

Optimal Surveillance Culture Sites for Detection of Methicillin-Resistant *Staphylococcus aureus* in Newborns[∇]

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Received 24 April 2006/Returned for modification 4 July 2006/Accepted 11 August 2006

We describe two outbreaks among newborns, one caused by community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) and the other by hospital-associated MRSA. The umbilicus, rectum, and nares were tested for colonization. We found that no single body site had optimal sensitivity when tested alone. The combination of umbilical and nasal swabs achieved a sensitivity of >90%.

Outbreaks of infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) in the neonatal intensive-care unit (NICU) setting are well documented (7, 9, 13, 16–18, 22, 23, 26). To prevent transmission and to identify individuals who are at risk for developing infection, it is important to perform surveillance cultures (6, 15). Surveillance cultures may be taken from a range of body sites (1, 2, 4, 7, 12, 17, 22), and practices vary in this regard.

Few publications have addressed the sensitivities of surveillance cultures taken from different sites in neonates. Singh et al. reported results from two MRSA outbreaks in the NICU setting in which nasal cultures were paired with rectal or axillary (with or without umbilical) cultures during active surveillance efforts (24). The authors concluded that the use of nasal cultures alone would have detected 97% of colonized infants and would have resulted in significant cost savings. Interestingly, there were no positive umbilical cultures (24). Back et al. found that the addition of rectal swabs to nasal swabs in neonates in the NICU appeared to improve detection of MRSA-colonized infants, although this finding was not statistically significant (2). Of 28 infants colonized with MRSA who had paired nasal and rectal cultures, 16 infants were positive in both sites, three were positive only in the nares, and nine were positive only in the rectum ($P = 0.15$). Umbilical swabbing was not performed. Jernigan et al. reported that the most common sites of MRSA colonization during an NICU outbreak were the nares (88%), umbilicus (56%), groin (50%), and axilla (31%) (11).

Community-associated MRSA (CA-MRSA) is increasingly recognized as a cause of serious infections in neonates (8), and outbreaks in the NICU have been reported (5, 20). More recently, an outbreak of CA-MRSA infections was reported among healthy newborns and maternity patients in a hospital setting (3). It is still not certain whether CA-MRSA strains colonize different body sites than hospital-acquired MRSA (HA-MRSA) strains.

Hospital no. 1 is a 430-bed community teaching hospital with over 5,000 babies delivered annually. The NICU is an advanced level II, 24-bed unit. In October 2004, there was a clonal outbreak of CA-MRSA (Canadian MRSA 10 or a USA300-related clone) among healthy newborns and their mothers. A smaller, related cluster emerged in January 2005. In an attempt to actively identify colonized and/or infected babies, mothers who had delivered during the outbreak periods were advised to bring their newborns to the hospital. There, they were examined for signs of infection and tested for MRSA colonization in the nares, umbilicus, and rectum. The nasal and rectal swabs were premoistened with sterile saline. Both nares were sampled sequentially with a single swab. The majority of parents brought their infants to the hospital. The rest chose to see their primary-care physician and to have the culture results forwarded to the infection control team at the hospital.

Hospital no. 2, a 220-bed community teaching hospital with approximately 2,800 deliveries annually, experienced an almost simultaneous outbreak of MRSA in their level II special-care newborn nursery. Similar call-back clinics and screening procedures were undertaken. The clonal outbreak at hospital no. 2 was determined to have been caused by a common HA-MRSA strain (Canadian MRSA-2, or USA100 related).

Samples from hospital no. 1 were collected and transported in clear Amies gel with charcoal (Copan, Brescia, Italy) and inoculated onto mannitol-salt agar plates containing 2 mg/liter of oxacillin, while those from hospital no. 2 were collected and transported in clear Amies gel (Starplex Diagnostics Inc., Etobicoke, Ontario, Canada) and plated onto mannitol-salt agar plates containing 8 mg/liter cefoxitin. *S. aureus* was identified in both laboratories by using Gram stain, catalase, Pastorex Staph Latex (Bio-Rad, Marnes-la-Coquette, France), and tube coagulase. Methicillin resistance was confirmed by latex agglutination for PBP 2a and by susceptibility testing by accepted methods (4).

