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Surveillance for Emerging Infection Epidemics in Developing Countries: The Early Warning Outbreak Recognition System (EWORS) and Alerta DISAMAR

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By mid-2006, a highly pathogenic strain of avian influenza, H5N1, had infected more than 200 people in Southeast, East, and Central Asia; the Middle East; and North Africa since emerging in Vietnam in 2003. More than half of these confirmed infections were fatal [1]. Although nearly all cases resulted from exposure to infected birds, the epidemic has generated serious international concern and resource commitments because influenza viruses undergo unpredictable genetic changes that influence pathogenicity and transmission characteristics. For example, an avian virus that acquired the ability to spread efficiently among humans probably caused the influenza pandemic of 1918-1919, in which around 50 million people died [2]. If genetic changes allow the H5N1 virus to spread efficiently from person-to-person (as seasonal influenza viruses do), the world would again face the possibility of a pandemic that could kill millions of people and devastate economies.

Avian influenza is an "emerging" infectious disease [3, 4] – the category includes diseases that have recently appeared (e.g., H5N1, which was first identified as a human

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pathogen in Hong Kong in 1997; and acquired immunodeficiency syndrome [AIDS]) and ones that are known but changing in significant ways (e.g., malaria, which is spreading to new areas and returning to areas where it was previously eliminated; and tuberculosis, which, like malaria, has developed resistance to many drugs). Effective public health response to emerging infections depends on surveillance systems to detect and characterize them and guide interventions [4, 5]. However, in much of the developing world, public health surveillance systems do not exist or are ineffective [5, 6]. Because many emerging infections, such as H5N1, spread easily beyond national borders, these deficiencies can have regional or global consequences. Heymann and Rodier of the World Health Organization (WHO) captured this interdependence in reflecting on the 2003 multi-country Severe Acute Respiratory Syndrome (SARS) epidemic: "Inadequate surveillance and response capacity in a single country can endanger national populations and the public health security of the entire world."[7]

This chapter explores strategies for implementing effective surveillance for emerging infection outbreaks in developing countries. After a general overview of challenges to effective surveillance in developing countries and possible solutions, it turns to two systems developed through host country-U.S. military collaboration. These case studies offer lessons that could be useful for developing countries, sponsoring agencies, and collaborators in developing and improving surveillance systems for emerging infections in resource-poor settings.

9.1 IMPROVING SURVEILLANCE IN RESOURCE-POOR SETTINGS

Developing countries face significant challenges in implementing effective public health surveillance systems. Some of these are similar in kind to, but of greater magnitude than, problems that developed countries encounter [8, 9]. For example, insufficient laboratory diagnostic capabilities [10, 11] and lack of personnel with necessary analytic skills [12] limit surveillance effectiveness in developing countries, but affect wealthy nations as well.

More specific to poor countries are infrastructure constraints that can make even rudimentary surveillance functions difficult. For example, poor roads and lack of transportation can prevent public health staff from investigating outbreaks; computerbased information systems may be difficult to implement because electrical power is unreliable; and communication systems (such as the Internet) may be very limited [9]. The bureaucratic structure of the health sector may obscure lines of accountability for surveillance functions [13]. When foreign assistance is provided to strengthen public health systems, well-intentioned donors may impose programmatic requirements that impede development of effective systems [9, 14].

Recent WHO efforts to strengthen global infectious disease surveillance depend on effective national and sub-national level systems [15, 16]. For example, the International Health Regulations, revised in 2005 to address SARS and other emerging infections that can spread rapidly through a globalized world, places broader obligations on countries to build surveillance and response capacities [17] (the original International Health Regulations, instituted in 1969, focused on monitoring and control of four diseases capable of causing serious international epidemics: cholera, yellow fever, plague, and smallpox). The Global Outbreak Alert and Response Network (GOARN), established in 2000 to facilitate collaboration among existing institutions and surveillance networks in identifying, confirming, and responding to epidemics of international importance [18], also can only be effective if component systems are effective.

Several innovative models have been developed for improving infectious disease surveillance in developing countries. A few successful, low-cost examples at the sub-national level are a community-based program in Cambodia that employs lay volunteers to identify outbreaks [19]; a hospital-based program in South Africa that trains infection control nurses to identify syndromes that require immediate public health action [20]; and a public-private hospital network that monitors a range of infectious diseases in India [21]. The success of these and other effective approaches owes, in part, to detailed understanding of local public health system problems and capabilities.

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9.2 U.S. MILITARY OVERSEAS PUBLIC HEALTH CAPACITY BUILDING

The U.S. military has long supported public health activities of foreign countries, though the formalization of an emerging infection-focused capacity building mission for the US Department of Defense (DoD) occurred relatively recently. A key DoD platform for public health capacity building abroad is a network of Overseas Medical Research Laboratories in Peru, Egypt, Kenya, Thailand, and Indonesia. DoD established these facilities between 1943 and 1983 to conduct tropical infectious disease research important to both host countries and the U.S. military. U.S. military and host country staff built on advanced laboratory capabilities, regional networks of field sites, and a spirit of collaboration and trust to produce medical advances of broad importance – including drugs for malaria and typhoid fever, fluid-electrolyte rehydration therapy for cholera, and vaccines for hepatitis A and Japanese encephalitis, among others [22, 23, 24, 25, 26, 27, 28, 29]. U.S. military scientists also supported host countries in responding to infectious disease outbreaks with laboratory diagnostics, epidemiologic field investigations, and training.

