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Brucellosis in the United States*

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THE ORIGINS OF BRUCELLOSIS IN THE UNITED STATES

The earliest human cases—In 1906 the first report of a case of brucellosis contracted in this country was published by Craig. Having seen other cases in this country among soldiers who had become infected in the Philippines, he recognized the disease in a nurse who, it was believed, had contracted the infection in Washington, D. C. Because at that time the belief prevailed that brucellosis did not exist in temperate climates, it was supposed that the patient must have contracted the infection while carrying on her work of caring for returned soldiers in hospitals. That explanation is hardly satisfactory now, for we know the unlikelihood of transmission of the disease from person to person. Furthermore, the nurse had never taken care of a recognized case of brucellosis.

In 1911 Ferenbaugh, and Gentry and Ferenbaugh reported 12 cases of brucellosis which they had seen that year in the goat-raising section of southwestern Texas. Ten of the patients were goatherds or ranchmen who worked with goats and lived in houses surrounded by them; two were boys who had often played in dusty goat-pens. Some of the patients had never drunk goat's milk.

On inquiry the investigators learned that similar cases had occurred in that locality for a long time, and that it was known among the people by various names, such as "goat fever" and "dust fever." The doctors of the region had realized that in many respects the fever was different from typhoid. In 1894 there had been an outbreak of 25 cases in one locality, occurring almost entirely in families that had goat-pens closely surrounding their houses.

In 1923 Holt and Reynolds studied the serologic evidence of brucellar infection of goats in the Southwest. From local laymen they learned of a human disease which was apparently brucellosis. Their inquiries led them to believe that it must have existed in that locality for at least 40 years.

According to Gentry and Ferenbaugh (1911) the goats of Texas are descended from goats imported from four countries —Spain, Malta, Asia Minor, and South

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Africa. That brucellosis is prevalent in the goats of the Mediterranean countries is common knowledge, and Gentry and Ferenbaugh quote South African investigators who proved that the disease existed in that country. Hence it may be assumed that the date of the first arrival of goats in Texas was followed shortly by cases of human brucellosis.

The first appearance of the disease in cattle—Brucellosis is known to have existed in the cattle of this country for more than a century. It is the subject of repeated discussion in the tenth volume of *The Cultivator,* published in Albany, N. Y., in 1843, edited by Gaylord and Taylor. At that early date many losses due to this bovine disease were reported from New York, Pennsylvania, Delaware, and Virginia.

Brucellosis may have been brought to this country in cattle very early, for according to Edwards (1921) it existed in the cattle of Great Britain before the settlement of the American Colonies. This author quotes Mascal, who wrote in 1567 that in some parts of Great Britain 50 to 60 per cent of the cows were "slipping" their calves.

The extent to which the bovine disease was transmitted to man prior to its recognition during recent decades can never be known. If the human disease were always as widely prevalent as it is today, it seems as if its derivation from cattle would have been suspected. It may be that the bovine strains of earlier times were of comparatively mild virulence for man, and that human infection occurred only rarely. The records of brucellar strains spreading through animal species which hitherto had been unaffected, as presented in the following pages, permits the supposition that man may have been relatively insusceptible to the strains of brucella which infected the cattle of this country a century ago.

However, Hardy, *et al.* (1930) were convinced that brucellosis was the protracted fever which was described during the latter part of the 19th century by a number of authors. Caulkins (1878), a doctor in rural Southeastern Michigan, wrote that a mild type of fever which differed from typhoid fever and malaria was first noted in certain sections of the country about 1861. He reported cases in which the symptoms were typical of acute brucellosis.

