THE ROLE OF NATIONWIDE NOSOCOMIAL INFECTION SURVEILLANCE IN DETECTING EPIDEMIC BACTEREMIA DUE TO CONTAMINATED INTRAVENOUS FLUIDS

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Since January, 1970, the Center for Disease Control (CDC) has coordinated surveillance of nosocomial infections in a group of voluntarily cooperating hospitals in the United States. In 1970, this surveillance system failed to realize one of its major goals: detection of a nationwide epidemic of septicemia caused by contaminated intravenous products. However, retrospective review of infections reported to CDC revealed that the data received were sufficient for the outbreak to have been recognized. Beginning in July, 1970, one month after the contaminated products were first distributed and five months before the outbreak was actually detected, CDC data showed a persistent increase in the incidence of *Enterobacter* and *Erwinia* (presently designated *Enterobacter agglomerans*) bacteremia. Furthermore, monthly rates of cases of bacteremia caused by these organisms were higher in hospitals using the contaminated intravenous products than for hospitals not using them. Failure to detect this outbreak at the time of its occurrence was due to delays in data processing and insufficiently sophisticated data analysis. Based on this experience, CDC has modified the surveillance system to aid recognition of future outbreaks.

In January, 1970, the National Nosocomial Infections Study (NNIS) was initiated to analyze nosocomial infection surveil-

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Abbreviations: CDC, Center for Disease Control; IV, Intravenous; NNIS, National Nosocomial Infections Study.

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erans. In 1970, it was generally designated Erwinia, and we have elected to use this term.)

**Methods**

In 1969, invitations to participate in NNIS were sent to the directors of infection control programs in several hundred United States hospitals that were known to have active surveillance and control programs (2). Between January, 1970, and July, 1971, the period of this review, 84 hospitals in 31 states joined NNIS. Although study institutions were not selected to be statistically representative of United States hospitals, a broad spectrum of hospitals participated; member hospitals ranged in size from fewer than 40 to greater than 1500 beds and included 57 community, 14 university, eight municipal, and five federal institutions.

Participating hospitals agreed to conduct prospective clinical surveillance of hospitalized patients following guidelines established by CDC (3). We did not evaluate surveillance efficiency during the study period. Surveillance personnel used standard CDC definitions of nosocomial infections (3). A case of bacteremia was designated as secondary or primary: a secondary case of bacteremia was defined as bacteremia resulting from a preceding infection with the same organism at another site; a primary case was defined as bacteremia in which no underlying infection could be documented. Organisms were reported only if they were felt to be responsible for clinical disease; reports of colonization were not accepted. Microbiology laboratories in participating institutions were encouraged to use standard nomenclature and, at a minimum, to identify isolates to the genus level.

A case abstract of each nosocomial infection was entered on a standard line-listing form supplied by CDC. Data reported included dates of admission and onset of infection, site of infection, and responsible pathogens. Accumulated line-listings were mailed to CDC monthly. In addition, the number of patients discharged from major clinical services each month was reported and served as a basis for calculating nosocomial infection rates. At CDC, line-listings were reviewed by physician-epidemiologists, coded, and verified. Coded data were transferred to magnetic tape for computer analysis.

To determine whether NNIS data reflected the epidemic of septicemia caused by contaminated IV fluids, we reviewed all nosocomial infection reports submitted by participants from January, 1970, to July, 1971. Cases of bacteremia due to Enterobacter were recalled from computer tape files. Because Erwinia had been coded as "other gram-negative rod," we manually reviewed line-listings to find cases of bacteremia caused by this organism.

Since participation in NNIS is voluntary, membership was initially in flux. Hospitals joined and left the study throughout the period from January, 1970, to July, 1971; others reported irregularly. Therefore, we have reviewed data from a subgroup of regularly reporting hospitals as well as from all participating institutions. Hospitals were included in the regularly reporting group if they submitted data for at least 13 of the 19 months in the study period, including either February or March, 1970, and either April or May, 1971. These criteria were structured to include at least one month of reporting both just before and after the recall of contaminated IV fluids on March 21.