At hospital no. 1, 542 neonates were screened. All had nasal and rectal swabs, and 530 had umbilical swabs collected. There were 37 neonates with MRSA identified, 25 colonized and 12 infected. Of the 25 colonized neonates, all had nasal swabs, 24 had rectal swabs, and 23 had umbilical swabs taken. The sensitivities for detection of MRSA colonization at the three sites

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[∇] Published ahead of print on 6 September 2006.

TABLE 1. Detection of MRSA colonization by site in two unrelated hospital outbreaks among healthy newborns

Outbreak ^a	Screening strategy	No. positive/no. of colonized infants tested	Sensitivity (%)
Hospital no. 1 (USA300-related outbreak)	Nares only	17/25	68
	Umbilicus only	14/23	61
	Rectum only	5/24	21
	Nares and umbilicus	23/23 ^b	100
	Nares and rectum	17/24 ^b	71
Hospital no. 2 (USA100-related outbreak)	Nares only	18/25	72
	Umbilicus only	18/25	72
	Rectum only	15/25	60
	Nares and umbilicus	23/25 ^b	92
	Nares and rectum	21/25 ^b	84

^a A total of 25 colonized infants (nasal and/or rectum and/or umbilicus) were detected in each of the two hospital outbreaks.

^b The number tested includes only those colonized infants tested at both sites.

were 68, 21, and 61%, respectively (Table 1). Of the eight colonized babies with negative nasal swabs, seven were positive based exclusively on the umbilical swab, while one was positive based on the rectal swab (an umbilical swab was not collected). All patients with MRSA infections had positive cultures from the infected site. Interestingly, 7 of 11 (64%) infected babies had negative nasal cultures.

At hospital no. 2, 250 neonates were screened and 26 colonized infants were detected. Culture data, by site, were available for 25 of the 26 infants. No infections were identified. All 25 infants were screened in the nares, umbilicus, and rectum. Eighteen infants were colonized in the nares, 15 were colonized in the rectum, and 18 were colonized in the umbilicus, with sensitivities of 72, 60, and 72%, respectively (Table 1). Of the seven colonized infants who tested negative nasally, five were identified based on the umbilical specimen, and three were identified based on the rectal specimen.

The majority of infants screened (colonized and noncolonized) were ≤ 3 weeks of age in both outbreaks. Of the colonized infants, 4 infants were ≤ 7 days old, 9 infants were 8 to 14 days old, 21 infants were 15 to 21 days old, 13 infants were 22 to 28 days old, and 3 infants were more than 4 weeks old. Although the numbers in the various age subgroups were small, there were no clinically or statistically significant differences between the sites of colonization. The combination of nasal and umbilical screening, in those who were sampled at both sites, led to sensitivities of 92% (12/13) in those ≤ 2 weeks of age, 100% (20/20) of those 2 to 3 weeks old, and 94% (15/16) of those 3 weeks old or older.

Our findings differ from those of Singh et al. in that nasal swabs alone did not appear sufficiently sensitive for active-surveillance purposes. In both hospital outbreaks described here, one caused by a CA-MRSA strain and the other by an HA-MRSA strain, moderate sensitivity was noted using either nasal cultures or umbilical cultures alone. The combination of umbilical swabs and nasal swabs improved the sensitivity for detecting colonized infants to 100% at hospital no. 1 and to 92% at hospital no. 2, whereas the combination of nares and rectum improved the sensitivity only to 71 and 84%, respectively. This is not surprising, given that the umbilicus is a common reservoir for *S. aureus* (10, 14, 27). *S. aureus* initially

colonizes the umbilical stump and readily spreads to the nose or other sites in neonates. Nasal colonization, however, may be more persistent than that of the umbilicus (7). This may help to explain the inconsistent findings of the various studies. The difference in the sensitivities of rectal swabs in the two outbreaks is interesting and may be related to hospital- and community-associated strains having predilections for different sites. It may also be due to the cefoxitin in the media used by the laboratory at hospital no. 2, as that antibiotic has been shown to improve the overall sensitivity and the suppression of normal flora in perineal specimens (19, 25). Differences in the swabbing techniques, the sensitivities of the screening plates used (21), inclusion of patients with clinical infections, and the age at the time of sampling may have contributed to this variability and may be areas of interest for future studies.

In conclusion, while it may be reasonable to limit routine surveillance cultures to the nares in the absence of an outbreak, we recommend pairing nasal swabs with umbilical swabs during outbreaks of either HA- or CA-MRSA to optimize detection of colonized newborns.

