

Treatment with Penicillin of Some Obstetric Cases

BY

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THE following account of the use of penicillin presents illustrations of its value in cases of sepsis in obstetrics. The patients, were all treated at the County

mary, Carmarthen, consisted of 5 cases of Group A haemolytic streptococcal infections of the genital tract with complications, and 2 cases of bullous impetigo in neonates. The 5 cases of streptococcal infection were first treated with sulphanilamide. The routine dosage employed was 2 g. initially, a further 2 g. in 4 hours and then 1 g. 4-hourly. This treatment was started as soon as there was rise of temperature or pulse-rate. Bacteriological examination was immediately carried out on vaginal, nose and throat swabs, and a catheter specimen of urine. Penicillin treatment was started only when it became clear that the infection was not being controlled by sulphanilamide.

CASE I.

Mrs. A. D., aged 35, a 5-gravida, had nothing relevant in her previous obstetric history. She was admitted at term as an emergency on September 12th, 1944, in the first stage of labour. There was a history that the patient had been in bed at home for a fortnight before admission with pyrexia and a left facial palsy. On admission to an isolation ward her temperature was 102.6°F. and her pulse-rate 120 per minute. Her general condition was poor; there was a left facial palsy and a dry, fibrosed perforation of the left tympanum. Other abnormal physical signs were not found. Her labour was uneventful and she was delivered naturally of a healthy infant an hour later. Sulphanilamide therapy was started immediately and bacteriological investigations were carried out. The

temperature settled the morning after delivery but the pulse-rate remained at 100 per minute. The bacteriological examination showed a heavy growth of Group A haemolytic streptococci in the vagina alone (the ear swab being among the negative findings). On September 14th (2nd day of puerperium) the patient's abdomen became distended and she developed generalized abdominal tenderness. Her general condition deteriorated. A provisional diagnosis of general streptococcal peritonitis was made, and the abdomen was opened the same day through a small low median incision. There was some serous exudate and the small bowel was distended. The exudate was aspirated and on direct culture grew Group A haemolytic streptococci. A tube drain was left in the abdominal wound for 3 days. On September 15th, as there was still further deterioration in the patient's general condition, penicillin therapy (15,000 units 3-hourly) was started and the sulphanilamide discontinued. The pulse-rate began to settle the day after penicillin was started. It was given for 4 days and then stopped. The haemoglobin level on September 18th was 52 per cent and the patient was given a transfusion of 2 pints of fresh blood.

There was a further rise of temperature and pulse-rate on September 22nd, and again on September 25th, when penicillin (15,000 units 3-hourly) was restarted for another 4 days. The temperature and pulse-rate again settled—this time in 3 days. At this stage the patient became fractious and was difficult to manage. She objected strongly to the pain of the penicillin injections and discharged herself against advice on October 2nd, the 20th day of the puerperium. Her general condition was then fairly good, the abdominal wound was healed and the facial palsy improved.

She was readmitted a fortnight later (on October 17th) with a history of intense headaches, vomiting, drowsiness and pyrexia for the previous

week. She was now running a remittent pyrexia. There was bilateral papilloedema with a patchy retinitis and a left facial weakness. The abdomen did not show any abnormality. The cervix was healthy, the uterus well involuted and the appendages normal. Routine bacteriological examination did not show haemolytic streptococci in the vaginal swab. Lumbar puncture revealed a normal cerebrospinal fluid. She was transferred to Oxford under the care of Mr. J. Pennybacker as a possible cerebral abscess. Investigations at Oxford showed that she had a cerebral thrombophlebitis. From October 26th to November 8th she had a further 1,900,000 units of penicillin at Oxford. She returned to Carmarthen on November 18th and went home on the 21st in good health.

Comment. There is considerable evidence that the sulphonamides have reduced the incidence of general peritonitis as a complication of streptococcal infections of the genital tract. Streptococcal peritonitis still has a high mortality even with sulphonamide therapy. It remains to be seen whether or not the use of penicillin—as illustrated above—will be a more effective form of treatment. In this particular case the initial course of penicillin was undoubtedly too short (penicillin at the time was difficult to get for civilian use).

CASE 2.

Mrs. H. M. L., a primigravida aged 26, was admitted on September 12th, 1944. She was a florid, obese patient who had hypertensive toxæmia throughout her pregnancy. She was admitted at the 38th week because of the sudden appearance of oedema and albuminuria in addition to the long-standing hypertension. In view of this and of the fact that her sister had had postnatal eclampsia 2 years previously, labour was induced by sweeping and rupturing the membranes after premedication. She had a spontaneous delivery of a live infant. An hour later she had an eclamptic fit and was given 500 c.cm. of 40 per cent glucose intravenously and morphia gr. $\frac{1}{4}$. She had 7 more eclamptic fits within 12 hours, was given more morphia and intravenous glucose and 1 pint of

blood was withdrawn by venesection. She eventually settled down 15 hours after delivery.