The first appearance of the disease in swine—Unlike the histories of brucellosis in goats and cattle, the history of the disease in the swine of this country is definite, for it began somewhat more than 30 years ago. In 1914 Traum published the statement that reports of the farrowing of hairless and immature pigs had been received by the United States Department of Agriculture from several of the western and middlewestern states. From the liver and other organs of a hairless pig received from Indiana, he obtained a culture which resembled the organism of contagious abortion of cattle. Two years later Good and Smith reported their study of the porcine disease and its causal agent in Kentucky. They stated that only three outbreaks had come to their attention. In 1920 Hayes and Traum reported that infectious abortion was becoming increasingly prevalent in the sows of California. They estimated that it might be present in 9 per cent of the herds of that state. In 1930 Hardy, *et al.* reported that of the 611 hogs which they examined in Iowa, 18 per cent gave serological evidence, and an additional 16 per cent gave doubtful evidence of infection. In the preceding year Theobald Smith reported that he had obtained cultures of the organism of contagious abortion from porcine fetuses in an outbreak which he believed was the first reported in the eastern part of the United States. According to Stone (1943) the hogs of New York State were free of brucellosis until 1941.

INVESTIGATIONS

When the scene of brucellar investigations shifted from European countries to the United States, about 1910, it was known that the human disease, called undulant, Malta, or Mediterranean fever, is prevalent in Mediterranean countries; that it is contracted by means of contact with infected goats, which, even when apparently in good health, excrete the causal organism, *Micrococcus melitensis,* in the milk and urine. From Mediterranean countries the disease was known to have spread to other subtropical regions, carried by exported goats.

Another fact known at that time, but entirely disconnected with the knowledge about "undulant fever" was that contagious abortion of cattle is due to an infection of the cow with an organism designated *Bacillus abortus,* which was discovered in 1897 by a Danish veterinarian named Bang.

The first publication to appear in this country on the causal organism of brucellosis in domestic animals was a confirmation of Bang's observation, by MacNeal and Kerr, in 1910. In the following year an important discovery was made by investigators of the Bureau of Animal Industry, United States Department of Agriculture. Schroeder and Cotton reported that they found the organism of contagious abortion in milk derived from apparently healthy cows. In that same year, Mohler and Traum examined the tonsils removed from 56 children, and succeeded in isolating the organism of contagious abortion from one. In commenting on these discoveries, Dr. Melvin, Chief of the Bureau of Animal Industry, made a prophetic statement: "The fact that this organism was found in 8 samples of market milk among 77 samples tested (over 11 per cent) and in the milk distributed by 6 among 31 dairies (over 19 per cent) leaves no doubt that we are dealing with a phenomenon that is ominously serious in its significance for public health."

Into the Dairy Division * of the Bureau of Animal Industry the writer came, and was assigned the task of studying the bacteria which occur in freshly drawn milk, that is, the bacteria which grow within the cow's udder and are excreted in the milk. Because the pathologists of the Bureau were deeply involved in investigations of Bang's disease, it was quite natural that the Gram-negative organisms which the Chief had "viewed with alarm" should become the object of keen interest to the dairy bacteriologist. Discussions with the pathologists were frequent and searching. One day in 1917 in a conversation with Dr. Adolph Eichhorn the idea evolved that it might be worth while to compare Bang's *"Bacillus abortus"* with the so-called *"Micrococcus melitensis."* It was the fact that both organisms were known to be excreted in the milk of apparently healthy animals that suggested their comparison.

Whose idea was it? It was one that neither the bacteriologist nor the pathologist could have formulated in solitary cogitation at that time. It developed when two minds, viewing the subject from different angles, were reciprocally stimulated in the search for facts bearing on related problems.

Immediately the bacteriologist set up simple experiments to test the idea, and with amazement noted that one result after another pointed to a close relationship between the strains of supposedly different genera. They were alike in morphology, in staining reactions, and in biochemical reactions. They were alike culturally, except that the strains of caprine and human origins produced a brownish discoloration of the medium after long incubation. They appeared alike when tested in an anti-

* Now designated the Bureau of Dairy Industry.

serum produced by a strain of bovine origin, for this serum agglutinated strains of bovine and human origin in equal titer. An antiserum produced by a strain of human origin also agglutinated antigens of both types, but the titer was somewhat higher when tested with antigen prepared with a strain of human or caprine origin. Pregnant guinea pigs inoculated with a strain of human origin aborted with the same degree of promptness as did those inoculated with a strain of bovine origin. Of all the tests applied at that time, that of agglutinin-absorption was the only one which could distinguish the strains of different origin.

