Neonatal streptococcal infections

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Summary

Most serious neonatal streptococcal infections are caused by group-B streptococci. The pattern of serious group-B neonatal disease in Britain resembles that described in other countries; both 'early-onset' and 'late-onset' forms are seen, but reliable incidence rates have not yet been determined.

Serological-type III strains predominate in neonatal meningitis in Britain, but not so markedly as in some parts of the U.S.A. A deficiency of group-II strains in meningitis is, however, apparent in both countries.

Present information about the carriage of group-B streptococci suggests that antibiotic prophylaxis administered to mothers or infants is unlikely to reduce greatly the frequency of 'early-onset' disease. The continuous presence of a suitable chemical disinfectant in the vagina during labour might be more effective.

Insufficient is known about the epidemiology of 'late-onset' neonatal disease for rational preventive measures to be designed. More information is required about the postnatal acquisition of group-B streptococci by neonates and its sources, and about passive transfer of type-specific antibody from the mother to her child.

By far the commonest streptococcus associated with serious disease in newborn infants is the group-B streptococcus. In a recent study of streptococci, other than pneumococci, associated with systemic disease in man (Parker and Ball, 1976), 543 isolates were examined from the blood and internal organs of patients suffering from a febrile or other apparently 'septic' illness and whose age was known; of these, fifty-five (10%) were from patients aged 6 weeks or less. Group-B streptococci comprised thirty-six (65%) of the streptococci from these neonates; the remainder included small numbers of a wide variety of other streptococci (Table 1).

Neonatal infection with group-B streptococci

For more than 80 years, the group-B streptococcus has been recognized, under the name *Streptococcus agalactiae,* as a widespread cause of mastitis in

TABLE 1. Systemic streptococcal infections (1972–74); isolates from blood or internal organs

Age	Number	Percentage
< 6 week.	55	10
Group A	1	
Group B	36	
Strep. sanguis	2	
Other 'viridans'	5	
Strep. milleri	1	
Enterococci	3	
Strep. bovis (biotype II)	6	
Other	1	
≤ 1 year	16	3
≤ 15 years	55	10
All ages	543	

cattle. The fact that similar organisms could be found in the human vagina has been known for more than 40 years (Lancefield and Hare, 1935), yet their importance as causes of serious disease in the newborn has been realized only recently. Some observers have therefore suggested that the frequency of neonatal group-B streptococcal disease must have increased greatly in recent years.

Early reports

It is of interest to look at published records of systemic infections with group-B streptococci between 1937, when Colebrook and Purdie first described the isolation of these organisms from a blood culture (in a case of puerperal endocarditis), and 1968, when Jones and Howells reported two cases of neonatal meningitis; this was the first account of serious neonatal disease due to group-B streptococci in the British literature.

Table 2 lists reports of systemic illnesses in which group-B streptococci were isolated from the blood or internal organs. Between 1937 and 1943 there were forty-two, but only three of them were stated to be in infants (Brown, 1939); of the remainder, over 50% were associated with childbirth and abortion, and most of these were cases of endocarditis. Only five cases of meningitis were recorded; none was stated to be in a neonate, but the clinical information

TABLE 2. Reports of systemic disease in which group-B streptococci were isolated from the blood or an internal organ

	Number of infections in				
	infants		older patients		
Years	Septi-caemia	Menin-gitis	Puer-peral or post-abortive sepsis	Other septi-caemia	Menin-gitis
1937–43*	3	0	20	14	5¶
1944–57†	0	0	1	9	0
1958–68‡	20	62	11	31	7
(Streptococcus Reference Laboratory)					
1964–67§	11	8	5	3	0
1970–75 (present series)	20	49	11	34	6

* Colebrook and Purdie, 1937; Fry, 1938; Brown, 1939; Hill and Butler, 1940; Rosenthal and Stone, 1940; Koletzky, 1941; Ramsay and Gillespie, 1941; Rantz and Keefer, 1941; Rantz, 1942; Rantz and Kirby, 1942; Gaustadt, 1942; Wheeler and Foley, 1943.

