SECTION ONE Introduction to Infectious Disease Surveillance

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Infectious disease surveillance: a cornerstone for prevention and control

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In view of the galloping pace of globalization that is transforming the world into a global village, close international co-operation is essential in the detection, prevention, and control of communicable diseases.

—Leung Pak-yin, Centre for Health Protection, Hong Kong [1]

Introduction

Throughout human history, infectious diseases have been a major force-continually changing as new human behaviors pose new risks, old pathogens adapt, and novel pathogens emerge. During the second half of the 20th century, the widespread availability of clean water, sanitation, vaccines, and antibiotics contributed to dramatic declines in morbidity and mortality associated with infectious diseases. This resulted in a mistaken view, expressed by some leaders in the late 1960s and 1970s, that infectious diseases would be conquered [2]. In the following decades, this optimism was replaced by a realization of the enormity of infectious diseases challenges. New pathogens, including human immunodeficiency virus (HIV), have erupted while known pathogens, such as drug-resistant tuberculosis (TB) and malaria, have re-emerged. Globally, infectious diseases are a leading cause of morbidity and mortality, accounting for approximately 11 million deaths each year worldwide [3].

The economic consequences associated with infectious diseases are enormous. Direct and indirect economic costs of the 2003 severe acute respiratory syndrome (SARS) pandemic were estimated at US\$80 billion [4]. More recently, the 2009 pandemic H1N1 influenza contributed to a decline in international travel, which undermined a fragile global economy. For example, the estimated cost of pandemic H1N1 influenza to the Mexican economy was over US\$2 billion, largely owing to a decline in trade and tourism. Endemic diseases also account for considerable human and economic costs [5]. In the USA, direct and indirect annual costs of seasonal influenza have been estimated at US\$87.1 billion (based on 2003 data), which included more than 3 million hospitalization days, 41 000 deaths, and 31.4 million outpatient visits [6].

In this chapter and throughout this book, we will demonstrate that, to confront threats from emerging and known endemic pathogens, systematic diseasetracking systems are crucial to guide prevention and control programs. Surveillance has played a critical role in controlling infectious diseases. Through careful surveillance for complete case detection and vaccination of contacts, smallpox has been eradicated (Figure 1.1). In May 2010, Margaret Chan [7], the Director General of the World Health Organization (WHO), unveiled a statue to commemorate the 30th anniversary of the eradication of smallpox and described the statue as a reminder of the "power of international health cooperation to do great and lasting good." In a recent reflection on successful

Infectious Disease Surveillance, Second Edition. Edited by Nkuchia M. M'ikanatha, Ruth Lynfield, Chris A. Van Beneden and Henriette de Valk. © 2013 John Wiley & Sons, Ltd. Published 2013 by Blackwell Publishing Ltd.



Figure 1.1 Local health department nurse immunizing a child. Vaccination against smallpox at a local health department in the USA. *Source:* Centers for Disease Control and Prevention.

eradication of smallpox in Ethiopia, de Quadros [8] credited international support for surveillance combined with innovation and persistence.

The idea that diseases such as plague and smallpox could be prevented by deliberate human actions became evident in 18th century Europe. Chapter 2 reviews major historical developments in the effort to track and control infectious diseases, including their application in public health practice. The evidence that surveillance results in undisputed public health benefits is made in Chapter 3, Part 1. During the final phases of the smallpox eradication efforts, timely reporting of cases was followed by swift, targeted vaccination response.

Guided by surveillance data, public health efforts have contributed to a reduction in the burden of a variety of infectious diseases. Chapter 3, Part 2, describes the use of surveillance to inform Guinea worm (*Dracunculus*) eradication efforts in South Sudan. The Guinea Worm Eradication Program has exceeded expectations by contributing to over 80% worldwide reduction in cases of Guinea worm disease from 20 581 cases in 2006 to 1060 cases in 2011 [9]. Commitment to a public health goal and regional cooperation coupled with sound surveillance programs also resulted in elimination of measles in the western hemisphere in 2002. Provided there is political and social commitment combined with heightened surveillance, measles elimination could be realized in Europe by 2015, despite recent setbacks [10]. The formidable nature of infectious diseases is illustrated in Chapter 3, Part 3.

We will introduce principles and methods that form the foundation of infectious disease surveillance. To portray the breadth of types of surveillance systems, we will provide a glimpse into the vast array of surveillance systems deployed around the world. The emphasis is on practical considerations including innovations that have enhanced surveillance over time.

Definition and scope of infectious disease surveillance

The general principles of public health surveillance are used in programs to prevent and control infectious diseases, chronic diseases, and injuries. In this book, we focus on surveillance for infectious diseases, primarily as communicable pathogens relate to human health but also with attention to pathogens in the interrelated veterinary realm and the environment (this is known as a "one health" approach). Public health authorities or infection prevention entities in healthcare institutions primarily carry out the infectious disease surveillance activities discussed; nevertheless, infectious disease surveillance requires collaboration with partners in a variety of fields, including veterinary medicine, information technology (IT), and law.

The conduct of surveillance can be conceived as a "three-legged stool" consisting of three main integrated activities: (1) systematic collection of significant data (e.g., case reports of a specific disease); (2) analyses of these data; and (3) timely dissemination of results to guide interventions. The three surveillance "legs" are contained both in the original 1969 International Health Regulations and in the most recent definition of surveillance in the current International Health Regulations (IHR 2005) [11]. The IHR 2005 define surveillance as "the systematic ongoing collection, collation and analysis of data for public health purposes and the timely dissemination of public health information for assessment and public health response as necessary." These components are considered central to public health surveillance system.

Besides the WHO, local, regional, and national agencies have embraced surveillance as a means to characterize and address endemic and emerging infectious disease threats. Although many of the examples covered in this book are from North America and Western Europe, infectious disease surveillance is conducted worldwide, albeit in varying degrees and forms.

What happens in the absence of infectious disease surveillance?

In considering the values of surveillance, it is instructive to ask, "What happens to public health in the absence of surveillance?" Where disease tracking is compromised, as is often the case during protracted armed conflicts, progress made in disease control efforts may be reversed.

For example, Afghanistan reported 80 cases of wild poliovirus in 2011, a threefold increase since 2010. The Global Polio Eradication Initiative cites continuing insecurity as the major reason for the setback in Afghanistan [12]. Presence of polio in one country undermines eradication efforts in neighboring countries.

The lack of surveillance and control programs contributed to resurgence of diseases such as human African trypanosomiasis in the Democratic Republic of Congo (DRC) in the 1990s [13]. Gains made earlier in the century were lost during war and socioeconomic deterioration—the incidence of trypanosomiasis rose to an estimated 34 400 in 1994, with neglected areas reporting the highest rates of the century. Over the past decade, 70% of the reported cases of trypanosomiasis occurred in the DRC, including 500 cases in 2010 [14]. Impromptu surveillance and disease control measures can be expected to be much more difficult to implement in countries that have suffered long-standing waves of violence and breakdown of the public sector infrastructure. Chapter 23 offers practical considerations for conducting surveillance in complex emergencies characterized by war or civil strife affecting large civilian populations. Examples are drawn from experiences in Albania, Basrah (Iraq), the Greater Darfur region (Sudan), and Haiti.

