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Surveillance for Newly Emerging Viruses

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Introduction and background

Newly emerging infectious diseases will pose an increasing global health threat over the next 20 years. However, the future impact of infectious diseases will be heavily influenced by the degree of success of global and national efforts to create public health infrastructure with effective systems of surveillance and response (Institute of Medicine of the National Academies, 2003).

Goals of surveillance

Surveillance is a fundamental tool for public health, producing information to guide actions. Modern surveillance tends to follow health measures such as the incidence of a disease or syndrome or even the occurrence of health-related behaviors. There are many reasons for conducting surveillance, and the data collected and the approach taken to analyzing those data are both influenced by the overall goal of a surveillance system. In the context of newly emerging viruses, surveillance may be performed to detect disease outbreaks, to monitor the spread or development of ongoing outbreaks, to evaluate the effectiveness of disease control measures, or to identify the determinants of infection and disease.

The focus of this chapter is on surveillance that will provide information useful for the detection of disease outbreaks due to newly emerging viruses. Surveillance systems aimed mainly at detection also provide information that may be useful for other purposes. The goal of detecting an outbreak of a newly emerging virus, however, places specific demands on the type of data collected and the types of analysis performed.

The term 'newly emerging' virus is different from 'emerging virus' in that a newly emerging virus has not yet been isolated in the laboratory (Barrett et al.,

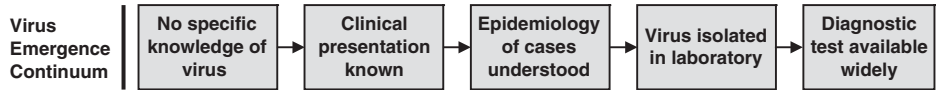

Fig. 1 Surveillance continuum for a newly emerging virus.

1998). Whether the virus has been isolated, and more importantly, whether a diagnostic test is available, have implications for surveillance. As a new virus becomes recognized (Fig. 1), or 'emerges,' it is initially recognized through the clinical presentation of infected individuals. Cases of an apparently novel infectious illness in humans will prompt epidemiological investigations and initiate efforts to isolate the causative agent. Once the agent has been isolated, effort often turns to development of methods for diagnosis. At some point in this progression, the virus is seen as an established cause of endemic or epidemic disease, and is no longer thought of as 'newly emerging.'

The distinction between 'newly emerging' and 'emerging' viruses is therefore important from the perspective of surveillance, because it determines what data a surveillance system can draw upon. For 'newly emerging viruses,' any case definition must rely on clinical and possibly epidemiological data because there are no recognized laboratory tests. Routine surveillance of laboratory test results is likely to be of little use in sounding the initial alarm in an outbreak due to a newly emerging virus. An exception might be if the newly emerging virus is genetically similar to an existing virus, to the extent that it can cross-react in an existing diagnostic test. However, laboratory testing will be useful for ruling out known viruses as the cause of illness, and ultimately to identify the virus. The surveillance system must follow data other than positive laboratory test results, such as reports of abnormal cases, or the incidence of non-specific symptoms, or syndromes that might occur following infection with a newly emerging virus.

This observation raises an important point, which is that the likelihood of identifying a newly emerging virus through surveillance will depend, among other factors, on the novelty and the severity of symptoms due to infection with the virus and the number of symptomatic cases. The surveillance approach that is most likely to detect an outbreak due to a newly emerging virus will vary with virus and outbreak characteristics. Depending on the combination of clinical presentation of those infected and the genotype of the virus (Fig. 2), different methods will be more or less efficient for early outbreak detection. Outbreaks of newly emerging viruses characterized by symptoms common to other infections already under surveillance may be detected by an existing surveillance system if the number infected is sufficiently large. Alternatively, infections with a newly emerging virus causing symptoms similar to another, known pathogen may be incorrectly attributed to the known pathogen, thereby obscuring the emerging epidemic. Genetic similarity to a known virus may hasten the identification of a newly emerging virus and the development of a diagnostic test as well as contribute to our understanding of its host range, natural reservoir, and transmission route.

