THE SECONDARY INFECTION OF SINUSES OCCURRING IN CASES OF NON-PULMONARY TUBERCULOSIS.

by

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THESIS PRESENTED

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INTRODUCTION.

The problem of tuberculosis is one which is intimately concerned with the general well being of the population. It, perhaps more than any other disease, is a reflex of the environmental conditions under which people live. A study of the statistical data shows that during the last 60 years the death-rate from this disease has declined in a striking fashion, and it would seem that the measures adopted during that period for the raising of the standard of living, hygienic as well as economic, were bearing fruit.

During this period the death-rate from all forms of tuberculosis occurring in the British Isles shows approximately a 70 per cent reduction: and the credit for this has been given to many factors. Of these factors social and economic improvements have undoubtedly played their part but probably the most beneficial power has been the application of medical knowledge to the health problems of the people.

When medicine laid aside mediaeval conceptions of disease and its causes and adopted in their place concise scientific facts the problem of the spread of disease by infection became evident. Practical experience had shown that certain diseases occurred and spread more readily in certain circumstances and steps were taken to minimise this spread by eradicating these adverse/

adverse circumstances. To this end reforms and improvements were being carried out in housing, sanitation, water supplies and other essential services.
In a word, the responsible governing bodies became 'Public Health conscious'. This quickening of the national interest resulted in the formation of Public Health organisations now scattered throughout the world; organisations staffed by specially trained men and women; whose particular duty it is to see that everything may be done to combat the conditions giving rise to, and helping, the spread of infectious disease.

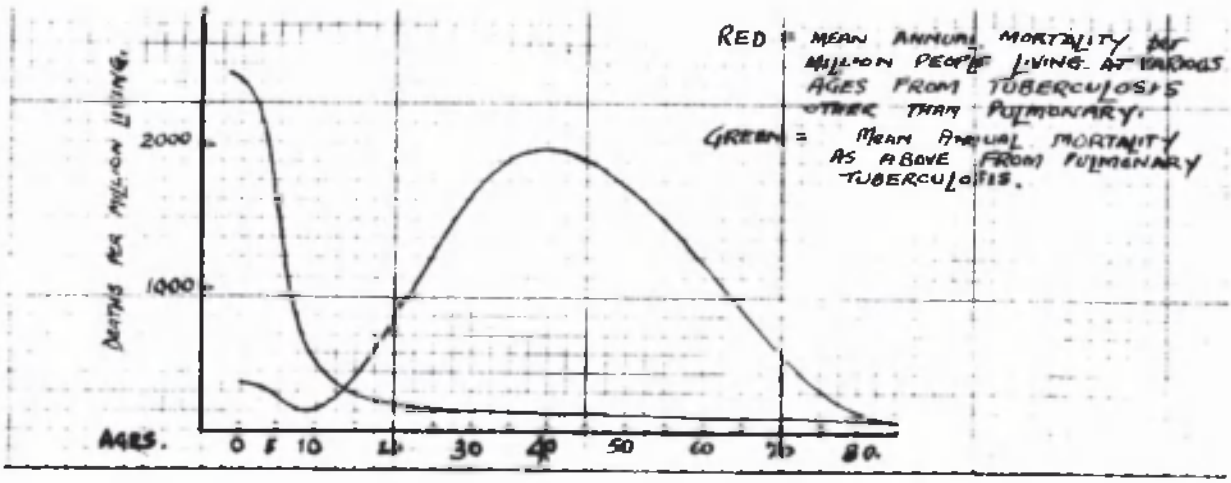
As it happened, tuberculosis was one of the earliest diseases in which a specific infection was proved but its significance was not appreciated by the administrative authorities, and fully thirty years elapsed after Koch's discovery, before it became a notifiable disease. This order intensified the upward trend which had already begun in the housing conditions and personal hygiene of the people. By providing hospital accommodation for segregation of those suffering from the disease or, at least training them to destroy contagious discharges, the way was further paved towards the improvement which now exists. Claims have been made that these efforts alone are not responsible for the improvement but that there are other factors also, yet whatever the cause, the fact remains that in tuberculosis there/

there has been a marked improvement in both incidence and mortality returns within a short number of years.

As it affects man this disease is roughly divided into two great groups, the PULMONARY and NON-PULMONARY forms and it is the latter which is the subject of this investigation.

Non-pulmonary tuberculosis is often called surgical tuberculosis because of its distribution and because, in contrast to the other, it lends itself particularly to surgical treatment. In addition it is a major problem only in the first ten to fifteen years of life; becoming distinctly rare at the ages when the pulmonary type takes its toll. The accompanying graph demonstrates the difference between the two types.

GRAPH 1.



Philip, quoting figures for Scotland showed that the most substantial reduction in tuberculosis fatality took place in the first year of life and the least at ages/

ages of 35 years and over. In view of the tables an inference may be drawn that an improvement occurred in the results of cases of non-pulmonary tuberculosis recorded and treated. This improvement may have been due to a change in the type of infection following tuberculisation of the population with a lowered fatality as suggested by some or, at the other extreme, to improved methods of treatment. One other potent factor is the supervision of the milk supply to the general public and it is also possible that earlier and more accurate diagnosis of the disease by trained observers, aided by modern radiology, plays a large part.

Despite this improvement tuberculosis of the bones and joints in children is still a grave problem and presents to the person treating it many anomalies. A patient with a simple lesion of this nature treated on modern lines may give a good result demanding no treatment other than rest and general care. On the other hand an apparently similar case may develop an abscess and eventually form a sinus. This complication may result in the development of amyloid disease and death; or, at the best it may be healed after much trouble with a residual crippling deformity. Complications of this type occur frequently and their importance cannot be over-rated. Fraser, in his book on Tuberculosis of the Bones and Joints, says that "abscess formation is serious/

serious in so far as it is so often the precursor of the next danger, viz. septic infection. In itself it increases the gravity of the disease and by its tendency to burrow it may open up to infection wide areas of soft tissue". In another part of the same book he says, "Mixed infection is the most serious complication which can occur. It follows abscess formation or imperfect surgical interference and its danger lies in the apparent impetus which it gives to the tuberculous process". Another author, Dudgeon, refers to the importance of mixed infections in bone and joint tuberculosis, remarking, "In the old days of mixed infections, due to errors in the surgical treatment, pyogenic vaccines were sometimes of use, but I have not employed such a vaccine since 1912" (Bact. vaccines and their post. in therapeutics, Dudgeon 1927).

Fraser is dealing with pre-war tuberculosis and Dudgeon's remark implies that some change has taken place in this form of tuberculosis since 1912. This change may have resulted from better methods of treatment or from a change in the type of the lesion.

With present day methods of treatment in use a superficial survey of a number of cases seemed to show that secondary infection of sinuses was not so important a factor as in former days. Yet certain sinuses developed complications and refused to heal while/

while others ran a short course and healed quickly. Information was sought upon the matter in the literature but it was found sadly lacking. Abscesses and their treatment received a full measure of care in all books but, in most, the question of sinuses, the reason for their troublesome course and the factors governing their formation and healing was not available. Even information relating to their effect upon the course of the primary focus of disease were lacking. One reference was found giving the infecting organisms in sinuses to include streptococci, diphtheroid bacilli and staphylococci but no evidence was given as to their relative importance.

It was thought, in view of the similarity between sinuses and wounds that some information might be found in works dealing with wound infections. Douglas, Fleming and Colebrook in an M.R.C. report on this subject state that "almost every secondary infection complication of any seriousness is caused by Strep. pyogenes, e.g. the persistence of sinuses, fever etc." As a result of random observations made upon sinuses suspicion had already fallen upon steptococci as the mischief making secondary infection and an investigation was planned primarily to answer the following questions.

I. The determination of the presence or absence of streptococci in sinuses.

II./

II. The classification of such streptococci.

III. The effect of these streptococci on the local and general condition of the patient.

IV. The method and time of infection

THE HISTORY OF THE STREPTOCOCCI IN RELATION TO DISEASE IN MAN.

Streptococci were first described and named by Billroth in 1874 and their existence was confirmed by other observers in the years which followed. Doubt lingered regarding their role in the tissues from which they were recovered and it was not until almost ten years had elapsed that Ogston of Aberdeen was able to prove their pathogenic power towards human beings. Coincident almost with this investigation was that of Cheyne who held that these organisms were non-pathogenic as he had found them in healthy wounds. Later investigations upheld these statements and the genus was enlarged by patient research and acknowledged to contain members which were widely different in their pathogenic powers. Even physical characteristics were found to vary and Veillon in 1893 described a strain which would not grow in the presence of air, the nucleus of a group which was similarly increased as time passed. Eventually, therefore, the genus was enlarged to contain strains which were very different in their biological requirements and pathogenic powers and which were widespread throughout nature particularly in reference to man.

A list of pathological conditions in man from which streptococci have been recovered would be very great/

great and the following is only representative of lesions in which it is the sole causal organism or in which it is a common causal organism.

1. Scarlet fever.
2. Puerperal sepsis.
3. Erysipelas.
4. Cellulitis.
5. Acute rheumatic fever.
6. Sub-acute ulcerative endocarditis.
7. Primary and secondary broncho pneumonia.
8. Tonsillitis.
9. Septic sore throat.
10. Otitis media, intracranial abscess, meningitis.
11. Various skin lesions.
12. Peritonitis.
13. Septicaemia.

Unfortunately from the view point of simplicity it was found impossible to say that a certain strain would bring about a certain lesion, as virulence, even over several generations of a particular strain, was found to vary. Reaction on the part of a host also varied and many interesting experiments have been carried out upon the immunity resultant from infection. This immunity was found to be of two forms, one local and the other general and these forms were sometimes developed separately. (Gay and Rhodes 1922). The existence of a general antitoxic immunity was first demonstrated/

demonstrated by the Dicks (1924) to occur in scarlet fever and on the basis of this discovery a diagnostic test was postulated and found successful.
A more widespread application of its general principles elicited several interesting facts regarding immunity in general to streptococcal infections. These were, (1) that the natural immunity to streptococcal infection was low (2) that variation in this immunity occurred from time to time (e.g. during pregnancy parturition and the puerperium) and (3) that exposure or illness reduced immunity.

Local immunity was found to vary in different sites of the body and was found to be purely transient in nature. A combination of these variable features and the variable virulence of streptococci makes it evident why no clear cut action could be ascribed to a particular strain. A general statement may be made that this genus contains many of the most dangerous pathogens of man.

Of particular interest in the present investigation was the problem of wound infection and with it, several of the cutaneous and general lesions caused by streptococci. The importance of these organisms in wounds of the skin and mucous membranes was brought out very forcibly during the Great War. During this time the possibilities for such an infection were enormously enhanced by the conditions under which the troops were living/

living and furthermore, ample facilities were present for adequate investigation. As a result of these investigations streptococci were given a place of importance in wound infections. Levaditi (1918) pointed out that delay in the healing of war wounds resulted if a streptococcal infection occurred. Bruce, Berlin and Lawrence (1918) found these organisms present in 24% of a series of 985 wounds and regarded their presence as the chief cause of the failure of secondary suture. In 1920 Douglas, Colebrook and Fleming reported that although often not present initially, S. pyogenes was found in practically every septic wound and was responsible for many of the complications and sequelae such as erysipelas and persisting suppurating sinuses. Anaerobic streptococci were also recovered in a percentage of cases but were assessed to be of low virulence and relatively unimportant. One exception to this was a fatal case reported by Marrwedel and Wehrsig in 1915.

It was thought that these organisms were very probably present as secondary infections in tuberculous sinuses although, as has already been remarked, no evidence exists regarding their role in this type of lesion. The probability is further enhanced by the widespread nature of the genus as was shown earlier in the chapter.

CHAPTER II.

THE HISTORY OF THE CLASSIFICATION OF STREPTOCOCCI.

Presenting many problems regarding their pathogenic powers these organisms presented still greater problems with regard to their classification and, it is safe to say, that more effort has been expended to this end than to investigating their relation to disease in recent years.

The first attempted classification of these organisms was on a morphological basis. When Fehleisen and Rosenback isolated the two strains, which they called the S. erysipelatis and the S. pyogenes respectively, the belief was that these strains were clearly differentiated and Rosenback made an attempted classification based on their growths on gelatin and agar. This method was found inadequate by Fraenkel (1889) and V. Lingelsheim (1891) and the latter and Kurth separately in 1891 produced papers attempting a classification on the appearances of streptococci broth media. In the years which followed the field was enlarged by the work of Veillon (1893) who described an anaerobic streptococcus while other investigators recovered other, and supposedly different, strains from various sources. Further confusion was caused by the work of Koch and Petrushky (1896) who proved that streptococci from a variety of sources were capable of producing erysipelas in animals provided the virulence was exalted sufficiently/

sufficiently by passage.

By now it was obvious that morphological tests as suggested were inadequate, and further tests were devised. Hiss (1902) introduced fermentation reactions and Schottmuller (1903) made a classification of a number of strains based on their action on blood agar. With improvement in knowledge and technique immunological tests were introduced, and now all these methods are in use for the classification of streptococci when recovered. For descriptive purposes, these tests may be dealt with under the following headings:-

I. Morphological and Cultural.

II. Biochemical: (A) Action on Blood.

(B) Fermentative Powers.

III. Immunological.

I. MORPHOLOGICAL AND CULTURAL.

When differentiating streptococci on the above grounds a primary division of the genus was made into those organisms which were aerobic and facultatively anaerobic and those which were strictly anaerobic. To these two groups, of which the former was the larger, further tests were applied. Strains which were aerobic or facultatively anaerobic were shown to have a relationship morphologically to their haemolytic powers and were further subdivided into Schottmuller's divisions of haemolytic and viridans strains and those which were inert towards blood.

II. THE HAEMOLYTIC STREPTOCOCCI.

Strains of this type were usually observed as well rounded cocci in chains of moderate length and were found to grow readily on agar and to yield cultures of good viability. It was further claimed that these organisms had the elements of the chain compressed so as to be longer in the axis at right angles to the chain (Holman 1916; Kinsella & Smith 1918; and McLeod). Morphological variations were noted by Tadder (1909) who described giant forms and Norton, Rogers and Georgieff (1921) described a bacillary form which they obtained under abnormal conditions. It was shown that the morphology varied in accordance with the recent environment/

environment as illustrated by the diplococcal form of a strain in an early superficial lesion as compared with the long chain form of a similar organism in a well-formed abscess. Capsule formation was shown to be absent with the exception of Baile & Kleinhans)1912) who claimed that a capsule may be observed irregularly around streptococci in the animal body but became visible 'in vitro' when the organisms were exposed simultaneously to the action of leucocytes and serum. When stained the organisms were shown to be Gram positive with occasional variations in intensity, especially in old cultures. Two strains were reported by Jaffe (1912) which gave Gram negative subcultures and Kinsella noted a tendency to loss of Gram positive staining when the strains increased in virulence.

The appearances when grown in 'broth media' were either a general turbidity or a granular deposit, and this feature was shown to be of no value in a differential sense. Weissenback (1918) showed that the presence of bile in fluid media inhibited growth and Wheatley proved that 40 per cent bile in agar inhibited the growth of S. haemolyticus whereas it had no effect on the S. faecalis.

The general observation was that haemolytic strains gave a distinct but not copious surface growth on the usual nutrient agar plate and a distinctive feature was the tendency for these colonies to remain discrete and

to stop growing after 24 hours. Colony form and its variations were intensively studied and some interesting observations were made. In strict chronological order those of Cowan (1922) come first. She maintained that by the repeated plating and selection of colonies it was possible to split several strains of streptococci into rough and smooth variants, the one with a translucent bluish flat colony and the other with a more opaque and roughly granular formation giving rise respectively to a diffuse turbidity and a granular deposit when grown in broth media. Secondly, Walker(1923) noted one or two colonies of a mucoid appearance occurring in a culture taken from the pleura of an animal into which a haemolytic streptococcus had been injected and observed that the strains grown from these colonies were more virulent and actively haemolytic than strains grown from the normal colonies. These hyper-virulent strains, however, lost their properties after a few generations. Thirdly - Eagles (1924) was of the opinion that two colony forms existed: (i) a small greyish pin point colony and (ii) a flat scale like colony. In the fourth place Griffith (1927) described 3 morphological types of colony, (i) an opaque, flat, rough and coherent colony; (ii) a colony with raised opaque centre and a thinner translucent margin which was never coherent and (iii) a large, more translucent, mucoid/

mucoid colony.

In contrast to Cowan, his rough colony on solid media gave rise to the uniform turbidity in broth characteristic of Cowan's smooth variant. He further claimed that, when his strains were classified on an antigenic basis, a degree of correspondence was shown to exist between the grouping so obtained and the morphology of the colonies. To cap these observations, Lancefield and Todd growing these organisms on blood agar, were able to differentiate morphologically a rough and a smooth colony form and came to the conclusion that a given strain could vary in colony form. Investigating further on an antigenic basis, they showed that it was only the rough colony which was capable of giving rise to a type specific antigen, and with this view F.W. Andrewes agreed. This last observation is the one most generally accepted.

THE VIRIDANS GROUP.

The viridans group may be subdivided into two: (i) streptococci whose habitat is the mouth and (ii) those whose habitat is in the bowel.

The mouth streptococci were shown to have the general characters of the genus under the microscope but formed chains intermediate in length between the haemolytic strains and the true bowel strains. When freshly/

freshly isolated strains were grown in liquid media, a deposit was formed, but this feature was lost on repeated subculture. The individual cocci within the chains were found to occur either singly or in pairs and were either spherical or slightly elongated and showed considerable variation in size. In solid media, small discrete colonies were formed which showed little tendency to coalesce as did the bowel streptococci and which grew less luxuriantly than S. haemolyticus. Capsule formation was not found to occur, and once again bile was found to inhabit growth in fluid media (Weissenbach).

The Bowel Streptococci. Under the microscope this organism was found to be a lanceolate diplococcus and which occurred in this form in broth cultures although occasional short chains of 6 to 8 elements were reported. The appearance of a broth culture was found to be that of uniform turbidity and growth was not interfered with if bile was present. On this feature Weissenbach suggested that these strains could be differentiated by using a 10 per cent bile peptone broth test medium. Growth on agar was found to be very good and colonies were produced larger than those of S. haemolyticus, sometimes 1 mm. in diameter after 24 hrs. growth. The presence of bile in solid media also was inhibitory and the organism was found to grow well on media like McConkeys.

Generally/

Generally speaking, the bowel streptococci were by far the most easy to keep in culture.

One final outstanding feature of this group was demonstrated by Dible in 1921 when he proved that these organisms were capable of surviving exposure to a temperature of 60°C. for 30 minutes, in distinction to the other streptococci which were killed by such a temperature after five minutes exposure.

The streptococci inert towards blood were found to have no particular morphological features and lastly the anaerobic streptococci remains to be described.

THE ANAEROBIC STREPTOCOCCI.

The existence of such organisms was, as has already been mentioned, shown by Veillon in 1893. Subsequent investigators, Rest, Halle & Guillemot, Kronig and Menge, Lewkowicy, etc., described other strains and a considerable morphological variation was shown to exist within the group. Certain of these strains viz: the M. foetidus of Veillon, the S. anaerobius and the S. putridus in special circumstances formed gas. Split into those which formed gas and those which did not, it was found that the gas formers strictly resembled the appearance of S. pyogenes and that in the case of the others the size of the coccus was the variable feature, all being small. When grown under anaerobic conditions

on/

on solid media, colonies were produced which were smooth, flat and semi-transparent with an occasional revised papilla in older colonies. In poured cultures the colonies appeared white or yellowish grey and were finely granular under the microscope - and in fluid media, under appropriate conditions, a slight general turbidity with a flocculent white deposit was noted.

The organisms of this group were found to be non-resistant to heat.

In conclusion it may be said that the features described above are of a certain value in differentiation but only as a preliminary step in the identification of a strain. It would seem to be a necessity to make a note of colony form under the microscope when a further immunological study is intended and the necessity is clear for a uniform technique in dealing with these organisms.

The following is a short resume of the position with regard to Biochemical tests.

A. ACTION ON BLOOD.

The action of different strains of streptococci in producing certain changes when grown on fresh blood agar plates is a factor of primary importance in any attempt to/

to classify these organisms. These changes are not limited to solid media but take place when a suspension of washed red blood corpuscles are exposed to the action of a filtrable substance called Haemolysin found in early broth cultures of certain strains of streptococci. It has been shown that a definite relationship exists between the reactions obtained by these two methods.

Historically, the haemolytic power of streptococci was first recognised by Knoor in 1893, when he observed evidence of this change in the blood of animals experimentally infected with strains of this organism. Three French investigators, (Bisredka, 1901; Marmorek, 1902; Breton, 1903) also showed that highly pathogenic streptococci had this power but the first classification of these changes was made by Schottmuller.

In a classical work published in 1903, the latter differentiated the streptococci into 3 main types basing his classification on pathogenic power, source of origin, morphology and the appearance of growths on fresh blood agar plates. Briefly, these types were as follows:- Type I: streptococcus longus pathogensive-erysipelatos, which included all highly pathogenic strains and was characterised by the development of clear colourless haloes around the colonies; Type II: Strep mitior sive viridans; which included strains mainly derived from the respiratory or digestive tracts, of/

of low pathogenicity and chiefly distinguished by their tendency to produce a green discolouration of the blood agar in the immediate vicinity of the colonies. In this case certain fallacies were found to exist, and they were the presence of narrow rings of cleaning around the colonies on agar of low blood content or when blood specially susceptible to disintegration was used in making the plates. Type III Streptococcus mucosus, of rarer occurrence than the foregoing, mainly characterised by its abundant colonies, and by the well-defined capsule seen in microscopic preparations even from cultures on solid media.

This method received general acclaim, especially when it was found to yield a separation into groups which corresponded to a degree with that obtained when the organisms were examined serologically. Dissatisfaction was expressed, however, and the subject received further study. As a result of this a monograph was produced by Brown (1915) in which the original classification was elaborated and wherein the necessity for a fixed and careful technique was stressed. Brown differentiated 3 types also which he named A, B, Y. Of these, his A & B. types corresponded with the Type II and Type I of Schottmuller respectively but in his Y type he laid stress upon a type which gave neither haemolysis nor green pigmentation when grown on blood

agar /

agar, a fact which was not made sufficiently clear by Schottmuller. Elaboration of Brown's classification finally yielded a differentiation of the A type into two groups and a later worker still (Bryant, 1927) claimed the existence of a type which gave green colouration around its colonies in the depths of a blood agar plate. Whether these elaborations were necessary is doubtful in view of the results which were obtained by others investigating the phenomenon in fluid media.

Using fluid media Lyall (1914) was able to split the streptococci into 3 groups: (i) those which produced haemolysin; (ii) those which produced methaemoglobin and (iii) those which produced no changes in blood, thus corresponding with the classification arrived at by Brown using solid media. Confirmation of Lyall's views was received from Mishulow (1921) and Cumming (1927). Other investigators when comparing the two methods for determining haemolysis found discrepancies to exist between them in which respect it is interesting to quote conclusions made by Cumming in 1927. He found that all streptococci from frankly suppurative lesions were equally haemolytic on human blood agar plates and on rabbits blood by either the plate or the tube method of observation but that a number of strains isolated from sputum were haemolytic only/

only on human blood agar plates. It was his suggestion that these strains should be termed pseudo-haemolytic and that this irregularity was the possible explanation of some of the discrepant results.

The observations of these gross changes were supplemented by an investigation into the chemical reactions bringing them about as a result of which it became apparent that many complex and, within limits, variable factors entered into their causation, thus again stressing the need for a fixed and careful technique. Claims were made that certain strains had been observed to change in haemolytic power from A to B. and vice versa, but no proof was advanced, and this change is considered unlikely.

Thus it may be said that in a classification of streptococci, it is important to know the haemolytic power of the strains and that this feature may be determined by either the plate or the fluid method but that this test in itself is not sufficient to render an identification of a strain possible. It does act, however, as a pointer to the virulence of the strain under observation (McLeod, 1923).

B./

B. FERMENTATION REACTIONS.

The possibility of differentiating the streptococci by means of their fermentative reactions was first suggested by Hiss in 1902. Employing various sugars, glucosides and alcohols, he showed that these organisms were possessed of wide fermentative activities. His experiments were repeated by Mervyn Gordon in 1903 who employed many different strains and succeeded in establishing a form of classification. The position was clarified to a considerable extent by an investigation conducted by Andrewes and Horder as a result of which they were able to indicate six main groups which they named as follows:- (i) S. equinsis; (ii) S. mitis; (iii) S. pyogenes; (iv) S. salivarius; (v) S. anginosus and (vi) S. faecalis. This grouping, which they obtained by the application of fermentation tests, was found to relate the fermentative powers of the organism to the source from which it was recovered. In addition the groups were not clearly defined but were found to merge into another with an intermediate series of strains which gave modified reactions under test conditions. These reactions were examined as to their reliability and both Hopkins and Lang working in collaboration and Lyall independently in 1914 reported favourably on this aspect. This mode of investigation, with its origin in England, was not pursued on the Continent with the same avidity, but the general opinion expressed/

expressed in France and Germany was unfavourable with regard to its differential value. In America, however, the subject attracted considerable attention and outstanding amongst the work done was that of Holman in 1916. He began by dividing the streptococci to be examined into those which were haemolytic and those which were non-haemolytic. Having determined this feature he applied to each group the fermentation of 3 'sugars' eventually producing a total of sixteen types, evolving a classification which became widely known and used.

The various investigations detailed above had all been favourable to the tests as a means of differentiation, but in the meantime strong criticism had been levelled at them. In France and Germany, as already quoted, the method was regarded with disfavour. Burnet and Weissenbach (1918) stated that after excluding the pneumococcus and the enterococcus from the field to be investigated, the remaining forms fell into two main categories, haemolytic and viridans strains, a classification which was supported by immunity reactions which is never the case in any grouping obtained by the fermentation tests. In Germany, Maass (1913) stated that there was no correspondence between groupings by sugar fermentation tests and the source of the pathogenic importance of the organisms. Blake(1917) was/

was practically of the same opinion as Burnet and Weissenbach but observed that he would reserve these fermentation tests for a further differentiation among the non haemolytic strains. Similar observations were made by Kinsella and Swift (1918) and Howell in the same year, who controlled their investigations by complement fixation tests. Another blow was struck by Douglas, Colebrook & Fleming in the M.R.C. Report No. 48 in which they pointed out that no serological difference existed between mannite fermenting streptococci of pyogenic type and those which did not ferment mannite.

Ritchie (1908) and Ainley Walker (1911) amongst others stated that in their opinion the fermentation reactions were not given constantly enough to serve as a basis of differentiation and Buerger (1907) showed that it was only necessary to give the streptococci more favourable conditions in order to enable them to ferment test substances previously unattacked. Taking secondary strains picked from separate colonies of a streptococcus Thro (1914) demonstrated that these varied in their reactions from time to time and McLachlan (1927) reported that he was unable to differentiate scarlatinal streptococci from other haemolytic strains by these methods. Holman's classification was criticised by Dible (1921) who stated that he found the former's fermentative types distributed equally

in/

in different lesions.

It will be seen from the above account that there is a considerable difference of opinion as to the value and significance of fermentative tests in the classification of streptococci. They are of doubtful value in relating the organism to disease and do not appear to agree with the results of serological tests. The consensus of opinion would appear to be in favour of their use as a subsidiary means of differentiation, supplementing for example, serological tests if necessary.

I M M U N O L O G I C A L.

