BRUCELLOSIS IN KRUGERSDORP, WITH A REVIEW OF THE PROBLEM IN SOUTHERN AFRICA

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'Brucellosis is a disease of mistakes. If we do not think of it we miss it, or we may think of it and test for it, yet find nothing. It eludes us. Nevertheless, as a cause of pyrexia of undetermined origin it is important, an obscure headache, lassitude, abdominal pain or arthritis may be due to its smouldering activity.'[1]

Dr. Wallis's apt description of a baffling disease is illustrated

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in the following reports of cases in Krugersdorp, Transvaal:

Case 1

A male European, aged 43 years, underground mine surveyor. In September 1946 had his tonsils removed for rheumatism. About March 1957 he had tick-bite fever with 2 tick-bite marks. Later he had pains in the back, and was diagnosed as having rheumatism. On 15 May 1957 he perspired excessively underground and came up to report ill. He had fever and chills for 4 days and was admitted to the Krugersdorp Provincial Hospital on 20 May under the description 'pyrexia of unknown origin'. He was given terramycin, 250 mg. 4-hourly. A specimen of blood submitted for agglutination tests on 21 May 1957 was reported by the SAIMR as agglutinating *Brucella melitensis* positive 1/50, end titre 1/400, *Br. abortus* positive 1/50, end titre 1/800, *B. proteus* positive 1/50.

He was discharged on 29 May feeling much improved. Repeat blood agglutination tests on 12 June 1957, gave *Br. melitensis* positive 1/50, end titre 1/400, *Br. abortus* positive 1/1600. The increasing high titres were taken as diagnostic of *Br. abortus*, but unfortunately no blood culture was performed during the stage of pyrexia. Agglutination tests on his family of wife, 3 children and mother-in-law (all resident in the same house) gave negative results.

The patient has a small agricultural holding at Chancliff Plots, Krugersdorp. Although he and his family live in the mine house, he spends much of his spare time on his farm, where he has a few pigs and 3 cows, whose milk supplies his own family and a few friends. The animals were examined by our veterinary officer, who reported that a Jersey cow was positive to contagious abortion on blood agglutination tests carried out by Onderstepoort laboratory. The animal was slaughtered. Blood agglutination of two persons supplied from this milk source were negative (SAIMR).

Case 2

On 24 July 1957 another case of Malta fever was notified—a male European, aged 18 years, apprentice fitter and turner in Krugersdorp. He had suffered from backache, which he attributed to the lifting of heavy iron rails at work. He was admitted to Cottesloe Hospital as a possible WCA case—injury to back. He developed pyrexia while in hospital. Blood agglutination, 12 June (SAIMR): *Rickettsia prowazeki* negative, *R. mooseri* positive 1/10, *R. rickettsii* negative, *R. burneti* negative, *R. akari* negative; on 14 June *Br. melitensis* positive 1/100, *Br. abortus* positive 1/200, Widal negative, Weil-Felix negative; on 20 June *Br. melitensis* positive 1/400, *Br. abortus* positive 1/400.

This patient's father is a friend of case 1, living on a neighbouring farm. He (the father) owns a cow which gives a blood agglutination test positive *Br. abortus* (29 August 1957). As from 1 March 1957, he supplemented his family's raw-milk supply from the herd of case 1. The milk from the town dairy which he owns is also not pasteurized. His son, case 2, is the member of the family most given to the drinking of raw milk.

Case 3

A Meat Control official at Krugersdorp abattoir, had brucellosis and was treated as a WCA case. He is a clerk, occasionally handling meat as part of his duty as issuing officer.

Case 4

On 7 November 1946 we were notified of a case of Malta fever in a 20-year-old immigrant Native mine labourer from the Portuguese North East Coast. Details are not available.

Case 5

An Angola Native mine labourer, he had worked 3 months at the West Rand Consolidated Mine when he developed 'pyrexia of unknown origin', enlarged spleen and liver, backache, and subacute arthritis of the knee. In March 1953 his agglutination report (SAIMR) was *Br. abortus* negative. He returned to hospital in May 1953 with an acute arthritis of the left ankle. Blood agglutinations (SAIMR) were *Br. melitensis* and *abortus* positive more than 1/6400; June 1953 the same result. He recovered on 46 capsules of 250 mg. of chloromycetin given over a week and did not return to hospital. His contract expired 7 months later. This was taken as a case of *Br. melitensis* infection.