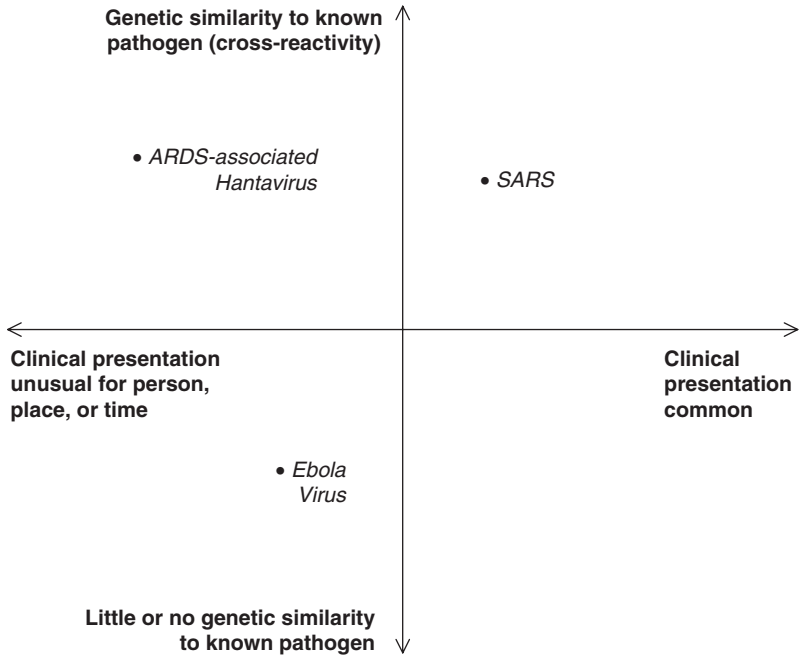

Fig. 2 Factors influencing the initial detection of outbreaks due to newly emerging viruses.

Relevant examples

The chronology of events surrounding the initial detection of two emerging viral disease, SARS-CoV and Hantavirus, illustrate how different approaches to surveillance contributed to the initial detection and early management of these outbreaks.

SARS

The emergence of severe acute respiratory syndrome (SARS) (Table 1; Brookes and Khan, 2005), caused by the SARS-CoV virus, was obscured because it appeared initially in the Chinese province of Guandong as cases of atypical pneumonia that were clinically similar to influenza and that occurred concurrently with an outbreak of avian influenza in chickens. The large number of cases and the circumstances similar to those of influenza outbreaks ensured that the SARS outbreak was detected, but the similarity of the clinical presentation to other diseases may have initially mislead public health officials about its etiology. Reports of an atypical pneumonia or influenza outbreak in China circulated as early as November 2002, disseminated via ProMED-mail (an Internet and email-based reporting and surveillance system), and picked up by the web-crawling surveillance system GPHIN (Global Public Health Intelligence Network, developed by Health Canada). The

Table 1

Timeline of SARS outbreak detection and virus identification (Brookes and Khan, 2005)

November 16, 2002	First known case of SARS occurs in Guandong Province, China
November 23, 2002	During a routine flu workshop in China, a participant informs the WHO Influenza Laboratory Network of a serious outbreak in Guandong, with high mortality and high involvement of health care staff
November 27, 2002	GPHIN (web-crawler developed by Health Canada) picks up rumors of avian influenza outbreak in mainland China
December 2002	Chinese Ministry of Health confirms outbreak of influenza B, now under control
February 10, 2003	An American infectious disease consultant receives an email from China concerning a rumor of closed hospitals and people dying due to an outbreak in Guangzhou. He posts the content of the e-mail on ProMED A relative of a former employee informs WHO of an epidemic involving over 100 fatalities in China. WHO contacts the Chinese Ministry of Health
February 11, 2003	The Chinese Ministry of Health in Beijing issues an official statement acknowledging an outbreak of atypical pneumonia dating back to November 2002 and involving 300 cases, of which 1/3 were health care workers
February 17, 2003	First SARS case introduced in Hong Kong
February 19, 2003	WHO issues an avian flu alert
February 26, 2003	First SARS case introduced in Vietnam
March 1, 2003	First SARS case introduced in Singapore
March 11, 2003	Outbreak of 'acute respiratory syndrome' among hospital workers in Hong Kong
March 13, 2003	SARS outbreak reaches Toronto
March 15, 2003	WHO confirms that SARS is a worldwide health threat, and that suspected cases have been identified in Canada, Indonesia, Philippines, Singapore, Thailand, and Vietnam
March 19, 2003	SARS spreads to the US, UK, Spain, Germany, and Slovenia
March 21, 2003	SARS coronavirus identified. Official identification announced on April 16
April 2003	PCR test to diagnose SARS from nasopharyngeal aspirate becomes available, followed by serological assay to diagnose SARS from blood sample

course of illness was rapid and its presentation severe; therefore the initial cases were not identified until infected persons sought the attention of health care professionals and a clinical assessment was made.

It was only when the outbreak spread beyond mainland China in February 2003 to hospital staff in Hong Kong that reliable information became available concerning the mysterious 'acute respiratory syndrome', allowing a novel etiology

to be hypothesized. It was recognized that the disease was unlike influenza when numerous health care professionals treating SARS patients fell ill themselves. As more became known about the illness, syndromic surveillance (i.e., surveillance of cases identified on the basis of clinical symptoms, in this case fever and respiratory symptoms), contact tracing, and quarantine were implemented.