Inadequate surveillance and consequent "blindness" to the health status of the population has contributed to the uncontrolled global spread of HIV/acquired immunodeficiency syndrome (AIDS), one of the worst pandemics in human history. Without accurate surveillance data to understand the true health status of their populations and to guide the use of limited public health resources, leaders can be grossly misinformed and, as in the case of HIV/AIDS, miss opportunities for early prevention and control before the virus becomes entrenched. Stigmatization, discrimination, and marginalization-all fueled by ignorance-have contributed simultaneously to the denial and, paradoxically, to the explosion of the HIV/AIDS pandemic. Three decades after recognition of HIV/AIDS, an estimated 34 million people were living with HIV worldwide and 1.8 million infected people died. There were 2.7 million new HIV infections in 2010 including approximately 390 000 among children (Figure 1.2) [15].

Complacency and diversion of resources have hindered maintenance of surveillance systems that can detect and control diseases prior to the development of widespread outbreaks. In the USA during the mid-1980s, waning support and resources for TB surveillance and control most likely contributed to a resurgence of TB, including subsequent multidrug-resistant TB, which resulted in more than \$700 million in direct costs for TB treatment in 1991 [16]. See Chapter 15 for a detailed discussion on methods used to monitor TB, including experiences from systems deployed in European countries.

Collecting surveillance data, which may include the collection of private data (e.g., age, home address, sexual contacts), is justified because these data are necessary for developing prevention and control measures

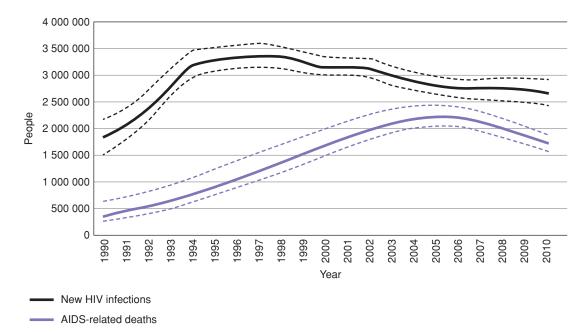


Figure 1.2 Globally, human immunodeficiency virus (HIV) infections continued to increase until 1997 when new infections peaked, whereas deaths peaked in the mid-2000s. Approximately 2.7 million new HIV infections and

and therefore protect the public's health. In return, the government has the responsibility to protect the confidentiality of data. Similarly, the use of isolation and quarantine by public health authorities, although impinging on an individual's liberty, may be needed at times to prevent the spread of highly contagious and virulent infections (e.g., SARS). Chapter 35 discusses the importance of basing public health actions on sound medical and epidemiologic evidence.

The value of surveillance

Because collection of data is a major undertaking, there is a risk that the data collection process itself may consume surveillance programs. However, merely collecting disease data has little impact. Instead, successful surveillance programs analyze and disseminate data to inform prevention and control activities. Specific programs, provided as examples here and further detailed later in this book, illustrate the value of appropriately utilized data from well-designed surveillance systems. 1.8 million deaths occurred in 2010 [15]. Used with permission from the Joint United Nations Programme on HIV/AIDS (UNAIDS).

Guide seasonal vaccine formulation

The WHO Global Influenza Surveillance Network, including five WHO Collaborating Centers for Reference and Research on Influenza and 136 laboratories in 106 countries, conducts annual surveillance for new strains of influenza (see Chapter 12). The results form the basis for WHO recommendations on the composition of influenza vaccine for the northern and southern hemispheres each year, enabling the vaccine to be antigenically similar to recently circulating influenza viruses [17].

Guide vaccination strategies

Characterization of risk factors for bacterial infections such as invasive pneumococcal and meningococcal disease and data on circulating serotypes guide the development of vaccination recommendations. For example, the US Advisory Committee on Immunization Practices uses data from active laboratoryand population-based surveillance to formulate guidelines for vaccination with a 7-valent pneumococcal

conjugate vaccine that was licensed in 2000 for use among young children. Continued surveillance then documented both the rapid decline in pneumococcal serotypes included in the 7-valent vaccine and the increase in disease due to non-vaccine serotypes [18]. This subsequently led to 2010 licensure of a 13-valent vaccine, which includes many of the serotypes that emerged [19]. Further details are presented in Chapters 6 and 10.

Assess vaccine safety

The success of vaccination recommendations depends on their acceptance by the public and by healthcare providers; an acceptable vaccine risk-benefit ratio is important in gaining this confidence. Surveillance for adverse events following vaccination enables public health authorities to investigate concerns and detect problems about specific vaccines. For example, data collected through Vaccine Adverse Event Reporting System (VAERS) enabled detection of intussusception related to rotavirus vaccine in 1999 (see background on VAERS at: http://vaers.hhs.gov/index/about/index). When evidence exists, this type of surveillance is also important for promotion of vaccines with good safety records. For details on post-licensure monitoring of vaccine safety, see Chapter 11.

Monitor adverse events associated with transfusion and transplantation

Advances in healthcare technology have enabled lifesaving procedures including blood transfusion, solid organ transplantation, and musculoskeletal allografts. These procedures, however, have an inherent risk of transmission of pathogens from donors to recipients. In 2011 public health authorities in New York City documented HIV transmission through organ transplantation from a living donor [20]. Surveillance for adverse events associated with the use of human tissues and development of strategies to reduce risk requires collaboration among stakeholders including regulators, the private sector, medical societies, and public health authorities. Project Notify, an initiative led by the WHO and expert societies in Europe, recently created an online database for exchange of information on adverse events associated with the use of substances derived from humans (e.g., solid organs and tissues) in medical procedures (details on Project Notify are available at: http://www.notifylibrary.org/). Chapter 17 discusses development of comprehensive surveillance to improve blood transfusion and transplantation safety.

Inform antimicrobial stewardship programs

The emergence of resistance to antimicrobial agents is an unresolved threat to public health worldwide. Thus, the European Parliament, the WHO, and other organizations call for deployment of surveillance systems to guide interventions [21]. As an example of this effort, data on antimicrobial consumption (e.g., antibiotics and antivirals) are collected in 32 countries through surveillance networks supported by the European Center for Disease Prevention and Control (ECDC). These data are used to guide facility-based antimicrobial stewardship programs and in campaigns to increase awareness about antimicrobial resistance in Europe; for more details, see Chapter 18.

Control emergence of antimicrobial-resistant organisms in domesticated animals

Widespread use of antimicrobial agents in animal husbandry is associated with increased resistance to antibiotics in bacteria isolated from animals and humans [22]. The European Food Safety Authority (EFSA) in collaboration with ECDC and other partners monitors antimicrobial resistance in organisms recovered from animals and food across Europe. In 2006, EFSA [23] standardized antimicrobial resistance surveillance for two important foodborne pathogens of animal origin: Salmonella and Campylobacter. In 2012, EFSA and the ECDC [24] released a joint report on antimicrobial resistance, which documented high prevalence of fluoroquinolone resistance in Campylobacter jejuni isolated from humans (51.6% among 9728 isolates from 13 Member States and Iceland) and food (50% among 670 isolates from seven Member States). The EFSA-ECDC report contributed to the European Union President's initiative to combat antimicrobial resistance [25]. Chapter 7, Part 3, discusses experiences from the National Antimicrobial Resistance Monitoring System. For the benefit of readers within and outside the USA, this chapter includes details about sampling methods, the

use of standard methods for susceptibility testing and interpretation, and strengths and limitations.

