J. Med. Microbiol. — Vol. 36 (1992), 117–120

Congenital bacterial sepsis in very preterm infants

P. J. THOMPSON, ANNE GREENOUGH*, H. R. GAMSU, K. H. NICOLAIDES† and J. PHILPOTT-HOWARD‡

Departments of Child Health, †Obstetrics and ‡Medical Microbiology, King's College Hospital, London SE5 9RS

Summary. The results of body fluid and surface cultures from 148 preterm infants < 33 weeks gestational age obtained routinely on admission to a neonatal intensive care unit were reviewed. The aim was to determine the occurrence of congenital bacterial sepsis in this population and to examine whether surface cultures yielded information helpful in management. Gastric aspirate and umbilical, nasal and ear swabs were cultured and the results were compared to those of blood cultures. Nine infants (5·4%) had congenital bacterial sepsis diagnosed by positive blood cultures. Only the results of microscopy of gastric aspirate were available within hours of birth and before the results of blood culture. Microscopy of gastric aspirate, demonstrating pus cells, alone had a sensitivity of 0·86 in predicting congenital sepsis but a specificity of 0·49; the specificity, however, rose to 0·80 if both organisms and pus cells were observed on microscopy. Thus, only this combination was a useful pre-indicator of congenital sepsis. In infants who did not develop septicaemia, treatment was modified only if *Streptococcus agalactiae* was cultured from surface sites; in all such cases, the organism was grown from the ear swab. Our results demonstrate that congenital bacterial sepsis is common amongst very preterm infants admitted for neonatal intensive care but routine screening of surface cultures should be restricted to an ear swab only.

Introduction

Intra-uterine infection has been implicated as a cause of premature labour and antenatal infection may be associated with as many as 40% of preterm deliveries.[1] This suggests that the incidence of congenital bacterial sepsis may be high amongst very preterm infants, but this has not been confirmed.

Body fluid and surface cultures are obtained routinely from preterm neonates when they are first admitted to a neonatal intensive care unit (NICU) in an attempt to identify potentially pathogenic organisms and guide antibiotic treatment, but their usefulness has not been evaluated. The results of such investigations, and of microscopy of gastric aspirate, may be used as screening tests for congenital sepsis. However, there has been disagreement about their usefulness as screening tests.[2,3] Mims *et al.*[2] examined the gastric aspirates from 207 neonates and reported that although 60% of gastric aspirates contained free bacteria and it was possible to culture pathogenic organisms from 14%, there were no cases of confirmed septicaemia. In contrast, Ablow *et al.*[3] suggested that analysis of gastric aspirate was useful because it enabled the differentiation of respiratory distress syndrome (RDS) from early onset group B streptococcal septicaemia. A further role of surface cultures is the detection of *Streptococcus agalactiae* infection. This organism causes such a severe multi-system illness that even if it is isolated only from surface sites and not from blood cultures, clinicians may institute or modify antibiotic therapy.[4,5] The frequency with which this organism is isolated from surface cultures alone in very preterm infants is not known, nor is it known whether restriction of cultures to those from only certain sites would still identify all such affected infants.

The aim of our study was to determine the incidence of congenital sepsis in very preterm infants admitted to the NICU. We also wished to assess, in this population, if surface cultures yielded information helpful in the management of these infants.

Received 28 June 1990; revised version accepted 9 May 1991.
*Correspondence should be sent to: Dr A. Greenough, Department of Child Health, King's College Hospital, Denmark Hill, London SE5 9RS.

Materials and methods

Patients

A review was made of the microbiological results of 168 infants of < 33 weeks gestation born at King's College Hospital and admitted consecutively to the NICU between 1 Jan. 1988 and 30 June 1989. The infants had a mean gestational age of 29 weeks (range

22–32 weeks) and a mean birthweight of 1·3 kg (range 0·43–2·52 kg).

Laboratory investigations

On admission, blood cultures, gastric aspirate, and ear, umbilical and nasal swabs were obtained from all infants and sent for microbiological examination. The transport medium used for swabs was a commercially available Amies' transport medium. These specimens were obtained as part of the routine practice of the unit. Lumbar puncture to obtain cerebrospinal fluid (CSF) was performed only if there was a specific clinical indication such as maternal pyrexia, prolonged rupture of the membranes (>48 h) associated with vaginal discharge, neonatal pyrexia or low white blood cell count ($<5\times10^9$/L). Blood was cultured by a radiometric method (Bactec). Gram-stained smears were prepared from gastric aspirates and samples were then innoculated on to horse-blood agar and incubated aerobically and anaerobically at 37°C. Enrichment media were not used and culture of mycoplasmas was not attempted. Other samples were processed by standard laboratory methods.

