

SEVEN-YEAR STUDY OF PNEUMOCOCCUS TYPE INCIDENCE IN THE ROYAL HOSPITAL FOR SICK CHILDREN, GLASGOW

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(With 1 Figure in the Text)

INTRODUCTION

Extensive investigations of pneumococcal type incidence in children, especially in pneumonia, are reported in American, Scandinavian and German literature, but we have been unable to find comparable data for British children. This article records the results of systematic typing of pneumococci isolated from children admitted to R.H.S.C., Glasgow, during the years 1938-44 inclusive. In order to obtain a comprehensive view of type distribution, typing was not confined to strains isolated from the respiratory tract, but included those cultured from pneumococcal pus wherever found, for example, in middle ears, meninges, joints, serous sacs and miscellaneous soft tissue lesions, together with strains from blood cultured before and after death.

In all, 1331 strains were isolated, a number small by comparison with American and Continental surveys, but as it represents the endemic pneumococcus type incidence in children over a period of seven years in one industrial area of Britain, it is of epidemiological value and may form a base line for further study, whether chemotherapeutic or bacteriological.

MATERIAL

Of the 1331 strains, 1178 were obtained from 870 patients and 153 strains from 127 normal controls. The children varied in age from 4 days to 12 years, and approximately two-thirds were under the age of 2 years; thirty infants were in the neonatal period; boys were rather more numerous than girls.

METHODS

Since the scope of this research was limited to discovering the local incidence of pneumococcal types, cultural methods were restricted to this object.

Specimens likely to yield a pure growth of pneumococcus, e.g. cerebrospinal fluid or empyema pus, were cultured on ordinary media, where an adequate growth was usually obtained. White mice were inoculated intraperitoneally with 3-4 hr. broth cultures of such specimens as were likely to give a mixed growth, e.g. throat swabs, lung puncture and middle-ear pus. Peritonitis generally developed in the mice within 48 hr. and the exudate sufficed for typing, but if pneumococci were scanty, the mouse peritoneal fluid and heart blood were cultured. The pneumococci obtained from these sources were typed on slides by the direct method (Neufeld reaction) using Lederle antisera. This method was employed for all strains, and each culture was tested with antisera from all the groups in order not to miss multiple types.

General distribution of pneumococcal strains

Fig. 1 shows the distribution by types of the 1331 strains isolated from patients and normal controls over the years 1938-44. Types 6 (19.3%), 19 (14.6%), 1 (8.2%) and 23 (6.2%) occurred most frequently, and amounted in all to 48.3% of the strains. Types 1, 2 and 3 comprised only 15.6% of the total.

Since various workers have stressed the fact that certain pneumococcal types are most prevalent in the early years of life, we, in conformity with other workers, have divided our cases into those under and over 2 years of age. Approximately, two-thirds of our strains were from patients under 2 years of age and the rest over 2 years, one-sixth being 5 years of age or more. In the youngest group the leading strains were types 6 (17%), 19 (15%), 23 (7%) and 22 (5%), while types 1, 2 and 3 together totalled 10% (type 1, 4%). In children over 2 years, type 6 was again the prevalent strain (24%), followed in order of frequency by types 1 (15%), 19 (10%) and

4 (5%): types 1, 2 and 3 amounted to 21%. There was thus a slight rise in the incidence of the 'fixed' types of pneumococcus in the older children, and this was more marked in the group of 144 patients over 5 years of age, where the 'fixed' types reached the figure of 33% (type 1, 26%). Conversely with the rise of type 1 in the older children, there was a fall in the incidence of the higher types (21-32), which in our series occurred only half as frequently in children over 2 years of age as in the younger age group. Pneumococcal types subdivided according to age for individual lesions are closely comparable.

monia. Types 1 and 6 each accounted for approximately one-third of the empyema strains and types 9, 14 and 19 each for 5%.

Otitis media and mastoiditis

Pus was derived from two sources, from the inflamed middle ears and mastoids during life, and from middle ears opened routinely at post-mortem, whether or not otitis media had been diagnosed clinically. From these combined sources 354 pneumococcal strains were obtained and the predominant types were 19 (19%), 6 (10.7%) and 23 (8.7%).