The virus was found to be a new coronavirus. Isolation of the virus did not occur initially, perhaps because the isolation of a coronavirus did not immediately raise suspicion because coronaviruses are commonly associated with milder respiratory illness. Laboratory-based surveillance did not become available until later in the outbreak, when diagnostic PCR and serology tests were developed. Population screening for SARS antibodies was instituted in some countries, with mixed results due to poor specificity of early versions of the tests.

Hantavirus

In contrast to the SARS outbreak, the May 1993 outbreak of acute respiratory distress syndrome (ARDS) in the Four Corners region of the western United States involved few cases and an unusual clinical presentation. According to many sources, the Four Corners epidemic would not have been detected, if not for one astute internist who saw a connection between an unusual death in his patient due to an acute respiratory syndrome, and the similar fatal illness of his fiancée. The illness was severe and the course rapid, therefore cases initially were identified only after infected persons sought medical attention. The internist sounded the alarm, alerting the state health department epidemiologist to a possible communicable disease outbreak; the epidemiologist launched a retrospective investigation to identify other similar recent cases, and instituted a mechanism for reporting suspected outbreak cases (Institute of Medicine of the National Academies, 2003).

Identification of the pathogen responsible for this outbreak was made easier and quicker because the virus was from a known virus family, and antibodies to the new virus cross-reacted with known viruses in the same family. The CDC's viral pathogens branch tested the clinical specimens received from Four Corners against antibodies for every known virus, and the test was positive for Hantavirus.

Hantaviruses had been discovered during the Korean War (1951–1954). Although they were known to cause renal impairment, they had never been associated with respiratory illness. Mice were known to be a reservoir for hantaviruses, so rodents were trapped in Four Corners and tested. PCR techniques were used to identify the deer mouse as the reservoir of Hantavirus in this outbreak.

Surveillance methodology and approaches to surveillance

The process of surveillance

All approaches to surveillance share some common principles. While some of the underlying methods used in public health surveillance have evolved considerably in

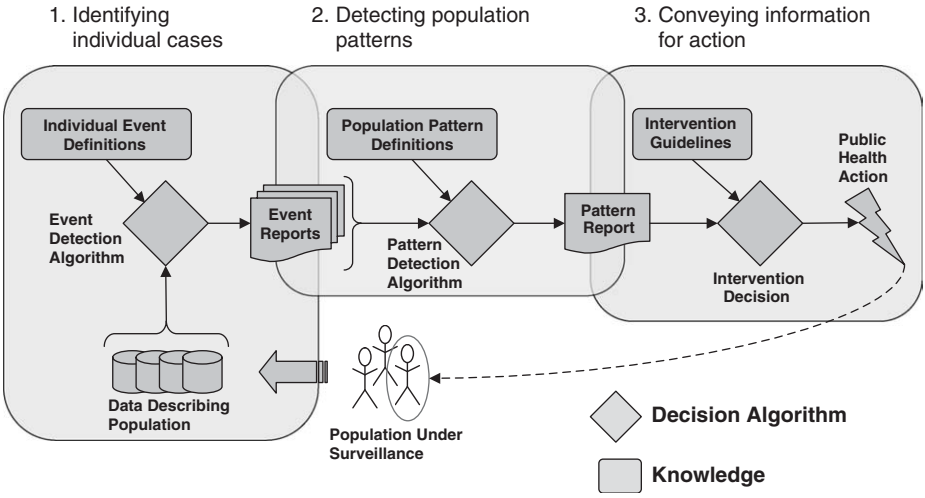

Fig. 3 The process of surveillance. Critical points in this process include the detection of events in individuals (e.g., a diagnosis of measles), the identification of patterns in the population (e.g., a rapid rise in incidence in a geographic location), and the incorporation of information about identified patterns into decisions about interventions. (For colour version: see Colour Section on page 357).

recent years, the general approach to surveillance has remained relatively constant. At a fundamental level, surveillance aims to (1) identify individual cases, (2) detect population patterns in identified cases, and then (3) convey information to decision-makers about population health patterns (Fig. 3).

Identification of individual cases

The definition of a case for a surveillance system (Fig. 3, Step 1) has important implications for the design and performance of the system. In settings where a surveillance system is intended to follow cases of a well-understood disease, it may be possible to make the case definition highly specific. For example, public health agencies in many developed countries conduct routine surveillance for communicable diseases such as measles. Definitions of cases in these systems tend to rely upon highly specific diagnostic tests. As a result, communicable disease surveillance systems tend to rely upon data from laboratory testing as opposed to data from clinical examinations (Koo and Wetterhall, 1996).

However, in many surveillance settings, it is not possible to rely on diagnostic tests as central components of a case definition. Worldwide surveillance for polio is an example in which, despite the existence of a specific diagnostic test, the case definition refers to a syndrome ('flaccid paralysis') as opposed to a laboratory test result (Kohler et al., 2002). Clinical data are used for the polio case definition because, in many countries, laboratory testing for polio is not readily available and because the clinical definition is highly sensitive. Newly emerging viruses present

another example of a situation where it is generally not possible to rely on a laboratory test for a case definition.

