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

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

Stephen N. White, Ph.D.
USDA-ARS Animal Disease Research Unit
Pullman, WA
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
• 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

- Ryan Oliveira
- Mehmet Ulas Cinar
- Kristy Pabilonia
- David Schneider
- Gary Haldorson
- Michelle Mousel
- Maggie Highland
- Bret Taylor
- Don Knowles
- Christina Weller

- Codie Durfee
- Caylee Birge
- Ralph Horn
- Lori Fuller
- James Allison
- ADRU staff
- Mark Williams
- Natalie Pierce
- Ella Ybarlucea
- USSES staff

Funding Sources: