Reduced use of surface cultures for suspected neonatal sepsis and surveillance

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Abstract

Data on infection in a neonatal unit were collected prospectively for seven years. After the first four years, the number of surface cultures obtained from neonates with suspected sepsis and for surveillance was reduced. Rates of systemic infection (sepsis and meningitis) were not significantly different in the four years before and the three years after this change. Reduction in surface culture information made no observable difference to detection of colonisation in neonates with early onset sepsis (within first 48 hours of life) nor to antibiotic choice in late onset sepsis. Decisions concerning the length of antibiotic course in suspected infection were not adversely affected. Reduction in the number of surface cultures led to considerable saving of time, effort, and cost while appearing safe in terms of clinical practice and outcome.

The use of surface cultures from neonates on intensive care units is controversial. Early studies suggested that routine surface cultures performed on individual infants at regular intervals as surveillance provided useful predictive information about the causative organism if an infant became septicaemic.¹ This has been challenged in a study by Evans *et al*, who found such cultures to be of little value in predicting the organisms causing true sepsis even if taken at the time of suspected sepsis.² Fulginiti and Ray describe surface culturing for the individual infant as an 'exercise in futility, wastefulness and inappropriate practice'.³ It may, however, be important to perform surface cultures to know what organisms are prevalent in a neonatal unit, their antibiotic sensitivity, and whether they are spreading from baby to baby.⁴ Preterm infants who receive artificial ventilation are at most risk of nosocomially acquired infections and comprise more than 80% of such cases,⁵ and surveillance cultures could be reserved for these babies. For early onset infection, the infant is usually heavily colonised with the invading organism, and culture from many sites may be unnecessary.

We have prospectively collected data on neonatal infections for seven years. Three years ago, we began an intervention study by reducing the number of surface cultures obtained from neonates for suspected sepsis and for surveillance. Effects on clinical practice and outcome were sought.

Methods

The neonatal unit serves a maternity department with a delivery rate that has increased

from 5750 to 6500 per annum over the seven years of the study and is the regional referral centre. There are approximately 550 admissions to the neonatal unit per annum, with about 10% of babies transferred from other hospitals.

DEFINITIONS AND DATA COLLECTION

Since April 1984, a weekly 'infectious diseases' ward round has been held on the neonatal unit. All microbiology reports for the previous week are collected and positive cultures recorded. All the babies are reviewed and episodes of systemic sepsis or other infection noted. If a baby is discharged during the week, the case notes are reviewed. The level of intensive care required and antibiotics prescribed are also recorded for each infant.

Early onset of sepsis is defined as septicaemia or meningitis in the first 48 hours of life. The unit policy is to stop antibiotic treatment in babies suspected of early onset sepsis if blood and cerebrospinal fluid cultures are negative after two to three days, unless the clinical state remains one of pneumonia or systemic infection in an infant heavily colonised with a pathogen such as group B streptococcus or *Listeria monocytogenes*. This has been termed 'very probable' early onset infection.^{6 7}

Late onset sepsis is defined as sepsis or meningitis occurring after 48 hours of age. Unit policy is to stop antibiotics on babies suspected of late onset sepsis if blood and cerebrospinal fluid cultures are negative after two days unless the clinical situation indicates otherwise: either the baby has continued to have signs suggesting systemic infection or a focus of infection has become apparent.

SURFACE CULTURES

In April 1988, we introduced a regimen that decreased the number of surface cultures performed for suspected early and late sepsis (table 1). For the 48 month period from April 1984 to March 1988 (period A) at least six surface sites were cultured, including aspirate of endotracheal secretions if the infant was intubated. For the 36 month period from April 1988 to March 1991 (period B) only two surface sites were cultured for suspected early onset sepsis: the external auditory canal and the throat. The urine was not cultured. For suspected late onset sepsis, no surface sites were cultured, but blood, cerebrospinal fluid, and urine were cultured. Surveillance cultures were decreased in this latter period from three times a week culture of tracheal aspirate from the endo-

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Table 1 Changes in surface cultures for babies with suspected sepsis and in surveillance cultures between periods A (1984–8) and B (1988–91)

Reason for culture	Period A	Period B	
	Early and late onset	Early onset	Late onset
Suspected sepsis	Blood Cerebrospinal fluid Ear Nose Eye Rectum Umbilicus Urine	Blood Cerebrospinal fluid Ear Throat	Blood Cerebrospinal fluid Urine
Surveillance	Endotracheal or nasopharyngeal (three per week)	Endotracheal (weekly)	

