TREATMENT OF BRUCELLA ABORTUS INFECTION WITH FOUADIN AND PRONTOSIL

BY

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Reports on the treatment of *Brucella abortus* infection with foudin and prontosil are gradually accumulating. Personal experience during the last year with the five cases here recorded supports the general impression that in the treatment of this disease both prontosil album and foudin are of value, and that the former may prove to be a simple specific remedy when the patient can tolerate it in moderate doses (about 3 grammes daily) for a week. In view of the tendency to relapse (Case III) it is probably wise to give short intermittent courses of the drug for two or three months after the fever has disappeared.

Case I

A man aged 37, a patient of Dr. W. C. Blackham of Moseley, was admitted to the General Hospital, Birmingham, on August 3, 1937. In January, 1929, he had pneumonia after influenza. Bilateral sterile pleural effusions followed; that on the left side recurred so often that an exploratory thoracotomy was done without effect. In September, 1929, a large abscess emptied itself through the operation wound; its origin was never determined, but it was thought to have tracked from the mediastinum. The sinus did not heal until 1931. He remained well and active until three weeks before admission, when he became febrile (temperature usually about 100° F. at night) and had transient slight pain in the right hypochondrium. Fever persisted at about the same level; there was some sweating at night, and the pulse varied between 72 and 80.

Physical examination was negative apart from flattening of the left chest—a consequence of the illness in 1929. The urine was normal. A radiograph of the chest showed nothing of significance; a cholecystogram was normal. There was slight leucopenia (polymorphs 50 per cent. in a count of 5,000). Agglutinations on August 5 were positive to *Br. melitensis* at 1 in 250, 1 in 500, and 1 in 1,250, but not at 1 in 50 or 1 in 2,500; to *Br. abortus* at 1 in 250 and (feebly) 1 in 500; and negative for the typhoid and Salmonella groups.

A week later without treatment his condition was unchanged, but the agglutination to *Br. melitensis* now occurred at 1 in 2,500 and to *Br. abortus* at 1 in 1,000. On August 13 he was given 1.5 c.cm. foudin, and the evening temperature fell to 99° F.; on the 16th 3.5 c.cm. of foudin was given, and his temperature fell to normal. Three further injections of foudin, each of 5 c.cm., were given at weekly intervals. After both the last two injections he had a rigor and his fever rose to 102° for a few hours; otherwise, apart from a trivial sore throat, his convalescence was uneventful. On September 7 agglutinations to *Br. abortus* and *Br. melitensis* were obtained at 1 in 5,000 dilution.

Case II

For the following notes I am indebted to Dr. M. I. Dick of Alvechurch. I did not see the patient myself, but advised treatment on the telephone.

The patient was a farmer's wife aged 45, and was the only member of the household who drank no milk except in her tea. She felt ill all through January. She was first seen on January 31, when she complained of aching all over. No abnormal physical signs were observed. Temperature 102° F.

During the following week her condition was unchanged, her temperature being round 101° F. in the morning and 103° F. in the evening. On February 7 strong positive agglutination to *Br. abortus* was obtained. The same day

the patient began to take one tablet of prontosil every four hours. Three days later she complained that the tablets made her sick, and as her condition was no better they were stopped, and on the 12th foudin was given, the first injection being 3.5 c.cm., and every other day afterwards 5 c.cm. On February 14 her temperature began to come down, and by the 18th was considerably lower. By February 26 she was much better, the morning temperature being normal and the evening temperature usually about 100°. The last injection was given on February 26, nine having been administered. On March 8 the patient was up for a few minutes, but was still having a slight evening rise and was feeling very weak. On March 25 she came downstairs.

Case III

A woman aged 61, a patient of Dr. C. Lowe of King's Heath, was admitted to the General Hospital, Birmingham, on May 24, 1938. She had been treated for pulmonary tuberculosis in 1918, but there was no subsequent ill-health. She had three children, one of whom had tuberculosis of the hip. For six weeks before admission she had high fever (between 102° and 103° F.), usually from midday until 10 p.m., when she sweated profusely. Shivering attacks occurred at intervals. Her appetite was poor; she lost weight and was unable to sleep. She also complained of a tongue that had been "sore and swollen."

