

THESIS PRESENTED BY

GARSWELL MARSHALL.

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Observations on the Treatment of Six Cases of Puerperal Sepsis  
by Autogenous Vaccines, with periodic Estimation of the Opsonic Index

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In the six cases which form the subject of these Observations no attempt was made at selection of the type of case treated. All were cases certified puerperal fever and admitted as such to the Puerperal Sepsis Ward of Belvidere Fever Hospital. In practice however, as the series of cases progressed, a very definite selection became evident, as the majority of cases admitted to the Ward were certified so late in their disease, or the infection was so acute, that death occurred shortly after their admission and before an autogenous vaccine could be prepared. With the possible exception therefore of Cases I and II which were admitted early in their diseases and before the clinical type was definable, the cases treated were of the subacute rather than the acute variety of Puerperal Sepsis.

The observations are mainly confined to the Vaccine and Opsonic Index aspect of the cases, but during the time of preparation of the vaccines and also throughout their administration, every therapeutic and surgical instrument was exhibited which gave prospect of alleviating or checking the progress of infection.

The routine local and general treatment adopted was that which had been found to give the best results prior to the commencement of Vaccine treatment and was in the main that recommended by Knyvett Gordon. (Brit. Med. Journal, April 1908).

On admission to Hospital the cases were put into the lithotomy position and after smears of discharge and cultures from the uterus had been taken, a thorough examination was made of the genital organs and other pelvic structures, if possible without the aid of a general anaesthetic but if necessary with it. Any debris found in the in the uterus was removed digitally or if the whole uterine cavity could not be explored with the finger, a blunt spoon-curette was introduced and passed lightly over the surface of the endometrium. Blood clot and any loosened debris were then removed with the hot, antiseptic, intrauterine douche, checking at the same time any tendency to haemorrhage, the cavity of the uterus being thereafter swabbed with pure IZAL.

In cases IV & VI, where there was persistent haemorrhage after the/

the use of the blunt curette the uterus was packed with sterile gauze rung out of Izal (1-20) solution.

Vaginal and intrauterine douching with Lysol solution was continued daily or oftener till all uterine discharge had ceased.

Constitutional treatment consisted in the administration of a mixture containing Quinine, Strychnine and Liquid extract of Ergot, and the exhibition of stimulants and sedatives as necessary. The diet was fluid as long as the temperature remained high, but more nourishing food was at once given as soon as the patient was able to digest it. Special attention was directed to keeping the body tissues well flushed with fluid and satisfaction was not felt until fluid to the extent of five pints or more was being taken daily.

#### PREPARATION OF VACCINES.

Cultures for the preparation of a Vaccine were taken at the primary examination on admission to Hospital.

The patient having been placed in the lithotomy position a duckbill speculum was inserted into the Vagina and all discharge removed by means of sterile swabs. The uterus was then manipulated bimanually, the index and second fingers of one hand being one on either side of the cervix, while the other hand compressed the fundus uteri through the abdominal wall. In this way some uterine discharge was expressed from the cervix and removed on a sterile handled swab to be transferred to glass slips for future microscopic examination.

The cervix was then wiped clean and the Vagina, with the speculum still in situ, irrigated with commercial methylated spirit which was allowed to remain in contact with the parts for two or three minutes. The cavity was then dried out with sterile swabs.

A Kelly's urethral speculum with the obturator in position, was next passed into the uterine cavity--the cervix being pulled down and fixed with forceps--the obturator withdrawn and a sterilised platinum loop introduced through the speculum till it came in contact with the fundus.

The loop was then withdrawn and inoculations made in both and on agar and blood-agar tubes. This technique was adopted in order to obviate as far as possible the danger of contamination from vaginal organisms.

In Case V. this method proved unsatisfactory and the organism used/

used for vaccine preparation was isolated from the blood.

The blood was taken under aseptic precautions from the Brachial Vein and transferred to both and to agar tubes which had been previously liquified and cooled to 40°C. in a water bath. The mixture of blood and agar was sloped prior to incubation.

Cultures from whatever source were examined after twenty four hours growth at 98.4°F. In five of the six cases more than one organism was present in the growths so obtained. The smears of uterine discharge were then examined and the organism which was present in the greatest numbers and which was, at the same time, the most probable etiological factor, was held to be the responsible cause of the infection and isolated from the cultures.

Isolation of the selected organism was carried out on agar plates, the inoculum being taken from the culture medium which showed it to be present in purist culture.

The method was as follows:-

A loopful of the mixed growth was introduced into one ounce of sterile .1% saline and thoroughly mixed with it. A loopful of the emulsion so obtained was transferred to a second similar quantity of sterile saline and 1cc. of this flooded over the surface of an agar plate, the excess being run to the edge and removed with a sterile pipette. The agar plate was then incubated for the time best suited to the growth of the selected organism. Colonies obtained by this method were invariably discrete and being all superficial, were easily handled.

From a colony of the selected organism inoculations were made on three agar tubes, and the resulting growth used for the preparation of the vaccine.

The organismal contents of the agar tubes were emulsified in a little sterile .1% saline, on the agar surface and the resulting emulsion, made up to about 5 c.cs. with .1% saline, transferred to a sterile centrifuge tube and clumps precipitated in the centrifugal machine. The supernacant fluid was then decanted and standardised.

In counting the standardisation films the smear was divided roughly into thirty two areas and a field counted in each area.

The emulsion was then diluted with sterile .1% saline; the calculation being so worked that .25 c.c. would contain a minimal dose of organisms. Sufficient Tricresol was added to make the diluted emulsion a .5% Tricresol solution. The diluted emulsion was then transferred to a sterile c.c. burette and by means of an aspirating-syringe/



syringe needle with rubber tubing and clip, quantities of .25c.c., .5 c.c., 1 c.c. and 2 c.c. were run into sterilised glass vials the latter being then sealed in the blowpipe flame.

The vaccine thus prepared was sterilised for 1½ hours at 60° c. in a paraffin incubator on two occasions:- first after decanting the initial emulsion off the clumps and second after tubing, twenty four hours being allowed to elapse between sterilisations.

After the last sterilisation a tube of vaccine was broken and an inoculation made on the culture medium best suited to the needs of the organism and no injection of vaccine was made into the patient until the result of this culture was known to be negative. Only in Case III where the organism was B. Coli was a third sterilisation necessary.

By the above method it was found impossible to prepare a vaccine in less than four days and if difficulties arose the time was proportionately longer.

#### OPSONIC INDEX TECHNIQUE.

The Opsonic Index Technique adopted was that recommended by Allen (2) the index being estimated to the organism obtained from the patient and from which the Vaccine had been prepared.