By definition, laboratory tests are not available for newly emerging viruses, so the case definition must focus on the clinical and epidemiological characteristics of disease. This is problematic, however, because newly emerging viruses may cause a variety of clinical presentations, depending on the characteristics of the virus and the host. In other words, the specific characteristics of a case are not known in advance when developing a surveillance system to detect newly emerging viruses. One approach to this problem is not to define cases in advance, but instead to monitor information sources (e.g., the World Wide Web, posts to electronic discussion boards, etc.) for reports of unusual cases that could be due to a newly emerging virus. However, if used, case definitions must be broad enough to ensure that the surveillance system will be sufficiently sensitive. In this setting, the cost of increased sensitivity is reduced specificity. In other words, to ensure that a case definition will identify cases of infection from a newly emerging virus, we must accept that the definition will also pick up cases of disease due to other causes.

Detection of population patterns among cases of the disease

The detection of population patterns (Fig. 3, Step 2) among cases generally refers to the detection of *unexpected* patterns in the incidence of cases. Surveillance analysts are interested usually in detecting an unexpected increases in overall incidence or an increase in incidence in a population subgroup or in a geographic region. There is a close relationship between the characteristics of the case definition and the detection of population patterns. When a case definition is highly specific, a large proportion of identified cases will be true cases and there will be very little 'noise' in the signal at the population level. When the signal is strong, it is easier to detect unexpected patterns. If the historical variation in the incidence rate of measles, for instance, is low, then an increased incidence of positive test results for measles virus infection should be detected relatively easily. Accordingly, the methods used to search prospectively for outbreaks using communicable disease surveillance data tend to be straightforward: mainly observation and statistical methods (Stroup et al., 1993; Hutwagner et al., 1997). However, the necessity for high sensitivity in the case definition for newly emerging viruses tends to result in low specificity.

Another potential source of 'noise' is the normal variation in the incidence of cases. In general, the greater this baseline normal variation, the more difficult it will be to detect an unexpected increase in the incidence. At one extreme, if no cases are expected under normal conditions, then the occurrence of a single case may be sufficient to trigger further action. For example, one case of hemorrhagic fever in a developed country is probably sufficient to attract notice. However, when cases present with more commonly encountered symptoms, a few cases may not be distinguished from the baseline incidence of those symptoms. For example, influenza-like symptoms due to a newly emerging disease agent might not attract notice.

In situations where an increase is observed in the incidence of cases with non-specific symptoms, appropriate public health action may be delayed (Duchin, 2003; Pavlin, 2003).

The public health response

The public health response is determined by the communicability and severity of the disease, and the susceptibility of the population. With a newly emerging virus, there are likely to be many unknown aspects about both the public health threat and potentially effective intervention measures. The cautious approach is to assume that the public health threat is serious, and, until the transmission dynamics are known, to use generic control measures such as isolation of infected cases and quarantine of exposed individuals.

Surveillance settings and mandates

An appreciation of the fundamental issues of surveillance is important, but it is also important to realize that surveillance occurs in a context that includes the geographic setting of the surveillance system and the mandate of the surveillance organization. Often the data collected through regional surveillance systems are transmitted to national systems, which provide a broader perspective and allow identification of disease outbreaks that span adjacent regions. The National Notifiable Disease Surveillance System (NNDSS) in the United States is an example of this model (Koo and Wetterhall, 1996). The communication between national and international systems generally involves aggregate data. The SARS outbreak in 2002–2003 provides examples of this cooperation as well as the role of political considerations, in terms of the initial detection in China, and the ongoing management of the outbreak in Canada.

Organizations conducting surveillance have differing mandates for data collection and for intervention. In most countries, the government has the legal authority and mandate to maintain public health, and this includes both surveillance and intervention to control disease outbreaks. However, the authority to conduct surveillance is often mandated in terms of known diseases; the surveillance to detect newly emerging diseases may not be explicitly described. This may pose practical problems for public health authorities as they attempt to develop surveillance systems, especially if the systems require clinical data whose use may be restricted by law. Similarly, the communication of surveillance information between countries and to international agencies may not be clearly permitted by law or policy in some countries. The Global Outbreak Alert and Response Network (GOARN), coordinated by the World Health Organization (WHO), was established in 1997 and formalized in 2000 to address issues of international cooperation in the face of outbreaks of emerging infectious diseases (Heymann, 2004).

