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Neonatal infections with *Haemophilus* species

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SUMMARY During a 27 month study seven non-serotypable strains of *Haemophilus influenzae* and two of *Haemophilus parainfluenzae* were isolated from nine neonates. Seven had early infection associated with respiratory distress or conjunctivitis; three had septicaemia one of whom died. The incidence of haemophilus septicaemia was 0.23 per 1000 live births.

The number of reports of infections caused by non-serotypable *Haemophilus influenzae* during the neonatal period is increasing.¹ Any series that includes only cases of bacteraemia or meningitis is likely to under report characteristic clinical features of infection with this organism.² We report a study conducted over 27 months of all haemophilus isolates in one unit.

Material and methods

On 1 January 1985 surveillance of haemophilus infections in our neonatal unit started and we report the results until 31 March 1987. When systemic sepsis was suspected we took samples of blood, urine, cerebrospinal fluid, nose, throat, umbilical, and rectal swabs before starting antibiotics. In addition, endotracheal secretions from babies requiring assisted ventilation were routinely cultured three times a week.

Blood cultures were performed using brain heart infusion broth with and without sodium thioglycolate (Gibco Ltd) with routine subculture to chocolate agar after 48 hours and five days' incubation at 37°C. *Haemophilus spp* were initially identified by their growth and morphology on chocolate agar

after primary culture or following enrichment in cooked meat medium. Strains were speciated and biotyped according to the method of Kilian using laboratory prepared media.³ Slide agglutination was used to attempt to serotype the strains using type specific antisera prepared by the Public Health Laboratory Service (type b) and Wellcome (types a, c, d, e, and f).

Antibiotic sensitivities were performed and interpreted using the comparative method.⁴ To prepare the inoculum six isolated colonies were touched and added to 2.5 ml of 1% tryptone water (Oxoid). *H influenzae* NCTC 11931 was used as the control organism. The test medium was Isosensitest (Oxoid) with 5% saponin lysed horse blood (Tissue Culture Services) and 10 mg/ml β nicotinamide adenine dinucleotide grade III (Sigma). Incubation was performed at 37°C in a 5% carbon dioxide incubator. Disc contents (measured in μ g) were ampicillin 2, cefuroxime 30, gentamicin 10, netilmicin 30, neomycin 10, trimethoprim 1.25, chloramphenicol 10 (Oxoid) and polymyxin B 250 units (Mast Laboratories Limited). The presence of β lactamase was detected with Intralactam strips (Mast Laboratories Limited).

Results

Throughout the study there were 12 910 live births in the hospital. The characteristics of the nine babies with *Haemophilus* are shown in the table. All neonates were born by spontaneous vertex delivery, except cases 1 and 9 who were delivered by caesarean section. Cases 1 and 2 grew *H influenzae* and *H parainfluenzae*, respectively, from respiratory secretions at 3 weeks of age. These were probably nosocomial infections as the two babies were not

Table *Clinical details of nine cases infected with Haemophilus spp*

Case No	Sex and gestational age (weeks)	Birth weight (g)	Risk factors for early onset sepsis; [duration of membrane rupture — hours]	Clinical diagnosis	Outcome	Site of positive culture
1	M, 29	570	None [0]	Right upper lobe pneumonia; chronic lung disease	Recovered	Endotracheal aspirate
2	F, 28	960	Spontaneous premature rupture of membranes [2]	Asymptomatic; recovered from severe respiratory distress syndrome	Recovered	Nasopharyngeal aspirate
3	F, 36	2660	Spontaneous premature rupture of membranes, maternal fever; antepartum haemorrhage six weeks earlier + small bleeds since [2]	Mild respiratory distress syndrome	Recovered	Gastric aspirate, nose, throat, naso-pharyngeal aspirate, placenta
4	M, 24	700	Spontaneous premature rupture of membranes [5]	Severe respiratory distress syndrome	Died; intraventricular haemorrhage; capsular liver tear at post mortem; early fetal pneumonia	Gastric aspirate, blood
5	F, 24	790	Spontaneous premature rupture of membranes; maternal fever [17]	Severe respiratory distress syndrome	Recovered	Blood, rectum, placenta, maternal vagina
6	F, 33	2210	Maternal fever [2]	Conjunctivitis	Recovered	Conjunctiva, blood, gastric aspirate, maternal vagina
7	M, 33	1960	Spontaneous premature rupture of membranes [2]	Conjunctivitis	Recovered	Conjunctiva
8	M, 34	2430	Spontaneous premature rupture of membranes [2]	Conjunctivitis	Recovered	Conjunctiva, gastric aspirate, placenta, maternal vagina
9	M, 41	3260	Prolonged rupture of membranes; antepartum haemorrhage; maternal fever; vaginal loss for two weeks	Conjunctivitis	Recovered	Conjunctiva, nose, throat, rectum, ears, umbilicus, placenta

colonised at birth. The remaining seven patients presented on the first day of life, and maternal specimens received from five of these patients yielded a *Haemophilus* of the same biotype.