Table 2 Comparison of incidence of early (under 48 hours old) and late onset septicaemia or meningitis between period A (1984–8) when multiple surface cultures were performed and period B (1988–91) when the number of surface cultures had been reduced

	Period A		Period B		p Value
	No	Per 1000 live births	No	Per 1000 live births	
Early onset sepsis					
Definite	42	1.7	19	1.0	0.058
Detected (95% CI)	38/39* (0.06 to 13.5)		17/18† (0.04 to 27)		0.53
Very probable (95% CI)	12 (6 to 21)	0.5	8 (3 to 16)	0.4	0.89
Late onset	64	2.6	57	3.0	0.69

*Three not tested, †one not tested. CI, confidence interval.

Table 3 Early onset sepsis: bacteraemia or bacterial meningitis in babies under 48 hours of age, in the neonatal unit 1984–91

	Group B streptococcus	Listeria monocytogenes	Gram negative	Other	Total	Incidence/1000 live births
1984/5	3 (3)	0	3	4	10	1.7
1985/6	5 (4)	1	2	4	12	2.1
1986/7	6 (2)	2	1	4	13	2.1
1987/8	2 (3)	3	0	2	7	1.1
1988/9	3 (4)	3	0	1	7	1.1
1989/90	4 (2)	1	1	0	6	1.0
1990/1	2 (1)	0	2	2	6	0.9

Figures in parentheses are cases of probable group B streptococcal infection (see text for definition).

tracheal tube in ventilated babies and nasopharyngeal secretions from all other babies receiving intensive care, to once weekly culture of only tracheal aspirates from ventilated babies.

Comparisons were sought between periods A and B for rates of infection (early onset, very probable early onset, and late onset sepsis); for cases of early onset sepsis where surface cultures failed to show surface colonisation; for outbreaks of sepsis with resistant organisms missed because of the decreased frequency of surveillance cultures, and for cases of missed sepsis where infants might have had relapse of infection if antibiotics were stopped inappropriately early.

Statistical analysis of significance of differences in proportions was by χ^2 test or by the Fisher's exact test if numbers being compared were insufficient for appropriate use of the χ^2 test.

Results

There was no change in the incidence of early onset infection between the two study periods. No significant change in detection rate occurred after the number of surface cultures was reduced. The false negative rate was similar; cultures from surface sites failed to detect colonisation in one of 38 septic infants in period A, compared with one of 18 infants in period B (table 2). There was no change of incidence in the 'very probable' infection in infants in whom blood and cerebrospinal fluid cultures were negative but who remained clinically infected and had surface cultures showing colonisation (table 2). Aside from those infants with proved sepsis and 'very probable' sepsis, antibiotics were routinely stopped at 48 hours irrespective of surface culture results. No infant subsequently relapsed with infection soon after antibiotics were stopped. The decrease in number of surface cultures from at least six to two did not result in any missed cases of early onset sepsis. The causative organisms are shown in table 3.

The incidence of late onset sepsis was also not significantly different between the two periods (tables 2 and 4). There were no occasions during period B, when less surface culture information was being collected, where an infant relapsed after stopping antibiotics.

During period B, there was one outbreak of infection with an organism resistant to multiple antibiotics. A preterm infant with severe necrotising enterocolitis, bowel perforation, and peritonitis grew *Escherichia coli* from both peritoneal fluid and tracheal aspirate that was resistant to ampicillin, netilmicin, and gentamicin. The weekly culture of tracheal aspirate showed that the infant in the adjacent cot was also colonised with this organism. All neighbouring babies had nasopharyngeal or, if ventilated, tracheal cultures taken to see if further spread had occurred undetected by the once weekly tracheal surveillance culture. No other colonised infants were found. Routine infection control precautions, in particular careful hand-washing, were re-emphasised and no further spread to other infants was found. On another occasion, two neighbouring ventilated infants became septicaemic within a few days of each other with a Gram negative organism, *Alcaligenes*

Table 4 Late onset sepsis: bacteraemia or bacterial meningitis in babies over 48 hours old, in the neonatal unit 1984–91

	Gram negative bacillus	Enterococci	Coagulase negative	Staphylococcus aureus	Other*	Total episodes	Incidence/100 live births
1984/5	14	2	1	0	0	15	2.5
1985/6	12	8	3	0	1	19	3.3
1986/7	8	5	5	1	1	16	2.6
1987/8	8	1	5	0	2	14	2.2
1988/9	2	0	13	2	0	17	2.7
1989/90	7	1	8	2	2	19	3.2
1990/1	3	0	13	2	3	21	3.2

