Review of Johne's Disease and Control Strategies

Part 1

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Topics

1. General information about Johne's
2. Diagnosis / current testing options
3. Prevalence
4. U.S. Voluntary Johne's control program
5. Current prevention / control methods
6. Economic relevance
7. Zoonotic concerns

What's the big deal about Johne's?

- 'Neglected' for over 100 years
  - Slow epidemic was predicted in 1924 *(Larson et al.)*
- Widespread across the US
  - ~22% of herds have prevalence > 10% *(NAHMS '96)*
  - Currently >70% of US dairy herds infected *(NAHMS 2007)*
- Economically important disease
  - Decreased milk production *(Lombard et al., Hendrick et al.)*
  - Increased risk of removal *(Lombard et al., Wilson et al.)*
  - Decreased weight at removal *(Whitlock et al.)*
  - NAHMS Dairy 1996 - $227/cow *(Ott et al.)*
- **Zoonotic concerns**

What is Johne's Disease?

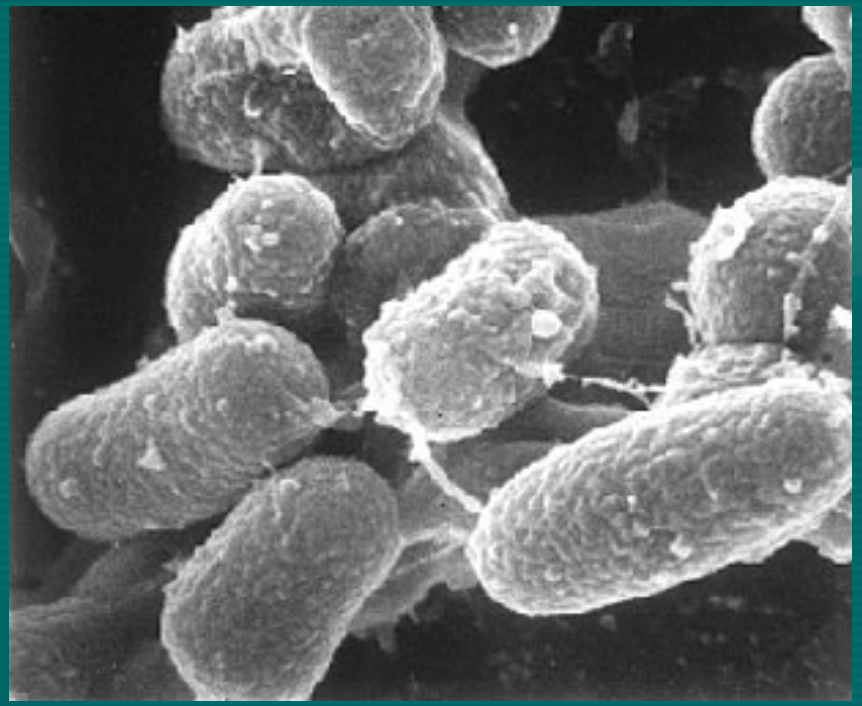
- First described by Drs. Johne and Frothingham in 1895 in Germany
- Caused by *Mycobacterium avium* subspecies *paratuberculosis* (*M. paratuberculosis, Paratb*, MAP)
- Chronic, infectious and "usually fatal" disease of ruminants and other animals

What is Johne's Disease?

- Animals usually infected before 6 mo. of age.
- Signs of disease usually >2 years of age
- Results in intermittent → persistent diarrhea and gradual weight loss
- Untreatable
  - Antibiotics not approved
  - Cost
- "Incubation" can last years!

Mycobacterium avium subspecies *paratuberculosis*

- Gram positive rod
- Acid fast
- Facultative intracellular pathogen
- Obligate parasitic pathogen
- Requires iron for growth
- Rough, thick, waxy cell wall



Courtesy of Johnes.org

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Survival and Dormancy of *Mycobacterium avium* subsp. *paratuberculosis* in the Environment

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The survival of *Mycobacterium avium* subsp. *paratuberculosis* was studied by culture of fecal material sampled at intervals for up to 117 weeks from soil and grass in pasture plots and boxes. Survival for up to 55 weeks was

Survived up to 55 weeks in pasture
Moisture and lime application – no effect on survival
Shade increased survival time

are involved in dormancy responses in other mycobacteria, are present in the *M. avium* subsp. *paratuberculosis* genome sequence, providing indirect evidence for the existence of physiological mechanisms enabling dormancy. However, survival of *M. avium* subsp. *paratuberculosis* in the environment is finite, consistent with its taxonomic description as an obligate parasite of animals.

How is Johne's Disease Transmitted?

- CALVES ARE MOST SUSCEPTIBLE!
  - Fecal Contamination
  - Colostrum & Milk
  - In Utero
  - Semen?
  - Embryo Transfer?
  - Rectal Palpation?

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Mycobacterium paratuberculosis Cultured from Milk and Supramammary Lymph Nodes of Infected Asymptomatic Cows

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"Shedding of *M. paratuberculosis* occurs in the milk of asymptomatic infected cows.."

prevalence of supramammary lymph node or milk infection was highest with heavy fecal shedding of *M. paratuberculosis* and lowest with light shedding. The serologic status of the cow was not useful for predicting the risk of supramammary lymph node or milk infection. Shedding of *M. paratuberculosis* occurs in the milk of asymptomatic infected cows but, apparently, less frequently than previously reported for symptomatic cows.