†Dawson, Hobby and Lipman, 1944; Dolphin and Cruick-shank, 1945; Loewe and Alture-Weber, 1946; Roemer and Grün, 1949; Kahler and Aicher, 1952.

‡Nyhan and Fousek, 1958; de Moor, 1960; Hood et al., 1961; Wahl et al., 1962; Mannik, Baringer and Stokes, 1962; Keitel et al., 1962; Eickhoff et al., 1964; Bret and Durieux, 1965; Sicherman, 1965; Etienne, Curioni and Laplane, 1965; Reinarz and Sanford, 1965; Hall, 1965; Lazarus, Sellers and Marine, 1965; Kexel, 1965; Kexel and Schönbaum, 1965; Winterbauer et al., 1966; Maher and Irwin, 1966; Butter and de Moor, 1967; Canet et al., 1967; Lafaix et al., 1968; Kvittingen, 1968; Toft and Jespersen, 1968; Jones and Howells, 1968.

§Harper, 1971.

¶Adults, postoperative, 2; 'children' with otitis media, 2; 'child' with hydrocephalus, 1.

given was incomplete and leaves slight doubts about this.

Very few cases were described in the next 14 years, but from 1958 onwards reports became frequent and most of them were of neonatal disease. In that year, Nyhan and Fousek recorded six isolations of group-B streptococci from the blood of newborn infants in one hospital in the space of 25 years, and gave the first clear account of neonatal meningitis in one of them; in 1961, Hood, Janney and Dameron de-scribed three cases of neonatal meningitis from one hospital within 3 months; and in 1962 Wahl, Cayeux and Derlot listed twelve cases of meningitis in 'babies' seen in France in the previous 8 years. By 1968, systemic neonatal disease due to group-B streptococci had been reported in the USA, Holland, France, Germany, Norway, Denmark, Britain and Senegal.

Septicaemic and meningitic neonatal disease; 'early-' and 'late-onset' disease

Most reports between 1958 and 1972 were con-

cerned separately with cases either of septicaemic or meningitic infection of neonates, and it was not until the end of this period that a comparison was made by American workers (Quirante and Cassady, 1972; Franciosi, Knostman and Zimmerman, 1973; Baker and Barrett, 1973) of the circumstances under which the two clinical types of infection occurred. It then became apparent that the natural history of 'early-onset' disease—in the first 10 days of life— and 'late-onset' disease were different. Early-onset disease might be either septicaemic or meningitic, was often associated with a long interval between rupture of the membranes and delivery, tended to affect infants of low birth weight, and had a high mortality despite prompt treatment; the infecting organism could nearly always be isolated from the mother's vagina. Late-onset disease was almost exclusively meningitic, affected apparently healthy infants after normal labour, and had a lower mortality if adequate treatment was given; information about vaginal carriage in the mother at or near the time of onset of disease is less complete, but a number of negative findings have been reported.

The so-called septicaemic disease is thus almost always early in onset. It is often associated with signs of respiratory distress and is difficult to distinguish from hyaline-membrane disease (Ablow et al., 1976; Katzenstein, Davis and Braude, 1976). It is often not recognized in life; for example, in seventeen cases, Quirante, Ceballos and Cassady (1974) made a bacteriological diagnosis on speci-mens collected before death in only five and identi-fied a further twelve *post mortem*. Meningitis, on the other hand, is a disease of the whole neonatal period, including the first few days of life, and continues to occur, though in smaller numbers, in the months following. It is thus an over-simplification to sub-divide group-B streptococcal neonatal disease into 'early' septicaemia and 'late' meningitis, as some authors have done.

In retrospect, there seems to be some evidence that the role of the group-B streptococcus in perinatal pathology has changed. Before 1958, many bacterio-logists were able to recognize the organism; although they were probably a minority, they included a number who were concerned in the study of puerperal sepsis. Lack of interest in possible bacteriological causes of perinatal death may account for the infre-quency with which 'early' septicaemic cases were recognized. It seems unlikely, however, that had neonatal meningitis been as common then as now, and particularly after the first week of life, it would not have been recorded. After 1958, accounts of neonatal meningitis appeared in quick succession, and several of the authors were clearly under the impression that the disease had not been recorded before.

