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OBSERVATIONS ON THE USE OF ANTISTREPTOCOCCUS SERUM IN THE TREATMENT OF PUERPERAL SEPSIS WITH A REPORT OF FIVE CASES.¹

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This paper has been prepared in the last few days as a consequence of your chairman asking me to report in a short paper my experience with the use of antistreptococcus serum in the treatment of puerperal sepsis. This paper is not, therefore, in any sense a review of the subject of puerperal septicemia, or even an expression of my views in regard to the treatment of the same, any more than may be pertinent in reporting the few cases in which the serum treatment has been employed, and in commenting on the results and treatment in these particular cases.

The antistreptococcus serum has now been in more or less general use for a number of years, and in this time has been subjected to a fair trial, by a large number of men and under varying conditions. In the aggregate, a considerable number of cases have been reported of its successful

use; for the most part, however, they are reports of single isolated cases, and not reports of series of cases treated on a rational basis. Two years ago the committee of the American Gynecological Society collected over 350 cases in which the serum had been used, among which cases there was a mortality of 33%. This is believed to be higher than the average normal mortality in similar cases.

I believe that the general opinion of the profession at large, on the use of antistreptococcus serum in puerperal sepsis, is, that as a therapeutic measure it is a resource of very uncertain value, not to be relied upon with any certainty of success, and applicable only to a few cases as an accessory in desperate conditions.

My observations are confined to the use of the serum in 5 cases, all occurring in the past year, and these 5 cases I have reported in some detail. Before last year there were a few cases, but the notes of these were not available for hurried reference.

CASE I. C. H., thirty years. First seen in consultation May 15, 1900. On May 4th, patient delivered of a full-term child in absence of physician, and no examinations made either before or after delivery by the attending physician. She was sent to hospital and admitted with a temperature of 103.8°, pulse 120 and respiration of 40. Face flushed, dazed and apathetic at times, at other times wildly delirious. Fine tremor of hands and of tongue when protruded. Abdomen slightly distended and tympanitic, not tender and no spasm. Uterus enlarged, os patulous with considerable discharge. Intra-uterine douches and later curettage was performed without finding any débris of consequence. Urine, albumin trace with few hyaline casts. Patient was pretty sick for ten days, running a temperature from 100° to 103°, and her mental condition at this time was rather bad, depressed at times, at others very delirious; but at no time was her condition considered desperate or her life despaired of. Patient did well while in the hospital, but her recovery of strength and mental equilibrium was very slow, and she remained in the hospital nearly three months before she was ready for discharge.

This patient, before entrance, was given three injections of antistreptococcus serum, one daily, 20 cubic centimetres each time, and these injections were followed by daily remissions of temperature to about normal, the temperature going up again at night. After her admission to the hospital no more serum was administered, because her condition was not considered severe enough to demand it. It is possible that the serum may have influenced the case in its favorable termination, although I have always thought, as I did at the time, that the patient would have recovered without it. Her convalescence was slower than uncomplicated cases of puerperal sepsis, but not longer than septic puerperal manias usually require for recovery.

CASE II. E. F., twenty-five years. Entered hospital October 1, 1900. Italian. No history

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obtainable, except that patient was sent in for a septicemia and peritonitis after miscarriage. Patient in poor condition, weak, with high temperature and pulse; slight abdominal distention and tenderness; uterus enlarged and soft; os patulous with a considerable foul discharge. Patient was curetted shortly after entrance because of condition of uterus, and much foul material was removed. After curettage patient seemed to improve slightly for about a week, when the uterine discharge practically ceased. She was brighter, less apathetic and a little stronger apparently, although the temperature still remained high and very irregular.

After some days, the patient's condition not at that time improving perceptibly, she was given a bottle, 20 cubic centimetres of antistreptococcus serum. The injection did not have any noticeable influence on the patient's general condition or in her pulse and temperature; but she seemed to be

Autopsy showed a general tubercular peritonitis while there were results of an extensive pelvic inflammation, the uterus being adherent to the bladder and drawn to the right and adherent to the right pelvic wall. The right tube and ovary were adherent to intestines, and the left tube to the pelvic wall.