Streeter et al., 1995 AJVR

M. paratuberculosis was isolated from colostrum (22.2% of FC+) more frequently than from milk (8.3% of FC+).

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In utero infection of cattle with *Mycobacterium avium* subsp. *paratuberculosis*: A critical review and meta-analysis

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Abstract

Mycobacterium avium subsp. *paratuberculosis* (*Mptb*) causes Johne's disease in ruminants. Disease control programmes aim to break the faecal–oral cow–calf transmission cycle through hygienic calf rearing and removal of affected cows from the herd, but these pro-
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to the value chosen for the proportion of clinical cases. In utero transmission of *Mptb* could retard the success of disease control programmes if the opportunities for post natal transmission via colostrum/milk and environmental contamination were able to be controlled. The consequences of fetal infection for the calves so infected are discussed in the context of diagnosis and vaccination together with recommendations for future research.

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In utero infection ranges from 0.44 - 9.3% of calves

"In utero transmission *Mptb* could retard the success of disease control programmes.."

Letters in Applied Microbiology 2001, **33**, 227–231

Bactericidal effect of chlorine on *Mycobacterium paratuberculosis* in drinking water

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2001/127: received 25 April 2001, revised 12 June 2001 and accepted 21 June 2001

L.B. WHAN, I.R. GRANT, H.J. BALL, R. SCOTT AND M.T. ROWE. 2001.

Aims: One possible route of transmission of *Mycobacterium paratuberculosis* from cattle to humans is via contaminated water supplies. The aim of this work was to determine whether this

"..when initial inoculums were high (106 CFU), neither *M. paratuberculosis* strain was completely killed at the free chlorine concentrations"

conditions the organism would experience in commercial water treatment operations.

Conclusions: The data showed that when initial inoculum levels were high (10^6 cfu ml^{-1}) neither *M. paratuberculosis* strain was completely killed at the free chlorine concentrations and contact times applied. Log_{10} reductions in the range 1·32–2·82 were observed. The greatest log_{10} reduction in cell numbers (2·82 and 2·35 for the bovine and human strains, respectively) was observed at the highest chlorine concentration (2 μg ml^{-1}) and longest contact time (30 min).

Significance and Impact of the Study: This work highlights the need for further research into the survival of *M. paratuberculosis* during water treatment.

Stages of Johne's Disease

- Silent Infection
  - Usually young cattle early in the disease
- Subclinical Disease
  - Infected but no diarrhea present
- Clinical Disease
  - Intermittent diarrhea
- Advanced Clinical Disease
  - Lethargic, weak and emaciated
  - "waterhose" or "pipestream" diarrhea

Stages of Johne's Disease
(Iceberg Effect)

