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Brucellosis: Consideration of Its Epidemiology, Diagnosis and Control*

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DURING 1930–1941, there were reported in the 48 states of this country 29,594 cases of brucellosis, an average annual rate of 1.87 per 100,000 population.† Officially notified cases in Iowa totaled 1,887 for the same 12 year period, the average annual rate being 6.25 per 100,000.

Direct contact with infected animals and use of raw milk products from infected dairy cows provide the chief means of transmission to man of brucellosis or undulant fever. This statement applies to Iowa, probably also to many if not all of the cattle and hog raising states. As pointed out by Hardy and associates,[1] direct contact with hogs must be considered a major factor to account for the relatively high incidence of brucellosis in the midwestern states of this country. Cases resulting from direct contact, whether with infected hogs or cows, are usually of sporadic nature; such cases in the aggregate, apparently exceed in number those traceable to contaminated dairy products.

Milk-borne brucellosis likewise, is nearly always of sporadic occurrence when *Brucella abortus,* the bovine type of organism, is the etiologic agent. On the other hand, when the porcine strain, *Brucella suis,* gains access to the udder of a dairy cow to contaminate a raw milk supply, multiple cases of the disease may be fully expected. This may be due to the fact that *Brucella suis* is more highly pathogenic than *Brucella abortus* and that the former multiplies more rapidly in a milk medium under ordinary atmospheric conditions than does the bovine strain of brucella.

Brucellosis lends itself favorably to epidemiologic study. The organism has

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† A table containing annual reports from the 48 states covering the 12 year period 1930–1941 may be had on request of the Iowa State Department of Health, Des Moines, Ia.

distinct morphologic and cultural characteristics, and can readily be isolated from blood, although such isolation may require several weeks to a month or longer. Agglutination, intradermal and other tests are available to throw light on the nature of infection and immunity. The disease in the animal reservoir and in the experimental animal also affords opportunity for determination of virulence, manner of spread and source of infection.

It is desired in this report to limit consideration to milk-borne brucellosis; information as presented is based on an investigation of two cases caused by *Brucella abortus* in Madrid (Boone County), Iowa, and on the study of an epidemic in Marcus, Iowa, in which *Brucella suis* was the inciting agent.

MADRID INVESTIGATION AND SURVEY (BRUCELLA ABORTUS)

On July 2, 1942, Mr. A. L., 68, a resident of Madrid (Pop. 2,074), Boone County, Iowa, began to complain of tired feeling, pain in back of neck, fever (102°), chills and sweats. Three weeks later, the patient's serum was found to agglutinate brucella antigen in a dilution of 1:1,280. The patient gave no history of direct contact with farm animals, but during the months antedating illness, had used two glasses daily of raw milk from a local, the C. S., dairy. Through coöperative arrangement between the State Department of Health, the Bureau of Animal Industry, and the State Department of Agriculture, local veterinarians were authorized to obtain blood specimens from dairy herds which supplied milk in the community. Of 13 cows in the C. S. dairy, 9 proved to be reactors to the agglutination test for Bang's disease. The dairyman concerned, a thoroughly coöperative person, sold no milk to patrons after July 31. Other herds were not tested at the same time, due mainly to misunderstanding on the part of producers with respect to accuracy of the agglutination test.

Although a blood culture from the patient failed to yield *Brucella abortus*, it is highly probable that infection was due to brucella of bovine type. This organism was later isolated from guinea pigs, following subcutaneous injection of cream from reactor cows.

While sporadic cases had developed from time to time in rural areas of the county, the case of brucellosis in Madrid was the first to come under observation of local physicians in a period of more than a decade. In addition to the patient, it was assumed that scores of children and adults in many homes had been exposed to the contaminated milk supply. With the interest and aid of local physicians, school superintendent, and parents, arrangements were made for blood specimens to be obtained for the agglutination test and for skin tests to be administered, using brucellergen. Such a survey was conducted in the school building on August 11, 1942, and again, for the most part on a different group, on September 29. Record was kept of the age and sex of volunteers, of residence in town or country, and of the source of milk supply.*

RESULTS OF AGGLUTINATION TESTS

The agglutination tests were carried out at the State Hygienic Laboratory, beginning with a titer of 1–5. The results as summarized for a group of 147 persons, are presented in Table 1. Males and females being considered equally susceptible to brucellosis of milk-borne character, the whole group was classified according to three age groups, 1–9, 10–19, 20 and over. Further classification was made under two headings, including on the one hand consumers of the "contaminated milk supply" and, on the other hand, those

* The authors desire to acknowledge the valued assistance in the investigation at Madrid of Glen M. Grout, Sup't of Schools, R. A. Gamble, M.D., M. M. Shaw, M.D., and J. O. Cook, M.D.

who had used "other milk supplies." "Other milk supplies" refers to five producers of raw milk and to "own cows" of those from the surrounding rural area.