Case 6

A medical man and his family came over from Canada on a cargo vessel shipping cattle in 1953. A few months later his wife developed undulant fever with arthritis of the knee joint, for which she was treated in Johannesburg. The case was not notified.

Case 7

A veterinary surgeon who fell ill in December 1950. He was confined to bed for 10 days with severe muscle and joint pains and extremely bad headache. Blood was positive (SAIMR) for *Br. abortus bovis* and *Br. melitensis* (titres not available). A 7-day course of aureomycin effected improvement

Case 8

Another veterinary surgeon, who contracted undulant fever in June 1950, with general malaise, headache and nausea. Blood tests: *Br. abortus* positive, *Br. melitensis* positive. A 4-day course of aureomycin effected improvement. Again in 1952 he had a milder attack of listlessness, continuous vague headache and malaise. Blood tests: *Br. abortus* positive and *Br. melitensis* positive. Patient elected to have no treatment because he preferred a state of immunity to develop rather than to sterilize his blood and render himself susceptible to reinfection.

It is considered that cases 7 and 8—veterinary surgeons in private practice at Krugersdorp—contracted the disease from cows while manually removing retained placentas. The route of infection may have been percutaneous or conjunctival.

Case 9

A Ventersdorp farmer, who had 1,000 cattle and frequently assisted his animals with calving, developed right-sided rheumatism with listlessness. He consulted a succession of doctors. A family friend, a veterinary surgeon, suggested brucellosis, and blood agglutination tests proved brucella-positive. Laparotomy was performed in a Johannesburg hospital in March 1950, revealing hard liver nodules and carcinoma of stomach, and also two liver abscesses containing *Staph. albus*, haemolytic streptococcus and *B. coli* on culture. He died in the following month from carcinomatosis.

Case 10

A farmer and business man, father of a health inspector in my department. In September 1942 he developed such pains in the shoulders that he could not put on his pyjama jacket. He felt as if he had a bad cold. A morning fever of 104°F would drop in the afternoon. He was severely ill until January 1943, when he was admitted to the Krugersdorp Hospital for special investigation. Blood tests were *Br. abortus* positive. He received 5 injections of killed brucellosis vaccine prepared by the SAIMR. On the second injection the fever subsided and he was cured.

Dr. J. L. B. Marais states that he remembers offhand at least 10 other cases, mostly from country areas surrounding Krugersdorp, that he has diagnosed as having brucellosis over the past decade. Case 10 is his only case that responded to brucella vaccine, subsequent cases having received antibiotics.

AFRICAN LITERATURE

The South African, Southern Rhodesian and Central African literature confirms that brucellosis abortus bovis has long been widespread, both among humans[2] and among dairy herds. Brucellosis melitensis, a more virulent infection, is encountered to a lesser degree and is known in South West Africa.

In 1937, Campbell and Greenfield,[3] of Cape Town, found the incidence of *Br. abortus bovis* to be 9·37% in patients with pyrexia of unknown origin. In 1939, Barnetson[4] found that out of 209 human sera submitted to the SAIMR, Johannesburg, from the Orange Free State, 1% gave a positive agglutination in a titre of 1 in 50; the corresponding percentages for the other regions were: Witwatersrand 1·9%, rest of Transvaal 5%, Cape Province 1·1%, South West Africa 24·9%.

Lewin, Bersohn and Richardson,[5] in 1948, reported 70% presence of brucella agglutinins in a total of 212 composite

samples of milk on the Witwatersrand submitted to whey agglutination tests. Of the 92 samples of milk tested, 3 were found to contain live brucella organisms. Human serum agglutinins were present amongst 200 normal blood donors as follows: 3 in 1/40 titre, 1 in 1/20 titre, and 4 in 1/10 titre. They suggest 1/100 as a diagnostic titre of active infection on the Witwatersrand. Meara[6]—Johannesburg 1950—reported 16·1% of 217 samples of milk as containing live *Br. abortus*.

