ProMED-mail: An Early Warning System for Emerging Diseases

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The Program for Monitoring Emerging Diseases (ProMED-mail) reports on outbreaks of diseases of infectious or toxic etiology, whether natural or intentionally released, that affect humans. Open to all sources, free of political constraints, and available to users free of charge, ProMED-mail exploits the speed and ubiquity of the Internet to serve as an early warning system for the detection of emerging disease outbreaks. ProMED-mail monitors diseases of plants and animals of agricultural importance in addition to zoonoses because of their key role in disease emergence. Reports are carefully screened for validity and are placed in an appropriate context by commentary and references from a panel of expert moderators. Reports are then posted to the Web and sent by e-mail to >32,000 subscribers in >150 countries.

> This morning I received this e-mail and then searched your archives and found nothing that pertained to it. Does anyone know anything about this problem?
>
> "Have you heard of an epidemic in Guangzhou? An acquaintance of mine from a teacher's chat room lives there and reports that the hospitals there have been closed and people are dying."
>
> (Posted by Stephen O. Cunnion, M.D., on ProMED-mail, 10 February 2003 [1])

This report marked the earliest public description of the outbreak of a disease that later became known as severe acute respiratory syndrome (SARS). SARS, which affected >8000 people worldwide and killed >900, was in many ways the prototype for emerging diseases of the new millennium. A novel disease, SARS is most likely a zoonosis that emerged in an area that had poor communication with other regions and that spread rapidly via international air travel. A government fearful of the political and economic consequences of its discovery actively suppressed news of the outbreak. Subscribers to the Program for Monitoring Emerging Diseases (ProMED-mail), a freely available service for the reporting of emerging infectious diseases, were among the first in the world to learn of this outbreak.

ProMED-mail continued to cover SARS throughout the outbreak, sending reports to our subscribers (>32,000 as of February 2004) on a near-daily basis. On 11 March 2003, ProMED-mail reported the illness of a businessman in Hanoi who appeared to have spread a respiratory illness to the staff of a hospital, forcing the closure of the hospital [2]. Officials were reassuring, saying that the disease was unlikely to spread. In a commentary accompanying the report, the ProMED-mail moderator wondered how the official could be sure of this.

ProMED-mail's ongoing reports of the SARS epidemic helped warn medical personnel halfway around the world of this contagious illness. In Toronto, medical staff who were regular readers of ProMED-mail's reports learned of the existence of this deadly and contagious illness. They were thus able to respond appropriately and to isolate patients when the disease first appeared there. In a report on the SARS epidemic in Toronto, local medical personnel credited Internet-based reporting in helping to contain SARS:

> The identification of SARS in Canada only a few weeks after an outbreak on another continent exemplifies the ease with which infectious agents can be transmitted in this era of international travel. It also demonstrates the importance and value of information and alert systems such as the Department of Communicable Disease Surveillance Response of the World Health Organization [WHO] and the Disease Outbreak News Web site (http://www.who.int/csr/don) and the ProMED-mail (Program for Monitoring Emerging Diseases) reporting net-

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work sponsored by the International Society for Infectious Diseases (http://www.promedmail.org) [3, pg. 2003].

In addition to serving as an early warning system, ProMED-mail became a communication network that allowed early collaboration among the laboratories around the world that were working to discover the etiologic agent of SARS. Virologists in Hong Kong, Germany, and Canada all used ProMED-mail to report their early results before the WHO's SARS laboratory network could be established. ProMED-mail also acted as a trusted intermediary, delivering information between parties who had no official channels of communication, such as Taiwan's government and the WHO.

ABOUT ProMED-mail

Founded in 1994 with only 40 subscribers, ProMED-mail was envisioned as a means of exploiting the Internet in the service of detecting emerging infectious or toxin-mediated diseases, either natural or intentionally caused, that threatened human beings. Its goal is to disseminate this information rapidly to a wide audience and allow for informed discussion in real time. As of February 2004, ProMED-mail has >32,000 subscribers in >150 countries who receive e-mail reports on outbreaks and disease emergence. Reports are selected and interpreted by a panel of specialist moderators who provide expert commentary, supply references to previous reports and to the scientific literature, and put the report in perspective for a diverse readership. Reports are simultaneously posted to ProMED-mail's Web site (http://www.promedmail.org), which receives thousands of visits each day. A program of the International Society for Infectious Diseases, ProMED-mail is provided free of charge to all and is supported by donations and foundation grants. Because it is without official ties to governments, it is entirely free of political constraints.

