HOSPITAL INFECTIONS

Second Edition

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24 INCIDENCE AND NATURE OF ENDEMIC AND EPIDEMIC NOSOCOMIAL INFECTIONS

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One of the central concepts of modern infection control is that one must have a thorough knowledge of the occurrence of infection problems to control them most effectively. Although there is no substitute for timely information on the current infection situation in one's own hospital from ongoing surveillance, a valuable perspective can be gained from studying the incidence and nature of nosocomial infections in the nation as a whole and in hospitals similar to one's own. Such information not only points out national infection problems and trends that are likely to be mirrored in local situations, but also alerts infection control personnel to potentially useful concepts and techniques that can be adopted and to potential pitfalls that can be avoided.

The problem of nosocomial infections is usually discussed in two different contexts: epidemics of infections and endemic occurrences. Epidemics have been very important in the development of the modern approach to hospital infection control by presenting emergency situations that have focused concern and effort on the problem, consequently epidemics of infections have received much attention from infection control personnel and have been the focus of much of the scientific literature on the subject. Since, however, only about 2 to 4 percent of nosocomial infections occur as part of epidemics [25,54], descriptions of nosocomial infections reflect almost entirely the nature of endemic infections and give little insight into epidemic problems. This does not mean that epidemics are not important, for when they are recognized they often provoke crises that call for intensive investigation and decisive control measures. It does mean, however, that an adequate description of nosocomial infections must deal with endemic and epidemic infections separately.

The purpose of this chapter is, first, to describe the nationwide incidence and distribution of endemic nosocomial infections in U.S. hospitals from several studies recently completed; second, to characterize the nature of epidemics and trends in their occurrence, including the troublesome problem of pseudoepidemics; and third, to discuss methods of estimating the adverse consequences of these problems in terms of prolongation of hospital stay, extra costs, and death.

ENDEMIC NOSOCOMIAL INFECTIONS

Overall Infection Rates

The effort to estimate rates of nosocomial infections began with surveillance studies of the prevalence [31] and incidence [11,49] of infections in individual hospitals. The first effort to estimate the magnitude of the problem on a wider scale was made by the Centers for Disease Control (CDC) in a collaborative study of eight community hospitals known as the Comprehensive Hospital Infections Project (CHIP) [11]. Performed in the late 1960s and early 1970s, this contract-supported study involved very intensive surveillance efforts to detect both nosocomial and community-acquired infections. Validation studies were performed by CDC epidemiologists who visited the hospitals on a regular basis to estimate the percentage of infections detected by the hospitals' surveillance personnel. Based on an overall rate of 3.2 infected patients per 100 discharges and an adjustment for the percentage of true infections detected, it was estimated that in 1970 approximately 5 percent of patients in community hospitals developed one or more nosocomial infections (the "infection percentage"—see Chapter 4) [4], an estimate that was subsequently widely held to be the national rate of nosocomial infection.

In 1970 the CDC studies were extended to a group of approximately 80 volunteer hospitals of diverse sizes and types and called the National Nosocomial Infections Study (NNIS). Although the same general surveillance methods were used, the quality-control techniques used in CHIP were not feasible in the NNIS, however, the advantages of the NNIS were that the group contained a substantial number of hospitals representing the major types of hospitals in the United States, and the system could continue reporting data over a number of years. The overall infection rates reported from the NNIS hospitals, unadjusted for completeness of ascertainment, have remained relatively stable at about 3.2 infections per 100 discharges (the "infection ratio"—see Chapter 4) from 1970 through 1982, although some interesting secular trends have been observed and are described in this section and in Secular Trends below. Assuming that the completeness of ascertainment of infections in the NNIS was similar to that in CHIP, we could derive an estimate of the nationwide infection rate in the same range as the 5 percent figure estimated from CHIP. Although the design of these two surveillance studies limited the precision of the estimates, they gave the first consistent estimates of the order of magnitude of the problem.

One of the objectives of the Study on the Efficacy of Nosocomial Infection Control (SENIC) Project (see Chapter 3) was to derive a more precise estimate of the nationwide nosocomial infection rate from a statistical sample of U.S. hospitals [22]. On the basis of direct estimates made in 338 randomly selected general medical and surgical hospitals with 50 beds or more and statistically derived extrapolations to groups of small and specialty hospitals, the report from the SENIC Project estimated that at least 2.1 million nosocomial infections occurred among the 37.7 million admissions to the 6449 acute-care U.S. hospitals in a 12-month period in 1975–76 [17]. Thus nationwide there were approximately 5.7 nosocomial infections per 100 admissions (the infection ratio), and approximately 4.5 percent of hospitalized patients experienced at least one nosocomial infection (the infection percentage). Given that patients stayed a total of almost 299 million days in U.S. hospitals in 1976, the incidence-density of infections was approximately seven infections per 1000 patient-days (see Chapter 4).

These figures should be considered lower-bounds estimates of the current infection rates for at least three reasons. First, the methods used in most studies of nosocomial infections appear to underestimate infection rates to some degree. Although the standardized procedures used in the SENIC Project were intended to minimize this bias, some underestimation is possible. Second, the fact that the nationwide infection rate appears to have increased by approximately 10 percent from 1970 to 1975–76 [18] suggests that infection rates in the 1980s can be expected to be higher than those estimated by the SENIC Project in the mid-1970s unless substantial improvement in hospitals' surveillance and control activities counterbalances this trend.

Third, since the estimates from the SENIC Project applied specifically to the 6449 acute-care U.S. hospitals, they do not account for a substantial number of additional institutional infections that occur each year in chronic-care hospitals and nursing homes (see Chapter 23). On the basis of the one study from which incidence rates in nursing homes can be estimated, as many as 3.3 infections per 1000 resident-days may be occurring, an incidence-density about half that in acute-care hospitals [17,33]. Since there are somewhat more total institutional days spent by residents in nursing homes than by patients in hospitals (approximately 451 million versus 299 million), nursing homes may be accounting for as many as 1.5 million institutional infections per year. If these figures and the secular trends are reasonably accurate, the total number of nosocomial and other institutional infections in the 1980s may exceed 4 million per year, a

number substantially larger than the total number of yearly hospital admissions for all cancers, accidents, and acute myocardial infarctions combined [50].

Rates by Site of Infection

Nosocomial infections involve diverse anatomic sites, but the risks of these various types of infections, and consequently their relative frequency, appear to be very similar in most hospitals. Table 24-1 lists the estimated nationwide infection rates and the relative frequency of the most common sites found in the SENIC Project [17]. These estimates, as well as those from past studies, support the following conclusions: nosocomial urinary tract infections make up about one-half of all nosocomial infections; surgical wound infections, about one-quarter; respiratory tract infections, about one-eighth; bacteremia, about one-sixteenth; and all other types of nosocomial infections collectively account for the remainder. Although these data are expected to vary from hospital to hospital, they have been remarkably consistent in most reported studies.

TABLE 24-1 Rates and relative frequencies of the major types of nosocomial infections, SENIC Project 1975–76

	Nationwide infection rates[a]	Percentage distribution
Urinary tract infection	2.39	42
Surgical wound infection	1.39[b]	24
Lower respiratory infection	0.60	11
Bacteremia[c]	0.27	5
Other sites	1.07	18
All sites	5.72	100

[a]Ratio of number of infections to number of admissions multiplied by 100 (i.e., number of nosocomial infections per 100 admissions). From Haley, R. W., et al. *Am. J. Epidemiol.* 121:159, 1985.
[b]The ratio of surgical wound infections to total operations was 2.79 per 100 operations.
[c]Includes primary and secondary bacteremias.

Rates by Pathogen

Currently the best source of information for gaining insight into the nationwide patterns of microorganisms involved in nosocomial infections is the NNIS. In the report of data from 1980–82, the epidemiology of the various nosocomial pathogens was particularly well analyzed [29]. Cultures were obtained in 90 percent of reported nosocomial infections, and in 85 percent at least one causative pathogen was isolated (a single pathogen in 65 percent and more than one in 20 percent). Among these infections of known cause, 91 percent involved aerobic bacteria; 2 percent, anaerobic bacteria; 6 percent, fungi; and the remaining 1 percent, a miscellaneous group of viruses, protozoa, and parasites. On the basis of other studies [26,51], it appears that viral nosocomial infections are substantially underreported in the NNIS, a fact that mirrors the underrecognition of viral infections in hospitals generally.

The relative frequency of the 12 most commonly isolated pathogens is shown for each of the four major sites of infection in Figure 24-1. In nosocomial urinary tract infections, *Escherichia coli* was by far the most commonly isolated pathogen, and this held true on all services. The second most common urinary pathogen was the enterococcus (*Streptococcus faecalis*), although it was slightly exceeded by *Pseudomonas* in surgical patients and by *Klebsiella* in pediatric patients, and was uncommonly seen in urinary tract infections of newborns.

In surgical wound infections *Staphylococcus aureus* was the most common because of its predominance on adult and pediatric surgical services. On the obstetric and gynecology services, however, *S. aureus* was far exceeded by wound infections with *E. coli*, the enterococcus, and *Bacteroides;* group-B streptococci also played a substantial role in wound infections on obstetrics services.

In lower respiratory infections *S. aureus*, *Pseudomonas aeruginosa*, and *Klebsiella* were encountered with about equal frequency overall, and the variation by service was not great. In cutaneous infections *S. aureus* strongly predominated, with little variation by service.

The microbiology was somewhat more complex for primary bacteremia (i.e., culture-documented bloodstream infections in which no other site of infection was found to be seeding the bloodstream with organisms). *S. aureus* and *E. coli* predominated overall and constituted between approximately 9 and 15 percent of primary bacteremias on all services. Coagulase-negative staphylococci made up about 10 percent of infections on all services, except pediatrics, on which they predominated (17 percent) and obstetrics, on which they were uncommonly isolated. *Bacteroides* predominated on gynecology services (24 percent), and along with other anaerobes were relatively common on obstetrics services but uncommonly isolated on the other services. Group-B streptococci were the most commonly isolated pathogens from primary bacteremia on obstetrics (16 percent) and newborn (25 percent) services but were virtually unseen on the other services. It should be noted that some primary bacteremias are in fact cases of secondary bacteremias in which the primary site of infection was never ascertained.

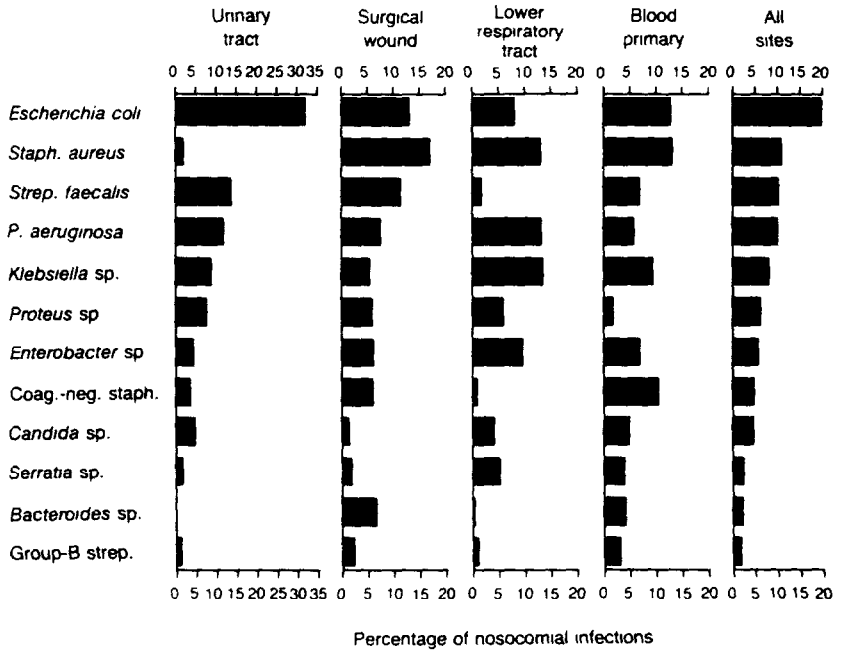

FIG. 24-1. Percentage distribution of nosocomial infections by primary pathogen at the major sites of infection, National Nosocomial Infection Study, 1980–82.

It is interesting that on the basis of its microbiology secondary bacteremia (not included in Fig. 24-1) appears to be a different disease from primary bacteremia. The risk of secondary bacteremia is highest following cardiovascular infections (e.g., endocarditis of a prosthetic valve), postoperative infections of the central nervous system, intraabdominal wound infections, and burns. Complication of infection by secondary bacteremia is most common on the newborn and pediatric services, of intermediate likelihood on the medical and surgical services, and least likely on the obstetrics and gynecologic services. Secondary bacteremia is also more likely in large teaching hospitals. The organisms most commonly involved are *Bacteroides* (12 percent); *Serratia* and *S. aureus* (each about 10 percent); group-B streptococci and coagulase-negative staphylococci (7 percent); and *Klebsiella*, *Enterobacter*, *Pseudomonas*, *Candida*, and *Acinetobacter* (each about 5 to 6 percent).

E. coli is the most commonly isolated pathogen from all nosocomial infections regardless of site because of its predominance in urinary tract infections and its substantial role in infections at all other sites. *S. aureus* is the second most commonly isolated pathogen overall, because of its frequent involvement in all types of infections except those of the urinary tract where it is uncommonly found. The high frequency of enterococci, the third leading pathogen, has perhaps not been well enough appreciated in the past. The important role of *Pseudomonas* as the fourth most common pathogen is not surprising because of its well-known involvement in all types of nosocomial infections. Improvements in surveillance and laboratory techniques are needed to clarify the roles of coagulase-negative staphylococci, anaerobic bacteria, and viruses, whose true frequencies have probably been misjudged, and perhaps more attention should be given to the endogenous mechanisms and nosocomial transmission of group-B streptococci in the obstetric and newborn areas.