On September 16th (4th day of the puerperium) she developed a temperature of 99.5°F. with a pulse-rate of 136 per minute and was isolated. Sulphanilamide was started. The vaginal swab showed a very heavy growth of Group A haemolytic streptococci. On the 7th day of the puerperium her temperature rose to 103°F. with a pulse-rate of 120 per minute. She developed abdominal distension and generalized abdominal tenderness. The abdomen was drained the same day through a small lower median incision. Fluid taken from the abdomen at operation did not grow any organisms, but fluid taken from the drainage tube 3 days later grew haemolytic streptococci.

The temperature began to show signs of settling, but rose again to 101°F. on September 26, and a vaginal swab on that day still showed a very heavy growth of Group A haemolytic streptococci. Sulphanilamide therapy was continued and repeated white-cell counts were done. On October 7th, after 21 days of sulphanilamide, came the first warning of agranulocytosis. The white cell count on that day was 4,550 per c.mm. with 30 per cent polymorphs and 51 per cent lymphocytes. The sulphanilamide was discontinued and Pentnucleotide (40 c.cm. daily and Vitamin C (600 mgm. daily) were given. Daily white cell counts showed gradual deterioration and on October 10th the total white cell count was 3,400 per c.cm. with only 4 per cent polymorph neutrophils and 1 per cent basophils.

In view of the facts that the patient still had a heavy streptococcal infection, that she was deprived of her natural cellular defences and that further treatment with sulphanilamide was dangerous, penicillin therapy was started on October 10th. The patient was given 15,000 units 3-hourly and this was continued until the white cell count returned to normal on October 17th, by which time the temperature and pulse-rate had also settled. Between October 10th and 17th the patient was also given alternate daily transfusions of 1 pint of fresh blood, daily parenteral liver ("Examen" 4 c.cm.), in addition to the Pentnucleotide and Vitamin C.

After October 17th the patient made steady progress. She had developed a superficial thrombophlebitis in the left leg on October 15th, which

gradually subsided. She was discharged in good health on November 10th. Postnatal examination on December 14th revealed a blood-pressure of 145/80, and a healthy pelvis.

Comment. In this case the general peritonitis had subsided before penicillin was started. It was the onset of a severe agranulocytosis with the heavy streptococcal infection persisting in the genital tract that provided the indication for penicillin. Superficial thrombophlebitis is a not uncommon complication of penicillin therapy.¹

CASE 3.

Mrs. W.B., a primigravida aged 32, was admitted on October 30th, 1944, and had a normal delivery of a full time infant. On the 3rd evening of the puerperium she developed a temperature of 103.6°F. and a pulse-rate of 120 per minute. She was isolated and given sulphanilamide therapy. Routine bacteriological examination showed a very heavy growth of Group A haemolytic streptococci in the vagina. The temperature and pulse settled gradually, but on the 10th day of the puerperium both rose again (temperature 101°F. to 102°F.; pulse 120 a minute). The temperature and pulse settled again in another 4 days, and on the 17th day the sulphanilamide was discontinued.

On the 24th day of the puerperium there was another sharp rise of temperature to 104.6°F. and of the pulse-rate to 136 per minute. The vaginal swab on that day still showed a heavy growth of haemolytic streptococci and sulphanilamide treatment was restarted. On the 25th day of the puerperium the white cell count was 6,000 per c.cm. with only 39 per cent polymorphs. Sulphanilamide was discontinued and penicillin (15,000 units 3-hourly) was given together with Pentnucleotide, 40 c.cm. daily. The Pentnucleotide was stopped after 3 days and the penicillin after 5 days. The pyrexia and rapid pulse-rate settled the day after penicillin therapy was begun. The clinical appearance of the patient improved rapidly and she was discharged in good health on December 5th; the 37th day of the puerperium. Postnatal examinations on December 23rd showed a healthy cervix, a uterus well involuted, and normal appendages.

Comment. The indication for penicillin in this case was similar to that in Case 2. The only difference was the degree of agranulocytosis.

CASE 4.

Mrs. E. A. J., aged 33, a 6-gravida, was admitted in labour on March 23rd, 1945, as a case of pre-eclamptic toxæmia. She was at term, her blood-pressure was 170/90, the urine was loaded with albumin and there was oedema of the legs. She had a spontaneous delivery. On the 3rd day of the puerperium she complained of a sore throat, had a temperature of 101.5°F. and a pulse-rate of 110 per minute. She was isolated and given sulphanilamide. Routine bacteriological investigations showed a very heavy growth of Group A streptococci in the vagina alone. On the 3rd day of treatment the haemoglobin was 50 per cent and the patient was transfused with 1 pint of fresh blood. There was no improvement after 6 days and penicillin was started. Both temperature and pulse settled on the following day. Penicillin was continued for another 5 days. On April 7th, 2 days after it was stopped, the temperature and pulse rose again. The left leg became oedematous and painful and there developed a clear picture of femoral thrombophlebitis. Bacteriological examination on April 7th did not show any haemolytic streptococci in the vaginal swab. Further penicillin was not given. The haemoglobin level was still only 64 per cent on April 8th, and a further transfusion of 1 pint of concentrated red cells was given. The thrombophlebitis subsided without incident, and the patient was discharged in good health on May 25th. Postnatal examination on that day showed an old laceration of the cervix, a well involuted uterus, and normal appendages.

