STREPTOCOCCAL AND STAPHYLOCOCCAL FEVERS.

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INTRODUCTION.

This short paper makes no pretence to state anything that is unknown to any of us. It contains few conclusions that we have not already reached. Its purpose is merely to emphasize some of the more important features of two very common but serious infections, namely streptococcal and staphylococcal fevers. A certain restriction of outlook having inevitably crept into our modern pathology, there was a tendency to regard the several manifestations of these infective processes as separate diseases. The primary lesion of each of these organisms was apt to obscure the composite clinical and pathological picture seen in the summation of their effects upon the body. This outlook, with its concentration upon the local disease processes, did not greatly influence practical therapy because treatment consisted of measures, more often than not surgical, directed towards the particular local disturbance and less towards the disease process as a whole. However, since the introduction of and the vast progress made in the use of specific chemotherapeutic substances as M & B 693, streptocide, sulphonamide, etc., the recognition of a general disease caused by streptococci and staphylococci has become of the utmost importance.

STREPTOCOCCAL FEVER.

Although minor grades of streptococcal infection such as tonsillitis and sinusitis are amongst the commonest of the human infirmities, the severer septicæmic and bacteræmic forms of the disease are not unknown to us, although mercifully they are not of everyday occurrence.

The following three cases show many of the salient features and from them we may be permitted to draw certain conclusions in regard to the natural history, course, prognosis and treatment of streptococcal fevers.

Case 1.—Private S., aged 24, an infantryman of approximately two years' service in Shanghai. This man was admitted at 4 a.m. to the British Military Hospital complaining of a very sore throat, which he had had for two days, high fever and a shivering attack just before admission, during which he vomited once. The patient looked ill and exhausted. His throat showed intense inflammation with marked swelling of both tonsils, temperature 102·4° F., pulse 100. His heart sounds were of poor quality. In view of a prevailing outbreak of diphtheria among the soldiers of his battalion at the time he received 20,000 units of anti-diphtheritic serum once pending the result of a throat swab. This was returned negative the following day. He was recognized as a case of streptococcal fever and
received 10 c.c. of anti-streptococcal serum the morning after admission. He received a further 20 c.c. eight hours later. Between the time of admission and midnight on the following day he received eight grammes of streptocide. His condition that evening was very poor. His temperature had risen to 103° F. and his pulse to 130. His white blood-count was 14,000 white cells per c.mm. He was a little better the following day, his temperature having dropped to 100-6° F. and his pulse to 110. His throat was still very dirty. He was receiving one gramm of streptocide four-hourly. The next day improvement was again noticed but his spleen had become palpable and tender and his urine contained albumin and red cells. His temperature rose again the following day. He looked worse and complained of pain and tenderness in his left knee. His spleen was still obvious. For seven days he continued with a high fever and rapid pulse. The same dosage of streptocide was continued. His temperature then subsided to normal and although his throat was still inflamed it was no longer painful. As he was showing a slight degree of cyanosis the streptocide was discontinued. Two days later he had an exacerbation of his fever. No further local signs were discovered and his urine was clear. He was once more placed on streptocide which was continued for a further five days. His temperature then subsided and convalescence commenced.

Case 2.—Corporal H., aged 35, clerk in the R.A.M.C. This man, while in hospital convalescing from a left basal pneumonia, for which he received M & B 693, developed a slight evening temperature and a mild sore throat. He had been getting up and was about the ward. He was a fat, flabby, unhealthy looking individual, and a W.B.C. taken during the course of his pneumonia revealed a count of 17,400 white cells per c.mm. His throat was inflamed, but this began to subside. Eight days after its onset he had a sudden shivering attack and developed: (1) an acute sore throat with pus-streaked tonsils, (2) tenderness and cutaneous hyperæsthesia in the right iliac fossa, and (3) acute tenderness over the gall-bladder. His temperature was 101.8° F., pulse 130. In addition, he complained of præcordial pain which radiated down the inner side of his left arm. His pulse was extremely rapid and his heart sounds were of very poor quality. A W.B.C. at this stage was 8,200 per c.mm. He was placed on tablets of streptocide, two four-hourly. The following day his condition was unchanged, except for quite a marked dypnsœa apparent on moving about in bed. His W.B.C. had risen to 10,000 per c.mm. His throat was still sore. A throat swab showed K.L.B., and he was transferred to the Isolation Division. He received 30,000 units A.D.S., and the dosage of streptocide was increased to four tablets four-hourly. The following day there was improvement and his temperature had subsided to 99-6° F., his W.B.C. to 12,400 per c.mm. The heart sounds were still poor and dypnsœa still present. His condition improved, streptocide was reduced to one tablet every four hours, and after six days more was discontinued. Improvement was maintained and his temperature remained normal, although his pulse still rose
on any slight effort or movement. His W.B.C. was now 8,200 per c.mm. He still remains in bed. Tenderness has left his appendix, but there is still a definite inspiratory catching of his breath on palpating the gall-bladder. Tachycardia and dyspnœa are still easily produced.

