T H E S I S

for the Degree of M. D.

by

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Affections of the Serous and Synovial Membranes in Scarlet Fever.

I.

INTRODUCTION

The cases reported on this paper occurred during the last two years in Ruchill Fever Hospital, where I have been resident in charge of Scarlet Fever Wards. For the reports of three of them I am indebted to my colleagues, namely to Dr Harrington for Case IV (of Empyema) to Dr Eadie for Case III (of Arthritis) and to Dr McKenzie for Case VI (of peritonitis).

For the histology of the last (case VI) I am personally responsible as well as for the remaining three cases the reports of which are given in full. The records of the cases of Scarlet Fever admitted to the Hospital - 3622 in number - since its opening in September 1900, have also been used and will be referred to.

To Dr Workman of the Pathological Department of the Glasgow Royal Infirmary I am also indebted for the use of apparatus in taking the accompanying photo-micrographs.

Lesions of the Serous Membranes in Scarlet Fever though known to occur cannot be regarded as common, whilst affections of the Synovial Membranes and joints (the benign forms being included) are among the complications most frequently met with in the course of the disease. Trousseau and Henoch both refer to the occurrence of pleurisy and pericarditis far on in the disease, and mention them as being malignant in nature; in regard to joint affections the former is of opinion that "articular rheumatism is an exceedingly common complication," and both describe the more unusual occurrence of suppuration in the joints. Lesions of these structures occurring from causes other than Scarlet Fever in a previously healthy person, are always serious; hence the outlook is all the more grave if they occur in the course of an acute attack of Scarlatina.

II.

INCIDENCE.

The majority of deaths from Scarlet Fever occur in children of from one to ten years of age[1]. It is in patients of this age that ulceration of the mucous membranes of the oral, nasal and pharyngeal cavities occurs most frequently and in its most severe form, such cases forming a class by themselves - the septic or anginose group of authors. It is about this age period that the serous and synovial membranes[2] are especially sensitive to all irritants reaching them from the blood stream. And it is held by most observers that the Scarlatinal toxin alone, circulating in the blood can cause inflammatory changes in the various organs.

A third factor in the production of these lesions is the subsequent predisposition of patients suffering from Scarlet Fever to infection by the ordinary pyogenic micro-organisms, and especially by the streptococcus pyogenes. So from these facts, viz: the severe ulceration of the pharyngeal and accessory cavities occurring in children of from one to ten years of age, the special sensitiveness of the serous and synovial membranes at this age to all irritants, and the subsequent/

subsequent predisposition to streptococcal infection - it follows that, among children of this age lesions of the serous and synovial membranes are most likely to occur. The ages of the cases mentioned in this paper fall within this period (one to ten years) and it is to be noted that, of the six cases recorded four were of the female sex.

III.

The Action of Toxins (A) and of Micro-organisms (B) in the production of lesions.

In the production of the lesions resulting from Scarlet Fever there are usually at least two factors to be distinguished, (A) the toxins circulating in the blood - these include the Scarlatinal toxin and those derived from the ulcerating process in the throat - and (B) the action of the ordinary pyogenic micro-organisms and especially of the streptococcus pyogenes.

Among the lesions caused by the first factor (A) the commonest is the simple synovitis of the joints occurring about the decline of the initial febrile disturbance. The joints most frequently involved are the wrist, the metacarpal and phalangeal articulations and the tendinous structures surrounding them. Other joints may be involved e.g. the knee, elbow and hip joints; and synovitis of the vertebral articulations has been described.

But the action of the toxins is not wholly limited in point of time to the first week or ten days during which the ordinary simple synovitis occurs, but may extend throughout the/

the whole course of the disease and cause more serious lesions of other organs such as pericarditis, endocarditis and possibly also nephritis(?).

Just as the toxins in diseases known to be microbic in origin have a special affinity for certain tissues e.g. the diphtheria toxin for nerve structures, so the Scarlatinal toxin would appear to attack by preference structures containing fibrous tissue - a tissue which enters largely into the formation of synovial and serous membranes.

This selective action for fibrous tissue structures is also one of the chief characteristics of the toxins in acute rheumatism, a disease now regarded by most observers as microbic in origin[3]. It is in the lesions of fibrous structures e.g. in ulcerated heart valves[4], in synovial membranes, and in rheumatic nodules that micro-organisms have been found most frequently in this disease; so that now many are of opinion that endocarditis is the direct result in every case of micro-organisms[5]. There are, however others who still think that the Scarlatinal toxin alone can cause lesions in the various tissues. Jurgensen[6] with regard to this point says that 'the Scarlatinal toxin alone is able to produce serious changes in the entire cardiac system', and speaks of the heart lesions as constituting a "Pancarditis" of/

of that organ. In support of this, he refers to the pathological findings of E. Romberg, who in the examination of ten cases found myocarditis, interstitial and parenchymatous in seven cases, pericarditis in six, and endocarditis in five. This last observer is also of opinion that the Scarlatinal toxin alone can cause all of the above mentioned lesions. Until however the primary infective agent of Scarlet Fever has been isolated, it is useless to try to assign to the Scarlatinal toxin or to a complicating organism each its separate role in the production of lesions for which, in the present state of our knowledge, they must both be held responsible.

Regarding now the action of the pyogenic micro-organisms (B), pyogenic infection of the serous and synovial cavities is necessarily of a more acute character and is more immediately dangerous to life than the lesions due to (A) the toxins in the blood.

In the production of the former lesions both factors (A & B) are concerned, the toxins in the blood first lowering the resistance of the tissues of the cavities, and thus rendering them more liable to infection by micro-organisms. Though both factors contribute to the production of these lesions their/

their gravity lies not so much in the severity of the Scarlatinal attack (though in a severe case this undoubtedly tells against the patient) as in the subsequent infection of the tissues by virulent micro-organisms. In many of these cases infection takes place through secondary lesions of the throat, as occurred in cases I and VI of this series.

During the first week or ten days of the acute attack of Scarlatina when active ulceration is going on in the fauces and pharynx, it can readily be understood that pyogenic infection of these cavities is very liable to occur e.g. in case II (Arthritis).

But infection of the other cavities - peritoneum, meninges, and pleura - is usually a late occurrence. Thus in case V infection of the meninges occurred after a reinfection of Scarlatina, and in case VI after a secondary ulcerated throat. So also in case IV (of empyema) the pleural infection did not come on till late in the disease.

A Nephritis accompanied the infection of the cavities in two cases viz: III and IV.

In case III the nephritis occurred along with infection of the second (the right) elbow joint; in case IV (empyema) it became evident on the day after the onset of the acute pleurisy. It is probable that the cause of infection of these/

these cavities contributed also to the occurrence of the nephritis. The only common channel by which these different structures could be almost simultaneously affected is the blood stream.

Most authors lay stress on this occurrence of pyogenic infection of the serous cavities during the course of a Scarlatinal nephritis. And considering the liability of these cavities in ordinary acute nephritis to simple effusions, and the known susceptibility of Scarlatinal patients to streptococcal infection, it can readily be understood that nephritis predisposes to pyogenic infection of these cavities.

In reference to this point, G. B. Smith and M. D. Sturge[7], from an analysis of nine cases of joint infections occurring in 5000 cases of Scarlet Fever, are of opinion that "both lesions (i.e. of joints and of kidneys) are probably expressions of the same general poisoning of the system."

Out of the 3622 cases of Scarlet Fever admitted to this Hospital, pyogenic infection of synovial cavities occurred in seven cases, of serous cavities also in seven.

Regarding the synovial infections: In one case, a septicaemia from which the patient died, both elbow joints and the sterno-clavicular were affected. In another case an interphalangeal joint was infected. This was opened and recovery/

recovery ensued. In two cases (II and III of this series) the corresponding joints on each side of the body were involved. In one pus was evacuated from both joints, and the patient recovered with perfect movement in the affected joints. The other case died.

Of the seven cases of infection of the serous cavities two occurred in the pleura, three in the peritoneum, and two in the meninges. No case of infection of the pericardium (excepting the terminal pyopericardium in case V) or of hydropericardium, conditions referred to by many writers, has ever been recorded in this Hospital.

Of the above mentioned complications of the serous membranes, pleurisy is described as by far the commonest, peritonitis much less common, and meningitis least of all. Most writers regard the two last conditions as rare.

Of the three cases of peritonitis, one occurred during convalescence forty four days after the acute attack of Scarlatina. Post mortem general peritonitis was found and one of the retroperitoneal glands was caseous. No culture was made of the exudate, and though it is included here, the case must be regarded as of doubtful Scarlatinal origin, i.e. peritonitis might have developed apart altogether from the attack of Scarlet Fever. In another the peritonitis developed ten/

ten days after a nephritis had occurred. Post mortem general peritonitis was found, the fluid from which shewed streptococci. One case of meningitis is reported below; the other, of streptococcal origin also, occurred after a secondary sore throat; it was published in the Glasgow Medical Journal for May 1905.

In the 3622 cases of Scarlet Fever, complications affecting the heart structures have been recorded in forty four cases, giving a per centage of 1.5 of the cases admitted.