A seminal report by the U.S. Institute of Medicine in 1992 drew attention to emerging infectious diseases as a threat to global health and U.S. security [4]. The report called for greater U.S. engagement with emerging infections overseas, and identified the DoD Overseas Medical Research Laboratories as the most broadlybased U.S. platforms for monitoring and responding to epidemics abroad. Building on this and subsequent reports, a 1996 Presidential directive formally expanded the mission of DoD and its Overseas Medical Research Laboratories to include surveillance, outbreak response, host country personnel training, and research for emerging infectious diseases [30]. DoD established the Global Emerging Infections Surveillance and Response System (DoD-GEIS) to coordinate and support these efforts at the DoD Overseas Medical Research Laboratories and in the Military Health System.

Current DoD-GEIS surveillance networks based at the DoD Overseas Medical Research Laboratories include more than 30 countries in South America, the Middle East, Sub-Sahara Africa, and Central and Southeast Asia [31]. A global, laboratorybased network monitors influenza [32], a top surveillance priority because of the ever-present pandemic threat. Other systems focus on malaria, dengue, diarrheal diseases, and sexually-transmitted infections. All surveillance networks rely on close U.S. military-host country collaboration, and must contend with the challenges described above of delivering accurate, timely information on emerging infections in resource-poor settings.

The following two sections focus on surveillance systems that host countries, DoD-GEIS, DoD Overseas Medical Research Laboratories, and other organizations have collaborated to develop and sustain. The purpose of both systems is to detect outbreaks of emerging infections early and to facilitate rapid public health intervention. The first, Early Warning Outbreak Recognition System (EWORS), was developed by the U.S. Naval Medical Research Unit-2 (NAMRU-2; Jakarta) and deployed in collaboration with host country ministries of health in Indonesia, Lao PDR, Cambodia, and Vietnam. U.S. Naval Medical Research Center Detachment (NMRCD; Lima) and the Peru Ministry of Health also have collaborated to implement a version of EWORS. The second case study focuses on Alerta DISAMAR, which was developed by NMRCD and deployed in collaboration with the Peruvian Navy and Army.

Several approaches to describing and evaluating public health surveillance systems have been proposed [33, 34, 35]. The case studies below draw on these approaches to present an overview of the systems and operating environment, focusing especially on data acquisition, information flow, the critical connection between the surveillance systems and public health response, and features that facilitate effective surveillance in resource-poor environments. Rather than provide comprehensive evaluations of many system attributes (e.g., simplicity, flexibility, data quality, acceptability, sensitivity, specificity, timeliness, stability), the case studies explore a key attribute for surveillance systems designed for emerging infections – flexibility. The U.S. Centers for Disease Control and Prevention (CDC) describes flexibility this way:

A flexible public health surveillance system can adapt to changing information needs or operating conditions with little additional time, personnel, or allocated funds. Flexible systems can accommodate, for example, new health-related events, changes

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in case definitions or technology, and variations in funding or reporting sources. In addition, systems that use standard data formats (e.g., in electronic data interchange) can be easily integrated with other systems and thus might be considered flexible [34].

Surveillance systems such as EWORS and Alerta DISAMAR, developed to detect outbreaks of emerging infections, must be flexible because clinical syndromes that signal the emergence of a new disease cannot be known in advance; systems must be configured so that "unusual" events – such as syndromes not normally seen in an area, or an increase in presentations of syndromes that are normally seen at lower rates – are identified and investigated. Ideally, systems should also allow for rapid implementation of new surveillance protocols; for example, after case definitions are established for a newly emerged disease, such as pandemic influenza. Finally, all surveillance systems, but especially those in resource-poor settings, should be able to adapt to temporal and spatial variability across important operating environment parameters – for example, variation in communication and transportation infrastructure across a system's catchment area; turnover of system operators; and infusion of new resources from sponsors. The case studies below illustrate different, important aspects of surveillance system flexibility.

9.3 CASE STUDY I: EWORS (SOUTHEAST ASIA AND PERU)

The Republic of Indonesia includes nearly 18,000 islands and over 200 million people. Jakarta and other areas of Java are among the most densely populated in the world (the island holds more than half of the country's population, in an area the size of New York state), but many people live in remote areas with very limited public infrastructure. Infectious diseases that cause localized epidemics across Indonesia and other Southeast Asian countries include malaria, dengue, and bacterial, parasitic, and viral diarrhea. Of global concern, influenza A/H5N1 was reported in humans in Indonesia in 2005. During the first half of 2006, Indonesia reported more human cases (N=37) and deaths (N=31) than any other country, and the second highest cumulative number of cases (N=54) and deaths (N=42) after Vietnam since 2003

[1]. Most cases are thought to have had contact with infected poultry. However, a small number of cases have been identified in self-limited family clusters, and human-to-human transmission is strongly suspected.

The U.S. Navy has supported public health programs of the Indonesia Ministry of Health since 1970, when Navy medical officers assigned to NAMRU-2 (then located in Taipei) assisted the government in responding to a plague outbreak. At the invitation of Indonesia, NAMRU-2 established a detachment in Jakarta following the outbreak to continue collaborations; this became the central NAMRU-2 facility in 1990.

NAMRU-2 staff and Ministry of Health colleagues have responded to numerous infectious disease epidemics [36, 37, 38, 39, 40, 41, 42], but often found that the response was launched too late for effective intervention. Newspapers often carried the initial reports of epidemics. For example, an outbreak of influenza-like illness in the remote jungle on Irian Jaya in 1995–1996, which involved more than 4,000 cases and 300 deaths, was noted first by local newspapers several months after the epidemic began [37]. This outbreak and other instances of delayed detection prompted NAMRU-2 and the Ministry of Health to develop a more timely system for detecting and responding to epidemics.