The pattern of clinical disease in Britain

The clinical manifestations of group-B streptococcal disease in this country appear to be similar to those reported elsewhere (Table 2). In the years before the first published account of neonatal disease in Britain, the Streptococcus Reference Laboratory at Colindale had received for identification a number of isolates of group-B streptococci from septicaemic and meningitic infections in neonates, and after 1970 that number increased. Of the cultures from 130 patients with systemic disease received in the years 1970–75, 120 were from patients who could be classified into neonates (<6 weeks old) and older persons (Table 3), although the exact date of onset in the neonates was not always known. Sixty-one (51%) of the isolates were from neonatal infections; of these eighteen (30%) were from septicaemic illnesses and forty-three (70%) from cases of meningitis. All of the septicaemic infections began within the first 5 days of life, but so did twelve (44%) of the meningitic infections in which the day of onset was known. Of fifty-five cases of meningitis, forty-three (78%) were in neonates, six (11%) in older infants, two (4%) in children, and four (7%) in adults.

TABLE 3. Age of patients suffering from systemic disease due to group-B streptococci from whom isolates were received at the Streptococcus Reference Laboratory in the years 1970–75

| | Number of patients with | |
Age	meningitis	other systemic disease
≤ 5 days	12	18
6–14 days	7	0
15 days–6 weeks	8	0
'Neonate'*	16	0
Total neonates	43	18
6 weeks–1 year	6	2
2–15 years	2	0
> 15 years	4	45
Total older patients	12	47
Grand total	**55**	**65**

* Age not further specified.

There is no way of knowing whether this is a representative sample of the disease, but the septicaemic neonatal disease is probably under represented. In three hospitals in the USA, Baker and Barrett (1974) recorded 116 cases of serious neonatal group-B streptococcal disease in 3·5 years; sixty-eight (59%) of these were of the septicaemic form.

Incidence

In the last 3 years, several estimates of the incidence of serious group-B streptococcal disease have been made in single hospitals or groups of neighbouring hospitals (Table 4), but in all of them the number of infections recorded was rather small. Despite this, and the fact that the frequency of detection of septicaemic disease might have been expected to vary between hospitals, the reported rates do not differ greatly (range 1·1–2·9/1000 births) and do not give evidence of systematic geographical variation. Nor do they appear to be related to reported vaginal carriage rates in the corresponding areas (see Table 8).

TABLE 4. Incidence of serious neonatal disease due to group-B streptococci

Authors	Geographical area	Rate per 1000
Franciosi, Knostman and Zimmerman, 1973	Colorado	2·1
Baker and Barrett, 1973	Houston, Texas	2·9
Howard and McCracken, 1974	Dallas, Texas	1·35
Reid, 1975	Aberdeen	2·7
Finch, French and Phillips, 1976	London	1·1

Distribution of serotypes among isolates

Lancefield (1934 and 1938) classified group-B streptococci into four serotypes possessing the polysaccharide antigens Ia, Ib, II and III respectively. Later, Wilkinson and Eagon (1971) added a further type Ic, characterized by the presence of a protein antigen in strains most of which would otherwise have been placed in type Ia (Lancefield, McCarty and Everly, 1975).

American workers have reported differences in the frequency of these types among strains from different categories of infection. Franciosi et al. (1973), in Colorado, reported that all of eleven isolates from cases of late-onset neonatal meningitis belonged to type III (Table 5). Baker and Barrett (1973 and 1974) examined a larger series from Houston, Texas, and observed a predominance of type III in both 'late' (93%) and 'early' meningitis (80%), and also in a very small number (100% of six) of 'late' septicaemic cases. In an even larger collection from various parts of the U.S.A. (Wilkinson, Facklam and Wortham, 1973), the percentage of type-III strains among isolates from meningitis (nearly all in infants) was somewhat lower (73%). The proportion of type-III strains among isolates from early septicaemic cases in Houston, Texas, was only 41%. Another feature common to the American series, first commented upon by Baker and Barrett (1973), was a marked deficiency of type II among isolates from meningitis in comparison with isolates from septicaemic disease.

