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M-I DRILLING FLUIDS
GREYBULL, WYOMING

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SUMMARY

In August 1992, the National Institute for Occupational Safety and Health (NIOSH) received a request from the Wyoming Department of Health to evaluate two cases of acute, febrile hepatitis among workers at a bentonite mine operated by M-I Drilling Fluids in Greybull, Wyoming. Subsequent blood tests indicated that the hepatitis was caused by *Coxiella burnetii*, the organism which causes Q fever. Q fever is a rickettsial disease, typically contracted by humans through the inhalation of dust or other materials contaminated by infected animal products. Q fever usually is manifested by fever, chills, muscle aches, and fatigue; occasionally, hepatitis, pneumonia, or other more serious disease results from infection by *C. burnetii*. For further information on Q fever, see appendix A.

From October 12-14, 1992, NIOSH representatives conducted a site visit to further characterize the cases of Q fever. NIOSH investigators surveyed 39 workers using a self-administered questionnaire and a blood test for antibodies to *C. burnetii*. Seven workers had serologic evidence of infection with *C. burnetii*, three displaying evidence of recent infection and four displaying evidence of past infection. Analysis of questionnaire data showed that the major risk factor significant for recent infection was sheep ownership. Risk factors suggestive of either recent or past infection included working outdoors, operating heavy equipment, and hunting.

As a comparison group, employees with similar demographic characteristics at a non-mining worksite were also tested and found to have fewer cases of infection; one case of past infection with *C. burnetii* was discovered.

Recommendations included maintaining a high index of suspicion for Q fever in persons with unexplained fever and influenza-like symptoms, hepatitis, or pneumonia; and reporting cases of Q fever to the state epidemiologist by physicians. Other recommendations, based on previous Q fever research, included avoiding contact with soil obviously contaminated with animal urine, feces, or birth products, as well as animals, particularly sheep and cats, who are giving birth. The last recommendation is directed in particular at pregnant women and persons with valvular heart disease.

On the basis of data obtained in this investigation, NIOSH investigators determined that a potential health hazard existed among employees working outdoors at the bentonite mining facility. A non-occupational risk factor, sheep ownership, was found to be important. The relative contribution of occupational and non-occupational risk factors could not be assessed. Recommendations for reducing morbidity and mortality associated with *Coxiella burnetii* infection include maintaining a high index of suspicion for Q fever in persons presenting with pneumonia, hepatitis, or unexplained fever; and avoiding contact with soil obviously contaminated with animal urine, feces, or birth products, as well as animals giving birth.

KEYWORDS: SIC 1459 (bentonite mining); Wyoming bentonite; Q fever; *Coxiella burnetii*; hepatitis, occupational, vector-borne

INTRODUCTION

In August 1992, the Wyoming Department of Health was notified of two cases of acute, febrile, non-A, non-B, non-C hepatitis in two men in northwestern Wyoming. Despite the hospitalization of one of the men and evaluation of the cases by an infectious disease consultant, the workers did not receive a specific diagnosis. Both men worked at a bentonite mine in Greybull, Wyoming, located about halfway between their respective homes. Suspecting a possible connection between the illness and the work site, the state epidemiologist contacted the National Institute for Occupational Safety and Health (NIOSH), requesting technical assistance in evaluating the potential occupational etiologies. After telephone interviews with the ill workers, a review of the medical records, and a discussion of the work site with the management, we requested that blood samples be sent for Q fever antibodies. The initial Q fever antibody titers, run at an outside lab, were negative in one of the workers and borderline in the other. Repeat samples were positive. NIOSH requested assistance from the Centers for Disease Control and Prevention (CDC), National Center for Infectious Disease (NCID), Division of Viral and Rickettsial Diseases (DVRD), Viral and Rickettsial Zoonoses Branch (VRZB), and made a coordinated visit to Wyoming on October 12, 1992.

BACKGROUND

Facility Description

The M-I Drilling Fluids facility consisted of the bentonite mine area, which covers a broad area of open land that is also used for grazing, the mill or processing area, and a storage area. At the time of our visit, 58 workers were employed--23 in the mine area, 22 in the mill area, and the rest in the office or lab areas.

Process Description

Bentonite is a naturally-occurring clay formed from volcanic ash. It has the property of being highly absorbent. It is used as a drying agent, as an animal feed additive, and in a variety of ointments. It is considered biologically inert. There are few reports of adverse reactions to it, limited mainly to skin and eye irritation. Bentonite is mined in open pits. It is piled up in the mine area, allowed to dry, and then transported to the processing and packaging areas. After additional moisture is removed, the bentonite is ground and then loaded or bagged.

