Nosocomial Infections in Pediatric Intensive Care Units in the United States

Michael J. Richards, MB, BS, FRACP; Jonathan R. Edwards, MS; David H. Culver, PhD; Robert P. Gaynes, MD; and the National Nosocomial Infections Surveillance System

ABSTRACT. Objectives. To describe the epidemiology of nosocomial infections in pediatric intensive care units (ICUs) in the United States.

Background. Patient and ICU characteristics in pediatric ICUs suggest the pattern of nosocomial infections experienced may differ from that seen in adult ICUs.

Methods. Data were collected between January 1992 and December 1997 from 61 pediatric ICUs in the United States using the standard surveillance protocols and nosocomial infection site definitions of the National Nosocomial Infections Surveillance System’s ICU surveillance component.

Results. Data on 110,709 patients with 6,290 nosocomial infections were analyzed. Primary bloodstream infections (28%), pneumonia (21%), and urinary tract infections (15%) were the most frequent and were almost always associated with an invasive device. Primary bloodstream infections and surgical site infections were reported more frequently in infants aged 2 months or less as compared with older children. Urinary tract infections were reported more frequently in children >5 years old compared with younger children. Coagulase-negative staphylococci (38%) were the most common bloodstream isolates, and aerobic Gram-negative bacilli were reported in 25% of primary bloodstream infections. Pseudomonas aeruginosa (22%) was the most common species reported from pneumonia and Escherichia coli (19%), from urinary tract infections. Enterobacter spp. were isolated with increasing frequency from pneumonia and were the most common Gram-negative isolates from bloodstream infections. Device-associated infection rates for bloodstream infections, pneumonia, and urinary tract infections did not correlate with length of stay, the number of hospital beds, or season.

Conclusions. In pediatric ICUs, bloodstream infections were the most common nosocomial infection. The distribution of infection sites and pathogens differed with age and from that reported from adult ICUs. Device-associated infection rates were the best rates currently available for comparisons between units, because they were not associated with length of stay, the number of beds in the hospital, or season. Pediatrics 1999;103(4).

METHODS

Data were collected on patients in PICUs in the NNIS system between January 1992 and December 1997. A PICU was defined as a unit in which >80% of patients were under the age of 18, but was not dedicated to the care of neonatal infants. The surveillance methods have been previously described. All patients in the ICU were monitored for nosocomial infection at all body sites for a period of at least 1 calendar month. On average, 9 months of data were contributed in a 12-month period. Standard Centers for Disease Control and Prevention/NNIS definitions of infection were used. The data collected on each infection included the date and site of infection, and patient demographics. In the NNIS system, primary bloodstream infection included both laboratory-confirmed infections, with a positive blood culture not related to infection at another site (excluding phlebitis), and clinical sepsis. Clinical sepsis was reported when a physician instituted treatment for sepsis and there was no apparent infection at another site, and a negative blood culture or no blood culture was taken. If a urinary tract infection (UTI) was associated with catheterization, pneumonia with mechanical ventilation, or bloodstream infection with a central intravascular line, it was recorded. Nosocomial infections were considered ICU-associated, if they developed in the ICU or within 48 hours of discharge from the unit, unless the clinical evidence strongly suggested otherwise. For patients with nosocomial infections in the PICU, age was collected. The patients were divided into five age groups as follows: newborn infants age 2 months or less, infants >2 months but <1 year, preschool children 1 year to 5 years, children >5 years to 12 years, and

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Table 1. Specific Infection Site Distribution in Pediatric Intensive Care Unit Patients (NNIS 1992–1997)

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<th>Infection</th>
<th>≤2 Months</th>
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<th>&gt;5 Years and ≤12 Years</th>
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<td>Pneumonia</td>
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<tr>
<td>Urinary tract infections</td>
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<td>Other</td>
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<td>Surgical site infections</td>
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<td>Skin</td>
<td>58</td>
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<td>Mediastinitis</td>
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<td>Eye, ear, nose, and throat infections</td>
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Abbreviations: NNIS, National Nosocomial Infections Surveillance (System); UTI, urinary tract infection.
advent of ages 13 years and older. Hospitals reported up to four pathogens associated with each nosocomial infection. Coagulase-negative staphylococci were reported as the cause of a primary bloodstream infection only if the patient had fever, chills, or hypotension; no clinical evidence of sepsis at another site; and had either two or more positive cultures drawn on separate occasions, or one positive blood culture and treatment was instituted.

