Major Trends in the Microbial Etiology of Nosocomial Infection

DENNIS R. SCHABERG, M.D., *Ann Arbor, Michigan,* DAVID H. CULVER, PH.D., ROBERT P. GAYNES, M.D., *Atlanta, Georgia*

To determine trends in the microbial etiology of nosocomial infections in the 1980s, surveillance data on the microbiology of documented nosocomial infection reported to the National Nosocomial Infections Surveillance System and from the University of Michigan Hospital were analyzed. Antimicrobial susceptibility data on selected pathogens from both sources were also reviewed. Overall, *Escherichia coli* decreased from 23% of infections in 1980 to 16% in 1986–1989, *Klebsiella pneumoniae* dropped from 7% to 5%, whereas coagulase negative staphylococci increased from 4% to 9% and *Candida albicans* increased from 2% to 5%. *Staphylococcus aureus, Pseudomonas aeruginosa,* Enterobacter species and enterococci had minor increases, but antimicrobial resistant strains for these pathogens as well as coagulase-negative staphylococci were seen more frequently. In contrast to the 1970s, major shifts in the etiology of nosocomial infection have occurred in the decade of the 1980s. Taken as a whole, the shifts are away from more easily treated pathogens toward more resistant pathogens with fewer options for therapy. These shifts underscore the continued need for prevention and control to accompany new developments in therapy.

From the Division of Infectious Diseases, Department of Internal Medicine, and Ann Arbor Veterans Administration Medical Center, University of Michigan Medical Center, Ann Arbor, Michigan, and Hospital Infections Program, Centers for Disease Control, Atlanta, Georgia.

Reprint requests should be addressed to Dennis R. Schaberg, M.D., University of Michigan Medical Center, 3110 Taubman Center, Box 0368, 1500 East Medical Center Drive, Ann Arbor, Michigan 48109-0368.

Nosocomial infection remains a significant consequence of hospitalization. Estimates are that from 3% to 5% of patients leave the hospital having acquired infection, depending on case mix, hospital size, and multiple other factors [1]. Examination of the microbial etiology of these infections provides important information in day-to-day decision making in individual hospitals regarding potential outbreaks, unusual pathogens, antimicrobial resistance, and local trends in the etiology of infection. It is also useful periodically to examine trends in the etiology of infection over more prolonged time periods to detect shifts in the cause of infection. This report uses two sources of data, pooled data from participants in the National Nosocomial Infections Surveillance (NNIS) System of the Centers for Disease Control (CDC) and single hospital data from a large tertiary referral teaching hospital, the University of Michigan Hospital, to examine trends in etiology of hospital-acquired infection in the decade of the 1980s.

METHODS

The NNIS system was established in January 1970 and is currently the only nationwide source of information on nosocomial infections in the United States [2,3]. This report examines surveillance among NNIS hospitals performing hospital-wide surveillance from 1980 to 1989. Patients were monitored for all nosocomial infections at all body sites. Standardized definitions for infection are provided to the participating hospitals [4] but a variety of case-finding methods were used. Various methods for performing antimicrobial susceptibilities, including disk diffusion, macrobroth, and microdilution are used, but each hospital must provide evidence of proficiency in the method being used. Data from each hospital are submitted monthly to the CDC.

The percentage of coagulase-negative staphylococci that were reported to be resistant to methicillin, oxacillin, or nafcillin (MRSE) was determined by estimating the mean percentage for 1989 for all hospitals that reported data. Hospitals that did not report susceptibility results for at least 20 coagulase-negative staphylococci in the year were ex-

TABLE I

Pathogen Distribution for Major Sites of Nosocomial Infection, National Nosocomial Infections Surveillance System, 1986–1989

