J. Roy. Coll. Phycns Vol. 10 No. 4 July 1976

Brucellosis in Veterinary Surgeons in Wales

EIRIAN WILLIAMS, MD, FRCP
Physician, Withybush Hospital, Haverfordwest, Pembrokeshire

Brucella abortus is the one species in the genus *Brucella* enzootic in Britain. Its natural host is the cow, and man, and several domestic and wild animals are infected directly or indirectly from the cow. The cost of bovine brucellosis in economic terms has long been recognised. A recent national survey showed that 25 to 30 per cent of dairy herds were infected (Animal Disease Surveys, 1964) and now, belatedly, a programme of eradication by slaughter has begun, with promise of an early conclusion.

Brucellosis in humans is primarily an occupational disease and veterinary surgeons are among those especially at risk (Barrett and Rickards, 1953). The cow's placenta, rich in erythritol, is an ideal culture medium for *Brucella abortus* (Williams *et al.*, 1962). It can penetrate the abraded skin, and cleansing or removing retained products of conception after abortion or calving therefore offers the greatest risk. Though in the calving season the veterinary surgeon confronted with an abortion storm may be asked to cleanse three or more times in a day, he has no real means of self-protection, for disposable shoulder-length gloves are liable to tear and some practitioners even refuse to wear them, on the grounds that they impair the sense of touch needed to separate placental cotyledons from the uterine wall. When infected cows give birth to healthy calves, help with calving calls for strenuous effort; gloves are then a hindrance, and almost invariably they tear. Inhalation of Brucella organisms and conjunctival contamination can also introduce infection but in routine veterinary practice masks and eye shields are rarely worn.

A live vaccine of the S 19 strain of *Br. abortus,* widely used since 1944, is claimed to halve the incidence of disease in immature animals (Morgan, 1970). An inactivated vaccine of strain 45/20, barred until recently in areas designated for eradication, is also effective. *Brucella* S 19 administration is a tedious repetitive task for veterinary surgeons. Individual doses, freeze-dried, are dispensed in sealed vacuum containers and, if air as well as diluent is added, a fine spray may follow the needle as it is withdrawn, soiling skin or conjunctiva. There is also a risk of self-inoculation. Loaded syringes are often carried carelessly and unguarded, the breast pocket and mouth serving as convenient repositories between injections. Wary practitioners, too, have cause to fear when calves are not properly restrained.

Most veterinary surgeons employed by Government have served in practice. Field officers take blood and vaginal smears from suspect cows, and investigators in laboratories examine plate isolations and carcasses. Thus, taking the risk overall, raw milk consumed on the farm is an unlikely source of brucellosis in veterinary surgeons.

At the Annual Congress of the British Veterinary Association in 1966 members were warned that the profession was heavily infected with *Brucella* organisms (Kerr *et al.*, 1966a) and they were urged to consider seriously this hazard to their health. Prompted by these and other expressions of concern, clinical surveys have since been carried out in County Cork (Foley and Corridan, 1968), in Northern Ireland (McDevitt, 1970b) and in Worcestershire (Henderson *et al.*, 1975) but the limitations of partly retrospective enquiries into the incidence of brucellosis in veterinary surgeons must be recognised. In occupational brucellosis serological tests are unhelpful for they are often positive in health. Attempts to isolate the organism, even in severe acute infection, usually fail and in chronic brucellosis especially the criteria for a confident clinical diagnosis may not be fulfilled. Characteristically, prolonged or recurring lassitude is associated with sweats, frontal headache and pain in back or limbs but lassitude may be the only symptom or there may be other unusual features with an uncertain overlay of anxiety or depression. Veterinary surgeons, furthermore, are hardy and reluctant patients, preferring sometimes to treat themselves.

SURVEY OF BRUCELLOSIS IN VETERINARY SURGEONS IN WALES

Method

Since 1966, 105 veterinary surgeons have been interviewed and examined and the great majority are still under observation. Another committed suicide five days before his arranged first appointment, and details of his illness were obtained. When first seen, 90 were practitioners, 12 were administrators and field officers for the Ministry of Agriculture, Fisheries and Food, and 3 worked in veterinary investigation centres; 3 practitioners were female. At each visit blood was examined for *Br. abortus* antibodies by the phenol saline agglutination test (PS), the mercapto ethanol test (ME), the anti-human globulin test (AHG) and the complement fixation test (CF) (Bradstreet *et al.*, 1970), and other investigations were requested when appropriate. To appreciate some of the hazards of large animal practice, veterinary surgeons were also accompanied during their work.