The fourth and last method of attempting to classify the streptococci is based on serum reactions. In the late nineteenth and early twentieth century bacteriologists, headed by Marmorek (1895) and Aronson (1896), discovered various properties in sera from animals which had been artificially infected with various organisms. Investigation into these properties revealed the presence of opsonins, bacteriotropins, precipitins, agglutinins, bacteriolysins and bactericidins; specific factors which were the animal response to the invading organism. Bacteria varied in their power to produce these substances, but it was determined at an early date that the streptococcus was capable of producing a serum in which these immunological substances were present in a fairly high degree. Tests were devised whereby the presence of these substances could be ascertained and estimated and of these the test most commonly used was that which dealt with the phenomenon of agglutination, supplemented later with the fixation of complement.

Using these tests, either singly or combined in some manner many investigators attempted to classify streptococci recovered from a variety of sources with, in many cases, confusing and incompatible results.

During/

During the inception of this method of investigation the validity of a classification of streptococci based on sugar fermentation reactions was being bitterly fought but the concensus of opinion was that a classification based on the immunological properties of strains was more certain and approximated more closely to the grouping obtained by haemolysis than that obtained by fermentation tests. This placed the value of the method on the highest plane as yet attained and the trend of investigation was to ascertain first of all the haemolytic power of the strain in question and then to examine it from a serological point of view, with, as an aid if required, an investigation into its sugar fermentation reactions.

In view of this it will be convenient to describe the serological properties of the streptococci under the following headings:-

I. STREP. HAEMOLYTICUS.

II. S. VIRIDANS: (a) MOUTH STREPTOCOCCI.

(b) BOWEL STREPTOCOCCI.

(c) THOSE WHICH PRODUCE NO CHANGE IN BLOOD.

III. ANAEROBIC STREPTOCOCCI.

I. S. Haemolyticus: This group contains the true haemolytic streptococci and following McLeod's statement/

statement that, although not all haemolytic streptococci were virulent, few virulent streptococci were not haemolytic, it may be taken to contain most of the highly pathogenic strains. The organisms within this group have been proved to give rise to scarlet fever and other acute infections such as puerperal fever, erysipelas etc. Attempts were made to relate each disease to a specific strain, but such specificity is still doubtful. Statements such as those of Bliss (1920) and Dochez (1925) who were of the opinion that 80% of scarlatina streptococci were of one group, were disproved by Griffiths (1926, 1927) and Smith (1927) who claimed that there were similar serological forms of haemolytic streptococci recovered from other sources.

McLachlan and Mackie (1928) in a more recent analysis found that, while strains presenting certain serological characteristics were more frequently associated with scarlatina than other lesions, haemolytic streptococci with common serological properties occurred both in scarlatina and in various other conditions. When investigation was extended to examining toxin formation for specificity, it was found by a number of workers (Rosenow 1924; Williams 1925; Birkhaug 1926; Eagles 1926) that culture filtrates of strains isolated from erysipelas, puerperal fever etc., produced reactions similar/

similar to those yielded by filtrates of scarlatina streptococci and McLachlan (1928) stated that the scarlatinal strains resembled each other mainly in their almost uniform power of producing a toxin active in high dilutions whereas only a minority of non-scarlatinal strains produced toxin in a similar degree and that these originated mainly in the throat.

The organisms isolated from cases of erysipelas were claimed to be highly specific and Birkhaug (1925) stated that 91.2% of erysipelas strains which he studied could be distinguished by agglutination tests from scarlatinal and puerperal strains. In this claim he was supported by Tunnicliff (1920) and Eagles (1924, 1926).

Against this there was the disproving of a similar claim with regard to scarlatinal strains and the observations of Stevens and Dochez (1926) who stated that no clear distinction could be made between erysipelas and scarlatina streptococci by agglutinin absorption tests.

In their opinion the antigenic individuality of each strain was a more marked feature than any group characteristic. Apart from these attempts to prove specificity attempts were being made to split the entire/

entire section into groups, but here again opinions were varied. Smith (1927) defined two groups by agglutination methods and described an association between the source of each strain and the group in which it was ultimately placed. In distinction was the statement of Douglas, Colebrook and Fleming in the M.R.C. Report No.57 who found that 24 haemolytic streptococci from war wounds were identical on examination, also by agglutination methods. Similarly, employing the complement fixation test, Kinsella and Swift (1918) claimed that all the Haemolytic streptococci which they examined were identical. Intermediate between these diverging results were those of Dochez, Avery and Lancefield (1919) while using agglutination methods. They examined 100 strains of haemolytic streptococci, mostly from the respiratory tract, and showed the existence of 4 well defined immunological groups in which the majority of these strains could be placed. A number of unclassified strains were found to remain, and where these strains were sufficiently virulent, it was found that animals were protected by the prophylactic injection of homologous serum but not by the injection of a serum belonging to another group.

The position, to a large extent, was clarified by the work of Lancefield in 1928. She applied to this group of organisms the method of preliminary chemical separation/

separation of antigens followed by the testing of the separated fractions by the precipitin reaction and succeeded in demonstrating that at least 3 antigenic components existed in various strains of S. haemolyticus. One of these was a nucleoprotein which showed a wide range of cross reactions with antisera prepared against related types, extending into the haemolytic group. Another was apparently a polysaccharide in nature and was specific for the species S. haemolyticus, but was shared in common by all the serological types within that species. The third was protein in nature and showed type specificity. A structure such as this would explain many confusing results particularly in view of the following observations. Todd (1928) showed that recently isolated, virulent strains of S. haemolyticus usually gave granular, coherent 'matt' colonies when grown on blood agar and that these strains could lose much of their virulence while retaining their colonial form but that after prolonged sub-culture these innate strains gave rise to 'glossy' or smoother variants which were permanently attenuated. Joint observations were made by Lancefield and Todd (1928) and it was shown that the change from the 'matt' to the glossy type was associated with the loss of the type specific acid extractable protein constituent. This was mentioned before when describing the morphological/

morphological features of streptococci and a note was made that these should be carefully recorded before departing on an antigenic classification. It is obvious that two antigenically dissimilar strains might be one and the same originally although one of them has deteriorated and lost the type specific factor. Investigations bearing this in mind,may finally enable the haemolytic streptococci to be differentiated among themselves, but at the present there is no proved grouping, and they are regarded by some as a large group of heterogenous strains.

S. VIRIDANS:

Mouth Streptococci.

These organisms were found mainly living a saprophytic existence in the mouth although pathogenic powers were ascribed to them in Rheumatic fever and sub-acute infective endocarditis. The technical difficulties of antigenic classification were less in this group than in the haemolytic group and the sera of animals immunised against these organisms contained considerable amounts of the ordinary antibacterial bodies.

In contradistinction to the results obtained in the S. haemolyticus group, it was the experience of many investigators that the members of this group showed/

showed considerable heterogeneity. Using agglutination tests (Klegler (1915) found that strains were to a large extent individual and did not form groups, an opinion which was confirmed by both Gordon (1922) and Norton (1923) using absorption agglutination tests. Kinsella and Swift (1917) using the complement-fixation test were also of the opinion that the group consisted of a large number of heterogeneous strains but thought that they were justified in dividing them into 2 large groups, the right and left hand groups as they appeared on their tables. These investigators at a later date claimed that a relationship existed between the haemolytic streptococci and their left hand group, and in 1925, Hitchcock, who was of the opinion that the relation between groups of streptococci depended upon the protein or protein lipoid fraction, confirmed this and further showed that the right hand group was apparently related to the pneumococcus. Lancefield (1925) showed that sera prepared against the protein fraction precipitated the proteins derived from the other green streptococci, haemolytic streptococci, pneumococci and to a certain extent staphylococci but not B. coli or C. diphtheriae. Utilising absorption tests she demonstrated that the protein fraction of the non-haemolytic streptococci consisted of 3 elements, one of which was common to all such organisms and peculiar to them; a

second/

second which was also found in haemolytic streptococci and a third which was present in all streptococci and also in staphylococci. There was some evidence to show that the protein of the individual strains differed slightly and the precise relation to the pneumococcal protein was undetermined. The non protein substance in each group was considered to be a polysaccharide and was strictly specific although it could not produce antibody when dissociated from the other constituents of the bacterium. It was only when the whole bacterium was injected that antibodies were produced which reacted with the carbohydrate to produce a typical precipitate as in the case of the pneumococcus. Sera produced against whole bacteria, contained a predominant amount of specific anticarbohydrate substance and a varying amount of antiprotein substance which gave rise to the cross reactions with members of the other groups.

In conclusion it may be said that, although there is some relationship among the organisms in the group, individuality is a marked feature.

(b) <u>The Bowel Streptococci:</u>

These organisms, as was shown by Dible (1921), have definite morphological, cultural and biochemical features associated with a very low virulence and a tendency to lead a saprophytic existence.

From a serological point of view Bagger (1926) found/

found that attempts at agglutination were unfruitful and that absorption agglutination experiments were equally valueless in attempting to classify the members of this group. These methods are unnecessary as the group is easily recognised.

THE ANAEROBIC STREPTOCOCCI.

Prevot in 1924 worked out the agglutination reactions of these organisms and arrived at the conclusion that, so far as we know its members, the individual strains were distinct but that some relationship to each other was in existence. Comparatively little is known of this group as their role in the causation of disease in the human subject is a limited one. Summarised, the antigenic picture may be put: I. A nucleoprotein antigen which is widely distributed yielding no means of serological identification; II. Various polysaccharide antigens which mark off the S. haemolyticus group as a whole from S. Viridans; III. Certain protein antigens which differentiate various serological types within the species S. haemolyticus.

By serological methods it is possible to determine the relationship of one strain of coccus to another and its place in the group generally but other criteria must be employed. In a classification, certain features/

features of the organism must be known. These are, morphological and cultural appearances, action on blood and serological reactions with, on occasion, particularly in the non-haemolytic group of streptococci, the sugar fermentation reactions. That is, all methods to hand may have to be used in a complete classification.

THE CASES FORMING THE BASIS OF THE INVESTIGATION.

The complete investigation dealt with 132 patients of both sexes. These patients ranged from one to seventeen years of age and were all suffering from non-pulmonary tuberculosis. That no doubt should exist regarding the tuberculous nature of the primary lesion bacteriological proof was obtained wherever possible. Tubercle bacilli were cultured from 81 patients and in the remaining 51 in which the specific organism was not recovered, the clinical and, in some cases, radiological data were considered adequate. All doubtful cases were excluded.

When the cases were divided into sexes and classified as simple 5 year age groups it was seen that the distribution over the first 15 years of life was good and that the sexes were equally represented.

TABLE I.

Age Group.	Male.	Female.
0 - 5 yrs.	14	19
5 - 10 yrs.	34	26
10 - 15 yrs.	17	17
15 yrs. +	1	4
Total	66	66

This last feature was purely fortuitous as no selection/

selection of material was made. It will also be seen from the table that the greatest number of cases occurs in the 5-10 year age group a feature which may be explained when it is remembered that the age of greatest incidence of major non-pulmonary lesions lies on the young side of this group, which, by the time sinus formation occurred, generally brought the patients within this later group.

In order to facilitate statistics the cases were classified in groups according to the site of the primary lesion.

These groups were:-

I. TUBERCULOSIS OF THE VERTEBRAL COLUMN: including all cases of disease involving the vertebrae, the sacrum and the sacro-iliac joints.

II. TUBERCULOSIS OF THE HIP JOINTS: including bone and soft tissue lesions involving the joint and those bone lesions of the pelvic girdle, excluding the sacrum and the sacro-iliac joints.

III. TUBERCULOSIS OF THE KNEE JOINTS: including soft tissue and bone lesions involving the joint.

IV. TUBERCULOSIS OF ANKLE JOINTS: including soft tissue and bone lesions involving the joint and lesions of the os-calcis.

V. TUBERCULOSIS OF LONG BONES: including lesions of all long bones in so far as they did not involve a joint.

VI./

VI. TUBERCULOUS DACTYLITIS: including bone lesions of the carpus, tarsus, metacarpus, metatarsus and phalanges but excluding lesions of the os-calcis.

VII. TUBERCULOSIS OF GLANDS AND OTHER SOFT TISSUES: including all glandular lesions except mesenteric and retroperitoneal and all soft tissue lesions not arising from joint capsules, and

VIII. MISCELLANEOUS: a heterogeneous collection including lesions of ribs, maxilla, mandible, mesenteric and retro-peritoneal glands and other structures not included in the first seven groups.

The number of cases in each of these groups is seen in Table II.

I.	Tuberculosis of Vertebral Column.	32.
II.	Hip Joints.	25.
III.	Knee "	8.
IV.	Ankle "	9.
V.	Dactylitis	11.
VI.	Long Bones.	15.
VII.	Glands and Soft Tissue.	20.
VIII.	Miscellaneous.	12.

Examples of disease in the Vertebral Column and Hip joints preponderate because abscesses in relation to them were common in the hospital during the investigation. Glandular and soft tissue lesions were also common/

common but only a representative number were taken. Abscesses in relation to the knee and ankle joints were rare which accounts for their poor representation in the series.

In order to obviate written case histories and to obtain pertinent data from the cases under observation their various features were tabulated under the following headings.

I. AGE: This was divided into 4 groups, viz. 0 - 5 years. 5 - 10 years. 10 - 15 years and 15 years +

II. SEX.

III. FAMILY HISTORY of Tuberculosis whether positive or negative.

IV. Presence or absence of bacteriological PROOF of tuberculosis and where possible the type of bacillus isolated.

V. Presence or absence of SINUS formation.

VI. The ACTIVITY of the primary tuberculous lesion.

No emphasis was laid upon the result of the Mantoux test as this was positive in every case.

The first five factors are self explanatory. The sixth and last was estimated from the history, clinical and radiological features presented by each case under observation up to the time of sinus formation. In some cases this observation period extended over one year/

year. Purely arbitrary divisions were made and the activity of each primary lesion was described as either ACUTE, SUB-ACUTE OR CHRONIC. Utilising these factors the Tables were prepared and are included as an Appendix for reference.

Dealing only with the activity of the primary tuberculosis lesion it was found that in 132 patients, this feature was classified as ACUTE in 46, SUB-ACUTE in 51 and CHRONIC in 35. That is, primary lesions classified as acute and sub-acute seemed to form more abscesses than those classified as chronic which is in accordance with expectation.

When comparative figures for each sex were taken it was seen that they approximated closely except in the lesions classified as 'sub-acute' where females had a majority. This majority was by virtue of the preponderance of female soft tissue lesions over male in which form of tuberculosis the activity was most commonly sub-acute.

TABLE IV.

Age Group	Acute		Sub-acute		Chronic	
	M.	F.	M.	F.	M.	F.
0 - 5	4	4	6	12	4	3
5 -10	13	11	12	10	9	5
10 -15	7	6	4	5	6	6
15 +	-	1	1	1	-	2
Total	24	22	23	28	19	16

Table IV shows these gross figures divided into age groups when it becomes apparent that the activity of the primary lesion varies in each group. From this the percentage of patients with acute, sub-acute and chronic/

chronic disease were calculated with results shown in Table V.

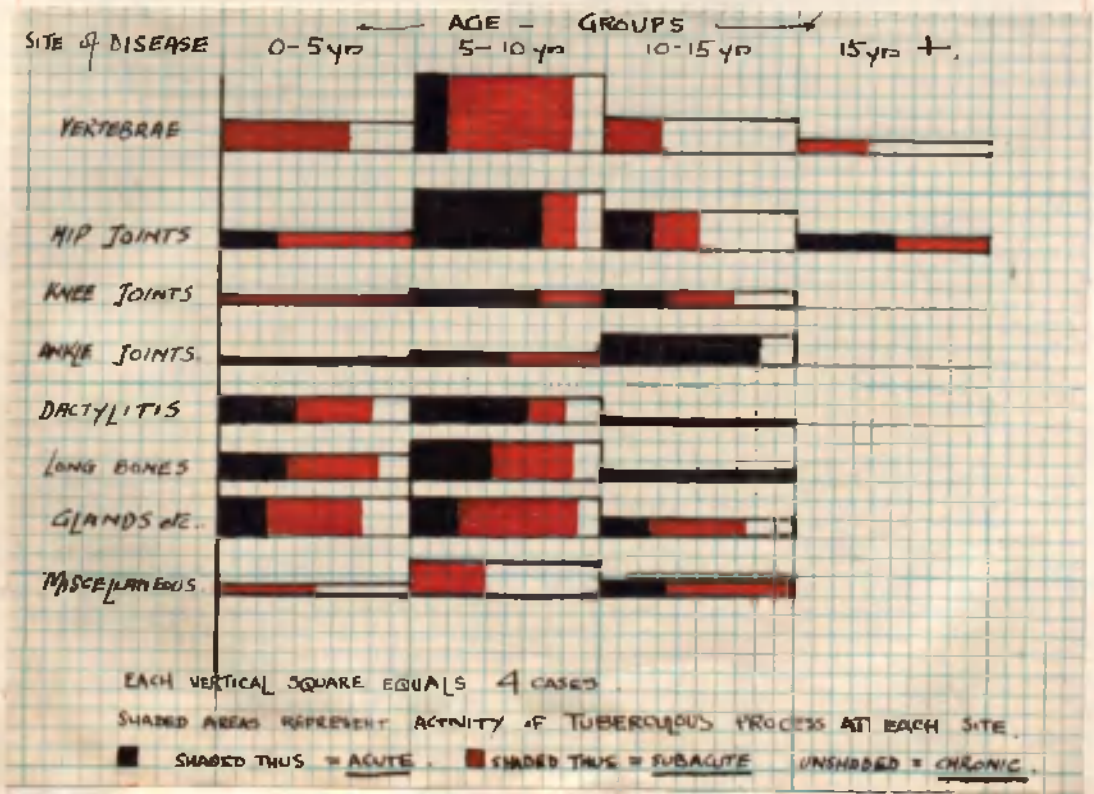
TABLE V.

Age Group	Acute %	Sub-acute %	Chronic %
1-5 yrs.	24.2	54.5	21.3
5-10 yrs.	40.0	36.6	23.4
10-15 yrs.	38.2	26.5	35.3
15 yrs. +	20.0	40.0	40.0

In view of the small numbers of patients over 15 years of age it was decided to neglect their results in a general consideration. Of the remainder, acute primary lesions were at their lowest between 0-5 years of age, reaching a maximum between 5-10 years of age and declining very slightly between 10-15 years of age. Tuberculosis graded as sub-acute was at its maximum in the youngest age group and declined steadily whereas chronic primary disease increased in incidence as the patients grew older. These figures relate only to the series under observation but no surprising feature was presented. Normally, it was expected that as age advanced the primary tuberculous lesion would decrease in acuity and such was the case with the exception of the phenomenally low figure for disease of an acute character in the first five years of life.

Even/

Even this exception was capable of explanation when the sites attacked by tuberculosis in the different age groups was considered. Thus, it was found that lesions of long bones, of glands and soft tissue and dactylitis occurred mainly in the first ten years of life, in contradistinction to ankle joint lesions which occurred mainly between 10 and 15 years of age. Lesions of the knee joints were scattered between 0 and 15 years of age with a slight increase in frequency between 5 and 15 years of age and lesions of the vertebrae and miscellaneous parts were mainly found between 5 and 10 years of age. Lesions of the hip joints were greatest between 5 - 10 years of age, but there were many sufferers between 10 and 15 years of age. This distribution was graphed (see graph) and an attempt made to indicate the relative proportion of acute, sub-acute, and chronic lesions forming each total.



From the graph it is clearly seen that tuberculosis of the ankle joints was mainly acute in character and was followed closely in this respect by lesions of the hip joints and dactylitis. In the knee joints and long bones a good balance between acute and sub-acute primary disease occurred with chronic disease in the minority. With glandular and soft tissue tuberculosis the predominating activity was sub-acute which degree of activity was also present, although overshadowed by acute disease, in dactylitis and long bones and to a lesser degree in the hip joints. Tuberculosis of sub-acute and chronic type predominated in disease affecting the vertebrae and miscellaneous parts with, in the case of vertebral lesions, a curious spate of acute disease between 5 and 10 years of age. It was this tendency for tuberculosis affecting different areas to do so mainly within set age groups and the fact that the activity of the disease varied so markedly for each site which resulted in the curious percentages obtained when the general figures for the activity of the primary lesions in age groups was taken.

General conclusions were drawn from these facts regarding the activity of primary lesions which give rise to abscess formation. It would appear that it requires an acute primary focus in the main to give rise to abscess formation in relation to hip joints, ankle joints and knee joints although in these sites

sub-acute/

sub-acute or chronic disease may originate a similar process. On the other hand when tuberculosis occurs on the hands or feet (Dactylitis), in the long bones, or in soft tissue sites generally, all degrees of acticity may give rise to abscess formation although the greatest number arise from disease classified as acute or sub-acute. At the other end of the scale come lesions of the vertebral column and miscellaneous parts where abscess formation may occur from tuberculosis of all grades of activity but where lesions classified as sub-acute and chronic have a greater tendency to do so than in any other area.

The effect of sex on all factors was considered and it was found that the activity of the tuberculosis in age groups was comparable except for the high incidence of sub-acute disease in females under 5 years of age and the high incidence of chronic disease in males between 5 and 10 years of age. In the female under 5 years of age sub-acute disease occurred in the hip joints, long bones, glands and soft tissue and dactylitis in greater numbers than in males. Similarly there was more disease of a chronic nature amongst males between 5 - 10 years of age with lesions of the vertebrae and miscellaneous parts than amongst females.

Taking each region separately it was found that more females than males were suffering from tuberculosis of the vertebral column under 5 years of age a feature which/

which was reversed within the next 5 years when the females also had lesions of a more acute character and that, between 10 and 15 years of age, the lesions were closely similar in activity. In the hip joints there was a tendency for the primary lesion to be more acute in males than in females at all ages but most markedly between 5 and 10 years of age. No distinguishing feature was noted between the sexes in the activity when the disease occurred in the knee and ankle joints, but tuberculous dactylitis affected more girls than boys at a younger age and the lesion in the male was of a more acute character. The next group, tuberculosis of the long bones, showed more males than females with a more acute lesion in the former, a series of facts which was completely reversed when the disease attacked the glands and soft tissues. The activity of the primary focus as it occurred in miscellaneous lesions was disregarded as the lesions were barely comparable. From the above it was impossible to generalise regarding the effect of sex upon incidence, site or activity of the primary lesion by virtue of the small number of cases.

The formation of sinuses was then considered. It was found that abscess formation did not inevitably lead to sinus formation although in 113 instances (86%) it did. This total comprised 56 males and 57 females which meant that 10 male and 9 female children had abscesses/

abscesses which healed without sinus formation and the following table shows the number and percentage of cases in each area in which this took place.

TABLE VI.

I. Vertebrae.	8 : 32	25%
II. Long bones.	3 : 15	20%
III. Hip Joints.	4 : 25	16%
IV. Knee joints.	1 : 8	12.5%
B. Ankle Joints.	1 : 9	11.1%
VI. Miscellaneous lesions.	1 : 12	8.5%
VII. Gland and Soft Tissue.	1 : 20	5.0%
VIII. Dactylitis	0 : 11	0%
Total	19 :132	14 Approx.

Of these 19 cases 3 were classified as having acute tuberculous processes, 4 sub-acute and 12 chronic. The acute lesions which did not form sinuses were composed of two cases where death occurred a short time after the onset of the disease and only one case which ran throughout its course and eventually healed. The lesions when death occurred were situated in the long bones and experience of infection of this site tended to the belief that, had the cases lived longer, sinus formation would have occurred inevitably. The residual case was one where the lesion was in the hip joint and in/

in this instance healing occurred. That is, only one example can be shown where a patient with an acute primary lesion and abscess formation did not form a sinus. Where the disease was sub-acute in nature sinus formation did not occur in 4 instances, a figure increased to 12 where the primary lesion was of a chronic type, although all these cases had a sufficiently long course to exclude the contingency of death preceding sinus formation. In short the greatest number of sinuses were formed where the primary lesion was of an acute nature, followed closely by lesions sub-acute in character and at a greater distance by lesions where the activity was classified as chronic.

The observation was also made that the great majority of sinuses were formed in the younger age groups. For example, excluding those cases where death intervened; 3 abscesses did not form sinuses under 5 years of age, 5 between 5 and 10 years of age and 9 between 10 and 15 years of age. Each of the few cases over 15 years of age formed sinuses but here, as was mentioned before, there are too few cases for a conclusion to be drawn. When percentages were calculated it was seen that the order of the age groups with regard to their tendency to sinus formation was I between 5 and 10 years of age. II under 5 years of age and III between 10 and 15 years of age. The outstanding feature was/

was that as the patients grew older the number of chronic primary lesions increased and that it was this grade of activity which had the least tendency to sinus formation.

Sex appeared to have no effect upon this occurrence as 10 Males and 9 Females did not form sinuses.

The next factor investigated was the family history of the patient as it was thought that a child with a positive family history might tend to form a sinus more readily than one in which this sinister omen was absent. The figures revealed that in those patients where sinus formation occurred the family history was positive in 22.1% of cases compared with 20.1% in those where sinuses were not formed. Thus the possibility of a hereditary predisposition to tuberculosis was shown to have no influence on sinus formation.

Reverting once more to the activity of primary lesion which gives rise to sinuses a similar result was obtained when the entire series of cases investigated was analysed.
For example.

TABLE 7./

TABLE 7. ACUTE PRIMARY LESIONS.

Site of Tuberculosis.	Sex of Patient.					
	Male			Female		
	Abscesses. No.	Sinuses No.	No Sinuses No.	Abscesses. No.	Sinuses No.	No Sinuses No.
Vertebrae	2	2	0	3	3	0
Long Bones	5	4	1	2	1	1
Hip Joints	8	7	1	4	4	0
Knee Joints	1	1	0	2	2	0
Ankle Joints	4	4	0	3	3	0
Miscellaneous	0	0	0	1	1	0
Glands etc.	1	1	0	4	4	0
Dactylitis	3	3	0	3	3	0

From the above it was seen that in each site, irrespective of age or sex, where the primary lesion was acute, abscess formation was almost inevitably followed by sinus formation. A notable exception was in lesions of the long bones but, as was already explained, death in these cases occurred first.

TABLE 8./

TABLE 8. SUB-ACUTE PRIMARY LESIONS.

Site of Tuberculosis.	Sex of Patient.					
	Male			Female		
	Abscesses. No.	Sinuses No.	No Sinuses No.	Abscesses. No.	Sinuses. No.	No Sinuses No.
Vertebrae	8	8	0	5	4	1
Long Bones	4	3	1	2	2	0
Hip Joints	3	3	0	4	3	1
Knee Joints	2	2	0	2	2	0
Ankle Joints	-	-	-	1	1	0
Miscellaneous	3	2	1	3	3	0
Glands etc.	3	3	0	8	8	0
Dactylitis	-	-	-	3	3	0

As in the case of acute disease, sinus formation was almost invariably the result of abscess formation.

TABLE 9./

TABLE 9. CHRONIC PRIMARY LESIONS.

Site of Tuberculosis.	Sex of Patient.					
	Male.			Female.		
	Abscesses. No.	Sinuses No.	No Sinuses No.	Abscesses No.	Sinuses No.	No Sinuses No.
Vertebrae	7	4	3	7	3	4
Long Bones	2	2	0	-	-	-
Hip Joints	3	2	1	3	2	1
Knee Joints	1	0	1	-	-	-
Ankle Joints	-	-	-	1	0	1
Miscellaneous	3	3	0	2	2	0
Glands etc.	3	2	1	1	1	0
Dactylitis	-	-	-	2	2	0

In contrast to the previous tables it was noted that there was a greater tendency for abscesses to heal without sinus formation. Notable exceptions were when the tuberculous process attacked the long bones, miscellaneous parts or the hands and feet. Particularly noticeable was the low incidence of sinus formation in relation to chronic disease affecting the vertebral column, a feature seen also to a lesser extent in relation to the hip joints. Thus, taken from another aspect, it again became evident that sinus formation was dependent upon the activity of the tuberculous process giving rise to the abscess.

