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## Surveillance of Infectious Diseases

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### Glossary

**active surveillance** Surveillance method in which health officials or other persons conducting surveillance take measures to ensure reporting occurs, for example, by collecting the data themselves. Generally, this approach has the advantage of providing more complete and better data, but it is more time-consuming and resource-intensive than passive surveillance.

**case definition** Specifies the event to be counted in surveillance, thereby providing uniform criteria for reporting of cases and improving ability to compare rates of disease from place to place and over time. Components of a case definition may vary depending on the characteristics of the disease or condition, and the particular purpose of surveillance.

**notifiable disease surveillance** A notifiable disease is one for which regular, frequent, and timely information regarding individual cases is considered necessary for the prevention and control of the disease. In many countries there is a government mandate or legal requirement to report notifiable diseases to public health jurisdictions. Notifiable disease surveillance systems are largely passive.

**passive surveillance** Surveillance method that relies on health-care providers (e.g., physicians, clinical laboratories) and others to report cases, based on a published list of conditions without follow-up to ensure reporting occurs. Generally, this approach has the advantage of being simple and inexpensive to implement, but it may be limited due to incompleteness of reporting, and variability in quality and timeliness.

**public health surveillance** The ongoing, systematic collection, analysis, and interpretation of data essential to the planning, implementation, and evaluation of public health practice, closely integrated with the timely dissemination of these data to those who need to know for public health action.

**population-based surveillance** Surveillance method in which the cases reported occur in a well enumerated population, which permits calculation of disease incidence rates. Population-based surveillance may be passive or active.

**public health informatics** An evolving discipline for the systematic application of information and computer science and technology to public health practice, research, and learning.

**sentinel surveillance** The collection of surveillance data from a limited number of reporting sites. The extent to which findings from a sentinel system can be generalized to a population is a key issue in evaluating sentinel systems. Sentinel reporting sites are often chosen based on practical considerations, such as sites where a disease is considered of particular public health importance and where reporters are willing to participate.

**syndromic surveillance** Surveillance that uses case definitions based on diseases syndromes and not specific diseases, for the purpose of identifying cases before a specific diagnosis can be made. Syndromic surveillance has been used in the context of terrorism preparedness in an attempt to initiate public health response as soon as possible.

### Abbreviations

| Abbreviation | Description |
|--------------|-------------|
| ABCs         | Active Bacterial Core surveillance          |
| CDC          | Centers for Disease Control and Prevention |
| EIP          | Emerging Infections Program                |
| GBS          | group B streptococcal                       |
| GISP         | Gonococcal Isolate Surveillance Project     |
| IDSR         | Integrated Disease Surveillance and Response|
| IEIP         | International Emerging Infections Program  |
| IHR          | International Health Regulations            |
| IPD          | Invasive pneumococcal disease               |
| MIRU         | mycobacterial interspersed repetitive units |
| MMR          | measles, mumps, and rubella                |
| PAHO         | Pan American Health Organization            |
| PCR          | polymerase chain reaction                   |
Defining Statement

Surveillance is the ongoing systematic collection, analysis, and interpretation of data essential to public health practice for public health action. This article describes important principles, techniques, and global trends in modern infectious disease surveillance. The article highlights the integration of laboratory and epidemiological methods, together with information technology.

Introduction

Surveillance is the cornerstone of preventing and controlling infectious diseases of public health significance. The foundation for modern surveillance was laid down by William Farr (1807–83). Farr created a system to record the cause of death in England and Wales, a precursor to vital statistics systems around the world today. In the United States, Lemuel Shattuck collected data in Massachusetts that linked infectious disease to poor living conditions, which he used in 1850 to report the impact of public health interventions. Compulsory reporting of infectious diseases was first introduced in Italy in 1881, followed by Great Britain in 1890, and the United States in 1893. The current practice of surveillance around the world was influenced by Alexander Langmuir, chief epidemiologist at Centers for Disease Control and Prevention (CDC) between 1949 and 1969 (called the communicable Disease Center at that time). Langmuir identified the three main features of surveillance as (1) systematic collection of data, (2) consolidation and evaluation of these data, and (3) prompt dissemination of results.

The dependence of the polio control program on surveillance in the 1950s focused attention on the critical role of reporting. Specifically, in 1955, several recipients of polio vaccine developed acute poliomyelitis, threatening national vaccination programs that were then in their early years. The United States developed an intensive national surveillance system, which assisted in demonstrating that the problem was limited to a single manufacturer of the vaccine, allowing the vaccination program to continue.

Surveillance was also the foundation for the successful global campaign to eradicate smallpox, launched by the World Health Organization (WHO) in 1967. Progressively more intensive surveillance for cases was conducted as the goal of eradication approached. The eradication program used surveillance information to target vaccination to specific areas. Reporting sources were established in schools, among agricultural extension workers and others, and toward the end of the campaign, house-to-house searches were conducted in the few areas where endemic smallpox was still suspected. The last natural case occurred in Somalia in 1977.

In spite of, or in part, because of these successes, surveillance efforts lagged in the United States and globally in the 1970s and 1980s as public health authorities perceived infectious diseases to be a receding threat. In the United States, the system of surveillance for drug-resistant tuberculosis (TB) ceased in 1986 and was not re instituted until the early 1990s when the problem had become evident. Continued surveillance with earlier detection of, and response to, the increase in multidrugresistant TB would have saved considerable public health resources and human suffering. Furthermore, even as new diseases such as Escherichia coli O157:H7 infection and cryptosporidiosis were recognized, surveillance was not undertaken in most states in the United States or in other countries during the mid-1980s and early 1990s until epidemiologic investigations revealed that outbreaks were often going unrecognized or detected late.