9.3.1 System Development, Configuration, and Operation

When development of what would become the Early Warning Outbreak Recognition System (EWORS) began in 1998, it was clear that implementing timely surveillance for disease-specific conditions would be difficult – in Indonesia, as elsewhere in Southeast Asia, many clinics and hospitals lacked even basic laboratory diagnostic capabilities, and training and experience of clinical staff varied widely [43]. Surveillance for reliably-defined syndromes offered an alternative, but advanced informatics capabilities for collecting and processing data, which support much of what is now called "syndromic surveillance," were not available.

System developers decided to focus on hospitals in urban or semi-urban areas, where the potential for epidemics to spread rapidly might be greatest and where data entry and communications capabilities would better support timely outbreak detec-

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tion. The information system they developed for such settings was a simple, menudriven software package that allows data entry at surveillance sites and graphical and statistical analysis at the Indonesia EWORS hub, a joint operation of NAMRU-2, the National Institute of Health Research and Development (NIHRD/LITBANGKES), and the Directorate General of Communicable Disease Control and Environmental Health and Sanitation (the Indonesian CDC).

At participating hospitals, medical staff in internal medicine and pediatrics clinics and the emergency department use a short, standardized questionnaire to collect demographic and clinical information from patients presenting with one or more of 29 syndromes (Fig. 9.1). Each participating hospital has at least one computer terminal where data is entered using EWORS software. EWORS data files are sent by email to the EWORS hub for analysis, ideally once per day. Medical staff and data entry personnel take approximately one minute each to complete each patient questionnaire. With a 56 Kbps modem, it takes approximately 10 minutes of Internet connectivity to transmit the data file to the hub.



Fig. 9.1 Country Outbreak Response Technical Unit.

Although experienced epidemiologists at NAMRU-2 and the Ministry of Health support the EWORS network, the software is designed to allow rapid, intuitive data interpretation by hospital-based operators with minimal epidemiologic training. For example, menus provide options for time series display based on surveillance sites, demographic groups, and syndromes (Fig. 9.2a-9.2c). Data are displayed in a line-chart format with observed case numbers by time, age group, or gender. Geographic information system (GIS) displays are easily generated for intuitive assessment of clustering over a period of time (Fig. 9.3). The software also allows users to output raw data to statistical packages for more detailed analysis.

EWORS Chart Wizard		
Hr.	You can limit data to analyze by using options below: Vues Time Range : From: 28/ Jul /2003	g Time Frame, Age, and Sex. Please select from To: 28/Agust/2003
	Travel History	Age Sex
	Cancel	< Back Next > Enish

Fig. 9.2a EWORS Chart Wizard (a)

EWORS pilot implementation in Indonesia began in 1999 with large public hospitals in Jakarta (on the island of Java), Medan (Sumatra), Denpasar (Bali), Pontianak (Kalimantan), and Ujung Pandag (Sulawesi). After the questionnaire was translated into Indonesian, this first-generation network enrolled more than 10,000 cases. This network facilitated identification of a large cholera outbreak [43]. With support from the Indonesia government, DoD, CDC, and the U.S. Agency for International

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	Primary Sign/Symptoms Additional Sign/Symptoms				
	Anuria / oliguria Cough Bloody cough Bubo-lymphadenitis Dehydration Fever Bloody diarrhea Diarrhea Mental status disturbances Hematemesis / melena Jaundice Stiff neck. Seizures Conjunctivitis Paralysis Malaise	Anuria / oliguria Cough Cough Bubo-lymphadenitis Dehydration Bloody diarrhea Diarrhea Mental status disturbances Hematemesis / melena Jaundice Stiff neck Seizures Conjunctivitis Paralysis Malaise Chills			
EWORS	Select <u>All</u> Clear	Select <u>All</u>			

Fig. 9.2b EWORS Chart Wizard (b)



Jumlah kasus bulanan gejala #1:Demam,#2:Mual,Perdarahan kulit,Sakit kepala,Sakit otot , di RSUD Soedarso, Pontianak, 01 Nopember 2001 -- 25 Oktober 2002

Fig. 9.2c EWORS Line Chart (c).

CASE STUDY I: EWORS (SOUTHEAST ASIA AND PERU) 9–11



Distribusi kasus gejala #1: Demam, #2: Mual, Pendarahan kulit, Sakit kepala dan Sakit otot di Kalimantan Barat yang berobat ke RSUD Dr. Soedarso 01 Oktober 2002 -- 31 Oktober 2002

Fig. 9.3 Number of All Cases from Pirngadi Hospital - North Sumatra.

Development, EWORS expanded to include 11 sites on the five islands (Fig. 9.4). Thereafter, NAMRU-2 collaborated with other Ministries of Health to translate software into local languages and implement EWORS in Lao PDR, Cambodia, and Vietnam. Together, these Southeast Asia EWORS networks have enrolled more than 5,000,000 cases. Although NAMRU-2 maintains a central EWORS hub that provides software and clinical protocol enhancements, technical support, and training for all of these systems, host countries have taken over responsibility for day-to-day operations, including outbreak identification and response. Thus, each country "owns" its EWORS data, and is not obligated to report to NAMRU-2; this has the double benefit of building analysis and decision-making experience in-country, and satisfying national privacy concerns.

In 2005, NAMRU-2 and NMRCD collaborated to initiate EWORS in Peru. Though still in pilot stage, EWORS-Peru includes modifications based on the EWORS experience in Southeast Asia (discussed below).

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Fig. 9.4 Influenza-Like Illness Surveillance Network.

9.3.2 Outbreak Detection and Response

At the Indonesia EWORS hub, up to two full-time analysts review daily reports from participating hospitals to identify increases in syndrome counts that could signify an outbreak. Downloading, processing, and analyzing daily data from all sites usually requires approximately one day (two days may be required if there are data file errors). If the analysts determine that an outbreak may be underway, the hub communicates with the affected site(s) to request additional information. Then, if warranted, the hub notifies the public health authorities responsible for responding to outbreaks. In addition to outbreak alerts, the EWORS hub also sends a monthly report to each participating hospital summarizing surveillance data for that hospital. Provincial health departments receive these reports for all participating hospitals in the province.