Guide allocation of resources for disease prevention and treatment programs

Surveillance data are used to guide allocation of resources to control infectious diseases at various levels. In the USA over \$2.2 billion from the Ryan White federal program are allocated to HIV-related services based in part on the number of cases reported by public health jurisdictions [26]. Chapter 20 provides lessons learned in surveillance including the impact of linking data to funds for medical care. Annual estimates of the burden of HIV/AIDS in different countries by the United Nations Program on HIV/AIDS has stimulated creation of organizations (e.g., The Global Fund to Fight AIDS, Tuberculosis and Malaria, and the Bill and Melinda Gates Foundation) focused on securing resources to expand public health programs in the countries that are most affected by HIV/AIDS [15,27].

Identify outbreaks and guide disease control interventions

Advancement in laboratory methods has enhanced the usefulness of surveillance in outbreak detection by linking bacterial isolates obtained from geographically dispersed cases. For example, PulseNet [28], a national network of public health and food regulatory agency laboratories in the USA, performs standardized molecular subtyping (or "fingerprinting") of disease-causing foodborne bacteria by pulsed-field gel electrophoresis (PFGE). PFGE patterns of isolates are compared with other patterns in the database to identify possible outbreaks. In a large multistate *Escherichia coli* O157:H7 outbreak in 1993, PFGE was first used to link cases with consumption of hamburgers from a restaurant chain (Figure 1.3) [29]. Public health action in Washington State prevented consumption of over 250 000 potentially contaminated hamburgers, preventing an estimated 800 cases [30].

Surveillance data can provide the historical baseline necessary to detect an outbreak, especially when PFGE patterns are common, as was the case with the 2011 multistate *Salmonella* Heidelberg outbreak in the USA (Figure 1.4). Combined with integrated surveillance data, PFGE enabled investigators to implicate consumption of ground turkey from a specific establishment, resulting in recalls of approximately 36 million pounds of ground turkey products that may have been contaminated with a multidrug-resistant strain of *Salmonella* Heidelberg [31]. See Chapter 7, Part 2, for further examples on the use of surveillance to guide outbreak investigations.

Public health laboratories are increasingly adapting new technologies to enhance detection of outbreaks. For example, whole-genome sequence typing was used recently to investigate a suspected cluster of transplantation-related *Coccidioides immitis* infections in three patients [32]. See Chapter 33 for detailed

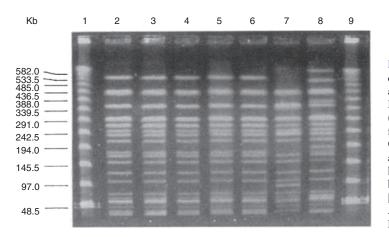


Figure 1.3 Pulsed-field gel electrophoresis of *Escherichia coli* 0157:H7 strains associated with a multistate outbreak. Lanes 1 and 9, molecular weight markers (lambda ladder); lanes 2–5, patient isolates from Washington, Idaho, Nevada, and California, respectively; lane 6, isolate from an incriminated lot of hamburger meat; lanes 7 and 8, isolates from lots of hamburger meat unrelated to the outbreak [29]. Used with permission from the American Society of Microbiology Journals Department.

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Figure 1.4 Pulsed-field gel electrophoresis (PFGE) pattern from the 2011 *Salmonella* Heidelberg outbreak linked to ground turkey. Ongoing surveillance provided the historical baseline necessary to detect an outbreak in this and other instances where PFGE patterns are common. Used with Permission from Carol Sandt, Pennsylvania Department of Health Bureau of Labs.

PFGE-Xbal Se

Serotype **PFGE-Xbal-pattern** Heidelberg JF6X01.0022 JF6X01.0022 Heidelberg Heidelberg JF6X01.0022 Heidelberg JF6X01.0022 Heidelberg JF6X01.0022 JF6X01.0022 Heidelberg Heidelberg JF6X01.0022

discussion on the use of new technologies to improve pathogen-specific surveillance.

Core infectious disease surveillance and disease-reporting systems

Students and those starting their careers in public health may perceive surveillance to be synonymous with a mandatory healthcare provider-based diseasereporting system. Although disease reporting is important, there are other components of surveillance. We will outline core disease-reporting systems as exemplified in the USA and other countries, and then introduce the breadth of other types of innovative systems used to monitor and respond to infectious diseases.

Disease reporters

In most countries, mandatory disease reporting relies upon physicians or other healthcare providers to diagnose and report specified diseases to public health authorities. Jurisdictions also mandate notification of suspected or confirmed disease and conditions by other professionals. Directors of clinical laboratories licensed in New York State are required to report HIVrelated test results, including patient demographic and provider information, to state public health authorities [33]. Many other jurisdictions in the USA, Europe, Australia, and other parts of the world require notification of specific test results to public health authorities. In addition, directors of schools, childcare centers, homes for the elderly, prisons, or other institutions are often required to notify public health officials of any clusters of disease, such as two or more cases of suspected food poisoning.

Despite being legally mandated, diseases are largely under-reported [34]. While failure to comply with reporting requirements can lead to criminal penalties, enforcement is rare. Moreover, physicians are often unaware of which diseases to report. Physicians may also not believe in the utility of surveillance, and the logistics of reporting cases can become unmanageable for busy clinicians. One key reason for sharing data with clinicians is to demonstrate the usefulness of disease reporting.

Creative means to motivate and support disease reporters can also be helpful. Until recently, physicians in England were given a modest financial incentive to notify public health authorities of suspected cases of reportable diseases [35]. To promote reporting of HIV, Michigan Department of Community Health (USA) maintains an active relationship with HIV care specialists through an email group that provides upto-date information on HIV and other infectious disease news (see Chapter 20). Surveillance, prevention, and control of healthcare-associated infections are new areas for many public health practitioners. Some jurisdictions in the USA, UK, and France have mandated reporting of healthcare-associated infections; state and local health departments have subsequently become more involved. Audits can be a component of assessing healthcare facility compliance with reporting requirements (see Chapter 16).

Laboratory-based surveillance

Clinical microbiology and public health laboratories can be rich sources of information on pathogens causing disease within a population. Compared with individual healthcare providers who are often spread across multiple clinics and acute and chronic care facilities, clinical laboratories are fewer and data are

better consolidated. Adaption of electronic information systems by clinical laboratories has created opportunities for new methods of submitting reportable conditions to public health authorities [36]. During the last decade, implementation of electronic laboratory reporting (ELR) has improved timeliness, completeness, and facilitated development of complementary laboratory-based surveillance systems for monitoring specific conditions. Today, secure ELR systems transfer test results for specified conditions to public health authorities in many jurisdictions in the USA. Nevertheless, deployment of ELR requires an understanding of its strengths, limitations, and strategies for analysis of increased data [37]. Chapter 29 provides principles and practical considerations for ELR with discussion of experiences from New York and Oregon.

Diseases selected for surveillance

In most European countries, diseases considered to be of public health significance and warranting systematic surveillance are selected at a national level (see Chapter 5). Provisions often do allow, however, for regional adaptation. For example, chikungunya was made a mandatory notifiable condition in mainland France and the overseas departments in the Caribbean, but not in the department La Réunion in the Indian Ocean in 2006, when a massive epidemic involving over 250 000 persons overwhelmed the diseasereporting structure. In the USA, the authority to require disease reporting is decentralized-states, territories, and independent local authorities legislate reportable diseases, and these vary by jurisdiction. For example, coccidiomycosis is typically reportable only in areas in the southwestern USA where the fungus is endemic.