The only detail in which Allen's Technique was departed from was in following the views of Copelli (3) that the Opsonising power of serum varies with the length of time it remains in contact with clot and reaches its maximum in 4 or 5 hours. The normal blood and the patients blood were therefore taken at the same time and as far as possible the serums separated and used four hours after withdrawal.

In estimating the Index a consecutive series of 50 leucocytes was counted in the normal and in the opsonic films and leucocytic clumps, so long as the outline of the individual members could be defined, were not excluded. No limit was placed on the number of organisms a leucocyte might contain.

Estimations of the Index were made prior to the injection of Vaccines and again 24 hours after the vaccine had been given. Thereafter they were made at such intervals as were suggested by the clinical symptoms or the possibility of the administration of another/

(2) Vaccine Therapy, Macmillan 1908.

(3) Il Policlinico sez. med. Rome 1909, XVI, P. 305.

another dose of vaccine.

In no case where a result was at Variance with what was expected— as long as the usual technique had been strictly adhered to and the resulting films were satisfactory—was a re-estimation made. The reason for this was that it was early recognised that the technique was at best faulty, and that if a sufficient number of series of 50 cells were counted in each film and the series with the maximum phagocytosis in the one film compared with the minimum series in the other, the Index could be manipulated within wide limits. It was therefore held that one might as well search through the already prepared films till a series of 50 cells was found that would give a credible result, as go through the whole technique again in the hope that the first series counted would give a result which would be more in keeping with ones preconceived notion of what the Index should be and as to have done so would have been absurd no re-estimation was made.

#### DETAILS OF CASES TREATED.

Case I Mrs V. Act 31, was admitted on the 6th day of her puerperium. She had been delivered of her fourth child at full time, the process being natural and conducted by two nurses. The first two days of the puerperium passed normally, but on the third day the patient, became feverish and suffered with headache. The next day the lochia became purulent and foulsmelling and remained so till admission. On the 5th day she became irrational in her behaviour and was very obstreperous in the evening. On the 6th day she was seen by a doctor who certified her as a case of Puerperal Fever and advised her removal to Hospital.

On admission patient was found to be a well nourished, but pallid woman. She was not in full possession of her mental faculties—wandering in her speech, singing to herself, and unable to give intelligent answers. She was continuously trying to get out of bed and showed her resentment to the necessary attention of the nurses by fighting and shouting. The condition was not delirium but gave the impression rather of early puerperal mania. The temperature was  $101^{\circ}$  F and the pulse 112 per minute.

Examination of the genitalia was performed under chloroform. The perinaeum and Vagina were intact but the cervix presented a deep fissure on the left side the edges of the wound being brawny and oedematous/

oedematous. The uterus, which was freely movable was enlarged to bimanual palpation and the sound passed 6 inches. The adnexa were normal to palpation.

Thick foetid discharge was expressed from the uterus and some shreds and small pieces of placental tissue were removed with the blunt curette prior to douching and swabbing with pure Izal. The fissure in the cervix was dressed with iodoform gauze.

The left leg was found to be the seat of a large annular syphilitic ulcer. No lesion of the Respiratory or Circulatory systems was discoverable.

The urine contained albumin to the extent of  $1\frac{1}{2}$  parts Esbach, but there were no tube casts present.

By the following morning the temperature had fallen to  $99.8^{\circ}$  F but rose again almost immediately to  $101^{\circ}$  F. The fall in temperature was accompanied by no remission of the mental symptoms.

The smears of uterine discharge showed a staphylococcus to be the principal organism present and the cultures gave a staphylococcus albus in almost pure growth.

The staphylococcus albus was therefore isolated and preparation of a vaccine immediately commenced. The Vaccine was ready by the 10th day of illness being four days from the time of admission.

During the interval of preparation of the Vaccine the temperature and pulse fell steadily as the result of local and general treatment and the mental symptoms abated considerably during the day but returned with full vigour in the evenings.

The uterine discharge remained copious but was sweeter smelling.

During the 9th day the temperature was subnormal but rose in the evening to  $99.2^{\circ}$  F.

On the 10th day a Vaccine injection of 200 Million organisms was made into the iliac region. The Opsonic Index prior to injection was .87. There was no local or general reaction as the result of the Vaccine injection, the highest point reached by the temperature in the succeeding 24 hours being  $99^{\circ}$  F. At the end of 24 hours the Opsonic Index had fallen to .69. On the 11th and 12th days of illness the patient's condition became much more satisfactory, her mental condition became practically normal and on the 13th day she complained of hunger and expressed a desire to be allowed to sit up. There was little difference in the quantity or quality of the uterine discharge/



discharge but the albumin which had been consistently plentiful in the urine prior to the Vaccine injection rapidly diminished and was only present as a trace on the evening of the 13th day.

On the 14th day the temperature rose abruptly to 102.6°F and the pulse to 140 per minute. The patient passed through a rigor lasting half an hour but, except for slight abdominal colic, neither at the time nor afterwards could anything be found to account for the exacerbation. The Opsonic Index estimated at the height of the rigor was found to be 1.17.

The further progress of the case was uninterrupted, the temperature remained normal and uterine discharge became very scanty. On the 17th day of illness a second injection of Vaccine was given. The dose was increased to 300 million organisms and was followed by no untoward symptoms either at the seat of injection or constitutionally, although the Opsonic Index fell to .8.

Two days after this second injection the uterine discharge finally ceased and intrauterine douching was discontinued.

The ulcer on the leg had meanwhile healed rapidly under local and internal administration of antisyphilitic remedies and by the 20th day when the patient was allowed to get up, was entirely covered with skin except over a small area the size of a sixpence.

On the 28th day from the confinement patient was discharged from Hospital, feeling strong and well, having been 22 days in residence and 18 days under Vaccine treatment. The Opsonic Index prior to discharge was 1.36.

This case presented on admission many of the symptoms of acute puerperal sepsis. The temperature however was only 101°F and the infecting organism proved to belong to a class which is not as a rule of very high virulence. Again the satisfactory reaction to local antiseptic treatment in the first four days, shows that the infection had not firmly established itself in the patients uterus. The presumption therefore is that the case belongs to the subacute class, but the infection being implanted on a host previously debilitated by syphilis, took on some of the characteristics of the more acute type.