IV fluids used by participants were determined in the fall of 1971 by questionnaire survey. Regularly reporting hospitals were divided into three groups: hospitals that used only IV fluids from Manufacturer A during the study period prior to product recall (Group A); hospitals that used only IV fluids from other manufacturers in that period (Group O); and hospitals that used a mixture of fluids supplied by Manufacturer A and other manufacturers in the period (Group M).
RESULTS

Based on previous CDC investigations, we consider the epidemic period to be from June, 1970, when contaminated IV fluids were apparently first distributed to hospitals, to March 21, 1971, when the contaminated fluids were recalled (1). Figure 1 shows the incidence of cases of Enterobacter and Erwinia primary bacteremia reported by all participating hospitals in the study period. Twenty-eight cases of bacteremia (0.6 per 10,000 discharged patients) were noted in the five months before the epidemic, and 28 (0.9 per 10,000) were reported in the four months following the epidemic. In the epidemic period, 169 cases of Enterobacter and Erwinia bacteremia (1.9 per 10,000) were reported, a 2.5-fold greater incidence than reported in the combined pre- and post-epidemic periods. The peak incidence of cases of Enterobacter and Erwinia bacteremia occurred in March, 1971, the month of recall, when 29 cases (5.3 per 10,000) were noted. Analysis of data from the 49 regularly reporting hospitals revealed similar rates of Enterobacter and Erwinia bacteremia during the study period.

The epidemic was not apparent when the incidence of all cases of primary bacteremia in the study period was examined (figure 2). Only 12.4 per cent of all cases of primary bacteremia noted during the epidemic were attributed to Enterobacter or Erwinia; therefore, the substantial increase in bacteremia caused by these organisms was obscured by the large number of cases of
bacteremia caused by pathogens not involved in the outbreak. Similarly, there was no significant change in overall nosocomial infection rates.

Of the 49 regularly reporting hospitals, 18 were in Group A, 19 in Group O, and 12 in Group M. Because of the varying product usage in Group M institutions, these hospitals have not been included in subsequent analyses. The increased incidence of Enterobacter and Erwinia bacteremia during the epidemic period was observed only in Group A institutions (figure 3). Of the Group A hospitals, 10 reported one or more
cases of Enterobacter or Erwinia bacteremia in the epidemic period. In contrast, only two of 19 group O hospitals reported such cases ($p = 0.005$, Fisher's Exact Test, two-tailed test). Erwinia was not reported as a cause of primary bacteremia until February, 1971. This late emergence of Erwinia was also seen in independent CDC investigations (1).

The increased rate of Enterobacter and Erwinia primary bacteremia in Group A hospitals was not associated with an increased nosocomial infection rate with these strains at other sites. In both the baseline and epidemic periods, Group A hospitals generally had a slightly higher monthly rate of Enterobacter and Erwinia infections than did Group O hospitals at sites other than blood, but this difference became less impressive during the time when the rate of bacteremia cases was sharply increasing.

The excess number of cases of Enterobacter and Erwinia primary bacteremia in Group A hospitals was not a reflection of a general increase in cases of bacteremia, per se, in these hospitals since Group O hospitals generally had higher rates of bacteremia caused by organisms unrelated to the outbreak than did Group A hospitals.

It is possible that the widespread publicity this outbreak received may have stimulated NNIS participants to identify and report cases of Enterobacter and Erwinia bacteremia. However, our experience in the five Group A hospitals which were among the 25 institutions independently investigated by CDC epidemiologists (1) does not suggest that there was a reporting artifact. One of these five hospitals learned in late February, 1971, that a nationwide epidemic of bacteremia was suspected, but the other four hospitals learned of the outbreak only after the first public announcement on March 13, 1971. Thus, prior knowledge of the existence of the nationwide problem could have influenced the collection and reporting of data prior to March, 1971, in only one of these five institutions. In that hospital the first cluster of cases was reported in July, 1970, and each month thereafter the hospital reported cases of Enterobacter bacteremia. Furthermore, in all participating hospitals infections were sought prospectively by surveillance personnel and were generally reported within two to 6 weeks of their onset. Thus, it is highly unlikely that infections occurring before February, 1971, were reported because of the publicity surrounding the outbreak.

**DISCUSSION**

Although contaminated intravenous fluids were first distributed in June, 1970, recognition of the resulting nationwide epidemic of Enterobacter and Erwinia bacteremia came slowly. In December, 1970, the initial report of a hospital outbreak of Enterobacter bacteremia reached CDC. Intravenous therapy was epidemiologically linked to cases of bacteremia in that hospital, but the source of contamination was not discovered. Only in January, 1971, after two additional hospitals had requested CDC's assistance in evaluating similar outbreaks, was contamination of Manufacturer A's IV fluids suspected.