Certain/

Certain exceptions to this rule were seen in the above table. For example, chronic primary disease situated in the long bones, miscellaneous parts, the hands and feet and to a lesser extent in glands and soft tissue formed sinuses in a number far greater than lesions of similar activity in the vertebral column or hip joints. The question arose, were there other factors which influenced sinus formation as well as the activity of the primary lesion? Examining many features it was decided that the site of the abscess arising from the primary lesion was of importance.

A tuberculous abscess is not merely a collection of inert material. Its walls are lined by a pyogenic membrane and it is in the walls that the tubercle bacilli are found in greatest number, actively enlarging the abscess by involving healthy tissue. When such an abscess approximates to the skin surface then that surface will be involved and eventually break down thus giving rise to sinus formation. Various local features may aid an abscess in its spread to involve a skin surface. Obviously abscesses originating from a primary bone or soft tissue lesion almost immediately subcutaneous will involve the skin early. Examples of this will be found when tuberculosis attacks the long bones such as the tibia, the bones or ligaments of the ankle and knee joints or the bones of the hands and feet. On the other hand those abscesses arising from tuberculosis of the vertebrae or the hip joints have

a/

a considerable amount of healthy soft tissue to traverse which forms a buffer and so hinders sinus formation. Thus site of the primary tuberculous lesion is a factor in sinus formation.

But abscesses are not disregarded when they form. Strenuous efforts are made in order to prevent their growth and these efforts take the form of aspiration of the abscess contents before they have had time to gather in great quantity and, in many cases, replacing them with various remedial solutions. No tuberculous abscess is aspirated through its central point unless an attempt is made to form a valve as is often illustrated in the text books of surgery. Even this can be bettered if a long needle is used and the abscess aspirated through a large area of healthy tissue. Employing this technique there is still a considerable risk of abscess material tracking through the needle puncture and it is obviously impossible to utilise this technique in an area where soft tissue is scanty and the abscess is almost subcutaneous. Finally, in an attempt to clean out the primary focus of the disease or where the skin is irreparably involved the abscess is incised. That is, abscesses may form sinuses naturally by extension and eventual erosion of a skin or mucous surface; by spreading through apertures left by an aspirating needle; and lastly by being incised. Details regarding the methods of origin of sinuses were taken for the cases under observation and have been tabulated as follows:-

TABLE 10..

Site of Disease	Site of Abscess.	No. of Cases	Method of Sinus Formation.		
			Incision	Needle Puncture	Erosion
Vertebrae	Neck	2	-	1	1
	Loin	3	-	3	-
	Back	1	-	1	-
	Groin and Upper Thigh	6	1	4	1
Hip Joint	Perineum	1	1	-	-
	Thigh (Ant.)	10	1	2	7
	Thigh (Lat. & Post.)	6	1	-	5
Knee Joint	Around Joint	5	2	-	3
Ankle Joint	Around Joint	4	4	-	-
	Heel	2	1	-	1
Long Bones	Subcutaneous	1	-	-	1
	In deep tissue	5	1	2	2
Glands etc.	All subcutaneous	6	5	-	1
TOTAL	-	52	17	13	22

It was found that many sinuses were caused by indiscriminate incision of abscesses before the cases reached hospital. Of those which came under treatment with abscesses or developed them in hospital sinuses were formed in a variety of ways. For example in lesions of the vertebral column the majority of sinuses were formed by pus leaking along aspiration needle tracks, whereas in lesions of the hip joints the most common method of sinus formation was by the abscess eroding the skin surface. Lesions of the knee joints and long bones were similar to hip joints in that erosion was the commonest method of sinus formation but in the case of disease in the ankle joints or the glands and soft tissues most sinuses were formed as a result of incision.

Why a certain manner of sinus formation should predominate in each group of cases was capable of explanation. Tuberculosis of the vertebral column we saw earlier was mainly sub-acute and chronic in activity thus tending to slow abscess formation and slow refilling of the abscess cavity when aspirated, conducive to many aspiration punctures and a consequently greater risk of leakage through the needle punctures. Added to this was the site of the abscesses. Those in the neck followed the fascial planes and were often close to the skin surface before their presence, as

indicated/

indicated by swelling, was suspected. In view of the numerous structures within the neck a long aspiration track was often impossible and no great variety of puncture sites were available so that the tissues around the abscess were damaged and a loophole for the escape of pus was presented. Similar conditions pertained in the back and loin. With psoas abscesses the position was different. They required aspiration at long range at first but, if the abscess was progressive, it led to very near the skin surface in which the punctures were most conveniently made and either spread through old needle tracks or through the later and, of necessity, shorter ones.

Abscesses arising from the hip joint were different. They were found to point almost impartially around the upper thigh with a slight preference for the front. Here the conditions for perfect aspiration were all present, long needle tracks were obtainable and bandaging was possible. But in these lesions we saw that the tuberculous process was mainly acute resulting in the steady progress of the abscess despite repeated aspiration and the eventual erosion of the skin surface.

With the remaining groups, excepting lesions of long bones, the abscesses were formed almost subcutaneously in the first place and involvement of the skin surface was early. As this surface when involved merely sloughed off, in order to save it incisions were made and/

and an attempt made to clean out the diseased tissue. That is, incision was merely to prevent erosion. This might have been done in the case of the hip joints but sinus formation in relation to this joint was feared so much more than in relation to these other areas that no opportunity was neglected in order to avoid its occurrence. Thus, sinuses relating to the knee joint were formed in two cases by incision and in 3 cases by erosion whereas needle puncture played no part. All sinuses arising from lesions of the ankle joints were formed by incision with one exception, which formed by erosion. Sinus formation as a result of incision with erosion as an alternative second was also the commonest method in lesions of glands and soft tissue and in dactylitis. Glandular and soft tissue tuberculosis giving rise to abscess formation was often treated by incision and scraping to obtain beneficial results rather than on conservative lines. With abscesses arising from lesions of the long bones sinus formation occurred in 3 cases by erosion, 2 cases by needle puncture and in 1 case by incision. The three sinuses formed by erosion and that which was formed as a result of incision all arose from abscesses which were immediately subcutaneous in origin and involved the skin surface early in their course. The two sinuses formed by needle puncture arose from deep-seated but progressive/

progressive abscesses resulting in the pus finding its exit in the easiest manner.

Therefore it may be said that the site of the primary tuberculous focus, its activity and the tissue through which abscesses track influence the particular manner in which sinus formation will occur.

THE TECHNIQUE EMPLOYED FOR EXAMINING THE SINUSES.

The investigation, dealing largely with the recovery of organisms from purulent discharges, necessitated a technique which would enable these organisms to be isolated readily and without fail. In a number of cases the secondary infection was purely streptococcal but in the majority of cases the infection was multiple and isolation of the various organisms was effected in the following manner.

When a dressing which had been in use for a period of from 4 to 24 hours was removed, the area of skin around the sinus was carefully cleansed with surgical spirit, care being taken to prevent the spirit from entering the sinus. One loopful, or sometimes more if it was known that the secondary infection was scanty, of the sinus exudate was taken with a freshly sterilised platinum loop at the bedside of the patient and immediately transferred to a tube containing Hartley's broth. Two of these tubes were thus inoculated and one was incubated aerobically and the other anaerobically at 37°C without loss of time. The tube which was incubated aerobically was allowed to remain in the incubator generally for 24 hours when it was removed and a loopful of the culture taken and stained and examined microscopically. A note was made of the organism

or/

or the various organisms growing therein and a loopful of the culture was then spread upon a serum-agar plate and incubated aerobically for a further 24 hours at 37°C when it was removed and the colonies examined either by the naked eye or with the aid of a lens. Subcultures of the various colonies were made on Hartley's broth and ordinary agar slopes and replaced in the incubator for a further 24 hours when they were re-examined to ascertain if they were pure cultures. In the event of them being pure cultures the next step in the examination was taken but if not then another attempt by plating was made to achieve such a desire.

Coincident with this the second tube inoculated was being incubated under anaerobic conditions for 48 hours. Anaerobic conditions were achieved by the use of sodium hydroxide and pyrogallic acid in a Buchanan tube. On the completion of 48 hours incubation the tube was opened and the organisms present determined by an examination under the microscope as in the case of the aerobic culture. When more than one morphological type of organism was present a loopful of the culture was spread over the surface of each of two serum-agar plates, one of which was immediately placed in the incubator under aerobic conditions and the other under anaerobic conditions. The plate which was incubated aerobically was removed after 24 hours and the/

the various colony forms noted and compared with those obtained by purely aerobic culture from the beginning when, if dissimilar, subcultures were taken. Anaerobic incubation was allowed to proceed for 48 hours and the colonies of this plate were examined and each transferred to two tubes of Hartley's broth, one of which was incubated aerobically and the other anaerobically for the usual periods of 24 and 48 hours respectively at the end of which time the cultures were stained and examined under the microscope. If the organism grew aerobically and anaerobically then the further subcultures were continued aerobically but if the organism grew only under anaerobic conditions then it was treated as such and subcultures and further examination was conducted under similar conditions. The occurrence of anaerobes was very rare.

It was thus possible in the great majority of cases to obtain a pure culture of the secondary infection infecting organisms in not more than 3 generations and thus obviate too great changes in the characters of the organisms by subculture.

When the investigation was extended to include the examination of pus removed from tuberculous abscesses a similar routine was observed. A difference was that more pus was used to inoculate the original broth media than in the case of the sinuses.

One more routine was evolved for the recovery of organisms/

organisms from the skin. A small piece of sterile absorbent gauze was soaked in nutrient broth and placed as a wet dressing on the skin surface to be examined. After two hours it was removed and cut into pieces which were added to ordinary broth in culture tubes. These tubes were then incubated aerobically and anaerobically at 37°C for varying periods. The difficulty of preventing streptococci from being rapidly overgrown by staphylococci was overcome by inspecting the culture tubes at regular, short intervals and examining a loopful of their content microscopically, when, if it was thought advisable, agar plates were inoculated and the required organisms picked off in the usual manner.

The other tests which were used at later stages in the course of the investigation were those of standard laboratory practice. It was felt that their detailed description might be omitted and they are mentioned as they appear.

THE SINUSES INFECTED WITH STREPTOCOCCI.

The central feature of the investigation was the microscopic and bacteriological examination of the discharge from sinuses arising from a representative series of tuberculous lesions. Some patients had multiple tuberculous foci giving rise to separate sinuses whereas others had one focus of disease resulting in multiple sinuses. In some instances numerous sinuses were examined in a single patient. It is for this reason that it is necessary to state that one hundred and ten sinuses, arising from one hundred and two patients, were examined. Of these patients fifty-five were females and 47 were males ranging in age from one to seventeen years. The presence of tuberculosis was proved bacteriologically in 60 cases and in the remaining 42 the specific organism was not recovered. Every patient in the present series was under discussion in the preceding chapter rendering it redundant to repeat at this point the features tabulated there.

As before no selection was made hence the relative incidence of males to females was accidental and not an indication that more females than males form sinuses.

Table I was constructed to demonstrate the origin of the sinuses which were examined.

TABLE 11./

TABLE 11.

Vertebrae . . .	25
Hip Joints . .	18
Knee Joints . .	8
Ankle Joints . .	9
Long Bones . .	13
Dactylitis . .	13
Glands and soft tissue	15
Miscellaneous . .	9
Total.	110

During the course of the investigation the method of examining the discharge from each sinus was standardised but differences existed in the times at which they were examined. Some sinuses were examined at their inception, some midway in their course and others when they were in the process of healing. Certain of them were examined at one or other of these periods and others at two or all of them. When repeated examinations were made the findings often varied and some difficulty was experienced classifying the results under a heading such as that of this chapter.

This was overcome by dividing the results into three large groups. For example, sinuses which yielded no secondary infection on examination were called 'sterile' and a second group was formed by those which yielded organisms other than streptococci, leaving a third/

third group from which streptococci were recovered. Under this classification a sinus which was once infected in any way was never classified as sterile irrespective of the result of an earlier or later examination and similarly, when streptococci were once isolated from the discharge, the sinus was included in that group for all time.

Tables were then made illustrating in percentages the following points, (1) the gross secondary infection of sinuses, (2) the infection by organisms other than streptococci and (3) the infection by streptococci.

TABLE I2.

Site of Primary Lesion.	% sinuses Gross Infection	% sinuses infected by orgs. other than Streps.	% sinuses infected by Streps.
Vertebrae	92%	32.0	60.0
Hip Joints	89.0	11.1	77.9
Knee Joints	87.5	0	87.5
Ankle Joints	89.0	0	89.0
Long Bones	91.6	33.3	58.3
Dactylitis	92.1	30.8	61.3
Glands and soft tissue	88.8	18.8	68.0
Miscellaneous	100.0	77.7	22.3

In/

In the first place it was seen that approximately 91% of all sinuses were secondarily infected and that, excluding those arising from miscellaneous parts, infection was approximately similar in extent in all of them irrespective of source of origin. From this it was inferred that the site of the sinus had no effect upon the onset of secondary infection generally. High though the incidence of infection was it was felt that it could have been still higher had certain sinuses, which were classified as 'sterile' been examined at earlier or later periods.

In the next column of the table it was seen that the percentage infection by organisms other than streptococci varied markedly and, in view of the standard percentage of sterility, in inverse proportion to that for streptococcal infection. Passing on to the third column it was noted that the percentage of sinuses which were infected by streptococci was high. Variation in the incidence occurred according to the site of the primary tuberculous lesion, being highest for those sinuses which arose in relation to knee and ankle joint lesions with those from the hip joints following closely. Those which arose from long bones, glands and soft tissues, dactylitis and the vertebral column were infected in a lower but closely similar degree whereas the percentage infection of this type in/

in miscellaneous lesions was low. Such a difference in figures suggested that there were factors controlling the type of secondary infection, for example streptococci, which gained entry to sinuses.

An attempt was made to ascertain if this was so and the cases were scrutinised in relation to age, sex, the activity of the primary tuberculous focus, the site of sinus, the nature of tissue through which the sinus ran and finally, the duration in time of existence of each sinus.

Dealing with these potential factors in the order enumerated above, that of age was first investigated. It was found, utilising age groups as before that 69.2% of sinuses in children under 5 years of age were infected with streptococci and that in the other 3 age groups the figures were 64%, 66% and 60% respectively. From these figures it was concluded that age had no influence upon the presence or absence of streptococci as a secondary infection in the sinuses examined.

The determination of the influence of sex necessitated fresh tabulation of the cases but it was found that no general conclusion could be made and that particular inference was impossible on account of the small numbers of each sex, in each site, in each age group. In view of the negative result obtained the table was omitted.

When/

When the activity of the primary lesion in each case was considered it was found that in 67 cases infected by streptococci the activity was gauged to be ACUTE in 36, SUBACUTE in 24 and CHRONIC in 7. In contrast were the corresponding figures in sinuses infected by organisms other than streptococci or those classified as sterile. These were ACUTE 5, SUBACUTE 16 and CHRONIC 15. From these figures it was inferred that sinuses which arose in relation to cases with an acute primary tuberculous lesion were more prone to streptococcal infection than those which arose in relation to a subacute focus, who were in their turn more vulnerable than those which arose from a chronic primary focus. These facts were capable of being proved in another manner, and to this end a fresh table was made.

TABLE 13./

TABLE 13.

	AGE GROUPS AND ACTIVITY OF DISEASE.														
	0 - 5.			5 - 10			10 - 15			15 +		
	Acute	Subacute	Chronic	A	S	C	A	S	C	A	S	C
VERTEBRAE.	0 0	3 3	1 0	5 5	4 2	3 0	0 0	2 0	2 2	0 0	1 0	2 1
HIP JOINTS.	1 0	2 2	0 0	7 7	2 2	1 0	1 1	1 1	2 0	1 1	1 1	0 0
KNEE JOINTS.	0 0	2 2	0 0	2 2	1 1	0 0	1 1	1 0	0 0	-	-	-
ANKLE JOINTS.	1 1	- -	- -	1 1	1 1	- -	5 5	- -	- -	-	-	-
LONG BONES.	2 2	3 2	1 -	2 2	3 1	1 0	- -	- -	- -	- -	- -	- -
DACTYLITIS.	2 0	2 2	1 0	3 3	1 0	1 0	1 1	- -	- -	-	-	-
GLANDS etc.	1 1	2 2	1 1	2 2	3 1	1 0	1 1	2 2	0 0	-	-	-
MISCELLANEOUS	-	-	-	-	3 0	4 2	1 0	2 0	-	-	-	-

N.B. The black numeral indicates the total number of patients with sinuses in each division and the adjacent red numeral shows the corresponding number infected by streptococci.

This table shows that the majority of sinuses arising from acute primary lesions, irrespective of the age of the patient or the site of the disease, were infected with streptococci, a feature which was less pronounced as the primary lesion became reduced in activity.

A conclusion was drawn once again, therefore, that the activity of the original lesion plays a part in the progress of each case and that it was a factor in determining the type of secondary infection which was recovered from the sinuses.

That a particular micro-organism was capable of selective activities did not seem to be reasonable and other factors were obviously existant.

The remaining factors, viz. site of sinus, duration of sinus and nature of tissue through which each sinus ran, were considered together and a survey revealed that sinuses arising from different areas were subject to different local conditions.

Assuming an Exogenous infection the first difference was found to exist on anatomical grounds alone. Sinuses arising from vertebral disease were found most commonly on the neck, back and loin and on the groin. Those in the neck were long with opposed walls and a narrow mouth, those in the back and loin varied from short to medium in length sometimes patent and sometimes with/

with opposed walls whereas those in the groin arising via the psoas muscle were long and widely patent. Those which arose from the hip joints were sometimes straight, long and patent and sometimes long,narrow and diffuse but in all cases they ran through vascular tissue, a feature which was shared by some sinuses arising from lesions of the long bones. Lesions in relation to the knee, ankle and elbow joints had features in common. These were, the short sinus surrounded often by diseased soft tissue and the close proximity to synovial cavities which would be a most suitable nidus for an added pyogenic infection. Somewhat similar in that the surrounding soft tissue was often involved, and the sinus was short, were sinuses such as arose from dactylitis, glands and soft tissue and some of the long bones. Those which arose from miscellaneous lesions were either short, or the disease was not extensive or had the feature that perfect cleansing was possible when dressing.

Another difference was found to exist in the time of onset of streptococcal infection and this was of importance as regards the duration in time over which the sinus was patent, a factor regarding which more will be said in a later chapter. Meantime it may be remarked that sinuses arising from the vertebrae were uncommonly infected early by streptococci but as time passed/

passed the possibility of recovering such an organism from the discharge increased. In miscellaneous lesions this infection was rare at any time whereas in lesions of the knee joint, ankle joint or hip joint it occurred at an early stage in the history of the sinus. The time of onset of the infection varied for each particular group of cases and it was supposed that each sinus was exposed to the same risk. A deduction was made that certain areas must be more suitable for the reception and retention of a streptococcal infection than others and that this encouraging factor must be local.

When the anatomical feature of each area were related to the activity of the primary tuberculous lesion some theories were formed. For example tuberculosis of the knee and ankle joints was to a large extent acute in character rendering a wide area of tissue devitalised and an easy prey to added infection against which the body had had no time to prepare. Similar conditions pertained to a degree in sinuses which arose from the hip joints whereas the comparative immunity to infection with complications which existed in the sinuses arising from psoas abscesses was due partly to the drainage afforded and partly to the efficient pyogenic membrane which had had time to form with the less active disease. Sinuses from the vertebrae arising in the neck and loin were similar to those from the

hip/

hip joint when once streptococcal infection had gained entry, although in the neck pocketing did not occur. Glands, dactylitis and some long bones were already compared to ankle and knee joints and here the only distinguishing features were the reduced extent and activity in some cases of the tuberculous process.

Thus a conclusion was made that the factors bearing upon the incidence of streptococcal infection in the sinuses were the site of the sinus and the nature of the tissue through which it ran and that these factors were governed solely in their effect by the activity of the primary tuberculous process all of which factors governed the duration of the sinuses in time.

THE STREPTOCOCCI WHICH WERE RECOVERED FROM THE SINUSES.

The task of typing the numerous strains of streptococci which were recovered was rendered difficult by the many divergent opinions expressed by authorities on the values of certain differential methods. It was finally decided that each strain which was recovered would have its morphological and cultural characteristics noted and its haemolytic power tested.

The morphology of a strain was taken from its growth in broth; the shape of the coccus and the length of the chain being noted. The cultural characteristics were noted on a 24 hours surface growth on an ordinary agar plate with, in some instances, an extended examination over a series of different media. Finally the haemolytic power was estimated on the changes caused by the strains when grown on a fresh blood agar plate.

In addition to these basic tests a number of strains were examined biochemically and certain others serologically.

When the investigation was completed 132 strains had been examined including a number of strains which had not been recovered from the sinuses but which were included for the purpose of comparison. Table 14 indicates the source of the various strains.

TABLE 14.

Source	Number of Strains.	Haemolytic Power.			
		a.	b.	nil.	query.
Type cultures	6	1	4	1	-
Faeces	1	1	-	-	-
Throats	7	2	5	-	-
Skin	2	1	-	1	-
Sinuses	116				
Vertebrae	25	-	19	3	3
Hip joints	31	-	23	7	1
Knee joints	9	-	9	-	-
Ankle joints	12	-	10	1	1
Long bones	11	-	10	1	-
Dactylitis	13	-	12	1	-
Glands etc.	13	-	10	3	-
Miscellaneous	2	-	-	2	-
Totals ..	132	5	102	20	5

There were 6 typed cultures from the Lister Institute including S. pyogenes, S. equi, S. infrequens, S. salivarius, S. faecalis and S. erysipelatosus. One other strain was recovered from the faeces of a patient with enteritis and two more from the skin surface of healthy children. Seven strains were recovered from the throats of various individuals. There is also shown on the table the particular source of origin of the strains recovered from sinuses.

The third column reveals the haemolytic powers of the various strains and the preponderance of B. haemolysis amongst the sinus strains is of interest as is the absence of strains a. haemolytic in character. Unfortunately haemolytic power was not always clearly defined and it was necessary to place a small number of the organisms under the heading 'query'. Variation in this power was well marked and in greater detail the tabulated results showed the following features. The type cultures gave definite readings with one exception. Streptococcus erysipelatosis, infrequens and equi were all definitely B. haemolytic with wide range of clearing around the colonies with blood cell destruction and a sharply defined margin. The exception was S. pyogenes when the clearing was small in extent but yet definite. a. haemolysis was shown by S. salivarius and S. faecalis exhibited no haemolytic powers. Those strains which were recovered from/

from throats showed B. haemolysis in four instances and a. haemolysis in three. 4 of them were recovered from patients with scarlatina and their haemolytic power was B. in character in 3 instances a. in one. One strain was recovered from a throat in health and was B. haemolytic whereas the remaining two were recovered from scarlatina contacts showing B. haemolysis in one instance and a. in the other. The strain which was recovered from the faeces showed a. haemolysis and those isolated from the skin surface showed a. haemolysis in one instance and no haemolytic power in the other.

These results were definite but it was amongst the strains which were recovered from the sinuses that variation occurred. It was noted that 102 showed B. haemolysis on culture, but the degree of change was not uniform in extent. Some showed extensive and undoubted clearing whereas others had only a small, though clear cut, reaction. None showed a. haemolysis on first culture and 20 strains were definitely devoid of haemolytic power. 5 strains were doubtful for the following reasons. When a strain exhibited no haemolysis or an a. reaction on first culture the test was always repeated in order to confirm the original observation and, where the second reading was confirmatory, the strain was classified as such. In 5 instances variations/

variations occurred during the course of these tests and these were the strains classified under 'query'. They exhibited the following characteristics.

Strain 1. N.S. 9.10.33. This organism was first isolated in pure culture on 13.10.33 and was plated on blood-agar when no haemolysis was observed. After repeated subculture the strain was again plated on blood-agar when haemolysis a. in type was noted on 8.11.33 and two days later another broth culture exhibited varying degrees of haemolysis on a similar medium.

Strain 2. N.S. 6.11.33. This strain was first obtained in pure culture on 9.11.33 by which date it exhibited no haemolysis on blood-agar. Re-inoculated it showed a. haemolysis on 10.11.33 and again on 14.11.33. Sugar fermentation. Acid and clot in lactose, maltose, glucose and acid in litmus milk. Morphologically and culturally similar to typical S. viridans, might be classed in this group.

Strain 3. M.M. 10.33. When this organism was first recovered it would not grow in air. Subculture however resulted in a fairly luxuriant growth under these conditions. Haemolysis was absent on 27.10.33 and 2.11.33, faintly present on 8.11.33 and definite of B. character by 11.11.33. Morphologically S. haemolyticus or S. viridans it was impossible to say clearly which on haemolytic power as exhibited.

Strain 4. D.L. 20.4.34. This strain was first recovered/

recovered on 22.4.34 from the anaerobe culture when it grew but sparingly in air. Subculture did not improve either in aerobic or anaerobic conditions and the strain died out on 30.4.34 having shown no reaction on blood-agar plates.

Strain 5. S.M. 10.34. This organism never gave proof of strong haemolytic power although always causing very faint clearing around its colonies. It was impossible to mention type although no definite methaemoglobin formation was noted. Again morphologically and culturally viridans or haemolyticus groups.

In some instances the haemolytic power of the strains varied directly as their apparent pathogenicity to the host. For example, it was noted that the most marked B. haemolysis was shown by organisms isolated from sinuses where an acute complication was occurring. To which rule, as to any other, there were a few exceptions. B. haemolysis was shown by organisms recovered from apparently normal clean wounds where they were leading a saprophytic existance.

Further classification was continued utilising haemolytic power as a primary division and adding cultural and morphological characteristics. It was found that the cooci were largely ovoid with the greatest diameter at right angles to the main axis of the chain with a minority truly ovoid. Their size was standard with very few exceptions but their chain length varied/

varied considerably. Colonies were mainly pin point, opaque and convex up with regular edges and another difference noted was the variation in granularity as seen under the microscope. On these combined features the following groups were produced.

Group I. B. haemolytic, finely granular, pin point colonies, long chains, transversely flattened cocci.

20 STRAINS.

Group II. As group I, medium length chains.

37 STRAINS.

Group III. As before, short chains.

26 STRAINS.

Utilising the granularity of the colonies under the microscope three further groups were found where this feature was more marked than in the preceding series.

Group IV. B. haemolytic moderately granular, pin point colonies, long chains, transversely flattened cocci.

1 STRAIN.

Group V. As group IV, medium chains.

3 STRAINS.

Group VI. As above, short chains.

5 STRAINS.

Still one more group was formed by colonies where granularity was very marked. All of these strains had chains medium in length.

Group VII.

4 STRAINS.

Finally, amongst the B. haemolytic strains were those where the individual cocci were truly ovoid.

Group VIII. B. Haemolytic, pin point, finely granular, ovoid cocci.

Long chain. NIL.

Medium chain. 3 STRAINS.

Short chain. NIL.

Group IX. Similar general features but with greater granularity in the colonies.

Long chain. NIL.

Medium chain. 3 STRAINS.

There were no organisms recovered from the sinuses which produced a. haemolysis but five strains were present within the series exhibiting this feature. Their details were -

1. C.B. Source, faeces.

Opaque, finely granular colonies up to 1 mm. in diameter. Short chains of transverely flattened cocci.

II. J.P. Source, skin.

Similar in detail to Strain I.

