

Laboratory Outbreak of Q Fever

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An outbreak of Q fever in a university department where sheep placentas were being used for research is described. Of six persons exposed to the sheep, four had positive titers with only one person developing an acute febrile illness and liver disease. This report illustrates the value of

the family physician obtaining an occupational history and conducting an outbreak investigation.

Key words. Sheep diseases; Q fever; occupational exposure; diagnosis, differential.

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Q fever is a zoonosis caused by a rickettsia (*Coxiella burnetii*). Its most common feature is a flulike illness, but it can also cause pneumonia, hepatitis, endocarditis, glomerulonephritis, and meningoencephalitis. Several outbreaks of Q fever have been reported in research laboratories using sheep.¹⁻³ We report an outbreak that occurred between May and August 1991 in a university department using sheep placentas for fetal respiratory studies. This case describes the investigation of the outbreak by a family physician, including case finding, work-site visit, and serologic and exposure survey. It also illustrates the value of obtaining an occupational history in making a prompt diagnosis.

Case Report

On May 6, 1991, a 31-year-old man presented to the family medicine center with diarrhea, fever, and mild abdominal distention. A presumptive diagnosis of viral gastroenteritis was made. A week later the patient returned with continued high fever, cough, mild shortness of breath, and worsening abdominal distention. His temperature was 39°C, and he had decreased breath sounds and an enlarged liver. A chest radiograph showed a hazy infiltrate in the right lower lobe.

A diagnosis of pneumonia with concurrent abdominal process was entertained, and the patient was admit-

ted for treatment and laboratory evaluation of his hepatomegaly. He was started on intravenous ceftriaxone.

Laboratory evaluation included tests for tuberculosis, viral hepatitis, syphilis, human immunodeficiency virus, and *Mycoplasma*, all of which were negative. Liver function tests were elevated, however, and an abdominal ultrasound showed a 17-cm liver span with reversal of flow in the hepatic veins, large amount of ascites, and a normal common bile duct. The ascitic fluid was sterile, and cytology showed mixed inflammatory cells. Liver biopsies showed periportal fibrosis and sinusoidal dilatation, but were negative for acid-fast bacilli.

Forty-eight hours after admission, the patient was afebrile. He was started on oral erythromycin, and by the 10th hospital day, he had no clinical ascites, no abdominal pain, and no fever. The cause of his illness remained unclear. Zoonosis was suspected when an occupational history revealed that he worked in a research laboratory caring for experimental animals including sheep, cats, and dogs. Serum titers for *Legionella*, tularemia, *Leptospira*, *Brucella*, and Q fever were collected before his discharge.

On follow-up 3 weeks later, an abdominal ultrasound showed complete resolution of the obstruction of the hepatic veins. The initial Q-fever titers were elevated, however, and convalescent serum confirmed a fourfold rise in titers from 1:1024 on day 45 after onset of the gastroenteritis-like illness to 1:4096. The patient was immediately started on a course of doxycycline.

The patient worked in an animal research laboratory with nine other employees. Three of these employees and two researchers were involved in sheep research. The sheep were received from two different suppliers; they were delivered to the building through a separate entrance with immediate access to an "animal elevator."

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Table 1. Comparison of Acute and Chronic Q Fever Syndromes

| | Acute Form (85%) | Chronic Form (15%) |
|------------------|---|---|
| Clinical picture | Asymptomatic Flulike (10%) Pneumonia (47%) Granulomatous hepatitis (42%) | Endocarditis (1%–11%) Nonspecific hepatitis |
| Serology | IgG, IgM, or IgA antibodies Phase II antibodies | IgG or mostly IgA, little IgM Phase I antibodies |
| Mortality | Less than 1% | Up to 60% with cardiac involvement |
| Therapy | Doxycycline | Requires two antibiotics: rifampin and doxycycline, or a quinolone |

NOTE: Percentages indicate averaged prevalence as derived from references 5–7. Prevalences vary with geographical area.

The elevator led to a slaughterhouse where the sheep were immediately slaughtered. The two researchers then removed the carotids, kidneys, and placentas for their research procedures. The animal care technicians dismembered the animals and disposed of them in special containers.

