there were induced well marked symptoms such as the patient had experienced during the early stage of an attack: sensation of fulness in the head, tendency to labored breathing, numbness and sweating of the hands, tendency to unconsciousness. Even after stimulation for from twelve to fourteen seconds, however, unconsciousness and convulsions were not induced. Pressure on the left carotid sinus produced a similar fall in blood pressure and slight bradycardia but no abnormal subjective effects. The patient was instructed to take phenobarbital and atropine and to carry with him readily soluble tablets of atropine (1/100 grain, or 0.0006 Gm.) to take when a severe attack impended.

In December the patient had a severe attack, which he believed was somewhat modified by the use of atropine. From this time until the end of May 1937 he had two milder episodes without loss of consciousness.

May 26, at midnight, the patient entered his car to drive home. Nothing remarkable had occurred during the earlier part of the evening; he had taken one glass of beer. After driving for a few minutes through a congested district he "felt an attack coming on." The preliminary symptoms were those already noted in the description of the attack of September 1936. He took one tablet of atropine and stopped his car. He then attempted to leave his car to defecate. At this point he lost consciousness. At 3:30 a. m. he was seen by an ambulance surgeon and at 4 o'clock I saw him. He had regained consciousness but complained of pain in the back of the neck, of intense fatigue and of headache. He again stated that his head felt "like a balloon."

On examination the face was flushed. The patient was fully conscious but slightly drowsy. There was no pain on movement of the neck, and no meningeal signs. The lower part of the back and the buttocks were soiled with feces. The blood pressure was 130 systolic, 90 diastolic. The pulse rate was 84 beats per minute, pounding in quality. The pupils were equal in size and were not dilated; the left pupil reacted more sharply to light than the right. The mouth was dry (the patient had taken atropine). The knee and ankle reflexes on the left were somewhat more brisk than on the right. There was a neutral plantar response on the right; the response on the left was normal.

Six hours later the patient appeared fully recovered. The blood pressure was 110 systolic, 80 diastolic. The pulse was from 76 to 80 beats per minute. A sense of fatigue was present which cleared up in the course of the next three days.

June 6, 1937, the patient was seen by Dr. Soma Weiss, who confirmed the observations of the carotid sinus reflexes previously recorded. Procainization of the right carotid sinus abolished its reflexes. The surgical indications were analyzed as follows: 1. Medical therapy with atropine, phenobarbital and, later, ephedrine had been essentially unsuccessful. 2. The velocity of evolution of the severe attacks precluded successful self medication with atropine. 3. There was obvious inherent danger in some of these sudden attacks, such as the one recorded in which the patient was driving an automobile.

Consequently, surgical denervation of the right carotid sinus was carried out June 17 by Dr. Donald Munro at the Boston City Hospital. No gross pathologic changes were encountered. Recovery was uneventful. No subsequent attacks have occurred. Four months and six months after operation pressure over the right carotid sinus region produced no symptoms and no fall in blood pressure or pulse rate.

COMMENT

The interesting features of this case may be outlined briefly. There was nothing in the history to point to the carotid sinus as the origin of the widespread autonomic disturbances. However, in only approximately 25 per cent of cases is an important lead obtained in the anamnesis.[9a] The avoidance of constriction of the neck by the use of loose collars is sometimes observed. Disturbances of the bowel such as occurred in this case are due, as has already been indicated, to severe widespread autonomic discharge with the afferent limb of the reflex arc in the carotid sinus. They are relatively unusual and may further confuse the differential diagnosis between hyperactive carotid sinus reflexes and idiopathic epilepsy. It is not unlikely, however, that with more general recognition of these disorders more cases of this type will be observed. Of interest was the prolonged duration of the attacks of syncope noted in this case, since ordinarily these are of relatively short duration, usually lasting only a few minutes.

Further intensive study of this and related conditions is of great importance, since it opens to improved clinical approach the field of frank and borderline autonomic and vegetative disorders.

