EPIDEMIOLOGICAL ASPECTS OF COMMON INFECTIOUS DISEASES*

BY

J. E. JAMESON, M.R.C.S., L.R.C.P.

Brighton

My terms of reference are epidemiological aspects of the common infectious diseases. If I were to try to say something about all of them I should end by having said very little about any of them. I am therefore going to limit my remarks to two groups of common infections.

Haemolytic Streptococcus

The first is infections caused by the haemolytic streptococcus belonging to Lancefield's Group A. I shall refer to this streptococcus as *Streptococcus pyogenes*. The commonest infection in the group is streptococcal throat infection. When fresh cases prove to be nasal carriers the infection is particularly apt to spread to others.

An untreated case commonly harbours *Str. pyogenes* for several weeks after clinical cure. It is not very surprising, therefore, that when a mass swabbing is done at a school during a fairly large outbreak most of the ambulant carriers detected are earlier victims of the outbreak who have since returned to normal school life. It may be inferred from this that I am an advocate of laboratory screening of convalescents. That would be a correct inference within limits, but I cannot overemphasize the point that, when laboratory screening is used, findings must not be allowed to form the basis of a rigid regime of exclusion from school life. Many highly reputable institutions make no attempt to screen convalescents, and many of these fare no worse than other institutions which do make this attempt.

How can these conflicting facts be reconciled? A clue is provided by the work of Brown and Allison (1935) and others some 20 years ago. These workers made a study of scarlet fever cases in hospital. They showed that something like 50% were carrying *Str. pyogenes* on discharge. In spite of this the return-case rate was low, in the region of 2%, though higher with children than with adults. Not surprisingly, it was found that heavy carriers were more often associated with return cases than light carriers. But it was also found that patients discharged from hospital during the fifth, sixth, and seventh weeks were more infective than those discharged earlier. By the use of serological typing it was shown that in these hospital cases the primary infecting strains disappeared on average just before the end of the third week. Of 47 hospital cases investigated, 33 became cross-infected with other strains present in the ward at that time, some being infected with as many as four different types in succession.

There is a weight of epidemiological evidence which indicates that the great majority of patients with streptococcal throat infections become relatively harmless to their fellows within three to four weeks. Griffith (1934) has plausibly suggested that this may be due to a process of antigenic degradation with loss of virulence occurring in the throat of a person who has acquired a type-specific immunity to the particular streptococcus with which he is infected. Such specific immunity would not be expected to cause loss of virulence in a cross-infecting strain until immunity had been built up against the latter strain also. Occasionally we encounter a case of scarlet fever or streptococcal tonsillitis which not only continues to harbour *Str. pyogenes* for months or years but also gives rise to return cases throughout the whole period the organism is carried.

Chronic Carriers

The existence of persistent carriers such as these is an embarrassment when one is asked whether a carrier convalescent for three to four weeks should be allowed to return to school. Various pointers help in this decision: the great majority of chronic carriers of virulent streptococci have an abnormality in the nose or throat, such as enlarged tonsils: unhappily, one cannot place total reliance on the absence of clinical abnormality, because normal-looking tonsils removed from chronic carriers have occasionally been found after excision to have been bags of pus with thin coverings of normal-looking tissue. An important pointer is the heaviness of the carrier state: the dangerous carrier yields abundant *Str. pyogenes* in almost all swabs taken. You will remember that the heavy nasal carrier is especially infective. When in doubt about whether or not to recommend that a known carrier of three to four weeks' duration should go back to school, as a calculated risk, I ask that the child should be sent to the laboratory. When the clinical examinations and the nose swab are negative and when I fail to isolate *Str. pyogenes* from the clothing, I recommend that the risk is a justifiable one, even though streptococci in the throat may be quite numerous.

I am sure many children are kept away from school unnecessarily. One girl I know of who yielded very scanty *Str. pyogenes* intermittently from her nose was kept away from school for three months on that account. There must also be instances when children return to school too soon for the safety of their schoolmates. The bugbear to this problem is that no laboratory test has yet been found which will give a direct answer to the question, "Is this particular strain of *Str. pyogenes* virulent?" The only court of appeal is the human community itself. It is not exceptional to find carriers of *Str. pyogenes* in a community clinically free from streptococcal infections. Other communities with no higher carrier rates may become victims to high, intermediate, or low streptococcal case morbidities which cannot reliably be predicted. But once clinical cases of streptococcal infection have occurred, it is reasonable to assume that contact-carriers of the type-strain causing the cases are infectious.