REFERENCES

- Andersen, B. M., R. Lindemann, K. Bergh, B. I. Nesheim, G. Syversen, N. Solheim, and F. Laugerud. 2002. Spread of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive unit associated with understaffing, overcrowding and mixing of patients. *J. Hosp. Infect.* **50**:18–24.
- Back, N. A., C. C. Linnemann, Jr., J. L. Staneck, and U. R. Kotagal. 1996. Control of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive-care unit: use of intensive microbiologic surveillance and mupirocin. *Infect. Control Hosp. Epidemiol.* **17**:227–231.
- Bratu, S., A. Eramo, R. Kopec, E. Coughlin, M. Ghitan, R. Yost, E. K. Chapnick, D. Landman, and J. Quale. 2005. Community-associated methicillin-resistant *Staphylococcus aureus* in hospital nursery and maternity units. *Emerg. Infect. Dis.* **11**:808–813.
- Clinical and Laboratory Standards Institute. 2005. Performance standards for antimicrobial susceptibility testing, 15th informational supplement M100-S15. Clinical and Laboratory Standards Institute, Wayne, Pa.
- Eckhardt, C., J. S. Halvosa, S. M. Ray, and H. M. Blumberg. 2003. Transmission of methicillin-resistant *Staphylococcus aureus* in the neonatal intensive care unit from a patient with community-acquired disease. *Infect. Control Hosp. Epidemiol.* **24**:460–461.
- Gerber, S. I., R. C. Jones, M. V. Scott, J. S. Price, M. S. Dworkin, M. B. Filippell, T. Rearick, S. L. Pur, J. B. McAuley, M. A. Lavin, S. F. Welbel, S. Garcia-Houchins, J. L. Bova, S. G. Weber, P. M. Arnow, J. A. Englund, P. J. Gavin, A. G. Fisher, R. B. Thomson, T. Vecchio, T. Chou, D. C. Johnson, M. B. Fry, A. H. Molloy, L. Bardowski, and G. A. Noskin. 2006. Management of outbreaks of methicillin-resistant *Staphylococcus aureus* infection in the neonatal intensive care unit: a consensus statement. *Infect. Control Hosp. Epidemiol.* **27**:139–145.
- Haddad, Q., E. I. Sobayo, O. B. Basit, and V. O. Rotimi. 1993. Outbreak of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive care unit. *J. Hosp. Infect.* **23**:211–222.
- Healy, C. M., K. G. Hulten, D. L. Palazzi, J. R. Campbell, and C. J. Baker. 2004. Emergence of new strains of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive care unit. *Clin. Infect. Dis.* **39**:1460–1466.
- Hitomi, S., M. Kubota, N. Mori, S. Baba, H. Yano, K. Okuzumi, and S. Kimura. 2000. Control of a methicillin-resistant *Staphylococcus aureus* outbreak in a neonatal intensive care unit by unselective use of nasal mupirocin ointment. *J. Hosp. Infect.* **46**:123–129.
- Jellard, J. 1957. Umbilical cord as reservoir of infection in a maternity hospital. *Br. Med. J.* **5024**:925–928.
- Jernigan, J. A., M. G. Titus, D. H. Groschel, S. Getchell-White, and B. M. Farr. 1996. Effectiveness of contact isolation during a hospital outbreak of methicillin-resistant *Staphylococcus aureus*. *Am. J. Epidemiol.* **143**:496–504.
- Khoury, J., M. Jones, A. Grim, W. M. Dunne, Jr., and V. Fraser. 2005. Eradication of methicillin-resistant *Staphylococcus aureus* from a neonatal intensive care unit by active surveillance and aggressive infection control measures. *Infect. Control Hosp. Epidemiol.* **26**:616–621.
- Lally, R. T., E. Lanz, and C. G. Schrock. 2004. Rapid control of an outbreak of *Staphylococcus aureus* on a neonatal intensive care department using standard infection control practices and nasal mupirocin. *Am. J. Infect. Control* **32**:44–47.
- Meberg, A., and R. Schoyen. 1985. Bacterial colonization and neonatal in-