941 Park Avenue.

CONCENTRATED STREPTOCOCCUS (HEMOLYTIC) ANTITOXIC SERUM IN PUERPERAL FEVER

FURTHER THERAPEUTIC STUDIES

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Many years passed between the time that Pasteur (1878) [1] first cultivated the hemolytic streptococcus from a patient with puerperal sepsis and the time that attempts were made to combat the disease with serum. Of all the bacteria that may produce puerperal sepsis, the hemolytic streptococcus has been found the most common invader in the fatal types of the infection. Since 1895, when Marmorek [2] produced a serum which was supposedly valuable in the treatment of all types of streptococcic infections, other investigators [3] employed polyvalent serums with discouraging results. Of all the types of serum therapy for puerperal sepsis subsequently reported,[4] the most promising employed human convalescent serum.[4b] However, the inadequacy of the supply made this mode of therapy impracticable.

The Dicks [5] demonstrated the importance of streptococcus antitoxin in the treatment of scarlet fever by a controlled therapeutic study. In one series of patients with moderately severe attacks (thirty-five controls and twenty-one treated), there were no deaths, but a higher incidence of complications occurred among the controls, or untreated patients. In another series of patients with severe attacks (fifteen controls and twenty-nine treated), there was a mortality of 20 per cent in the control group and of only 3.4 per cent in the treated group.

The demonstration in 1925 of the production of toxin by hemolytic streptococci from patients with puerperal sepsis [6] and the subsequent production of an antitoxin [7] introduced a new and rational basis for serum therapy

Eli Lilly & Co. prepared the serum and furnished the author with an adequate supply for this study.

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2. Marmorek: Ann. Inst. Pasteur. **9**: 593, 1895.
3. These include:
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5. Dick, G. F., and Dick, Gladys Henry: Therapeutic Results with Concentrated Scarlet Fever Antitoxin, J. A. M. A. **84**: 803 (March 14) 1925.
6. Lash, A. F., and Kaplan, Bertha: Puerperal Fever, J. A. M. A. **84**: 1991 (June 27) 1925.
7. Lash, A. F., and Kaplan, Bertha: Puerperal Fever: J. A. M. A. **86**: 1197 (April 17) 1926.

for puerperal sepsis. Subsequent clinical studies of the effect of the antitoxic serum on puerperal sepsis indicated its therapeutic value in the early stages.[8] The contemporary studies of Warnekros, Louros and Becker[9] and Gaessler[10] corroborated the definitely favorable effect of treatment with antitoxic serum. That the serum was of value only when used early in the course of the disease was in accord with the experience with serum therapy for any toxin-produced disease, such as diphtheria, infection with Bacillus welchii, scarlet fever and erysipelas. Although an advance was made over the old antistreptococcus nonantitoxic serum, the therapeutic evaluation of the preparation was very difficult because of known spontaneous recoveries from streptococcic infections and the absence of any published studies checked by adequate controls. The present study, begun in 1928, was undertaken to check the value of serum therapy in a series of patients with puerperal sepsis in which alternate patients were treated with serum.

TABLE 1.—*Predisposing Etiologic Factors in Puerperal Sepsis*

	Treated Group (40)	Control Group (33)
Race		
White	21	11
Negro	19	22
Age		
20	13	11
21-25	13	8
26-30	7	8
31-35	5	4
36-40	1	2
41	1	0
Gravida		
I	21	15
II	4	5
III	5	5
IV	1	3
V	3	1
VI	4	1
VII	1	0
VIII	0	0
IX	1	2
X	0	1
Character of Labor		
Spontaneous	24	20
Operative	16	13

TABLE 2.—*Clinicopathologic Diagnosis of Puerperal Sepsis*

	Treated Group (40)	Control Group (33)
Acute metritis	29	18
With toxemia	4	4
With early peritonitis and septicemia	6	7
With early parametritis	1	4
With early generalized peritonitis		

