

"THE SERUM THERAPY OF PYOGENIC AFFECTIONS"

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by

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The treatment of pyogenic affections by antistreptococcus serum is of comparatively recent date the first recorded case in England being that of a case of Puerperal Septicaemia recorded by Angus Kennedy in the Lancet of Nov: 2nd 1895. To Marmorek working at the Pasteur Institute at Paris appears to be due the credit of having first prepared an antistreptococcus serum that is practically of a constant strength and character.

✓ Annales de
l'Institut Pasteur
1895 p 593.

I propose to review & criticise the literature & published cases & to record the notes of some cases that have come under my own observation.

Marmorek rendered horses, asses & sheep immune against an extremely virulent streptococcic infection.

✓ Soc de Biol
April 5th 1895.

Bokenham in B M J of July 4th 1896 records briefly the nature, mode of preparation and the means employed for estimating the activity of the antistreptococcus serum he states that it is serum obtained from the blood of an ass which has received during several months repeated and increasing injections of living virulent streptococci. Marmorek states that virulence and toxicity of the microbes are indispensable conditions for the production of a truly active serum. The difficulty in the preparation of this serum arises from that the fact that the microbes readily lose their virulence when grown in the ordinary culture media

such as bouillon. Bokenham tried hydrocele fluid, ascitic fluid decalcified blood plasma and the serum from the ass and the horse. None of these media were entirely satisfactory the best of them was serum obtained from the ass. Bokenham found that a mixture of bouillon (in which the microbes grow well but lose their virulence) and of asses serum (in which growth is less satisfactory but virulence is less affected) was satisfactory, a similar mixture prepared with horses serum being not nearly so satisfactory.

The principle involved differs from that involved in the preparation of antidiphtheritic serum for the antistreptococcus serum acts rather by destroying the streptococci themselves or bringing about changes which lead to their destruction than by neutralizing their chemical products as in the case of Diphtheria and Tetanus. The antistreptococcus serum appears to be more analogous to the serums employed against Cholera and Typhoid Fever.

In both the horse and the ass the reaction to even minute doses is far more virulent than with Diphtheria toxin although similar in kind.

Bullock records the results obtained in the process of immunising large animals against streptococcus pyogenes for the purpose of obtaining a specific therapeutic serum. Working at the British Institute of Preventive Medicine in conjunction with Arnard Ruffer he found that the best medium for cultivation

✓ Lancet
May 2nd 1896

was human blood serum (Two parts) and peptonised bouillon (one part) but owing to the difficulty of obtaining human blood serum ascitic fluid was substituted. In comparison with antidiphtheritic or antistreptococcus serum (1) the curative effect is slight (2) the serum is specific against streptococcus only.

Sims Woodhead states that six organisms under the name of streptococcus pyogenes have been described almost identical as regards their microscopic and naked eye appearances & it is only when the products of these organisms and their relative pathogenicity are enquired into that any distinctive characters are found. They may be divided into three groups.

V Treves Superior
Vol 1 9127.

Group I. S Pyogenes found wherever there is progressive erysipeloid suppuration, in very acute abscesses and in certain cases of Ulcerative Endocarditis.

(1) The cocci vary very much in size and are arranged in pairs or in chains (2) In gelatine tube cultures there is a delicate growth on the surface while in depth a number of minute granules are seen (3) It grows slowly at room temperature and best at temperature of body (4) does not liquefy gelatine (5) Stains well by Grams method (6) Is pathogenic to both mice and rabbits (2) S. Pyogenes malignus - found by Fleufel in necrotic foci of lencaenic spleen similar to above but grows more slowly (3) S. Septicus the

micrococci form chains which break up into diplococci
Group II. *S. erysipelatis* and *S. septo-pyanicus* have
 been described as separate species though probably
 the same (1) Grown in gelatine appear as minute points
 with scant surface growth (2) *S. erysipelatis* does not
 grow on potato while dirty white colonies appear when
S. septicus is grown (3) Either of these organisms
 when inoculated set up an erysipeloid inflammation
 unaccompanied by suppuration (4) Nenck maintains
 that the difference in the products of the two
 organisms when grown in various media indicates that
 the *S. Pyogenes* and the *S. Erysipelatis* are distinct
 species.

Group III. *S. Articulorum* separated by Loeffler in
 cases of Diphtheria from the mucous membrane. It
 occurs in long chains of which each segment consists
 of two hemispheres with intermediate Zone. It is
 pathogenic for mice but not for guinea pigs, when
 injected into veins of a rabbit, joints specially
 affected.

For a long while the view was generally accepted that
 there were several varieties of streptococci each of
 which was capable of producing distinct pathological
 effects thus the *S. Erysipelatis* when injected into
 susceptible animals would only produce erysipelas &
 the *S. Pyogenes* in a similar way would produce

abscesses or at any rate pus. Cultural differences were also noticed corresponding with these differences in action & a difference in size of the individual micrococci or variations in length of the chains formed by them were also quoted as supporting the above views but later investigations have cast considerable doubt on the above views for by altering the nutrient medium the character in many cases will become quite changed e.g. *S. Erysipelatis* may be grown on nutrient bouillon then change the medium to artificial serum and lastly employ for several successive generations the living tissues of rabbits in such a series it is possible to get first of all erysipelas then later on pus production and lastly a general streptococcus infection.

This is important with regard to serum therapy for if the above holds good that is to say that the differences observed between streptococci obtained from different sources are not in any sense specific in character it does away with one of the difficulties that would arise in preparing a serum which would possess antitoxic powers against the various forms of streptococcic poisoning.

I propose to discuss and analyse the cases published and described as having been treated with antistreptococcus serum under the following headings.

- (a) Erysipelas (b) Septicaemia (c) Puerperal Fever
- (d) Scarlatina (e) Ulcerative Endocarditis (f)

Miscellaneous cases treated with the serum.

Erysipelas - Fehleissen proved Erysipelas due to a streptococcus closely allied to if not identical with streptococcus pyogenes, he was the first to describe accurately & to isolate a specific streptococcus to cultivate it in pure cultivations outside the body & to demonstrate its direct causal relationship with the disease - Fehleissen asserts that cultivations obtained on blood serum, jellies and potatoes are characteristic, but most observers have failed to detect any difference between this growth & that of S. Pyogenes this point is of considerable interest and importance in considering the treatment of erysipelas by antistreptococcus serum - no doubt the two organisms are closely allied but that they are identical is opposed to clinical experience in man, on the one hand there is no evidence to show that the erysipelas cocci can cause suppuration in man ~~or~~ on the other hand inoculation into the skin ~~of~~ streptococcus pyogenes has produced suppuration but not Erysipelas M. Marmorek adopts the view that Erysipelas is purely streptococcic in origin & so chooses it to commence his observations on the therapeutic value of the serum.

✓ Watson Cheyne
 in Clifford Allbutt's
 Syst of Medicine
 Vol 1.

Cobbet & Melsome have made some important observations on the streptococcus of Erysipelas which

✓ Soc de Biol
 April 5th 1895.