It should be pointed out, however, that in an earlier series of isolates from Holland (Butter and

TABLE 5. Distribution of serotypes among group-B streptococci* from groups of patients with systemic diseases in the U.S.A. and Holland

Geographical area (authors)	Clinical character of group	No. of isolates examined	Percentage of isolates of serotype†				
			Ia	Ib	II	III	NT
Colorado (Franciosi, Knostman and Zimmerman, 1973)	'Late' neonatal meningitis	11	0	0	0	100	0
Houston, Texas (Baker and Barrett, 1974)	Meningitis (≤10 days)	15	20	0	0	80	0
	Meningitis (> 10 days)	33	7	0	0	93	0
	Septicaemia (≤10 days)	56	13	5	44	33	5
	Septicaemia (> 10 days)	6	0	0	0	100	0
California (Anthony and Concepcion, 1975)	Neonatal meningitis	6	0	0	0	100	0
	Neonatal septicaemia	8	0	13	25	62	0
U.S.A. (Wilkinson, Facklam and Wortham, 1973)	Meningitis‡	97	16	2	0	73	8
	Septicaemia‡	103	22	4	16	41	17
Holland (Butter and de Moor, 1967)	Neonates§	26	76	4	0	19	0
	Adults§	23	70	13	4	4	9

* One isolate from each patient.
† Type Ic included in type Ia; NT, untypable.
‡ Meningitis: 94 from infants; septicaemia: 'two-thirds' from infants.
§ Neonates: 22 with meningitis; adults: 20 with septicaemia.

de Moor, 1967) an entirely different type distribution had been observed. Type III was uncommon both in neonatal meningitis and in septicaemic disease of adults; some 75% of all isolates in both categories belonged to type Ia.

The present findings (Table 6) show trends similar to those in the American series, but less extreme. Thus, at all ages, type-III strains formed 50% of isolates from meningitis and 26% from other septicaemic diseases; the corresponding figures for type II were 5% and 26%. There was no evidence that age affected type distribution, although the numbers in some categories were rather small. Thus, the percentages of type-III strains were 53 (twenty-three of forty-three) for neonatal meningitis and 50 (six of twelve) for meningitis in older persons. The type distribution in early neonatal septicaemic disease and in septicaemia in older persons, nearly all of whom were adults (see Table 3), was similar.

The type distribution in neonatal septicaemia shows a general correspondence with that in isolates from the female genital tract. Table 7 gives some representative figures; the samples are probably too small to justify detailed comparisons with type distributions in neonatal disease in corresponding geographical areas (Tables 5 and 6), but the rather high percentage of type Ia among isolates from Dutch women should be noted; unfortunately information about the age of onset of the Dutch cases of neonatal meningitis was not given. Franciosi *et al.* (1973), who found a high proportion of type Ia in the vagina, drew attention to the great clinical severity of neonatal septicaemia due to this type.

The difference in type distribution in meningitic and septicaemic disease in the U.S.A. has been attributed to qualitative differences in the pathogenicity of individual streptococcal strains; the present findings give limited support to this view.

TABLE 6. Distribution of serotypes among group-B streptococci* from patients with systemic disease received at the Streptococcus Reference Laboratory, Colindale, 1970–75

Category	No. of isolates examined	No. (and percentage) of serotype†				
		Ia	Ib	II	III	NT and other
All systemic infections	130	33	25	17	48	7
Meningitis: all ages	60	11 (18)	14 (23)	3 (5)	30 (50)	2 (3)
Other systemic: all ages	70	22 (31)	11 (16)	14 (20)	18 (26)	5 (7)
Meningitis: all ≤6 weeks	43	9	8	1	23	2
Meningitis: <5 days	12	2	4	0	6	0
Meningitis: 6–14 days	7	2	1	1	2	1
Meningitis: 15 days–6 weeks	8	2	1	0	5	0
Meningitis: all > 6 weeks	12	0	5	1	6	0
Other systemic: ≤5 days	18	7	0	5	4	2
Other systemic: > 6 weeks	47	12	10	8	14	3

* One isolate from each patient.   † Type Ic included in type Ia; NT, untypable; other, reaction with two antisera.