TABLE 3.—*Results of Antitoxic Streptococcus Serum Therapy*

Mortality	Complications	
40 treated patients 4 (10 per cent)	Unilateral parametritis, 3	Pyelitis, 2
33 control patients 13 (39.4 per cent)	Parametritis: Unilateral, 7; Bilateral, 2	Pyelitis, 1

PREPARATION AND DOSAGE OF SERUM

The serum was prepared by immunization of horses with the toxin and organisms isolated from the blood and cervices of women with severe puerperal sepsis due to the hemolytic streptococcus. The details have been described in another study.[8] The immune serum was utilized when a high antitoxic titer was demonstrated, as compared with scarlet fever antitoxin and after concentration. The initial dose was 40 cc. of the concentrated serum. It was given after the patient was tested and found to be free of idiosyncrasy to horse serum.

TABLE 4.—*Abstracts of Deaths in Treated Series*

Patient	Character of Delivery	Onset of Puerperal Sepsis	Clinicopathologic Diagnosis	Bacteriology: Cervix	Bacteriology: Blood	Serum Therapy	Comment
D. T., white, aged 25, P-I, G-II	Self induced abortion with catheter	3d day post abortion entered hospital; 104.2, 118, 22; chills, lower abdominal pain for 48 hours	Acute metritis; early peritonitis	Str. hem.	Neg.	5th day post abortion 40 cc. intravenously; 6th day post abortion 20 cc. intramuscularly; 7th day post abortion 40 cc. intravenously (104, 160, 44)	Died 8th day post abortion; generalized peritonitis; no autopsy
S. J., white, aged 21, P-I, G-II	Self induced abortion with catheter	5th day post abortion; pains in lower abdomen; 6th day post abortion entered hospital; 103.4, 124, 40	Acute metritis; early peritonitis	Str. hem.	Neg.	7th day post abortion 40 cc. intravenously; 8th day post abortion 40 cc. intramuscularly; 9th day post abortion 20 cc. intramuscularly	Died 12th day post abortion; autopsy: generalized peritonitis
M. M., white, aged 22, P-V, G-V	Forceps delivery at home followed by daily douches for chills, fever	6th day P.P. entered hospital; 104.4, 182, 32; toxic; abdomen slightly distended but soft	Acute metritis; early parametritis; peritonitis	Str. hem.	Str. hem.	7th day P.P. 40 cc. intravenously; 8th day P.P.; 40 cc. intramuscularly; 9th day P.P. 20 cc. intramuscularly; 10th day P.P. 20 cc. intravenously	Died 11th day P.P.; generalized peritonitis; septicemia; no autopsy
M. S., white, aged 40, P-V, G-VI	Spontaneous delivery, 6 hours 27 min. labor	3d day P.P.; 103.4, 120, 20; pain in lower abdomen	Acute metritis	Str. hem.	Neg.	8th day P.P. 60 cc. intramuscularly	Died 9th day P.P.; generalized peritonitis; no autopsy

The intravenous route was used if the patient was very toxic, but usually the intramuscular route was chosen. The same dose was repeated in twenty-four hours if the clinical course of the patient required it. A third dose of 20 cc. was given twenty-four hours later if necessary. From clinical experiences it was observed that as a rule 100 cc. of the concentrated antitoxic serum was sufficient to obtain a favorable response.

CLINICAL MATERIAL

The patients treated were all in the sepsis ward of the Cook County Hospital, having been delivered there or elsewhere. All of them had cultures taken of material from the cervix which yielded hemolytic streptococci. Cultures of the blood were also taken. In order for a patient to receive serum therapy or to be included in our series for study, the comprehensive diagnosis had to be puerperal sepsis, acute metritis, septicemia or toxemia, hemolytic streptococcus infection. Although the plan followed was to give serum to alternate patients, in compiling my statistics I found several more in the serum group, the reason being that

8. Lash, A. F.: Am. J. Obst. & Gynec. **17**: 297 (March) 1929.
9. Warnekros, K.; Louros, N., and Becker, M.: München. med. Wchnschr. **73**: 2155 (Dec. 17) 1926.
10. Gaessler, E.: München. med. Wchnschr. **75**: 164 (Jan. 27) 1928.