III. Type culture S. salivarius.

Similar to Strains I and II.

IV./

IV. R. Similar to the first 3.

V. G. a. haemolytic, finely granular colonies, 1 mm. diameter, ovoid cocci in short chains.

The remaining strains, all non-haemolytic when similarly classified resulted in the following grouping.

Group X. Non-haemolytic, finely granular colonies, 1 mm. diameter, medium chains, transversely flattened cocci.

8 STRAINS.

Group XI. Similar but with moderately granular colonies.

4 STRAINS.

Group XII. Granular colonies.

1 STRAIN.

Finally there were the non-haemolytic strains with ovoid cocci.

Group XIII. Long chains.

2 STRAINS.

Group XIV. Medium chains.

3 STRAINS.

Group XV. Short chains.

2 STRAINS.

Outstanding/

Outstanding as a result of this grouping was the close relationship exhibited between the majority of the strains when morphology and haemolysis were taken as factors for classification. Equally noticeable was the morphological similarity amongst the strains which were B haemolytic and the absence, with one exception, of any strain which might be streptococcus faecalis. Another feature was the shape of the individual cocci. Opinion has been expressed that cocci with their long axis at right angles to the chain are more virulent than those showing the standard ovoid form, in which case most of the strains examined were of this slightly more virulent nature. In opposition, however was the evidence afforded by the granularity of the colonies under the microscope, when the vast majority were so finely granular as to be almost smooth, a feature reputed to indicate an avirulent stage in the life of an organism.

Support was given to this assumption when the virulence of some of the strains recovered was tested in mice. The method in use was to inject intraperitoneally into a healthy mouse 0.5 cc. of a 24 hours ordinary broth culture of the organism to be tested. Twenty-five strains were then examined and all were found to be avirulent with two exceptions. The following table indicates the source and characters of the various strains tested.

TABLE 15./

TABLE 15.

Source of Organism.	No.	Haem.Power	Avirulent	Virulent
In lesions from which an acute disturbance was in process.	21	B.	20	1
From quiescent lesions	4	B.	3	1
	25	B.	23	2

The broth cultures used were those which showed the best growth from a series of 3 tubes which were inoculated. One mouse only was used for each test.

A conclusion, based on all the previous details was that morphological and cultural characteristics appeared to be of value but only as an accessory to the haemolysis test.

Exact differentiation of a certain number of strains was then attempted utilising the biochemical properties of the organisms. The test medium used was Hiss' serum water in which was dissolved various sugars and glucosides and the technique was such as would be followed in standard laboratory practice. Twenty-six strains were subjected to this test with results as in Table 16./

TABLE 16. (+ = A.C.)

	Lactose	Saccharose	Raffinose	Salicin	Mannite	Maltose	Glucose	Litmus Milk
G. P. 11.33	+	+	-	-	-	+	+	A
S. M. II.	+	+	-	-	-	+	+	A
A. McD. 11.33	+	+	-	-	-	+	+	A
A. M.	+	+	-	+	-	+	+	A
M. C.	+	+	-	+	-	+	+	A
K. C. C.	+	+	-	+	-	+	+	A
K. C. F.	+	-	-	+	-	+	+	A
J. McL.	+	+	-	+	-	+	+	A
M. M. 2) 11:33	+	+	-	+	-	+	+	A
M. C. 10:33	+	+	-	+	+	+	+	A
Do. 12.33	+	+	-	+	+	+	+	A
A. N. 11.33	+	+	-	+	+	+	+	A
I. R. 11.33	+	-	-	-	-	+	+	A
M. M. 11.33 1)	+	-	-	-	-	+	+	A
I. W.	+	-	-	-	-	+	+	A
J. N.	+	-	-	-	-	+	+	A
R. B. M.	+	-	-	+	-	+	+	A
S. Mastitidis	+	-	-	+	+	-	-	A
S. Infrequens	-	-	-	+	+	-	-	A
S. Equi	-	-	-	+	-	-	-	A
D. S. I.	-	-	-	-	-	+	+	-
D. S. II.	-	-	-	-	-	+	+	-
A. W. L.	+	-	-	-	+	+	+	A
A. W. R.	+	-	-	-	+	+	+	A
I. R. 1.34	-	-	-	-	-	+	+	A
J. S.	+	+	+	+	-	+	+	A

When these strains were grouped on the basis of their haemolytic powers, two large groups were formed. Group I contained those which showed B. haemolysis on blood agar and Group II those which were a. haemolytic in character. No non-haemolytic strains were examined in this manner.

Group I contained the following sections, named according to the typical reactions suggested in Topley & Wilson's Test book of Bacteriology.

Section I. Strains fermenting lactose, maltose and glucose with the formation of a clot and producing acid in litmus milk.

		Effect on Patient.
S.M. 11.33	Group form S. ANGINOSUS.	Cellulitis.
I.R. 11.33		Cellulitis.
M.M.I 11.33		Cellulitis & Acute Abscess formation.
S.M.I 11.33		Cellulitis.
I.W. 11.33		Surgical Scarlatina.
J.N.		Scarlatina.

Section II. Strains fermenting saccharose with the production of a clot, in addition the reactions of Section I.

G.P. 11.33	Group form S.PYOGENES.	Acute Arthritis.
S.M. 11.33		Cellulitis.
A.McD. 11.33		Cellulitis.

Section III./

Section III. fermenting as Section II with, in addition, mannite.

A.M.		Cellulitis.
M.C. 1) 10.33	Group form S. PYOGENES.	Cellulitis.
K.C. C. 11.33		Erysipelas.
J. McL.		Scarlatina.

Section IV. Reacting only with lactose, salicin, maltose, glucose and litmus milk.

K. C. F.		Erysipelas.
M. M. 2) 11.33	Group form S.PYOGENES	Cellulitis, Acute Abscess Formation.
R.B.M.		Nil

Section V. Strains fermenting, lactose, saccharose, salicin, mannite, maltose and glucose, and producing acid in litmus milk.

M. C. 10.33	Group form S. INFREQUENS.	Cellulitis.
M. C. 12.33		Cellulitis.

Section VI. Strains fermenting lactose, mannite, maltose and glucose with the production of acid in litmus milk.

A. W. (L. ankle)	Probable group form S.INFREQUENS.	Cellulitis.
A. W. (R. ankle)		Cellulitis.

Section VII. Strain fermenting only maltose and glucose and producing acid in litmus milk.

D. S. I.	Impossible to name.	Nil.
D. S. II.		Nil.
I. R. 1.34		Cellulitis very slight.

Finally there was one strain (J.S.) recovered from the throat of a patient with Scarlatina which fermented lactose, saccharose, raffinose, salicin, maltose and glucose with the production of a clot and produced acid in litmus milk. In view of this reaction the culture tested was thought to have contained strains of S. viridans in addition to S. haemolyticus.

For the purpose of comparison three type cultures were also subjected to the test. Their reactions were -
S. Mastitidis. A. C. in lactose, salicin, mannite, maltose, and glucose and A in litmus milk.
S. Infrequens. A. C. in salicin, mannite, maltose and glucose and A. in L.M.
S. Equi. A. C. in salicin only.
Group II contained the few strains which were haemolytic in nature. All three fermented lactose, saccharose raffinose, salicin, maltose and glucose with the production of a clot, and acid in litmus milk. From this it was impossible to say more than that they were strains of S. viridans, a fact already elicited from the blood agar plate. Two of these strains were recovered from throats, one during an attack of scarlatina and one from a contact. The third was recovered from the faeces. Appended to each strain in Group I was a short note regarding its source and activity within the host and it shows clearly that the more active strains in a fermentative respect were cultured generally/

generally from lesions where the local upset was greatest. Decisive reactions were obtained with the majority of strains tested, notable exceptions being those falling into Sections VI and VII. Of these the strains falling into Section VII showed no evidence of virulence on clinical grounds. It was also worthy of note that the type cultures reacted as expected in the instances of S. equi and S. mastitidis but that S. infrequens failed to attack lactose for a typical reaction.

Utilising all the known features of these strains tables were made to see if the morphological and cultural characteristics were of differential value but the conclusion was drawn that these features were capable of too considerable variation. The value of the haemolytic test was upheld being only upset once as noted before.

At the onset of the sugar fermentation test doubt was entertained as to their value. Opinions were read which stated that the results were unstable and liable to variation with the medium in which the culture had been grown. In order to obviate this source of error all strains were cultured on a precisely similar manner and to obviate variations in the fermentative powers of the strains, each test was triplicated with, in all cases, similar results. Encouraged by these results an extension of the technique was made to include strains which had been grown previously on ordinary agar/

agar, blood agar and 3%, 6% and 9% glycerine agar. The results were once more uniform with very occasional variation and an opinion was formed that the biochemical tests appeared to offer an accurate and consistent differentiation between the strains which were being recovered during the course of the investigation.

Complement fixation tests were then applied to a further series of organisms, the method and technique employed again being that of standard laboratory practice. Each test was carried out in the form illustrated (V.1) and a positive result was noted only when lysis occurred throughout the full range of tubes. Forty-seven strains were selected including type cultures and tested using antisera produced against the type cultures. The results of these tests were tabulated.

EXAMPLE OF TEST CONDUCTED.

0.25 cc.	S.E.	+	0.05 cc.	I.S.	+	1	M.H.D.	C.	Incubated	+	1 cc.	S.R.C.	Result
"	"	+	"	"	+	2	"	"	with	+	"	"	
"	"	+	"	"	+	3	"	"	Frequent	+	"	"	
"	"	+	"	"	+	4	"	"	Shaking for	+	"	"	
"	"	+	"	"	+	5	"	"	90 minutes at 37°C.	+	"	"	

S.E.= Streptococcal Emulsion. I.S. Immune Serum.
C.= Complement. S.R.C. Sensitised Red Corpuscles.

TABLE 17.

Name.	S.pyog.	S.inf.	S.equi.	S.eng.	S.Sal.	S.Faec.
H. McK. 10.34	+	+	+	-	-	-
W. G. 10.34	-	+	-	+	-	-
A. C. 10.34	-	+	-	-	-	-
S. M.	-	-	+	-	-	-
J. B.	+	+	-	-	-	+
M. McC.	-	+	-	-	-	-
H. R.	-	-	-	-	-	-
J. S.	-	-	+	-	-	-
A. McD.	-	-	-	-	-	-
S.M. II.	-	-	-	-	-	-
S.M. III.	-	-	-	-	-	-
J. G.	-	-	-	-	-	-
R. P. 11.34	-	+	-	-	-	-
B.C.	-	+	-	-	-	-
H. J.	-	-	+	-	-	-
J. G.	-	+	-	-	-	-
M. B.	-	+	-	-	-	-
C. D. 11/34	-	-	-	-	-	-
M.McC.11.34	-	-	-	-	-	-
do. 3.35	-	-	-	-	-	-
C.D. 3.35	-	+	+	-	-	-
M. M.	+	-	-	-	-	-
I. R. I.	+	+	-	-	-	-
I. R. II.	-	-	-	-	-	-

Table 17. contd.

Name.	S.pyog.	S.inf.	S.equi.	S.ang.	S.Sal.	S.Faec.
J.A. 1.	-	-	-	-	-	-
B.H.	-	-	-	-	-	-
A. McM.	-	-	+	-	-	-
C.B.	-	-	-	-	-	-
A.McD. 'B'	-	+	-	-	-	-
W.G.	-	-	+	-	-	-
A.S.	-	-	-	-	-	-
G.D.	-	+	+	-	-	-
R.B.M.	-	-	-	+	-	-
J.P. 111.	-	-	-	-	-	-
M.H. 3.35.	+	-	-	-	-	-
R.K.	-	-	-	-	-	-
R.P. 3.3.35	-	-	-	-	-	-
J.B. 6.35.	-	-	-	-	-	-
H.McK. 7.35	-	-	-	-	-	-
D.McN.	-	-	-	+	-	-
C.H.	+	-	-	-	-	-

Based on the results of this test it was possible to form groups relating the various strains to the type culture.

Group 1./

Group I. Relating of S. erysipelatosis.
R.B.M. and D. McN. 7.35.

Group II. Relating to S. pyogenes.
M.H. 3.35. C.H. and M.M. 11.34.

Group III. Relating to S. pyogenes and
S. infrequens. I.R. 1.

Group IV. Relating to S. infrequens.
A.C. 10.34: A. McD. 'B': M. McC. 7.35
B.C.: R.P. 10.34: R.P. 3.35: J.G.:
and M.B.

Group V. Relating to S.infrequens and S.equi
H.McK. 10.34: W.G.: C.D. 1.35: and
C.D. 3.35.

Group VI. Relating to S. equi
S.M.: W.G.: H.J.: J.S.: A.McL.

Group VII. Indeterminate strains relating to none
of the type cultures.
H.R: M.McC.3.35: S.M. 11: S.M. III,
I.R. 11: J.A. 1: J.G: C.D. 11.34
B.H: M.McC. 11.34: C.B: J.P. 111,
R.K: J.B: 6.35 H.McK. 7.35: A.S.

That is, reasonably clear cut reactions were given in approximately one half of the strains examined.

Features of interest were:-

1. The large number of strains which appeared to be unrelated to the type cultures.

11. The strains which were related to 2 type cultures.

111./

111. The overturning of the haemolysis test on 2 occasions.

IV. The substantiation serologically of previously ascertained bio-chemical features (R.B.M.= S.pyogenes).

V. The classification as S.equi of one strain where the haemolysis test was doubtful.

The failure to relate each strain examined to a type culture resulted in an attempt being made to discover the relationship between the various strains which were isolated from the sinuses. This was done as in the previous instance utilising antisera prepared against selected sinus strains in place of those against the type culture. The results were tabulated and appear in Table 18.

TABLE 18.

Strain.	S.M.	M.M.	J.S.	I.R.	C.D.
W.G.	+	+	+	+	+
A.C.	+	+	+	-	+
S.N.	+	+	+	+	-
J.B.	+	+	+	+	-
H.R. 1.	+	+	1	+	-
J.S.	+	+	+	-	+
S.M. 11.	+	-	-	+	-
J.G.	+	-	-	-	-
R.P. 10.34	+	+	-	-	-
C.D. 11.34	+	+	+	+	+

TABLE 18. (continued)

Strain.	S.M.	M.M.	J.S.	I.R.	C.D.
C.D. 3.35	+	+	+	+	+
M.M.	+	+	+	-	-
M. McC. 1.35	-	+	-	+	+
I.R. 1.	+	-	-	+	-
I.R. 11.	+	-	-	+	-
J.A. 1.	+	-	-	-	+
A. McM.	+	+	-	-	+
A. McD. 'B'	-	-	-	+	-
W.G.	+	+	-	-	+
A.S.	+	-	-	-	+
G.D.	+	+	-	-	-
R.B.M.	-	-	-	-	-
M.H. 3.35	+	-	-	+	-
R.K.	+	-	-	-	-
R.P. 3.35	-	-	-	-	-
J.B. 7.35	+	-	-	-	-
D. McN.	+	-	-	-	+
C.H.	+	-	-	-	+
S.infrequens.	+	+	-	-	+
S.erysip.	+	+	-	-	-
S.faec.	+	-	+	-	+
S.pyogenes	-	-	+	+	+
S.equi	-	-	-	-	-

A considerable group association was shown amongst these organisms and in only a few instances was a clear relationship exhibited between the various strains. These isolated examples were -

I. J.A. 1. = C. D.

II. J.G.: R.K.: J.B.: = S. M.

III. A. McD. 'B' = I.R. 1.

Agglutination tests were then conducted. The dilutions used were 1 in 100, 1 in 200, 1 in 400 and 1 in 800 which were found by previous experiment to be within the titre of the various antisera but otherwise the technique was standard. The results were tabulated, numerals up to 4 being used to indicate the dilution at which agglutination was occurring.

TABLE 19./

TABLE 19.

Strain	S.pyogenes	S.infrequens	S.Mastitidis	S.Equi	S.Erysipelatosus	S.Salivarius	S.faecalis
H.McK. 10.34	-	-	11	-	1	-	111
W.G.	-	-	-	-	11	1	111
A.C.	11	-	-	-	111	-	-
J.S.	-	-	-	-	11	-	IV
J.G.	-	-	-	-	111	-	-
R.P. 10.34	-	-	-	-	-	-	-
C.D. 11.34	-	-	11	-	11	-	11
M.N.	IV	-	-	-	-	-	-
M.McC. 1.35	IV	IV	-	-	111	-	-
I.R. 1.	111	-	-	IV	11	-	1
I.R. 11.	IV	-	-	-	IV	-	III
J.A. 1.	IV	111	-	-	IV	-	-
A.McM.	111	-	-	-	111	-	IV

TABLE 19. (continued)

Strain.	S.pyogenes	S.infrequens	S.Mastitidis	S.Equi	S.Erysipelatosus	S.Salivarius	S.faecalis
C.B.	-	-	-	-	-	-	IV
A. McD. 'B'	-	-	-	-	-	-	III
W.G.	II	-	-	-	II	-	III
G.D.	III	-	-	-	IV	-	-
R.B.M.	-	-	-	-	IV	-	-
R.K.	II	-	-	-	III	-	IV
J.B. 6.35	II	-	-	-	IV	-	II
H. McK. 7.35	-	-	-	IV	II	-	-
C.H.	II	-	-	-	IV	-	IV
D.McN.	-	0	-	IV	IV	-	III

Group agglutinins were common yet full agglutination occurred with a considerable number of the antigens.

The type cultures, on these tests, were capable of differentiation with the exception of S.salivarius. In 2 instances (S.erysipelatosus and S.equi) these tests appeared to give a clear line of demarcation but in other 3 (S.pyogenes, S.faecalis and S.infrequens) the complement fixation tests allowed a wide relationship which was annulled by the agglutination test. It was interesting to note that S.pyogenes and S.faecalis were indistinctly separated. The serological reactions of S.salivarius were general and non-specific.

Of the other strains of streptococci which were examined in a similar manner, two which were recovered from sinuses and were similar on morphological and cultural grounds were consistent in their reactions. These strains were M.M. 11.34 and D.McN. 6.35 and corresponded respectively with S.pyogenes and S.erysipelatosus. Only one other strain, recovered from a throat in health and situated in group III, was clearly demarcated. This was strain R.B.M. which corresponded with S.erysipelatosus. The remainder of the organisms examined appeared to lack specific characters and beyond being able to say that a close relationship existed between them and other members of the group S. haemolyticus, was impossible on their reaction.

Confusion occurred in some instances where a strain/

strain related to the group S. haemolyticus on one test was more closely allied to group S.faecalis on another and vice versa.

In view of the inability of the preceding tests to differentiate the various strains of streptococci which were recovered from the sinuses absorption-agglutinin tests were carried out amongst the 6 strains against which antisera had been prepared. The results were entirely negative each antigen being capable of absorbing the agglutinin present in the antisera against which it was being tested.

The lack of specificity amongst these sinus strains was thought to be due to their avirulent nature, a feature which was suspected from the almost exclusive appearance of a colony form on culture which coincided with the 'smooth' form described by Cowan. Variants on this colony form were rare but occurred on 3 occasions. In one of them the 'rough' variant was virulent on injection into a mouse whereas the colony exhibiting the more common 'smooth' features was avirulent.

It appeared that the sinuses were infected with streptococci largely belonging to the group S. haemolyticus and therefore potentially pathogenic, although their appearance on culture and their reaction on testing indicated that their pathogenic power was low.

OTHER ORGANISMS IN ASSOCIATION WITH STREPTOCOCCI.

Hitherto mentioned only in passing, organisms other than streptococci were recovered from the sinuses which were investigated. These were mainly varieties of staphylococci and diphtheroid bacilli with a few coliform bacilli and some others which it was found impossible to name. Gross statistics revealed that these organisms were recovered in the following numbers.

Staphylococci	86
Diphtheroid bacilli	21
Coliform bacilli	6
Others	5

Whilst these bacteria were not made the subject of an investigation so detailed as that in the case of the streptococci, steps were taken towards establishing a particular identity in many instances.

Staphylococci, the largest group, were subjected to the following tests.

(I) The colour of the colonies grown on an ordinary agar plate for 24 hours at 37°C. was noted in all instances.

(II) Several strains were examined biochemically, utilising a range of sugars and glucosides similar to that in the case of the streptococci.

(III) A few strains were tested for virulence, by injecting/

injecting 0.5 cc. of a 24 hour broth culture into a mouse (intraperitoneally).

The first test revealed that there were 20 strains of staphylococcus aureus, 65 strains of staph. albus and 1 strain of staph. citreus. Acknowledging the general opinion that staph. aureus is the most pathogenic with staph. albus as a very feeble pathogenic and staph. citreus a non-pathogenic saprophyte, it was inferred that the majority of the sinuses were infected with strains potentially pathogenic. The relative incidence of aureus to albus strains modified this inference by indicating that the pathogenicity was of a low order. The marked rarity of strains classified as staph. citreus was of interest, it being expected that a variety which abounds on the skin surface would be present in a greater incidence.

Strains examined under the second heading were eleven in number. Here the wide fermentative powers of the staphylococci necessitated the adoption of a classification outlined in the M.R.C's System of Bacteriology. Utilising mannite fermentation as the differential factor and neglecting colony pigmentation this method delineates four varieties of staphylococci: (1) Pyogenic. (2) Skin. (3) Scurf A and (4) Scurf B.

From the eleven strains examined 9 were 'pyogenic' and two were 'skin'. Introducing the previously noted feature of pigmentation the 'pyogenic' strains were 'albus'/

'albus' in 6 instances and 'aureus' in three and the 'skin' strains were 'aureus' in one instance and 'albus' in the other. In this latter respect a loss of virulence would account for the presence of an aureus strain which did not ferment mannite. From these tests it was felt that the majority of the strains isolated were potential pathogens in view of the high percentage classified as 'pyogenic' in a non-selected sample.

The third test was applied to 8 strains, three of which were 'aureus' and the remainder 'albus' on the pigmentation test (one of the latter was 'pyogenic' biochemically). None of these eight strains tested were virulent biologically. The animals used were mice as rabbits were not available for this test despite their known greater suitability.

From an aggregate of all the features it was concluded that the sinuses were largely infected by potentially pathogenic staphylococci but that this power was very low.

The next largest group of organisms isolated were the diphtheroid bacilli where 21 strains were isolated in pure culture. The differential features utilised here were:

(I) Morphological; the appearance of a 24 hour aerobic growth at 37°C. both on an ordinary Agar plate and on Loeffler's serum.

(II) The appearance of the bacilli in these colonies when stained by Grams' and Pugh's methods.

(III)/

(III) The Biochemical features over the same range of sugars as the staphylococci and the streptococci and

(IV) The virulence in mice utilising quantities as before.

Unfortunately these organisms proved more diverse in their characteristics than any of the others recovered. Finally from the data of section (1) and (2) above, 19 strains were divided into 6 groups as follows:-

Group I.

One example.. Circular smooth surface, 1 mm. diameter colonies on Loefflers medium. A similar growth with a rough surface on ordinary agar. Typical Chinese letter arrangement, of Gram Positive Bacilli which were stained uniformly by Pugh's stain with the exception of a clear central septum.

Group II.

Two examples. Loeffler: Circular irregular edged rough surface colonies 1 mm. diameter; Ordinary agar: small pin point colonies. Gram positive: Pughs: medium size uniformly staining rods.

Group III.

Two examples. Loeffler: Large, flat, shiny colonies. Ordinary agar: A similar growth with irregular edges. Gram positive. Pughs: Small uniformly staining bacilli.

Group IV./

Group IV.

Loeffler. Shiny, opaque, convex up colonies 1 mm. diameter. Ordinary agar: A similar but less luxuriant growth. Gram positive. Pughs: Generally small uniformly staining rods with pleomorphic forms exhibiting granular marking and occasional Bipolar staining.

Group V.

Loeffler: Large irregularly circular flat, shiny colonies, naples white in colour: Ordinary agar: A similar but less luxuriant growth. Gram positive. Pughs: Large uniformly stained bacilli with a few markedly granular variants.

Group VI.

Loeffler: Small white stringy colonies. Ordinary agar: similar but less luxuriant growths. Gram positive. Pughs: Small slightly curved bacilli uniformly stained.

It will be noted that only 19 strains were thus classified. The two remaining were insufficiently examined to admit of this differentiation.

The biochemical features were ascertained in thirteen of the nineteen strains grouped above and when related to the morphological and cultural characteristics gave the following results.

Group I.

The organism which gave these features was C. Hoffmann.

Group II./

Group II.

Each of the two strains gave different fermentation reactions.

Group III.

Similar to Group II. One of the strains fermented saccharose whereas the other did not.

Group IV.

Contained a number of different biochemical results only two strains being similar.

Group V.

4 strains giving rise to two pairs similar biochemically.

The strains in Group VI were not examined biochemically.

The features adopted for classification were those suggested in Topley and Wilson's Principles of Bacteriology and immunity resulting in the exact definition of one strain only. In view of this, recourse was had to the groups suggested by Andrewes (M.R.C. Monograph 1923) resulting in two of the *sinus* strains falling into his suggested Group V and Group VI. The fermentative features of the various strains examined are shown in the accompanying Table:-

TABLE 20.

REACTIONS IN HISS' SERUM WATER.

Strain No.	Lact.	Sacc.	Raf.	Inulin	Sal.	Mann.	Malt	Gluc.	Glyc.	Lit.Milk
I.	A	-	-	-	-	-	A	A	-	SL.A.
II.	A	A	-	-	-	-	A	A	-	SL.A.
III.	-	-	-	-	-	-	A	A	-	SL.A.
IX.	A	A	-	-	-	-	A	A	-	SL.A.
XI.	A	-	-	-	-	-	A	A	-	-
XII.	A	-	-	-	-	-	A	A	-	-
XIV.	A	-	-	-	A	-	A	A	A	-
XV.	A	-	-	-	-	-	A	A	A	-
XVII.	A	A	-	-	-	-	A	A	-	A
XVIII.	A	-	A	A	-	-	A	A	-	-
XX.	A	-	-	-	A	-	A	A	A	-
XXI.	A	-	-	-	-	-	A	A	A	-

A conclusion was formed that the diphtheroid bacilli infecting the sinuses were different in their reaction from the various strains recorded in the literature.

The foregoing details were of academic interest only but the virulence test, utilising mice as before, was of practical importance and the results showed that of eight unselected strains, none were virulent. It was concluded therefore on these results that the sinuses were infected by a series of diphtheroid bacilli, including C. Hoffmann but that these were either saprophytic or of low pathogenic power. Their role within the tissues of the host will be more fully discussed in a succeeding chapter.

The third group of organisms isolated, much smaller than either of the foregoing, comprised the Coliform bacilli. These were 6 in number and were subjected to the routine biochemical laboratory tests for organisms of this group. So tested they were:

(I)		B. pneumoniae	(Friedlander)
(II)	N.S.10/33.	B. Neapolitanus.	(Emmerich)
(III)		B. rhinoscleromatis.	
(IV)	M.L.10/34	B. proteus. vulgaris.	
(V)	D.McN.3/34.	B. Neapolitanus.	(Emmerich)
(VI)	M.McV.12/34	B. Neapolitanus.	(Emmerich)

All of them were recovered from lesions opening upon/

upon the abdominal wall, upper thigh or buttocks. In one instance a faecal fistula was forming and in another they were recovered from a healing appendicectomy wound. A feature of note was their remarkable scarcity.

Finally there were the organisms isolated but unidentified. They were 5 in number and presented the following features.

Series I.

