SUCCESSFUL USE OF PRONTOSIL IN A SEVERE CASE OF STREPTOCOCCUS SEPTICEMIA FOLLOWING CYSTOSCOPY AND PERI-URETHRAL ABSCESS

CHARLES C. HIGGINS, M.D., AND F. C. SCHLUMBERGER, M.D.

Several months ago there was introduced into our therapeutic armamentarium a new chemical agent said to be specific for an organism which has always presented a problem to the physician—the Streptococcus. The trade name of this substance—disodium 4-sulphamidophnyl-2-azo-7-acetylamino-1-hydroxynaphthalene 3, 6-disulphonate—is Prontosil. Convincing clinical as well as pharmacologic evidence has thoroughly established its efficacy in Germany and England. In England, its value in infections due to Streptococcus haemolyticus has been particularly stressed and even in cases of well developed blood stream infections, as in puerperal septicemia, recovery has frequently occurred and the mortality rate has been greatly reduced. It has been shown to be effective in the treatment of severe infections due to other forms of Streptococci, and it has been reported to be specific for the Gonococcus.

The following is a striking demonstration of the promptness of action and rapid reduction of temperature following the administration of Prontosil. Perhaps an even more striking result would have been obtained had the dosage been adequate from the beginning.

REPORT OF CASE

The patient was a young man, 20 years of age, who was brought to the Cleveland Clinic Hospital in an ambulance. He was admitted on the general surgical service with the following complaints: chills and fever and abscess at the base of the penis which had been present for two weeks and pain over the left kidney during the preceding four months.

Past history revealed that, at the age of 4 years, he had had scarlet fever and this was followed by mild nephritis. At the age of 15 years a ureteral calculus had been passed. A stormy convalescence followed a cystoscopic examination and ureteral catheterization at this time, and severe cystitis persisted for several months. Possibly several small stones were passed during this period. Following this, the patent's health was good until one year previous to admittance to the hospital when he began to pass cloudy urine and, on analysis, a definite pyuria was found. He was attending school at the time and no further investigation was made. Associated with the pyuria was a chronic aching pain over the left kidney. The pyuria persisted and several severe attacks of pain simulating renal colic occurred.

The patient was taken to the local hospital where an attempt was made to pass a cystoscope but an obstruction was encountered in the membranous urethra. A number 18 Wishard catheter was passed and it was concluded that a urethral stricture was present. The following day he had a severe chill followed by fever of 103° F. The chills continued, as many as two or three occurring each day, and these were followed by a marked elevation in temperature. No further

cystoscopic examinations were made. A roentgenogram of the kidneys, ureters, and bladder showed no evidence of renal lithiasis. The patient was discharged from the hospital after ten days, at which time his temperature was 103° F. During the preceding two months 35 pounds in weight had been lost.

After the patient had been home for two days, he found a soft, painful mass along the urethra at the scrotal junction, extending along the left side of the scrotum. He also experienced some difficulty in passing urine. A physician passed a catheter and the mass was incised. About 60 cc. of creamy pus exuded and a quantity of urine. A drain was placed in the incision and urine continued to drain from the opening. The chills continued to occur and each time the temperature seemed to rise a little higher, reaching 104.8° F. at times.

The patient entered the Cleveland Clinic Hospital on January 31, 1937. The temperature was 101.8° F. and the pulse rate was 108 beats per minute; the blood pressure in millimeters of mercury was 112 systolic, 60 diastolic. His weight was 200 pounds. His appearance was that of a chronically ill but well nourished, sallow male who was perspiring freely and gave evidence of the presence of pain on every movement.

Examination of the head, neck, and chest, aside from those findings described, revealed no abnormalities. The abdomen was flat and soft and no masses or areas of tenderness were palpable. The fist percussion over both costovertebral angles was very painful, especially on the left side and even light palpation on this side produced pain. There was some suggestion of fullness in the left costovertebral angle. An indwelling catheter was in place and some urine also came from an opening just to the left at the base of the penis. It was at this point that the peri-urethral abscess had been opened and there remained an area of redness and induration but there was no purulent drainage. The genitalia were otherwise negative. There were no other positive physical findings.

Diagnoses of urethral fistula, acute cystitis, and acute bilateral pyelonephritis were made. The patient was then transferred to the urological service.

Laboratory findings at this time were: Blood count, red blood cells 4,240,000; hemoglobin 78 per cent; white blood cells 6,100 with 83 per cent neutrophils and 15 per cent lymphocytes; blood urea 51 mg. per hundred cubic centimeters; blood sugar 106 mg. per hundred cubic centimeters, icterus index 10.0. The Wassermann reaction of the blood was negative. A blood culture was taken on entrance and was reported negative for seven consecutive days. The sedimentation rate was elevated to 1.10, and agglutinations for tuluremia and undulant fever were negative. Analysis of the urine showed a specific gravity of 1.017, 2+ albumin, negative for sugar, 5 to 10 red blood cells per high power field and loaded with pus cells, negative for acid-fast bacilli.