Renewed efforts in surveillance of infectious diseases show its importance for public health, especially when epidemiology and laboratory science together form the basis for surveillance. For example, advances in virology have been instrumental in improving the usefulness of surveillance data to understand the epidemiology of viral hepatitis (Figure 1). While experts previously believed that the syndrome of acute hepatitis was probably caused by multiple viruses, nationally reported surveillance data on viral hepatitis could not distinguish between them until serologic and virologic tests for hepatitis A and hepatitis B became available.

Internationally, strengthening surveillance is recognized as a priority for the global control of measles. Available data confirm that vaccination programs were successful in reducing illness and death (Figure 2). However, many countries have limited data about the number of cases, deaths, or children vaccinated. Although mathematical models are used to estimate the number of cases and deaths due to measles where data are

| PFGE | pulsed-field gel electrophoresis |
| STD  | sexually transmitted diseases   |
| TB    | tuberculosis                   |
| WHO   | World Health Organization      |
| WRS   | Weekly Returns Service         |
not available, robust surveillance data are needed to inform those models, monitor intervention progress, and plan vaccination programs.

In the first decade of the twenty-first century, surveillance of infectious diseases has never been more vital for identifying and addressing new and emerging public health threats. These threats include zoonoses, such as West Nile virus, a mosquito-borne infection that has spread across the United States after the first case was recognized in New York in 1999, and bovine spongiform encephalopathy (BSE or mad cow disease) in the United Kingdom that was transmitted from cows fed meat-and-bone meal containing scrapie-infected sheep products; pandemic or global outbreak threats such as influenza, SARS (severe acute respiratory syndrome) and HIV/AIDS; bacteria that have developed resistance to antibiotics, such as extensively drug-resistant TB and methicillin-resistant *Staphylococcus aureus*; and the deliberate release of bioterrorist agents such as anthrax. Global recognition of the continued importance of public health surveillance to address infectious diseases and threats of emergence led to an extensive revision of the International Health Regulations (IHR, 2005), which came into force on 15 June 2007. The IHR (2005) require, among other things, that countries develop and maintain core public health capacities for surveillance and report health emergencies of international concern to WHO.

**Elements of Public Health Surveillance of Infectious Diseases**

**Purposes and Uses of Public Health Surveillance**

Public health surveillance serves a variety of purposes (Table 1). Although surveillance data have common uses at the local, regional, and national public health levels, different governmental levels may place differing emphases on how surveillance data are used. For example, individual case investigation is often more critical at the local and regional levels than at the national level, while...
evaluation of larger scale prevention and control measures (e.g., the impact of new vaccines) is a high national priority. Data from surveillance systems also support medical practice by providing information on antimicrobial resistance for development of treatment guidelines. Similarly, findings from surveillance systems may alert health professionals when an intervention is not working.

Sources of Data for Surveillance

Fulfilling the objectives of public health surveillance requires information from numerous data sources. For any given disease, a complete picture of the problem may require combining information from a variety of sources. Health-care providers and laboratories frequently provide data on individuals with reportable diseases such as measles, syphilis, TB, and salmonellosis. Other sources of medical data that are useful for surveillance include hospital discharge data, medical records of ambulatory patients, and emergency department encounters.

In addition, public health surveillance may utilize data from outside the traditional health-care system. For example, collecting disease data from animals or vectors may constitute part of surveillance for zoonotic and vector-borne diseases, such as rabies or the arboviral encephalitides. Vital statistics such as death certificate data or other sources of data not expressly collected for infectious diseases surveillance can nonetheless provide important information. For example, death certificate data can elucidate trends in infectious disease mortality (Figure 3).

In many developed countries, changes to health-care systems may impact surveillance systems for infectious diseases. For example, decreases in laboratory testing for diarrheal illnesses may result in decreased notification of enteric illnesses, such as salmonellosis and shigellosis, which in turn may result in decreased or delayed detection of outbreaks. In addition, hospital use of rapid testing may lead to a lack of available specimens for public health or other laboratories to perform molecular typing or antimicrobial resistance testing. Such specimens are helpful in evaluating which prevention and control measures are most effective.

In developing countries, conducting surveillance of infectious disease can be particularly challenging due to the lack of suitable, timely data sources, and limited public health resources. Where health systems are not strong, the reliability and validity of data may be compromised. Laboratory facilities may be minimal or nonexistent, precluding the use of laboratory confirmation or strain
characterization data to identify cases and outbreaks. Recently, much effort has been directed toward strengthening infectious disease surveillance in developing countries by integrating multiple surveillance systems when appropriate and training local public health professionals to collect and analyze data.

**Case Definitions for Public Health Surveillance**

A surveillance case definition specifies the event to be counted and thus is a fundamental requirement of any surveillance system. Case definitions provide uniform criteria for reporting cases thereby enabling valid comparisons of disease rates over time and from place to place. Components of a surveillance case definition include clinical signs and symptoms and laboratory data, and may include other defining features such as epidemiologic characteristics (person, place, and time). The choice of a surveillance case definition is a trade-off between the desire to capture all relevant health events (sensitivity) while not including nonrelevant health events (specificity), within the limitations of time, material, and personnel resources.

Surveillance case definitions vary depending on the characteristics of the disease or condition, the role and availability of laboratory testing, the method of reporting or data collection, and the purpose of surveillance. For example, isolation of *Neisseria meningitidis* from a normally sterile site (e.g., blood or cerebrospinal fluid) might define a case of meningococcal disease for a laboratory-based surveillance system; however, for surveillance during an epidemic of meningococcal disease in a developing country with limited laboratory resources, a clinical case definition (e.g., fever and a stiff neck) would be more appropriate after initial cases were culture-confirmed. The case definition may also depend on the epidemiologic circumstances; for example, surveillance for foodborne diseases may include criteria such as exposure to a point source of infection, such as a restaurant, to define cases. When a surveillance case definition is modified or updated, following the implementation of new laboratory methods, it may result in an apparent increase or decrease of disease rates over time. It is therefore important to always know the case definition and any subsequent modifications made to it when interpreting surveillance data.

