

Q Fever

2015 LRN Meeting

Bandera, TX

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Texas Department of State Health Services

Canyon, TX

EVALUATION OF *COXIELLA BURNETII* IN RURAL AND URBAN ENVIRONMENTS

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Q Fever

1937

**Febrile illness in abattoir workers
in Queensland, Australia**

(query fever)

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

Coxiella burnetii

- n **Obligate intracellular** bacteria
- n **Infects humans and many animal species**
- n **Worldwide distribution**
- n **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

- n **Both DHHS and USDA select agent**
- n **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**
- n **Category B bioterrorism agent**
 - **Treatable – doxycycline**
 - **Few fatalities from acute infection**

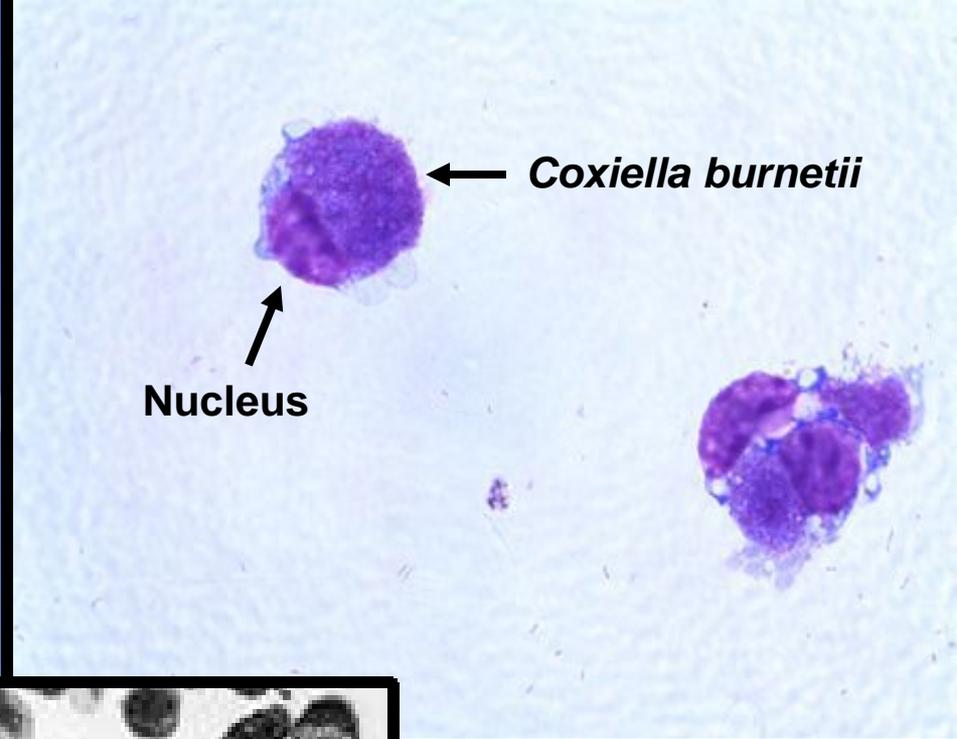
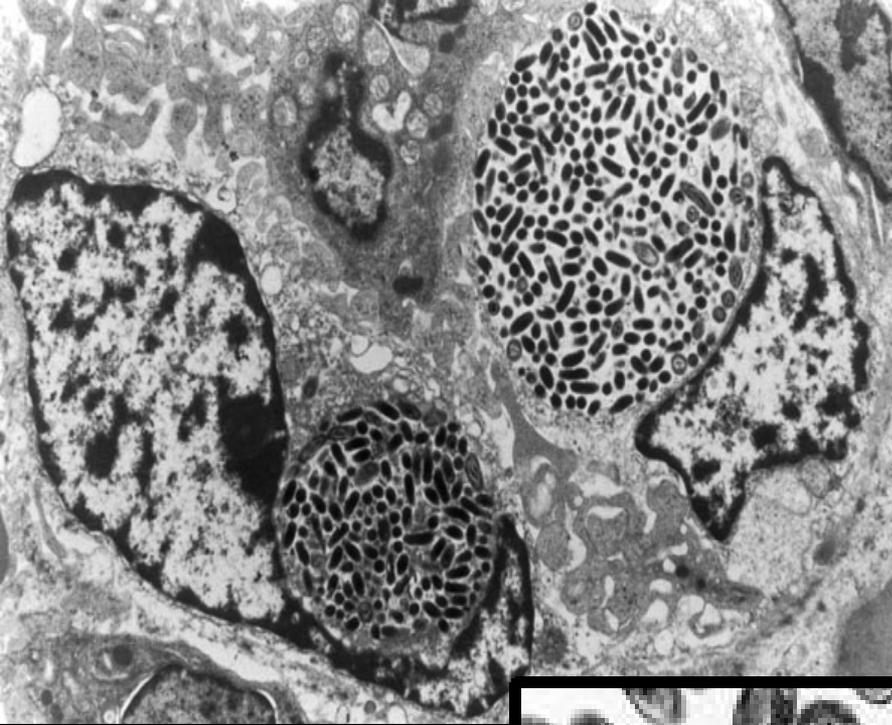
US

