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# Is Bloodstream Infection Preventable Among Premature Infants? A Tale of Two Cities

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**ABSTRACT.** *Background.* Bloodstream infection (BSI) is a significant cause of morbidity and death encountered in the NICU. The rates of BSIs vary significantly in NICUs across the nation. However, no attempt has been made to correlate this variation with specific infection-control practices and policies. We experienced a significant increase in BSIs in the NICU at the George Washington University Hospital and were seeking additional precautionary measures to reduce BSI rates. Our objective was to review policies and practices associated with lower infection rates nationally and to test their reproducibility in our unit.

*Design and Methods.* Data on BSI rates in 16 NICUs were reviewed. The BSI rate at Connecticut Children's Medical Center (CCMC) was the lowest among those reviewed. A team from George Washington University Hospital conducted a site visit to CCMC to examine their practices. Differences in the aseptic precautions used for intravenous line management were noted at CCMC, where a closed medication system is used. This system was applied at George Washington University Hospital starting January 1, 2001. Infection rates among low birth weight infants (<2500 g) at George Washington University Hospital in the period from January 1998 to December 2000 (group 1) were compared with those in the period from January 2001 to December 2003 (group 2). Comparisons between the 2 cohorts were made with Fisher's exact test, the Kruskal-Wallis test, and Student's *t* test. Multivariate analysis was used to control for differences in birth weight, gestational age, central line days, and ventilator days. Analyses were repeated for the subgroup of very low birth weight infants (<1500 g).

*Results.* A total of 536 inborn low birth weight infants were included in this retrospective study (group 1, *N* = 169 infants; group 2, *N* = 367). The incidence of sepsis decreased significantly from group 1 to group 2 (25.4% and 2.2%, respectively). The reduction of sepsis observed in association with the new practice was statistically significant after controlling for birth weight, central line days, and ventilator days in a multiple regression model (regression coefficient:  $0.95 \pm 0.29$ ). The odds ratio of reduction in sepsis after implementation of the new practice was 2.6 (95% confidence interval: 1.5–4.5).

The central line-related BSI rate decreased from 15.17 infections per 1000 line days to 2.1 infections per 1000 line days. The study included 233 very low birth weight infants, ie, 90 in group 1 and 143 in group 2. The rate of BSIs decreased significantly from group 1 to group 2 (46.7% and 5.6%, respectively). The decrease in sepsis rate remained significant in a multiple regression model (regression coefficient:  $1.42 \pm 0.35$ ). The odds ratio of decreased sepsis in relation to the new policy application among the very low birth weight infants was 4.15 (95% confidence interval: 2.1–8.3).

*Conclusion.* Applying the closed medication system was associated with reduced BSI rates in our unit. This protocol was easily reproducible in our environment and showed immediate results. Serious attempts to share data can potentially optimize outcomes and standardize policies and practices among NICUs. *Pediatrics* 2005;115: 1513–1518; *infection, sepsis, closed medication system, premature infants.*

ABBREVIATIONS. BSI, bloodstream infection; CVC, central venous catheter; CCMC, Connecticut Children's Medical Center.

Neonatal sepsis is a commonly encountered complication among premature infants, particularly those who require a central venous catheter (CVC).<sup>1,2</sup> Critically ill premature infants are especially vulnerable to bloodstream infections (BSIs), because of their immature immune systems, poor skin integrity, repeated invasive procedures, and exposure to numerous caregivers and an environment conducive to bacterial colonization.<sup>2–5</sup> There is no agreement regarding the acceptable range, if any, for the incidence of nosocomially acquired infections in NICUs. This is because of the wide variability in reported rates of sepsis in different NICUs.<sup>6,7</sup> The National Nosocomial Infection Surveillance System reported an overall line-related infection rate of 8.4 BSIs per 1000 catheter days.<sup>8</sup> In comparison, the BSI rate in our NICU in 1998–2000 ranged from 14.3 to 16 BSIs per 1000 catheter days. This higher BSI rate led us to pursue potential strategies to reduce the incidence of sepsis.