Case 3.—Private G., aged 24. This patient was admitted complaining of fever, shivering and a very sore throat, temperature 102.2° F., and pulse 120. Speech was difficult owing to a gross inflammation of the tonsils andœdema of the surrounding tissues. The urine contained large quantities of albumin (5 gr. per litre). A throat swab was negative for K.L.B. Streptococcal fever was diagnosed and he received two tablets of streptocide every four hours for four days. His temperature then subsided and he felt better. Three days later his temperature rose again to 100° F., and remained up for two days. During this period he received only local treatment to the throat condition. He was then placed again on streptocide, two tablets three times a day. The fever did not subside and his condition deteriorated, and the dosage was increased to two tablets four-hourly. In addition he received 10 c.c. of anti-streptococcal serum. This dosage of streptocide was continued for four days and for a further day after his temperature had subsided to normal. His fever subsided gradually. The dosage was then cut down to one tablet four-hourly for three days, and then one three times a day for two days, and his recovery was complete. Throughout the acute stage of his illness his urine was loaded with albumin, but no casts or R.B.C.s were ever seen. Quantities of albumin up to 1 gr. per litre were noted.

These three cases all have certain features in common; each of them demonstrates incidents which may occur in any case of streptococcal fever. They all had the same original focus of infection, the mucous surface of unhealthy tonsils. In Case 1 the portal of entry had been well prepared for the streptococcal invasion by a previous attack of Vincent’s angina and ulcerative gingivitis.

In streptococcal fever, however, the portal of entry varies widely, the large raw area of the placental site contrasting with the insignificant hangnail of the overworked medical man, while the unhealthy cryptic tonsils of cases such as the three just quoted occupy an intermediate position.

The onset of the disease is sudden and is characterized by the occurrence of high fever, malaise, chilliness and actual rigors. This was a marked feature in all these cases. The organism spreads rapidly throughout the body. The fever remains high, rarely descending to the base line, while the pulse is extremely rapid. There is a marked systemic disturbance. In all these cases there was a marked primary local infection of the tonsils.

In two cases, one of which I have not reported, there was a marked secondary disturbance which resulted in rapid splenic enlargement, which was accompanied by a considerable degree of pain and abdominal discomfort, due no doubt to an accompanying amount of perisplenitis. Further secondary manifestations were observed in Case 2. Here, after an initial tonsilitis, the appendix, the myocardium and the gall-bladder were all rapidly and
successively involved. The tendency for these fevers to have metastatic manifestations in organs with mucous surfaces was well marked in this case. Although the appendix has more or less settled down, the gall-bladder is still inflamed, and will, I think, come to another acute exacerbation. This patient is going to present a considerable problem as to his future treatment as one is left a little uncertain where to start. At present the consensus of opinion leans towards his tonsils.

Metastases into the serous sacs are a further feature of streptococcal fevers and although in this small series there was no actual incidence of this, in Case 1 the occurrence of pain and tenderness in the left knee was suggestive of an abortive attempt at an arthritis and an effusion into the joint by the streptococcus which was wandering through the body. Did chemotherapy abort this occurrence? I am tempted to think that it did.

In one other case, about which I was unable to obtain any notes, a severe diarrhoea with blood and mucus in the stools, occurred. This case was in many aspects similar to Case 1. A general infection followed a very septic throat and after a few days' illness characterized by rigors, sweating, fever and a rapid and painful enlargement of the spleen, he developed a quite marked distension with tympanites and discomfort and this was accompanied by dysenteric manifestations, the stool growing nothing on culture. This case, by the way, also received anti-streptococcal serum and large doses of streptocide and made a good recovery.

There is a further secondary manifestation upon the body in these streptococcal fevers. I refer to the effects of the infection upon the kidneys. In two of the three cases quoted, urinary changes were recorded. In Case 3, a severe infection of the throat, a very heavy albuminuria was noted, which subsided and disappeared with his recovery. At no time were red blood cells or casts discovered. Contrast this with the first case reported, where albumin and red blood corpuscles were observed. This case also cleared up. These two cases show two types of renal involvement. The first one, with the heavy albuminuria with no red cells or casts, I am inclined to regard as a larval nephrosis, the pathological change probably being a severe degree of cloudy swelling of the kidney tubules. The second case showing albumin and red cells was probably a focal glomerulonephritis and would have shown the corresponding pathological changes. Not all cases clear up as did these two. Diffuse glomerulonephritis can, and does, occur as a manifestation of streptococcal fever and permanent renal damage may ensue.