Pathogen	Urinary Tract Infection	Wound	Pneumonia	Bloodstream	Total
E. coli	11,135 (26)*	1,951 (10)	946 (6)	733 (6)	14,765 (16)
Enterococci	6,720 (16)	2,645 (13)	342 (2)	1,037 (8)	10,744 (12)
P. aeruginosa	5,127 (12)	1,668 (8)	2,598 (17)	543 (4)	9,936 (11)
• *S. aureus*	823 (2)	3,439 (17)	2,401 (16)	• 1,984 (16)	8,647 (10)
Coagulase negative staphylococci	1,634 (4)	2,472 (12)	293 (2)	3,384 (27)	7,783 (9)
Enterobacter sp.	2,339 (6)	1,529 (8)	1,625 (11)	610 (5)	6,103 (7)
K. pneumoniae	2,664 (6)	618 (3)	1,042 (7)	548 (4)	4,872 (5)
C. albicans	2,978 (7)	481 (2)	615 (4)	617 (5)	4,691 (5)
P. mirabilis	2,312 (5)	712 (4)	503 (3)	105 (1)	3,632 (4)
Streptococcal species	207 (0)	539 (3)	231 (1)	465 (4)	1,442 (2)
Citrobacter sp.	812 (2)	321 (2)	226 (1)	82 (1)	1,441 (2)
Candida sp.	853 (2)	81 (0)	109 (1)	330 (3)	1,373 (2)
S. marcescens	367 (1)	271 (1)	579 (4)	152 (1)	1,369 (2)

*Number (percent). Note: a site may have up to four pathogens.

cluded from the analysis. Changes in percent of MRSE between two consecutive years were estimated using only the data from hospitals that reported to NNIS in both years. In this way, the estimated change in percent MRSE over the period 1980–1989 was not biased by the effects of sample migration, i.e., hospitals joining and leaving NNIS.

The University of Michigan Hospital is a 588 bed adult medical and surgical tertiary care hospital. Separate hospitals house the obstetrics service, the neonatal unit, and pediatric patients, which are not included in the data in this report. Definitions for nosocomial infection identical to those in NNIS are used [4]. Antimicrobial susceptibilities are performed by microbroth dilution.

RESULTS

When the overall pathogen distribution for the four major sites of hospital-acquired infections reported to NNIS from 1986–1989 is examined, *Escherichia coli* remains the most common isolate (**Table I**). The other pathogens accounting for greater than 10% of infections are enterococci, *Pseudomonas aeruginosa,* and *Staphylococcus aureus*. These same four pathogens also dominate at the University of Michigan Hospital but the order differs slightly. *E. coli* also is most common, accounting for 23% of infections, but *P. aeruginosa* is second at 20% followed by the other two. Although *E. coli* still is the most frequent isolate, it has dropped in overall frequency comparing NNIS data from 1980 with 1986–1989 (**Figure 1**). Two of the top 10 pathogens have dropped in percentage, *E. coli* from 23% to 16% and *Klebsiella pneumoniae* from 7% to 5% of isolates. In contrast, coagulase-negative staphylococci have increased from 4% to 9%, almost all as a function of increase in bloodstream infections. *Candida albicans* also increased from 2% in 1980 to 5% in 1986–1989, with the increase occurring across all major sites of infection. Slight increases have occurred with *S. aureus, P. aeruginosa,* enterococci and *Enterobacter* species, with the overall change of 1–2% in each instance.

In addition to the overall changes noted, there have been changes as well within a given genus, in particular in antimicrobial resistance phenotype. For example, 1982 was the first full year of susceptibility data for cefotaxime at the University of Michigan with 91% of isolates of *P. aeruginosa* susceptible in contrast to only 65% in 1989 and 93% of *Enterobacter cloacae* susceptible in 1982 versus 76% in 1989. Similarly, 97% of *P. aeruginosa* were sensitive to gentamicin in 1982 versus 88% in 1989. Changes in phenotype in the gram-positive nosocomial pathogens have been seen as well. At the University of Michigan, in 1980 less than 1% of *S. aureus* isolates were methicillin-resistant, but in 1989 17% were resistant. In 1981, a single clinical isolate of high-level gentamicin-resistant enterococci was identified in our hospital. In 1989, 20% of all enterococcal isolates displayed this phenotype. Currently, more than 60% of coagulase-negative staphylococci at the University hospital are methicillin-resistant. This increasing resistance is also reflected in the pooled data from NNIS (**Figure 2**).