Case definitions

To standardize surveillance data within and across public health jurisdictions, case definitions are used with specific clinical and laboratory criteria. In the USA, the Council of State and Territorial Epidemiologists, an organization representing public health epidemiologists, establishes and periodically updates case definitions used in surveillance for nationally notifiable infectious diseases [38]; a current list is available on the US Centers for Disease Control and Prevention's (CDC) website (www.cdc.gov). Case classifications range from "suspected" to "confirmed," depending on the availability of supporting data.

Case definitions for over 80% of nationally notifiable diseases in the USA require a positive laboratory test for confirmation. An epidemiologic link to a laboratory-confirmed case is typically required for designating a case as "probable" [38]. Guidance on identifying "epidemiologically linked" cases is provided in Figure 1.5, based on Australian case definitions [39]. For some diseases, such as tetanus, surveillance is primarily based on clinical criteria (e.g., an acute onset of hypertonia or painful muscular contractions, usually of the muscles of the jaw and neck, and generalized muscle spasms without other apparent medical cause).

The sensitivity and specificity of a case definition are influenced by the availability of reliable laboratory diagnostic assays to support clinical criteria, and by epidemiologic factors. In an outbreak or in other settings where confirmatory laboratory assays do not exist or are not practical, sensitive but less specific case definitions may be selected. For example, a gastrointestinal illness can be counted as a case of salmonellosis if epidemiologically linked to a laboratory-confirmed case of *Salmonella*. By contrast, when a single case has major public health implications, the case definition may be quite rigorous with strict laboratory criteria, e.g., vancomycinresistant *Staphylococcus aureus* or human infection with influenza A (H5N1) virus.

Case definitions are subject to evolution in response to diagnostic and therapeutic advances—for example, the case definition for HIV/AIDS has been refined several times [40]. Caution is necessary when interpreting data following a change in case definitions because any observed changes might be surveillance artifacts (i.e., due to the change in case definition rather than a change in the true incidence of disease). See Chapter 20 for a discussion of how the case definition for HIV surveillance in the USA has evolved over time.

Data flow

Reporters telephone, fax, mail, or electronically transmit case reports to local health jurisdictions that investigate cases. Public health officials then ensure that case definitions are met, and initiate appropriate

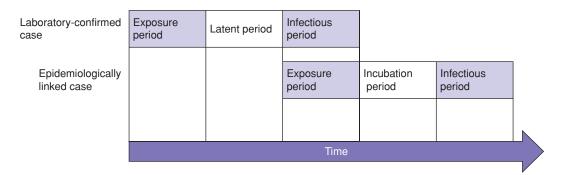


Figure 1.5 Guidance for defining an epidemiologically linked case prospectively. An epidemiologic link is established when there is contact between two people involving a plausible mode of transmission at a time when: (1) one of them is likely to be infectious and (2) the other

interventions. In the USA, case reports for diseases that are deemed "nationally notifiable" are forwarded to the National Notifiable Disease Surveillance System (NNDSS) at the CDC. Submission of data to the national system in the USA is voluntary; nevertheless, all jurisdictions participate. In countries where the disease-reporting authority is centralized at the national level, all cases confirmed at the local jurisdiction are forwarded to the national surveillance system.

Dissemination of data

Surveillance data are compiled, analyzed, and presented at many levels. A prominent outlet in the USA is the Morbidity and Mortality Weekly Report (MMWR) where surveillance summaries on notifiable diseases are published both on a freely accessible website (http://www.cdc.gov/mmwr/) and in printed copies that are mailed to subscribers. In the UK, surveillance data are published regularly in the Health Protection Report, available on the Health Protection Agency website (http://www.hpa.org.uk/hpr/), and by email subscription. States, territories, and local health departments in the USA have a variety of methods to share surveillance data; use of the Web is discussed in Chapter 26. Because sharing surveillance data with healthcare providers and the public is crucial, public health jurisdictions are increasingly taking advantage of Facebook, YouTube, Twitter, and other social media tools to achieve this objective. Chapter 41 covers this topic in two parts: Part 1 provides strategies to enhance public health communication including

has an illness onset within the incubation period after this contact. At least one case in the chain of epidemiologically linked cases (which may involve many cases) must be laboratory confirmed [34]. Used with permission of the Australian Government Department of Health and Aging.

best practices for relations with mass media and use of social networking tools; Part 2 describes a public awareness campaign.

Internationally notifiable diseases—International Health Regulations

In most countries, public health agencies operate independently. Because infectious pathogens do not respect national borders, concerns about some events extend beyond the "index" country; the international public health response may therefore be essential to controlling an outbreak. The IHR, as originally articulated by the World Health Assembly in 1969, required countries to report cases of yellow fever, plague, and cholera to the WHO. The current IHR (2005) expanded this obligation to include not only known pathogens but also as of yet undefined new or re-emerging diseases that can spread rapidly with enormous impact to global public health. IHR (2005) also addresses international emergencies caused by non-infectious diseases.

The current IHR calls for strengthening of capacity to conduct surveillance in each country. This approach would facilitate assessment and reporting within 24 hours—of events that constitute public emergency of international concern. These regulations also mandated creation of specific national IHR focal points (for States Parties) and WHO IHR contact points to facilitate efficient and effective exchanges of event-related information at all times. By 2007, virtually all members of the United Nations (194 countries)

had implemented IHR and progress has been made in key areas including establishment of national IHR focal points. For details about implementation of IHR including steps taken by the WHO and member countries during the 2009 influenza pandemic, see Chapter 4.

Additional types of surveillance systems and emerging technologies

Limitations encountered by the core disease-reporting systems include delays in notification, underreporting, lack of representativeness, and exclusive focus on human diseases. Some of the deficiencies of core disease-reporting systems can be addressed by surveillance conducted by alternative modalities.

Active surveillance

Describing surveillance systems as "passive" is a misnomer because it suggests minimal effort on anyone's part. Customarily, the intent of labeling some surveillance systems as "passive" and others as "active" is to distinguish the intensity of public health agency effort in finding and investigating cases. Systems based on mandatory disease reporting, while obviously relying on healthcare-provider energies, generally involve minimal public health effort to solicit case reports, and thus are described as "passive." Under-reporting is a major limitation of this type of surveillance system. In practice, however, no surveillance system should be entirely "passive," even from the point of view of the public health agency, as regular communication and feedback to healthcare providers are necessary to ensure a successful system.

By contrast, "active" surveillance signifies intensive public health efforts to identify cases needed to determine incidences and epidemiologic characteristics of specific conditions within defined regions. Populationbased surveillance aims to capture every case diagnosed within a population living in a defined geographic catchment area and thus can best describe the epidemiology and measure rates of a disease under surveillance. To be sufficiently comprehensive, active and population-based surveillance sometimes involves retesting of isolates submitted by clinical laboratories and collection of additional epidemiologic and clinical information. The benefits of population-based surveillance to public health are clear; however, the additional resources required to conduct this type of surveillance limits widespread implementation of this approach.