EVALUATION PROCEDURES

Environmental

A tour of the facility, including a walking tour of the enclosed structures and a driving tour of the main mine roads, was conducted to look for potential sources of *C. burnetii*, such as areas in which workers might have come into contact with animals. Six soil samples were taken from different sites throughout the mine area for analysis for *C. burnetii* by polymerase chain reaction (PCR).

Medical

Although NIOSH and NCID conducted a joint investigation, each had separate goals. The goals of the NIOSH investigation were to determine the number of workers currently infected with Coxiella burnetii, either recently or remotely, as well as the number of workers who had experienced symptoms consistent with Q fever over the six months prior to our visit. We also wanted to look for possible sources of infection, identify possible workplace risk factors, and educate management and employees about Q fever.
The goal of the NCID investigation was primarily to conduct a community investigation, consisting of case-finding, testing possible animal reservoirs in the area, and locating a comparison group for the miners' study. The NCID investigator also wanted to educate local health care workers about Q fever.

NIOSH

A self-administered questionnaire was distributed to current employees; it sought information concerning demographic variables, work practices, exposure to animals in and out of the workplace, as well as medical history, with emphasis on symptoms of Q fever. A 10-milliliter (ml) blood sample was requested from each person after informed consent was obtained. The blood samples were analyzed antigens at NCID laboratories using an indirect fluorescent antibody (IFA) assay. Each blood sample was screened for IgG antibodies to phase II antigen. A positive sample was defined as having a titer greater than or equal to 1:64. The positive samples were then further tested for IgM antibodies to phase II antigen and IgG antibodies to phase I antigen in an effort to determine whether the infection was recent or remote.

NCID

The NCID investigation began with case-finding. The study population included mine-workers' family members who had heard about the investigation and came forward for testing; persons identified through medical record research as possibly having Q fever; and a number of "volunteers" from the community who sought out the NCID investigator upon hearing of the study. A total of 27 participants completed questionnaires and had blood samples drawn for Q fever testing.

Animal testing was accomplished by collecting blood samples from deer, elk, and antelope carcasses brought to the two meat processing facilities in the Greybull area. Twenty-five of the samples collected from deer were suitable for testing. In addition, serum from local cattle herds, collected for routine brucellosis testing, was requested to be forwarded to NCID for *C. burnetii* antibody testing.

Employees of the Wyoming Transportation Department (WTD), located in Basin, eight miles south of Greybull, were selected as a comparison group for the bentonite mine workers. They were selected because they were an easily identifiable group, since the highway department was one of the few large employers in the area, and the outdoor work activities of this group were

similar to those of the mine employees. Of the 43 employees present on the day of the survey, 27 (63%) completed questionnaires, and of these, 25 (58%) submitted a blood sample for Q fever testing.

Case definition

The case definition for Q fever was based entirely on the results of serological testing, using the same case definition used by CDC in the laboratory-based surveillance of 1985.[1] A case of recent or current acute Q fever was defined as a single IgM titer of ≥1:64, or a single IgG titer of ≥1:256. Persons with an IgG titer of at least 1:64 but below 1:256 were considered to have had past infection with *C. burnetii*. This was also called "remote" infection.

Analysis

Univariate analysis of the workers' questionnaires was performed using EpiInfo version 5.01a[2] to define risk factors for infection with *C. burnetii* in our populations. A variety of exposures were examined to determine risk factors for infection with *C. burnetii*, separately analyzed for recent or remote infection. These exposures included where the workers spent the majority of their work day, type of equipment used, contact with animals in the workplace or away from work, and hobbies.

RESULTS AND DISCUSSION

Participation

Forty-seven (81%) of the 58 current mine employees completed the questionnaire. Thirty-nine (67%) submitted serum samples for testing.

Thirty-six of the 39 participants (78%) were white men; the mean age was 46 years (range of 24-64 years). Most lived in Greybull; others lived within a 50 mile radius of the town. The mean length of employment was 15 years (range of 1-40 years). Most worked 9-12 hour days, 4-5 days per week. (See Table 1.)

Serological results

Three mine employees met the case definition for recent or current acute Q fever. Included in this number were the two "index" cases. All three affected workers had experienced symptoms consistent with Q fever in the six months prior to our investigation. Two of these workers had both elevated IgG and IgM titers; the third had only an elevated IgG titer. Three other mine employees had IgG titers of 1:64, and another had an IgG titer of 1:128, indicating past infection. These persons had not experienced symptoms of Q fever in the six months prior to the investigation.