The ultimate result would doubtless have been recovery if the antiseptic treatment alone had been persisted in, but the promptitude with/

Journal Reference,

Case I

Sex,

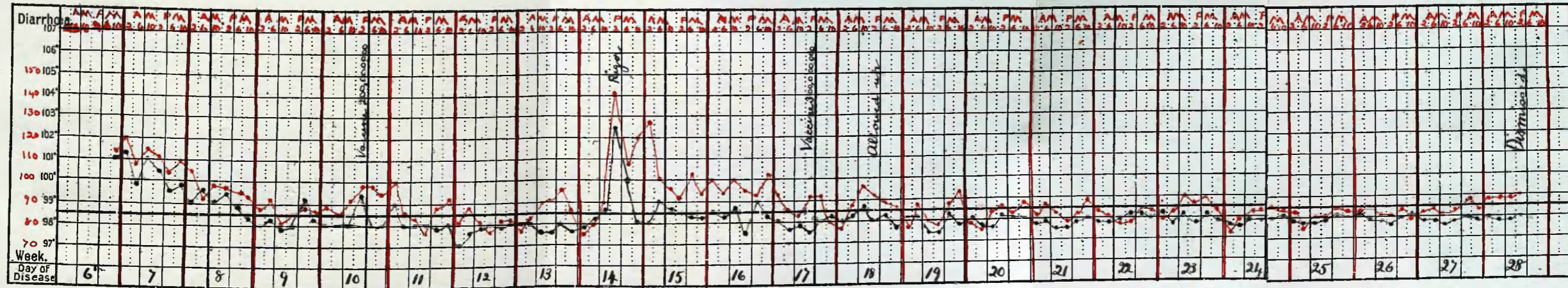
Age,

Result,

Complications,

Remarks,

- Temperature
- Pulse.



with which the more acute symptoms disappeared after the first Vaccine injection lead one to suppose that the rapidity of the cure was considerably influenced by its administration. The most striking feature of the case was the rapid disappearance of albumin from the urine. The presence of considerable albumin in the urine of such a case as this argues- in the absence of tubecasts- a high degree of Toxæmia and its disappearance argues some agency at work which has enabled the tissues to deal with the infecting organism and its by-products more satisfactorily. In this case the disappearance following immediately on the Vaccine injection seems to indicate that the Vaccine was the agency at work.

The absence of all circumuterine complications may also be attributed to the rapidity of the cure as one has frequently noted that low virulence cases if they do not react quickly to treatment are very liable to develop pelvic cellulitis.

The healing of a syphilitic ulcer even of large size, in twenty days is not unusual if the patient is at absolute rest and undergoing local and general antisyphilitic treatment; but it may be that in this case the administration of a Vaccine consisting of an organism of such general epidermal distribution as the Staphylococcus Albus influenced the secondary infection of the ulcer, while the mercury and iodide dealt with the primary etiological factor.



CASE II. Mrs U. act 37 was admitted on the 4th day of the puerperium, her 7th pregnancy having terminated at the end of the fourth month in a miscarriage.

Delivery had been accompanied by considerable haemorrhage which recurred at intervals during the two succeeding days. On the third day the lochia became foul smelling and in the evening patient felt feverish and had a shivering fit. She called in a doctor the following day who certified her Puerperal fever, and advised removal to Hospital.

On admission temperature was  $99.8^{\circ}$  F and the pulse 116 per minute. She was a well nourished woman but the colour was very pale. The only subjective symptom was severe headache.

Examination of the genitalia discovered a normal perinaeum and Vagina, except that the latter contained considerable purulent discharge. The cervix was deeply fissured on the left side evidently the result of some of her previous labours, two of which had been instrumental. The fissure was healed in its greater extent but the apex was raw and had apparently been recently torn. The uterus was of normal size the sound passing 3" and there was no limitation of movement in any direction. The cervix was dilated to admit the index finger and the uterine cavity found to be free of foetal tissue, there was however considerable purulent discharge present.

Apart from the genitalia the patients organs were normal to physical examination.

Examination of the films of uterine discharge showed a staphylococcus and a long rodshaped bacillus to be the only organisms present. On agar the staphylococci were almost completely grown down by the bacillus but in both the latter proved to be non-motile and consequently B. Coli could be eliminated from the consideration. As the bacillus did not correspond to any of the pus forming bacilli with which one was familiar it was considered a saprophyte and the staphylococci isolated for Vaccine preparation. When obtained in pure culture they proved to belong to the Aureus variety.

The Vaccine was ready on the 4th day after admission being the 8th day of the puerperium.

On the 8th day a dose of 200 million organisms was given. The condition of the patient had improved considerably during the interval of Vaccine preparation, the temperature after a preliminary rise/



rise to 102.6° F, probably due to uterine manipulation, having fallen steadily to normal. There was occasional complaint of sickness but no vomiting, and on two occasions the catheter had to be passed for retention of urine. Uterine discharge remained fairly profuse but the headache which was the most distressing symptom on admission had entirely disappeared.

The Opsonic Index prior to the injection of Vaccine was 1.02 and showed, if the estimation was correct, that the patients resisting powers had the infection well in hand.

The Vaccine administration was followed by no untoward symptoms but the Index fell to .88 at the end of 24 hours. On the 10th day the appetite returned and by the 13th day all uterine discharge having ceased, douching was stopped and the patient allowed to get up for a little in a chair. The Opsonic Index by that time had risen to 1.3.

The further progress of the case was uninterrupted and the patient was discharged on the 18th day of the puerperium feeling strong and well.

This case belongs to the unfortunately rare class in which the potential gravity of the infection is recognised early and steps taken to have it removed to some place where the somewhat elaborate technique of uterine antiseptic treatment can be properly carried out. The infecting organism was a Virulent one and possibly in the course of a few days would have given rise to all the symptoms of acute puerperal sepsis. The simple routine treatment of intrauterine medication and douching was however sufficient to arrest the further progress of the infection and to put the patient well on the high road to recovery before an autogenous vaccine could be got ready.

The improvement under antiseptic treatment coupled with the fact that the state of the patients defensive mechanism, as estimated by the Opsonic Index, was above normal prior to the injection of Vaccine leaves only the hypothetical conclusion to be advanced that the further progress was hastened by its administration. This conclusion is however supported by the fact that it was not until after the Vaccine had been given that the uterine discharge began to diminish rapidly, and also by the consideration that although postabortive sepsis is seldom fatal, if treated by ordinary antiseptic measures, yet there is no more fertile source of all the chronic endometrial and/

