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Early neonatal bacteraemia

Comparison of group B streptococcal, other Gram-positive and Gram-negative infections

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SUMMARY All cases of neonatal bacteraemia associated with clinical illness occurring at Hammersmith Hospital, over a 9-year period 1967–1975 inclusive, have been reviewed. The infants studied were those born in the hospital's maternity unit and those admitted from other hospitals from a wide area round London who were ill or of low birthweight. Positive blood cultures occurred in 91 infants, 47 of them in the first 48 hours of life. These 47 infants were analysed separately and divided into three groups, 13 with group B streptococcal infections, 11 with other Gram-positive infections, and 23 with Gram-negative infections. There were no significant differences in birthweight or gestation, in mortality, in incidence of clinically diagnosed respiratory distress syndrome or recurrent apnoea, or in the need for mechanical ventilation between the three groups. The age at which a diagnosis of infection was suspected, and the age at death were both significantly earlier in the group infected with group B streptococcus than in those infected with other organisms ($P<0.01$ for both comparisons). There were no significant differences in the incidence of hyaline membrane formation or pneumonia seen at necropsy among the three groups. In some of the earliest deaths in the Gram-negative bacteraemic group, Gram-negative rods comprised the bulk of the hyaline membrane as did cocci in the group B streptococcal group.

The features of group B streptococcal (GBS) infection in the newborn have been described in numerous recent reports (Franciosi *et al.*, 1973; Barton *et al.*, 1973; Quirante *et al.*, 1974; Howard and McCracken, 1974; Lloyd and Reid, 1976). These tend to consider the organism and the patterns of illness it engenders in isolation, perhaps because it has become one of the most frequent causes of neonatal sepsis. For instance, it has been suggested that when the disease has an early onset, it frequently mimics the respiratory distress syndrome, even to the extent of hyaline membrane formation (Ablow *et al.*, 1976). To restore a balanced outlook, we have examined all cases of early neonatal bacteraemia occurring in our hospital over a 9-year period.

Patients and methods

The study extended from 1967 to 1975 inclusive, and the infants studied were (1) those born to mothers delivered in the maternity unit of Hammersmith Hospital. There were 16 240 live births during this time. (2) Those admitted from other hospitals to the neonatal intensive care unit, which in addition to catering for its own maternity unit, acts as a referral centre for ill and/or low birthweight babies from an approximately 50 mile radius round London, and occasionally from farther afield. Admissions to this unit from other hospitals and elsewhere numbered 849.

Blood was drawn for culture as part of the routine investigations for any suspected infection, before antibacterial therapy was started. If an infant died, whether infection was suspected or not blood was also drawn immediately after death, usually by direct cardiac puncture. The records of all infants with positive blood cultures were reviewed, and details of their clinical course abstracted. Those in whom positive culture had occurred within 48 hours of birth were selected for further analysis. We also compared birthweight and gestation of those early-infected infants with that of 254 infants held on our computerized perinatal data bank who had come to

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necropsy over a similar time period with hyaline membrane disease.

Results

Ninety-one of all infants studied had illness associated with a positive blood culture; this occurred in 26 of the inborn infants, and in 65 of those born elsewhere, giving rates of 1·6/1000 live hospital births, and 76/1000 outside admissions. We cannot be certain that our routine for drawing blood culture before starting antibacterial therapy and/or at death was always followed, therefore we give these figures as a minimum rather than as an exact incidence. 47 of the 91 infants (52%) had positive cultures within the first 48 hours of life. Details of the isolates are given in Table 1, and their distribution among inborn and outborn infants in Table 2. Clinical features of the 47 infants are given in Table 3. It can be seen that there were no significant differences between those with GBS, other Gram-positive, or Gram-negative infections, in birthweight or gestation, in the frequency with which respiratory distress or recurrent apnoea were diagnosed, or in need for mechanical ventilation. Intubation at birth was necessary in only 13% of GBS infections as compared with 45% of those with other Gram-positive infections and 65% of those with Gram-negative infections ($P<0·05$). The distributions of age at diagnosis and, in fatal cases, age at death were highly skewed. The median age at diagnosis was 13, 24, and 39 hours for infants with GBS, other Gram-positive and Gram-negative infections respectively. The corresponding ages at death were 21, 33, and 42 hours respectively. The differences between the three groups of infants were significant ($P<0·01$ and $P<0·025$ for age at diagnosis and death respectively) using Kruskal-Wallis rank analysis of variance (Siegel, 1956). The GBS infants were diagnosed earlier and died more rapidly than the infants with other infections ($P<0·01$ for both comparisons using the Wilcoxon rank test). Of the 254 cases who died of hyaline membrane disease without infection, mean birthweight (±SEM) was

Table 1 *Isolations from infants with early onset (<48 hours) bacteraemia*

Gram-positive		*Gram-negative*	
Species	*No. of infants*	*Species*	*No. of infants*
Group B streptococcus	13		
Staphylococcus albus	4	*Escherichia coli*	8
Staphylococcus aureus	2	*Pseudomonas aeruginosa*	7
Clostridium welchii	1	Klebsiella-Enterobacter-Serratia group	5
Group G streptococcus	1	*Haemophilus influenzae*	2
Listeria monocytogenes	1	*Pseudomonas alcaligenes*	1
Streptococcus faecalis	1		
Streptococcus viridans	1		
Total	24		23

Table 2 *Isolations from inborn and outborn infants with early onset (<48 hours) bacteraemia*