ProMED-mail focuses on newly described or unknown diseases, epidemics, and outbreaks and on the emergence of diseases in new areas or populations. Because of their ample coverage in other forums, tuberculosis, HIV infection, and vaccine-preventable diseases are not covered by ProMED-mail except in unusual circumstances. In addition to its focus on human disease, one of the unique features of ProMED-mail is its emphasis on diseases of plants and animals that might affect human populations. ProMED-mail espouses the "one medicine" concept and recognizes the importance of diseases that affect plants and animals of agricultural importance, as well as zoonoses. For example, ProMED-mail provided extensive coverage of the outbreak of foot-and-mouth disease that devastated livestock in the United Kingdom, as well as the recent outbreaks of avian influenza in Europe, Southeast Asia, and the United States. Of course, ProMED-mail provides extensive coverage of less sensational but equally important illnesses, such as dengue fever and norovirus infection (table 1).

Table 1. Number of ProMED-mail reports, 1994–2003, by disease category.

Disease	No. of reports
Dengue	749
West Nile virus infection	728
Foot-and-mouth disease	597
Cholera	578
Bovine spongiform encephalopathy	578
Rabies	557
Anthrax	474
Ebola virus infection	424
Escherichia coli O157 infection	422
Hantavirus infection	340
Creutzfeldt-Jakob disease	332
Influenza	329
Salmonella	308
Malaria	279
Yellow Fever	265
Unknown illness	209

NOTE. Data are for the 16 disease categories with the greatest number of ProMED-mail reports, 1994–2003.

It has been estimated that >70% of emerging diseases are zoonoses (e.g., *Escherichia coli* O157, Monkeypox, Nipah virus, SARS, and spongiform encephalopathies) [4]. For this reason, ProMED-mail's staff includes 4 veterinarians with diverse expertise to help us sift through the news of diseases among animals.

INFORMATION FLOW AT ProMED-mail

Receipt of information. Each day, ProMED-mail receives dozens of e-mails, many from subscribers, that contain new data on outbreaks or diseases, some of which are reported firsthand and some of which are reported from other sources (figure 1). In addition, our staff combs through the Internet and traditional media for relevant items and scans a variety of official and unofficial Web sites (e.g., the Web sites of ministries of health; federal, state and local health departments; and international organizations) looking for recent updates. ProMED-mail's staff of >20 individuals in 9 countries collaborates virtually; all information is relayed via the Internet, using both e-mail and Web-based systems.

Review and verification. All incoming information is filtered through the "top moderator"—either the editor, or one of the associate editors—who is on duty on a given day. Some reports are rejected immediately because they contain information that is irrelevant, not credible, or outdated or duplicates information contained in previous reports. Most reports are examined carefully and then sent to one of the expert subject moderators for further review. ProMED-mail's panel of spe-