Patient Risk Factors

The strongest determinants of the risk of nosocomial infection are the characteristics and exposures of patients that predispose them to infection. Like the so-called chronic diseases, such as coronary heart disease and cancer, nosocomial infections arise from the complex interactions of multiple causal factors, and these factors interact differently in predisposing to the different types of infection (see Chapter 1). Much epidemiologic and clinical research has been devoted to studying the characteristics associated with the oc-

currence of nosocomial infection [7,9,10,13,14,16, 20,27,28,32,35,47]. It has not always been clear whether the associations are truly causal, however, and these characteristics are often referred to as "risk factors," that is, factors associated with, but not necessarily causing, infection. Undoubtedly, some of these risk factors are true causes of infection; others are only coincidentally associated with infection because they frequently follow infection or occur along with the truly causal factors. Complicating matters additionally is the fact that two or more risk factors often occur simultaneously in the same patient, sometimes exerting additive, or even synergistic, effects. In this respect it is said that these risk factors are strongly intercorrelated.

To design strategies for preventing infections, it is important to try to differentiate among coincidental indicators of risk, independent causal factors, and synergistic interactions of causal factors. There have been several attempts to study multiple risk factors using modern techniques of multivariate statistical analysis. Much of this work can be illustrated by the results of analyses of risk factors performed on a group of 169,526 patients who made up a representative sample of patients admitted to acute-care U.S. hospitals in 1975–76 as part of the SENIC Project [16, 20,27]. In an initial descriptive analysis, population estimates of infection rates for each of the four major types of infection were calculated within each category of exposure to between 10 and 20 separate risk factors [20]. A striking finding was that all of the risk factors were associated with infection at all four sites. At first this seems surprising since one would not expect a direct causal association between being treated on a respirator, for example, and acquiring a urinary tract infection. The explanation, of course, is that some of the associations are indicative of direct causal relationships; others are indicative of partial causal relationships, potentiated or diminished by other concurrent influences; and others (such as that between respirators and urinary tract infection) represent largely coincidental associations (most patients on respirators also have indwelling urinary catheters that predispose them to urinary tract infection).

The two factors that appeared to exert the strongest causal influences in all four sites of infection were indicators of the degree of the patient's underlying illness. (1) in surgical patients, the duration of the patient's operation and (2) an index of the number and type of distinct diagnoses and surgical procedures recorded (intrinsic risk index). After these, several factors were strongly associated with infections at one or two sites but not with all four. Having a combined thoracic-abdominal operation was strongly associated with pneumonia and surgical wound infection; undergoing a "dirty" or "contaminated" operation was associated with surgical wound infection; having an indwelling urinary catheter was linked to urinary tract infection; being on a respirator, with pneumonia and bacteremia; previous nosocomial infection, with bacteremia; and receiving immunosuppressive therapy, with bacteremia. Examples of risk factors that had weaker associations with all four sites were age, sex, previous community-acquired infection, and length of preoperative hospitalization.

Another way of viewing these complex multivariate associations is to hypothesize that there are two general categories of causes: those that allow microorganisms access to vulnerable areas of the patient (e.g., operations, catheters, and endotracheal tubes) and those that reduce the patient's capacity for resisting the multiplication and injurious effects of the microorganisms (e.g., immunosuppressive therapy and metabolic sequelae of lengthy operations). In a later multivariate analysis of the SENIC data, this concept was tested using surgical wound infection as an example [16]. The resulting multivariate model indicated that 2 factors—the familiar surgical wound classification [2] and undergoing an abdominal operation—both represent the likely degree of contamination of the operative wound. These measured a portion of the risk of surgical wound infection largely separate from that measured by the other two factors—the duration of the operation and the number of diagnoses recorded. These later 2 factors represent the patient's degree of susceptibility to infection. Moreover, one might infer that the degree of contamination of the wound and the patient's susceptibility were of about equal importance in the genesis of surgical wound infections because each of these four factors was about equally important in the multivariate model.

Although multivariate modeling of risk factors for nosocomial infection is still in an early stage, several conclusions appear reasonable, pending additional research. The risk of infection is primarily determined by definable causal factors reflecting the patient's underlying susceptibility to infection or the degree to which microorganisms have access to vulnerable body sites. Modification of one or more of these factors can alter a patient's risk. Multivariate statistical models can be developed to predict accurately a patient's risk of nosocomial infection from measurable risk factors. The aggregate infection risk of a hospital, or of a subgroup of patients in a hospital—measured by its overall nosocomial infection rate—is primarily determined by the mix of patients, that is, by the causal factors present when patients are admitted and to

which they are exposed in diagnosis and treatment. These conclusions form the basis for understanding much of the variation in nosocomial infection rates described in the following sections.

Rates by Service

Differences in the average risk of infection among groups have been most readily noticed in relation to the well-known differences in infection rates of different services, or specialty areas. Analyses of the SENIC data showed that surgical patients were not only at highest risk of surgical wound infections but also had rates of infection for the other main sites almost three times higher than medical patients (approximately four times higher for pneumonia and approximately one and one-half times higher for urinary tract infection and bacteremia). Moreover, even though surgical patients constituted only 42 percent of general medical and surgical patients, they accounted for 71 percent of nosocomial infections of the four major types (virtually all surgical wound infections, 74 percent of pneumonias, 56 percent of urinary tract infections, and 54 percent of bacteremias) [20]. Analyses of data collected in the NNIS from 1980–82 showed a stepwise decrease of nosocomial infection rates by service from surgical to medical, to gynecology and obstetrics, with the lowest rates on pediatric and newborn services [30]. Other investigators have quantitated the inordinately high risks of patients in special care units (see Chapter 18).

Rates by Type of Hospital

It has long been apparent that overall nosocomial infection rates differ substantially from one hospital to another. In the midnineteenth century Sir James Y. Simpson found that the rate of death from infection of amputated extremities varied directly with the size of the hospital in which the operation was performed (with larger hospitals having higher rates), a phenomenon he called "hospitalism" [46]. The rates of surgical wound infection in the five hospitals participating in the National Research Council's prospective evaluation of ultraviolet light were found to vary from 3.2 to 11.0 percent [28]. The average infection rates of hospitals participating in the NNIS were reported to vary from 1.7 percent in small community hospitals to over 11 percent in chronic disease hospitals [4].

A multivariate analysis of the SENIC data was performed to determine what institutional characteristics of the hospitals best predicted their nosocomial infection rates. Of the many characteristics studied, those found to differentiate best were affiliation with a medical school (teaching vs. nonteaching), size of the hospital (indicated by the number of beds), type of control or ownership of the hospital (municipal, nonprofit, investor-owned), and region of the country [21]. The overall nosocomial infection rates averaged 3.7 percent in small ($<$ 200 beds) nonteaching hospitals, 5.1 percent in large ($\geq$ 200 beds) nonteaching ones, 7.6 percent in nonprofit teaching hospitals, and 8.5 percent in the municipal teaching hospitals. These relationships tended to be consistent for each of the four major sites of infection. Since nonprofit teaching hospitals tend to have fewer than 500 beds, and municipal teaching hospitals tend to have more than 500, teaching hospitals could be subclassified almost as well by size as by ownership-control. In addition, within these four hospital groups rates of urinary tract infection, surgical wound infection, and bacteremia were generally higher in the northeast and north central regions, whereas rates of pneumonia were higher in the West. A similar analysis of NNIS data from 1980–82 found the lowest rates in nonteaching hospitals, intermediate levels in teaching hospitals with less than 500 beds, and highest rates in teaching hospitals with 500 beds or more [29]. This relationship held consistently for infection rates at each site, on every service, and for all pathogens.

To test the hypothesis that these differences were largely due to differences in the mix of patients typically treated in the different types of hospitals, the SENIC data were additionally analyzed to try to explain the differences. Indeed, indexes of the patients' risk factors explained the greatest part of the interhospital differences, and after controlling for indexes of patients' risk factors, average length of stay, and measures of the completeness of diagnostic workups for infection (e.g., culturing rates), the differences in the average infection rates of the various hospital groups virtually disappeared. These findings indicate that much of the difference in observable infection rates of different types of hospitals is due to differences in the intrinsic degree of illness of their patients and related factors, and because of this the overall infection rate per se usually gives little insight into whether the hospital's infection control efforts are effective.

Trends Over Time

The occurrence of nosocomial infections is a dynamic process. Changes are constantly occurring in the types of patients admitted to hospitals, risk factors to which they are exposed, character of the pathogens predominating in the hospital milieu, quality of patient care, thrust of infection control efforts, and other important factors. Two indicators of the dynamic nature

of the problem are the seasonality of certain types of nosocomial infections and the long-term secular trends that may occur.

SEASONALITY Analysis of the data from NNIS has repeatedly shown seasonal variations in the occurrence of nosocomial infections involving certain gram-negative rods [1,29,39]. The report of the 1980–82 results shows clear seasonal peaks of infections in the summer and early fall with certain gram-negative bacteria, specifically—*Klebsiella*, *Enterobacter*, *Serratia*, and *Acinetobacter* species as well as *P. aeruginosa*. In contrast to the seasonal occurrence of pyogenic infections in the community [3], staphylococcal and streptococcal infections show no significant seasonal variation in the hospital. There also seems to be no seasonality of infections with other common bacteria, such as *E. coli*, enterococcus, *Enterobacter*, and anaerobes. Nosocomial viral respiratory infections occur mostly during the seasons in which they occur in the community (e.g., influenza and respiratory syncytial virus infections in the winter and early spring) [26].

SECULAR TRENDS Changes in nosocomial infection rates over time are difficult to study. In prevalence studies performed over several decades, the relatively small sample sizes have hampered the detection of secular changes. An analysis of secular trends in the NNIS from 1970–79 suggested that surgical wound infections may have decreased slightly over the decade, bacteremias may have increased, and other types of infections remained unchanged [1]. The inability to control these analyses for other factors that could have accounted for the changes, however, rendered these findings difficult to interpret.

To address this issue, the rates from the two time periods of the SENIC Project, 1970 and 1975–76, were compared after controlling for the most likely biasing factors [18]. After controlling for changes in levels of patient risk, length of stay, and completeness of ascertainment of infections, overall nosocomial infection rates in acute-care hospitals were found to have increased by a statistically significant 10 percent over the five-year period. Additional analysis, however, revealed three contrasting trends in different groups of hospitals. In the group that established no substantial infection surveillance and control programs, the overall infection rate increased by 18 percent; in the group in which moderately intensive programs were established, the rates tended to show no significant change; and in the group that established very intensive programs for preventing infections at all four of the major sites, the overall rate decreased by 36 percent. These findings suggest strongly that the overall nationwide trend of a 10 percent increase was really the result of two forces that were affecting the nationwide rate in opposite directions: (1) the continuing introduction of more invasive and immunocompromising techniques into the care of hospitalized patients, which tended to increase the infection rates and (2) the efficacy of newly established infection surveillance and control programs, which tended to decrease them. This indicates that future secular trends in the rates of endemic nosocomial infections could be in either direction, depending strongly on the balance that hospitals achieve between technologic innovations in patient care, and investments in infection surveillance and control programs.

EPIDEMIC NOSOCOMIAL INFECTIONS

Incidence, Recognition, and Control

While many scientific articles have been written to describe individual outbreaks of nosocomial infections, very little work has been done to estimate the frequency of these epidemics. The earliest study on this subject was performed in the CDC's CHIP study in the early 1970s [25]. Among seven community hospitals participating in CHIP during 12 months in 1972–73, a computerized threshold program screened the regularly reported cases of nosocomial infection for clusters of infection that might indicate an outbreak, and a CDC epidemiologist additionally analyzed the data to eliminate purely coincidental clusters. Then CDC staff members visited the hospitals that had potential outbreaks to confirm the nature of the problem and suggest control measures if needed. From these data it was estimated that one true outbreak occurred for every 10,000 hospital admissions and that outbreaks accounted for somewhere in the range of 2 percent of patients with nosocomial infections. More recently, Wenzel and colleagues [54] estimated that 3.7 percent of nosocomial infections in a large university-affiliated referral hospital occurred in outbreaks. Although confined to a relatively small number of hospitals, these estimates appear to confirm the prevailing view that outbreaks account for a relatively small proportion of nosocomial infections.

Besides the attention often provoked by outbreaks, one of the main reasons for infection control personnel to be concerned about them is that, if recognized and investigated, control measures can often stop them, thus bringing about demonstrable reductions in mor-

bidity and mortality. In the CHIP investigations, despite the fact that the seven hospitals had very active surveillance systems, one-third of the clusters had not been recognized before the CDC visit. This fact points out the difficulty of recognizing outbreaks even in the best of circumstances and suggests the usefulness of inventive computerized systems to screen surveillance data for potential epidemics (see the Role of Computers in Surveillance, Chapter 4). It also suggests that hospitals that appear never to have outbreaks may simply be failing to recognize them.

The CHIP investigations also demonstrated that 40 percent of the outbreaks appeared to have resolved spontaneously, while the remaining 60 percent continued until control measures were instituted [25]. Half of the outbreaks that continued were controlled by measures taken by the hospitals' infection control staff and the other half were completely resolved only after measures suggested by the outside investigators. While the rate of spontaneous resolution explains the origin of opinions against surveillance expressed by some persons, if these figures are representative of community hospitals in general—and it must be recalled that these were hospitals with very active infection surveillance systems—then a large number of outbreaks may currently be going unrecognized and uncontrolled, despite the advanced state of infection surveillance and control programs.