In these heart complications the pericardium was involved in two cases, the endocardium in twenty six, the pericardium and endocardium combined in six. Rheumatism in association with pericarditis was noted once, with endocarditis three times.

Case I is one of the cases of endocarditis in which during the course of the heart involvement, a hemiplegia occurred. It is the only one of the six cases in which the lesion found was caused by the toxins in the blood. In all the other cases micro-organisms were shewn to be the causal agents, either during life or post mortem.

SUMMARY OF III.

Action of Toxins (A) and of Micro-organisms

(B) Lesions due to A - synovitis, pericarditis, endocarditis, nephritis (?).

Toxins have selective action for fibrous tissue.

Comparison with Acute Rheumatism.

Can the Scarlatinal toxin alone produce lesions?

Both factors (A & B) are concerned in pyogenic lesions.

Their danger lies in infection of tissues with virulent organisms.

Infection occurs often through secondary lesions.

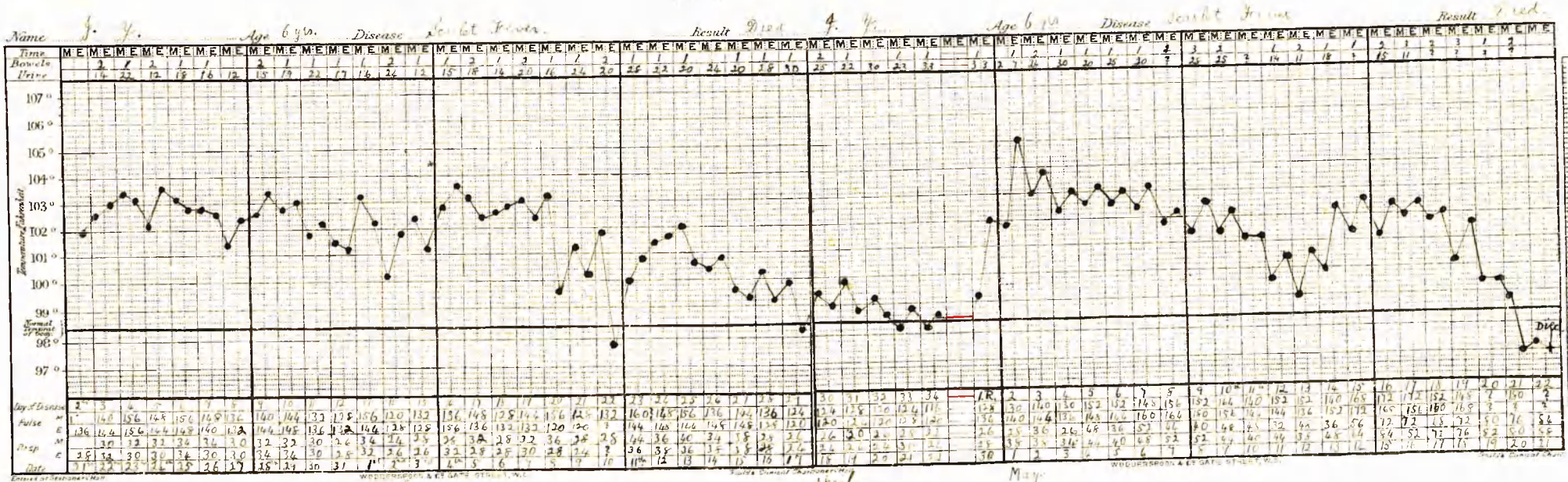
Infection of Serous Cavities a late occurrence.

Nephritis predisposes to these infections.

Pyogenic infection of Serous and Synovial Cavities occurred each seven times in 3622 cases of Scarlet Fever.

Heart complications occurred in forty-four cases.

Case I of endocarditis the only case in this series due to toxins.


Name J. Y.
Age 6 yrs.
Disease Scarlet Fever.
Result Died
Name H. Y.
Age 6 yrs
Disease Scarlet Fever
Result Died
Time
Bowels
Urine
Temperature Fahrenheit
Normal Temperature of Body
Pulse
Resp
Date
March
April
April.
May
DIED

IV.

Reports of Cases.

Case I.

J. Y. (female)
age 6 years
36 Port Dundas Road.

Admitted March 21st, 1904.

Present illness started on March 20th with sore throat; a rash was also noticed on the chest. Later in the evening she was sick, and vomited.

She suffered from whooping cough, diphtheria and measles in infancy.

Patient is one of a family of two (her sister was admitted with her suffering from Scarlet Fever) and has always been considered healthy. There is no evidence of rheumatism in the family history.

On admission - Her temperature is 102.2; pulse 136 and respirations 28 per minute.

She/

She is very restless in bed and objects strongly to all treatment.

She is fairly well developed, but is poorly nourished.

A brilliant scarlatiniform rash is present on trunk and extremities.

The skin papillae over extensor surfaces of both elbows are prominent, giving the skin a "rough" feeling.

The tongue in the anterior third is reddened, and has its surface epithelium denuded exposing the prominent dorsal papillae. A white fur covers the posterior two thirds.

The fauces and tonsils are congested, swollen and oedematous; on the surfaces of the latter, little points of white secretion are present.

The submaxillary glands on each side of the neck are enlarged and tender.

Lungs: Nothing abnormal can be detected.

Heart: The apex beat is in the 5th interspace, 2" from midsternum.

The cardiac dullness is within normal limits.

Both sounds of the heart are well heard and are free from murmur.

Urine, is straw coloured, of S. G. 1018, and contains a/

a haze of albumin, but no blood.

Ulceration of the tonsils and fauces was severe and extensive, and superficial parts of former necrosed and came away as sloughs. Nasal discharge was profuse and purulent, and temperature kept high—102-103. On 27th March urine contained albumin in fair amount but blood was not present. On the 28th March both ears had commenced to discharge, and the purulent nasal secretion had not lessened any in amount; the temperature was still keeping high. On April 4th temperature reached 103.6 and pulse was keeping at from 120-140 per minute. On April 6th the pulse was found to be irregular for the first time, and the cardiac condition was noted as follows:

Apex beat was diffuse, and was present in the 5th and 6th interspaces, $2\frac{1}{8}$" from mid-sternum.

The borders of cardiac dullness were: The right was at the right margin of sternum, the outer was immediately outside the nipple line, the upper was at the lower border of 3rd rib. Transversely the cardiac dullness measured $2\frac{1}{2}$". The heart's sounds were very rapid, 136 per minute, and on auscultation the first sound was thought to be "blurred."

No precordial pain or discomfort had ever been complained of by the patient. On 8th April, a small subcutaneous abscess/

abscess on the outer aspect of the left arm was opened. Cardiac condition was as noted on 6th, except that the first sound was now almost obliterated; no murmur could be detected.

On April 10th about 5 p.m. patient suddenly complained of pain in the head,and this was so severe that she cried out. Her colour was very bad,and her pulse had become almost imperceptible. She could not be roused, nor did she answer when spoken to. The pupils were unequal, the left being more dilated than the right, and they did not react to light. Some spasmodic jerkings of the muscles of the left arm were noticed, but there were no convulsions. Meanwhile the temperature had dropped to 97.8, and the pulse was still uncountable. The muscles of the left arm and to some extent those of the left leg were flaccid,and the limbs dropped from the hand to the bed in a very 'limp' manner.

Next morning April 11th, the paresis of the muscles of the left leg, arm and left side of face was more marked, but patient had not yet regained consciousness and was in a very critical condition. The knee jerks could not be obtained in either leg,nor could ankle clonus be elicited. The fundi oculorum shewed nothing abnormal. During the next three days the pulse was very rapid, 130-150 per minute, and of poor quality. On auscultation the first sound of the/

the heart could not be distinguished.

After this patient's condition rapidly improved so that by April 21st her temperature had reached normal, though the pulse still continued to keep a high rate - 116 to 120 per minute. On auscultating the heart a short, soft murmur was heard to follow the first sound. It could be detected round in the axilla. The urine still contained a slight haze of albumin. Though patient could use neither the left arm nor leg, the paralysis was thought to be not quite so absolute as on April 10th. Her general condition was improved and child was brighter.

This improvement continued till the evening of April 30th when her temperature suddenly rose to 102 and she was sick and vomited. On the evening of next day (May 1st) the temperature was 105 and a scarlatiniform rash was present on the trunk and extremities and by the 2nd was well out. The throat was again inflamed and oedematous, and the sub-maxillary glands on each side of the neck were enlarged. Patient was now evidently suffering from a reinfection of Scarlet Fever.

Up to May 6th temperature level was at about 103, pulse rate 130-160 per minute and of poor quality. On auscultating the heart it was impossible to distinguish the sounds/

sounds,and to say whether or not a murmur was actually present. Patient's general condition was bad, and the throat had not yet cleaned up. By May 12th the temperature had fallen to 99° but pulse still kept rapid, 140-150 per minute on an average. The temperature now continued to go steadily up reaching 102.6 though the throat and nose were now healed.

On 16th patient's colour had commenced to fail and her general condition was worse.