Str. pyogenes is a versatile organism and causes infections as diverse as scarlet fever and tonsillitis on the one hand, and as erysipelas, puerperal fever, cellulitis, rheumatic fever, acute nephritis, septicaemia, otitis media, and impetigo on the other. Any particular strain of *Str. pyogenes* may under appropriate conditions give rise to more than one of the varied types of infection just mentioned. In any outbreak one should therefore be on the look-out for more than one clinical manifestation of the infection. A familiar example is puerperal pyrexia following a case of streptococcal tonsillitis.

In spite of their versatility, individual strains of streptococci have predilections. A case of scarlet fever is more likely than a case of streptococcal tonsillitis to give rise to a further case of scarlet fever. This is not a good example, because in scarlet fever the clinical result of the infection also depends largely upon the individual patient. A person who has circulating antitoxin as a result of a previous attack of scarlet fever will not develop a second scarlet rash no matter what strain of streptococcus he picks up, though he can and does succumb to streptococcal throat infections. In some instances the association between the infecting strain and the site of election is stronger; haemolytic streptococci isolated from impetiginous lesions fall predominantly into two closely related serological groups, one of which is rarely encountered in other situations. An equally close strain relationship exists between acute nephritis and *Str. pyogenes* of serological type 12.

Reservoirs of Infection

In an outbreak that has become established there are three reservoirs of infection to be taken care of. Firstly, the clinical cases themselves; secondly, the convalescent carriers

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and chronic carriers; and thirdly, bedding, floor dust, etc. Spread of infection from these reservoirs is facilitated by overcrowding, so often seen in class-rooms and dormitories to-day, and by inadequate ventilation. If one could eliminate all the reservoirs the outbreak would die out rapidly. In practice total elimination is never possible, but the more complete the elimination the greater the chance of success. The balance between the hosts and the infecting organisms is often critical, and only a partial elimination of the reservoirs of infection may be sufficient to tilt the scales in favour of the community.

Laboratory aid for the elimination of ambulant carriers is sometimes sought after an outbreak has given rise to substantial inconvenience or anxiety. When this state of affairs has been reached it is worth while removing from the community all heavy carriers of the type-strain which has given rise to the clinical cases. Removal of these carriers does not necessarily entail their segregation; a similar result is obtained if the carriers can be rendered non-infective. This is possible temporarily in most, and in some carriers permanently, by an umbrella of parenteral penicillin held over them for a week or two. The penicillin umbrella is impermanent and leaky, but it does enable ambulant carriers to continue their normal occupations, and it may tilt the scales firmly in the right direction, provided the other reservoirs are not overlooked. Long-acting penicillin, such as benzathine penicillin, has considerable theoretical possibilities in this field, but I think its main practical disadvantage is that the injections are painful.

I hope I have conveyed reasons why I have discussed streptococcal outbreaks in general terms. Each outbreak is influenced by many variables, and each must be judged on its own merits as it gradually unfolds. The pattern of the big outbreaks in schools has generally been a gradual build-up of infection over several weeks. I am convinced that these outbreaks would have been brought under control more easily if the schools concerned had started taking serious preventive measures sooner.

Bacterial Infections of the Bowel

The second group of infections I have chosen are bacterial infections of the bowel, including typhoid and paratyphoid fevers, salmonella infections, and Sonne dysentery.

Typhoid and Paratyphoid Fevers

The key to the epidemiology of typhoid fever lies in the fact that, unlike paratyphoid, a few viable typhoid bacilli taken in food or drink are able to set up disease in man. This explains the differences in the epidemiology of the two diseases. A polluted drinking-water may readily give rise to an outbreak of typhoid fever, as it did in Croydon, but, though water supplies are polluted with paratyphoid bacilli as often as they are with typhoid, water-borne outbreaks of paratyphoid fever are very uncommon. This is because pollution in drinking water is highly diluted and the number of pathogenic organisms in a gallon is small, high enough to infect with typhoid bacilli, but not high enough for paratyphoid. For the same reason typhoid fever, but not paratyphoid, is spread by lettuce and by watercress which has been exposed to remote pollution. Shellfish can spread both diseases, the reason being that they filter large volumes of water in a day and thus ingest a large number of organisms. Though these various means of typhoid infection are mentioned in textbooks they do not together account for a very significant proportion of typhoid fever cases. Typhoid fever is conveyed by means other than sewage. Owing to the permeability of toilet paper, typhoid bacilli can readily get on to the fingers of carriers, and thence directly or indirectly on to foods not destined for further cooking.

The channels by which paratyphoid infection is spread are necessarily more limited. An article of food is seldom at the outset contaminated by a sufficient number of bacilli to produce clinical paratyphoid fever. For the latter to

ensue a chain of circumstances must act together. Firstly, the food must become infected; secondly, the conditions must be favourable for bacterial multiplication in food; and, thirdly, the food must be consumed without a further period of cooking sufficient to kill the paratyphoid bacilli.

