briefly to an important recent contribution by J. C. White of Boston (1935) on this subject. White has shown that the pain of angina pectoris and of aneurysm of the aortic arch can be abolished by injection with alcohol or surgical excision of the upper five thoracic sympathetic ganglia and by division of the upper five posterior thoracic spinal roots. Experimental confirmation was obtained in dogs. By passing a silk ligature under the left coronary artery and bringing it out through the chest wall in a glass tube, temporary occlusion of the coronary could be produced with ease, and gave rise to obvious signs of cardiac distress within a few seconds. When the four upper pairs of thoracic ganglia were excised, or the upper five pairs of posterior spinal roots divided, the occlusion caused no manifestations of distress. Division of the vagi, the upper six intercostal nerves, and bilateral stellate ganglionectomy all failed to prevent the discomfort, and it is plain that the afferent pain fibres from the heart pass through the thoracic cardiac nerves entering the upper five thoracic segments.

White believes that cardio-aortic pain is produced in part by the viscerocutaneous reflex postulated by Mackenzie, but also in large part by direct transmission over visceral afferent pathways, or, in other words, as a true visceral pain. He gives both clinical and experimental evidence against the axon reflex as a factor in cardiac pain.

Dual Mechanism of Abdominal Pain

Whatever the ultimate truth may be as to the mechanism of referred pain in angina, I think we must admit the probability that it differs fundamentally from the mechanism of pain in the gastro-intestinal tract. In that tract we have certainly a dual mechanism. On the one hand we see true visceral pain as part of a defence against the threat of obstruction. It is primitive in the scale of evolution, is in no sense referred to the superficial somatic nerves, and is imperfectly and vaguely localized. On the other hand we find referred pain, the stimulus for which arises not from the visceral afferent nerves at all but from the somatic nerves of the parietal peritoneum. It has been evolved as a protection against bacterial infection of the peritoneum, either by penetrating wounds from without or by perforation of the intestine within. It is later in the scale of evolution, and produces a radiation of pain to the superficial somatic nerves and a reflex protective rigidity of the overlying muscles, both of which are accurately localized.

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In a report issued as Water Pollution Research Technical Paper No. 6 by the Department of Scientific and Industrial Research (H.M. Stationery Office, 12s. 6d.) a detailed description is given of the results of a chemical and biological investigation of the non-tidal reaches of the River Tees. This investigation, which occupied about four years, formed part of a comprehensive chemical, biological, and hydrographical survey of the whole of the river and its tributaries from its source to the sea. The object of the survey was to obtain data on the effects of the various discharges of sewage and trade effluents on the river and on the extent to which these liquids should be purified before discharge if serious pollution of the river water is to be avoided.

BRUCELLOSIS IN MAN AND ANIMALS IN STAFFORDSHIRE LABORATORY OBSERVATIONS

BY

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The incidence, bacteriology, and epidemiology of undulant fever vary in different countries. In many lands the disease is more prevalent than in Great Britain. On the Mediterranean littoral *Br. melitensis* predominates. In the United States of America *Br. melitensis*, *Br. suis*, and *Br. abortus* all occur. In this country *Br. abortus* prevails. The animal vectors also show geographical variation. In southern Europe the goat is pre-eminent. In America the goat, pig, cow, and sheep play a part. In England the cow is considered the main reservoir of infection, for although horses suffering from poll evil and fistulous withers also harbour *Brucella* they are not regarded as of grave epidemiological importance. While these fundamental differences are clearly recognized and accepted, there are other discrepancies which arise from unstandardized and varied techniques. Also a great deal of work remains to be done in this country on the comparative aspects of brucellosis in relation to human infection, and the findings and conclusions of distant authorities are often accepted too readily as applying universally.

The aims of this local investigation were: (A) to ascertain the prevalence of agglutinins to *Brucella* in the sera of man and of some of the animals presumed to have been in contact with infected cattle; (B) to assess the accuracy of the agglutination test as a diagnostic procedure; (C) to find out the incidence of *Brucella* organisms in the milk of the cow and of the goat; (D) to investigate the species and virulence of the organisms recovered.