This mention of renal involvement in streptococcal fever brings to our notice another well-defined type of case. I refer to scarlet fever.

This is a streptococcal fever with the initial lesion in the mucous membrane of the throat. It has a well-marked onset with fever and vomiting, accompanied by a considerable degree of tachycardia. It has, as a secondary manifestation, the evidence of renal damage. In short, it presents every feature shown by the cases reported earlier on in this paper, but it has a characteristic skin manifestation.
Why this should occur in some individuals who have a streptococcal fever and not in others with identically the same fever, gives rise to some thought.

Is the erythema of scarlet fever an outward and visible sign of a pre-existing sensitivity in certain individuals towards the streptococcal exotoxin?

Should we regard all streptococcal fevers accompanied by a tonsillitis as legally defined infectious diseases and act accordingly?

It is on this note of interrogation that I will leave the clinical aspect of the streptococcal fevers and pass on to some consideration of their prognosis and treatment.

PROGNOSIS AND TREATMENT.

Since the introduction of the sulphonamide group of drugs the prognosis of the streptococcal fevers has improved out of all knowledge. Take for example Case 2. This case had a poor leucocytosis even with his initial pneumonia. He was a type ill-adapted to deal with a severe infection and his chances in the pre-sulphonamide days would indeed have been gloomy. We have now a potent weapon forged to our hands for the prevention of the development of those localizing manifestations for which we used to wait with mixed feelings of hope and fear; hope, that their development would assist the patient in his struggle against the disease; fear, that they would develop in sites which would render us impotent to interfere surgically. The constitution of the individual and the leucocytic response are guides to prognosis, but specific chemotherapy and its immediate effects are more often the key.

TREATMENT.

Although in this connexion any contribution of mine will not be original, there are one or two points well worth emphasizing, particularly in connexion with the chemotherapy of these fevers.

The first point is this: that no matter what brand or type of sulphonamide is employed, the initial dosage must be high and the dosage must be maintained at a high level during the early stages of the disease. These drugs are rapidly excreted in the urine and it is of the utmost importance that a high serum concentration of them be obtained in the early stages. If given in small doses such a serum concentration as would be adequate to interfere with the metabolism of the circulating bacteria (as indeed is the probable mode of action of these drugs), is never obtained in severe cases. Its premature withdrawal has the same effect and the infection once again regains the upper hand. This is shown in Cases 1 and 3. In both these cases the drug was stopped too soon and a recurrence of the fever occurred.

The next point is the incidence of cyanosis in cases receiving these drugs. Case 1, when on the way to recovery, showed a slight cyanosis which resulted in the stoppage of the drug. He relapsed as soon as it was discontinued,
improving again on the drug being readministered to the point where a mild cyanosis re-occurred. I am of the opinion that cyanosis in a moderate degree does not matter and that it may be taken as a sign of adequate dosage and sufficiently high plasma content of the drug for bactericidal purposes.

In any case it can be dispersed by the administration of methylene blue. White blood-counts carried out on these patients, although perhaps on the low side for an adequate natural aid to recovery, showed no evidence of agranulocytosis. This complication is, I think, rare, and is a possibility more to be aware of, than to be afraid of, in connexion with the use of these drugs.

Finally, the place of anti-streptococcal serum. Two of the cases quoted were considered ill enough to receive serum in addition to streptocide. Some authorities regard serum as a life-saving measure, others deny its use to be of value. I think its use is best regarded in the following way. "Serum by itself is effective, streptocide by itself is effective, but both together, they are an extremely powerful weapon."

Last, but not least, comes the consideration of general treatment. This is mainly directed towards mobilizing the natural defences to meet the emergency. An adequate fluid intake of sweetened drinks, attention to the pain and discomfort of the local lesion and the maintenance of the general well being of the patient all have their place. Above all, do not let us forget the treatment, during convalescence, of the inevitable anaemia which has occurred and will always occur in every case of streptococcal fever.

**Staphylococcal Fever.**

By contrast to the preceding type of infection the portal of entry of the staphylococcus is the skin. The primary lesion is on the body surface and takes the form of a boil, carbuncle or minor pimple. Mucosal infection is rare. Staphylococcal infections such as these constitute a considerable proportion of the infirmities with which we are called upon to deal, more especially in military practice where minor injuries and abrasions, with a superadded staphylococcal infection, are extremely common. The familiar diagnosis of I.A.T. has its origin in the majority of cases from the *Staphylococcus aureus*. Such infective processes, fortunately, rarely proceed further than the local lesion. Localization is generally good, there is a sound tissue response and the affair ends at this point.