Blood samples were obtained from 91 doctors to form a control group for the interpretation of serological tests. The 84 males were asked whether they had suffered from epididymo-orchitis not due to mumps while in practice but no other clinical details were sought.

Results

When first examined, 71 veterinary surgeons were well and they have remained well throughout the period of the enquiry; 14 presented with a variety of illnesses, mostly minor, although after six years, one died of senility and heart failure and another of hepatic cirrhosis. Twenty-two, 16 in the former group and 6 in the latter, described earlier episodes of ill-health, suggesting a probable diagnosis of brucellosis. Most had first complained of symptoms soon after starting in veterinary practice. They had stayed at work and after months or years had recovered completely.

Brucellosis During the Enquiry

A diagnosis of acute or chronic brucellosis was made in 13 patients during the enquiry. In 5, symptoms had recurred for four to twelve years but in none were they sufficiently severe to cause long absences from work. Another, a retired practitioner, was admitted with brucellosis in relapse but the most severe observed long illness remained undiagnosed until epididymo-orchitis was a late complication. The one veterinary surgeon with brucellosis whose spleen was palpable owned only to a vague unaccountable lassitude, insomnia, anorexia and weight loss, present for six months. In four patients with acute brucellosis disability was also relatively mild. A fifth had epididymo-orchitis and was therefore one of two with this complication during the enquiry.

A veterinary investigations officer aged 46 years presented 14 months after first complaining of backache and pain in the knees and left shoulder. Tiredness he had blamed on pressure of work and headache on sinusitis. He had also become irritable, anxious, depressed and forgetful – forgetting his destination when called to a farm and failing to recognise hitherto familiar landmarks. Four months before he had attended a veterinary congress in Exeter and on his return could not recall the journey or an occasion when he dined with friends. When reminded by them it served only to increase his anxiety. He now had insomnia and his sleep was also disturbed by nightmares of frightening intensity. On one Saturday he had sat at home intending to read. Two hours later his wife saw that the page of his book had not been turned and helped him to bed. He soon awoke, agitated, confused and unaware of his surroundings. Urgent psychiatric advice was obtained and tranquillisers and antidepressants were prescribed. A diagnosis of brucellosis was not considered. After seven weeks he returned to work believing he was better but again complained of lassitude, headache and muscle pains. For nine days before attending, his right testicle had been painful and swollen. He denied sweating, but according to his wife for months he had sweated freely in bed. He looked anxious, tired, and ill. The upper pole of the right epididymis was swollen and tender. His spleen could not be felt but *Brucella* antibody tests were positive – PS 40 ME 40 AHG > 5120 CF 80. (The reciprocals of the dilutions are shown.) Treated with

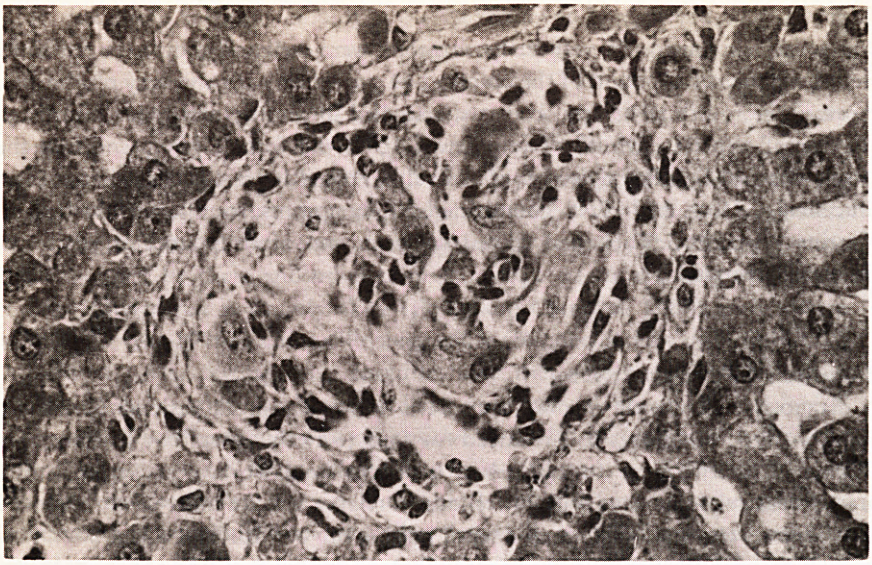

Fig. 1. A histiocytic and giant cell granuloma in the parenchyma of the liver. The patient was a young veterinary surgeon with mild acute brucellosis. (x 520).