✓ Journal of
 Pathology Vol 3.

show that there may be a local as well as a general immunity. They found that an attack of cutaneous Erysipelas produced by injecting streptococci into the ear of a rabbit completely protected that ear from a second inoculation although the rest of the body was only slightly or not at all immune. The second injection from an ear which has recovered from a first attack causes a very rapid and short inflammatory reaction.

These facts form a strong argument against any theory of the purely chemical action of the blood or lymph and point to increased resistance of the tissue cells. General immunity was more readily attained by the injection of attenuated cultures or their toxins into the peritoneal cavity.

Watson Cheyne states that there is the closest clinical relationship between cutaneous erysipelas and cellulitis & that they are both due to streptococcal infection further that streptococci are also the cause of diffuse cellulitis which however it is to be noted may be caused by other kinds of infection, the importance of this last point will be considered later on - for the failure of the serum to do any good in some of the cases of cellulitis may I think be fairly attributed to the fact that the case was one of mixed infection.

✓ Treves Scapery
Vol 1 3167.

Marmorek reports on 46 cases treated in Paris at a special hospital for such cases.

V Soc de Biol
1895. S230-

These 46 cases were selected during a given period out of a large number of cases just because they were all serious cases some of them very serious. Marmorek has not the least doubt of the value of the treatment "all our patients, he says, rapidly recovered with one exception that of a woman 63 years old who died ten hours after an injection not of the Erysipelas but of a pneumonia from which she was suffering on admission. In every case the temperature fell rapidly usually within 24 hours after an injection of from 5- 20 cc and at the same time the general condition became more satisfactory. When there had been Albuminuria it rapidly disappeared. Desquamation of the erysipelalous patches was noted & a regular rapid disappearance of the signs of inflammation.

He adds that the formation of abscesses which often happened before the beginning of the treatment, ceased altogether after it & that some of the patients treated were in so grave a condition they were not expected to recover.

M.M. Charrin and Roger record the treatment of a case of Erysipelas Neonatorum in a child age three weeks - born on Feb 24th - on 25th T was 101° - on 26th Erysipelas of upper lip appeared - on the 27th the Erysipelas invaded the cheeks 5 cc were injected -

V Soc de Biol
1895. S225.

on the 28th lip normal and cheeks less red - on March 1st Erysipelas has faded on the cheeks but gained the ears - on March 4th the Erysipelas has quite gone.

Steele records the case of a child age three weeks with well marked Erysipelas spreading from umbilicus which was not yet healed - with T 102 & pulse 150 - an injection of 6 cc was given & it was noted the following day (1) the T was reduced to 101 (2) the redness had not extended (3) three days after redness appeared on left thigh the T was normal (4) no other treatment was adopted. Steele specially remarks on the good result obtained in this case owing to the large number of these cases seen at the Plaiston Maternity and previously with very fatal results.

Cheatle records the case of a girl suffering from facial erysipelas who had been ill for two days, age 16, diplococci, streptococci and staphylococci were found 60 cc in doses of 10 cc were given - the rash continued to spread and no improvement followed.

M.M. Charrin and Roger state that it is somewhat difficult to estimate its true value in Erysipelas as it is often of a benign nature in adults but that the fact that it had a very marked effect in the cases of Erysipelas Neonatorum treated with it is of importance as the mortality in that disease is very great.

✓ B. de. Journal
Dec 7th 1895.

✓ Lancet Jan
2nd 1897.

✓ Soc de
Biol 1895
P 225.

Septicaemia.

Lockwood states that of 94 cases treated at St Bartholomew's Hospital in 16 years 66 died. The statistics of Gussenbauer show that out of 50 cases 44 died.

V Treves Surgery
Vol 1 p. 171.

Pyæmia very rare in children and hardly occurs during the first five years of life - it is commonest between 16 and 30. In Senns summary of the investigations of Rosenbach, Pawlorky and Schillier 69 cases were mentioned.

Streptococci found in 37

Staphylococci ,, ,, 23

a mixed infection of the above in 5

Staphylococcus Aureus in 4.

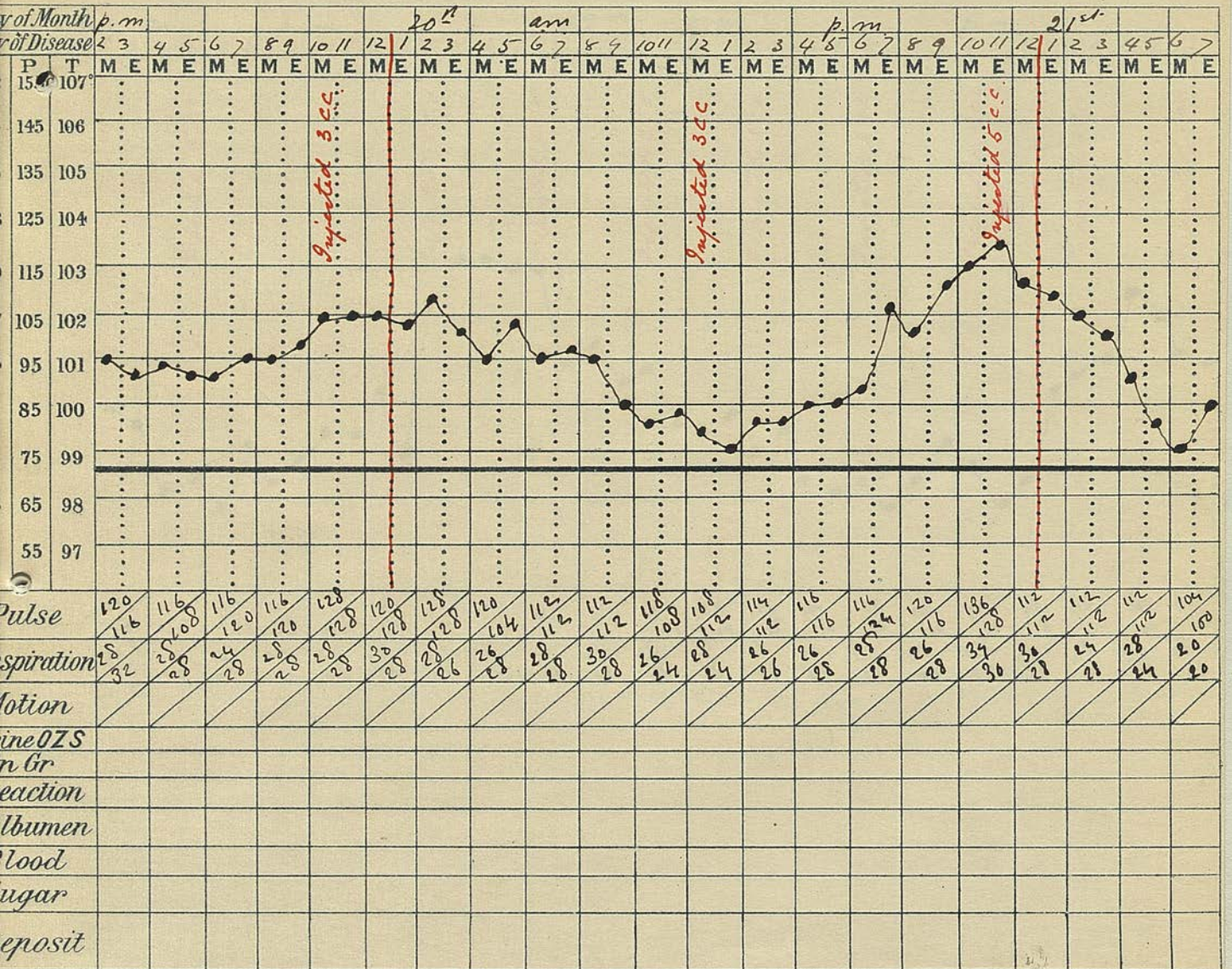
There is the closest relationship between Pyæmia and acute Osteomyelitis - the average duration of life in 41 cases complicating acute infective Osteomyelitis was 12 days. In 133 cases of ordinary Pyæmia it was 10 days. It is beginning to be recognized that in streptococcus poisoning the joints are usually affected while staphylococcus poisoning especially prone to cause suppurative periostitis or Osteomyelitis.