Occasionally, however, such infections may catch the body "napping" as it were and a bacteremia supervenes. A general infection is now complicating a local lesion. Occasionally it happens that the local lesion may not be discoverable at the time of onset of the fever. It has come and gone but not before it has left its fingerprints. In suspected cases of staphylococcal fever, therefore, a careful clinical history is of the utmost value in diagnosis and the forgotten occurrence, a short time previously, of a local septic lesion may be the clue required to solve the puzzle in an unknown febrile disorder. Generally speaking, the onset of a staphylococcal fever is quite sudden.
The initial bacteræmia giving rise to fever, shivering and malaise, sometimes even rigors occurring. This is less usual and not so often the case as in a streptococcal fever. The pulse, although rapid, is never raised to the same extent and consequently other infections, such as the enteric group or influenza, may be suspected.

There is no enlargement of the spleen and localizing signs are generally rapid in making their appearance. In nearly all cases there is a bacteræmia with ultimately a demonstrable metastasis or fixation abscess. Such a metastasis may be solitary or it may multiply in various tissues of the body, depending on how the body itself is dealing with the temporarily circulating organism.

Staphylococcal metastases show a preference for the more solid tissues. We are familiar with the organism settling down in the capillary loops at the diaphyseal ends of the bones, giving rise to a picture of acute osteomyelitis. We know only too well of the possibilities of perinephric infection. We have seen from time to time collections of staphylococcal pus in the muscles and tissue planes.

Contrast this with the streptococcus whose choice falls upon the serous lined cavities and the mucous membrane of internal organs.

The continued fever, in the absence of rigors or sweats, with the fairly rapid formation of a local abscess, is in favour of a staphylococcal bacteræmia, more especially if the fever clears up upon drainage of that local abscess. It is the occurrence of these local collections of pus or the pre-purulent stage of tissue infection which places such a high diagnostic value upon an early leucocyte count. It has been stated previously that the pulse-rate is slow in proportion to the degree of fever and this early white count will be of material assistance in excluding infections such as the enteric group which have an initial leucopenia.

Furthermore, it is a guide to treatment with particular reference to surgical interference as I will try to show from the case reported below.

This case in many ways shows most of the features of a typical staphylococcal fever. The clinical history, its onset, its course, diagnosis and treatment present a picture of the natural history of the disorder almost in its entirety.

Case 1.—Private R. This patient was a sturdy well-built soldier, aged 23. His duties as an orderly in the dining hall, cookhouse and with the dishwashing plant entailed heavy work and fairly long hours. Three weeks prior to his admission to hospital, I had incised and drained a local abscess on one of his fingers. A large slough was removed and the hand recovered rapidly. He returned to work and forgot completely about it.

On January 2 he reported sick saying he had been shivering and felt ill, and that he had a severe pain in his right loin. He was doubled over to the affected side and all around the right renal area he was acutely tender. His temperature was 100°F, and his pulse 90. He had frequency of micturition. The urine was acid and contained a few pus cells. He was admitted at once
to hospital and placed on fluids and alkalis, four-hourly. The diagnosis of acute pyelitis was made. The following day he had red cells in his urine. The pain was worse and his fever still high. It remained up between 100° F., and 102° F., and never subsided to the base line. Three days after admission his W.B.C. was 8,000 per c.mm. (82 per cent polymorphs). A straight X-ray of the renal area showed nothing. His fever continued and he had one or two severe sweats. His urine became clear. A diagnosis of perinephric abscess was considered at this stage. Ten days after admission he was placed on M & B 693 two tablets four-hourly, and received this quantity for seven days. It had no effect at all on his fever and was discontinued. During this period his respirations were raised and a dullness developed at the right lung base. Aspiration failed to reveal any fluid. Seventeen days after admission his W.B.C. was 13,600 per c.mm. An intravenous pyelogram was done and showed no abnormality. The next day his W.B.C. was 14,200 per c.mm.

Operation and exploration of the right renal area were considered at this point, but the fact that the W.B.C. never reached a really high figure decided us against it and natural resolution was considered a possibility. Besides it was thought that in all probability no pus would be present, or at the most about a drachm among oedematous perirenal fat. Twenty-three days after admission his temperature started to subside and on the twenty-seventh day of his illness it was normal, and his W.B.C. had dropped to 11,400 per c.mm. Retrograde pyelography showed nothing. His temperature has remained down and his recovery has been uneventful. Except in the initial stage of the fever his urine remained clear.

