



Original Contribution

Fifty-Five Years of International Epidemic-Assistance Investigations Conducted by CDC's Disease Detectives

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For more than 60 years, the Centers for Disease Control and Prevention (CDC) has used its scientific expertise to help people throughout the world live healthier, safer, longer lives through science-based health action. In 1951, CDC officially established the Epidemic Intelligence Service to help build public health capacity. During 1950–2005, CDC's Epidemic Intelligence Service officers conducted 462 international epidemiologic field investigations in 131 foreign countries and 7 territories. Investigations have included responding to emerging infectious and non-infectious disease outbreaks, assisting in disaster response, and evaluating core components of public health programs worldwide. Approximately 81% of investigations were responses to infectious disease outbreaks, but the proportion of investigations related to chronic and other noninfectious conditions increased 7-fold (6%–45%). These investigations have contributed to detecting and characterizing new pathogens (e.g., severe acute respiratory syndrome–associated coronavirus) and conditions, provided insights regarding factors that cause or contribute to disease acquisition (e.g., Ebola hemorrhagic fever), led to development of new diagnostics and surveillance technologies, and provided information upon which global health policies and regulations can be based. CDC's disease detectives will undoubtedly continue to play a critical role in global health and in responding to emerging global disease threats.

Centers for Disease Control and Prevention (U.S.); epidemics; epidemiologic methods; world health; World Health Organization

Abbreviations: CDC, Centers for Disease Control and Prevention; EIS, Epidemic Intelligence Service; EISOs, Epidemic Intelligence Service officers; Epi-Aids, epidemic-assistance investigations; FELTP, Field Epidemiology and Laboratory Training Program; FETPs, Field Epidemiology Training Programs; SARS, severe acute respiratory syndrome; WHO, World Health Organization.

Global health has been defined as placing priority on improving health and achieving health equity for all persons worldwide without regard for the concerns and perspectives of individual nations (1, 2). Societal and environmental trends have highlighted the importance of a borderless, collaborative approach to addressing disease threats. For example, globalization of travel, trade, and communications has resulted in enhanced global connectivity and facilitated global dissemination of infectious and other disease threats (3–6). A review of emerging infectious disease events during 1940–2004 revealed hot spots in tropical Africa, Latin America, and Asia (7). Climate change can result in injuries or illness attributable to floods and heat exposure, increase respiratory problems or

vectorborne illnesses, and threaten the safety and availability of food and water supplies (8). Historically, infectious diseases have dominated the global public health landscape, but noncommunicable diseases (e.g., heart disease, diabetes, and cancer) are increasing in alarming numbers in developing countries as a result of changing dietary habits, decreased physical activity, and increased life expectancy (9, 10).

For more than 60 years, the Centers for Disease Control and Prevention (CDC), an agency of the US Department of Health and Human Services, has used its scientific expertise to help people throughout the world live healthier, safer, longer lives through science-based health action. CDC contributes to global health efforts through activities that include

1) developing surveillance and strategic information systems, 2) strengthening laboratory systems and networks, 3) building the capacity of the public health workforce, 4) participating in public health emergency responses, 5) translating research into public health policy, and 6) monitoring and evaluating public health programs (11).

In 1951, CDC officially established the Epidemic Intelligence Service (EIS) Program as a means of building public health capacity in the United States and abroad (12–16). The 2-year training program in applied epidemiology and public health provides EIS officers (EISOs) with opportunities to conduct epidemic-assistance investigations (Epi-Aids) and provide epidemiologic assistance domestically as well as internationally. CDC's EISOs, sometimes called "disease detectives", are selected from a variety of disciplines and include physicians, nurses, doctoral-level scientists, and veterinarians from the United States and other countries.

Since the inception of the EIS Program, requests from foreign countries for onsite epidemiologic assistance have increased steadily. When CDC receives a request for epidemiologic assistance from a foreign government, the response is usually provided by subject-matter experts related to the public health problem. The majority of requests for assistance are related to an acute disease outbreak and thus are handled through CDC's Epi-Aid system (13). EISOs and other CDC staff who are deployed in response to the request work closely with public health officials from the host country's ministry of health to identify the cause of the outbreak/public health problem, implement control measures, and provide recommendations to prevent future outbreaks or public health problems (13).

EISOs have assisted nations worldwide in responding to novel, emerging, and established infectious and noninfectious disease threats (17–21). In this paper, we summarize and describe the evolution of international epidemiologic field investigations conducted by EISOs during 1946–2005 and highlight selected investigations that illustrate the contribution of these investigations to global health efforts, including disease prevention and control, public health science, and health policy.

MATERIALS AND METHODS

To identify CDC's international Epi-Aids, we reviewed an electronic database of all field investigations and available published and unpublished reports conducted by CDC during the 1946–2005 period. For this review, an international Epi-Aid was defined as one that occurred in countries or territories other than the United States and Puerto Rico. An Epi-Aid that occurred in multiple countries or locations but was linked to a single etiology was counted as a single investigation and was attributed to the location where the problem was first identified. We excluded investigations linked to travelers returning ill to the United States from a foreign country or cruise ships because the investigation began in the United States and not the foreign country.

To characterize the Epi-Aids, we extracted information on the location (i.e., country and World Health Organization (WHO) region), year, number of cases and outbreak-related

deaths, type (i.e., infectious, noninfectious, or other), and, when available, the specific etiology (e.g., pathogen or toxin). Epi-Aids during which the investigators were unable to attribute the outbreak or condition to an identifiable cause were classified as being of unknown etiology.

To highlight the number of outbreaks that might have been prevented or that might be amenable to recognized public health interventions, we also grouped investigations into the following categories: cancer (e.g., cervical dysplasia or leukemia); noncancerous chronic conditions (e.g., multiple sclerosis); disaster (e.g., wars or floods); foodborne/enteric (e.g., botulism or cholera); injury (e.g., violence); nosocomial (e.g., aspergillosis or *Clostridium difficile*); nutrition (e.g., anemia or goiter); other infectious (e.g., Brazilian purpuric fever or hepatitis C); parasitic (e.g., malaria or balantidiasis); refugee (e.g., health assessments); reproductive health (e.g., maternal mortality or pregnancy); respiratory (e.g., legionellosis or tuberculosis); sexually transmitted infections (e.g., human immunodeficiency virus or syphilis); surveillance (e.g., nonspecific regarding disease); toxin/poisoning (e.g., aflatoxicosis or cadmium poisoning); vaccine-preventable diseases (e.g., diphtheria, hepatitis B), vectorborne diseases (e.g., dengue fever or yellow fever); zoonotic diseases (e.g., anthrax or Ebola virus); and other/unknown. If available from published reports, we also extracted information regarding factors implicated as causing or contributing to the outbreak, the corrective actions taken, and their public health impact. Note that not all Epi-Aids reports have been published in the scientific literature.

Data extracted from reports were entered into an Excel spreadsheet (Microsoft Corporation, Redmond, Washington), imported into STATA version 9 (StataCorp LP, College Station, Texas), and analyzed to provide summary descriptive statistics.