Case definitions for surveillance case reporting are not intended to be used for establishing clinical diagnoses, determining treatments for individual patients, providing standards for reimbursement or quality assurance, or as rigid standards to dictate when public health action is warranted.

**Public Health Informatics**

Public health informatics is a relatively new discipline that has developed out of the related disciplines of medical informatics and bioinformatics. It is defined as the systematic application of information, computer science, and technology to public health practice, research, and learning. With the rapid pace of information technology development, new applications of public health informatics contribute to more timely and accurate data for disease surveillance. Examples include electronic laboratory reporting of notifiable diseases, aided by new data transmission standards and vocabularies; personal digital assistants or handheld computers to collect data in the field that can be downloaded into a database with no further data entry requirements; geographic information systems integrated with satellite images to provide information about the spread of diseases; use of mobile telephones to report surveillance data from the field, especially in resource-limited countries; and use of the Internet as an effective way to share surveillance data with health professionals, researchers, members of the public, and the media.

Along with these new opportunities, increasing use of information technology for public health surveillance faces many challenges, such as ensuring appropriate governance structures to protect confidentiality and privacy; providing storage capacity for increasingly large quantities of data; managing increasingly complex and costly systems associated with computer software and hardware; and the growing need for trained public health informatics professionals. As many health systems move toward the implementation of electronic patient medical records, specialists in public health informatics are needed to realize the potential of such data for public health surveillance. While the application of public health informatics has been more prominent in richer countries, the Health Metrics Network was created as a global partnership of countries, donors, and charitable foundations, to support the development of health information systems and standards worldwide, provide technical and financial support for countries with limited health informatics structure, and promote access to information by users at the local, regional, and global levels.

**Communicating Findings from Public Health Surveillance**

The purpose of public health surveillance is to provide information for action. This can only be achieved if findings from surveillance systems are communicated to the appropriate audience in a timely manner. Generally, health professionals are the main users of communications about surveillance results. Many countries produce routine national surveillance reports, such as the *Morbidity and Mortality Weekly Report* in the United States. Direct and regular communication with individuals who collect and process surveillance data not only enhances their motivation, but is also important for identifying whether unusual
or unexpected patterns in the data are caused by changes in the way data are collected. When an increase in cases detected through surveillance appears to be due to an actual increase in disease incidence, this should be promptly communicated with the relevant health authorities so that appropriate action can be taken. Promoting close working relationships with data providers and public health partners should be considered a goal in the management of any surveillance system because such relationships increase the use of surveillance data for public health action. A clear interpretation of reported surveillance findings must be provided by the responsible public health professional because factors such as changes in the case definitions for public health surveillance, different mechanisms for identifying cases (i.e., active vs. passive), the introduction of new diagnostic tests, or the discovery of new disease entities may cause changes in disease reporting that are independent of the true incidence of disease.

**Approaches to Surveillance**

There are a variety of approaches for infectious disease surveillance. The particular approach used depends on purposes of the surveillance, characteristics of the disease, sources of information, and available resources. This section highlights several approaches frequently used for infectious disease surveillance, with representative examples of each approach.

**Notifiable Disease Surveillance**

Traditionally, public health surveillance is based on notifiable disease reporting. In many countries there is a government mandate or legal requirement to report certain diseases or conditions to public health jurisdictions. Notifiable disease systems are largely passive, relying on health-care providers, clinicians, or laboratories to report cases of disease. Within public health systems, there is usually a chain of reporting from local to more central public health authorities.

While notifiable diseases data are useful for analyzing disease trends and determining relative disease burden, the data must be interpreted in light of reporting practices, which may vary from place to place. Diseases that cause severe clinical illness (e.g., plague or meningitis), if diagnosed by a clinician, are most likely to be reported accurately. When these diseases are diagnosed in a less severe form, they are less likely to be reported. In addition, persons who have diseases that are clinically mild and infrequently associated with serious consequences (e.g., salmonellosis) may not even seek medical care from a health-care provider. The degree of completeness of reporting is also influenced by factors such as the availability and use of diagnostic tests; control measures that are in effect; public awareness of a specific disease; the interests, resources, and priorities of government officials responsible for disease control and public health surveillance; and the quality of relationships between health-care providers and public health agencies.

**National Notifiable Disease Surveillance in the United States**

One of the oldest surveillance systems in the United States, the National Notifiable Diseases Surveillance System, is built upon a long-standing partnership between the CDC and state and local health departments. Public health officials at state health departments and CDC collaborate to determine which diseases should be nationally notifiable. The Council of State and Territorial Epidemiologists, with input from CDC, makes recommendations annually for additions and deletions to the list of nationally notifiable diseases. A disease may be added to the national list as a new pathogen emerges (e.g., SARS in 2003 and novel influenza A infections in 2007), and a disease may be deleted as its incidence declines (e.g., rheumatic fever in 1994). Reporting of nationally notifiable diseases to CDC by the states is voluntary. However, reporting by providers and laboratories to states is mandated by state legislation or regulation, and the list of diseases that are considered notifiable, therefore, varies slightly by state.

