The Epidemiology of Q Fever in Iowa

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REPORTS of Q fever in California in the 1940's called attention to the public health significance of the disease (*1–3*). Likewise, experiences of World War II demonstrated its military implications (*4, 5*). Q fever has consequently become a subject of investigation in many areas, military and civilian, both in this country and abroad. An important reason for the recent increases in Q fever surveys and research was the development of the Luoto capillary-agglutination test (CAT) as a rapid and reliable method for the serodiagnosis of Q fever in man and animals (*6, 7*). In addition, this technique provides an economically feasible method for conducting large-scale human and animal serologic surveys for evidence of Q fever infections.

Naturally occurring Q fever in man and animals has recently been detected in a number of States previously presumed free of the disease (*8–10*). The nationwide occurrence of Q fever in dairy cattle has been reported (*11*). Available information indicates the disease is enzootic in most sections of the country with reservoirs in dairy cattle and sheep. Reports of sporadic human infections suggest the possible occurrence of endemic Q fever in some areas (*10, 12*). Relatively few reported studies have sought to identify and confirm human infections in recently recognized enzootic areas.

Q fever in both animals and man was first reported in Iowa in 1957–58. Initial studies revealed that 0.7 percent of dairy cattle were serologically positive while 3.25 percent of dairy herds contained reactors (*13*). During this same period the first case of human Q fever in Iowa was identified (*14*). Subsequent studies (*15*) were conducted to investigate the epizootiology of the disease in dairy cattle, to confirm the infection status of serologically positive cattle by isolation of *Coxiella burnetii*, and to evaluate the CAT method with milk samples as an epizootiologic tool (*16*). More recently, the prevalence of CAT positives among the human population of Iowa was investigated; a number of acute human infections were identified and subjected to detailed epidemiologic study. In addition, another survey of bovine serums was performed to detect any recent changes in the prevalence of bovine Q fever. This report presents the results of these studies.

Materials and Methods

Human serum specimens were selected at random from the routine daily samples submitted to the Iowa State Hygienic Laboratory for diagnostic serology of febrile diseases (febrile agglutinations), such as brucellosis and typhoid fever. Serums were collected and tested daily during February through May 1958 and October 1958 through July 1959. A number of routine premarital blood specimens were similarly collected and tested during the same periods until May 1959. The serums were tested by the CAT method (*6, 7*) in a screen test at a 1:2 dilution, a level indicative of

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specific and reproducible evidence of Q fever antibodies; positive serums were titrated to end point.

The positive specimens were identified as to patient, submitting physician, and the results of other serologic tests. Repeat specimens were obtained from all patients positive for Q fever in an effort to demonstrate serologic stability or fluctuation. In those few patients found serologically positive for Q fever and brucellosis or typhoid fever, tests on successive serums implicated the responsible etiologic agent. For purposes of field investigations, Q fever reactive serums were arbitrarily divided into two categories on the basis of end point titer. Specimens reacting at a titer of 1:8 or less were identified, and explanatory letters requesting repeat specimens in approximately 10 days were sent to the submitting physicians. Specimens reacting at a titer of 1:16 or greater were identified, and the submitting physicians were interviewed by telephone. The clinical features of the patient were defined, and, if similar to active Q fever, a detailed field investigation was initiated.

Epidemiologic investigations included recording clinical signs and symptoms supplied by the physician or patient, abstracts of hospital and clinic records, collection of serial blood specimens, and a detailed patient interview regarding occupational and environmental history. When warranted, the routine dairy cattle and sheep contacts of the patient were identified and investigated as possible exposure sources. Cases were evaluated by clinical and serologic criteria; a compatible clinical syndrome supported by either a fourfold rise in antibody titer or a stable titer of 1:128 or greater was accepted as evidence of current or recent acute infection.

