

## Streptococcal infection in a Junior Detention Centre: a five-year study

BY A. COLLING, IDA KERR,

*Kirklevington Detention Centre, Yarm, Cleveland*

W. R. MAXTED AND JEAN P. WIDDOWSON

*Division of Hospital Infection, Central Public Health Laboratory,  
Colindale Avenue, London NW9 5HT*

(Received 14 March 1980)

### SUMMARY

In 1972 more than 20% of boys admitted to a closed community (Junior Detention Centre) developed acute tonsillitis and group-A streptococci were isolated from more than 40% of all boys at some time during their stay of two months. The most common serotype was M-type 5, which has frequently been associated with rheumatic fever in other epidemics; four cases of rheumatic fever occurred between 1972 and 1977. Various methods were tried to eliminate the infection, but only full penicillin prophylaxis (0.25 g oral penicillin 4 times a day for 10 days) to all boys on entry appeared to be effective.

In a sample of cases of acute tonsillitis, group-A haemolytic streptococci were isolated from 31.7% by the use of dry swabs or unenriched transport medium, but with enrichment medium duplicate swabs, 77.6% yielded positive results. We question the current practice in some laboratories of reporting positive cultures only when more than ten colonies of  $\beta$ -haemolytic streptococci are present. In this survey viruses did not appear to be an important cause of acute tonsillitis.

High titres of streptococcal antibodies (antistreptolysin O, anti-desoxyribonuclease B and anti-M associated protein) were found, not only in cases and carriers, but in boys on entry to the centre. This supports epidemiological evidence that adolescent boys are particularly prone to streptococcal throat infections.

### INTRODUCTION

In September 1972 the Medical Officer at the Kirklevington Detention Centre, Yarm, Cleveland, grew worried about the number of boys admitted to the sick bay with acute tonsillitis. A preliminary investigation of 100 boys showed that 30% harboured group-A streptococci at some time during their two-month stay. We considered that this warranted a more detailed study, and present this report on the incidence of streptococcal carriage, tonsillitis and rheumatic fever in the centre during the period October 1972 to June 1977, together with relevant information on the prevalence of different streptococcal serotypes and a detailed study of the streptococcal antibody titres of newly admitted boys, carriers and boys with tonsillitis.

## MATERIALS AND METHODS

*Kirklevington Detention Centre, Yarm, Cleveland*

The Junior Detention Centre at Kirklevington receives boys aged 15–17 years from a large area of the North of England, roughly north of a line from the Mersey to the Humber. More than half the boys are at home until sentencing by the Courts, whilst the remainder are detained in remand centres for a matter of weeks awaiting trial or sentencing.

*Collection of swabs*

Boys usually remained in the centre for 8 weeks (reduced in September 1975 to 6 weeks). Swabs were taken from the noses and throats of all boys on entry, after 4 weeks and before discharge. The cultures were sent as dry swabs to the local laboratory and cultured for 24 h at 37 °C on blood agar. Any cultures positive for group-A streptococci were sent to the Streptococcus Reference Laboratory at the Central Public Health Laboratory, Colindale, London NW9 5HT, for type identification.

After May 1975 all swabs were taken in duplicate; one was sent to the local laboratory in transport medium (Stuart, 1956) and the other sent directly to the Reference Laboratory in an enriched culture medium (5.0% horse serum, 0.5% glucose, 0.7% ion agar in a Hartley Digest Base).

Swabs for virus isolation (carried out only from September 1972 to September 1975) were taken from all boys with acute tonsillitis, placed in Amies transport medium with charcoal (Difco Ltd, West Moseley, Surrey) and kept at 4 °C until collected by the local laboratory – usually within 2 h.

The effectiveness of penicillin therapy was tested in a sample (50) of carriers and cases of acute tonsillitis by taking swabs from the throat, ear, nose and perineum on the 14th day after treatment was begun, i.e. 4 days after completing treatment. The swabs were transported to the Reference Laboratory in serum glucose agar.