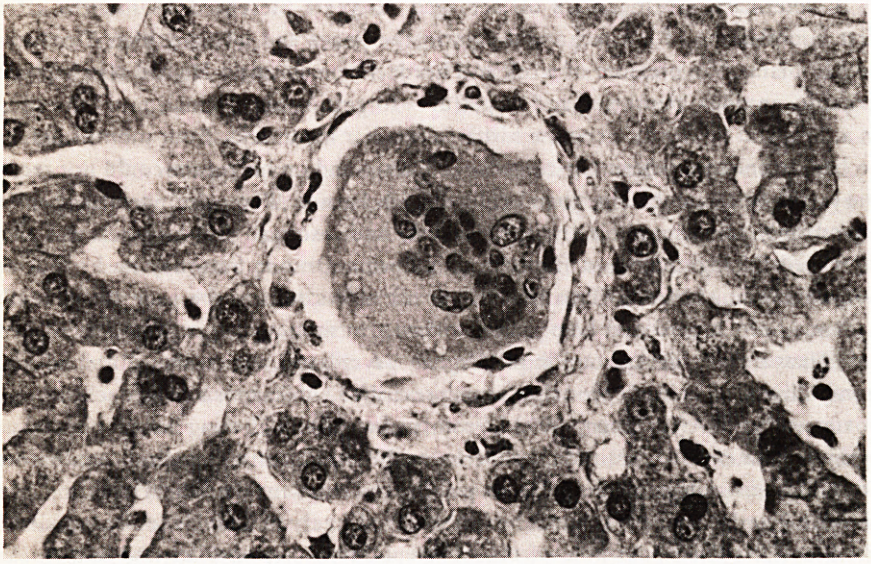

Fig. 2. A granuloma consisting of one large giant cell and a few histiocytes and lymphocytes. The same patient as in Fig. 1. (x 520).

tetracycline he recovered and when recalled two and a half years later, he was well: PS 0 ME 0 AHG 40 CF 40.

A young assistant in practice was a victim of mild uncomplicated acute brucellosis. When first seen he denied symptoms but *Brucella* antibody tests were strongly positive – PS 1280 ME 1280 AHG 5120 CF 320. A fortnight before, he had been unwell for a week with headache, pain in both knees, sweats, and attacks of shivering, but he had recovered without treatment. Four months before splenectomy had been performed for traumatic rupture, the result of a road traffic accident. Three months after examination, though still at work, he was again complaining of drenching sweats, especially at night. Liver biopsy showed numerous granulomas and intrasinusoidal collections of lymphocytes (Figs 1, 2, 3). A few weeks later he returned to Ireland and has since been well. Seven and a half years later the results of *Brucella* antibody tests were as follows: PS 20 ME 20 AHG 20 CF 20.