I. The following case was a case of acute E-piphysitis of neck of femur with subsequent symptoms of Septicaemia.

A boy, age 8 was admitted into the General Hospital Birmingham with a history that two days previously

Name _____ Age _____ Ward _____

Surgeon _____ Admitted _____



when at school was seized with pain in the right thigh he returned home & was in great pain and delirious at night. There was no history of injury or previous illness. On admission complained of great pain in the right thigh - on the anterior aspect just below Ponparts ligament but no fluctuation or swelling to be made out. Box splint and extension was applied -

Nov: 14th no improvement, was delirious at night -

Nov: 15th Anterior incision was made over hip when about two drachms of pus were evacuated & drainage tube inserted & wound left open and packed with gauze. The wound dressed at night - no pus in the dressing but there was abundant foul smelling watery discharge

Nov: 16th continues in much the same state T up, quick pulse, foul tongue and sordes round mouth, breath very offensive and delirium at night. Injections of antistreptococcus serum begun to-night (Nov: 17th) 63cc altogether were given - chart - on Nov: 19th it was noted that the tongue was not so foul & the wound looks better & more healthy - Nov: 20th wound looks better and there are granulations round the edge. The general condition is much the same.

Nov: 21st tongue is quite clean to-day - From this time the boy continued to improve steadily & was discharged on Jan: 9th.

The following appear to be the chief points of interest connected with this case.

(1) The boy appeared to be getting steadily worse his general condition was one of Septicaemia in spite of the surgical treatment.

(2) Acute Epiphysitis of neck of femur is generally a very fatal disease.

(3) The boy reacted well to the serum as is shown by the hourly temperature chart although only temporarily.

(4) The general condition was certainly improved, the delirium disappeared - tongue cleared up & the appetite improved.

(5) On the whole I think I may assume that good was done in this case although an incision was made and a small amount of pus evacuated, the condition of the boy at the time was one of Septicaemia rather than Saproaemia.

2. For being allowed to record and treat this case I am indebted to Mr Gilbert Barling.

The patient, a man age 36 was admitted on Feb: 16th to the General Hospital Birmingham at 6pm with a history that a week previous to admission he scratched his right hand while at work he felt unwell but continued to work up till three days previous to admission. He was a temperate man & had previously enjoyed good health. On admission his T was 100 - he was semi comatose & sweating profusely with furred tongue and sordes round the mouth. The arm was intensely swollen and inflamed as far as the axilla

free incisions were made under CHC⁰ & the usual local & general treatment adopted 5cc of serum were injected.

Feb: 17th passed a very bad night with noisy delirium T in the morning was 103 - continued in much the same condition all day but takes his nourishment.

Feb: 18th no improvement in his condition, is passing his motions involuntarily still delirious & tongue very foul - Injections of serum were begun at 2pm & given regularly - chart.

Feb: 19th injections of serum continued throughout the day - Pulse very rapid and respirations quick Is a good deal cyanosed - Continues to take nourishment well. Ordered Strychnine & Diptalis every 4 hours - wound dressed no further spreading of the oedema.

Feb: 20th Injections stopped as pulse is 140 & respirations 40 per minute - Is much weaker more cyanosed & does not take his nourishment so well - Oxygen inhalations given at 1pm with injections of Strychnine - Haemorrhagic patches noticed on both legs, wound dressed & in parts was gangrenous.

Death took place at 2-30 pm.

(1) In this case the serum apparently did no good whatever (2) when treatment was begun the disease was very far advanced & apparently very virulent.

(3) Active local & general treatment was adopted

(4) 43cc of serum were used in doses of 5cc (5) The serum had not even a temporary effect on pulse or temperature.

3. For being allowed to record the two following cases I am indebted to Mr Stephen Paget.

J.W. age 32 admitted into West London Hospital on Jan: 4th suffering from suppuration of upper lip - was well up three days before admission - On admission T 104°, rigors, upper lip much swollen, hard and durky, very little pus on incision - Jan: 5th condition much the same 10+10cc given.

Jan: 6th 3am - 10cc T 103.8°, 6am 10cc T 102.2°, 12 noon 10cc - breath is less foul & tongue cleaner, very restless.

Jan 7th the lip is less swollen but brawny indurated swelling all over left side of face - the tissues over Sterno-mastoid and Supraclavicular space beginning to be involved. At 3pm 10cc given - Patient anaesthetised & swollen tissues incised freely - Delirium at night & sweating freely - Jan: 8th wandering all day T 100° pulse 148 very weak the seventh injection of 22cc at 5pm an eighth injection of 20cc at 8-40pm. T at midnight 105.4° - Death 12-30 am.

Bacteriological examination mixed infection probably.

(1) The serum apparently had no effect. (2) It is to be noted that the infection was probably a mixed one.

(3) Before treatment began the general condition was very bad.

4. Mr Stephen Paget allows me to record his own case where after operating on a case of septia peritonitis his finger began to throb - about 24 hours after infection he had a sharp rigor and T of 103°, within an hour of the rigor 20cc of antitoxin were injected & on the four following days 10cc were given on each day making 60cc altogether. A year and a half previously he had a similar infection of the same hand leading to a slow tedious suppuration of the axillary glands - at that time the whole mass of axillary glands were cleared out & the vein explored thus it was interesting to see what would happen to a man with poisoned wound of hand but no axillary glands. For three days T ran high rising on the third day to 104° on fourth day it fell to 99°, there was no swelling of hand or arm & no red streaks up the arm, on the second day there came diffuse patches of lymphagitis over the deltoid and along the anterior fold of the axilla with some swelling & oedema below the clavicle on the fourth day the whole attack came suddenly to an end.

This was the fourth occasion on which hand had been poisoned during operation or while doing a post mortem examination previously there had been suppuration & wound was slow to heal. It is to be noted in this case (1) The infection was virulent (2) onset rapid (3) no axillary glands (4) was well in four days

(5) no headache (6) the treatment was commenced early within 24 hours of onset of disease.