Because trends in many infectious diseases have the potential to shift, surveillance needs to be as timely as required. Reports from health-care providers and laboratories regarding individual cases of notifiable diseases, such as measles, hepatitis, syphilis, and *E. coli* O157:H7 infection, are essential to the function of this surveillance system at local, state, and national levels. These reports are generally communicated to the local health department, which passes the information on to the state health department. Each state health department, in turn, reports their data to CDC on a weekly basis. Data exchange is done using a national electronic reporting system capable of capturing data already in electronic form, such as laboratory results. Urgent matters requiring rapid public health response, cases of botulism or meningococcal meningitis, or a multistate outbreak of foodborne disease, for example, are reported immediately to the local, state, or federal jurisdiction.

**Integrated Disease Surveillance and Response**

Integrated Disease Surveillance and Response (IDSR) is a strategy of the WHO African Regional Office. Specifically designed for African countries with limited notifiable disease surveillance systems, IDSR aims to reduce mortality, disability, and morbidity from infectious diseases by informing timely public health action. IDSR does this by integrating surveillance systems...
already established by single-disease control programs, integrating laboratory and epidemiology efforts, and developing human resource capacity at the district level. IDSR targets 20 priority infectious diseases, which are broadly categorized as epidemic-prone diseases, diseases targeted for elimination and eradication (both are defined as a reduction of new infections to zero, but elimination requires continued measures to prevent reestablishment of disease), diseases that are endemic, and pandemic influenza.

Linking surveillance to action is a primary goal of IDSR. This is carried out by using a surveillance threshold approach to alert public health professionals about situations where action is needed. These thresholds are defined by each country based on the epidemiology of the disease. The success of IDSR relies on building capacity for epidemiologic surveillance at the local level, which is achieved through a combination of developing technical manuals and implementing training programs. Monitoring and evaluation of IDSR using standard indicators for all countries promotes continued quality improvement. Underpinning IDSR is the development of standard laboratory diagnostic methods for confirming priority diseases. This includes an external quality assessment program for health laboratories in the WHO Africa region that is modeled on the Canadian Microbiology Proficiency Training Program and organized by the National Institute for Communicable Diseases in South Africa.

An example of how IDSR works can be illustrated by an outbreak of meningitis in Burkina Faso, an African country located within an area known as the ‘meningitis belt’ that stretches across central Africa. Burkina Faso uses an alert threshold of 3 cases per 100,000 persons per week, which is recommended by WHO when epidemic activity is confirmed in neighboring countries. In January 2008, four districts within the country exceeded the alert threshold: Mangodara 7.6 cases per 100,000; Sapouy 8.4 cases per 100,000; Segueneba 6.5 cases per 100,000; Gaoua 6.2 cases per 100,000. A national outbreak management committee was formed to direct the public health response. Based on the data from IDSR surveillance, in conjunction with findings from epidemiologic and laboratory investigations, a mass vaccination campaign was undertaken in the affected districts.

**Active Population-Based Surveillance**

In contrast to passive surveillance, which relies on public health officials to initiate the reporting of cases of disease, health officials conducting active surveillance take measures to ensure reporting. Active population-based surveillance is often considered the ‘gold standard’ of surveillance because in addition to capturing close to 100% of cases, the population under surveillance (e.g., in a district or province) is well enumerated. This means that active population-based surveillance systems generate more complete, better quality data; enable the accurate calculation of disease rates to monitor disease trends, especially in population subgroups; and can be used for robust evaluations of the impact of public health interventions. However, because active population-based surveillance is more time-consuming and resource-intensive than passive surveillance, it is usually limited to select geographic areas rather than an entire country.

**The United States Emerging Infections Program Network**

The Emerging Infections Program (EIP) is a network of CDC and ten state health departments, along with collaborators in academic institutions, infection control practitioners, and other federal agencies. The network conducts active population-based surveillance; engages in applied laboratory and epidemiologic research, and pilot tests; and evaluates prevention and control measures. This network, with special surveillance efforts in targeted areas, complements national passive notifiable disease surveillance. Here we present two examples from the Active Bacterial Core surveillance (ABCs), an EIP project that links laboratory isolates to active population-based surveillance data about invasive diseases caused by emerging, vaccine-preventable, and drug-resistant bacterial diseases.

Invasive pneumococcal disease (IPD) is a major cause of meningitis, pneumonia, and bacteremia, mostly affecting young children and the elderly. In 2000, a pneumococcal conjugate vaccine for use in infants and young children was introduced in the United States. The vaccine targets seven pneumococcal serotypes that cause most IPD cases in the United States. The impact of the new vaccine could be measured by ABCs, where a case is defined as isolation of *Streptococcus pneumoniae* from normally sterile sites (usually blood or cerebrospinal fluid). Between 1998–99 and 2005, the incidence of IPD (all serotypes) among children <5 years declined from 98.7 to 23.2 cases per 100,000 (Figure 4). Use of the vaccine also reduced IPD among unvaccinated children and adults by reducing nasopharyngeal colonization and transmission of vaccine-type pneumococci from vaccinated children (i.e., indirect or herd effects). The reduction in IPD was driven by reductions in vaccine serotypes, resulting in an estimated 14,200 fewer IPD cases in children <5 years nationally. In contrast, the rate of IPD in children <5 years caused by nonvaccine serotypes increased from 16.8 to 21.7 cases per 100,000, largely due to an increase in serotype 19A. Results from ABCs suggest that the emergence of nonvaccine serotypes has occurred following the introduction of the vaccine and that including additional serotypes in pneumococcal
vaccines, especially 19A, would further contribute to the reduction of IPD in the United States.