A small Gram positive bacillus, which grew sparingly under aerobic and anaerobic conditions on ordinary media, produced a slight but uniform turbidity on ordinary broth and grew sparingly in blood agar plates without any action on the corpuscles, was recovered in 3 instances. One strain was from a healing sinus and was present in association with a few streptococci. The other two were from sinuses very early in their course and were obtained in pure culture. Tests on sugar ranges suitable for Coliform bacilli or streptooccci failed to reveal any fermentative powers. They did not grow on McConkeys agar. In two instances they were tested for virulence in mice and found **avirulent**.

Series II.

The other two examples were Gram positive diplocccci, lanceolate in shape, capsulated and producing a haemolysis on blood agar plates. One grew in the presence of bile and fermented inulin but the absence/

absence of a virulence test made it impossible to call the organism a pneumococcus. Subsequent attempts to recover this organism failed.

The other did not grow on bile and was so friable that it died out in 3 generations of culture. It grew both aerobically and anaerobically and was recovered on several occasions. It appeared to have no fermentative power on sugars and was avirulent when injected into a mouse.

That is, the sinuses investigated were open to a secondary infection by organisms other than streptococci but when these organisms were investigated bacteriologically they were found to be of low pathogenic power with the exception of the coliform bacilli.

An attempt made to discover which organism was most commonly present, and the results of 100 microscopic examinations of sinus exudates were collected. These results were tabulated (Table 21) showing that the most common organism and that present in greatest numbers in the discharge was the streptococcus, being followed by staphylococci and finally diphtheroid bacilli. It was also noted that a secondary infection was present microscopically in the vast majority of cases indicating that it was not a very minor feature recovered only as a result of careful culture of the pus from the sinuses. Another feature was the inability, with one exception, to discern tubercle bacilli/

bacilli microscopically although they were recovered biologically in many instances. Lastly the number 58 referring to streptococci does not indicate that in the majority of instances when they were seen they were present in a degree much greater than occurred with any of the other organisms.

T A B L E 21.

No. of Examinations	100
No. showing secondary infection microscopically	77
No. of occasions on which Orgs. were seen:-	
I. Staphylococci	31
II. Streptococci	58
III. Diphtheroid Bacilli	6
IV. Others	2
V. Tubercle Bacilli	1

Some attention was also paid to the cytology of the discharge, and it was noted that in the majority of instances this resembled that of an acute inflammatory process. In fact, over a series of examinations of any particular sinus it was noted repeatedly that, as a secondary infection appeared, the discharge lost its tuberculous character gradually. In cases where this infection was by staphylococci or diphtheroid bacilli this feature was often not marked although present to some degree but in almost each instance where a streptococcus was recovered it was a marked feature. An example of such an occurrence was selected and is seen in Table 22.

T A B L E 22.

DATE	INFECTION RECOVERED.				CELL-TYPE OF DISCHARGE.						
	Staph.	Strep.	Diphs	Others	Poly	Mono	Lymph	Tissue Cells.	R.B.C.	Phago-cytosis	Debris
17/11/33	-	-	-	-	-	++	+	+	-	-	-
1/12/33	-	-	+	-	+	+	+	-	++	-	+++
1/2/34	-	++	-	-	+	+++	-	-	-	-	-
19/3/34	-	++++	-	-	+++	++	-	-	-	++	-
10/11/34	++	+	-	-	++	+	+	-	++	-	-

TABLE 23.

VERTEBRAE.

Name	Age	Site of Dis.	Onset of Sinus	TIME OF EXAMINATION IN MONTHS AND ORGANISMS RECOVERED. 1	2	3	4	5	6	7	8	9	10	-11	-12	-15	-18	21	24	2 years & over.
I.L. C		CV.4-7	25/ 2/32														*	*	*	*Capsulated Cocci.
R.K. C.		CV.7 DV.1	6/ 2/34													*St Alb. B.Haem. Strep. Diph.		Sterile (Unnamed)		
P.P. O		CV.4-7	9/ 2/33		*Staph.Alb															
J.S. C		CV.6-DV.1	?																	*Staph.Alb. Strep.(Non haem.) *Sterile.
J.B. O		CV.4-6	32																	
P.O. O		DV.1,2,3.	11/ 6/34				*Staph.Alb.													
I.R. C.		DV.5-10	1929/30																	*Streps.i)Do.ii)S.Anginosus * i)B.Haem. * i)B. ii) B.Haem. Staph Alb.
W.McD.C		DV.4-6	1930																	*Streps (B)
M.G. O.		DV.12 LV.1.	1/34		*Staph Aur.															
Do. C.		Do.	30/ 4/35			*Staph.Alb.														
A.McM.C		DV.10 LV.1	21/ 4/33			*Staph.Alb.(P)						Staph.Alb.(P) *Diph.							*Staph.Alb. Streps.(B)	
J.McB.O		DV.12 LV.1 & 2.	28/11/33			*Staph. (Alb) Diph.														
N.S. C.		DV.12 LV.1 & 2.	8/ 9/33			*Streps										*Streps.				
D.M. C.		LV.1-5	23/ 6/31 9/ 6/31														*Staph.Alb. Streps.			
N.S. C.		LV.3-5	7/ 1/31																	*Streps(?) Diph.B. Coliform Bacilli. (2)
A.G. C.		L.V.4	27/ 2/33											*St.Alb. Streps (non haem)				*St.Alb		
A.McN.C		LV.4	1/ 5/33									*Staph.Alb Diph.					X Streps (not cultured)			
H.R. C.		LV.3-4	15/11/32																	*Staph.Alb. Streps.I & II B.Haem.
J.S. C.		LV.4-5	14/12/34				* *		*Streps.All B.Haem.											
M.L. C.		LV.2-3	10/34		B.Proteus Vulg. *Staph.Alb. Strep. ?															
M.M. C.		Sacro-Iliac.	1930																	Staph.Alb. *Strep.(?) (*Diph. *Strep 10/34 (Groin B.Haem. (
C.		Do.																		Staph.Aur. B.Haem.Strep.*11/34. (Rt.Leg
D.McN.C		Do.	2 /11/31														*Staph Alb. Coliform	*Staph		(Thigh
Do. C		Do.	6 / 8/32																	*Streps i)ii)non haem. (Groin *Staph.Aur.
J.B. O.		Sacrum	11/10/34	*Sterile																*Streps. B.Haem.
P.A. O.		LV3-5	9/30.																	*Staph. Alb.

The reaction of the tissues of the host was also estimated from the degree of phagocytosis which was occurring. In about 30% of cases this feature was present in varying degree and generally in response to an infection by streptococci. In numerous instances however the invading organism seemed to have the upper hand, destroying the attacking cells. The more general lack of antagonism to staphylococcci and diphtheroid bacilli was felt to underline the saprophytic or lowly-pathogenic role they filled in the sinuses as indicated bacteriologically earlier.

The combination of these organisms in the sinuses was also of interest and in order to illustrate this point each area was taken separately.

TABLE 23 - opposite.

The results of examinations of sinuses arising from tuberculosis of the vertebrae were shown in Table 23 related to the period of time at which the examinations were made. Clearly shown was the fact that the bulk of these cases were investigated at periods around 2 years or more after the inception of the sinus and that those examined at periods earlier than this harboured mainly staphylococci in pure culture or staphylococci in association with diphtheroid bacilli. In four out of fourteen instances streptococci were recovered/

recovered in pure culture and only in two sinuses.

Staphylococci were recovered in pure culture in five instances and only within the first four months of the course of the sinus. One very early examination showed the sinus to be free from secondary infection whereas another showed the association of staphylococci and diphtheroid bacilli. This combination appeared in 3 instances in all, the other two being in the eighth and ninth months of the course of a sinus. The association of staphylococci with streptococci, non haemolytic in character, appeared for the first time in the twelfth month. The examinations which were conducted later showed more examples of the presence of streptococci, mainly B. haemolytic in pure culture, of staphylococci in association with streptococci (again mainly B. haemolytic) and fewer examples of staphylococci in pure culture or in association with diphtheroid bacilli. In other words streptococci were present in greater numbers in the sinuses which were examined after a prolonged period of activity, a feature which will be referred to again.

TABLE 24.

HIP JOINTS.

TIME AND RESULT OF EXAMINATIONS.

No.	Name.	Site of Disease.	Date of formation of Sinus.	1	2	3	4	5	6	7	8	9	10	11	12	15	18	21	24	2 years & over.
I.	M.M. C.	R.Hip.	17/10/32				*Streps.	10 S.Anginosus 11 S.Pyog.										Staph.Alb. *Streps. B.		P.M. Streps.
2.	P.T. C.	R.Hip.	5/12/33	*Sterile *Streps.(non) St. Alb.			*Streps B.			*Streps B.			*Streps B.							
3.	J.B. C.	R.Hip.	7/12/33	*Streps (B)													*Staph.Alb. Streps (B)			
4.	R.L. O.	R.Hip.	1/12/33					*Staph.Alb. Streps (mainly anaerobe)												
5.	C.H. O.	R.Hip.	10/ 3/33							*Straph.Alb. (P)							*Staph.Alb.(P) Streps.		Doubtful.	
6.	J.F. C.	R.Hip.	2/31																	*Staph. Alb.
7.	W.G. O.	R.Hip.	3/34				*St.Alb. Streps (B)													
8.	M.McC.C.	R.Hip.	14/ 9/34		*B Streps. *Streps.				*B Streps.											
9.	M.H. C.	R.Hip.	12/34	*Sterile			*Streps.(B)				*G-ve Bacilli Few Streps.									
10.	J.McL.O.	L.Hip.	1/ 6/35	*Sterile.																
11.	C.D. C.	L.Hip.	10/34	*Staph.Alb. Streps.					Staph.Aureus. *Streps. B.											
12.	W.K. C.	L.Hip.	16/12/32										*Staph.Alb. Streps.(non haem.) 3 strains.							
13.	J.B. C.	L.Hip.	2/ 4/31																	*Streps. (B)
14.	W.L. O.	L.Hip.	25/12/33			*Staph.Aureus. Diph.														
15.	M.P. C.	L.Hip.	22/ 6/33.					*Streps B.			*Streps B.					*	*Sterile.			
16.	J.A. C.	L.Hip.	13/12/31.	2 years *Streps (did not grow) Dipths.						9 months later only (onset of cellulitis)				B.Haem.Streps.				Do. 6 months. later still.		A.*Streps.B. (doubtful) Diph. B.*Streps.B. C.*Streps.B.
17.	M.S. C.	L.Ilium	8/34										*Sterile.							
18.	A.S. O.	L.Ischium	9/34.	*Staph.Alb. Streps. (non haem.)																

TABLE 25

KNEE JOINT.

TIME AND RESULT OF EXAMINATIONS.

No.	Name	Site	Onset of Sinus.	1	2	3	4	5	6	7	8	9	10	11	12	15	18	21	24	2 years & over.
1.	M.B. C.	L.Knee	9/11/33	*Sterile Diph.		*Strep. B.	*St. Alb. Strep. B								*St. Aureus. Streps B.					
2.	B.H. C.	L.Knee	19/10/33	*St Alb. Diph.						St.Alb. *Diph. Streps (Could not culture.)					*Steps (B)					
3.	M.C. C.	L.Knee	5/ 6/34	*St Alb. Streps	(B)															
4.	" C.	R.Knee	5/ 6/34	*St Alb. Streps	(B)															
5.	W.H. C.	L.Knee	12/34							*St.Alb. St.Citreus Strep. (unknown) B.Proteus "										
6.	A.C. P.	R.Knee.	8/34							*Sterile.										
7.	M.C. C.	R.Knee.	14/8/33	*Streps.(S.Inf.)			*Streps (S.Inf.)								*St.Alb.					
8.	G.P. C.	L.Knee. (lower end of femur)	18/ 8/33	*St.Aureus. Streps. (S.Pyog.)																

TABLE 24.

A similar table was made for sinuses arising from tuberculosis of the hip joints but in this example the majority of examinations were conducted within the first year and almost all within the first two years. Here the majority of sinuses were infected with streptococci, mainly B. haemolytic at an early stage in their course and no gradual change of type of infection was seen such as was exhibited in the case of the vertebrae. Three cases examined very early were free from secondary infection as were two at a very late stage. Only one example of the association of staphylococci and diphtheroid bacilli was seen whereas the association of staphylococci and streptococci was of frequent occurrence. Staphylococci in pure culture were recovered in two instances only, one fairly early and the other late. The onset of secondary infection in this area seemed to be much more rapid than in the case of the vertebrae.

Table 25 shows the results which were obtained when sinuses around the knee joints were examined.

TABLE 26

ANKLE JOINT

TIME AND RESULT OF EXAMINATION.

No.	Name	Site of Disease.	Onset of Sinus.	1	2	3	4	5	6	7	8	9	10	11	12	15	18	21	24	Over 2 years.
I.	I.G. O	L.Ankle (Soft tissue & bones)	14/11/33					*Sterile (Healed 1 month)												
2.	A.W. C.	L.Ankle (Soft tissue & bones also peri-ostitis.)	7/ 6/32															*Streps (B) (few)		
3.	A.W. C.	R. Ankle do.	24/ 9/32													*Streps B.	*St.Alb. Streps.B.			
4.	J.McI. C.	L.Ankle.	20/11/31																	*St.Aureus Streps. (Non Haem.)
5.	S.M. C.	L.Ankle (os calcis)	17/ 9/32													*St.Alb. Pneumococci Streps.(B.Haem.)				*St.Alb. St.Aureus. Streps.(strongly probable B.)
6.	J.G. C.	R.Ankle. Soft tissue.	18/ 6/34					*Streps (B)												
7.	A.M. C.	R.Ankle. (os Calcis)	4/31																	*Streps.(S.Pyog.)
8.	M.McC. C.	R.Ankle. (os calcis)	27/ 5/32																	i) Streps. B. St.Alb. * St.Aureus. ii) Streps. B.
9.	H.McK. C.	R.Ankle.	31/ 7/34			*Streps. (B)									*Streps. (B)					

In this instance, on account of the shorter course of the disease all examinations except one were conducted within 1 year of the formation of the sinus. The features were rather similar to those shown by hip joint sinuses but, in one instance the association of staphylococci and diphtheroid bacilli, being replaced later by B. haemolytic streptococci, was seen. Staphylococci were recovered in pure culture in one instance only, viz: the latest examination made, in a healing wound.

Sinuses arising from the ankle joint were examined at a period mainly after one year's duration and here the features noted previously were reversed.

TABLE 26..

TABLE 27

ARM LONG BONES.

TIME AND RESULT OF EXAMINATIONS.

No.	Name		Site	Date of Onset.	1	2	3	4	5	6	7	8	9	10	11	12	15	18	21	24	2 years & over
1	D.P.	C.	L.Tibia	27/ 6/33							*St.Alb. Strepe. (B)										
2.	S.M.	C.	L.Tibia.	9/33	*Staph.Alb.(P) Strepe.i) S.Ang. ii) S.Prog.							*St.Alb. (P) Strepe. (B)									
3.	A.McD.	C.	R.Fibula.	28/ 8/34												*Streps.(B)					
4.	J.G.	C.	R.Humerus	18/ 6/32						*Staph.Alb.											
5.	J.S.	O.	Humerus	3/35			*St.Alb.														
6.	R.McK.	O.	L.Elbow	26/9 /34	*Sterile																
7.	H.J.	C.	R.Humerus (lower ⅓ elbow.)	5/11/34	Staph.Alb. *Streps.(B)																
8.	J.McL.	O.	R.Ulna	1/ 6/33									*Streps.(B)								
9.	T.S.	C.	R.Elbow	About 1930.																	*St.Aur.
10.	A.K.		L.Tibia	9/33		*Staph.Aur (Skin) Diph. Streps. Non Haem.															
11.	G.D.	G.	L.Tibia lower ⅓.	5/11/34	*Sterile *Strepe. (B) * do. (B)																
12.	G.J.	C.	Remur R.	10/ 4/34						*Strepe. (B)											

TABLE 28

DACTYLITIS.

TIME AND RESULT OF EXAMINATIONS.

No.	Name.		Site.	Sinus Onset	1	2	3	4	5	6	7	8	9	10	11	12	15	18	21	24	2 years & over
I.	M.L.	O.	Left 2nd metacarp. & prox. phalanx.	7/33				Staph.Alb. *Strepts. Non. Haem.													
2.	R.McM.	O.	L. 5th prox. phalanx & Hand.	5/34		*G-ve bacilli.															
3.	N.P.	C.	Prox.Phalanx 3rd.Finger.	2/34	*St.Alb.																
4.	B.C.	C.	Prex.Phalanx L. Thumb.	5/34						*Streps (B)											
5.	M.C.	C.	L. Hand 3 & 4 Metacarp.	4/33								*Streps.B.(Spyog.)									
6.	A.McD.	C.	L.Cuboid.	8/33		Staph. *St.Aureus Diph. *St.Alb.Pyog. St.Alb.Skin.	*Streps.(very friable)St.Aur							*St.Alb. Streps.B.Haem.	S.Ang.						*B.Haem.Streps.	
7.	R.P.	C.	Rt. 4 & 5 Metatarsals.	8/34		*Streps.(B)					*St.Alb. St.Aureus. Streps.(B)										
8.	D.S.	C.	Rt. Cuboid.	26/7/32														*St.Aureus. Diph. i) Strepsii) B. Haem.			
9.	J.B.	C.	Rt.Navicular	11/33	*St.Aureus.					*Streps.(B)									*Streps. (B)		
10.	M.C.	C.	Metatarsus.	4/33								*Streps. (B)									
11.	R.S.	O.	L.1st Metatars	10/33	*Staph.Alb. Diph.																
12.	T.H.	O.	Rt.Prox. Phalanx 1st Toe	6/33						*Sterile											
13.	A.C.	O.	L.1st Meta-tarsal.	1/32																*S.Alb.	

The earlier examinations demonstrated the presence of B. haemolytic streptococci in pure culture and only those conducted at a later stage yielded mixed cultures of staphylococci and streptococci. No instance was found of staphylococci in pure culture or even of the presence of diphtheroid bacilli in the lesions. One sinus was free from secondary infection and this sinus was a very minor one which healed within one month after the examination.

The secondary infection recovered from sinuses arising from the long bones were very variable and are shown in Table 27. . Once again all examinations except one were conducted within the first year of the course of the sinus. Staphylococci were recovered in pure culture in 3 instances, two early and one late, and all in healing wounds. Diphtheroid bacilli were recovered in one instance only and that early and in association with a staphylococcus and a non-haemolytic streptococcus. Two sinuses were free from secondary infection, both being examined very early in their course. One of these healed quickly but the other became infected by B. haemolytic streptococci before a month had elapsed. Streptococci in pure culture and in association with staphylococci were the commonest infection, the streptococci being all B.haemolytic.

The features of the results of examination of sinuses/

TABLE 30.

MISCELLANEOUS LESIONS.

TIME AND RESULT OF EXAMINATIONS.

No.	Name.	Site of Disease.	Onset of Sinus.	1	2	3	4	5	6	7	8	9	10	11	12	15	18	21	24	2 years & over
		ABDOMINAL T.B.																		
1.	J.McL. O.	T.B.Abdomen					*St.Alb.													
2.	W.A. C.	do.	6/ 7/33								*Streps. Non Haem.									
3.	M.M'V. O.	do.	10/12/34	*Coliforms																
		MAXILLA																		
4.	R.McH. O.	Left.	6/34				*St.Aureus. St.Albus.													
5.	C.McC. C.	Left.	28/ 6/32														*Diph.i) ii)			
		MANDIBLE.																		
6.	R.B. C.	Asc.Ramus L.Mandible.	2/12/33				*Streps.(Non Haem.													
7.	E.A. O.	L.Mandible.	12/10/34	*Staph.Alb.							*Sterile.									
		RIB.																		
8.	S.N. O.	R. 7th.	2/10/34	*St.Albus.																
		PERINEPHRIC ABSCESS.																		
9.	E.B. C.	Right.	7/ 8/33						*St.Aureus St.Albus.											

sinuses of the hands and feet were seen in Table 28 and no hitherto unremarked feature was noted. The change of secondary infecting organisms over a period was shown very well in one instance.

Glandular and soft tissue tuberculosis gave rise to sinuses which ran a short course hence all the examinations took place within one year. Two sinuses had no secondary infection and both were healing at the time of the examination. One sinus showed the transition when healing from a pure infection with streptococci to an infection by staphylococci. A rare example of the association of diphtheroid bacilli and a B. haemolytic streptococcus occurred and only in one instance was there an association between staphs, and streps. The general tendency appeared to be for whatever organism was present in the sinus to remain there in pure culture. These features are seen in Table 29

Sinuses which arose from miscellaneous parts were outstanding in the almost complete absence of streptococci. These organisms were present on only two occasions, both times in pure culture and both were non-haemolytic. Staphylococci were recovered in pure culture on 5 occasions, diphtheroid bacilli on one, and staphylococci combined with coliform bacilli on one other occasion. There was also an example here of an infected sinus becoming 'sterile' in the process of healing. Table 30 illustrates these facts.

As/

As a result of these tables it was seen that different sites varied in the rapidity with which infection gained ingress (for example vertebral and miscellaneous sinuses c.f. knee or hip joints) but that the most common early infection was one by staphylococci alone. At a later stage these were sometimes joined by diphtheroid bacilli but much more commonly by streptococci and that streptococci in association with diphtheroid bacilli were seen very rarely. There was a tendency for streptococci to persist as an infection and at times to banish the other organisms from the sinuses. Further, it was noticed that sinuses which were healing or almost healed tended to be free from secondary infection or contain staphylococci in pure culture, even in instances where, for a long period of their course, the secondary infection was a streptococcus. These features related to the microscopic evidence regarding the type of organism most commonly present and the bacteriological evidence of the nature and virulence of the organisms other than streptococci led to a conclusion that these latter organisms were the most potent of the secondary infections. That is, the others were purely incidental.

The clinical data on this statement will be given later.

THE EFFECT OF INFECTION.

Tuberculosis is commonly a chronic illness and the non-pulmonary type with which the investigation deals proves no exception to the rule. Cases admitted to hospital for treatment remain there for varying periods of time which periods may be increased by the occurrence of any untoward complications in the course of the illness. Such a complication is a formation of a sinus a feature common to the majority of cases which have been discussed previously. A survey of the cases revealed that residence was prolonged in many instances but that the figures varied according to the site of the primary tuberculous lesion. The lengths of time over which sinuses remained patent when they arose in each area were estimated approximately and tabulated and compared with the average duration of residence of all cases of disease in a similar area which were dismissed from the hospital in which the investigation was conducted.

TABLE 31./

TABLE 31.

Cases with Sinuses.			All Cases.
Site of Tuberculosis.	Duration of Sinuses.	Average duration of sinuses.	Average Residence.
Vertebrae	2 yrs.- 10 yrs.	4 yrs. approx.	800 days approx.
Hip joints	4/12 yrs.- 6 yrs.	2½ yrs. "	770 " "
Knee joints	7/12 yrs.- 1 7/12 yrs.	1 yr.. "	600 " "
Ankle joints	8/12 yrs.- 3 yrs.	2½ yrs. "	570 " "
Long bones	4/12 yrs.- 2 yrs.	1½ yrs. "	400 " "
Dactylitis	6/12 yrs.- 3 yrs.	1 yr. "	400 " "
Glands etc.	1/12 yrs.- 1 5/12 yrs.	6/12 yrs. "	230 " "
Miscellaneous	4/12 yrs.- 1 yr.	5/12 yrs. "	No comparable figures.

From the table it will be seen that sinuses sometimes remain patent for very long periods and that in disease of some areas the sinuses remain patent for periods in excess of the average total duration of treatment of all similar cases. This feature is most marked in disease of the vertebrae and of the ankle joints and to a minor degree in the lesions of the hip joints.

In disease affecting the knee joints and dactylitis the opposite pertains and in lesions of the long bones and of glands or soft tissue the periods almost synchronise. A possible explanation of the figures for knee joints lay in the fact that much time is expended in this particular lesion in excising the joint after the lesion has healed thus adding appreciably to the period of residence. Similarly in the instance of dactylitis this lesion is often multiple and dismissal may be impeded either by a fresh lesion forming or by one of multiple lesions not healing quickly. Lesions of the long bones and glands share the common feature of a very high incidence of abscess and sinus formation (approximately 80% of all cases) thus rendering the cases within the scope of the investigation almost typical of the disease as it occurred generally. Generally speaking however sinus formation prolonged the residence of the cases and was therefore/

therefore an important factor in the economics of treatment.

Regarded from another aspect the table reveals that these patients had open wounds over periods of years which were, as has been shown, infected with pyogenic bacteria. These organisms were not entirely saprophytic but attacked the tissues of the host giving rise to disturbances called 'acute complications' which were relatively frequent and serious. The complications were 6 in number and were:-

1. Toxaemia.
2. Cellulitis, superficial and deep.
3. Acute abscess formation, tracking from a sinus.
4. Acute lymphadenitis.
5. Erysipelas.
6. Surgical Scarlatina.

Their degree varied markedly. Toxaemia, for example was a marked feature throughout the course of some cases whereas in others it was slight and transitory. Its presence was gauged from the temperature of the patient in the absence of any other disturbance such as marked cellulitis. Cellulitis was often present in the skin surrounding the sinus mouth varying in extent from a small localised patch to an area many inches in diameter. In these instances particular care was taken to distinguish it from erysipelas. Its occurrence/

occurrence was not infrequent in the deeper tissues and presented a little difficulty in its differentiation from localised acute abscess formation in the depths of a sinus. This latter complication occurred most frequently in long sinuses which ran through a considerable mass of soft tissue and was felt to be due to the accumulation of pyogenic material in an inaccessible and undrained area of the sinus. When it occurred the process rapidly extended necessitating fresh incisions being made for drainage purposes. In areas which were the site of previous complications acute inflammation sometimes occurred in the lymph glands which drained the area and its occurrence, purely in response to the secondary infected, was noted. As already stated it was remarkably rare. The fifth complication, erysipelas, appeared on several occasions and like cellulitis it was very varied in degree. The most marked cases were two in number where a 'migrans' form of the disease involved an entire arm and leg respectively. Surgical scarlatina occurred in only one instance but was sufficiently marked to be worthy of record.

These features therefore, completely transformed the charts of the patients from those of children suffering from an illness of low toxicity into a likeness of those of sufferers from very acute illnesses. Their occurrence was noted in each case throughout its course and a table constructed relating their occurrence to the type of secondary infection recovered from the sinuses.

TABLE 32.

Type of Infection.	Origin of Sinus.								Nature of Complication.
	Vertebrae	Hips	Knees	Ankles	Long Bones	Dactylitis	Glands etc.	Miscellaneous	
Section 1	1	4	-	-	1	-	2	-	Nil
Sinuses infected by strep-tococci	17	10	7	8	7	8	8	2	Toxaemia
	6	8	6	6	5	8	2	1	Cellulitis.
	3	10	5	2	1	-	-	-	Acute abscess formation.
	-	1	1	1	-	-	1	-	Erysipelas
	-	-	-	-	-	-	1	-	Surgical Scarlatina
Section 2	5	1	-	-	1	3	3	5	Nil
Orgs. other than strepto-cocci.	2	1	-	-	2	1	-	2	Toxaemia
Section 3	2	1	1	1	1	1	2	-	Nil
Sterile	-	1	-	-	-	-	-	-	Toxaemia

The table shows that the incidence of complications was highest in sinuses from which a streptococcus was recovered and that the only complication occurring in the other two groups was toxaemia. A straightforward statement based on these 'figures' that streptococci were the causal organisms of these complications was prevented by the occurrence in Section 1 of a few cases in which no complication occurred. These cases showed the following features.