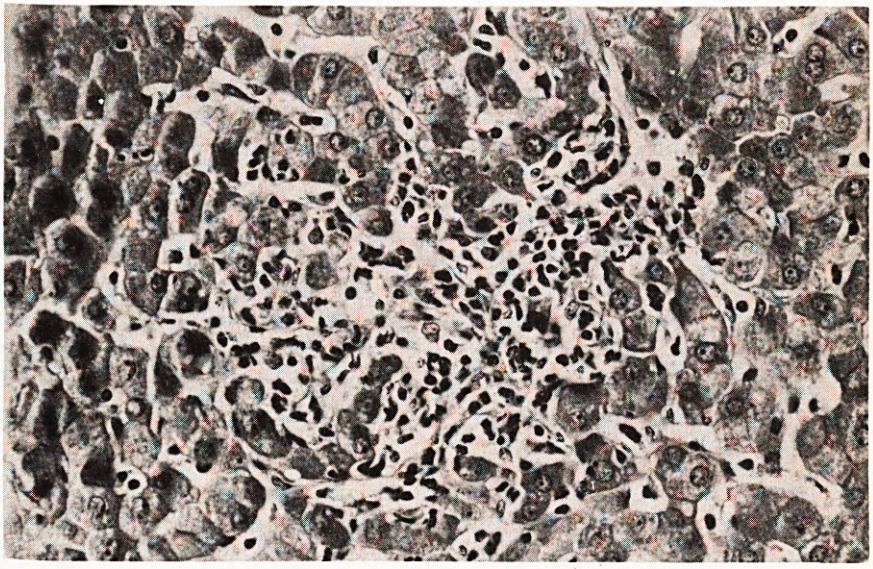

Fig. 3. An intra-sinusoidal lymphocytic focus in acute brucellosis. The same patient as in Figs. 1 and 2. (x 450).

Brucellosis and Suicide

A practitioner, aged 47 years, stayed in bed for one day with 'influenza' and then insisted on returning to work. He remained unwell. Backache which had recurred for several years was unusually severe. He became increasingly tired, with chills, sweats and intractable insomnia. After a month he looked pale and drawn and though advised to take a holiday he refused. He was now severely depressed and

told his wife of other veterinary surgeons whom he believed had been forced to retire as a result of brucellosis. In the seventh week, after learning that his own *Brucella* antibody tests were positive and agreeing to attend in consultation, he took his own life.

Brucellosis as an Unlikely Diagnosis

In seven veterinary surgeons, six with positive antibody tests, brucellosis was considered an unlikely diagnosis although it could not be ruled out with certainty as a contributory cause of symptoms. Three had recurring mild anxiety and depression. A fourth for six years had complained of severe pain in his back and limbs. He had no other symptoms of disease and there were no abnormal signs. Recurring lassitude, sweats and fever in a fifth were invariably associated with tracheitis, suggesting that brucellosis was not the cause. A veterinary surgeon, aged 47 years, was tired and depressed, complaining of vague muscle pains. Two years earlier he had been admitted with severe psittacosis pneumonia which was followed by cardiac infarction. He had then returned too soon to a busy practice. In a seventh patient, with early rheumatoid disease, the cause of splenomegaly was uncertain. Tetracycline was prescribed but a year later his spleen was still enlarged. After eight years he had left a large animal practice because of severe rheumatoid deformity of his hands. His spleen was no longer palpable.

Epididymo-orchitis

Two veterinary surgeons presented with brucellosis complicated by unilateral epididymo-orchitis and four others recalled this complication of brucellosis in earlier years. Two had suffered a relapse. Two of 84 doctors questioned had had epididymo-orchitis. In one a diagnosis of brucellosis had been made. In the other, the diagnosis had not been considered but, fifteen months after his illness, tests for *Brucella* antibodies were positive: PS 160 ME 160 AHG 320 CF 0.

Splenomegaly

Marked enlargement of the spleen, four fingersbreadth, of one veterinary surgeon was due to haemochromatosis, hitherto undiagnosed. The spleen was enlarged one to two fingersbreadth in six others when first examined. All showed serological evidence of *Brucella* infection. Splenomegaly in one, with symptoms of brucellosis, disappeared in response to treatment. Another, attending seven years after effective treatment, still had an enlarged spleen but on re-examination one year later it was no longer palpable. In a patient with progressive rheumatoid disease the role of brucellosis as a cause of transient splenomegaly was uncertain. Three veterinary surgeons denied all symptoms: the spleen in one was felt once only; in two it was still palpable after five years, and liver biopsy in one of these showed no evidence of cirrhosis.

Alcohol

The veterinary surgeon with 'idiopathic' haemochromatosis consumed eight pints of beer a day. One veterinary surgeon died of alcoholic cirrhosis during the enquiry. Three others have needed treatment for alcoholism, two in hospital during episodes of acute psychosis. Two who first took alcohol to alleviate evening fatigue, depression and other symptoms of brucellosis, have recovered, and one firmly believes that brucellosis was the main cause of his addiction.