Types of surveillance

The appropriateness of a surveillance method for an emerging virus is determined to a large extent by the specificity of the case definition (Fig. 4). Any surveillance system searching for new viruses must follow cases with unusual presentations or must follow the incidence of non-specific syndromes. Once the clinical presentation and epidemiology of a newly emerging virus are understood, this knowledge can be incorporated into a more specific case definition. Even greater specificity in the case definition can be achieved once the virus is isolated and diagnostic tests have been developed.

Initial detection and early stage surveillance

For unknown viruses or those early in emergence, the focus of surveillance can follow either of two approaches. One is 'information surveillance', by which information about disease outbreaks is sought on the Internet or through other sources. The other is syndromic surveillance, which follows pre-diagnostic data generated when individuals use health care services.

Information surveillance. The Internet has enabled novel approaches to collecting public health data, both passively and actively. Passive approaches rely on submission of disease reports, usually via e-mail, to a single location; active approaches involve searches of the Internet for posted information about disease outbreaks. These systems conduct 'information surveillance', in that they follow information about outbreaks, as opposed to relying on the case definitions traditionally used in disease surveillance. One system that has been used is ProMED-mail, which relies on both submission of outbreak reports and manual review of Internet sources, and the resulting information is reviewed by experts who then disseminate their conclusions. Another system, GPHIN, relies on active computer search of the

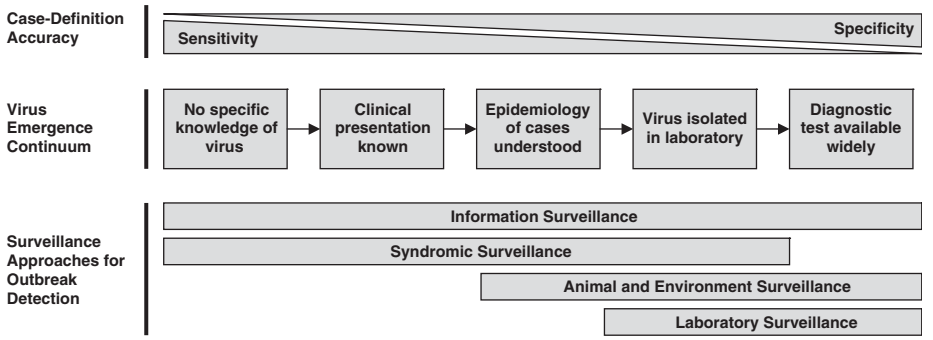

Fig. 4 The continuum of emergence for a virus showing the change in the sensitivity and specificity of the case definition for surveillance, and the appropriate approaches to surveillance, at different points along the continuum.

Internet for reports of disease outbreaks. Both of these systems have successfully identified recent outbreaks of newly emerging viruses, but neither approach to surveillance has been the subject of a rigorous peer-reviewed evaluation.

The Program for Monitoring Emerging Diseases (ProMED) and ProMED-mail: The Program for Monitoring Emerging Diseases (ProMED) was founded in 1993, and an e-mail list for sharing news about emerging diseases (ProMED-mail) was created in the following year (Madoff and Woodall, 2005). ProMED-mail now has >32,000 subscribers in more than 150 countries, and it has developed into a mature system for receiving, analyzing, and disseminating information about newly described or unknown diseases and epidemics (Madoff, 2004). More than 20 staff members around the world search the Internet and traditional media daily for disease information and file reports on relevant findings. Spontaneous reports can also be submitted electronically to ProMED, and approximately 30 spontaneous reports of disease activity are received each day. Each report is reviewed by an editor and in many cases by a subject expert, and approximately seven reports and accompanying editorial comments are posted each day through e-mail lists and on the website. Posted reports are also stored in an archival database for future reference.

ProMED-mail relies in part on a community of interested individuals to submit information about unusual disease activity, and on a small group of experts to analyze this information and disseminate reports of interest. In terms of the surveillance process (Fig. 3), ProMED-mail does not operate with specific case definitions. Events of interest for ProMED-mail are defined loosely as 'newly described or unknown diseases, epidemics and outbreaks and diseases emerging in new areas or populations' (Madoff, 2004). Dissemination is rapid and broad, without political oversight or interference. This approach to surveillance is likely to be sensitive, rapid, and reasonably specific due to the expert analysis.

The Global Public Health Intelligence Network (GPHIN): The Global Public Health Intelligence Network (GPHIN) was initially developed in 1998 by Health Canada in partnership with the WHO for the collection, filtering and sorting, and review of emerging disease information. In the collection step, automated software is used to search the Internet for selected disease-specific words. An average of 8000–10,000 items of interest per month are identified in this way. In the filtering and sorting step, irrelevant and duplicate information are discarded, and each relevant item is categorized. In the review step, 9000 pieces of information are reviewed each month and posted on the Internet. The most recent version of the GPHIN software, placed into service in 2004, can process information in Arabic, English, French, Russian, Chinese, and Spanish. GPHIN is now operated by WHO Epidemic and Pandemic Alert and Response (EPR) in collaboration with Health Canada, and provides approximately 40% of the information that WHO receives about disease outbreaks.