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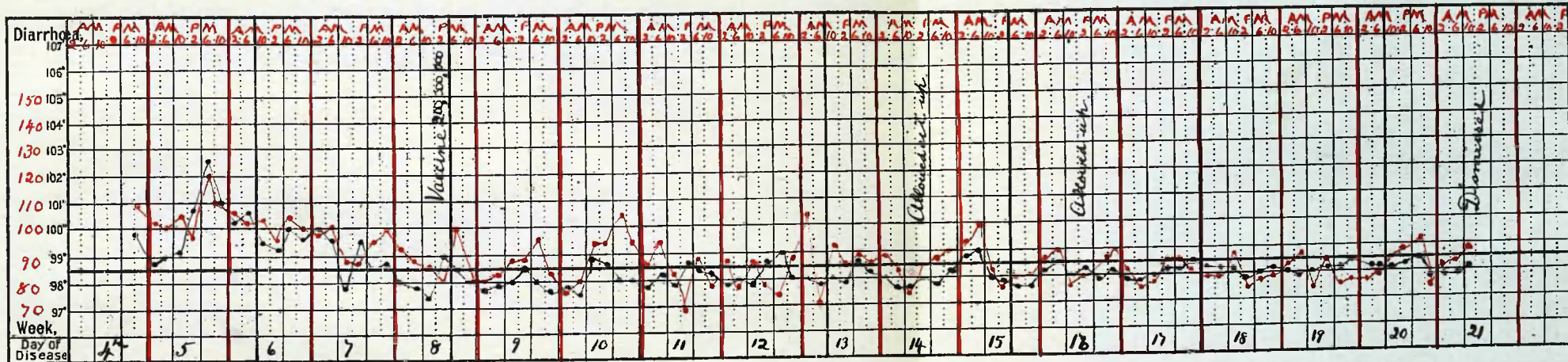
Case II

Sex, Age,

Result,

Complications,

Remarks,



- Temperature
- Pulse

and tubal troubles which owe their existence to organismal activity in the cavity of the uterus. These features being absent in the present case it is not beyond the limit of probability that the single dose of Vaccine was a useful adjunct to the antiseptic and constitutional treatment and the fact that the Opsonic Index had risen to well above normal a few days after its administration, seems so far as it can be relied on as an estimate of the patient's capacity for dealing with organismal infection, to support the contention.

GASE III. Mrs C. was admitted on the 19th day of the puerperium. She had been delivered of her third child at full time and birth had occurred before the arrival of assistance. A nurse arrived in time to witness the birth of the placenta, but gave no assistance further than was necessary to make the patient clean and comfortable. The patient got up on the third day and assisted in the work of the house and continued to do so daily until the seventh day of the puerperium. About that time the lochia began to be offensive and she suffered from vague discomfort and occasional sickness.

This condition of affairs got gradually worse- the patient being one day in bed and the next up. She had frequent attacks of "bilious" vomiting often accompanied by severe abdominal colic and occasional diarrhoea. In the third week she called in her doctor who ultimately certified her Puerperal Sepsis and advised her removal to Hospital.

On admission the temperature was  $100.4^{\circ}$  F and the pulse numbered 112 per minute. She was found to be a pale, poorly nourished woman and the subject of marked osseous deformity from infantile rickets. Her colour was a dirty lemon-yellow and the nails, lips and conjunctivae were blanched. Haemoglobin was only present to the extent of 54% of normal and the red corpuscles numbered 2,800,000 per cmm. The tongue was covered with a dirty brown fur and the breath very offensive. The teeth were moderately clean but covered with sordes. The abdomen was considerably distended and tympanitic all over- there was no abdominal tenderness.

The vagina contained very offensive purulent discharge but was otherwise normal. The uterus, which was enlarged, the sound passing 4 inches, was of firm consistency and freely movable in all directions. No lesion was discoverable on palpation of the tubes and ovaries. The uterus contained no foetal tissue but the endometrium was greatly thickened and necrotic in places. The endometrium was removed with the curette and the usual medication carried out.

The circulatory, respiratory and urinary systems presented no discoverable lesion.

The smears of uterine discharge showed a bacillus and cocci to be <sup>present</sup> ~~actively motile~~. The bacillus was isolated and found to conform to many of the cultural peculiarities of B. Coli- it grew on potato as a brownish streak; but did not form gas in gelatine stab cultures. In/



In lactose-litmus gelatine the litmus was turned red. From this organism a Vaccine was prepared and a 50 million dose injected on the 29th day of illness being 10 days from the date of admission.

During the preparation of the Vaccine no improvement took place in the patient's condition. The temperature presented a typically septic appearance sometimes reaching 103 F. in the evenings. Sickness was a prominent feature and diarrhoea an occasional symptom. Milk prepared with Hungarian lactic acid ~~and~~ bacillus was not tolerated by the stomach and the diet consisted in the main of peptonised milk and albumin water.

Intestinal antiseptics did not seem to effect the intestinal fermentation much, but as all medicine was liable to aggravate the sickness, they hardly got a proper chance. Uterine discharge persisted and was as foetid as on admission.

On the 29th day the Vaccine was injected and the Opsonic Index which immediately before injection was .51 fell in 24 hours to .46. There was no constitutional disturbance as the result of the injection in fact the temperature although still swinging did so within narrower limits. At the seat of injection a little redness and tenderness developed but had completely disappeared four days after the injection.

On the 32nd day the temperature rose to 102.6° but fell again immediately and fell to normal. On the 33rd and 34th days the temperature ranged between normal and 100° F.

By that time there had taken place a very decided improvement in the patient's condition. The sickness and diarrhoea had ceased and milk foods were able to be taken and retained. Uterine discharge was still present but not so copious nor so offensive.

On the 35th and 36th days the temperature again ranged higher but on the following day this was found to be due to an abscess which had developed over the sacral region. Under a local anaesthetic this was incised and about two ounces of pus evacuated. The organism in the pus was found to be a staphylococcus. Drainage of the abscess was followed by a prompt fall of the temperature to normal.

By the 37th day the Opsonic Index had risen to .71 and the following day an injection of 100 million organisms was given. In the evening the temperature rose to 99.6° but this was attributed to the/

the abscess rather than to the Vaccine.

The Opsonic Index estimated 24 hours after injection was found to be 1.3 and although entirely out of keeping with what was expected no re-estimation was made for the reason above stated.

The further progress of the case was straightforward there being no recurrence of sickness nor diarrhoea nor any appreciable rise of temperature. All uterine discharge ceased on the 40th day and on the 44th vaginal examination being unable to detect any abnormality about the genitalia, the patient was allowed to get up in a chair. Her opsonic index at that time was 1.2.

On the 51st day a third Vaccine injection was given. The dose was 200 million organisms and it was followed by an Opsonic fall to normal in 24 hours with a subsequent rise which on the 61st day reached 1.24.

The patient was discharged on the 62nd day from her confinement feeling strong and well. The haemoglobin had risen to 72% of normal and the red corpuscles to 4,200,000 per cmm.

In this case the uterine condition seems to have been part and parcel of a general B. Coli intoxication. The absence of all interference at the time of delivery points to an autoinoculation either by the blood stream or else by absorption from the neighbouring hollow viscera. The presence of staphylococci in the uterine discharge is probably referable to vaginal douching, which the patient carried out in her own home prior to admission to Hospital.

The persistent sickness and diarrhoea associated with abdominal distension all argue active organismal life in the digestive system. In this B. Coli would play an active part. The failure of intestinal antiseptics to limit the fermentative processes going on in the digestive system is in the main due to the intolerance of the patients stomach and consequent vomiting of everything taken by the mouth.

