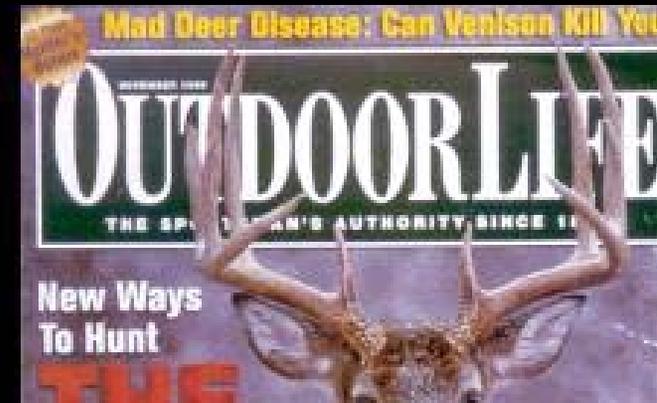
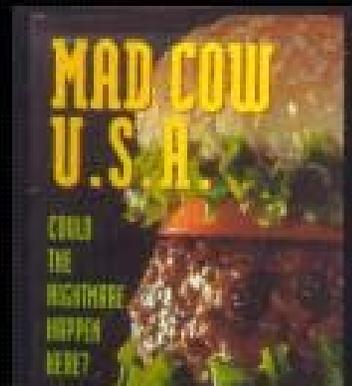
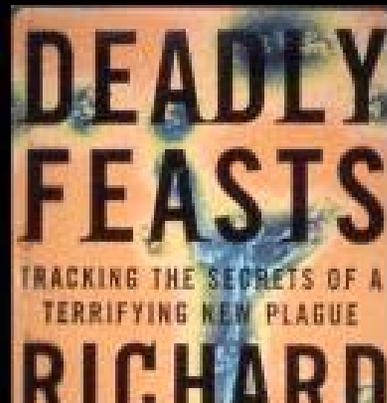
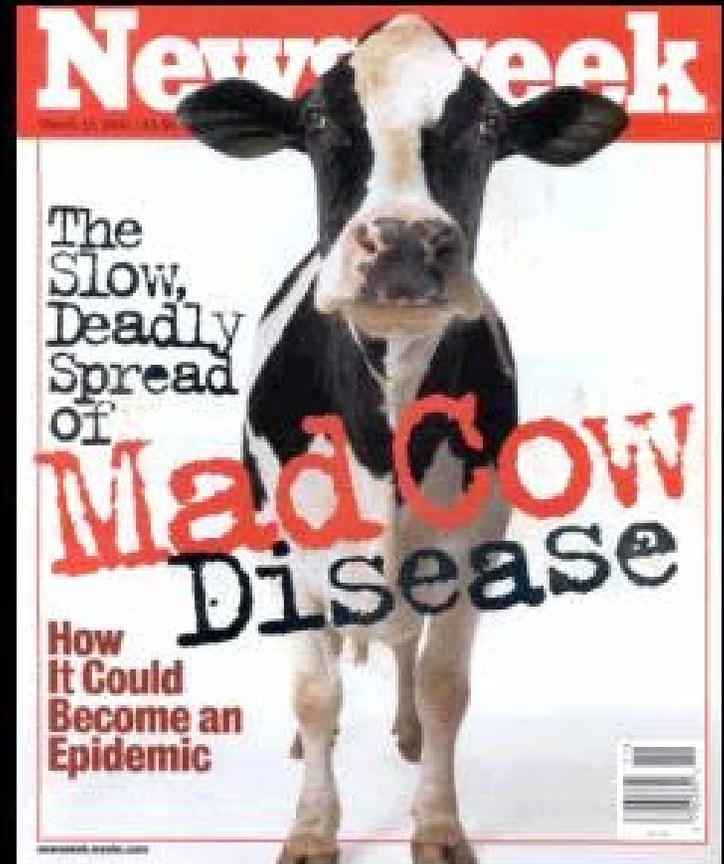


Bovine Spongiform Encephalopathies (BSE): A Review of Actions in North America

**Linda A. Detwiler, DVM
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University of Maryland
Animal Health Consultant**

MAD DEER DISEASE
CAN VENISON KILL YOU?