There were two patients with *H parainfluenzae*, (cases 2 and 9). Case 2 was probably asymptotically colonised with the organism and case 9 had conjunctivitis. The other seven babies grew *H influenzae*, and all the isolates were non-capsulate. They comprised biotype I (n=1), II (n=2), III (n=2), V (n=1), and unknown (n=1).

Three babies (cases 4, 5, and 6) had septicaemia

and received penicillin and gentamicin, ampicillin and netilmicin, and ampicillin, respectively. Two presented with clinical and radiological features indistinguishable from hyaline membrane disease, and case 4 died on day 2, pneumonia being confirmed at necropsy. The third septicaemic baby had bilateral conjunctivitis at birth but was otherwise well. The four cases of conjunctivitis were treated with trimethoprim and polymyxin B eye drops and all resolved.

All strains examined were sensitive to neomycin, gentamicin, cefuroxime, and polymyxin B, but two

were resistant to chloramphenicol, one to ampicillin due to the production of β lactamase, and one to trimethoprim.

Discussion

The number of reports of *H influenzae* sepsis in the newborn has increased. In one study *H influenzae* caused 1.4% of cases of neonatal sepsis seen in the early 1960s, rising to 3.8% over the next 10 years.² In a study from Houston the proportion rose from 0.3% in the early 1970s to 2.6% over the next five years. The incidence of neonatal haemophilus bacteraemia in 1976-81 in Houston was 0.14 per 1000 live births,¹ and we found an incidence of 0.23. Any apparent increase, however, may be due as much to increased awareness as to a true rise in incidence.

One study described 10 cases of neonatal bacteraemia due to *H influenzae*, and in four cases biotype IV was isolated.¹ Non-serotypable strains are rarely biotype IV unless they are of neonatal, maternal, or genital origin. Non-serotypable strains belonging to biotype IV may have a special affinity for the genital tract.¹ Biotypes II and III have also been isolated from cases of neonatal sepsis. In contrast, we found several biotypes but no cases due to biotype IV.

Early neonatal sepsis with haemophilus is likely to arise by maternal vaginal carriage. The reported rate of vaginal carriage during pregnancy is less than 1%.¹ If the incidence of neonatal sepsis due to *Haemophilus* continues to rise there may be a case for introducing selective media to increase its detection from vaginal swabs, as is used for sputum bacteriology.

Ophthalmia neonatorum is a common condition and occurred in 12% of newborn babies in Southampton and 8.2% in Harrow.⁵ In the Southampton study three of 42 patients grew *Haemophilus* spp (two *H influenzae* and one *Haemophilus* spp), but in Harrow the organism was not isolated. In most studies in developed countries about one third of cases of neonatal conjunctivitis are associated with bacterial pathogens other than *Neisseria gonorrhoeae* or *Chlamydia trachomatis*.

When this occurs, it is usually treated with neomycin or chloramphenicol eye drops.⁵ Chloramphenicol resistance occurs in up to 1% of non-capsulate *H influenzae*, although it is rarely found among capsulate strains.⁶ Two strains in our series (*H influenzae* and *H parainfluenzae*) were chloramphenicol resistant. Standard first line antibacterial treatment for sticky eye in Oxford was trimethoprim and polymyxin B sulphate eye drops because an endemic *Klebsiella oxytoca* strain, which was chloramphenicol, neo-mycin, and gentamicin resistant, often colonised babies in our unit.

Penicillin or ampicillin and an aminoglycoside are often used in the treatment of neonatal infection of unknown cause. Only one strain of *H influenzae* in this study was a β lactamase producer, and ampicillin resistant strains of *H influenzae* are fortunately uncommon in this setting.¹ A change of standard empirical antibiotic treatment is not indicated by the results of this study, except if a baby fails to respond.

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