RESULTS

Characteristics and trends in Epi-Aids

A total of 462 international Epi-Aids, representing 131 countries and 7 territories, were identified for the 1946–2005 period; the first occurred in 1950. Readers should note that an EISO did not participate in this investigation because the EIS Program officially began in 1951; it is included as CDC's first international investigation. During a 55-year period beginning with the first international Epi-Aid in 1950, CDC conducted a median of 9 (range: 1–23) international Epi-Aids annually. The distribution of international Epi-Aids by WHO region is displayed in Figure 1.

The Americas accounted for 213 (46%) investigations; the western Pacific region, 78 (17%); the African region, 77 (17%); the European region, 49 (11%); the Southeast Asia region, 26 (6%); and the eastern Mediterranean region, 19 (4%). The African, Americas, and western Pacific regions demonstrate an increasing trend in Epi-Aids, whereas the European and Southeast Asia regions do not reflect consistent increasing trends in the number of Epi-Aids during 1946–2005 (Figure 2). Of the 462 field investigations conducted, 376 (81%) were infectious disease related, 79 (17%) were noninfectious disease related, and 7 (2%) were of

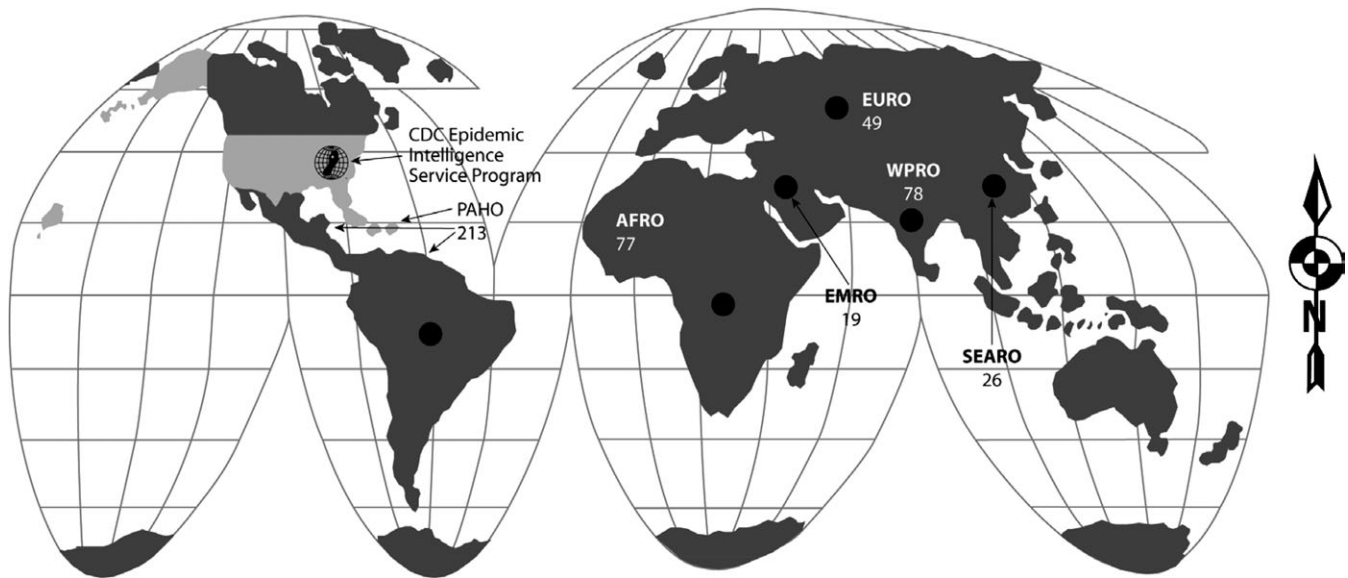


Figure 1. Global distribution of epidemic-assistance investigations conducted by the Centers for Disease Control and Prevention's (CDC's) Epidemic Intelligence Service officers—1950–2005. Black circles indicate the presence of Field Epidemiology Training Programs in the World Health Organization regions, as follows: AFRO, Regional Office for Africa; EMRO, Office for the Eastern Mediterranean; EURO, Regional Office for Europe; PAHO, Pan American Health Organization (also known as the Regional Office for the Americas); SEARO, Regional Office for the South-East Asia; WPRO, Regional Office for the Western Pacific.

unclear etiology. Although infectious diseases accounted for the majority of Epi-Aids during all decades, the proportion of investigations conducted in response to noninfectious causes increased 7-fold (6%–45%) from 1966–1975 to 1995–2005 (Figure 3).

Overall, foodborne/enteric infections was the most common category of infection, accounting for 27.1% ($n = 125$ Epi-Aids) of all investigations and representing the largest specific category of investigations in each decade. Vaccine-preventable diseases were the next most frequent, accounting for 21.0% ($n = 97$) of all investigations. Vectorborne and zoonotic infections accounted for 6.9% and 6.5% of investigations, respectively; respiratory infections, 6.5%; parasitic infections, 5%; nosocomial infections, 2.4%; sexually transmitted infections, 1.1%; and other infectious diseases, 5.2%. Among the investigations of noninfectious diseases and conditions, disaster response (5.4%) and outbreaks caused by toxins/poisonings (4.8%) were the most common (Table 1).

Further examination of selected Epi-Aids

Selected investigations obtained from a literature review highlight CDC's global health contributions by EISOs. Key findings are discussed in the following sections and are summarized in Tables 2–5 by year, location, category, etiology, number of cases (deaths, case-fatality, and attack rates), risk factors, public health actions, and collaborators.

1946–1975

During the period 1946–1975 (Table 2), 4 investigations are highlighted. An outbreak of poliomyelitis in Barbados in

1963 illustrated the importance of implementing vaccination campaigns to interrupt the outbreak. This outbreak did not end until a second mass immunization campaign was conducted (22). The first international investigation of a noninfectious disease occurred in New Zealand in 1967. An EISO investigated a cancer cluster; however, the results were inconclusive (CDC, unpublished data, 1966). In 1971, an outbreak of rubella in Bermuda investigated by EISOs ended 19 days after a vaccination campaign was implemented (23). Before 1971, the island had not conducted any mass campaigns for rubella vaccine (23). Investigation of the Lassa fever outbreak in Sierra Leone was notable because fewer deaths occurred than in previous outbreaks in Nigeria and Liberia; a proportion of the population apparently had evidence of prior infection with Lassa fever virus (24). During this investigation, both nosocomial transmission and person-to-person transmission occurred among families. The investigators recommended use of protective guards in the hospital and quarantining persons with fever to prevent transmission of the disease.