Bevan[7] (1955) reports a number of dairy-herd outbreaks in Southern Rhodesia since 1905. Besides bovine, he describes many human cases, and the difficulties he met in getting the occurrence of human cases accepted by the medical profession. He mentions two butchers becoming infected, and one farmer who developed infection of his seminal vesicles, a very common site of infection in bulls. He emphasizes that the disease is not always recognized but is mistaken for influenza, rheumatism, tuberculosis, malaria and a dozen other complaints. The problem calls for the closest cooperation between the medical and veterinary professions.

Daneel and Meyer[8] describe a case of abortus fever in a Zulu male aged 32 years presenting as headache with weakness and abdominal pains. Eales[9] describes *Br. melitensis* infection of an 11-year-old Coloured boy of Rehoboth, South West Africa, presenting as an arthritis of the hip joint. The boy was in the habit of consuming large quantities of goat's milk. Trevor Jones,[10] in a brief survey of the orthopaedic aspects of brucellosis in Central Africa, describes its protean bone and joint complications, many crippling in effect. The chronicity of skeletal brucellosis, such as spondylitis, has been stressed and its resistance to treatment. No specific cure for the chronic case is known.

Treatment

In the treatment of human cases most authors[9-11] endorse the efficacy, especially in acute cases, of aureomycin, terramycin and chloromycetin, sometimes combined with streptomycin and cortisone. Latterly cathomycin has been held to be most effective in Malta fever. There is little or no response to penicillin, sulpha drugs, arsenicals or atebrin.[12] Antigen therapy is still in dispute but may be useful.

The treatment of chronic cases is difficult. General measures, vaccines, serum from immune donors, and hyperthermia, have yielded variable and often disappointing results.

Diagnosis

No reliable, early, quick diagnostic test for brucellosis has been developed. 'All tests other than culture—particularly the skin test—must be interpreted with caution, and negative laboratory tests do not exclude the presence of the disease.'[13]

A leucopenia with a low polymorph count may be suggestive.

(*a*) *Culture tests.* Our most decisive criterion is the isolation of the organism in culture. Because of the frequent early disappearance of brucella from the blood stream, specimens of urine and stool, blood, bone marrow, joint fluid, lymphatic gland, or splenic puncture material, must be submitted for culture at an early stage of pyrexia. This is not being sufficiently practised. Special laboratory culture-methods are required. Carrere and Roux, in France, have obtained up to 30% positive blood cultures in chronic cases, using a 5-day chick embryo as culture medium. Where positive cultures are obtained, identification of the brucella strain and investigation of the animal source is desirable. The primary culture of organisms may require from 5-10 days up to 4 weeks.

(*b*) *Animal inoculation* (guinea-pigs) should be reserved for difficult cases.

(*c*) *Agglutination tests.* 'Absence of agglutinins is without significance. In the chronic phase of brucellosis the finding of a positive blood agglutination reaction in a significant titre is the exception rather than the rule. Brucella has been cultured by many workers from patients with negative blood-agglutination reactions.'[13] Repeated early and late agglutination tests (with a wide range of titres to avoid negative agglutination zones) are advisable; a rising titre of brucella agglutinins is helpful in diagnosis. Positive agglutination results may be delayed 30 days and longer after initial symptoms, or they may never be obtained. In cases where antibiotics have been given in the acute phase, the patient may escape the initial diagnostic net of clinician and laboratory. Brucella antigens may persist for years in humans. Fleeting positive blood tests are sometimes produced by the ingestion of milk or meat containing dead organisms. 'In animals the agglutinin is the first to appear in the blood, followed in a few days by the complement-binding substances. They disappear from the blood in the same order.'[14] Abortus and suis strains cannot be differentiated by means of agglutination tests. 'It is an erroneous concept that lessening of the agglutination titre is of favourable prognostic import.'[13]

(*d*) *Allergic tests.* A multiple-puncture device (Allen and Hanbury) used for the intradermal test with 1,000-fold concentrated brucella solution is reported by Wallis[1] to be more reliable than the routine intradermal test. It must be borne in mind that allergic tests may upset agglutination results and therefore should be delayed. The size of an allergic reaction is not an index to immunity.

(*e*) *Other tests* such as the opsonocytophagic test[13] measuring the phagocytic power of the white cells to brucella are difficult and not so reliable.