Characteristics of Epidemics

To recognize, investigate, and control epidemics most effectively, it is helpful to understand their nature, likely problems, and mechanisms. Although there are many reports of individual outbreak investigations, the only body of information large enough to study the characteristics of epidemics is the series of investigations performed by the CDC in response to hospitals that request assistance. Recently reviewed by Stamm and colleagues [48], this series included 252 hospital investigations performed between 1956 and 1979. Since various factors influence the types of investigations undertaken by the CDC, this series should be considered only an approximate reflection of the mix of outbreaks that occur routinely in U.S. hospitals. The studies probably reflect the types of problems that infection control personnel find particularly urgent, perplexing, or difficult to control.

In the early phase of these investigations—1958 through 1962—the outbreak investigations were divided between epidemics of gastrointestinal disease—mainly due to *Salmonella* and enteropathogenic *E. coli*—and outbreaks of staphylococcal infections. Almost all these problems were centered in newborn nurseries. From the mid-1960s on, investigations of staphylococcal infections diminished abruptly dc to an occasional yearly episode, and by the early 19 outbreaks of gastroenteritis similarly diminishec a continuing low level. From the late 1960s u the present, there has been an increasing trend tow involvement of gram-negative pathogens, bac emia, and surgical wound infections in outbrea and toward problems related to intensive care newly introduced medical devices and related te nologies. For example, during the 1970s the typ infection most commonly investigated was bac emia. Also noteworthy was an increase in inve gations of hepatitis outbreaks that peaked in 1 and 1976. Other interesting groupings included c breaks of necrotizing enterocolitis in nurseries sternal wound infections following open-heart s gery—both beginning in the mid-1970s—and c breaks of legionnaires' disease, about half of wh occurred in hospitals. From the late 1960s on, increasingly important issue in many of these in tigations was the resistance of epidemic pathogen multiple antimicrobial agents, particularly resista of gram-negative bacilli to aminoglycosides and o *aureus* to methicillin and/or gentamicin.

One of the most striking characteristics of the idemics was that the percentage distribution of ty of infections and pathogens involved bore little semblance to the percentage distributions in ende infections. Eight types of nosocomial infections curred with roughly the same frequency in the CI investigated epidemics, whereas three or four m types predominate in endemic infections (Table 2). Moreover, except for *S. aureus*, which constitu about 10 to 12 percent of both endemic and epide infections, the pathogens found most commonly the CDC-investigated epidemics—*Salmonella*, he titis B, *Serratia*, and *Enterobacter*—were among least common pathogens in endemic infections (T 24-2). This interesting relationship probably refl in part the fact that outbreaks occur by epidemiol mechanisms different from those that cause ende infections. It may also be due to the greater likelih that clusters of unusual pathogens or site-patho combinations will be recognized by infection con personnel, and conversely that outbreaks of infect similar to the most common endemic infections not as easily recognized. The selection factors get the CDC involved in investigations also undo edly contribute to this profile of epidemic proble

Of most practical value is the information that investigatory experience provides for identifying modes of transmission of future outbreaks. The breaks can be classified into five groups accordin the most likely mode of transmission: (1) comm

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source, (2) human transmitter (carrier), (3) person to person (cross-infection), (4) airborne (microorganisms traveling more than a few feet), and (5) uncertain mode of transmission. After outbreaks were classified in this manner, it became apparent that certain site-pathogen combinations, sometimes specific to a patient group, could be rather specifically identified with particular modes of transmission. These combinations are listed in Table 24-3.

Knowledge of these unique combinations can be useful in focusing on the most likely mode of transmission early in an outbreak investigation. For example, outbreaks of *Salmonella* gastroenteritis among adult patients are most likely to be spread by a common source (e.g., food), whereas a similar outbreak in a newborn nursery is most likely to be spread by person-to-person contact, although the roles of hospital-prepared formula or breast-milk banks must be ruled out (see Chapter 32). Similarly, outbre
hepatitis A are most likely to be due to a cor
source, whereas outbreaks of hepatitis B are
likely to be caused by either a human dissem
(e.g., a surgeon who is a carrier) or person-to-p
spread (e.g., poor blood-handling techniques
Chapter 35). Surgical wound infections caused
group-A streptococci are very likely to be rela
a human disseminator (e.g., an anal carrier), w
wound infections due to *S. aureus* may be du
human disseminator or other factors (see Chapte
It is noteworthy that no human disseminato
implicated in 68 outbreaks involving gram-ne
bacilli. Perhaps half the outbreaks of staphylo
infections in nurseries can be attributed to cro
fection and about one-quarter to human dissemi
(see Chapter 19). Outbreaks of bacteremia d
gram-negative bacilli, particularly if they oc
intensive care units, are very likely to be du
common source (e.g., contaminated devices), w
outbreaks involving other types of infections
gram-negative bacilli (particularly urinary tra
fections) are most likely to be due to cross-inf
(e.g., inadequate care of urinary catheters) (see
ter 18). The types of outbreaks likely to invol
borne spread are varicella infections, *Aspergill*
fections, and legionnaires' pneumonia, partic
in immunosuppressed patients (see Chapter 37
pulmonary tuberculosis, particularly in hospit
sonnel working in emergency rooms (see Chap

TABLE 24-2. Comparison of types of infections and pathogens involved in endemic and epidemic infections

	Endemic infections[a] (%)	Epidemic infections[b] (%)
Type of infection		
Urinary tract infection	38	10
Surgical wound infection	27	9
Pneumonia	16	12
Cutaneous infection	6	11
Bacteremia	4	16
Meningitis	<1	6
Gastroenteritis	<1	17
Hepatitis	<1	12
Other	8	7
Total	100	100
Pathogen		
Escherichia coli	19	3
Enterococcus	10	<1
Staphylococcus aureus	10	12
Pseudomonas	9	4
Proteus	8	<1
Klebsiella	8	3
Enterobacter	4	7
Group-A streptococci	2	3
Serratia	2	8
Salmonella	<1	11
Hepatitis B virus	<1	10
Total	100	100

[a]National Nosocomial Infection Study, 1975 through 1978
[b]1971 through 1979
Source. Adapted from Stamm, W E , et al *Am J Med.* 70:393, 1981

Multihospital Epidemics

An issue of increasing concern is the involvem
multiple hospitals in an epidemic. This occur
commonly by interhospital spread and less com
through the nationwide distribution of produc
cause or predispose to infection. First, a pat
involved in an epidemic in one hospital may
troduced into the patient population of anothe
pital, generally by one of three modes of transm
(1) transfer of infected or colonized patients,
ularly those with burns or decubitus ulcers [
41,44,53], (2) transfer of colonized or ir
medical house staff [45,51], and (3) transie
onization of hands of nurses and technicians w
ternate working at different hospitals [42]. Sir
transfer of house staff and seriously ill patients
primarily among large, university-affiliated, t
referral hospitals, interhospital spread appears
cur most frequently in these and less commonly
smaller community hospitals [19]; however,
creasing trend of nurses and technicians toward
ing in cooperatives serving several hospitals m
courage more interhospital spread.

TABLE 24-3. Likely modes of transmission of the most common types of nosocomial infection epidemics

Mode of transmission	Site or type of infection	Pathogen	Service or patient group	CDC investigations[a] Number[b]
Common source	Gastroenteritis	*Salmonella*	Adults	11/13
	Hepatitis	Hepatitis A virus	Any	3/3
	Urinary tract or bacteremia	*Pseudomonas cepacia*	Any	4/4
	Pulmonary	*Pseudomonas aeruginosa*	Any	4/5
	Bacteremia	Gram-negative bacilli	Any	10/13
Human disseminator	Bacteremia	Any	ICU	6/7[c]
	Surgical wound	Group-A streptococci	Any	5/6
	Surgical wound	*Staphylococcus aureus*	Surgery	3/8
	Cutaneous	*S. aureus*	Nursery	5/24
	Hepatitis	Hepatitis B virus	Any	3/12
Cross-infection	Gastroenteritis	*Salmonella* or enteropathic *Escherichia coli*	Nursery	16/17
	Cutaneous	*S. aureus*	Nursery	12/24
	Urinary tract	Gram-negative bacilli	Any	10/14
	Hepatitis	Hepatitis B virus	Any	8/12
Airborne	Varicella	V-Z virus	Any	—
	Pulmonary	*Aspergillus*	Any	—
	Pulmonary	*Mycobacterium tuberculosis*	Any	—
	Pulmonary	*Legionella*	Any	—

V-Z = varicella-zoster, ICU = intensive care unit.
[a]From Stamm, W. E., et al. *J Infect Dis.* 136(Suppl):S151, 1977
[b]Of the 13 outbreaks of gastroenteritis due to *Salmonella* among adults, 11 were transmitted by the common-source mode.
[c]From Wenzel, R. P., et al. *IC Infect Control* 4:371, 1983

Interhospital transmission of outbreaks has been observed primarily in epidemics involving pathogens with important antimicrobial resistance patterns, such as multiply resistant *Serratia* [42], aminoglycoside-resistant gram-negative bacilli [53], and methicillin-resistant *S. aureus* [19] (see Chapter 12). This association could be due to the genetic colinkage of antimicrobial resistance with factors that facilitate spread. For example, strains of diverse genera that are prevalent in nosocomial infections have been shown to share the genetic information that confers resistance to important antimicrobial agents [43]. Similarly, the diversity of phage types involved in epidemiologically clear outbreaks of methicillin-resistant *S. aureus* infections suggests the spread of genetic information among different strains that have strong predispositions to infect hospital patients. Alternatively, the association could be due merely to the fact that resistance provides a dramatic marker that increases the likelihood that an epidemic will be recognized. If so, as infection control personnel in hospitals develop more sensitive means for recogn outbreaks and more effectively share surveillance with their counterparts in other local hospitals (through area-wide surveillance systems supporte local health departments), interhospital transmi of infection will probably be recognized more monly.

In the second type of multiple-hospital inv ment, a widely distributed product used in pa care may cause infections in many hospitals si taneously, due to either intrinsic contaminati the product in the factory [34] or design fla common usage errors that encourage in-use con ination in the hospitals [5,8] (see Chapters 3 38). After a series of nationwide epidemics d intrinsically contaminated products in the early 1 it appeared that intrinsic product contamination become a common problem [34]. Subsequent rience has shown, however, that in-use contamin is a far more common explanation for infectio lated to newly introduced products and devices

ics

CDC investigations[a]	
umber[b]	(%)
11/13	85
3/3	100
4/4	100
4/5	80
10/13	77
6/7[c]	86
5/6	83
3/8	38
5/24	20
3/12	25
16/17	94
12/24	50
10/14	71
8/12	67
—	›
—	›
—	100
—	›

e mode

› for recognizing surveillance data l hospitals (e.g., ms supported by al transmission ılized more com-

ıospital involve- used in patient hospitals simul- ntamination of design flaws or : in-use contam- Chapters 36 and ıidemics due to the early 1970s, mination would bsequent expe- e mination or fections re- and devices.

Pseudoepidemics

Not all clusters of reported nosocomial infections constitute true epidemics of disease. In the prospective study of outbreaks in the CDC's CHIP project, about 80 percent of the clusters of infection identified statistically by a computerized threshold program were judged to be coincidental, illustrating the need for epidemiologic evaluation of surveillance data to detect outbreaks [25]. More important, of those clusters that appeared to represent real outbreaks epidemiologically, approximately one-third (37 percent) were found not to be true outbreaks after thorough investigations. Most of these pseudoepidemics were traced to systematic errors or changes in clinical diagnosis of infections or in reporting of infections by the infection surveillance staff; systematic errors in the microbiology laboratory explained fewer than one-quarter of them. In the series of epidemic investigations performed by the CDC, pseudoepidemics accounted for only 11 percent of the presumed outbreaks for which hospitals requested epidemiologic assistance, and about one-half of these were attributed to processing errors in the microbiology laboratories [48,52].

The difference in results between these two studies is probably due to the more extensive investigation usually done by hospital personnel to rule out artifactual problems before the CDC epidemiologists undertake a formal investigation. Consequently in the routine practice of infection control in most hospitals, the majority of pseudoepidemics may be due to diagnostic and reporting errors as reflected by the CHIP investigation, although truly perplexing pseudoepidemics may more often be traced to contaminated equipment or errors in the microbiology laboratory, as reflected in the CDC investigations (see Chapter 5).

ADVERSE CONSEQUENCES OF NOSOCOMIAL INFECTIONS

In reading the scientific literature on the subject of nosocomial infections, one is struck by the disproportionately large number of articles on the adverse consequences—prolongation of hospital stay, extra hospital costs or charges, and deaths—of these infections. The importance of these studies stems from two factors: first, in contrast to most other hospital services, hospitals have not traditionally been able to charge patients or their insurance carriers directly for the costs of their infection surveillance and control programs; and second, it has been difficult to demonstrate how many nosocomial infections these programs prevent. Consequently it has been necessary, or at least very helpful, in many hospitals to demonstrate how costly the infections are for the patients to justify the expenditures of mounting and sustaining a preventive program.

Estimates of extra costs attributable to nosocomial infections must be interpreted with some caution. Because the actual costs of hospitals are difficult to study, their charges to patients are usually used as a substitute for their actual costs. However, hospitals commonly redistribute charges among different cost centers to recover costs not fully reimbursed by public and private reimbursement agencies, so charges to the patient may not accurately represent the hospital's costs of treatment [12]. In addition, estimates expressed in dollars must be constantly adjusted for inflation to be meaningful in the current context.

The studies on this subject have used one of three methods to estimate the prolongation of hospital stay, extra charges, and number of deaths attributable to nosocomial infections: concurrent assessments of infected patients, unmatched comparisons of infected and uninfected patients, and matched comparisons [24]. Each approach has its own strengths and weaknesses, which may lead to a biased estimate.