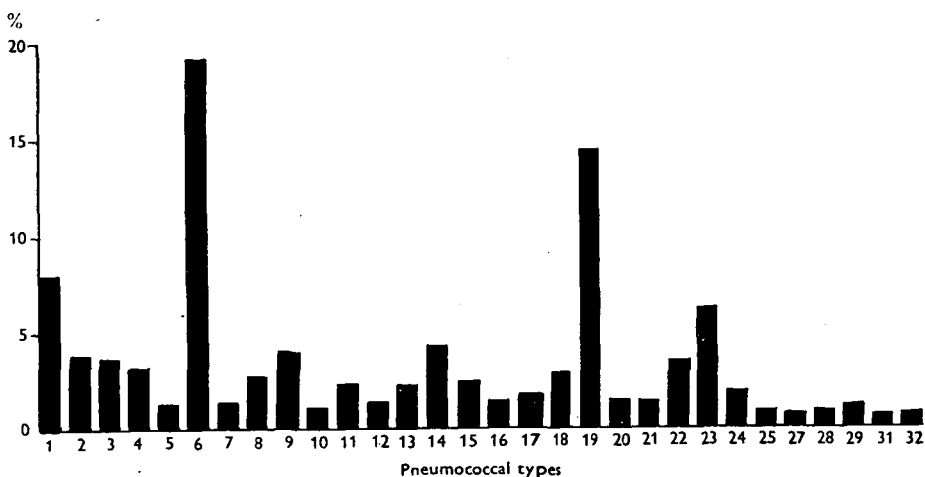


Fig. 1. R.H.S.C., Glasgow, 1331 pneumococcal strains, type of distribution (1938-44).

Respiratory tract

The material comprised fifty-five samples of sputum, 447 throat swabs (which in young children take the place of sputum in older children and adults), and 155 lung punctures mostly obtained at autopsy. From these sources 617 strains were isolated, and types 6 (19.5%) and 19 (15%) predominated. Types 1 (5.3%), 23 (5%) and 22 (3.9%) were next in order of frequency, and types 1, 2 and 3 together amounted to 12.6%. Thus, approximately one-half of the strains in this series occurred with frequency of less than 4%, and were mostly of the higher groups. In sixty-seven instances more than one strain of pneumococcus was isolated.

Consolidation of the lungs was mostly broncho-pneumonic, sometimes ill-defined and confluent: lesions were examined microscopically in most cases. Both from throat and lung cultures pneumococci of types 6 and 19 were most frequent.

In addition, 106 specimens of empyema pus were examined, and these are dealt with in this section even although there was not always clinical evidence of pneumonia, since in our experience pneumococcal empyema is almost invariably secondary to pneu-

Types 1, 2 and 3 together totalled 10.6%. There was no noteworthy difference in the type incidence between the ante-mortem and autopsy strains.

Pericarditis and peritonitis

Of the eight strains from pericardial pus, three belonged to type 6, two to type 14 and one each to types 2, 19 and 25. Sixteen pneumococcal strains were isolated from the peritonium and of these seven belonged to type 1, three to type 15, two each to types 6 and 19, one to type 16 and one to type 22. From two of these type 1 cases, type 1 pneumococcus was obtained also by vaginal swabbing.

Arthritis

From pus in acute arthritis thirty pneumococcal strains were cultured, mostly in young children under 2 years of age, and the predominant types were 6 (20%), 1 (16.6%), 2 and 23 (each 13.2%).

Meningitis

Forty-nine strains were obtained from acute pneumococcal meningitis which was generally secondary to pneumonia or otitis media, and the

pneumococcus in the cerebrospinal fluid was usually of the same type as in the primary lesion. Of these strains, 20.4% belonged to type 2, 18% to type 6 and 10.2% to type 23. Types 17 and 19 each totalled 9.6%.

Miscellaneous

We have been impressed by the occurrence of the pneumococcus in pure culture from miscellaneous lesions in young children, none of whom had a respiratory tract infection. Purulent pneumococcal orchitis was present in two infants, one aged 3, and the other 6 months: the types were respectively 2 and 6. Pneumococcal cellulitis affected the soft tissues in twelve patients, of whom eight were infants mostly under the age of 6 months: the pneumococcal strains isolated belonged usually to the higher types. In two cases, a pneumococcus was isolated from the gall bladder, one type 2 strain in a 5 weeks old infant with a pneumococcal septicaemia, the other a type 6 strain occurring in a girl aged 3½ years, again with septicaemia. Pneumococcal osteomyelitis due to type 2 occurred in two children, aged respectively 10 months and 1 year. A conjunctival swab in a 3 weeks old infant yielded a type 10 strain, while type 4 was isolated from a retropharyngeal abscess in a girl aged 7½ years. Finally, a type 19 strain was isolated repeatedly from the urine in a 2½ months old female infant.

