Q Fever

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Bandera, TX
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Texas Department of State Health Services
Canyon, TX
EVALUATION OF COXIELLA BURNETII IN RURAL AND URBAN ENVIRONMENTS

Q Fever

1937

Febrile illness in abattoir workers in Queensland, Australia

(query fever)

Coxiella burnetti (Cox and Burnet)
**Coxiella burnetii**

- **Obligate intracellular bacteria**
- **Infects humans and many animal species**
- **Worldwide distribution**
- **Human disease = Q fever**
  - Monocyte/macrophage infected
  - Acute - flu-like febrile illness
    - Pneumonia
    - Hepatitis
  - Chronic - endocarditis
    - France
      - 348 cases of culture negative endocarditis
      - 167 (48%) Q fever
**Coxiella burnetii**

- Both DHHS and USDA select agent
- Potential bioterrorism weapon:
  - Spore-like form (small cell variant)
  - Resistant to environmental conditions and many disinfectants
  - Aerosol route of infection
  - Single particle infectious
  - *C. burnetii* weaponized in 1960’s
- Category B bioterrorism agent
  - Treatable – doxycycline
  - Few fatalities from acute infection
US

1946

Outbreaks in:
Packing house workers in Chicago
Livestock sale yard employees and packing house workers in Amarillo
Coxiella burnetii

Nucleus

SCV

LCV
**Affected Species**

- Cattle
- Goats
- Sheep
- Cats
- Dogs
- Avian
- Rodents
- Ticks
- Horses
- Camels
- Rabbits
- Swine
- Water Buffalo
Some Key Q Fever Symptoms

Almost all patients suffering from acute Q fever pneumonia present with a fever, usually associated with fatigue, chills, headaches, myalgia, and sweats.

Headaches are often severe and retroorbital

Radiographic findings may include single or multiple opacities of rounded configuration, increased reticular markings, atelectasis, and pleural effusion

Cough was recorded in 24 to 90% of infected patients in different series of Q fever patients

Human Exposure

Method

- Aerosol – inhalation, m.m.
- Ingestion
- Transplacental
- Autopsies
- Intradermal inoculation
- Blood transfusion
- Abortion/Parturition
- Arthropod ???
Sources of Exposure/Environmental Contamination

Animal parturition:

$>10^9$ bacteria/gram of placenta

(4.5 x $10^{12}$ bacteria/avg. bovine placenta)

Feces

Urine
Q-fever Infection

- Dose, strain and host factor dependent
  - (1 cell is all that is needed to infect)

- Agricultural association

- 1-3 week incubation

- “flu-like illness”

- Multiple syndromes
# Q-fever Infection

## Acute
- Fever - Prolonged/Undulating
- Pneumonia
- Hepatitis
- Myocarditis
- Pericarditis
- Skin Rash
- Meningoencephalitis
- 13 others

## Chronic
- Endocarditis
- Vascular Inf.
- Osteoarticular Inf.
- Hepatitis
- Pulmonary Inf.
- Chronic fatigue syndrome
Q Fever in the USA?

- Prevalence in cattle (McQuiston et al, 2005)
  - Milk from veterinary school dairy herds tested
  - 92% of herds seropositive

- North Dakota sheep ranchers – 3.4% positive

- Montana dairy farmers – 19.5-38.2%

- Manitoba, Canada – 15.9% general population

- Colorado 2005 – 10% general population

Active surveillance needed
# Community Acquired Pneumonia

- Generally affects patients \( \geq 65 \) years
- \( \sim 5 \times 10^6 \) cases annually (CDC estimate)

**Major bacterial spp. seen in:**

<table>
<thead>
<tr>
<th>Outpatients</th>
<th>Non-ICU:</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td><em>Streptococcus pneumoniae</em></td>
</tr>
<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td><em>Mycoplasma pneumoniae</em></td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td><em>Haemophilus influenzae</em></td>
</tr>
<tr>
<td><em>Chlamydophila pneumoniae</em></td>
<td><em>Chlamydophila pneumoniae</em></td>
</tr>
</tbody>
</table>

- UK estimation of 1% of CAP due to *C. burnetii*
Q Fever Cases in USA?