TABLE 7. Distribution of serotypes among group-B streptococci isolated from healthy females

Geographical area (authors)	Sources of isolates	No. of isolates examined	Percentage of isolates of serotype*				
			Ia	Ib	II	III NT	or other
Colorado (Franciosi, Knostman and Zimmerman, 1973)	Vagina: parturient	45	40	9	15	29	7
Houston, Texas (Baker and Barrett, 1973)	Vagina: parturient	46	17	11	35	37	0
California (Anthony and Concepcion, 1975)	Vagina: parturient	57	16	10	35	39	0
Holland (Butter and de Moor, 1967)	Throat and nipple: puerperal	33	52	6	21	18	3
London† (Finch, French and Phillips, 1976)	Vagina‡	115	11	12	22	40	15

* Type Ic included in type Ia; NT, untypable; other, reaction with two typing sera.
† Typed at the Streptococcus Reference Laboratory, Colindale.
‡ Only seven from pregnant women.

Thus, some type-III strains might have an enhanced ability to invade the meninges or to establish infection at a site from which the meninges are easily invaded. Additionally, or alternatively, type-II strains might lack this. But the differences in strain character are clearly not absolute, and the Dutch findings suggest that they are not invariably type-associated.

Another suggestion is that early-onset infection reflects contamination from a maternal source at birth but that late-onset meningitis is a consequence of subsequent contamination from some other source. A necessary corollary would be that type-III strains predominate in the alternate source. The question of hospital spread of group-B streptococci will be discussed later.

The source of infection for neonates

It has never been seriously thought that human group-B streptococci are derived to a significant extent from animal sources. Pattison, Matthews and Maxted (1955) showed that there are considerable differences in the frequency of individual type antigens in human and bovine strains, and Butter and de Moor (1967), by a combination of serotyping, biochemical tests, and bacitracin-sensitivity tests, showed that the human and bovine populations exhibit almost no overlapping of characters.

Carriage in adults. Early observers found low carriage rates in the female genital tract—few in excess of 5% and most considerably lower. The first report of a high rate (12·4%) was by Kexel and Beck (1965), who used a selective plating medium and enrichment culture. This rate was obtained, perhaps significantly, from vulval swabs; the percentages for vaginal swabs and cervical swabs were 9·5 and 6·7 respectively. Other genital carriage rates are given in Table

8. These show wide variations, only some of which are easily explicable by variations in technique. Thus, the low rate (4·6%) for parturient women in Colorado was obtained on non-selective medium and without enrichment culture, and the high rate (22·5%) in Houston, Texas, after enrichment in selective broth containing gentamicin and nalidixic acid. The moderately low rate (8·3%) in Minnesota was from direct culture on selective agar medium containing colistin and nalidixic acid; in a small series in which the Texan selective enrichment broth was also used, the isolation rate was almost doubled. However, Finch, French and Phillips (1976) obtained a carriage rate of only 6·4% in parturient women—admittedly from the examination of high vaginal swabs—by the use of a selective plating medium, and an enrichment broth similar to the Texan medium. It is notable that several groups of workers have observed considerably higher carriage rates in various classes of non-pregnant women, including female members of the hospital staff, than in parturient women.

Vaginal carriage in late pregnancy appears to be somewhat unstable. Ferreiri et al. (1977) found that 42% of women positive in labour had given negative swabs when last seen in the antenatal clinic, and that 19% of those positive in late pregnancy were negative in labour; yet, when the organism was isolated on both occasions, it was almost invariably of the same type. This finding, and the frequency with which isolations are made only by enrichment culture, suggest that in many women the vagina is not the primary site of carriage.