To Ballace & Abbot belong the credit of bringing under the notice of the profession a well marked case of Haemorrhagic Septicaemia treated successfully with antitoxin.

*V B. L. Journal
July 4th 1896.*

Dr M age 30 pinched his thumb making a p m examination, the following day showed all the signs of an acute Septicaemia with a T of 103° & drowsiness. Three days after commencement of illness 3.5cc of serum were injected & six hours after injection certain signs of improvement were manifest (1) mind was clear (2) respirations regular and less rapid (3) pulse slower (4) tongue moist along the edges. The next day dose was increased to 7cc every four hours and gradual convalescence of the patient took place.

The chief points in this case seem to be (1) the severe type of the disease (2) no local reaction except slight urticaria (3) although pulse much improved T not much affected (4) surgical & general means adopted (5) this case certainly appeared to be going to end fatally before the commencement of the use of the serum.

6. Coleman & Wakeling record a case of acute Septicaemia treated with the serum, a middle aged medical man fifteen days after attending a fatal case of

*V B. L. Journal
Sept 12th 1896.*

puerperal Septicaemia was attacked with all the usual signs of a virulent Septicaemia. It was noted in this case that the pulse became slower, fuller & more regular (2) the patient became conscious (3) the tongue became cleaner (4) the T after an initial rise began to fall (5) the mind became clearer (6) the diagnosis was confined bacteriologically.

7. Heatherley in B M Journal records a case of well marked Cellulitis of face and neck treated with Marmorek's serum in a boy age 15 commencing as a suppurating boil at the angle of the mouth & spreading with great rapidity over the whole of the side of the face. The ordinary treatment of Cellulitis was carried out including incisions. This treatment was carried out for nine days. On the tenth day of the disease an injection of 10cc was given - the next day 13cc & after this injection the oedema appeared to be less & the neck softer, as however the pulse & T remained up 21cc more were given but the next day the patient was much worse & suffering from diarrhoea & death took place the following day.

V B - M - Journal
Dec 7th 1895.

In this case the serum appears to have had little or no effect, at any rate only a temporary effect on the pulse and temperature for after the injections the pulse reached as high as 156 & the respirations ranged between 38 & 52. It was noted that locally the disease appeared to cease to spread after the first injection

Bacteriological examination showed the presence of a Streptococcus in the serum obtained from the wound probably the Streptococcus Pyogenes Albus. It is to be noted in this case (1) the serum treatment was begun very late (2) the boy was evidently in a very advanced stage of septic infection when the treatment was commenced.

8. Cook records the case of a man, age 56 with Cellulitis of the leg with T of 104° & signs of general septicaemia. Six days after admission the inflammation was rapidly extending up the leg & T 101° - 20cc were ~~in~~jected. The T fell next day to 98°. Further incisions were made during the next three days & the general state of the health improved. Three weeks after owing to a fresh spread of the inflammation - another 16cc were injected with a good result the T falling to normal with no further spread of the inflammation. In this case the effect of the serum seems to be doubtful as the fall of the T was more probably due to surgical interference.

9. In the same number Cook records another case but only one injection was given & that 17 days after the commencement of the Cellulitis so that this case is of little or no value.

V B-le-four
Oct 31st 1896

10. Cheatle records the case of a man age 46 suffering from general symptoms of Septicaemia. He was treated for six days & altogether had 138cc - Bacteriological examination was made & Streptococci found in abundance. Surgical means were employed. In this case the serum seems to have had absolutely no effect either on temperature, pulse or general condition. Patient had however been ill 18 days before the serum was used.

V Lancet
Jan 2nd 1897

11. Cheatle records the case of a woman age 30 suffering from a wound of the finger

Ibid.

(1) Serum used four days after admission in a dose of 35cc (2) Diplococci and streptococci found (3) Surgical means adopted (4) T came down following day & remained down with exception of one day when it went up to 104° (5) Large doses adopted 30 + 35cc.

12. Cheatle records the case of a man suffering from Chronic Septicaemia (1) the injections were commenced forty days after admission the T at that time being 99° in the morning & 102° at night (2) during the next ten days 140cc were used in doses varying from 10- 75cc (3) there was no improvement death took place.

Ibid.

13. Boake records a case of septicaemia from wound of finger (1) five injections given very late in the

V B. L. Journal
Dec 27th 1897

disease three weeks after illness commenced (2) after the injections local improvement noted, the swelling of forearm was much less (3) Urticaria noted (4) case ended fatally.

Scarlatina.

The published cases of Scarlatina treated with the serum are fairly numerous most of them however coming from abroad.

Marmorek in an interesting paper records a series of 96 cases of Scarlatina treated with the serum at the Trousseau Hospital - in all of these cases bacteriological examination was made. He relates one interesting case where a child was admitted with Albuminuria of three weeks duration & had not been treated with the serum - his two sisters who fell ill from the same disease - Scarlatina were admitted & treated with the serum & no complications followed. Out of the 96 children treated with the serum, bacteriological examination showed the streptococcus present either alone or associated with other microbes. In 17 cases the bacillus of Loeffler was found associated with streptococcus.

Four out of this number entered with signs of Diphtheria & were treated with the two serums but without effect and another child died of acute double Pneumonia - Injections of 10cc were given on admission and doubled if the general condition was bad.

V Annales de
l'Institut Pasteur
Jan 1896.

Injections were given daily and usually two injections were sufficient but as soon as glandular swellings or traces of albumen in the urine were found - the injections were begun again and not stopped till they disappeared.

Marmorek advises care in looking out for the complications which may occur at a late stage of the disease. No local treatment with the exception of mouth washes was adopted.

The total quantity of serum used was

in ordinary cases 10-30 cc

in severe cases up to 80cc

The most marked effect was on glandular swellings of the neck. 19 cases showed them on or soon after admission they however soon settled down & in no case went on to suppuration.

As a rule albumen in the urine disappeared after one or two injections (33 cases had Albuminuria) which disappeared after two injections. Four cases on admission had discharge from both ears which soon ceased, in one case only did a discharge from the ear come on after admission.

Marmorek concludes that the serum

(I) Not only stops grave complications but produced rapid disappearance of inflammation of the throat.

(2) Mental state improved (3) Pulse stronger & slower
 (4) When T was due to streptococci it fell after injection of the serum while if due to the poison of Scarlatina it continued its ordinary course and the rash does the same.

(5) Fugitive erythenas were rarely noted & the use of the serum was not followed by any bad results.

(6) Marmorek states that the number of cases treated is too small to come to any definite conclusion but that it had a favourable action on (a) glandular swellings (b) albuminuria (c) the grave complications of Scarlatina,

Baginsky records a series of cases treated with the serum. He treated 48 cases. In 27 cases he noted after the use of the serum (1) T was notably lowered (2) No deaths (3) No grave complications followed (4) That the sore throat & glandular enlargement disappeared at an early stage (5) with regard to Nephritis he states that owing to the strict milk enforced in hospital it is difficult to estimate its value but that in the cases treated kidney complications were rare.

In another group of 16 cases the serum had no appreciable effect & several of them died rapidly in spite of its use in large doses & others had supplicative adenitis.