*Other=anaerobes, fungi, other Gram positive organisms; some episodes were polymicrobial.

denitrificans. Culture of the tip of the umbilical arterial catheter from one of the infants grew the organism. As this was an unusual infecting organism, a search was made for a likely source. Sites such as parenteral nutrition bags, sinks, humidifiers, and incubators were cultured. All babies in that particular room of the intensive care unit had their nasopharyngeal or, if ventilated, tracheal secretions cultured. No evidence of environmental or surface colonisation was discovered and no further episodes of sepsis with this organism occurred. The reduction in number of surface cultures to once a week from the endotracheal tube of artificially ventilated infants appeared to give adequate information about the prevailing organisms colonising the most 'at risk' babies on the unit.

Annually, approximately 310 'septic screens' were performed for suspected early onset sepsis and 150 for late onset. On average there were four intubated babies from whom the weekly surveillance culture was collected. Reducing the surface cultures as shown in table 1 and reducing routine surveillance cultures of endotracheal secretions from three times to once per week, led to a fall of 75% in the number of surface cultures from approximately 3800 to 960 per year. We estimated that each surface culture processed in the microbiology unit of this hospital costs £10 (using a time and motion study). The approximate annual saving from reducing the number of cultures was £28 000.

Discussion

Culturing of multiple body surface sites is widely practised in neonatal units.² This is done both at the time of suspected sepsis and at frequent intervals as a surveillance of potential pathogens. With increasing length of stay in a unit, a baby becomes sequentially colonised with a number of organisms but colonisation has been shown to correlate neither with the likelihood of occurrence of infection in that particular baby nor with the organism actually causing infection when it occurs.⁸⁻¹³ Evans *et al*² showed that even surface cultures performed on the day of suspected sepsis were poorly predictive of the organism actually causing infection of normally sterile body fluids. The longer the period between culture and infection, the more poorly predictive were the cultures. We have shown in this study that the number and frequency of surface cultures can be greatly decreased without compromising patient care.

One way in which a reduction of surface cultures was effected was to decrease the number of sites cultured at the time of suspected sepsis. Infants with early onset infection acquire the infecting organism from the birth canal either before or during birth. As they are likely to be heavily colonised, it was not unexpected that we found a culture of throat and external auditory canal to be as reliable as the culture of six or more sites previously performed. Colonisation with a potential pathogen at birth does not of itself predict infection. It could be argued that surface culture information is completely redundant. The septic screen is performed on the basis of clinical symptoms and signs of

infection and/or recognised risk factors for early onset infection.

A decision to stop antibiotics is usually made at 48-72 hours if blood and spinal fluid cultures are negative and the clinical picture allows. There is a group of babies in whom there is presumptive evidence of infection such as pneumonia but the body fluid cultures are negative. Philip *et al* termed these babies as having 'very probable' infection.⁶ It was to detect an aetiological organism for these infants that we retained some surface cultures. With the reduced number of sampling sites, we did not see a change in incidence of prospectively diagnosed cases of 'very probable' infection between the two study periods. However, a much larger study, of approximately 700 patients, would be necessary to have an 80% chance of detecting a change of statistical significance. Urine infection is unusual in the first two days of life.¹⁴ In the first four years of study (1984-8), we had no positive cultures of urine from babies with early onset sepsis, other than as part of generalised sepsis such as group B streptococcal septicæmia, and we therefore decided to stop culturing urine for suspected early onset sepsis.

We abandoned entirely the use of surface cultures for babies with suspected late onset infection in the light of the study of Evans *et al*.² Surface cultures on an individual baby do not help in predicting either an infective episode or the aetiology of an actual episode even when the culture site is contiguous with the infected surface—for example, the endotracheal secretions from intubated infants with pneumonia.¹² Our antibody policy for suspected late onset sepsis (a semisynthetic penicillinase resistant penicillin, flucloxacillin, and an aminoglycoside), is based mainly on the organisms which have caused sepsis in the past.⁷ The antibiotics used may have to be changed if there are frequent episodes of systemic sepsis with resistant organisms.⁴ Sometimes an outbreak with resistant organisms may be predicted by finding widespread colonisation with the organism,⁴ although Slagle *et al* found correlation between organisms in endotracheal isolates and those causing systemic sepsis in only 19% of cases.¹³ Nevertheless, we have encountered situations where knowledge of endotracheal colonisation, combined with episodes of sepsis with resistant organisms, enabled us to change the antibiotic procedure rapidly.⁴

As it is the smallest, most premature, most intensively nursed infants who are at greatest risk of late onset sepsis,⁵ we decided to retain a once weekly endotracheal culture as our sole routine surveillance culture compared with the previous three times weekly cultures. The incidence of late onset sepsis was unchanged in the two periods. In period B, when surveillance was reduced, there were no major omissions in terms of the range of coverage with antibiotics for suspects sepsis.