Carriage in the upper respiratory tract has been recognized for many years, but on the whole appears to be less common than carriage in the genital tract. Thus, Franciosi et al. (1973) found 5·2% of throat carriers among females who had a vaginal carriage rate of 13·0% (see also Baker and

TABLE 8. Frequency of isolation of group-B streptococci from the female genital tract

Geographical area	Authors	Percentage isolation rate		
		Pregnant women	Non-pregnant women	
		Late pregnancy in labour, puerperium	Hospital staff	Outside hospital
West Germany	Kexel and Beck (1965)	12·4	—	—
Colorado	Franciosi, Knostman and Zimmerman (1973)	4·6	13·0	11·6
Houston, Texas	Baker and Barrett (1973)	22·5	30·0	—
Minnesota	Ferreiri, Cleary and Seeds (1977)	8·3	—	—
Aberdeen	Reid (1975)	4·5	—	—
London	Finch, French and Phillips (1976)	6·4	—	17·1† 36·0‡
Sweden	Wallin and Forsgren (1975)	—	—	20·6*‡

* Includes urethral swabs.
† Family-planning clinic.
‡ Clinic for sexually transmitted diseases.

Barrett, 1973). There is little evidence that throat carriers are of significance as sources of infection for infants.

The importance of anal carriage appears, however, to have been underestimated. Franciosi *et al.* (1973) recorded an anal carriage rate of 16·8% in female hospital staff. More recently, Badri *et al.* (1976) observed in pregnant women a vaginal carrier rate of 10·2% and a rectal carrier rate of 17·9%; and of 142 women with group-B streptococci in the anal swab, only sixty-one had a positive vaginal swab. They suggest that the bowel is the main carriage site of the organism; if this is confirmed, much vaginal 'carriage' may have to be looked upon as contamination, and this will greatly influence our ideas about the prevention of neonatal disease.

Colonization of infants. In general, early colonization of infants is with group-B streptococci of types found in the mother's vagina. Baker and Barrett (1973) found that 72% of the infants of vaginally positive mothers, and 12% of the infants of mothers with negative vaginal swabs, yielded group-B streptococci from one or more body sites 18 hours after delivery. When cultured at the time of birth, over 50% of all positive cultures from umbilicus, nose or ears yielded fifty or more colony-forming units of group-B streptococci; the greatest number of positive swabs was obtained from the external auditory canals (Ferreiri *et al.*, 1977). The initial contamination rate in this series was 3·4% of all infants examined, but when nasal and umbilical swabbing was repeated on the third day of life a further 2·1% of infants gave positive swabs. When a group-B streptococcus had been isolated from the mother, the early and late acquisitions by the infants were almost invariably of strains of the same type.

Infection from other sources. The possibility that infants may acquire group-B streptococci from sources other than the mother has been repeatedly raised, but little evidence for this has so far been obtained. Winterbauer, Fortuine and Eickhoff (1966) described two cases of meningitis that occurred within one week in a small hospital; the second child was delivered by staff who were concurrently attending the first case of meningitis. Steere *et al.* (1975) investigated three cases of meningitis due to type-III organisms that had occurred within a period of 7 days, and produced some evidence that the infecting strain might have spread among healthy infants in the hospital. None of the mothers of the affected infants yielded group-B streptococci, but the swabs were taken several weeks after the incident. Of the infants who had been present in the nursery during the month in which the incident had occurred, 36% were carriers of group-B streptococci and 20% type-III organisms; in the following month, after control measures had been instituted, the corresponding carrier rates were 9% and 2%.

Adequate retrospective investigation of possible hospital sources of late-onset infections is difficult to perform. When the disease develops, the affected infant and his contemporaries have usually left hospital. Comprehensive bacteriological screening of hospital staff may present practical difficulties. If this is performed, numerous carriers are likely to be found, but the present serological typing system is not sufficiently discriminatory for effective studies of sources and routes of infection. The paucity of information about intra-hospital spread of group-B streptococci must therefore not be taken as evidence that this is unimportant.

Susceptibility to infection
The association of low birth weight with the risk of

early septicaemic infection has already been mentioned. The possible relationship between the formation of hyaline membrane and the multiplication of group-B streptococci in the lung has yet to be investigated fully (see Katzenstein *et al.*, 1976). Other predisposing obstetric factors seem likely to act by increasing the dose of the infecting organism or the length of time the infant is in contact with it. No predisposing factors for late-onset meningitis have yet been identified.