Cleansing Rashes

Fifty-eight veterinary surgeons described rashes after cleansings or calvings: in 12 a diffuse erythema, in 13 discrete papules, and in 33 pustules as well as papules; 7 attributed their rashes to *Brucella* allergy resulting from direct contact with cows, though on no occasion had bovine infection been confirmed; 7 blamed repeated exposure to bactericides and detergents. *Salmonella dublin* was isolated from pustules on the arms of four veterinary surgeons attending routinely, one on a second occasion after an interval of three years. The herd source of four of these infections was confirmed. One veterinary surgeon had worn a shoulder length disposable glove but it had torn and three had tried to achieve asepsis by washing repeatedly with a solution of povidone iodine.

Accidental Self-inoculation with Brucella Strains S 19 and 45/20

Sixty-two veterinary surgeons recalled pricking or scratching their hands with needles containing *Brucella* S 19. Three, from syringes in dust jacket pockets, had injected an arm in the axilla, the praecordium on bending, and a thigh on climbing a fence. One had found the helping hand of a farmer. A lasting tender subcutaneous nodule was a common sequel but in nine veterinary surgeons the local and systemic effects of *Brucella* S 19 were more severe.

A veterinary surgeon, age 49 years, carelessly, by his own admission, injected *Brucella* S 19 into the base of his left thumb (Fig. 4). Within an hour his hand was swollen, he felt faint and weak and complained of intense headache. Tetracycline was prescribed, the thumb was incised and the limb immobilised. For two weeks he was delirious and sweated profusely. After five weeks tetracycline was replaced with co-trimoxazole and he then improved but for four months a sinus continued to discharge. Now, after five years, there is marked thenar wasting (Fig. 5).

A veterinary surgeon, age 36 years, jogged by a calf, inserted a needle into the base of the middle finger of his left hand. Within three hours he was feverish and his hand was painful and swollen. He was treated promptly with penicillin, streptomycin and chloramphenicol and on the fifth day the finger was incised. Chlortetracycline was then added, and the limb was immobilised. Skin necrosis occurred over the proximal third of the finger, exposing flexor tendons (Fig. 6) and skin grafting was performed but was unsuccessful. The proximal inter-

Fig. 4. The hand of a veterinary surgeon ten days after self inoculation with *Brucella* S 19.

Fig. 5. The same hand as in Fig. 4 five years later, showing atrophy of thenar muscles.

phalangeal joint became fixed in flexion and six months after the accident the finger was amputated.

One of four veterinary surgeons who had directed *Brucella* S 19 into an eye attended with acute conjunctivitis. He had no symptoms of generalised infection. Three veterinary surgeons described accidents with *Brucella* 45/20. One reported

Fig. 6. Necrosis of skin due to *Brucella* S 19, exposing the tendons of flexor digitorum profundus and flexor digitorum sublimus. The finger was later amputated.

from Ireland that skin on a finger had sloughed, exposing bone. Grafting and amputation were considered but the finger healed.

THE RESULTS OF LABORATORY TESTS

Anaemia in one veterinary surgeon was due to hiatus hernia. Eosinophilia in another, persisting for two years, was unexplained. Leucopenia was not observed. The erythrocyte sedimentation rate was 46 mm in one hour (Westergren) in one

patient with brucellosis in relapse. It was also raised in two patients with rheumatoid arthritis but was normal in all other subjects.

Brucella Antibody Tests

Positive results were obtained in 97 of the 105 veterinary surgeons examined. Fifty-five of 71, well throughout the enquiry, could not recall an earlier illness to suggest a diagnosis of brucellosis. Of these, 22 had positive results in a titre of 1/80 or above in the phenol saline test, 21 in the mercapto ethanol test, 46 in the AHG test and 30 in the complement fixation test. However, in 89 of 91 doctors, *Brucella* antibody tests were negative. In one, the AHG test alone was positive in low dilution, PS 0 ME 0 AHG 40 CF 0. In another, whose positive results have already been described, they were obtained 15 months after an attack of epididymo-orchitis.