*Serum samples*

Serum samples were collected for streptococcal antibody tests during the first two years of the survey (October 1972–4) from three categories of boys:

(i) *Normal boys*. 146 boys were bled immediately on entry to the centre to give 'baseline' information on the antibody titres in boys of this age from the north of England.

(ii) *Carriers*. Single samples of sera were taken as soon as possible (usually about 2 days) after the isolation of a group-A streptococcus from 187 boys who were without symptoms. Thirteen carriers were bled again 4 weeks later.

(iii) *Boys with acute tonsillitis*. Paired sera (the first sample taken as soon as possible after the isolation of a group-A streptococcus and the second 4 weeks later) were collected from 113 boys considered to have tonsillitis, mainly those who complained of sore throat, were febrile (temperature > 37 °C) and had inflamed tonsils. In boys without tonsils, an inflamed pharynx was accepted. The group also included a few boys who were ill but afebrile and had grossly inflamed tonsils, adenitis and exudate.

*Identification of streptococci*

Beta-haemolytic streptococci were grouped by Fuller's method (Fuller, 1938) at the North Tees General Hospital, Stockton, Cleveland. Group-A strains were T-typed (Griffith, 1934), M-typed (Rotta *et al.* 1970) and certain strains identified by opacity-factor neutralization tests (Maxted *et al.* 1973) at the Streptococcus Reference Laboratory.

*Identification of viruses*

The specimens were inoculated into three different cell lines (Rhesus monkey kidney, Teesside embryonic lung and HeLa cells) and incubated for 14 days at 33 °C. Cytopathogenic agents were looked for and, before the cultures were discarded, they were also examined for CPE-negative haemadsorbing agents.

*Streptococcal antibody tests*

All sera were tested for antistreptolysin O (ASO) (Goode & Williams, 1961), for anti-desoxyribonuclease B (anti-DNAase B) (Nelson, Ayoub & Wannamaker, 1968) and for antibody to M-associated protein (MAP) (Widdowson, Maxted & Pinney, 1971). The antibody titres for the sera of the various groups of boys were compared by plotting cumulative percentage curves for each group and calculating the 50% values (the titre exceeded by 50% of the sera in the group). Arbitrary 'upper limits of normal' for each antibody were defined from the curves for the sera of a group of boys sampled on entry to the centre, as the value exceeded by 15% of the sera in the group.

*Penicillin treatment*

Boys with tonsillitis were treated with intra-muscular penicillin 0.6 g twice a day until symptoms cleared, and then oral penicillin 0.25 g four times a day for 10 days. Carriers were treated with oral penicillin 0.25 g four times a day for 10 days.\*

*Penicillin prophylaxis*

From December 1974 until the end of the survey (June 1977) all boys were treated with 0.25 g of oral penicillin four times a day for 10 days, beginning the morning after they entered the centre.\*

## RESULTS

*Incidence of acute tonsillitis, 'sore throat' and streptococcal carriage (October 1972 to November 1974)*

During the first six months of the survey (Period 1, October 1972 to March 1973) the incidence of tonsillitis and 'sore throat' was high (see Table 1). Sixty-five boys (20.6%) out of a possible 316 admitted to the centre during that period developed

\* Erythromycin 0.25 g four times a day was given if there was a history of penicillin allergy.

Table 1. Incidence of tonsillitis, 'sore throat' and carriage of group-A streptococci among the boys of Kirklevington Detention Centre, October 1972 to June 1977