As the older bacteriologists will remember, these findings, which were reported at the annual meeting of the Society of American Bacteriologists, held in Washington, D. C., in December, 1917, encountered skepticism when they were published in July, 1918. The only reason which the writer ever heard given to account for their tardy acceptance was that if there was a close relationship between the two supposed genera, other bacteriologists would have noted it. Although the accuracy of some of the statements in question could have been confirmed in a few hours, one distinguished bacteriologist continued for seven years to deplore the confusion caused by what he considered hasty publication. Even the writer's colleagues, the pathologists of the Bureau of Animal Industry, did not believe that the results could have been accurate. This statement was confirmed recently by one of them * who at the time was one of the younger members of the staff.

The skepticism ought to have been dispelled earlier than it was, because the original observation of a close relationship between the organisms of bovine contagious abortion and human "undulant fever" was confirmed by Meyer and Shaw in 1920, and by 10 other investigators in 7 foreign countries within the next four years. (This literature was reviewed by the writer in an earlier publication [1925].)

The close relationship between the two organisms raised a question as to why no cases of disease were ever traced to cattle. There was no satisfactory answer for a number of years. We could only ask: "Are we sure that cases of glandular disease, or cases of abortion, or possibly diseases of the respiratory tract may not sometimes occur among human subjects in this country as a result of drinking raw cow's milk?" (Evans, 1918.)

Human cases of proved brucellar infection—The beginning of an answer came in the fall of 1922, when a culture was received from Dr. Harold L. Amoss of the Johns Hopkins Hospital. It had been isolated from the blood of a patient with the symptoms of undulant fever who denied having had any association with goats or their products. The culture came with the request that it be studied to determine whether it was *Micrococcus melitensis* or *Bacillus abortus*. According to the agglutinin-absorption test, the culture was unquestionably not of the caprine type.

This case, which was reported by Keefer (1924) was the first to be reported in medical annals in which brucella not of caprine origin were proved to be the cause of human disease. Later information revealed that the patient had contracted the disease from tissues obtained from a slaughter house. As an assistant in the histological laboratory of Johns Hopkins Medical School, he went frequently to a slaughter house to obtain tissues for purposes of teaching. Subsequent studies showed that his infection was with the porcine type of the organism, and that the mode of his infection, which resulted

* Dr. Harry Schoening, in a discussion at a meeting of the Bacteriological Seminar, University of Maryland, June 7, 1945.

from the handling of infected hogs or their carcasses, is typical of a large percentage of cases occurring in this country.

The finding of one human case of brucellosis due to the organism of contagious abortion stimulated a prompt search for others. The writer collected the remnants of samples of serum obtained routinely in Washington hospitals for the Wassermann test, and tested them for brucellar agglutinins. Among 500 samples, one serum gave a strongly positive reaction, and two gave positive reactions in the dilution of 1 to 40 (Evans, 1924). At that time we did not know how to interpret such a low reaction. We know now that it may be suggestive of infection (Evans, Robinson, and Baumgartner, 1938). In the case of the strongly positive reaction, the doctor in charge made a diagnosis of brucellosis, for the history and symptoms agreed with that disease. The patient, who lived in Clarendon, Va., stated that he drank raw cow's milk habitually, but that he had never consumed goat's milk or any of its products. Agglutinin-absorption tests made on his blood serum indicated that the infection was of the bovine type. This second case of brucellosis caused by the organism of contagious abortion was recognized in March, 1923. The clinical history of this case was not reported, but the laboratory findings were reported (Evans, 1924).

Keefer's report of the first recognized case of brucellosis in this country not of caprine origin is frequently mentioned in the literature. The order of sequence of the third, fourth, and fifth cases is established by the dates on which cultures were sent to the writer for identification, and it is confirmed by the dates given in the published reports. The dates of publication of the reports follow one another in a different order.

The third case was reported by Gage and Gregory (1926). A culture obtained from the blood was received in May, 1924. Agglutinin-absorption tests showed that it was not of caprine origin. The patient, whose job was the killing of hogs, had worked for five years in a slaughterhouse in Sioux Falls, S. D.

Also the history of the fourth case, which was reported by Knowlton (1925) indicated that the infection was confracted from hogs in a slaughterhouse. A blood culture was received by the writer in August, 1924. Agglutinin-absorption tests showed that it was not of caprine origin.

