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Changing Pathogen Profile among Early- and Late-Onset Bloodstream Infections in High-Risk Nursery Patients \_ United States, 1995-2004

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**Background:**

Bloodstream infections (BSIs) account for approximately 45% of neonatal healthcare-associated infections, and they result in significant morbidity and mortality. The widespread use, in recent years, of intrapartum antibiotics to prevent Group B streptococcal sepsis and broad-spectrum antibiotics to treat healthcare-associated infections has raised concerns that organisms causing neonatal BSIs have changed.

**Objective:**

To determine whether a change in pathogen distribution causing early- and late-onset neonatal BSIs has occurred in the United States.

**Methods:**

We analyzed neonatal BSIs reported by 146 High-Risk Nurseries participating in the National Nosocomial Infections Surveillance (NNIS) system from 1995 through 2004. BSI was defined using standard NNIS criteria. We calculated overall BSI rates by birth weight category ( $\leq 1000g$ , 1001-1500g, 1501-2500g and  $>2500g$ ). We examined pathogen distribution for early-onset (occurring within 3 days of age) and late-onset (occurring after 3 days of age) BSIs. We then statistically assessed differences in these distributions over three time periods (Period 1: 1995-1997, Period 2: 1998-2000, Period 3: 2001-2004). Periods were selected based on publication of national guidelines for intrapartum prophylaxis first in 1996 and later in 2002.

**Results:**

From 1995 through 2004, 19,825 neonatal BSIs among 5,858,301 patient-days were reported. The pooled mean BSI rates per 1000 patient-days were 5.8 for neonates  $\leq 1000g$ , 3.1 for neonates of 1001-1500g, 1.6 for neonates of 1501-2500g, and 2.1 for neonates  $>2500g$ . An etiologic agent was identified in 17,288 (87%) neonatal BSIs. For the 1,488 early-onset BSIs where a pathogen was isolated, the most common organisms were Group B streptococci (GBS) (34%), *Escherichia coli* (19%), and coagulase-negative staphylococci (CNS) (17%). Between Period 1 and Period 2, the proportion of early-onset BSIs caused by GBS decreased ( $p < 0.001$ ), while those caused by *E. coli* increased ( $p = 0.002$ ). For the 15,800 late-onset BSIs where a pathogen was isolated, the most common organisms were CNS (54%), *Staphylococcus aureus* (9%), and enterococci (6%). There was a significant decrease in the proportion of late-onset BSIs caused by CNS ( $p < 0.001$ ) between Period 1 and Period 2, and a significant increase in the proportions caused by *S. aureus* ( $p < 0.001$ ) and enterococci ( $p = 0.03$ ) between Period 2 and Period 3.

**Conclusions:**

There was a shift in the proportion of GBS and *E. coli* early-onset BSIs after publication of first guidelines for intrapartum prophylaxis in 1996. Among late-onset BSIs, reasons

for the increase in the proportions of *S. aureus* and enterococci in recent years need further exploration. Confirmation of these changes in pathogen profile by ongoing surveillance and assessment of antibiotic resistance for these organisms may help to guide future neonatal BSIs prevention efforts.

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Do Clinical Cultures Reflect Burden of Methicillin-Resistant *Staphylococcus aureus* (MRSA) and Vancomycin-Resistant Enterococci (VRE) in a Pediatric Intensive Care Unit (PICU)?

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#### Background:

MRSA and VRE are major pathogens in adult ICUs. Active surveillance cultures at time of hospital admission are an effective tool to identify patients (pts) colonized with MRSA or VRE. A recent study suggested that clinical cultures of MRSA may correlate with the MRSA burden in an adult population. Little is known about the burden of MRSA and VRE in the PICU.

#### Objective:

To determine the prevalence of MRSA and VRE in a tertiary care PICU and to evaluate whether clinical microbiological cultures were a good indicator of MRSA and VRE burden in the unit.

#### Methods:

For 16 weeks in 2006 weekly nasal and rectal cultures were obtained from patients in the PICU. During the same time period, clinical cultures growing MRSA or VRE were identified. Based on surveillance and clinical culture results, the prevalence density rate (PR) was estimated by number of pts with a culture growing an organism per 100 patient-days (pd). Appropriate statistical tests were performed to examine the significance of PR ratio (PRR).