It will be noted that among 63 users of the contaminated milk supply, 18, or 28.6 per cent, showed agglutination in titers ranging from 1:5 to 1:40, the titer of but one person being 1:40. Of 84 individuals of all ages, representing consumers of "other milk supplies," 17, or 20.2 per cent, showed positive agglutination, 16 in titers of 1:5–1:20 and one in the 1:40 dilution.

These results, based as they are on a comparatively small number of people, some of whom used milk and cream only sparingly, are hardly remarkable. A similar agglutination survey, in a sanatorium or institution with an abundant per capita use of raw milk from infected dairy cows, would probably be accompanied by more significant evidence of latent infection.[2]

RESULTS OF SKIN TESTS

Intradermal tests were administered with brucella nucleoprotein, known as brucellergen and made according to the method of I. Forest Huddleson, D.V.M., Research Professor in Bacteriology, Michigan State College, East Lansing, Mich. Two types of antigen were supplied for this survey through the courtesy of Dr. Huddleson, prepared separately from *Brucella abortus* (dilution 1:12,000) and *Brucella suis* (1:4,000). Each person received two intradermal tests (0.1 ml.) on the inner aspect of the forearm, brucellergen abortus above and brucellergen suis below. Each preparation was further diluted to 1:60,000 and 1:20,000 respectively to avoid the possibility of a severe reaction in those who might be markedly allergic.

Skin reactions were observed and measured after an interval of 48 hours, an area 2 x 2 cm. in diameter, with redness, induration, and tenderness being recorded as positive. The results are set forth in Table 2. As in Table 1, those tested were divided into three age groups, 1–9, 10–19, 20 and above, and according to use of "contaminated" and "other milk supplies." Skin tests were performed on 170 volunteers. Among 71 who had used the contaminated milk supply, 10, or 14.1 per cent, had positive reactions; of 99 consumers of other milk supplies, 12 or 12.1 per cent, showed allergic response.

It is of interest to note that among 27 children of the age group 1–9, 13 of whom used the contaminated milk, all showed negative skin reactions.

There was no notable difference in size, redness, or induration between the reaction produced by brucellergen abortus and that resulting from brucellergen suis.

OCCURRENCE OF A SECOND CLINICAL CASE

Among those who participated in the agglutination and skin test survey on August 11 were Mr. and Mrs. D, aged 40+, residents of the city and exposed to the contaminated milk supply. Mr. D's agglutination test was negative, his skin tests strongly positive. Agglutination and skin tests were both negative in the case of Mrs. D, but she began to complain of fever and indisposition about September 1. On September 10, a second blood specimen showed agglutination of brucella in a dilution of 1:320, and the skin test had become positive. It seems probable that this woman carried a latent infection on August 11, in spite of negative skin and agglutination tests. Among 30 other individuals whose serum when taken August 11 showed no agglutinins or titers not higher than 1:5 or 1:10, 21, or 70 per cent, were entirely negative when the agglutination test was repeated on September 29.

TABLE 1

Agglutination Tests for Brucellosis in Relation to (1) a Raw Milk Supply Contaminated with Brucella Abortus and to (2) Other Milk Supplies in Madrid, Boone County, Iowa, 1942

Age Group	Contaminated Milk Supply Agglutination Reaction						Other Milk Supplies Agglutination Reaction						All Milk Supplies Agglutination Reaction					
	No. Tested	Negative		Positive			No. Tested	Negative		Positive			No. Tested	Negative		Positive		
		No.	%	1:5 1:20	1:40 1:80	%		No.	%	1:5 1:20	1:40 1:80	%		No.	%	1:5 1:20	1:40 1:80	%
1– 9	1	1	100.0				4	4	100.0				5	5	100.0			
				0	0	0.0				0	0	0.0				0	0	0.0
10–19	14	10	71.4				46	36	78.3				60	46	76.7			
				4	0	28.6				9	1	21.7				13	1	23.3
20 and over	48	34	70.8				34	27	79.4				82	61	74.4			
				13	1	29.2				7	0	20.6				20	1	25.6
Totals	63	45	71.4				84	67	79.8				147	112	76.2			
				17	1	28.6				16	1	20.2				33	2	23.8