1976–1985

Eleven international Epi-Aids are highlighted during 1976–1985 (Table 3). A drought in Haiti further exacerbated living conditions in communities of low socioeconomic status and having limited safe-water supplies during predrought conditions (25). A survey conducted for the investigation revealed that illness during the drought was related to having a low income and being unemployed, having a large family size, and being in a household with fewer than one 5-gallon (18.9-L) can of water (25). The findings from this investigation in

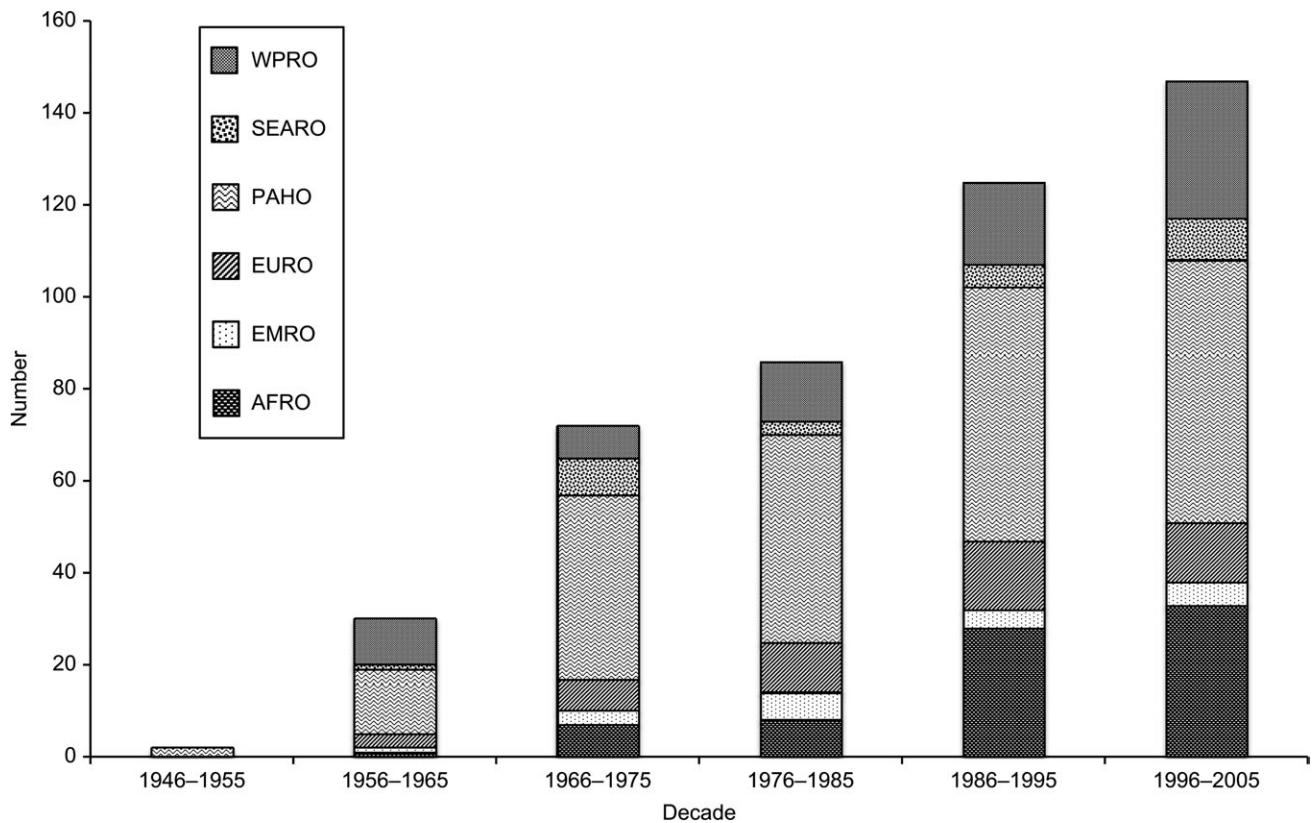


Figure 2. Number of international epidemic-assistance investigations conducted by the Centers for Disease Control and Prevention's Epidemic Intelligence Service officers, by decade and World Health Organization region—1950–2005. AFRO, Regional Office for Africa; EMRO, Office for the Eastern Mediterranean; EURO, Regional Office for Europe; PAHO, Pan American Health Organization (also known as the Regional Office for the Americas); SEARO, Regional Office for the South-East Asia; WPRO, Regional Office for the Western Pacific.

Haiti confirmed the importance of using data to inform government planners.

The 1977 Ebola investigation was the second documented investigation of a disease that had not been observed before in the communities in which the outbreak began or in other countries around the world (26). The ensuing outbreak in the Democratic Republic of Congo was closely linked to a hospital where the first group of patients had received injections. Secondary transmission of Ebola virus also occurred among families and within the community. As a result of a thorough investigation that included surveillance, epidemiology, laboratory analysis, contact tracing, and ecologic testing, Ebola was declared a new virus with characteristics comparable to other hemorrhagic fevers (e.g., Lassa fever). Recommendations from the international commission of public health specialists included national campaigns to inform health personnel of correct methods for sterilizing needles and syringes to prevent disease spread, developing and maintaining a list of experienced local staff who can react quickly to another epidemic, and having a ready supply of medicine and personal protective equipment.

A third outbreak of Ebola occurred again in South Sudan in 1979 (27). The investigators determined that patients in a hospital had infected their family members with the disease.

Recommendations to prevent Ebola again included quarantine practices and increased surveillance for hemorrhagic fever-like illness. In 3 of the investigations during the 1970s (Lassa fever and Ebola), avoidable deaths occurred among health care staff who had not worn personal protective equipment and who had practiced unsafe standards (e.g., reuse of syringes).

In Venezuela, a rural population of Yucpa Indians was affected by an outbreak of hepatitis for 3 years (28). The investigation concluded that it was the delta virus infection that needed hepatitis B to survive as the etiologic agent in this epidemic. An injury-related investigation in Canada sought to determine the cause of pediatric deaths among children with severe congenital heart disease (29). A nurse was implicated in the deaths, but the cause of the epidemic was inconclusive. This investigation demonstrated the link between forensic science and epidemiology. The return of an American tourist to the United States from Cancun, Mexico, with cholera resulted in an Epi-Aid examining whether cholera was a problem in the community where the tourist had stayed during vacation (30). Testing revealed non-01 *Vibrio cholerae* isolated from 22 samples of 134 stool and rectal swabs, 92% of sewage samples (58/63), 86% of untreated well-water samples (12/14), 1 home storage tank, and 21% of