1. J.S. Disease of cervical vertebrae; chronic in nature with an old discharging sinus. Secondary infection; a few non-haemolytic streptococci.
2. R.L. Bone disease of hip joint; healed clinically and radiologically with the temporary recurrence of a sinus. Secondary infection; a few anaerobic streptococci.
3. C.H. As R. L. Secondary infection; a few non-haemolytic streptococci.
4. W.G. Almost healed bone disease of hip joint. Abscess reappeared shortly after an attack of scarlatina and eroded its way through. Minimal discharge from resultant sinus which healed quickly. Secondary infection; few B. haemolytic streptococci.

5./

5. A.S. Bone disease of ischium; short open sinus which healed very rapidly upon removal of diseased bone. Secondary infection; few non-haemolytic streptococci.

6. J. McL. Bone disease of ulna which was removed entirely leaving an open gutter on the surface of the bone which remained clean and healed rapidly. Secondary infection; B. haemolytic streptococci.

7. J.McQ. Tuberculosis of glands of neck which were incised and thoroughly cleaned out and healed rapidly. Secondary infection; few non-haemolytic streptococci.

8. L.C. Small localised soft tissue abscess also thoroughly scraped out and healed rapidly. Secondary infection; few B. haemolytic streptococci.

In no instance therefore was the secondary infection gross and in most the suitable soil for the continued residence of the organisms was removed by eradicating the tuberculous focus. Also in four instances the streptococci recovered were non-haemolytic in type and it was a fortuitous combination of these factors which probably prevented serious complications.

A similar routine was undertaken with regard to the cases falling within Sections 2 and 3 of the table which/

which showed complications. Dealing firstly with Section 2 the cases presented the following histories.

1. I.L. Suffering from subacute tuberculosis of the cervical spine with an old standing profusely discharging sinus on his neck. Frequent examination yielded no bacteria but finally an unidentified Gram positive diplococcus was isolated before death. This organism was very difficult to culture and may have been present in the deeper parts of the sinus throughout.

2. M.G. Suffering from subacute disease of the dorso-lumbar spine with a recurrent sinus in the loin. Toxaemia became more marked after a bacteriological examination of the sinus had revealed only the presence of staphylocci and the probability of an added streptococcal infection was great. Unfortunately an examination of the sinus at this stage was impossible.

3. M.L. Suffering from acute tuberculosis of the lumbar spine with an abscess extending widely in the buttocks and pointing to a sinus in the natal cleft. Accurate isolation of secondary infecting organisms was nullified on account of the preponderance of B. proteus in the discharge. The toxaemia here was marked and the presence of streptococci in small numbers was suspected.

4./

4. J.F. A boy with a small sinus arising bone disease of the head and neck of femur and acetabulum which was almost cured at the time of examination. Culture revealed only staphylococci and there was no disturbance at the time of the examination. Cellulitis had occurred in the past when the lesion was very active and the possibility of an earlier streptococcal infection being present then and disappearing as the lesion healed was great. This feature was remarked upon earlier.

5. T.S. Suffering from disease of the elbow joint and displaying exactly the same features and history as case No.4.

6. J.G. Had extensive bone disease of the shafts of the humerus with a profusely discharging sinus which yielded only staphylococci. This case had a marked toxaemia and was thought to be one of osteomyelitis until the development of a tuberculous hip joint. The complication present was very possible on account of the extent of bone involved in the arm.

7. M.P. Suffering from dactylitis with very extensive destruction of soft tissue over the diseased bone. Here the examination was conducted early revealing only staphylococci but the area involved was sufficient to account for the toxaemia which occurred.

8./

8. E.P. With a perinephric abscess and a wide, feebly discharging sinus which yielded only staphylococci. These organisms formed a small acute abscess in the depth of the sinus, which, when incised, healed rapidly.

9. C.M. With extensive tuberculosis of the maxilla and extensive sequestration with a widely patent profusely discharging sinus which yielded only diphtheroid bacilli. In this instance toxaemia was slight and not incompatible with the facilities offered for absorption of toxins.

The conclusion was formed that these cases contained some in whom it was impossible to exclude the possibility of streptococci aiding the presence of the complication but also that there were some in whom staphylococci were exhibiting faint pathogenic powers.

Section 3 examined likewise revealed only one example of a toxaemia occurring and in this case it was so transient that it might have been brought about by any minor intercurrent infection.

Thus, in no instance, was any complication except a degree of toxaemia brought about in the absence of streptotocci. Positive proof of their pathogenic role was afforded when the bacteriological findings in a number of sinuses which had been examined in the course of an acute complication were tabulated.

TABLE 33.

VERTEBRAE.

Name.	Date of Complication.	Nature of Complication.	Date of Examination.	Organisms Recovered.
1 N.S.	11.33	Toxaemia	11.33	Streptococci
2 D.McN.	7.35	Cellulitis, acute abscess formation.	7.35	Streptococci
3 J.S.	6.34	Toxaemia	6.35	Streptococci
4 M.M.	10.33 5.34	Toxaemia, acute abscess formation	10.33 10.34	Streptococci Do.
		HIP JOINTS.		
5 P.T.	1.34	Toxaemia, acute abscess formation.	1.34 3.34 9.34	Streptococci Do. Do.
6 J.B.	General	Toxaemia	4.34	Streptococci
7 W.K.	General	Cellulitis Toxaemia	11.33	Streptococci ++++ St. Alb +
8 M.McC.	1.35	Acute abscess formation	11.34) 3.35)	Streptococci
9 C.D.	11.35 3.35 5.35	Acute abscess formation Erysipelas	10.34 2.35 4.35	Streptococci Streptococci ++++++ St. Aur +
10 M.H.	3.35	Acute abscess formation	3.35	Streptococci
11 M.P.	10.33	Toxaemia	11.33	Streptococci
12 M.M.	General	Toxaemia, cellulitis acute abscess formation	11.33 6.34	Streptococci Streptococci +++++ Staph +

TABLE 33 contd. KNEE JOINTS.

Name	Date of Complication	Nature of Complication.	Date of Examination	Organisms Recovered.
13 H.B.	1.34 6.34	Cellulitis and acute abscess formation	2.34) 3.34)	Streptococci
14 M.C.	10.33 11.33	Cellulitis Septic Arthritis	10.33) 12.33)	Streptococci
15 G.P.	9.33	Septic Arthritis	10.33	Streptococci +++++ Staph. few
		ANKLE JOINTS.		
16 J.G.	11.34	Cellulitis acute abscess formation.	11.34	Streptococci
17 M.McC.	General	Toxaemia, cellulitis acute abscess formation	5.34) 4.35)	Streptococci
18 A.M.	2.34	Cellulitis	2.34	Streptococci
19 A.W.L.	11.33	Cellulitis	11.33	Streptococci
20 A.W.R.	11.33	Cellulitis	11.33	Streptococci
21 H.McK.	General	Cellulitis do.	10.34) 7.35)	Streptococci

LONG BONES./

TABLE 33 contd. LONG BONES.

Name	Date of Complication	Nature of Complication	Date of Examination	Organisms Recovered.
22 G.D.	12.34	Cellulitis and acute abscess formation	12.33	Streptococci
23 J.G.	10.34	Acute abscess formation	10.34	Streptococci
24 S.M.	10.33	Cellulitis	10.33	Streptococci
		DACTYLITIS.		
25 B.C.	11.34	Cellulitis	11.34	Streptococci
26 R.P.	10.34	Cellulitis	10.34	Streptococci
27 J.B.	1.34 5.34	Cellulitis surgical Scarlatina	12.33) 5.34)	Streptococci
28 M.C.	9.33	Cellulitis	10.33	Streptococci
		GLANDS etc.		
29 I.C.	10.33	Acute abscess formation	12.33	Streptococci
30 K.C.	10.33	Erysipelas	11.33	Streptococci

This shows clearly that the organisms recovered during these phases were mainly streptococci and in pure culture although in a few instances they had associated with them a few staphylococci. It was worthy of note that in these examples the streptococci were in huge preponderance over the latter a reversal of the common finding in quiescent sinuses. The streptococci which were isolated in these examples were B. haemolytic with one exception which was a haemolytic in nature. During the entire course of the investigation seven other examples of a or non-haemolytic streptococci were recovered from sinuses in which there had been previous activity but in all of them the organisms, on clinical grounds, appeared to be leading saprophytic existences at the time of examination, which period was remote from the period when disturbances were occurring. The conclusion was formed therefore, that the serious complications which occurred in tuberculous sinuses were purely related to the presence of streptococci as a secondary infection and that it was organisms of the type S. haemolyticus which were the most common and greatest pathogens.

Apart from these obvious defects secondary infection had other and more far-reaching effects upon the patient and an attempt was made to determine the effect of this factor upon:-

1./

1. The local spread of tuberculosis.
2. The general spread of tuberculosis.
3. The activity of the primary focus.
4. The general health and resistance of the patient.

Considerable difficulty was experienced in estimating these factors, particularly in the instance of estimating local spread. The fact that abscess formation had originally taken place meant that more body tissue was involved in the tuberculous process than would have been the case in a simple lesion. These abscesses were lined with an active tubercular membrane capable of attacking more healthy tissue and so increasing their dimensions, a facility which was retained after the formation of a sinus by the sinus walls. This meant that the sinus was not a static tube but was more akin to a healthy shoot with its roots deep in the body tissues and capable of branching out at any part of its length which, occurring as it did, accounted for the tortuous course of many sinuses. When secondary infection was added these off-shoots carried it with them, a process normal to the sinus and not accelerated in any way by the presence of the infection. Yet, if one of these branches became blocked and a process akin to acute abscess formation occurred, resulting in a rapid spread necessitating incision and fresh sinus formation/

formation, then the secondary infection was judged to have aided in the local spread of tuberculosis through healthy tissue. Surrounding cellulitis and acute adenitis sometimes gave similar results and they too were included in this category.

It was also difficult to estimate when a general spread of tuberculosis resulted and in order to do this the entire cause of each case was considered and its features compared with those of other cases in whom there was no secondary infection. This meant that, if, by virtue of the nature of the primary lesion and its course it was considered possible for a general spread to have taken place without the aid of a secondarily infected sinus then such a spread was ascribed to that reason and examples of this were not infrequent. If, however, a patient developed multiple lesions or even a military tuberculosis outwith the expected course of his or her type of disease and in association with an infected sinus then the credit for the spread was laid upon the infection. The same process of elimination was continued in estimating the spread of the primary focus and the feature used to determine the effect upon the patients general health was the weight record.

These factors were tabulated for disease affecting the vertebrae and an attempt made to answer the various questions.

TABLE 34./

TABLE 34.

VERTEBRAE.

Column I. Effect of sinus formation and secondary infection on local spread of tuberculosis.
II. General spread.
III. On activity of primary focus.
shown + or 0.

H. R.	+	0	0	Loss at first, gained later.
M. G.	0	0	0	Gr. gain.
A. G.	+	0	0	Loss first then a grad. gain.
J. McB.	0	0	0	Gain, loss, gain.
A. McM.	0	0	0	I.S.Q.
A. McM.	0	0	0	I.S.Q.
D. M.	?	0	0	I.S.Q. at first loss later.
P. P.	0	0	0	Sl. gr. gain.
M. L.	+	0	0	Sl. gain.
J. B.	0	0	0	Sl. gr. gain.
M. M.	+	0	0	I.S.Q. then loss.
D. McN.	+	0	0	Fluct. at first, final sl. gain then loss.
J. S.	0	0	0	I.S.Q. then sl. gain.
J. S.	0	0	0	V. sl. gain.
R. K.	0	0	0	I.S.Q. Sl. loss.
N. S.	0	0	0	I.S.Q.
N. S.	0	0	0	Sl. loss.
P. O.	0	0	0	Sl. wt. gain.
J. C.	0	0	0	Gain.
I. R.	0	0	0	Sl. gain.
I. L.	0	0	0	I.S.Q. loss.
P. A.	0	0	0	Sl. loss.
W. McD.	0	0	0	I.S.Q. loss.

I. The effect of local spread.

In six instances a degree of local spread was attributed to the secondary infection. It did not occur in sinuses relating to the cervical and dorsal vertebrae but only in relation to lesions of the lumbar region and sacro-iliac joints and then only in sinuses where there was a streptococcal secondary infection. On four of the occasions the tuberculous abscess tracked through the sacro-sciatic foramen and reached the abundant soft tissues of the buttock and upper thigh where, lacking drainage, an acute process resulted with extensive destruction of soft tissue and the eventual formation of fresh sinuses through the counter incisions which had to be made. In one other case the abscess tracked through the soft tissues of the buttock where the secondary infection became very virulent in the sheltered areas afforded there and in the final case a small off-shoot from an infected psoas abscess tracked over the iliac crest to the gluteal muscles where an acute abscess was formed once more necessitating incision and drainage. No other examples like the above were seen although normal extension of a sinus through the soft tissues was noted often.

II. The general spread of tuberculosis.

No evidence was afforded that this occurred in response to the stimulus of secondary infection.

III. The primary focus was not advanced or stimulated in any way by the presence of infection.

IV. The effect of sinus formation upon the course of the illness and the patient's resistance was illuminating. It was found, where the secondary infection was of a subsidiary and parasitic nature or absent, that sinus formation appeared to have no deterrent effect as the patient continued to gain steadily in weight. A similar effect was seen in two instances where there was a streptococcal infection in the sinus. One was a patient who had a short open sinus free from acute complication although harbouring B. haemolytic streptococci, and the other was a patient with an old chronic sinus harbouring non-haemolytic streptococci. The remaining cases, particularly those with a heavy secondary infection and visible complication, lost weight at first, or equivalent to losing weight in a child, remained at a stationary weight for some time. As the infection died out and healing occurred some of these cases commenced to gain weight but where the activity of the sinuses were maintained weight was steadily lost. The majority of these latter cases died. One case which developed amyloid disease appeared to gain weight in the last few months of life due to the amyloid changes and the subsequent oedema. It remains to be remarked that the most serious secondary infecting organism was the B. haemolytic streptococci.

TABLE 35/

TABLE 35.

Hips.	L.S.	G.S.	P.F.	Weight	Remarks.
W. G.	0	0	0	Sl. gr. gain	
P. T.	+	0	0	Loss then a sl. gain.	
W. L.	0	0	0	Sl. gr. gain	Recurrence sinus.
M. H.	+	0	0	Loss steady then gain.	
M. M.	+	0	0	Gr. loss.	
J. McL.	0	0	0	Gain.	
M. S.	+	0	0	Wt. I.S.Q.	Second sinus formed.
C. D.	+	0	0	Sl. gain	
M. McC.	+	+	0	I.S.Q. then loss.	
A. S.	0	0	0	Sl. gain.	
J. A.	+	0	0	Sl. gr. gain	Adenitis here
J. B.	0	0	0	Gain.	
W. K.	+	0	+?	Sl. loss later a steady rise.	
C. H.	0	0	0	Sl. rise lost when sinus re-opened gained on healing.	
M. P.	0	0	0	Sl. loss.	
D. L.	0	0	0	Gain.	
J. B.	0	0	0	Sl. loss.	
J. F.	0	0	0	Sl. gr. gain spreading later.	

This table gives facts regarding the hip joint similar to those given in Table 34 for the vertebrae.

I. The local spread of tuberculosis was aided in eight instances, a higher figure than in the previous series. All the sinuses which showed this feature were in positions similar to the vertebral sinuses with a similar clinical course. Of interest was the fact that on two occasions an acute inguinal adenitis occurred and broke down to be subsequently involved in the tuberculous process.

II. The secondary infection was an adjuvant to the general spread of tuberculosis in one instance only.

III. A stimulation of the activity of the primary lesion was suspected in one instance although here the primary lesion was almost sufficiently acute to justify an unaided spread.

IV. The effect upon the health of the patient was similar to that seen in the case of the vertbrae with this difference that a greater number of cases continued to gain weight despite the occurrence of a sinus. In two instances sinuses recurred associated with streptococci in the discharge and further reference will be made to phenomena of this type. As in the case of sinuses arising from the vertebrae, the streptococcus was the pathogen responsible for all serious mischief.

TABLE 36.

Knees.	L.S.	G.S.	P.F.	Weight	Remarks.
M.C. (R)	0	0	0	Sl. gr. gain.	-
M.C. (1)	0	0	0	Sl. gr. gain.	-
M.B.	+	0	0	I.S.Q. then a gain later.	Acute abscess around joint.
G.P.	+	0	0	Loss.	Amputation.
A.C.	0	0	0	Sl. gain.	-
B.H.	+	0	0	I.S.Q. fluctuation late gain.	-
M.C.	+	0	0	loss - gr. gain.	-
W.H.	0	0	0	I.S.Q. - sl. gain.	-

I. Sinus formation and secondary infection was considered responsible for the local spread of tuberculosis in four examples in this series. On each occasion the spread occurred to include the bony structures around the joint and the primary lesion was of an acute character. This local spread occurred in the form of acute abscesses in the upper calf and behind the joint resulting from a gravitational spread of infection in two instances and in the remaining two took the form of an acute arthritis. In all these cases ankylosis of the/

the joint with deformity was the result except one where an amputation in mid-thigh was performed.

II. General spread of tuberculosis occurred in one of the examples cited above.

III. The activity of the primary lesion was thought to have been increased in one example where a small sinus leading from soft tissue disease became secondarily infected and before healing occurred all the structures of the joint were involved.

IV. The effect on the general health corresponded with previous findings.

TABLE 37.

THE ANKLE JOINTS.

	L.S.	G.S.	P.F.	Weight.
A.M.	0	0	0	Sl. gr. gain.
H.McK.	+	0	0	Loss.
A.W. (L)	+	0	0	Sl. gr. gain.
A.W. (R)	+	0	0	Do.
I.G.	0	0	0	Gr. gain.
S.M.	+	0	0	Loss - I.S.Q. rapid gain.
M.McC.	+	0	0	I.S.Q. - gain.
J.G.	+	0?	0	Sl. gain.
J.McL.	+	0?	0	Sl. gain.

Disease of this joint was found to be profoundly affected by the addition of secondary infection.

I. Local spread of tuberculosis was noted on seven occasions.

II. Doubt existed as to whether a general spread was aided in two occasions.

III. In no instance was there any evidence that the primary lesion was effected in its course in any way.

IV. The weight charts exhibited that, as a general rule, infection super-added to sinus formation was less formidable to the patient than in any series so far examined as a greater number continued to gain slowly in weight throughout the course of the disease. Yet toxaemia and weight loss was marked in two examples where amputation was finally performed resulting in an excellent demonstration of the detrimental effect of a discharging sinus upon the general health and resistance. In the first of these two cases 7 lbs. weight was gained within the first two months after the amputation and in the other 5 lbs was gained in 3 months.

TABLE 38./

TABLE 38.

DACTYLITIS.

	L.S.	C.S.	P.L.	Weight.
J.B.	+	0	?	Loss, late gain.
A.C.	0	0	0	Sl. Gr. gain.
T.H.	+	0	0	Do.
M.C. (H)	0	0	0	Sl. gr. gain.
M.C. (F)	0	0	0	
B.C.	0	0	0	Loss - gain later.
R.McM.	0	0	0	Loss.
M.P.	0	0	0	I.S.Q. sl. gain.
M.L.	0	0	0	Sl. gr. gain.
R.S.	0	0	0	Do.
R.P.	+	0	0	Loss gain.
D.S.	0	0	0	Do.
A.McD.	+	+?	0	Loss I.S.Q.

I. Local spread occurred in 4 instances only. In 1 instance it was slight but resulted in amputation of the offending digit in order to prevent further spread but in the remaining 3 instances it was extensive and resulted in very marked cellulitis and localised abscess formation in the soft tissues of the feet necessitating fresh sinus formation for drainage.

In/

In 2 of these cases an inguinal adenitis arose in relation to the affected sinuses in one of which it was acute and due entirely to streptococci but in the other it was primarily tuberculous.

II. No example was seen of a general spread of tuberculosis hastened or brought about by secondary infection.

III. In one case (J.B.) the secondary infection was held to be responsible for the rapid dissemination of disease throughout the bones of the foot. Here the primary lesion was so chronic that it was thought to be Kohler's disease until the formation of a sinus, when, after the onset of an acute secondary infection a widespread tuberculosis resulted.

IV. Detriment to the patients' health was noted in a number of cases, the initial slight loss being generally followed by slow gain in weight. In sinuses not infected by streptococci the weight continued to increase gradually a feature shared by some others in which there was a streptococcal infection. Where serious complications occurred the secondary infecting organism was invariably a streptococcus.

TABLE 39.

TUBERCULOSIS OF THE LONG BONES.

	L.S.	G.S.	P.L.	Weight.	Remarks.
R.McK.	0	0	0	Sl. gr. gain	-
J.S.	0	0	0	Steady loss	-
J.McL.	0	0	0	Steady gain	-
S.M.	+	0	0	Loss - slow gain.	-
A.K.	0	0	0	I.S.Q.	-
H.J.	0	0	0	Slow gain	-
G.D.	+	+?	0	Loss	-
T.S.	0	0	0	Sl. gain	Ankylosed
J.G.	0	0	0	Sl. gain	-
D.P.	+	0	0	Loss - sl. gain.	-
J.G.	+	0	0	Gr. gain.	-
A.McD.	0	0	0	Loss - I.S.Q.	-

I. Only 4 examples were seen where a local spread was aided.

II. One doubtful example occurred where a general spread was aided.

III. No example was seen of any change in the activity of the primary lesion as a result of infection.

IV. Once again the weight features conformed to those seen previously although marked detrimental effects were absent. The important pathogen throughout was the streptococcus.

GLANDULAR AND SOFT TISSUE TUBERCULOSIS.

Lesions of this nature escape more lightly from the depredations of secondary infection than other sites.

TABLE 40.

	L.S.	G.S.	P.L.	Weight.
C.W.	+	0	0	I.S.Q. - gain
L.C.	0	0	0	Sl. gain
J.B.	0	0	0	Loss
J.McG.	0	0	0	Steady gain
J.McC.	0	0	0	I.S.Q - gr. gain.
C.C.	0	0	0	I.S.Q. - gain
I.C.	0	0	0	Steady gain
C.W.	+?	0	0	Loss - gain
M.D.	0	0	0	Gain
M.F.	0	0	0	Gain
J.L.	+	0	0	I.S.Q. - gain
M.H.	0	0	0	Do.
A.C.	+?	0	0	Steady gain
I.W.	0	0	0	Do.
A.McD.	0	0	0	Loss - I.S.Q.

I. A local spread occurred in 2 instances as a result of gravitational pocketing of pus which required fresh sinus formation for draining.

II. & III. There was no evidence of general spread or of any change being effected on the tuberculous process by infection.

IV./

IV. Weight loss was seen in 3 instances in one of which it was probably due to the pulmonary lesion which caused death and in another it was due to the presence of multiple lesions and unlikely to be influenced by the minor glandular lesion. The remaining cases all gained weight steadily throughout the course of their illness, exhibiting thereby the relative impotence of their lesion.

TABLE XI.

MISCELLANEOUS LESIONS.

	L.S.	G.S.	P.L.	Weight	Remarks
W.A.	+	+	0	Sl. gain	Died.
R.B.	0	0	0	Do.	
C.McC.	0	0	0	Do.	
E.B.	0	0	0	Do.	
E.A.	0	0	0	Do.	
M.McV.	0	0	0	Do.	
S.M.	0	0	0	Do.	
J.McL.	0	0	0	Do.	
F.McH.	0	0	0	Do.	

These lesions escaped what was eventually regarded as serious secondary infection and in no example was there any evidence of a local spread of tuberculosis or any change in the primary lesion caused by the infection. General spread resulting in death from miliary tuberculosis/

tuberculosis was felt to have resulted from an infected abdominal sinus in a case with tabes mesenterica. Each patient gained weight gradually throughout the course of the disease.

In the aggregate the following conclusions were made:-

I. That abscess and sinus formation undoubtedly opened up fresh tissues to the risk of infection and that local spread of the disease was seen on numerous occasions and most markedly in lesions in which the primary focus was acute and deep lying with a sinus track running through an extent of soft tissue.

II. That general spread resulted from infection in very few instances and even then was not definitely caused by it.

III. That on only 3 occasions was there incomplete evidence that the addition of a secondary infection to a sinus acted as a stimulus to the primary focus.

IV. That sinus formation plus secondary infection was detrimental to the patients' general health and was a definite deterrent to recovery in a number of cases but that in the majority the effect was minimal and was overcome by the patient quite readily. On this basis the most serious sites with added infection were vertebrae, hip joints, knee joints and ankle joints.

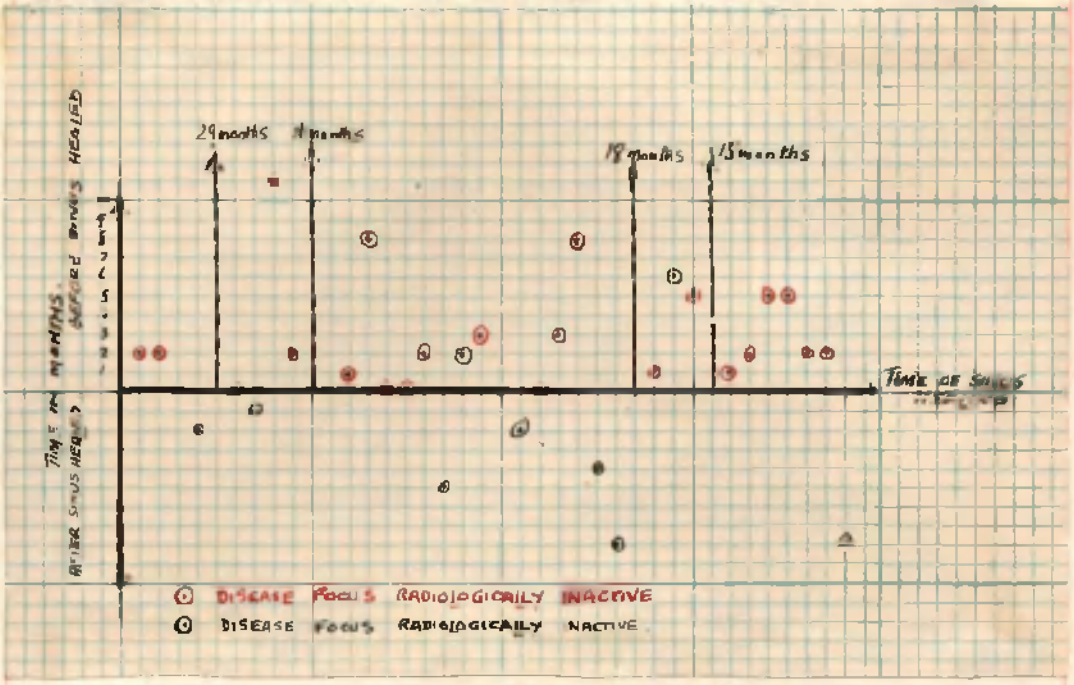
V./

V. That in every example showing any detrimental feature the secondary infection was a streptococcus and that in all serious cases this organism was B. haemolytic in character.

There remains to be discussed one more feature shown by sinuses, namely, their recurrence. This feature has been ascribed to many factors including the recrudescence of a dormant secondary infection. An examination of several of these sinuses bacteriologically, after their recurrence, revealed the presence of very friable and very sparse organisms. In certain instances streptococci were recovered but they were either non-haemolytic in character or so friable that culture was impossible, factors which augured ill for their ability to reopen a sinus track by virtue of their pathogenic powers. Accordingly attention was directed to other features presented by the cases within the investigation and a graph was prepared comparing the dates on which sinuses healed with the dates on which the tuberculous lesion corresponding became inactive clinically and radiologically.

GRAPH 3./

GRAPH 3.