| Period  | No. of boys admitted*  | Acute tonsillitis |        |                       |        |               |        |                  |        |
|---|--|-------------------|--------|-----------------------|--------|---------------|--------|------------------|--------|
|   |  |                   |        | Streptococci isolated |        | 'Sore throat' |        | Group-A carriers |        |
|   |  | No.               | %      | No.                   | %      | No.           | %      | No.              | %      |
| (1) Oct. 1972 to Mar. 1973                      | 316  | 65                | (20.6) | 30                    | (46.2) | 181           | (57.3) | 98               | (31.0) |
| Hygienic measures taken                         |  |                   |        |                       |        |               |        |                  |        |
| (2) May 1973 to Oct. 1973                       | 357  | 86                | (24.1) | 27                    | (31.4) | 237           | (66.4) | 94               | (26.3) |
| (3) Jan. 1974 to June 1974                      | 352  | 75                | (21.3) | 24                    | (32.0) | 196           | (55.7) | 47               | (13.4) |
| (4) July 1974 to November 1974                  | No action taken. Permission to give penicillin prophylaxis sought. |                   |        |                       |        |               |        |                  |        |
| Penicillin prophylaxis introduced December 1974 |  |                   |        |                       |        |               |        |                  |        |
| (5) Dec. 1974 to May 1975                       | 335  | 70                | (20.9) | 7                     | (10.0) | 225           | (67.2) | 23               | (6.9)  |
| (6) June 1975 to Aug. 1975                      | 210  | 27                | (12.9) | 8                     | (20.6) | 16            | (7.6)  | 33               | (15.7) |
| (7) Oct. 1975 to Mar. 1976                      | 419  | 71                | (16.9) | 24                    | (33.8) | 51            | (12.2) | 31               | (7.4)  |
| (8) Jan. 1977 to June 1977                      | 570  | 27                | (4.7)  | —                     | (—)    | 18            | (3.2)  | —                | (—)    |

\* Each boy remained at the Centre for 8 weeks during periods 1-6. The sentence was reduced to 6 weeks during periods 7 and 8.

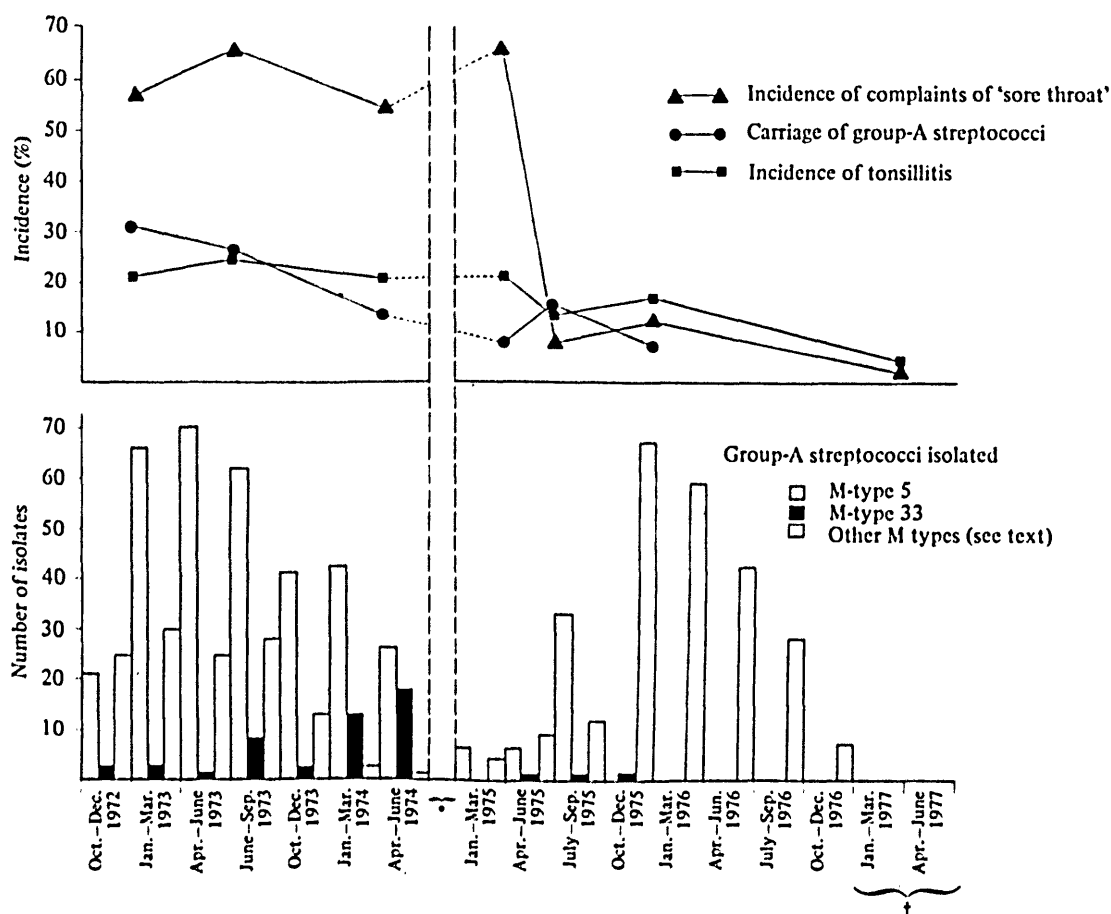
— = not done.