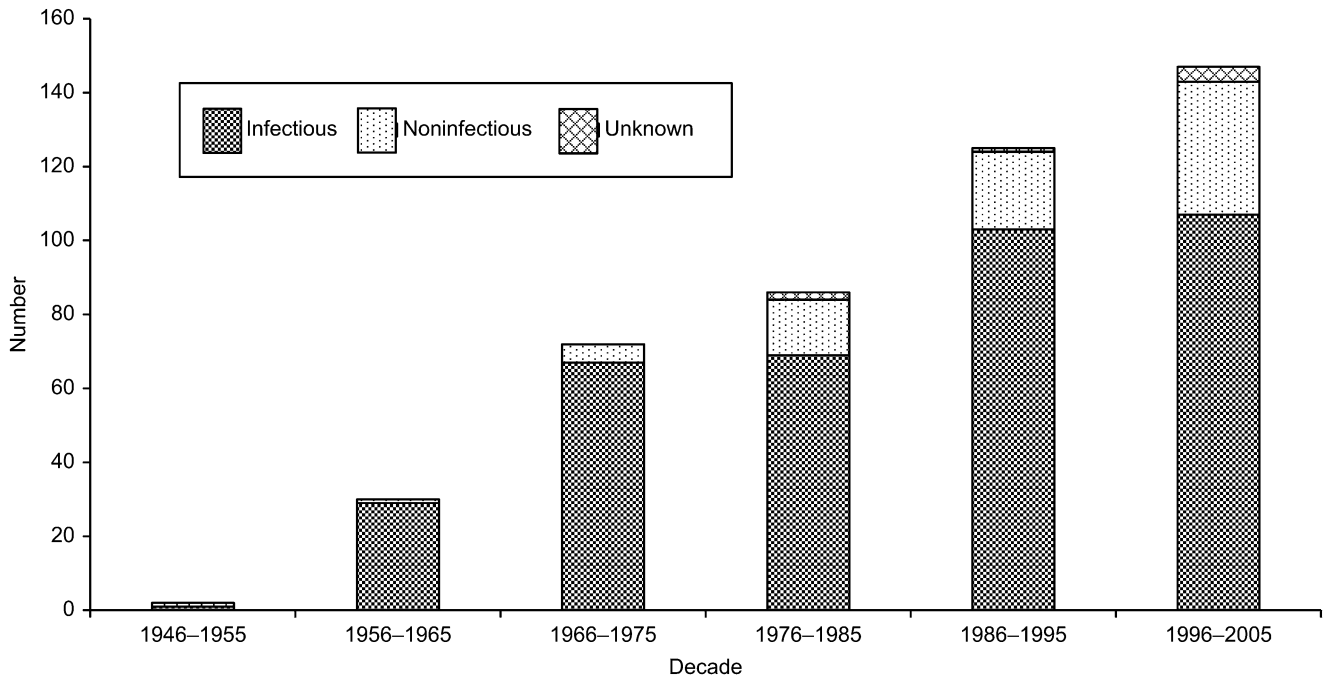


Figure 3. International epidemic-assistance investigations conducted by the Centers for Disease Control and Prevention's Epidemic Intelligence Service officers, by decade and infectious disease status—1950–2005.

raw seafood samples (5/24). The investigation determined that non-01 *V. cholerae* was an important cause of diarrhea among Mexican children, and additional studies were needed to determine modes of transmission and reservoirs.

An interesting, but also sad investigation was of a Peace Corps volunteer in Kenya who died of rabies (31). The Peace Corps worker had received preexposure rabies prophylaxis with the standard 3-dose intradermal series of human diploid cell rabies vaccine, but she still experienced rabies within 8 months of receiving the vaccine. Investigators noted the Peace Corps worker had been tested for antibody rabies titer, and her test indicated no signs of a response to the vaccine. As a result of her death, a serosurvey was conducted of other Peace Corps volunteers who had received the rabies vaccine in the United States and other developing countries. Those vaccinated in developing countries had lower levels of rabies antibodies. No reasons could be identified, and emphasis was placed on persons in developing countries being tested after receiving the rabies vaccine.

A short report in 1985 alerted physicians to botulism poisoning in British Columbia and requested physicians to report suspect cases (32). A new disease, Brazilian purpuric fever, was discovered in Sao Paulo, Brazil, in 1985 (33). The newly recognized illness, purpura fulminans, was determined to be potentially associated with *Haemophilus aegyptius*. The disease is thought to be rare and is characterized by purpura, fever, and hypotension.

In France, as a result of an investigation that implicated nosocomial infection by *Aspergillus*, the importance of recognizing pseudoepidemics was highlighted (34). This outbreak

was a result of specimens being contaminated in the laboratory. Negative outcomes included unnecessarily treating persons thought to be infected. In Haiti in 1985, an outbreak of diarrheal illness was linked to shigellosis at a hotel (35).

1986–1995

Nine investigations are highlighted for the 1986–1995 period (Table 4). An outbreak of hepatitis in a Somalia refugee camp was one of the first to indicate that this disease is a health concern in refugee settings (36). Parathion contamination of flour in Sierra Leone demonstrated the need to preserve potential sources of contamination (37). One bakery closed immediately after persons became ill, which led investigators to test the flour and other items and to confirm parathion contamination. One key recommendation based on this investigation is that countries establish laws to regulate the shipment and use of such toxic pesticides as parathion. In Nigeria, data from a survey of 9 villages during an outbreak of yellow fever highlighted the need to undertake mass vaccination campaigns before the next rainy season to prevent future outbreaks (38).

Another pseudoepidemic occurred in Georgetown, Guyana, in 1987 (39). Local test results indicated a dramatic increase in thallium poisoning cases, but additional testing by CDC demonstrated no evidence of thallium poisoning. Recommendations from this investigation included that the international environmental health community focus on training epidemiologists and that adequate laboratory resources are needed to detect environmental toxicants accurately to identify

Table 1. Number of International Epidemic-Assistance Investigations Conducted by the Centers for Disease Control and Prevention's Epidemic Intelligence Service Officers, by Decade and Etiologic Category, 1946–2005

Etiology	Decade						Total	Overall, %
	1946–1955	1956–1965	1966–1975	1976–1985	1986–1995	1996–2005		
Cancer	0	0	3	1	2	1	7	1.5
Noncancerous malignant chronic conditions	0	0	0	1	1	1	3	0.6
Disaster	1	1	2	3	10	8	25	5.4
Foodborne/enteric	0	7	22	34	35	27	125	27.1
Injury	0	0	0	2	0	1	3	0.6
Nosocomial infections	0	0	0	3	2	6	11	2.4
Nutrition	0	0	0	0	0	6	6	1.3
Other infectious	0	1	2	6	10	5	24	5.2
Parasitic	0	1	6	2	6	8	23	5.0
Reproductive	0	0	0	0	1	3	4	0.9
Respiratory	0	0	0	7	4	19	30	6.5
Refugee health	0	0	0	1	0	6	7	1.5
Sexually transmitted infections	0	0	0	0	2	3	5	1.1
Surveillance	0	0	0	0	2	0	2	0.4
Toxin/poisoning	0	0	0	7	6	9	22	4.8
Vectorborne	0	2	4	3	11	12	32	6.9
Vectorborne diseases	0	18	26	12	24	17	97	21.0
Zoonotic	0	0	7	4	8	11	30	6.5
Other/unknown	1	0	0	0	1	4	6	1.3

affected persons but also to rule out false cases. In Senegal, an investigation revealed the necessity of providing the 2-dose regimen of polio vaccine instead of 1 to confer immunity (40). A measles epidemic in Hungary perhaps was caused in part by vaccine failure (41). The investigators recommended additional studies.

An elevated maternal mortality rate was investigated in 1990 in Mexico (CDC, unpublished data, 1989). However, the investigation revealed that the apparent substantial increase in maternal mortality perhaps was caused by overreporting of deaths and incomplete reporting in certain areas. An investigation in Sierra Leone resulted in a recommendation that, for developing countries, providing Papanicolaou smear screening on a national basis was impractical when a shortage of trained cytotechnologists existed (CDC, unpublished data, 1991). An additional Ebola outbreak occurred in the Democratic Republic of Congo in 1995 (42). Injections were not identified as a major risk factor for transmission, as was the case in the 1976 outbreak. Instead, transmission was primarily associated with person-to-person contact. Of note, this was the fourth major outbreak of Ebola documented and the first to occur in a large population center. Recommendations arising from this investigation again called for use of personal protective equipment by health care workers, development and implementation of improved surveillance for infectious diseases, better communication between hospitals and public health officials, and quick action to control diseases associated with high case-fatality rates (42).