For bacterial multiplication to take place various conditions must obtain together; the food must contain a sufficiency of moisture and nutrients for bacterial growth, it must remain at a suitable temperature for a long enough time, and it must not be too acidic. When the temperature of the food is above 70° F. (21.1° C.) half a day may suffice for the necessary bacterial multiplication. When the temperature is near to blood-heat multiplication takes place within a few hours; below 50° F. (10° C.) multiplication is slow, and at refrigerator temperature it is negligible. These facts explain why paratyphoid fever is mainly prevalent during late summer and autumn, though we must remember that food does not always remain at atmospheric temperature. When a large mass of food is warmed up, cooling takes place slowly and the temperature-time combination in the centre is often favourable for multiplication of those bacteria that have not been destroyed by the cooking. An article of food often incriminated in outbreaks of paratyphoid fever is cream cakes. The reason for this is that the cream filling acts as a culture medium and unlike most bakery products is not subjected to baking. Cream cakes are often eaten after a lapse of hours or days from the time the cream fillings are prepared in the bakery.

Though both in typhoid and in paratyphoid fever the reservoir of infection is always human, careful examination of the staff of a bakery implicated in a paratyphoid outbreak often fails to reveal the presence of the carrier. Paratyphoid bacilli can enter bakeries in imported foodstuffs, especially in egg products used in confectionery. Working conditions may be crude. Appliances such as muslin strainers are infrequently sterilized, and are used for straining successive mixes of different kinds. It may thus happen that infection in one kind of mix passes to another kind of mix not destined for baking. Cream cakes may thus leave a bakery infected, although the ingredients from which they were made were free from infection and there were no carriers in the bakery.

Cream cakes are only one vehicle for the dissemination of paratyphoid infection. Similar principles apply to others—namely, a breakdown of hygiene leading to contamination, multiplication of the bacilli in the contaminated food, and consumption of the food in the absence of adequate cooking. I have used the word adequate because some cooking processes sterilize only the surface of the food. The uncoagulated yolk of a soft-boiled egg and the unaltered haemoglobin in the centre of a lightly done steak bear eloquent testimony to the absence of severe heating. A sausage must be very well grilled or fried if vegetative organisms near its centre are to be destroyed.

Salmonella Infections; Sonne Dysentery

Salmonella infections were formerly associated with names such as Aertryck or Gaertner. They are referred to now as *Salmonella typhi-murium*, *Salmonella enteritidis*, or as *Salmonella x*, *x* being a place-name. The epidemiology of salmonella infections has much in common with that of paratyphoid, for the reason that a relatively large number of salmonellae have to be ingested before clinical infection ensues. Apart from the shorter incubation period, the difference lies in the reservoirs of infection. In the case of salmonellae there is an extensive animal reservoir, especially rats and mice, poultry, pigs, and cattle. Other animals, including unlikely ones such as the tortoise, harbour salmonellae; cats and dogs occasionally fall victims to salmonella infection, and both have been known to pass this infection to man, but fortunately this is rare. Infected rats and mice leave droppings in any food to which they have access. An infected farmyard animal may itself become an article of food, and poultry eggs may carry infection. Hen eggs are rarely infected, but when bulked in large numbers, as in the preparation of dried egg, frozen liquid egg, or egg

albumen, the risk of salmonella infection is increased proportionately. Duck eggs are notorious for their association with *Salmonella typhi-murium*. In any large collection of hen eggs a few duck eggs are often to be found; this adds to the risk of salmonella infection in bulked-egg products. One would expect pork sausages to be a good vehicle for the spread of salmonella infections, and this is so in practice.

The most prevalent type of dysentery in Britain by far is Sonne dysentery. It accounts for over 95% of the cases. As in salmonella infections, the incubation period is a short one, from one to three days. In common with typhoid and paratyphoid fever there is no animal reservoir. As in typhoid fever the infective dose is probably a small one. Bacterial multiplication in food is not an important factor in its transmission, and it is noteworthy that this disease is now commoner in Britain in the early spring than it is in the summer. The factors which govern its spread are not yet fully understood, though soiling of lavatory seats by children is believed to play a part. In Scandinavia it is still a summer disease, as it was in Britain until the end of the war. There is a closer case-to-case linkage than with salmonella infections, and it is uncommon for an outbreak of Sonne dysentery to involve widely scattered households between which there is no link, as occurs in typhoid and paratyphoid outbreaks.

Discussion

In outbreaks of all these intestinal infections it is the rule and not the exception to find that there are persons exposed to risk but clinically unaffected who are excreting the organisms in their stools. In common with streptococcal infections of the throat, convalescents remain infective to others after clinical recovery. In intestinal infections these periods of infectivity tend to be long. The tendency for a prolonged carrier state is greatest with typhoid and paratyphoid, intermediate with salmonella, and least with Sonne dysentery bacilli, in which a carrier state lasting more than three months is rare. An outbreak of paratyphoid fever in Eastbourne was followed up eight years later. At the end of 18 months, 5% of the patients were still excreting paratyphoid bacilli. These persistent excretors were mainly among the under 5's and over 70's. One of the over 70's is still alive and still excreting paratyphoid bacilli.