Media Attention to the TSEs



Transmissible Spongiform Encephalopathies: Family

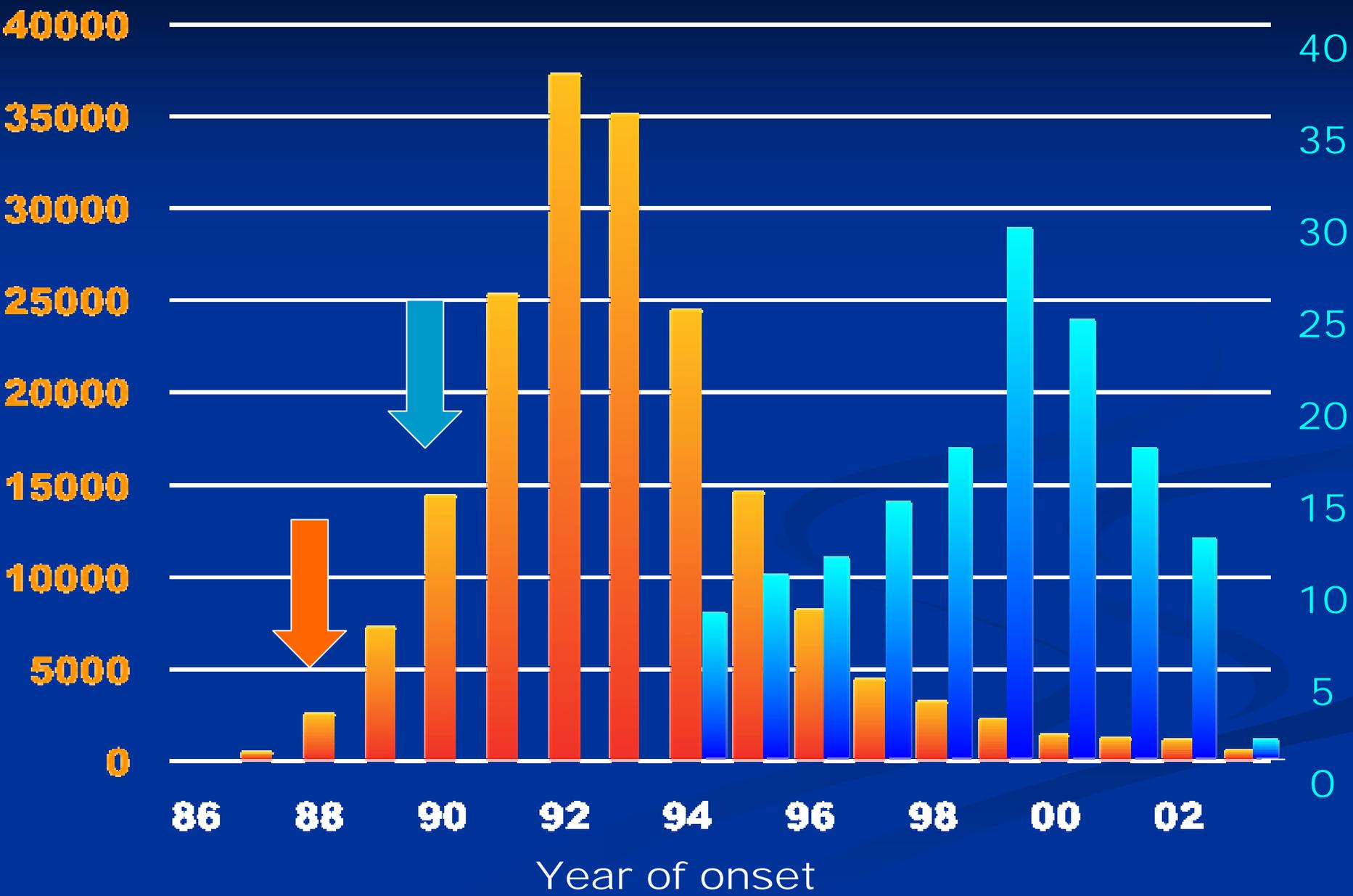
Long incubation diseases with limits to preclinical test

Think - if I knew disease would be here tomorrow, what should I have done yesterday