Few of the infants who are contaminated with group-B streptococci subsequently develop serious disease. Estimates of that proportion vary between 1 in 20 and 1 in 100 according to the colonization rate. It seems possible that maternally acquired antibody may protect some infants against invasion. Antibody against type-specific polysaccharide, and against the protein antigen Ic, protects mice (Lancefield *et al.*, 1975) against lethal infection. *In vitro* studies of the blood of parturient women reveal several factors that might be concerned in defence against the organism (Klesius *et al.*, 1973; Mathews, Klesius and Zimmerman, 1974). According to Baker and Kasper (1976), the sera of women whose infants suffered from invasive type-III infection were devoid of antibody against this type but it was present in the sera of vaginal carriers of type-III organisms.

Possible preventive measures

Present information about the carriage of group-B streptococci makes it unlikely that some of the preventive measures being advocated would be effective in preventing early-onset disease. If the 'at-risk' group could be detected by culture of the vagina in late pregnancy, and this group is reasonably small, antibiotic prophylaxis might be considered, but in some areas it might be necessary to treat up to 25% of all mothers. The vaginal swab in late pregnancy appears, however, to have a poor predictive value for detecting at-risk infants. Furthermore, there is little certainty that systemic antibiotic would eliminate carriage, particularly if the primary source is the bowel. It is unlikely that the detection and prophylactic treatment of contaminated or colonized infants could be performed quickly enough to prevent early-onset disease; present evidence suggests that systemic penicillin treatment seldom eliminates carriage by infants (Steere *et al.*, 1975; Paredes *et al.*, 1976).

If infection from the maternal source is to be eliminated or minimized, therefore, it should be by some measure that can be applied to all mothers; for this purpose, antibiotic prophylaxis is certainly unacceptable. The most logical approach would be the local application of a bland but persistent chemical disinfectant that could be kept continuously in contact with the vaginal wall for as long as possible in labour. Comparative studies should therefore be made of the effects of likely agents, in various formulations, on the group-B streptococcal population of the vagina during labour.

Not enough is yet known about the epidemiology of late-onset disease for rational means for its prevention to be suggested. Its relation to initial and subsequent contamination with group-B streptococci must be explored by large-scale prospective studies in which infants are followed-up after they leave the maternity hospital, and linked with similar studies of possible intra-hospital sources of infection. If the relation of late-onset disease of neonates to antibody deficiency in the mother is confirmed, the possibility of vaccination during pregnancy will have to be investigated.

Other streptococcal infection in neonates

Sporadic cases and occasionally small outbreaks of septicaemia and meningitis due to group-A streptococci have been recognized for many years but are now less common than formerly. Nyhan and Fousek (1958) recorded sixteen group-A streptococci among thirty-seven isolates from blood cultures of neonates in 1933–43, but only five among sixty-nine such isolates in 1944–57. The present author encountered only one in 1972–75 (Table 1). Infections in infants may be associated with outbreaks of puerperal sepsis or with symptomless vaginal carriage in the mother, but both of these events are unusual. Many group-A streptococcal infections of neonates are almost symptomless; on a number of occasions, widespread umbilical colonization in nurseries has been revealed only when a serious infection in an infant or an outbreak of puerperal sepsis occurred (Gray, 1956; Kwantes and James, 1956; Boissard and Eton, 1956; Langewisch, 1956). There is some evidence that the rarity of serious group-A streptococcal disease among neonates is attributable to the presence of maternally acquired protective antibody (Zimmerman and Hill, 1969). Occasional sporadic cases of pneumococcal septicaemia and meningitis occur, and in some of them the source of infection is the mother's vagina (see Keitel *et al.*, 1962).

Systemic enterococcal infections occasionally occur, usually in neonates with serious underlying disease or as a postoperative complication. Another group-D streptococcus, the dextran-negative biotype II of *Strep. bovis*, is not uncommonly found in blood cultures of neonates. It formed 11% of the series of isolates from newborn infants (Table 1), but was rarely found in systemic diseases of older patients; its presence was not associated with a distinctive pattern of illness in the infants.

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