Isolations	*Infants born in Hammersmith Hospital*	*Infants born elsewhere*
Group B streptococcus	5	8
Other Gram-positive	5	6
Gram-negative	6	17
Total	16	31

Table 3 *Clinical details in early onset (<48 hours) bacteraemia*

	Group B streptococcus		*Other Gram-positive*		*Gram-negative*		*P for heterogeneity*
	No.	%	*No.*	%	*No.*	%	
Total no. of infants	13	100	11	100	23	100	
Deaths	10	77	5	45	20	87	NS
Intubation at birth	2	15	5	45	15	65	<0·05
RDS diagnosed	10	77	8	73	17	74	NS
Recurrent apnoea	10	77	8	73	17	74	NS
Mechanical ventilation	9	69	6	55	19	83	NS
Birthweight (g)							
Mean	1786		1972		1689		NS
Range	720–3060		900–3720		780–3250		
Gestational age (w)							
Mean	32·3		33·5		31·9		NS
Range	24–40		27–41		26–42		
Age at diagnosis (h)							
Median	13		24		39		<0·01*
Range	3–38		5–48		7–47		
Age at death (h)							
Median	21		33		42		<0·025*
Range	7–51		13–221		13–106		

*Using Kruskal-Wallis one-way analysis of variance by ranks.
RDS=respiratory distress syndrome.

1607±41 g, and mean gestation 31·5±0·2 weeks. These values were slightly lower than those in the infected babies but the differences were not significant.

Thirty-five of the 47 infants who had positive cultures within 48 hours of birth died, and permission for necropsy was obtained in 31. The incidence of pneumonia and hyaline membrane formation is shown in Table 4. Hyaline membrane formation

Table 4 *Incidence of hyaline membranes and pneumonia at necropsy according to infecting organism*

Necropsy findings	*Group B streptococcus*	*Other Gram-positive*	*Gram-negative*
Total necropsies	8	4	19
Hyaline membranes only	3	0	8
Pneumonia only	4	0	3
Hyaline membranes + pneumonia	1	2	2

and/or pneumonia was present in all cases of GBS infection, in half of those with other Gram-positive infections and in two-thirds of those with Gram-negative infections. Masses of cocci within the lungs were a feature of babies with GBS infection, and were seen mainly in those who had received less than 6 hours of antibiotic treatment before death. The cocci were usually seen within the hyaline membranes. These membranes did not differ morphologically from those present in lungs of babies with other Gram-positive or Gram-negative infections. 2 infants with *Haemophilus influenzae* bacteraemia who died at an early age (10 and 14 hours) with clinically diagnosed hyaline membrane disease had pulmonary hyaline membranes infiltrated with masses of organisms in a similar fashion to the appearance seen in lungs of babies with GBS infection.

Discussion

It is well known that neonatal bacterial infection occurs significantly more often among those of low birthweight, after prolonged rupture of membranes, and in the course of other neonatal illness. Streptococcal infection, prevalent at the beginning of the century in both the newborn infant *and* his mother, has again become one of the most numerically important of the neonatal period. Recent reports (Franciosi *et al.*, 1973; Barton *et al.*, 1973; Quirante *et al.*, 1974; Howard and McCracken, 1974; Lloyd and Reid, 1976) have suggested that GBS gives rise to characteristic patterns of illness, the most devastating of which is an early septicaemic form, often presenting as respiratory distress, in which maternal transmission is frequently proven. Infective illness due to GBS starting later may be more insidious in onset, and is more often associated with meningitis.

We do not believe the patterns of illness due to GBS infection differ markedly in general from those in other neonatal bacterial infections, and have examined particularly those infants with bacteraemia occurring within 48 hours of birth over a 9-year period to seek support for this contention. No significant differences are present in mean birthweight or gestation, in mortality, or in the frequency with which respiratory distress or recurrent apnoea were diagnosed when infants with GBS infection were compared with infants having other Gram-positive or Gram-negative bacteraemia. Lung findings at necropsy in the three groups did not differ significantly, though GBS infants all had hyaline membrane formation and/or pneumonia. Katzenstein *et al.* (1976) using fluorescein-labelled antisera to study lung sections in infants who had died of GBS infection, have shown that the cocci may on occasions be so numerous that they comprise the bulk of the membrane. They have postulated that the membranes form because of pulmonary alveolar damage by the organism. Our experience suggests that such damage is not necessarily confined to GBS, but may occur in other overwhelming neonatal infections, whether Gram-positive or Gram-negative.

Streptococcal bacteraemia did, however, differ from other Gram-positive and Gram-negative bacteraemias in the age at onset and the age at death, which were both significantly earlier. This means that more widespread use will have to be made of ancillary investigations such as quantitative and qualitative changes in the polymorphonuclear leucocytes (Xanthou, 1972; Zipursky *et al.*, 1976; Kuchler *et al.*, 1976), and stained smears of pharyngeal, gastric, or ear canal aspirate (Scanlon, 1972), if diagnosis is to be made soon enough for antibacterial therapy to be effective. We do not as yet have enough information on lecithin/sphingomyelin ratios performed on pharyngeal aspirates to know to what extent they would be helpful in differentiating infection from genuine respiratory distress, though we are able to say that low ratios and infection coexist. Symptoms of respiratory distress in infants of over 32 weeks' gestation should always prompt a rapid search for confirmatory evidence of infection so that effective treatment can be started without delay.

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