One might wonder, in view of the long period convalescents remain infective, why it is that these diseases are not universal. Some of them are indeed at times widespread, and there is always a submerged number of undiagnosed cases the size of which we can only guess. But even taking this into consideration, only a minute fraction of the total population is ever infected at one time. The main limiting factor apart from hygiene is, I believe, natural immunity. We have much evidence that the ingestion of small numbers of paratyphoid and salmonella bacilli is followed by no undesirable clinical effects. Though with typhoid fever and Sonne dysentery the threshold of infection is lower, the prevalence of symptomless excretors in both these diseases is also strongly indicative of the natural resistance.

Further evidence of this resistance is the rarity of outbreaks in which the morbidity of adults exposed to risk reaches 50%. Similar evidence of a more direct kind is provided by the sauce chef of one of Brighton's leading hotels. There is retrospective evidence that this chef remained a heavy excretor of *Salmonella typhi-murium* for several months before he infected the residents and visitors to the hotel, although sauces, which are his whole-time professional occupation, may be an excellent vehicle for the dissemination of salmonellae.

Now a few words only on the treatment of intestinal carriers. Cholecystectomy is sometimes successful for typhoid and paratyphoid carriers, but not by any means always. Antibiotic treatment has in the main proved disappointing in its long-term results for chronic carriers. It is true that many temporary intestinal carriers appear to have responded permanently to antibiotic treatment, but we must not forget that the great majority of intestinal

carriers stop excreting in their own good time, whatever it may be, without treatment. An attitude of healthy scepticism rather than of blind faith is called for.

Before I end there is one more fact I should mention: the sauce chef I spoke of has now disappeared from Brighton and has not been traced by our health department. Doubtless he is now pursuing his culinary art in some other town.

In preparing this paper I should like to acknowledge my indebtedness to Topley and Wilson's *Principles of Bacteriology and Immunity*, by Wilson and Miles (4th edition, 1955), for some of the information relating to streptococcal infections.

Summary

Two groups of infections have been considered, those due to *Str. pyogenes* and those due to enteric bacilli.

Str. pyogenes, though versatile, has predilections. The most frequent site of infection is the throat, but nasal carriers are more infective. Throat cases usually become non-infective within three weeks, but exceptions occur and are discussed. In outbreaks there are three reservoirs of streptococcal infection. Though complete elimination of all the reservoirs is never possible, partial elimination, including removal or neutralization of contact carriers of the type-strain causing the clinical cases, may limit the outbreak. If these measures are applied early enough an outbreak may be prevented.

An attempt has been made to rationalize the known epidemiological facts concerning typhoid and paratyphoid fevers, salmonella infections, and Sonne dysentery. This has been made in relation to the relative infective doses of the organisms concerned, their reservoirs of infection, natural immunity in the population at risk, and current hygienic (and unhygienic) practices.

REFERENCES

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Griffith, F. (1934). *Ibid.*, 34, 542.

RHEUMATIC DISORDERS

HEBERDEN SOCIETY MEETING

Among the topics discussed at the Heberden Society's two-day scientific and annual general meeting last month were the reason for the persistently high E.S.R. sometimes found in patients with degenerative arthritis and a hitherto little commented upon complication of ankylosing spondylitis—namely, spontaneous atlanto-axial dislocation, of which 10 cases were reported. The meeting was held in London on December 14 and 15 at University College Hospital Medical School and the Wellcome Foundation, under the presidency of Dr. ERNEST FLETCHER. On the first day Professor R. E. TUNBRIDGE, of Leeds, delivered the Heberden Oration, on this occasion a review of recent advances in our knowledge of the connective tissue and its constituents. In the evening the society's annual dinner was held at the Apothecaries' Hall (*Journal*, December 29, 1956, p. 1557). Eight scientific papers were presented during the meeting, and here we summarize a few of them.

Unexplained Elevation of the E.S.R.

Dr. B. M. ANSELL and Dr. E. G. L. BYWATERS described a three-year study at the Postgraduate Medical School of London of patients with an unexpectedly high erythrocyte sedimentation rate. Sometimes, they said, routine estimation of the E.S.R. by the Westergren technique in new patients attending the rheumatic clinic had revealed a reading which could not be explained on the basis of the original diagnosis—for example, degenerative joint disease. Of 51 patients with such readings, out of approximately 900, they had now satisfactorily investigated and followed 45. These