- fections. Effects of skin and umbilical disinfection in the nursery. *Acta Paediatr. Scand.* **74**:366–371.
15. Muto, C. A., J. A. Jernigan, B. E. Ostrowsky, H. M. Richet, W. R. Jarvis, J. M. Boyce, and B. M. Farr. 2003. SHEA guideline for preventing nosocomial transmission of multidrug-resistant strains of *Staphylococcus aureus* and enterococcus. *Infect. Control Hosp. Epidemiol.* **24**:362–386.
 16. Nakano, M., H. Miyazawa, Y. Kawano, M. Kawagishi, K. Torii, T. Hasegawa, Y. Iinuma, and M. Ohta. 2002. An outbreak of neonatal toxic shock syndrome-like exanthematous disease (NTED) caused by methicillin-resistant *Staphylococcus aureus* (MRSA) in a neonatal intensive care unit. *Microbiol. Immunol.* **46**:277–284.
 17. Nambiar, S., L. A. Herwaldt, and N. Singh. 2003. Outbreak of invasive disease caused by methicillin-resistant *Staphylococcus aureus* in neonates and prevalence in the neonatal intensive care unit. *Pediatr. Crit. Care Med.* **4**:220–226.
 18. Noel, G. J., B. N. Kreiswirth, P. J. Edelson, M. Nesin, S. Projan, W. Eisner, D. J. Bauer, H. de Lencastre, A. M. sa Figueiredo, and A. Tomasz. 1992. Multiple methicillin-resistant *Staphylococcus aureus* strains as a cause for a single outbreak of severe disease in hospitalized neonates. *Pediatr. Infect. Dis. J.* **11**:184–188.
 19. Perry, J. D., A. Davies, L. A. Butterworth, A. L. Hopley, A. Nicholson, and F. K. Gould. 2004. Development and evaluation of a chromogenic agar medium for methicillin-resistant *Staphylococcus aureus*. *J. Clin. Microbiol.* **42**:4519–4523.
 20. Regev-Yochay, G., E. Rubinstein, A. Barzilai, Y. Carmeli, J. Kuint, J. Etienne, M. Blech, G. Smollen, A. Maayan-Metzger, A. Leavitt, G. Rahav, and N. Keller. 2005. Methicillin-resistant *Staphylococcus aureus* in neonatal intensive care unit. *Emerg. Infect. Dis.* **11**:453–456.
 21. Safdar, N., L. Narans, B. Gordon, and D. G. Maki. 2003. Comparison of culture screening methods for detection of nasal carriage of methicillin-resistant *Staphylococcus aureus*: a prospective study comparing 32 methods. *J. Clin. Microbiol.* **41**:3163–3166.
 22. Saiman, L., A. Cronquist, F. Wu, J. Zhou, D. Rubenstein, W. Eisner, B. N. Kreiswirth, and P. Della-Latta. 2003. An outbreak of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive care unit. *Infect. Control Hosp. Epidemiol.* **24**:317–321.
 23. Shiojima, T., Y. Ohki, Y. Nako, A. Morikawa, T. Okubo, and S. Iyobe. 2003. Immediate control of a methicillin-resistant *Staphylococcus aureus* outbreak in a neonatal intensive care unit. *J. Infect. Chemother.* **9**:243–247.
 24. Singh, K., P. J. Gavin, T. Vescio, J. R. Thomson, Jr., R. B. Deddish, A. Fisher, G. A. Noskin, and L. R. Peterson. 2003. Microbiologic surveillance using nasal cultures alone is sufficient for detection of methicillin-resistant *Staphylococcus aureus* isolates in neonates. *J. Clin. Microbiol.* **41**:2755–2757.
 25. Stoakes, L., R. Reyes, J. Daniel, G. Lennox, M. A. John, R. Lannigan, and Z. Hussain. 2006. Prospective comparison of a new chromogenic medium, MRSASelect, to CHROMagar MRSA and mannitol-salt medium supplemented with oxacillin or cefoxitin for detection of methicillin-resistant *Staphylococcus aureus*. *J. Clin. Microbiol.* **44**:637–639.
 26. Tan, K. W., L. Tay, and S. H. Lim. 1994. An outbreak of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive care unit in Singapore: a 20-month study of clinical characteristics and control. *Singapore Med. J.* **35**:277–282.
 27. Watkinson, M., and A. Dyas. 1992. *Staphylococcus aureus* still colonizes the untreated neonatal umbilicus. *J. Hosp. Infect.* **21**:131–136.