Comment. Clinical response to sulphonamide therapy was not evident after 6 days, and on this indication penicillin was started with striking effect.

CASE 5.

Mrs. F.O., aged 23, a primigravida, was admitted on September 28th, 1944, at the 39th week of a twin pregnancy for pre-eclamptic toxæmia. Labour was induced by sweeping and rupturing the mem-

branes and live infants were delivered without incident. On the 4th day of the puerperium she developed a temperature of 103°F. and a pulse-rate of 130 per minute. She was isolated and given sulphanimide. Routine bacteriological examination showed a very heavy growth of Group A haemolytic streptococci in the vagina. She ran an intermittent pyrexia which settled on the 12th day of the puerperium and she discharged herself against advice on the 13th day (October 14th).

She remained at home in indifferent health and 3 weeks later she became acutely ill and was re-admitted to hospital on November 7th. On admission she had a temperature of 104.8°F. and a pulse-rate of 128 per minute. She complained of a great deal of pelvic pain. She had a large, tender, fixed mass in the right side of the pelvis and the uterus was pushed over to the left. Penicillin (15,000 units 3-hourly) was started at once. The temperature was normal the next day but the pulse-rate was still high—118 per minute. The same day (November 8th) the pouch of Douglas was explored by a posterior colpotomy. Pus was not found and a small de Pezzer tube drain was left in the incision for 3 days. The fluid from the tube was sterile and the vaginal swab grew coliform bacilli only. The pulse-rate gradually settled and the temperature did not rise again. The pelvic mass gradually resolved, and during its resolution it became more and more obvious that it was a parametritis. Penicillin was stopped after 7 days. A striking feature of this case was the marked improvement in the clinical condition of the patient effected by penicillin in 1 week. She was discharged on November 27th in good health. Postnatal examination on December 16th revealed a healthy cervix, the colpotomy wound healed, and the uterus, parametrium and appendages all normal.

Comment. The swift response to penicillin suggests that the parametritis, which followed a streptococcal genital tract infection, was due to a penicillin-sensitive organism. The swabs from the de Pezzer tube drain and the vagina were taken 20 hours after penicillin was started. It is possible that the negative swab findings may have resulted from this amount of penicillin therapy.

CASE 7.

Infant B. was born on July 23rd, 1944. The delivery was at term and was normal. On July 27th the baby developed bullous impetigo—first in the folds of the neck and eventually over most of the body. Swabs showed a very heavy growth of *Staphylococcus aureus*. At the time there was an outbreak of bullous impetigo in the nursery. The affected infants were isolated and their lesions and cord stumps were dusted with sulphathiazole powder. The ruptured bullae were dried before the powder was applied. Most of the infants responded to this treatment. In the case of Infant B the lesions kept on spreading, and red indurated areas developed round some of them. Penicillin ointment was applied after 8 days of sulphathiazole powder and the condition began to subside. The ointment was applied 8-hourly, and the lesions were cleared in 6 days. The infant's general condition was much improved.

CASE 8.

Infant J., born on July 29th, 1944, was a similar case. Penicillin ointment was applied to the lesions after 3 days initial trial with sulphathiazole powder. The rash cleared in 7 days.

Comment. Staphylococcal bullous impetigo has been a troublesome infection in nurseries in the last few years. Its control has been thoroughly investigated recently.² Penicillin ointment, properly prepared³ and handled, offers a simple therapeutic measure well worthy of further trial.

CONCLUSIONS.

In the cases described the patients were very ill. The first 2 patients, in spite of early sulphonamide-treatment, developed peritonitis. In Cases 2 and 3 sulphonamides were pushed to the stage at which agranulocytosis developed—a complication as dangerous as the original infection. Before penicillin was available there was no further line of treatment, and it is probable that Case 1, and possible that Cases 2 and 3, would have died. The rapid

improvement with penicillin was therefore all the more striking.

The cases are few in number and it will be some time yet before the value of penicillin can be fully assessed and compared with that of the sulphonamides.

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REFERENCES.

1. Florey, H. W. and M. A. Jennings. *Brit. Journ. Surg.*, 1944, xxxii, 112.
2. Knott, F. A. and J. B. Blaikley. *Journ. Obstet. and Gynaecol. Brit. Emp.*, 1944, li, 386.
3. Gough, J. B., M. Still and C. J. H. Wozencroft. *Lancet*, 1945, ii, 91.