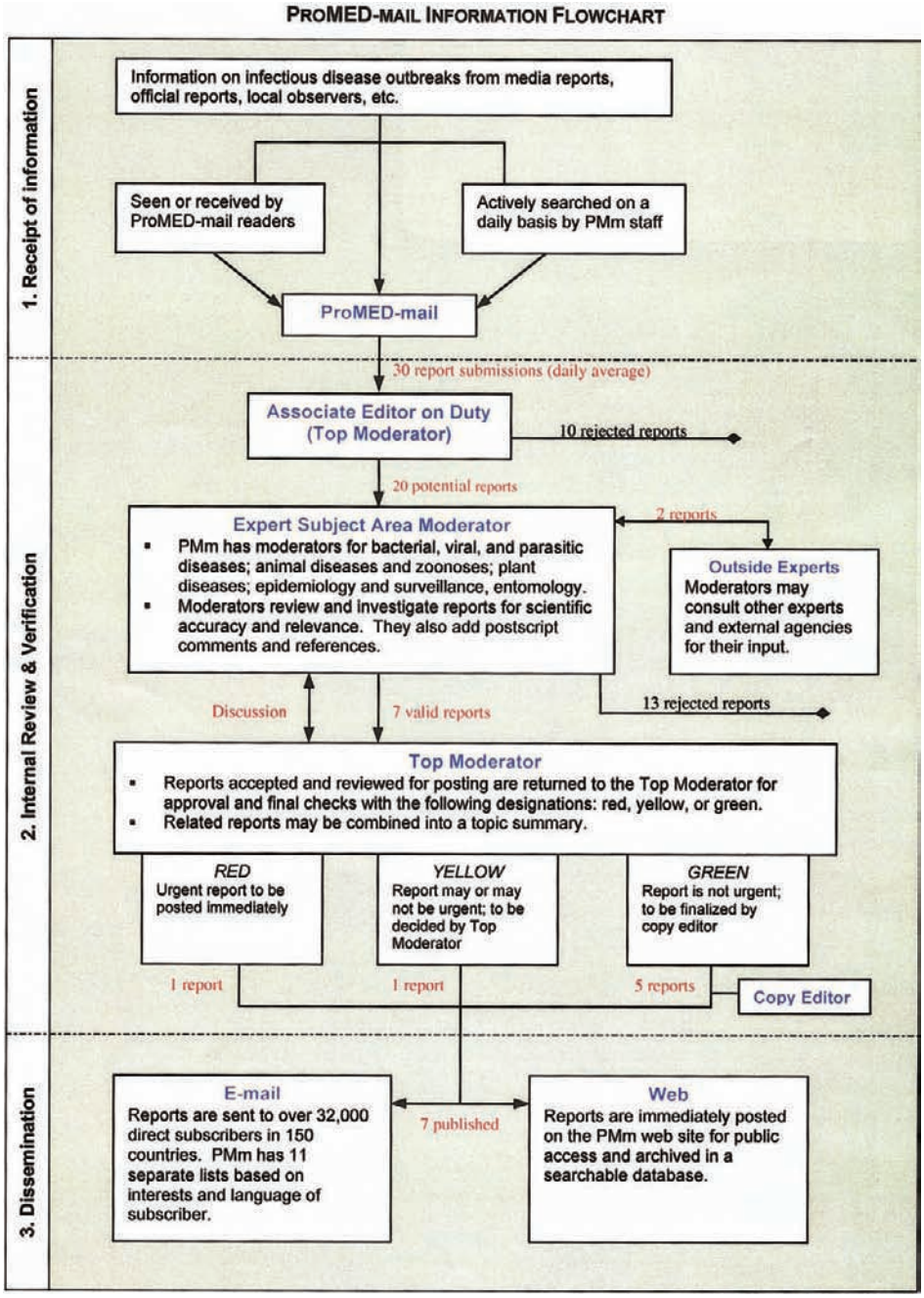

Figure 1. ProMED-mail information flowchart. Reports are received by ProMED-mail and passed electronically among the ProMED-mail staff. Numbers of reports represent typical values.

cialty moderators includes experts in viral diseases, bacterial diseases, plant diseases, veterinary diseases and zoonoses, epidemiology, and medical entomology. Reports are frequently sent to >1 moderator. For example, a report on trypanosomiasis might be relayed to a veterinary moderator, the parasitic diseases moderator, and the medical entomologist. Sometimes reports are sent for translation and, on occasion, to outside experts for their opinions.

The specialty moderator then has several tasks. The foremost of these is to assess the reliability and accuracy of the information. At times, this may involve verification of the report from another source, including direct contact with a colleague who might possess first-hand knowledge. The moderator edits the piece for content, provides pertinent references (both from prior ProMED-mail reports and from the scientific literature), and adds commentary. This commentary is usually brief, with the intention of providing background and perspective. Sometimes multiple reports of the same outbreak or disease entity