In terms of the surveillance process model (Fig. 3), the keywords and word arrangements used to identify potentially relevant information are essentially the case definitions in GPHIN. These case definitions are highly sensitive but not very specific, and so retrieved information must be filtered, first automatically, and then manually. The events of interest to GPHIN are also quite broad, including not only infectious disease outbreaks, but also illnesses related to consumer products, radiation, food and water, and other causes. The filtering and human review steps in GPHIN correspond to the analysis step in the surveillance process.

While ProMED-mail and GPHIN can both be thought of as approaches to 'information surveillance', their differences are noteworthy. Neither system uses a case definition in the traditional sense, but GPHIN does use a pre-defined set of terms to identify information of potential interest. A precisely specified list of terms is required by GPHIN because it is an automated system. In contrast, ProMED-mail does not specify in detail what constitutes relevant information, and this degree of precision is not required because ProMED-mail relies on humans to identify and submit information. As a consequence of their different approaches to data collection, GPHIN collects more information than ProMED-mail, but it also collects more irrelevant information, which subsequently must be filtered. In both systems, the final assessment of relevance is manual.

From a management perspective, GPHIN is operated by governmental and international public health agencies, while ProMED-mail is operated by a non-governmental organization. As a result, information posted through ProMED-mail is not subject to any political review. In practice, however, the two systems are linked; since ProMED-mail posts information on a website, this information is included in that collected by GPHIN on the Internet. In addition, individuals may submit to ProMED-mail relevant information identified by the GPHIN website. Thus, in many ways these two approaches to information surveillance are complementary. The main strength of GPHIN is the breadth and volume of information that it can consider, whereas the main strengths of ProMED-mail are its expert analysis of information, and independence from governmental supervision. Both systems have performed well in identifying recent outbreaks due to newly emerging viruses, including the SARS outbreak in 2002–2003.

Syndromic surveillance. Advances in the electronic capture of health data have led to surveillance using data generated through the routine administration of health care services. This practice is known as 'syndromic surveillance' because cases are defined in terms of non-specific administrative codes or conditions, which can be thought of as syndromes (Mandl et al., 2004). Although using syndromes for case definitions has been practiced for many years, this 'syndromic surveillance' is novel in that it relies on the automated capture, transmission, and analysis of non-specific patterns of information in pre-diagnostic health data. For example, many syndromic surveillance systems follow administrative data from emergency room visits. The records are automatically obtained from hospital records and forwarded to a public health agency, automatically grouped into designated 'syndromes' such

as 'respiratory disease' or 'gastrointestinal disease', and then analyzed to look for unexpected increases in the number of visits.

Rapid development of syndromic surveillance systems has occurred as a result of developing preparedness to detect episodes of bioterrorism, and the systems are equally useful for detecting emerging viruses (Institute of Medicine of the National Academies, 2003). The US Centers for Disease Control and Prevention (CDC) has supported demonstration projects in syndromic surveillance (Yih et al., 2004), and is developing an operational system to monitor several data sources, including emergency department visits, laboratory test orders, and pharmaceutical prescriptions (Loonsk, 2004; United States Government Accountability Office, 2005). A variety of other systems are also being operated by governmental and non-governmental organizations in the US (Lombardo et al., 2003; Wagner et al., 2003; Heffernan et al., 2004), in the United Kingdom (Cooper et al., 2004), and in Canada.

It is difficult to establish the utility of different types of syndromic surveillance systems because of the variation in data characteristics across locations. Data from early disease events, such as sales of over-the-counter pharmaceuticals and calls to telephone-based medical triage systems, offer promise due to their timeliness and the prevalence of these responses to symptoms. However, these data contain little specific clinical information, and outbreak signals are likely to be masked by considerable noise. For these reasons, many syndromic surveillance systems now rely on more specific data such as records of visits to emergency departments. Ideally, many available data sources would be used simultaneously, but further research is needed to identify the optimal approach to combining information from multiple types of data within single surveillance systems.

In terms of the framework for surveillance (Fig. 3), the case definition used in syndromic surveillance is usually a set of codes or keywords that correspond to a syndrome, and grouping of records into syndromes is usually conducted automatically. Outbreak detection algorithms consider the chronology of different syndromes (Buckeridge et al., 2005a), but some researchers have examined the use of algorithms that search for outbreaks over geographic space (Kulldorff et al., 2005), and other covariates found in medical records, such as age and gender (Wong et al., 2003). The link of surveillance systems of these types to public health decision-making is variable, and many public health agencies are still determining the best policy for the follow-up of alarms that are often non-specific (Duchin, 2003; Pavlin, 2003).