In an effort to improve the quality of care in the NICU, a comprehensive literature search was conducted to identify the unit reporting the lowest rate of nosocomial sepsis nationally. An in-depth analysis of the practices of this unit resulted in significant modifications of our standard of care for CVC management. Changes in our practices were associated with a very significant reduction in the rate of sepsis

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in our unit. Our report of this experience may validate a new model of quality improvement through the sharing of practices associated with improved patient outcomes.<sup>9</sup>

## METHODS

### Study Design

An effort was made to identify data sources reporting rates of nosocomial sepsis nationally. The report by Medical Management Planning, Inc, of 16 NICUs located in children's hospitals in the United States identified Connecticut Children's Medical Center (CCMC) (Hartford, CT) as the unit reporting the lowest infection rate. A team from George Washington University Hospital traveled to CCMC to examine their infection-control practices and to compare them with those at the former hospital, to identify potential areas for improvement. We identified differences in several practices, namely, use of a closed medication system and procedures for dressing changes and ongoing care of CVCs. These procedures were incorporated into our patient care practices and are outlined below.

### Closed Medication System

#### Before 2001

A standard procedure for medication administration did not exist. Commonly, nurses accessed the central line by inserting a needle through a rubber hub located on the line tubing close to the patient. Alternatively, a Y-connector piece or a 3-way stopcock was connected directly to the central line, through which medications were administered after alcohol sterilization of the site.

#### Starting in January 2001

Preparation of the closed medication system is performed with sterile techniques. Normal saline solution is drawn into a 10-mL syringe, which is then connected aseptically to a 3-way stopcock, a 3-mL syringe, microbore infusion tubing (ICU Medical, San Clemente, CA), and a tri-fuse connector (Fig 1). Saline solution is flushed through to the end of the tubing, which is then connected to the central intravenous catheter site. The other 2 limbs of the tri-fuse connector are attached to parenteral nutrition and intravenous lipid solutions. The exact medication volume is then pre-

pared. The 3-mL syringe is removed, and the medication syringe is attached to the stopcock in a sterile manner. The medication syringe is placed in the infusion pump while the stopcock is in the off position. The infusion pump is programmed for the desired hourly rate of medication administration, plus an extra 1 mL of flush solution. The stopcock is turned off to the flush solution for medication administration. After the medication has been infused, the stopcock is turned off to the tubing and 1 mL of saline flush solution is withdrawn from the 10-mL syringe and added to the medication syringe. The stopcock is then closed to the flush syringe, and the flush solution is infused from the medication syringe. The empty syringe is left in place until the next medication dose is due.

### Care of Peripherally Inserted CVCs

#### Before 2001

Fluids and tubing were changed daily. Entry into the central line was not limited strictly, however, and the central line was interrupted occasionally for infants who required several medications and/or multiple fluid pushes.

#### Starting in January 2001

Once a CVC is inserted, new fluids and tubing should be used. Entry into the CVC is then limited to once every 24 hours. All intravenous fluids and tubing are changed daily. The site of insertion, the integrity of the dressing, and the extremity involved are assessed and documented every hour.

