

## OBSERVATIONS ON HUMAN BRUCELLOSIS IN GENERAL PRACTICE

H. P. KIRSTEN, M.B., CH.B. (CAPE TOWN), *Beaufort West*

This paper is a review of the findings and observations I made in the treatment of human brucellosis during 11 years in private practice as a general practitioner in South West Africa. Over this period I treated an estimated 350-500 patients with this disease, from an area of more than 80,000 square miles.

*Geographical Distribution*

Brucellosis is a widespread disease in South West Africa and a very frequent cause of ill health, both in man and animals. Although found in every part of the territory, it occurs mainly in the southern half and north-western section where karakul farming is almost the sole industry.

*Animal Incidence*

Cattle, pigs, goats and sheep are all subject to infection. Of all domestic animals in the territory the karakul is, without doubt, the main carrier. In newly infected flocks the disease may cause up to 60% of premature or full-term stillbirths for 2-4 lambing seasons, after which the ewes, although still infected, give birth to live offspring at term.

*Human Incidence*

No age is immune, but in the absence of a proper survey it is futile even to guess at the amount of human brucellosis in highly endemic areas. However, on a single farm 4 members of a family of 9, together with 2 African shepherds out of 3, were found to suffer from Malta fever at approximately the same time as an entire family of 5 on another farm 130 miles away. It seems obvious to me from these findings that the incidence of the disease is far higher than is generally recognized.

*Mode of Infection*

In animals the disease is transmitted venereally. Whether or not this is the main or only route of transmission I do not know. Orthodox teaching states that man acquires the disease by ingesting infected dairy products or meat, of which goat's milk appears to be the chief offender. In South West Africa this is not true. The high incidence of human brucellosis in the territory undoubtedly results from the handling of highly infective material, such as newborn lambs or recently skinned pelts. The apparent predilection of the disease for karakul farmers, compared with cattle or goat farmers, could not be explained otherwise.

Moreover, I have a strong suspicion that in man transmission by the venereal route is likewise possible—a conclusion arrived at after close questioning of several female patients who had neither handled infective material nor ingested possibly infected dairy products, but whose husbands were known to suffer from Malta fever.

*Symptomatology*

In the acute and subacute stages the main signs and symptoms, viz. fever, malaise, painful swelling of one or more of the large joints, swelling of the liver and/or the spleen, and unilateral disabling sciatic pain, are almost identical in man and animal.

In newly infected flocks of sheep, for instance, a considerable number are often observed to be temporarily lame in a hind leg. In my own experience, intractable pain in the hip was so common that a patient presenting with such a complaint was investigated serologically as a matter of routine unless some other cause for the pain was demonstrable.

Pain and swelling of a knee joint is common enough to be borne in mind as a possible sign of Malta fever. Some obviously chronic cases present with annually recurring acute arthritis of a knee joint—almost invariably confined to the same knee year after year, even when the systemic infection has long been burnt out and serological reactions have been negative for years.

Onset of the disease may be sudden, and is then easily recognized. On the other hand, it may be so insidious that the patient is often unaware of being infected for months or even years. In a disease of such protean character even those well versed in its deceptiveness sometimes find it impossible to recognize it for what it is. The following are two cases in point:

1. Mr. M., a European male aged 46. Seen by chance when his car broke down on the way to the coast where he had been sent by his doctor to receive further treatment for acute cardiac failure. The findings were: Heart grossly enlarged, with to-and-fro murmurs at all valvular areas. Hepatomegaly and splenomegaly. Blood smear for malaria negative.

I was asked to examine the patient's second youngest child who presented with fever and was thought to have caught a cold. The child's liver was grossly enlarged. This made me suspect Malta fever and the patient's wife and other two children were, therefore, also examined. In the children unmistakable signs of Malta fever were found. No clinical signs were detectable in the mother. For confirmation the blood sera of the husband and wife were forwarded to the South African Institute for Medical Research and strongly positive reactions were eventually returned in both cases. Treatment of the family was started forthwith, and Mr. M.'s cardiac condition cleared up. He returned to his farm without proceeding to the coast.

2. Miss de B., a European schoolgirl aged 14. No previous illnesses and no preceding symptoms. She unexpectedly collapsed in the classroom with epileptiform fits, and was rushed to hospital where her doctor described the fits as Jacksonian in type. A tentative diagnosis of a space-occupying brain tumour led to arrangements for transfer to Groote Schuur Hospital. The patient improved in hospital and was sent home to await transfer to Cape Town. I was asked to keep her under observation. Since her mother and two younger brothers were at the time still under treatment for Malta fever, I forwarded her blood serum to the SAIMR. A positive reaction was returned of 1 in 7,200 for *Br. melitensis* and 1 in 3,200 for *Br. abortus*. Treatment was started immediately and the condition cleared up completely. There was no recurrence.

*Effect on Pregnancy*

The following cases are reported for consideration:

1. Mrs. R., a European female aged 33. Married 6 years. No children. 3 previous miscarriages in October 1947, July 1948, and August 1950. A suspicion that strong retroversion and retroflexion of the uterus had been responsible for the abortions had led to ventral suspension of the uterus in November 1950. The Wassermann reaction was repeatedly negative.

Fertilization occurred for the fourth time in August 1952. She consulted me for the first time when she was 10 weeks' pregnant and had just commenced bleeding again. All the previous

pregnancies had terminated spontaneously at 6-8 weeks. On this occasion she aborted at 10½ weeks in spite of treatment in hospital.