TABLE 2

Skin Tests with Brucellergen in Relation to (1) a Raw Milk Supply Contaminated with Brucella Abortus and to (2) Other Milk Supplies in Madrid, Boone County, Iowa, 1942

Age Group	Contaminated Milk Supply Skin Test Reading					Other Milk Supplies Skin Test Reading					All Milk Supplies Skin Test Reading				
	No. Tested	Negative		Positive		No. Tested	Negative		Positive		No. Tested	Negative		Positive	
		No.	%	No.	%		No.	%	No.	%		No.	%	No.	%
1– 9	13	13	100.0			14	14	100.0			27	27	100.0		
				0	0.0				0	0.0				0	0.0
10–19	14	14	100.0			57	50	87.7			71	64	90.1		
				0	0.0				7	12.3				7	9.9
20 and over	44	34	77.3			28	23	82.1			72	57	79.2		
				10	22.7				5	17.9				15	20.8
Totals	71	61	85.9			99	87	87.9			170	148	87.1		
				10	14.1				12	12.1				22	12.9

MARCUS INVESTIGATION AND SURVEY (BRUCELLA SUIS)

On September 10, 1941, investigation was made in Marcus (population 1,206), Cherokee County, Iowa, of 13 cases of brucellosis. These cases, verified by positive agglutination findings at the State Hygienic Laboratory, were reported by the local health officer and attending physician, to the District Health Service and to the State Department of Health. All of the patients gave the history of having been supplied with milk from the W. H. dairy, distributor of raw milk. Delivery of milk from this dairy was stopped September 10, 1941. In spite of early removal of the contaminated milk supply, additional cases came to attention through the remaining months of 1941. In the entire outbreak, 77 persons were found to have active or latent infection as confirmed by positive agglutination tests. Of a series of 29 blood cultures, 13 yielded brucella, all strains being identified as *Brucella suis*.

Agglutination tests for Bang's disease, performed on serum of cows in the W. H. dairy, showed three positive (and one suspicious) reactors. *Brucella suis* was isolated from the cream of two reactors. Hogs on the dairy farm were also found to be infected.[4]

The Marcus milk-borne epidemic caused by *Brucella suis* was the second of its kind to be investigated in Iowa; the first outbreak occurred in 1933 and was reported by Beattie and Rice.[5]

In order to obtain additional information as to the extent of infection in the Marcus community, blood specimens for agglutination were secured and skin tests performed on students and adults in the public and parochial schools.*

RESULTS OF AGGLUTINATION TESTS

Findings of the agglutination survey are presented in Table 3. Here also, those contributing specimens have been classified into the age groups 1–9, 10–19, 20 and above, and according to whether the "contaminated milk supply" or "other milk supplies" were used during the months preceding the epidemic. The group totalled 204; among 33 who had been exposed to contaminated milk, 12, or 36.3 per cent, showed positive agglutination for brucellosis, all in diagnostic dilutions varying from 1:80 to 1:2,560. Five children were under 10 years, the remaining 7 between 10 and 19 years of age. There was no instance of agglutination in diagnostic titer among 171 consumers of other milk supplies.

RESULTS OF SKIN TESTS

Material for performing intradermal tests with brucellergen, was supplied through the courtesy of Dr. Huddleson of Michigan State College. Two separate antigens were used without further dilution, one prepared from *Brucella abortus* (1:12,000), the other from *Brucella suis* (1:4,000). One girl of teen age whose agglutination test was negative, but who was apparently very allergic, showed a severe reaction, with subsequent necrosis of the skin and subcutaneous tissues. In a few instances, individuals showed a more marked reaction with brucellergen suis than with brucellergen abortus.

A summary of results of the series of intradermal tests is contained in Table 4. A striking difference will be noted in the percentage of positive skin tests among those using contaminated milk as compared with those whose milk came from other sources. Among 57 persons of all ages who used the contaminated milk supply, 42, 73.7 per cent, showed positive skin reactions, whereas 17, or 10.8 per cent, of 158

* Acknowledgment is made of the valued assistance in the investigation at Marcus of Father E. M. McEvoy, H. Wood, Sup't of Public Schools, and M. F. Joynt, M.D.