Congenital sepsis was defined as the isolation of a single organism from blood cultures or CSF, or an excess of white blood cells in the CSF taken in the first 24 h of life. The results of the superficial cultures and gastric aspirates were compared with the occurrence of congenital sepsis. The sensitivity and specificity of these investigations in predicting congenital sepsis were calculated:[6]

$$\text{Sensitivity} = \frac{\text{septic infants with positive test result}}{\text{all septic infants tested}}$$

$$\text{Specificity} = \frac{\text{non-septic infants with negative test result}}{\text{all non-septic infants tested}}$$

Infants who developed signs of respiratory distress (tachypnoea, grunting, retraction) or had a maternal history suggestive of infection were commenced on parenteral penicillin and gentamicin; these antibiotics were discontinued after 48 h if all culture results were negative. If blood cultures were positive or *S. agalactiae* was isolated from surface cultures despite negative blood cultures, antibiotics were continued and, when necessary, modified according to microbiological results and clinical progress.

Results

Blood culture and surface swabs were obtained from 148 of the 168 infants. In the remaining 20 cases there was no clinical indication and review of the medical notes confirmed that there had been no evidence of septicaemia. Positive blood culture results were found in nine of the infants—6·1% of the 148 tested, 5·4% of all 168 infants. The organisms isolated were *S. agalactiae* (4 cases), *Listeria monocytogenes* (2), *Escherichia coli* (1), *Haemophilus influenzae* (1) and *Enterobacter intermedium*. Lumbar puncture was performed on 13 infants; indications were prolonged rupture of membranes in 10 and pyrexia in three. Only one infant had a positive CSF result; *L. monocytogenes* was cultured from blood and CSF. Lumbar puncture was performed on only one of the other eight infants with septicaemia and there were no positive CSF findings. The mortality in the neonates with congenital sepsis was 33% (3 of the 9 infants) compared with 17% (24 of 139 infants) without proven sepsis (not significant; χ^2 test with Yates's correction).

Culture results from 127 gastric aspirates, 130 nasal swabs, 136 umbilical swabs and 134 ear swabs were available from the neonates who had blood taken for culture. In the nine infants with congenital sepsis no organism, other than that identified from the blood culture, was isolated from the surface cultures or gastric aspirate (table I). *S. agalactiae* was isolated from ear swabs from another three babies. Antibiotic therapy was maintained in all three infants for 10 days; none had further neonatal problems. In the four neonates with proven streptococcal septicaemia, although the organism was not isolated from all surface sites, in all four infants it was isolated from the ear swab. Other organisms were isolated from surface sites from other infants but were not associated with septicaemia (table II). The sensitivity and specificity

Table I. Positive surface cultures from very preterm neonates

Species isolated	Number of infants with positive cultures from							
	gastric aspirate		nasal swab		umbilical swab		ear swab	
	PS	NS	PS	NS	PS	NS	PS	NS
S. agalactiae	3	3	3	1	4	1	4	3
E. coli	0	3	1	0	1	0	1	2
H. influenzae	1	0	0	0	0	0	0	0
Ent. intermedium	0	0	0	0	0	0	0	0
L. monocytogenes	2	0	1	0	2	0	2	0

PS, proven septicaemia; NS, non-septicaemic.

Table II. Positive surface cultures with organisms not associated with septicaemia

Species isolated	Number of infants with positive cultures from			
	gastric aspirate	nasal swab	umbilical swab	ear swab
Gardnerella vaginalis	1	...	...	...
Streptococcus milleri	1	1	1	1
Non-haemolytic streptococcus	...	...	...	1
S. sanguis	1	2	2	2
Acinetobacter sp.	...	...	...	1
Staphylococcus aureus	1	1	1	...
Enterococcus faecalis	...	...	2	...
Proteus sp.	...	...	...	1
Viridans streptococcus	2	1	3	2
Staph. epidermidis	2	...	...	...
Bacteroides sp.	2	...	...	...
Klebsiella sp.	1	...	...	...
Citrobacter sp.	1	...	...	...

of surface cultures in predicting congenital sepsis are shown in table III.

Discussion

In this series of 168 infants delivered at < 33 weeks gestation, the incidence of septicaemia was 5·4%. This is much higher than the 0·4% incidence reported for neonatal sepsis in infants born before 37 weeks gestation.[7] However, by restricting our report to infants of < 33 weeks gestation who were admitted to the NICU, we have concentrated upon a sub-group of premature babies who are at greater risk of this complication. Boyle *et al.*[8] also found a high incidence (8%) of congenital septicaemia in a selected group of preterm infants with RDS. The incidence of meningitis has previously been reported as 0·4–1/1000;[3,9] only one infant in our study developed meningitis and comparison is inappropriate.

In our survey, the sensitivity for prediction of septicaemia of cultures from surface swabs was 0·71–0·78 and the specificity was 0·90–0·97. These values are better than those of Evans *et al.*[10] (0·56 and 0·86, respectively). Our surface swabs were obtained on the first day of life, whereas Evans *et al.*[10] used the data from all cultures performed on infants throughout their stay in the NICU. Our results confirm those of Pacifico *et al.*[11] who also found that surface swabs were most useful as a screening test for neonatal infection when performed on the first day of life.