Cases

Advanced Clinical = 1

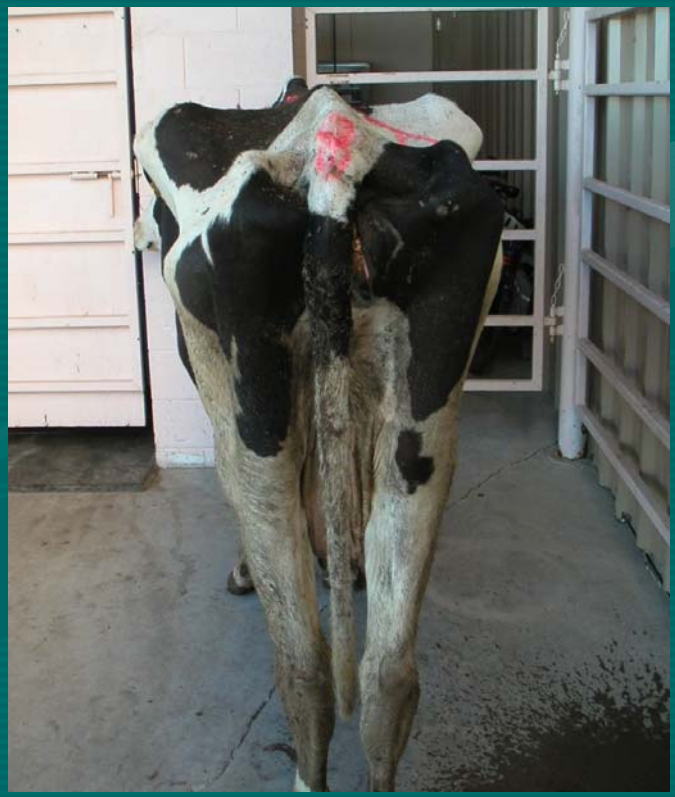
Clinical = 2

Subclinical = 6

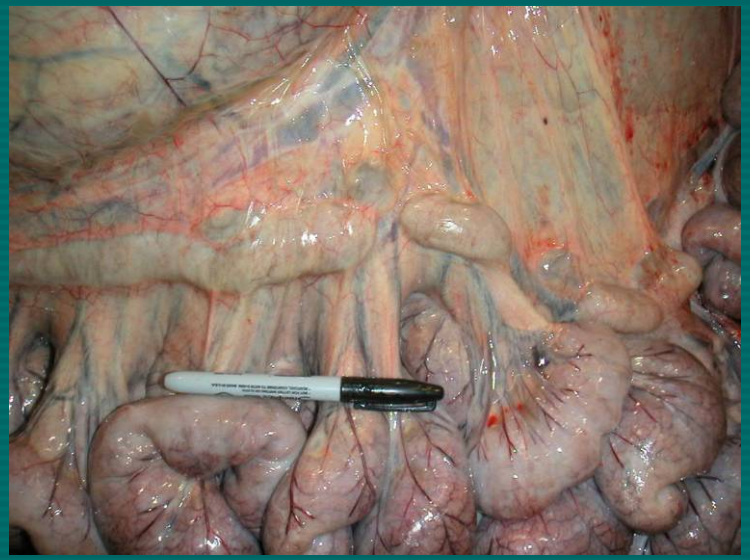
Silent = 12

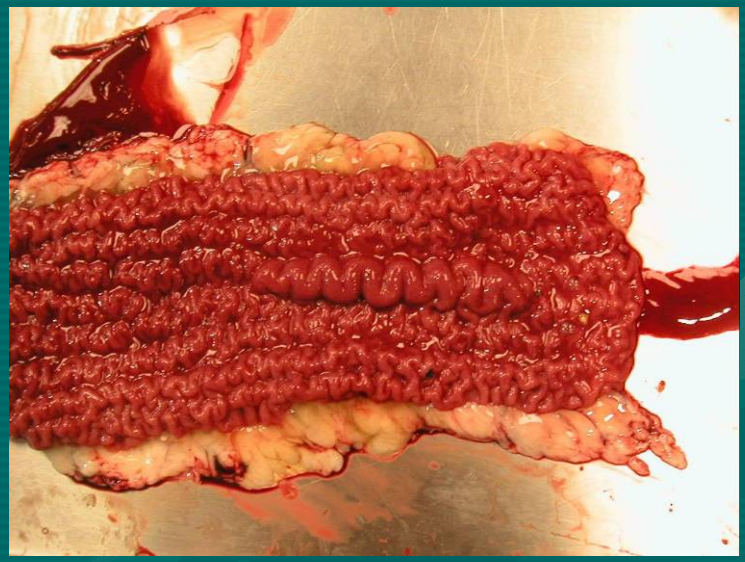
Total Cases = 21

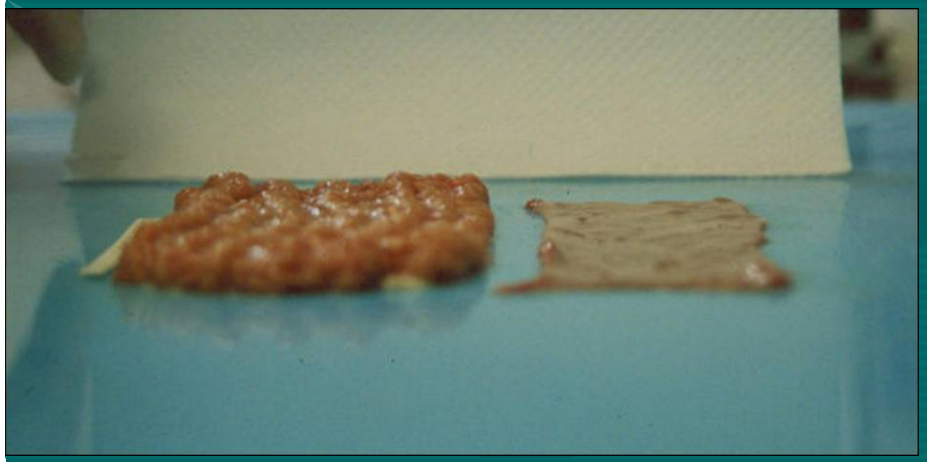
Advanced Clinical Disease

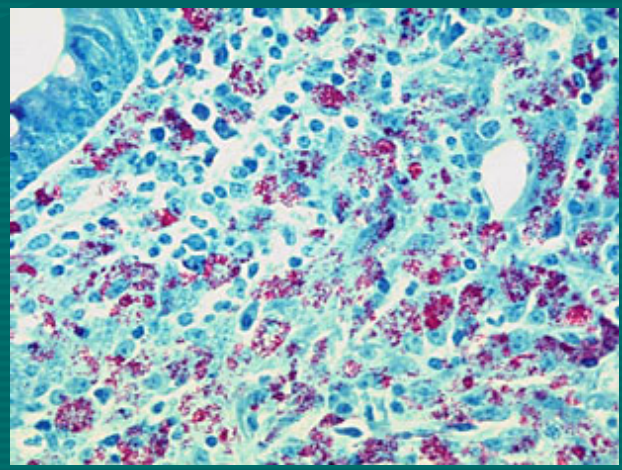


Pathology









Clinical Disease

Diagnosis of Johne's Disease

- Clinical Signs
- Blood Tests (ELISA, AGID, CF, γ - IFN)
- Milk Tests (ELISA, PCR)
- Fecal Culture / PCR
- Biopsy
- Necropsy

Diagnostic Tests

- No tests are perfect (for any disease)
- Repeatable
- Adequate to assist in controlling disease
  - "Size matters!"
- Consistently identify the most infectious animals

