

PROBLEMS IN THE PRIMARY PREVENTION OF RHEUMATIC FEVER: EXPERIENCE FROM JERUSALEM

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This paper will report an attempt to answer the question "can first attacks of rheumatic fever in school children be prevented by early diagnosis and treatment of streptococcal sore throats through a school health service?" To this end, 7,500 school children, aged initially 7-11, were followed prospectively for three school years. Forty two percent of the 65,655 absences from school were due to upper respiratory infections (URI) an average of 3.7 per child over the 3 years, and from 12.7% of these cases, throat swabs yielded *Streptococcus pyogenes*. Children belonging to the 40% systematic sample, selected a priori, had their sore throats treated by the research team: the remainder were referred, with the laboratory report, to their family doctors.

Absence from school due to URI was affected by age, sex, school, season, social class and certain attributes of the home environment. Similar factors affected streptococcal recovery although here, the severity of symptoms was the deciding factor. There were considerable temporal fluctuations in the predominant types among the 3,700 strains recovered as well as in the proportion of strains typable by anti-M sera.

During the 3 years of the survey, 32 of the children suffered a first attack of possible or probable rheumatic fever. Twenty three of these occurred during the school year and in 16, a definite diagnosis could be made. Only three of these definite cases however, were preceded by a clinical pharyngitis and streptococcal recovery.

Interpretation of our results raises a number of questions. The questions deal with the definition, diagnosis and treatment of streptococcal sore throat and while they are primarily of clinical importance, they can only be discussed adequately, in my opinion, against a background of bacteriological, serological and epidemiological studies.

I shall discuss the problems of clinical diagnosis of streptococcal sore throat, the interpretation of bacteriological and serological findings and shall then pose the questions.

CLINICAL DIAGNOSIS

The physician who believes in his ability to make a clinical diagnosis of streptococcal sore throat has never put his skill to objective tests. Fig. 1 shows the degree of redness of the throat of nearly 10,000 children, aged 7-13 who complained of upper respiratory infections, as recorded by trained public health nurses, 1-3 days after onset of symptoms. While there is a correlation between the degree of severity and the percentage of throat swabs positive for group A streptococci (Fig. 2), 10% of children with no redness at the time of examination yielded streptococci while three quarters of the children with severe pharyngitis did not do so. Some children of all groups (Fig. 3) had received antibiotics before we saw them—for those who had not, the percentage of positive swabs was 11% in the mildest cases, to 34% in the most severe.

While the presence of increasing fever, dysphagia and swollen tender glands is associated with increased streptococcal recovery and antibody response, the correlation is poor and selection of the more clinically severe cases for treatment would reduce the work load but miss the majority. As Fig. 4 shows, 38% of children with upper respiratory infections had received antibio-

tics from their family doctor—although only half of them were given penicillin—but there was no correlation between the treatment and the bacteriological findings.

BACTERIOLOGICAL FINDINGS

It is generally assumed that the culture of group A streptococci from a throat swab is certain evidence of streptococcal pharyngitis while a negative swab excludes the diagnosis. This assumption is contradicted by everyday experience. If 8-10% of children are normally streptococcal carriers, they might remain so even when suffering from a vital infection although there is evidence that the rate of streptococcal recovery from throats decreases during an epidemic of influenza.

More commonly, the streptococcus may be present yet missed. Among factors contributing to false negative results are the technique of swabbing, bacteriostatic substances in the cotton of the swab and the use of human blood for blood agar plates. We have shown that the fluorescent antibody test is more sensitive in detection of small numbers of streptococci than usual culture methods and its use could increase the yield of positive swabs by 5-15%. Furthermore the use of a single throat swab, as compared to duplicate swabs, might miss 13.5% of the positive cases. There is a correlation between the "degree of positivity" of the throat swabs and the antibody response; the higher the yield of streptococci the greater the response, (Figure 5) but even when very few colonies were recovered on only one of the two swabs, 10% of the children still showed a significant rise in ASO titres.

SEROLOGICAL FINDINGS

Much of our knowledge of antibody response to streptococcal infection derives from studies of rheumatic children and is based on anti-streptolysin O titres, still the test most commonly performed. It may be asked whether the conclusions need necessarily apply to normal children, the vast majority of whom are not susceptible to rheumatic fever.

Most clinicians are aware of the clinical limitations of a single antibody measurement although many still accept an ASO titer of 1:200 or more, based on a single reading as significant evidence of recent streptococcal infection. In a study of 647 paired sera, 35% showed an acute phase, initial titer of 1:240 or more and 25% of 1:340 or more.