To calculate nosocomial infection rates, hospital personnel collected monthly the number of patients in the ICU and the total number of patient days, urinary catheter days, ventilator days, and central line days. The overall nosocomial infection patient and patient-day rates were calculated by dividing the total number of nosocomial ICU infections pooled throughout all months by the total number of ICU patients (×100) and patient-days (×1000), respectively, at each hospital ICU. For pneumonia, bloodstream, and UTIs, device-associated infection rates were calculated by dividing the number of device-associated infections (×1000) by the total number of appropriate device-days. We also calculated device utilization ratios for central lines, ventilators, and urinary catheters by dividing the number of days of device use by the number of patient-days. Seasonal variation in the three device-associated infection rates was examined by calculating infection rates for each 3-month season of each year of the study.

Statistical analysis was performed using the χ² test for independence, Fisher’s exact test, and, where appropriate, the Spearman rank correlation coefficients and the χ² test for linear trend. The influence of multiple risk factors was assessed by performing linear regression analysis.

### RESULTS

#### Nosocomial Infections

From January 1992 to December 1997, 61 PICUs in 54 hospitals submitted data on 110,709 patients with 427,811 patient-days. Fifty-six (92%) of the units were in teaching hospitals. Fourteen PICUs (23%) were in hospitals exclusively devoted to pediatric patients. Forty-eight units (79%) were in hospitals with high-risk nurseries. The mean number of beds in the hospitals was 519 ± 238 and the mean number of beds in the PICUs was 10.8 ± 5.7. During this 6-year period, the median length of stay fell from 4.8 days in 1992 to 4.3 days in 1997 (P < .05). Data on 6290 nosocomial infections were submitted from this period.

#### Distribution of Nosocomial Infections by Site

The distribution of infections was examined by the major site of infection. Three major infection sites represented 64% of all reported infections; primary bloodstream infections were most frequent, followed by pneumonia and UTIs. The distribution of nosocomial infections by age showed 1145 (18%) infections were reported in children age 2 months or less, 2433 (39%) in children >2 months but <1 year, 1049 (17%) in children aged 1 year up to 5 years, 935 (15%) in children >5 years to 12 years, and 728 (11%) in children 13 years and older. The distribution of major infection sites differed between most age groups (Fig 1). As the distribution of infection sites for infants aged >2 months but <1 year and children 1 year up to 5 years was not different (P = .613), these two groups were combined.

Differences in distribution of major infection sites were observed between each of these four new age groups (P = .001). Primary bloodstream infections and surgical site infections were reported more frequently in infants 2 months or less as compared with older children (386/1145 [33.7%] vs 1352/5145 [26.3%], P < .001, and 116/1145 [10.1%] vs 330/5145 [6.4%], P < .001, respectively). UTIs accounted for a smaller percentage of infections in those children <5 years compared with older children (626/4627 [13.5%] vs 317/1663 [19.1%], P < .001).

We examined the type of surgical procedure pre-
ceeding surgical site infections in the PICU. The most frequent types of preceding surgical procedure were chest surgery, including cardiovascular surgery (41%); gastrointestinal surgery (24%); neurosurgery (13%); transplant surgery (8%); orthopedic surgery (5%); vascular surgery (3%); and head and neck surgery (3%).

The distribution of specific sites of infection within selected common major infection sites (Table 1) was similar across the age groups, with a few exceptions. Of infections of the eyes, ears, nose, and throat, ear infections and conjunctivitis were more frequent in children 5 years and younger than older children: (87/311 [28.0%] vs 15/115 [13.0%], P < .001, and 60/311 [19.3%] vs 8/115 [7.0%], P < .001, respectively), whereas sinusitis was more frequently reported in children >5 years compared with younger children (61/115 [53.0%] vs 52/311[16.7%], P < .001). Of surgical site infections, intraabdominal infections were more frequent in children >2 months than in younger children (79/330 [23.9%] vs 8/116 [6.9%, P < .001), and mediastinitis was more common in children 5 years or younger than in older children (44/341 [12.9%] vs 3/105 [2.9%], P = .001). Twenty-two episodes of nosocomial endocarditis were reported, 18 in patients <1 year of age. Twelve episodes of necrotizing enterocolitis were reported, all in children <1 year of age.