Physical examination was negative. The pulse was 110. The urine contained a few pus cells, hyaline casts, and streptococci. Radiographs of the chest were normal. The blood count showed a slight simple anaemia and leucopenia (polymorphs 46 per cent. in a total count of 3,800). Agglutinations were positive to *Br. abortus* at all dilutions to 1 in 2,500 and to *Br. melitensis* to 1 in 1,250; negative to the typhoid and Salmonella groups.

From May 28 to June 5 she was given 3 grammes of prontosil album daily; from June 6 to 10 she had 1 gramme daily. The temperature fell to normal on June 2, and remained so (six days after the first dose of prontosil). In hospital the highest fever recorded was 101° on the day before treatment began. On June 15 agglutination to *Br. abortus* could only be obtained up to 1,250; at this date the leucopenia persisted (3,900) at the same level as before treatment.

The patient left hospital apparently well on June 18. A fortnight later she had a recurrence of symptomless fever, which disappeared after a few days' treatment at home with prontosil album under the care of Dr. Lowe. There has been no relapse since.

Case IV

A woman aged 62, a patient of Dr. Jessiman of Malvern. She had had typhoid in her youth, and her gall-bladder had been drained in 1920. She had been subject to migraine all her life. Rheumatic pains occurred in the right shoulder and sacro-iliac joints for a year, and she "had not been quite well" for some months.

History of Present Illness.—She has been feverish for five weeks (temperature at first between 100° and 101° F. at night and about normal in the morning, but during the last five days has been continuously between 101° and 102° F.). There have been profuse night sweats with an unpleasant odour and occasional "shivers," some neuralgic pain in the face and indefinite pains about the body, a little cough but no sputum, but no other symptoms apart from a sense of severe illness. A radiograph of the chest was normal, and the urine was sterile and otherwise normal. A blood count showed a leucopenia (polymorphs 60 per cent. of total count of 3,600). Blood culture proved sterile: the Widal test proved negative to the typhoid group; and the Mantoux test was also negative. A little dullness was found at the right base; subphrenic abscess was considered, but exploration proved negative (Dr. Jessiman).

The patient was first seen on May 24, 1938, on admission to a nursing home, being very collapsed after an ambulance journey of forty miles, and having a sense of impending death. Physical examination proved negative. On the evening of

May 25 her temperature was 103° F. and pulse 106. On May 26 agglutination to *Br. abortus* was positive in dilutions of 1 in 250 to 1 in 1,000 (Dr. J. H. Ebbs). Prontosil album (1 gramme daily) was given on May 26 and 27. Subsequently the dose was increased to 1.3 grammes daily until May 31, from which date 1 gramme daily was given to June 6. The temperature reached 103° F. during the first three days of treatment, but then fell rapidly to normal in the next three days; convalescence was rapid and apparently complete. On June 10 (after ten days of normal temperature) agglutination to *Br. abortus* occurred only in dilutions of 1 in 25 and 1 in 50. The blood count on that date was: haemoglobin, 78 per cent.; erythrocytes, 4,500,000 per c.mm.; leucocytes, 6,400 per c.mm. (polymorphs 42 per cent. with slight toxic granularity) (Dr. J. H. Ebbs).

The patient went to Yorkshire for a holiday on June 19. Towards the end of the month she developed symptoms of cystitis with a high temperature (103° F.). Dr. J. MacGowan of Shipley saw her in consultation and kindly wrote to me on July 8: "Clinically her illness has been solely due to the cystitis, and had she not given a history of having had undulant fever this would never have entered my head. The cystitis has reacted well to sodium mandelate, and she has been afebrile for about a week." In a specimen of blood taken by Dr. MacGowan during the acute stage of the cystitis agglutination to *Br. abortus* up to 1 in 2,560 and to *Br. melitensis* to 1 in 320 was found by Dr. J. C. Young of Bradford and also by Dr. J. H. Ebbs of Birmingham. The patient has been well since.