The process described has encountered three important challenges. First, linking EWORS-detected suspected outbreaks with outbreak response actions can require coordination of complex bureaucracies when agencies within the Ministry of Health have compartmentalized roles and responsibilities. The administrative decentralization that followed President Suharto's 32-year reign, which ended in 1998, makes difficult a strong connection between central outbreak detection at the EWORS hub and outbreak response at affected hospitals, for which the provincial health department has primary responsibility. The Ministry of Health must be invited or be granted permission by the provincial authorities to assist in an outbreak response. There is bureaucratic complexity at the national level too – within the Ministry of Health, three agencies coordinate outbreak response. One has responsibility for public health surveillance and outbreak investigation, another for research and development, and the third for public hospital management.

In contrast to Indonesia, EWORS in Lao PDR is based in a more centralized public health system. There, the EWORS hub is hosted by the National Center for Laboratory and Epidemiology, which is responsible for conducting public health surveillance across the country and has authority to investigate all outbreaks. This centralized system appears to have allowed a stronger connection between surveillance and outbreak response in Lao PDR. However, the scarcity of human and financial resources impacts investigations.

A second challenge has been standardizing procedures at the EWORS hub for identifying possible outbreaks. Early versions of EWORS software emphasized simplicity and user-friendliness, but the decision of whether to issue an outbreak alert was not based on validated statistical procedures. With the lack of statistical thresholds to define a possible outbreak, EWORS staff with variable epidemiological training made entirely subjective conclusions about outbreaks. For example, at one national hub, EWORS staff calculated historical means and standard deviations of case counts to define statistical thresholds for issuing alerts. Another national hub's process was to define an outbreak as a two-fold rise in cases over a two-week period. There was no validation performed as to how sensitive and specific such thresholds were. This lack of standardization brought uncertainty into alerts. In the context of

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scarce public health resources, committing those resources to subjective conclusions can be difficult for Ministries of Health.

To address this problem, NAMRU-2 and NMRCD have collaborated to incorporate automated statistical outbreak detection algorithms into EWORS software. The goal is to preserve the opportunity for intuitive, qualitative data assessment through graphical displays, but to offer quantitative assessments and automatic "flags" using algorithms currently employed in syndromic surveillance systems in the United States. Software developers and epidemiologists at NMRCD are evaluating several algorithms using archived EWORS data.

The third challenge has been validating an outbreak detection system in a developing country with limited laboratory diagnostic capabilities (in fact, a primary purpose of EWORS is to fill a surveillance gap where there is no laboratory network) and scarce resources to investigate possible outbreaks. It is too costly to send outbreak investigations teams out on every EWORS alert. And, without constant surveillance from other systems, it is difficult to determine whether outbreaks are being missed.

In practice, EWORS in Southeast Asia has been useful less in generating the initial identification of an outbreak, and more in guiding the deployment of scarce resources from central and provincial offices. Because 1 or 2 days may elapse between a patient presenting to a hospital with a syndrome under surveillance and analysis of the data at the EWORS hub, hospitals often have been aware that outbreaks are underway before an alert could be sent. Although hospital staff may know that an outbreak is underway, persuading provincial and central offices to provide epidemiologic or laboratory support can be difficult without convincing data – for example, the number of patients suspected of having the disease; the usual number of patients with similar presentations seen during a given timeframe; and patient clinical and demographic information. For hospitals that participate in EWORS, such data can be provided rapidly; in contrast, hospitals that do not routinely participate in EWORS or other surveillance systems can become too overwhelmed with patient care to produce such data during an outbreak. EWORS has been especially useful in demonstrating the geographic scope of outbreaks that have affected several hospitals and required mobilization of significant resources from provincial or central levels.

Although NMRCD implemented EWORS in Peru recently (2005), several features of that short experience are noteworthy. In Peru, the Ministry of Health's primary goal in supporting implementation of EWORS was improving outbreak detection at the hospital and district level. For this reason, participating sites send surveillance data to the EWORS hub at NMRCD infrequently, and are responsible for managing and interpreting data for their site using EWORS software adapted from Indonesia. This arrangement provided additional impetus to incorporate automated statistical detection algorithms into the software, and requires the EWORS hub to provide more training to participating sites that would be needed if data management and interpretation occurred centrally. An indirect benefit of this training, but one welcome by the Ministry of Health, has been improvement in outbreak preparedness in general – by learning the clinical, epidemiologic, and computer skills necessary to take an active role in EWORS, hospital staff have become better able to identify and investigate "unusual" events, whether or not they are reportable in EWORS.

In addition, the EWORS training program in Peru strengthens feelings of professional competence among hospital staff. This has been an important incentive for sites to participate in the system, especially because NMRCD staff made a strategic decision early in EWORS implementation not to provide financial or resource incentives to participating hospitals (e.g., salaries and computers) – a policy that has dissuaded some hospitals from participating, but ensured that ones that elect to participate are committed to the system and professional development, and not seeking ancillary benefits.

9.3.3 System Flexibility

NAMRU-2 and host countries developed EWORS to improve surveillance for a wide range of emerging infectious diseases. With concern growing for an influenza pandemic beginning in Asia, however, EWORS has been identified as a system that might provide an early warning capability critical for effective pandemic response. For example, the U.S. National Strategy for Pandemic Influenza calls for continued support of EWORS as part of efforts to strengthen pandemic influenza surveillance

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overseas [44]. In the national influenza strategy of Lao PDR, EWORS is included as a major component of surveillance.