### Procedure for Tubing Changes

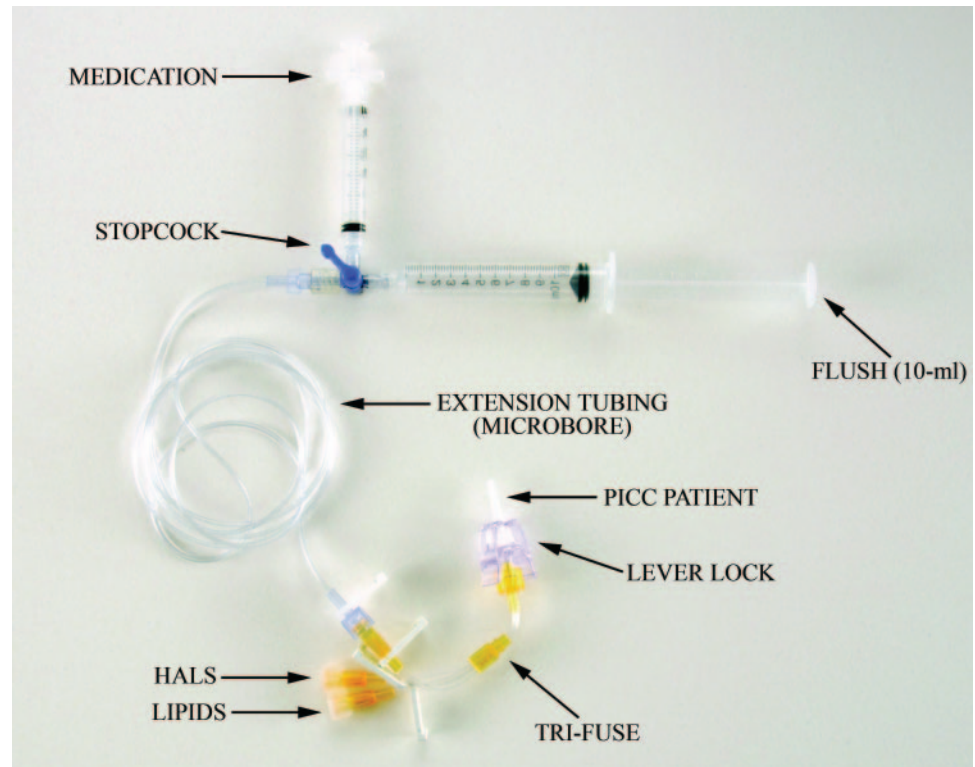
#### Before 2001

Tubing was changed daily. The bedside nurse used sterile gloves and performed the entire procedure without a second nurse to assist. Therefore, the procedure did not necessarily occur in a strict sterile field.

#### Starting in January 2001

Two nurses check all intravenous fluid orders for accuracy and perform the daily tubing changes with sterile techniques. One nurse wears a mask and sterile gloves, whereas the other wears a mask and acts as the assistant. Sterile gauze pads, alcohol pads,

**Fig 1.** System used for administration of medications through a central line. PICC indicates peripherally inserted central catheter; HALS, hyperalimentation; LIPIDS, intralipids.



and povidone-iodine swabs are opened and placed in a sterile field. The new fluids are primed through the tubing, with the end of the tubing kept protected to avoid contamination. Priming is performed through intravenous pumps, to verify successful infusion. A sterile towel is placed under the CVC. With sterile gloves, the lever lock is attached to the proximal end of the tri-fuse connector. The parenteral fluid reservoir is attached to one tri-fuse port and fluid is flushed through. The intravenous lipid reservoir is primed in the same manner and attached to another tri-fuse port. A new medication administration set is attached to the third tri-fuse port and flushed. The junction of the interlink adapter and the lever lock is wiped 3 times with povidone-iodine and allowed to air dry for 2 minutes. The new tubing is then connected to the central line through insertion of the interlink adapter into the lever lock. The lever lock is changed every 7 days.

## Dressing Changes for the Central Line

### Before 2001

Dressing for the central line was not changed unless it was grossly loose and the line was insecure. In that case, the physician performed the entire change alone, without a second person to assist with maintaining sterile procedures. Masks were not used during dressing changes.

### Starting in January 2001

Dressing changes are performed within 24 hours after insertion and then weekly. Two people conduct the dressing changes; one person uses sterile protection, whereas the other wears a mask and acts as the assistant. Sterile supplies are opened into a sterile field. The old dressing is removed, and the site is assessed for erythema, edema, or drainage. The site is cleansed with povidone-iodine swabs, in concentric circles from the site, 3 times for a total of 2 minutes. The catheter is then coiled, secured for its entire length, including the hub, and covered with a transparent dressing. Care is taken to ensure that the dressing does not encircle the extremity. The infant is returned to the incubator, and the procedure is documented.