The concurrent assessment method relies on a physician to visit each infected patient frequently enough to enumerate all extra days and extra services that were performed to treat the infection but would not have occurred if the infection had not supervened. By applying the routine per diem room charge to each extra day and the actual charge for each ancillary service from the patient's hospital bill, the physician can estimate directly the total extra charges attributable to the nosocomial infection. The advantage of this method is that the identifiable charges are directly itemized; the disadvantage is that, by relying on the physician's clinical judgment to determine what days and services are attributable, the results may be biased in either direction depending on how conservative the judgments are. For example, for some days or services the circumstances are too ambiguous to make a clear determination; if the ambiguous circumstances are always considered nonattributable to infection, the final results will be underestimates.

In the unmatched comparison approach, the average extra stay (or charge) is estimated after the completion of a study by subtracting the average total length of stay (or total hospital charges) of uninfected patients from that of infected patients. This method always substantially overestimates the attributable extra stay (and charges) because of a strong selection bias: patients who contract nosocomial infections tend strongly to have been more seriously ill at the be-

ginning of hospitalization (and thus more strongly predisposed to long hospital stays, higher charges, and death) than those who are likely to be discharged without an infectious complication.

The matched comparison approach is similar to the comparison approach except that for each infected patient the investigator selects one or more uninfected patients who are similar to their match on several selected characteristics. The advantage of this approach, like the unmatched comparison, is that it avoids use of clinical judgment to decide what is attributable to infection. The disadvantage is that it is extremely difficult to match uninfected patients with infected patients closely enough to overcome the powerful selection bias. To the degree that the matching fails to control for this underlying noncomparability of infected and uninfected patients, the study will overestimate the magnitude of extra stay, extra charges, or deaths attributable to infection.

One fundamental reason that the matched comparison studies performed to date have failed to control for the large disparity in degree of underlying illness is that they have generally matched infected and uninfected patients on the wrong characteristics. These studies have used as matching criteria such predictors of infection risk as age, sex, service, first diagnosis, and first surgical procedure. To control for the underlying predisposition to an extended hospital stay, the matching characteristics should include the major factors that determine prolonged hospital stay (or death), which are not necessarily the same as those that predispose to nosocomial infection. For example, it was pointed out in one of the earliest concurrent assessment studies that some of the main factors that increase length of stay apart from nosocomial infection include severe underlying illness, development of unexpected complications such as venous thrombosis or pulmonary embolism, and social factors that delay discharge [6]; these appear frequently to be colinked with the severity-of-illness factors that also predispose to nosocomial infections. For matching comparisons to be useful, it must be shown that the matching characteristics are sufficiently complete predictors of prolonged hospital stay, high total hospital costs, or the probability of death to control completely for the bias caused by the greater complexity of the infected patients' underlying conditions.

In a study comparing all three methods in the same cohort of patients, the estimates were lowest by the concurrent assessment, intermediate for the matched approach, and highest for the unmatched approach [24]. Published estimates of the prolongation of stay for surgical wound infections by the concurrent assessment method have ranged from 1.5 to 11 days; by the matched comparison approach, from 7 to 1[illegible] days; and by the unmatched comparison approach from 5 to 26 days.

Nationwide estimates of the number of deaths attributable to nosocomial infections have varied even more widely. By combining data from the SENIC project [17] and from a concurrent assessment of mortality performed in NNIS [30], 19,000 deaths nationwide per year were estimated to be directly attributable to nosocomial infections, and in 58,000 more deaths nosocomial infections contributed but were not the only cause (Table 24-4). At the other extreme, a recent study using multivariate logistic regression techniques, with the same drawbacks as the matched comparison approach, estimated 300,000 deaths per year nationwide attributable to nosocomial urinary tract infections alone [37]. Regardless of which estimates are used, however, the large number of deaths from nosocomial infections is a cause for concern. Counting only the 19,000 deaths directly caused by nosocomial infections—the lowest estimate derived from NNIS and SENIC—would place it just below the tenth leading cause of death in the U.S. population; whereas, if one also counts the 58,000 deaths to which nosocomial infections contribute but are not the only cause, it would rank as the fourth leading cause of death, just behind heart disease, cancer, and stroke. These figures indicate the need for an accurate counting of nosocomial infections in our national systems for vital and health statistics [17].

Until the serious methodologic problems are solved it seems prudent to use the more conservative estimates derived from concurrent assessments even though they may underestimate the magnitude of the problem. Table 24-4 lists the estimates of extra days and costs derived from concurrent assessments in the SENIC pilot studies [23] and estimates of deaths derived from the NNIS [30] and SENIC [17]. In view of the new strategies of prospective reimbursement for hospital care and the evidence for the efficacy of infection surveillance and control programs, it is likely that the direct cost reductions produced by infection control will be sufficiently obvious even if derived from the most conservative estimates.

Preventability

That large numbers of endemic as well as epidemic nosocomial infections are preventable has periodically been reaffirmed by milestone reports such as that of Semmelweis, studies on the effects of proper care of urinary catheters and respirators, and the virtual elimination of epidemic bacteremia caused by intrinsic contamination of commercial intravenous solu

TABLE 24-4 Estimated extra days, extra charges, and deaths attributable to nosocomial infections annually in U S hospitals

	Extra days		Extra charges			Deaths			
						Infections directly causing death		Infections contributing to death	
	Avg. per infection[a]	Est. U.S total[b]	Avg extra charges per infection in 1975 dollars[a]	Avg extra charges per infection in 1985 dollars[c]	Est U S total in 1985 dollars[b]	Percent[d]	Est. U S total[b]	Percent[d]	Est U S total[b]
Surgical wound infection	7.3	3,726,000	$838	$2,734	$1,395,000,000	0 64	3,251	1 91	9,726
Pneumonia	5.9	1,339,000	$1,511	$4,947	$1,123,000,000	3 12	7,087	10 13	22,983
Bacteremia	7 4	762,000	$935	$3,061	$315,000,000	4 37	4,496	8.59	8,844
Urinary tract infection	1.0	903,000	$181	$593	$535,000,000	0 10	947	0 72	6,503
Other site	4.8	1,946,000	$430	$1,408	$571,000,000	0 80	3,246	2.48	10,036
All sites	4 0[e]	8,676,000	$560[e]	$1,833[e]	$3,939,000,000	0 90[e]	19,026	2.70[e]	58,092

[a]Adapted from Haley, R W , et al *Am J Med* 70 51, 1981, by pooling data from the three SENIC pilot study hospitals

[b]Estimated by multiplying the total number of nosocomial infections estimated in the SENIC Project (Haley, R W , et al *Am J Epidemiol* 121 159, 1985) by the average extra days, average extra charges, or percentage of infections causing or contributing to death, respectively

[c]1985 dollars estimated from Haley, R W , et al *Am J Med* 70 51, 1981, by pooling data from the three hospitals and adjusting for the annual rate of inflation of hospital expenses from 1976 to 1985 (range 4 9 to 19 1 percent) obtained from the American Hospital Association's National Panel Survey

[d]Unpublished analyses of data reported to the National Nosocomial Infections Study (NNIS) in 1980–1982 (Hughes, J M , et al *Abstracts of the Twenty-Second Interscience Conference on Antimicrobial Agents and Chemotherapy, 1982*)

[e]Nationwide estimate obtained by summing the products of the site-specific estimate of the average extra days, average extra charges, or the percentage of infections causing or contributing to death, respectively, from the SENIC pilot studies (Haley, R W , et al *Am J Med* 70 51, 1981), and the nationwide estimate of the proportion of nosocomial infections affecting the site from the main SENIC analysis (Haley, R W , et al *Am J Epidemiol* 121.159, 1985)

tions. Yet when a representative sample of infection control program heads were asked to estimate the percentage of nosocomial infections presently occurring in U.S. hospitals that are preventable, the responses varied from 1 percent to 100 percent, with a mean of approximately 50 percent, the program heads who had served in their positions longer and who were more knowledgeable about infection control tended to give lower estimates [15]. There are at least two reasons for this lack of agreement among those working most closely with the problem. First, it is difficult to demonstrate that infections have been prevented or to infer whether active infections were preventable [36]. Second, because new risk factors for infection are constantly appearing, necessary control measures are continually evolving, and ability to manage the patient-care behavior of hospital personnel is changing, the true percentage of infections that are preventable probably changes from time to time.

Consequently the only meaningful way of framing the preventability question is to ask what percentage of nosocomial infections can be prevented by maintaining an intensive infection surveillance and control program that continually adjusts to the new risks and attempts to manage patient-care behavior. Since this was precisely the question framed in the SENIC Project, there is an approximate answer. Among U.S. hospitals in the 1970s, approximately one-third of all nosocomial infections were preventable by maintaining infection surveillance and control programs with particular characteristics [18] (see Chapter 3). The fact that the approaches found to be effective were general preventive strategies aimed at managing infection control (i.e., surveillance and control programs), rather than individual preventive practices (e.g., catheter care), suggests that the SENIC estimate of preventability will remain reasonably accurate for the foreseeable future.

REFERENCES

1. Allen, J. R., Hightower, A. W., Martin, S. M., and Dixon, R. E. Secular trends in nosocomial infections: 1970–79. *Am. J. Med.* 70:389, 1981.
2. Altemeir, W A., Burke, J. F., Pruitt, B. A., et al. (Eds.). *Manual on the Control of Infection in Surgical Patients.* Philadelphia: Lippincott, 1976, pp. 29–30.
3. Benenson, A. S. Staphylococcal Disease. In Benenson, A. S. (Ed.), *Control of Communicable Diseases in Man* (14th ed.). Washington, DC: American Public Health Association, 1985, pp. 358–366.
4. Bennett, J. V., Scheckler, W. E., Maki, D. G., and Brachman, P. S. Current National Patterns: United States. In *Proceedings of the International Conference on Nosocomial Infections,* August 3–6, 1970. Chicago: American Hospital Association, 1971, pp. 42–49.
5. Centers for Disease Control. Nosocomial Bacteremia from Intravascular Pressure Monitoring Systems. *National Nosocomial Infections Study Report,* 1977, issued 1979, pp. 31–36.
6. Clarke, S. Sepsis in surgical wounds with particular reference to *Staphylococcus aureus. Br. J. Surg.* 44:592, 1957.
7. Cruse, P. J. E., and Foord, R. The epidemiology of wound infection: A 10-year prospective study of 62,939 wounds. *Surg. Clin. North Am.* 60:27, 1980.
8. Donowitz, L. G., Marsik, F. J., Hoyt, J. W., and Wenzel, R. P. *Serratia marcescens* bacteremia from contaminated pressure transducers. *J.A.M.A.* 242:1749, 1979.
9. Dukes, C. Urinary infections after excision of the rectum: Their cause and prevention. *Proc. R. Soc. Med.* 22:259, 1928.
10. Ehrenkrantz, N. J. Surgical wound infection occurrence in clean operations: Risk stratification for interhospital comparisons. *Am. J. Med.* 70:909, 1981.
11. Eickhoff, T. C., Brachman, P. S., Bennett, J. V , and Brown, J. F. Surveillance of nosocomial infections in community hospitals. I. Surveillance methods, effectiveness, and initial results. *J. Infect. Dis.* 120:305, 1969.
12. Finkler, S. A. The distinction between costs and charges. *Ann. Intern. Med.* 96:102, 1982.
13. Freeman, J., and McGowan, J. E., Jr. Risk factors for nosocomial infection. *J. Infect. Dis* 138:811, 1978.
14. Garibaldi, R. A., Britt, R. A., Coleman, M. L. Reading, J. C., and Pace, N. L. Risk factors fo predicting postoperative pneumonia. *Am. J. Med* 70:677, 1981.
15. Haley, R. W. The "hospital epidemiologist" i U.S. hospitals, 1976–1977: A description of th head of the infection surveillance and control pro gram. *Infect. Control* 1:21, 1980.
16. Haley, R. W., Culver, D. H., Morgan, W. M. White, J. W., Emori, T. G., and Hooton T. M. Identifying patients at high risk of surgica wound infection: A simple multivariate index c patient susceptibility and wound contamination *Am. J. Epidemiol.* 121.206, 1985.
17. Haley, R. W., Culver, D. H., White, J. W. Morgan, W. M., and Emori, T. G. The natior