Roentgen examination revealed the chest to be normal. A urogram made five days after admission showed prompt function from both kidneys. The right kidney was apparently normal and emptied in one hour while the left showed some dilatation and retention after one hour. The appearance of the calices was somewhat characteristic of that seen in an infectious process.

At cystoscopic examination a number 18 McCarthy cystoscope was passed very easily. The bladder showed evidence of marked cystitis; both ureteral orifices were seen and a catheter was passed to the left kidney. A specimen of urine from this kidney was quite cloudy in appearance. The pH of the urine was 6.5, a few red blood cells were present, 2+ pus, and many organisms, but there were no acid-fast bacilli. A culture of this urine revealed B. coli and B. pyocyaneous.

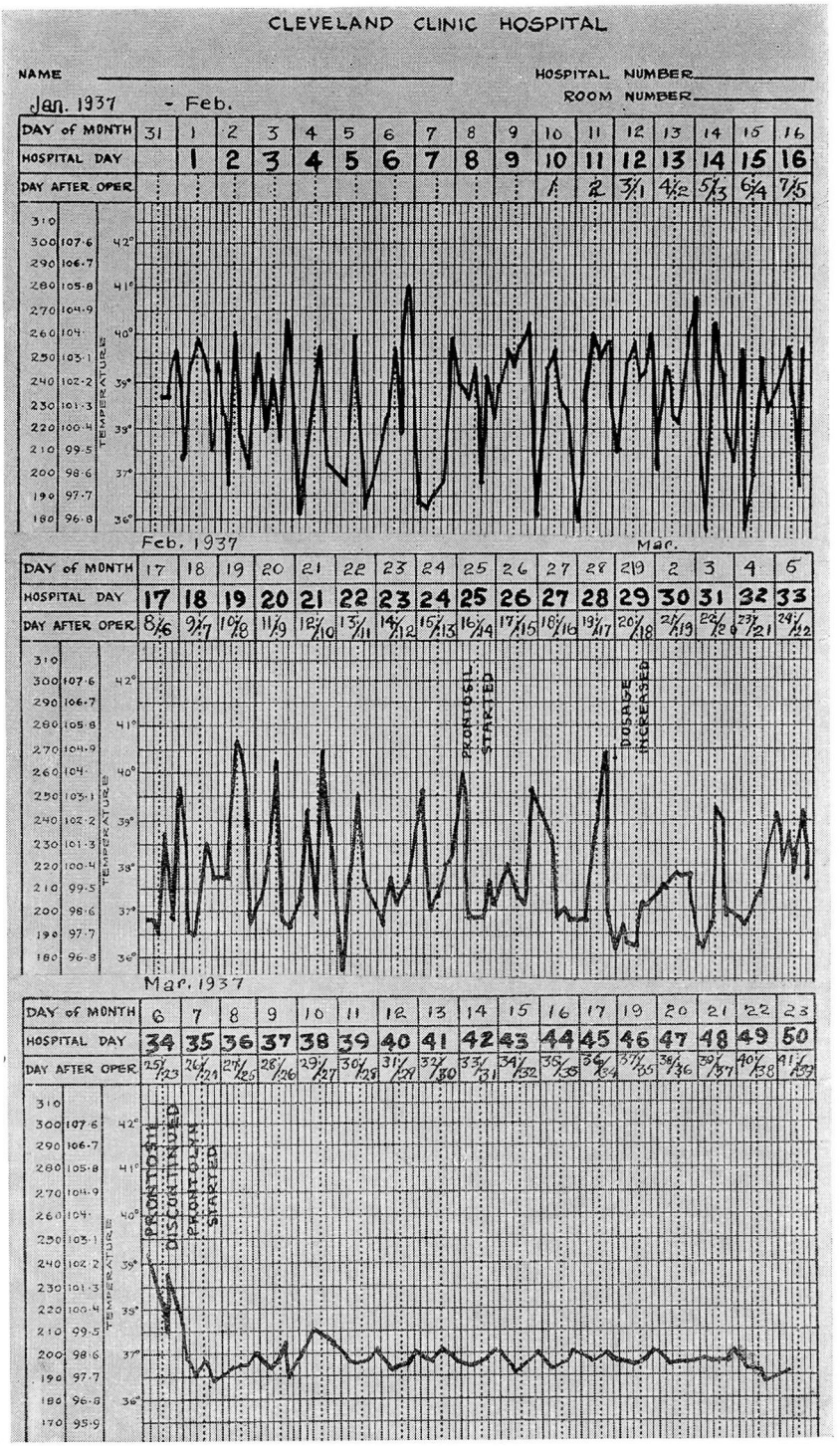

FIGURE 1: Temperature curve from time of admission to time of discharge.