The length of time taken in preparing the vaccine having allowed ample opportunity for the trial of ordinary therapeutic measures without success, the rapid amelioration in the distressing features of the case must be attributed to the Vaccine, following as it did immediately on the administration of the latter.

The development of the sacral abscess is not out of keeping with the improvement of the general condition, for although the resistance/



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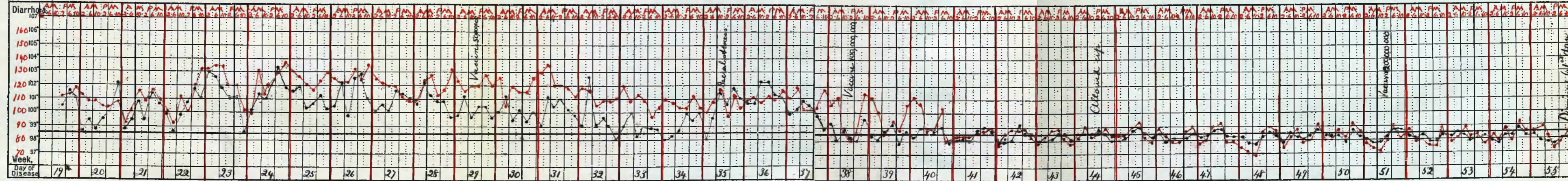
Case III

Sex, Age,

Result,

Complications,

Remarks,



- Pulse
- Temperature

Dismissed 61<sup>st</sup> day

resistance to B. Coli was rising the patients general resistance must have been much below par and at the time she had been confined for fifteen days to the dorsal decubitus, exercising continuous pressure on the sacrum.

The rise of the Opsonic Index was slow but its steady advance after each injection shows that the patient was reaching to the treatment.

The rapid increase in the haemoglobin and red corpuscles is attributable to two causes both presumably due to the Vaccine treatment. First, the patient from the date of the first injection was able to retain and digest nourishing food <sup>the cessation of excessive organometal activity in</sup> and secondly the stomach and intestines must have checked the active haemolysis which would be taking place as the result of the circulation of toxic products in the blood stream and solid organs.

It therefore seems justifiable to attribute the cure of this case primarily to the Vaccine treatment.



CASE IV. Mrs McK., act 26, was admitted on the 12th day of the puerperium having been confined of her fourth child at full time. The birth was easy and natural and was conducted by a doctor and nurse.

Discharge was profuse from the first and became purulent on the third day. On that day she was sick and vomited and felt feverish in the evening. On the 4th day intrauterine douching was commenced by her medical attendant and continued daily till admission. Progress was steadily in the wrong direction, sickness was occasional but feverishness was continuous and "shivering fits" not infrequent.

On admission on the 12th day the temperature was  $103^{\circ}\text{F}$  and the pulse 112 per minute and full and soft in character. The face was flushed and the tongue furred and dry. Pain was complained of in the head and also in the right iliac region. Patient had an occasional cough accompanied by a thick mucoid spit.

On physical examination the uterus was palpable at the level of the umbilicus and tenderness<sup>area</sup> was experienced over the right half of the lower abdomen. On auscultation moist rales were found over both lung bases behind. The heart was rapid in action but free from organic lesion. The urine presented a trace of albumin.

Pelvic examination confirmed the enlargement of the uterus and discovered that it was drawn to the right side and fixed by a mass of pelvic cellulitis in the right broad ligament. The sound passed  $5\frac{1}{2}$  inches.

There was no retained foetal tissue in the uterine cavity but the endometrium was thickened and in places soft and necrotic. Removal of the endometrium with the blunt curette caused considerable haemorrhage so after the usual medication the cavity was packed with sterile gauze soaked in 1-20 Izal solution.

The smears of uterine discharge showed streptococci to be abundant and there was also present a minute bacillus not unlike *B. Pyocyaneus*. There was however no green colour in the uterine discharge and the latter organism on agar cultures did not form pyocyanin.

On the agar slopes no streptococci could be found but an organism which was at first thought to be a staphylococcus was plentiful although the colonies were very minute. In broth, streptococci were numerous and it was only after some delay that it was recognised/

recognised that the organism which was taken for a staphylococcus on agar was in reality a streptococcus which would not form chains on agar but did so readily in broth.

The streptococcus was isolated and from it a Vaccine prepared which however was not ready till the 28th day of illness being 16 days from the time of admission to Hospital (4)

During the time of preparation of the Vaccine there was no improvement in the patient's condition. The temperature frequently rose to 105°F, delirium was invariably present in the evenings and rigors were a frequent occurrence. Fluid nourishment was borne well but there was occasional vomiting. Pain and swelling appeared in both shoulder joints on the 15th day of illness but were relieved by local applications of ichthyol ointment and internal administration of Asperin. An abscess developed on the left arm, a little above the lower end of the Humerus and was incised. No communication was found with the elbow joint. The organism present was a pure streptococcus.

The temperature continued to swing wildly sometimes passing through a range of 6°F in the twenty four hours. The pelvic cellulitis extended but frequent puncture with an aspirating syringe failed to localise any pus.

On the 28th day a dose of 10 million streptococci was given. The Opsonic Index prior to injection, was estimated at .81 and 24 hours after injection at .67. In no other respect did the Vaccine have any effect on the patient. The temperature continued its wild excursions and uterine discharge remained as before. It was however noticed that the wound on the arm which had practically ceased discharging, commenced to discharge again two days after the injection. By the 32nd day the Opsonic Index had risen to 1.4 but there was no corresponding improvement in the patients condition.

On the 36th day a second injection of 20 million organisms was given and was followed by an Opsonic Index fall to .67. After this injection the pelvic cellulitis became less tense and began to diminish. The other features of the case however showed no improvement, in fact from the 36th day the downward progress was more rapid.

On the 39th day pain was complained of in the sacral region but nothing definite was discovered on examination. The bronchitis, which/

(4) Personal considerations compelled my absence from Hospital for over a week.

*worse & the spit was more copious & had*

which was present on admission had by this time become assumed a purulent character. Dulness to percussion developed at the left base and in the following days extended till the whole lower lobe of the lung became affected.

The sacral pain was persistent and on the 41st day it was thought that there was a suspicious fulness about the left buttock. Under chloroform this region was incised and pus to the extent of 15 oz. evacuated. The abscess was situated below the Gluteus Maximus but no communication could be found with the interior of the pelvis. After evacuating the left buttock the right one seemed unduly prominent and it also was incised and a similar though smaller abscess found. On the following day a small swelling was noticed over the lower end of the left Radius and on incision this also proved to be of abscess formation.

After incision of the abscesses the temperature which had for some days previously been higher and less fluctuant, commenced to swing again.

On the 43rd day of illness, being 7 days from the second Vaccine injection the Opsonic Index was estimated and found to be 1.0.