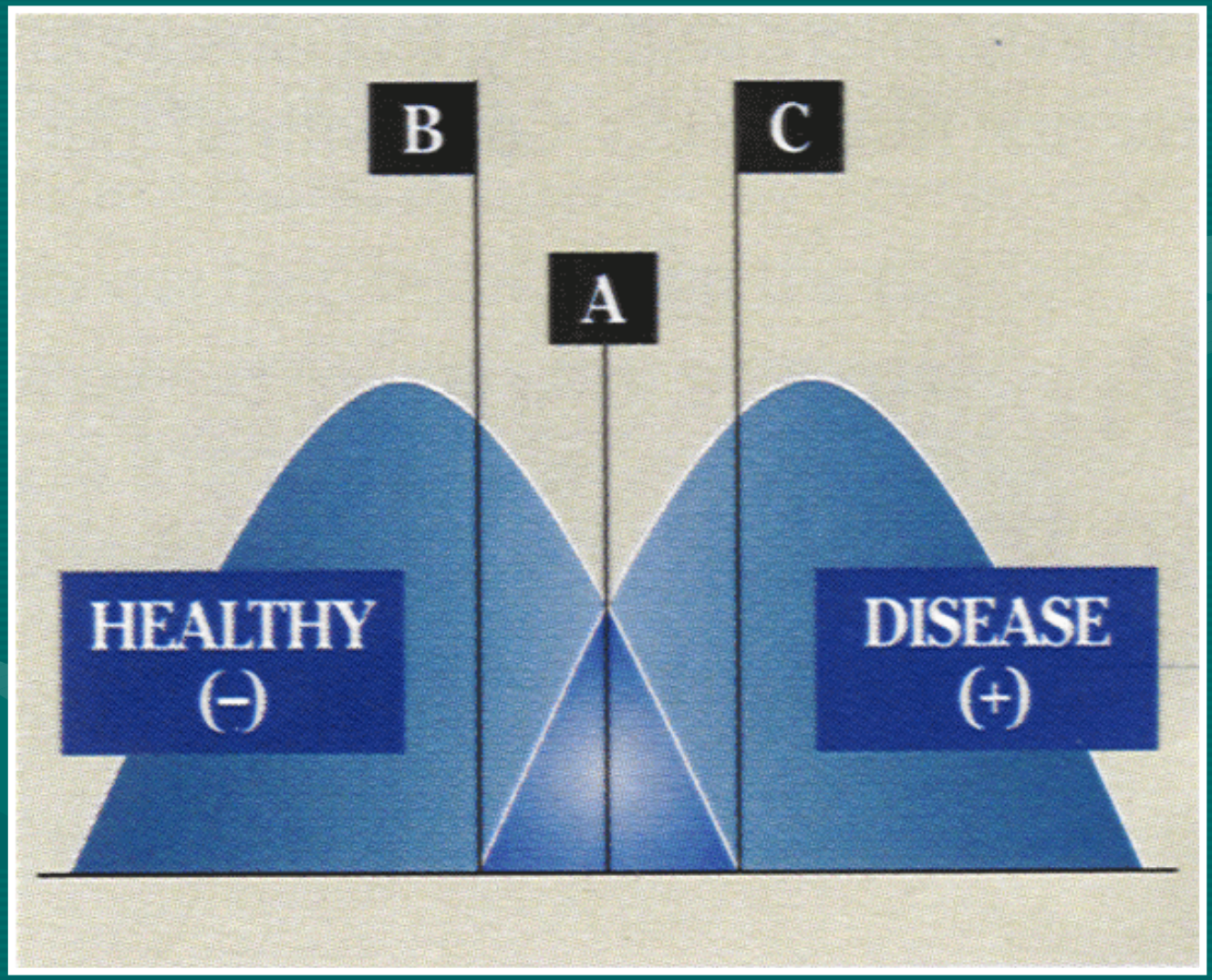
- **The problem is the organism, not the tests!**

Diagnostic Tests

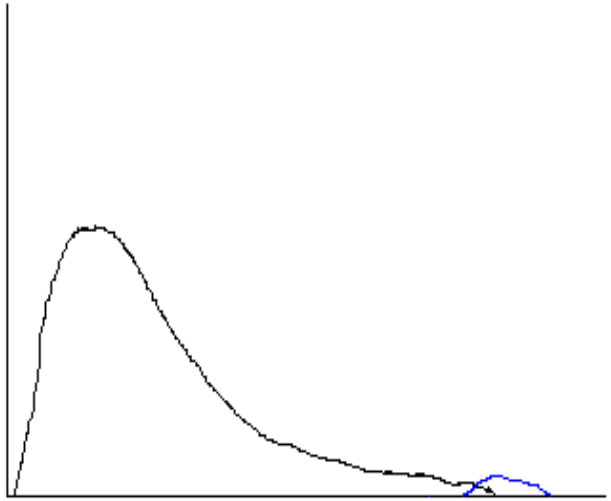
- *Antibody detection – rapid and economical*
  - *Serum ELISA (SE) (Se=15-85%, Sp=97-100%)*
  - *Milk ELISA (ME) (Se=21-64%, Sp=80-99%)*