Since its emergence in the 1970s, group B streptococcal (GBS) disease has been the leading bacterial infection associated with illness and death among newborns in the United States. ABCs has played a key role in guiding and monitoring the impact of neonatal GBS disease prevention efforts. ABCs defines a case of invasive GBS disease as the isolation of GBS from a normally sterile site or from the placenta or amniotic fluid in instances of fetal death. ABCs documented a 70% decline in the incidence of invasive GBS disease in the first week of life after the issuance of the first national consensus prevention guidelines in 1996, which recommended either screening pregnant women using prenatal cultures or assessing obstetric risk factors intrapartum. In 2002, ABCs data contributed to the issuance of revised national guidelines for the prevention of prenatal GBS disease, which recommends universal screening of pregnant women by culture for rectovaginal GBS colonization at 35–37 weeks' gestation and the use of intrapartum antibiotic prophylaxis for GBS carriers. Since the implementation of these guidelines there has been a further decline in GBS. From 2002 to 2005 ABCs identified 1020 cases of early-onset disease (in the first week of life). Compared to the period 2000–01, before the guidelines were introduced, incidence of early-onset disease during 2003–05 was 33% lower (0.33 vs. 0.49 cases per 1000 live births) (Figure 5). However, further analysis indicated that while incidence decreased among white infants, it increased among black infants. These surveillance findings highlight that the revised guidelines have contributed to a reduction in neonatal GBS disease, but not in all racial groups, and that further strategies are needed for prevention and to reduce racial disparities in GBS disease.

International Emerging Infections Program

The International Emerging Infections Program (IEIP) was established in Thailand, Kenya, China, Guatemala, and Egypt (as of 2006) as a collaboration with the Ministries of Health in those countries and CDC to address emerging infections. A core component of IEIP is active population-based surveillance for diseases of local and international importance, such as pneumonia and diarrhea, together with strengthened laboratory capacity. This is particularly important for countries as high-quality data on the incidence and cost of infectious disease can be used to prioritize the development and evaluation of control programs, including vaccination. Without reliable surveillance data, the relative importance of certain infectious diseases may be obscured; poor data may not reveal the effectiveness of public health measures already in place.
When planning a new active population-based surveillance system, it is important to understand how local people use health-care services. As this differs from country to country, a 'one-size-fits-all' approach is not possible. Understanding how people seek medical care can be performed by conducting health-care utilization surveys. For example, in Thailand people with pneumonia often go to hospital to seek care. Therefore, the IEIP pneumonia surveillance system in Thailand was set up in 20 hospitals in two provinces that serve a population of 1.2 million people. In contrast, in rural Kenya, people with pneumonia do not often go to hospital and so community-based surveillance is more appropriate. To accomplish this, surveillance officers collect data about approximately 62,000 individuals by visiting their households every 2 weeks. Building the necessary surveillance infrastructure requires training of surveillance personnel; creating systems and procedures for the collection, transmission, and storage of data; building epidemiological and laboratory capacity within the country; and developing high-quality reference laboratory testing. A further strength of IEIP active population-based surveillance is that it provides a platform upon which research activities can be built, including etiology studies, intervention studies, and cost-effectiveness studies.

The work of IEIP Thailand, established in 2001, has led to new insights about influenza epidemiology in the tropics. Previously, influenza was considered to be a mild and a relatively less important disease in Thailand. However, active population-based surveillance revealed that the incidence of hospitalized influenza-related pneumonia may be as high as 111 per 100,000 persons and outpatient influenza 1420 per 100,000 persons, compared to between 64 and 91 cases of influenza per 100,000 persons (inpatient and outpatient combined) during the years 1993–2002 as measured by the national passive surveillance system. Those with the highest risk of hospital admission due to influenza-related pneumonia were the young, elderly, and those with chronic diseases. Overall, the public health burden of influenza in Thailand was estimated at US$63 million per year. The surveillance system also documented clear seasonal trends in influenza incidence with a peak in July, breaking the dogma that influenza occurred at low levels year round in the tropics. Data from other tropical countries support this finding and have important implications for vaccine timing. In Thailand, these data contributed to the formulation of health policy in Thailand in 2008 in favor of seasonal influenza vaccine in persons >65 years with underlying disease.

Sentinel Surveillance

Sentinel surveillance systems collect data from a limited number of reporting sites. For example, a sentinel surveillance system may only include a few hospitals within a country or state. This approach is advantageous where it is not feasible to include all reporting sites, or due to constraints of public health resources, such as in low- and middle-income countries. The extent to which findings can be generalized to a population is a key issue in evaluating sentinel systems. Selection of sentinel reporting sites is often based on practical considerations, such as sites where the disease is considered of particular public health importance and where reporters are willing to participate. However, this typically means that not all reporting sites (and hence individuals with disease) have an equal probability of being included in the surveillance system, which limits the ability to make statistically representative disease estimates using sentinel surveillance data.

In the United States, the Gonococcal Isolate Surveillance Project (GISP) was established in 1986 to monitor trends in antimicrobial susceptibilities of strains of *Neisseria gonorrhoeae* and to establish a rational basis for the selection of gonococcal therapies. GISP is a collaborative project among selected sexually transmitted diseases (STD) clinics, five regional laboratories, and CDC. During 2006, GISP included *N. gonorrhoeae* isolates collected from the first 25 men with urethral gonorrhea attending STD clinics each month in 28 clinics around the United States (Figure 6). Findings from GISP have included the continued high prevalence of
resistance to both penicillin and tetracycline, which has remained above 22%; the emergence and increasing prevalence of resistance to the fluoroquinolones; the appearance and increasing prevalence of decreased susceptibility to the macrolides; and the emergence of multidrug-resistant isolates (resistant to penicillin, tetracycline, and fluoroquinolone) with decreased susceptibility to cefixime. GISP findings have directly contributed to STD Treatment Guidelines in 1993, 1998, 2002, and 2006 and updates to the guidelines in 2004 and 2007.