BSE

vCJD

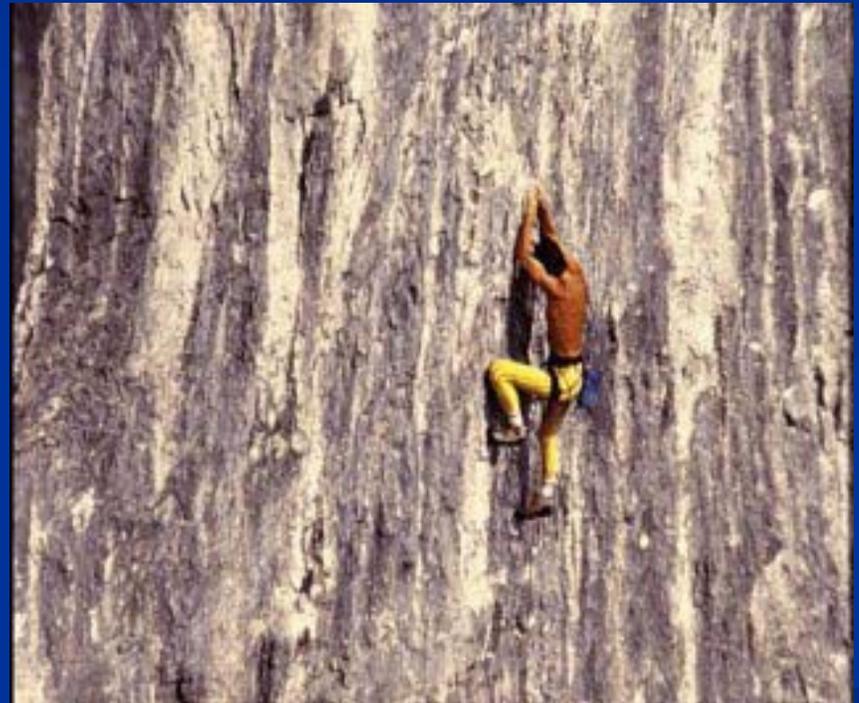


BSE in North America

- 1 imported UK case (1993)
- 2 native cases (2003) – Angus and Holstein
- All nonambulatory disabled
- 2003 cases born Spring 1997 (6-6.5 yrs old)
- Most likely exposed within first year of life (pre feed ban?)
- Both born in Canada and sold from herds of birth

BSE in North America (cont.)

- Both presented for slaughter with no overt signs of BSE
- Both submitted as routine surveillance
- Canadian case into rendering
- Case in US into food and feed chain



Canada's Action

- **Epidemiological Investigation**
 - Trace forwards
 - Trace backs
 - Disposition of index cow investigation
 - Investigation into source of infection
- **Depopulations - approximately 2700 animals (index herd, all aqua line; portion of yellow line, over 100 from trace forwards; 3 herds connected to feed)**

Canada's Action (*continued*)

● International Review

- Team from Switzerland, US and New Zealand

- Reviewed Epi investigation - thorough and complete

● Recommendations:

- SRM ban – urgent - **DONE**
- Increase surveillance - high risk not healthy
- Prevent cross contamination in animal feed chain

Canada's Action *(continued)*

- Increase testing 2004 to 8000
- Increase to 30,000 in subsequent years
- Enhanced enforcement activities associated with current identification systems
- Accelerated development over the next two years of a more comprehensive cattle ID program that uses new technologies

Canada: Future Directions

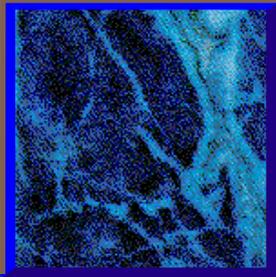
- Feed ban:
 - SRMs from animal feed????
 - On farm compliance

US Actions

- Epi Investigation
- Trace progeny:
 - 2 living (1 in herd, 1 in feeding operation not identified)
- herd cohorts: 28 of 80 identified; (birth cohorts (25 – 13 located, 1 index)
- product:
 - Meat recalled
 - Offals to MBM traced and destroyed by FDA

US Actions

- Prohibit SRMs for human consumption (Canadian list)
- No vertebral column or skull from animals >30 months in AMR
- No spinal cord or DRG from animals <30 months in AMR
- Prohibit “downers” from entering human food chain
- NO MSP or air injected stunning
- Increase surveillance
- Institute system of tracing ASAP



BSE detected in US: Future Actions

FDA and the feed ban??????

FDA – human products



Surveillance: Why do it?