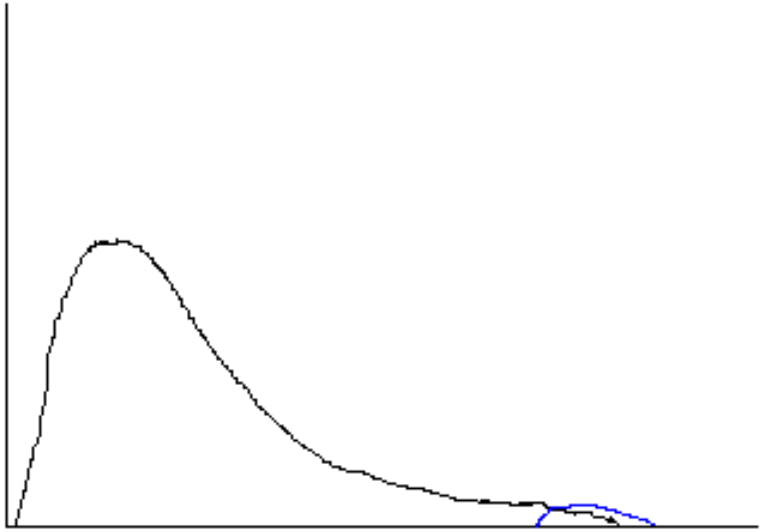
- *Organism detection – slow and expensive*
  - *Fecal Culture (FC) (Se=50%, Sp=100%)*
  - *Histopathology*
  - *PCR*

Population Distribution

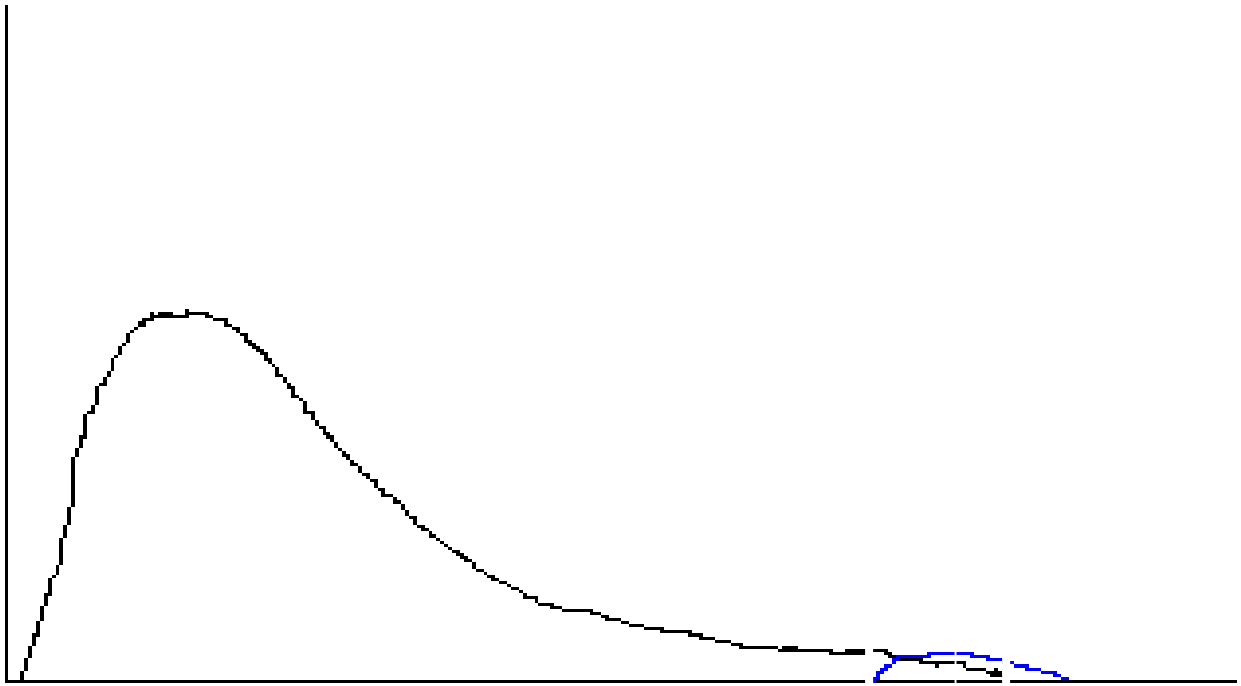


Population Comparison





Test Interpretation



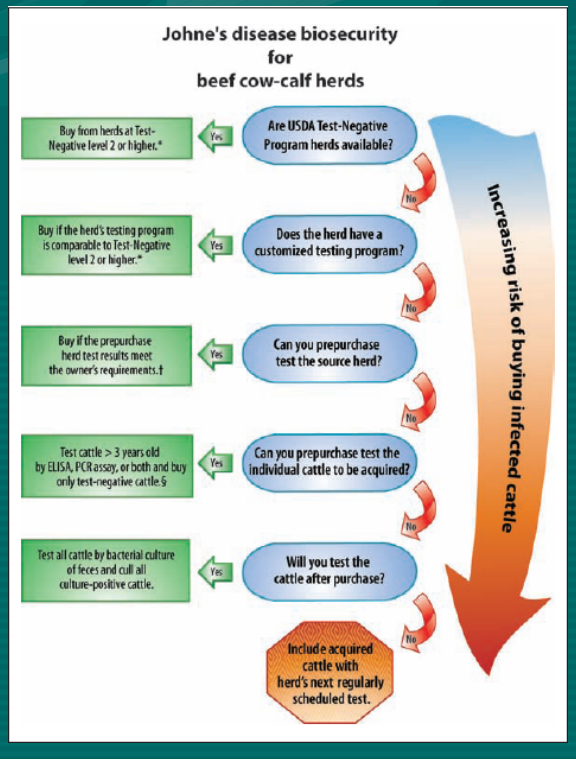
Special Report

Consensus recommendations on diagnostic testing for the detection of paratuberculosis in cattle in the United States

Michael T. Collins, DVM, PhD, DACVM; Ian A. Gardner, BVSc, MPVM, PhD; Franklyn B. Garry, DVM, MS, DACVIM; Allen J. Roussel, DVM, MS, DACVIM; Scott J. Wells, DVM, PhD, DACVPM

Table 3—Recommended test regimen for the detection of paratuberculosis in cattle on the basis of herd type and testing purpose.