## Clinical Definitions

The incidence of BSIs refers to the number of episodes of culture-proven BSI in comparison with the total number of infants in that cohort. The incidence of central line-related BSIs is defined as the number of culture-proven infection episodes among infants with indwelling central lines and no other identifiable source of infection per 1000 days of total cumulative duration of central lines in the cohort. Line use is defined as the ratio of central line days to total patient days in the NICU. Cultures of organisms usually considered contaminants were excluded only if the managing physician did not maintain antibiotic treatment for >72 hours. This definition of contaminants minimized the possibility of bias in excluding positive cultures. Physicians in our unit were likely to confirm a positive blood culture for an otherwise asymptomatic infant by repeating the culture before initiating treatment. If the repeat culture was negative within 72 hours, then treatment was stopped.

## Statistical Analyses

All low birth weight infants (<2500 g) admitted to the NICU in the period of January 1998 through December 2003 were included in this retrospective study. The incidences of BSIs were calculated for the period before (January 1998 to December 2000) and after (January 2001 to December 2003) institution of the closed medication system. Univariate analyses were conducted to compare the 2 groups with respect to gestational age, birth weight, race, gender, average CVC days per infant, length of hospital stay, and average days of mechanical ventilation per infant. Fisher's exact test and the  $\chi^2$  test were used for comparisons of categorical variables. The Kruskal-Wallis test was used for nonparametric continuous variables, and Student's 2-tailed *t* test was used for parametric continuous variables. Nosocomial sepsis rates were compared between the 2 groups after controlling for other variables in a multivariate regression analysis. Odds ratios for the contribution to sepsis were also calculated. Analyses were repeated for the subgroup of infants weighing <1500 g. The annual rates of central line-related BSIs were also determined and compared for these 6 years. This study was approved by the institutional review board at George Washington University and was conducted in compliance with Health Insurance Portability and Accountability Act of 1996 regulations.

## RESULTS

A total of 536 inborn, low birth weight infants were included in this retrospective study. One hundred sixty-nine infants were admitted before the revised infection-control policy (group 1), and 367 infants were admitted after implementation of the new policy (group 2). Survival rates were comparable for groups 1 and 2 (91.7% and 94%, respectively; *P* = .354). The size difference between the 2 cohorts is a reflection of changes in labor and delivery censuses related to shifts in third-party contractual agreements in the District of Columbia with time. These changes resulted in a significant increase in the Medicaid population from group 1 to group 2 (13% and 31.3%, respectively; *P* < .001). Potential confounding factors that might have influenced infection rates were examined and controlled for as necessary (Tables 1 and 2). Gestational age, birth weight, and length of stay differed significantly between groups.

The incidence of BSIs decreased significantly from group 1 to group 2 (from 25.4% to 2.2%, *P* < .0001). There were 43 episodes of culture-proven sepsis in group 1. The most common organisms were coagulase-negative *Staphylococcus* (*n* = 29), *Staphylococcus aureus* (*n* = 4), and *Klebsiella* (*n* = 2). Infants in group 2 had 8 episodes of culture-proven sepsis, 6 attribut-

TABLE 1. Clinical Characteristics of the Study Population (*n* = 536)

	Group 1 ( <i>n</i> = 169)	Group 2 ( <i>n</i> = 367)	<i>P</i>
Birth weight, g	1393 ± 576.1	1594.1 ± 585.9	<.001*
Gestational age, wk	30.1 ± 3.6	31.2 ± 4.0	.002*
VLBW, %	53	39	.003†
Male, %	46.8	49.3	.642
White, %	28.6	25.6	.527
Black, %	64.9	60.5	.34
Apgar score at 1 min	5.8 ± 2.3	6 ± 2.3	.163
Apgar score at 5 min	7.9 ± 1.3	7.8 ± 1.6	.673
Survival rate, %	91.7	94	.354
LOS, d	32.4 ± 28.2	26.5 ± 25.1	.024*
Medicaid, %	13	31.3	<.001†

LOS indicates length of hospital stay; VLBW, very low birth weight.

\* Kruskal-Wallis test.

† Fisher's exact test.