UK
- ~ 1% of community-acquired pneumonia (CAP) estimated due to Q fever = 700 cases
- > 100 q fever cases/year

USA
- ~ 5 million cases CAP/year
- 1% estimate = 50,000 cases of Q fever
Number of Annual Q Fever Cases, 1998-2010

- **Q Fever, Before 2008**
- **Acute Q-Fever**
- **Chronic Q-Fever**

**Year of Report**

- 1998
- 1999
- 2000
- 2001
- 2002
- 2003
- 2004
- 2005
- 2006
- 2007
- 2008
- 2009
- 2010
Issues for the Attending Physician

The list of primary drugs of choice for the most common causes of CAP generally does not include the drug of choice for acute Q fever – *doxycycline*

Some *C. burnetii* strains are resistant to the drugs commonly used for CAP

Improper treatment may lead to chronic infection

Sero-conversion may take 3-4 weeks:
- 2nd week: 10%
- 3rd week: 50%
- 4th week: 70%
Effects of Stress

Guinea Pig Model

Infected animals became culture and sero-negative

Treatment with cyclophosphamide, high steroid doses or radiation resulted in recrudescence of infection
Q Fever Diagnosis

- Patient history
- Age
- Environment
- Paired sera
1999: Q fever became a nationally notifiable disease.

Natural prevalence of *C. burnetii* unknown.

Preliminary study undertaken to determine background levels as a baseline for testing in the event of a bioterrorism attack.
Study Design

3 locations selected in cooperation with the state and local public health departments.

9 sample sites - urban and rural sites.

~10 environmental samples were taken from each site.
Sites Sampled

- Governmental
- Commercial
- Agricultural
- Social
Sites

- Dairies – 3 Cattle, 1 Goat
- Feedlot – 1 Cattle, 1 Sheep
- Ranch - 1
- Sale Yard – 1
- Research Farms – 2
- Veterinary Clinic – 1
- Post Office – 1
- Schools – 3
- Social Clubs – 2
- Livestock Exhibition venues – 2
- Businesses – 5
- Animal Control -1
- FFA club site – 1
- Local Health Dept. - 1
Samples

Surface swabs taken with pre-moistened sponges

Bulk soil samples

Vacuum filter samples

Type of samples determined by what was most appropriate for each site
Floor Mats
Bulk Samples
# Results

<table>
<thead>
<tr>
<th></th>
<th>Non-Ag Positive</th>
<th>Ag Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sites</td>
<td>69% (9/13)</td>
<td>50% (7/14)</td>
</tr>
<tr>
<td>Samples</td>
<td>17% (29/173)</td>
<td>8% (14/165)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined Positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sites</td>
<td>59% (16/27)</td>
<td></td>
</tr>
<tr>
<td>Samples</td>
<td>12% (43/338)</td>
<td></td>
</tr>
</tbody>
</table>
Q Fever

M. Maurin and D. Raoult

*Clinical Microbiology Reviews, Oct. 1999, p. 518-553*
Investigation of a Q Fever Outbreak in the Texas Panhandle

Investigating A Suspected Q Fever Outbreak

James L. Alexander, DVM, MPVM
Zoonosis Control Division
Texas Department of Health
Canyon, Texas
Coxiella burnetii

Source of Organism

Birthing fluids, urine and feces of livestock and cats and dogs
The Panhandle has an abundance of livestock.

*Coxiella burnetii*
Coxiella burnetii

- The Panhandle has an abundance of wind
Coxiella burnetii

- Spreads by aerosolization of contaminated dust/soil

- West Texas has plenty of aerosolized dust and soil
A Light Breeze in the Panhandle
June 12, 2008

Late in the day began receiving calls about an illness at an ethanol plant construction site at Hereford, Texas.

Symptoms reported were more consistent with food-poisoning.