A blood culture from the fifth case, which was reported by Carpenter and Merriam (1926) was received in February, 1925. Agglutinin-absorption tests showed that it was not of caprine origin. In this case, which occurred in Ithaca, N. Y., the history pointed to cow's milk as the source of the infection.

Human cases are recognized in South Africa also—Almost simultaneous with these events in this country was the recognition of brucellosis in South Africa in cases in which goats could not be implicated. According to the veterinarian, Bevan (1933), after he had read, in 1921, of the relationship between the causal organisms of Bang's disease and undulant fever, it occurred to him that certain hospitalized patients of his acquaintance might be infected with the bovine type of the organism. The results of agglutinative reactions strengthened that supposition, and in November, 1921, he reported at a meeting of the Southern Rhodesian Veterinary Association that he had tested the blood of a patient, and obtained a rapid and marked agglutination with Bang's organism in dilutions as high as 1:200. This seems to have been the first reported observation anywhere in the world of evidence of human infection with Bang's organism. The report was published in January, 1922. It mentions other human cases which were detected in a certain district "within the

last few months." In 1924 Bevan wrote that cases similar to the one mentioned in his earlier publication continued to occur. In 1925 he wrote that 35 cases of undulant fever had been recognized in persons in Southern Rhodesia who could not have been infected from goats. At that time only 5 such cases had been recognized in the United States.

Working in the same area with Bevan was the bacteriologist Orpen. In 1923 he described the method by which he obtained brucella from Rhodesian patients with undulant fever. By agglutinin-absorption tests he identified these strains with the bovine type of the organism (1924). Orpen does not give the date when he first obtained cultures of brucella from patients. Hence it cannot be stated whether this proof of human infection of bovine origin antedated the cultivation of brucella from the Baltimore case.

Many cases of brucellosis are found—Following these observations an occasional human case of brucellosis of other than caprine origin was recognized here and there in the United States and in other parts of the world. Usually the recognition of one case aroused interest, which resulted in finding other cases in the neighborhood. In April, 1925, an editorial appeared in the *Journal of the American Medical Association* calling the attention of physicians to the existence of brucellosis in parts of the United States where it was hitherto unsuspected. Probably as a result of this editorial, recognition of cases became more frequent. By the end of 1926, data were available on 20 cases from which a sample of serum and/or a culture was sent to the writer for study. These were examined by means of the agglutinin absorption test, and the result indicated the type of infection. A report of the findings was published in the *Journal of the American Medical Association* in February, 1927.

Then the number of recognized cases began to multiply by leaps and bounds. In 1927, 217 cases were reported in *Public Health Reports;* in 1928, 649 cases; in 1929, 1,301 cases; in 1934, about 2,000 cases; in 1938, more than 4,000 cases. Since then, there has been no increase in the number reported. The discrepancy between the actual number and the reported number is discussed further on.

NOMENCLATURE

Nomenclature has played the mischief with brucellosis. Familiar names which suggested erroneous ideas made impressions so deep that they could hardly be obliterated by contrary facts. The two generic names, Micrococcus, implying a spherical form of the causal organism of "Malta fever" and Bacillus, implying an elongated form of the causal organism of contagious abortion, prevented their comparison until twenty years had passed after Bang's discovery. The names "Malta fever" and "Mediterranean fever" suggested a limited distribution of the disease, and this helped to prevent its recognition in other parts of the world. The name "undulant fever," suggesting that in every case there must be a significant rise of temperature tracing an undulating curve, exerts an influence now against the recognition of the chronic disease.

Some of the unfortunate names have been dropped. When Meyer and Shaw (1920) confirmed the close relationship between strains of caprine and bovine origin, they suggested for this group of organisms the generic name Brucella, derived from Bruce, the name of the Englishman who first cultivated the organism from a human case on the island of Malta. This name was accepted, and it is now used in all scientific publications.

