# Q Fever/Coxiellosis in Goats: Outbreak Report and Update on Tool Development

http://www.express.co.uk/news/world/664685/goat-human-face-mutant-faun-farmer-Malaysia viewed 01/24/17

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# Outline

- Overview of *C. burnetii* problem
  - In human beings
  - In livestock
- Outbreak history
  - Lessons and needs
- Research to date
- Proposed solutions

# Overview: Billion with a B – Part 1

- Pathogen causes disease in both ruminant livestock and human beings
- Ruminant livestock blamed for most outbreaks
- Endemic in the U.S. (and around the world)
- Common pathogen: multiple studies show presence in ~95% bulk tank milk
- Up to 1 Billion organisms per gram of placenta

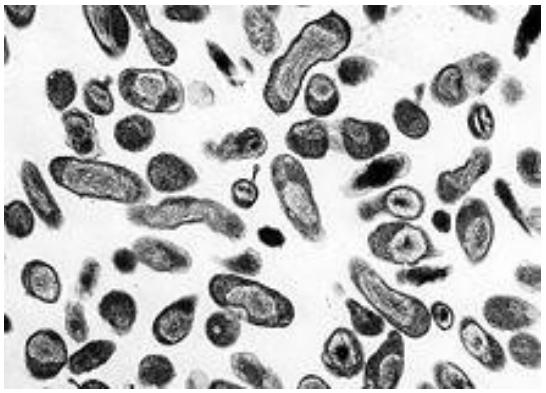
- Minimum infectious dose = 1 organism
- Airborne transmission over miles

# Overview: Billion with a B – Part 2

- Single outbreak cost Netherlands €307 million in 2005-2011
- Adjust for size of national flock & inflation suggests:
- $1 Billion potential for a single outbreak in the U.S.

# Q Fever Pathogen: *Coxiella burnetii*

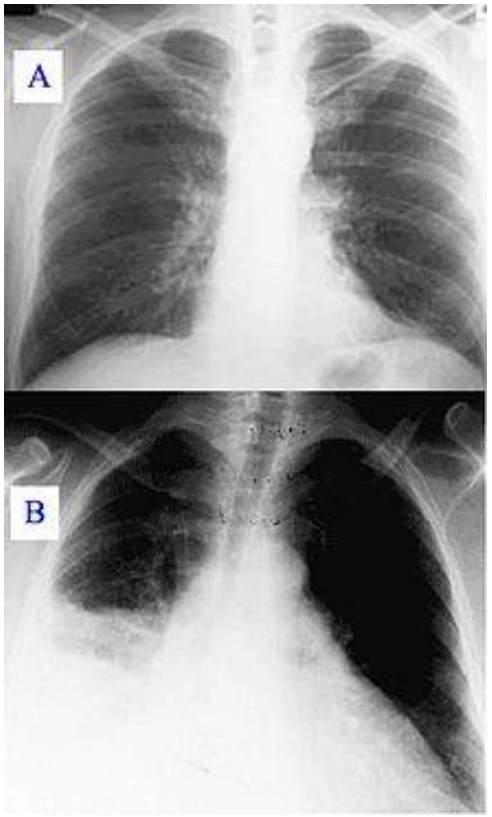
- Endemic worldwide (except New Zealand)
- Intracellular bacterium that lives in phagolysosomes of macrophages and trophoblasts
- Has a form that is resistant to drying and heat, and can persist in the environment for months or even years



https://en.wikipedia.org/wiki/Q_fever viewed 01/24/17

# Q Fever: Disease in Humans

- More than half of infected people have no symptoms
- Acute
  - –Flu-like illness, self-limiting
  - –Fever, cough, headache, muscle pain, joint pain, chills, sweats
  - –Pneumonia or hepatitis
  - –Antibiotic treatment




https://en.wikipedia.org/wiki/Q_fever viewed 01/24/17

# Q Fever: Chronic Disease

- 1-5% of acute Q Fever cases progress to chronic disease
- Endocarditis with fever, hepatitis, weight loss, and heart failure or stroke
- Most susceptible include immunosuppressed, immunocompromised, pregnant, or those possessing heart valve defects, vascular grafts, or arterial aneurysms
- People can develop chronic Q fever despite antibiotic use in the acute phase

# Disease in Livestock: Coxiellosis

- Usually asymptomatic
- Abortion/Stillbirth
  - –Release of *C. burnetii*
  - –Transmission to flock mates and human beings
- Weak young

http://www.goatworld.com/articles/abortion/abortion1.shtml viewed 01/24/17

# Economic Impact: Agriculture

- Production losses in millions per year for industry
- Including:
  - Abortion, stillbirth, weak offspring
  - Loss of milk and offspring sales
  - Costs for diagnostics, treatment, cull replacement
- Estimated up to $10k per year per farm when present, depending on level of *C. burnetii* exposure