1996–2005

Fourteen published manuscripts and other unpublished CDC data were reviewed for the period 1996–2005 (Table 5). In Haiti, a diethylene glycol-associated outbreak emphasized the need for pharmaceutical producers worldwide to be aware of possible contamination of glycerin and other raw materials containing diethylene glycol and to use quality control measures to identify and prevent potential contamination (43). A woman's health investigation in Tanzania included determining the incidence and risk factors for infant mortality and low birth weight among Burundi refugees (44). Adverse pregnancy outcomes were higher among the refugees compared with women in Tanzania, underscoring the need for including quality reproductive health care for women in refugee settings.

In 1998, Jamaica's Violence-Related Injury Surveillance System was reviewed by CDC's disease detectives by using CDC's guidelines for evaluating surveillance systems during the pilot testing of the system (45). Results indicated that the system was simple, flexible, and sensitive, with a positive predictive value of 86%. After the Violence-Related Injury Surveillance System was reviewed, CDC recommended that the system include additional hospitals and that the abstraction form be adapted to include other injury data. After a hurricane in the US Virgin Islands, reported conjunctivitis cases surged (46). The investigation did not link the outbreak of conjunctivitis with the hurricane but demonstrated that residents should avoid social contact with persons who have

Table 2. Selected International Epidemic-Assistance Investigations and Response Efforts Conducted by the Centers for Disease Control and Prevention's Epidemic Intelligence Service Officers, 1946–1975

Year	Location (Reference No.)	Category	Etiology	No. of Cases, Deaths, Case-Fatality and Attack Rates, if Available	Risk Factors	Public Health Actions	Collaborators
1963	Barbados (22)	VPD	Poliomyelitis	68 cases of paralytic poliomyelitis; attack rate: 29.3/100,000 persons; 4 deaths; case-fatality rate: 5.9%	Children aged 0–5 years (52 cases)	Two mass vaccination campaigns (oral vaccine); epidemic ended 6 days after the second campaign	WHO, Barbados General Hospital, Barbados Medical Services
1967	New Zealand ^a	Cancer	Leukemia	6 leukemia cases over 15 years (1952–1966); 5 cases among children = acute leukemia; 1 case in an adult = chronic granulocytic leukemia	Close proximity of cases, community elementary school, and access to a vineyard	Further studies needed to examine this potential cancer cluster	New Zealand Department of Health
1971	Bermuda (23)	VPD	Rubella	260 cases	Age group most affected: 15–24 years; infection associated with school classroom, ill contacts including family, work, and social settings	Island-wide rubella vaccination campaign; >80% of elementary and nursery school children reached (aged 2–12 years)	Bermuda Ministry of Health
1973	Sierra Leone (24)	Zoonotic	Lassa fever	63 suspect cases (10 confirmed) identified over a 2-year period admitted to 2 hospitals	Associated with hospital setting	Use of personal protective equipment (gown, gloves, and masks) to prevent nosocomial transmission of Lassa fever in hospitals	Sierra Leone Ministry of Health

Abbreviations: VPD, vaccine-preventable disease; WHO, World Health Organization.

^a CDC, unpublished data.

conjunctivitis and that ill persons be restricted from attending school and work; hand washing was also advocated strongly (46).

On the island of Mauritius, with a population of 51,000 persons, a measles epidemic occurred in 2000 (47). A study confirmed that vaccine efficacy for 1 and 2 measles-mumps-rubella vaccine doses was 92% and 95%, respectively. The study findings indicate that even with highly effective vaccines, widespread outbreaks still can occur because of the high transmissibility of measles virus in crowded communities.

An investigation related to severe acute respiratory syndrome (SARS) conducted in 3 countries—Laos, Taiwan, and Thailand—revealed that only 5 (25%) hospitals studied had implemented WHO recommendations for private negative-pressure isolation rooms, minimal personal protective equipment for all staff entering the patient's room, and ineffective visitor policies during the early stage of the SARS epidemic (48). Another SARS-related study conducted in Taiwan also in 2003 evaluated the effectiveness of using a call hotline to identify persons at risk of SARS (49). Data collection from the hotline was not systematic, which limited how many callers were identified as being at risk of SARS. Of note, the 18 callers at high risk of SARS were not followed up for outcome to determine whether they met the WHO suspected or probable SARS case definition. The hotline was viewed as promising but required detailed documentation of the callers and had a lack of careful follow-up of persons identified at being at risk of SARS.

An examination of maternal mortality in Afghanistan determined that direct causes for maternal death included hemorrhage, obstructed labor, pregnancy-induced hypertension, cardiomyopathy, sepsis, obstetric embolism, and early pregnancy outcome (50). A strategy in response to the investigation developed by the Afghanistan Ministry of Health planned to provide effective antenatal care for all pregnant women by focusing on improved availability of skilled attendants at birth and the coverage, use, and quality of emergency obstetric care, particularly in rural areas.

The avian influenza epidemic in a Vietnam investigation indicated that H5N1 viruses were not readily transmitted from person to person (51, 52). In Bangladesh, a reported epidemic of encephalitis was confirmed, with the assistance of CDC EISOs, to be caused by the Nipah virus (53). The Epi-Aid investigation included a matched case-control study, environmental assessment, and laboratory testing. The groups that the investigation determined to be at risk were males less than 15 years of age, persons participating in tree climbing, and having contact with persons with Nipah virus. Investigators hypothesized that cases were likely infected from contact with fruit bats or their secretions. This emerging infectious disease was first documented in 1998 and 1999 in Malaysia and Singapore. A famine in Niger documented the coping strategies of families and observed that half of the deaths among children during this time were in part caused by malnutrition (54).

The results of a joint investigation by CDC, the Kenya Field Epidemiology and Laboratory Training Program (FELTP), Kenya's Ministry of Health, and the US Department of Agriculture demonstrated a substantial outbreak associated with aflatoxin-contaminated maize that occurred in eastern

Table 3. Selected International Epidemic-Assistance Investigations and Response Efforts Conducted by the Centers for Disease Control and Prevention's Epidemic Intelligence Service Officers, 1976–1985