In the USA, the Emerging Infections Program (EIP) supports active, population-based surveillance for selected pathogens conducted in a representative population of approximately 44 million or 14% of the total population in 2012 [41]. This approach involves 10 EIP sites distributed throughout the USA that conduct surveillance activities in collaboration with state and local health departments, academic institutions, clinical laboratories, and healthcare providers. The Active Bacterial Core surveillance (ABCs), which tracks selected invasive disease (e.g., Streptococcus pneumoniae, groups A and B Streptococcus, Haemophilus influenzae, and Neisseria meningitidis), is an example of populationbased surveillance activities conducted by EIP sites. For detailed discussions on ABCs, see Chapter 6. The EIP sites also monitor the incidence of selected foodborne pathogens (e.g., Salmonella, Campylobacter, and Shiga toxin-producing E. coli). For an example of use of population-based surveillance to estimate the burden of foodborne illnesses due to specific pathogens, see Chapter 7, Part 1.

Sentinel surveillance

The intensive public health resources required to conduct population-based surveillance are often not readily available; as an alternative strategy, sentinel surveillance involves collection of data from a "sentinel" or subset of a larger population. The strategy of focusing on a small population subset can be conceived as a type of "sampling." To generalize these data to larger populations, it is necessary to ensure (1) that the sentinel population is representative and (2) that the sentinel data are linked to denominator information on a predefined population under surveillance; see further discussion in Chapter 19.

The Gonococcal Isolate Surveillance Project systematically monitors antimicrobial resistance among *Neisseria gonorrhoeae* isolates collected from 25–30 sentinel US cities. Antimicrobial susceptibility testing is performed on the first 25 isolates per month from male patients with gonococcal urethritis (approximately 5900 isolates annually). Rising resistance documented by this surveillance system has contributed

to recommendations that fluoroquinolones should no longer be used to treat gonococcal infections in the USA. Recent concerns about *N. gonorrhoeae* resistant to cephalosporins warrant vigilance in monitoring patients for treatment failures, and prompt reporting of isolates with decreased cefixime or ceftriaxone susceptibility ($\geq 0.5 \ \mu$ g/mL) to public health authorities [42]; see the detailed discussion in Chapter 22.

In France, a network of sentinel primary care physicians report information at weekly intervals on a selected group of health events that are relatively common in general practice such as influenza-like illness, acute gastroenteritis, mumps, chickenpox, herpes zoster, male urethritis, and Lyme disease. Data are extrapolated to regional and national levels. The system, known as "Sentinelles," describes the occurrence and progression of regional and national outbreaks. For details on this system, see Chapter 27.

Multiple "sentinel" surveillance methods have been used to estimate the prevalence of HIV in India, South Africa, and other countries. Testing for HIV in women presenting for antenatal care is common. However, for strategies used to address biases inherent to antenatal sentinel surveillance data, see Chapter 21, Part 3.

Targeted sentinel surveillance for HIV is also conducted in high-risk groups (e.g., female sex workers and single male migrants); see Chapter 21, Part 1. Sentinel surveillance for HIV among street youth in St. Petersburg, Russia, is presented in Chapter 21, Part 2.

Animal reservoir and vector surveillance

Because of the central role of wildlife, domestic animals, and vectors (e.g., ticks and mosquitoes), zoonotic diseases cannot be adequately understood and controlled by only monitoring the disease in human populations. With increasing recognition of the importance of zoonotic diseases, surveillance systems have been designed to monitor pathogens as they circulate in various human and non-human hosts. Brucellosis control in the USA has been successful because of the focus on animal health as a way to protect human health: comprehensive animal testing, vaccination of breeding animals, and depopulation of affected herds (see Chapter 8). Surveillance for vector-borne diseases (e.g., West Nile virus, Lyme disease, and dengue) involves different complementary modalities. During the past decade, surveillance for West Nile Virus in the USA has evolved with a recent decline in utility of dead bird monitoring and an increase in entomologic capacity. Still, recognition of transplantation as a new mode of West Nile virus transmission demonstrates the need for robust monitoring of risk factors (see Chapter 9).

Detection of pathogens in the environment

The identification of the fungus Cryptococcus gattii in British Columbia, Canada, illustrates the use of surveillance to define an emerging pathogen intrinsically linked to the environment. Previously only known in tropical and subtropical climates, the fungus emerged in approximately 1999 in Vancouver Island as a pathogen in humans and domestic and wild animals. Environmental sampling identified the fungus on trees, in soil, in air samples, and in water, and helped to define the evolving realm of this new pathogen [43]. During the past decade, C. gattii expanded to the Pacific Northwest region of the USA. Studies of isolates from patients revealed that genetically similar strains of C. gattii caused outbreaks in the US Pacific Northwest while other strains caused disease in a wider geographical area [44] (Figure 1.6). See Chapter 37, Part 2, for a case study on application of a geographic information system in North America and East Africa.

Surveillance across borders and mobile populations

Conventional surveillance systems may not fully capture infectious diseases among border or mobile populations. The Early Warning Infectious Disease Surveillance (EWIDS), a cross-border surveillance system involving 20 public health jurisdictions in the USA, Canada, and Mexico, is an example of a regional effort to improve timeliness of public health response through early detection of pathogens. An example of surveillance activities carried out by EWIDS collaborators is sharing of molecular laboratory test results through PulseNet [45] and sharing data on biologic agents that are of concern in bioterrorism. The Border Infectious Disease Surveillance, along the USA-Mexico border, is another example of a system coordinated by public health jurisdictions in two countries (see Chapter 24 for details).

Surveillance for infectious disease associated with mass gathering presents challenges to traditional surveillance systems. Mass gatherings involve potentially thousands of persons in an inherently

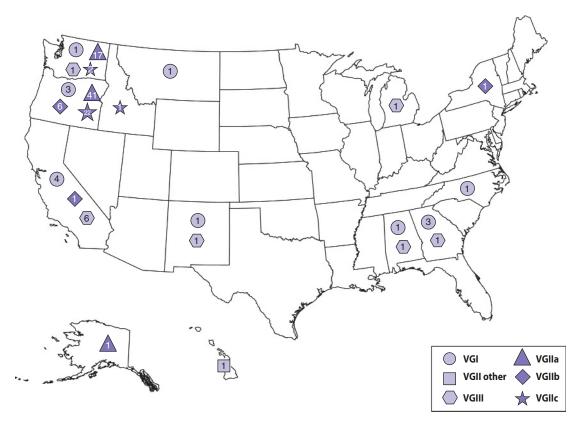


Figure 1.6 Distribution of *Cryptococcus gattii* human cases by outbreak and non-outbreak strain, USA, 2011. The various strains of *C. gattii* cause illnesses that may differ in clinical manifestation. *C. gattii* strains—outbreak: VGIIa,

transient population; in the case of the Hajj, the Muslim annual pilgrimage to Mecca, the gathering is estimated at 2.5 million people. Experiences from systems deployed during winter and summer Olympic Games and the 2009 Hajj, which took place during the influenza H1N1 pandemic, provide lessons for enhancing surveillance during mass gatherings [46]. These lessons include integration of new sources of data from Internet-based systems (see Chapter 25).