On the 46th day a third Vaccine injection was made. The dose given was 50 million organisms and the Opsonic Index 24 hours later was .98.

At this time the dulness to percussion had extended throughout the whole left lung and the breath sounds which had previously been tubular and accompanied by moist crepitations, became entirely lost.

Aspiration of the chest at the level of the 7th and 9th ribs failed to find any free fluid in the pleural cavity, so the condition was considered to be absolute hepatisation of the lung, due to septic pneumonia. Albumin which had been present in the urine all along had by this time increased to  $1\frac{1}{2}$  parts Esbach and although the urine remained acid pus cells were present in the deposit.

There was no beneficial result after the Vaccine administration and on the 48th day cyanosis became marked, the pulse became very feeble and patient was only semiconscious.

Death occurred in the early morning of the 50th day of illness - the Opsonic Index a few hours before falling to .69.

Post mortem it was verified that the abscess cavities in the gluteal region had no communication with internal structures. The left/

left pleural cavity contained about 2 oz. of opalescent fluid. The left lung was solid and dripped pus on section. The right lung except for a few old pleuritic adhesions was healthy.

The Spleen was enlarged, (12½ oz.) very dark in colour and diff-  
luent in consistency. The liver showed fatty degeneration but no  
abscess formation.

Both kidneys were enlarged and pale—the left weighed 6½oz. and  
contained a little pus in its pelvis.

The uterus was enlarged weighing 6½oz. There were no adhesions  
on the peritoneal surface but both broad ligaments were thickened  
and indurated. In removing the uterus numerous small abscesses were  
opened in either broad ligament and a rather larger one was found in  
the connective tissue between the uterus and bladder. In consistency  
the uterus was soft and tore like a piece of sponge. Numerous  
minute collections of pus were found in its walls. The brain, heart,  
and alimentary tract appeared to be normal.

Microscopic sections were cut of the left lung, the left kidney  
and uterus.

The lung showed advanced cellular exudation into the air cells.  
In places the individual cell walls had been ruptured and the exudate  
occupied the space of three or four cells.

In the kidney sections, no necrotic foci could be found but  
there was considerable leucocytic infiltration along many of the  
tubules and round the glomeruli. Free leucocytes were noted in  
some of the glomerular capsules.

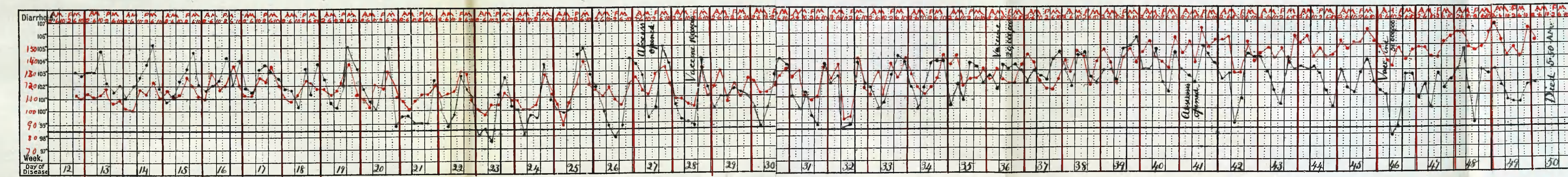
The uterine sections showed dense cellular infiltration at the  
endometrial surface, with large areas of necrosis. Scattered  
throughout the thickness of the uterine wall were necrotic foci of  
various sizes.

Except in its duration this case presented all the features of  
Acute Puerperal Sepsis.

The post mortem condition of the uterine wall and the wide  
spread distribution of secondary abscesses show the futility of in-  
trauterine medication alone, as suitable treatment for the advanced  
cases of Puerperal Sepsis. The only treatment likely to be attended  
by success was that calculated to raise the general resistance and  
to stimulate phagocytic activity. Tonic treatment and Vaccine  
therapy/



Journal Reference,  
**Case IV**  
 Sex, Age,



Remarks,  
 • Temperature  
 • Pulse

therapy theoretically fulfil these requirements and their failure to avert a fatal issue, gives rise to some speculation.

It may be that the wrong organism was chosen for the preparation of the Vaccine but the presence of streptococci in the secondary abscesses shows that they at least played an important part in the progress of the disease. The most probable explanation however of the failure of the Vaccine lies in the lateness of its exhibition. For 28 days the patient's defensive powers had been struggling with the invading organism and probably the administration of Vaccine only acted as an additional stimulus to an already overstimulated mechanism. If this view be correct then the failure of response is a natural sequence.

The deciding factor in the fatal issue was undoubtedly the condition of the left lung, and as this was probably due to the numerous organisms which hang about the respiratory passages obtaining a pathological footing, in the debilitated condition of the patient, a streptococcal Vaccine could not be expected to influence the consequent pneumonia in any way.

The behaviour of the Opsonic Index is difficult to explain. After the first Vaccine injection the Index rose to well above normal, without any corresponding improvement in the patient's condition and after the second, it ultimately rose to normal although at that time the patient was rapidly getting worse. The obvious conclusions are that either the technique was faulty, and as far as possible this was revised- recounts of the films being made and corresponding fairly accurately with the first counts thus eliminating any idea of subvoluntary manipulation of the Index, or else there was a sufficiency of free opsonin in the blood, of which the leucocytes were unable to avail themselves.

Whichever be the true explanation the fact remains that despite the estimated high index the downward progress of the case was persistent and wholly uninfluenced either by the Vaccine or other therapeutic measures.



CASE V. Mrs P. Act 34, was admitted on the 33rd day of the puerperium, having been confined of her second child at full time. The birth had been easy and natural and was conducted by a doctor and nurse.

During the pregnancy the left leg had been troublesome, being swollen and painful whenever the patient had been any length of time on her feet. It was found on inquiry that she had had enteric 22 years previously and convalescence had at that time been protracted owing to swelling of the left leg. After her confinement the uterine discharge persisted and was purulent in character and intra uterine douching was carried out daily in her own home. She did not regain her health after confinement but suffered no acute discomfort till a week prior to admission to Hospital. At that time the left leg became swollen and acutely painful and later redness developed along the inner side of the thigh. At the same time she became feverish, had several rigors and was delirious in the evenings.

On admission the temperature was  $102.4^{\circ}$  F and the pulse numbered 106 per minute. The face was flushed and the tongue dry but clean.

The left leg was greatly swollen and an area of dusky red discoloration and acute tenderness about 4 inches wide, extended from Poupart's ligament to the knee along the course of the Saphenous Vein. The leg below the knee was swollen and oedematous but not tender.

The perinaeum and Vagina were intact. The uterus was enlarged of firm consistency and freely movable. The sound passed  $3\frac{1}{2}$  inches.

