

## Brucellosis

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Britain is among the rapidly dwindling number of countries that have not eradicated brucellosis, which is now the major remaining zoonosis in this country. Denmark, Finland, Norway and Sweden have long been clear of the disease and many other countries are becoming so.

Brucellosis in man has been recognized for over 37 years, and has a diversity of signs and symptoms. Sometimes it occurs as an undulant fever, but often the temperature does not show the undulant pattern but tends to be irregular. The disease is apt to be diagnosed late, it often becomes chronic, and the response to antibiotic therapy is unpredictable.

Infection with the organism *Brucella abortus* is due to contact with infected cattle either directly, as in the case of veterinary surgeons; by being in an environment in which the brucella are lying in dust in a byre, as in the case of agricultural workers or children playing on holiday; or by the drinking of infected milk in the case of anyone drinking non-pasteurized milk which is not safe from this infection.

The difficulty in diagnosing the disease is due to the behaviour of the infecting organism which tends to live intra-cellularly and is not easily cultured, the only practicable method of isolation being by blood culture, which usually proves unsuccessful. Diagnosis is therefore dependent on immunological methods, and these fall into two groups, serological and hypersensitivity.

Laboratory diagnosis in man is by three methods:

The first is blood culture, 10 ml of blood taken from the antecubital vein with strict aseptic precautions is injected into two blood culture bottles, 5 ml into each. In the laboratory they are incubated at 37°C, one of them in an atmosphere of 5–10 per cent CO<sub>2</sub>, for at least two weeks, subcultures on suitable media being made from time to time. If a *Brucella* is present, it appears as a tiny Gram negative bacillus which can be typed by a variety of methods. In Great Britain human cases are due to strains of *Brucella abortus*.

The second method of diagnosis is the use of serological tests, and three types are employed. They are:

1. Standard agglutination test (SA)
2. Indirect agglutination test (AHG)
3. Complement fixation test (CF)

The third method of diagnosis is the use of the brucellin test. This is a delayed hypersensitivity reaction produced by the intradermal injection of brucellin (an antigen prepared from brucella organisms). The test is comparable to the Mantoux test in tuberculosis and a positive response is indicative of a past infection with the organism, but not necessarily of a current one.

We are left, because of the uncertainty of the meaning of the brucellin reaction with the second method of diagnosis, with the use of serological tests to determine whether a person is suffering from a current brucella infection. We may ask why three serological tests have to be employed instead of just the standard agglutination test which has been in use for a long period. The reason is that the other two indicate the presence of different types of antibody in the patient's serum, and these are found in different stages of infection.

Following any infection, specific antibodies are produced. The important immunoglobulins from the point of view of resistance to infection are: IgG with a molecular

weight of 160,000, IgM with a molecular weight of 900,000 and IgA with a molecular weight which varies from 160,000 to about 800,000.

Following brucella infection, the first antibody to appear is IgM, which can be demonstrated in the standard agglutination test. After the infection has been going on for some time IgG antibodies appear, and the IgM tend to diminish and disappear. IgG is most clearly demonstrated by complement fixation. Later in the disease IgA antibodies appear and these are demonstrated by the indirect agglutination test which can also be used for estimation of IgM and IgG.

In *acute brucellosis* (see table I) the patient usually has a pyrexia, and the isolation of *Brucella* by blood culture is the most convincing evidence of infection. If the standard agglutination test is positive to 1/160 or more this indicates the presence of the IgM

TABLE I  
ACUTE BRUCELLOSIS IN MAN

(1) Blood culture <i>may</i> be positive, and isolation of a <i>Brucella</i> from the patient is the most convincing evidence of infection.
(2) <i>Serological tests</i> . The standard agglutination test is positive to 1/160 or more; the indirect agglutination and complement fixation tests are usually also positive.
(3) Brucellin test is not normally performed.