This case was undoubtedly one of general peritoneal tuberculosis and tuberculosis of the uterus, with which occurred a puerperal infection of severe type. Because of these complications occurring together, it is scarcely fair to judge the action of the serum in this case by the patient's death, for had the existence of the tuberculosis been known before the serum was injected it would not have been used. It is probable that the woman was in very poor condition from the tubercular peritonitis, and the puerperal infection was merely the means of hastening her death.

holding her own after its use without any especial change, although being very weak.

Soon after the injection of the serum, a report on the products of the curettage was received from the pathologist, stating the condition to be tuberculosis of the uterus. This report rather nonplussed us at first, and it was with considerable skepticism that the report was received, as the case seemed clinically a typical puerperal septicemia, not only from the history, but also from the course of the disease and the uterine discharge. The patient was, therefore, kept under observation in the gynecological ward for nearly three weeks, and then, nothing new developing, she was seen by Dr. Sears, who agreed that the condition might be one of tuberculosis, and she was transferred to his service. At this time the abdomen was slightly distended, tender and tympanitic, and her condition generally resembling sepsis. She, however, died two weeks later.

CASE III. M. R., twenty years. First seen October 2, 1900. Six days before, on September 26th, patient was delivered by forceps of a full-term child. Increasing pain, temperature and discomfort since delivery, when a consultation was held and she was removed to the hospital, having a temperature of 104.2° and pulse of 124. At entrance, pulse and temperature were elevated, eyes sunken, face anxious and there was mania present.

On examination, the abdomen was rigid and tender, not much distended. The uterus was enlarged, the os patulous, admitting the finger, and there was tenderness in both broad ligaments. The uterus seemed empty to the finger, although there was considerable discharge, and intra-uterine douches brought away some shreds. A curette was passed over the inner surface of the uterus, without ether, but nothing was obtained. The patient developed a pronounced mania, so that

constant restraint was necessary for her in the ward. The urine was normal in amount, containing a trace of albumin and a few hyaline and granular casts. The intra-uterine douches were continued twice daily. The patient failed gradually, in spite of all treatment, when on the sixth day she became entirely rational, no longer needing restraint, and remarked several times that she was glad to be again in her right mind.

On this day, October 8th, 20 cubic centimetres of antistreptococcus serum was injected, 10 cubic centimetres in the morning and 10 cubic centimetres in the evening. The temperature chart is particularly interesting at this point, for while the regular chart shows a gradual decline from the first administration of the serum, yet the four-hour chart shows evening exacerbations on each day,

whether or not the serum was injected, varying between 103° and 104°.

On October 9th, the next day, there being no apparent improvement, 20 cubic centimetres of serum was injected in the morning and 20 cubic centimetres in the evening without any noticeable change. At this time, 60 cubic centimetres of serum had been given in all; there had been no change for the better in any respect. On the other hand, the patient had been growing steadily weaker and the pulse intermittent, so that the serum was discontinued, and the patient stimulated merely, until she died three days later, on October 12th, without any marked change having occurred in the symptoms.

The chart of this case is an interesting one, as I have already brought to your attention. The

decline in the temperature and pulse following the injection of the serum, ordinarily favorable symptoms, without any amelioration of the patient's condition. I find we are very apt to look at a patient's chart, and, seeing a lower pulse and temperature, to at once conclude that there is improvement in the condition. I believe it is particularly true of septic conditions that the pulse and temperature chart is a poor guide in many cases, as the normal point is not infrequently reached only to react again shortly. I have also seen a patient die of sepsis in whom the temperature never rose above 100°.

CASE IV. F. S., thirty-seven years. Entered hospital on October 4, 1900. Six days before entrance, patient was delivered of a fetus of between four and five months for placenta previa. She was curetted soon after delivery for early sepsis. Patient was in a very poor condition and evidently profoundly septic. The uterus was enlarged, the os patulous, and the lochial discharge somewhat foul. The temperature was 104.2°, the pulse 118. There was dullness at the left base with marked bronchial breathing and numerous râles. Respiration at this time was not much

increased, but the next day it rose to 40, and patient unquestionably developed a septic pneumonia. The uterus was 5 inches in depth, the os admitting the finger, and a considerable amount of debris could be felt inside the uterus. The patient was therefore curetted, and the uterus washed out and packed with iodoform gauze.