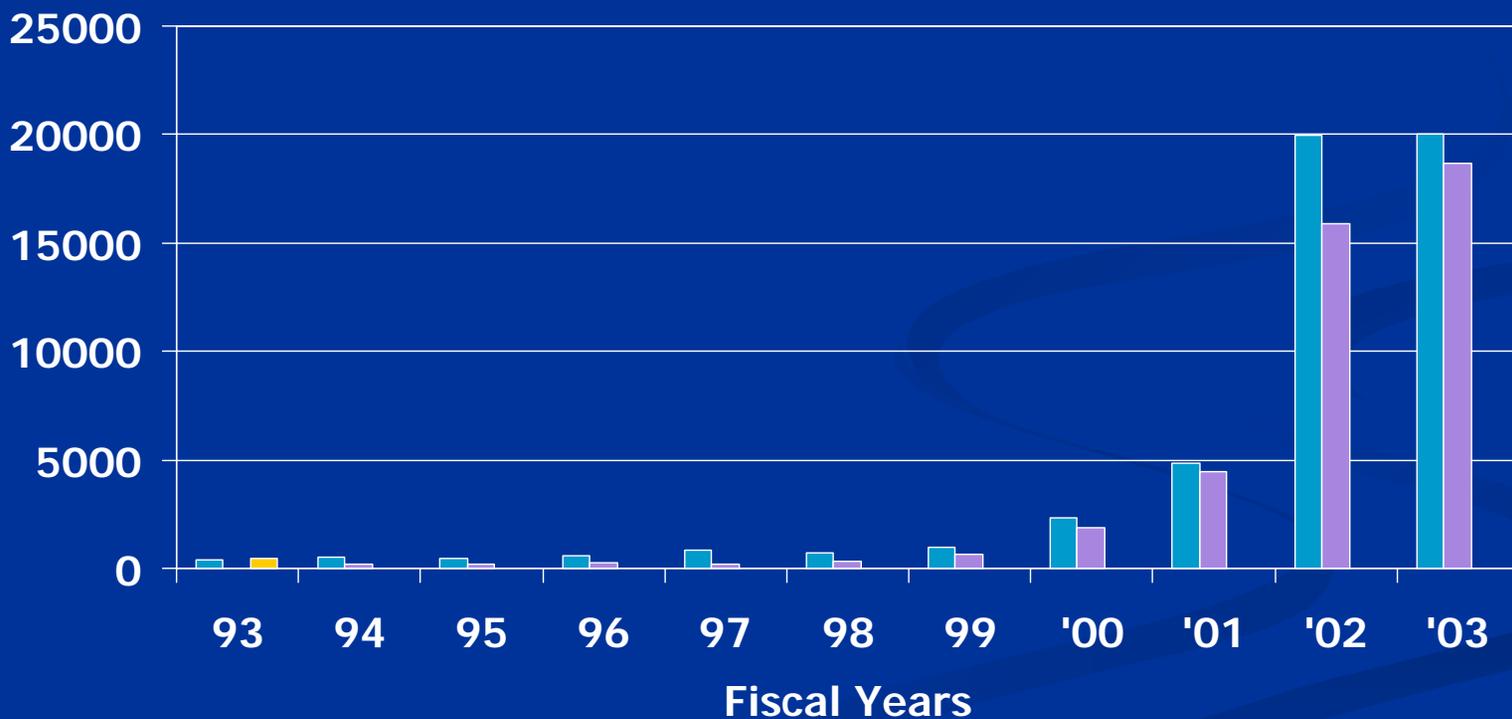
- Is the disease present?
- Will tell you if prevention is successful
- Will tell you if control is working
- Buyer confidence
- Trade confidence



Past Surveillance:

NVSL Bovine Brain Submissions FY 93-03

(as of Sept 30, 2003)



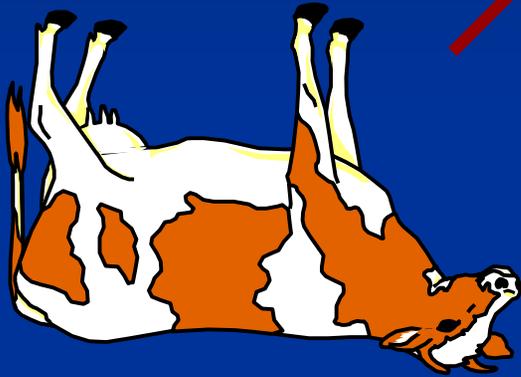
■ Total Submissions ■ "Downers" (fallen stock) ■ OIE Goal