wide nosocomial infection rate: A new need for vital statistics. *Am. J. Epidemiol.* 121:159, 1985.
18. Haley, R. W., Culver, D. H., White, J. W., Morgan, W. M., Emori, T. G., Munn, V P., and Hooton, T. M. The efficacy of infection surveillance and control programs in preventing nosocomial infections in U.S. hospitals. *Am. J. Epidemiol.* 121.182, 1985.
19. Haley, R. W., Hightower, A., Khabbaz, R. F., Thornsberry, C., Martone, W. J., Allen, J. R., and Hughes, J. M. The emergence of methicillin-resistant *Staphylococcus aureus* infections in United States hospitals: Possible role of the house staff–patient transfer circuit. *Ann. Intern. Med.* 97:297, 1982.
20. Haley, R. W., Hooton, T. M., Culver, D. H., et al. Nosocomial infections in U.S. hospitals, 1975–1976: Estimated frequency by selected characteristics of patients. *Am. J. Med.* 70:947, 1981.
21. Haley, R. W., Morgan, W. M., Culver, D. H., and Schaberg, D. R. Differences in nosocomial infection rates by type of hospital: The influence of patient mix and diagnostic medical practices. (Unpublished data presented at Interscience Conference on Antimicrobial Agents and Chemotherapy Miami, Fla., October 4, 1982.)
22. Haley, R. W., Quade, D. H., Freeman, H. E., and the CDC SENIC Planning Committee. Study on the efficacy of nosocomial infection control (SENIC Project): Summary of study design. *Am. J. Epidemiol.* 111.472, 1980.
23. Haley, R. W., Schaberg, D. R., Crossley, K. B., Von Allmen, S. D., and McGowan, J. E., Jr. Extra days and prolongation of stay attributable to nosocomial infections: A prospective interhospital comparison. *Am. J. Med.* 70:51, 1981.
24. Haley, R. W., Schaberg, D. R., Von Allmen, S. D., and McGowan, J. E., Jr. Estimating the extra charges and prolongation of hospitalization due to nosocomial infections: A comparison of methods. *J. Infect. Dis.* 141:248, 1980.
25. Haley, R. W., Tenney, J. H., Lindsey, J. O. II, Garner, J. S., and Bennett, J V. How frequent are outbreaks of nosocomial infection in community hospitals? *Infect. Control* 6:233, 1985.
26. Hall, C. B. Nosocomial viral respiratory infections: Perennial weeds on pediatric wards. *Am. J. Med.* 70.670, 1981.
27. Hooton, T. M., Haley, R. W , Culver, D. H., White, J. W , and Morgan, W. M. The joint associations of multiple risk factors with the occurrence of nosocomial infection *Am J. Med.* 70 960, 1981.
28. Howard, J. M., Barker, W. F., Culberts W. R., et al. Postoperative wound infecti The influence of ultraviolet irradiation of operating room and of various other fact *Ann. Surg.* 160(Suppl.):1, 1964.
29. Hughes, J. M., Culver, D. H., White, J. V et al. Nosocomial infections surveillar 1980–1982. *Morbid. Mortal. Weekly Rep.* 32:1 1983.
30. Hughes, J. M., Munn, V., Jarvis, W., Cul D. H., and Haley, R. W. Mortality Associa with Nosocomial Infections in the United Sta 1975–1981. *Abstracts of the Twenty-Second In science Conference on Antimicrobial Agents and Ch otherapy*, October 4–6, 1982, Miami Beach, Fl ida, p. 189.
31. Kislak, J. W., Eickhoff, T. C., and Finland, Hospital-acquired infections and antibiotic us in the Boston City Hospital. *N. Engl. J. M* 271:834, 1964.
32. Lidwell, O. M. Sepsis in surgical wounds: M tiple regression analysis applied to records of p operative hospital sepsis. *J. Hyg. (Camb.)* 59:2 1961.
33. Magnussen, M. H., and Robb, S. S. Nosocon infections in a long-term care facility. *Am. Infect. Control* 2:12, 1980.
34. Maki, D. G., Rhame, F. S., Mackel, D. C., Bennett, J. V. Nationwide epidemic of se cemia caused by contaminated intravenous pr ucts. I. Epidemiologic and clinical features. *J. Med.* 60:471, 1976.
35. McCabe, W. R., and Jackson, G. C. Gr negative bacteremia. I. Etiology and ecology. A *Intern. Med.* 110:847, 1962.
36. McGowan, J. E., Jr., Parrott, P. L., and D V. P. Nosocomial bacteremia: Potential for vention of procedure-related cases. *J.A.M* 237:2737, 1977.
37. Platt, R., Polk, B. F., Murdock, B. S., et Mortality associated with nosocomial urinary t infection. *N. Engl. J. Med.* 307:637, 1982.
38. Price, E. H., Brain, A., and Dickson, J. A An outbreak of infection with a gentamicin-methicillin-resistant *Staphylococcus aureus* in a natal unit. *J. Hosp. Infect.* 1:221, 1980.
39. Retailliau, H. F., Hightower, A. W., Khabl R. F., et al. *Acinetobacter calcoaceticus:* A nos mial pathogen with an unusual seasonal patt *J. Infect. Dis.* 139:371, 1979.
40. Sapico, F. L., Montgomerie, J. Z., Canaw H. N., and Aeilts, G. Methicillin-resis *Staphylococcus aureus* bacteriuria. *Am. J. Med.* 281:101, 1980.

41. Saraglou, G., Cromer, M., and Bisno, A. L. Methicillin-resistant *Staphylococcus aureus*. Interstate spread of nosocomial infections with emergence of gentamicin-methicillin-resistant strains. *Infect. Control* 1:81, 1980.
42. Schaberg, D. R., Alford, R. H., Anderson, R., Farmer, J. J., Melly, M. A., and Schaffner, W. An outbreak of nosocomial infection due to multiply resistant *Serratia marcescens:* Evidence of interhospital spread. *J. Infect. Dis.* 134 181, 1976.
43. Schaberg, D. R., Rubens, C. R., Alford, R. H., Farrar, E. D., Schaffner, W., and McGee, Z. A. Evolution of antimicrobial resistance and nosocomial infection: Lessons from the Vanderbilt experience. *Am. J. Med.* 70:445, 1981.
44. Shanson, D. C. Antibiotic-resistant *Staphylococcus aureus*. *J. Hosp. Infect.* 2.11, 1981.
45. Shanson, D. C., and McSwiggan, D. A. Operating theatre–acquired infection with a gentamicin-resistant strain of *Staphylococcus aureus*. Outbreaks in two hospitals attributable to one surgeon. *J. Hosp. Infect.* 1:171, 1980.
46. Simpson, J. Y. Our existing system of hospitalism and its effects. Part I. *Edinburgh Med. J* 14:816, 1869.
47. Stamm, W. E., Martin, S. M., and Bennett, J. V. Epidemiology of nosocomial infections due to gram-negative bacilli: Aspects relevant to development and use of vaccines. *J. Infect. Dis.* 136(Suppl.):S151, 1977.
48. Stamm, W. E., Weinstein, R. A., and Dixon, R. E. Comparison of endemic and epidemic nosocomial infections. *Am. J Med.* 70:393, 1981.
49. Thoburn, R., Fekety, F R., Cluff, L. E., and Melvin, V B. Infections acquired by hospitalized patients. *Arch Intern. Med.* 121·1, 1968.
50. United States National Center for Health Statistics. *Utilization Patterns and Financial Characteristics of Nursing Homes in the United States: 1977 National Nursing Home Survey*. Hyattsville, MD: National Center for Health Statistics, 1981. (Data from the National Health Survey, Series 13, No. 53. DHHS publication no. [PHS]81-1714.)
51. Valenti, W. M., Meneges, M. A., Hall, C. B., et al. Nosocomial viral infections: Epidemiology and significance. *Infect. Control* 1:33, 1980.
52. Weinstein, R. A. Pseudoepidemics in hospital. *Lancet* 2:862, 1977.
53. Weinstein, R. A., and Kabins, S. A. Strategies for prevention and control of multiple drug-resistant nosocomial infection. *Am. J. Med.* 70:449, 1981.
54. Wenzel, R. P., Thompson, R. L., Landry, S. M., Russell, B. S., Miller, P. J., Ponce de Leon, S. P., and Miller, G. B. Hospital acquired infections in intensive care unit patients: An overview with emphasis on epidemics. *Infect. Control* 4:371, 1983.
55 Winn, R. E., Ward, T. T., Hartstein, A. I., et al. Epidemiological, bacteriological, and clinical observations on an interhospital outbreak of nafcillin-resistant *Staphylococcus aureus*. *Curr. Chemother.* 2:1096, 1979.

Infectious and Parasitic Diseases

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Most of the health problems identified in *Closing the Gap* relate directly or indirectly to infectious diseases. Infections and infection-related deaths are important contributors to circulatory, respiratory, and gastrointestinal diseases, to infant morbidity and mortality, and to arthritis. Infections also play an important role in morbidity and mortality that may complicate unintentional injuries, malignancies, attempted homicides or suicides, and diabetes mellitus. Microbial agents probably play a crucial role in dental caries and periodontal disease. Further, in the past few years viruses have been found to cause malignancies in humans, and other oncogenic viruses will no doubt be identified. Because of these interrelationships, the information in this report overlaps with and complements information in other position papers of the Carter Center Health Policy Project.

The effective control of each health problem will reduce the morbidity and mortality associated with infectious disease. Conversely, improvements in infection prevention and treatment will reduce the morbidity and mortality associated with other health problems.

DATA SELECTION

Infectious and parasitic diseases occupy the International Code of Diseases (ICD) codes 1–113, but at least 125 additional specific ICD codes reflect infections. Indeed, only 17 percent of all deaths from infections can be identified within ICD codes 1–113. Some ICD codes represent entities that are not always caused by infectious agents (for example, bronchitis), and some codes encompass situations in which infections may be either primary events or secondary to other inciting episodes (for example, peritonitis). These deficiencies in classification make it difficult to obtain a clear picture of the true magnitude of infections from data systems based on ICD codes. For this reason, we relied on other data to establish the burden of illness caused by infections.

To estimate the negative impact of infectious diseases in the United States, we first divided all infectious diseases into mutually exclusive groupings, then used published material and survey data from the National Center for Health Statistics to derive morbidity and mortality estimates for each grouping. The groupings were then combined to give totals for all infectious diseases. We refer to this information as the consultants' data. (The details of this data set are presented in a 361-page appendix which is on file with the Carter Center.)

The second group of data, referred to as CDC Survey Data, was collected from experts in the various divisions of the Center for Infectious Diseases and the Center for Prevention Services, Centers for Disease Control (CDC). Data were provided in 1985 on the current incidence of symptomatic infections, current and estimated future case-fatality ratios attributable to these infections, and current and estimated future overall efficiency in preventing infections caused by 117 specific microbial agents or agent groupings (Table 1, first five columns). Estimates included the morbidity and mortality averted by use of all applicable intervention strategies in both the public and private sectors. Estimates are given of current effectiveness as well as likely future effectiveness deriving from known or likely upcoming improvements in the effectiveness of various intervention strategies. Estimates of the effectiveness of prevention efforts vary in reliability. In some instances, such as nosocomial infections, these estimates are well established. In other instances, such as rotaviruses, they are based on the assumed efficacy of a yet-to-be-fully-devel-

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oped vaccine. Some estimates represent solely the cautious guesses of experts.

The data provided in the CDC survey were then used to derive additional parameters by which prevention could be assessed as described in Table 2. The resulting estimates of the numbers of cases and deaths prevented now and in the future and other derivative data appear in the last nine columns of Table 1.

The 117 specific infections or infection groupings were assigned subsequently to appropriate, mutually exclusive etiologic groups and to one or more of 13 additional infection categories that were not necessarily mutually exclusive (Table 3). In some instances, such as the category "zoonotic," all infections potentially transmissible from animals to humans were included. In other instances, such as the category "foodborne," the proportion of each specific infection acquired in that fashion was estimated as indicated in Table 3, and only that proportion of overall morbidity and mortality attributable to foodborne acquisition was included under the "foodborne" heading. "Vaccine-preventable" infection data could not be apportioned reliably in this fashion, although it is recognized that the vaccine itself may sometimes not be responsible for all prevented cases (e.g., anthrax).

In general, the CID survey data underestimated the overall magnitude of infections compared with the consultants' data, since not all known specific infectious agents were included in the survey results, and clinically diagnosed infections of known and unknown causes were encompassed in the consultants' data. Thus, we have relied primarily on the consultants' data for estimates of negative impact and on the CDC survey data for prevention estimates.

SCOPE OF THE PROBLEM

The consultants' data indicate that more than 740 million infectious disease events and nearly 200,000 attributable deaths occur annually in the United States (Table 4). Included in the total incidence are infections that, although not life threatening for persons who have normal host defenses, may result in days lost from work (or other major activities) or that incur a direct financial burden. The total number of deaths attributed to infectious diseases includes those cases for which either prevention or successful treatment would have prolonged the life of the affected person.

We estimate that each year infectious diseases result in more than 2 million years of life lost before the age of 65, more than 52 million hospital days, and nearly 2 billion days lost from work, school, and other major activities. The total direct cost of infectious diseases—not including the cost of deaths, lost wages and productivity, reactions to treatment, or other indirect costs—exceeds $17 billion annually.

The leading contributors to these negative impacts, as assessed from the CDC survey data, are listed by nonexclusive category in Table 5. The five most important contributors to mortality from infections, in decreasing order of magnitude, are: bacterial infections, lower respiratory infections (pneumonia and influenza), nosocomial infections, vaccine-preventable infections, and viral infections. The five major causes of symptomatic infections, in decreasing order of magnitude of cases, are: viral, upper respiratory, cutaneous, vaccine-preventable, and bacterial infections.

The annual monetary costs of infectious diseases derive largely from the cost of hospital care. Nosocomial infections themselves account for the greatest direct costs; they complicate the course of recovery among hospitalized patients, increase the severity of illness, increase mortality, or prolong hospital stay, thus adding substantially to the consumption of expensive hospital services.

The consultants' data indicate that nosocomial infections account for almost 12 million excess hospital days annually and pose direct costs of close to $3.5 billion. Enteric and lower respiratory infections account for 9 million and 7.5 million hospital days, respectively, and are estimated to involve direct costs of $3 billion and more than $2 billion, respectively. Genitourinary tract infections, soft-tissue infections, and upper respiratory infections are not major causes of death. However, they result in appreciable costs for outpatient care. Approximately $5 billion was spent on genitourinary tract and upper respiratory infections, and $2 billion on soft-tissue infections.