A. Serological Investigations

Three different antigens were used in this investigation: standardized Oxford suspensions; a local laboratory strain; and the special antigen used by Huddleson (1932) in his rapid method of field testing.

Human Sera.—These specimens consisted of two groups: (I) those taken from patients suffering from or with a recent history of an infection causing pyrexia and submitted to the laboratory for the routine Widal reaction; (II) those from people with no history of recent infection with fever.

Group I comprised 500 sera. Fifty reacted to *Br. abortus*, ninety-eight to different members of the typhoid-paratyphoid-salmonella-dysentery group, and the remainder were completely negative to all the twenty-seven micro-organisms used in the routine tests. The fifty sera agglutinating *Br. abortus* reacted in the following titres:

TABLE I

1/25	1/50	1/125	1/250	1/500	1/1,250	1/2,500	1/5,000
6	9	5	2	5	15	4	4

Group II consisted of two batches of 500 sera, one examined in 1932-3 and the other in 1937. They reacted to *Br. abortus* in the following numbers and dilutions:

TABLE II

Years	1/25	1/50	1/125	1/500	Negative
1932-3	—	1	3	1	495
1937	3	2	—	—	495

Of pyrexial patients 10 per cent. showed agglutinins to *Br. abortus*, as compared with 1 per cent. of those not giving a history of recent rise of temperature.

Animal Sera (Sheep, Pigs, Rats, and Poultry).—The different classes of sheep included two rams which were negative; 372 were under 3 years of age, and 203 were 3 years or older. The pigs were aged 6 to 9 months, with the exception of three sows which were over 3 years old. The estimated ages of the rats ranged from 2 months to 3 years, and the hens among which the doubtful positives occurred fell within the age group of 16 to 18 months. The sheep and pig sera were collected from slaughterhouses dealing with good-quality animals. The serological reactions of these animals were:

TABLE III

	Number Tested	+	Titre of Agglutination for <i>Brucella abortus</i>				
			1/10	1/25	1/50	1/125	1/250
Sheep ..	575	21	2	9	7	—	3
Pigs ..	920	20	8	10	2	—	—
Rats ..	200	—	—	—	—	—	—
Poultry ..	100	2	2	—	—	—	—

The 1 in 10 reactions have in the meantime been included among the positives.

B. The Relation of Active Infection to the Presence of Serological Agglutination

As it would be difficult to conduct exhaustive culture work on patients and animals away from the laboratory, guinea-pigs were utilized for this part of the investigation. It is not claimed that the reactions of small laboratory animals are exactly comparable to those of man and the larger animals, but there is every reason to think that the advantages of controlled experiment far outweigh the other considerations.

Seventy-five cavies were killed six weeks after inoculation with infected milk sediment, the blood sera collected, and cultures sown, in some instances from the spleen and other large organs, the lymph glands, and the bone marrow. As the investigation proceeded it became evident that positive cultures were more likely to be obtained from the spleen, bone marrow, and lymphatic glands than elsewhere. The following serological reactions* to *Br. abortus* were obtained in the sera of those animals from which this micro-organism was recovered.

TABLE IV

Negative	1/25	1/50	1/125	1/250	1/500	1/1,250	1/2,500	1/5,000	1/12,500
3	2	4	12	6	24	11	6	6	1

It is interesting that three sera—that is, 4 per cent. of the total actually examined—were completely negative serologically. The wheys of the three inoculated milks in these instances were also negative, but so were thirty-two of the other wheys, which produced positive cultures and agglutination titres in the animals varying from 1 in 25 to 1 in 5,000. There was not much correlation between the agglutinin content of the wheys and that of the sera when the wheys were positive. The lapse of six weeks, and the fact that mainly milk sediment and not actual whey or milk was inoculated, ruled out any passive transference of whey agglutinins.