The more severe the clinical signs, the greater the chance of significant antibody response (Fig. 6) but the ability of a child to show an increase in titre was affected markedly by the initial antibody level. When this was ASO 1:120 or less, 47% of children with a sore throat from whom group A streptococci had been recovered, showed a significant increase in titer. When the initial titer was 1:340 or more the percentage responding was only 26. (Fig. 7). The same general picture was true of two other streptococcal antibodies, antihyaluronidase and anti DPNase (now called anti NADG or nicotinamide adenine dinucleotide glycohydrolase) which brings up the question as to the sensitivity of the ASO test alone in detecting response to streptococcal infection. In a study of 326 duplicate sera, taken in the acute phase and 3 weeks later, three tests were performed, ASO, AH and ADPNase. As may be seen from Fig. 8, 132 of them or 40% showed a rise in one or more of the antibodies. But while 25% showed a rise in ASO, only 12 sera, or 3.7% showed a rise in all three tests. Part of the discrepancy is due to the fact that many streptococcal strains produce little or no hyaluronidase or DPNase so that the

DEGREE OF REDNESS OF THROAT IN 9735 CASES OF UPPER RESPIRATORY INFECTION

UPPER RESPIRATORY INFECTIONS, STREPTOCOCCAL RECOVERY AND ANTIBIOTIC TREATMENT (9735 EPISODES)

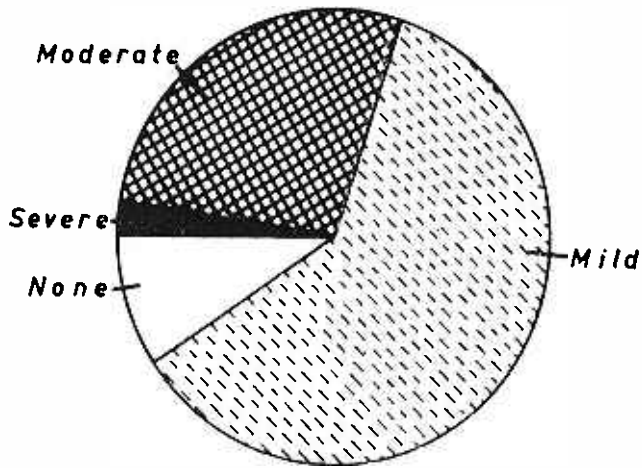


Fig. 1.

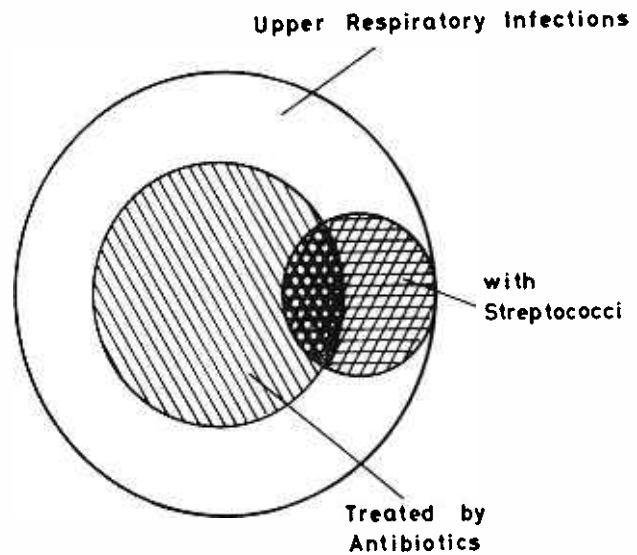


Fig. 4.

PERCENTAGE OF POSITIVE SWABS BY DEGREE OF REDNESS OF THROAT

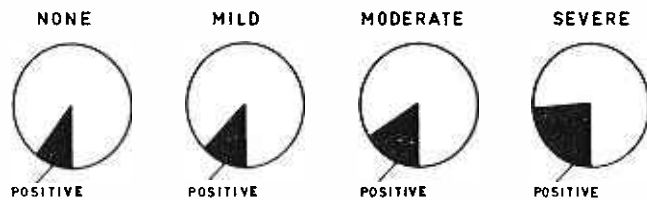


Fig. 2.