Patient died suddenly on May 21st at 2.30 p.m.

A post mortem examination was made on the 22nd May. In the right hemisphere of the brain an area of softening was present. It involved the internal capsule and stretched from beyond the grey matter in front, 1½" into the grey matter behind. In the centre of the softened area was a dark greyish mass almost like a slough. None of the larger vessels were found thrombosed. A culture from the fluid remained sterile.

Heart: There was no excess of fluid in the pericardium.

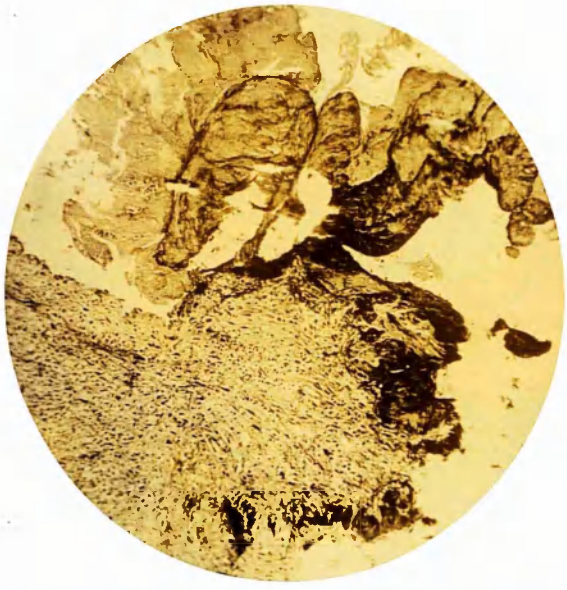
Viewed in situ its area was enlarged. The enlargement involved chiefly the area of the left ventricle. The aortic valves were incompetent.

On cutting into the ventricle the cardiac muscle was found/

p19A

Note:

The sections from which these micro-photographs have been taken, are stained with Heidenhain's Iron Haematoxylin, unless where otherwise stated



No. 1

Microphotograph of section of aortic valve showing vegetation.

120 Diams.

found to be pale, but its thickness was normal.

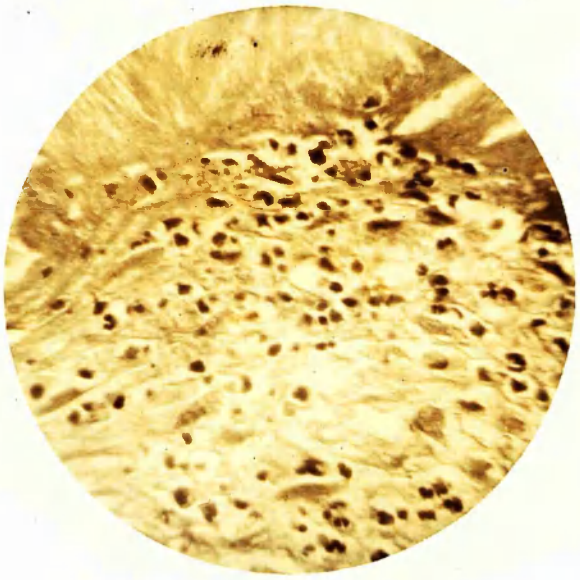
On the cusps of the mitral and aortic valves fresh reddish white vegetations were present along the line of contact of the valve curtains; they were situated some little distance up from the edges of the curtains. The vegetations were each about the size of a split pea. Those on the mitral valve were on the auricular surfaces, those on the aortic valves on the ventricular aspects of the valve curtains. The latter vegetations were of somewhat larger size than the former, and were very friable and easily detached.

The tricuspid and pulmonic valves were healthy.

The lungs shewed hypostatic congestion at their bases, but were otherwise normal. On the surface of the left kidney were three linear indentations. Under the microscope they were seen not to be infarctions. The liver shewed some white areas of degeneration. The spleen was enlarged but contained no infarctions.

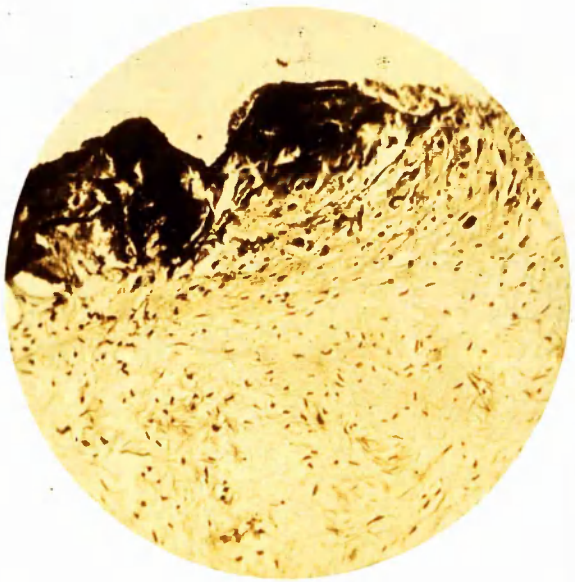
Histology: Section of aortic valve and vegetation (low power). From the free margin of the valve curtain up to the base of the vegetation the surface endothelium is continuous and is normal in appearance. Immediately before the point of attachment of the vegetation the cells in the subendothelial tissue have undergone active proliferation. The vegetation is composed of fibrin having a 'dendritic'

p.208.



No. 2.

Microphotograph of section of aortic valve, showing vegetation and round celled infiltration. Stained with haematoxylin and Eosin.
400 Diams.



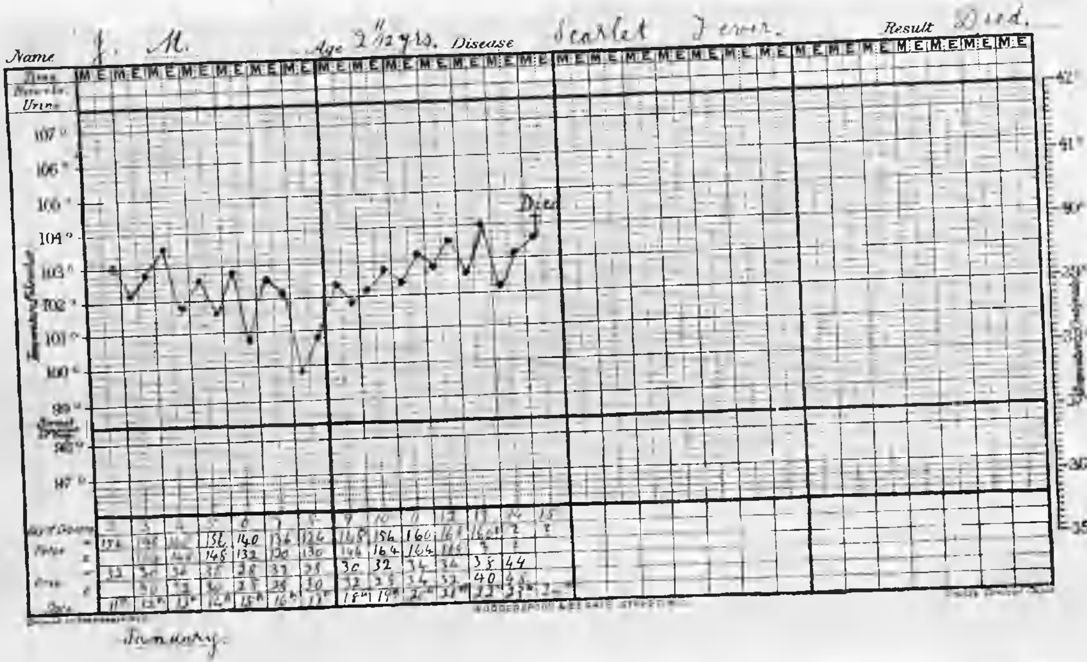
No. 3.

Micro-photograph of section of mitral valve. showing vegetation and round celled infiltration. 130 Diams.

arrangement and in some places it has 'eaten into' the substance of the valve.

High Power: The vegetation is attached along a broad base so that a large part of the free margin of the valve is involved in the ulcerative process; the mass of fibrin spreads out beyond its base, thus overhanging the healthy endothelium. In the subendothelial layers there are present proliferated connective tissue corpuscles and round cells. These extend deep into the valve structure. In the free margin of the vegetation, whose edges in some places are very rough, are present red and white blood corpuscles evidently derived from the blood stream. Stained with Gram's and other bacterial stains, no organisms can be detected.

Section of Mitral valve and vegetation shews similar inflammatory changes, but the infiltration with round cells does not extend so deeply into the valve structures, being confined to the neighbourhood of the vegetation. The vegetation itself is not so large, though the line of the endothelium is interrupted for some distance. At the junction of the fibrous valve structure with the myocardium there is seen to be an infiltration with round cells of the interstitial tissue between the muscle cells. Many of the latter stain only very faintly, and the normal transverse striation in them has disappeared.


Name J. M.
Age 2½ yrs.
Disease Scarlet Fever.
Result Died.
Died
January.

CASE II.

J. M. (female)
age 2 11/12 years
575 Alexandra Parade.

Admitted January 11th, 1904.