Bovine blood samples were obtained from the Iowa State-Federal Brucellosis Laboratory on a random selection basis in weekly lots of 1,500 to 2,000 and identified as to county of origin. The samples were collected and examined by CAT techniques from April 6 to May 4, 1960, essentially as during an earlier survey in 1957 (*13*). Groups of specimens submitted by private veterinarians were accepted as representing individual, but not necessarily com-

Table 1. Results of serologic survey for Q fever in Iowa, 1958 and 1959

Month	Specimen source								Total number tested	Total number reactors [2]		
	Febrile agglutination [1]				Premarital							
	Number tested	Number of reactors [2]			Number tested	Number of reactors [2]						
		1:2	1:4>	Total		1:2	1:4>	Total		1:2	1:4>	Total
1958												
February	870	0	2	2	445	1	1	2	1,315	1	3	4
March	1,483	1	6	7	1,442	0	1	1	2,925	1	7	8
April	1,669	1	4	5	1,777	0	2	2	3,446	1	6	7
May	807	0	1	1	1,149	0	3	3	1,956	0	4	4
October	351	0	0	0	471	1	0	1	822	1	0	1
November	1,345	1	4	5	1,998	1	5	6	3,343	2	9	11
December	1,259	2	6	8	2,039	2	4	6	3,298	4	10	14
1959												
January	1,448	0	4	4	1,768	0	2	2	3,216	0	6	6
February	1,476	0	3	3	1,582	1	5	6	3,058	1	8	9
March	1,696	0	2	2	1,838	0	1	1	3,534	0	3	3
April	1,860	1	8	9	1,829	3	6	9	3,689	4	14	18
May	1,565	2	3	5	1,394	0	3	3	2,959	2	6	8
June	1,991	3	7	10	----	----	----	----	1,991	3	7	10
July	1,369	1	6	7	----	----	----	----	1,369	1	6	7
Totals	19,189	12	56	68	17,732	9	33	42	36,921	21	89	110

[1] Specimens submitted to the Iowa State Hygienic Laboratory for brucellosis or typhoid serology, or both.
[2] Agglutination in the Luoto capillary-agglutination test.

plete, herd samples. Although it was not possible to identify bovine serums as being of dairy or beef cattle origin, all specimens were considered of dairy origin in computing the prevalence of positive serums (*13*).

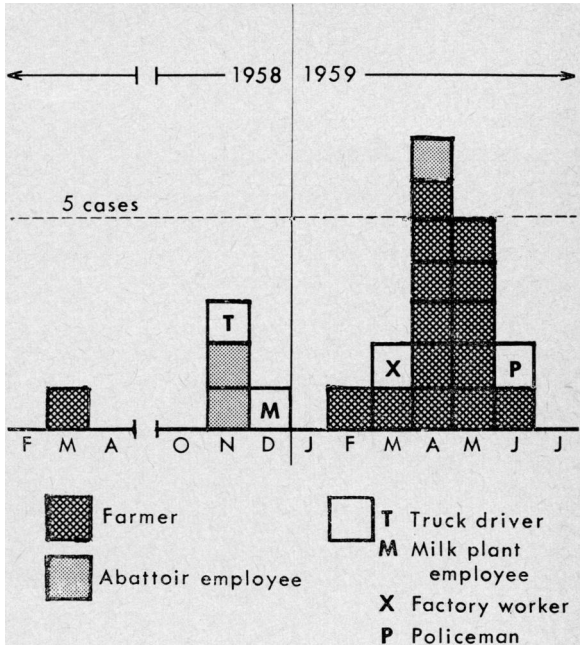
Results

Human serum survey. Survey results (table 1) showed that 110 serums (0.30 percent) of 36,921 human serums contained Q fever antibody detectable at the 1:2 level of the screen test. Sixty-eight (0.35 percent) of 19,189 febrile-agglutination serums and 42 (0.24 percent) of 17,732 premarital samples contained antibody. At titers of 1:4 or greater 89 (0.24 percent), 56 of febrile (0.29 percent) and 33 of premarital serums (0.19 percent), respectively, were reactive. The distribution of end point titers of the survey specimens is shown in table 2. Titers among the febrile patients were, in general, higher than those of the premarital group—23.4 percent (16 of 68) of the febrile serums were positive at 1:32 or greater, and 20.6 percent at 1:64, as compared with 14.2 percent (6 of 42) and 7.1 percent (3 of 42) among the premarital serums, respectively.

Fifty-nine percent of the specimens from the febrile group were from males and 41 percent from females; however, 61 of the 68 positive serums were obtained from males. Among the premarital specimens, equally contributed by males and females, 28 of 42 positives were from males.