Thus of 43 cases of bone tuberculosis with discharging sinuses the primary lesion was inactive clinically and radiologically before or at the same time as the sinus healed in 30 instances and a feature of note was the close relationship exhibited between these two factors. Where this order was reversed, as it was in 12 instances, firm healing occurred in 8 and repeated recurrence took place in 4. In one instance the primary lesion was inactive but the sinus was still patent after a period of one year. An inference was drawn that the healing of a sinus was closely/

closely related to the healing of a primary lesion which caused it. Adding to this the previous observations that secondary infection tended to disappear in healing sinuses and that the most grave infection with serious consequences almost invariably occurred in acute forms of tuberculosis it was felt that the secondary infections were aptly named as they were only capable of their greatest destructive powers in the suitable soil provided for them by the tuberculous process. Examples of this were seen in the uncomplicated course followed, even by wide sinuses, when the primary focus was thoroughly removed such as was possible in some long bone and glandular lesions.

Continuing the investigation over a long period enabled the end results of the illness to be appreciated, as with comparatively few exceptions a definite result was achieved with the cases under observation.

TABLE 42./

TABLE 42.

	I.	II.			III.		
		Streptococci +			Streptococci -		
		Activity of Tuberculosis.					
Result	Total	Ac.	S.Ac.	Ch.	Ac.	S.Ac.	Ch.
Died	12	6	2	2	1	1	0
Deteriorated	7	2	3	1	0	1	0
I. S. Q.	10	5	0	0	1	2	2
Improved	8	2	3	1	1	1	0
Healed	62	17	16	3	2	11	13
Amputated	3	3	0	0	0	0	0
	102	35	24	7	5	16	15

Embodying the results, revealed that there was a mortality of approximately 12% and a complete recovery of approximately 65%. Certain cases were still active and of these 7% were deteriorating, 8% were improving and 10% were in statu quo ante. These results appear good but compare unfavourably with those taken from the total dismissals of comparable cases from the same hospital for two consecutive years in the middle of the investigation. These were, in approximate figures: Died 7.4%, Irregularly dismissed 2.2%, Healed 90.4%. Of the cases investigated 65 had had a streptococcal secondary infection and 37 had not and the figures in the columns II and III of the table showed the very much better results obtained in patients who remained free from streptococcal secondary infections. Entering into these results was the activity of the primary lesion and these figures give definite proof of an earlier statement that streptococci were more commonly found in association with the more acute cases of tuberculosis. It was to be expected that the more active primary lesions would have a greater mortality than the less active yet the series of figures suggest that those sinuses infected with streptococci showed a relatively greater mortality than a strict proportion would have allowed.

The result of treatment varied according to the site/

site affected by the disease and when these figures were abstracted it was seen that the most disappointing occurred in relation to disease of the vertebrae.

VERTEBRAL TUBERCULOSIS.

Of 23 patients with disease in this area there were 6 who died, 5 who were deteriorating, 4 in a stationary condition , 2 who were improving and only 6 in whom the disease was healed, figures which compare unfavourably with the results of treatment of all cases of disease of the vertebrae where there were 10 deaths and 61 cases healed out of 73 dismissals. All 6 patients who died were extremely toxic from their secondarily infected sinuses and all were suffering from amyloid disease. Amongst those whose condition was deteriorating 2 had developed amyloid disease and, with one exception, were extremely toxic from their sinuses. The exception was a case with chronic disease of the cervical vertebrae which had been in existence for 10 years. The 4 which remained stationary had the common feature of a mild infection in their sinuses and still active primary lesions and, in all in whom improvement occurred, the secondary infection was mild in degree and the resistance of the patient good. Those which healed had a streptococcal secondary infection in only one instance, the remainder being either sterile or harbouring less pathogenic organisms. Within this series was a patient who made a recovery from what was clinically/

clinically amyloid disease. This patient was admitted with discharging sinuses and active tuberculosis. He was toxic and developed an enlarged liver, a 'waxy' appearance and albuminuria. Following an attack of jaundice his symptoms and signs abated and he slowly improved to be dismissed, healed.

On the whole these results were very disappointing and displayed the gravity of the secondary infection as a factor militating against recovery.

TUBERCULOSIS OF THE HIP JOINT.

Within this series there were 18 cases of whom 2 died, 2 deteriorated, 1 remained stationary, 2 improved and 11 healed. Comparative figures for all cases of this area were 3 deaths, 1 irregular dismissal and 60 who healed out of 64 cases, still showing poorer results within the series investigated but not so markedly inferior as were the previous results. Death occurred in two instances where there was acute progressive tuberculosis with heavily infected sinuses and amyloid disease as a terminal feature. Both examples where deterioration occurred were still suffering from active tuberculosis when the investigation was concluded and in both there was a heavy secondary infection by streptococci with marked toxaemia and other complications, features also shown by the cases which

were/

were remaining in a stationary condition. Improvement occurred in 2 and healing in 7 instances where there was a streptococcal secondary infection on the sinuses and in some of them the effect of thos infection was only overcome after long and careful treatment. In disease of this joint, even with a serious secondary infection, the results of treatment were better despite the fact that the infection was as severe, if not more severe, than in many of the vertebral lesions. The only difference lay in the relatively shorter course of the tuberculous process in the hip joints with, as was pointed out,a shorter course for the sinuses resulting in a less prolonged drain upon the patient's resistance.

TUBERCULOSIS OF THE KNEE JOINT.

This lesion showed much better results. Of 7 patients, 1 died, 1 was improving and 5 were healed. Still worse, however, than 2 deaths in 33 patients which were the general results. The case in which death occurred was one in which the streptococcal secondary infection was held partly responsible for the rapid deterioration of the patient and the general spread of tuberculosis which resulted in death. The case in which improvement was recorded was only under observation for a relatively short period of time but it was felt that a satisfactory result was under way. Once more the secondary infections were gross and caused/

caused extensive damage which was fortunately limited by the relatively short course of the illness.

TUBERCULOSIS OF THE ANKLE JOINTS.

The results here were excellent and 100% recovery was achieved, thus equalling the figures achieved over all types of this lesion. Again, however, the secondary infections and complications were severe, necessitating amputation in 2 instances as a curative measure. At the beginning of the chapter a note was made on the relatively long course of lesions of this region. Observation revealed that this was due to the tendency for the os calcis to fragment and form sequestra which came away from time to time.

TUBERCULOSIS OF THE LONG BONES.

Lesions of these areas were satisfactory in their termination as, of 12 cases, 8 healed, 1 was healing and 3 were stationary. These cases call for no remark except that of the stationary cases 2 were under observation for relatively short periods of time.

TUBERCULOUS DACTYLITIS.

Dactylitis did not yield such satisfactory results mainly on account of the damage caused by the secondary infection. Of 11 cases, 1 died, 1 suffered an amputation, 3 showed an improvement and 6 healed, yielding a comparison with 3 deaths and 17 recoveries from 20 unselected/

unselected patients. The death occurred purely by reason of the virulent nature of the tuberculous infection.

TUBERCULOSIS OF GLANDS AND SOFT TISSUES.

From a total of 14 patients, 1 died and 13 recovered; figures comparable with 2 deaths and 58 recoveries out of a gross total of 60 patients treated over a number of years in the hospital when it was remembered that the death which occurred was due to added pulmonary disease. It was to be expected that these results would correspond very closely as approximately 80% of glandular lesions form abscesses and sinuses.

MISCELLANEOUS LESIONS.

In this group of 9 cases, 1 died, 1 was improving and 7 healed beyond which statement no more can be said as no comparable series of cases were possible.

A conclusion was formed that the gravity of a case depended upon the site of the primary lesion and that lesions of glands, soft tissues, long bones and miscellaneous parts pursued their course regardless of additional pyogenic infection. Also that the reverse held in examples of disease of the vertebrae or hip joints to a marked degree and less markably in the instances of the knee and ankle joints. In short, sinus formation/

formation and secondary infection were to be feared where the site, nature and course of the primary lesion afforded the infection a prolonged residence and activity. It was also concluded, in view of the experimentally ascertained low virulence of the most dangerous secondary infection, namely streptococci, that the local resistance of the affected parts was markedly diminished.

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bacteriologically for secondary infection from their inception until they formed sinuses. Accordingly the pus which was aspirated from 57 abscesses was examined in this manner with a total of 188 examinations. In some instances one specimen only was examined whereas others were examined on numerous occasions, the greatest number of serial examinations in one abscess being 23. These 57 abscesses were grouped as follows:-

I. Those which were traced to breaking point or incision. . . . 21

II. Those which healed without sinus formation or failed for other reasons to form sinuses. 30

III. Those which were in close relation to sinuses 6

and the relevant details were tabulated.

TABLE 43./

TABLE 43.

Name	Site of disease.	No. of Exams.	Date of Last examination	Date of Sinus Formation	Result.
J.B	Sacrum	1	15.10.33	18.10.33	Sterile
J.B.	Thigh	18	18.11.34	1.7.34	Do.
J.S.	Lv.	8	11.2.34	14.2.34	Do.
J.McB.	Dorsal spine	2	13.11.33	28.11.33	Do.
J.A	Rt. hip	23	12.6.34	14.6.34	Do.
R.K.	Cerv. spine	1	30.1.34	2.2.34	Do.
W.G.	Hip	7	24.3.34	28.3.34	Do.
P.T.	Hip	1	3.12.33	5.12.33	Do.
T.C.O.	Hip	1	7.4.34	24.4.34	Do.
W.L.	Hip	1	23.11.33	25.12.33	Do.
J.G.	Knee	9	10.4.34	10.4.34	Do.
M.C.	Knee	4	15.5.34	5.6.34	Do.
M.B.	Knee	1	9.11.33	9.11.33	Do.
I.G.	Ankle	5	18.12.33	19.12.33	Do.
J.G.	Ankle	8	12.6.34	18.6.34	Do.
H.McK.	Ankle	3	22.7.34	23.7.34	Do.
J.R.	Glands	1	31.10.33	Just before incision 27.3.34	Do.
J.McG.	Glands	2	25.3.34	27.3.34	Do.
J.C.	Soft tissues	3	23.5.34	28.5.34	Streptococci.
D.R.	Rib	1	25.6.34	2.8.34 incised	Sterile
A.K.	Left elbow	8	29.3.34	1.4.34	Do.

Table 43. was based on the cases falling into Group I above, and shows the bacteriological results and dates of the last examination of the abscess contents which was made before sinus formation occurred. In separate columns are shown the number of occasions on which each abscess was examined and the dates on which the sinuses formed. The majority of the cases formed sinuses shortly after the date of the last examination but in some instances the period was prolonged. One example included shows that a period of two and a half months elapsed between the last examination and sinus formation because in this instance no appreciable amount of pus gathered in the intervening period, the sinus being formed by a very small leak through an old needle puncture. The other examinations however, were sufficiently close to the date of sinus formation to be certain that the possibility of a secondary infection entering and multiplying in the interval, sufficiently to be harmful, was negligible. Yet in all instances except two the examinations failed to reveal the presence of any secondary infection. The exceptions were:-

I. a groin abscess, subcutaneous in its later stages and difficult to aspirate and

II. a small subcutaneous soft tissue abscess of the lower calf.

The infections recovered were respectively:-

I./

I. a small unnamed Gram negative bacillus and
II. a faintly B. haemolytic streptococcus,
but in neither case was there any clinical manifestation of the presence of a secondary infection. In both the integrity of the skin surface over the abscess was doubtful.

Therefore in Group I, 21 tuberculous abscesses formed sinuses under observation and in 19 no bacteriological evidence of any secondary infection occurring prior to sinus formation was noted. In 2 where this infection was found the clinical features cast doubt upon the integrity of the abscess at the time of the examination and showed no evidence that these organisms were an aid to sinus formation. From this it was inferred that the pyogenic cocci and other organisms which were isolated from the sinuses must gain ingress after the sinus had formed.

The cases comprising Group II were tabulated as were those in Group I, and twenty-seven of them showed no evidence of a secondary infection gaining ingress to the abscess.

TABLE 44./

TABLE 44.

Name.	Site of disease.	Site of abscess	No. of Exams.	Date of 1st & last exam.	Result of Exam.	Final Result.
J.B.	Sacrum	Rt.groin	4	13.2.23-20.3.34	Sterile	Healed
G.McC.	Dorsal L. spine	Back	1	1.2.34	Sterile	No sinus died.
J.M.	D.L.spine	Psoas	1	31.1.34	Sterile	Healed
A.C.	Dorsal spine	Lumbar	10	22.1.34-11.7.34	Sterile	Healed
J.McG.	L.sacro-iliac	Back	1	25.11.33	Sterile	Healed
H.A.	Lumbar spine	Psoas	1	6.33	Sterile	Healed
M.S.	LV3-5	Psoas	1	13.1.34	Sterile	Healed
D.H.	LV5 SV.I.	Psoas	3	19.1.34	Sterile	Healed
T.K.	L.hip	Thigh	2	15.1.34 12.3.34	Sterile	Healed
E.McI.	L.hip	Thigh	11	12.1.34-4.7.34	Sterile	Healed
G.M.	L.hip	Thigh	13	11.11.33-24.6.34	Sterile	Healed
E.W.	L.hip	Thigh	5	11.33-7.1.34	Sterile	Healed
W.G.	Hip	Thigh	2	16.2.34-7.1.34	Sterile	Healed
R.C.	Knee		1	13.11.33	Sterile	Healed
A.B.	Msent. Glos.	Groin	1	19.1.34	Sterile	Healed
J.F.	Ing. gland	Groin	1	26.8.34	Sterile	Healed
J.C.	Cerv. gld.	Neck	4	4.1.34-12.1.34	Sterile	Healed

TABLE 44. (continued)

Name.	Site of disease.	Site of abscess	No. of Exams.	Date of 1st & last exam.	Result of Exam.	Final result.
M.S.	Cerv. gld.	Neck	1	24.4.34	Sterile	Healed
H.McD.	Do.	Do.	1	13.2.23	Sterile	Healed
E.M.	Do.	Do.	5	18.5.34-26.8.34	Sterile	I.D.
H.C.	Wrist		1	11.11.33	Sterile	Died
I.D.	Ribs	Chest wall	1	16.11.35	Sterile	Sinus & I.D.
J.H.	Wrist		1	13.3.34	Sterile	Healed
M.T.	Os Calcis	Heel	1	26.3.34	Sterile	Healed
L.B.	Ribs	Chest wall	2	12.8.34-15.8.34	Staphs. and G.-ve bacilli	Acute abscess.
J.N.	Dorsal spine	Back	3		Sterile	Healed finally sinus
R.McK.	Elbow		3	14.2.34-21.4.34	Sterile	Healed.
W.H.	L.tibia	Leg	3	6.7.34 19.7.34	Sterile	Died.
J.B.	Groin		1	19.5.34	Streptococci	Acute Abscess Healed.
L.C.	Ear		1	.4.34	Streptococci	Do.

Three exceptions occurred but their clinical and bacteriological features suggested that they were acute inflammatory processes and not tuberculous. Their details were:-

I. An abscess of the chest wall, purely staphylococcal in origin and negative for tuberculous when tested biologically.

II. An abscess behind the ear in relation to an acute mastoid.

III. An acute inguinal adenitis occurring in relation to a severely infected sinus in a foot. These last two both yielded pure cultures of B. haemolytic streptococci. Therefore, disregarding the exceptions, it was again shown that no secondary infections gained ingress to tuberculous abscesses during treatment. Finally there were the few cases in Group III, different from the others in that these abscesses were in close proximity but not communicating with existing sinuses.

TABLE 45../

TABLE 45..

Name	Lesion	Sinus Infection.	Abscess Examination.
N.P.	Dactylitis	Staph. albus	Sterile.
A.C.	Axiliary Adenitis	Staph. albus Non-haem. Strep.	Sterile.
M.D.	Cerv. Adenitis	Staph. Aureus	Sterile.
J.McC.	Do.	Sterile	Sterile.
C.W.	Do.	Staph. albus & B. Haem. Streps.	Staph. albus) Diphtheroids)
M.F.	Do.	Sterile	Sterile.

These adjoining sinuses were secondarily infected in four instances and 'Sterile' in two and the pus aspirated from the abscesses which were in proximity to the last two was also free from added infection. In three instances where the sinuses were secondarily infected the abscess contents were sterile but one was secondarily infected. This abscess yielded staph. albus and diphtheroid bacilli with the bacilli in the minority and the sinus was infected with staph. albus and B. haemolytic streptococci in the same order. In view of the close proximity of the abscess and sinus in this instance the possibility of an infection spreading from one to the other was high, yet the streptococci isolated from the sinus were not present in the abscess. Therefore, if a comparatively rooted organism like a staphylococcus was able to cross the intervening tissue then the likelihood of a streptococcus doing this was much greater and its failure to do so suggested that the organisms recovered from the abscess did not originate in the sinus.

The abscess was covered only by the thinnest layer of skin and an infection may have been carried through when aspirating. Another feature was that there were no clinical signs of secondary infection in the abscess.

A tentative conclusion was made from this small number of cases that the soft tissue intervening between the sinuses and the abscesses formed an efficient barrier/

barrier to the spread of infecting organisms from one to the other and that the organisms within the sinuses were very closely limited in their distribution to the confines of the sinus. Further proof of this last statement was demonstrated by the almost complete absence of acute lymphadenitis occurring in the glands draining areas containing a profusely discharging sinus. From the combined results it was concluded that secondary infections occurred after sinus formation in all but a very few cases and also that the precautions taken in aspirating the abscesses were sufficiently good to prevent the ingress of infection.

Attention was next focussed on the sinuses which were examined at varying periods of time after their inception and certain results were tabulated.

TABLE 46./

TABLE 46.

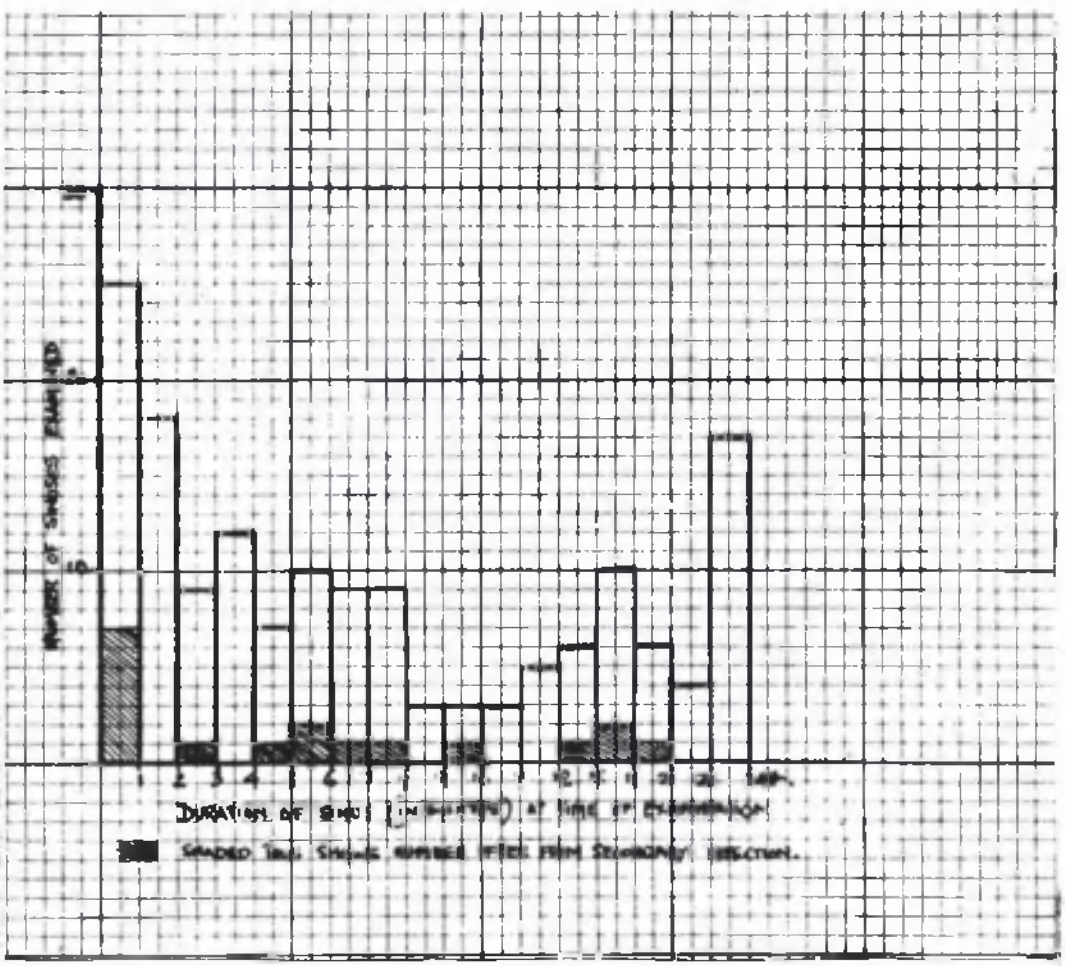
Name.	Site of lesion.	Date of Examination.
J.McG.	Glands (neck)	10.3.34 25.3.34 26.3.34 27.3.34.
C.W.	do.	Abscess before incision.
I.C.	Do.	13.12.33 16.12.33.
W.L.	L. hip	23.12.33 25.12.33 10.2.34.
M.B.	R. knee	Not aspirated. 9.11.33 17.11.33 1.12.33 1.2.34 19.3.34 10.11.34
P.T.	L. hip	3.12.33 5.12.33 12.1.34 19.3.34
J.McB.	Spine	29.10.33 13.11.33 28.11.33 10.1.34
R.McK.	Elbow	21.3.34 21.4.34 5.6.34 13.7.34 Healed uninfected.
W.G.	R. hip	19.1.34 2.2.34 19.2.34 20.2.34 Do.
Reaccumulation.		10.3.34 24.3.34 28.3.34 19.6.34
J.R.	Glands (neck)	31.10.33 Healed uninfected.
J.McL.	L. hip	27.4.35 9.5.35 1.6.35 17.6.35 Healed uninfected.
M.G.	Spine	4.5.34 Do.
J.S.	Spine	4.2.34 11.2.34 14.2.34 19.2.34 21.6.34
H.McK.	Ankle	19.7.34 22.7.34 23.7.34 30.7.34 13.10.34
J.G.	Femur	25.3.34 10.4.34 10.4.34 21.10.34
J.G.	Ankle	12.6.34 18.6.34 29.6.34 12.11.34
B.H.	Knee	19.10.33 17.11.33 14.5.34 9.11.34 8.12.34 22.12.34

Date underlined in red is date of sinus formation and Date underlined in black is that on which secondary infection was recovered from the sinus discharge.

From the table it was seen that the onset of infection varied in time and did not occur automatically upon the formation of a sinus. In a few instances such was the case but in nearly all instances infection inevitably occurred.

Departing from this small series of cases and utilising data obtained from the tables in the preceding chapter the results of all the examinations which were conducted were graphed to show the relative proportion of secondarily infected sinuses to those free from infection at different periods of time.

GRAPH 4.



From the graph it was seen that non-infected sinuses were found rarely after the first month although a few examples were noted at late periods. Recalling the observation made in the preceding chapter that healing sinuses were often free from infection these latter results were re-examined and it was found that all the examples reported up to the tenth month were healing lesions. This left four examples in the later months still, but these were capable of explanation as follows. That in the 12 - 15 months period was in a toxic patient who had had a previous heavy secondary infection by streptococci. Clinically the child was secondarily infected but the sinus was capable of complete cleansing in its upper reaches and it was felt that the failure to recover pyogenic cocci was due to the concentration of antiseptics in this region. This case also accounted for a similar example in the 15-18 month period as a further attempt was made to recover a secondary infection which again failed. There was also the possibility in this instance of the infection terminating itself. A single case with disease of the cervical vertebrae accounted for the remaining two sterile sinuses occurring in the 15-18 months and the 18-21 months period. Here the features also suggested a secondary infection although none/

none was cultured. Finally, however, a gram positive unnamed diplococcus was recovered which proved very friable and which died out in subculture. This organism may have been present earlier and defied culture. Therefore a secondary infection was present in every sinus which was not almost healed after it had been in existence more than one month with one notable exception in the instance of a sinus arising from a hip joint lesion which was maintained free from infection throughout its four month course. This was done by observing scrupulous care in dressing and the short duration of the sinus was interesting to note. A general conclusion was formed that secondary infecting organisms were superadded shortly after sinus formation had occurred. The source of this infection was then sought and the two possible sources which existed, endogenous and exogenous, were examined.

Endogenous infection was possible in normal health but was much more likely to occur in the course of an acute illness or in a septicaemic condition. The only acute illness which occurred during the investigation was Scarlatina and here the clinical appearances in certain patients suggested the possibility of an added infection stimulating the activity of the tuberculous process. Three patients only showed these features.

I. J.N. Tuberculosis of dorso lumbar vertebrae with a re-accumulation of pus within an abscess which had/

had been quiescent for eight months. This occurred 7 days after the onset of Scarlatina.

II. W.G. Almost inactive bone lesion of R. hip. Fresh abscess appeared in thigh 10 days after onset of Scarlatina.

III. J.B. Tuberculosis of sacrum with an abscess of thigh which increased vastly in size, starting 3 days after the onset of Scarlatina.

All these cases prevented the common feature of a rapid accumulation of pus in their abscesses closely following an attack of Scarlatina. An obvious inference was that streptococci might be responsible for this and the abscess contents were examined bacteriologically on several occasions for the presence of such infection with negative results. This seemed to exclude the possibility of an endogenous infection in tuberculous abscesses even in these eminently suitable cases. A possible explanation of the increased activity of the tuberculous process lay in the fact that in none of these cases was the primary lesion inactive and that the unwonted movement plus the suspension of normal treatment which took place during the course of the intercurrent illness was detrimental to the healing process. Other cases, numbering 21, were also observed/

observed during and after an attack of Scarlatina but in none was there any change in the tuberculous lesion clinically or radiologically. A note was therefore made that Scarlatina as a complication of surgical tuberculosis was a detrimental factor, although only in a minor degree.

These cases were not thought to be sufficient evidence to discountenance the possibility of endogenous infection and the problem was approached in another manner. It was thought that a septicaemia might occur amongst these cases in relation to other acute streptococcal infections in the sinuses such as erysipelas and cellulitis. Accordingly blood cultures were made from 8 patients where this possibility was present and the relevant details were tabulated.

TABLE 47.

Name.	Acute Lesion.	Result.
M.H.	Cellulitis, Acute abscess formation, toxaemia.	Sterile.
M.McG.	ditto.	Do.
P.T.	ditto.	Do.
M.McG.	ditto.	Do.
J.S.	ditto.	Do.
S.M.	ditto.	Do.
C.D.	Erysipelas	Do.
C.D.	ditto.	Do.
J.S.	Chronic toxaemia	Do.

In these examples no evidence of a septicaemia was found. A conclusion was made, based on all the examinations which were made that secondary infection occurring in tuberculous abscesses and sinuses was not endogenous in origin.

The only remaining source of infection was therefore exogenous which meant from the skin surface or from the air. With regard to the former Haxthausen showed that streptococci could be recovered from the skin surface in 5% of cases and that these organisms were potentially pathogenic. Utilising a simple technique an attempt was made to recover these organisms from the skin surface of 21 patients. The results were tabulated and appear as follows:-

TABLE 48.

Attempts to Recover Streptococci from Skin.