**TABLE 2.** Data on Central Lines and BSIs in the Study Population ( $n = 536$ )

	Group 1 ( $n = 169$ )	Group 2 ( $n = 367$ )	$P$
Sepsis, %	25.4	2.2	<.001*
BSIs, $n$	43	8	<.001*
Central line days	$8.5 \pm 11.7$	$7.1 \pm 12.7$	.025†
Line use	$0.29 \pm 0.6$	$0.22 \pm 0.4$	.066†
Central line-related BSIs, infections per 1000 line days	15.17	2.1	<.001*

\* Kruskal-Wallis test.

† Fisher's exact test.

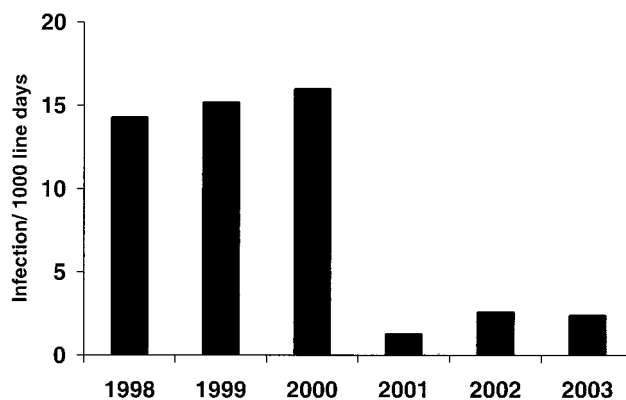
able to coagulase-negative *Staphylococcus* and 2 attributable to *S aureus*. The average central line duration was 1.4 days greater for infants in group 1, compared with group 2 ( $8.5 \pm 11.7$  days and  $7.1 \pm 12.7$  days, respectively;  $P = .025$ ) (Table 2). There was a trend toward a difference in line use that did not reach significance. In the logistic-regression model, birth weight, central line days, and ventilator days significantly influenced the rate of sepsis. The reduction in sepsis rate observed in association with the new policy was statistically significant after controlling for other factors in the regression model (regression coefficient:  $0.95 \pm 0.29$ ;  $P < .001$ ) (Table 3). The odds ratio of reduction in BSIs after the implementation of the new policy was 2.6 (95% confidence interval: 1.5–4.5). The incidence of central line-related BSIs decreased significantly from group 1 to group 2 (15.17 BSIs per 1000 line days and 2.1 BSIs per 1000 line days, respectively;  $P < .001$ ) (Fig 2).

The study included 233 very low birth weight infants (<1500 g), ie, 90 in group 1 and 143 in group 2. The 2 groups were similar with respect to birth weight, gestational age, central line days, line use, and ventilator use (Table 4). The culture-proven sepsis rate decreased significantly from group 1 to group 2 (46.7% and 5.6%, respectively;  $P < .0001$ ). The number of episodes of culture-proven sepsis decreased from 42 to 8 (Table 5). The decrease in sepsis rate remained significant in the logistic-regression model (regression coefficient:  $1.42 \pm 0.35$ ;  $P = .0001$ ) (Table 6). The odds ratio of decreased sepsis in relation to the new policy application among the very low birth weight infants was 4.15 (95% confidence interval: 2.1–8.3).

**TABLE 3.** Logistic-Regression Analysis of Factors Affecting Sepsis ( $n = 536$ )

	Regression Coefficient	SEM	$P$
Group 1 vs 2	0.95	0.29	<.001
Birth weight	1.2	0.33	<.001
Gender	-0.2	0.29	.489
White race	0.13	0.55	.819
Ventilator days	-0.05	0.03	.086
Central line days	-0.05	0.01	<.001
Maternal infection	-0.44	0.31	.157
PROM	-0.27	0.3	.376
Maternal diabetes mellitus	-0.65	0.49	.178

PROM indicates prolonged rupture of membranes.