There was no pelvic cellulitis, but digital examination of the left lateral fornix was painful. The uterus contained copious, foul smelling discharge but no solid material. Thickened unhealthy endometrium was removed with the blunt curette and the usual medication carried out. The course of the left Saphenous Vein was dressed with Ichthyol ointment and the limb padded and elevated.

The smears of uterine discharge showed a profusion of organisms in which staphylococci predominated, Streptococci and two varieties of bacilli were also present. The cultures gave similar results and as vaginal contamination was suspected smears and cultures were retaken but the same organisms were again found present.

As it was impossible to decide which organism or organisms to isolate for Vaccine preparation, recourse was had to blood cultures and/

and a pure staphylococcus Aureus obtained. To prove that the organism was not due to accidental infection while drawing off the blood, the process was repeated with a similar result.

From this organism a Vaccine was prepared and was ready by the 45th day of illness being 12 days from the date of admission to Hospital.

During the preparation of the Vaccine the condition of the limb improved somewhat. As the result of postural treatment and absolute rest the oedema entirely disappeared from the lower limb and the redness and tenderness along the course of the vein became slightly less acute. As the swelling went down the vein became palpable as a hard cord. The uterine discharge remained copious but was less offensive. The condition on Vaginal examination was unaltered. The temperature had settled and remained almost constant between  $99^{\circ}\text{F}$  and  $100^{\circ}\text{F}$  with an occasional rise to  $101^{\circ}\text{F}$ .

The Opsonic Index immediately before the injection of Vaccine at the commencement of the 7th week of illness, was .96 and 24 hours after the injection of 200 million organisms was again estimated and found to be .97. There was no local reaction as the result of the injection but the temperature began to rise after 36 hours and eventually reached  $101.8^{\circ}\text{F}$ . The patient complained of feeling weaker and although not delirious at night, was very restless and required a hypnotic. The temperature remained high for a period of three days and then fell gradually to normal which it reached in four days more. From that time it remained absolutely normal till the next injection was given on the second last day of the 8th week.

As the temperature reached normal the patient lost her feeling weakness and became much brighter in her general demeanour.

While the temperature was high, discharge from the uterus practically ceased but returned again as it reached normal. The leg improved rapidly and at the time of the second injection the redness and tenderness had gone, leaving only a brownish discoloration of the skin. The vein could be freely palpated as a firm fibrous cord throughout its whole length.

Prior to the second injection the Opsonic Index rose to 1.27.

On the second last day of the 8th week a dose of 400 million was given. In 18 hours the temperature rose to  $101.6$  but after 30 hours had again fallen to normal. With this rise there were no subjective/



Journal Reference.

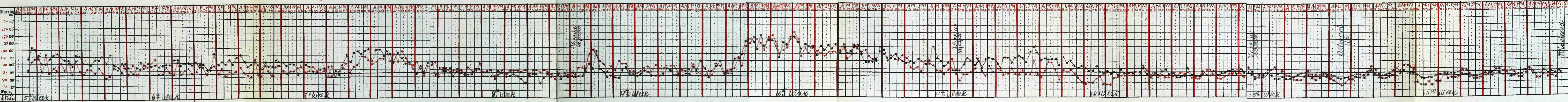
Case V

Sex, Age,

Result,

Complications,

Remarks.



• Temperature  
• Pulse



subjective symptoms, ~~or in the affected limb~~. Twenty four hours after the injection the Opsonic Index had fallen to .90, but by three days later had again risen to 1.58.

About the middle of the 9th week the temperature began to swing again and by the end of the week reached 103 F. The reason was not long in doubt. Pain and tenderness at the right Saphenous opening and also in the right lateral fornix gave conclusive evidence of septic thrombosis in the right iliac and femoral veins. The patient redeveloped all the symptoms she had had on admission, except that there was no discoloration of the right thigh. The Opsonic Index estimated at the beginning of the pyrexia was 1.16.

Sickness, vomiting and nocturnal delirium appeared and continued throughout the 10th week. At the beginning of the 11th week the Opsonic Index was 1.14 and a third injection of Vaccine was given. The original dose of 100 million organisms was gone back to and although the Index fell to .65 at the end of 24 hours there were no ill effects of any kind. Five days after the injection the Opsonic Index had risen to 1.09.

After this third injection the right leg rapidly became easier and the patient returned to the condition in which she had been previous to the right leg becoming involved. The temperature took some time to settle but by the beginning of the 12th week normal was reached. By this time the uterine discharge had entirely ceased and involution of the uterus had become complete, the sound only passing 2½ inches.

On the 1st day of the 13th week the Opsonic Index having risen to 1.35 a fourth and final injection of 200 million organisms was given. There were no untoward symptoms following the injection and four days later the patient was allowed up. There was no swelling of the legs on reassuming the erect posture, although the left vein *was completely blocked.* *Progress being satisfactory - the patient* was dismissed at the end of the 14th week feeling strong and well. The Opsonic Index on the day of discharge was 1.64.

This was a case in which a subacute septic infection spreading to tissue damaged by previous illness set up a violent conflagration which might well have proved fatal.

The extent of vein involved and the violent nature of the inflammation set up, together with the resistance shown to local and general therapeutic measures, present a clinical picture the outlook in/

CASE VI. Act 18, was admitted on the 15th day of the puerperium, having been delivered of her first child, at full time, with the aid of chloroform and forceps. The lochia became purulent on the third day after delivery but there was no constitutional disturbance. On the 6th day the patient got up, but feeling weak returned immediately to bed and in doing so knocked her left leg against the bedstead and "barked her skin". At the time of this accident she was wearing her stockings and continued to do so for the next two days. The stocking became adherent to the abrasion and when removed it was found that there was considerable redness round the wound. By the 14th day after confinement, the redness had extended over the whole area between the knee and the ankle and the leg was considerably swollen. The following day she called in her doctor who advised removal to Hospital.

On admission the temperature was 102°F and pulse 124 per minute. She was a well nourished healthy looking girl, but of very nervous temperament. The left leg was red, swollen and oedematous from the toes to the knee joint. An area of dusky discoloration and excoriation was found on the anterior aspect of the limb rather below the middle of the shaft of the tibia.

On pelvic examination the vagina and perinaeum were intact but the Vagina contained purulent discharge. The cervix uteri which was soft and oedematous, presented a deep inflamed fissure on the left side. The uterine cavity contained no solid matter, but withdrawal of the examining finger was followed by a flow of pure pus. The uterus was enlarged and flabby, but was freely movable. The sound passed 4½ inches. Use of the blunt curette caused considerable haemorrhage and after the usual medication, the uterine cavity was packed with 1-20 IZAL gauze.

The smears of uterine discharge showed a staphylococcus to be the only organism present. The cultures giving the same result a Vaccine was prepared and was ready by the 21st day of illness being 7 days from the date of admission to Hospital.