Case V

A woman of 50, a patient of Dr. H. V. Jessop of Burton-on-Trent, was first seen on June 22, 1938. She had led an active vigorous life with no illness of significance until six weeks previously. She then felt vaguely unwell and sweated profusely at night, the sweats having a sour, unpleasant smell. Despite this she went for a holiday to the seaside. On her return her temperature was taken for the first time and was found to be 102° F. The fever persisted and was often highest in the mornings. Physical examination was completely negative. The pulse was relatively slow (88 to 96), and the urine was normal. Agglutinations were positive to *Br. abortus* from 1 in 25 to 1 in 900 (Dr. J. H. Ebbs); negative to typhoid and Salmonella groups.

Two grammes of prontosil album were given daily from June 22 to July 2; then for three days 2½ grammes daily. From July 5 she took 1½ grammes daily until the 9th, when the drug was discontinued. During the first five days of this treatment there was high continuous fever (from 100° to 103° F.), with severe headache and pains in the limbs. On June 27 physical examination was still negative. On the 28th the temperature fell to normal, and subsequently was raised at times to about 99° F. until July 6, when the fever ended. Her general condition rapidly improved, convalescence being uneventful. A blood count on June 27, after 10 grammes of prontosil, showed no leucopenia (polymorphs 63 per cent. in a total count of 9,900).

In view of the relapse in Case III I advised that prontosil (1½ grammes daily) should be taken during one week of each of the two following months.

Summary

Five cases of infection with *Br. abortus* are reported. One was treated with fouadin alone with apparent benefit (Case I). It was a mild case, but fever had been continuous for four weeks, and the titre of the specific agglutination rose steadily in the week before treatment began.

Case II took prontosil album (3 grammes daily) for three days without improvement, and as she then began to vomit treatment by fouadin was adopted. Dr. Dick considers that she undoubtedly benefited, and her fever declined considerably in five days, though it did not become normal for a fortnight.

Cases III, IV, and V were treated with prontosil alone, and in all of them improvement was rapid and in the most severe one (Case IV) was dramatic. The temperature fell to normal in all of them in less than a week. In view of the tendency to leucopenia in *Br. abortus* infection the dose of prontosil album used was comparatively small; in none of the cases were any toxic symptoms observed, and there was no increase in the leucopenia found in two of them.

Case III had a relapse three weeks after prontosil was discontinued, but it was rapidly controlled by a further course of the drug.

Case IV had acute cystitis during convalescence; this cleared up under treatment with sodium mandelate.

In Cases II and IV the specific agglutinations declined to negligible titres after prontosil treatment; this was not observed in Case I, which was treated with fouadin alone.

In Case IV the specific agglutination rose again to a high titre during the febrile reaction to the cystitis. Topley and Wilson state: "Agglutinins are generally present in a suggestive titre by the end of the second week, and in frank cases of undulant fever they generally rise to 1 in 640 or over. After the attack is over they tend to fall fairly rapidly, and may sink to a low level within three months. There is evidence that in chronic cases they may fall even during the period of active infection."

It would be interesting to know if a fall in the agglutination titre is common after prontosil treatment.

[Since this article was written Case V had a slight relapse early in September. Fever persisted only three days and was rapidly controlled by prontosil.]

REPORT ON FIVE CASES OF BRUCELLA ABORTUS INFECTION

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Infection by *Brucella abortus* is uncommon enough in this country to justify the recording of the occurrence and treatment of five cases in one practice.

History of the Disease and its Mode of Spread

Brucella abortus was first identified by Bang in 1897, and it was shown by him to be the cause of contagious abortion in cattle. It was then called "Bang's bacillus." Kennedy in 1914 demonstrated agglutinins for *Brucella melitensis* in milk and serum of cows in London—which cows were no doubt infected by *Br. abortus*. But it was not until 1921 that Bevan, in Rhodesia, demonstrated agglutinins in human serum. Cases were first reported in England in 1928–9.

It is stated by experienced workers that the usual mode of spread of the disease is by infected unpasteurized milk and cream, but it can also be spread by contact with infected animals, their carcasses, discharges, or excreta. It appears that a healthy cow may continue to yield milk which is infected long after all symptoms of abortus fever have cleared up. The disease may also be disseminated by farm hands, butchers, sausage-makers, and veterinary surgeons: the latter's serum often contains agglutinins, though activity of the disease has never been manifest. Infection in such cases is probably latent. Contact from man to man has never been demonstrated (Beckman, 1938).