TABLE 3

Agglutination Tests for Brucellosis in Relation to (1) a Raw Milk Supply Contaminated with Brucella Suis and to (2) Other Sources of Milk in and near Marcus (Pop. 1,200), Cherokee County, Iowa, 1941

Age Group	Contaminated Milk Supply Agglutination Reaction					Other Milk Supplies Agglutination Reaction					Total Tested Agglutination Reaction				
		Negative		Positive			Negative		Positive			Negative		Positive	
	No. Tested	No.	%	1:80 1:2,560	%	No. Tested	No.	%	1:80 1:2,560	%	No. Tested	No.	%	1:80 1:2,560	%
1– 9	14	9	64.3	5	35.7	42	42	100.0	0	0.0	56	51	91.1	5	8.9
10–19	18	11	61.1	7	38.9	126	126	100.0	0	0.0	144	137	95.1	7	4.9
20 and over	1	1	100.0	0	0.0	3	3	100.0	0	0.0	4	4	100.0	0	0.0
Totals	33	21	63.7	12	36.3	171	171	100.0	0	0.0	204	192	94.1	12	5.9

TABLE 4

Skin Tests with Brucellergen in Relation to (1) a Raw Milk Supply Contaminated with Brucella Suis and to (2) Other Milk Supplies at Marcus (Pop. 1,200), Cherokee County, Iowa, 1941

Age	Contaminated Milk Skin Test Reading					Other Supplies Skin Test Reading					Total Tested Skin Test Reading				
		Negative		Positive			Negative		Positive			Negative		Positive	
	No. Tested	No.	%	No.	%	No. Tested	No.	%	No.	%	No. Tested	No.	%	No.	%
1– 9	23	8	34.6	15	65.2	70	65	92.9	5	7.1	93	73	78.5	20	21.5
10–19	33	7	21.2	26	78.8	85	75	88.2	10	11.8	118	82	69.5	36	30.5
20 and over	1	0	0.0	1	100.0	3	1	33.3	2	66.7	4	1	25.0	3	75.0
Total	57	15	26.3	42	73.7	158	141	89.2	17	10.8	215	156	72.6	59	27.4

consumers of other milk showed a positive or an allergic response.

FOLLOW-UP OF AGGLUTINATION REACTIONS

On October 18, 1942, another blood specimen for agglutination was obtained by one of us (D.M.H.) with the coöperation of M. F. Joynt, M.D., of Marcus. Of 27 patients, whose serum showed agglutination of brucella antigen in titers from 1:160 to 1:1,280 during the late months of 1941, 7 showed negative agglutination and 16 had titers down to 1:10, 1:20, or 1:40 in October, 1942.

DIAGNOSIS, CONTROL, AND PREVENTION

The isolation of brucella from the blood stream stands first among laboratory aids which confirm the physician's clinical diagnosis of brucellosis. Finding of the organism makes possible its species identification, which in turn helps to establish the source of infection in hogs, cows, or other animals.

The presence of agglutination in diagnostic dilution is second only to the blood culture as an aid in clinical diagnosis. Both rapid and slow methods of agglutination are dependable. Should a first specimen show negative or weakly positive agglutination, taking of subsequent specimens will frequently result in strongly positive agglutination reports.

A positive intradermal test with brucella antigen signifies exposure to brucella infection in the recent or remote past. Simpson [6] advises against overemphasizing the diagnostic significance of this test, stating that the intradermal test when positive " does not mean that the symptoms from which the patient is suffering at the time are necessarily due to brucellosis."

Findings of the opsonocytophagic test are probably most dependable when observed soon after onset of symptoms. Results need to be interpreted with caution.

Economically and from a health standpoint, brucellosis is one of the most important diseases transmissible from animals to man. Measures for eradication of Bang's disease need to be pursued vigorously in coöperation with veterinarians, the Federal Bureau of Animal Industry, and state departments of agriculture.

Use of none but carefully pasteurized dairy products and enforcement by cities and communities of the *Standard Milk Ordinance* as recommended by the U. S. Public Health Service, afford the best assurance against the possibility of milk-borne disease.

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