Name.	Site.	Staph.	Strep.	Diph.
M.C.	Thigh	Albus	-	-
M.McC.	Thigh	Albus	-	+
M.H.	Thigh	Albus	-	-
J.P.	Groin	Citreus albus	a. haem.	-
E.B.	Groin	Albus	-	+
H.A.	Thigh	Albus Aureus	-	-
L.C.	Groin	Albus	Non-haem.	-
S.M.	Groin	Albus	-	-

TABLE 48. (continued)

Name.	Site	Staph.	Strep.	Diph.
H.G.	Groin	Albus	-	-
S.M.	Groin	Albus	-	+
J.McL.	Thigh	Albus citreus	-	+
A.F.	Arm	Albus citreus	-	+
M.B.	Groin	Aureus	-	-
C.M.	Groin	Albus Aureus	-	-
H.C.	Groin	Citreus albus	-	-
R.McK.	Groin	Aureus	-	+
J.B.	Groin	Citreus albus	-	-
S.S.	Arm	albus aureus	-	-
R.J.	Groin	Albus	-	-
S.B.	Groin	Albus	-	+
P.D.	Thigh	Albus	-	-

Staphylococci, sometimes more than one type, were recovered in every instance, diphtheroid bacilli in 7 instances and streptococci in 2. Twenty-nine strains of staphylococci were isolated, 20 being St. albus, 4 St. aureus and 5 St. citreus. Beyond noting the colour/

colour no further observations were made of these organisms and the feature of interest was the high incidence of St. citreus. No attempt was made to classify the diphtheroid bacilli but an examination was made of the streptococci. One was a. haemolytic on blood agar and the other was a non-haemolytic organism which grew in short chains. Only the first of these was typed. On its biochemical characteristics it was an indeterminate strain of S. viridans which, when examined serologically, showed itself to have no relation to any of the type cultures by complement fixation tests but was most nearly related to S. equi on its agglutination features.

This examination showed that it was possible for the secondary infecting organisms to gain access to the sinus from the skin surface particularly in the instance of staphylococci and diphtheroid bacilli. The absence of haemolytic streptococci from the surface and their marked preponderance within the sinuses inferred that these organisms must gain ingress from some other source.

The only remaining source was air borne and the conclusion was formed that such an infection originated from the buccal spray, a route which was shown to be of importance by obstetricians particularly with regard to streptococci. Attempts were made to culture streptococci/

streptococci from the buccal spray and the method adopted was to ask 8 people to cough over exposed blood agar plates. Streptococci were recovered in 3 instances, 2 from patients with Scarlatina and 1 from a person in good health. The details of these strains were -

I. W.G. B. haemolytic streptococcus.
Complement fixation test = S. equi.
Agglutination - incomplete S. faecalis and S. pyogenes.
Related to several sinus strains.

II. R.B.M. B. haemolytic streptococcus.
Biochemically = S. pyogenes.
Complement fixation test = S. erysipelatosus.
Agglutination test = S. erysipelatosus.

III. J.S. B. haemolytic streptococcus.
Biochemically indefinite.
Serologically indefinite.
(probably a mixed strain)

These organisms bore a distinct resemblance to those which were isolated from the sinuses increasing the possibility of a droplet infection of sinuses, a possibility which was further enhanced by the behaviour of sinuses in the vicinity of Scarlatina.

In this respect there were 9 examples of streptococcal/

streptococcal complications occurring in the sinuses and related to a definite outbreak of Scarlatina. Attention was first drawn to this relationship in the instance of a child with a discharging sinus of the ankle when the following events were noted.-
In February 1933 a case of Scarlatina occurred in a ward and within the next 24 hours a well marked cellulitis appeared around the ankle sinus of the patient occupying a neighbouring bed. Examination of the sinus discharge revealed that the complication was associated with the sole presence of streptococci in great numbers. This organism was typed with the aid of biochemical tests and was shown to be S. pyogenes. Cultures were taken from the throats of 2 healthy children occupying similarly adjacent beds yielding S. pyogenes in one instance and S. viridans in the other. The inference was that infection gained access to the sinus from the air when this medium was heavily infected. Had this association occurred only once then it might have been said to be a co-incidence but further examples arose. Another child suffering from dactylitis with a discharging sinus on her hand developed Scarlatina on 26.9.33 when, within 3 days, marginal cellulitis occurred around this sinus and the discharge increased in amount. An examination in this instance yielded streptococci in pure culture of the type S. pyogenes. Still further evidence was shown

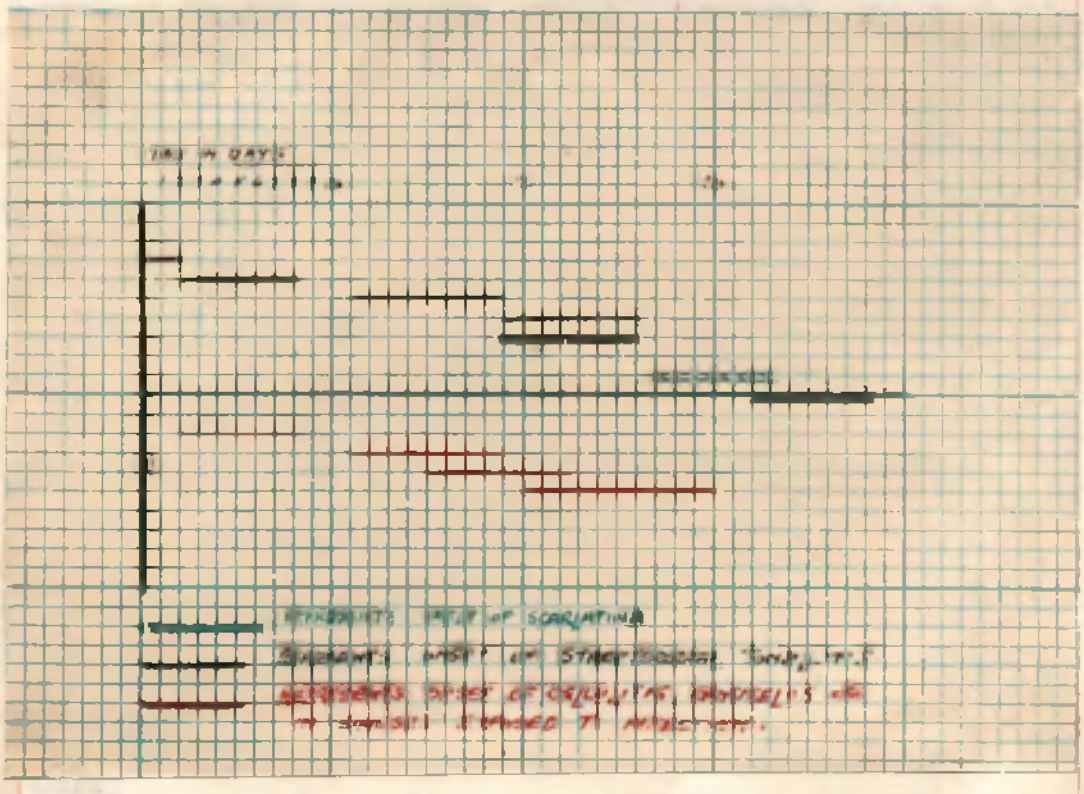
by/

by a child who had soft tissue tuberculosis of the knee joints with a small discharging wound. She developed mild Scarlatina on 5.10.33 which was followed one day later by the onset of cellulitis around the diseased joint. These fresh symptoms were associated with the presence of streptococci of the group S. infrequens. Another patient in the adjacent bed who had an axillary adenitis incised on 16.10.33 developed erysipelas from the sinus on 21.10.33 and the organisms recovered here were of the group S. pyogenes. This association was more remote yet this latter patient's dressing was done by the staff in attendance upon the case of Scarlatina and the precautions in use eliminated all source of infection other than that carried by air or from the buccal spray.

Sporadic cases of Scarlatina were of infrequent occurrence but in 3 further instances the features appearing in the wards in which they occurred were of interest. In one ward these were as follows.- The disease appeared in one case on 8.10.34 and was associated with increased activity from the sinuses of 2 adjacent patients, one on 6.10.34 and the other on 13.10.34 and in both of these cases the discharge from the sinus yielded[a] pure culture of streptococci. In another ward the disease appeared on 3.1.34 and an acute inflammation occurred in the sinus of the neighbouring/

neighbouring patient on 8.1.34 from which once again a pure culture of streptococci was obtained. In the third and last instance, where the occurrence of a 'carrier' was proved, complications in sinuses were cellulitis around an ankle and a definite increase in the activity of a groin sinus associated in both instances with the appearance of haemolytic streptococci in the discharges. These features were charted as was the occurrence of streptococcal throats and Scarlatina amongst the staff and patients. From the chart the relationship of the sinus complications to an increase from the air borne infection in the ward was clearly seen.

CHART 5.



In order to discover if this relationship existed between Scarlatina and sinus complications due to streptococci the details of each patient with a discharging sinus who developed this disease were obtained. Five cases apart from those recorded fell into this category, and no change took place in the course of sinus.

In conclusion, endogenous infection of abscesses and sinuses was shown to be absent and also that abscesses were almost entirely free from secondary infection which, when it occurred was most probably of exogenous origin. Exogenous infection was shown to be possible from the skin surface which, however, was incapable of explaining the presence of the streptococci which were recovered from the sinuses and in this respect it was shown that these organisms most probably originated from throats by droplet infection. This possibility was enhanced by the fact that a sinus which remained active and patent for a considerable period almost certainly had an infection by these organisms. In short, these wounds, different from most in that they receive considerable care before and after their onset, were open to infection such as is feared by gynaecologists and general surgeons, namely droplet infection, and this source of infection was one of importance judging from the seeming inevitability of additional secondary infection occurring in suitable soil.

THE TREATMENT OF THE CASES.

The basic principle of all treatment was the normal routine of a sanatorium. Each case was placed under conditions as nearly ideal as possible, rested adequately, fed suitably and given as much exposure to sun and air as possible. These features plus the necessary immobilisation of the diseased area were designed to build up the patient's bodily health and to increase his or her general resistance to the tuberculous infection.

Abscess formation, when it occurred was combatted mainly by aspiration, the technique and aims of which were described in an earlier chapter. Efforts were made to prevent abscesses occurring and certain forms of tuberculosis lent themselves particularly to this end. For example, if a small area of disease was seen radiologically in the centre of the neck of the femur, not involving the joint cavity but threatening to do so, then an attempt was made to remove it surgically, avoiding the joint cavity. This measure was applicable only in a limited number of sites, generally long bones such as the ulna, tibia and the lower end of the femur above the knee joint, as well as the example cited. In many instances it was successful in cutting short the progress of the disease. Next when abscess formation had taken place and progressed to involve the skin surface/

surface and appeared likely to form a sinus then the skin was incised and an attempt made to remove the underlying tuberculosis. An added value in this was that skin surface, difficult to replace, was conserved. As a measure this was not a distinct success but showed its greatest value in glandular and soft tissue lesions. No other interference was conducted with abscesses.

When a sinus had formed and sequestration was taking place in its depths the sequestra were removed. In instances where the sequestrum was single its removal hastened healing but if gradual and prolonged sequestration occurred then repeated interference was necessary. This, in an infected sinus and particularly one in which there were streptococci, often resulted in a fresh activity of the secondary infection some days later, which, fortunately, was never marked in degree. An explanation of this occurrence was thought to be in the fact that interference removed the tuberculous membrane of the sinus and exposed healthy body tissues to the action of the secondary infecting organisms. As has already been mentioned this membrane was felt to be a definite barrier to the activities of these organisms. At the other end of their history when sinuses were progressing towards healing they were carefully watched to see that no epithelium grew down their walls and they were subjected to an occasional scrape with a spoon. This appeared to hasten healing/

healing and, as it has been shown that these sinuses lacked a dangerous secondary infection, no aftermath occurred.

When the toxaemia from infection was grave the major surgical measure of amputation of the diseased member was carried out. This procedure was applicable in some cases with a primary lesion situated in the hip joint or the knee joint but was more commonly used where the disease affected either the hands or feet or the ankle joint. Its greatest value was seen when used in the last three examples, probably because it was only attempted as a last resort when the disease affected the hip or knee joints. The marked improvement which resulted in suitable cases tended to encourage its use in many instances where conservative measures and patience achieved an eventual cure. This was particularly marked in tuberculosis of the ankle joint where the source of the disease was protracted and the local disturbances great, yet many severe cases healed without amputation. No other major surgical measures were employed.

The common complications arising from a sinus such as cellulitis and acute abscess formation were treated on ordinary surgical principles and orthodox treatment was given to the few cases of erysipelas which arose.

The general treatment which the sinuses received

was a routine daily dressing with an antiseptic, the most common being carbolic lotion or eusol. Where the sinuses ran deeply into the tissues packing was inserted to assist drainage. 'Pocketing' was prevented as far as possible by careful probing with sinus forceps and attempting to increase the drainage of pus from the 'pocket' into the general sinus track. Counter incisions to assist drainage were made but mainly in an emergency such as acute abscess formation. During a phase of activity in a sinus it was necessary in many instances to have more frequent changes of dressing.

With regard to the materials used when dressing it was already remarked that the favourites were carbolic lotion or eusol. During the investigation all manners of special fluids and pastes were used but they did not have any marked effect. Amongst those which were used were B.I.P.P., Beck's paste, Morton's fluid and Calots fluids and pastes. The last named, used purely empirically, appeared to be of value as a surface dressing on the type of lesion caused by infected sinuses arising around the wrist or ankle joints.

Continuous irrigation of sinuses was attempted using weak eusol or normal saline solution without improvement but complete immersion of lesions of the hands, feet or ankle joints was found to be of value in isolated cases.

Heliotherapy/

Heliotherapy, or exposure of the wound to the sun's rays was similarly tried, again without marked change in the local condition and, in view of the risk of further infection being added, it was discontinued.

The chemical armament reduced itself to carbolic lotion, eusol, normal saline solution, Calot's paste and occasionally a 1/1000 acriflavine emulsion. Their value especially when the infection was gross was doubtful in view of the fact that the secondary infecting organisms were present in the deepest recesses of the sinuses where the antiseptic would reach only in a great dilution, if at all. In superficial lesions, capable of thorough cleansing their action was similar to what it would have been in a normal wound and rapid cleaning occurred. This was particularly noticeable in superficial glandular lesions.

The high degree of infection noted in the sinuses impressed the dangers of an infection being carried from one sinus to another by defective dressing technique and this point was carefully watched during dressing. A routine was evolved whereby those sinuses which were free from secondary infection were dressed first; those which contained organisms other than streptococci next; and finally, those infected by streptococcci.

This care was felt to be responsible for maintaining certain lesions free from streptococci and, in one instance/

instance, for maintaining complete 'sterility' in a sinus arising from a hip joint during the four months over which it remained patent.

In short, it was felt that the secondary infection of sinuses need not occur but that when it did the most suitable treatment appeared to be that founded on ordinary surgical principles.

C O N C L U S I O N S.

I. A series of 132 cases of non-pulmonary tuberculosis in children complicated by the presence of abscess or sinus formation was investigated from the clinical and bacteriological aspects.

II. The rationale of formation of 'cold' abscesses was observed and it was found that they were dependent upon the acuity of the initial infection and also on its 'site'. In the series under consideration they occurred more frequently in the younger children but sex did not appear to play any part, nor did the family history qua tuberculosis.

III. When a sinus resulted it was found to be determined by the same factors but the site of the lesion was more significant.

IV. 86% (113) of the cases investigated formed sinuses and it was found that in 91% of these sinuses there was present a secondary infection but that the serious secondary infecting organism was the streptococcus which was present in 64.8% of all the cases.

V./

V. The types of streptococci recovered from the sinuses varied considerably in their cultural and biological characters but were, in a preponderance, capable of being classified within the group Streptococcus haemolyticus.

VI. The effect of the presence of these streptococci on the local and general conditions of the patients was observed when it was found that they were responsible for all the acute complications occurring in the sinus. It was also found that they increased the risk of local spread of the tuberculous process and aided in its more widespread dissemination. There was no evidence that they influenced the 'activity' of the primary lesion itself. The toxaemia arising from their presence in the tissues was thought to diminish the natural resistance of the patients to the tuberculous process, thereby protracting the illness in many cases, while in others contributing in some measure to the fatal issue.

VII. Organisms other than streptococci were found as secondary infections and these were, in order of incidence, staphylococci, diphtheroid bacilli, coliform bacilli and some unnamed organisms. They were with the exception of the/

the coliform bacilli, avirulent or of low virulence. Symbiosis was thought to occur mainly between staphylococci and streptococci, rarely between the latter and diphtheroid bacilli although it was noted that the streptococci were capable of ousting the others from their habitat.

VIII. Of almost equal importance was the time at which secondary infection took place and its source. It was found to be absent in all cold abscesses examined in the series and occurred subsequent to the breaking down of the skin. The source of the infecting organisms was difficult to determine but in the bulk of the cases it was exogenous in origin and could only be attributed, in the case of streptococci, to droplet infection or perhaps to faulty technique during dressing.

In a certain number of cases it was highly probable, more especially in the diphtheroid, staphylococcal and coliform groups, that the source of infection was the patient's skin.

It was an interesting observation that the commonest early infection was staphylococcal and diphtheroid in character but the streptococci, appearing later, dominated the condition during/

during the highly active period and seemed to lead to the disappearance of the others, with a tendency for the reverse process to take place during the stage of healing.

IX. Lastly sinuses generally healed in close relationship to the healing of the underlying tuberculous process and that quick healing, and an uncomplicated course resulted in every instance where it was possible to eradicate the tuberculous process entirely.

REFERENCES.

Andrewes et al. M.R.C. Monograph. Diphtheria. 1923.

Andrewes and Horder. 1906. Lanc., ii, 708, 775, 852.

Brown. 1919. Mono. Rock. Inst. Med. Res., No.9.

Chalot. Indispensable Orthopoedics.

Dible. 1921. J. Path. and Bact., xxiv, 3.

Dochez, Avery, Lancefield. 1919. J. Exp. Med., xxx, 159.

Douglas, Colebrook and Fleming. M.R.C. Report No.48.

Dudgeon. Bact. Vacc. and their position in Therapeutics.

Eagles. 1926. B.J.Exp. Path., vii, 286.

Fraser. Tuberculosis of the Bones and Joints.

Griffith (1926. J. Hyg., xxv, 385.
(1927. J. Hyg., xxvi, 363.

Holman. 1916. J. Med. Res., xxxiv, 377.

Hopkins and Lang. 1914. J. Inf. Dis., xv, 63.

Lancefield. 1928. J. Exp. Med. xlvii, 91.

ibid. xlvii, 469.

ibid. xlvii, 481.

Lyall. 1914. J. Med. Res., xxx, 487.

McLeod. 1912. J. Path. and Bact., xvi, 321.

ibid. xix, 392.

McLachlan & Mackie. 1928. J. Hyg., xxvii, 225.

M.R.C. System of Bacteriology.

Smith. 1927. J. Hyg., xxiv, 420.

Thro. 1914. J. Inf. Dis., xv, 234.

Todd. 1928. J. Exp. Med., xlviii, 493.

Topley & Wilson. 'The Principles of Bacteriology and Immunity.'

Walker. 1911. Proc. Roy. Soc. B., lxxxiii, 541.

APPENDIX.

To abbreviate case histories and give only relevant details the following tables were made.

Column 1. gives initials of patients.

2. Family history.

3. Type of primary lesion:-

Acute = A

Subacute = S

Chronic = C

4. Result of search for tubercle bacilli - if present and typed then Human (H) or Bovine (B) entered in first column: if cultured and not typed '+' in second column, if neither cultured nor seen microscopically '0' in second column.

5. Formation of sinus from abscess.

6. Result of treatment.

EXAMPLE.

1	2		3	4		5		6
	F	H						
J.M^{C}B.	+	-	A.S.C.	+	0	+	0	+

MALES VERTEBRAE.

1	2		3			4		5		6	
Name	F. H.		Lesion			T. B.		Sinus		Result.	Age Group
	+	-	A	S	C	H.B.	O	+	-		
J.McB		-			+	H		+		Healed	0-5 yrs.
R.K.		-		+			+	+		Died	
A.G.		-		+			+	+		I.S.Q.	
A.M.	+		+				+	+		Improving	
M.S.		-	+				+	+		Died	
J.B.		-			+		O	+		Improving	
P.O.		-		+			O	+		Deterior-ating.	5-10 yrs.
J.B.	+				+		O	+		Healed	
D.M.	+			+			+	+		Deterior-ating.	
W.M.		-		+			+	+		Died	
P.A.		-		+			O	+		Healed	
P.H.		-			+	B.			-	Healed	
I.M.		-			+		O		-	Healed	
J.N.		-		+		H		+		Healed	
I.R.		-			+		O	+		I.S.Q.	
I.L.		-		+			O	+		Died	10-15 hrs
G.M.		-			+	H			-	Died	

FEMALES VERTEBRAE.

1	2		3			4		5		6	
Name	F.H.		Lesion A	S	C	T. B.		Sinus		Result	Age Group
H.S.		-		+		H		+		Deteriorating	
A.McM		-		+		H		+		I.S,Q.	0-5 yrs.
H.A.		-		+		H			-	Healed.	
M.S.	+				+		0		-	I.S.Q.	
D.M.		-	+				0	+		Died.	
H.R.		-	+				0	+		Healed.	5-10 yrs
J.S.		-	+				+	+		Deteriorating	
M.C.		-			+	H			-	Healed.	
J.S.		-			+		0	+		Deteriorating	
M.L.	+		+				+	+		Healed.	10-15 yrs
J.T.		-			+		0		-	Healed.	
H.M.		-			+		+		-	Healed.	
M.M.	+				+	H		+		Died.	
M.G.		-		+		H		+		I.S.Q.	15 yrs +
P.P.	+				+		0	+		Healed	

FEMALES - HIP JOINT.

1	2		3			4		5		6	
Name	F.H.		Lesion A	S	C	T.B.		Sinus		Result	Age Group.
N.G.		-		+		H		+		Healed.	
M.M.		-	+				+	+		Died.	
C.D.	+		+				+	+		Deteriorating	5-10 yrs.
M.H.	+		+				+	+		Healed.	
N.S.		-			+		O	+		Healed.	
A.S.		-		+			O	+		Healed.	
C.H.		-		+		H		+		Healed.	
J.M.		-			+		+	+		Healed.	10-15 yrs.
C.W.	+				+	H			-	Healed.	
E.M.		-		+		H			-	Healed.	
M.M.		-	+			H		+		Died	15 + yrs.

MALES - KNEE JOINT.

1 Name	2 F.H.		3 Lesion A	S	C	4 T.B.		5 Sinus		6 Result	Age Group.
W.H.		-		+			+	+		Healed	0-5 yrs.
C.P.		-	+			H		+		Died.	
A.C.		-		+			+	+		Improved	10-15 yrs.
R.C.	+				+	H			-	Healed.	

Females - Knee Joint.

1	2		3			4		5		6	
M.C.		-		+		H		+		Healed.	0-5 yrs.
M.B.		-		+		H		+		Healed.	
R.H.		-	+				O	+		Healed.	5-10 yrs.
M.C.	+		+				+	+		Healed.	

MALES - ANKLE JOINT.

1 Name	2 F.H.		3 Lesion A	S	C	4 T.B.		5 Sinus		6 Result	Age Group.
J.G.	+		+			H		+		Healed	0-5 yrs.
I.G.		-	+			H		+		Healed	
M.M.		-	+			B		+		Amputated.	10-15 yrs.
A.M.		-	+				O	+		Healed.	

FEMALES - ANKLE JOINT.

1 Name	2 F.H.		3 Lesion A	S	C	4 T.B.		5 Sinus		6 Result	Age Group.
S.M.		-	+			H		+		Amputated.	5-10 yrs.
J.M.	+			+			O	+		Healed.	
A.W.		-	+			H		+		Healed.	
H.M.		-	+				+	+		Healed.	10-15 yrs.
M.T.		-			+	H			-	Healed.	

MALES - LONG BONES.

1 Name	2 F.H.		3 Lesion A	S	C	4 T.B.		5 Sinus		6 Result	Age Group.
H.J.		-		+			+	+		I.S.Q.	
S.M.	+				+		O	+		Healed.	0-5 yrs.
G.D.		-		+			+	+		Healed.	
J.G.		-		+			O	+		Healed.	
T.S.	+				+		O	+		Healed.	
J.M.		-		+			+	+		Healed.	
D.P.		-	+				+	+		Improving	5-10 yrs.
J.G.	+		+			H		+		Healed.	
J.H.		-		+		H			-	Healed.	
W.H.		-	+			B			-	Died.	
J.S.		-	+				O	+		I.S.Q.	10-15 yrs.

FEMALES - LONG BONES.

1	2		3			4		5		6	
S.M.		-		+			+	+		Healed.	
R.M.		-		+		H		+		Healed.	0-5 yrs.
A.K.	+		+			H		+		I.S.Q.	
H,C.	+		+			H		+		Died.	10-15 yrs.

MALES - DACTYLITIS.

1. Name	2 F.H.		3 Lesion A	S	C	4 T.B.		5 Sinus		6 Result	Age Group
R.P.		-	+				+	+		Amputated	5-10 yrs.
D.S.		-	+				O	+		Healed	
J.B.		-	+			H		+		Healed.	

FEMALES - DACTYLITIS.

M.L.		-		+			o	+		Healed.	0-5 yrs.
R.McM.		-	+				+	+		Died.	
R.S.		-			+		O	+		Improving.	
N.P.	+		+				O	+		Improving.	
B.C.	+			+			+	+		Healed.	
T.H.		-		+		H		+		Healed.	5-10 yrs.
A.C.		-			+		O	+		Healed.	
A.M.		-	+			H		+		Improving	10-15 yrs.

MALES - GLANDS AND SOFT TISSUES.

1	2		3			4		5		6	
Name	F.H.		Lesion A	S	C	T.B.		Sinus		Result	Age Group
J.L.		-			+		0	+		Healed.	0-5 yrs.
J.R.		-		+			+	+		Healed.	
G.M.		-	+			H		+		Healed.	
J.C.	+				+		0	+		Healed.	
J.M.		-		+			+	+		Healed.	5-10 yrs.
J.M.	+			+		B		+		Healed.	
H.M.		-			+		0		-	Healed.	10-15 yrs.

FEMALES - GLANDS AND SOFT TISSUES.

1	2		3			4		5		6	
I.C.	+		+				+	+		Healed	0-5 yrs.
M.M.		-		+			+	+		Healed	
A.C.		-		+			+	+		Healed	
L.C.		-		+			+	+		Healed.	
J.B.		-	+				0	+		Died.	5-10 yrs.
M.F.		-			+	H		+		Healed	
C.W.		-	+			B		+		Healed	
M.D.		-		+			0	+		Healed	
E.M.		-		+			+	+		Healed	
M.S.		-		+			+	+		Healed	
C.W.		-		+			0	+		Healed	10-15 yrs.
K.C.	+		+				0	+		Healed	
I.W.		-		+			0	+		Healed	

MALES - MISCELLANEOUS.

1 Name	2 F.H.		3 Lesion A	S	C	4 T.B.		5 Sinus		6 Result	Age Group.
W.A.		-			+		O	+		Died.	5-10 yrs.
R.B.		-			+		O	+		Healed	
J.M.		-			+		O	+		Healed	
F.M.		-		+			O	+		Healed	
I.D.		-		+			O		-	Healed	10-15 yrs.
D.R.		-		+			+	+		Healed	

FEMALES - MISCELLANEOUS.

1	2		3			4		5		6	
E.A.		-		+			+	+		Improving	0-5 yrs.
E.B.	+				+		+	+		Healed	
M.M.		-			+		O	+		Healed	5-10 yrs.
C.M.		-		+			O	+		Healed	
S.N.		-		+			O	+		Healed	
A.B.	+		+				O	+		Healed	10-15 yrs.