#### Results:

During the 1963 pd over the 16 week study period, weekly cultures were obtained from 329 pts. Compliance was 98% and 96% for nares and rectal cultures, respectively. Estimated MRSA PR based on weekly surveillance cultures was 0.87/100-pd, compared to 0.71/100-pd based on clinical cultures (PRR=1.21,  $p>0.05$ ). The estimated VRE PR rate was 0.56/100-pd based on weekly surveillance cultures, 0.15/100-pd based on clinical cultures (PRR=3.67,  $p=0.04$ ). If surveillance cultures were conducted once a month instead of weekly, PR would be underestimated by 18% for MRSA and 73% for VRE. Combining results from monthly surveillance culture with clinical cultures improved PR, overestimating MRSA by 6% and underestimating VRE by 45% compared to weekly surveillance cultures. For patients identified as newly colonized or infected with MRSA or VRE, 67% with MRSA and 90% with VRE were identified by surveillance culture. Patients with a surveillance culture growing MRSA (4 pts) or VRE (2 pts) had a subsequent clinical culture grow on average 24 or 49 days later, respectively.

#### Conclusions:

The prevalence of MRSA and VRE may be underestimated in pediatric ICUs that use clinical culture results to estimate the reservoir of colonization. Surveillance cultures can identify colonized individuals weeks before clinical cultures enabling early isolation of patients. Results of monthly surveillance cultures plus clinical cultures may be adequate to estimate colonization rates of MRSA in pediatric ICUs with limited resources. We will expand our observations to assure that these findings are maintained over time.

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#### Community-Associated Methicillin-Resistant *Staphylococcus aureus* Among Personnel at a Pediatric Clinic

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#### Background:

Ambulatory-care visits for skin and soft-tissue infections have increased dramatically in the United States, and community-associated (CA) methicillin-resistant *Staphylococcus aureus* (MRSA) is a frequent cause of these infections. Health-care workers (HCWs) are exposed to an increasing number of MRSA-infected persons and can be at increased risk for infection.

#### Objectives:

We investigated a group of MRSA infections among personnel of a pediatric outpatient clinic in order to determine the extent of the outbreak and the risk to HCWs and to recommend control measures.

#### Methods:

Isolates from a clinic worker who died of MRSA sepsis were compared with isolates from nasal-swab cultures from other personnel and a sample of clinic patients using pulsed-field gel electrophoresis (PFGE). Environmental samples were cultured to identify contamination by *S. aureus* in the clinic. A questionnaire concerning hygiene and work practices was administered to clinic personnel.

#### Results:

We identified 16 skin and soft tissue infections in a 6 month period among 45 clinic staff with a completed questionnaire; three, including the deceased employee, had laboratory-confirmed MRSA. Nasal swabs indicated that 15/45 (33%) personnel were colonized with *S. aureus*, and 2/45 (4.4%) isolates were identified as MRSA. PFGE patterns of these two isolates were indistinguishable from the USA800 strain and did not match the pattern from the deceased employee's isolate (USA300). Among the sample of 262 patient swabs, 97 (37%) yielded *S. aureus*. Nine (3.4%) were identified as MRSA and represented a variety of PFGE patterns, with three indistinguishable from the USA300 strain. Of 71 environmental surfaces cultured, eight (11%) were contaminated with *S. aureus* (none were MRSA). The questionnaire indicated that standard precautions had been inconsistently applied when dealing with skin and soft-tissue infections among patients.

#### Conclusions:

HCWs in outpatient settings are exposed to increasing numbers of persons infected with CA-MRSA. Standard precautions and environmental controls in outpatient clinics are important methods of limiting HCW exposure.

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Different Outcomes After Active Surveillance Culture Implementation for Control of Methicillin Resistant *Staphylococcus Aureus* Transmission in Two Neonatal Intensive Care Units

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#### Background:

Nosocomial transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) infections has been frequently reported, especially among intensive care patients. Active surveillance cultures (ASC) for patients with MRSA risk factors have been recommended as a strategy to prevent MRSA transmission.

#### Objective:

To describe our experience using ASC to bring an outbreak of MRSA in two NICUs under control.