acute tonsillitis and were treated with penicillin. Of these 65 boys, 30 (46.2%) had group-A streptococci isolated from their throats.

A further 181 boys (57.3%) complained of 'sore throat' but they were afebrile and their throats appeared normal. In the prison population many boys report sick with apparently trivial complaints; they were not given penicillin. However, when throat swabs from a sample of these boys were sent to Colindale in enriched medium, group-A streptococci were isolated from 14 out of 18 samples (78%).

The predominant organism isolated from cases and carriers during this period was M-type 5 (Fig. 1). The same organism was isolated from the air and blankets in the dormitories, and from clothes and blankets in the stores. These possible sources of infection were eliminated, but in spite of the 'clean-up' and the fact that all cases and carriers were treated promptly with penicillin, the attack rate for tonsillitis continued to be high during the two subsequent six-month survey periods (May-October 1973 and January-June 1974). The carriage rate of group-A streptococci, which was 31% during the first six months, had, however, been reduced to 13.4% by the third period (January-June 1974).

" As expected, a few boys (4%) entered the centre carrying a group-A streptococcus. A surprisingly high proportion of these belonged to M-type 5. Six out of 16



\* No swabs taken from June to November 1974. Penicillin prophylaxis started December 1974.

† No swabs taken between January and June 1977.

Fig. 1. Provalence of different serotypes of group-A streptococci and the incidence of tonsillitis, group-A carriage and complaints of 'sore throat'.

(37.5%) group-A carriers admitted from seven other remand centres had M-type 5. This type is not very common according to recent surveys of the type distribution of group-A streptococci in this country, and type 5 accounted for only 2% of group-A streptococci sent to the Streptococcus Reference Laboratory for typing in the years 1972-7 (M. T. Parker, personal communication), but has been described in connexion with outbreaks of tonsillitis and rheumatic fever in closed communities in this country (Widdowson *et al.* 1974a, b).

*Prophylactic penicillin treatment (December 1974 to June 1977)*

During periods 1, 2 and 3 (Table 1) group-A streptococci were isolated from 31% of all boys at sometime during their sentence. Since the attack rate of tonsillitis was high (20%) and we had seen three cases of rheumatic fever in two years, we introduced penicillin prophylaxis in December 1974 after permission had

been granted by the prison authorities. A course of oral penicillin (see Materials and Methods) was given to all boys on entry to the centre before the results of the throat swabs were known. The attack rate of tonsillitis remained high (21.0%) for the first six months after prophylaxis was introduced, but then fell gradually over the next 18 months until it was reduced to 4.7% in the period January–June 1977. The most striking effect of penicillin prophylaxis was that the incidence of boys complaining of ‘sore throat’ fell from over 67% to only 3.2% during the two years of prophylaxis.

Although penicillin prophylaxis seemed successful in the long term in reducing the incidence of tonsillitis, the treatment failure rate, i.e. failure to eradicate the streptococcus from individual patients, was about 50% in a small sample of 50 cases and carriers sampled 4 days after penicillin treatment had ceased.