Present illness started on January 10th when she complained of sore throat and was sick and vomited. On the morning of 11th patient was again sick and a rash was noticed for the first time on her chest.

She has had no previous infectious diseases and has always been very healthy.

She is one of a family of four who are all alive and healthy. There is no history of tubercle or rheumatism in the family.

On admission: Her temperature is 103, pulse 156, respirations 32.

Patient is very restless. Her cheeks are flushed and there is marked circum oral pallor present.

She is a well developed and well nourished child.

A commencing scarlatiniform rash is present on the trunk and extremities.

The tongue is covered with a thick white fur on the posterior /

posterior third, while the anterior third is congested and has its surface epithelium denuded, shewing the prominent papillae beneath. The tonsils are reddened and oedematous; their free margins are covered with secretion.

There is nothing abnormal in heart or lungs.

Urine: Straw coloured S.G. 1016, contains a haze of albumin.

By January 14th ulceration of fauces and tonsils had commenced and extended deeply into the tissues. Nasal discharge was also present and was very profuse and purulent.

On the 18th both ears had commenced to discharge. Up to this time temperature had been keeping high - above 102 and pulse rate 140-150 per minute. On 21st temperature and pulse were still high and the latter was of poor quality. The child screamed when the legs were moved, but there was no evidence of fluid in either knee joint.

On the evening of the 22nd the right knee joint was found to contain fluid, but patient was in a very critical state, her pulse running and at time uncountable; her colour had also failed once or twice.

On the 23rd the right knee joint was more swollen and tender, and the skin over the internal condyle was reddened. The left knee joint was also found to be swollen and was thought /

thought to contain an excess of fluid. It also was painful when moved. On 24th the left knee joint was more swollen. Patient died on this day.

Post mortem examination made on the 25th.

The right knee joint contained pus which yielded a pure culture of short chained streptococci. The left knee joint contained yellowish turbid fluid, a smear from which shewed a short chained streptococcus.

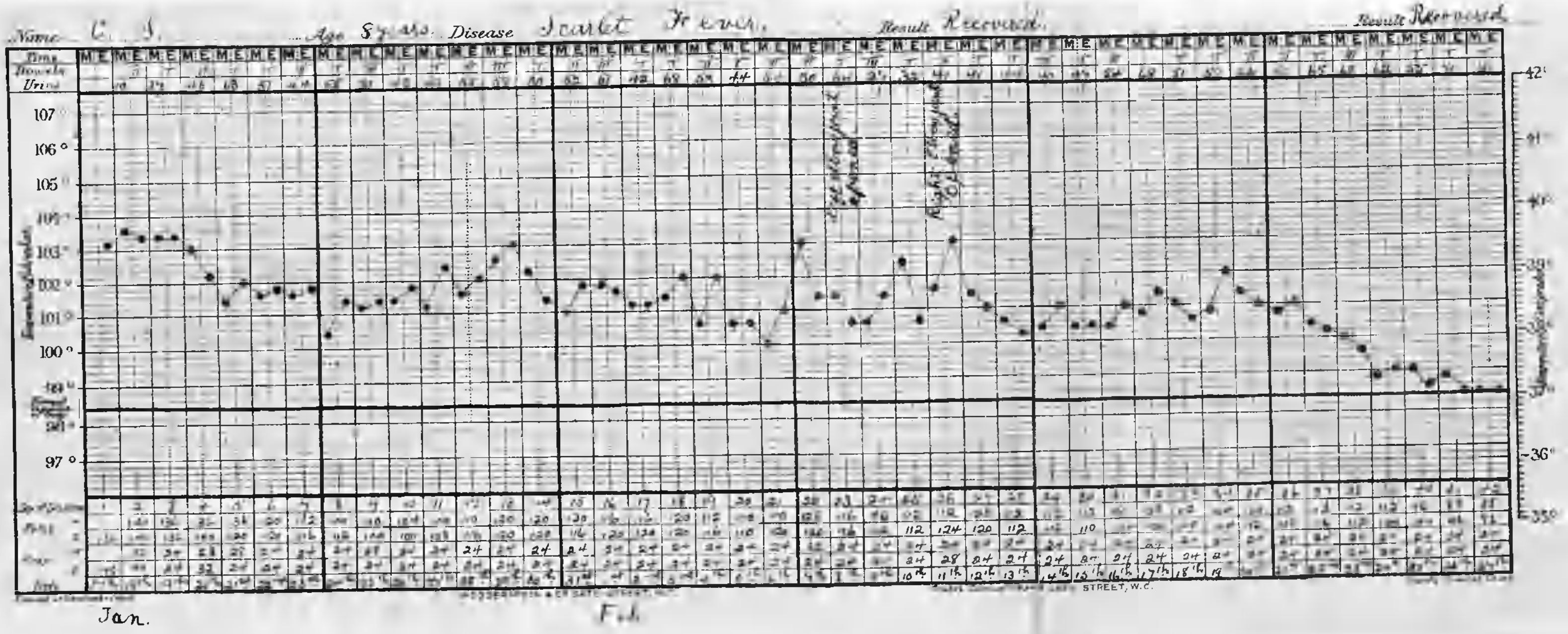
The synovial membranes, especially that of the right knee joint, were swollen and reddened. The articular cartilages appeared normal. The heart was healthy, the spleen was enlarged and there were some white areas of degeneration in the liver.

There was some cloudy swelling of the tubules of the kidneys.

The bases of both lungs shewed hypostatic congestion.

COMMENT.

This case (II) is to be classified as belonging to the group of 'Acute Septic Arthritis' of Marsden[8], in that (1) the age of the patient was under 5 years, (2) ulceration of the throat tissues was severe and deep with high temperature, and (3) the times of occurrence of the infections were the 12th and the 13th days of the disease. Ashby[9], who in 500 cases of Scarlet Fever saw only two cases of septic joint lesions, records one of them a similar case, in which in a boy of 5 years, infection of both ankle joints occurred on the 13th day of the disease, the patient dying on the 19th.


Name C. S.
Age 8 years
Disease Scarlet Fever
Result Recovered
Result Recovered
Time
Bowels
Urine
107°
106°
105°
100°
97°
42°
41°
40°
39°
36°
35°
Left Elbow joint affected
Right Elbow joint affected
Jan.
Feb.

CASE III

C.S. (Female)
Aged 8 years
48 Well Road.

Admitted on 17th January, 1904, suffering from Scarlet Fever.

The illness had commenced on the day of admission with sickness and vomiting and sore throat. A rash was also noticed on this day.

The case turned out to be a sever anginose one with continuous temperature, and deep ulceration of the fauces and tissues of the throat. This was the state of matters up to February 7th, the 22nd day of the disease. On this day temperature suddenly rose to 103 and patient complained of pain in the left elbow joint. On 8th the joint was greatly swollen; it was tender to the touch, and there was slight oedema of the surrounding tissues. The joint was opened and purulent fluid evacuated. From the pus a culture was made, and on examination showed a short chained streptococcus. On this day (8th) a large amount of albumin was present in the urine.

On the 9th February patient complained of pain in the/

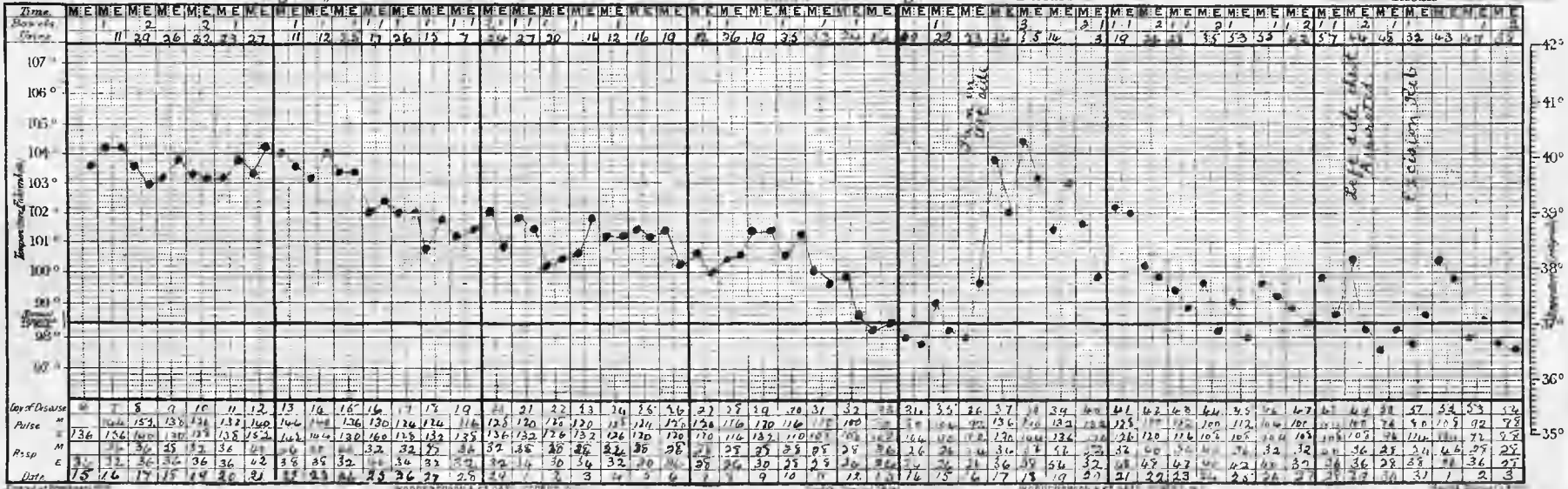
the opposite (the right) elbow joint; the temperature was 102.6. On 10th the temperature had fallen, but had risen again on the 11th to 103°.