the inclination of the house physician occasionally was to use the serum in cases of severe involvement despite the rule. All the patients fulfilled the criteria of having early severe sepsis on the basis of clinical, pathologic and bacteriologic changes, as discussed in a previous publication on nomenclature.[11] There were forty patients in the treated group and thirty-three in the control group. Although the stage of the disease was judged early, on the basis of duration of fever and symptoms, careful examination and the clinical course demonstrated variations in the rate of the progression of the infection and resulting pathologic changes. Thus acute metritis and toxemia were usually present from three to five days after the onset of the infection, but in some instances generalized peritonitis or septicemia occurred within the same time. Therefore, the evaluation of the clinical material of puerperal sepsis was difficult, but these factors were considered in the analysis of the two groups. There were seven positive blood cultures for hemolytic streptococci in the control group and six positive blood cultures in the treated group.

TABLE 5.—*Abstracts in Deaths in Control Series*

Patient	Character of Delivery	Onset of Puerperal Sepsis	Clinico-pathologic Diagnosis	Bacteriology: Cervix	Bacteriology: Blood	Comment
K. D., Negress, aged 18, P-I, G-II	Spontaneous delivery at home	4th day P.P. 103; 124; 22, chills	Acute metritis	Str. hem.	Neg.	Died 22 days P.P.; septicemia; no autopsy
A. D., white, aged 28, P-IV, G-V	Spontaneous 5½ months miscarriage at home; placenta removed by doctor	2d day P.P. 104.4; 124; 24	Acute metritis; early parametritis; septicemia	Str. hem.	Str. hem.	Died 17 days P.P.; septicemia; no autopsy
A. S., white, aged 40, P-XIII, G-XIII	Attempted forceps, version and extraction at home; craniotomy and manual removal of placenta in hospital; spontaneous delivery	2d day P.P. 101.4; 132; 40	Acute metritis	Str. hem.	Neg.	Died 62 days P.P.; autopsy; subacute P.P. metritis; purulent parametritis; recent thrombo-endocarditis of mitral valve; thrombosis of left sigmoidal petrosal and cavernous sinus plus usual general pathologic changes of sepsis
M. J., Negress, aged 26, P-II, G-II	Spontaneous delivery	4th day P.P. 103; 124; 22	Acute metritis	Str. hem.	Neg.	Died 18 days P.P.; septicemia; no autopsy
B. S., Negress, aged 17, P-I, G-I	Spontaneous delivery; artificial rupture of B.O.W.	3d day P.P. 103.4; 124; 32	Acute metritis; early peritonitis; septicemia	Str. hem.	Str. hem.	Died 7 days P.P.; generalized peritonitis; septicemia
L. G., Negress, aged 30, P-I, G-II	Classic cesarean section	2d day P.P. 101.4, 120; 26	Acute metritis; early peritonitis	Str. hem.	Neg.	Died 5 days P.P.; autopsy: diffuse fibrinopurulent peritonitis metritis
G. B., white, aged 33, P-IV, G-V	Self induced abortion	3d day post abortion; 102.4; 124; 22	Acute metritis	Str. hem.	Neg.	Died 91 days post abortion; autopsy; suppurative thrombophlebitis of uterine, iliac, femoral veins and inferior vena cava, plus generalized appearances of septicopyemia
I. C., Negress, aged 31, P-IX, G-IX	Spontaneous delivery	4th day post partum; 102.2; 110; 16	Acute metritis	Str. hem.	Neg.	Died 14 days P.P.; autopsy: pseudomembranous suppurative endometritis metritis, thrombophlebitis left ovarian vein, right ovarian vein and inferior vena cava; multiple lung abscesses
M. G., Negress, aged 30, P-IV, G-IV	Spontaneous delivery	4th day post partum; 103; 100; 88	Acute metritis; septicemia	Str. hem.	Str. hem.	Died 31 days P.P.; septicemia
A. D., Negress, aged 16, P-I, G-II,	Self induced abortion with penholder	5th day post abortion; 102.8; 112; 24	Acute metritis; early peritonitis	Str. hem.	Neg.	Died 11 days post abortion; generalized peritonitis
T. A., Negress, aged 21, P-III, G-V	Spontaneous delivery	3d day post partum 103.2; 102; 22	Acute metritis; early peritonitis	Str. hem.	Neg.	Died 14 days P.P.; generalized peritonitis
L. T., Negress, aged 32, P-III, G-IV	Spontaneous delivery at home	4th day post partum 104.8; 126; 22	Acute metritis; septicemia	Str. hem.	Str. hem.	Died 6 days P.P.; autopsy: acute metritis, septicemia
L. S., white, aged 24, P-III, G-IV	Spontaneous delivery	2d day post partum 103.2; 128; 22	Acute metritis	Str. hem. also in throat	Str. hem.	Died 7 days P.P.; septicemia