V. La Semaine
 Médicale
 March 18^e 1899

In another group of five cases the serum was not employed at the commencement of the illness but only when complications had arisen, the serum seemed to have some influence but the number of cases was too small to come to a definite conclusion.

Previous to the employment of the serum the mortality was from 22 - 24% since then it has been reduced to 14 % but that the number of cases is too small to draw any deductions as to the diminution in the mortality.

He states also that it has no influence on the Scarlatina itself but only on the complications e-g sore throat Nephritis and otitis.

He noted (1) rapid fall of T after the injections (2) suppurations ear occurred in four cases (3) albuminuria was rare (4) only one case of acute Nephritis.

The mortality in 230 other cases in the same epidemic not treated with serum was 24.9% & the mortality from Scarlet Fever in four preceding years ranged from 22.6 to 34%.

Gordon records the case of a boy age 6 suffering from Scarlet Fever with well marked symptoms of Septicaemia developing on 2nd day of illness (1) Streptococci and Staphylococci found (2) two doses of

V Lancet Jan
2nd 1897.

10cc each were given (3) T came down in 48 hours

(4) pulse, rash and general condition much improved

(5) recovery.

Lemoine (Soc: Med: des Hopitaux) from a long series of researches on the complications of Scarlet Fever confirms Marmorek's view though the specific organism of the disease is still unknown to us, the complications of the disease are dependant on the agency of the streptococcus which after being localised in the pharyngeal canal can invade the skin, the serous membrane & the kidneys.

*V. Lemoine de
Méd 1896.*

Puerperal Septicaemia

The treatment of puerperal septicaemia with antistreptococcus serum although of recent date is of considerable importance for anything that would tend to lessen the mortality from this most fatal disease, deserves our closest attention. The annexed table recently published by Cullingworth shows that the unsatisfactory state of affairs which exists even at the present time with regard to this disease for the mortality is little if at all decreased from that of between 40 and 50 years ago. Unfortunately the difficulties arising in estimating the results of this treatment are for various reasons great for in many of the published cases the treatment seems to have commenced

very late in the disease and frequently no bacteriological examination was made for according to Bullock recent researches show that a puerperal fever may be set up by the gonococcus, the bacillus coli communis the Talamon Fraenkel coccus & the staphylococcus this is of importance as the serum is said to be of no use in cases of mixed infection and Playfair states that no one microbe has been proved as the specific cause but that in the majority of cases the disease appears to be caused by the streptococcus pyogenes, further very active local and general treatment was adopted in a large number of the cases and as at first the infection is local it is important to make sure in estimating the value of the treatment that the infection is of a general character as distance from a local one.

Mortality from Puerperal Fever in England & Wales.

Table showing actual number of deaths from above disease with the death rate estimated in relation to the number of registered births.

Year.	No of deaths.	Per 1,000 births.
1847	784	1.5
1848	1,365	2.4
1849	1,165	2.0
1850	1,113	1.9

✓ Lancet i 1896
p 84.

✓ Clifford Allbutt
Syst of medicine
Vol i 1869.

✓ B. M. Journal
March 6th 1897

Year.	No of deaths.	Per 1,000 births.
1851	1,009	1.6
1852	972	1.6
1853	795	1.3
1854	954	1.7
1855	1,079	1.7
1856	1,67	1.6
1857	836	1.3
1858	1,068	1.6
1859	1,238	1.8
1860	987	1.4
1861	886	1.3
1862	940	1.3
1863	1,115	1.6
1864	1,489	2.0
1865	1,333	1.8
1866	1,197	1.5
1867	1,066	1.4
1868	1,196	1.5
1869	1,181	1.5
1870	1,492	1.9
1871	1,464	1.8
1872	1,400	1.7
1873	1,740	2.1
1874	3,108	3.6
1875	2,504	2.9
1876	1,746	2.0
1877	1,444	1.6

Year.	Deaths.	Per 1,000 births.
1878	1,415	1.6
1879	1,464	1.7
1880	1,659	1.9
1881	2,287	2.6
1882	2,564	2.9
1883	2,616	2.9
1884	2,468	2.7
1885	2,420	2.7
1886	2,078	2.3
1887	2,450	2.8
1888	2,386	2.7
1889	1,852	2.1
1890	1,956	2.2
1891	1,973	2.2
1892	2,356	2.6
1893	3,023	3.3
1894	2,167	2.7
1895	1,849	2.0

The following are brief notes of the published cases.

Williams publishes six cases.

Case I. Age 24, primipara, female child born Dec: 14th presentation normal, labour instrumental, perineum slightly torn, progressed well till 7th day when T 101°, rigors, quinine was given - on 8th day was better - on 9th day T 103° - on 11th day T 104° pulse 135, lochia scanty but not offensive had daily douches of

V B. L. Journal
Oct 31st 1896.

perchloride of mercury (Iin 4,000) at 5pm I0cc injected at 11pm T I02° pulse I25 - on I2th day T I03° pulse I30 20cc injected at 5pm T normal, from this time onwards made a smooth recovery - no bacteriological examination was made.

Case 2. Age 28, primipara, confined Jan 29th normal labour, perineum slightly torn continued to do well till the 5th day - local & general treatment continued till 8th day when T I04° pulse I30 & respirations 36 & with general symptoms of septicaemia - at 3pm 30cc injected, on the 9th day T I01°, pulse I00 & respirations 25 - on the I0th day morning T I03°, pulse I20, respirations 30 - on I1th day foul Vaginal discharge with diarrhoea and bed sores - I2th day T I02° 30cc injected - on I3th day T 99° patient better lochia not offensive - between the I4th day & I7th day patient's condition varied but T never rose above I01° on the I7th day T I03° pulse I08 respirations 38. signs of Pneumonia at basis of both lungs - between the I7th & 24th days T varied between I03° and I08° - between the 24th & 29th days T varied between I00° and I02°, on the 30th day it was normal from this time onward convalescence took place. No Bacteriological examination was made.

Case 3. Age 22, primipara, instrumental labour, perineum slightly torn - on 8th day rigors T I04°,

pulse 115 - on the 9th day T 102° pulse 120 - on the 10th day T 100°, pulse 110 continued much worse till 14th day when T was 104° pulse 140 & respirations 40 with all the symptoms of general septicaemia - 35cc injected at 12pm, at 6pm T 104 at 6am 102 & at 2am following day 99 on the 15th day T was 99° from this time onward recovery was rapid. Bacteriological examination of the lochia was made when streptococci were detected in great abundance.

Case 4. Age 24, aborted at third month in first pregnancy between the 3rd and 5th days T was 103° - 30cc injected, on 6th day T was 99°, pulse 100 - on 7th day T 102° pulse 130, 30cc injected this was followed by an erythematous rash on the 8th day T subnormal - from this time T never rose above 100 & made an uninterrupted recovery. No bacteriological examination was made.

Case 5. Age 22, primipara, confined of twins, perineum torn, febrile symptoms appeared between 3rd & 6th days on the 7th day T 104°, pulse 140 & symptoms of septicaemia 28cc were injected - on the 8th day T 100°, pulse 120 erythematous rash appeared - on the 9th day T 100° rapid improvement from this time onwards. No bacteriological examination.

