Unexplained Deaths and Critical Illnesses of Suspected Infectious Cause, Taiwan, 2000–2005

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We report 5 years’ surveillance data from the Taiwan Centers for Disease Control on unexplained deaths and critical illnesses suspected of being caused by infection. A total of 130 cases were reported; the incidence rate was 0.12 per 100,000 person-years; and infectious causes were identified for 81 cases (62%).

In 2003, the outbreak of severe acute respiratory syndrome (SARS) demonstrated that the world has become a global village in which human risk for exposure to different kinds of biological hazards is increased through frequent travel and commercial activities (1–5). Historically, emerging diseases occur abruptly in outbreaks of unknown cause. Although various efforts have been proposed and conducted to analyze secondary data periodically (6–9), they generally provide information for the less urgent decision making in health policy and may not be in time for infectious disease control. Thus, a task force is needed to provide timely and accurate diagnosis for early control of any potential epidemic infection, especially in a newly developed country like Taiwan, where the healthcare resources may not be evenly distributed and autopsy for diagnosis is not widely accepted culturally.

In 2000, the Taiwan Centers for Disease Control collaborated with academic institutions, medical examiners, local health authorities, and experts from different fields to establish a nationwide surveillance center for outbreak and unexplained death investigation due to unknown infectious causes (COUNEX) (Figure). This effort was to build

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Taiwan’s capacity for detecting and responding to uncommon and unrecognized pathogens, which was conceptually the same as that of the study of Hajjeh et al. (10). We defined the surveillance case-patient as a previously healthy resident who died or was admitted to a hospital with a life-threatening illness possibly caused by infection of unidentified etiology. Usually the death occurred within 3 days of the patient’s admission. Patients were excluded if the cause of death was noninfectious. A life-threatening illness was defined as any illness requiring admission to an intensive care unit or reported as being critical. An infectious disease is generally suspected if the case-patient has ≥1 of the characteristics such as fever, leukocytosis, histopathologic evidence of an acute infectious process or more specific symptom patterns, or infection precipitating adult respiratory distress syndrome, renal failure, or sepsis.

A total of 130 cases were reported during 2000–2005, for an annual average rate of 0.12 cases per 100,000 persons. The annual incidence rates varied by year and among 4 branches of Taiwan Centers for Disease Control (Table). The highest rate was in the eastern branch, where surveillance was conducted in a well-defined population of ≈596,119 persons. Ninety-five (73%) of the case-patients died. For 47 (49%) of those who died, an autopsy was performed, a rate much higher than the national autopsy rate of <11% (12). The mean age of case-patients was 33.8 years. The incidence rates varied by age group; it was highest in those 85–89 years of age, followed by those <1–4 years, and then 65–69 years, with 0.48, 0.30, and 0.23 per 100,000 person-years, respectively. Men had a higher incidence rate than women (0.16 vs. 0.10 per 100,000 person-years).

Approximately 10% of 130 case-patients and 16% of 81 patients with cases of infection had a history of animal contact; 9% of 130 case-patients and 10% of infection case-patients had a history of travel outside Taiwan within the previous 3 months. The most common initial syndromes were acute respiratory (59%), acute neurologic (22%), and acute diarrhea-related syndrome (13%). Initially, 8 patients had acute heart-related syndrome, and 11 had acute kidney-related syndrome; both of these syndromes had a 100% case-fatality rate.

The online Appendix Table (www.cdc.gov/EID/content/14/10/1653-appT.htm) lists all the infectious pathogens and noninfectious causes identified among 95 fatal cases. One third were related to bacterial infection and one fourth to viral infection; 22 remained unclassified. The proportion of explained cases was lower among patients who survived (74%) than that among patients who died (77%). The proportion of explained cases was also higher for patients who underwent autopsy (83%) than for non-autopsied patients (71%) but not statistically significantly so. Explained cases were similar to unexplained cases in terms of patient age and interval between dates of disease onset and report (median 7.2 and 6.8 days, for explained and unexplained cases, respectively). Although the overall case-fatality rate was 73%, patients were more likely to die if they had multiple organ system involvement.

We have established the infrastructure needed to detect critical and fatal cases of unknown causes; such a surveillance system is essential to identify early potential infectious threats in a period of globalization and increasing travel between countries. The contributions of our surveillance system are demonstrated by early detection and control of at least 3 outbreaks of serious viral diseases: hantavirus pulmonary syndrome, rabies, and SARS.

In 2001, a family cluster occurred in Huanlian city; dyspnea, cough, leukopenia, and pulmonary edema developed in both parents, who died. Their 16-year-old daughter was also ill, but she survived. COUNEX quickly intervened, and hantavirus pulmonary syndrome was confirmed by positive serologic test results, which led to an early control of local rodents and spread of the disease.

Taiwan has been free of human and animal rabies since 1961. However in 2002, a 45-year-old woman from mainland People’s Republic of China was admitted to a hospital because of difficulty in swallowing, fear of wind (aerophobia), and numbness of the arms. Her condition was reported to the surveillance system as suspected rabies. Our

Table. Incidence rate of case-patients detected by surveillance and proportions of deaths, possible infectious causes, and autopsy.

| Category                                      | Total | Northern | Middle | Southern | Eastern |
|-----------------------------------------------|-------|----------|--------|----------|---------|
| Incidence/100,000 person-years†               | 0.12  | 0.09     | 0.16   | 0.09     | 0.64    |
| Proportion of deaths among all case-patients, % | 73    | 75       | 64     | 79       | 83      |
| Proportion of infectious causes identified, %  | 65    | 63       | 68     | 68       | 39      |
| Viral agents among infection cases, %         | 42    | 56       | 30     | 37       | 57      |
| Bacterial agents among infection cases, %     | 46    | 36       | 57     | 47       | 36      |
| *Rickettsia* spp. among infection cases, %    | 4     | 4        | 3      | 0        | 14      |
| Proportion of causes remaining unknown, %     | 23    | 25       | 16     | 29       | 25      |
| Autopsy rate among patients who died, %      | 49    | 53       | 43     | 41       | 67      |

†Denominators for the population under surveillance, obtained from the 2002 intercensuses (11) and approximately the midpoint of this study period, included all people in the age groups under surveillance at the various sites and were used to calculate the incidence rate.

*TCDC, Taiwan Centers for Disease Control.
personnel quickly confirmed the diagnosis by reverse transcription–PCR and DNA sequence analysis of the samples from cerebrospinal fluid, saliva, and trachea while the patient was still alive (13). The patient had been bitten by a domesticated dog in mainland China 2 months earlier.

During the SARS outbreak in 2003, the surveillance system received reports of 6 cases; autopsies were performed on 3 patients. As a result, the correlation between infection control at remote regions with limited resources. Most physicians in the rural eastern part of the country have less access to consultation and referral to other specialties in medical centers and teaching hospitals. Thus, they rely more on this kind of surveillance system for early detection of potential infectious threats. This was especially important for acute unexpected deaths, as was demonstrated by a higher incidence and autopsy rates in eastern Taiwan.

Throughout this project, we have increased the autopsy rate and established a population-based bank of specimens for future research. This collection could provide a better opportunity for corroboration or refutation of any previous diagnosis of infectious disease. This improved decision making in regard to control of infections was demonstrated in November 2003, when influenza virus (H5N1) was diagnosed in a patient who had a previous misdiagnosis of SARS (15).

Because emerging and reemerging infectious diseases may quickly travel between different countries, the system is becoming more crucial for early detection and control of potential health hazards. The system depends on close cooperation among different disciplines and staff from different agencies. Thus, education, empowerment, and good feedback incentives should be continually offered to keep this system sustainable.

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