The clinical statistics given in table 1 indicate a similar incidence of the usual etiologic factors of puerperal sepsis, particularly the high incidence of operative deliveries. Table 2 shows the incidence of the pathologic stages in the two series of patients studied when first seen. The diagnosis of early puerperal sepsis was a chronologic one; that is, a duration of from two to five days. The varying rate of progression of the infection during this interval is evident from table 2. The two groups of patients were, however, similar, allowing for the determination of the value of serum therapy.

The results of the antitoxic streptococcus serum therapy are given in table 3. The residual pathologic changes found clinically when the patients were discharged are also given. The favorable effect of the serum therapy is apparent in a comparison not only of the mortality but also of the incidence and extent of the residual pathologic changes. When the early cases of my last report were included, the total number of patients treated was sixty, with a mortality of 8 per cent (five patients), and there were forty-four control patients, with a mortality of 48 per cent (twenty-one patients); the latter rate is comparable to the mortality reported by Fitzgibbon and Bigger[12] (51 per cent in fifty-seven patients not treated with serum).

The amount of serum used depended on the clinical response. Of the forty patients, twelve received 40 cc., nine received 60 cc., six received 80 cc., six received 100 cc., five received 120 cc. and one received 160 cc. No immediate reaction followed the use of the concentrated serum. Although the intravenous injection gave a quicker therapeutic response, the intramuscular route was most often chosen for the sake of safety. The difference in rate of absorption between the two may not be great, but the effect is much more striking with intravenous administration. Late serum sickness, that is, erythema, urticaria and swollen and tender joints, occurred from six to nine days after the administration of the serum in 40 per cent of the patients, which is a high incidence. No serious consequence followed the serum sickness, except in two patients: one had persistent sciatica and the other had toxic encephalitis (no organisms on smear or culture). They recovered, and the relation to serum therapy was dubious.

An analysis of the deaths in the treated group (table 4) shows that the cause of death was generalized peritonitis. The negative value of the serum in this group was not due to the delay in the administration of

11. Lash, A. F.: Am. J. Obst. & Gynec. **27**: 793 (June) 1934.
12. Fitzgibbon, G., and Bigger, J. W.: J. Obst. & Gynaec. Brit. Emp. **32**: 298, 1925.

the serum except in probably one instance (M. S.) but rather due to the rapidity of the extension of the infection (generalized peritonitis). It is again evident that serum is of no value in the treatment of this type of infection.

The deaths in the control group (table 5) may be considered as those due to early fulminant peritonitis and, in a larger group, to delayed development of peritonitis and other pathologic states. The assumption might be warranted that in the latter group the early use of serum might have prevented the progression to peritonitis and the other fatal complications (septicemia, thrombophlebitis and septicopyemia). There were no deaths from septicemia or thrombophlebitis with septicopyemia in the treated group.