No Evidence of BSE Detected

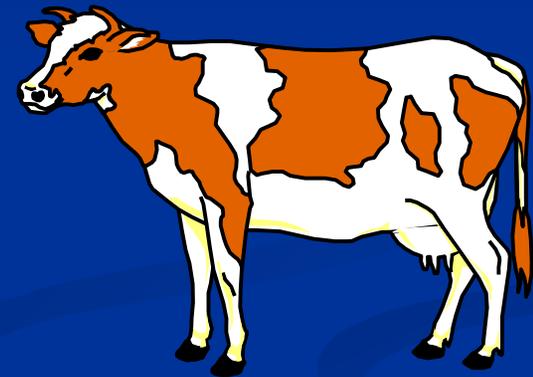
BSE Surveillance: Plan

- Announced by USDA March 15, 2003
- Result of recommendation by International Committee
- Testing of all high risk population and percentage of older cattle to slaughter
- Estimated high risk – 446,000/yr
- Attempts to sample as many as possible
- Realistic goal – 201,000-268,000 samples
- NVSL and TSE Network
- Approval of rapid tests

USDA Surveillance Goal = 268,000



248,000 diseased,
down, dying, dead
(from farms, renderers,
etc)



20,000 healthy cattle
presented for routine slaughter
(Randomly selected from 40
cow plants)

Summary of Actions

- **New regulations for human food supply**
 - No downers
 - SRMs out
 - Stunning
 - AMR restrictions and prohibitions
- **Increased Surveillance**

What More?

- Identification and traceability – pilots starting
- FDA regulated human products – rules in draft
- USDA regulated human food – is it enough?
- Food – cross contamination
- Animal Feed - ??????



Animal Feed: Current Rule

- Prohibits most mammalian protein to ruminants
- Exceptions:
 - Pure porcine
 - Pure equine
 - Milk
 - Blood
 - Gelatin
 - Tallow – containing protein?

Animal Feed: Current Rule

- Prohibits most mammalian protein to ruminants
- Exemptions:
 - Poultry litter
 - Plate waste
 - Unfiltered tallow

Animal Feed: Are there still risks?

- Legal Exemptions
 - Poultry litter
 - Plate Waste
 - Unfiltered tallow
 - Blood
- Cross contamination
- Cross Feeding
- Other Species



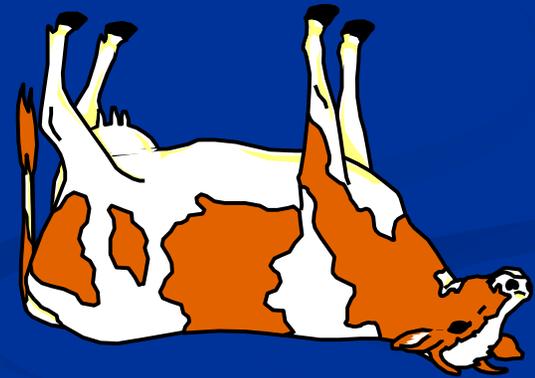
Animal Feed: Where does the risk come from

- SRMs
- Down and dead cattle



What poses a risk: 3D/4D cattle

- More than 50% of cases in EU from 3D/4D population
- Down or dead from BSE – at highest level of infectivity