The patient continued in a very serious condition, although for a few days she seemed to be improving slightly; but as this was only temporary, and her condition continuing very precarious, four days after entrance, on October 8th, 10 cubic centimetres of serum were given morning and evening without apparent result, and on the following day, October 9th, 20 cubic centimetres were given at one injection. Early the next day the patient's pulse and temperature fell rapidly to normal, and she almost collapsed, while the respiration remained unchanged at about 40 per minute. Under vigorous and free stimulation the patient rallied temporarily, while the pulse and temperature rose rapidly again to their former line. No more serum was administered, owing to its marked depressing effects. The patient died two days later.

This was a very critical case from the onset of the disease. The general septicemia was complicated by a septic pneumonia, which helped bring about the fatal result. No improvement of any sort was observed from the serum injection, 40 cubic centimetres being used altogether, while its use did result in marked depression of the vital forces, bordering on collapse.

CASE V. A. C., twenty-six years. Admitted to hospital on December 31, 1900, for pelvic abscess and septicemia after childbirth. Confined by midwife 40 days before entrance, and operated for vaginal puncture a few days before being sent to the hospital. Patient was poorly developed and nourished, and her general condition was very seedy. Chest negative, except for a soft systolic murmur at apex. Pulse poor and feeble, 92 per minute, temperature 98°. Abdomen rigid with considerable tenderness, which prevented any satisfactory examination, except that there could be felt a mass in abdomen of considerable size extending half way to the umbilicus. Urine contained trace of albumin, much pus, and numerous hyaline and granular casts and a few brown granular casts. Just to the left and posterior to the cervix was a small opening in the vagina, extending into a cavity into which was inserted a small iodoform wick with not much discharge. This wick was removed daily, the cavity irrigated through a small tube with normal salt solution, and a new wick inserted, while the patient, being in a very poor general condition, was nourished and stimulated. This treatment was continued until the seventh day, when her evening temperature reached 104.4°, having before this maintained a general tendency upwards, as may be seen by a study of the chart. As there was little discharge from the cavity through the vaginal sinus at this time, it seemed probable from the continued rise in temperature that there was an

accumulation of pus in the pelvis which was dammed up and not finding a ready exit. Therefore, it seemed best to give the patient a little ether, which was done, and an incision made posterior to the uterus transversely about one inch long from the side of the old opening through the vaginal wall. Through this opening, with my finger, I carefully separated the tissue up into the cavity which had previously been punctured and was being drained by the wick. No accumulation of pus was found there or elsewhere in the pelvis. The uterus was large, firm and anterior. The cavity was irrigated with salt solution and packed with iodoform gauze, the whole operation not lasting longer than ten minutes at the outside, and very little ether being used.

After the vaginal section the temperature ranged between 101° and 102° for three or four days. There was no marked change in the patient's condition, except it was evident there was no im-

provement, while on the whole the pulse was averaging a little higher, being about 120 per minute, and there seemed to be some loss of strength.

Other measures having failed, I thought it would be at least worth while to give the serum treatment a trial; accordingly, on the fourth day, 20 cubic centimetres of antistreptococcus serum was injected. This injection was repeated on the fifth, the sixth and the eighth days, when there was a marked decline in the temperature, and the patient seemed brighter and better, although still very weak. No more serum was injected, 80 cubic centimetres having been used in all. The temperature was subnormal on the ninth day, being 97.6°; but, nevertheless, the patient appeared to gain a little during the next few days, and seemed to be making fair progress on the road to recovery, when she suddenly collapsed and died in the morning, four days after the last serum was administered, twelve days after the operation, and about sixty days after delivery.

This case illustrates fully the disadvantages under which many of these cases are received into the hospital and treated there, entering in a very weak condition after a period of prolonged septicemia, already continued nearly six weeks, with probably only the most meagre care and surroundings through it all.

It seems fair to assume, and I am willing to admit, that the second operation which I performed was in a measure detrimental to the patient's interests, as it resulted in no improvement, and the probable conditions were not found as expected. On the other hand, the condition was gone over very carefully, and without relief in some form she seemed to be rapidly approaching a fatal termination.