#### Methods:

Children's Hospitals and Clinics of Minnesota (CHC) initiated ASC after identification of case clusters of MRSA infection/colonization in both the Minneapolis (MP) and St. Paul (SP) neonatal intensive care units (NICU). ASC were obtained from the nares and perirectum of patients on admission and weekly thereafter from Jan 04 to Dec 2006. MRSA colonized patients were placed in contact precautions. Other interventions included gloving with all patient contact, education, heightened cleaning, environmental culturing, employee culturing and treatment (SP only), and treatment of colonized patients (SP only).

#### Results:

MP NICU: Prior to the outbreak the MRSA case rate was 0.4 per 1000 NICU admissions. Upon initiating ASC, the MRSA case rate was 26.9 cases per 1000 NICU admissions. 2581 patients were admitted during the study period. 33 patients with MRSA were identified by ASC (3 on admission and 30 during hospitalization). 8 additional MRSA patients were identified by clinical cultures. The case rate increased to 61.9 in 4<sup>th</sup> quarter 2004 followed by a decrease to 0.0 cases per 1000 NICU admissions by 4<sup>th</sup> quarter 2006.

SP NICU: Prior to the outbreak the MRSA case rate was 3.3 per 1000 NICU admissions. Upon initiating ASC, the MRSA case rate was 26.0 cases per 1000 NICU admissions. 2380 patients were admitted during the study period. 64 patients with MRSA were identified by ASC (5 on admission and 59 during hospitalization). 10 additional MRSA patients were identified by clinical culture. Despite ongoing ASC as well as many other measures, MRSA cases increased, reaching a peak incidence of 69.1 per 1000 NICU admissions in 2<sup>nd</sup> quarter 2006. A significant decrease to 12.9 cases per 1000 NICU admissions was finally achieved by the 4<sup>th</sup> quarter of 2006.

#### Conclusions:

ASC allows prompt identification of MRSA colonized patients and targeted use of contact precautions. Implementation of ASC, along with multiple other infection control strategies, was temporally associated with different outcomes in each NICU. Our experience underscores the complex nature of healthcare associated MRSA transmission. Even with multiple intervention strategies, including ASC, outbreak control can remain elusive.

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#### Gram-negative Surveillance Revisited in the NICU

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#### Background

Colonization of the gastrointestinal (GI) tract of low-birth weight (VLBW) (birth weight <1,500 grams) infants is thought to be integral to the pathogenesis of late onset sepsis caused by Gram-negative bacilli.

#### Objectives

We sought to determine if Gram-negative bacilli colonizing the GI tracts of VLBW infants cause subsequent bloodstream infections (BSIs) and to determine the frequency of gentamicin resistance as this agent is commonly used for empiric therapy of late onset sepsis.

#### Methods

From January 2004-September 2005 weekly surveillance cultures of the GI tract were performed by swabbing the rectal verge of VLBW infants in the NICUs at the Children's Hospital of New York-Presbyterian and the Weill-Cornell Medical Center. Selective media for Gram-negative bacilli were inoculated, examined for growth at 24 and 48 hours, and the most predominant phenotype(s) was identified and susceptibility testing performed using the Vitek® II System. Blood cultures (Bactec Peds Plus®) were obtained as clinically indicated. To determine the genetic relatedness of Gram-negative bacilli causing BSIs and antecedent colonizing flora, pulsed-field gel electrophoresis (PFGE) was performed.

#### Results

During the study period, 15 (6.8%) of 220 VLBW infants developed 20 BSIs with Gram-negative bacilli. All invasive isolates were the same species as the most recent species detected in surveillance although 9 infants had two colonizing organisms detected. Two infants had  $\geq 2$  BSIs. Strains associated with 19 of 20 episodes of BSI and surveillance isolates (1-17 days prior to BSI) were available for PFGE. Seventeen of the 19 strain pairs had indistinguishable PFGE patterns, one pair was closely related, and one pair was unrelated. Shared clones occurred infrequently. Twin infants developed BSIs with *S. marcescens* and two infants hospitalized in the same room developed BSIs with *E. cloacae*. Twenty-five percent of colonizing-infecting pairs demonstrated gentamicin resistance; gentamicin resistance was 100% concordant in the colonizing flora and infecting strains of individual infants.

