Public Health School Without Walls is an innovative and sustainable model of worker development, conceived in 1994 in partnership with Makerere University, which houses the program; the Ministry of Health; and the development partners, notably, the Rockefeller Foundation, the Centers for Disease Control and Prevention (CDC), and the World Health Organization (WHO). Up to 145 professionals from medical, biologic, and social sciences have been trained in a 10-year period. The curriculum is flexible and is constantly reviewed and adapted to the local situation. The program is 75% field-based, during which trainees are placed in 15 district training sites under professional working conditions and they also rotate through various Ministry of Health programs, where they get hands-on training. The program emphasizes operational research, dissemination of findings to policymakers, and evidence-based management decisions, features that have translated into marked improvements in the quality of the delivery of health systems in the country. Students participate in both national and international outbreak investigations. Challenges include increasing the numbers of students to match the high demand and increasing the number of learning facilities. Ensuring effective mentorship, appropriate recruitment, career paths for graduates, and sustainability of the program with reduced donor funding are also problems.

Other examples of international public health worker development initiated by WHO and its Communicable Disease Surveillance Response unit for development of training materials in partnership with CDC are the Lyon 2-year training program for laboratory specialists and epidemiologists, Global Outbreak Alert and Response Network, and various internships.

The Council of State and Territorial Epidemiologists (CSTE) conducted an Epidemiology Capacity Assessment survey of all states and territories. As of November 2001, a total of 1,366 persons were employed as epidemiologists in the 44 responding state and territorial health departments; almost half (47.7%) of these epidemiologists were working in infectious disease. The survey found that 42%

[1]Presenters: Margaret Lamunu, World Health Organization; Matt Boulton, Michigan Department of Community Health; and Lou Turner, North Carolina Public Health Laboratory.

of all epidemiologists working in state and territorial health department have no formal academic training in that discipline. States reported that approximately 48% of epidemiologists work in infectious diseases (a figure that is close to optimal), but that the rest of the public health disciplines, such as chronic disease, maternal child health, occupational health, oral health, bioterrorism/emergency preparedness, injury, and environmental health, are far below optimal capacity; further, >60% of states epidemiologic funding support comes from federal sources. Most states reported having an insufficient number of epidemiology staff and resources to carry out essential public health services.

In response to the training needs identified by this assessment, CSTE, CDC, and Association of Schools of Public Health developed a 2-year applied epidemiology training fellowship that places trainees in state health departments. CSTE hosted the first national epidemiology workforce summit in January 2004 to identify strategies for building epidemiologic capacity in the U.S. public health system.

Infectious disease testing is one of the core capacities of public health laboratories. Such laboratories play a key role in supporting outbreak investigation and surveillance activities. Public health laboratory staff must meet unique requirements and posses technical skills that require a long learning curve. Staff also need to have the knowledge of public health principals and relevance of their work to public health activities. Special recruitment and retention issues are challenging the public health laboratory workforce, including increasing vacancy rates and an increasing demand for skilled workers in light of the Select Agent Rule. At the same time, technology is changing rapidly, with new tests emerging almost daily. Solutions offered were salary parity with the private sector, innovative training, creation of interest in laboratory sciences, and continuing education. The National Laboratory Training Network has helped by offering courses, and Emerging Infectious Diseases fellowships are also attracting new workers. In 2000, Association of Public Health Laboratories survey of state laboratory directors led to the "Green Book," which forecasts impending vacancies up to 40% in certain public health laboratory areas. This finding led to the development of the Center for Public Health Laboratory Leadership, which offers corrective courses and ventures.

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Methicillin-Resistant *Staphylococcus aureus*[1]

Methicillin-resistant *Staphylococcus aureus* (MRSA) is first and foremost a pathogen of healthcare settings. It is the most common pathogen associated with nosocomial infections in the United States, particularly nosocomial pneumonia and surgical site infections. It is also a frequent cause of bloodstream and skin and soft tissue infections. The percentage of *S. aureus* isolates resistant to oxacillin/methicillin in U.S. intensive care units increased from 30% to 40% in the mid-1990s to 57% in 2002.