Each of the three major sites of nosocomial infection, bloodstream infection, pneumonia, and UTI, was strongly associated with use of an invasive device. Of bloodstream infections, 91% were in patients with a central intravenous line present. Of episodes of nosocomial pneumonia, 95% were in patients on mechanical ventilation. Of nosocomial UTIs, 77% were in patients with urinary tract catheters.

Pathogen Distributions Among Nosocomial Infections

Primary Bloodstream Infections

Coagulase-negative staphylococci (38%) were the most common pathogens reported (Table 2). Gram-negative aerobic bacilli were reported frequently (25% of all isolates for all species); Enterobacter spp. was the most commonly reported species.

Nosocomial Pneumonia

Sixty-seven percent of reported isolates were Gram-negative aerobic bacilli. Pseudomonas aeruginosa (22%) was the most frequently reported isolate, followed by Staphylococcus aureus (17%). Of 36 viral isolates reported from children with nosocomial pneumonia, 27 (75%) were respiratory syncytial virus. Of 94 viral isolates reported from children with nosocomial lower respiratory tract infections other than pneumonia, 77 (82%) were respiratory syncytial virus.

UTIs

Fifty-seven percent of reported isolates were aerobic Gram-negative bacilli. Escherichia coli was the most frequently reported isolate (19%). Twenty-three percent of reported isolates were fungi, most frequently Candida albicans (14%).

Surgical Site Infections

The pathogens reported from surgical site infections differed according to the type of procedure. P aeruginosa (16%) was the most common pathogen reported after gastrointestinal tract surgery, followed by S aureus (10%). S aureus (34%) was the most common pathogen reported after chest and cardiovascular surgery, followed by coagulase-negative staphylococci (18%). Coagulase-negative staphylococci (23%) were the most common pathogens reported after neurosurgery, followed by S aureus (19%).

Other Specific Sites

Of 190 pathogens reported from 194 episodes of nosocomial gastroenteritis, 99 (52%) were reported as Gram-positive anaerobes, presumably Clostridium difficile. Eighty-four (44%) were viruses. Of these, 62 (74%) were rotaviruses and 11 (13%) enteroviruses. Of 62 pathogens reported from 113 episodes of nosocomial sinusitis, 33 (53%) were Gram-negative aerobic bacilli and the most frequent of these were P aeruginosa (18%) and Enterobacter spp. (13%). Sixteen percent of pathogens were S aureus. Of 89 pathogens reported from 51 episodes of nosocomial meningitis or ventriculitis, 36 (40%) were coagulase-negative staphylococci, 10 (11%) were S aureus, and 36 (40%) were aerobic Gram-negative bacilli. Of 27 pathogens reported from 22 episodes of nosocomial endocarditis, 7 (26%) were coagulase-negative staphylococci, 6 (22%) were S aureus, 6 (22%) enterococci, and 4 (15%) aerobic Gram-negative bacilli.

Changes in the Pathogen Distribution With Use of Invasive Devices

We noted a difference in the pathogen distribution in patients with device-associated infections compared with patients with infections when an invasive device was not present. Fungal bloodstream infections were more commonly reported in primary bloodstream infections associated with central lines than in noncentral line-associated bloodstream infections (173/1710 [10.1%] vs 8/176 [4.5%], P = .008, respectively). Viral pneumonia was less commonly reported in pneumonia associated with mechanical ventilation than nonventilator-associated pneumonia (27/1379 [2.0%] vs 9/80 [11.3%, P < .001, respectively), P aeruginosa and C albicans UTIs were more commonly reported in UTIs associated with urinary catheters than in noncatheter-associated UTIs (115/800 [14.4%] vs 22/245 [9.0%, P = .02, 133/800 [16.6%] vs 16/245 [6.5%, P < .001, respectively).

Temporal Changes in Pathogen Distribution

We examined changes in the frequency of pathogens from all infection sites during the 6 years. Enterobacter spp. was more frequently reported in later years, increasing from 7% to 12% of reported pathogens (χ² value for linear trend, P < .001). This change was most marked in respiratory infections, ie, the frequency of reports of Enterobacter spp. from pneumonia increased in the 6-year period from 7.4% to 13% (χ² test for trend, P = .02). For bloodstream infection isolates, P aeruginosa was reported more
frequently later in the 6-year period (3.0% to 7.4%, \( P = .02 \)). \textit{S. aureus} was more frequently reported in earlier years, decreasing from 16% to 10% of all pathogens in all infection sites (\( P = .001 \)).