Case investigations. Epidemiologic field investigations resulted in the detection and confirmation of a total of 22 acute human infections. Among these patients, all located through tests of diagnostic serums from ill persons, were 12 persons with at least a fourfold increase in serum titers after illness and 10 with stable titers of 1:128 or greater who had clinical symptoms compatible with acute Q fever infection. The routine testing of febrile-agglutination specimens led to identification and confirmation of 16 cases, while 6 cases were provisionally diagnosed by physicians after practitioners were alerted to the possible occurrence of infections.

Distribution of occurrence of 22 cases of Q fever in Iowa, by occupation of patients and month of onset, 1958 and 1959



The 22 confirmed cases occurred in males. Their age distribution within 10-year age group increments was: 2 patients, from 11 to 20 years; 3 patients, from 21 to 30 years; 8, 31 to 40 years; 3, 41 to 50 years; 1, 51 to 60 years; and 5 pa-

Table 2. Titer distribution of positive [1] human specimens, Q fever survey, Iowa

Specimen source	Number tested	Total positive	Percent positive	Number of specimens positive at titers of—									
				1:2	1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:512	1:1024
Febrile agglutination specimens	19, 189	68	0. 35	12	11	17	12	2	6	2	4	1	1
Premarital specimens	17, 732	42	. 24	9	11	10	6	3	2	1	0	0	0
Totals	36, 921	110	. 30	21	22	27	18	5	8	3	4	1	1

[1] In the Luoto capillary-agglutination test.

tients over 61 years of age. The patients were not concentrated geographically. The chart shows the distribution of occurrence by occupation and month of onset; 5 infections were detected in 1958 and 17 in 1959. Of the 17 episodes occurring from January to July 1959, 12 had onset during April and May. By occupation, the 22 patients consisted of 15 farmers, 3 abattoir employees, 1 milk plant employee, 1 policeman, 1 truck driver, and 1 factory worker.

Of the 22 patients, a history of routine contacts with dairy cattle or sheep, or both, was obtained in 16, 13 farmers and 3 abattoir employees. Testing of animal contacts associated with the 13 infected farmers resulted in identification of three positive dairy herds. Consumption of raw milk was reported by only one patient, a dairy farmer; the dairy herd in question proved to be serologically negative for Q fever.

The clinical signs and symptoms reported by physicians or patients are listed below.

Sign or symptom	*Number of patients*
Fever	22
Anorexia	22
Headache	20
Myalgia	13
Cough	11
Nausea	8
Chest pain	8
Vomiting	6
Vertigo	4
Dyspnea	2
Sore throat	2

Illnesses were characterized by abrupt onset with initial headache, fever, and anorexia. Most patients reported intense, persistent headache of several days' duration as their most severe symptom. Generalized myalgia occurred in 13 patients and cough was a prominent sign in 11. Nausea and vomiting, as well as generally severe chest pain occurring 4 to 6 days after onset of illness, were reported by less than half the patients. Chest X-rays taken on seven patients during the course of acute illness revealed pulmonary lesions in only one patient. Urine and blood studies were essentially normal for 12 patients. The mean duration of acute illness was approximately 14 days, followed in most instances by several weeks of general malaise and weakness. Observations on the effectiveness of chemotherapy were complicated by variations in the agents used and in the dosages and duration of administration. Complete recovery without complications occurred in 21 of the 22 patients; the single possible exception was a 78-year-old patient who died of unverified causes 1 month after apparent clinical recovery from Q fever (*14*).

Bovine serum survey. Of 9,359 bovine blood specimens from 94 of the 99 Iowa counties tested for Q fever antibody in 1960, 149 serums (1.6 percent) were positive, while 62 herds, or 9.6 percent, contained serologically positive animals. The geographic distribution of positive herds was indicative of widespread foci of infection. Comparison of these findings (table 3) with those of similar surveys (*13*) during 1957, when 0.7 percent and 3.2 percent of dairy cows and herds were infected, shows a significant increase and spread of animal Q fever within the State.