**Fig 2.** Annual rates of central line-related BSIs at George Washington University Hospital.

**TABLE 4.** Clinical Characteristics of the Very Low Birth Weight Subgroup of Infants ( $n = 233$ )

	Group 1 ( $n = 90$ )	Group 2 ( $n = 143$ )	$P$
Birth weight, g	$937.8 \pm 294.8$	$996.4 \pm 306.3$	.156
Gestational age, wk	$27.5 \pm 2.6$	$27.7 \pm 2.8$	.609
Male, %	40.2	47.1	.353
White, %	29.4	22.9	.289
Black, %	67.4	66.7	1.00
Apgar score at 1 min	$5.3 \pm 2.2$	$5.2 \pm 2.4$	.943
Apgar score at 5 min	$7.6 \pm 1.4$	$7.4 \pm 1.7$	.515
LOS, d	$47.1 \pm 29.9$	$45.2 \pm 28$	.645

LOS indicates length of hospital stay.

**TABLE 5.** Data on Central Lines and BSIs Among Very Low Birth Weight Infants ( $n = 233$ )

	Group 1 ( $n = 90$ )	Group 2 ( $n = 143$ )	$P$
Sepsis, %	46.7	5.6	<.001*
BSIs, $n$	42	8	<.001*
Central line days	$14.9 \pm 12.6$	$16 \pm 16$	.883
Line use	$0.51 \pm 0.8$	$0.45 \pm 0.5$	.857

\* Fisher's exact test.

**TABLE 6.** Logistic Regression Analysis of Factors Affecting Sepsis Among Very Low Birth Weight Infants ( $n = 233$ )

	Regression Coefficient	SEM	$P$
Group 1 vs group 2	1.42	0.35	<.001
Birth weight	1.38	0.64	.031
Gender	-0.14	0.34	.683
White race	0.81	0.66	.221
Ventilator days	-0.04	0.03	.136
Central line days	-0.05	0.01	<.001
Maternal infection	-0.47	0.38	.208
PROM	-0.03	0.36	.928
Maternal diabetes mellitus	-1.42	0.36	.040

PROM indicates prolonged rupture of membranes.

## DISCUSSION

In this report, we affirm the effectiveness of applying a self-critical approach in monitoring and improving infection rates in our NICU. Infection rates were reduced significantly through the identification of optimal benchmark results and clinical practices in another unit and application of these practices in our own unit. A dramatic improvement in infection rates

was observed in the absence of other, chronologically parallel changes in our NICU practice.

Nosocomial infection is a major problem facing premature infants in the NICU. Premature infants are particularly vulnerable to sepsis because of their underdeveloped immune systems, repeated handling and exposure to multiple personnel, and invasive interventions.<sup>1-5</sup> CVCs are among the most common interventions thought to contribute to nosocomial infections.<sup>10</sup> The patients inherently at highest risk for sepsis (very low birth weight infants) usually require CVC placement, which increases their risk for sepsis.<sup>11</sup> Strategies to reduce or prevent catheter-related BSIs have included the use of antibiotic-coated catheters<sup>12</sup> and prophylactic administration of systemic antibiotics.<sup>13</sup> Such strategies may contribute to antibiotic resistance and toxicity. There continues to be a role for alternative strategies in the control of nosocomial infections, to improve the quality of care delivered to these vulnerable infants.<sup>4,14</sup> The wide variability in infection rates in comparable NICUs across the nation emphasizes the importance of identifying best practice guidelines and testing their effectiveness.

The implementation of the closed medication system and associated policies was associated with a significant decrease in the nosocomial infection rate in our unit, similar to the experience at CCMC.<sup>15</sup> Such a system prevents direct contact of medications and flush solutions with the hub of the catheter. Contamination of the hub has been correlated closely with the occurrence of sepsis, with the same organism cultured at the hub.<sup>16</sup> Administration of medication at a site distal to the patient is difficult, because it requires a significant amount of fluid to deliver these medications through the line to the patient. The tubing used in this closed medication system possesses a very narrow-lumen "microbore," which allows flushing of the 1.5-m line with only 0.4 mL of fluid. Nosocomial sepsis has been associated not only with CVCs but also with peripheral intravenous cannulae. Some studies showed equal risks for sepsis with either vehicle.<sup>17</sup> Therefore, we used the same closed medication system for both peripheral intravenous lines and CVCs. This might have been responsible for the decrease in sepsis rates for both infants with and without CVCs in the George Washington University Hospital population. We recommend uniform implementation of this practice.