1946

Outbreaks in:

Packing house workers in Chicago

**Livestock sale yard employees and
packing house workers in Amarillo**



SCV
LCV



SAFER • HEALTHIER • PEOPLE™



Affected Species

n **Cattle**

n **Goats**

n **Sheep**

n **Cats**

n **Dogs**

n **Avian**

n **Rodents**

n **Ticks**

n **Horses**

n **Camels**

n **Rabbits**

n **Swine**

n **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

- n **Aerosol – inhalation, m.m.**
- n **Ingestion**
- n **Transplacental**
- n **Autopsies**
- n **Intradermal inoculation**
- n **Blood transfusion**
- n **Abortion/Parturition**
- n **Arthropod ???**

Sources of Exposure/Environmental Contamination

Animal parturition:

$>10^9$ bacteria/gram of placenta

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

Feces

Urine

Q-fever Infection

- n **Dose, strain and host factor dependent**
 - (1 cell is all that is needed to infect)
- n **Agricultural association**
- n **1-3 week incubation**
- n **"flu-like illness"**
- n **Multiple syndromes**

Q-fever Infection

Acute

- n **Fever -
Prolonged/Undulating**
- n **Pneumonia**
- n **Hepatitis**
- n **Myocarditis**
- n **Pericarditis**
- n **Skin Rash**
- n **Meningoencephalitis**
- n **13 others**

Chronic

- **Endocarditis**
- **Vascular Inf.**
- **Osteoarticular Inf.**
- **Hepatitis**
- **Pulmonary Inf.**
- **Chronic fatigue
syndrome**

Q Fever in the USA?

- n **Prevalence in cattle (McQuiston et al, 2005)**
 - **Milk from veterinary school dairy herds tested**
 - **92% of herds seropositive**
- n **North Dakota sheep ranchers – 3.4% positive**
- n **Montana dairy farmers – 19.5-38.2%**
- n **Manitoba, Canada – 15.9% general population**
- n **Colorado 2005 – 10% general population**
- n **Active surveillance needed**

Community Acquired Pneumonia

- n Generally affects patients ≥ 65 years
- n $\sim 5 \times 10^6$ cases annually (CDC estimate)
- n Major bacterial spp. seen in:

Outpatients

Streptococcus pneumoniae
Mycoplasma pneumoniae
Haemophilus influenzae
Chlamydophila pneumoniae

Non-ICU:

Streptococcus pneumoniae
Mycoplasma pneumoniae
Haemophilus influenzae
Chlamydophila pneumoniae
Legionella spp.

- n UK estimation of 1% of CAP due to *C. burnetii*

Q Fever Cases in USA?