Computer simulation studies showing that rapid detection and public health intervention might contain an emerging pandemic suggest the utility of an early warning system [45, 46]. A draft WHO plan [47], based in part on such work, calls on countries to rapidly identify and report clusters of people with symptoms and exposures that could represent human-to-human transmission of a novel influenza virus – possibly the first indication of an emerging pandemic. WHO also has established large stockpiles of antiviral drugs to be deployed for pandemic containment, but only if the emerging pandemic is detected early enough for containment to be feasible [47].

Whether EWORS, in its current forms, could provide timely detection of an emerging influenza pandemic, or whether it is sufficiently flexible to accommodate modifications that would enhance early pandemic detection, is unknown. To investigate these questions, DoD-GEIS, NAMRU-2, NMRCD, and The Johns Hopkins University/Applied Physics Laboratory (JHU/APL) initiated an "end-to-end" system evaluation in 2006. Because the success of pandemic containment is time-dependent, with computer simulations providing guidance on how soon interventions must begin [45, 46], the evaluation team is using quantitative modeling approaches in addition to qualitative epidemiological assessments to understand how EWORS might perform in the face of an emerging pandemic. The system modeling framework will allow assessment of various EWORS modifications that could improve performance. One of the project's objectives is to guide future development of EWORS and of other systems that countries may implement to improve early detection for pandemic influenza or other epidemic-prone respiratory viruses.

Though in early stages, the EWORS evaluation has identified several features of EWORS and its operating environment that are likely to influence its effectiveness as an early warning system for an emerging influenza pandemic. For example, important system features could include the number and type of clinics at sentinel hospitals that participate in EWORS; the time lag between patient admission and data analysis; the background rate of syndromes for which an increase might indicate an outbreak of a viral respiratory illness such as influenza; and many others. Approaches

for evaluating syndromic surveillance systems in the United States [48, 49] will be adapted for evaluating such features in EWORS.

A realistic projection of EWORS performance for pandemic influenza, though, also requires analysis of factors that are external to the system. For example, local preferences for traditional medicine (which could reduce the effectiveness of a hospital-based surveillance system such as EWORS), referral patterns for patients with suspected avian influenza infection (which could direct such patients towards, or away from sentinel hospitals), population density (which could affect the rate of epidemic progression), location and type of laboratory testing capabilities (which could affect how rapidly a suspected outbreak is verified), and the administrative relationships between the EWORS surveillance hub and outbreak response offices are a few of the extra-system factors that a thorough evaluation should consider. Epidemiologic capabilities of the host country also are critical, and will affect the number and skill of personnel available for surveillance activities.

A tool expected to result from this evaluation is a generic framework for establishing, enhancing, and evaluating surveillance activities in developing countries. When applied, a key consideration must be the ability of the system's host agency to sustain and validate recommended capabilities. While it is possible to suggest many enhancements to a system with limited existing capability, it is important to assess the ability of the host agency to sustain the new features. If enhancements are accepted and sustained, they should be validated over time – to continue improving the system, and to assess the potential utility of such features for other systems.

9.3.4 Summary

A key lesson from several years of EWORS experience in Southeast Asia is the importance of the system's administrative context as a determinant of usefulness. In addition, providing actionable information using validated procedures is critical to developing confidence in a system that can trigger expenditures of human and financial resources. EWORS, in its present or in modified forms, may facilitate rapid detection and containment of pandemic influenza, but rigorous evaluation of

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the system and its operating environment is needed to define its role in pandemic influenza preparedness.

9.4 CASE STUDY II: ALERTA DISAMAR (PERU)

The Peruvian Navy maintains dozens of training facilities, ports, and other bases across the country, from modern facilities in Lima to remote bases in border areas. Crowded living conditions and challenges to maintaining hygiene, which militaries in wealthy and developing countries alike may contend with, contribute to outbreaks of respiratory and diarrheal diseases among Peruvian Naval personnel. The tropical, jungle environment poses additional risks of malaria, yellow fever, dengue, and other vector-borne diseases. Outbreaks of such diseases can render a large proportion of a base population ill, and can significantly impact the Peruvian Navy's ability to execute missions.

Before 2002, the Peruvian Navy's public health surveillance system did not facilitate rapid detection, investigation, and control of infectious disease outbreaks among medical beneficiaries (approximately 25,000 active duty personnel and 100,000 family members in 2006). At each base, a medical officer recorded diseases targeted for surveillance by the Navy. Paper reports were mailed each month to the central Naval medical office in Lima. Because of the long reporting interval and time required for mailed reports to reach Lima (especially for ones sent from remote border areas), surveillance data indicating infectious disease outbreaks often did not reach the central office until outbreaks were far along or over. Even if reports could reach the central office more rapidly, though, timely public health action may not have occurred because the Navy lacked an information system to support the small central staff in managing, analyzing, and interpreting the data. The cost of delayed outbreak response was great: the Peruvian Navy spent substantial amounts of money evacuating patients to the central hospital and treating patients with severe disease.

After a severe *Plasmodium falciparum* malaria outbreak at a base along the Colombian border in 2001, the Peruvian Navy acknowledged the need for more timely outbreak detection and response and committed to developing a more effective infectious disease surveillance system. For assistance, the Navy turned to NMRCD, which the Peruvian Navy has hosted at its national medical campus in Lima since 1983.

9.4.1 System Development, Configuration, and Operation

NMRCD and Peruvian Navy system planners recognized communications infrastructure as a key consideration in generating timely information. Developing a nationwide system that would cover all Navy facilities was an essential objective, but communication capabilities varied widely across the Navy. Some facilities had Internet access, but remote bases did not. Some of these even lacked telephones, and used radio to communicate with higher-level commands. After considering several possible solutions, system planners settled on an innovative, commercial technology that could integrate surveillance data across diverse communications platforms.