The main argument for conducting syndromic surveillance rests on the assumption that this approach to surveillance will detect a disease outbreak more rapidly than other surveillance systems. Because syndromic surveillance systems follow data from events that occur before diagnosis, it is assumed that they will detect outbreaks earlier because the incidence of pre-diagnostic events, such as purchase of over-the-counter medications, will increase before the incidence of diagnoses will increase. In general, these assumptions may hold true under some conditions, but not under other conditions. The limited research on these systems suggests that the

results are affected by the clinical course of the disease, the number of individuals exposed, the type of data source monitored, whether an applicable routine test is positive in the disease, and the outbreak detection algorithm used (Buehler et al., 2003; Reis et al., 2003; Stoto et al., 2004; Buckeridge et al., 2005b). Syndromic surveillance is likely to be more rapid than clinical detection in detecting an outbreak when the clinical symptoms mimic an existing disease with a low incidence, when a clinical data source is being monitored, and when there is no routine diagnostic test for the disease. This is a conceivable scenario for the initial presentation of a newly emerging virus, and so it is reasonable to expect that syndromic surveillance systems may be useful in the initial detection of an outbreak due to a newly emerging virus.

Intermediate stage surveillance

Once public health personnel know more about the epidemiology and genetics of an emerging virus, additional surveillance approaches become feasible. One such approach, surveillance of animals and the environment, capitalizes on knowledge about the epidemiology of the virus to identify when and where human infection is likely to occur. A second approach, surveillance of laboratory test results, makes use of results from diagnostic testing to follow with high specificity the development of an epidemic or endemic disease.

Surveillance of animals and the environment. Many emerging viruses cause zoonotic diseases. Once a newly emerging virus is understood to have a vertebrate animal host, and the vector of transmission has been identified, it may be informative to conduct surveillance of the animal hosts of the disease, of the vector, or even the habitat of the animal host or vector. For example, researchers have found that the spatial and temporal patterns of human dengue virus infections follow known entomological risk factors (Tran et al., 2004). Other researchers have observed the same phenomenon with West Nile virus (WNV), for which deaths among birds and the distribution of habitats suitable for adult mosquitoes have both been shown to correlate well with virus-positive mosquito samples and the occurrence of human infections (Eidson et al., 2001; Brownstein et al., 2002; Mostashari et al., 2003). In fact, surveillance of these factors are now a component of many programs for WNV surveillance.

Laboratory-based surveillance. After diagnostic methods are available, surveillance of positive laboratory tests becomes possible. This approach to surveillance is likely to be highly specific, but it will identify only those cases that are tested at laboratories participating in the surveillance system. Automated surveillance of positive laboratory test results (Effler et al., 1999) and monitoring the incidence of emerging pathogens through laboratory methods (Bravata et al., 2004) can be a highly effective form of surveillance.

Ongoing surveillance

Surveillance, in practice, capitalizes on different approaches at different points in the emergence of a virus (Fig. 3).

West Nile virus

WNV was first isolated and identified in 1937, in samples from a febrile person in the West Nile district of Uganda. Prior to 1999, the virus was found only in the Eastern Hemisphere, with wide distribution in Africa, Asia, the Middle East, and Europe. In late summer 1999, the US documented its first domestically acquired human cases of West Nile encephalitis (Anderson et al., 1999; Briese, 1999; Jia et al., 1999; Lanciotti et al., 1999; Nash et al., 2001). The WNV epidemic of 2002 was the largest epidemic of WNV meningoencephalitis on record, and the largest recognized arboviral meningoencephalitis epidemic ever recorded in the Western Hemisphere. Significant human disease activity was recorded in Canada for the first time, in the Caribbean basin, and in Mexico. A program of surveillance is now in place for WNV detection in North America using data from human, avian, equine, and mosquito samples.

Human surveillance: Health care providers report all probable and confirmed cases of WNV infection to designated health authorities. In the absence of WNV activity in an area, passive surveillance is used for the reporting of hospitalized cases of encephalitis, and for patients who test positive for IgM antibodies to WNV. In areas with known WNV activity, active surveillance may take place, in which (1) public health professionals contact physicians in appropriate specialties and hospital infection control staff on a regular basis to inquire about patients with potential arboviral infections, and (2) laboratory-based surveillance is implemented to identify CSF specimens meeting sensitive but non-specific criteria for arboviral infections. Special surveillance projects can be used to supplement WNV surveillance, including the Emerging Infections Network of the Infectious Diseases Society of America (IDSA EIN), Emergency Department Sentinel Network for Emerging Infections (EMERGEncy ID NET), Unexplained Deaths and Critical Illnesses Surveillance of the Emerging Infections Programs (EIP), and the Global Emerging Infections Sentinel Network of the International Society of Travel Medicine (GeoSentinel). In addition, blood banks in the United States routinely screen all donated blood for WNV using PCR.