A pyelogram disclosed findings similar to those seen on the urogram and a questionable diagnosis of early tuberculosis of the left kidney was made by the roentgenologist.

During this investigative period which occupied approximately nine days, the patient had one and sometimes two chills each day (Fig. 1). His temperature rose to 104° F. each time with one exception, at which time it reached 105.8° F. The chills seemed to become more severe each day. Between chills, he was quite comfortable, maintained a very good appetite, and his fluid intake and output were very good. Daily analyses of the urine continued to show the same findings as on admission. Repeated cultures of the blood gave negative findings even though the clinical picture was that of septicemia. The white count varied from 8,000 to 15,000 but never became exceedingly high. The value for hemoglobin gradually fell from 78 to 58 per cent and two transfusions, one of 300 cc. and the other of 500 cc. of citrated blood were given during the first week in the hospital.

In view of the clinical and laboratory findings referable to the left kidney, it was explored on the eleventh hospital day in the belief that a perinephritic abscess, carbuncle of the kidney, or possibly multiple abscesses of the kidney might be found. The only abnormality encountered was a marked perinephritis with considerable edema of the fatty tissue about the kidney. The kidney tissue proper appeared grossly quite normal. A No. 16 rubber catheter was sutured into the kidney pelvis, however, in order that the pelvis might be lavaged, thus promoting adequate drainage. The postoperative convalescence was uneventful and the general condition continued as it was before the surgical intervention. Four days after operation, another transfusion of 800 cc. of citrated blood was given. All types of urinary antiseptics, including mendelic acid therapy, gave no results.

On the sixteenth hospital day, another blood culture was taken and on the twenty-fourth hospital day it was reported positive for Streptococcus, nonhemolytic. Another transfusion of 800 cc. citrated blood was given.

At this time the new therapeutic agent, Prontosil, was introduced and 5 cc. of the substance was given every four hours by deep intramuscular injection in the gluteal muscles. Some response followed and for thirty-six hours the patient had no chills. This medication was continued for 4 days until a total of 120 cc. of Prontosil had been given. The temperature then began to rise again and another chill ensued. It was realized that the dosage had been inadequate so it was increased to 20 cc. every four hours, being given in the same manner. This was continued for five days until the total amount of Prontosil given had reached 720 cc. Definite response then began to be evident; only one chill had occurred during this time, and, on the thirty-fifth hospital day the temperature was normal. Prontolyn was then given by mouth, gr. 5, three times daily until the patient left the hospital and the temperature continued to remain normal. Repeated blood cultures gave negative findings.

The general condition immediately began to improve following the increase in the dosage of Prontosil and the urethral fistula closed entirely. During the hospital stay, 70 pounds in weight were lost. On the forty-fourth hospital day, the patient was up, walking about his room, and on the fiftieth day he was discharged from the hospital. Four weeks after discharge, word was received from the patient's mother stating he had been feeling fine, had gained 25 pounds in weight, and was normal in every respect.

Discussion

Considering the severity of the infection in this case and the general condition of the patient, it is difficult to resist the conclusion that the remarkable improvement was due chiefly to the introduction of treatment with Prontosil. After having almost despaired of saving this young man, as it was quite evident that he was in the terminal stages of a fatal infection, his prompt recovery was astonishing.

No severe toxic effects followed administration of the drug even though it was given in very large doses. Irritation of the urinary tract existed to a mild degree before this treatment was instituted but it was slightly more severe following the fifth day of Prontosil therapy. A few red blood cells were found in the urine and there were numerous epithelial cells. These disappeared following cessation of treatment with Prontosil.

The value for hemoglobin diminished slightly when Prontosil therapy was begun and it continued to be below normal even at the time of discharge. No definite determination was made to establish the presence of sulphemoglobinemia. Several such cases have been reported following the use of Prontosil. Such a finding is most likely to occur, however, when some form of magnesium sulphate is administered during the period when Prontosil is given.

Prontosil and Prontolyn have been employed at the Cleveland Clinic in the treatment of septic sore throat, suppurative otitis media, streptococcic infections of the hand, brain abscess, and several cases of Streptococcus septicemia. In all cases there has been a striking reduction of temperature and general improvement of the patient. Its use in the treatment of gonorrhea has been encouraging but not definitely verified at this time.

A tremendous interest has been manifested in Prontosil and Prontolyn and they are worthy of consideration by every physician who is treating infections due to the Streptococcus.