The right elbow joint was swollen, tender, and painful. This joint also was opened and drained.

On the same day (11th) blood and albumin were present in the urine, and a nephritis had developed.

By March 27th both elbow joints had healed and the movements in each were perfect. Patient was dismissed well on April 16th.

Name [illegible] D. Age 7 yrs. Disease Scarlet Fever. Result Recovered.



CASE IV

A. S. (male)
age 7 years
7 Doncaster Street.

Admitted on February 15th, 1904, suffering from Scarlet Fever.

Illness had commenced on 15th February with vomiting and sore throat.

Ulceration of the throat tissues was severe and some sloughing of the tonsils occurred. Nasal discharge was profuse and purulent, and on 27th both ears had commenced to discharge. There was much glandular enlargement on both sides of the neck, and pus was evacuated from the right side on February 29th, and from the left on March 8th. Temperature gradually subsided and on 12th March reached normal. It remained so until the morning of March 17th, when it reached 103.6 and patient complained of pain in the left inframammary region. A pleurisy with effusion now developed on the left side. On 19th March a nephritis had also occurred. In the fluid withdrawn from the left side of the chest streptococci and diplococci were found.

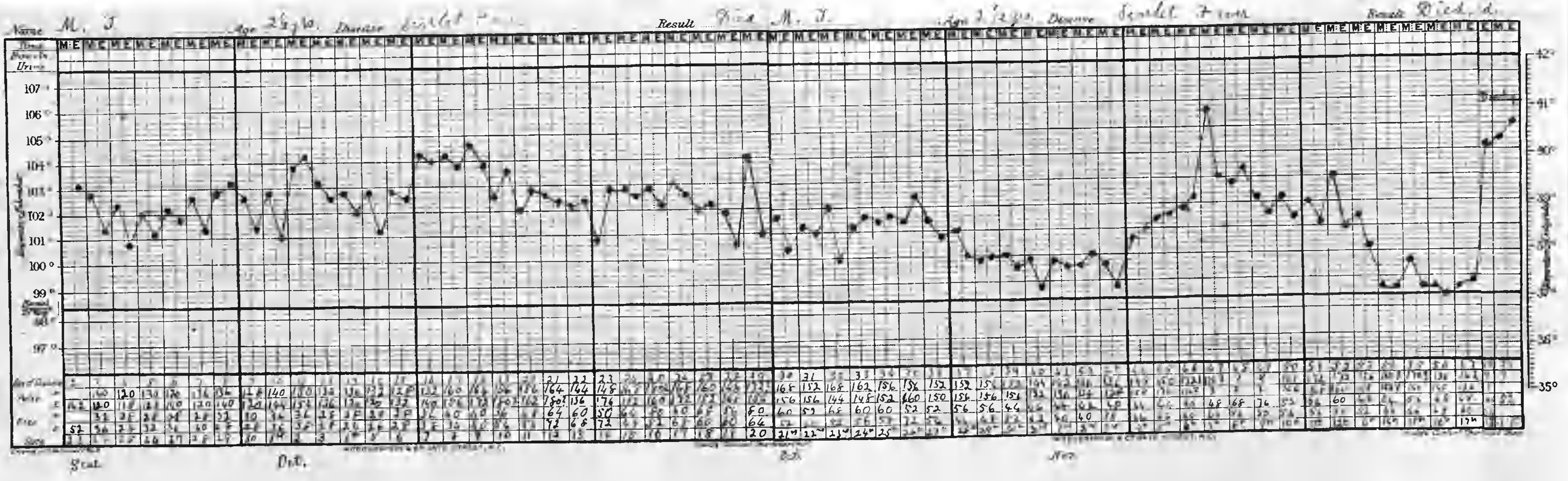
By March 23rd the throat had healed, but temperature was/

was going up to 99 and 100 at some period of the 24 hours.

On March 31st, the 50th day of illness a portion of rib on the left side of chest was excised and the cavity drained.

On April 6th the urine had become clear and by 19th May the wound of the left side of chest had healed.

Patient was dismissed well on 25th June.


Name M. J.
Age 2½ yrs.
Disease Scarlet Fever
Result
Result Died
Bowels
Urine
107°
106°
105°
104°
103°
102°
101°
100°
99°
98°
97°
42°
41°
40°
39°
38°
37°
36°
35°
Pulse
Resp.
Sept.
Oct.
Nov.

CASE V

M.T. (female)
age 2½ years
116 North Frederick St.

Admitted 23rd September, 1904.

On 22nd September she complained of sore throat and was sick and vomited. Later in the evening a rash was seen on her chest.

She suffered from measles and whooping cough in infancy, and has always been considered a healthy child.

Beyond the fact that a brother of patient's aged 5 years, died of 'bronchitis' the family history is good.

On admission: Patient's temperature is 103; pulse 142; and respirations 52 per minute.

Patient's cheeks are flushed and she is very restless in bed.

She is fairly well nourished and is slightly rachitic. On the trunk and limbs a brilliant scarlatiniform rash is present.

The tongue is furred in centre; its edges and tip are reddened and have the surface epithelium denuded, shewing the prominent dorsal papillae. Fauces and tonsils are reddened/

reddened and oedematous. On the right tonsil is a small area of white exudate.

The submaxillary glands on each side of the neck are enlarged and tender.

There is nothing abnormal present in the heart and lungs.

Urine: Is Amber coloured; S. G. 1016, contains a trace of albumin but no blood.

The case proved to be a severe anginose one. Ulceration of the throat tissues was severe and extensive, and sloughing of superficial parts of both tonsils occurred. Nasal discharge commenced on 25th September and was both profuse and purulent. Considerable glandular enlargement of both sides of the neck was present, but no suppuration ever occurred in this region. The raw granulating surface in the throat was so painful to the patient, that she had to be nasally fed from 13th October onwards. The temperature remained at about the level of 102° with exacerbations to 103 and over, and corresponding remissions to 100-101. On 29th October the right ear had commenced to discharge and the left on 30th. Throat was still dirty and nasal discharge still present.

On 14th October crepitant rales had appeared at the bases/

bases of both lungs, respirations being 40 to 60 per minute, pulse 150 to 160.

On October 25th, 28th, and 30th subcutaneous abscesses appeared over the right trochanter major, right fore arm in its upper half, and on the middle of left forearm respectively. These were opened and drained. Temperature had now fallen to 100 and was keeping at this level. On November 3rd another abscess on the skin of left forearm was opened; the temperature on this day fell to normal. Ulceration of the throat still continued but was less severe than on admission; the discharges from both ears and from the nostrils were still present. Patient was now much exhausted and her general condition was bad. On the morning of November 4th other two abscesses were present in the skin of the abdomen, one on each side of the umbilicus. On the morning of 5th November the left side of patient's face commenced to twitch, the angle of the mouth being pulled convulsively upwards and outwards. These movements soon affected all the face muscles. Three hours later the muscles of the left arm and leg became affected and the convulsive movements continued with an interval of rest of some few minutes, for the next two hours. During the convulsive movements both eyes were turned to the left and upwards, the pupils were widely dilated and did not react/

react to light. The patient was unconscious for the next three or four hours. By the following day she had recovered somewhat, and on examination paresis of the muscles of the left leg, arm and left side of face was found to be present. The knee jerk was absent on the left side, and ankle clonus could not be elicited. With the patient in a sitting posture Kernig's sign was easily obtained. The fundi oculorum were examined, but neither at this nor on subsequent occasions was anything abnormal detected in them. The leucocytes were increased in number - 15,600 per c.mm.

Other two abscesses were opened on the 1st and 13th November. On November 7th patient's temperature touched 105.6 with pulse 180? per minute; it kept at about the level of 102 until November 12th when it commenced to subside.

From November 13th the temperature remained practically normal with pulse rate 130-140 per minute, but patient's condition was getting steadily worse. On November 18th twitchings of muscles of left side of face and convulsive movements of left arm and leg again occurred. On the morning of November 19th similar movements occurred and patient died suddenly at 3.30 a.m.

A post mortem examination was made on the 20th. The head cavity was opened first. On removing the calvarium with/

with the dura mater, the meningeal surfaces were seen to be of a whitish colour and to be 'bulging,' owing to the exudation beneath them. The vessels of the meninges were engorged, and a white area could be traced along their whole length shewing the presence of exudate there.