This case demonstrates well, I think, several features of a staphylococcal fever. The history of a septic lesion in the hand revealed a point in its etiology. The fact that he forgot about it shows the value of a careful clinical history, particularly with reference to the occurrence of local septic conditions. Its sudden onset, with the initial bacteremic symptoms and its rapidly developing metastatic manifestation in the solid tissues surrounding the kidney are all part of the same picture. The high fever, with its relatively slow pulse, the rising leucocyte count and its aid to diagnosis are all points which I wish to stress.

A further point in this case which weighed against operation was the negative finding with X-rays. There was no loss or blurring of the outline of the border of the psoas muscle on the affected side. In a well-developed perinephric abscess, this is quite a constant feature and is of considerable diagnostic value.

There is one feature of this case which is not in accord with the true picture of a well-defined staphylococcal perinephric metastasis. It will have occurred to the reader that the urinary findings are not quite consistent with a perinephric abscess of this type. On admission this patient had pus cells in his urine and the following day he had red blood corpuscles in addition. This is the exception rather than the rule. It will be recalled that
it is the streptococcal fevers which prefer the actual kidney tissue and which can inflict an actual nephritis. This occurrence can be explained, however, if we pause to consider the various ways in which a perinephritis can occur. There are, generally speaking, three ways in which this may happen:—

(1) By blood-borne infections. Here the organism reaches the renal cortex via the blood-stream from a primary local lesion. It forms a subcortical abscess, which bursts outwards through the tissue planes to give rise to perinephric cellulitis.

(2) From an already infected and disorganized kidney, the infection arising by a direct outward extension.

(3) From an infection, co-existing in the pelvis, for example, a pyosalpinx, spreading upwards via the retroperitoneal lymphatics.

In those cases having their origin under group (1) (infection via the blood from a distant focus) urinary findings are unlikely although there is no reason for them not to occur, as indeed they did in this case by the subcortical abscess touching the tip of a calyx and giving rise to some degree of inflammation of the renal pelvis.

In group (2) urinary findings are generally refreshingly obvious while in group (3) their occurrence depends on the relationship of the urinary apparatus to the initial focus.

Although much of what I have just said may appear rather far from the point in a discussion upon staphylococcal fever, it may be stated that, apart from the occurrence of osteomyelitis, perinephric abscess is one of the commonest, and at the same time one of the most obscure, manifestations of staphylococcal fever and gives rise to a very real difficulty in diagnosis.

Features enabling us to point a finger in its direction are the onset of a fever following the occurrence of a local skin infection, the finding of a tender spot, the raised white cell count, and, generally, the negative urine findings. Radiography, in a well-developed case, reveals loss of clearness in the outline of the psoas muscle, while pyelography both intravenous and retrograde in a classical case, generally reveals a normal pelvis and calyces, as it did in this case. In one case, however, which occurred recently in the military hospital a slight degree of hydronephosis was observed. This case came to operation and a large quantity of pus was evacuated from the perirenal area. The degree of hydronephrosis in this case may be explained, I think, by the large amount of perirenal oedema and consequent slight pressure upon the ureto-pelvic junction which must occur in such cases and will almost invariably interfere with adequate natural function at this point. I do not think that there were any positive urinary findings in this case prior to operation.

Such statement and speculation as I may have put forward have resulted from the consideration of two cases of staphylococcal fever. Their natural history has been noted and the value of urinary findings and X-rays discussed in connexion with the diagnosis of such manifestations of staphylococcal infection.
The question of treatment now obtrudes itself. With regard to these fevers we are not so fortunate in our therapeutic armament, as a modification of streptocide or M & B which is equally effective for staphylococcal as well as streptococcal infection remains to be discovered. In staphylococcal fevers the results of chemotherapy are disappointing. Both the cases received adequate doses of these drugs which were continued for an adequate time for their effects to be observed. In neither case did they have any effect upon the fever although whether or not they saved Case 1 from operation is a matter for some thought.

The use of staphylococcal toxoid has not fulfilled its early promise, more particularly in those types of fevers due to repeated staphylococcal skin infections. So we are forced back upon the general treatment of these cases, with careful nursing and observation, and with surgical intervention at such times and in such places as we may deem suitable.

CONCLUSION.

It will have been seen from these few observations that the clinical features of streptococcal and staphylococcal fevers are painted on a large canvas with a very generous brush. The local lesion of each is only a part, and a very small part of this picture.

The difference in their choice of site for metastasis, their secondary manifestations, particularly in regard to the kidney, together with their chemotherapy, are all features which compel our attention to these two disorders and which to some extent exercise us in taking what Sir William Gull has so concisely called "the General View."