**Nosocomial Infection Rates and Device Utilization**

The mean overall patient nosocomial infection rate was 6.1 infections per 100 patients, and the mean infection rate per 1000 patient days was 14.1. However, these overall rates were strongly correlated with other measures, ie, with length of stay (\( r = 0.45, \ P = .0002 \)) and central line, ventilator, and urinary catheter use (\( r = 0.65, 0.56, 0.40; \ P = .0001, .0001, .001 \), respectively). After we controlled for device exposure by calculating device-associated infection rates, central line-associated bloodstream infections, ventilator-associated pneumonia, and catheter-associated UTIs did not correlate with length of stay (\( r = 0.11, −0.04, −0.005; \ P = .39, .77, .97 \), respectively), with associated-device utilization (\( r = −0.01, 0.09, −0.09; \ P = .92, .48, .47 \), respectively), or hospital size by number of beds (\( r = 0.07, 0.12, 0.07; \ P = .59, .37, .58 \), respectively, for each device). On univariate analysis we found a weak, negative association between rates of catheter-associated UTIs with ICU size (\( r = −0.31, \ P < .02 \)) but no such association for ventilator-associated pneumonia or line-associated bloodstream infections (\( r = −0.19, 0.19; \ P = .08, .08 \), respectively). The distribution of the device-associated rates is shown in Figs 2, 3, and 4. The distribution of each of the three device-associated rates in the PICUs in pediatric as compared with nonpediatric hospitals did not differ.

We used linear regression modeling to further assess potential associations with the three device-associated infection rates and total number of hospital beds, rates of associated device utilization, ICU bedsize, and the average length of stay in the ICU. There was no significant association between the device-associated infection rates and any of these variables with the exception of ICU bedsize. We found a negative association with ICU bedsize for both catheter-associated UTI and ventilator-associated pneumonia rates (\( P < .002 \)). We examined the three nosocomial device-associated infection rates for the four 3-month seasons. Controlling for length of ICU stay, year of infection, hospital size, and ICU size, we found no seasonal variation.

**Use of Invasive Devices**

Device utilization varied greatly between the PICUs (Table 3). Urinary catheter utilization was the lowest among the three devices.

**DISCUSSION**

Our analysis suggests that the epidemiology of nosocomial infections in PICUs differs from that seen in other critical care areas. The distribution of infection sites lies between what we have previously reported in neonatal ICUs\(^7\) and adult medical ICUs.\(^8\) First, primary bloodstream infections were the most common sites of infection, followed by pneumonia and UTIs. In adult medical ICUs, UTIs were most frequently reported. In neonatal ICUs, bloodstream infections were an even greater proportion of all infections than in pediatric units. We saw a transition between the two patterns with age, although bloodstream infections remained the most frequent nosocomial infections in adolescents. This distribution may in part reflect lower rates of urinary catheter use in PICUs; the pooled mean rate of urinary catheter utilization in PICUs was 0.32, as compared with 0.69 in medical ICUs. Surgical site infections, particularly skin infections and mediastinitis, were more frequent in neonates, reflecting early surgery for congenital defects. Nosocomial lower respiratory tract infections not classified as pneumonia were reported more frequently in PICUs (12% vs 4.4%), and cardiovascular infections, usually phlebitis, less frequently (1.9% vs 4.2% of major sites of infection) than in adult medical ICUs. Also, sinusitis was reported predominantly in older children.

The distribution of pathogens in PICUs differed from that we have observed in adults, and within the PICUs and changed with age. In primary nosocomial bacteremia, Gram-negative bacteria were more frequently reported in PICUs than in adult medical ICUs (25% vs 17%). \textit{Enterobacter} spp. was the most common Gram-negative species reported in PICU patients with primary bacteremia and cardiovascular infections. Others have suggested that enterococci are infrequent bloodstream pathogens in pediatric settings,\(^9\) but enterococci were reported more frequently than \textit{S. aureus}. In nosocomial respiratory infections, \textit{Enterobacter} spp. was reported more frequently in neonates. Viral infections were reported...
as important pediatric nosocomial respiratory pathogens, but are rarely reported as adult ICU nosocomial pathogens. Others have noted that viruses are less frequent as nosocomial pathogens in PICUs than in other areas of pediatric hospitals. This may, in part, explain the lack of seasonal variation in device-associated infection rates. Fungal pathogens were reported more commonly in bloodstream infections in school-aged children, but much less frequently in UTIs than we have recently reported in adult medical ICUs (23% vs 39%). These differences in pathogen distribution seem likely to be, in part, an effect of age but also to reflect other patient-related factors, including underlying medical and surgical conditions, previous hospital stay, and antibiotic exposure.