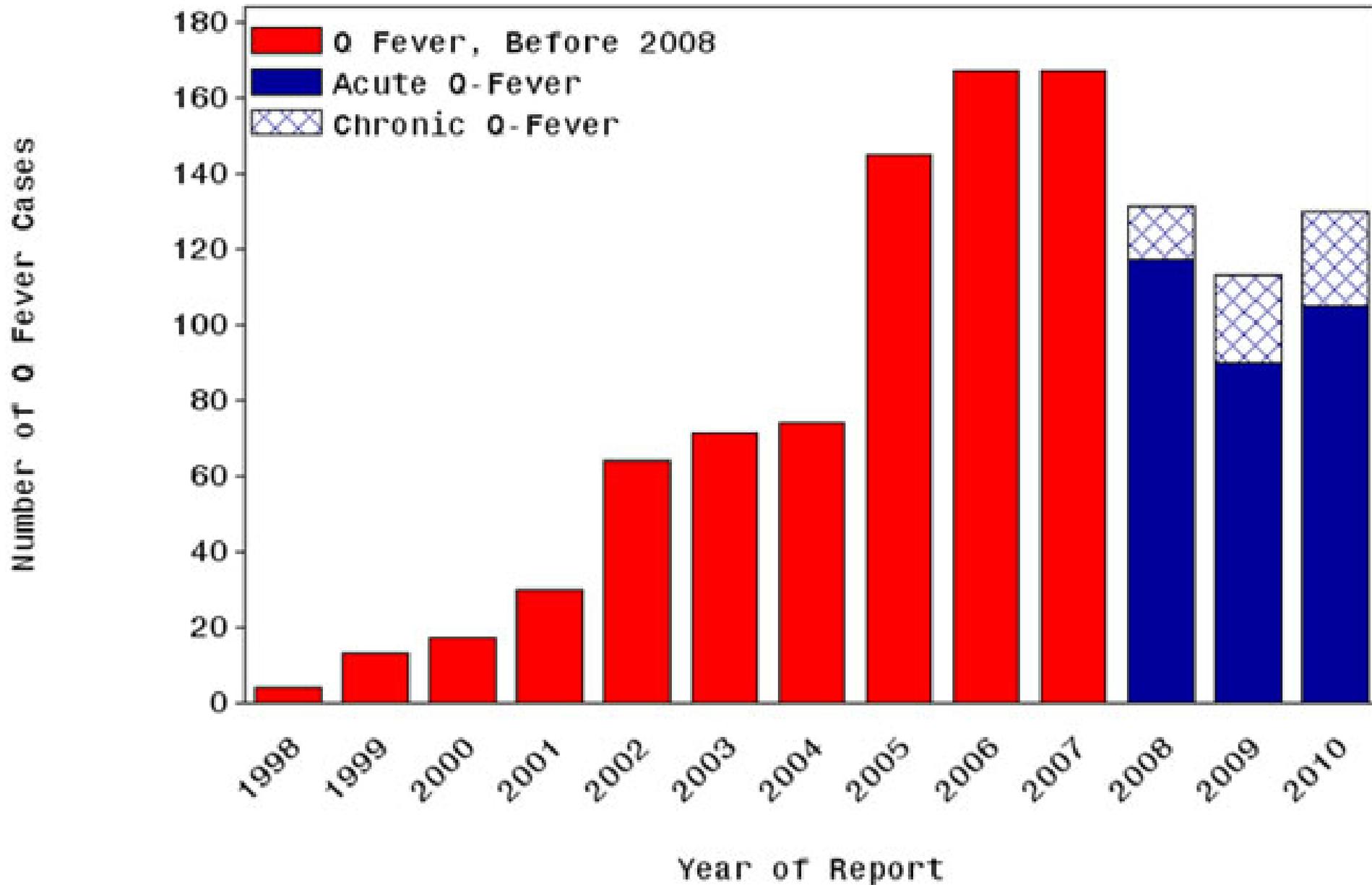
n UK

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

n USA

- ~ 5 million cases CAP/year
- 1% estimate = 50,000 cases of Q fever

Number of Annual Q Fever Cases, 1998-2010



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

- n **Patient history**

- n **Age**

- n **Environment**

- n **Paired sera**

2006 Study

1999: Q fever became a nationally notifiable disease.

Natural prevalence of *C. burnetii* unknown.

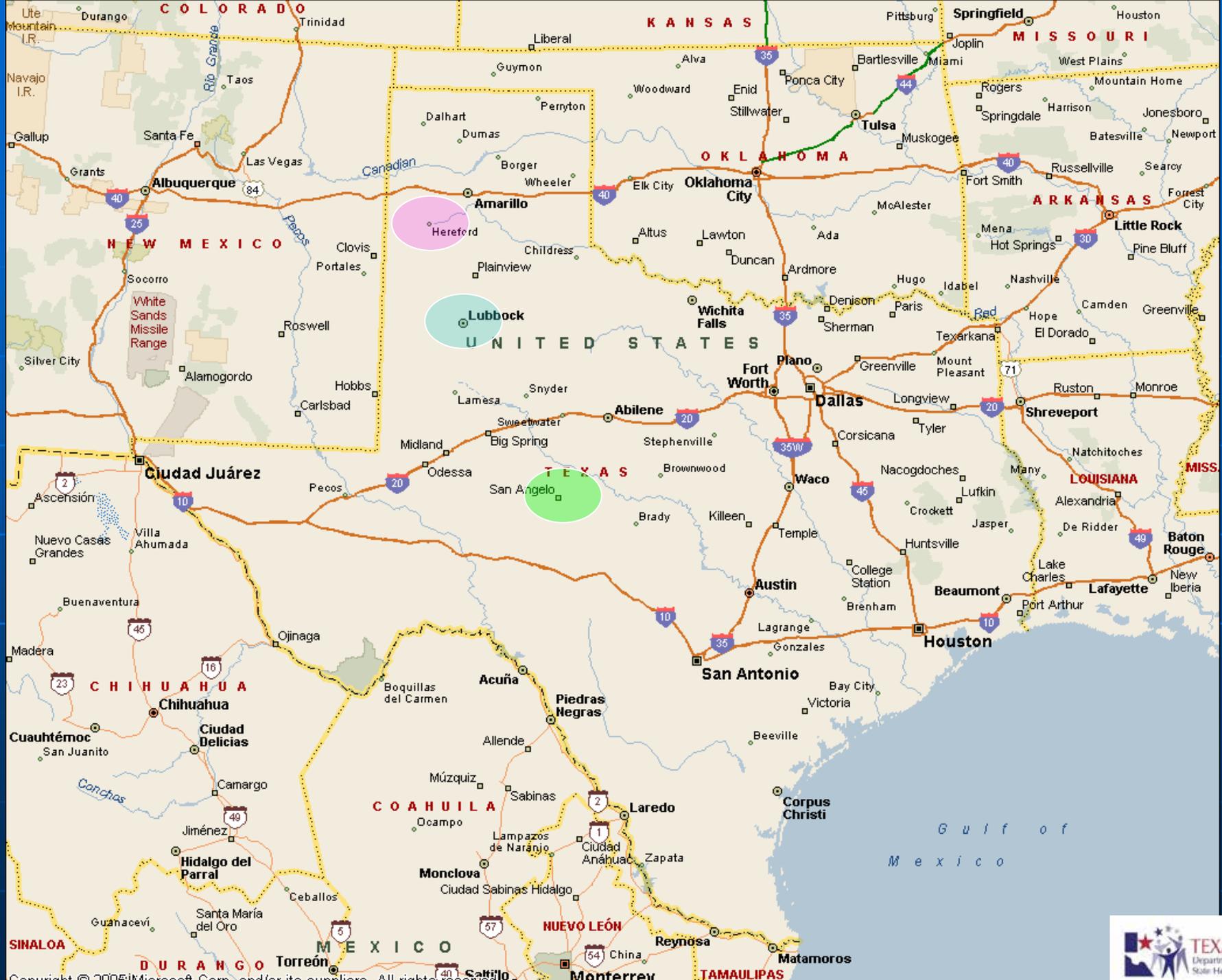
Preliminary study undertaken to determine background levels as a baseline for testing in the event of a bioterrorism attack.