Developed by Voxiva, the system allows real-time data transmission by Internet or telephone [50]. Alerta DISAMAR was built around this information system in 2002, beginning with 11 reporting Navy facilities. The surveillance system has since expanded to 69 reporting units (including several Navy vessels) across the country, covering 97.5% of the Peruvian Navy medical beneficiary population (Fig. 9.5). Based on successful implementation in the Navy, the Peruvian Army recently has enrolled sites into the system, giving priority to posts in remote areas with endemic tropical diseases, such as in the Amazon basin. The Air Force has requested incorporation into the system.

Fig. 9.10 summarizes information flow through Alerta DISAMAR (the figure and the remainder of the case study focus on the more mature and extensive Navy network). At each site, a medical officer (physician or nurse) employed by the Peruvian Navy transmits data to the Alerta DISAMAR central hub at NMRCD by the most convenient means available – Internet or telephone (the call is toll-free from public land lines). Sites without access to either mechanism transmit reports by radio to regional hubs, where they are sent by Internet or telephone to the central hub.

Reports consist of demographic and clinical data for clinically suspected or laboratory-confirmed cases of diseases/syndromes identified as surveillance priorities by the Peruvian Ministry of Health or Navy (Fig. 9.7; approximately one-third

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Fig. 9.5 Reporting units (including several Navy vessels) across Peru.

of cases are laboratory-confirmed during routine surveillance, depending on on-site and nearby laboratory capabilities). Reporting frequency depends on the disease – some diseases require a daily report with demographic and clinical information on each case, while common syndromes (such as acute diarrhea or respiratory illness) are reported twice per week in batches to reduce data transmission time. All units



Fig. 9.6 Information fbw through Alerta DISAMAR.

must send a twice-per-week "zero report" if no reportable diseases are identified. The medical officer at each site devotes approximately 10–30 minutes per day to medical record review in preparation for reporting, and approximately 2–3 minutes to transmit data on each case (or batch of cases for the twice-per-week report).

The Alerta DISAMAR hub staff includes one full-time physician employed by NMRCD and a senior noncommissioned officer and two part-time physicians assigned by the Peruvian Navy. The hub uses Voxiva software to convert data reported by different communication platforms into a common format to facilitate management and analysis. Quality assurance includes weekly manual review of automated

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INDIVIDUAL REPORT							
ERUPTIVE BARTONELLOSIS	LEPTOSPIROSIS *	CONGENITAL SYPHLIS					
SYSTEMIC BARTONELLOSIS	P. FALCIPARUM MALARIA	TETANUS					
BRUCELLOSIS *	P. VIVAX MALARIA	NEONATAL TETANUS					
ANTHRAX	MENINGOCOCIC MENINGITIS	EPIDEMIC TY PHUS					
CHAGAS DISEASE	TB MENINGITIS	WHOOPING COUGH					
DENGUE FEVER	MATERNAL DEATH	PULMONARY TB*					
DHF	SNAKEBITES	HIV					
DIPHTERIA	PLAGUE	TRAUMA					
YELLOW FEVER	ACUTE FLACCID PARALY SIS						
TYPHOID FEVER *	RABIES	COLLECTIVE NEPONT					
HEPATITISA *	RUBELLA	CHOLERA					
HEPATITIS B	CONGENITAL RUBELLA	ADD (Acute diarrheal disease)					
STD*	MEASLES	ARI(Acute respiratory infection)					
CUTANEOUS LEISHMANIASIS	SARS	PNEUMONIA					
MUCOCUTANEOUS LEISHMANIASI	ASTHMA						

Daily report

Biweekly report

Fig. 9.7 Alerta DISAMAR Diseases under surveillance individual reports.

procedures that track reporting timeliness (including "zero reporting"), completeness, and error rates (e.g., invalid diagnostic codes) by site (Figs. 9.8 and 9.9). All the data can be exported to Excel for further analysis. To rapidly identify excess cases, graphs are automatically generated in Excel with weekly counts of the most common diseases and expected counts based on historical averages, by site within each Navy region (Fig. 9.10). The staff evaluates the graphs to assess whether additional follow-up is needed. Each week, reports summarizing epidemiologic data and quality assurance metrics for each site are generated automatically; these include counts of the most common diseases/syndromes and timely report rates (Fig. 9.11). Medical officers at reporting units and the central Peruvian Navy medical leadership can access these reports on a restricted, password-protected Internet site. Alerta DISAMAR personnel who lack Internet access may elect to receive compressed, text reports by cellular telephone.



Fig. 9.8 Alerta DISAMAR Attributes: Timeliness.

9.4.2 Outbreak Detection and Response

When Alerta DISAMAR graphical displays of observed and usual case counts suggest that an outbreak may be underway, the central hub staff first checks the reports for obvious errors. The next step is to make contact with the reporting site's medical officer by telephone or radio, to verify the accuracy of the report, gather additional clinical information, and identify any additional cases not yet formally reported. Based on this assessment, the central hub team decides whether to launch an outbreak investigation. Frequently, discussion between central hub and field site staff results in a decision not to initiate an investigation – for example, if the etiology already is known, morbidity is not severe, and effective control measures are in-place. Investigations launched as a result of Alerta DISAMAR have identified outbreaks of various infectious diseases, including malaria [51], dengue [52], and cyclosporiasis [53] (Fig. 9.12).



Fig. 9.9 Alerta DISAMAR Attributes: Data Quality.