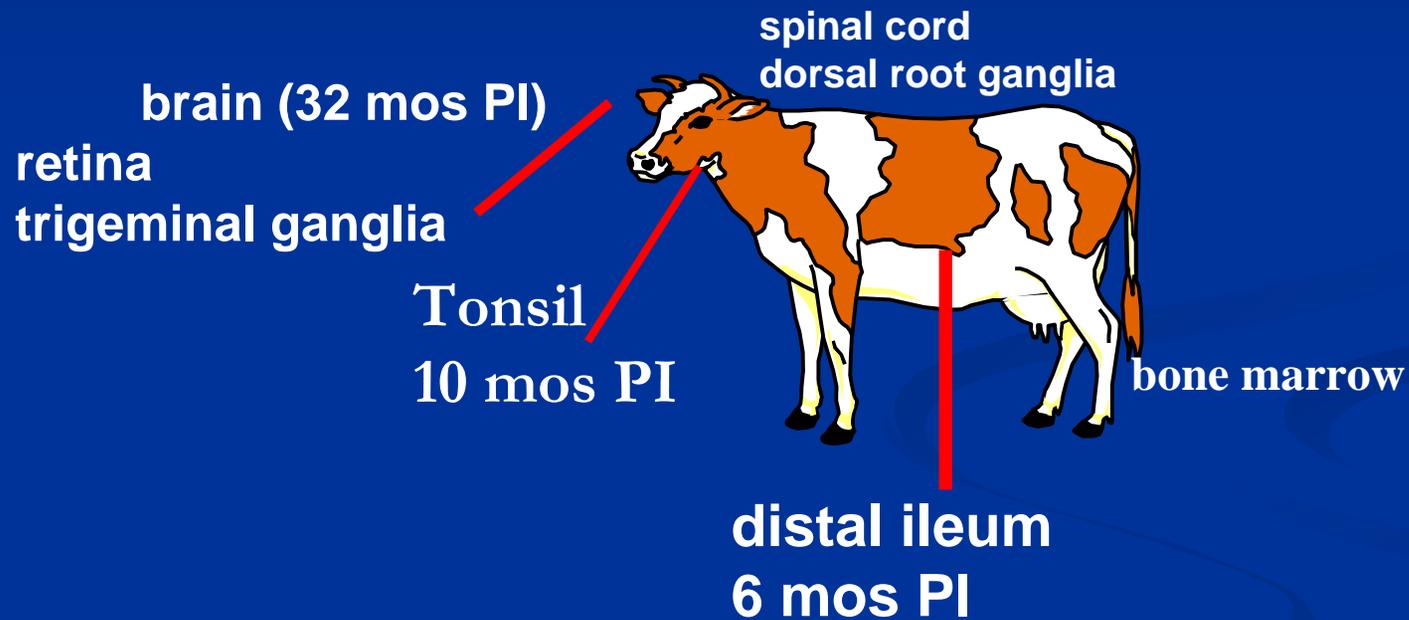


Per the Executive Summary of the 2001 Harvard risk assessment: “Our evaluation of potential risk mitigation actions highlights potential measures to further reduce the already low likelihood that BSE could spread to cattle or contaminate human food if it were to arise. **Prohibiting the rendering of animals that die on the farm, possibly of BSE, removes a great deal of potential contamination in the animal feed chain and reduces average predicted cases of BSE following introduction of ten infected cattle by 77%.**

What poses a risk: SRMs (to date)

- Brain
- Spinal Cord
- Eye
- Trigeminal Ganglia
- Dorsal Root Ganglia
- Distal Ileum (Intestine)
- Vertebral Column
- Skull
- Tonsil
- 3rd eyelid (Nictitating membrane)

Distribution of Infectivity: Experimental



to date not in cattle muscle - UK DEFRA
mouse muscle (Bosque et al., 2002)

Per the Executive Summary of the 2001 Harvard risk assessment: “Our evaluation of potential risk mitigation actions highlights potential measures to further reduce the already low likelihood that BSE could spread to cattle or contaminate human food if it were to arise.

Implementation of a UK-style ban on specified risk material (e.g., spinal cords, brains, vertebral columns) from both human food and animal feed reduces the predicted number of BSE cases in cattle by 80% and the potential human exposure by 95%.”

Cross Contamination: Why risks are difficult if not impossible to eliminate

- Attack rate study
- Inactivation of agent



BSE Transmission: Attack Rate

- studies underway: .1 gr; .01 gr; .001 gr
- .1 gr – 3 of 15 affected
- .01 gr – 1 of 15 (50+ mos incubation)
- .001 gr – 1 of 15 (71 mos)



TSE Inactivation

- “TSE agents are unusually resistant to disinfection and sterilization by most of the physical and chemical methods in common use for decontamination of infectious pathogens.”

WHO Infection Control Guidelines for the TSEs (1999)

WHO Guidelines: Disinfectants

Ineffective vs. TSEs

- Ineffective
 - alcohol
 - ammonia
 - β -propiolactone
 - formalin
 - hydrochloric acid
 - hydrogen peroxide
 - peracetic acid
 - phenolics
 - sodium dodecyl sulfate (SDS) (5%)
 - ethylene oxide
 - formaldehyde
- Ineffective
 - boiling
 - dry heat (<600°C)
 - ionising, UV or microwave radiation
- Variably or partially effective
 - autoclaving at 121°C for 15 minutes
 - boiling in 3% sodium dodecyl sulfate (SDS)
 - Certain rendering systems

Rendering

- Most effective is not 100% effective
- Most effect 133 C, 3 bar, 20 minutes
- Systems very limited in US