#### *Failure to isolate group-A streptococci from routine swabs*

Although the attack rate for tonsillitis was high (21.0%) in the first six months of prophylaxis, the isolation rate of group-A streptococci from dry swabs during this period was extremely low (10% compared with 30–40% before prophylaxis started). Therefore, from May 1975 onwards the swabs were taken in duplicate: one was sent in Stuart’s transport medium to the local laboratory and the other in enrichment medium to the Streptococcus Reference Laboratory at Colindale. The enrichment medium produced a striking increase in the frequency of isolation of group-A streptococci from the tonsillitis patients and, in the 11 months when the swabs were being taken in duplicate, 77.6% of swabs were positive after transport in enrichment medium compared with 31.7% for transport in Stuart’s medium.

#### *Virus isolation*

There were only two isolations, both of influenza B, between September 1972 and September 1975 when virus studies were undertaken.

#### *Group-A streptococcal serotypes (October 1972 to June 1974 and January 1975 to December 1976) (Fig. 1)*

M-type 5 (‘T’-pattern 5/27/44 or no ‘T’-antigen) was present at the start of the survey in October 1972 when it accounted for 14% of the group-A streptococci isolated. It started to predominate in December 1972 (65% of group A strains) and remained by far the most frequently isolated type (58–73%) throughout the next 18 months. During this period the only other serotype that accounted for > 2% of the group-A strains was M-type 33 (‘T’-pattern 3/13/B3264). For the first 18 months about 5% of strains belonged to this type, but later, in the first six months of 1974, an average of 30% were type 33. A mixture of other group-A serotypes (none occurring at a frequency of > 1%) accounted for about 30% of the strains isolated during the first year of the survey, but this figure gradually decreased in late 1973, so that in 1974 only 2–3% of the group-A streptococci belonged to serotypes other than M5 or M33.

No swabs were taken between July and December 1974 when discussions were in progress on the best way to cut down streptococcal infection in the Centre.

Penicillin prophylaxis began in December 1974. From January to September 1975 the number of group-A streptococci isolated was small but M-type 5 still remained the predominant organism, occurring in 43 cases (72%), whereas type 33 was isolated only once. After October 1975 type 5 disappeared and then the most frequently isolated organism had the T-pattern 3/13/B3264 (91%). However, these cultures were M-untypable and we cannot conclude that they all belonged to the same M-type. The fact that some were OF-positive and some OF-negative suggests that there were at least two M-types present (Maxted *et al.* 1973).

#### *Streptococcal antibody titres of boys on entry to the Detention Centre*

Of the 146 boys sampled on entry to Kirklevington 77% had evidence of recent streptococcal infection by virtue of an ASO titre  $\geq 200$  units/ml or an anti-DNAase B titre of  $\geq 400$  or both. The antibody titres of 86 boys admitted directly from their own homes were slightly lower (72% with raised titres) than those of a group of 60 boys admitted from other remand centres (83% with raised titres). The arbitrary upper limits of normal (titre exceeded by 15% of the sera in the group) calculated for this entry population were: ASO = 375, anti-DNAase B = 1300 and anti-MAP = 80. These values are greatly in excess of the arbitrary upper limits of normal generally adopted (Widdowson *et al.* 1974a).

#### *Antibody titres of carriers*

The 50% values for all three antibodies tested were raised in a group of 187 carriers bled 2 days after a group-A streptococcus was isolated (Table 2). Thirteen of the carriers were bled again 4 weeks later and six (46%) of these showed a rise (of greater than one doubling dilution) in ASO or anti-DNAase B or both. No rises in anti-MAP were observed.

#### *Antibody titres in boys with acute tonsillitis*

Sera taken from boys with tonsillitis, 2 days after a positive swab, had 50% values that did not exceed those of the intake population. However convalescent sera from these cases taken a month later showed a marked increase in 50% values for all three antibodies, and 47% of the sera showed a rise in ASO or anti-DNAase B or both. Anti-MAP titres showed a more than twofold rise in 40% of the sera, and in 12% of the sera anti-MAP was the only antibody that increased in titre. In all, 60% of the sera showed a rise in one or more of the three antibodies.