*Enterobacter* spp. was reported with increasing frequency throughout the 6 years examined, particularly in respiratory tract infections and were the most frequently reported Gram-negative pathogens after *P. aeruginosa* in surgical site infections and eye, ear, nose, and throat infections. Individual institutions have reported nosocomial outbreaks of *E. cloacae* in neonatal and pediatric ICUs and increased *Enterobacter* spp. bacteremia in pediatric patients. Enterobacter organisms are intrinsically resistant to first-generation cephalosporins and their prominence in these units may reflect selective pressure of these frequently used agents. Emergence in adults of broadly resistant *Enterobacter* spp. through high level production of chromosomal β-lactamase seems to develop in individual patients through mutation rather than crossinfection. In adults, this has been associated with previous therapy with a third-generation cephalosporin rather than with an aminoglycoside or extended-spectrum penicillin.

We noted a mean overall patient infection rate of 6.1%. Brown et al reported 7% of patients admitted to a PICU developed an ICU-acquired infection, in a study using NNIS definitions and methods. In previous studies in other ICU types, overall nosocomial infection rates were confounded by average length of stay and rates of device utilization. However, device-associated infection rates in PICUs were not confounded by these factors or by the hospital bed-size. We noted slightly lower rates of catheter-associated UTIs and ventilator-associated pneumonia rates in larger PICUs although the significance of this finding for purposes of comparing rates is not clear. This may reflect differences in intrinsic risk factors including differences in the severity of illness in patients using these urinary catheters or ventilators, differences in the duration of urinary catheterization in patients after, for example, surgical procedures, or differences in reporting. We observed a considerable variation in these rates that our current NNIS data collection does not explain. More detailed surveillance to investigate other risk factors, both intrinsic to the patient and relating to the ICU environment and procedures, may explain these variations but involves a further burden of data collection.

Differences in nosocomial infection rates according to the type of ICU have been previously de-
The rates of ventilator-associated pneumonia and catheter-associated UTIs in PICUs were less than we reported recently in adult medical ICUs (pooled mean, 5.9 vs 9.1 and 5.9 vs 9.5), and the central line-associated bloodstream infection rate was higher (pooled mean, 7.3 vs 3.1). Others have reported that children under 2 years of age have the highest nosocomial infection rates in PICUs with up to 25% of children in this group infected. Our data show the distribution of infection sites differed with age. Thus, differences in the age distribution among PICUs may explain some differences between nosocomial infection rates in different PICUs.

Device utilization in PICUs was comparable to that in adult medical ICUs, apart from lower rates of urinary catheter utilization. Within PICUs, we found considerable variation in rates of device utilization. High ventilator utilization ratios may reflect severity of illness that may explain, in part, some of the variation. Also, there may be step-down facilities in certain institutions, allowing earlier discharge from the PICU, reducing nondevice-days, and increasing the utilization ratio.

These surveillance data have several limitations. These ICUs were generally in large hospitals with academic departments and may not be representative of smaller institutions. Pulmonary infection in the ICU often is particularly difficult to differentiate from nonpulmonary pulmonary infiltrates and the microbiology reported from sputum cultures may be contaminated by upper respiratory tract flora. Viral infections were underreported because appropriate cultures were not always performed. Data reported here may reflect underreporting of infections at sites other than the three most frequent sites, as noted in a recent evaluation study of NNIS hospitals. We reported the types of surgery preceding surgical site infections, but lack denominator data on the number and details of these procedures to evaluate the risk of infection after the procedure. For that information to be most useful, surgical site infection data collection should not be restricted to the ICU. We did not collect denominator data on risk factors apart from device use, which limits comparison of rates between units.

CONCLUSIONS

In PICUs, the distribution of infection sites and of pathogens lay between that reported in neonatal ICUs and adult ICUs, and changed with the age of the patients. Device-associated infection rates were the best available rates for comparisons between units because they were not confounded by length of stay, total number of hospital beds, or differences in the associated device utilization.

REFERENCES

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*Pediatrics* 1999;103;e39

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