Two ill community members had IgG titers of 1:256 or above. One of these was an adult member of a mine employee's family, and the other had been identified through the medical record search. One employee of the Wyoming Transportation Department had a titer of 1:64. He had not been ill in the previous six months.

Cattle from two ranches, one in Big Horn County, where Greybull is located, and one in an adjacent county, were tested for antibodies to C. burnetii. Three (21%) of the 14 cattle sera from the ranch in Big Horn County were positive for IgG antibodies at ≥1:64. None of the 12 cattle sera from the ranch in the adjacent county was positive. None of the 25 deer sera was positive for antibodies to Coxiella burnetii.

Risk factors

Sheep ownership was the only statistically significant factor which correlated with recent infection (odds ratio (OR)=70.0; confidence interval (CI)=2.0-13500). (See Table 2.)

Spending the majority of the workday outdoors was a suggestive but not statistically significant risk factor for being infected with *C. burnetii* either recently or remotely (OR 8.8; CI=0.9-425.1). (See Table 3.) Two of the three recently ill employees worked outdoors in the mine area; the third worked in the packaging area. The four employees who had evidence of past infection worked in the mine area. Among those who worked outdoors, heavy equipment operation was not a statistically significant risk factor, although five of the six outdoor workers infected with *C. burnetii* operated heavy, earth-moving equipment. This work was associated with an odds ratio of 2.2, but a confidence interval which included one. (See Table 3.) Given the plausibility of such dust-generating activity being a risk factor for infection, it is possible that, with a larger sample size, this would be a true association.

The hobby of hunting was associated with recent or remote infection (OR 7.8; lower 95% confidence limit 1.04; p=0.045). Fishing was associated with an odds ratio of 6.9 (lower 95% confidence limit 0.91; p=0.0625). (See Table 2.) It should be noted that these are not independent variables, as persons who hunt were much more likely to fish, and vice versa, in this population.

The following difference between the "outdoor" workers and the "indoor" workers was noted: 95% of "outdoor" workers owned animals compared with 75% of the "indoor" workers. This may be a confounder. A confounder is something which is related to exposure and affects the outcome being studied, but which is not included in the original hypothesis. In this case, owning animals provides an additional potential exposure to *C. burnetii*, which may place animal owners at higher risk for infection; the fact that more "outdoor" workers than "indoor" workers own animals may explain their higher rate of infection, rather than the fact that they are "outdoor" workers. This difference in animal ownership failed to achieve statistical significance. The numbers were too small to permit further analysis to answer this question. An equal proportion of "outdoor" and "indoor" workers hunted or fished. (See Table 4.)

Comparison

The bentonite mine workers were compared to the Transportation Department workers to test the hypothesis that the mine area was a risk factor for infection with *C. burnetii*.If the infection rates are compared, the prevalence odds ratio for recent infection was 2.6 (lower 95% CI=0.27). Three of 39 mine workers and none of 25 Transportation Department workers tested positive for recent Q fever. The risk of ever being infected with *C. burnetii*, however, appeared to be higher among the miners, although this prevalence odds ratio of 4.6 had a 95% confidence interval which included one. (See Table 5.) Seven of 39 mine workers and one of 25 Transportation Department workers tested positive for infection with *C. burnetii*.

The workers at the Wyoming Department of Transportation were demographically similar to the bentonite miners studied. Twenty-one of the 25 workers were white men; the mean age

was 45 years (range of 25-64). Most lived in Basin. Mean length of employment was 10 years (range 1-31 years). (See Table 1.)
A similar proportion of mine workers and Transportation Department workers worked outdoors--49% versus 40%. This difference was not statistically significant. However, a significantly higher proportion of the mine workers reported having contact with animals in the workplace--59% versus 32%. Also, a significantly greater percentage of mine workers operated earth-moving, heavy equipment--36% versus 12%. (See Table 6.)

A smaller percentage of the mine workers owned animals, 87% compared to 92%, but a higher percentage--72% versus 52%--reported having contact with animals away from the workplace. (See Table 7.) Neither of these differences was statistically significant. Equal proportions of the mine workers and the Transportation Department workers hunted or fished. (See Table 7.)

Environmental

Due to technical problems with the PCR equipment, the soil samples were not analyzed.

Limitations

The study was limited by a number of factors. The number of workers studied was small, which limited the statistical power and ability to perform more sophisticated analysis. The small numbers may also have influenced the confidence intervals, because they affect the standard error measurement (make it larger) upon which the confidence interval calculation is based. The major risk factor for Q fever, contact with animals, is common among the members of the study population, both at and away from the workplace, making the relative contributions of occupational and non-occupational contact difficult to assess. Quantifying exposure to animals is difficult to do, and so the reliability of our exposure information is uncertain. In addition, difficulties in making the diagnosis of Q fever, even with serologic testing, makes it possible that there were a number of false negatives. Several of the persons may not yet have mounted an antibody response despite being infected.