#### *Incidence of rheumatic fever (October 1972 to June 1977)*

The family doctors of all boys were notified on their discharge by the probation officer if a group-A streptococcus had been isolated. During the five years of the survey 3582 boys passed through the detention centre, 648 boys (18%) had tonsillitis and, of these, four (0.6%) developed rheumatic fever. All four of the rheumatic fever cases met the revised Jones's criteria (Stollerman, Markowitz & Taranta, 1965) with fever, raised ESR, and swollen, painful joints. Three of the four boys had heart murmurs and two of these had some ECG abnormalities. Two of the four had positive throat swabs for group-A streptococci (one M-type 5 and

Table 2. *Streptococcal antibody levels (50% values) in boys with tonsillitis, carriers of group-A streptococci and normal boys on admission to Kirklevington Detention Centre*

| Category       | No. tested | 50% values* of titres |               |          |
|----------------|------------|-----------------------|---------------|----------|
|                |            | ASO                   | Anti-DNAase B | Anti-MAP |
| 'Entry' boys   | 146        | 200                   | 600           | 35       |
| Carriers       | 187        | 267                   | 1043          | 73       |
| Tonsillitis    |            |                       |               |          |
| 1st serum†     | 113        | 183                   | 533           | 42       |
| 2nd serum      | 113        | 350                   | 1316          | 78       |
| Normal adults‡ | 122        | 50                    | 65            | 8        |

\* Titre exceeded by 50% of the sera in the group.

† First serum taken at acute stage of disease and the second one month later.

‡ 50% values taken from Widdowson *et al.* (1974*b*).

the other not typed). There was serological evidence of recent streptococcal infection in all four boys by virtue of rising titres of all, or some, of the three streptococcal antibodies tested. All four boys had ASO and/or anti-DNAase B titres in excess of the generally accepted arbitrary upper limits of normal. However, in three cases the rise of ASO titre was only slight and in only two of the four cases did the titre at any time exceed the upper limit of normal as defined by the intake population.

#### DISCUSSION

The problems of the eradication of group-A streptococci from closed and semi-closed communities are well known (Frank, Stollerman & Miller, 1965). Our measures to reduce the prevalence of tonsillitis and carriage at Kirklevington by prompt penicillin treatment of cases and carriers failed, and we had to adopt the more extreme measure of treating all the boys with penicillin on admission. In the long run this was successful and the attack rate for tonsillitis fell from 21.0% to 4.7% during the 18 months after penicillin prophylaxis was introduced. However, the regime was slow to take effect and it was six months before we saw any reduction in the number of tonsillitis cases. A possible reason for this may have been the high incidence of treatment failures. Although this was not studied in detail, we estimated from a small sample that the failure rate was about 50%. The reason for this is not known, but a recent report (Kaplan *et al.* 1979) suggests that a high incidence of *bona fide* treatment failures (i.e. failure that could not be attributed to non-compliance) may occur when the treated population contains a high proportion of transient or convalescent carriers. There are also indications (Rosenstein *et al.* 1968) that certain serotypes of streptococci are more difficult to eradicate than others.

A striking feature of the streptococci isolated at Kirklevington was the long-term predominance of M-type 5. One of the reasons why we considered penicillin prophylaxis to be justified was that M-type 5 had been associated with outbreaks of tonsillitis and some cases of rheumatic fever in closed communities (Widdowson *et al.* 1974*a, b*). Other types of streptococci were continually being introduced by



boys who were carriers on admission but these did not appear to get a hold. It was difficult to explain why type 5 was so common even among the new admissions, because only about 2% of strains submitted for typing to the Streptococcus Reference Laboratory in the years 1972-7 belonged to this serotype. After penicillin prophylaxis was introduced M-type 5 persisted for about eight months, but was then replaced by other group-A serotypes.