I have never seen but one case up to the present time in which I have felt that hysterectomy was justified for puerperal sepsis, but possibly this case which I have just recounted might have survived under it if performed early.

The study of the results in these 5 cases, while not in themselves sufficient to determine the permanent value of antistreptococcus serum, is of considerable interest and may be of some value. In the observation of these cases, I think we cannot fail to be disappointed in the results of the serum treatment, and also cannot but conclude that as a curative agent its power is limited to a very narrow line of cases. It has also impressed me that the serum has a marked depressing effect on the patient, and is not to be administered to a very sick patient offhand in large and frequent amounts, as the directions are given which come with the serum. When used, I believe it is best endured by the patient and less depression follows, in doses of 10 cubic centimetres, repeated not oftener than every twelve hours until some result is observed. This is usually shown by a marked decline in pulse and temperature. In amounts of 20 cubic centimetres administered repeatedly to a patient in a critical state, the serum is a remedy not without danger and one likely to result in dangerous symptoms.

It is important to bear in mind that these cases of mine were all extremely sick, and in very critical, if not desperate, condition at the time the serum treatment was begun. But none of these cases were moribund, or even so critically ill that it was not considered at least that there was a good fighting chance. It is certainly in these cases that we should expect the serum to assist, if at all, as the milder cases recover without its use.

The mortality of puerperal sepsis, of all cases, mild and severe, is usually believed to be about 25%. In the City Hospital, where we see every year a large number of cases of this class, it certainly is not greater than this, and my impression is that it is somewhat lower. On this subject I hope to present a paper at a later date. In some cases much importance has been attached to the fall of the pulse and temperature which often follows the injection of the antistreptococcus serum. This fall in pulse and temperature does seem to be an attendant symptom on the injection of the

serum, but that is not always an entirely favorable symptom and is not unattended by danger. I am convinced that it is rather a signal of danger and an indication of impending collapse. This occurred in 2 of my cases, only shortly before death, and in one of these the pulse and temperature rose immediately, after touching normal, to 160° and 103.6° respectively. Moreover, severe cases of puerperal sepsis treated, without the use of serum, have frequently in the course of the disease remissions of pulse and temperature, only to recur again in a day or two when one is just ready to conclude that the disease has about run its course.

In every case of puerperal septicemia the virulence of each particular infection, the extent of the constitutional infection and the ability of the individual patient to combat the trouble, all have a direct bearing on the severity of the disease and on the ultimate result.

In puerperal sepsis the streptococcus is generally recognized as the main etiological factor, while a few other varieties of bacteria, as the staphylococcus and the colon bacillus, are believed to be the cause in certain cases, and in others the so-called mixed infections, when two or more of these bacteria are believed to be the exciting causes. In a few cases of pure streptococcus infections the antistreptococcus serum is apparently of great value as a life-saving measure. The varieties of the streptococcus are so many that it is only an occasional case that will be helped by the serum treatment. While in the majority of cases of streptococcus infection, and in all cases of mixed infections, it is useless to expect the serum to cure the disease.

I believe that the serum treatment has no place in the routine treatment of puerperal sepsis, that it should be used only in desperate cases after failure to obtain improvement by other and usually more efficient methods, and that if no improvement is shown after use for two or at most three days and the injection of 40 cubic centimetres to 60 cubic centimetres, it should be discontinued. I believe that its use is not free from danger, that it usually lowers the pulse and temperature, but at the same time it has a correspondingly depressing effect upon the patient, and that it has not apparently lowered the mortality of the disease.

With regard to the general treatment of puerperal sepsis, early curettage of the uterus carefully performed as soon as the diagnosis is established is, I believe, of primary importance, and the same result is not accomplished in my opinion by any other method of procedure. If carefully done it can result in no harm, and if efficiently performed it always removes the primary focus of the disease, and not infrequently removes the disease at its outer limits.

Following curettage, and sometimes in place of it in the mild cases, intra-uterine douches have proved to be of much value.

For constitutional treatment we must mainly rely on stimulation, tonics and forced feeding, with moderate diuresis and catharsis.