In the interval of Vaccine preparation the condition of the patient had not improved. The uterine discharge continued to be profuse and the cellulitis of the leg extended to mid thigh. Limb baths of 1-150 carbolic lotion had been tried and were followed by carboluria in 24 hours so recourse was had to dressings enveloping the/

the whole limb, of 10% Ichthyol ointment on gutta percha tissue. On the 21st day of illness the limb presented a dull red appearance from mid thigh to toes, but there was nowhere any localisation of pus. The temperature was usually 103° F in the evenings and although swinging considerably never remitted till after the Vaccine injection.

On the 22nd day 100 million organisms were injected, the Opsonic Index immediately before being .61. The injection was followed by a prompt fall of temperature to normal and although it rapidly rose again, a daily remittance was thereafter invariable. In six days after the Vaccine administrations the uterine discharge had become very slight and the uterus smaller in size, the sound only passing 3½ inches. Vaginal examinations discovered no development in the way of complications so uterine douching which till that time had been carried out twice daily, was cut down to once a day. There was however no improvement in the leg condition in fact the redness had extended to the hip, although the swelling was more localised to the knee and ankle joints.

Four days after the injection the Opsonic Index had risen to .74.

On the 27th day a second injection of 200 million was given. It was followed by no change in the character of the temperature but by the 29th day the Opsonic Index had risen to 1.08 and the uterine discharge had become very scanty.

On the 33rd day a third injection of 400 million was given and was followed by an Opsonic fall to .73 in 24 hours. In four days time the Index had risen to 1.73 and all uterine discharge had ceased. The fissure in the cervix had healed and the uterine sound only passed 3 inches.

The character of the leg meanwhile had changed. The redness had disappeared from the thigh and calf and was now limited to the knee and ankle joints which were more swollen. On the 36th day fluid was localised in the prepatellar bursa and under Chloroform this was incised and synovio-purulent fluid evacuated. Drainage of the septic bursa caused no reduction in temperature, which continued to swing between 103° F and normal.

On the 40th day aspiration localised pus in both knee and ankle joints and the case passed out of my hands.

Free incision of both joints was followed by no improvement and the patient died 13 days later.

The/



Journal Reference,

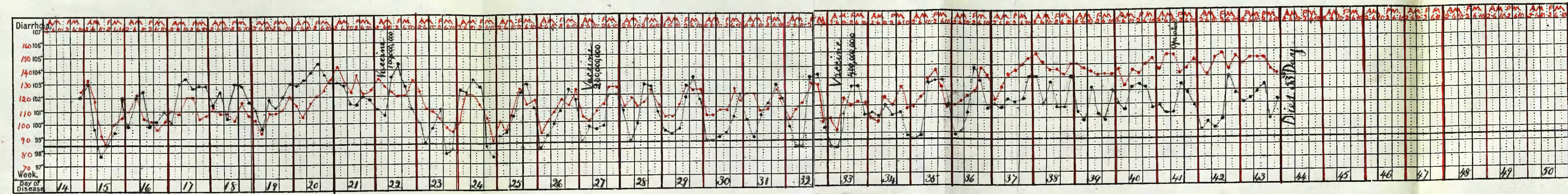
Case VI

Sex, Age,

Result,

Complications,

Remarks,



- Temperature
- Pulse

The organism present in the pus in all three collections was a pure streptococcus.

Post mortem examination revealed no further lesion and the pathologist stated that the genitalia were normal.

This case on admission to Hospital was evidently suffering from two distinct infections. The possibility of the uterine condition being secondary to the leg condition is precluded by the fact that the uterine discharge appeared before the leg injury was received. That the cellulitis of the leg was secondary to the uterine condition is improbable, considering the history of injury and the fact that the cellulitis radiated from the site of injury. Further the organisms present in the two situations were of different species.

As no severe constitutional disturbance appeared till after the leg became involved it seems probable that in the after developments of the case the leg was the paramount factor, and to it the wild excursions of temperature must be attributed.

From the fact however that the patient got better of septic infection in one situation, while similar infection in another became progressively worse, it is possible to deduce slight evidence in favour of the <sup>part</sup> played by Vaccine.

Before any such inference can be drawn it is however necessary to consider the relative virulence of the two infections and this seems to have been greater in the case of the leg condition. In the first place streptococci are as a rule more violent in their action than staphylococci and secondly the synovial surfaces seem to be situations in which organismal life flourishes par excellence. The uterus in its puerperal state is however also a favourable situation for organismal activity and the implantation of staphylococci in a uterus at or immediately after parturition must be considered a serious infection.

Allowing then that the leg was the more virulent, condition it is still suggestive that all uterine discharge, which had remained unchanged under antiseptic treatment alone, disappeared when the exhibition of Vaccine was added to the antiseptic treatment and that improvement was taking place while the leg was progressively becoming worse. Both centres of infection were treated to the limit of antiseptic and surgical resource and the fact that in the uterine condition, where treatment calculated to raise the patients resistance against the invading organism was used and a cure eventually brought about/



about; while the leg infection in which no artificial stimulation of Opsonin formation was attempted resulted in death, seems to argue something in favour of the Vaccine administration.

#### GENERAL CONCLUSIONS.

This series of cases treated by Autogenous Vaccines is too limited and the types of case comprising it too diverse to permit of any sweeping generalisations. Several points have however suggested themselves and may be tentatively put forward.

1. The treatment is only possible in the less acute forms of Puerperal Sepsis as the acute cases are so rapidly fatal that time is not given for the preparation of an Autogenous Vaccine.
2. It is possible that something might be done by means of stock Vaccines, till Autogenous ones could be prepared, but the diversity of organisms present in Puerperal Sepsis renders this a matter of some difficulty.
3. The choosing of one organism for the preparation of a Vaccine where several are coincident in the uterus, is not beyond criticism and yet the alternative of making a combined Vaccine of all the organisms present raises the question as to whether harm might not be done by injecting a Vaccine composed of organisms some of which might only be saprophytic and not pathogenic.
4. Cases 1 & 11 show that routine antiseptic treatment is of the utmost importance and that the administration of Vaccine should only be looked upon as an adjuvant to that treatment..
5. The results of the six cases treated show that some benefit may be anticipated from the administration of Autogenous Vaccines, but the result does not always justify the anticipation (Case IV). Further the negative phase which follows the administration of Vaccine is a potential source of danger (Case V).
6. In the hands of the ordinary observer at least the estimation of the Opsonic Index is not reliable, but if taken in conjunction with the clinical aspect of the case is of assistance in the regulation of dosage and helps to buttress ones confidence in the management of the case. The amount of time required for the estimation however, is a serious drawback to its routine use and the compensating advantages so slight that it can safely be neglected and the Vaccine administration regulated by the clinical symptoms alone.