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

n **Governmental**

n **Commercial**

n **Agricultural**

n **Social**

Sites

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

Non-Ag Positive

69% (9/13) Sites

17% (29/173) Samples

Ag Positive

50% (7/14) Sites

8% (14/165) Samples

Combined Positive

59% (16/27) Sites

12% (43/338) Samples

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
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Canyon, Texas



Coxiella burnetii

Source of Organism

**Birthing fluids, urine and feces
of livestock and cats and dogs**



Coxiella burnetii

- The Panhandle has an abundance of livestock



Coxiella burnetii

- n **The Panhandle has an abundance of wind**



Coxiella burnetii

- n Spreads by aerosolization of contaminated dust/soil
- n West Texas has plenty of aerosolized dust and soil



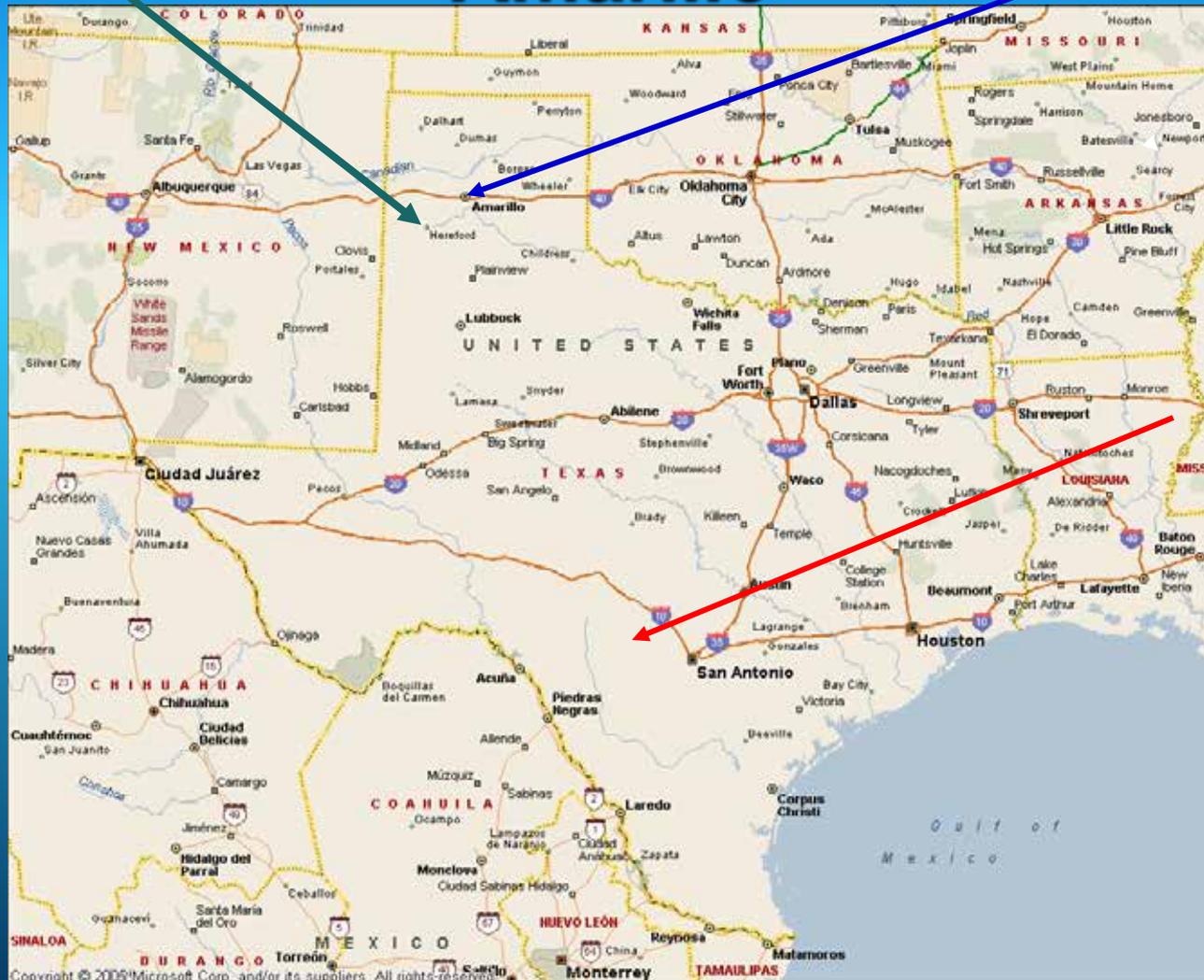
A Light Breeze in the Panhandle



June 12, 2008

- n Late in the day began receiving calls about an illness at an ethanol plant construction site at Hereford, Texas
- n Symptoms reported were more consistent with food-poisoning
- n Workers were going to the hospital to be tested for q fever

Hereford, Texas – ~ 40 miles SW of Amarillo



You are
here

June 13, 2008

- nMet with personnel from the company that owned the ethanol plant**
- nMet with Hereford City Officials**
- nParticipated in media interviews**
- nVisited Infection Control Nurse @ hospital**

Hereford is known for feedlots “The Beef Capital of the World”







Manure-fueled Ethanol Plant







05.19.2008 10:14



05.19.2008 10:17



06/08/2008 06:42



06/08/2008 06:43



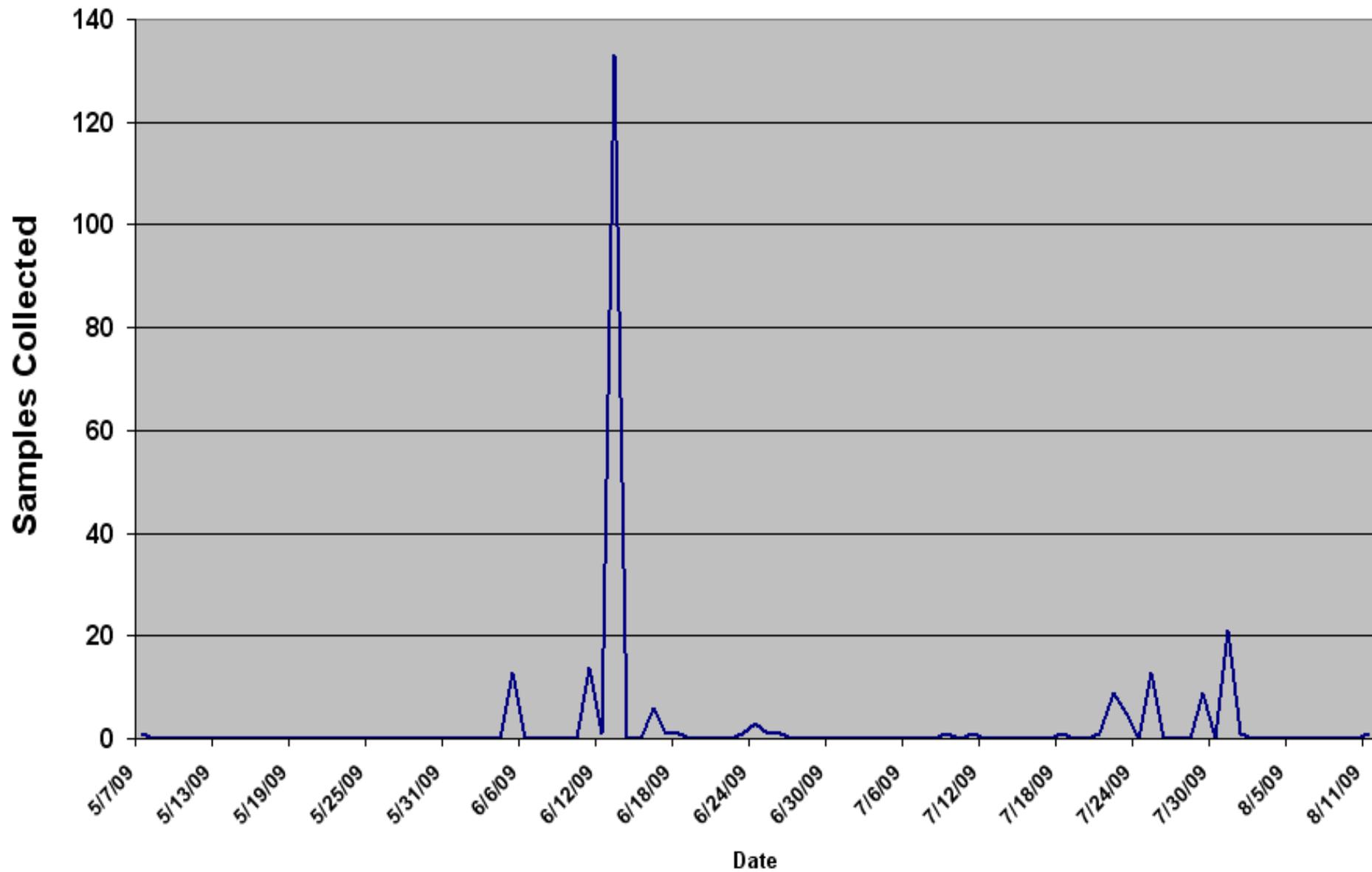
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Companies