Workers were going to the hospital to be tested for Q fever.
June 13, 2008

- Met with personnel from the company that owned the ethanol plant
- Met with Hereford City Officials
- Participated in media interviews
- Visited Infection Control Nurse @ hospital
Hereford is known for feedlots
“The Beef Capital of the World”
Manure-fueled Ethanol Plant
Companies

14 were on site during the 60 days prior to the "discovery" of q fever titers in the work force

The majority left that Friday or in the next week

Interviews and follow-up testing delayed

Many returned in late July but some were lost to follow-up
Investigation

198 people received at least 1 test

- 36 people received at least 2 tests
- 5 people were tested 3 times
- 238 samples collected
- No one that did not already have a titer of $\geq 128$ developed a higher titer
Surveyed Population

Of 198 Workers Tested

- 17 had titers ≥ 128 (8.6%)
- 1:4096 was the highest titer based on a retest of the index case
122 (62%) of the “Tested” people were interviewed

- 15 of the 17 with titers
- 5 asymptomatic (33.3%)
- 10 symptomatic (67.7%)

• 42 interviewees with compatible symptoms (32 w/o titers)
• 80 interviewees without compatible symptoms (5 with titers)
Tested Population

- 15 Females (7.6%)
  - Age: 22 - 52
    - 2 with ≥ 128 (13.3%)
      - Ages 22 and 48 (mean = 35)
  - 13 without titers
    - Ages 23-52 (mean = 37.8)
Tested Population

- **183 Males (92%)**
  - **Age:** 18 - 69
    - **15 with ≥ 128 (8.2%)**
      - **Age:** 19-61 (mean = 40.6)
    - **168 without titers**
      - **Ages 18 - 69 (mean = 39.8)**
Information Obtained

- Demographics and health history
- Work location on site
- Job title/occupation
- Past livestock exposure
- Animal exposure in past 60 days
- Exposure to aborting animal
- Illness and symptoms
- Use of PPE
- Proximity to manure
# Predominant Symptoms of “Cases” and Non-titered People Reporting Illness

<table>
<thead>
<tr>
<th>Symptom</th>
<th>“10 Cases”</th>
<th>“32 Non-cases”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weakness</td>
<td>10 (100%)</td>
<td>24 (75%)</td>
</tr>
<tr>
<td>Malaise</td>
<td>8 (80%)</td>
<td>22 (69%)</td>
</tr>
<tr>
<td>Chills</td>
<td>7 (70%)</td>
<td>22 (69%)</td>
</tr>
<tr>
<td>Sweating</td>
<td>7 (70%)</td>
<td>21 (66%)</td>
</tr>
<tr>
<td>Headache</td>
<td>6 (60%)</td>
<td>27 (75%)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>4 (40%)</td>
<td>17 (53%)</td>
</tr>
<tr>
<td>Lymphadenitis</td>
<td>3 (30%)</td>
<td>4 (12.5%)</td>
</tr>
</tbody>
</table>
Evaluated

- Proximity to manure – not significant
- Employer – not significant
- Prior contact with livestock – not significant
Plant Owner Modifications

- Tarp to block wind at unloading site
- Water misting during manure unloading
- Removal of grinder from manure processing system
- Halting manure delivery when wind direction was from the manure site toward areas occupied by personnel
Actions Taken by Contractor

- Invited OSHA to visit - declined
- Invited NIOSH to visit – accepted
- Required Tyvek© suits and respirators
- Established PPE zones
NIOSH Recommendations

- No Tyvek suits
- Shower and laundry facilities on-site
- No work clothes or footwear to leave the site
- Move the contractor office trailers and install running water to improve hand sanitation
- Medical screening for symptomatic personnel
- Cleaning shoes at office doorways and proper cleaning techniques for offices
- Appropriate respiratory-protection equipment based on the job function
Q FEVER IN THE PANHANDLE
THE SAGA CONTINUES