C. Incidence of *Brucella* in Cows' and Goats' Milk

Cows' Milk.—Several batches of cows' milk were investigated some time ago. Over 1,000 samples were tested biologically, and *Br. abortus* was recovered in 5 per cent.

It was then felt that the efforts to isolate the organism had not been exhaustive enough, and recently of 397 guinea-pigs inoculated with the sediments of routine milk samples for the purpose of excluding tuberculosis 6.3 per cent. revealed the presence of *Br. abortus*.

Goats' Milk.—Fifty-seven samples of goats' milk from different parts of the country were found to be devoid of whey agglutinins and failed to produce any serological reactions to *Br. abortus* or positive cultures in guinea-pigs.

D. Species and Virulence

All the strains proved by differential tests to be *Br. abortus*. One hundred per cent. of the organisms tested behaved consistently to the carbon dioxide and to the bacteriostatic dye tests in primary culture (Huddleson, 1934). Three failed to produce hydrogen sulphide, but the remaining strains reacted to this test according to rule. The glucose utilization test of McAlpine and Slanetz (1928), although cross-checked by the Somogyi and Benedict methods, showed many discrepancies.

Of the seventy-five guinea-pigs from which the micro-organism was isolated six weeks after injection only 32 per cent. showed macroscopic pathological changes, and these were limited to enlarged spleen and lymphatic glands, but many of the animals which showed no naked-eye changes had in various organs small mononuclear accumulations which were discernible microscopically. All the lesions caused by infected milk were slight compared with those resulting in a guinea-pig inoculated with a strain from a dead calf foetus. This animal developed extensive proliferative lesions, haemorrhages, abscesses, and areas of necrosis three weeks after inoculation.

Discussion

The results obtained from the sera of people suffering from pyrexia were interesting, and illustrated the value of including a test for undulant fever in all routine diagnostic work. Atypical clinical forms of this disease were fairly frequent, and the symptoms were so protean that they were sometimes attributed to typhoid fever, tuberculosis, chronic rheumatism, or even neurasthenia. Two of the fifty positive sera were from children aged 7 and 8 years respectively, and these patients were suffering from undulant fever at the time of test. These facts are mentioned as some authorities believe that this disease is very rare in childhood. The low percentage of positives in Group II sera correlated to some extent with the results obtained by Hardy, Jordan, Borts, and Hardy (1931), who obtained in Iowa 1.3 per cent. reactions in dilutions over 1 in 20.

That nineteen of 575 sheep reacted to titres of 1 in 25 or over came as a surprise, for while in France and other countries these animals are often infected, yet in England they are regarded as almost free from the disease. In the United States and Denmark, where *Br. suis* occurs, pigs are heavily infected. Huddleson, Johnson, and Hamann (1933) consider that the incidence varies from 0 to 23 per cent. in different parts of the United States. Gwatkin in Canada (1931) found among 501 sows 0.6 per cent. positive and 0.8 per cent. suspicious. In this country very few positives have been as yet reported, but in the present investigation 1.3 per cent. of young pigs reacted in a dilution of 1 in 25 or more.

Karkadinovsky (1936) examined thirty-four wild rats from infected farms and isolated *Br. abortus* from eleven. Many of my group of 200 rats came from infected farms and from a slaughterhouse where infected animals were killed, and not even one suspicious agglutination reaction

was obtained; but further work must be done before asserting that rats play no part in the spread of this disease.

The two positive reactions of 1 in 10 in hens were of no significance. According to Beller and Stockmayer (1933) normal fowl sera may contain agglutinins to *Br. abortus*. On the other hand, Emmel and Huddleson (1929, 1930) consider that poultry infection is common in the United States. Italian observers have reported a *melitensis* infection in poultry in Messina, and Dubois (1931) a similar infection at Nîmes contracted from sheep.

When the diagnosis was definitely established in guinea-pigs by culture the agglutination test showed an accuracy amounting to 96 per cent. A 1 in 25 reaction may indicate a very recent or an old infection, and to establish the diagnosis repeated testing is necessary in all low-titre agglutination, combined with the estimation of the opsono-cytophagic index and attempts to isolate the micro-organisms, although the significance of low-titre agglutination can often be settled by repeated serological examination alone.