DISCUSSION

Though in America and Scandinavia the proportion of pneumococcal strains not conforming to the original Cooper 1929 classification appears to be considerable (Kaufmann, Mørch & Schmith, 1940; Walter, Guevin, Beattie, Cotler & Bucca, 1941; Mørch, 1944), in this hospital very few pneumococci failed to give a Neufeld reaction. In our material types 6 and 19 are clearly the prevalent pathogenic strains, since they predominate throughout the entire series of specimens from various sources, and their incidence is more or less constant year by year. This uniform picture throughout the period of investigation is remarkable in children from the densely populated area of Glasgow and the Clyde valley, and similar results were obtained by Hendry (1942), working independently in this hospital, who also isolated types 19 and 6 most frequently from 186 children with pneumonia.

The uniformity of our results is the more striking when contrasted with those of many authors in various countries, who, in recording large investigations over periods of several years, found considerable fluctuation in the annual incidence of pneumococcus types. This variable incidence is evident in the review by Mørch (1943), of pneumococcus type-distribution in different countries. In America, also,

Cecil, Baldwin & Larsen (1927); Bullova & Wilcox (1937) and Finland (1937) record considerable annual fluctuation. On this account Friderichsen (1939), who had a similar experience in Denmark, advocates 5 years as the minimum period in which to study pneumococcal incidence.

Variation in type frequently is not only annual, but also geographical. For example, Möller (1942) states that type 2 is much less prevalent in Sweden than in America, and, according to Mørch (1943), type 2 is especially liable to vary in incidence from place to place and year to year. Type 14 occupies a place of much greater prominence in America than in Glasgow, where it is comparatively rare. In the States it is the most frequent cause of pneumonia in infants and young children; Reiman (1938) found type 14 responsible for 20% of infantile pneumonias in America; Bullova & Gleich (1938) and Curnen (1939) give similar figures, and all these authors regard type 14 as a remarkably virulent strain.

Various workers have correlated type-prevalence with age—the high incidence of type 14 in infancy has been cited above—and have selected the ages of 2 and 3 years as dividing lines. Thus, Nemir, Andrews & Vinograd (1936), in America, found type 19 almost exclusively under the age of 2 years and, in Denmark, Friderichsen reported types 6 and 23 as leading strains in that age group, with types 1 and 7 most prevalent over 2 years. Vammen (1939), in Copenhagen, found that types 6 and 19 were predominant in his pneumonia patients under 3 years of age, and types 1 and 7 were the most frequent strains over 3 years and in adult cases.

In our series the leading strains in children under 2 years were types 6, 19, 23 and 22. Over 2 years the four main types in order of frequency were types 6, 1, 19 and 4. Regarding the incidence of the 'fixed' types in the two groups, types 2 and 3 showed a comparable low figure in both, but type 1 occurred nearly four times as often in children over 2 as in those under 2, and in children from the older group, aged 5 years or more, the incidence of type 1 strains had risen still further to approximately six times the figure in the youngest age group. While type 1 increased in frequency with age, the higher types, 21–32 inclusive, showed a corresponding but less marked decline. These combined types together represented 21% of the total strains in the patients under 2, while this figure was approximately halved in those over 2. The varying incidence of type 1 in the two age groups is the only significant difference in our series.

Just as types 6 and 19 predominated over our entire series of strains from patients, irrespective of age, so too were they most prevalent in the 153 strains isolated from normal children's throats, where most of the children were over 2 years of age. There are

few comparable records, but Straker, Hill & Lovell (1939) had similar figures for normal children in London and south-east England. Gundel (1932-3), in Heidelberg, cultured multiple throat swabs from healthy school children over 12 years of age, and again found type 6 to be among the four most prevalent strains. When normal throats are swabbed repeatedly at intervals it is often found in children and in adults that an individual carries one particular pneumococcal type over a considerable period (Straker, Hill & Lovell 1939; Webster & Hughes, 1931; Gundel & Linden, 1931; Smillie, Calderone & Onslow, 1943), and this is true even of young infants (Neufeld & Ettinger-Tulczynska, 1932; Sutliff & Davis, 1937). On the other hand, more than one type of pneumococcus may be found in the sputum; according to Finland (1942) infants and young children are particularly prone to harbour multiple types of pneumococcus, and not infrequently we found two and occasionally three and four strains in specimens, both from sick and healthy children, and other workers have had the same experience. Cockrell & Ruegsegger (1941) record the case of a schoolboy with pneumonia, from whose sputum six different pneumococcal types were simultaneously isolated by mouse inoculation.