In England and Wales, sentinel surveillance of infectious diseases has been conducted by the Royal College of General Practitioners since 1957. The Weekly Returns Service (WRS) is a network of over 100 primary care clinics, covering a patient population of almost 1 million persons. Weekly, data are extracted from electronic medical records for all patients attending a primary care clinic within the network. Clinical diagnoses are recorded using Read codes, a hierarchical coding schema especially designed for primary care in the United Kingdom and cross-referenced to ICD-9. WRS plays an important role in national influenza surveillance by tracking incidence of patients presenting with influenza-like illness each week. Moreover, laboratory specimens from these patients are tested to monitor circulating strains of seasonal influenza.

GeoSentinel is an international sentinel surveillance network of travel and tropical medicine clinics. Established in 1995 by the International Society of Travel Medicine and CDC, GeoSentinel currently includes 39 clinics in 25 countries. The aim is to monitor disease trends among travelers and other globally mobile populations around the world. For example, over one-fourth of returned travelers attending a GeoSentinel clinic between 1997 and 2006 presented with fever, of which 17% was due to a vaccine-preventable illness or malaria, highlighting the importance of pretravel preventive medicine.

**Syndromic Surveillance**

Syndromic surveillance uses case definitions that specify disease syndromes and not specific diseases. Since the terrorist attacks on 11 September 2001 and the anthrax attacks in the same year, the US government has made considerable investment in automated statistical analysis of disease syndromes in an effort to detect disease events earlier than traditional surveillance systems, with a focus on detection of possible bioterrorism events.

Syndromic surveillance typically involves daily analysis of data from hospital emergency departments or other sources about the number of patients presenting with one of a collection of disease symptoms (i.e., a syndrome). Early symptoms of many outbreak-prone diseases and bioterrorist agents are not specific. Thus syndromic surveillance may focus on common symptoms such as sore throat, headache, muscle pain, and malaise. Although sophisticated statistical methods are being developed to analyze these data, in essence they assess whether the number of cases averaged over several days exceeds a predetermined alarm threshold.

In Boston, Massachusetts, a syndromic surveillance system was developed for the 2004 Democratic National Convention and has subsequently been incorporated into
the routine public health surveillance system. Each day, patient visit data are electronically transmitted from ten hospital emergency departments in Boston. For each patient, the automated system classifies information on chief complaints into seven infectious disease syndromes, along with gender, zip code, age, and race. These data are analyzed daily by an automated software program to look for unusual patterns. The Boston system has been expanded to include daily data from death certificates, emergency medical services, and Boston-based calls to the Regional Center for Poison Control and Prevention.

Syndromic surveillance faces many challenges. Current syndromic surveillance systems are not good at identifying an insidious ‘rising tide’ of cases. Detecting bioterrorist events from the routine patient caseload of an emergency room is most reliable when large spontaneous events occur. However, these events would most likely be noted by clinicians whether or not a surveillance system was in place. To be timelier than traditional surveillance systems or reports from clinicians, syndromic surveillance monitors nonspecific health data from which it may be difficult to identify bioterrorist-related events and outbreaks. The problem is that reducing the alarm threshold to identify events involving fewer patients will produce more false alarms. Finally, the utility of syndromic surveillance systems depends entirely on rapid public health investigation once an alarm threshold is exceeded, which requires integration with routine public health surveillance and availability of public health professionals to conduct investigations.

In addition to using emergency department visits, attempts have been made to use other data sources for syndromic surveillance, including purchases of over-the-counter medications and the number of laboratory tests requested by doctors. The Global Public Health Information Network scans web pages for media stories about infectious disease outbreaks and events of public health significance around the world. ProMed is an Internet listserv moderated by the International Society for Infectious Diseases, which collects reports from clinicians and public health professionals globally. While reports are not substantiated by the moderators, ProMed may provide an early indication of a new health problem: the first report of SARS was posted on ProMed in February 2003. Prediction markets have been proposed as a novel way of predicting seasonal influenza activity: expert health professionals can trade on an artificial market, which is interpreted as the consensus professional belief about future events.

**Multinational Surveillance Systems**

The potential for diseases to spread between countries is increased by global trade and international travel. For example, air travel facilitated the spread of SARS from southern China to 29 countries around the world between November 2002 and July 2003. Multinational surveillance systems represent collaborative efforts by countries to control and respond to transnational disease threats. They do so through reporting cases of a disease in one country to alert other countries about possible outbreaks; identifying outbreaks where cases are distributed in small numbers across several countries; facilitating the investigation of common sources of infection, such as contaminated food or medicines; allowing tracking of disease trends at supranational or regional levels; and measuring the impact of control measures employed by different countries.

Multinational surveillance systems may be created through a network of linked national surveillance systems. Enter-net, an international surveillance network for gastrointestinal infections, includes 15 countries in the European Union, in addition to Australia, Canada, Japan, South Africa, Switzerland, and Norway. Each country submits monthly data on laboratory-confirmed cases of verocytotoxin producing *E. coli*, *Salmonella*, and *Campylobacter*. In 2001, Enter-net was used to investigate an outbreak in seven countries that led to identification of over 500 cases and was caused by chocolate contaminated by *Salmonella* Oranienburg. The Regional Immunization Program of the Americas, coordinated by the Pan American Health Organization (PAHO, the WHO Regional Office for the Americas), is a multinational network with the aim of protecting children from vaccine-preventable diseases. A central component of the program is surveillance, whereby each country provides weekly surveillance data on vaccine-preventable diseases, which are analyzed by PAHO, and communicated to member countries via a weekly bulletin. Other regional surveillance networks include the European Centre for Disease Prevention and Control, the Caribbean Epidemiology Centre, and the Pacific Public Health Surveillance Network. Challenges for multinational surveillance networks include differences in case definitions, laboratory methods, health-care systems, health-care utilization patterns, and public health priorities.