	Dairy		Beef	
Testing purpose	**Commercial**	**Seedstock**	**Cow-calf**	**Seedstock**
Herd classification (infected or not infected)	Bacterial culture by ENV-HEY or ENV-LIQ	Bacterial culture by ENV-HEY or ENV-LIQ	Whole-herd testing, target testing, or bacterial culture by ENV-HEY or ENV-LIQ	Whole-herd testing, target testing, or bacterial culture by ENV-HEY or ENV-LIQ
Precise estimation of within-herd prevalence	NR	NR	NR	NR
Control disease in herd with known infection, high prevalence (> 10% positive results on ELISA), and clinical disease, or owner is concerned	ELISA	Bacterial culture by IND-HEY or IND-LIQ	ELISA	Bacterial culture by IND-HEY or IND-LIQ



Prevalence Estimates

- Beef cattle
  - Animal level = 0.5 – 10%
    - Belgium, Canada, Spain, US
  - Herd level = 3 – 63%
    - Belgium, Canada, US
- Dairy cattle
  - Animal level = 1 – 20%
    - Austria, Belgium, Canada, Denmark, Netherlands, US
  - Herd level = 22 – 94%
    - Austria, Belgium, Canada, Denmark, Netherlands, Switzerland, US

- Approved in 2001 by USAHA
- Template for state programs
- Each state has opportunity to customize their plan
- 48 states now have programs

Program Elements

1. **EDUCATION**
2. **MANAGEMENT**
   - Risk Assessment & Management Plan
3. Testing
   - Test Negative Component
     - Level 1 – 4
   - Test Positive Component
     - Management component

Culture and Cull Procedure for Control of Paratuberculosis

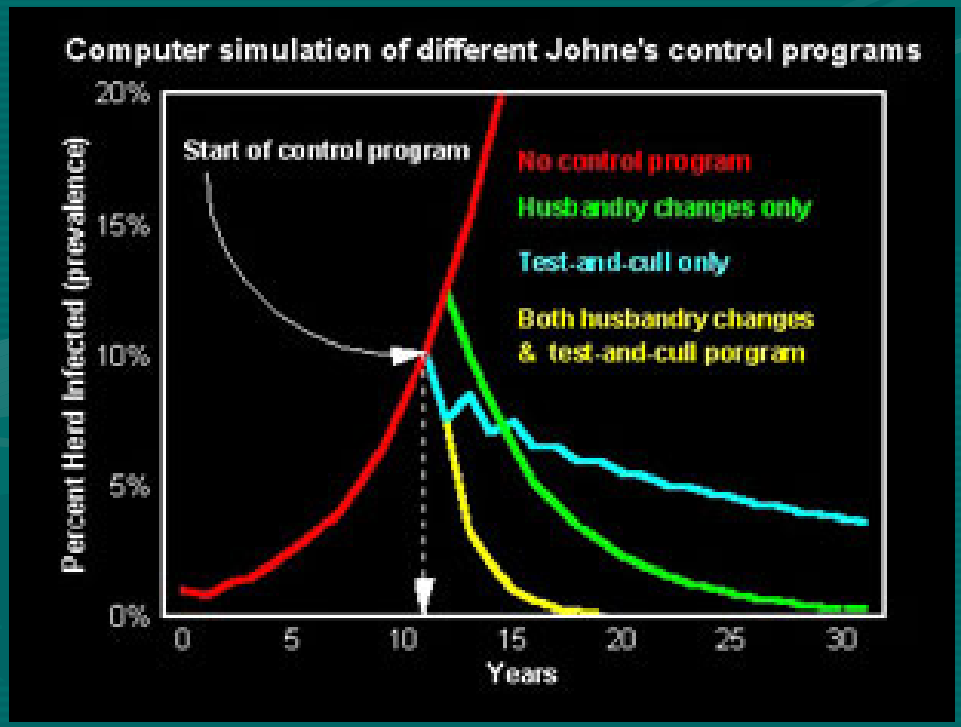
TABLE 1—Guidelines for Eradication of Paratuberculosis