James L. Alexander, DSHS
Kelly Fitzpatrick, CDC
Lindsay Oliver, CDC
Gilbert Kersh, CDC
Robert Massung, CDC
Kevin McClaran, DSHS
“What is the prevalence of antibodies to q fever in the Panhandle population?”
Netherlands

- 2009: 2,357 new human q fever cases
  - US 43,855 (109)

- Slaughtered about 62,500 pregnant goats and sheep

- 455,000 doses of vaccine distributed

- Vaccinated about 90% of sheep/goat herds
DSHS collaborated with the local blood bank

IRB approval obtained

Donors were apprised of the project, given a fact sheet and asked if they would participate

DSHS provided a vacuum tube which the phlebotomists used when collecting the routine samples for screening tests.

A questionnaire was administered by a DSHS representative.
2009 Sero-survey for Q-fever

- 589 donors in the study
- 19 blood drive events in 17 counties
Residents from 23 counties participated

Tubes were centrifuged, serum was pipetted and samples were stored on dry ice until they could be placed in a Revco® @ -80° C

Held @ -80° C until shipped to CDC for testing.
2009 Sero-survey for Q-fever

CDC Test Protocol

- All samples screened by ELISA
- All ELISA positive/equivocal samples tested by IFA @ 1:16
- Samples reactive @ 1:16 were titrated to their endpoint
Prevalence

589 samples utilized in the study

Antibody prevalence:

10.7% in 589 people from 23 Counties
# Prevalence

<table>
<thead>
<tr>
<th>Counties</th>
<th>Donation Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>6 Counties with 0%</strong></td>
<td><strong>2 Sites with 0%</strong></td>
</tr>
<tr>
<td>1-6 donors (14)</td>
<td>8 and 35 donors (43)</td>
</tr>
<tr>
<td><strong>9 Counties with 3-8%</strong></td>
<td><strong>10 Sites with 3-8%</strong></td>
</tr>
<tr>
<td>19-99 donors (385)</td>
<td>12-80 donors (350)</td>
</tr>
<tr>
<td><strong>8 Counties with 16-50%</strong></td>
<td><strong>8 Sites with 19-43%</strong></td>
</tr>
<tr>
<td>5-68 donors (190)</td>
<td>4-72 donors (196)</td>
</tr>
</tbody>
</table>
Symptoms

Do you recall having an illness, possibly lasting 7 days or more, that began suddenly with fever, chills, profuse sweating, muscle and joint pains, severe headache and fatigue for which a definitive diagnosis was not made?
Symptoms

11.1% of people with sero-positive results said “Yes”

Male (6): 14%
Female (1): 5%
All White Non-Hispanic
Symptoms

10.3% of people with negative results also said “Yes”

Male (23): 8.7%

Female (31): 12%
# Age Data

<table>
<thead>
<tr>
<th>Positives:</th>
<th>All</th>
<th>Pos</th>
<th>Neg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>18-82</td>
<td>18-76</td>
<td>18-82</td>
</tr>
<tr>
<td>Mean</td>
<td>46.3</td>
<td>46.4</td>
<td>46.2</td>
</tr>
<tr>
<td>Median</td>
<td>48</td>
<td>49</td>
<td>48</td>
</tr>
<tr>
<td>Mode</td>
<td>53, 55</td>
<td>38, 49, 51</td>
<td>55</td>
</tr>
</tbody>
</table>
## Demographics
### Racial Percentages

<table>
<thead>
<tr>
<th>Race</th>
<th>Survey</th>
<th>Popn</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Non-Hispanic</td>
<td>85.6</td>
<td>62.8</td>
</tr>
<tr>
<td>Hispanic</td>
<td>12.7</td>
<td>29.3</td>
</tr>
<tr>
<td>Black Non-Hispanic</td>
<td>0.3</td>
<td>5.4</td>
</tr>
<tr>
<td>Amer. Indian/Alaskan Native</td>
<td>0.7</td>
<td>1.0</td>
</tr>
<tr>
<td>Asian-Pacific Islander</td>
<td>0.2</td>
<td>1.4</td>
</tr>
<tr>
<td>Black Hispanic</td>
<td>0.2</td>
<td>NA</td>
</tr>
<tr>
<td>None Provided</td>
<td>0.3</td>
<td>NA</td>
</tr>
</tbody>
</table>
US Sero-prevalence Study