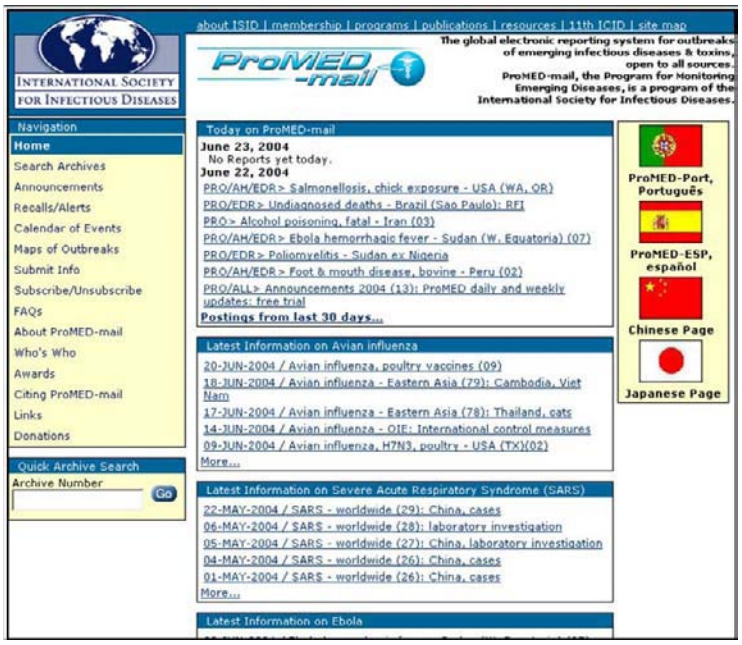

Figure 2. The ProMED-mail Web site (http://www.promedmail.org)

may be grouped into a single report to enhance clarity and minimize the number of e-mails our readers receive.

Edited reports are returned to the top moderator for final editing (in collaboration with a copy editor), verification, and additional commentary. Reports of normal priority (coded "green") are handled routinely and will normally transit the system, from initial report to final posting, within 24 h (ProMED-mail is in operation 7 days a week, 365 days a year). Reports of greater urgency—for example, a report of an outbreak of a potentially epidemic disease in a new location—could be coded "yellow." These reports receive expedited review and are posted as quickly as possible. Reports that are extremely urgent are coded "red" and may bypass parts of the editorial process to be posted immediately.

Dissemination of information. Finalized reports are simultaneously posted to the ProMED-mail Web site (figure 2) and distributed to ⩾1 of 11 mailing lists that are based on the interests and languages of the subscribers. Approximately one-third of our readers receive the main ProMED-mail list; they receive every report as it is distributed. Other lists are oriented toward animal diseases (ProMED-Animal Health and Emerging Animal Diseases [ProMED-AHEAD]) or plant diseases. ProMED-Emerging Disease Reports (ProMED-EDR) is designed for readers who want to receive only reports of disease occurrences and do not want to receive discussion, background reports, or announcements. Digest forms of each list are also available. Digest subscribers receive an assemblage of reports approximately once each day. This minimizes the number of e-mails but may delay the receipt of a given report. Finally, specialized lists for readers in Latin America are available. ProMED-Port and ProMED-ESP deliver emerging disease news specifically oriented to readers in this region in Portuguese and Spanish, respectively. E-mails are sent as "plain text" so that all readers, particularly those in low-resource countries, are able to view and use the information as quickly as possible.

ARCHIVES AND WEB SITE

All ProMED-mail reports, dating from the inception of the service in 1994 to the present, are available to readers in a searchable database. This powerful archive feature, housed on the ProMED-mail Web site (developed and maintained by Oracle [Redwood Shores, CA]), allows users to search ~20,000 reports using text, dates, and geographic locations. For example, a user wishing to find reports of Nipah virus in Malaysia could enter these 2 search terms and receive a list of accessible links (figure 3). Reports are internally cross-referenced, so that a single mouse-click on a reference to another report will bring up that report in a browser window. Archives can also be retrieved by e-mail (although without search capability) for those whose Internet connection does not permit Web browser access.

Other features available through ProMED-mail's Web site include a listing of recent reports (listed in reverse chronological order), a "who's who" of the ProMED-mail staff (including their contact information), instructions on how to submit in-