Year	Location (Reference No.)	Category	Etiology	No. of Cases, Deaths, Case-Fatality and Attack Rates, if Available	Risk Factors	Public Health Actions	Collaborators
1977	Haiti (25)	Disaster	Drought	400 families selected for study to examine the impact of drought on water restriction	Diarrhea rate higher for children from homes with less than one 5-gallon (18.9-L) can of water/person per day	Concluded that the field epidemiologist can provide much needed information to planners concerned with providing adequate water supplies	Haiti Ministry of Health, Agency for International Development
1977	DRC (26)	Zoonotic	Ebola	318 cases; 280 deaths; 38 serologically confirmed survivors	Injections received at hospital, contact with infected patient	Recommendations included active national surveillance and disseminating information to medical personnel regarding surveillance	Institut de Medecine Tropicale (Belgium), Commissariat de la Sante Publique (Zaire/DRC), Institut Pasteur (France), Fonds Medical Tropical (Zaire/DRC), South African Institute of Medical Research
1979	South Sudan (27)	Zoonotic	Ebola	34 cases; 22 deaths (65% case-fatality rate)	5 families primarily affected; 21 females, 13 males; nosocomial acquired infection	Contact tracing for patients; laboratory testing to identify Ebola	WHO, Belgian Assistance Program Sleeping Sickness Project
1981	Venezuela (28)	Other infectious	Delta-agent superinfection with hepatitis B	149 Yucpa Indians; 34 died; 22 experienced chronic hepatitis	Ages 1–14 years	NA	Venezuela Ministry of Health, Pan American Health Organization
1982	Canada (29)	Injury	Pediatric deaths	Case-fatality rate elevated; 43.1 deaths/10,000 patient-days; 25/33 infant deaths occurred during 12:00–6:00 AM	Children with severe congenital heart disease; for 4 patients, investigation indicated possible intravenous overdose of digoxin	Recommendations that hospital strengthen control for dispensing medicines and implement a system for monitoring deaths by time and place within the hospital	Ontario Ministry of Health, Ontario Ministry of Labour, Laboratory Centre for Disease Control, Health and Welfare Canada
1983	Mexico (30)	Foodborne/enteric	Non-O1 cholera	Case-control study conducted; exact numbers unavailable	Compared with controls, more cases had eaten home-prepared gelatin during the 5 days before illness onset	NA	Mexican Ministry of Health, Pan American Health Organization
1983	Kenya (31)	Zoonotic	Rabies	Female American Peace Corps volunteer died 20 days after illness onset	Bitten by her puppy who had rabies	Recommendation for persons in developing countries to test their rabies antibody for seroconversion	US Peace Corps, Kenya Medical Research Institute, US Department of State, US Army Medical Research Unit
1985	Canada (32)	Foodborne/enteric	Botulism	1 confirmed and 20 suspected cases of botulism	Cases associated with eating at a Vancouver restaurant, August 27–September 11, 1985	Physicians told to be aware of the outbreak and to report suspect cases to local and state public health authorities	Department of National Health and Welfare, Ottawa, Canada, US Food and Drug Administration

1985	Sao Paulo, Brazil (33)	Other infectious	Brazilian purpuric fever	10 cases among children, 100% case-fatality rate	Antecedent purulent conjunctivitis more present among ill children than controls (2 case-control studies conducted); children aged 1–4 years at higher risk	Disease investigated: working case definition used for surveillance and to identify other cases	Pan American Health Organization, Sao Paulo Ministry of Health
1985	France (34)	Nosocomial	Aspergillus	7 cases	Epidemiologic study did not reveal the risk factors; study affected by laboratory contamination of other samples being tested for Aspergillus	Transplant unit closed to new admissions; testing undertaken; substantial numbers of additional cases above the norm led investigators to discover that laboratory testing was false	Service de Microbiologie Medicale, Institut Gustave Roussy, Direction de l'Action Sociale de l'Hygiene et de la Sante de la ville de Paris
1985	Haiti (35)	Foodborne/enteric	Shigellosis	339 cases of diarrheal illness among tourists and hotel employees	Case-control study; illness associated with being of North American origin and eating raw or rare hamburger	Ill kitchen staff no longer allowed to work in the kitchen	Pan American Health Organization, Government of Haiti

Abbreviations: CDC, Centers for Disease Control and Prevention; DRC, Democratic Republic of Congo; NA, information unavailable; WHO, World Health Organization.

and central Kenya in 2004 (55). This investigation included not only a descriptive study but also a case-control study and laboratory testing of maize that had been sold in the local market. Recommendations based on findings from the investigation included improving food safety standards in the country to avoid future outbreaks. The contaminated maize was believed to represent a continued exposure to aflatoxin because the homegrown maize implicated in the outbreak had been consumed or discarded. Finally, a rotavirus investigation revealed that if the rotavirus vaccine had been available in Nicaragua, severe rotavirus cases and deaths could have been avoided during the epidemic (56). In all of the highlighted Epi-Aids, CDC worked with its partners (e.g., ministries of health and WHO) to conduct the investigations.

DISCUSSION

In summary, this review of international Epi-Aids provides insight into the impact of CDC and its EISOs in the field of global health. The discipline of global health has been defined as transcending boundaries, reflecting the modern reality of globalization, encouraging collaboration, opposing all health threats, emphasizing homegrown solutions, and seeking equity for all (1). Effective responses to global health threats will require a trained public health workforce and effective surveillance systems to detect, prevent, and control the emergence and reemergence of infectious diseases and other disease threats. CDC's EISOs are a unique cadre of public health professionals who possess such skills, and CDC's EIS Program and the public health response efforts and activities presented in this review embody the desired attributes of global health (1, 57).

During its first 55 years, CDC EISOs conducted 462 international epidemiologic field investigations in 131 countries and 7 territories; these field investigations addressed a wide range of infectious and noninfectious health conditions, many preventable by public health measures (e.g., vaccines, clean water, vector control, and food security). Through Epi-Aids, EISOs have helped to detect, characterize, and control new and existing disease threats as well as assess the uptake and impact of such effective interventions as vaccinations to eradicate or prevent vaccine-preventable diseases.

Throughout the 55-year period, infectious diseases predominated the international Epi-Aids, but the number of responses to noncommunicable and chronic disease conditions increased substantially, consistent with the increasing prevalence of chronic disease conditions globally. Cardiovascular disease now accounts for approximately 30% of deaths in low- and middle-income countries each year and is accompanied by critical economic repercussions. Building public health infrastructure and health systems with the capacity to implement programs to address cardiovascular disease and other chronic disease risk will be required. These programs should consist of evidence-based prevention strategies, including behavior modification and health policy interventions developed for chronic diseases (e.g., heart disease, diabetes, and obesity) and unhealthy behaviors (e.g., smoking) (58).

This review had certain limitations. We did not have detailed information on all investigations because not all Epi-Aids

Table 4. Selected International Epidemic-Assistance Investigations and Response Efforts Conducted by the Centers for Disease Control and Prevention's Epidemic Intelligence Service Officers, 1986–1995