While pneumococcal pneumonia in children is thus often endemic, localized small epidemics due to specific strains occur from time to time. Such outbreaks due to type 1 pneumococcus in children's homes are recorded by Strøm (1932), and by Joppich (1934). Schroder & Cooper (1930) describe a pneumococcus type 5 epidemic, and Dauer, Dowling & Noble (1941) report a type 2 epidemic in a school. Rarely have outbreaks been caused by higher types, but Smillie & Jewett (1941) record one due to type 14 in an orphanage; further, Finland (1942) cites many instances of familial infection with various group IV strains.

On surveying the types of pneumococci isolated from the various lesions in our material, we recovered altogether 130 pneumococcal strains from the serous sacs. These comprised 106 specimens of pus from pleura, eight from pericardium and sixteen from peritoneum. Types 1 and 6 each accounted for one-third of the empyema strains. The former is well known to be an invasive pyogenic type in adults, and Glynn & Digby (1923) found that it accounted for 40% of thirty empyemata in children. Fairbrother (1935) also isolated type 1 pneumococcus from fifty-one of fifty-nine empyemata in children, and Blacklock & Guthrie (1933) found that the incidence of type 1 empyema rose with the increasing age of the children, although group IV strains predominated in the empyemata following broncho-pneumonia. These authors also collected seventy-two cases of pneumococcal peritonitis from the literature, including fifteen of their own. Nearly 75% of the

combined cases were due to type 1 infection, and about 12% to type 2 and to group IV respectively. Pahmer (1940) divided his twenty-nine cases of pneumococcal peritonitis into those which were primary and those complicating nephrosis; the former were mostly due to type 1 strains, while in the latter group IV strains predominated.

Pneumococcal arthritis is essentially a disease of young children, and most of our thirty cases were under 2 years of age. Pneumococci of types 6 and 1 occurred most frequently. Finland (1937) records three cases of purulent arthritis in children due respectively to types 1, 12 and 14, and Hendry had two cases, one due to a type 6 and one to a type 9 strain.

Pneumococcus meningitis also is most frequent in early infancy (Fothergill & Sweet, 1933). Their youngest case was only a day old and the youngest patient in our series of forty-nine cases was aged 4 days. Our cases were generally secondary to pneumonia or otitis media, and the cerebrospinal fluid yielded a pneumococcus of the same type as the primary infection. Gundel (1932-3), Finland (1937), Finland, Brown & Rauh (1938), Joppich (1938), Nemir *et al.* (1936) and v. Heukelom & Beeuwkes (1942) all failed to find striking prevalence of any one type of pneumococcus in meningitis, though where the infection complicated otitis media or mastoiditis type 3 was a common strain, particularly in adults in whom it is frequently found in suppurative conditions of the ear. Mørch (1944) records eighty-seven cases of meningitis, due mostly to the higher pneumococcal types.

It is evident from our experience, and from that of others, that the prevalent nasopharyngeal pneumococcus strains in healthy children belong to group IV, and that similar types are met with in respiratory disease. This fact is important in more ways than one. First, it may be inferred that the diagnostic significance of group IV strains in children is uncertain merely from throat swabs, but if the organism is isolated also from pus in an acute otitis, due almost certainly to a pharyngeal strain, the invasive power of such a strain is proved. We found an identical pneumococcus in 95% of cases where a strain was isolated from pus in the middle ear as well as from a lung lesion in the same child, and the almost complete identity of otitic, pharyngeal and pulmonary strains seems to confirm the view that in children the same organism affects the entire respiratory tract. Moreover, in our series where multiple specimens of pus were typed from the same case, for example, from various serous sacs or from the lung or pleura, there was agreement in practically every instance. In adults, Andrews (1937) had similar findings and Plummer, Raia & Shultz (1930) isolated the same pneumococcal type from sputum, and from some other focus of infection in 84% of their juvenile