2003-2004

Stratified for age

Part of the National Health and Nutrition Examination Survey program
## Comparison of Studies

<table>
<thead>
<tr>
<th></th>
<th>Anderson, et al(^1) (≥20 y.o.)</th>
<th>Panhandle (≥ 18 y.o.)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sample Size</strong></td>
<td>4437</td>
<td>589</td>
</tr>
<tr>
<td><strong>Sero-prevalence</strong></td>
<td>3.1%* ((≥1:16))</td>
<td>10.7% ((≥1:128))</td>
</tr>
</tbody>
</table>

* Weighted pop\(^n\) estimate

1 Seroprevalence of Q Fever in the United States, 2003–2004
# Comparison of Studies

<table>
<thead>
<tr>
<th></th>
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<th>Panhandle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male +</td>
<td>3.8%</td>
<td>14%</td>
</tr>
<tr>
<td>Female +</td>
<td>2.4%</td>
<td>7%</td>
</tr>
<tr>
<td>Male:Female</td>
<td>1.5:1</td>
<td>2:1</td>
</tr>
<tr>
<td>Age Risk</td>
<td>Age Risk</td>
<td>No Effect</td>
</tr>
</tbody>
</table>

**Seroprevalence of Q Fever in the United States, 20**
### Comparison of Studies

<table>
<thead>
<tr>
<th></th>
<th>Anderson, et al</th>
<th>Panhandle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male vs Female</td>
<td>1.5 OR (1.0-2.3)</td>
<td>2.1 OR (1.2-3.8)</td>
</tr>
<tr>
<td>White Non-Hispanic</td>
<td>2.8%</td>
<td>10.4%</td>
</tr>
<tr>
<td>Hispanics</td>
<td>7.4%</td>
<td>10.7%</td>
</tr>
<tr>
<td>Geometric mean (Phase II IgG)</td>
<td>95 (16 - 4096)</td>
<td>597 (64 - 65536)</td>
</tr>
</tbody>
</table>
Panhandle Study Limitations

- Of 19 counties with more than 1 participant, 5 were under-represented and 14 were over-represented.

- Residents of 4 counties provided 50% of the samples

- 2 of those counties (large pop) were over represented and 2 (moderate pop) were under represented
Study Limitations

- Used healthy blood donors
- Racial/ethnic representation did not match the area’s diversity
- Convenience sample
- Not stratified for age
Conclusions

- Exposure to *Coxiella burnetii* appears to be significant in some parts of the Texas Panhandle.

- If the healthy, blood donor population has a 10.7% prevalence, it is logical to suspect that a random sample across our population might detect a higher prevalence.

- Analysis continues to examine risk factors, including occupation, association with livestock and location of residence.
Important Points About Q-fever

• *C. burnetii* prevalence is high in both urban and rural settings that were sampled

• Q-fever is under diagnosed

• Q-fever seroconversion may be delayed
  - 2\(^{nd}\) week: 10%
  - 3\(^{rd}\) week: 50%
  - 4\(^{th}\) week: 70%

• CAP cases in US should be evaluated

• Cats should be surveyed
Important Points About Q-fever

- Dahlgren, et al, estimate that at least 13 cases of q fever are undiagnosed for everyone detected.

- They also estimated that in two reporting systems, deaths are underreported by factors of 5 (MCD) and 14 (CRF).

- Healy, et al, found only a 35% concordance between three reference labs on the same samples.
Unidentified Agent in the Panhandle

- 3 Patients with pneumonia treated with standard antibiotic protocols
- All with symptoms compatible with Q Fever
- All lived in Hereford, TX
- All were on vents and considered terminal
- Doxycycline was added to regimen
- All recovered
- All negative for Q Fever on serology
James L. Alexander, DVM, MPVM, DACVPM

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