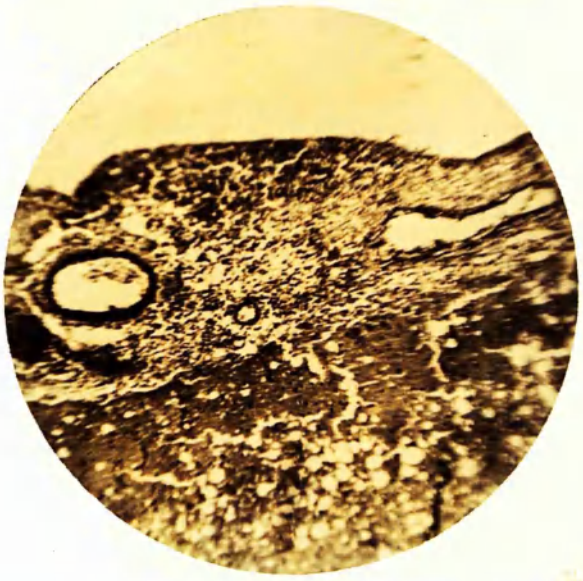
The exudate while uniformly present on both sides of the brain was most abundant on the right. It extended down over the surface of the cerebellum, and also invaded the base. It was present on the medulla and upper part of the cord.

The spinal canal was not opened. The dura mater over the base of the skull shewed no break in its continuity. Nothing abnormal was present in the internal auditory meatus of either side.

Heart: The pericardium was seen to contain fluid. It amounted to three ounces, was clear and contained flakes of lymph, free in it. The visceral layer of the pericardium was reddened and the heart's surface was covered by a layer of fibrinous exudate presenting a honey combed appearance. The heart muscle on section was pale and flabby. The valves were competent and there was no break in their endothelial surfaces. The bases of both lungs shewed marked hypostatic congestion. The spleen was large and diffluent.

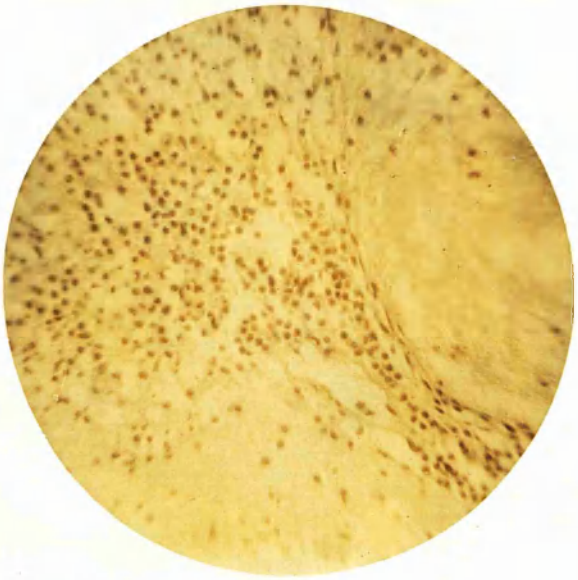
The kidneys shewed some cloudy swelling in the cortex.

There were no enlarged bronchial glands, nor other evidence/



No 4.

Microphotograph of section of cerebrum and meninges, shewing exudate in subarachnoid space. 120 Diams.



No. 5.

Microphotograph of same, shewing cells of the exudate and their massing round a vessel. Stained with haematoxylin and Eosin. 350 Diams.

evidence of tubercle.

Bacteriology. Cultures from the exudate on the cerebral hemispheres shewed the presence of staphylococci and streptococci. Cultures from the fluid in the pericardium shewed streptococci only.

Histology: Section of Meninges and cerebrum (low power).

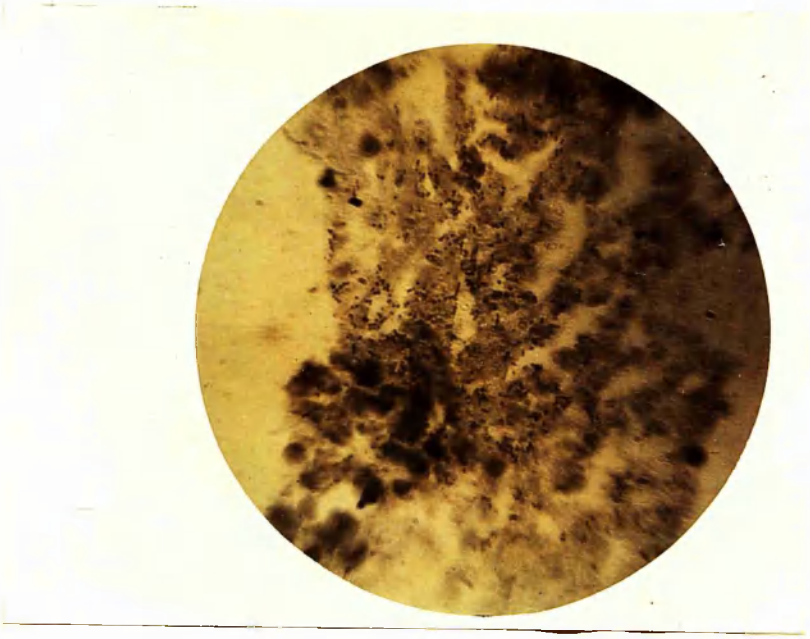
The subarachnoid space is filled with exudate which is composed of leucocytes and round cells. Sections of vessels are seen cut transversely. Round some of these the cellular elements are massed.

High Power: The cells of the exudate are composed of round cells, polymorphonuclear leucocytes, lymphocytes and a few red blood corpuscles. Many of the leucocytes stain very faintly. They invade the cerebral cortex and are present in great numbers in the perivascular lymphatic spaces. Stained with Gram's stain, a short chained streptococcus and staphycocci are shewn.

Masses of these organisms are present in the deeper layers of the exudate, down between the cerebral convolutions.

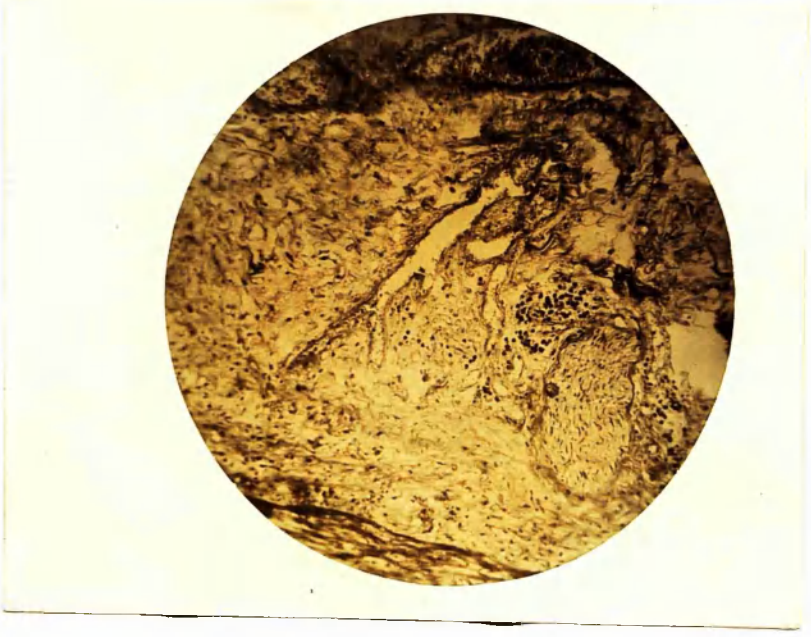
Section of Pericardium (low power):

The pericardium is acutely inflamed and has become practically disorganised. It is infiltrated by large numbers/



No. 6.

Microphotograph of section of meningeal exudate, showing streptococci and staphylococci. Gram's stain. 650 Diams



No 7.

Microphotograph of section of heart wall and pericardium shewing latter inflamed and disorganised. 140 Diams.

large numbers of leucocytes and round cells and shews newly formed blood vessels cut in various planes. On its free surface is an exudate composed of fibrin and containing many leucocytes. At some places in the section, parts of the disintegrated pericardium can be seen surrounded by leucocytes.