ESTIMATES OF PREVENTION GAPS

We can prevent many additional infections every year simply by expanding our current efforts in prevention and utilizing recent technological advances. Specific infections or infection groupings where more than a million additional future cases may be preventable each year include infections caused by rotaviruses, enteroviruses, Norwalk and other 27-nanometer particles, campylobacter, salmonella, and toxoplasma (Table 1, column 12 minus

Table 1. Domestic infections, United States, 1985

Disease or agent	Current incidence[a]	Case/fatality ratio (%)[b]		Effectiveness[c]		Deaths now
		Now	Future	Now	Future	
Bacterial						
Chlamydia neonatal	50,000	0.0001	0.0001	0	35	0
Psittacosis	700	1.0	0.5	40	50	7
Trachoma	100	0.0	0.0	50	50	0
Mycoplasma pneumonia	1,000,000	0.01	0.01	0	1	100
Anthrax	1	5.0	5.0	99	99	0
Bacillus cereus	5,000	0.0	0.0	80	84	0
Botulism incl. infants	200	4.0	2.0	99	99.3	8
Brucellosis	400	0.5	0.5	97	99	2
Campylobacteriosis	2,100,000	0.1	0.02	75	95	2,100
Chancroid	4,000	0.0005	0.0001	50	80	0
Chlamydia trach. gen. inf.	2,200,000	0.05	0.02	5	50	1,100
Cholera	25	1.0	0.0	95	98	3
Clost. perfringens	10,000	1.0	0.0	80	85	100
Dial. pyrogen, py. reac., sep.	5,000	0.1	0.08	10	15	5
Diphtheria	10	10.0	3.0	>99.9	>99.9	1
E. coli–enteric.	200,000	0.2	0.1	90	98	400
End. bact.–aer. and anaer.	10,000	0.05	0.05	10	10	5
Gardnerella vaginale inf.	6,000,000	0.0	0.0	1	10	0
Gonococcal infection	2,000,000	0.05	0.02	40	65	1,000
H. influ. incl. menin.	20,000	5.0	5.0	3	75	1,000
Legionellosis	75,000	15.0	15.0	3	12	11,250
Leprosy	400	1.5	1.0	4	4	6
Leptospirosis	1,100	3.0	1.0	55	60	33
Listeriosis	220	12.5	12.5	1	35	28
Meningococcal inv.	6,000	10.0	10.0	4	50	600
Misc. unclass.	1,000	0.05	0.05	0	1	1
Miscellaneous enteric	200,000	1.0	0.5	50	80	2,000
Miscellaneous zoonotic	2,000	1.0	0.5	5	10	20
Mycobacteria nontb.	10,000	0.5	0.4	1	2	50
Mycoplasma hom. genital	100,000	0.002	0.001	1	25	2
Mycoplasma/ureaplasma,	250,000	0.001	0.001	1	7.5	3
Pasteurella multocida	14,000	0.25	0.2	20	25	35
Pertussis	34,000	0.2	0.2	80	85	68
Plague	50	15.0	10.0	50	75	8
Pneumococcal invasive	400,000	8.0	6.0	4	55	32,000
Relapsing FVR.–tick/louse	264	0.5	0.5	5	5	1
Rickettsioses	2,000	5.6	5.0	5	10	112
S. aureus–TSS	4,500	3.0	1.5	75	90	135
S. aureus excl. TSS	8,900,000	0.08	0.05	3	5	7,120
Salmonellosis, nontyphi.	2,000,000	0.1	0.05	80	95	2,000
Shigella	300,000	0.2	0.2	55	75	600
Strep. Group A	10,000,000	0.03	0.02	1	1.5	3,000
Strep. Group B neonatal	7,000	20.0	15.0	5	25	1,400
Syphilis	70,000	0.08	0.01	75	85	56
Tetanus	150	30.0	30.0	98	99	45
Tuberculosis	27,000	5.0	4.0	40	40	1,350
Tularemia	402	1.0	0.8	15	17	4
Typhoid	600	6.0	5.5	95	99	36
Vibrio inf. excl. cholera	10,000	4.0	2.0	80	95	400
Yersiniosis excl. plague	5,000	0.05	0.04	0.5	2	3
Fungal						
Actinomycotic diseases	1,400	5.0	4.0	10	10	70
Aspergillosis	2,300	7.0	4.0	5	5	161
Blastomycosis	100	7.0	4.0	5	5	7
Candidiasis	4,000	10.0	2.0	5	5	400
Chromoblastomycosis	50	0.0	0.0	5	5	0
Coccidioidomycosis	8,000	4.0	2.0	10	10	320
Cryptococcosis	1,000	10.0	10.0	4	4	100
Dermatophytoses	18,000,000	0.0	0.0	1	1	0
Histoplasmosis	10,000	1.0	1.0	5	7	100
Mycetomas	25	0.0	0.0	0	0	0

	Without prevention		With prevention		Preventable annually[d]		Future incidence[e]	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
Bacterial								
Chla. neon.	50,000	0	0	0	17,500	0	32,500	0
Psittacosis	1,167	12	467	45	583	9	584	3
Trachoma	200	0	100	0	100	0	100	0
Mycopl. pneu.	1,000,000	100	0	0	10,000	1	990,000	99
Anthrax	100	5	99	5	99	5	1	0
B. cereus	25,000	0	20,000	0	21,000	0	4,000	0
Bot. in infant	20,000	800	19,800	792	19,860	797	140	3
Brucellosis	13,333	67	12,933	65	13,200	66	133	1
Campylobact.	8,400,000	8,400	6,300,000	6,300	7,980,000	8,316	420,000	84
Chancroid	8,000	0	4,000	0	6,400	0	1,600	0
Chla. tra. gen.	2,315,789	1,158	115,789	58	1,157,894	926	1,157,895	232
Cholera	500	5	475	2	490	5	10	0
C. perfring.	50,000	500	40,000	400	42,500	500	7,500	0
Dial. pyro.-sep.	5,556	6	556	1	833	2	4,723	4
Diphtheria	15,000	1,500	14,990	1,499	14,990	1,500	10	0
E. coli.-ent.	2,000,000	4,000	1,800,000	3,600	1,960,000	3,960	40,000	40
End. bac.-Ae&An	11,111	6	1,111	1	1,111	1	10,000	5
Gardner. vag.	6,060,606	0	60,606	0	606,060	0	5,454,546	0
Gonococcus	3,333,333	1,667	1,333,333	667	2,166,666	1,434	1,166,667	233
H. inf. in men	20,619	1,031	619	31	15,464	773	5,155	258
Legionellosis	77,320	11,598	2,320	348	9,278	1,392	68,042	10,206
Leprosy	417	6	17	0	16	2	401	4
Leptospirosis	2,444	73	1,344	40	1,467	63	977	10
Listeriosis	222	28	2	0	78	10	144	18
Meningo. inv.	6,250	625	250	25	3,125	312	3,125	313
Misc. unclass.	1,000	1	0	0	10	1	990	0
Misc. ent.	400,000	4,000	200,000	2,000	320,000	3,600	80,000	400
Misc. zoo.	2,105	21	105	1	211	12	1,894	9
Mycobac. nontb.	10,101	51	101	1	202	11	9,899	40
Mycop. hom. gen.	101,010	2	1,010	0	25,252	1	75,758	1
Mycop./ureapla.	252,525	3	2,525	0	18,939	1	233,586	2
Pasteur. multoc.	17,500	44	3,500	9	4,375	18	13,125	26
Pertussis	170,000	340	136,000	272	144,500	289	25,500	51
Plague	100	15	50	7	75	12	25	3
Pneumo. inv.	416,667	33,333	16,667	1,333	229,167	22,083	187,500	11,250
Relap. fever	278	1	14	0	14	0	264	1
Rickettsioses	2,105	118	105	6	210	23	1,895	95
S. aur.—TSS	18,000	540	13,500	405	16,200	513	1,800	27
S. aur. ex TSS	9,175,258	7,340	275,258	220	458,763	2,982	8,716,495	4,358
Salm.-nontyphi.	10,000,000	10,000	8,000,000	8,000	9,500,000	9,750	500,000	250
Shigellosis	666,667	1,333	366,667	733	500,000	1,000	166,667	333
Strep. gp. A	10,101,010	3,030	101,010	30	151,515	1,040	9,949,495	1,990
Strep. gp. B neo	7,638	1,528	638	128	1,974	678	5,664	850
Syphilis	280,000	224	210,000	168	238,000	220	42,000	4
Tetanus	7,500	2,250	7,350	2,205	7,425	2,227	75	23
Tuberculosis	45,000	2,250	18,000	900	18,000	1,170	27,000	1,080
Tularemia	473	5	71	1	80	2	393	3
Typhoid	12,000	720	11,400	684	11,880	713	120	7
Vibrio ex. chol.	50,000	2,000	40,000	1,600	47,500	1,950	2,500	50
Yersinio ex. pl.	5,025	3	25	0	100	1	4,925	2
Fungal								
Actinomycosis	1,556	78	156	8	156	22	1,400	56
Aspergillosis	2,421	169	121	8	121	77	2,300	92
Blastomycosis	105	7	5	0	5	3	100	4
Candidiasis	4,211	421	211	21	211	341	4,000	80
Chromoblastomy.	53	0	3	0	3	0	50	0
Coccidioidomyc.	8,889	356	889	36	889	196	8,000	160
Cryptococcosis	1,042	104	42	4	42	4	1,000	100
Dermatophytos.	18,181,818	0	181,818	0	181,818	0	18,000,000	0
Histoplasmosis	10,526	105	526	5	737	7	9,789	98
Mycetomas	25	0	0	0	0	0	25	0

Table 1. Continued

Disease or agent	Current incidence[a]	Case/fatality ratio (%)[b]		Effectiveness[c]		Deaths now
		Now	Future	Now	Future	
Paracoccidioidomycosis	2	0.0	0.0	0	3	0
Sporotrichosis	200	6.0	4.0	3	4	12
Zygomycosis	100	15.0	15.0	0	5	15
Nosocomial						
Acute care	2,200,000	1.2	1.2	6	32	26,400
Chron. care	1,900,000	1.3	1.3	1	16	24,700
Parasitic						
Amebiasis	12,000	0.3	0.01	50	50	36
Ascariasis	50,000	0.1	0.01	20	50	50
Babesiosis	20	10.0	10.0	10	10	2
Cryptosporidiosis	50	50.0	50.0	20	50	25
Echinococcosis	200	1.5	0.75	50	60	3
Filariasis	300	0.001	0.001	0	0	0
Flukes	9,000	0.001	0.0001	0	0	0
Giardiasis	120,000	0.0001	0.0001	50	90	0
Hookworm	200	0.0001	0.0001	90	95	0
Leishmaniasis	35	0.1	0.1	0	0	0
Malaria	2,500	1.0	1.0	75	98	25
Meningoencephal., amoebic	4	99.99999	50.0	0	10	4
Pediculosis	9,000,000	0.0	0.0	10	10	0
Pneumocystis	600	20.0	1.0	90	90	120
Scabies	10,000,000	0.0	0.0	1	1	0
Schistosomiasis	1,000	0.001	0.0001	75	90	0
Strongyloidiasis	10,000	1.0	1.0	1	20	100
Taeniesis/cysticercosis	1,000	1.0	0.2	50	80	10
Toxocariasis VLM	10,000	0.0001	0.0001	1	80	0
Toxoplasma congenital	3,000	15.0	2.0	5	50	450
Toxoplasmosis excl. cong.	2,300,000	0.0001	0.0001	5	50	2
Trichinosis	100,000	1.0	0.001	10	90	1,000
Trichomoniasis	5,000,000	0.0	0.0	5	10	0
Trypanosomiasis, African	2	10.0	5.0	0	0	0
Trypanosomiasis, Amer.,	1	10.0	5.0	0	0	0
Viral						
Adenovirus	10,000,000	0.01	0.01	10	15	1,000
CMV congenital	1,900	15.0	10.0	30	60	285
Colorado tick fever	2,500	0.01	0.01	1	20	0
Coronavirus	18,080,000	0.0	0.0	0	0	0
Dengue–classical	46	0.0	0.0	25	60	0
Encephalitides, N.A.	5,000	12.0	1.0	20	75	600
Enteroviral dis.–nonpolio	6,000,000	0.001	0.0001	50	80	60
Hepatitis A	48,000	0.3	0.3	40	50	144
Hepatitis B	128,000	3.0	3.0	15	80	3,840
Hepatitis non-A non-B	50,000	0.4	0.4	0	15	200
Herpes simplex (gen.)	400,000	0.00001	0.00001	5	30	0
HIV	80,000	10.0	10.0	20	50	8,000
HSV neonatal	1,000	50.0	20.0	30	80	500
Influenza	20,000,000	0.005	0.005	5	7.5	1,000
Lymphocytic choriormenin.	200	1.0	0.01	10	10	2
Measles	2,500	0.01	0.01	>99.9	>99.9	0
Mumps	10,000	0.004	0.004	99.6	99.9	0
Norwalk/other 27 nmpar.	6,000,000	0.0001	0.0001	30	50	6
Papilloma virus	3,000,000	0.001	0.001	0	0	30
Poliomyelitis	7	10.0	10.0	99.9	99.9	1
Rabies	10	99.0	99.0	99	99	10
Rhinovirus	125,000,000	0.00001	0.00001	10	10	13
Rotavirus	8,000,000	0.01	0.01	0	50	800
Rubella congenital	70	50.0	50.0	99	100	35
Rubella excl. congenital	20,000	0.0001	0.0001	98.6	99.9	0
Varicella	3,500,000	0.003	0.0002	0	2	105
Virus, respiratory sync.	7,000,000	0.005	0.005	0	30	350