1. Remove calves to clean quarters immediately after birth. Natural nursing must not be permitted.
2. Thoroughly wash udder and sides of dam to remove all manure before drawing colostrum to be used for initial feedings of calf.
3. Protect young cattle from all adult feed and waste material. Wear clean clothing and footwear in calf rearing quarters.
4. Use only clean utensils for feeding calves. Use only clean, uncontaminated bedding. Use cleaning tools maintained for clean group only.
5. Be sure that feed is not visibly contaminated with animal waste.
6. Pasture on clean, uncontaminated areas and maintain in winter quarters separate from adults until necessary to add to the milking line.
7. Protect young cattle from all drainage that may come from area occupied by adult cattle.
8. Remove any unnecessary shade from areas occupied by either the young, clean group or the adult group. Allow for sun to reach any shaded areas at some time during the day.
9. Fence or fill with earth any stagnant pools. Allow cattle to drink from uncontaminated tanks or free-flowing streams only.
10. Separate any unthrifty cattle from the herd until condition is diagnosed. Handle these cattle after normal cattle in routine chores. Do not return these cattle to the herd unless possibility of paratuberculosis is eliminated.
11. Remove immediately for slaughter any animal or offspring of any cows with recurrent diarrhea.
12. Culture feces from all mature cattle in infected herds twice annually.
13. Remove all culture-positive cattle and their offspring from the herd.
14. Use semen from noninfected bulls. Extreme care must be taken that a bull comes from a paratuberculosis-free herd, and frequent changes in sires are desirable.
15. Clean and disinfect areas where infected cattle have been kept with US Department of Agriculture-approved disinfectant.
16. If necessary to purchase replacement cattle, obtain mature individuals from herds with no history of paratuberculosis.
17. Sale of known infected cattle for dairy or breeding purposes may subject the owner to civil liability.

April 1, 1975

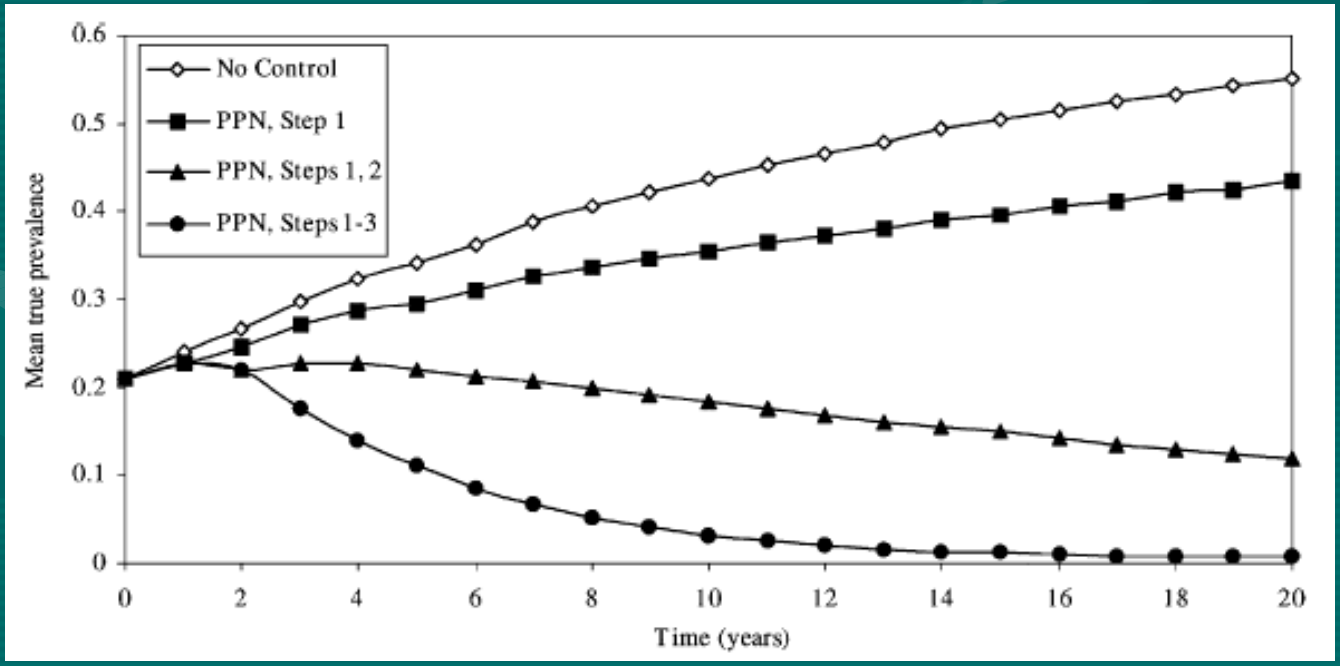
Herd Based Models

- Collins and Morgan (1992)
  - Calf management was most important in reducing prevalence
  - Test and Cull also decreased prevalence, but at a slower rate
  - 70% Se was predicted to reduce prevalence to less than 1%



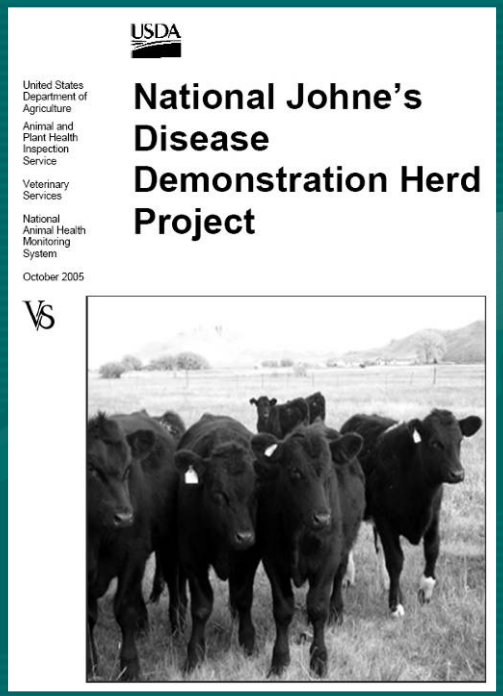
Herd Based Models

- Groenendaal et al (2002, ,2003, 2004)
  - Excellent calf management required to reduce prevalence over 20 years
  - Test and cull – usually economically unattractive
  - Vaccination – usually economically attractive