Several global surveillance systems created for specific diseases are coordinated by WHO. The Global Influenza Surveillance Network was established in 1952 and comprises four WHO Collaborating Centers and 121 institutions in 93 countries. Laboratories in these countries collect clinical specimens and perform primary virus isolation and preliminary antigenic characterization. Newly isolated strains are sent to one of the four collaborating centers for further laboratory antigenic and genetic analysis. The results from the network inform the composition of influenza vaccine each year. Another example is global surveillance of poliomyelitis, which is a core component of the Global Polio Eradication Initiative. Polio-endemic areas conduct active surveillance.
for cases of acute flaccid paralysis in children <15 years, which includes testing of clinical specimens by a WHO accredited laboratory. In addition, all nonendemic countries are required to report cases of polio to WHO under the IHR.

In 2005, WHO published a major revision of the IHR. Originally adopted by WHO Member States in 1969, with minor revisions in 1973 and 1981, the IHR were created to address the international spread of epidemics. (The IHR were preceded in 1951 by the International Sanitary Regulations.) The IHR included a set of legal obligations for WHO Member States, which broadly encompassed the reporting of human cases of cholera, plague, and yellow fever, and adherence to specified sanitary requirements for international ports and airports. In 1995, the World Health Assembly agreed to fully revise the IHR, a process that took 10 years. The IHR (2005) have a much broader scope and new obligations for WHO Member States, largely influenced by recent global trends, including increased international trade and movement of people; the emergence and reemergence of infectious diseases; increasing drug resistance; environmental changes; civil conflicts; natural and man-made disasters; and deliberate acts involving chemical, radiological, or infectious agents. To conduct surveillance of such a wide variety of events, IHR (2005) mandates the reporting of all ‘public health emergencies of international concern’ (Figure 7).

Four infectious diseases must always be reported to WHO: smallpox, poliomyelitis due to wild-type poliovirus, human influenza caused by a new subtype (e.g., H5N1 in humans), and SARS. Other significant features of IHR (2005) include the requirement for Member States to provide detailed information in order that WHO may conduct an assessment of risk, a mandate allowing WHO to seek verification of events under IHR (2005), and an obligation for all Member States to maintain core public health capacities for surveillance.

**Laboratory and Epidemiology Integration as a Critical Element of Infectious Disease Surveillance**

Laboratory-based surveillance refers to surveillance systems that identify cases using laboratory results. The value of laboratory-based surveillance systems is somewhat dependent on the disease under surveillance. For example, most patients in the United States with meningococcal disease will have an isolate from a sterile site (cerebrospinal fluid or blood) sent for laboratory investigation. Therefore, a surveillance system that includes all cases of laboratory confirmed *N. meningitidis* is likely to identify most cases. In contrast, relatively few cases of foodborne illness are identified by a laboratory and supplemental sources of surveillance data and epidemiologic surveys are needed to capture other cases (Figure 8). The role of laboratory-based surveillance also depends on the frequency and clinical presentation of the disease. For example, measles is a relatively uncommon disease following the introduction of the measles, mumps, and rubella (MMR) vaccine and new cases should be confirmed by laboratory testing.

Molecular methods are now widely used by public health laboratories for surveillance. These methods enable routine classification of microorganisms at the subspecies level to help identify outbreaks and disease trends. Molecular methods are an integral part of surveillance for several diseases, such as influenza, *Salmonella*, polio, and TB. However, interpreting strain characterization is not always straightforward and depends on the genetic diversity of the agent, the prevalence of the strain, the stability of genetic markers used to compare strains, and the ecology of the microorganism in question. Therefore, the contribution of molecular methods for infectious disease surveillance depends on a good understanding of epidemiologic factors.

**PulseNet**

Foodborne outbreaks have traditionally been considered as occurring in a defined population at a single point in time, such as a *salmonella* outbreak at a party. With the advent of modern food processing, low-level contamination of a widely distributed product may occur over wide geographic areas and among diverse populations. To detect and control these outbreaks, CDC initiated PulseNet, a national network of public health laboratories that perform pulsed-field gel electrophoresis (PFGE) subtyping of *Salmonella*, *E. coli* O157:H7, *Listeria monocytogenes*, *Streptococcus*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Campylobacter jejuni*, and *Yersinia pestis*. Since 1995, PulseNet has used standardized PFGE methods to create a national database of PFGE patterns from laboratories across the country. Today more than 70 local public health and federal food regulatory agency laboratories participate in PulseNet and each one of them has their own local database with online access to the national database. This makes it possible to perform searches of local and national databases for clusters of PFGE patterns that are indistinguishable. PulseNet enables surveillance for foodborne outbreaks that previously were difficult to detect due to the physical distance between cases, and to differentiate disease outbreaks from sporadic cases of disease. PulseNet has revolutionized the detection of case clusters representing outbreaks of foodborne infections.

A multistate outbreak of *Salmonella* infections in 2006–07 demonstrates the power of PulseNet. In November 2006, public health officials at CDC and state health departments noticed a substantial increase in infections caused by *Salmonella* Tennessee. Infections due to this
A case of the following diseases is unusual or unexpected and may have serious public health impact, and thus shall be notified:
- Smallpox
- Poliomyelitis due to wild-type poliovirus
- Human influenza caused by a new subtype
- Severe acute respiratory syndrome (SARS)

Any event of potential international public health concern including those of unknown causes or sources and those involving other events or diseases than those listed in the box on the left and the box on the right shall lead to utilization of the algorithm

Is the public health impact of the event serious?

Is the event unusual or unexpected?

Is there significant risk of international spread?

Is there significant risk of international travel or trade restrictions?