CORRELATION BETWEEN ANTIBODY RESPONSE AND STREPTOCOCCAL RECOVERY

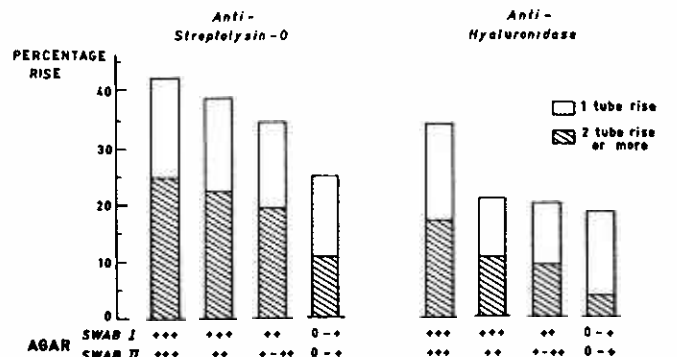
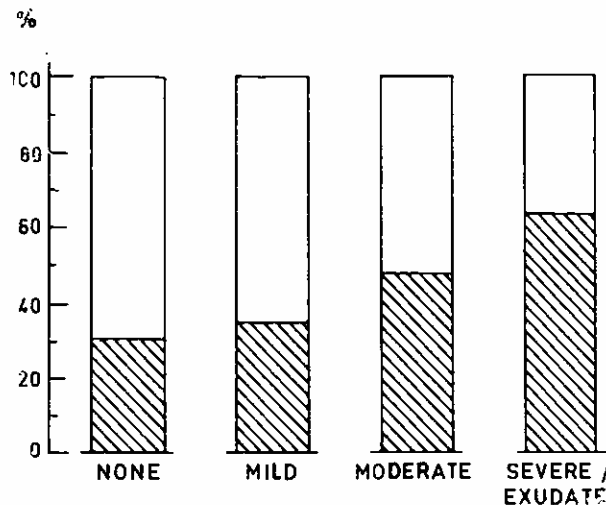


Fig. 5.

PERCENT RECEIVING ANTIBIOTICS BEFORE FIRST THROAT SWAB BY DEGREE OF REDNESS

▨ ANTIBIOTICS BEFORE SWAB



Redness

Fig. 3.

CORRELATION BETWEEN DEGREE OF REDNESS OF THROAT AND ANTIBODY RESPONSE

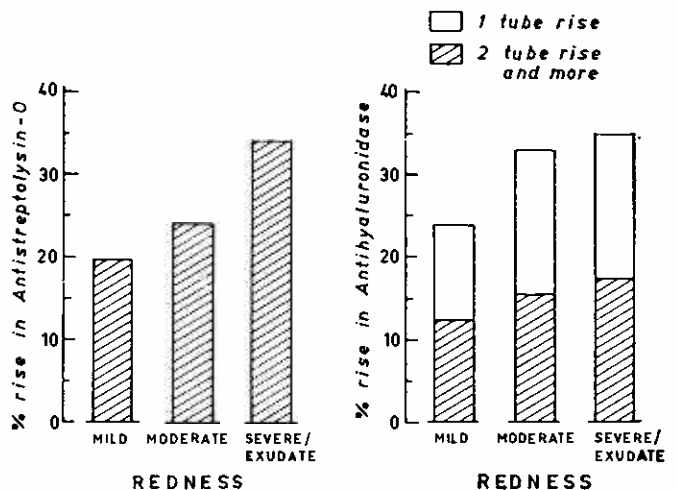


Fig. 6.

EFFECT OF ACUTE PHASE TITERS ON ANTIBODY RISE IN CHILDREN WITH STREPTOCOCCAL SORE THROAT

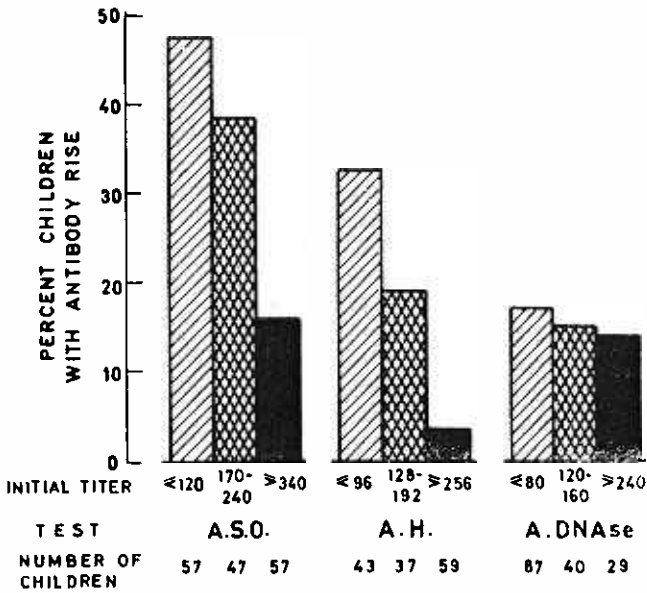


Fig. 7.