A critical element in this decision-making process is the Peruvian Naval senior non-commissioned officer assigned to the Alerta DISAMAR central hub. This individual maintains close contact with each site in the surveillance network (a full-time job) – to provide feedback on reports, respond to requests for technical assistance, and assess whether an outbreak investigation is warranted. As a Naval servicemember, his understanding of the surveillance sites facilitates communication with the sites and interpretation of surveillance data. The Peruvian Navy's decision to detail a senior non-commissioned officer to the Alerta DISAMAR central hub attests to its support for the system. Efforts are ongoing to persuade other Peruvian government agencies enrolling sites into Alerta DISAMAR to assign such an individual to the central hub.

Once the central hub team reaches a decision to investigate a potential outbreak, it must obtain permission from the military installation commander or higher levels of command. The close relationship between NMRCD and Peruvian Naval leadership



Fig. 9.10 ADD cases 2006 Second Navy Region.

facilitates this process as well. Rather than seek permission at the installation level (which could be problematic, as installation commanders may not always feel they have the time or interest to host an outbreak investigation), the central hub team briefs the central Naval medical leadership, which has authority to approve an investigation at any Navy facility. The medical leadership has approved all requests for facility access to investigate outbreaks since Alerta DISAMAR was initiated. To facilitate collaboration with installation personnel, the investigation team, on arrival to the facility, provides a briefing to the facility commander on why the investigation is needed and how it will be executed.

Because outbreaks often are first identified as an increase in clinically suspected cases of an infectious disease, an early step in outbreak investigation is collection of specimens and submission to a competent laboratory for confirmatory diagnosis; frequently, the medical staff at the affected site can accomplish this before the investigation team arrives. Most Peruvian Naval medical facilities lack advanced diagnostic

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SE 2006 - 30		SE 2006 - 31		SE 2006 - 32		SE 2006 - 33	
Daño	Nro Casos	Daño	Nro Casos	Daño	Nro Casos	Daño	Nro Casos
IRA	435	IRA	729	IRA	598	IRA	687
EDA	128	EDA	144	EDA	102	EDA	142
Asma-SOB	3	Asma-SOB	8	Asma-SOB	4	Asma-SOB	6
Malaria Vivax	1	Malaria Vivax	2	Malaria Vivax	4	Malaria Vivax	3
Dengue Clasico	2	Dengue Clasico	3	Dengue Clasico	4	Dengue Clasico	3
Otros	0	Otros	2	Otros	1	Otros	2
Neumonia	0	Neumonia	0	Neumonia	0	Neumonia	2
Malaria Falciparum	0	Malaria Falciparum	0	Malaria Falciparum	0	Malaria Falciparum	1
TBC Pulmonar	0	TBC Pulmonar	1	TBC Pulmonar	2	TBC Pulmonar	1
Reporte Negativo *	28	Reporte Negativo *	25	Reporte Negativo *	26	Reporte Negativo *	30

Reporte de los daños mas frecuentes notificados en las cuatro últimas semanas epidemiológicas Alerta DISAMAR 2006

Fig. 9.11 Example of report summarizing epidemiologic data and quality assurance for each site.

capabilities, so Alerta DISAMAR interfaces with national laboratory networks to identify outbreak etiology: public health laboratories operated by the Ministry of Health, and a nation-wide laboratory-based surveillance network operated by NM-RCD in collaboration with the Ministry of Health.

This laboratory-based network, the Febrile Syndromic Surveillance System, enrolls patients presenting with febrile, respiratory, gastrointestinal, or hemorrhagic syndromes to 10 clinical sites across the country. Site staff collect demographic, historical, and clinical data; and diagnostic specimens appropriate for the presenting syndrome. Data and specimens are sent at regular intervals to the central laboratory at NMRCD or an NMRCD field laboratory in Iquitos (northeastern Peru, in the Amazon basin), which use virological, serological, and polymerase chain reaction (PCR) methods to test for a wide range of likely pathogens. The transportation protocols established for this ongoing surveillance program facilitate transfer of specimens collected in an Alerta DISAMAR outbreak investigation to a competent laboratory,

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Fig. 9.12 Alerta DISAMAR usefulness: outbreaks detected.

if specimens can be directed to a Febrile Syndromic Surveillance System enrollment site.

On completion of the outbreak investigation, the Alerta DISAMAR central hub team prepares a report on its findings and recommendations for preventing or responding to future outbreaks to the central Naval medical leadership, which may direct the affected facility (or others) to implement recommendations. Understanding and respecting such chain-of-command relationships has been critical for NMRCD's success in developing and expanding Alerta DISAMAR in the Peruvian Navy.

9.4.3 System Flexibility

Voxiva-developed Alerta DISAMAR software provides for system flexibility in key domains. As discussed earlier, the system's ability to integrate surveillance data from internet and telephone is important because communication capabilities vary

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markedly across the Alerta DISAMAR network. The software also allows the central hub to define new reportable diseases and syndromes as the Peruvian Navy recognizes new health threats. This is an important capability for a system focused on emerging infectious diseases, which (by definition) are new or changing. However, experience in adding leptospirosis, sexually-transmitted infections, and other diseases to the original list has shown the process to impose significant requirements on the surveillance sites. Central software modification allows all sites to report new diagnostic codes, but generating those new data requires busy medical staff to implement new clinical procedures (e.g., additional questions or physical examination components).

Voxiva and its software also have proven adaptable to the needs of the Peruvian Navy and central hub by incorporating new ways of entering and visualizing data. For example, the latest software upgrade allows staff at sites with intermittent Internet access to perform data entry offline on a PC, then upload the data to the central hub when an Internet connection is available. Reporting platforms are being expanded to include smart phones and PDAs. SMS/text messaging will provide another means of reporting to the central hub and of communicating from the central hub to notify sites of new diseases to include in surveillance or of emergency procedures (e.g., if there is concern for SARS, pandemic influenza, or another novel, dangerous disease in the region).