EVENT SHALL BE NOTIFIED TO WHO UNDER THE INTERNATIONAL HEALTH REGULATIONS

Figure 7  International Health Regulations (2005) decision instrument for the assessment and notification of events that may constitute a public health emergency of international concern.

serotype are rare, with an average of 52 cases reported each year in the United States between 1994 and 2004, about 0.1% of all reported Salmonella strains. However, between July 2006 and May 2007, a total of 628 cases were reported to PulseNet. Cases were reported from 47 states (Figure 9). Twenty percent of patients were hospitalized; no deaths due to Salmonella Tennessee were reported. Interviews with patients identified many who had eaten peanut butter in the week before illness onset. A case-control investigation of 65 patients and 124 controls concluded that cases were more likely to have eaten Peter Pan or Great Value brand peanut butter (matched odds ratio = 10.9, 95% confidence interval = 3.8–43.0). Immediately, the Food and Drug Administration issued a health alert to consumers warning them not to eat these brands of peanut butter, and the manufacturer voluntarily recalled the products and ceased production. A search of patient isolates in the PulseNet database found three closely related PFGE patterns associated with this outbreak. Two of these outbreak strains were isolated from 21 unopened jars of peanut butter collected from 13 states. This was the first outbreak of a foodborne illness caused
by peanut butter in the United States and demonstrates the potential for widespread illness due to the distribution of contaminated food as well as the potential for prevention of foodborne disease through responsive surveillance and timely public health action.

TB Genotyping Service

TB control programs in 50 states and two major cities (New York and San Diego) participate in CDC’s TB genotyping service. Since 2004, two laboratories, one in Michigan and the other in California, have been contracted by CDC to conduct genotyping of isolates from culture-positive patients. The genotyping laboratories use two polymerase chain reaction (PCR) genotyping methods for DNA analysis: spoligotyping, a hybridization assay that detects variability in the direct repeat region in the DNA; and mycobacterial interspersed repetitive units (MIRU) analysis, which identifies the number of copies of DNA segments containing tandem repeated sequences. A further method, IS6110-based restriction fragment length polymorphism analysis, which compares the number of copies and positions of the insertion element IS6110 in the genome, is used to further discriminate between two isolates with identical PCR results. Automated instruments determine the spoligotype and MIRU type, and the results are directly imported into a genotyping laboratory-tracking database. The database compares spoligotype and MIRU type with all other isolates previously submitted from the same TB program and emits a report directly to that program.

Figure 8  Schematic representation of the burden of foodborne diseases and corresponding surveillance data sources.

Figure 9  Number of confirmed cases ($N = 628$) (cases with an outbreak-associated pulsed-field gel electrophoresis (PFGE) pattern) of *Salmonella* Tennessee infection associated with consumption of peanut butter, by state – United States, 1 August 2006 to 22 May 2007.
TB genotyping identifies genetic relationships between *Mycobacterium tuberculosis* isolates from different TB patients. If the genotypes from two TB patients do not match they are unlikely to be involved in the same chain of recent transmission (within the previous 2 years). Two patients who have isolates with matching genotypes may be involved in the same chain of recent transmission, but this can be confirmed only if patients share epidemiologic links that can explain where and how they transmitted TB among themselves. Patients with matching genotypes that share no known epidemiological links are not likely to be involved in the same chain of recent transmission.

In an outbreak of TB in a homeless shelter in New York, TB genotyping was used to identify possible chains of transmission. From January to July 2003, four TB cases were reported in a 1001-bed homeless shelter operated by the New York City Department of Homeless Services and located in Orange County, New York. Further review of health records revealed four additional cases of TB among residents in the same period. A further six cases were identified by matching the list of residents at the shelter with the statewide TB register and six more cases were identified among former residents. The *M. tuberculosis* genotyping database at the New York State Department of Health was searched for strains matching isolates from the reported cases and five additional TB cases among former residents were found. Active case finding among shelter residents identified another four culture-positive pulmonary TB cases. In total, 29 TB cases were identified. Of the 26 TB cases with genotyping data available, 11 shared the same genotype associated with the homeless shelter, 8 shared a different genotype, and 7 had genotypes not matching other residents. In this outbreak, genotyping helped characterize the transmission of TB among homeless shelter residents and suggested that multiple chains of transmission occurred simultaneously. This investigation demonstrates the importance of TB screening for existing and new residents of homeless shelters.

**Conclusion**

Surveillance of infectious diseases remains crucial for providing high-quality information on which to base and evaluate public health actions. The adoption of the IHR (2005) underscores the continued importance of public health surveillance as well as the ongoing commitment from countries around the world to track the occurrence of infectious diseases. However, modern surveillance systems must keep pace with the dynamic emergence of infectious diseases and the factors that influence it: human demographics and behavior; technology, economic development, and land use; international travel and commerce; microbial adaptation and change; and breakdown of public health measures. Included in these modern challenges is the need for preparedness to detect and respond to potential acts of bioterrorism. Modern technology also offers opportunities to further develop surveillance systems. For example, continued development of diagnostic and molecular laboratory methods, when effectively combined with epidemiologic information, can make prevention, recognition, and response to outbreaks faster and more precise. Furthermore, developments in information technology can facilitate linking diverse sources of data, rapid analysis and synthesis of large amounts of information, and development of the communications and networks needed globally for surveillance and response to infectious diseases.

Disclaimer: The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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**See also:** AIDS, Historical; Cholera, Historical; Epidemiological Concepts and Historical Examples; Global Burden of Infectious Diseases; Hepatitis Viruses; History of Microbiology; Respiratory Viruses; Smallpox, Historical; Teaching Resources, Microbiology; Vaccines, Viral; Zoonoses

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