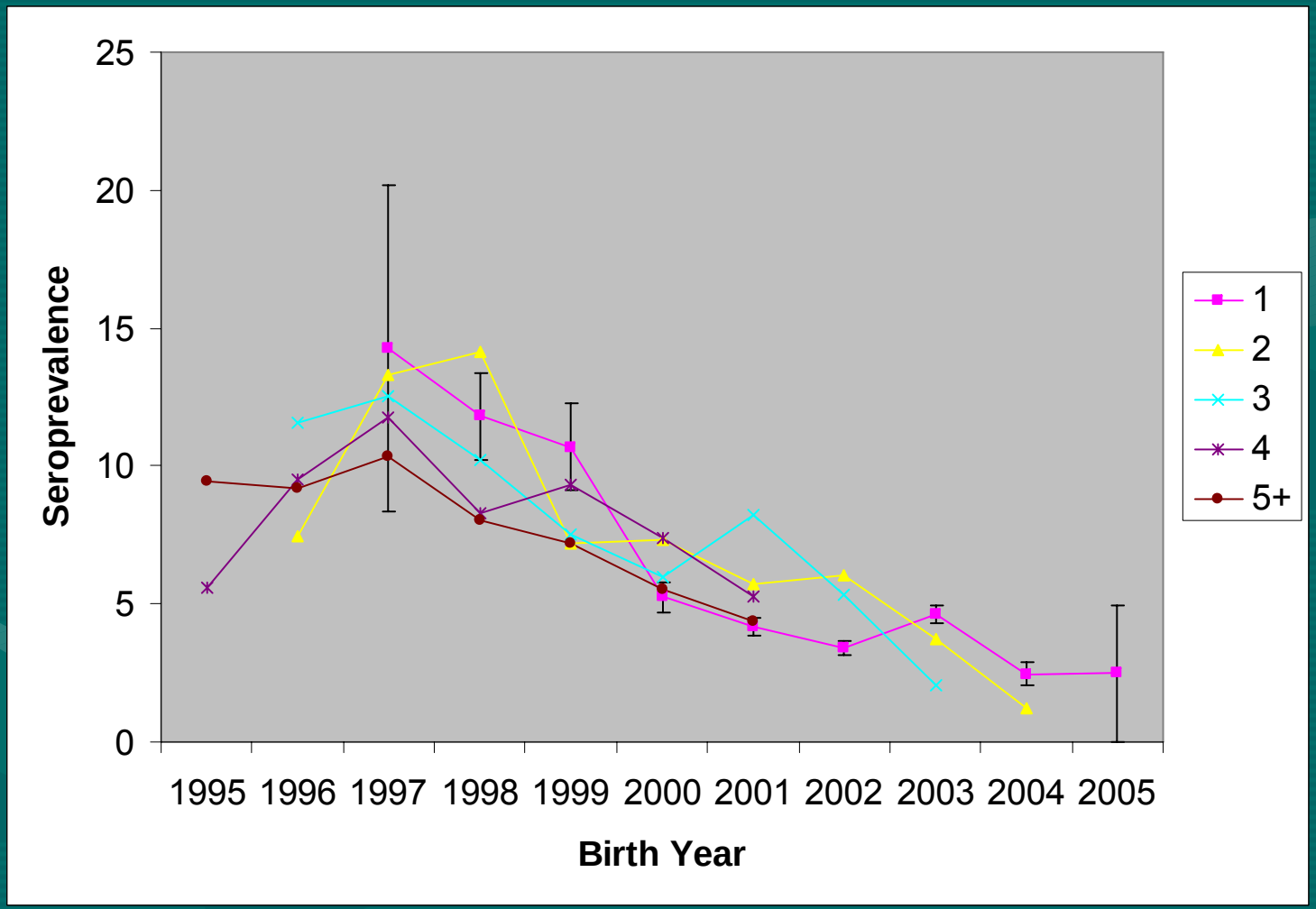
National Johne's Disease Demonstration Herd Project

- Third year of study
- 66 dairy herds (~74,000 animals)
- 25 beef herds (~6,400 animals)



- Data
  - Risk Assessments and Management Plans (RAMPS), animal information, removal information, testing information, etc

Lactation Cohort Seroprevalence Dairy



National Johne's Disease Demonstration Herd Project

- Calves from fecal-culture positive (FC+) dams are at increased risk of being FC+ later in life
  - **Cull calves from FC+ cows?**
- Cows from operations where JD clinical cows are allowed in calving area are at increased risk of being FC+.
  - **Remove JD clinical cows immediately; prior to culling, keep them as far away from calving area as possible.**
- Cows on operations where calves are allowed to nurse and /or udder hygiene is poor, are at increased risk of testing FC+.
  - **Remove calves immediately after birth, before they have a chance to nurse; keep udders clean, or clean them prior to collecting colostrum.**

Johne's Prevention and Control

- Implement good hygiene practices
- Prevent animals (especially newborns) from contacting / ingesting the bacteria
  - **Manure, Colostrum, Milk, Feed, Water**
- Decrease contamination by testing and culling test-positive animals
  - In utero Infection - Cull when Pregnant if Positive
- Vaccination
  - Reduces fecal shedding and incidence of clinical signs