Year	Location (Reference No.)	Category	Etiology	No. of Cases, Deaths, Case-Fatality and Attack Rates, if Available	Risk Factors	Public Health Actions	Collaborators
1986	Somalia (36)	Other infectious	Hepatitis B	>2,000 cases of clinical hepatitis during study period; survey in refugee camp revealed 3% point prevalence of jaundice; attack rate: 8%	None mentioned	Survey conducted and disease identified; report indicated this as the first time hepatitis was described as a problem in a refugee camp	None mentioned
1986	Sierra Leone (37)	Toxin	Parathion poisoning	49 cases; 14 persons died	Case-control study with 21 cases and 22 controls; cases were more likely to have eaten bread 4 hours before becoming ill; flour contaminated with parathion; highest rate of illness for children aged 1–10 years	Case-control study identified risk factors; one bakery was locked and not used after the onset of illness, which helped investigators take samples because other bakeries had remained open	Sierra Leone Ministry of Health
1987	Nigeria (38)	VPD	Yellow fever	126 probable cases from treatment centers/hospital, case-fatality rate: 47%; highest attack rate among persons aged 20–29 years; mean mortality rate: 2.8% among villages	<i>Aedes africanus</i> mosquitoes appeared to be the transmission vector	Outbreak investigated; 9 villages surveyed; vector identified; mass vaccination recommended before the next rainy season and including the yellow fever vaccine in the Expanded Program on Immunizations	Nigerian Ministry of Health, World Health Organization
1987	Guyana (39)	Toxin	Thallium poisoning	No specimens identified by CDC to be positive for thallium	7 persons met the case definition by CDC and also 68 blood and urine specimens tested by the Guyanese health system indicated thallium poisoning	Government laboratory had indicated the specimens were positive, but further testing by CDC revealed no thallium; no evidence of an epidemic of thallium poisoning	Guyana Ministry of Health, Pan American Health Organization, Caribbean Epidemiology Center
1987	Senegal (40)	VPD	Poliomyelitis	618 cases; crude attack rate: 9.6/100,000 persons	Case-control study to estimate efficacy of 1–2 doses of inactivated polio vaccine combined with diphtheria, tetanus, and pertussis vaccine	22% of cases and 18% of controls had 1 dose; 12% of cases and 24% of controls had 2 doses; clinical efficacy of 1 dose was 5% and 2 doses was 76%	Senegal Ministry of Health, Task Force for Child Survival, Atlanta, Association Pour la Promotion de la Médecine Préventive, Senegal, France
1989	Hungary (41)	VPD	Measles	19,080 cases (December 1, 1988–May 14, 1989); 6 deaths (0.03% case-fatality rate)	75% of patients aged 16–22 years	Vaccine efficacy: 83%; control measures included mass revaccination of persons aged 16–22 years regardless of vaccination history	Hungary Ministry of Health and Social Affairs, National Institute of Hygiene, Hungary, WHO Regional office

1990	Mexico ^a	Reproductive health	Maternal mortality	Initially, data from Mexico indicated substantial increases in maternal deaths; CDC determined that the maternal mortality ratio of 43.1/100,000 livebirths in 1989 was only 3% higher than 1988 data	Protocols for diagnosing and managing conditions not followed in each health facility; limited or no anesthesia, inconsistent laboratory and blood banking facilities, emergency land and air transportation, and necessary pharmaceuticals; preeclampsia a possible problem	Recommended a study to identify the prevalence of preeclampsia/eclampsia	Bureau of Family Planning and Reproductive Health, Mexican Institute of Social Security, Pan American Health Organization
1992	Sierra Leone ^a	Cancer	Cervical dysplasia	3 squamous cell cervical cancers in 1,403 women provided with Papanicolaou smears; other 6 cancers detected included 3 adenocarcinoma, 1 rectal squamous cell carcinoma, 1 sarcoma, and 1 unknown-origin squamous cell; 12% positive for gonorrhoea	Cancers not previously discovered because of limited cancer screening programs	Recommendations included screening and treatment for gonorrhoea and chlamydia	Sierra Leone Ministry of Health
1995	DRC (42)	Zoonotic	Ebola	316 cases	Matched case-control study (44 cases, 1:3 match); risk factors: admission to health care center for illness during 3 weeks before onset of Ebola, visiting a person with fever and bleeding	Before Ebola determined to be the cause of outbreak, no precautions taken when family members cared for their ill relatives; after Ebola was identified, precautions taken	Institut Supérieur du Kikwit, Mosango Hospital, DRC

Abbreviations: CDC, Centers for Disease Control and Prevention; DRC, Democratic Republic of Congo; VPD, vaccine-preventable disease; WHO, World Health Organization.
^a CDC, unpublished data.

resulted in published papers. The categories used to classify the etiology of the investigations were mutually exclusive; however, investigations might have fallen into more than one category used. In addition, we might have underestimated the number of international investigations conducted by EISOs because field investigations and requests for technical assistance can be processed through means other than the Epi-Aid mechanism used for acute responses. Although we might not have captured all of the international activities performed by EISOs during the 60-year period, this review clearly demonstrates the depth and breadth of their response efforts globally.

Through its field investigations, the EIS Program has served as an example to the global health community by showing how epidemiologic principles can be applied to address epidemic and nonepidemic conditions. Since 1980, approximately 40 countries, with support from CDC, have established Field Epidemiology Training Programs (FETPs) and FELTPs (59); all were modeled on CDC's EIS Program (60, 61). Figure 1 indicates that FETPs have developed in each region in which Epi-Aids have been conducted. FETPs/FELTPs help to improve global public health capacity by developing a trained cadre of public health professionals in low- and medium-income countries. Similar to the EIS Program, FETPs and FELTPs provide training in core public health competencies, including epidemiology, biostatistics, public health surveillance, laboratory practice, communication, computer technology, management and leadership, and prevention effectiveness (62–64). CDC continues to provide financial support and technical assistance to 18 programs in 34 countries (includes regional programs) with FETPs and FELTPs (59). Six other countries (Zimbabwe, Jordan, Saudi Arabia, Thailand, Brazil, and Egypt) were once supported by CDC but now have self-sustaining programs managed by the host country (59). FETPs also exist in developed countries (e.g., Australia, Canada, Germany, and Spain).

Certain challenges lie ahead in the effort to promote and ensure global health and health equity, including globalization, climate change, limited human resources, and lack of established and functioning health and public health systems. Multinational, multidisciplinary collaborations between private, public (governmental and nongovernmental) organizations will be required to strengthen health systems effectively, increase adoption of proven interventions, monitor disease threats and trends, and make efficient use of available resources (57). Developing a public health workforce trained in the core public health competencies is critical to the success of global health efforts (58).

Certain areas of the world are likely to remain hot spots for emerging infectious disease threats (7) (e.g., drug resistance and vectorborne infections). This review of the first 60 years of Epi-Aids demonstrates the impact that an adequately trained public health workforce can have on global health. Additionally, it confirms the adaptability of the EIS Program and the methods it uses to address emerging and changing disease trends and illustrates the rich contributions that CDC EISOs have made to global health. CDC's disease detectives, working in partnership with WHO, ministries of health, and other organizations, will undoubtedly continue to play a critical role in global health and in responding to future global disease threats.

Table 5. Selected International Epidemic-Assistance Investigations and Response Efforts Conducted by the Centers for Disease Control and Prevention's Epidemic Intelligence Service Officers, 1996–2005