Case 6. Age 30, primipara, normal labour, seen on 6th day with signs of septicaemia 20cc injected - on 10th, 11th & 12th days Diarrhoea & vomiting throughout. Death on 14th day. No bacteriological examination was made.

Case 7. Garland in an article "Sérotérapie dans la Fievre Puerperale" records the case of a rickety woman with contracted pelvis who had a prolonged labour and perineum torn, on 7th day T rose to 105° & remained there for four days - on the 11th day T still 105° & pulse 140, uterus curetted & packed with gauze - on 12th day T 102° on 13th day T rose further 10cc of Marmoreks serum injected, on 14th day T lower & 2cc were injected, from this date T fell slowly & patient soon well.

Case 8. recorded by same observer in same journal a multipara delivered instrumentally, on 2nd & 3rd day T 104° uterus swabbed out, on 4th day cultures of streptococci got from vaginal discharge & T 104.9° 10cc of Marmorek's serum injected - on 5th day 10cc on 6th day 10cc T 102.9° on 7th day 10cc on 8th day T 101° on evening of 9th day T normal but was seized with bilious vomiting, next day condition much worse, death took place on 11th day. He believes after post mortem examination too much serum was given which caused the vomiting.

V Irene M
Nov 30th 1893

Vinay records four cases, I however exclude the last one which was a case of puerperal mania & which in my opinion was not a fair case for trial of the serum.

*V Lyon
Medical
Jan 26th 1896*

Case 9. F. age 27, Sept: 7th miscarriage, Sept: 11th rigors & vomiting T 104° first seen on the 15th - condition very grave, profound sepsis, abdominal pain, thirst & sleeplessness T 105° no peritonitis, on the 16th curettage, on the 17th no improvement in general condition T 105.4 pulse 124 with sordes on lips, dry tongue & pinched expression, 20cc were injected, on the 18th day T 101.5° pulse 100, in the evening T 104.7° 20cc were injected, on the 19th was going on well on the 20th 20cc injected, on the 21st 10cc from the 22nd there was steady improvement & recovery.

Case 10. Age 27, primipara with long labour and albuminuria, Nov: 9th delivery, same evening T 103° continued till the 16th with usual symptoms of septicaemia, on three following days 20+20+15cc given, T fell in 6 hours & general condition improved, recovery.

Case 11. Age 38, delivery Aug: 31st on 4th day symptoms of septicaemia, three weeks after had rheumatism of shoulder with albuminuria & T 105° 15cc given, on Sept:22nd same general condition. Death

on the 24th. The post mortem showed endocarditis with renal degeneration. This case appears to have been more a case of rheumatism of septic origin.

Case 12. Jacquet records the case of a woman age 23, normal labour, signs of septicaemia 2nd day after delivery active local treatment up till 9th day when T in evening was 40.8° 35cc given & T fell three degrees, 25-25cc given as T went up & patient went on well for next four days. Nine days after the accouchement the mother who had been nursing her daughter was seized with erysipelas & was isolated, two days later the daughter had a rigor (the T having been normal for the last four days) & the T went up at night to 40° & was the same the following night, another injection of 25cc was given & the T did not go up again.

V Soc de Biol
May 11th 1895.

This case is interesting as showing the close relationship between Puerperal Septicaemia & Erysipelas.

Jacquet concludes (1) although the case might have been cured otherwise the T came down rapidly & stopped the course of a Septicaemia which would probably have been prolonged (2) He advanced the theory that the Erysipelas in the mother allowed the streptococcus to renew its virulence in a new host (the mother) & was then transmitted to the daughter, in other words

draws attention to the close relationship of the micro-organism of Erysipelas and Puerperal Fever.

Case 13. Kennedy publishes the first case in England the case of a primipara age 28, labour Aug: 28 showed signs of septicaemia Sept: 4th & continued on & off better & worse till Sept: 17th when T 103° & pulse 120. No local symptoms whatever & distension had disappeared but pulse no better & general condition much worse, 40cc given at once T fell to 99° in 6 hours & in 24 hours was normal & since then there has been constant improvement.

✓ Lancet Nov
2nd 1895.

Case 14. M. M. Charrin et Roger record the case of a woman with all the symptoms of puerperal septicaemia & T of 103° she had 8+8+25cc three days after the injections the woman was practically well.

✓ Soc de Biol
1895. p. 124.

Case 15. A woman delivered Feb: 18th symptoms of fever, on the 19th admitted into hospital, on the 22nd with T of 39° between the 22nd & 26th had five injections 26+20+20+10+10 by the 25th was much better and by the 26th T was normal.

Ibid 1894.

Case 16. M.M. Josue et Hernary record the case of a raelitic woman who had symphysiotomy performed the cervix was lacerated, next morning had fever and

Ibid 1895.

was curetted on the 3rd day T was 103.6 pulse 140, nervous excitement & general health very bad, on 5th day 30-30cc given on 6th day 20-15. Rapid improvement of general condition. After first two injections excitement gone, good sleep & rapid improvement right away. The day after last injection the cervix which was covered with unhealthy granulations began to heal & on the 17th day was walking about.

Case 17. M. Jacquet records the case of a woman age 23 had slight laceration of the vulva. Forty four hours later had a rigor & T 102.2 all sorts of local & general treatment were adopted up till eight day after confinement without avail the T at that time was 105.2 . On the 9th day 30cc given, on the 10th day 25cc on the 11th day 25cc the T then remained normal till five days later when there was a fresh rigor & T 104 , 25cc more were given & from that time there was steady recovery.

Case 18. Sheen records the case of a primipara age 25 delivered Oct: 14th, on the evening of 15th T 103 , douching, curettage etc was adopted the general condition was much worse. Between the 21st & 24th 10-10-10- 10-10cc were given. Patient died on that day. Pneumonia set in a few days before death.

leid 6358

*V B. de fowred
Dec 10th 1896.*

Case 19. Adam records a case of puerperal septicaemia followed by Typhoid Fever in a primipara age 26, labour Aug 15th, feverish on 6th day, T kept at 104- 105° on the 26th 5cc given & altogether 107cc given in doses of from 4-17cc. At beginning of 4th week Typhoid Fever. Ultimate recovery. The impression given was that the serum kept the patient from losing ground & that the most expensive Lyons brand had a very decided effect on the T.

V B. L. Journal
Dec 26th 1896.

Case 20. Leask records case of a primipara delivered instrumentally on March 19th, on 7th day shivering but no abdominal tenderness but T rose steadily on 11th day it was 106° & pulse 120, 4cc of serum injected, next day T 100° & pulse 96 & patient had slept well & was much better & ultimately recovered.

V B. L. Journal
i 9 1500.

Case 21. M.M. Charrin and Roger record the case of a woman delivered on the 18th & admitted into hospital Feb 23rd, T 39C° lochia offensive 26-20cc given on 25th general state excellent 10cc given making altogether 96cc T 37C° & other came to normal. It was noted (1) prompt improvement in general state (2) feeling of bien etre (3) convalescence rapid.