It is unclear how the system affected the incidence of BSIs. We did not conduct cultures of the catheter hub to prove lower rates of line colonization or colonization at the connecting site.<sup>17</sup> In addition, the microbore extension tubing itself could have created a barrier for bacterial loads to be transported from the connecting site to the patient, because of the very small volumes of flushing fluid required in the system. These potential mechanisms deserve additional investigation. Of note, infections caused by *Candida* have been controlled in our unit for several years. This is probably a result of the longstanding policy in our unit to start oral nystatin prophylaxis for infants of <1000-g birth weight until they are receiving full enteral feeding. A previous study of our NICU in-

fants correlated acquired *Candida* sepsis with gastrointestinal colonization by *Candida parapsilosis*.<sup>18</sup>

The major limitation of this study is the lack of randomization. The multivariate regression analysis controlled for many risk factors known to be associated with nosocomial sepsis, such as body weight, CVC use, and mechanical ventilation. We cannot exclude the potential confounding effect of the new CVC policy influencing general motivation in the unit to decrease infection rates. However, the observational period of 3 years after implementation of this practice decreases the potential confounding. It is noteworthy that we searched for other changes that could parallel the dramatic reduction in BSI rates from the first time period to the second time period. There were no changes in the blood culture methods, brand of CVC used, brand of antiseptic used for hand-washing, or approach to antibiotic use. Both cohorts were inborn at our level 3 unit. There were no changes in staffing ratios or hospital infection-control or cohort practices.

The encouraging results of this study add to the growing body of literature emphasizing the value of benchmarking and collaboration in the quality improvement process.<sup>9,19</sup> Although dissemination of practice guidelines based on prospective randomized trials remains the standard method, the experience and knowledge of units with consistent excellence with respect to particular focused outcomes ("best/better practices") are valuable. This study emphasizes how quickly the successes of one such unit can be reproduced in another, underscoring the value of accessible shared outcome data.

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### A BONUS FOR HEALTH, PAYABLE TO THE DOCTOR TO CUT COSTS: MEDICARE TRIES INCENTIVES TO MEET STANDARDS

"A quiet revolution is taking place in Medicare, one that could set a new standard for the way medicine is practiced in this country. For the first time in its history, Medicare is starting to embrace an approach that has changed industries as diverse as carmakers and fast-food restaurants—giving employees financial incentives to meet goals for quality. By the end of this year, more than 600,000 Medicare recipients will be in test programs that pay doctors and hospitals bonuses for achieving better results, like increasing the number of diabetic patients whose blood sugar is under control. . . . Under the doctors' test program, which involves 10 large groups covering around 200,000 patients, physicians will receive bonuses if they measurably improve care for patients with common chronic diseases, including congestive heart failure, coronary disease, diabetes and high blood pressure. To qualify for the bonuses, the doctors must also provide preventive services like vaccines and cancer screening and they must save Medicare money by keeping patients out of the hospital and eliminating unnecessary procedures. A similar pay-for-performance program involving 280 hospitals is already under way. Later this spring, Medicare will post on its Web site ([www.HospitalCompare.hhs.gov](http://www.HospitalCompare.hhs.gov)) scores on 34 measures of performance for those hospitals. The Web site recently posted general performance data on 3,800 hospitals across the country. A third pilot program to begin later this year will focus on chronic-care management companies that help patients cope with diabetes and other long-term illnesses. 'It's hard to convey how big this is going to be, but it's going to be big,' said Dr. Mark B. McClellan, Medicare's top administrator."

Kolata G, Abelson R. *New York Times*. April 15, 2005

Noted by JFL, MD

## Is Bloodstream Infection Preventable Among Premature Infants? A Tale of Two Cities

Hany Aly, Victor Herson, Anne Duncan, Jill Herr, Jean Bender, Kantilal Patel and Ayman A. E. El-Mohandes

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