cases. Group IV strains in infancy and childhood are thus potential pathogens capable of infecting the lung, and pneumococcal pneumonia in childhood is often an endogenous infection, particularly in the first 6 months of life (Cruikshank, 1945). In contrast, the pneumonia of adults both in this country and in America is most commonly due to pneumococci of types 1 and 2 (Christie, 1932; Cruikshank, 1933; Anderson, 1945); such types are rarely met with in the throats of healthy subjects. On the other hand, group IV strains are commensals of the adult throat. Since carriers of pneumococci are widespread in the community, they probably represent an important source of infection in children. A chronic lesion in tonsils or nasal sinuses renders carriers more highly infective since the pneumococci proliferate rapidly in the throat and nose during attacks of coryza to which such persons are liable.

Of the 870 patients in our series, thirty only were neonatal infants. Of these, twenty-seven died, eighteen with pneumonia, sometimes associated with empyema, otitis media, or meningitis; and nine with acute purulent otitis media. Of the three survivors one had conjunctivitis and cellulitis and two had purulent arthritis. There were no predominant pneumococcal strains but most belonged to one or other of the higher types.

Like many observers, we have been impressed by the comparative immunity of newborn infants to pneumococcal infection. This is the more remarkable when contrasted with the high carrier rate of staphylococcus in the early days of life (Cruikshank, 1946; Guthrie & Montgomery, 1947), and the frequency of outbreaks of staphylococcal sepsis and pneumonia in maternity nurseries. It is impossible to say whether opportunities for pneumococcal infection in the newborn are less frequent than for staphylococcal, but in the investigation undertaken by Torrey & Reese (1945), although 22.8% of seventy mothers harboured pneumococci in their nasopharynx, this organism was isolated from only about one-fifth of their babies. It would appear that the newborn infant is relatively resistant to the pneumococcus. Rimington & Bickford (1947), in explanation, quote Hirsfeld's (1927) theory of 'humoral immunity'. Sutliff & Finland (1932) state that immune bodies to the pneumococcus are present in the blood of infants immediately after birth and disappear about the end of the first month. These early type-specific antibodies are similar to those of the mothers, and are probably acquired by placental transmission. Although direct cultural observations of the neonatal respiratory and mouth flora such as those of Thaysen (1914), Johnson & Meyer (1925) and Kneeland (1930), using cultural methods only, indicate that the pneumococcus is amongst the last organisms to

become established, Gundel & Schwarz (1931-2) employing mice, isolated the pneumococcus from a premature infant within 6 hr. of birth and from three other infants before the age of 24 hr.; by the twelfth day 59% of fifty-two infants harboured pneumococci, mostly group IV strains.

Knowledge of pneumococcal infections of the lower respiratory tract in the neonatal period is also scanty. Macgregor (1939) rarely isolated the pneumococcus from the lungs of children with neonatal pneumonia unless the lesion was typically alveolar in character. One of us (K. J. G.), investigating a staphylococcal epidemic in a maternity nursery, isolated pneumococci twice only on inoculating mice with bronchial exudate and lung puncture material from thirty infants.

Compared with that of other age groups, the field of neonatal bacteriology is relatively unexplored, and it is possible that a systematic search for the pneumococcus might disclose a higher incidence than is so far apparent from the literature.

SUMMARY

This paper records the results of systematic pneumococcus typing over a 7-year period in children from 4 days to 12 years of age in the R.H.S.C., Glasgow. Strains typed include those from respiratory tract lesions, from pus in middle ears, meninges, joints, serous sacs and miscellaneous purulent foci. A series of strains from normal throats serves for comparison.

The constant prevalence year by year of types 6, 19, 1 and 23 in all types of disease is striking. On dividing the cases into those under and over 2 years, the incidence of type 1 in the older children is four times that in the younger group. Conversely in those over 2 the incidence of the higher types (21-32) is only half that in the younger patients. No other significant difference in type distribution is observed on comparing the two age groups. Group IV pneumococci are commonly carried in the healthy nasopharynx, and are potential pathogens in young children in whom broncho-pneumonia is generally an endogenous infection. There is evidence that the same type of pneumococcus frequently invades the entire respiratory tract and the middle ears. Only thirty of our cases were in the neonatal period and the apparent immunity of the newborn to the pneumococcus is discussed.

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