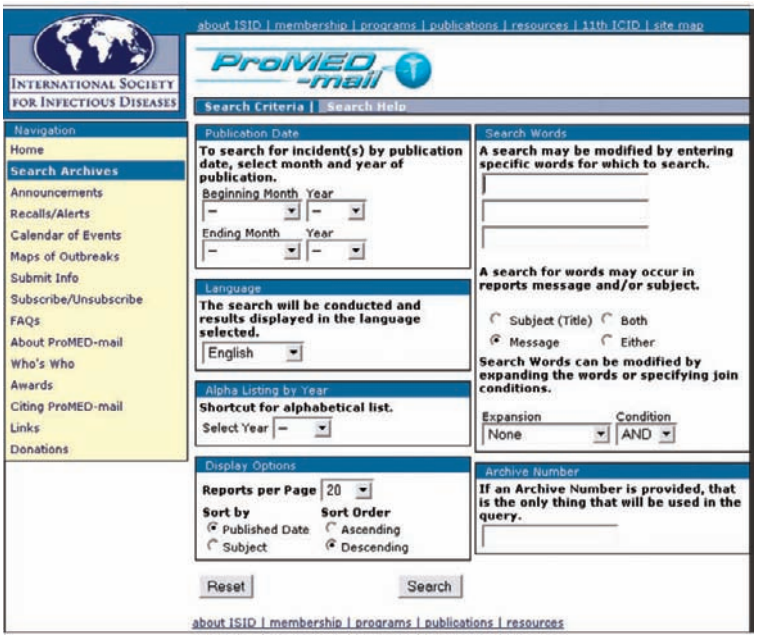

Figure 3. The ProMED-mail search page. The ability to search ~20,000 archived reports is an important feature of ProMED-mail's Web site.

formation to ProMED-mail, easy access to free subscription to the various mailing lists, and many links to relevant sources of information on emerging infectious diseases.

THE CONTEXT OF ProMED-mail

ProMED-mail is a powerful tool, and its growth (~20% net new subscribers between February 2003 and February 2004) is testimony to the value of the services it provides. However, it is clear that no single system can fulfill the mission of detecting and reporting every outbreak of infectious disease worldwide. All who work in this area acknowledge the need for multiple networks and surveillance systems. The WHO's Global Outbreak Alert and Response Network draws on numerous sources, including its own teams of public health workers, to report on and respond to outbreaks of public health significance. A portion of the information gathered is made available on the WHO's Web site. The Global Public Health Intelligence Network, a service of Health Canada, automatically searches the Internet for news stories involving emerging disease threats. However, its use is restricted to a select group of public health officials, and it is not publicly accessible. Epi-X, provided by the US Centers for Disease Control and Prevention (Atlanta, GA), is a Web-based communications system designed to allow public health professionals (including state and local public health departments) to communicate quickly and securely. It does not seek or allow input from most health practitioners or the general public. Numerous other surveillance systems exist, some directed at specific diseases or regions, some oriented toward a particular population or interest group. The Emerging Infections Network is a collaboration between the Infectious Diseases Society of America and public agencies that is designed to allow infectious diseases physicians to act as sentinels of disease outbreaks.

The existence of multiple surveillance systems, official and unofficial, is beneficial from a number of standpoints. First, the complementary flow of information on the basis of the reporting interests and biases of each network makes it more likely that a given outbreak or emergence of disease will be discovered and reported in a timely way. Moreover, each system serves as an important validation tool for the others. Outbreaks of disease that are uncovered by one surveillance system but not by another lead to the recognition of gaps in the detection of disease. Partial redundancy helps to insure that the overall goal of disease detection is accomplished.

FUTURE INITIATIVES

To further the primary mission of ProMED-mail, which is to detect emerging disease, we plan to form alliances with regional disease surveillance networks. One such collaboration that is already under way involves a consortium of countries in Southeast Asia and is called the Mekong Basin Disease Surveillance Group. Supported by a grant from the Rockefeller Foundation, this project seeks to improve the detection of outbreaks of disease in this region and facilitate interaction within the group

using ProMED-mail's experience in building and running moderated networks. Another project, sponsored by the Nuclear Threat Initiative, is engaged in building a Russian-language version of ProMED-mail that will improve the surveillance of emerging diseases in the newly independent states of the former Soviet Union.

A third project, in collaboration with the Center for Applied Microbiology Research in the United Kingdom, envisions building an information system that will provide a geographic representation of ProMED-mail's reports. This will allow ProMED-mail users to "see" where outbreaks of disease are occurring and to query the archives through a geographic interface.

The surveillance of outbreaks of newly emerging diseases is of more than academic importance. The sooner a disease outbreak is recognized, the sooner appropriate public health measures can be taken to control its spread. ProMED-mail—open to all sources of information and unique in its freedom from political constraints and its free availability to all—will continue to serve as an international early warning system for emerging infectious diseases.

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