TABLE II  
CHRONIC BRUCELLOSIS IN MAN

(1) Blood culture is negative.
(2) <i>Serological tests</i> . The standard agglutination test may be negative, but the indirect agglutination and complement fixation tests are positive.
(3) The Brucellin test is positive.

antibody; the indirect agglutination and complement fixation tests are usually positive also, and the brucellin test is not done. In *chronic brucellosis* (see table II) the patient has vague symptoms of malaise and depression, and may even be regarded as having a psychiatric problem. The blood culture is generally negative, because the organisms are not free in the circulation but lie in the cells of the reticulo-endothelial system. This also means that antibiotics to eradicate the infection must be given for at least a month.

Serological tests are of great value. The standard agglutination test may be negative but the indirect agglutination and complement fixation tests are both positive. A positive complement fixation test denotes the presence of IgG antibodies indicating *active* infection. The brucellin test is positive in chronic brucellosis, but shows only that infection has taken place.

Several series of serological tests have been carried out in the last year or two and they show a different prevalence of chronic brucellosis in different types of community, urban having least cases and agricultural most cases. In Dundee and district, we carried out serological tests on 132 patients between July 1967 and August 1968 and table III shows that 15 per cent of these patients appear to have been suffering from brucellosis. At least 20 per cent of the patients tested had been infected at one time

TABLE III  
BRUCELLA ANTIBODIES (DUNDEE)  
July 1967–August 1968

S.A.	Serological test		Total
	A.H.G.	C.F.	
+	+	+	= 15
—	+	+	= 5
—	+	—	= 5
+	+	—	= 3
—	—	—	= 104
Total number			132

S.A. = Standard agglutination: + = 160 or more  
A.H.G. = Anti-human globulin test: + = 160 or more

C.F. = Complement fixation test: + = 8 or more

At least 20 per cent of the patients tested had been infected at one time

or another in the past.

The highest percentage of positive tests is found among veterinary surgeons. At a Veterinary Association congress in 1966 it was reported that 63 per cent of 309 veterinary surgeons showed serological evidence of present or past brucella infection.

## Brucellosis in cattle

### Mr H. Davidson (*Veterinary surgeon*)

In this country cattle are the main animals affected with brucellosis. There is little evidence of the disease in sheep and pigs, though it has been reported in dogs which may show almost human symptoms of undulant fever.

In cattle the disease is termed 'contagious abortion' as this is the most important clinical sign of infection.

In 1960 it was suggested that 2.1 per cent of the animals in the national dairy herd were affected with brucellosis; since then the incidence appears to have risen but this may only be because of greater awareness.

In the cow the gestation period is nine months and abortion due to *Brucella abortus* occurs typically after the fifth and up to the eighth month. In subsequent pregnancies the foetus is usually carried to full term but a second or even third abortion may occur.

The organism has a predilection for the pregnant uterus, testes, lymphnodes, joint capsules and bursae. It localizes in one of these sites after a bacteraemia of some 7-10 days duration.

In the bull the lesions are an orchitis and epidymitis with resulting sterility, though in many infected bulls no lesions are seen and the animal may remain fertile. The bull can transmit the organism at coitus but abortus fever is not considered to be a true venereal disease and infection by the bull is not the most important method of transmission. In the cow the chief lesion is placentitis, which leads to expulsion of the foetus. When abortion occurs there is usually a yellow-brown, flocculant, odourless discharge, the placental cotyledons have a yellow necrotic appearance, the chorion is thickened and opaque often with a characteristic leathery texture; and discharges at this stage contain large numbers of *Br. abortus*. The foetal membranes are often retained, predisposing to secondary bacterial infection and this causes an endometritis which interferes with subsequent attempts to get the cow in calf again.

The presence of *Br. abortus* in the mammary gland is not normally associated with any clinical changes and the milk appears normal. The organism has been recovered from bursae and joint capsules; cows tied up in byres frequently bruise their knees on the feeding troughs, and it is important when opening or attending to these lesions that the infection is not spread.

*Diagnosis.* By no means all abortions in cows are due to *Br. abortus*. There are many possible reasons for abortion, probably only about 50 per cent being caused by *Brucella* infection. In suspected *Brucella* abortion the best sources of organisms are the stomach and lungs of the foetus, where an almost pure culture of *Br. abortus* may be found. Where the foetus has been lost smears from the genital tract may provide evidence.

The organisms can be got from scrapings of the chorion, but these membranes