- n 14 were on site during the 60 days prior to the "discovery" of q fever titers in the work force
- n The majority left that Friday or in the next week
- n Interviews and follow-up testing delayed
- n Many returned in late July but some were lost to follow-up

Number of Samples Drawn



Investigation

198 people received at least 1 test

- n 36 people received at least 2 tests**
- n 5 people were tested 3 times**
- n 238 samples collected**
- n No one that did not already have a titer of ≥ 128 developed a higher titer**

Surveyed Population

n Of 198 Workers Tested

- 17 had titers ≥ 128 (8.6%)
- 1:4096 was the highest titer based on a retest of the index case

Surveyed Population

122 (62%) of the "Tested" people were interviewed

- n 15 of the 17 with titers**
- n 5 asymptomatic (33.3%)**
- n 10 symptomatic (67.7%)**
- 42 interviewees with compatible symptoms (32 w/o titers)**
- 80 interviewees without compatible symptoms (5 with titers)**

Tested Population

n 15 Females (7.6%)

- Age: 22 - 52

 - n 2 with ≥ 128 (13.3%)

 - Ages 22 and 48 (mean = 35)

 - n 13 without titers

 - Ages 23-52 (mean = 37.8)

Tested Population

n **183 Males (92%)**

- **Age: 18 - 69**

- n **15 with ≥ 128 (8.2%)**

- **Age: 19-61 (mean = 40.6)**

- n **168 without titers**

- **Ages 18 - 69 (mean = 39.8)**

Information Obtained

- n Demographics and health history
- n Work location on site
- n Job title/occupation
- n Past livestock exposure
- n Animal exposure in past 60 days
- n Exposure to aborting animal
- n Illness and symptoms
- n Use of PPE
- n Proximity to manure

Predominant Symptoms of “Cases” and Non-titered People Reporting Illness

	“10 Cases”	“32 Non-cases”
n Weakness	10 (100%)	24 (75%)
n Malaise	8 (80%)	22 (69%)
n Chills	7 (70%)	22 (69%)
n Sweating	7 (70%)	21 (66%)
n Headache	6 (60%)	27 (75%)
n Myalgia	4 (40%)	17 (53%)
n Lymphadenitis	3 (30%)	4 (12.5%)

Evaluated

- n Proximity to manure – not significant
- n Employer – not significant
- n Prior contact with livestock – not significant

Plant Owner Modifications

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

Actions Taken by Contractor

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



08-13-2008 14:26

NIOSH Recommendations

- n **No Tyvek suits**
- n Shower and laundry facilities on-site
- n No work clothes or footwear to leave the site
- n Move the contractor office trailers and install running water to improve hand sanitation
- n Medical screening for symptomatic personnel
- n Cleaning shoes at office doorways and proper cleaning techniques for offices
- n 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

- n **2009: 2,357 new human q fever cases**
 - **US 43,855 (109)**
- n **Slaughtered about 62,500 pregnant goats and sheep**
- n **455,000 doses of vaccine distributed**
- n **Vaccinated about 90% of sheep/goat herds**

2009 Sero-survey for Q-fever

- n DSHS collaborated with the local blood bank
- n IRB approval obtained
- n Donors were apprised of the project, given a fact sheet and asked if they would participate
- n DSHS provided a vacuum tube which the phlebotomists used when collecting the routine samples for screening tests.
- n A questionnaire was administered by a DSHS representative.