During the period of the enquiry a number of veterinary surgeons moved to other practices. Thirty-nine, examined before 1971, had remained in the district and were still visiting the same farms when recalled in 1975. Raised antibody titres (1/80 or above) before 1971 and in 1975 were as follows: 23 reducing to 2 for the phenol saline test, 19 reducing to 2 for the mercapto-ethanol test, 39 reducing to 24 for the AHG test and 31 reducing to 21 for the complement fixation test. The AHG test was initially positive in all and the complement fixation test was negative in only one. In 1975 the AHG test was negative in 11 and the complement fixation test was negative in 12.

Liver Biopsy

Biopsy sections from one patient with mild acute brucellosis contained histiocytic and giant cell granulomas (Figs 1 and 2) (Hunt and Bothwell, 1967) and foci of intrasinusoidal collections of lymphocytes (Fig. 3). Another patient was a retired veterinary surgeon with brucellosis in relapse. Microgranulomas were seen (Weinbren, 1975). In one veterinary surgeon with recurring anxiety and depression the role of brucellosis as a cause of symptoms was uncertain. Liver biopsy showed one large giant cell granuloma, an intrasinusoidal collection of lymphocytes and scanty foci of necrotic parenchymal cells. Biopsies in seven others showed scanty or single microgranulomas with lipogranulomas in four. Five of the seven had received prolonged antibiotic treatment and in none was there clear clinical evidence of disease when biopsy was performed.

Hepatosplenomegaly in one symptomless veterinary surgeon was attributed to haemochromatosis.

DISCUSSION

Antibody tests in brucellosis reflect changes in immunoglobulins IgG, IgA and IgM (Coghlan and Weir, 1967) and the suggestion that IgG antibodies are present only during active infection (Reddin *et al.*, 1965; Kerr *et al.*, 1966b), the cause of much of the anxiety expressed at the British Veterinary Association Congress in

1966, has not been confirmed (Kerr *et al.*, 1966a). Thus, the antiglobulin and complement fixation tests for IgG are often positive in health (McDevitt, 1970a), as in the majority of veterinary surgeons in the present series. It has also been shown that, rarely, they are negative (Payne, 1974) or positive only in low dilution (Poole, 1975) when infection is proved by blood culture.

When antibody levels are persistently raised, continuing exposure to *Brucella* organisms or vaccines may be the cause. *Br.* S 19 is still widely used and the fact that practitioners in south west Wales who still visit the same farms show a fall in antibody titres may be an encouraging indication of progress in the eradication scheme.

In reports on brucellosis in veterinary surgeons no clear picture of its clinical importance has emerged. Though rarely fatal, it caused one death from suicide in the present series. Epididymo-orchitis is a common complication but others, more serious, are rare. One overworked Government Officer presented with acute delirium, and only with hindsight was it properly attributed to brucellosis. Depression in this disease is a known cause of alcoholism (Spink, 1956), as in one or possibly two veterinary surgeons in the present series. Hepatic cirrhosis is described (McCullough and Eisele, 1951) but in one patient who died of cirrhosis its cause was alcohol which may also have been a contributory cause of haemochromatosis in another. Liver biopsy in 23 veterinary surgeons reassuringly showed no evidence of cirrhosis.

A high incidence of brucellosis in rural Britain has been questioned (Henderson, 1967). In veterinary surgeons especially it is wrongly diagnosed if undue emphasis is placed on laboratory tests. Furthermore, splenomegaly can occur without symptoms and it can persist long after effective cure. But brucellosis is not always severe or disabling and mild symptoms are perhaps less likely to be misinterpreted if surveillance is maintained. A clinical diagnosis was made in a third of the veterinary surgeons in the present series. In many the illness was mild and eventual recovery was the rule.

The risks from self inoculation with *Brucella* S 19 are known (Spink and Thompson, 1953) and are often publicised in veterinary journals (Harvey, 1969). Accidents, however, are not always the result of negligence. Calf vaccination is believed to be an essential prerequisite to effective eradication and *Brucella* 45/20 is not a safe alternative (Price, 1973).