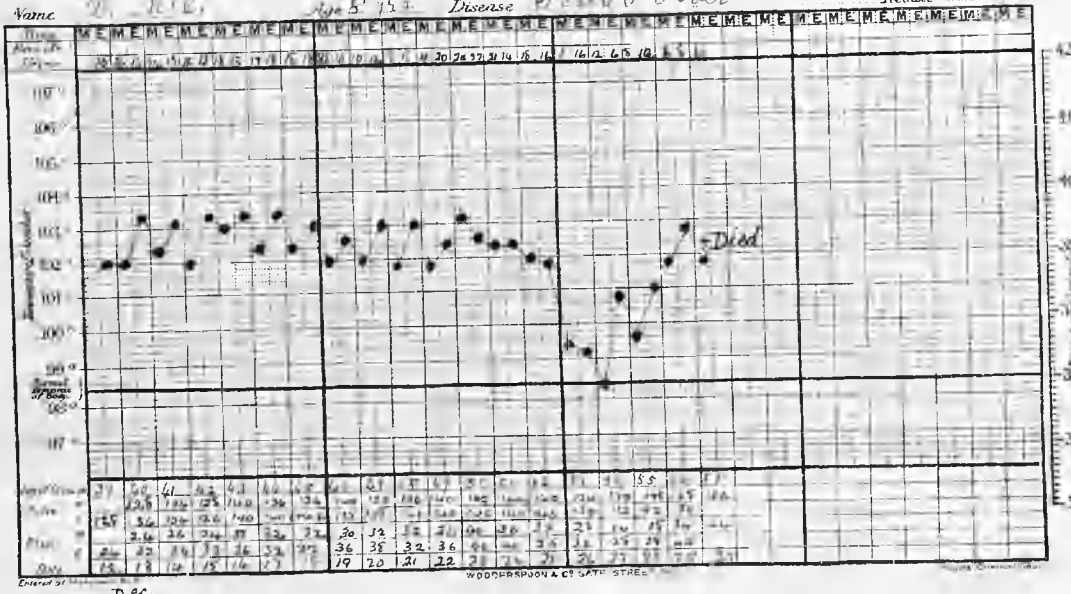
High Power: The connective tissue cells of the pericardium have undergone active proliferation and in most places round cells have invaded the heart muscle. The cells of the exudate lying between the meshes of fibrin are composed of red and white blood corpuscles and proliferated connective tissue cells. Stained with Gram's stain no organisms can be detected.

COMMENT.

This was evidently a case of 'chronic pyaemia'[10] having lasted for twenty five days from the appearance of the first subcutaneous abscess. Two serous cavities were infected, the meningeal and the pericardial, though the latter was only discovered post mortem and presented no physical signs during life. The first demonstration of such a condition post mortem is not an uncommon occurrence[11]. The absence of optic neuritis, retraction of the head, tonic spasms of the limbs and back, vomiting - symptoms usually present in meningitis - and the occurrence of a terminal pyopericardium, would make this case be classified as one of the 'vertical class' of Lees and Barlow.[12]

That meningitis is a rare complication of Scarlet Fever is shewn by the references to it in various text books. Thus in Allbutt's system of Medicine no mention of meningitis is made in the complications affecting 4015 cases.

Forchheimer mentions all serous membranes as liable to infection in Scarlet Fever. Thomas, in von Ziemsson's handbook, mentions it as a complication of the disease.


Name
Age 5 yrs
Disease Pleuritic Fever
Result Died
Died
WODDERSPOON & Co SATE STREET
Dec

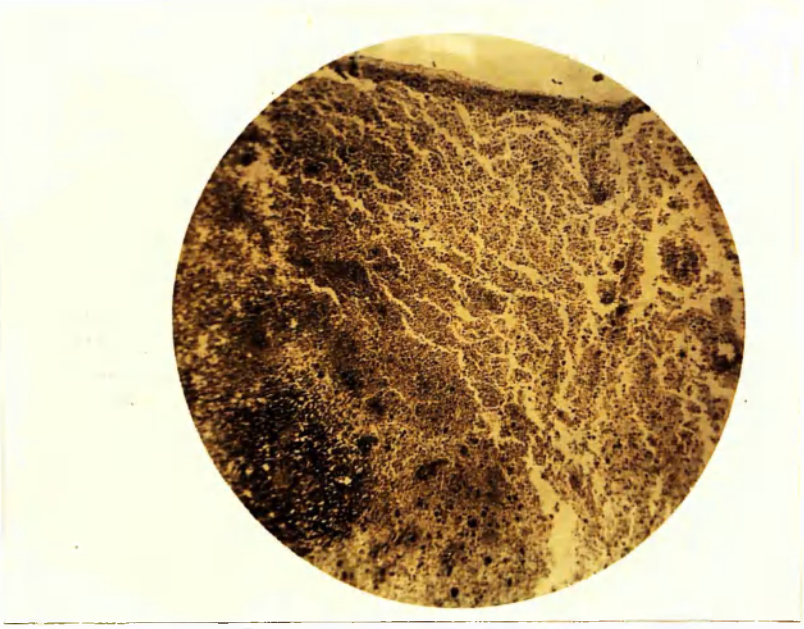
CASE VI

D. McC. (male)
aged 8 years
22 Houston Street.

Admitted November 7th 1904, suffering from Scarlet Fever. The illness had commenced on November 3rd with sore throat.

On the 24th November it was noted that patient was desquamating in a characteristic manner.

On the 12th December i.e., 39 days from the onset of his first attack, patient developed a reinfection of Scarlet Fever, and this turned out to be of a severe anginose type with ulceration of the tissues of the throat. Temperature kept continuously high, between 102 and 103 on an average. On 26th December temperature had dropped gradually to normal and pulse rate with it. On 28th it was noted that the throat was improving, but that a septic rash was present on the body. Also that pericarditis and endocarditis had developed though no accumulation of fluid could be anywhere detected. On 29th December the signs of pericarditis could not be detected, but those of endocarditis were still present. There was tenderness in the splenic region and friction was evident on palpation and auscultation. The patient's condition was evidently getting/



No 8.

Microphotograph of section of spleen, showing infarction.

130 Diams.

getting worse. On the morning of 30th December the septic condition was more marked. The abdomen was slightly distended and was tender in the left flank. The pulse was very feeble and the heart's sounds were heard with difficulty.

The patient died at 11.20 a.m.

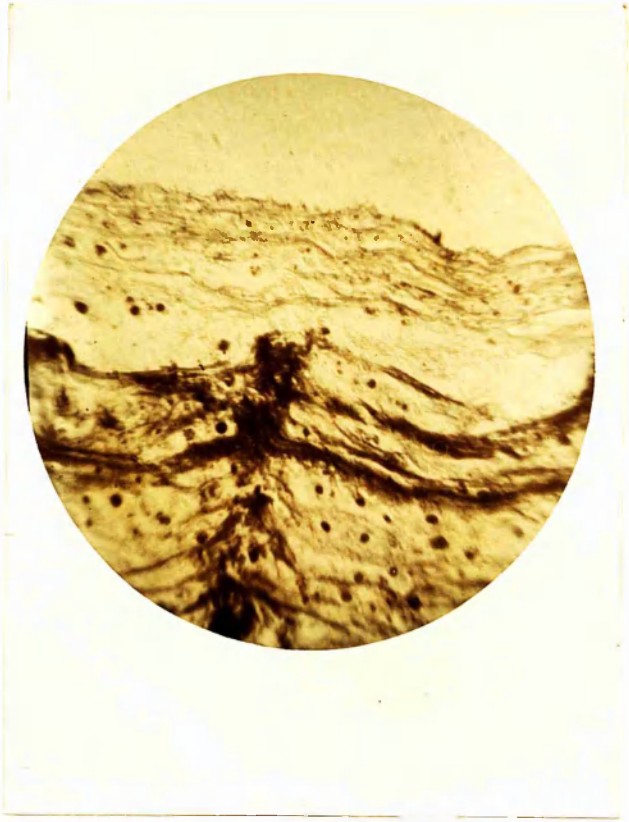
A post mortem examination was made. The abdominal cavity contained free fluid, which yielded a pure culture of the streptococcus pyogenes; it amounted to about a pint. The peritoneal coats of all the organs were reddened.

The spleen contained a large infarction which involved part of its free margin, and there was some inflammatory exudate on the surface of its capsule. The liver was pale and shewed some areas of degeneration in its substance.

The heart was pale and flabby, and there was some roughening of the pericardial surfaces at its base. The mitral valves had the appearance of having vegetations on their endocardial surfaces.

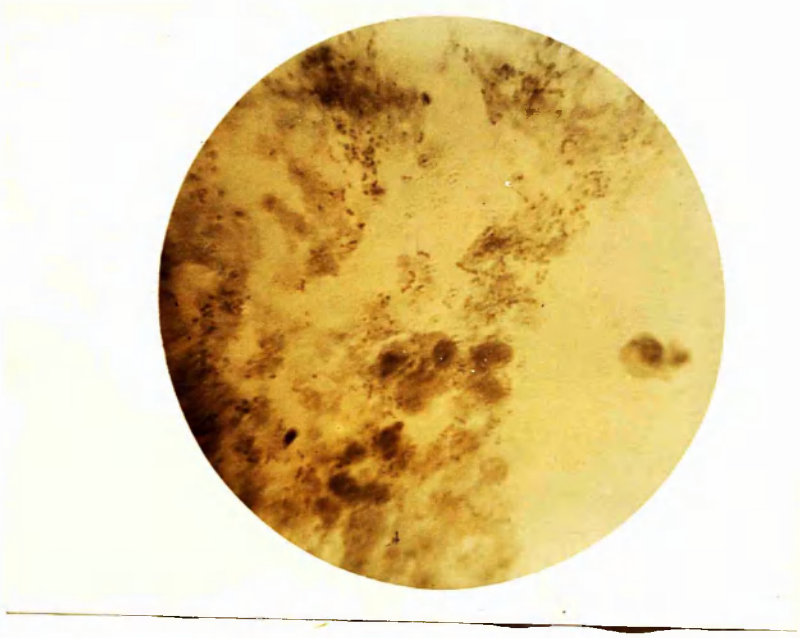
The lungs shewed hypostatic congestion of both bases.