ANTIBODY RISE TO THREE STREPTOCOCCAL ANTIGENS (326 duplicate sera)

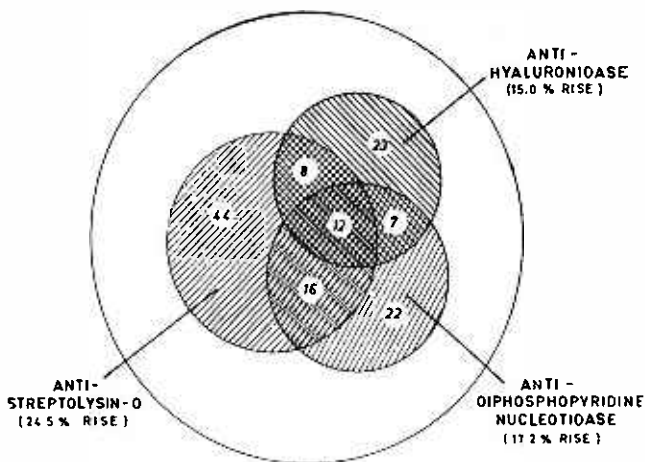


Fig. 8.

CORRELATION BETWEEN DPNase PRODUCTION OF STREPTOCOCCAL TYPES AND ANTIBODY RESPONSE

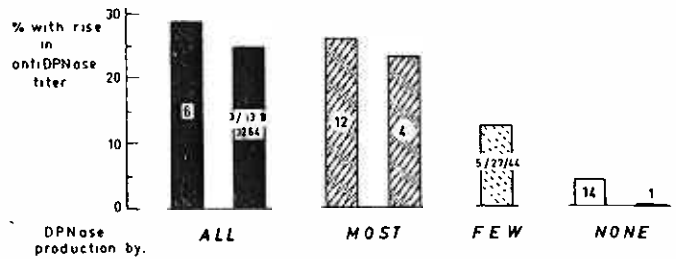


Fig. 9.

STREPTOCOCCAL CARRIAGE AND ANTIBODY RESPONSE

(257 CHILDREN SWABBED WEEKLY 25-32 TIMES, BLED EVERY 2 MONTHS. SERA TITERED FOR A.S.O., A.H., A.D.P.N.)

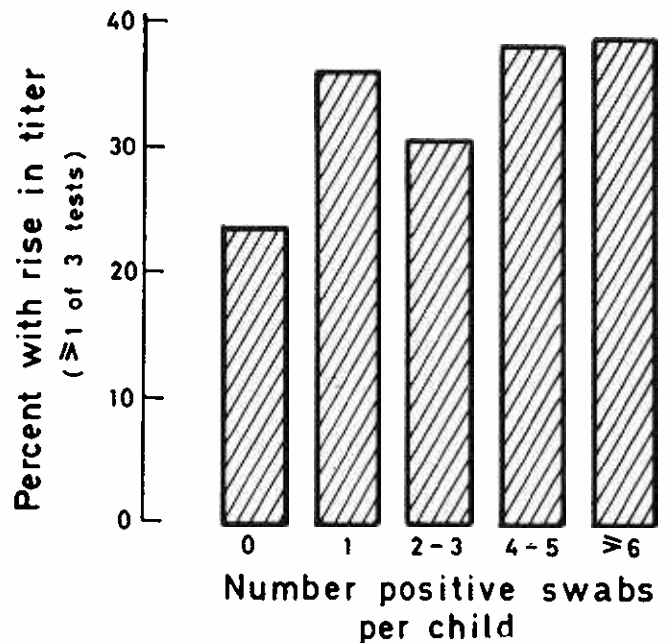


Fig. 10.

antigenic stimulus is lacking. (Fig. 9). The more tests performed, the larger the number of responders detected although there is a law of diminishing returns and considerably increasing costs. Recently, we have studied 165 children in depth, using a battery of 4 tests, the three already referred to and a new one, the streptozyme test, which itself measures the titer of 5 antibodies. If we take as reactors the 75 children who showed a significant increase in titer in one or more tests, then a rise in ASO detected 64% of them, the use of 2 tests detected 80% and three tests, 85%. Thus, if we rely on ASO alone, we may miss over a third of the cases.

DEFINITION AND TREATMENT OF SORE THROATS

These findings which are by no means unique or unusual, have been reviewed as an introduction to the discussion of two questions of paramount importance in the prevention of rheumatic fever.

- (a) what is the definition of a streptococcal sore throat? Is it enough to recover streptococci from cases with symptoms or is it necessary to demonstrate a rise in antibodies? And what action should be taken in the case of carriers? As Fig. 10 shows, they, too, may show an antibody rise even without any clinical infection.
- (b) should the physician treat every case of sore throat with an antibiotic, preferably penicillin? And if not, which cases may he neglect?