	Without prevention		With current prevention		Preventable annually[d]		Future incidence[e]	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
Paracoccidioid.	2	0	0	0	0	0	2	0
Sporotrichosis	206	12	6	0	8	4	198	8
Zygomycosis	100	15	0	0	5	1	95	14
Nosocomial								
Acute care	2,340,426	28,085	140,426	1,685	748,936	8,987	1,591,490	19,098
Chron. care	1,919,192	24,950	19,192	250	307,070	3,992	1,612,122	20,958
Parasitic								
Amebiasis	24,000	72	12,000	36	12,000	71	12,000	1
Ascariasis	62,500	63	12,500	13	31,250	60	31,250	3
Babesiosis	22	2	2	0	2	0	20	2
Cryptosporidio.	63	32	13	7	31	16	32	16
Echinococcosis	400	6	200	3	240	5	160	1
Filariasis	300	0	0	0	0	0	300	0
Flukes	9,000	0	0	0	0	0	9,000	0
Giardiasis	240,000	0	120,000	0	216,000	0	24,000	0
Hookworm	2,000	0	1,800	0	1,900	0	100	0
Leishmaniasis	35	0	0	0	0	0	35	0
Malaria	10,000	100	7,500	75	9,800	98	200	2
Meningoenc.–amo.	4	4	0	0	0	2	4	2
Pediculosis	10,000,000	0	1,000,000	0	1,000,000	0	9,000,000	0
Pneumocystis	6,000	1,200	5,400	1,080	5,400	1,194	600	6
Scabies	10,101,010	0	101,010	0	101,010	0	10,000,000	0
Schistosomiasis	4,000	0	3,000	0	3,600	0	400	0
Strongyloidiasis	10,101	101	101	1	2,020	20	8,081	81
Taeniasis/cys.	2,000	20	1,000	10	1,600	19	400	1
Toxocara vlm.	10,101	0	101	0	8,081	0	2,020	0
Toxoplas. cong.	3,158	474	158	24	1,579	442	1,579	32
Toxopla. ex. con.	2,421,053	2	121,053	0	1,210,526	1	1,210,527	1
Trichinosis	111,111	1,111	11,111	111	100,000	1,111	11,111	0
Trichomoniasis	5,263,157	0	263,157	0	526,316	0	4,736,841	0
Trypanosom.–Af	2	0	0	0	0	0	2	0
Trypanosom.–Am	1	0	0	0	0	0	1	0
Viral								
Adenovirus	11,111,111	1,111	1,111,111	111	1,666,667	167	9,444,444	944
CMV congenital	2,714	407	814	122	1,629	298	1,085	109
Colorado tk. fv.	2,525	0	25	0	505	0	2,020	0
Coronavirus	18,080,000	0	0	0	0	0	18,080,000	0
Dengue–classic	61	0	15	0	37	0	24	0
Encephaliti.–NA	6,250	750	1,250	150	4,688	734	1,562	16
Enterov. non-po.	12,000,000	120	6,000,000	60	9,600,000	118	2,400,000	2
Hepatitis A	80,000	240	32,000	96	40,000	120	40,000	120
Hepatitis B	150,588	4,518	22,588	678	120,471	3,614	30,117	904
Hepa. non-A non-B	50,000	200	0	0	7,500	30	42,500	170
Herpes sim.–gen.	421,053	0	21,053	0	126,316	0	294,737	0
HIV	100,000	10,000	20,000	2,000	50,000	5,000	50,000	5,000
HSV neonatal	1,429	714	429	214	1,142	657	287	57
Influenza	21,052,632	1,053	1,052,632	53	1,578,947	79	19,473,685	974
Lymph. choriom.	222	2	22	0	22	2	200	0
Measles	3,500,000	350	3,497,500	350	3,497,500	350	2,500	0
Mumps	2,500,000	100	2,490,000	100	2,497,500	100	2,500	0
Nor./oth. 27 nmp.	8,571,429	9	2,571,429	3	4,285,714	5	4,285,715	4
Papillomavirus	3,000,000	30	0	0	0	0	3,000,000	30
Poliomyelitis	7,000	700	6,993	699	6,993	699	7	1
Rabies	1,000	990	990	980	990	980	10	10
Rhinovirus	138,888,889	14	13,888,889	1	13,888,889	2	125,000,000	12
Rotavirus	8,000,000	800	0	0	4,000,000	400	4,000,000	400
Rubella congen.	7,000	3,500	6,930	3,465	7,000	3,500	0	0
Rubella ex. con.	1,428,571	1	1,408,571	1	1,427,142	1	1,429	0
Varicella	3,500,000	105	0	0	70,000	98	3,430,000	7
Virus–resp. syn.	7,000,000	350	0	0	2,100,000	105	4,900,000	245

Data from CDC survey

[a] Estimated true annual number of clinically significant infections.

[b] Attributable to the infection.

[c] Total effectiveness, in percent, of all public and private interventions in preventing cases.

[d] Assuming future effectiveness and case-fatality ratios.

[e] Unprevented morbidity and mortality.

column 10). Similarly, more than a thousand additional deaths might be preventable each year by improved prevention of infections caused by pneumococci, HIV-1 (human immunodeficiency virus–type 1), hepatitis B, *Staphylococcus aureus*, campylobacter, salmonella, and miscellaneous bacterial enteric pathogens (Table 1, column 13 versus column 11).

Similar analyses can be applied to categories of infection (Figure 1). Substantial increments are possible in the number of prevented cases of enteric (13 million), viral (12.9 million), bacterial (6.6 million), vaccine-preventable (5.4 million), zoonotic (4.3 million), foodborne (3.5 million), lower respiratory (3.0 million), and sexually transmitted infectious diseases (2.9 million). Marked increases in the proportion of infections prevented (cases prevented in the future divided by cases prevented now) are envisioned for nosocomial infections (6.9-fold), meningitis (5.1-fold), perinatal infections (3.4-fold but not shown in Figure 1 because numbers are too small for the scale used), lower respiratory infections (3.3-fold), sexually transmitted infections (2.5-fold), and day-care-center-related infections (2.4-fold).

Impressive gains in the numbers of deaths prevented (in decreasing order) can be achieved (Figure 2) with bacterial diseases (35,900), vaccine-preventable infections (25,300), lower respiratory infections (23,300), and nosocomial infections (11,100). The largest proportional gains in deaths prevented are envisioned with meningitis (10.5-fold), fungal infections (7.0-fold), nosocomial infections (6.8-fold), lower respiratory infections (6.7-fold), cutaneous infections (5.9-fold), day-care-center-related infections (4.2-fold), and vaccine-preventable infections (3.1-fold).

Prevention of infection translates readily into economic savings. The results of applying current and achievable effectiveness in preventing cases (from CDC survey data) to negative impacts (from the consultants' data) are depicted in Figure 3. Despite impressive accomplishments in prevention, substantial gaps between what we are achieving and what we could achieve in preventing infection remain. For example, we estimate that an additional $1.3 billion in direct costs, 56 million cases of infection, 3.2 million hospital days, and 144 million disability days could be saved merely by broader application of available or soon-to-be-available interventions.

The estimated gaps between current and future achievements in preventing deaths and reducing the number of years of life lost are shown in Figure 4. An additional 80,000 deaths and nearly 1 million years of life lost may be saved annually. Indeed, more than twice as many deaths as are annually prevented now are likely to be prevented in the future. These gains result both from improved primary prevention of cases and from improved diagnosis and treatment of cases that do occur. However, such gains could occur simultaneously with and be offset by increases in unprecedented deaths from any expanding lethal infection problem. Only HIV infections are foreseen to pose such a threat.

Table 2. Derivations of additional parameters from CDC survey data

Deaths now	= (*current cases*) (*current case-fatality ratio*[a,b])
Cases in absence of prevention	= (*current cases*) ÷ (1 − *current effectiveness*[a])
Deaths in absence of prevention	= (cases in absence of prevention) (*current case-fatality-ratio*[a])
Cases prevented now	= (cases in absence of prevention) (*current effectiveness*[a])
Deaths prevented now	= (deaths in absence of prevention) − (deaths now)
Cases prevented in the future	= (cases in absence of prevention) (*future effectiveness*[a])
Future annual cases	= (cases in absence of prevention) − (cases prevented in the future)
Future annual deaths	= (future annual cases) (*future case-fatality-ratio*[a])
Deaths prevented in the future	= (deaths in absence of prevention) − (future annual deaths)

[a] Expressed as a decimal.
[b] Italics: data provided by CDC survey.

NARROWING THE GAPS

Each prevention estimate in the foregoing material depends on the composite efficacy of applicable interventions. Thus, a detailed scrutiny of each intervention capable of preventing morbidity or mortality from infection seems appropriate.

Intervention strategies for preventing infectious diseases can be divided into two basic groups: (1) strategies that are generically applicable to all infectious diseases (indeed, to all diseases), such as disease surveillance, epidemiologic investigations, diagnosis, and treatment; and (2) strategies that are applicable to subsets of infectious diseases, such as immunization, chemo- or immunoprophylaxis,

screening, contact tracing, control of environmental sources and vehicles (food, water, air, medical devices), control of insect and animal reservoirs and vectors, isolation precautions and quarantine, and behavior modification. These 12 strategies interact synergistically with each other.

Rapid and accurate identification, both of individual cases and of clusters of disease, is important in preventing new cases as well as in initiating early and appropriate treatment of those who are already ill. The potential for the rapid identification of specific infectious diseases has been greatly enhanced in recent years by developments in the microbiology laboratory and by the revolution in data pro-

Table 3. Domestic infections, United States, 1985: percentage attributed to various infection categories

Disease or agent	Pneumonia and lower respiratory	Upper respiratory	Perinatal	Zoonotic	Cutaneous	Foodborne	Enteric	Waterborne	STD	Meningitis	Vectorborne	Day care	Vaccine preventable
Bacterial													
Chlamydia neonatal	100		100										
Psittacosis	100			100									
Trachoma					100								
Mycoplasma pneumonia	100												
Anthrax				100									100
Bacillus cereus						100	100						
Botulism incl infants						90	100						
Brucellosis				100		5							
Campylobacteriosis				100		100	100	15					
Chancroid									100				
Chlamydia trach. gen. inf.									100				
Cholera						100	100						
Clost. perfringens						100	100						
Dial. pyrogen, py reac, sep.													
Diphtheria		100								•			100
E. coli–enteric.						25	100	75				5	
End. bact.–aer. and anaer.	50									5			
Gardnerella vaginale inf.									100				
Gonococcal infection									100				
H. influ. incl. menin.	12									50		30	100
Legionellosis	98												
Leprosy					100								
Leptospirosis				100									
Listeriosis				100						60			
Meningococcal inv.										80		5	100
Misc. unclass.	1									1			
Miscellaneous enteric						95	100	5					
Miscellaneous zoonotic				100									
Mycobacteria nontb.	20									1			
Mycoplasma hom. genital									100				
Mycoplasma/ureaplasma									100				
Pasteurella multocida				100									
Pertussis	100											0.5	100
Plague	20			100						10	100		
Pneumococcal invasive	95									5		5	100
Relapsing FVR – tick/louse				100							100		
Rickettsioses			•								100		
S. aureus–TSS													
S. aureus excl. TSS	1				75	17				1		2	
Salmonellosis, nontyphi				100		96	100	3				1	
Shigella						30	100	10				25	
Strep Group A	1	75			25	5			\	1		2	
Strep. Group B neonatal	20		100							50			
Syphilis									100				
Tetanus													100
Tuberculosis	85									0.6			
Tularemia				100							100		
Typhoid						80	100	10					
Vibrio inf excl. cholera						90	100	10					
Yersiniosis excl. plague				100		65		35					
Fungal													
Actinomycotic diseases													
Aspergillosis	100												
Blastomycosis	95												
Candidiasis												5	
Chromoblastomycosis					100								

Table 3. Continued

Disease or agent	Pneumonia and lower respiratory	Upper respiratory	Perinatal	Zoonotic	Cutaneous	Foodborne	Enteric	Waterborne	STD	Meningitis	Vectorborne	Day care	Vaccine preventable
Coccidioidomycosis	100												
Cryptococcosis										60			
Dermatophytoses					100							5	
Histoplasmosis	100												
Mycetomas					100								
Paracoccidioidomycosis	100												
Sporotrichosis					100								
Zygomycosis					100								
Nosocomial													
Acute care	15				6								
Chron care	11				16		8						
Parasitic													
Amebiasis							100					0 5	
Ascariasis							100					5	
Babesiosis											100		
Cryptosporidiosis							100					2	
Echinococcosis				100									
Filariasis											100		
Flukes							100						
Giardiasis							100	60				15	
Hookworm							100						
Leishmaniasis					90						100		
Malaria											100		100
Meningoencephal , amoebic										100			
Pediculosis					100							0 5	
Pneumocystis	100												
Scabies					100							0.5	
Schistosomiasis													
Strongyloidiasis							100						
Taeniesis/cysticercosis				100									
Toxocariasis VLM				100									
Toxoplasma congenital			100										
Toxoplasmosis excl cong				100									
Trichinosis				100		100							
Trichomoniasis									100				
Trypanosomiasis, African											100		
Trypanosomiasis, Amer.											100		
Viral													
Adenovirus		100										2	100
CMV congenital			100										
Colorado tick fever											100		
Coronavirus		100										1	
Dengue-classical											100		
Encephalitides, N.A.											100		
Enteroviral dis -nonpolio							100					2	
Hepatitis A						10	100					15	
Hepatitis B			1										100
Hepatitis non-A non-B													
Herpes simplex (gen.)					100				100				
HIV			1						75				
HSV neonatal			100										
Influenza	100											1	100
Lymphocytic chonormenin				100						95			
Measles					100								100
Mumps		100											100
Norwalk/other 27 nmpar.							100	5				0.5	
Papilloma virus					100				5				
Poliomyelitis							100						100
Rabies				100									100
Rhinovirus		100											
Rotavirus							100					10	100
Rubella congenital			100										100
Rubella excl. congenital					100								100
Varicella					100								
Virus, respiratory sync	100											5	

Table 4. The annual negative impact of infections, United States: consultants' data

Cases	742,248,261
Deaths	194,704
Years lost before the age of 65	2,192,370
Hospital days	42,029,624
Disability days[a]	1,901,847,705
Cost[b]	$17,191,400,000

[a] Days lost from work, school, preschool, or housekeeping.
[b] Excludes costs of death, sequelae of infections, home care, and reactions to treatment.