Avian surveillance: While most birds survive WNV infection, mortality in a wide variety of bird species has been a hallmark of WNV activity in North America. Avian mortality due to WNV is a sensitive indicator of ongoing enzootic transmission, such that public health agencies can use bird mortality to track effectively the spread of WNV. Avian morbidity and mortality surveillance includes the

reporting and analysis of dead bird sightings, and the submission of selected birds for WNV testing. Detection of seroconversion in sentinel live-captive chickens or free-ranging birds can also be used for surveillance.

Equine surveillance: Among large land mammals, horses are particularly susceptible to WNV infection. Horses appear to be important sentinels of WNV epizootic activity and human risk, at least in some geographic regions. Veterinarians, veterinary service agencies, and state agriculture departments are essential partners in any surveillance activities involving equine WNV disease.

Mosquito surveillance: Surveillance of mosquitoes is the primary tool for quantifying the intensity of virus transmission in an area. WNV is transmitted principally by *Culex* spp. mosquitoes, though greater than 36 species of mosquitoes can be infected with WNV. In areas where WNV has never been detected, mosquito surveillance focuses on establishing which mosquito species are present, and how many are in the area. In areas where WNV has been detected, mosquitoes are collected and tested for WNV.

SARS

Health Canada's GPHIN system first recognized the outbreak of atypical pneumonia emerging in southern China, later identified as SARS and later shown to be caused by the coronavirus, SARS-CoV. During the 2003 SARS outbreak, surveillance relied heavily on passive reporting by health care providers of suspected and confirmed cases, active contact tracing, and active syndromic surveillance of quarantined contacts. Some countries also conducted serological screening of large segments of the population.

Since the end of the 2003 outbreak, SARS surveillance has focused on (1) persons with a potential epidemiologic link who are hospitalized with severe respiratory illness, (2) clusters of severe respiratory illness, (3) persons with laboratory evidence of SARS-CoV infection, and (4) in Canada, where there is joint surveillance for human cases of SARS and avian influenza, persons with laboratory confirmed influenza A (serotype H5N1) or other novel influenza virus infection. As more is learned about the natural reservoir, host species, and transmission of SARS-CoV, SARS surveillance will likely expand to include surveillance of host animal species. Global SARS surveillance uses GPHIN technology, passive reporting of laboratory-confirmed cases to WHO as well as special studies of SARS-CoV infection in areas at increased risk of reemergence.

Implications for future policy, practice, and research

The convergence of human disease ecologies resulting from increasing globalization is thought to be a driving force behind emerging viral diseases (Barrett et al., 1998).

Outbreaks arising in distant countries can be exported by jet travel, making it imperative that global and local outbreak detection and response be closely interrelated. Improved global infectious disease surveillance is needed to ensure adequate local outbreak detection and response (Institute of Medicine of the National Academies, 2003; United States Government Accountability Office, 2004). Improvement of global surveillance should focus on building surveillance capacity in many countries, especially in resource-poor regions (United States Government Accountability Office, 2004), establishing networks of expertise (The SARS Commission, 2004; World Health Organization, 2003), and improving case reporting to the WHO, permitting the issuance of timely alerts to prevent international spread (World Health Organization, 2003).

Many governments also seek to improve domestic surveillance through better case and contact reporting by health care professionals (Institute of Medicine of the National Academies, 2003; The SARS Commission, 2005), and through enhanced coordination between different government agencies at national and local levels (The SARS Commission, 2004, 2005; United States Government Accountability Office, 2004, 2005). Astute clinicians can be the first line of defense for identifying emerging viral threats, but many health care providers do not understand their potential role as a source of valuable disease data (Institute of Medicine of the National Academies, 2003). Solutions to enhance timeliness, accuracy, and completeness of disease reporting by health care providers include the development of secure, web-based reporting, implementation of automated laboratory reporting, and standardization and consolidation of local reporting systems (United States Government Accountability Office, 2004, 2005; The SARS Commission, 2005).

There is also a need to explore innovative systems of surveillance, such as those incorporating remote sensing, and automated systems of syndrome surveillance (Institute of Medicine of the National Academies, 2003). Careful evaluation of novel surveillance systems should be conducted to determine their accuracy and effectiveness (United States Government Accountability Office, 2004). Because the majority of emerging infectious diseases are zoonoses (Institute of Medicine of the National Academies, 2003), vector-borne and zoonotic disease surveillance and control should be improved (Institute of Medicine of the National Academies, 2003; United States Government Accountability Office, 2004). Significant improvements could be achieved by using robust models for predicting and preventing vector-borne and zoonotic diseases, and by adding veterinary laboratories to laboratory surveillance networks (Institute of Medicine of the National Academies, 2003).

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