

## COMMENT

### Streptococcal infection in general practice

The last 30 years have seen changes in emphasis in the study of streptococci and streptococcal diseases. Earlier work concentrated mainly on the sources and methods of cross-infection and descriptive epidemiology of *Streptococcus pyogenes* in its major manifestations of respiratory, cutaneous and invasive infection and in the complications of rheumatic fever (RF), scarlet fever (SF) and post-streptococcal glomerulonephritis (PSGN).

Since the 1960s there has been both extension and consolidation in this field of study. The introduction of Lancefield grouping and rapid streptococcal identification kits for routine use in diagnostic laboratories has led to increased interest in the role of non-group A and non-haemolytic streptococci in human and animal infections. Contemporary advances in molecular biology and immunology have led to a much more detailed understanding than was previously possible of streptococcal pathogenicity and the closely-associated issues of host immunity.

Much of the recent work on streptococci has been of a molecular or genetic nature and carried out by laboratory-based researchers but a strong interest has been maintained in the general epidemiology, clinical manifestations and management problems posed by these common organisms. In many parts of the industrialised world there has been a resurgence in serious streptococcal infection during the 1980s [1] and an unexpected increase in the incidence of RF has been reported from many localities [2]. In addition, new settings for epidemic streptococcal infection in our society have been reported, such as in meat handlers [3], new associations recognised, such as that between non-group A streptococci and PSGN [4], and new clinical syndromes have been described, such as the toxic shock-like syndrome (TSLs) [5, 6].

In this issue of the journal three papers from general medical practice in England describe the clinical findings in patients with *S. pyogenes* upper respiratory infections directly observed over a period of several years in the early 1960s. Single observer studies such as these allow a highly consistent approach to be taken over prolonged periods although the number of patients studied is necessarily limited. Several novel observations are set out and discussed in these papers, particularly with regard to PSGN, splenic enlargement and the possible role of dual infection of the patient with streptococci and viruses.

How relevant are findings from the 1960s to present-day thinking on streptococci and do the data hold true? Certainly changes have occurred in the predominant strains of streptococci circulating in our community since that time and such changes are often associated with alterations in the pattern of streptococcal diseases. Typical changes in the prevailing T/M-types of *S. pyogenes* circulating in the community were illustrated in a study in Oxfordshire in the late

1970s [7] which showed transient epidemics with particular types occurring over months or years against a background of more persistent endemic infection with other types. Studies of *S. pyogenes* isolates sent to national reference laboratories in the UK and USA in the 1980s [8, 9] correlated the rise and fall of particular prevailing streptococcal types with the parallel occurrence of particular streptococcal diseases, including invasive infection, RF, SF and TSLs, and features such as antibiotic resistance. Overt PSGN is now less commonly encountered in the UK than in the 1960s, even after infection with streptococci of M-types, such as 4, 12 and 49, that were then regularly associated with the complication [8, 10]; strains of streptococci within particular T/M-types probably vary in their ability to produce nephritogenic products and the state of immunity of the population to these substances may also be an important determinant of the prevalence of overt disease [11, 12]. In this light, local resurgence of streptococcal diseases, including PSGN, can be expected to occur from time to time in industrialized countries; in less developed parts of the world they have remained generally common throughout the recent period. The determining factors for splenomegaly in streptococcal infection are not yet known; if there is a relationship to particular T/M-types of *S. pyogenes* some periodic variation in the occurrence of this clinical feature may also be expected.

Many of the classic studies of earlier years on streptococcal infection and epidemiology gave fundamental information the value of which endures to this day. In similar manner, although the particular setting of infecting strains of streptococci may have changed, the findings of 30 years ago discussed in the present papers remain relevant.

The observations in these papers on dual bacterial and viral infection contribute to the growing debate on this subject. The facilities available for viral diagnosis in the 1960s were relatively unsophisticated but they were more likely to underestimate than to over-estimate the occurrence of dual infection. Common bacterial and viral infections are likely to occur together by chance in some individuals, particularly in the childhood years, and the combined effects, even without specific pathogenic interactions, may produce unusual arrays of symptoms and signs [13]. In the present paper numbers are small and the effects observed on kidney and spleen might simply indicate the ability of one or other agent to produce such complications alone or by addition. Proper study of the interactions which may occur between these two groups of agents has always been bedevilled by the problem of recruiting adequate numbers of comparable cases and appropriate controls. Despite these difficulties a number of reports now suggest that significant synergistic interactions may occur. Bacterial infections might promote infection with viruses by enhancing ingress to the body, such as for HIV infection in genital ulcerative disease [14], or by enhancing surface virulence factors, such as the processing of surface precursor haemagglutinins of the influenza virus by enzymes from *Staphylococcus aureus* [15]. Viruses might promote bacterial infection by the immunosuppression they may cause [16, 17], by the production of local tissue damage which provides suitable local conditions for bacterial adherence, multiplication and invasion [18] and by enhancing transmission [19]. In clinical research on streptococci dual infections have been reported in a number of studies of serious, invasive disease [20, 21] and associations

with measles, varicella and acute enterovirus infection have been noted with some regularity [22–24]. The possibility of enhancement of local streptococcal infection and its complications by concurrent acute viral infection deserves further exploration.

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