O'Neill 2012

# *C. Burnetii* Shedding/Transmission

- Shedding usual for another year after abortion event, possibly for life
- Placenta is major source of transmission
- Additional transmission routes
  - Milk
  - Urine
  - Feces

http://popsci.typepad.com/popsci/2007/07/goat-milk-does-.html viewed 01/24/17

- Goat does that shed *C. burnetii* can still have healthy kids/lack of abortion

# US Dairy Goat Outbreak

- An abortion diagnosed as *C. burnetii*
- Ongoing abortion storm
  - Severe: more than half of kids were aborted or died in first half of kidding season, survival gradually improved as kidding season progressed
- Recent additions to herd

- >300 total goats on premises
- Commercial dairy
- All milk pasteurized

# Sample Collection

- USDA-ARS coordinated with owners, USDA-APHIS, State Veterinarian, CDC
- Collected samples:
  - Placenta: Cotyledon, intercotyledonary membrane
  - Vaginal swabs: Mid-kidding season, End of kidding season
  - Milk samples (individual)
  - Blood (for serology)

# High Prevalence

- Serology
  - 74% seropositive, additional 5% suspect: 79% seropositive or suspect
- Shedding (qPCR): Overall >95% positive for everything done to date
  - Placenta: >95% positive
  - Vaginal swabs
    - Mid-Kidding: >95% positive
    - End of Kidding: >95% positive
  - Milk: >95% positive

# Shedding from Young Nulliparous Does

- Animal Groups
  - –Milking does
  - –Kidding area
  - –Yearling does (never bred)

- 52/57 (91%) yearling does had detectable shedding by vaginal swab
  - –They can transmit *C. burnetii*

# Implications for Surveillance

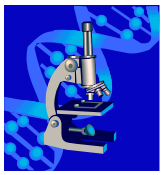
- Experimental inoculation study: no vaginal shedding until after birth (Roest et al 2012)
- One study: vaginal shedding from young nulliparous goats during depopulation in Netherlands (Hogerwerf et al 2011)
  - –not emphasized
- Many studies have examined shedding in vaginal mucus, but very few even looked in never bred animals
- But we must consider this route

# Much More Coming Soon

- One of very few studies on *C. burnetii* to incorporate sizable placenta collection
- Correlation of shedding amounts
  - Enable prediction of total shedding from easier to obtain samples
- Genome-wide scan of all chromosomes for gene regions important in determining amount of *C. burnetii* shedding by all routes

# Program Goals for Integrated Management

- Vaccine
  - BSL2 production for cost-effectiveness without subsidy
  - Prevent or reduce *C. burnetii* shedding from ruminant livestock
  - Prior data suggest may be most helpful in females who have never been pregnant
- Antibiotic Treatments
  - Improved disease management
  - Reduced shedding



- Host Genetics
  - Identify low risk genetics
  - Sire side tools for rapid deployment
  - May provide meaningful risk reduction even for females who have been pregnant before
  - Breed away from *C. burnetii* shedding before an outbreak occurs
  - Basic information about host-pathogen interaction

# BSL3 Production: Reason Coxiella Vaccine $$$

- BioSafety Level 2 (BSL2: ordinary laboratory) is safer, faster, & cheaper!
- We need a Coxiella vaccine that can be made in BSL2
- [Note: Some research testing will still need to be done in BSL3]

https://www.envirosafetyproducts.com/bullard-eva-papr-system-eva20tics.html viewed 01/21/2020

# Model Development: Experimental Design

Day 0: Mating
Confirmation via copulatory plug

Day 6: Infection
$1x10^8$ *C. burnetii* in 400 µL PBS
Intraperitoneal injection

Day 19: Euthanasia and procurement of tissues

IL-6, IL1β ELISA

COX-2 enzyme activity assay

$PGE_2$ immunoassay

*C. burnetii* qPCR

Histology, scoring

# Progress: First Mice Now

- Mouse breeding colonies established
- First inoculated mice finishing now
  - Had fevers, as expected
  - Placenta data soon
- Establish the role of the placental immune system and *C. burnetii*

# 2020 USDA-ARS Animal Health National Program

# Assessment and Priorities Evaluation Form

# Purpose

- The purpose of the survey is both retrospective as well as prospective
- It gives the ARS Office of National Programs information that is used to define the next 5-years of Animal Health Research
  - **Retrospective**- Measurement of impact; Did we accomplish what we said we would?
  - **Prospective**- What animal health disease research would have the most impact for your industry? What research should we be doing or continue to do?

# Details

- A link will be shared electronically (target date is February-March pending approvals)
- Targeted towards stakeholders (producers, researchers, veterinarians, government agencies etc.)
- Will remain open until we get over 500 respondents.
- ~15 minutes to complete

# Thank You

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