Table III. Sensitivity and specificity of surface cultures in predicting congenital sepsis

Test	Sensitivity	Specificity
Gastric aspirate		
Microscopy		
pus cells	0·86	0·49
pus cells +organisms	0·86	0·80
Culture	0·75	0·84
Surface swabs		
Umbilicus	0·78	0·92
Nose	0·71	0·97
Ear	0·78	0·90

To be most useful in the prediction of congenital sepsis, results from screening tests should be available before the results of blood cultures; thus, microscopy of gastric aspirate is potentially the best test. Microscopy of gastric aspirate revealing the presence of pus cells (polymorphonuclear leucocytes) had the lowest specificity of the potential screening tests reported in the present study. This finding was not unexpected because previous studies[12,13] have shown that pus cells may be present in the gastric aspirate within the first 6 h of life as a result of conditions other than infection, in particular, fetal asphyxia. Our results demonstrate that only the presence of both pus cells and organisms accurately predicts congenital sepsis.

In our cohort, four neonates had proven streptococcal septicaemia and the organism was identified from surface sites only in a further three. Although *S. agalactiae* organism was not isolated from all surface sites, in all seven infants it was isolated from the ear swab. The usefulness of culturing the ear swab has been recommended previously because, theoretically, at birth the ear contains a small amount of amniotic fluid and would seem likely to be the surface site from which organisms are most likely to be cultured in congenital sepsis.[14,15]

Culture of ear, nasal and umbilical swabs costs *c.* £3 per swab and examination and culture of the gastric aspirate is *c.* £6.50. Thus, these tests cost *c.* £15.50 per patient; this does not include the cost of medical, nursing or technologist time in performing and analysing these tests. Each year, large numbers of preterm infants are admitted to NICUs; it is important that the most sensitive and specific screening tests, or those which reveal data that would modify treatment

are employed. Therefore, we conclude that routine cultures of preterm neonates of < 33 weeks gestation on admission should be restricted to examination of the blood and an ear swab.

P. J. T. (Research Fellow) was supported by Children Nationwide Medical Research Fund. We are grateful to all the nursing and medical staff of Frederic Still Ward, without whose help this study would not have been possible, and we thank Ms Sue Williams for secretarial assistance.

References

1. Morales WJ, Angel JL, O'Brien WF, Knuppel RA, Finazzo M. A randomized study of antibiotic therapy in idiopathic preterm labor. *Obstet Gynecol* 1988; **72**: 829–833.
2. Mims LC, Medawar MS, Perkins JR, Grubb WR. Predicting neonatal infections by evaluation of the gastric aspirate: a study in two hundred and seven patients. *Am J Obstet Gynecol* 1972; **114**: 232–238.
3. Ablow RC, Driscoll SG, Effmann EL, Gross J *et al.* A comparison of early-onset group B streptococcal neonatal infection and the respiratory-distress syndrome of the newborn. *N Engl J Med* 1976; **294**: 65–70.
4. Pyati SP, Pildes RS, Ramamurthy RS, Jacobs N. Decreasing mortality in neonates with early-onset group B streptococcal infection: reality or artefact. *J Pediatr* 1981; **98**: 625–627.
5. Schmidt M, Bors Z, Kis É. Bacterial colonization of newborn infants in an intensive care unit. *Acta Microbiol Hung* 1983; **30**: 259–262.
6. Thorner RM, Remein QR. Principles and procedures in the evaluation of screening for disease. US Public Health Service, Division of Chronic Diseases. Washington DC, Government Printing Office 1961. Monograph no. 67: 24 pp.
7. Wientzen RL, McCracken GH. Pathogenesis and management of neonatal sepsis and meningitis. *Current Problems in Pediatrics* 1977; VIII Dec.
8. Boyle RJ, Chandler BD, Stonestreet BS, Oh W. Early identification of sepsis in infants with respiratory distress. *Pediatrics* 1978; **62**: 744–750.
9. Overall JC. Neonatal bacterial meningitis. *J Pediatr* 1970; **76**: 499–511.
10. Evans EM, Schaffner W, Federspiel CF, Cotton RB, McKee KT, Stratton CW. Sensitivity, specificity, and predictive value of body surface cultures in a neonatal intensive care unit. *JAMA* 1988; **259**: 248–252.
11. Pacifico L, Chiesa C, Cianfrano V, Panero A, Bucci G, Midulla M. Body surface cultures in the neonatal intensive care unit. *JAMA* 1989; **261**: 46.
12. Maudsley RF, Brix GA, Hinton NA, Robertson EM, Bryans AM, Haust MD. Placental inflammation and infection. *Am J Obstet Gynecol* 1966; **95**: 648–659.
13. Pole G, McAllister TA. Gastric aspirate analysis in the newborn. *Acta Paediatr Scand* 1975; **64**: 109–112.
14. Scanlon J. The early detection of neonatal sepsis by examination of liquid obtained from the external ear canal. *J Pediatr* 1971; **79**: 247–249.
15. MacGregor RR, Tunnessen WW. The incidence of pathogenic organisms in the normal flora of the neonate's external ear and nasopharynx. *Clin Pediatr* 1973; **12**: 697–700.