CONCLUSIONS

1. *Coxiella burnetii* is present in Big Horn County, and persons there are at risk for contracting Q fever.2.Outdoor work was a risk factor for acquiring Q fever among the workers at the bentonite facility, as was hunting. Operation of heavy equipment may also be a risk factor.

3. Ownership of sheep correlated with recent acute Q fever in this investigation. Ownership of animals, especially small pets, may also be a risk factor for infection with *C. burnetii*.

4. Working at the bentonite mine may have been a risk factor for infection with *C. burnetii*.

RECOMMENDATIONS

1. Physicians and other health-care providers should maintain a high index of suspicion for Q fever in persons presenting with hepatitis, pneumonia, or unexplained febrile or influenza-like illness, especially if there is a history of contact with or work near animals or areas in which animals live.

2. Avoid contact with soil obviously contaminated with animal urine, feces, milk, or birth products. This is directed especially at persons with valvular heart disease or pregnant women.

3. Because Q fever is a notifiable disease in Wyoming, physicians, laboratory workers, and other health-care providers should report cases to the state epidemiologist.

4. Further study may help answer some of the questions raised by this investigation. For example, a limited active surveillance study in an endemic area such as this would yield useful information about incidence and prevalence as well as more specific data on risk factors.

AUTHORSHIP AND ACKNOWLEDGMENTS

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2. Wyoming Department of Health
3. Employee representatives
4. OSHA Regional Office

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TABLE 1

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DEMOGRAPHICS

39 Mine Workers

Mean age (range)	46 years	(24-64)
Sex	36 men	3 women
Race	38 white	1 Hispanic
Mean employment length (range)	15 years	(1-40)

25 Wyoming Transportation Department Workers

Mean age (range)	45 years	(25-64)
Sex	21 men	4 women
Race	25 white	0 other
Mean employment length (range)	11 years	(1-31)

TABLE 2

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NON-WORKPLACE RISK FACTORS

Recent Infection

Exposure	Odds Ratio	95% CI*
Sheep ownership	70.0	2.0-13,500

Recent or Remote Infection

Exposure	Odds Ratio	Lower 95% CL**
Hunting	7.8	1.04
Fishing	6.9	0.91

*Confidence interval
**Lower 95% confidence limit (CL) used because an empty cell was present. These values were obtained using log exact methods (LogXact).[3]

TABLE 3

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WORKPLACE RISK FACTORS

Recent or Remote Infection

Exposure	Odds Ratio	95% CI*
Outdoor work --heavy equipment use	8.8 2.2	0.9-425.1 0.2-131.0

*Confidence interval

TABLE 4

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POSSIBLE CONFOUNDERS: OUTDOOR *VS.* INDOOR WORKERS

39 Mine Workers

Exposure	Outdoor 19 participants	Indoor 20 participants
Own animals	18 (95%)	15 (75%)
--livestock	9 (47%)	13 (65%)
--sheep	1 (5%)	0
--pets	18 (95%)	14 (70%)
Hunt	12 (63%)	12 (60%)
Fish	12 (63%)	13 (65%)

TABLE 5

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OCCURRENCE OF INFECTION: MINE WORKERS *VS*. WTD WORKERS

Mine Workers vs. WTD Workers

Infection	Prevalence Odds Ratio	95% CI*
Recent	2.6	0.27**
Remote	4.6	0.5-212.8

*Confidence interval
**Lower 95% confidence limit used because an empty cell was present. These values were obtained using log exact methods (LogXact).[3]

TABLE 6

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EXPOSURE COMPARISON: WORKPLACE EXPOSURES

Mine Workers vs. WTD* Workers

Exposure	Mine Workers 39 participants	WTD Workers 25 participants
Outdoor work	19 (49%)	10 (40%)
Work contact with animals	23 (59%)	8 (32%)
Heavy equipment	14 (36%)	3 (12%)

*Wyoming Transportation Department

TABLE 7

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EXPOSURE COMPARISON: NON-WORKPLACE EXPOSURES

Mine Workers vs. WTD* Workers

Exposure	Mine Workers 39 participants	WTD Workers 25 participants
Own animals	34 (87%)	23 (92%)
Non-work contact with animals	28 (72%)	13 (52%)
Hunt	24 (61%)	15 (60%)
Fish	25 (64%)	16 (64%)