Year	Location (Reference No.)	Category	Etiology	No. of Cases, Deaths, Case-Fatality and Attack Rates, if Available	Risk Factors	Public Health Actions	Collaborators
1996	Haiti (43)	Toxin	Diethylene glycol	86 children; 85% aged ≤ 5 years; preliminary investigation suggests only 1 survivor	Determined that 79% of children consumed 1 of 2 locally manufactured acetaminophen syrup preparations contaminated with diethylene glycol	Government issued alert to parents to not administer the syrup products to their children and prohibited sale of the items; public awareness campaign initiated; after recall and campaign, new cases declined	Pan American Health Organization, Caribbean Epidemiology Center, Haiti Ministry of Health, Port-au-Prince University General hospital, US Food and Drug Administration
1998	Tanzania (44)	Reproductive health	Refugee surveillance	Of 138 deaths September 1, 1997–January 31, 1998, 16% maternal and neonatal deaths; 538 women completed survey; fetal death rate: 39/1,000 births; neonatal mortality rate: 23.2/1,000 births, and low birth weight was 22.6% among all livebirths	Having a first or second pregnancy, prior high socioeconomic status, and ≥ 3 episodes of malaria during pregnancy	Findings highlight importance of reproductive health in refugee settings	International Rescue Committee
1998	Jamaica (45)	Injury	Surveillance, interpersonal violence	In 1997, homicide rate was 45/100,000 persons in Jamaica compared with 7.9/100,000 persons in the United States	Lacked data for planning interventions and resource allocation; established the Violence-Related Injury Surveillance System using patient registration data from Kingston's public hospital	Conducted an evaluation of the surveillance system; system determined to be flexible, acceptable to clinical staff and ministry of health officials; was moderately sensitive, detected 62%–69% of violent records identified from clinical records and a patient survey; positive predictive value: 86%	Jamaica Ministry of Health, Pan American Health Organization, University of the West Indies
1999	US Virgin Islands (46)	Other infectious	Conjunctivitis	1,051 cases after Hurricane Georges, based on 3 health facilities; survey of 600 households reported 10% of households had at least 1 case of conjunctivitis	Laboratory testing indicated agent as coxsackievirus A24 variant	Disseminating public health information by press release, radio interviews, and distribution of fact sheets by physician's offices, public health clinics, and schools	US Virgin Islands Department of Health
2003	Marshall Islands (47)	VPD	Measles	> 800 cases; 3 deaths; 41% of cases previously vaccinated; household secondary rate used to evaluate vaccine efficacy; secondary cases occurred in 24/72 households (33.3%)	Risk factors included large household sizes, high overall population density, older siblings, and adults and infected infants	$> 35,000$ persons vaccinated	Republic of the Marshall Islands Ministry of Health

2003	Taiwan, Laos, Thailand (48)	Respiratory	SARS	355 probable cases reported in the 3 countries (November 2002–July 2003); control practices were investigated during early stage of the epidemic	Mobile SARS teams organized to investigate cases of SARS and assess hospital infection control practices (retrospective study)	Mobile teams investigated 22 reports of SARS in 20 hospitals; hospitals did not consistently have written policies for SARS infection control practices, triage of patients with possible SARS, and visitation requirements to rooms of patients with possible SARS; use of personal protective equipment varied among the hospitals	Thailand Ministry of Health, Taiwan Center for Disease Control, WHO, International Emerging Infections Program, Thailand, Lao People's Democratic Republic, International Field Epidemiology Training Program, Thailand, Emory University
2003	Taiwan (49)	Respiratory	SARS	Population-wide fever hotline received 11,228 calls; 28% of callers advised to seek further medical evaluation; 21% advised to remain at their residence and monitor symptoms (June 1–10, 2003)	Taipei fever hotline: 1,966 calls, body temperature recorded for 51% of calls; temperature of $\geq 38^{\circ}\text{C}$ recorded in 37% of calls; 18 (0.9%) at high risk of SARS	Innovative interventions included population-wide body temperature and fever hotline, increased public awareness about SARS, improved early detection of fever, and provision of medical triage; from the population-based survey, 71% knew about the fever hotline	Taiwan National Bureau for Health Insurance
2003	Afghanistan (50)	Reproductive health	Maternal mortality	Retrospective cohort study; 154 of 357 deaths were among women (reproductive age); population: 90,816 persons; extremely high maternal mortality rates	Risk factors first-level barrier, being illiterate, living in rural areas; other problems included no attendant at birth	Afghan Ministry of Health developed a comprehensive national reproductive health strategy for lowering maternal mortality, guided by this study's preliminary findings and other research	UNICEF
2004	Vietnam (51)	Respiratory	Avian influenza, H5N1	Matched case-control study; 28 cases with confirmed H5N1 infection during 2004 and 106 age-, sex-, and location-matched controls	Risk factors included preparing sick or dead poultry for consumption before illness onset, having sick or dead poultry in the household before illness onset, and lack of an indoor water source	None reported	WHO, National Institute of Hygiene and Epidemiology, Vietnam; Vietnam Ministry of Health
2004	Vietnam (52)	Respiratory	Avian influenza, H5N1	Cross-sectional seroprevalence survey among hospital employees exposed to 4 confirmed and 1 probable H5N1 cases or their clinical specimens; 83/87 (95%) completed questionnaire and provided serum sample	95% reported exposure to H5N1 cases; 59 (72%) reported symptoms, and 2 (2.4%) fulfilled the definition for a possible H5N1 secondary case	Persons providing care for H5N1 patients should continue to take measures to protect themselves	WHO International Avian influenza Investigation Team

Table continues

Table 5. Continued

Year	Location (Reference No.)	Category	Etiology	No. of Cases, Deaths, Case-Fatality and Attack Rates, if Available	Risk Factors	Public Health Actions	Collaborators
2004	Bangladesh (53)	Zoonotic	Nipah virus	12 patients with Nipah virus encephalitis identified in January 2004; 10 deaths; case-control study to identify risk factors	Males aged <15 years affected; risk factors included climbing trees and contact with another patient with Nipah virus encephalitis	Recommend personal protective equipment when contacting patients; avoiding contact with fruit bats and their secretions/excretions; encourage persons to wash or peel fruit in addition to washing their hands before preparing meals or consuming fruit	International Centre for Diarrheal Diseases Research, WHO, Institute of Epidemiology Disease Control and Research, Bangladesh; Bangladesh Ministry of Health
2005	Niger (54)	Nutrition	Famine/nutrition	2-stage cluster survey; 4,003 households surveyed; crude mortality rate: 0.4/10,000 persons/day; mortality rate for ages <5 years: 1.7 deaths/10,000 persons per day	Deaths of children aged <5 years attributed to diarrhea, acute respiratory illness, and meningitis; of the children who died, caregivers thought 51.6% were malnourished	Survival techniques used by families to cope with food crisis; further research needed	Office of US Foreign Disaster Assistance, UNICEF, United Nations Development Program
2005	Kenya (55)	Toxin	Aflatoxicosis	317 cases; 125 deaths; conducted cross-sectional survey to assess extent of contamination and evaluate contamination of maize with outbreak	Aflatoxin-contaminated, homegrown maize identified by laboratory testing; contamination located throughout the local markets; previous case-control study did not associate market maize with aflatoxicosis in the outbreak	Recommended establishment of long-term interventions (e.g., comprehensive food safety program) and target both market vendors and local farmers to prevent or minimize future aflatoxicosis outbreaks and reduce long-term exposure to aflatoxins	US Department of Agriculture, Kenya National Public Health Laboratory, Kenya Field Epidemiology and Laboratory Training Program, Kenya Ministry of Health
2005	Nicaragua (56)	Foodborne/enteric	Rotavirus	47,470 clinic visits related to diarrhea between epidemiology weeks 6–18 in 2005; 41 deaths during weeks 1–9 in early 2005	Deaths associated with incorrect treatment of severe disease by traditional healers, malnutrition, and lack of indoor plumbing	Despite not knowing the etiology of the outbreak, recommended boiling water and improving hygiene, both of which are ineffective for interrupting transmission of rotavirus	Minsiterio de Salud, Nicaragua; Pan American Health Organization

Abbreviations: SARS, severe acute respiratory syndrome; VPD, vaccine-preventable disease; WHO, World Health Organization.

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