During the first six months of prophylaxis the attack rate of tonsillitis was still high (21%) but the isolation rate of group-A streptococci from suspected cases was very low (only 10% compared with over 30% before prophylaxis started). As virus infection did not appear to be the cause of the sore throats, we tried to improve our isolation of group-A streptococci. The introduction of an enrichment medium produced a striking increase in the number of isolations of group-A streptococci from tonsillitis cases over the following year. Thus, 77.6% of cases yielded group-A streptococci by enrichment compared with 31.7% by the routine method. This suggested that approximately half the positive swabs, presumably those containing only small numbers of streptococci, were being missed by the routine method, but it is difficult to judge the significance of this without further work. At present, some laboratories report a positive isolation of group-A streptococci only if the culture contains more than ten colonies because a small number of colonies is thought to be clinically insignificant (Bell & Smith, 1976; Breese *et al.* 1970). However, the difficulties of making a diagnosis of streptococcal pharyngitis and distinguishing active infection from the carrier state in patients with symptoms has been stressed by Kaplan *et al.* (1971) who found that about one third of patients with fewer than 10 streptococci in their swabs still showed a rise in streptococcal antibody titre, suggesting that infection had, in fact, occurred.

The streptococcal antibody levels were extremely high even among the new admissions to Kirkclevington, which made the interpretation of raised titres in single sera very difficult. The antibody titres of single sera from carriers were higher than the values obtained for the intake population. This is in agreement with the results of Kaplan *et al.* (1971), who suggested that the high titres in carriers were the result of streptococcal infection in the recent past in patients who were still harbouring the streptococcus. Similarly, at Kirkclevington many of the carriers had type 5 with high antibody titres one month after entry. Since their swabs were negative on entry it is reasonable to assume that they acquired type 5 sometime during that month, but did not appear to have had a clinical infection. Paired sera were obtained from a small number of carriers and of 13 pairs tested, six (46%) showed a more than twofold rise in titre of ASO or anti-DNAase B or both, suggesting that subclinical infection might have occurred in about half the carriers. This figure (46%) does not differ from the value (47%) obtained from 113 paired sera from boys with tonsillitis and a positive throat swab. However, none of the carriers tested showed a rise in anti-MAP titre compared with 40% of the boys with tonsillitis, and among the tonsillitis cases 12% showed a rise in anti-MAP alone, with no other serological evidence of infection. This requires further study, but it is possible that because antibody to the cellular antigen MAP rises more slowly than antibody to the extracellular products, we

observed more rises in anti-MAP than in ASO or anti-DNAase B, due to the timing of our bleedings relative to the time of infection. It also seems possible that, although 'carriage' (or subclinical infection) elicits antibody to the extracellular products of the streptococcus, overt infection is required to stimulate antibody to the cellular antigen MAP.

The peak age for the occurrence of tonsillitis associated with group-A streptococci is 5-7 years, but a second peak seems to occur in adolescence (Glezen *et al.* 1967; Kaplan *et al.* 1971; Fry, 1979), which might perhaps explain the high antibody titres of boys on admission to Kirklevington. It is clear that closed communities for adolescents are a special problem as regards the prevention of streptococcal infection. We saw four cases of rheumatic fever (but no cases of nephritis) in five years, which represents an incidence rate of 0.6% of those who suffered from tonsillitis, a figure which increases threefold if expressed as a percentage of those with tonsillitis and a positive throat swab. Of the preventive measures tried we found that only full penicillin prophylaxis to all boys on admission effectively reduced the attack rate for tonsillitis to acceptable levels. Work is still in progress to determine the minimum amount of penicillin cover required to keep streptococcal infection under control at Kirklevington.

Our thanks are due to: the Wardens and Prison Staff of Kirklevington Detention Centre for their continued interest and help, Dr E. Walton and staff in the Pathology Department at North Tees General Hospital, the staff of the Streptococcus Reference Laboratory, Colindale, and Mr T. Cashmore and Mr J. Bashford, Virology Department, Middlesbrough General Hospital. We are also grateful to part-time medical officers Dr A. Bird, Dr W. G. Davies and Dr D. Redman for their help at Kirklevington.