COMMENTS

Surveillance, including bacteriologic surveillance to provide background information in order to recognize nosocomial infection problems requiring control measures or interventions, remains important to current infection control efforts in hospitals. As has been noted by Stamm and coworkers [5], the bacteriology of epidemic nosocomial infection is dramatically different from endemic infection. The trends noted in this report pool bacteriology from both types of infections but endemic infections overwhelm any impact of out-

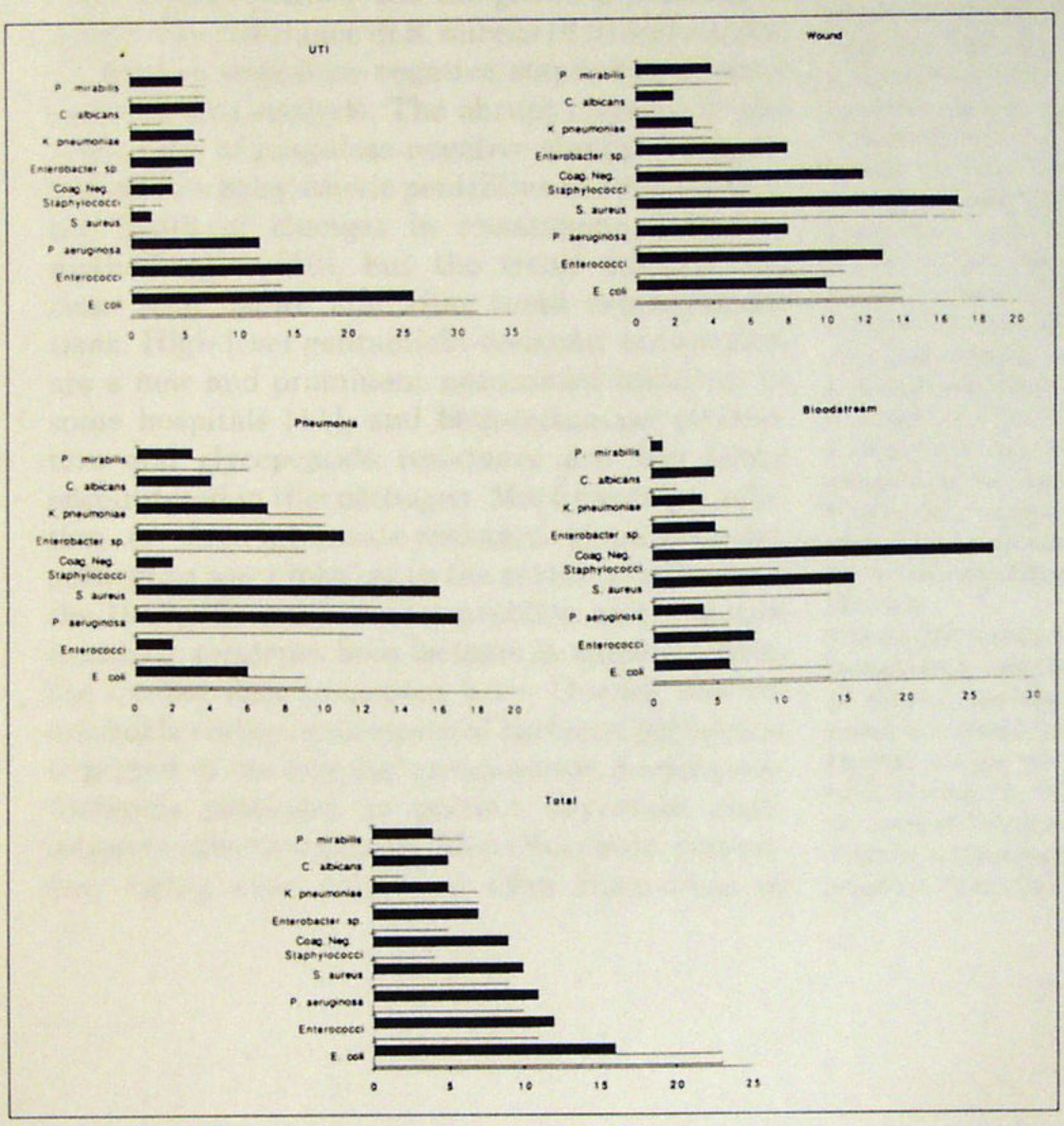

Figure 1. Comparative percentage of pathogen distribution for nosocomial infections, National Nosocomial Infections Surveillance System, 1980 (**white bars**) versus 1986–89 (**black bars**). UTI = urinary tract infection.