Discussion

Although the prevalence of Q fever antibodies was relatively low among survey groups of routine febrile-agglutination and premarital serum specimens, the survey results reflect a

Table 3. Comparison of bovine infections during two sampling periods for Q fever in Iowa

Survey period	Serums tested [1]			Herds tested [1]		
	Number	Positive	Percent positive	Number	Positive	Percent positive
November 1956 to June 1957	11,779	84	0.7	767	25	3.25
April to May 1960	9,359	149	1.6	646	62	9.6

[1] By the Luoto capillary-agglutination test.

definite degree and frequency of human exposure to *C. burnetii* in Iowa. Epidemiologic investigation of suspect Q fever cases, as determined by serum titer, proved to be an efficient method of identifying human infection. Similar surveys and epidemiologic studies are indicated in other recently identified areas of enzootic Q fever.

To our knowledge, the use of the CAT method in human beings has been limited. In both Luoto's and the Institute of Agricultural Medicine's laboratories, comparisons have been conducted with respect to the complement fixation (CF) and CAT methods of testing human serum in cases of suspected Q fever. Experience to date (*17*), has indicated close and significant agreement where both the CF and CAT methods have been applied. Further and more solid confirmation of the value of the CAT method in the testing of serums from supposed human cases must rest on isolation of the causative organism. Unfortunately, the nature of the human illness and the complicated and sometimes risky laboratory procedures involved tend to make the isolation of Q fever rickettsiae from human cases a rather difficult undertaking (*18*).

The greater occurrence of Q fever identified serologically among males, in both the febrile-agglutination and premarital survey groups, suggests occupational exposure to the disease. Further, the fact that all 22 identified cases of Q fever occurred in males is indicative of occupational exposure. Investigation of their occupational backgrounds resulted in the identification of specific exposure sources for only three patients, farmers who had routine contact with dairy cattle serologically positive for Q fever. Abattoir employees accounted for three cases; although it was not possible to determine the infection status of the animals implicated as possible exposure sources, it may be assumed, on the basis of the known prevalence of Q fever among Iowa dairy cattle, that these men were occupationally exposed. Also, occupational exposure to Q fever probably occurred with the milk plant employee having routine contact with raw milk. No specific exposure source could be identified for the remaining 15 patients. However, each patient recalled occasional, if not regular, contact with dairy cattle or sheep, or both, or their environs. Thus, multiple and diverse opportunities for exposure to Q fever occurred in animal environments.

Clinical signs and symptoms among the 22 patients were essentially typical of Q fever. As illustrated in the chart, the distribution of patients during the survey period suggests an increasing infection rate as a function of time. However, the limited number of patients, as well as the interrupted 1958 summer survey, precluded valid comparison of case rates. Of the 17 infections confirmed in 1959, 12 occurred during April or May; 11 of the 12 patients who became ill during the 2-month period were farmers. One possible explanation for the apparent seasonal concentration of cases, along with winter cases, among farmers in this sample is the fact that the majority of Iowa dairy cattle deliver their calves in the spring. The parturition of infected cattle or sheep is well recognized as an effective mechanism for aerosol dissemination of *C. burnetii* (*19–21*). The status of sheep infections remains unknown in Iowa.

The second Q fever serologic survey of Iowa dairy cattle from the same general areas revealed a significant increase in individual and herd positive rates. The proportion of positive bovine serums increased from 0.7 percent in 1956–57 to 1.6 percent in 1960, while the herd positive reactor rate increased from 3.25 percent to 9.6 percent. The negative influence provided by the presence of incomplete herd tests and beef cattle blood samples in the bovine blood specimens has been discussed previously (*13*).

These data strongly suggest the progressive spread of Q fever among Iowa dairy cattle during the last 4 years. The bovine disease may be expected to spread more rapidly in the future since transmission is facilitated by increases in reservoirs of infected animals. Consequently, an increase in the number of human Q fever infections may result.

Summary

A serologic survey for Q fever in Iowa of 36,921 human serums, consisting of 19,189 diagnostic specimens from febrile patients and

17,732 premarital specimens, revealed a reactor rate of 0.30 percent positive.

Epidemiologic investigations of suspect infections, confirmed by private physicians, using clinical and bacteriological criteria, resulted in the identification and diagnosis of Q fever in 22 males. Investigation of suspect exposure sources for these patients revealed contact with infected dairy cattle for 3 farmers, and presumptive occupational exposure for 3 abattoir employees and 1 milk plant employee; no specific exposure source could be identified for the remaining 15 patients.