Data from a recent Duke Infection Control Outreach Network survey indicate that of patients with healthcare-associated MRSA infections, 39% were from nursing homes, 37% had been hospitalized in the previous 90 days, 10% had received home health care, and 10% received dialysis. Data suggest that MRSA bacteremia is associated with an increased likelihood of death, longer hospital stays, and increased cost of hospitalization, when compared with bacteremia levels caused by methicillin-susceptible strains. Increasing resistance to vancomycin among MRSA also complicates therapy, which is already difficult because of multidrug resistance among healthcare-associated MRSA. Because spread of MRSA in healthcare settings is often clonal, hand hygiene and barrier precautions are often effective in interrupting spread. Targeted surveillance for MRSA is also a useful aid for infection control. Data from the Duke network indicate that the spread of MRSA can be curtailed in healthcare settings, given vigilance and adequate funding of infection control activities.

MRSA is now spreading in community settings. Reports from the early 1980s indicate that patients in the community without established risk factors for MRSA (i.e., recent hospitalization, residence in a long-term care facility, or dialysis) sought medical care with MRSA infections. In the late 1990s, four children in Minnesota and North Dakota died from community-associated MRSA

[1]Presenters: Keith Kaye, Duke University; Ruth Lynnfield, Minnesota State Department of Heath; and Barry Kreiswirth, New York University Public Heath Research Institute.

infections. The isolates were susceptible to most non-β-lactam drugs, had pulsed-field gel electrophoresis (PFGE) profiles that differed from typical healthcare-associated MRSA, and contained the Panton-Valentine leukocidin toxin. Prospective surveillance for MRSA in Minnesota at 12 sentinel hospitals (6 in metropolitan areas and 6 in rural areas) indicated that community-associated MRSA patients were significantly younger than healthcare-associated MRSA patients and more likely to have skin and soft tissue infections than respiratory or urinary tract infections. A study in Texas showed that incision and drainage of abscesses due to community-associated MRSA was more effective management than administering antimicrobial agents alone, particularly since many patients were given ineffective antimicrobial agents (i.e., β-lactam agents).

Molecular analysis of the community-associated MRSA strains showed that the methicillin resistance gene *mecA* is typically carried on a much smaller genetic element than is seen in healthcare-associated MRSA. Four distinct elements, called staphylococcal chromosome cassette mec (or SCCmec), have been described. In the United States, SCCmec type II, which is approximately 60 kb in size and also carries an erythromycin resistance determinant, predominates among healthcare-associated MRSA, while SCCmec type IV, which is only 23 kb in length and carries no other resistance determinants, is typically associated with community-associated MRSA. Three major strain typing methods, PFGE, multi-locus sequence typing (MLST), and staphylococcal protein A typing (spa typing), are used to study the spread of MRSA. MLST identified a series of five major lineages (also called clonal complexes) of MRSA globally, while spa typing and PFGE subdivide this group into approximately a dozen epidemic clones. Virulence determinates for MRSA include a series of enterotoxins, toxic shock toxin, and the Panton-Valentine leukocidin toxin.

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Battling 21st-Century Scourges with a 14th-Century Toolbox[1]

A range of quarantine approaches were used in five jurisdictions heavily affected by the outbreak of severe acute respiratory syndrome (SARS) in 2003. Implementation of modern quarantine was resource intensive, involved coordination of multiple sectors of society, frequently required new legislative actions or authorities, and was highly dependent on effective communication.

In Toronto, Ontario, Canada, quarantine ranged from home quarantine with active surveillance to enhanced passive surveillance augmented by education about prevention and a contact number to call if symptoms developed. Healthcare workers were occasionally required to adhere to "work quarantine." New legislation in Ontario authorized compulsory quarantine with active follow-up for compliance. Although 30,000 people in Toronto were recommended for quarantine, enforcement orders had to be issued in only 27 instances. A comprehensive infrastructure was developed to support those in quarantine; masks, thermometers, food, and financial assistance, as well as psychosocial support, were provided. Should SARS return to Toronto, the same measures would be used to ensure that close contacts of infected persons are isolated and actively monitored.