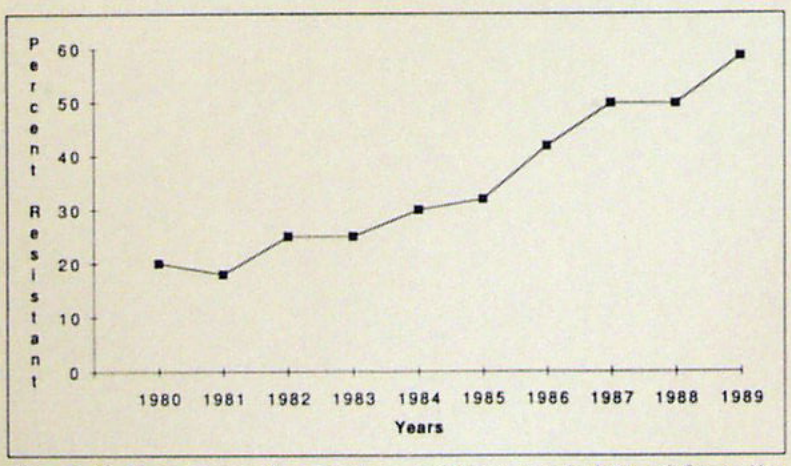

Figure 2. Proportion of coagulase-negative staphylococci from the National Nosocomial Infections Surveillance System reported as resistant to methicillin, oxacillin, or nafcillin, 1980–1989 (n = 27,150).

breaks. The changes noted thus appear to be gradual shifts in the pathogens isolated from hospital-acquired infection. It should be noted that these shifts are in contrast to similar analysis over the last decade where no secular or periodic trends were found [6].

One explanation for the shifts noted would be selective prevention of infections due to *E. coli* and *K. pneumoniae*. These organisms do share in common a similar reservoir, the gastrointestinal tract, and endogenous acquisition as mode of infection. Antimicrobial prophylaxis or therapy with agents active against these organisms but not more resistant organisms, such as *Enterobacter* species, if used widely might explain the shift away from them as causes of infection. An antimicrobial group with such a spectrum is the so-called first-generation cephalosporins, which are often chosen as prophylaxis for a variety of procedures in hospitals, but whether this explains the observed shift away from *Klebsiella* and *E. coli* is speculation.

Another major change is the increasing importance of coagulase-negative staphylococci. This change is almost entirely due to the increase in bloodstream infection. This may in part be due to the growing appreciation of this organism as a pathogen [7] and thus a willingness to report positive cultures as true infections. It also may in part be due to the increasing reliance on a variety of devices, especially intravascular devices, to aid in the care of seriously ill hospital patients. A report by Gaynes *et al* [2] examines this secular trend.

The most disturbing trend occurring in the 1980s was a move away from more susceptible toward more resistant pathogens. This occurred both between and within genera. Genera that tend

to be more susceptible to antimicrobials, *Proteus mirabilis*, *E. coli*, and *K. pneumoniae*, all decreased in prevalence, whereas *Enterobacter*, *Pseudomonas*, *Enterococcus*, and *Candida* increased. Within genera, traditional etiologies in some instances changed little, but phenotype did. Several studies have already pointed out the growing problem of methicillin resistance in *S. aureus* [8,9] and similar changes in coagulase-negative staphylococci were found in this analysis. The abrupt increase in the proportion of coagulase-negative staphylococci resistant to semisynthetic penicillins in 1986 is likely the result of changes in recommended testing methodologies [10], but the trend upward was clear both before and after these recommendations. High-level gentamicin-resistant enterococci are a new and prominent nosocomial infection in some hospitals [11], and beta-lactamase production and glycopeptide resistance are also being encountered in this pathogen. More frequent isolation of aminoglycoside-resistant gram-negative pathogens was hinted at in the review of data from the 1970s [6] and a similar problem with the new extended spectrum beta-lactams is apparent from the limited data presented here. Overall, the remarkable ability of nosocomial bacterial pathogens to persist in the hospital environment despite new therapies continues to present important challenges to infection control. More than ever, prevention rather than treatment after occurrence of nosocomial infection should remain a primary goal.

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