V Soc de Biol
April 5th 1895

Case 22. Allisan records the case of a woman delivered on Jan 9th by the 13th symptoms of septicaemia on the

V B. L. Journal
March 6th 1896
S 639.

14th T 101° P 120, wound unhealthy, nervous excitement abdomen tender 4cc given by mouth an hour after T fell to 98° - Jan 15th T 99° it never rose again above normal. Urticarial rash appeared after a few days on face & body. Apparently not inert after passing through gastro-intestinal tract.

Case 23. Reddy records the case of a woman age 20, normal labour, two days after T 101° P 90 no local cause for T could be found, next day T 104° P 106, rigors a varicose vein was seen to have burst on the vulva & a whitish membrane was noticed the membrane bacteriologically was found to be streptococcic, the membrane spread to right side, on the 7th day 10cc of Marmorek's serum given, for 48 hours after there was numbness & tingling of the extremities no rash was observed - T at time of injection was 103° ten hours later 101.4° & following morning was 99° & the membrane on both sides had disappeared leaving a raw surface the following day severe haematuria appeared & continued for three days, ten days later patient discharged from hospital cured.

Case 24. Sharp records the case of a woman age 23
 (1) Injections begun on 5th day (2) T previously 105°
 (3) doses of 10cc given on three days and one dose of 30cc on 4th day the last dose reduced T 2½° (4) T

V Canada
 Medical Record
 Record 1896

V B. L. Journal
 Feb 27th 1897

reached normal on 30th day (5) No streptococci found in the blood.

Case 25. Coombs records a case in which two injections were given on the 8th day of illness of 10cc each, patient was evidently moribund when injections began.

V B. L. Journal
Feb 27th 1897.

Case 26. Ashley Cummins records the case of a woman age 23 who previous to the use of the serum had a T of 105° with vomiting, delirium, hiccough with erysipelalous eruption round manna she had eleven injections of 10cc each in eight days - it was noted (1) the general symptoms vomiting etc disappeared rapidly (2) the T was unaffected not coming down till twelve days after serum was stopped (3) it had a marked influence on the rash as it ceased to spread (4) local treatment was adopted.

V B. L. Journal
Feb 13th 1897.

Case 27. Mc Kerron records three cases of puerperal septicaemia treated with the serum. A woman age 22, instrumental labour, continued well till 9th day when T was 100° on 26th had a rigor & T 105° T continued up & had rigors till the 30th when 10cc were injected a slight fall of T followed, another injection of 10cc given the same night the next day was better & had had sleep the T however next day was 103° & a third injection of 10cc was given - a considerable improvement in T & pulse followed & the following morning

V B. L. Journal
Feb 10th 1896

T was normal. The T however continued above normal for five weeks with however ultimate recovery.

Case 28. A woman age 43, normal labour on 4th day T 102.5° Pulse 180, six days after labour a bright rash resembling measles seen on chest on 8th day at noon T 104° 10½ 10 given, next day T 101° - patient had a good night 10cc more given on next day a 4th injection 10cc the next day however T continued to rise & was at 106° before death.

Ibid.

Case 29. A woman age 26, normal labour convalescence satisfactory till three days after when T began to go up for the next four days T ascillated between 101° & 104°, 8 days after delivery 10cc given in the morning & again at night the next day T fell & a 3rd injection of 10cc given for the four following days T was normal or subnormal & there was ultimate recovery.

Ibid.

Ulcerative Endocarditis.

Drenchfield states that according to observations published between 1885 & 1888 among others by Cornish & Baber, Frankel, Drenchfield & Rosenbach the following is a summary of the results obtained.

v Cliffnd Allerts
Supt of Medicine
Vol i

1. In nearly all cases of "Infective Endocarditis" whether ulcerative or not microbes were found.
2. In most cases only one organism found but in a few more than one.
3. That the organism found was not the same in all cases.
4. The organisms most often found were (1) streptococcus pyogenes (2) staphylococcus (3) Pneumococcus. The first two found most often in cases of puerperal disease, pyaemia & septicaemia.
5. Endocarditis sometimes due to a mixed infection.
6. Experiments on animals led to diverse results sometimes injections of pure cultivations gave no results, at others produced septic symptoms.

As regards the nature of infective endocarditis the conclusions are.

- (1) It is due to micro-organisms (2) the disease is not produced by one specific microbe alone (3) The organisms which are most frequently the cause of the disease are streptococci and staphylococci.
- (4) Of other organisms the diplococcus of pneumonia often gives rise to infective endocarditis, the specific organisms of enteric fever, gonorrhoea, diphtheria tuberculosis do so very rarely.

Miscellaneous cases.

1. Boucheron records a case of chronic Dacryocystitis which had resisted treatment for several years, two injections given & great improvement noted.

V Semaine
Méd
Nov 18th 1896.

Boucheron suggests that prophylactic injections should be given in ocular suppuration wounds of the eye etc.

2. Law records a case of acute septic general Peritonitis with septic Metritis with typical symptoms, rigors, diarrhoea & T of 104°, abdomen distended & tympanitic an injection of 3cc was given the T & pulse next day were much improved & four more injections of 3cc each were given, peritoneal friction could be felt all over the abdomen - for the next two days the same amount of serum was given making 35cc altogether there was ultimate recovery in six weeks time.

V B. d. Journal
Jan 2nd 1897

3. M.M.Charrin et Roger record the case of a woman who 23 days after delivery was attacked with an "Auguine preudo-membranense" bacteriological examination showed a mixed infection of strepto and staphylococcus the T varied between 39 & 40C° & pulse 148, two injections of 30cc each were given on 9th March & on the next day another injection of 30cc the local treatment was simply boric acid gargles. Thirty six hours after first injection T fell to 38,5° & next day to normal & stopped there.

V Soc de Biol
1895 J 226.

4. Boucheron records a successful case of extraction of cataract in a diabetic woman age 70. She had 48 grammes of sugar per litre of urine but under treatment this was reduced to 18 per litre, she however contracted a lymphangitis of foot and leg - M.Marmorek was consulted & recommended the use of his serum - two injections of 5cc each were given & the lymphangitis was terminated in four days, however to complete the action of the serum on the streptococcus two injections of 10cc each were given five days after the first injection as it was supposed that the patient had got over the streptococci infection the operation was performed with a perfect result.

Boucheron states that he believes this is the first time a cataract has been extracted with success in spite of glycosuria & streptococcic infection.

5. Steele reports the case of a child age $1\frac{1}{2}$ with acute spreading Gangreul of forehead, the child had rigors & was drowsy & had a high temperature, two injections of 5cc each were given although the T remained high for three days after the injections there was sudden & striking cessation of the gangreul & phagedaemic ulceration - & immediate improvement in the child's general condition - large numbers of streptococci were found in the skin round the edges of the gangrenous patches.

V Soc de Privil
1896 1432

V B. de Fourne
Dec 17th 1896

Table of cases treated.

Erysipelas - - 49 cases.

Recovery - 47 cases..

No improvement - I,,

Death - - I ,

Pyæmia - - 13 cases.