2009 Sero-survey for Q-fever

- n 589 donors in the study
- n 19 blood drive events in 17 counties

2009 Sero-survey for Q-fever

- n Residents from 23 counties participated
- n Tubes were centrifuged, serum was pipetted and samples were stored on dry ice until they could be placed in a Revco[®] @ -80° C
- n 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

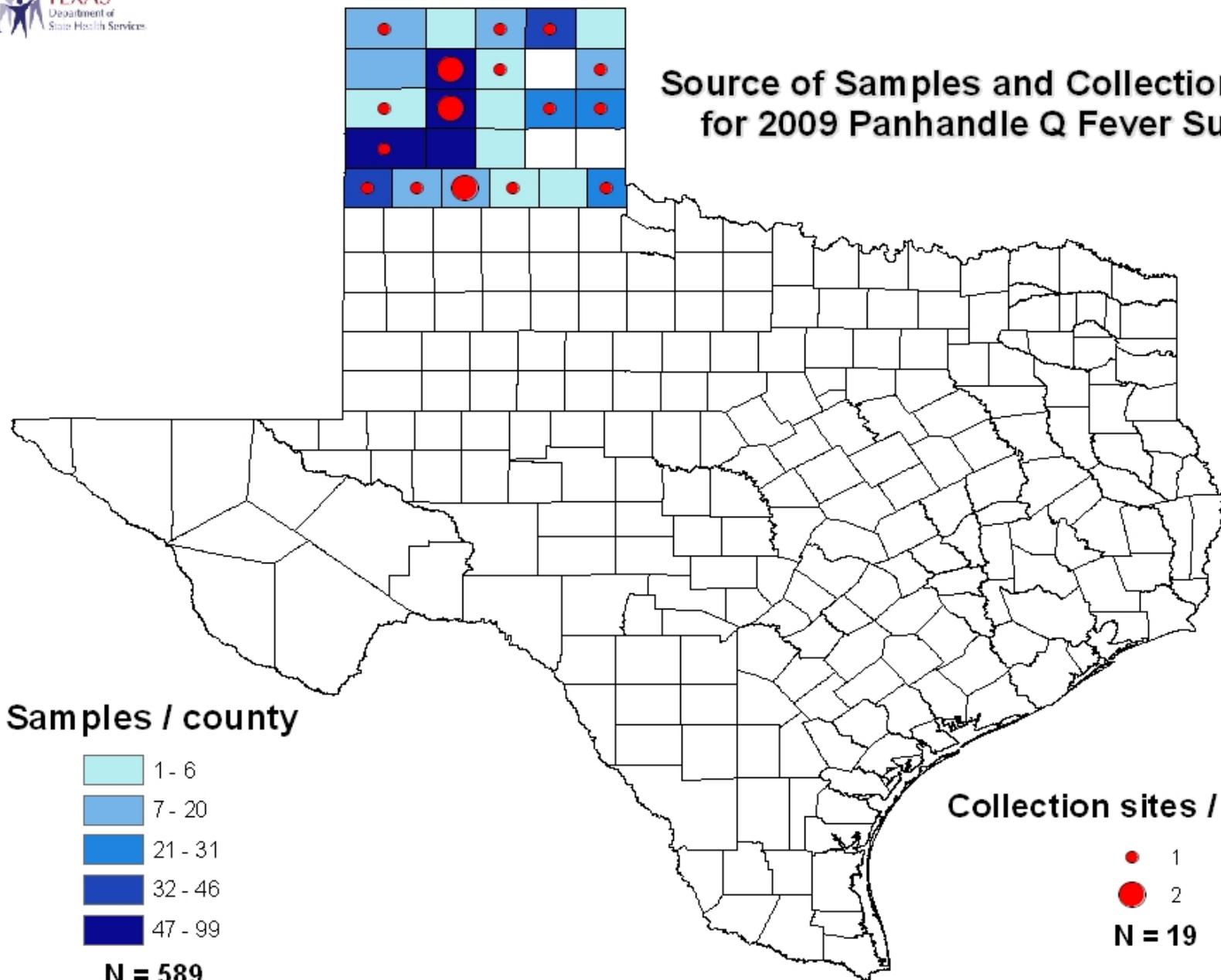
n 589 samples utilized in the study

Antibody prevalence:

10.7% in 589 people
from 23 Counties



Source of Samples and Collection Sites for 2009 Panhandle Q Fever Survey



Prevalence

Counties

- n 6 Counties with 0%
1-6 donors (14)
- n 9 Counties with 3-8%
19-99 donors (385)
- n 8 Counties with 16-50%
5-68 donors (190)