Use of health services and administrative data for disease surveillance

Infectious disease surveillance systems have sometimes incorporated administrative and vital statistics data that are being collected for other purposes. To bill for services, healthcare facilities in the USA assign

VGIIb, VGIIc; non-outbreak, VGI, VGIII, and VGII other. Used with permission from the US Centers for Disease Control and Prevention.

diagnosis codes to clinical care encounters (i.e., International Classification of Diseases, 10th revision). This is a potential source for surveillance activities for a range of diseases (see Chapter 22). Hospital admission data can also complement routine surveillance data. In Germany, national surveillance systems extract records on diagnoses and treatment of specific diseases under surveillance from healthcare reimbursement databases. For an example of a system used by the Robert Koch Institute, see Chapter 28. In England, hospital admission data have been used to monitor end-stage liver disease where the underlying cause is chronic viral hepatitis (see Chapter 19). Monitoring of drug utilization and drug sales may be an indirect measure of disease activity. At the US CDC, where a supply of "orphan" drugs are housed for treatment of rare diseases, increased requests for pentamidine in

the 1980s led to an investigation of a cluster of pneumocystis pneumonia which, in turn, led to the first detection of AIDS in the world [47].

To complement core surveillance systems that are based on reporting of specific diagnoses, public health authorities use syndromic surveillance data to monitor selected indicators. Syndromic surveillance systems typically use automated data extraction and analytic methods to detect aberrations from expected levels of various syndromes. For example, in Virginia the chief complaints recorded at emergency department visits are used to track influenza-like illness during the flu season [48]. Pharmaceutical databases have been explored for a variety of syndromic surveillance systems (see Chapter 32).

In the USA, initiatives under the 2009 Health Information Technology for Economic and Clinical Health (HITECH) Act will likely accelerate use of health records for surveillance purposes. This law provides incentives to promote "meaningful use" of electronic health records to improve clinical outcomes for patients and public health (www.cms.gov). For example, HITECH offers healthcare facilities and providers incentives for submitting specified electronic immunization data to registries. The law also provides incentives for developing statewide Health Information Exchange (HIE) to enable healthcare organizations to seamlessly share and receive electronic immunization and other forms of data. The use of data from HIE in public health settings was in the early stages development as of the end of 2012.

Risk factor surveillance

Although most surveillance systems focus on disease occurrences or circulation of pathogens causing disease, several surveillance systems have focused on behaviors that pose risk for specific diseases. Two examples relate to HIV/AIDS surveillance in the USA [49]. The National HIV Behavioral Surveillance system includes interviews of a sample of persons to assess the prevalence of sexual behaviors, drug use, and testing history for other sexually transmitted infections [50]. Data from this system examine the front end of the HIV/AIDS epidemic and may guide and assess prevention programs. The other is the Medical Monitoring Project, designed to produce national estimates about people living with HIV/AIDS in the USA. It involves collection of self-reported behavioral and selected clinical data through in-person interviews (see Chapter 35). Similarly, the Youth Risk Behavior Survey measures the prevalence of health risk behaviors among adolescents through self-administered, school-based surveys. Reports of sex without condoms and sex associated with drug and alcohol use are among the data collected (www.cdc.gov/yrbs) [51]; for additional discussion, see Chapter 22.

Emerging mobile technologies

The convergence of mobile technology and the Internet coupled with declining costs of portable wireless devices present new approaches for tracking emerging and endemic pathogens. By 2011, over 85% of the world's population (5.9 billion people) subscribed to mobile telephones and 1.2 billion were using these devices to access the Internet [52]. For examples of wireless device systems deployed to monitor outbreaks in post-disaster emergencies in China and Haiti, see Chapter 30.

Surveillance based on media reports and computer algorithms

The availability and speed of information transmission over the Internet has also allowed development of innovative electronic media-based surveillance systems. For example, the Global Public Health Intelligence Network (GPHIN) uses automated algorithms to filter electronic media reports, in seven languages, of occurrence of diseases on a real-time, 24-hour basis. Although the electronically gathered information requires further verification by trained personnel, GPHIN is used extensively as an early source of outbreak information by Health Canada, the WHO, the US CDC, and others (see Chapter 31).

Surveillance collaborations with partners outside traditional human public health systems

As illustrated by the broad variety of infectious disease surveillance systems, diverse sources of information can be utilized. The development of these systems relies upon new collaborations between human public health agencies and non-traditional partners. For example, human health agencies have traditionally

acted as separate entities from domesticated and wildlife animal health agencies. When West Nile virus emerged in the USA, public health officials who customarily focused only on human diseases began forging collaborations with entomologists, veterinarians, and wildlife oversight agencies [53]. Human health agencies often do not have these diversely skilled personnel, but instead depend upon common goals and national agendas to facilitate collaborations.

As described in Chapter 14, medical examiners have the authority to investigate sudden, unattended, and unexplained deaths. Although the focus of these investigations has traditionally been on intentional or accidental deaths, public health agencies have collaborated with medical examiners to systematize specimen collection and diagnostic testing relevant for detection of reportable, emerging, or bioterrorism-related infectious diseases. Chapter 13 also discusses collaboration with regional poison control centers in monitoring suspicious reports.

Today's increasingly complex surveillance methods require robust information systems and data management support. Optimal use of Internet-based systems and mobile technologies also requires close collaboration with IT specialists and computer scientists. Because of the heightened need for privacy of surveillance data that use certain types of mobile technologies (e.g., smart phones), input from cyber wireless system engineers may be necessary. To meet surveillance objectives, however, involvement of end-users in all phases of system design and testing is critical to ensure the viability of these potentially multimillion dollar systems (see discussion in Chapter 26).

Data analyses require statistical software (see Chapter 34, Part 1) and may necessitate input from individuals with a strong background in biostatistics; see also Chapter 34, Part 2. This chapter introduces common analytic methods including graphic presentation of data and summary statistics. Chapter 37, Part 1, provides details about tools and methods for geospatial analysis of surveillance data, and approaches to analysis of surveillance data on HIV/AIDS are discussed in Chapter 35. For an introduction to time series analysis, including specific examples, see Chapter 36.

The need for review of public health surveillance practices from an ethicist's perspective is discussed in Chapter 40. What constitutes research and unlinked anonymous testing for HIV are examples of persistent ethical quandaries in infectious disease surveillance.

In the USA and elsewhere, surveillance is not exclusively a government function and involves working with multiple private entities. For example, private hospital laboratories transmit large amounts of reportable disease information to health departments at their own cost. Another example of public–private partnership is the US Vaccine Adverse Events Reporting System, as is detailed in Chapter 44. While federal public health agencies set programmatic objectives and provide technical oversight, the for-profit Constella Group is contracted to support this surveillance system's data collection processes [54]. These types of "mixed model" partnerships may be able to harness private sector energy and efficiency while remaining faithful to public health objectives.

Challenges and promises for the future of infectious disease surveillance

Progress in development of surveillance systems supports disease prevention and control, a primary obligation of governments to their citizens. Moreover, to meet their obligation to the global community, all countries were required by IHR to have core capacity for surveillance by June 2012. While there are improvements, persistent challenges in surveillance and disease control remain around the globe. Countries with limited resources struggle with a balance between providing basic medical services and efforts to control infectious diseases-it may appear more logical to address the needs of those suffering from diseases than divert resources to monitoring activities. Infectious disease surveillance in all countries requires political will to allocate adequate resources to sustain ongoing activities.

The gap between data collection and effective use of data for disease control and prevention is among the most formidable challenges faced by surveillance programs. An unfortunate reality of public health surveillance is that substantial efforts are devoted to collection of data while sufficient resources are often not expended on timely dissemination and constructive use of the information. If these data are not appropriately analyzed, disseminated, and applied, surveillance will be perceived as categorically ineffective. As William Foege [55], former director of

the CDC, once remarked, "The reason for collecting, analyzing, and disseminating information on a disease is to control that disease. Collection and analysis should not be allowed to consume resources if action does not follow."