Although NNIS played no part in the recognition of the epidemic, our review indicates that NNIS data did contain dramatic evidence of the outbreak. Analysis of data from all reporting hospitals clearly showed an increase in the incidence of Enterobacter bacteremia beginning in July, 1970, more than four months before the first epidemic was reported to CDC. Moreover, NNIS data revealed that the increased incidence of Enterobacter and Erwinia bacteremia was confined to hospitals using IV fluids from Manufacturer A. Thus, the failure of NNIS to fulfill one of its major goals, the detection of an outbreak caused by widely-distributed contaminated medical products, was not due to limitations in the data collected.

In order to improve the ability of NNIS to recognize future outbreaks, we have eval-
uated the possible reasons why, in spite of adequate data, an epidemic of considerable magnitude was not detected at the time of its occurrence. Two aspects of NNIS data management seem to have been responsible: a delay in data retrieval and analysis and a failure to perform data analyses of sufficient sophistication.

At the time of the outbreak, surveillance data were reported only monthly and were accepted up to 30 days after the end of a reporting month. Thus, an infection noted at the beginning of one month often was not reported to CDC until the end of the following month. In addition, there were considerable delays in coding, checking, and entering data into the computer file. As a result, infections were not available for analysis until approximately three months after they had been recognized by participating hospitals. Based on this experience, we have completely revised data processing. Hospital surveillance personnel now dictate infection reports directly into a recorder that can be accessed by telephone from CDC at any time. We request personnel to report new cases of infection at least several times a week. Trained clerk-coders call the dictating stations at participating hospitals twice each week and enter reports immediately into a computer file. Newly-entered reports are checked nightly by computer to be sure that valid codes have been selected and that criteria for data consistency have been met. Infection reports are then available for retrieval and analysis. Thus, it is possible for an infection to be reported to CDC and analyzed within several days of its recognition.

Delays in data processing do not fully explain the failure of NNIS to detect the outbreak. Although rates of all nosocomial infections, primary bacteremia, and Enterobacter infection were calculated, these rates were not significantly altered by the epidemic. To detect the outbreak, analysis of Enterobacter bacteremia rates would have been necessary, but such analyses were not performed at that time. Subsequently, routine analysis of temporal changes in pathogen rates, by site of infection, has been initiated.

Although our changes in data management and analysis would have allowed recognition of this outbreak, it is likely that an epidemic of more commonly reported infections, such as *Escherichia coli* urinary tract infections, would be missed unless the problem were of great magnitude. Detection would generally be facilitated if hospitals characterized strains of bacteria more precisely in reports to NNIS. For example, epidemic strains usually have consistent—and often unique—antimicrobial susceptibility patterns (1), so NNIS hospitals are now requested to include these data with infection reports. Other epidemiologic markers such as phage types, serotypes, and biotypes would be useful but cannot be determined by most institutions on a routine basis. However, many hospitals do perform an expanded standardized series of biochemical tests (for example, the API 20E identification system for gram-negative bacteria) which may prove to be epidemiologically valuable.

As we have expanded the number of coded pathogen-site combinations because of the increasing importance of previously obscure organisms, it has become impractical for CDC epidemiologists to manually review data for significant changes in infection rates. Thus, we are developing and evaluating computer-based analytical systems that will identify potential problems. One simple, but useful, program which has recently been introduced flags clusters of two or more cases of bacteremia, meningitis, or neonatal infection caused by the same microbial species in the same hospital in a single month. Had this program been operational in 1970, clusters of Enterobacter bacteremia would have been flagged beginning in July, 1970. To identify other potential problems, computer-assisted programs are being refined that compare cur-
rent infection rates for each site-pathogen combination with comparable rates observed in prior, selected baseline periods.

In summary, this retrospective analysis demonstrates the potential usefulness of NNIS in identifying nationwide outbreaks of nosocomial infection caused by widely-distributed medical products contaminated in low frequencies. However, prompt and appropriate analysis of surveillance data is mandatory if this potential is to be fully realized.

REFERENCES