Donation Sites

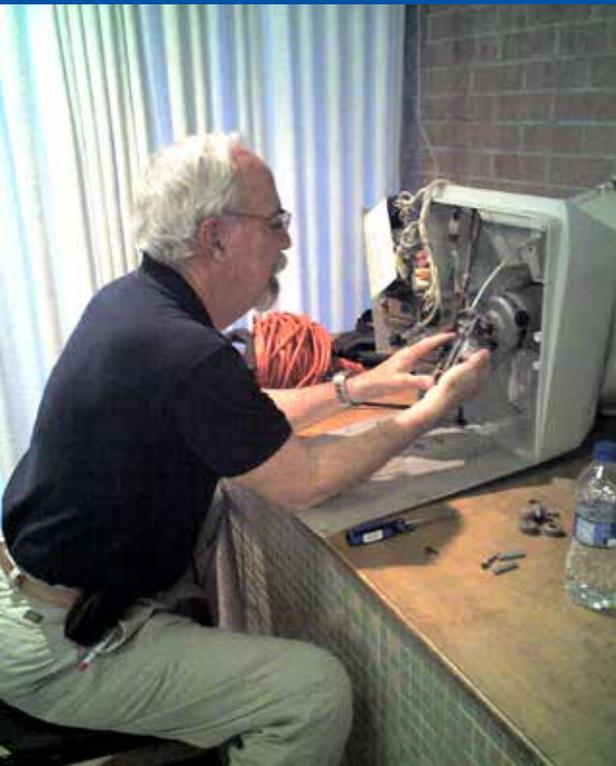
- 2 Sites with 0%
8 and 35 donors (43)
- 10 Sites with 3-8%
12-80 donors (350)
- 8 Sites with 19-43%
4-72 donors (196)

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

Positives:

	All	Pos	Neg
Range	18-82	18-76	18-82
Mean	46.3	46.4	46.2
Median	48	49	48
Mode	53, 55	38, 49, 51	55

Demographics

Racial Percentages

	Survey	Pop ⁿ
White Non-Hispanic	85.6	62.8
Hispanic	12.7	29.3
Black Non-Hispanic	0.3	5.4
Amer. Indian/Alaskan Native	0.7	1.0
Asian-Pacific Islander	0.2	1.4
Black Hispanic	0.2	NA
None Provided	0.3	NA

US Sero-prevalence Study

- n *Seroprevalence of Q Fever in the United States, 2003–2004, Anderson, et al*
- n 2003-2004
- n Stratified for age
- n Part of the National Health and Nutrition Examination Survey program

Comparison of Studies

	Anderson, et al ¹ (≥ 20 y.o.)	Panhandle (≥ 18 y.o.)
Sample Size	4437	589
Sero-prevalence	3.1%* (≥1:16)	10.7% (≥1:128)

* Weighted popⁿ estimate

Comparison of Studies

	Anderson, et al	Panhandle
Male +	3.8%	14%
Female +	2.4%	7%
Male:Female	1.5:1	2:1
Age	Age ↑ Risk	No Effect

Seroprevalence of Q Fever in the United States, 20

Comparison of Studies

	Anderson, et al	Panhandle
Male vs Female	1.5 OR (1.0-2.3)	2.1 OR (1.2-3.8)
White Non-Hispanic	2.8%	10.4%
Hispanics	7.4%	10.7%
Geometric mean (Phase II IgG)	95 (16 - 4096)	597 (64 - 65536)

Panhandle Study Limitations

- n Of 19 counties with more than 1 participant, 5 were under-represented and 14 were over-represented.
- n Residents of 4 counties provided 50% of the samples
- n 2 of those counties (large popⁿ) were over represented and 2 (moderate popⁿ) were under represented

Study Limitations

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

Conclusions

- n Exposure to *Coxiella burnetii* appears to be significant in some parts of the Texas Panhandle
- n 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
- n 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
 - 2nd week: 10%
 - 3rd week: 50%
 - 4th week: 70%
- CAP cases in US should be evaluated
- Cats should be surveyed

Important Points About Q-fever

- n **Dahlgren, et al, estimate that at least 13 cases of q fever are undiagnosed for everyone detected.**
- n **They also estimated that in two reporting systems, deaths are underreported by factors of 5 (MCD) and 14 (CRF).**
- n **Healy, et al, found only a 35% concordance between three reference labs on the same samples.**

Unidentified Agent in the Panhandle

- n **3 Patients with pneumonia treated with standard antibiotic protocols**
- n **All with symptoms compatible with Q Fever**
- n **All lived in Hereford, TX**
- n **All were on vents and considered terminal**
- n **Doxycycline was added to regimen**
- n **All recovered**
- n **All negative for Q Fever on serology**

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