Recovery in 6 cases.

Death - 6 ,

Doubtful - I ,,

Scarlatina - - 145 cases.

Recovery in 124 cases.

Death in 21 ,,

Ulcerative Endocarditis - - 3 cases.

Recovery in 1 case.

Death in 2 ,,

Puerperal Septicaemia. - - 29 cases excluding

case 25 - 28.

Recovery - 24 cases

Death - 4 ,,

Miscellaneous cases - - 5

Recovery in all.

Total cases - - 344.

In summarising the results obtained it will be convenient to discuss the subject under the following heads.

Nature of cases. Erysipelas - the cases treated by this method were on the whole successful for out of 49 cases 47 recovered all being of a severe type. As the disease is one in which at any rate in the purely cutaneous forms, the streptococcus plays an important if not the only part in its causation it would appear that it is specially suitable for this treatment & the account given of the above cases - more especially those of Erysipelas Neonatorum - a disease which has a markedly high mortality is I think hopeful in the extreme - although one must admit that the prognosis in simple cutaneous Erysipelas is by no means grave yet any mode of treatment that tends to shorten the duration & severity of the disease more especially in the aged must be considered a distinct advance in the treatment of this disorder. In those cases of traumatic erysipelas e.g following scalp wounds in which the mortality is so high there seems to be a distinct indication for its use. The general effect seems to have been (1) a rapid fall in the temperature usually within 24 hours (2) Improvement in the general condition (3) Local suppuration ceased.

Pyæmia.- the cases only number 13 and out of this number six recovered, the effect of the serum is not so marked in these cases chiefly because I think in many of them the treatment was begun very late and the infection in several of the cases was probably a mixed one. The case recorded by Ballace & Abbot & that of Mr Paget make it impossible to believe however that the serum can have other than a beneficial effect in certain cases of this disease, however, to be of any good it appears to me that the serum should be used early say within 48 hours of the onset of the disease and not, as in many of the recorded cases as late as a week for by that time the patient has as a rule become so weak & the poison so virulent that it is impossible to expect any satisfactory reaction to the serum. In none of the recorded cases does the serum appear to have had any bad effect and in some of them it appears to have certainly saved the patient's life. The effect on the T in most of the cases was not very rapid the general & mental condition however usually rapidly improved when the serum was going to prove of any value.

Scarlatina. the cases numbered 145 with 124 recoveries the serum does not appear to have had any effect on the course of the fever itself but certainly seems to have had a beneficial effect on the complications met with more especially on the throat and ear troubles

so frequently met with. Albuminuria was rare and in only four of the cases was otitis media noted.

The serum certainly seems to have had a beneficial effect on the complications met with in this disease which are of a septicaemic nature - and gives encouragement to hope that by its use not only that the mortality may be lessened but that the bad after effects of this disease may be diminished.

Ulcerative Endocarditis. the number of cases of this disease treated with the serum is too small to form any opinion as to its value but it would appear from the nature & pathology of this disease it might effect a temporary improvement.

Puerperal Septicaemia. the case number 28 with 4 deaths and the results on the whole are I think very favourable for many of the cases were of a severe type and in the majority of the cases active local treatment had been adopted without avail. The effect on the T and pulse in most of the cases was rapid, the T coming down and the pulse becoming slower and stronger. Where the lochia were offensive it was frequently noted that they became less so after the use of the serum.

2. Dose employed varied from 3cc to 75cc the latter

dose being given in a case of Septicaemia by Cheatle the average dose given was however 10cc to an adult and 5cc to a child, this however must vary somewhat depending on the source of the serum thus making it desirable that there should be a uniform system of standardising so that a maximum and minimum dose may be arrived at on a proper basis.

3. Mode of administration. In all the cases the serum was given subcutaneously with the exception of one case where it was given by the mouth with apparently good results.

4. Complications following use of serum, in only one case, that recorded by Gaulard (case 8) puerperal Septicaemia is the serum said to have done harm, but from the account given I should think it is doubtful. Urticaria and erythematous rashes of a fugitive character were noted in some cases but did not cause any serious inconvenience. The serum was injected subcutaneously with full antiseptic precautions & in no case did it give rise to any local trouble.

5. The effect on temperature & pulse. was somewhat variable, although as a rule after each injection there was a fall of the temperature, there was as a rule a decrease in the frequency of the pulse & its character in favourable cases usually improved.

6. Effect on general condition was as a rule beneficial the disappearance of headache and insomnia was frequently noted.

The use of antistreptococcic serum in pyogenic affections as a prophylactic has been advocated by Boucheron and others, at present however this treatment has not been adopted to any extent possibly it may prove of benefit & if so a smaller dose would probably be sufficient as obviously a larger dose is required to remove a lesion than to prevent an infection or intoxication.

The difficulties in the employment of a curative serum for the treatment of streptococcic are greater than the employment of a serum in the treatment of say, Diphtheria or Tetanus for the former are due to micro-organisms which have a marked tendency to infect the blood & tissues generally (hence the futility of treating these cases late) while the Tetanus bacilli always & the Diphtheria bacilli generally remain at the seat of inoculation multiplying to a limited extent & manufacturing their more active poisons.

Again we are unable to detect essential differences between processes connected with one or other group of cocci yet it is known that a serum antagonist to an infection by one is useless against infection by others & so a practical difficulty enters in the

use of these serums for frequently it is not possible to obtain a bacteriological examination at the time when it is most essential that is to say at the commencement of the disease.

While it appears to me probable that the serum treatment of pyogenic affections will never be as satisfactory from a clinical point of view as that of Diphtheria, yet it seems to me to give promise of success in a certain number of cases under given conditions which hitherto have failed to be benefited by the usual mode of treatment.

The following points appear to me to be essential in carrying out this mode of treatment.

1. Owing to the impossibility of estimating the amount of toxin & the number of bacteria present in the tissues a large initial dose at any rate should be given & then according to whether reaction to the serum is noted or not , infections - the following doses should be regulated accordingly.

2. Early treatment is most important for by adopting it we have a constitution much better able to withstand the toxins produced in the system.

3, Local & general treatment should be just as vigorously carried out as when the serum is not used for it is to be remembered that the serum in this class of cases is not to be used as a substitute

but only as an aid to other forms of treatment.

4. Bacteriological examination should be made whenever possible for it is to be noted that the serum is only said to be active in purely streptococcic affections and not in cases of mixed infection.

5. The serum should be given regularly and steadily not in one or two doses as in some of the recorded cases and then allowing a considerable interval to elapse. The general condition of the patient in this respect appears to be as important as the pulse & temperature for in many cases the temperature does not appear to be reduced for some considerable time whereas the general condition often improves rapidly.

6. Strict antiseptic precautions should be taken in using the serum and not more than 20cc should be injected at one spot.

In conclusion although there are yet many difficulties to be solved in the use of a serum in the treatment of pyogenic affections, yet I think that from the cases recorded above we may fairly hope that with the advancement of knowledge with regard to the more accurate methods of preparation and standardisation of these serums we may look for results more favourable in the treatment of this class of disease than have hitherto been recorded.