Rashes after cleansings and calvings have been blamed on *Brucella* allergy (Huddleson, 1943), an attractive hypothesis without proof. There is proof that a papular and pustular dermatitis can be caused by *Listeria monocytogenes* (Dijkstra, 1959; Owen *et al.*, 1960), *Salmonella dublin* (Williams, 1969), *S. typhimurium* (McCoy, 1969) and *S. abortus equi* (Clarenburg, 1964). Veterinary obstetricians are therefore vectors of common bovine pathogens, which is an indictment of modern materials and techniques. Most brands of disposable shoulder-length gloves, though accepted by a tolerant profession, are liable to tear, and ritual washing with povidone iodine does not create an effective bactericidal

barrier. Asepsis in large animal practice, however, is illusive for other immutable reasons and brucellosis is an occupational hazard that will remain until eradication is achieved. As a rare exotic illness it will then present an even greater diagnostic challenge.

ACKNOWLEDGEMENTS

This report is based on a study of brucellosis carried out in conjunction with Dr David Morgan, Public Health Laboratory, Carmarthen, and Mr Arthur Clark, Withybush Hospital, Haverfordwest, and Professor Kenneth Weinbren gave guidance in the interpretation of liver biopsies.

I am especially indebted to my colleagues in veterinary medicine and in general practice for their co-operation.

References

Animal Disease Surveys (1964) *Brucellosis in the British Dairy Herd.* Report No. 4. London: HMSO.

Barrett, G. M. and Rickards, A. G. (1953) *Quarterly Journal of Medicine,* **22**, 23.

Bradstreet, C. M. P., Tannahill, A. J., Pollock, T. M. and Mogford, H. E. (1970) *Lancet,* **2**, 653.

Clarenburg, A. (1964) In *Zoonosis.* (Ed. J. Van Der Hoeden). Amsterdam and London: Elsevier.

Coghlan, J. D. and Weir, D. M. (1967) *British Medical Journal,* **2**, 269.

Dijkstra, R. G. (1959) *Tijdschrift Voor Diergeneeskunde,* **84**, 719.

Foley, B. V. and Corridan, J. P. (1968) *British Journal of Industrial Medicine,* **25**, 126.

Harvey, T. R. (1969) *Veterinary Record,* **84**, 563.

Henderson, R. J. (1967) *Lancet,* **2**, 353.

Henderson, R. J., Hill, D. M., Vickers, A. A., Edwards, J. M. B. and Tillett, H. E. (1975) *British Medical Journal,* **2**, 656.

Huddleson, I. F. (1943) *Brucellosis in Man and Animals.* New York: Commonwealth Fund.

Hunt, A. C. and Bothwell, P. W. (1967) *Journal of Clinical Pathology,* **20**, 267.

Kerr, W. R., Coghlan, J. D., Payne, D. J. H. and Robertson, L. (1966a) *Veterinary Record,* **79**, 602.

Kerr, W. R., Coghlan, J. D., Payne, D. J. H. and Robertson, L. (1966b) *Lancet,* **2**, 1181.

McCoy, J. H. Personal Communication. (Reported in Williams, E. (1969) *Lancet,* **2**, 737.)

McCullough, N. B. and Eisele, C. W. (1951) *Archives of Internal Medicine,* **88**, 793.

McDevitt, D. G. (1970a) *Journal of Hygiene,* **68**, 173.

McDevitt, D. G. (1970b) *Irish Journal of Medical Science,* **3**, 181.

Morgan, W. J. B. (1970) *Journal of Dairy Research,* **37**, 303.

Owen, C. R., Meis, A., Jackson, J. W. and Stoenner, H. G. (1960) *New England Journal of Medicine,* **262**, 1026.

Payne, D. J. H. (1974) *British Medical Journal,* **2**, 221.

Poole, P. M. (1975) *Postgraduate Medical Journal,* **51**, 433.

Price, T. P. (1973) *Veterinary Record,* **93**, 524.

Reddin, J. L., Anderson, R. K., Jenness, R. and Spink, W. W. (1965) *New England Journal of Medicine,* **272**, 1263.

Spink, W. W. (1956) *The Nature of Brucellosis.* London: O.U.P.

Spink, W. W. and Thompson, H. (1953) *Journal of the American Medical Association,* **153**, 1162.

Weinbren, K. (1975) In *Recent Advances in Pathology*, Number 9. (Ed. C. V. Harrison and K. Weinbren). Edinburgh and London: Churchill Livingstone.

Williams, A. E., Keppie, J. and Smith. H. (1962) *British Journal of Experimental Pathology,* **43**, 530.

Williams, E. (1969) *Lancet,* **2**, 737.