#### REFERENCES

- BELL, S. M. & SMITH, D. D. (1976). Quantitative throat swab cultures in the diagnosis of streptococcal pharyngitis in children. *Lancet* *ii*, 61-3.
- BRESE, B. B., DISNEY, F. A., TAPLEY, W. B. & GREEN, J. L. (1970). Beta-haemolytic streptococcal infection. The clinical and epidemiologic importance of the number of organisms found in cultures. *American Journal of Diseases of Children* **119**, 18-26.
- FRANK, P. F., STOLLERMAN, G. H. & MILLER, L. F. (1965). Protection of a military population from rheumatic fever. Routine administration of benzathine penicillin G to healthy individuals. *Journal of the American Medical Association* **193**, 775-83.
- FRY, J. (1979). Acute throat infection. *Update*, May 1979, p. 1181.
- FULLER, A. T. (1938). The formamide method for extraction of polysaccharide from haemolytic streptococci. *British Journal of Experimental Pathology* **19**, 131-9.
- GLEZEN, W. P., CLYDE, W. A., SENIOR, R. J., SHEAFFER, C. I. & DAVEY, F. W. (1967). Group-A streptococci, mycoplasmas and viruses associated with acute pharyngitis. *Journal of the American Medical Association* **202**, 455-60.
- GOODER, H. & WILLIAMS, R. E. O. (1961). Titration of anti-streptolysin O. Broadsheet no. 34 (new series). London: The Association of Clinical Pathologists.
- GRIFFITH, F. (1934). The seriological classification of *Streptococcus pyogenes*. *Journal of Hygiene* **34**, 542-83.
- KAPLAN, E. L., TOP, F. H., DUDGING, B. A. & WANNAMAKER, L. W. (1971). Diagnosis of streptococcal pharyngitis: differentiation of active infection from the carrier state in the symptomatic child. *Journal of Infectious Diseases* **123**, 490-501.

- KAPLAN, E. L., GASTANADUY, A., MCKAY, C. & WANNAMAHER, L. W. (1979). High treatment-failure rate in patients with group-A streptococcal pharyngitis. In *Pathogenic Streptococci* (ed. M. T. Parker), pp. 113-14. Chertsey, Surrey: Reedbooks.
- MAXTED, W. R., WIDDOWSON, J. P., FRASER, C. A. M., BALL, L. C. & BASSETT, D. C. J. (1973). The use of the serum opacity reaction in the typing of group-A streptococci. *Journal of Medical Microbiology* 6, 83-90.
- NELSON, J., AYOUB, E. M. & WANNAMAHER, L. W. (1968). Streptococcal anti-deoxyribonuclease B: microtechnique determination. *Journal of Laboratory and Clinical Medicine* 71, 867-73.
- ROSENSTEIN, B. J., MARKOWITZ, M., GOLDSTEIN, E., KRAMER, I., O'MANSKEY, B., SEIDEL, H., SIGLER, A. & TRAMER, A. (1968). Factors involved in treatment failures following oral penicillin therapy of streptococcal pharyngitis. *Journal of Pediatrics* 73, 513-20.
- ROTTA, J., KRAUSE, R. M., LANCEFIELD, R. C., EVERLY, W. & LACKLAND, H. (1970). New approaches for the laboratory recognition of M types of group-A streptococci. *Journal of Experimental Medicine* 134, 1298-315.
- STOLLERMAN, G. H., MARKOWITZ, M. & TARANTA, A. (1965). Jones' criteria (revised) for guidance in the diagnosis of rheumatic fever. *Circulation* 32, 664-8.
- STUART, R. D. (1956). The use of transport media and other devices to maintain the viability of bacteria in specimens. *Canadian Journal of Public Health* 47, 114-22.
- WIDDOWSON, J. P., MAXTED, W. R. & PINNEY, A. M. (1971). An M-associated protein antigen (MAP) of group-A streptococci. *Journal of Hygiene* 69, 553-64.
- WIDDOWSON, J. P., MAXTED, W. R., NEWRICK, C. & PARKIN, D. (1974a). An outbreak of streptococcal sore throat and rheumatic fever in a Royal Air Force Training Camp; significance of antibody to M-associated protein. *Journal of Hygiene* 72, 1-12.
- WIDDOWSON, J. P., MAXTED, W. R., NOTLEY, C. M. & PINNEY, A. M. (1974b). Antibody response in man to infection with different serotypes of group-A streptococci. *Journal of Medical Microbiology* 7, 483-96.