Strengthening core surveillance systems requires public health officials with sufficient training in principles and practical aspects of monitoring diseases. Grasp of applied epidemiology and skills in data analysis and communication are among the basic prerequisites for those engaged in surveillance activities. The modern concepts and public health surveillance, however, is relatively young (see Chapter 2). While much of the practice of surveillance may be learned on the job as newly hired personnel begin careers in public health, formal training offers tremendous advantages.

Training in public health surveillance and epidemiology

Two epidemiology training programs that combine didactic training with hands-on experience are covered in Chapter 42. Through formal evaluations of in-use surveillance programs, Epidemic Intelligence Service officers not only begin to understand real-life surveillance but also bring fresh perspective to systems that may have become stagnant. The European Programme for Intervention Epidemiology Training also includes joint training with the European Public Health Microbiology Training Programme. Another example of a formal training fellowship is covered in Chapter 43. This program provides didactic training on surveillance courses at Albany, NY, in combination with a home country experience in assessing surveillance systems. In collaboration with Ministries of Health in several countries, the US CDC offers two applied epidemiology programs that have a surveillance component: the Field Epidemiology Training Program and the Field Epidemiology and Laboratory Training Program (FELTP) (available on the CDC website at: http://www.cdc.gov/globalhealth/fetp/). Practical training on actionable surveillance should also be an emphasis in schools of public health and other educational arenas.

Evaluating and improving surveillance systems

Ongoing evaluations are a core component of living surveillance systems. Systematic evaluations should

assess whether surveillance systems are operating as effectively as possible, and, if not, determine what changes can be made. Evaluations can also highlight achievements and in this way demonstrate their value to stakeholders. For example, the US CDC Global Disease Detection Program recently described an evaluation by FELTP-Kenya of Eritrea's pediatric bacterial meningitis surveillance system. This effort eventually led to creation of a laboratory-based surveillance system for rotavirus and bacterial meningitis [56]. For an introduction to formal evaluation of surveillance systems, see Chapter 38. Surveillance systems face the challenges of chasing moving targets-as more is learned about the epidemiology of a disease, surveillance strategies must be adapted. Emerging pathogens add further complexities. Surveillance systems need to be regularly reviewed, refined, and re-energized.

On the frontiers of public health, technical advancements facilitate efforts to improve surveillance systems. In addition to sophisticated IT instruments mentioned previously, molecular fingerprinting has improved the epidemiologic understanding of links between human cases, management of outbreaks, and links to animal reservoirs (see Chapter 33). In the future, geographic information systems may be used (see Chapter 37) to analyze multiple layers of geographical, ecologic, and climatic information, linking the epidemiology of zoonotic and other diseases to environmental conditions. New tools to enhance infectious disease surveillance continue to be developed. How to optimize the use of both old and new surveillance tools to inform disease prevention and control remains both an ongoing challenge and an opportunity.

References

- news-medical.net. Hong Kong Health Commitment Pledged in Sweden. Available at: http://www.newsmedical.net/?id=5119. Accessed September 5, 2012.
- 2 Petersdorf RG. The doctors' dilemma. N Engl J Med 1978;299:628-34.
- 3 National Institutes of Health. Infectious Diseases and Biodefense. Available at: http://report.nih.gov/ biennialreport/ViewSection.aspx?sid=9&ccid=2. Accessed September 5, 2012.
- 4 Knobler S, Mahmoud A, Lemon S, et al. (eds.). Learning from SARS: Preparing for the Next Disease

Outbreak: Workshop Summary. Washington, DC: National Academies Press, 2004: 11.

- 5 Food and Agricultural Organization. *Emerging and Transboundary Animal Diseases Funding Requests to Donors.* Available at: http://www.fao.org/avianflu/en/ funding.html. Accessed September 5, 2012.
- 6 Molinari NA, Ortega-Sanchez IR, Messonnier ML, et al. The annual impact of seasonal influenza in the US: measuring disease burden and costs. Vaccine 2007;25:5086– 96.
- 7 World Health Organization. *Statue Commemorates Smallpox Eradication*. Available at: http://www.who. int/mediacentre/news/notes/2010/smallpox_20100517/ en/index.html. Accessed September 5, 2012.
- 8 de Quadros CA. Experiences with smallpox eradication in Ethiopia. *Vaccine* 2011; 29(Suppl. 4):D30–5.
- 9 World Health Organization. Dracunculiasis. Available at: http://www.who.int/dracunculiasis/en/. Accessed September 5, 2012.
- 10 Centers for Disease Control and Prevention. Increased transmission and outbreaks of measles: European Region, 2011. MMWR Morb Mortal Wkly Rep 2011;60:1605–10.
- 11 World Health Organization. WHA58.3: Revision of the International Health Regulations. Available at: http://www.who.int/gb/ebwha/pdf_files/WHA58-REC1/english/Resolutions.pdf. Accessed September 5, 2012.
- 12 The Global Polio Eradication Initiative. Global data and monitoring: polio this week. Available at: http:// www.polioeradication.org/Dataandmonitoring/Poliothis week.aspx. Accessed September 5, 2012.
- 13 Ekwanzala M, Pepin J, Khonde N, *et al.* In the heart of darkness: sleeping sickness in Zaire. *Lancet* 1996;348(9039):1427–30.
- 14 World Health Organization. Human African Trypanosomiasis (Sleeping Sickness). Available at: http://www. who.int/mediacentre/factsheets/fs259/en/. Accessed September 5, 2012.
- 15 Joint United Nations Programme on HIV/AIDS (UNAIDS). UNAIDS 2011 World AIDS Day Report. Available at: http://www.unaids.org/en/resources/ publications/2011. Accessed September 5, 2012.
- 16 Berkelman RL, Bryan RT, Osterholm MT, et al. Infectious disease surveillance: a crumbling foundation. Science 1994;264:368–70.
- 17 World Health Organization. Recommended Composition of Influenza Virus Vaccines for Use in the 2012–2013 Northern Hemisphere Influenza Season. Available at: http://www.who.int/influenza/vaccines/ virus/recommendations/2012_13_north/en/index.html. Accessed September 5, 2012.