The disease is now correctly called brucellosis, a satisfactory name which identifies brucella infection in any of its manifold manifestations in man or ani-

mals. The writer was unable to find the first use of the term "brucellosis," but in 1930 Hasseltine stated that the synonymous terms "brucellosis" and "brucelliasis," signifying the state of being infected with brucella, had recently appeared in the literature, and that the latter term was preferred by classical scholars. Both of these names were used frequently until 1934, when Giltner published a monograph on "brucellosis." In a footnote he explained that "brucellosis" is preferable to "brucelliasis" because the ending *iasis* is used commonly for names of diseases due to protozoan infections, whereas *osis* is used commonly for names of diseases due to vegetable pathogens.

"Brucellosis" is gradually replacing other names, although "undulant fever" still appears in official records in this country. If it should be discarded, that would help to clear the way toward a recognition of the chronic disease.

THE SPECIES OF BRUCELLA

When the close relationship between the causal organisms of "undulant fever" and contagious abortion of cattle was first recognized, the only available test which could distinguish the bovine from the caprine type was the agglutinin-absorption test, which does not distinguish strains of bovine and porcine origins. Later, other tests were devised which enable that distinction to be made, the most practical being the bacteriostatic tests devised by Huddleson.

For the sake of convenience, the various types of *Brucella* have been given specific names. There are three species, *melitensis*, *abortus*, and *suis*. Actually, in the opinion of the writer, they are too closely related to justify the recognition of three species. They differ, however, enough to justify varietal distinctions.

Because trinomials are awkward, recognition of the distinctions as varietal was not acceptable to the taxonomists.

Susceptibilities of host species—The present incomplete knowledge of susceptibilities to brucellar infection of man and those species of domestic animals in which infection is known to be widespread may be outlined as follows:

Species	*Primary Host*	*Secondary Hosts*
B. abortus	cattle	man horse
B. suis	swine	man cattle
B. melitensis	goats (sheep)	man cattle swine

Information is limited on transmission from animal to animal in other than the primary host species. However, a few facts are known.

Although cattle are susceptible to infection with *B. suis*, swine are insusceptible to infection with *B. abortus*. This explains why the disease can exist in the cattle of localities where the porcine disease is nonexistent.

We do not hear of human cases resulting from contact with horses, and this suggests that the infection may not be readily transmitted from the equine to the human subject. A number of investigators (Fitch and Dodge, 1939; Stone, 1941; and others) believe that the disease is transmissible from horses to cattle.

Cattle infected with *B. melitensis* or *B. suis* transmit these organisms to man through the milk. They are more virulent for man than is *B. abortus*, and apparently they do not lose virulence for man on passage through the cow.

Infection of cattle with *B. melitensis* has extended to regions remote from the goat raising country of the Southwest. In 1934 Carpenter and Boak reported that among 122 samples of raw milk from 3 counties in Central New York, brucella were found in 25 samples, and 3 of the strains were proved to be *B.*

melitensis. They came from herds in 3 widely separated localities.

According to data published by Jordan and Borts (1946) it appears that the earliest infections of the swine of this country with *B. melitensis* are of recent occurrence. The first culture of *B. melitensis* from a human case in which the infection was contracted from swine in Iowa was obtained in December, 1943. Since then many cultures of *B. melitensis* have been obtained from human cases in packinghouse workers and farmers. The data suggest that in most of these cases the infection was derived from swine.

The relative percentages of the three brucellar species in the human infections of any locality depend largely on the extent of the development of the hog-raising and/or goat-raising industries. The two following surveys were made in middlewestern states, where the hogs are commonly infected. Kabler and MacLanahan (1936) studied 38 strains which came to the laboratories of the Minnesota Department of Health. Twenty-four were *B. suis*, 12 were *B. abortus*, and 2 could not be satisfactorily classified. Jordan and Borts (1946) reported the distribution of species among 339 strains isolated from the blood in cases of the human disease and studied at Iowa Department of Health from July, 1927, to June, 1945. The distribution was as follows: 67.3 per cent *B. suis;* 24.5 per cent *B. abortus;* 7.7 per cent *B. melitensis;* 0.5 per cent unidentified. That *B. suis* has spread to states where the raising of hogs is not a well developed industry is shown by the data reported from Alabama which were published by Hutchings (1944). Among the cultures from 91 human cases occurring in that state, 69, or 75.8 per cent, were *B. suis*.