Viability[14, 15]

Brucella organisms are most frequently found in the cream layers of milk. They may survive 2-15 days in sour milk, 2 weeks in chilled milk and butter, 2 weeks in animal flesh, and up to 147 days in the animal afterbirth. In overripe cheese they cannot be detected. Under conditions of desiccation *B. abortus* will perish in 3 days. Brucella is rapidly destroyed by sunlight and by most ordinary disinfectants; *Br. abortus* will withstand heating at 55°C for 20 minutes. In urine, and dried cow dung, brucella dies in 24 hours but in moist dung it survives for 75 days.

Occurrence and Transmission in Animals

Brucellosis affects only sexually mature animals, susceptibility being greatest during periods of gestation and lactation. Non-pregnant cows and maiden heifers are not so readily infected, and rarely become carriers after infection. After one abortion the animal is unlikely to abort again, but may remain infected for life. Generally, the organisms disappear from the uterus a few weeks after abortion or parturition.[15]

Br. abortus possesses special predilection for embryonic tissue, placenta and placental fluids, which are invaded during pregnancy; but subsequently the organisms lodge in the udder of the cow, in the testicles, epididymis and seminal vesicles of the bull, and in various lymphatic glands. The mucous membranes of the uterus and the ovaries apparently remain

free from invasion. Even when large numbers of *Br. abortus* are eliminated with the milk the mammary tissue may remain perfectly healthy.[15] Of infected cows, *Br. abortus* has been found in the pregnant uterus, uterine and vaginal discharges, foetal parts, lochia, afterbirth and membranes of live and dead calves, and the urine. It has also been found in the faeces of a calf feeding on infected milk, and in the semen of a bull whose epididymis and testicles were infected.

According to Huddleson,[16] brucellosis is sometimes transmitted by mosquitoes and biting flies. The incubation period in bovines varies from 14 to 227 days. The usual portals of entry are intestinal and through the skin. Conjectival inoculation may be successful. Sexual transmission by mechanical means is possible.

Br. melitensis, *Br. abortus bovis* and *Br. abortus suis* are not confined to goats, cattle and pigs respectively; cross infection of animals occurs. *Br. abortus* may affect other domestic animals such as pigs, equines, sheep, dogs, ducks, turkeys, pheasants and fowls. Guinea-pigs are highly susceptible. There is much justification for the view that the various strains of the genus *Brucella* should be regarded as varieties.

VETERINARY AND PUBLIC HEALTH CONTROL

The Public Health Act 1919 makes Malta fever a notifiable disease in South Africa, but has not been amended to cover the modern terminology of brucellosis. This partly explains the failure to notify on the part of practitioners, who probably consider that 'Malta fever' means *Br. melitensis* infection and does not include *suis* and *bovis* strains. Only 4 cases have been officially notified in Krugersdorp since 1933; knowledge of the other cases has been gleaned by questioning colleagues and members of the public.

Contagious abortion has not been included amongst the scheduled diseases in the Stock Diseases Regulations since 1919.[15] 'It is strange that the Public Health Act was promulgated at the same time as the stage was being set for relaxation of veterinary control of brucellosis and the subsequent alarming increase in South Africa.' 'It now surpasses by far in veterinary economic importance the majority of maladies at present included in the Stock Diseases Act.'[15]

Immunization of Herds[16]

For the immunization of herds the attenuated *Br. abortus* strain No. 19 is used as a vaccine for calves between the ages of 4 and 8 months; it protects at least 90% against the natural disease during the first pregnancy, and a high degree of immunity persists during the second and third pregnancies. Vaccination of calves, maiden heifers and non-pregnant cows does not lead to the establishment of the organisms in the animal body, and does not produce carriers. The sera of calves and young heifers react positively for not more than a few months after the inoculation, which obviates any confusion that may result if the agglutination test is later applied for diagnostic purposes.

If adult cattle are vaccinated with this attenuated strain, the resulting resistance is equal to that produced in calves. In pregnant animals there is some danger of abortion. The agglutinins may persist in the animals' serum so that the agglutination test cannot subsequently be used for diagnostic purposes. Vaccinated animals are not considered to be a source of infection. A second vaccination is recommended after a year or two.[15]

Infections of humans with *Br. abortus* occurs in laboratory workers and in persons that handle infective material. The infection is said to occur most commonly by the cutaneous route. In Russia a special variant of strain 19 is used for the protective inoculation of humans. More than a million persons have been inoculated, apparently with success.