- 18 Pilishivili T, Lexau C, Farley MM, et al. Sustained reductions in invasive pneumococcal disease in the era of conjugate vaccine. J Infect Dis 2010;201:32–41.
- 19 Centers for Disease Control and Prevention. Licensure of a 13-valent pneumococcal conjugate vaccine (PCV13) and recommendations for use among children: Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep* 2010;59(9):258–61.
- 20 Centers for Disease Control and Prevention. HIV transmitted from a living organ donor: New York City, 2009. MMWR Morb Mortal Wkly Rep 2011;60:297– 301.
- 21 European Parliament. European Parliament resolution of 27 October 2011 on the public health threat of antimicrobial resistance. Available at: http:// www.europarl.europa.eu/sides/getDoc.do?pubRef=-// EP//TEXT + TA + P7-TA-2011-0473 + 0 + DOC + XML + V0//EN. Accessed September 27, 2012.
- 22 Fey PD, Safranek TJ, Rupp ME, et al. Ceftriaxoneresistant salmonella infection acquired by a child from cattle. N Engl J Med 2000;342:1242–9.
- 23 European Food Safety Authority. Antimicrobial Resistance. Available at: http://www.efsa.europa.eu/en/ topics/topic/amr.htm. Accessed September 5, 2012.
- 24 European Food Safety Authority. European Union Summary Report on Antimicrobial Resistance in Zoonotic and Indicator Bacteria from Humans, Animals and Food in 2010. Available at: http://www.efsa.europa.eu/ en/efsajournal/doc/2598.pdf. Accessed September 5, 2012.
- 25 Danish Presidency of the European Union 2012. Combating Antimicrobial Resistance: Time for Joint Action. Available at: http://eu2012.dk/en/Meetings/ Conferences/Mar/Bekaempelse-af-antibiotikaresistens en-faelles-indsats. Accessed September 5, 2012.
- 26 Department of Health and Human Services. *Health Resources and Services Administration. Ryan White HIV/AIDS Program.* Available at: http://hab.hrsa. gov/abouthab/aboutprogram.htm. Accessed September 27, 2012.
- 27 The Global Fund to Fight AIDS, Tuberculosis and Malaria. About. Available at: http://www. theglobalfund.org/en/about/. Accessed September 5, 2012.
- 28 Centers for Disease Control and Prevention. PulseNet. Available at: http://www.cdc.gov/pulsenet/whatis.htm# interlaboratory. Accessed September 5, 2012.
- 29 Barrett TJ, Lior H, Green JH, et al. Laboratory investigation of a multistate food-borne outbreak of Escherichia coli O157:H7 by using pulsed-field gel electrophoresis and phage typing. J Clin Microbiol 1994;32:3013– 17.

- 30 Bell BP, Goldoft M, Griffin PM, *et al.* A multistate outbreak of Escherichia coli O157:H7-associated bloody diarrhea and hemolytic uremic syndrome from hamburgers. The Washington experience. *JAMA* 1994;272:1349–53.
- 31 Centers for Disease Control and Prevention. Investigation Update: Multistate Outbreak of Human Salmonella Heidelberg Infections Linked to Ground Turkey. Available at: http://www.cdc.gov/salmonella/ heidelberg/index.html. Accessed September 5, 2012.
- 32 Engelthaler DM, Chiller T, Schupp JA, et al. Nextgeneration sequencing of Coccidioides immitis isolated during cluster investigation. *Emerg Infect Dis* 2011;17(2):227–32.
- 33 New York State Department of Health. HIV/AIDS reporting. Available at: http://www.health.ny.gov/ professionals/reportable_diseases/eclrs/hiv/index.htm. Accessed September 5, 2012.
- 34 Doyle TJ, Glynn MK, Groseclose SL. Completeness of notifiable infectious disease reporting in the United States: an analytical literature review. *Am J Epidemiol* 2002;155:866–74.
- 35 Health Protection Agency. Notifications of Infectious Diseases (NOIDs). Available at: http://www.hpa.org. uk/Topics/InfectiousDiseases/InfectionsAZ/Notifications OfInfectiousDiseases/. Accessed September 5, 2012.
- 36 Centers for Disease Control and Prevention. Case definitions for infectious conditions under public health surveillance. MMWR Recomm Rep 1997;46(RR-10):1–55.
- 37 Nguyen TQ, Thorpe L, Makki HA, Mostashari F. Benefits and barriers to electronic laboratory results reporting for notifiable diseases: the New York City Department of Health and Mental Hygiene experience. *Am J Public Health* 2007;97(Suppl. 1):S142–5.
- 38 Centers for Disease Control and Prevention. Case definitions for infectious conditions under public health surveillance. MMWR Recomm Rep 1997;46(RR-10):1-55.
- 39 Commonwealth of Australia. Australian Notifiable Diseases Case Definitions. Available at: http://www. health.gov.au/internet/main/publishing.nsf/Content/cdasurveil-nndss-casedefs-epilink.htm#epi. Accessed September 5, 2012.
- 40 Schneider E, Whitmore S, Glynn KM, *et al.* Revised surveillance case definitions for HIV infection among adults, adolescents, and children aged <18 months and for HIV infection and AIDS among children aged 18 months to <13 years: United States, 2008. *MMWR Recomm Rep* 2008;57(RR-10):1–12.
- 41 Centers for Disease Control and Prevention. Emerging Infections Programs. Available at: http://www.

cdc.gov/ncezid/dpei/eip/index.html. Accessed September 5, 2012.

- 42 Centers for Disease Control and Prevention. Cephalosporin susceptibility among Neisseria gonorrhoeae isolates: United States, 2000–2010. MMWR Morb Mortal Wkly Rep 2011;60:873–7.
- 43 MacDougall L, Fyfe M. Emergence of Cryptococcus gattii in a novel environment provides clues to its incubation period. *J Clin Microbiol* 2006;44: 1851–2.
- 44 Harris JR, Lockhart SR, Debess E, et al. Cryptococcus gattii in the United States: clinical aspects of infection with an emerging pathogen. Clin Infect Dis 2011;53:1188–95.
- 45 Centers for Disease Control and Prevention. Early Warning Infectious Disease Surveillance (EWIDS) Program Activities on the Northern and Southern Border States. Available at: http://www.bt.cdc.gov/surveillance/ ewids/. Accessed September 5, 2012.
- 46 Khan K, McNabb SJ, Memish ZA, et al. Infectious disease surveillance and modelling across geographic frontiers and scientific specialties. Lancet Infect Dis 2012;12:222–30.
- 47 Centers for Disease Control and Prevention. Pneumocystis pneumonia: Los Angeles. 1981. MMWR Morb Mortal Wkly Rep 1996;45:729–33.
- 48 Commonwealth of Virginia. Electronic Health Record Incentive Program ("Meaningful Use"). Available at: http://www.vdh.state.va.us/clinicians/meaningfuluse/ index.htm. Accessed September 5, 2012.
- 49 Centers for Disease Control and Prevention. Surveillance Brief: Surveillance Systems Supported by the Division of HIV/AIDS Prevention. Available at: http://www. cdc.gov/hiv/topics/surveillance/resources/factsheets/ surveillance.htm. Accessed September 5, 2012.
- 50 Centers for Disease Control and Prevention. HIV surveillance: United States, 1981–2008. MMWR Morb Mortal Wkly Rep 2011;60:689–93.
- 51 Eaton DK, Kann L, Kinchen S, *et al.* Youth risk behavior surveillance: United States, 2009. *MMWR Surveill Summ* 2010;59:1–142.
- 52 International Telecommunications Union. Facts and figures. Available at: http://www.itu.int/ITU-D/ict/facts/ 2011/index.html. Accessed September 5, 2012.
- 53 Fine A, Layton M. Lessons from the West Nile viral encephalitis outbreak in New York City, 1999: implications for bioterrorism preparedness. *Clin Infect Dis* 2001;32:277–82.
- 54 Constella Group. Constella Health Sciences Rewins CDC and FDA's \$21 Million Vaccine Adverse Event Reporting System Contract. Available at: http://phx.corporate-ir.net/phoenix.zhtml?c=131092

&p=irol-newsArticle&ID=1149532&highlight=. Accessed September 27, 2012.

- 55 Foege WH, Hogan RC, Newton LH. Surveillance projects for selected diseases. Int J Epidemiol 1976;5:29– 37.
- 56 Centers for Disease Control and Prevention. Global Disease Detection Program. 2010 Monitoring And Evaluation Report. Available at: http://www.cdc. gov/globalhealth/GDDER/pdf/mande2010.pdf. Accessed September 27, 2012.