Many infected milks may be devoid of whey agglutinins, as shown in this investigation, and agglutination tests on milks have not the same diagnostic value as the serological reactions. The percentage of milks yielding *Brucella* in culture was small. Starr (1934) estimates that 20 to 50 per cent. of cattle in the United States are infected. As this investigation was coincident with the biological test for tuberculosis the milk sediments only were injected, and many *Brucella* go up with the cream during centrifugalization. The cream was, however, repeatedly broken.

Although the goat is pre-eminently the host for *Br. melitensis*, it can deal effectively with moderate doses of *Br. abortus*, and makes a quick recovery when so infected. In this investigation the negative findings suggest that goats in this country are in a similar position to those in Sweden. Henricsson (1931) considers that the goat is not responsible for undulant fever in Sweden. This disease is most prevalent there in the middle and south-west parts, where goats are seldom seen. The goats are kept in north Sweden, where undulant fever is rare. Goats' sera from different parts of that country were negative to agglutination and complement fixation.

The statement that a supposed *melitensis* infection was said to have been acquired from a goat in England a few years ago cannot be maintained, for, in the light of present-day knowledge and simply judging by the details actually reported, there was no evidence that either the patient or the goat had undulant fever. The apparent freedom from *Brucella* infections of goats in this country is of the utmost importance from the economic point of view.

All the strains isolated in the present investigation were *Br. abortus*. (*Br. suis* and *Br. melitensis* can infect cows and appear in the milk.) They were only mildly pathogenic to the guinea-pig even when administered parenterally. The prevalence of such strains may explain the comparative rarity of human infections, and perhaps other factors such as the diluted dosage in bulk milks and the bactericidal effects of the gastric juice may play their parts:

Before concluding I would like to make a plea for closer co-operation between the medical and veterinary professions in dealing with animal diseases which are communicable to man. With the disease under discussion this is essential, otherwise the public health and economic aspects may each become segregated, with ultimate detri-

ment to both. Most veterinary authorities are agreed that infected cows do not go on aborting indefinitely, but after one or two abortions they may settle down and produce healthy calves. The quantity of the milk may then be unimpaired, and the animals may appear healthy. Investigation has shown, however, that such milk may contain *Brucella*, so that for once in a way economics and public health do not seem to go hand in hand. In Staffordshire co-operation has been close and the carrier condition has received some attention, and it may be that the harmonious co-ordination of the medical staff, the veterinary surgeons, and the farmers has contributed to the small percentage of infected milks revealed during this research.

Summary

1. Of sera from pyrexial patients 10 per cent. agglutinated *Br. abortus*. Samples from people who were not pyrexial showed 1 per cent. positives. Nineteen of 575 sheep and twelve of 920 pigs reacted in 1 in 25 or higher. The sera of 200 rats and 100 poultry showed no significant agglutination.

2. In animals yielding positive cultures the accuracy of the serological agglutination test reached 96 per cent. Many infected milks did not contain agglutinins.

3. *Br. abortus* was recovered from 6.3 per cent. of samples of cows' milk. No positive cultures were obtained from fifty-seven samples of goats' milk.

4. All the strains of *Brucella* isolated were *Br. abortus*, and all exhibited a low degree of virulence for the guinea-pig.

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N. Carrara and A. Previtera (*Pediatrics*, Naples, September 1, 1937) record their observations on the relation of the type of *C. diphtheriae* to the clinical course of the disease in twenty-eight cases, their conclusions being as follows: (1) the classification of the types of *C. diphtheriae* adopted by Anderson and his co-workers should be accepted with reserve, especially as regards the suggested existence of a relation between the individual types of the organism and the course of the disease; (2) the isolation of the so-called *gravis* type has not settled the problem of malignant diphtheria; other factors connected with the constitution and with treatment and immunity are of much greater importance; (3) in view of the great variations in the results obtained by different observers, further examination of the problem on a large scale is desirable.