Milk-borne Infection

Pasteurization or boiling of milk is the only satisfactory safeguard against the milk-borne spread of brucellosis, as of tuberculosis.

'At Seattle, Washington, in 1937, a man who had contracted brucellosis from infected milk was awarded 1,946 dollars in a suit against the company which distributed the milk, and the farmer who produced it (Harris—1941, 1950[13]). In London, in 1939, a man was awarded £195 damages against a dairyman in a similar suit (*The Times*, 1939).'[1]

According to van Drimmelen, of Onderstepoort, the use of the *Br. abortus* ring test on fresh incoming milk at urban depots may to some extent assist in locating sources of infection, but is not so accurate as the blood agglutination test.

Tuberculous disease of the joints is common in Native children of the Border Area, Eastern Cape. I suggest that some of the children that are diagnosed as suffering from this condition are cases not of tuberculosis but of brucellosis.

SUMMARY

A series of Krugersdorp cases of brucellosis bovis is described.

The Central and South African medical literature on brucellosis among animals and humans is briefly reviewed.

Brucellosis is widespread and likely to be conveyed by our daily raw-milk supply; heat treatment of milk is our most satisfactory public-health safeguard against milk-borne infection of animals and humans alike. Raw milk should be sold only from herds certified as free from brucella infection.

Percutaneous infection of persons handling infected animals is well known.

Serious bone and joint complications are recorded.[4] Brucellosis is more important in public health than we are wont to believe.[17]

Brucellosis may be confused with influenza, tuberculosis, typhoid, rheumatism, septic sore throat, malaria, disc lesions, other joint infections and epididymal infections, etc.[5]

Few of the overt human cases are being reported. Searching and authoritative investigation of the incidence of human cases is called for, especially in country areas. Reference is made to protective inoculation as a means of securing immunity in dairy and other herds. Too much reliance should not be placed on this procedure for reinfection is known to occur.

General practitioners, health departments and veterinary surgeons are urged to keep one another informed of the occurrence and behaviour of brucellosis.[6]

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REFERENCES

1. Wallis, H. R. E. (1957): Brit. Med. J., **1**, 617.
2. Gelfand, M. (1948): *The Sick African*, 2nd ed. Cape Town: Stewart Printing Company (Pty.) Ltd.
3. Campbell, W. and Greenfield, E. C. (1937): S. Afr. Med. J., **11**, 192.
4. Sacks, I. and Neser, A. T. (1945): *Ibid.*, **19**, 25.
5. Lewin, W., Bersohn, I. and Richardson, N. (1948): *Ibid.*, **22**, 763.
6. Meara, P. J. (1950): *Ibid.*, **29**, 593.
7. Bevan, L. E. W. (1955): Cent. Afr. J. Med., **1**, 173.
8. Daniel, J. and Meyer, J. (1944): Leech, **15**, 27.
9. Eales, L. (1951): S. Afr. Med. J., **25**, 143.
10. Jones, R. T. (1955): Cent. Afr. J. Med., **1**, 16.
11. Editorial (1954): S. Afr. Med. J., **28**, 431.
11. (*a*) Questions Answered (1949): *Ibid.*, **23**, 503.
11. (*b*) Editorial (1958): *Ibid.*, **32**, 535.
12. Campbell, W. and Gilchrist, F. G. (1943): *Ibid.*, **17**, 389.
13. Harris, H. J. (1950): *Brucellosis Clinical and Subclinical*, 2nd ed., pp. 278-279, 282-283. New York: Paul B. Hoeber Inc.
14. Greig, R. (1938): *Special Pathology and Therapeutics of the Diseases of Domestic Animals*, 4th ed., vol. I, p. 795. London: Ballière, Tindall and Cox.
15. Henning, M. W. (1948): *Animal Diseases in South Africa*, 2nd ed., pp. 28-60. South Africa: Central News Agency Ltd.
16. Huddleson, I. F. (1943): *Brucellosis in Men and Animals*. New York: The Commonwealth Fund.
17. Davies, J. E. (1957): Brit Med. J., **2**, 1082.