The study coincided with coagulase negative staphylococci emerging as the single commonest pathogen responsible for late onset sepsis. Forty per cent of these isolates were methicillin resistant (data not shown), though no clinical

deterioration occurred before vancomycin was substituted for the semisynthetic penicillin, probably because of sensitivity to the aminoglycoside, and the removal of any central venous catheters. Given the variety and ubiquity of coagulase negative staphylococci colonising infants, the prediction of the invasive isolate by surveillance would have been impossible. The limited surveillance did detect the localised spread between babies of an organism resistant to multiple antibiotics, but more extensive surface culturing failed to detect any further spread. When there was an outbreak of late onset sepsis with an unusual organism, not detected by the once weekly endotracheal culture, nor a part of the prevalent flora, a more extensive search was made (including the use of surface cultures of the babies in the same room as the index case), but no evidence of surface colonisation was found. Both episodes suggested that the limited surveillance was sufficient.

The cost of procedures that are considered routine and part of the rituals of an institution are often the last to be scrutinised. In this study, we considered only the financial savings made in processing the specimens in the laboratory. There was also considerable saving in effort for nursing staff who take the swabs, and laboratory staff who decide how far to characterise, identify, and establish the sensitivity of each organism cultured. The thinner sheaf of results returned to the neonatal medical staff could be considered more thoughtfully by them and filed more easily by the clerical staff.

The collation of bacteriological and clinical information from a neonatal intensive care unit is straightforward. Over a period of time, it can

be used to assess changes in management critically. In this instance, we have used the monitoring system to show that the number of surface cultures performed can be reduced without detriment to patient care and with considerable saving in time, effort, and cost.

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- 1 Sprunt K, Leidy G, Redman W. Abnormal colonization of neonates in an intensive care unit: means of identifying neonates at risk of infection. *Pediatr Res* 1978;12:998-1002.
- 2 Evans ME, Schaffner W, Federspiel CF, et al. Sensitivity, specificity and predictive value of body surface cultures in a neonatal intensive care unit. *JAMA* 1988;259:249-53.
- 3 Fulginiti VA, Ray CG. Body surface cultures in the newborn infant. *Am J Dis Child* 1988;142:19-20.
- 4 Isaacs D, Catterton J, Hope PL, Moxon ER, Wilkinson AR. Factors influencing colonisation with gentamicin resistant Gram negative organisms in the neonatal unit. *Arch Dis Child* 1988;63:533-5.
- 5 Isaacs D, Wilkinson AR, Moxon ER. Surveillance of colonisation and late onset septicaemia in neonates. *J Hosp Infect* 1987;10:114-9.
- 6 Philip AGS, Hewitt JR. Early diagnosis of neonatal sepsis. *Pediatrics* 1980;65:1036-41.
- 7 Isaacs D, Wilkinson AR. Antibiotic use in the neonatal unit. *Arch Dis Child* 1987;62:204-8.
- 8 MacGregor RR, Tunnessen WW. The incidence of pathogenic organisms in the normal flora of the neonate's external ear and nasopharynx. *Clin Pediatr (Phila)* 1973;12:697-700.
- 9 Townsend TR, Wenzel RP. Nosocomial bloodstream infections in a newborn intensive care unit: a case matched control study of morbidity, mortality and risk. *Am J Epidemiol* 1981;114:73-80.
- 10 Goldmann DA, Leclair J, Maccone A. Bacterial colonization of neonates admitted to an intensive care environment. *J Pediatr* 1978;93:288-92.
- 11 Goldmann DA. Bacterial colonization and infection in the neonate. *Am J Med* 1981;70:417-22.
- 12 Webber S, Wilkinson AR, Lindsell D, et al. Neonatal pneumonia. *Arch Dis Child* 1990;65:207-11.
- 13 Slagle TA, Bifano EM, Wolf JW, Gross SJ. Routine endotracheal cultures for the prediction of sepsis in ventilated babies. *Arch Dis Child* 1989;64:34-8.
- 14 Visser VE, Hall RT. Urine culture in the evaluation of suspected neonatal sepsis. *J Pediatr* 1979;94:635-8.