The patient's husband had been vaguely ill for some years and had been treated for acute Malta fever in 1951. Although she herself had never complained of illness, her blood serum was forwarded for investigation some 8 days after she had aborted for the fourth time. The SAIMR returned a positive finding of 1 in 6,400 for *Br. melitensis* and 1 in 1,600 for *Br. abortus*.\* She was given a full course of 'chloromycetin' in January 1953, with an initial dosage of 75 mg. per kg. bodyweight, to a total of 36 G. She fell pregnant again in August 1953 and had an uneventful pregnancy, ending at term on 6 May 1954.

2. Mrs. M., a European female aged 37. Married 14 years with 4 children and no previous miscarriages. She aborted spontaneously, with massive, almost fatal, haemorrhage at approximately 8 weeks, in October 1954. The uterus was evacuated by curettage. Subsequently she developed metrorrhagia which gradually became worse, until curettage was repeated in the belief that some product of gestation had remained behind. The second curettage yielded nothing abnormal. Concomitant symptoms led to the suspicion of Malta fever. Serological investigation, completed on 13 July 1955, yielded a titre of 1 in 400 for *Br. melitensis*. The test for *Br. abortus* was negative.

I can recall several other patients with a history of repeated spontaneous abortions in which serological investigation confirmed a diagnosis of brucellosis. One of these, too, an African woman, gave birth to a live baby subsequent to treatment.

#### Long-term Effects

Untreated brucellosis in man is seldom fatal, but is always a long-drawn-out affair; the most crippling long-term effect being recurrent acute arthritis in the knee or hip joint. Even where no permanent disablement results, the untreated or inadequately treated patient remains a person of low physical productivity for a long time.

#### TREATMENT

In view of the foregoing, it is, in my opinion, important to treat Malta fever quickly and energetically as soon as the diagnosis is established. Here I want to stress the fact that my observations were made in a region more than a thousand miles from the nearest laboratory, where communications were as uncertain as one could imagine. Consequently, after sufficient experience in practice, I seldom waited for serological confirmation of the clinical diagnosis. The patient was usually back at work before the serological results were known.

Various methods of treatment were tried, with sulphonamides, streptomycin, and broad-spectrum antibiotics all taking their turn as they became available. I found chloromycetin to be the drug of choice. In the dosage advocated it is better tolerated, and will cure brucellosis faster and more lastingly than all the others I tried. I am well aware that exponents of other antibiotics may challenge this statement. I can only reiterate that these were personal observations, and that by a method of trial and error certain conclusions forced themselves upon me.

Chloromycetin should be used in massive doses from the outset to ensure destruction of the organisms. The patient must be weighed and the course commenced with 75-100 mg. per kg. bodyweight per day in divided doses at 4- or 6-hourly intervals. This high initial dosage is decided upon

arbitrarily according to the clinical severity of the case and maintained until the temperature approaches or reaches normal, which usually occurs within 48 hours. At this stage the dosage is reduced by 500-1,000 mg. per day, depending upon the response of the patient. Levelling-off occurs at 1,000 mg. per day and this is maintained until the patient has been afebrile for a week. For children under 12 years of age, the final dosage level depends to some extent on the weight, but should never be lower than 500 mg. per day. For the adult, the total dosage varies between 25 and 40 G., being lower or higher at the opposite ends of the age scale.

With this régime the number of relapses, in my experience, were few indeed, and I cannot recall a single patient who developed a toxic reaction to the drug, nor did I ever have a case of intolerance, although I had been told in the past that chloromycetin in such doses may be dangerous.

#### Socio-economic Aspects of Treatment

In private practice the patient expects to be returned to duty at the earliest possible date. The quicker an infection is knocked out, the sooner the patient will be out of hospital and back at work. The course of treatment should last approximately 10 days and not 10 weeks. Accordingly, the use of an expensive drug in massive doses is justified by the absolute minimal period of incapacity of the patient. A final case is quoted to illustrate this point:

Mr. B., a European farmer aged 54. Admitted to hospital in September 1951. The patient had been receiving treatment with streptomycin, 'terramycin' and 'aureomycin' for more than two months in two different hospitals. On admission his condition was extremely poor, and he was unable to walk. He was seen in consultation a day or two after admission. Medication was switched over to the régime advocated above. Response was dramatic and the patient made a complete recovery in 14 days. Owing to his very poor initial condition he stayed in hospital for three weeks.

#### CONCLUSION

1. Experience gained from treatment of a large number of patients has taught me that chloromycetin, if administered in adequate amounts, is the drug of choice in the treatment of human brucellosis. The reasons for this I do not know, but to me there seems to be some relationship between its effect on typhoid and paratyphoid organisms on the one hand, and brucella organisms on the other.

2. Apart from the oral route of infection, I am convinced that the mere handling of infective material is sufficient to transmit the disease from animal to man, although it is possible that even then infection takes place *via* the gastro-intestinal tract. In addition, however, I would suggest that transmission by the venereal route is possible.

3. I have long had a suspicion that brucellosis in the human female may have an effect on pregnancy similar to that in animals. I have never been able to understand the argument that an organism which affects humans and animals alike in all other respects, is said to cause spontaneous abortion in animals only. Admittedly, it is unwise to draw inferences from such a small number of cases. Nevertheless, it is significant that work done in England some years ago by a bacteriologist (later attached to the South African Bureau of Standards), revealed that about 20% of placentas from a series of spontaneous abortions in an endemic area were found to show positive agglutination tests. It is my belief that brucellosis cannot be entirely disregarded as a cause of spontaneous abortion in humans,

\* SAIMR reference no. 249437 dated 27 November 1952.

and the matter should receive closer attention from research workers and medical practitioners in endemic areas.

4. Finally, I wish to point out that these are personal observations, the interpretation of which I leave to those

who are better qualified to assess or determine their validity or scientific value.

For his encouragement, I wish to thank Dr. F. E. Hofmeyr, of the College of General Practitioners in Cape Town, at whose request this paper has been written.