Serologic surveys for Q fever in dairy cattle revealed an increase in prevalence from 0.7 percent in 1956–57 to 1.6 percent in 1960, while the herd positive reactor rate increased from 3.25 percent to 9.6 percent.

REFERENCES

(1) Young, F. W.: Q fever in Artesia, California. California Med. 69: 89–90 (1948).

(2) Lennette, E. H.: Q fever in California. California Med. 69: 91–95 (1948).

(3) Beck, M. D., Bell, J. A., Shaw, E. W., and Huebner, R. J.: Q fever studies in southern California; epidemiologic study of 300 cases. Pub. Health Rep. 64: 41–56 (1949).

(4) Robbins, F. C., and Ragan, C.: Q fever in Mediterranean area; report of its occurrence in allied troops; clinical features of disease. Am. J. Hyg. 44: 6–22 (1946).

(5) Commission on Acute Respiratory Diseases, Fort Bragg, North Carolina: Epidemics of Q fever among troops returning from Italy in spring of 1945. II. Epidemiological studies. Am. J. Hyg. 44: 88–102 (1946).

(6) Luoto, L.: Capillary agglutination test for bovine Q fever. J. Immunol. 71: 226–236 (1953).

(7) Luoto, L.: Capillary-tube test for antibody against *Coxiella burnetii* in human, guinea pig and sheep sera. J. Immunol. 77: 294–298 (1956).

(8) Reed, C. F., and Wentworth, B. B.: Q fever studies in Ohio. J. Am. Vet. M. A. 130: 458–461 (1957).

(9) Kitze, L. K., Hiemstra, H. C., and Moore, M. S.: Q fever in Wisconsin; serologic evidence of infection in cattle and in human beings and recovery of *C. burnetii* from cattle. Am. J. Hyg. 65: 239–247 (1957).

(10) Luoto, L.: The epidemiology of Q fever in the United States. Am. J. Pub. Health 49: 334–338 (1959).

(11) Luoto, L.: Report on the nationwide occurrence of Q fever infections in cattle. Pub. Health Rep. 75: 135–140 (1960).

(12) Stoenner, H. G., Jellison, W. L., Lackman, D. B., Brock, D., and Casey, M.: Q fever in Idaho. Am. J. Hyg. 69: 202–213 (1959).

(13) Tjalma, R. A., and Smith, I. M.: Q fever in Iowa dairy cattle. J. Am. Vet. M. A. 133: 606–610 (1958).

(14) Tjalma, R. A.: A review of Q fever with a report on a recent human case in Iowa. J. Iowa M. Soc.: 542–546, October 1958.

(15) Tjalma, R. A., and Braun, J. L.: Application of the Luoto capillary agglutination milk test to the study of bovine Q fever. Am. J. Pub. Health 49: 1025–1031 (1959).

(16) Luoto, L., and Mason, D. M.: Agglutination test for bovine Q fever performed on milk samples. J. Immunol. 74: 222–227 (1950).

(17) Tjalma, R. A.: Q fever in animals and man in Iowa. Institute of Agricultural Medicine, Department of Hygiene and Preventive Medicine, Bull. No. 3. State University of Iowa, August 1958.

(18) Rivers, T. M., and Horsfall, F. L.: Viral and rickettsial infections of man. Ed. 3. J. B. Lippincott Co., Philadelphia, Pa., 1959, p. 887.

(19) Luoto, L., and Huebner, R. J.: Q fever studies in southern California. IX. Isolation of Q fever organisms from parturient placentas of naturally infected dairy cows. Pub. Health Rep. 65: 541–544 (1950).

(20) Welsh, H. H., Lennette, E. H., Abinanti, F. R., and Winn, J. F.: Q fever in California. IV. Occurrence of *Coxiella burnetii* in the placenta of naturally infected sheep. Pub. Health Rep. 66: 1473–1477 (1951).

(21) DeLay, P. D., Lennette, E. H., and DeOme, K. B.: Q fever in California. II. Recovery of *Coxiella burnetii* from naturally infected airborne dust. J. Immunol. 65: 211–220 (1950).