Histology: Section of Infarct of Spleen (low power). The tissue of the infarct is very friable and has apparently broken up into smaller areas on section. At the edge of the infarct on one side is seen the normal spleen structure with/



No. 9.

Microphotograph of section of splen, showing exudate on its peritoneal surface. 400 Diams.



No. 10

Microphotograph of section of splen, showing streptococci and staphylococci in peritoneal exudate.

Grams stain. 650 Diams.

with trabeculae running through it and masses of leucocytes in the Malpighian corpuscles. The tissue of the infarct presents nothing of the normal structure of the spleen; its fibrous tissue capsule stains faintly and trabeculae running into its substance are absent. Here and there the tissue of the capsule has some exudate with leucocytes adhering to it. The whole of the tissue elements of the infarct stain only faintly.

High Power: The tissue of the infarct is composed of red blood corpuscles in various stages of degeneration; they stain faintly. Traces of trabeculae can be made out, mostly in and around the altered Malpighian bodies. In the infarcted tissue no blood vessels are present.

Section of spleen shewing Peritonitis (High Power).

On the surface of the capsule there is exudation. This is composed mainly of fibrin and leucocytes. The fibrous capsule is infiltrated with leucocytes, and at some parts separation of its layers has taken place. Stained with Gram's stain streptococci and staphylococci are present in the exudate on the surface of the capsule. These can also be seen blocking the lumen of some of the vessels.

Sections of various parts of the mitral valves shewed no inflammatory changes, nor could organisms be demonstrated in them.

Comment.

This case was of the anginose type and the peritonitis occurred late in the disease - 56 days from the first acute attack and 17 days from the reinfection, the patient dying on the 57th day of the disease.

In two cases of peritonitis occurring in Scarlet Fever recorded by McCollom and Blake[13], the streptococcus in pure culture was recovered from both. In one, a child of five years, the peritonitis developed on the twenty-third day of illness. Paracentesis of the abdomen was performed on the forty-first day of disease. On the next day leaking of fluid occurred from the umbilicus and continued for several days. The patient made a good recovery.

In the other case, a man of thirty-one years, the peritonitis occurred on the twenty-third day of the disease. The abdomen was opened but the patient died. These observers consider that in both cases infection occurred via the blood stream.

In the case of D. McC. (Case VI) given above it is probable that the blood was first infected, and that the infection of the peritoneum occurred secondarily from the septic infarction in the spleen.

According/

According to Nothnagel the haematogenous form of peritonitis is exceedingly rare, even in infectious diseases, and this author is of opinion that infection of the cavity is almost always from a local source e.g. a gland or one of the contained visceral organs.

V.

Discussion

In the cases recorded in this paper (excepting case I) the streptococcus alone or along with other organisms was the cause of infection of the various cavities, and ulceration of the throat tissues was severe in all of them. Now at a first glance it is not easy to see how ulceration of the mucous membranes of the fauces and pharynx should cause such serious lesions in other organs of the body, remote from the original focus of disease. But in this, Scarlet Fever is on a level with diseases known to be microbic in origin. In these diseases involvement of the serous and synovial cavities is well known to occur. For example: In infection of the urethra or other mucous membrane by the gonococcus the organism has been recovered from the knee joint[14], and peritonitis and more rarely meningitis[15] have been described in connection with it. In Enteric Fever meningitis and peritonitis[16] are well known complications; arthritis also, due to the Bacillus Typhosus, has occurred in some few cases. In Epidemic Cerebro Spinal Meningitis[17] infection of the pleura occurred in some outbreaks, in others arthritis of various/

various joints was common, and occasionally pericarditis and even endocarditis were found, the causal agent in each instance being the Diplococcus of Weichselbaum. In Rheumatism, besides the joint involvements pleurisy is well known, and peritonitis[18] is now generally recognised as a possible complication of the disease; and other examples might be given.

In such diseases infection of the blood stream takes place at some period of the malady, and subsequently the serous and synovial cavities become involved. In some of these diseases the causal organism has been actually recovered from the blood in severe cases e.g. in pneumococcal infection[19]and in severe cases of Enteric Fever[20]. This has been actually done in one case of Scarlet Fever by Baginsky and Sommerfeld[21], in which during life, lumbar puncture was performed as a therapeutic measure on account of coma and convulsions. In the fluid withdrawn and subsequently in the blood streptococci were demonstrated. Post mortem too streptococci have also been demonstrated in the tissues by these same observers.

In a series of 42 cases examined by them within from two to three hours after death, streptococci were found in some one organ in all the cases, the tissues examined being:- blood/

blood from the heart, bone marrow, spleen, kidney, liver, gall bladder and mesenteric glands.

Similarly Gordon[21] in the examination of 10 cases found streptococci in nearly all the organs examined.

Hence it is to be concluded that in severe anginose cases of Scarlet Fever streptococci are often present in the blood stream, and also that in the cases reported in this paper such a blood infection actually occurred.

Another point in which such cases of Scarlet Fever as we are considering, are analogous to some of the above microbic diseases, is that the primary lesion is situated in a mucous membrane - that of the mouth, and infection takes place from this. Thus in Enteric Fever the mucous membrane of the bowel, in gonorrhoea that lining the genito-urinary tract is the original focus of disease, and in pneumonia a serous membrane, the pleura, is almost invariably involved with the lung tissue.

Hence Scarlet Fever is analogous to other diseases of known microbic origin in that in severe cases (1) A mucous membrane undergoes prolonged ulceration (2) a blood infection occurs and subsequently (3) infection of the serous and synovial cavities.

Now when the blood stream has become invaded by organisms

why/

why should the serous and synovial cavities become infected?

For this a consideration of the anatomical and physiological relations of the various cavities, besides the reaction of the blood and tissues to the invading organism and its toxin is necessary.

Developmentally the pleural, pericardial, and peritoneal cavities are all part of one larger cavity - the pleuroperitoneal[22] which ultimately becomes split up into these smaller divisions. They are not 'cavities' in reality but only potentially so, and this applies equally to the various synovial cavities as well as to the subarachnoid space[23].

They all serve a common purpose, namely to insure free gliding movement between the various organs they contain, or between the articulations of bones. For this purpose of free movement a constant exudation and reabsorption of lymph goes on in their lining membranes, and this fluid in health is never in excess. If however an irritant gain access to them, then the balance between exudation and reabsorption is disturbed and fluid tends to accumulate, a true cavity thus being formed. If the irritant be chemical or toxic in nature then reabsorption of the effused fluid is possible and often actually occurs. For example, in the exudates into the serous cavities occurring in ordinary acute nephritis this is almost always the course of events.

But/

But, if the irritant be bacterial in nature, then the effused fluid furnishes a most suitable pabulum for organisms to grow in, and infection of the cavity thus progresses. This is the mode of infection in many cases e.g. in synovial membranes. And it is to be remembered that the occurrence of nephritis along with a blood infection as in Cases III & IV, predisposes to the occurrence of infection of these cavities. But in the case of the peritoneum the lodgement of organisms is not so easily effected, though its extensive superficies favours this; for it is known that from the phagocytic power of its own cells and that of effused leucocytes the peritoneum can overcome a certain number of micro-organisms, and that it can even acquire a certain degree of immunity under prolonged irritation.[18] This same power would seem to be present to some extent at least, in the pleura and pericardium and also in the vascular lining of the subarachnoid space. In the case of the pleura however, it is negatived to some extent by its intimate anatomical connection with the lungs - tissues which are very liable to undergo inflammatory changes in the variety of Scarlatina under consideration.

The synovial membranes on the contrary are comparatively avascular structures, are more liable to simple effusions, and so their resisting powers against microbic invasion are lower/

lower than those of serous membranes. We would therefore expect them to be infected oftener than the serous cavities. And this is actually what occurs, since infections of the pericardial, meningeal and peritoneal cavities are rare compared with the frequency of occurrence of infections of the joints.

The reaction of the blood and tissues to the invading micro-roganism, the streptococcus pyogenes, has also to be considered. Regarding the relation of the streptococcus to Scarlet Fever F.F.Caiger[1] says that "in anginose cases its presence may be demonstrated with tolerable certainty in the ulcerated mucous membrane, in abscesses, and discharges from an otitis media."

We would therefore expect, from the long continued suppuration caused by the streptococcus, that antibodies antagonistic to its vitality in the tissues would be present in the blood.

And this is the case, since it has been found that 'during the disease the serum of such patients invariable agglutinates streptococci derived from Scarlet Fever.'[24] This heightened resistance of the tissues to the streptococcus would account for the comparative nonvirulence of the infection in joint structures. It is also of some importance practically

in/

in the treatment of such infections, for in one of the cases of peritonitis of McCollom and Blake quoted on p. 39, recovery ensued after paracentesis only of the abdomen had been performed. From this it may be inferred that the virulence of the streptococcus found was of a low degree, either from the antibodies present in the blood inhibiting its growth, or from the altered character of the micro-organism, whose virulence in pure culture in peritoneal infections is known to be very great.

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