Human infections with *B. abortus* tend to be sporadic; those caused by *B. melitensis* and *B. suis* ingested in raw milk are more apt to occur in groups. In this country many of the outbreaks of human brucellosis traced to cattle have been caused by *B. suis* in raw milk. An outbreak of 11 cases occurred in Georgia in 1929 (Atwood and Hasseltine); one of 30 cases occurred in Iowa in 1933 (Beattie and Rice); one of 14 cases with 3 deaths occurred in a home for elderly persons in Connecticut in 1934–1935 (Horning); one in which 77 persons gave evidence of infection occurred in Iowa in 1941 (Borts, *et al.*).

In 1922 an outbreak of 37 definite and additional suspected cases of brucellosis caused by *B. melitensis* occurred in Arizona. There were two deaths of patients in whom the brucellar infection was superimposed on other chronic disease. In 32 cases the source of the infection was traced to goat's milk (Watkins and Lake, 1927).

THE PREVALENCE OF BRUCELLOSIS

The prevalence of brucellosis in man depends on its prevalence in animals. Hence it is predominantly a rural disease.

Prevalence of brucellosis in cattle—On July 1, 1934, the U. S. Department of Agriculture initiated a campaign for the eradication of the disease from cattle which has been carried on in every state. The criterion of infection is a positive agglutinative reaction of the specific organism in the cow's serum in a titer of 1:100. Reacting animals are slaughtered, and the owner receives partial indemnity. During the first ten years of the campaign about 65,000,000 cattle were tested; more than 2,500,000 were found to be reactors, and were slaughtered. During the first year of the campaign about 10 per cent of cattle reacted to the test, involving 40 per cent of the herds that were tested. The fact that ten years later only about 4.5 per cent of reactors were found attests the success of the campaign in reducing the number of infected cattle.

Prevalence of brucellosis in other

animals—Extensive data comparable to those relating to cattle are unavailable for estimation of the prevalence of brucellosis in other animals. However, limited surveys have been made.

The incidence of brucellosis in swine differs in various parts of the country, being highest in the hog raising states of the Middlewest. Likewise, the incidence of brucellosis in goats is unevenly distributed, being highest in the goat raising states of the Southwest. Holt and Reynolds (1925) found serological evidence of infection in 16.7 per cent of 1,130 goats examined in 22 counties along the Mexican border. Recently Stiles (1945) examined the blood serum of 14,339 animals representing 131 herds in southwestern Colorado, and found evidence of infection in 8.5 per cent of them.

That brucellar infection is common in the horses of this country was shown by several investigators, including Carpenter and Boak (1937) in New York State, and Deem (1937) in Ohio. These investigators found a positive agglutinative reaction in a high percentage of cases of fistula of the withers and poll evil, and in a considerable percentage of horses which appeared normal.

Although brucellar infection of sheep exists in France and in other Mediterranean countries, the disease is almost unknown in the sheep of this country. However, it has begun to make its appearance here. Bruce (1930) reported that he had cultivated brucella from a dead lamb received in February, 1927, from Vancouver Island. It came from a flock in which some trouble with lambing had occurred. Apparently the culture was not studied to determine the species of *Brucella*. Bruce believed that this was the first report in North America of brucellar infection of sheep. Jordan and Borts (1946) believe that the recent introduction into Iowa of *B. melitensis* infection of swine was through sheep imported from western and southern sections of this country. They report one human case of *B. melitensis* infection in which the patient had contact with no animals other than sheep.

A few cases of brucellar infection in dogs have been reported in this country, and the possibility of human infection from dogs is shown by several reports of the transmission of the disease from dogs to man in foreign countries (Dargein and Plazy; Menzani; Mühlenbeck).

Brucellar infection of domestic fowl is reviewed by Huddleson (1943). Little is known, however, of its significance as a source of infection of domestic animals. Infection of rodents, and the possibility that they may serve as a reservoir of infection of domestic animals has been considered by many investigators in foreign countries, and by Fitch and Bishop (1938) in this country. Katz (1941) reviewed the literature on brucellosis in various species of wild animals and discussed the possibility that they may serve as a source of perpetuation of the disease in domestic animals.