In Taiwan, from April 28 to July 4, 2003, travelers arriving from World Health Organization–designated SARS-affected areas were quarantined for 10 days (level B quarantine). During the SARS epidemic, 50,319 persons who were close contacts of SARS patients were placed under level A quarantine; suspected or probable SARS was diagnosed for 112 (0.22%). A total of 80,813 persons were placed under level B quarantine; 21 (0.03%) of these cases were diagnosed as suspected or probable SARS. The strategies were later modified as understanding of the infectivity of SARS increased, so that close contacts and travelers from local transmission areas were required to follow guidelines of self health management, including isolation at home only when they had a fever. Fever monitoring at international ports initially continued year-round; its ongoing utility will be further examined.

Singapore relied on effective quarantine of all persons who had unprotected close contact with symptomatic case-patients. Critical systems were implemented for quarantine

[1]Presenters: Bonnie Henry, Toronto Public Health; Ih-Jen Su, Center for Disease Control, Taipei; Souk Kai Chew, Medical Services Epidemiology and Disease Control, Singapore; Thomas Tsang, Hong Kong Department of Health; and Zonghan Zhu, Beijing Municipal Health Bureau.

policy and practice, legislative backing, communications, enforcement and surveillance, safeguards on public transport and hospital visits, financial support, operational costs, and compensation. As the gravity of the situation became clear, the Infectious Diseases Act was invoked to impose quarantine on exposed, potentially infectious persons. A Quarantine Board was set up to assist with decisions on a case-by-case basis. An important lesson was the value of clear communication. As part of a comprehensive financial and social support system, the government offered an allowance to self-employed persons to compensate for part of their lost income and to establishments with affected employees.

In Hong Kong, medical services were severely disrupted when 380 healthcare workers became ill with SARS. From April to June 2003, the economy lost an estimated U.S.$3 billion, gross domestic product growth fell by 3.7%, and exports slumped by 13.9%. SARS was controlled by a combination of measures, including disease surveillance, isolation of cases, heightened infection control, contact tracing, quarantine, entry and exit screening, and community engagement. Hospital isolation facilities and infection control training were strengthened by adding 1,000 extra isolation beds and a U.S. $20 million training fund. Retrospective analysis showed that SARS developed in 2.7% of household contacts in home quarantine, and approximately 90% of all case-patients had an identifiable epidemiologic link. Entry and exit screenings that use health declarations and temperature checks, which detected only two cases during the outbreak, have covered 90 million passengers, 5,000 of whom had fever. Addressing surge capacity was a key issue, in which the private medical sector and nongovernmental organizations proved pivotal in providing medical services, community education, and support for emergency operations, including quarantine both at home and at dedicated residential facilities.

Beijing, China, experienced the world's largest outbreak of SARS in spring 2003 with 2,521 reported probable cases. Quarantine played an important role in controlling the outbreak. By July 1, a total of 30,178 persons, 0.21% of the Beijing population, had been quarantined. Most close contacts were quarantined at home (60%); the rest were at designated sites, including hotels, universities, and construction worksites. In late April, fever checks were instituted at the airport, major train stations, and all 71 roads connecting Beijing to other areas; these sites used infrared thermometers to screen and axillary thermometers to confirm fever among passengers. As of June 30, 2003, of almost 14 million people screened, only 12 probable cases of SARS were identified. All healthcare workers in SARS-designated hospitals had to stay in designated hotels close to the hospitals rather than at home. After finishing their work with SARS patients, they were sent to resort areas for 2 more weeks. Top challenges for implementing quarantine included tracing contacts, maintaining movement restrictions even at home, and finding the resources to provide 10,000 people with supplies and psychological care. Nonetheless, the same quarantine measures will be implemented if SARS returns.

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