*Wyoming Transportation Department

APPENDIX A

Q Fever

Q fever is a disease caused by the rickettsia *Coxiella burnetii*. *C. burnetii* is extremely infectious; a single inhaled organism may be all that is necessary to initiate disease.[4] The organism is hardier than most rickettsiae, resistant to desiccation as well as most physical and chemical agents. It has been reported to survive for months in the soil.[4]
Natural reservoirs for *C. burnetii* include ticks[5]--Dermacentor, Amblyomma, Ixodes, and Haemaphysalis--and a variety of animals, including cattle, sheep, goats, and cats. Animals typically have a subclinical course, even while shedding the organism in high numbers in urine, feces, milk, and, especially, amniotic fluid.[4]

Q fever is usually contracted through direct or indirect contact with infected animals or animal products. Most often, this occurs through inhalation of dust contaminated by the urine, feces, milk, or amniotic fluid of an infected animal.[4] There are reports of disease occurring after handling infected animal skins or drinking contaminated unpasteurized milk.[6] There is no documented transmission of *C. burnetii* from ticks to humans, although it is possible that ticks are responsible for spreading the organism among animals.[4] There have been no reports of human to human transmission of Q fever, with the exception of one report of spread by blood transfusion.[5]

The incubation period for Q fever averages 19-20 days, with a range of 14-39 days.[6] The clinical manifestations vary from mild (it can go almost unnoticed) to debilitating. Typically, the symptoms are similar to influenza. The first symptom is often chills, perhaps rigors, accompanying a fever of up to 105°F.[4] Headache, muscle aches, fatigue, anorexia, and malaise predominate. Chest pain, cough, and abdominal pain may also occur. These symptoms may last days to weeks, but rarely last longer than two weeks. Elderly persons are more likely to have a more protracted course,[4] with symptoms lasting up to four weeks. Even after resolution of the acute symptoms, many persons continue to feel generally weak. However, these symptoms, too, typically resolve within 4-6 weeks. Another manifestation of Q fever is pneumonia. Also, up to 1/3 of persons infected with *C. burnetii* develop hepatitis.[5]

Acute Q fever, including pneumonia and hepatitis, usually resolves over a period of weeks without intervention.[6] In a small proportion of persons, however, Q fever becomes a chronic disease typically manifested by endocarditis. This usually evolves slowly, occurring up to 20 years after acute infection. Persons at higher risk include those with heart valve abnormalities.[4] Q fever endocarditis is a much more serious disease than acute Q fever. It is difficult to treat, responding poorly to antibiotics, often requires surgical valve replacement, and is frequently fatal.[4]

Some unusual manifestations of infection with *C. burnetii* include neurologic manifestations, such as encephalitis in children, hemolytic anemia, and infertility and miscarriage.[6]

Epidemiology

The incidence and prevalence of infection with *C. burnetii* among humans and other animals is not entirely clear. It has been described throughout the world.[4] Several attempts have been made at estimating the incidence of Q fever or prevalence of infection with *C. burnetii* among humans, cattle, and sheep. Among humans, reports have ranged from less than 1% to 30%, with rural areas having a higher seroprevalence. Animal seroprevalence varies by region and species.[7]

In the United States, where reporting of Q fever cases to CDC is voluntary, several efforts have been made to determine the occurrence and distribution of cases. Conclusions from these investigations included that it is difficult to determine the incidence and distribution of Q fever in the U.S.; that it may occur more often than it is reported or diagnosed; but, that it occurs infrequently.[8] Wyoming, where Q fever is a reportable disease, has only two recorded cases in the past 11 years. Prior to that, in the years 1948-1977, 10 cases had been reported.[8]

Diagnosis

The diagnosis of Q fever rests primarily on serologic testing. Although complement fixation (CF) and enzyme-linked immunosorbent assay (ELISA) methods are used, the indirect fluorescent antibody assay (IFA) is the most widely used test and allows detection of various immunoglobulin isotypes, as well as the antigenic phase variation.[6] This can be helpful in establishing the acuteness of the infection. Specific IgM antibodies can be detected as early as 7 days after exposure.[5] Most people appear to have an IgM antibody response within the first two weeks, but others may have a delayed response. IgG antibodies may persist for a longer period of time.

Therapy

In acute Q fever, tetracycline or doxycycline, if administered within the first three days of illness, may reduce the duration of fever.[6]

In Q fever endocarditis, optimal antimicrobial therapy has not been fully defined. Various combinations have been suggested, with treatment duration ranging from 12 months to an indefinite period.[6]

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