The prevalence of brucellosis in man—Approximately 4,000 cases of human brucellosis are reported annually to the state departments of health, and the data are summarized in *Public Health Reports*.

The reported disease, designated "undulant fever," includes acute cases with an undulating temperature curve. It would be impossible to estimate how nearly the reported figure approximates the actual number of such cases, for according to Hughes (1897) and numerous subsequent authors, diagnosis is difficult, even in acute cases. No doubt many acute cases are being missed.

The chronic form of brucellosis is extremely difficult to diagnose. The following lines of evidence indicate, however, that an unrecognized mild form of brucellosis is a common ailment in this country: First, the disease has a

tendency to become chronic in every species of domestic animal in which it has been studied. Second, in many human cases in which the correct diagnosis is finally attained it is only after years of poor health for which no cause could be found. Third, many physicians have found numerous cases after they became aware that there is a chronic form of the disease.

CHRONIC BRUCELLOSIS

A mild form of brucellosis in domestic animals—A general understanding of the course of brucellosis is available without experimentation, for the disease as it occurs spontaneously in domestic animals is known to veterinarians. Its most important feature is the common failure of complete recovery. Every farmer knows the depreciated value of a cow, horse, or hog which has contracted this disease. According to Wight, who has charge of the program of eradication, only one-third to one-half of the cows which become infected with brucella ever recover fully.

In other animals also, brucellar infection is apt to occur in a mild, chronic form, with no obvious signs of disease. Polding (1940) found evidence of latent localized infections persisting in goats for several years following acute infection. Several investigators (Hardy, *et al.*, 1930; Feldman and Olson, 1934; McNutt, 1934) noted that brucella may exist in the tissues of apparently healthy swine. Rice (1944) stated that the exhibition at state and county fairs of infected swine, which appear healthy, is a means of dissemination of the porcine disease. Carpenter and Boak (1937) tested the blood serum of a group of mares repeatedly during a period of two years and found evidence that some of them had become infected without presenting clinical evidence of disease.

A mild form of brucellosis in man—Bearing in mind the tendency of brucellosis to become chronic in various species of animals which appear healthy in spite of infection, it should be expected that in man also the disease would have a tendency to become chronic. In man, a mild form of brucellosis does occur without obvious signs of disease. It generally fails to be recognized because characteristic signs are lacking and laboratory diagnostic techniques are inadequate.

The following experience, beginning more than twenty years ago, when human brucellosis was almost unknown in this part of the world, is typical of that of many patients at the present time, as revealed in letters requesting information on brucellosis which come to the National Institute of Health. Similar cases are described repeatedly in the growing literature on chronic brucellosis.

In October, 1922, the writer became infected while working on cultures of *Brucella melitensis* received from Phoenix, Ariz. For the first nine months the disease was mild. Medical aid was sought, and after examinations failed to reveal any cause for complaint, a diagnosis of "neurasthenia" was received. Then came an acute exacerbation of typical "undulant fever," so diagnosed when a culture of brucella was obtained from the blood. Then five years of poor health, with complete incapacitation much of the time. Again, medical aid was sought in four successive hospitals. The outcome was always the same, the patient was regarded as "neurasthenic." Finally the impasse was broken by the intervention of another disease which necessitated an operation, during which brucellar lesions were found, from which *B. melitensis* was cultivated. Thus accidentally, at last, came relief from the misunderstandings which must inevitably arise when a patient is said to be suffering from imaginary ills. These misunderstandings are a feature of chronic brucellosis that tries the patient almost beyond endurance.

The literature on chronic brucellosis—The first paper on chronic brucellosis to be published in this country appeared in 1934 (Evans). Since then, numerous authors have discussed the subject (Cameron and Wells, 1934; Angle, 1935; Goldfain, 1938; Roberts and Roberts, 1939; Calder, 1939; Robinson and Evans, 1939; Angle and Algie, 1939; McGinty and Gambrell, 1939; Dustin and Weyler, 1940; Harris, 1941; Goss, 1941; Simpson, 1941; Holbrook, 1942; Manchester, 1942; Hartsock, 1942; Davis, 1942; Urschel, 1943; Griggs, 1943; Schmidt, 1943; Lehr, 1944; Staub, 1944; Chuinard, 1944; Rice, 1944; Benning, 1946). All are convinced that chronic brucellosis is a common disease. Most of them comment on the frequency of the diagnosis of neurasthenia.