Serologic samples from all the animal laboratory personnel (10 employees) and the two researchers were obtained. The testing was done using the immunofluorescent assay technique. Out of six persons exposed to the sheep, four had positive titers. The six persons not exposed to sheep had negative titers.

Discussion

In 1937, Derrick⁴ described Q fever in a group of slaughterhouse workers in Australia. Its agent, *Coxiella burnetii*, is endemic throughout the world; it commonly affects the genital tract of animals, including cows, sheep, goats, and cats, but rarely causes disease. Spread to man occurs usually by inhalation of the organism or contact with parturient material. It is believed that a single inhaled organism is sufficient to initiate infection.⁵

The incubation period of *C. burnetii* varies from 14 to 39 days, following which the illness may be asymptomatic, acute, or chronic.⁵ The variety in clinical presentations is believed to be due to both different *C. burnetii* isolates and unknown host factors.^{6,7} A comparison of acute and chronic syndromes is shown in Table 1. The commonest presentation is that of an atypical pneumonia with a benign illness resolving in 2 weeks. If the liver is involved, its histology shows a characteristic doughnut granuloma. In the chronic form the histology is nonspecific hepatitis and very rarely granulomatous.^{8,9} Our patient was found on biopsy to have periportal fibrosis, but no granulomas were detected.

The diagnosis of Q fever is usually based on serology. *C. burnetii* can exist in either of two antigenic states, labeled phase I and phase II. Antibodies to phases I and II are measured using an immunofluorescent assay technique. Acute Q fever is serologically confirmed when there are antibodies to phase II on the order of 256 or more of IgG, or of 64 or more of IgM, or when there is a fourfold rise in the IgG titers. Chronic Q fever is confirmed either when phase I titers are higher than phase II titers or when phase I titers meet the same criteria as described for phase II in the acute form.¹⁰

Outbreaks of Q fever in the United States usually occur in occupational settings in persons working in animal research laboratories or slaughterhouses.³ In our laboratory, the four persons with positive titers (phase II *Coxiella* titers higher than 256) were involved with animal surgery. The two with negative titers who had been exposed to sheep had participated in organ removal but were not involved in extensive surgery. Only one worker had symptoms (the identified case). The other three were asymptomatic. All animal handlers wore appropriate gowns and gloves, but some did not consistently wear surgical masks. The patient in our case had worn masks, gloves, and gown.

It is conjectured that the workers were infected through inhalation of particles splashed during surgery or dismembering of the animals. The precautions taken by providing separate access to the surgical room and disposal of the remains seem to have been appropriate since none of the other workers in the area had any change in the titers.

Identifying the illness in the one patient who had symptoms was difficult. This case illustrates the importance of obtaining an occupational history. The delay in diagnosis was due to ignorance about the patient's work with sheep and reliance on the fact that the suppliers test

the sheep for Q fever. It is important to keep in mind that testing of sheep is done randomly and does not fully guarantee safety, as even seronegative sheep may shed rickettsia.^{3,11} Using sheep from a closed flock known to be disease-free may be a safe approach, but following guidelines set for work with sheep in research³ is even more reassuring to workers. The recommendations are for a program of serosurveillance of persons at risk, skin tests for those who are nonimmune, the option of vaccination, and the evaluation and confirmation of suspect cases.³ It is only with such measures that clinical cases can be prevented, or detected and treated at an early stage.

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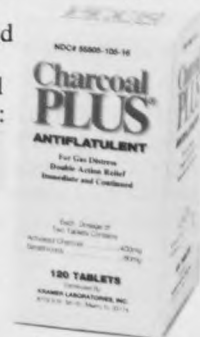
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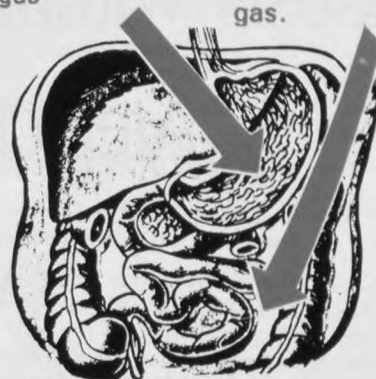
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