#### Conclusions

The majority of BSIs caused by Gram-negative bacilli in the study NICUs were endemic

infections caused by endogenous GI tract flora with relatively high rates of resistance to gentamicin. Future studies should address the impact of targeted surveillance on empiric treatment for late onset sepsis and transmission of resistant organisms.

Table: Surveillance and Clinical Isolates

Infant #	Organism	Surveillance clone	Bloodstream infection (BSI) Clone	Days between surveillance/ BSI	Gent MIC $\geq 8^{\#}$
1	<i>Klebsiella pneumoniae</i>	O	O2 <sup>‡</sup>	4	
2	<i>Escherichia coli</i>	C	C	3	
3	<i>K. oxytoca</i>	J	J	9	+
4	<i>Enterobacter cloacae</i>	B*	B*	1	
5	<i>Citrobacter koseri</i>	A	A	1	
6	<i>K. pneumoniae</i>	N	N	7	
7	<i>E. coli</i>	E	E	2	
8	<i>K. pneumoniae</i>	M	M	2	+
9	<i>K. pneumoniae</i>	L	L	5	
10	<i>E. coli</i>	H	H	2	
11	<i>K. oxytoca</i>	I	I	7	
12	<i>Serratia marcescens</i>	P*	P*	17	
13	<i>S. marcescens</i>	P*	P*	6	
14 <sup>^</sup>	<i>E. coli</i>	F	G	8	
14 <sup>^</sup>	<i>S. marcescens</i>	Q	Q	7	+
15 <sup>^</sup>	<i>K. pneumoniae</i>	K	K	1	
15 <sup>^</sup>	<i>K. pneumoniae</i>	K	K	12	+
15 <sup>^</sup>	<i>K. pneumoniae</i>	K	K	1	+
15 <sup>^</sup>	<i>E. coli</i>	N/A <sup>†</sup>	N/A <sup>†</sup>	3	
15 <sup>^</sup>	<i>E. cloacae</i>	B*	B*	4	

# Intermediate or resistant

‡ 1 band difference from Clone O

\* Clones shared with another infant

<sup>^</sup> Infants with more than one infection

<sup>†</sup> Not-available

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#### Risk Factors for Healthcare-acquired Influenza in Hospitalized Children

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#### Background:

Community-acquired influenza is a common cause of hospitalization for children and adults. Hospitals are reservoirs of infection while influenza is circulating in the community and put patients at risk of nosocomial infection. However, little is known about the risk factors for nosocomial transmission of influenza.

#### Objective:

To identify modifiable risk factors associated with the transmission of influenza.

#### Methods:

A nested case-control study was conducted over 4 influenza seasons. In this large children's hospital, we conduct active surveillance for nosocomial respiratory infections and commonly utilize viral diagnostic testing. Nosocomial influenza was defined as laboratory-confirmed infection with the onset of symptoms > 72 hrs after hospital admission or within 72 hours of prior hospitalization. Control patients were randomly selected from rosters of patients who were hospitalized for > 72 hrs and were matched for hospitalization during the exposure window. The exposure window was defined as the 3 days prior to the onset of nosocomial influenza. Detailed chart review was conducted to identify both in-room and out-of-room activities during the exposure window.

#### Results:

A total of 56 case and 112 control patients were identified. Most patients were infected with influenza A (n=40, 71%). The median length of hospitalization prior to the onset of influenza was 7.0 days (IQR 4.5, 16.0). Case, as compared to control, patients were more likely to have been admitted from the Emergency Department (50% vs. 28%; OR 2.6, 95%CI: 1.3, 5.1). The frequencies of specific in-room contacts with healthcare providers (such as vital signs, medication administration, or administration of respiratory therapies) were similar for case and control patients. There was a tendency for case patients to require assistance for feeding (79% vs. 67%, p=0.12). The frequency of out-of-room contacts (including transfer to another unit, visit to the Radiology Department or Operating Room) was similar for case and control patients.

#### Conclusions:

No specific clinical activity was associated with the acquisition of nosocomial influenza. However, patients with nosocomial influenza were more likely to be admitted from the Emergency Department. Additional analysis is required to determine whether exposure to the Emergency Department is an independent risk factor for nosocomial influenza.