Estimations of the incidence of chronic brucellosis—Obviously, estimations of the prevalence of a disease which is so difficult to diagnose as is chronic brucellosis can be only grossly approximate. It seems worth while, however, to record such estimations as can be made.

In 1936, a survey was made of the incidence of chronic brucellosis in Charlotte, N. C. (Robinson and Evans). At the time of the investigation, this city of about 92,000 inhabitants was supplied with raw milk, although many of the herds of cattle in the neighborhood were known to be infected with Bang's disease. Dr. Robinson, who conducted the investigation lasting six months, requested the local physicians to permit him to coöperate with them in studying cases of obscure chronic disease, and he received their generous coöperation.

Although the survey could not cover the entire population of Charlotte, 325 cases of chronic disease were investigated, and among them 22 were regarded as probably chronic brucellosis. In some of the cases this diagnosis was confirmed by a positive agglutinative reaction. In 5 cases, blood cultures confirmed the diagnosis.

Considering these results, it would appear to be a conservative estimate to assume that there were at least 25 cases of chronic brucellosis in Charlotte at the time of the survey. If the incidence of the chronic disease in the entire rural population of the United States of approximately 57,000,000 resembles the incidence in Charlotte at the time of the survey, there would be about 35,000 cases in the entire country.

A similar figure is obtained if an estimation is based on the data reported by Lehr (1944). He found that two physicians of St. Clair County, Illinois, who had established a reputation for skill in the diagnosis of brucellosis, together had diagnosed about 100 cases during a period of 2½ years, although they had reported only 2. Lehr studied 24 of their cases, and reported that most of the patients had suffered from ill health for 1 to 4 years before coming under the care of a physician.

All of the 100 cases considered by Lehr were from the rural area of St. Clair County, Illinois, with a population of about 70,000. (The urban population of the county was not considered in these figures because it was protected by an ordinance which required pasteurization of milk.) At the rate of 40 cases per year in an area with a rural population of about 70,000, about 33,000 cases would occur each year in the rural areas of the entire country.

Again, a somewhat similar figure is obtained in an estimation based on a statement made by Gilbert and Coleman (1934). They doubted whether more than one-tenth of the cases that occur in New York State are recognized. It happens that in Italy also, an investigator (Alessandrini, 1938) held the opinion that the number of reported cases should be multiplied by ten, at least, to represent the actual number.

At that rate, the three or four thousand cases reported annually in *Public Health Reports* would represent 30,000 to 40,000 actual cases.

Data published by Huddleson, *et al.* (1937) may be used to obtain a much higher figure for the prevalence of brucellosis. They carried out an investigation in a county hospital in Michigan where a part of the supply of milk was known to be infected with brucella. These investigators found evidence that 7.1 per cent of the 8,124 inmates were infected. If that percentage of the entire rural population of the United States were infected, the total figure would be approximately 4,000,000.

The actual number of persons suffering from brucellar infection in this country during any year probably lies somewhere between 40,000 and 4,000,000. Perhaps the smaller figure may represent approximately the number of persons who are disabled or partially disabled for a considerable time during the year. In other words, it may roughly represent the number of patients with brucellosis who consult a doctor. Perhaps the larger figure may not be too high if it is taken to include mild cases of transitory infection in which recovery is complete after a few days of indisposition, and cases of the chronic disease in which the general health is impaired by a localized infection of many years' standing.

RESEARCH PROBLEMS

A fundamental problem of brucellosis is the discovery of methods for the control of the disease in animals. Urgent from the point of view of both the human and animal disease is the discovery of an effective therapeutic agent. The development of laboratory techniques to facilitate the recognition of the mild form of the disease is important. Many other brucellar problems on which information is incomplete should be investigated. Some of them were suggested in the preceding pages.

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