Table 5. Current annual impacts by infection category, United States: CDC survey data

Infection group	Deaths[a]	Incidence[b]
Bacterial	68,200	36,026,000
Cutaneous	11,800	53,534,000
Day-care-related	2,600	3,713,000
Enteric	10,800	25,227,000
Food-borne	9,100	6,496,000
Fungi	1,200	18,027,000
Meningitis	3,500	229,000
Nosocomial	51,100	4,100,000
Parasitic	1,800	26,620,000
Perinatal	2,800	65,000
Pneumonia and lower respiratory	52,000	29,321,000
Sexually transmitted	8,200	16,234,000
Upper respiratory	3,300	160,590,000
Vaccine-preventable	40,400	38,623,000
Vector-borne	800	13,000
Viral	17,000	207,329,000
Water-borne	900	940,000
Zoonotic	5,300	6,536,000

[a] Rounded to the nearest 100.
[b] Rounded to the nearest 1,000.

cessing. Advances in molecular biology and microbial genetics have led to the development of rapid, sensitive, and specific diagnostic tests, and additional discoveries are imminent.

Surveillance and epidemiologic investigations establish risk factors for disease by defining the sources of infection, the means by which the causative agent is spread, and the host factors that make people susceptible to infection. Surveillance identifies new problems, focuses control efforts, and provides a means to monitor the effectiveness of control efforts.

Our ability to perform surveillance has been greatly enhanced by advances in data processing, which permit rapid transmission of data among public health agencies and health care providers and allow for immediate analysis of large amounts of data as they are gathered. Disease surveillance and investigation, combined with new diagnostic techniques, permit the other interventions discussed to be performed efficiently and effectively for specific infections. Potentially communicable persons and reservoirs within the environment can be identified, treatment or decontamination can be

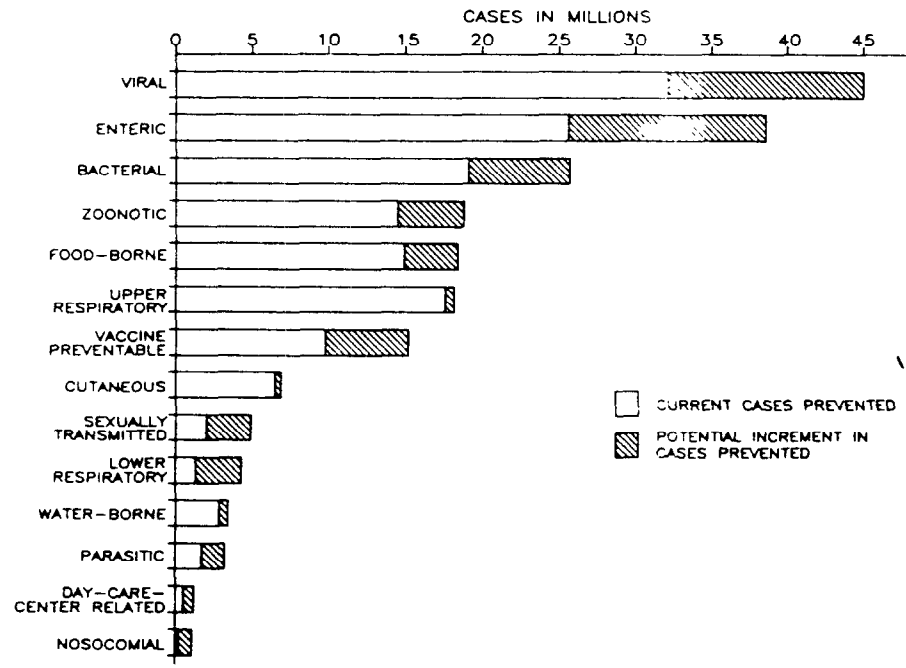


Figure 1. The prevention of infectious diseases in the United States, current and potential: number of cases prevented annually, by infection categories, based on CDC survey data.

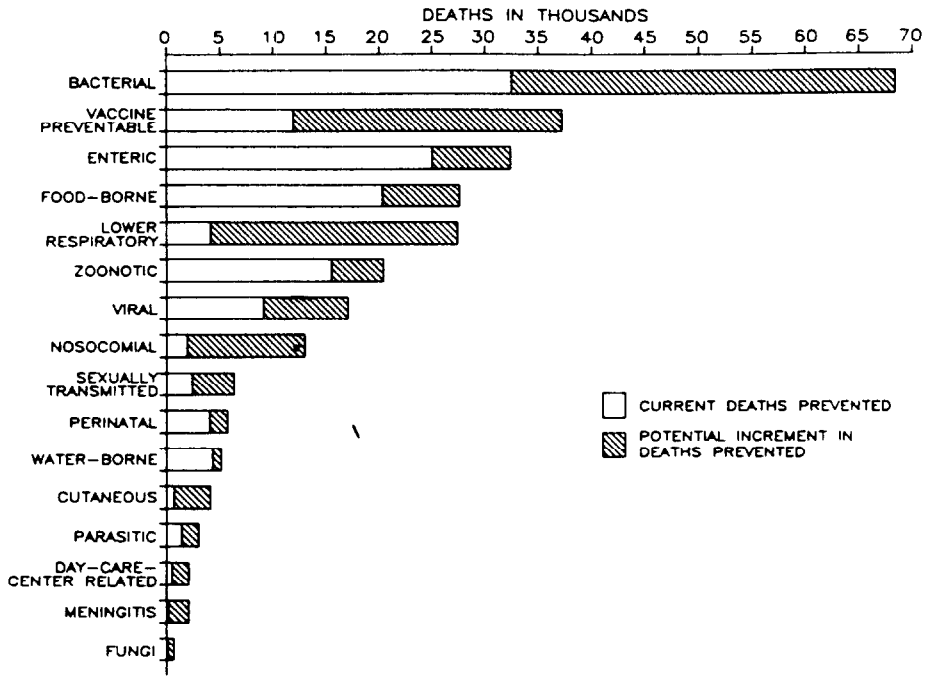
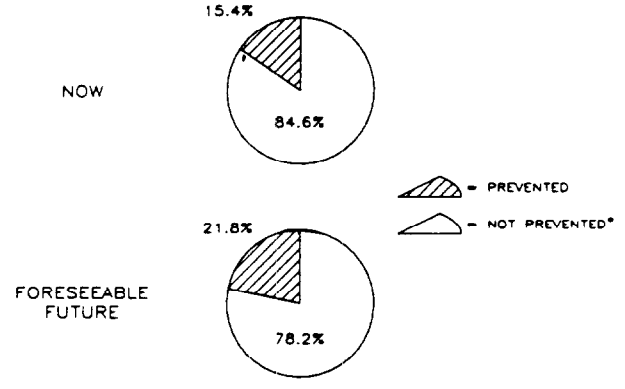


Figure 2. The prevention of infectious diseases in the United States, current and potential: number of deaths prevented annually, by infection categories, based on CDC survey data.

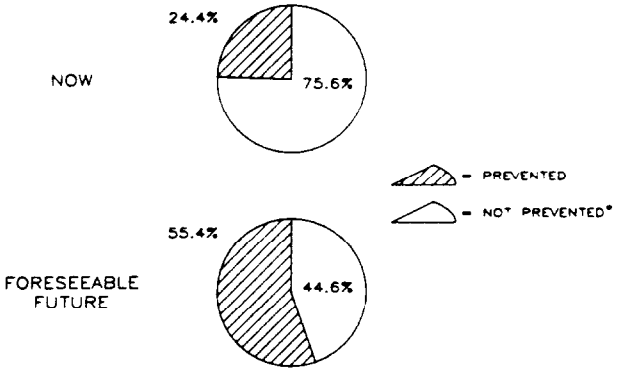
initiated, and, when necessary, chemoprophylaxis and immunoprophylaxis can be offered to exposed and potentially exposed persons. Disease investigations continue to identify new sources of transmission for well-known agents.



NEGATIVE IMPACTS	PREVENTED		NOT PREVENTED	
	NOW**	FUTURE**	NOW*	FUTURE**
COSTS (BILLIONS)	3.1	4.4	17.2	15 9
CASES (MILLIONS)	135.1	191.3	742 2	686 0
HOSPITAL DAYS (MILLIONS)	7.6	10.8	42.0	38.8
DISABILITY DAYS (MILLIONS)	346.2	490.1	1901.8	1757 9

*Figure 3. Annual morbidity from infections, United States. *Unprevented morbidity is equivalent to the current negative morbidity impacts shown in Table 4. **Derived from above prevention estimates and current negative morbidity impacts.*

Advances in molecular biology offer great opportunities to improve the immunogenicity, safety, and quantity of older vaccines and to develop highly effective and safe new ones. The production of more effective vaccines with a longer duration of protection in large quantities at low cost may ulti-



NEGATIVE IMPACTS	PREVENTED		NOT PREVENTED	
	NOW**	FUTURE**	NOW*	FUTURE**
DEATHS (THOUSANDS)	62.8	142 7	194.7	114.8
YEARS OF LIFE LOST (MILLIONS)	.7	1.6	2.2	1.3

*Figure 4. Annual mortality from infections, United States. *Unprevented mortality is equivalent to current negative mortality impacts in Table 4. **Derived from above prevention estimates and current negative mortality impacts.*

mately make routine immunization of the entire population with a variety of vaccines (e.g., hepatitis B, meningococcal vaccine) economically feasible. Improved vaccines might also play major roles in management of persons known or likely to be exposed to particular infectious agents, and make it possible to develop highly effective immunoprophylactic agents.

Ongoing research has led to new antimicrobial agents, especially antiviral and antifungal drugs, that are available or undergoing experimental trials. These drugs offer the promise of successful therapy for persons who have infections that until now have been untreatable. Such therapy will lessen the burden of illness and reduce the likelihood that the diseases will be communicated to others. Surveillance of microbial resistance of infectious agents improves the appropriateness and thus the effectiveness of both treatment and prophylaxis.

Contact tracing is often associated with finding persons exposed to sexually transmitted diseases. This method may also be used to identify people who are at risk for other infections, such as infections caused by eating contaminated food, by contact with persons who have communicable diseases in day care centers or institutions, or by exposure to contaminated pharmaceutical products and medical devices. The rapid institution of effective therapy in persons already infected, at times before the onset of symptoms, may be critical to the prevention of disability, mortality, and spread of infection.

Screening, the systematic and routine use of tests to detect infection, is especially useful when a large percentage of infected persons are without clinical symptoms, and the progress or spread of the infection can be influenced if its presence is known. Infections detected through screening contribute to surveillance and contact tracing and may lead to chemo- or immunoprophylaxis, immunization, or counseling to influence changes in behavior.

Environmental control is the process of ensuring that food, water, and air do not become a source of infectious diseases. Examples of areas where further progress can be made include finding ways to reduce antibiotic-resistant salmonella in meat products and developing new approaches to reduce the hazard of legionella in cooling towers and potable water.

The control of insects and animals involved in arthropod-borne and zoonotic infections continues to be of great importance. Expanded efforts at prevention will further reduce the impact of illnesses as diverse as campylobacteriosis, plague, rabies, and infectious encephalitis.

Quarantine, the detection and total physical isolation of infected persons, has some applicability in preventing the introduction of certain hazardous communicable infections from other parts of the world into the United States. However, it plays little part in the prevention of domestic infections. Isolation, the implementation of precautions appropriate for the known ways in which infections are spread, is effective in preventing spread from patients to other patients, hospital staff, and visitors.

The final intervention strategy is behavior modification. Convincing people to alter aspects of their lifestyles that predispose them to infectious diseases or that enable them to spread infections to others is difficult. Personal hygiene, sexual behavior, and the use of tobacco products, alcoholic beverages, and licit and ilicit drugs, as well as a person's willingness to make appropriate use of health care providers and public health services, profoundly affect one's risk of becoming a victim of an infectious disease.

We believe that the interventions likely to have the most impact on closing the demonstrated gap between current achievements and future attainments in preventing cases and deaths from infections include improved epidemiologic services, improved diagnosis and treatment, more widespread immunization, more effective environmental control, and more effective behavior modification. The risks for infectious disease are multifactorial, and a broad-based approach to prevention that uses many intervention strategies will yield the best results.

SUMMARY

More than 740 million symptomatic infections occur annually in the United States, resulting in 200,000 deaths a year. Such infections result in more than $17 billion annually in direct costs, not including cost of deaths, lost wages and productivity, reactions to treatment, and other indirect costs. About 135 million infections, 63,000 deaths, and $3.1 billion in direct costs are now prevented annually, but an additional 56 million cases, 80,000 deaths, and $1.3 billion in direct costs could be prevented by using currently and soon-to-be-available interventions.

The advances made in preventing infectious diseases during this century have been among the most dramatic developments in medicine. However, it is likely that we will be able in the future to prevent nearly one and a half times more infections

and more than twice as many deaths as can be prevented now. Indeed, it is conceivable that we will be able during the next decade to match the entire accumulated progress to date in preventing morbidity and mortality from infections. Unfortunately, the presently expanding mortality from HIV infection will lessen the net effects of these remarkable advances in prevention.

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