Mention may be made of the procedure of sending an adequate supply of serum to ten different obstetric clinics for further clinical evaluation. The reports were incomplete and could not be used for any statistical study.

CONCLUSIONS

1. The value of antitoxic serum therapy in the treatment of early hemolytic streptococcus puerperal sepsis is demonstrated by the marked reduction in mortality and residual pathologic changes in a controlled series of cases.

2. The early diagnosis of hemolytic streptococcus puerperal sepsis is essential for the successful use of the antitoxic (hemolytic) streptococcus serum.

3. Failures despite early therapy may be due to the abnormally rapid progression of the infection (fulminant form of generalized peritonitis).

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PEPTIC ULCER IN SYPHILIS OF THE CENTRAL NERVOUS SYSTEM

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While studying a series of cases of syphilis of the central nervous system we were impressed by the number of patients who entered the hospital complaining of nausea, vomiting, hematemesis and epigastric pain. Complete study of these cases gave results which are at variance with our previous conceptions and constitute the basis for this report.

MATERIAL AND METHOD

All cases of syphilis of the central nervous system admitted to an active, large general hospital during a period of approximately four years were studied. Each case was examined by one or more of us. A few of these cases presented other primary causes for hospitalization, such as pulmonary tuberculosis. In each case complete examination facilities were utilized, so that gastric analyses and roentgenologic study of the gastrointestinal tract were accomplished in all indicated cases. All pathologic changes found on roentgen examination were verified after the administration of belladonna and atropine. Only patients in whom abnormalities were found on repeated roentgen examination and who had definite gastric symptoms were placed in the ulcer group.

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All cases presented clear-cut neurologic, psychiatric and spinal fluid signs of syphilis of the central nervous system. A minimum of two examinations of the spinal fluid was made in each case included in the series. Wassermann and Kahn reactions of the blood were both obtained at least twice in each case. These serologic reactions of the blood were negative or only incompletely positive in approximately 30 per cent of our cases. Cases incompletely studied or those presenting questionable clinical conditions were excluded from the series. This accounts for an additional thirty-seven cases. Two hundred cases of syphilis of the central nervous system remained for study.

TABLE 1.—*Incidence of Peptic Ulcers in Syphilis of Central Nervous System and Control Groups*

	Syphilis of Central Nervous System	Latent Syphilis	Pulmonary Tuberculosis	Serial Admissions
Average age, years	40.8	38.9	34	35.2
Total cases	200	200	100	100
Total peptic ulcers	21	3	1	3
Incidence of peptic ulcer, per cent	10.5	1.5	1.0	3.0

The controls for our observations on these patients with syphilis of the central nervous system were three other groups of patients in the hospital during the period of study. The method of study was identical with that outlined for the neurosyphilis group. These control groups consisted of:

1. Two hundred patients with latent syphilis. Each of these patients repeatedly had completely positive blood Wassermann and Kahn reactions without any demonstrable clinical or serologic involvement of the cardiovascular or central nervous systems.

2. One hundred patients with pulmonary tuberculosis, none of whom had syphilis.

3. One hundred patients consecutively admitted to this hospital.

In addition to the basic study of 200 patients with syphilis of the central nervous system and the control groups, we studied the records of 100 patients with peptic ulcer, who had been examined and treated in the hospital, for evidence of syphilis of any type.

OBSERVATIONS

The incidence of peptic ulcer in our series of cases of syphilis of the central nervous system was 10.5 per cent, while this condition occurred in the control series in from 1 to 3 per cent of the cases, as shown in table 1.

The characteristics of peptic ulcer as we observed them in our series of patients with syphilis of the central nervous system were of interest and, we believe, of significance. The symptoms presented in this group were characteristic of ulcer of the duodenal, gastric or anastomotic areas. The roentgenologic aspects were those of peptic ulcer of these areas without reference to any underlying or accompanying systemic disease. The gastric analyses were, however, of considerable interest in that thirteen of the twenty-three patients having both syphilis of the central nervous system and peptic ulcer had repeatedly low determinations of total and