The web-based interface provides data visualization from anywhere with Internet access. Multiple "dashboards" have been created to customize data views for users with different needs (e.g., surveillance site staff versus central Naval leadership). These web-based interfaces display key information using indicators, graphs, alerts, and an interactive GIS map. Charts can be generated automatically that use standard epidemiologic formats, or custom-made with user-specified data and formats. Data can be exported to standard statistical software packages for further analysis.

As a military surveillance system, an important challenge that Alerta DISAMAR contends with is personnel turnover. While most central hub staff members have worked there for several years, many medical officers at Navy surveillance sites are young physicians or nurses performing short, required national service duty. Although such frequent turnover demands frequent training, the central Peruvian Naval command allocates time to Alerta DISAMAR training during initial medical officer training, which occurs in Lima over two days before assignment to facilities across the country (an example of training material developed by the central hub is shown in Fig. 9.13). This arrangement allows the central hub to conduct one group basic training session each year for a new cohort of surveillance site medical officers, and is another example of how high system acceptability by the major stakeholder, the Peruvian Navy, contributes to efficiency and effectiveness.



Fig. 9.13 Alerta DISAMAR Training Material.

Finally, broadly-based training of surveillance site staff allows them to respond appropriately to possible outbreaks, even if that requires modification of usual system procedures. In one recent example, the medical officer on a Naval ship noticed an increase in diarrhea cases during a two-day period over what normally occurs on the ship. Because diarrhea is not uncommon in the population and Alerta DISAMAR reporting draws staff away from other important clinical duties, system procedures call for reporting of diarrhea cases twice per week. The medical officer, though,

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had completed an NMRCD outbreak response course as part of Alerta DISAMAR training, and recognized the increase as a possible outbreak requiring immediate reporting. She contacted the Peruvian Naval representative at the central hub, who quickly verified that other ships in the area that had shared a training environment were experiencing excess diarrhea cases as well.

9.4.4 Summary

The Peruvian Navy and NMRCD have found Alerta DISAMAR to be useful for timely detection of emerging infectious disease outbreaks [54]. Key factors that contribute to the system's effectiveness are software that integrates surveillance data across diverse communication platforms, which extends surveillance to remote facilities with minimal communication capabilities; broadly-based training of system operators, which prepares them to respond appropriately to situations that require modification of usual system procedures; and, perhaps most importantly, strong stakeholder support, which facilitates communication with surveillance sites, addition of new sites to the network, physical access to sites for outbreak investigation, and centralized training of surveillance site medical officers. As with many infectious disease surveillance systems in developing countries, Alerta DISAMAR often reports clinically-suspected rather than laboratory-confirmed diagnoses. In outbreak scenarios, though, integration with laboratory-based networks can provide diagnostic confirmation.

9.5 CONCLUSION

The two short case studies presented in this chapter illustrate a few common themes – the importance of gaining visible endorsement for the surveillance system from offices whose authority is recognized by clinical and public health personnel who may participate in the system; the utility of broadly-based training for system operators, which will prepare them to address new situations not covered by the system's standard operating procedures; and the need for integrating laboratory-based and

syndromic surveillance. Although the case studies covered surveillance systems in developing countries, these points apply to systems in wealthy countries as well.

It would be wrong to assume, though, that evaluations of and experience with surveillance systems in wealthy countries provides sufficient guidance for implementing systems in resource-poor settings. While challenges and solutions may appear similar at a high level of abstraction, the brief treatment in this chapter of EWORS and ALERTA Disamar shows that some features of the developing country environment call for technological or administrative strategies that might not be needed in, for example, a county health department in the United States. There are significant challenges that money alone cannot solve – for example, lack of skilled personnel to operate surveillance systems, and issues of legal authority in outbreak investigations or implementing new systems.

The need for surveillance system evaluations in developing countries is greater than ever, as concern for an influenza pandemic has driven wealthy countries to provide substantial resources for improvement of public health capacity in developing countries. Fundamentally, there is a need to identify the advantages, disadvantages, and appropriate applications of various sponsorship and support models. For example, how useful is direct aid in developing public health capacity in poor countries? How does this compare with the experience of overseas platforms like NAMRU-2, NMRCD, and other broadly-based laboratories? What models not yet implemented might work best? Analyses that answer such questions could prove very useful in guiding efficient, effective investment in the public health systems of developing countries.

9.6 STUDY QUESTIONS

9.6.1 Incentives can be a useful tool in enrolling and maintaining sites in a surveillance system. But they can increase system sustainment cost and might introduce threats to data validity (for example, if incentives are based on number of events reported).

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Q: Besides financial and equipment incentives, what are some ways that busy hospitals or clinics in developing countries could be persuaded to participate in a surveillance system?

9.6.2 In many developing countries, people may seek care at hospitals only after pursuing other options (e.g., treatment at home, or by a traditional healer or pharmacist).

Q: In such places, how could surveillance systems be designed to capture timely and accurate information?

9.6.3 This chapter described one system (Alerta DISAMAR) that uses the internet and telephones to communicate surveillance data from remote locations.

Q: What are some other methods of communicating surveillance data that could be implemented in resource-poor settings?

9.6.4 Developing country ministries of health usually have small budgets for investigating outbreaks. Even if a surveillance system is in place and provides convincing evidence that an outbreak is underway, decision-makers may elect not to expend precious resources on a response.

Q: What data could a surveillance system in a developing country collect to help authorities decide whether to launch an investigation?

9.6.5 Several approaches to evaluating surveillance systems have been proposed. Some have been informed primarily by experience in high-income countries.

Q: What are some features of surveillance systems (or their operating environments) in developing countries that might require special attention in an evaluation?

Disclaimer

The views expressed here are the private views of the authors, and are not intended to be construed as official, or as reflecting the true views of the US Department of the Army, US Department of the Navy, or US Department of Defense.

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