Cross Contamination: Feed

- Methods of processing can theoretically increase the risk to products via cross contamination
- Feed: throughout processing chain: rendering, feed manufacturer, transport, on farm mills, equipment
- Alterations in practices can reduce cross contamination

Significance of cross contamination

- UK experience – predicted 60 cases through 2005
- Switzerland – Feed tests still finding MMBM in feed



Cross Feeding

- Definition: The feeding of rations made for a certain species to a different species. Ie. The feeding of pig or poultry feed to cattle
- Human Error
- Europe
- Canada
- US

BSE: Other animal species

- Feline Spongiform Encephalopathy
- TSE of Exotic Ruminants

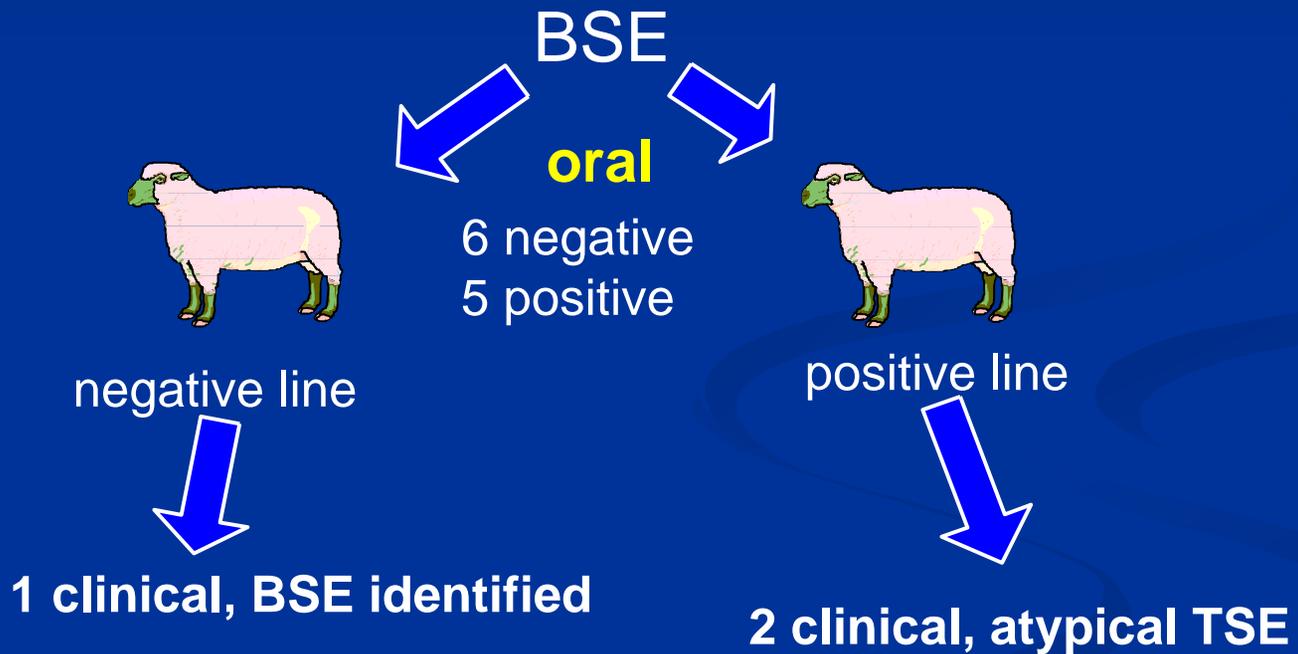


domestic cats
large cats

kudu
nyala
gemsbok
bison



BSE in Sheep: Research (Foster et. al.)

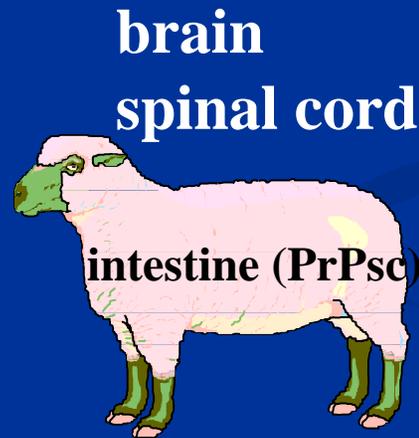


BSE in Sheep: Research

Distribution of Infectivity

Results thus far like scrapie – publication in press (UK)

**blood- via
transfusion
(Houston et
al., 2000;
Hunter et
al., 2002)**



**spleen
(Foster
et al.,
1996)**

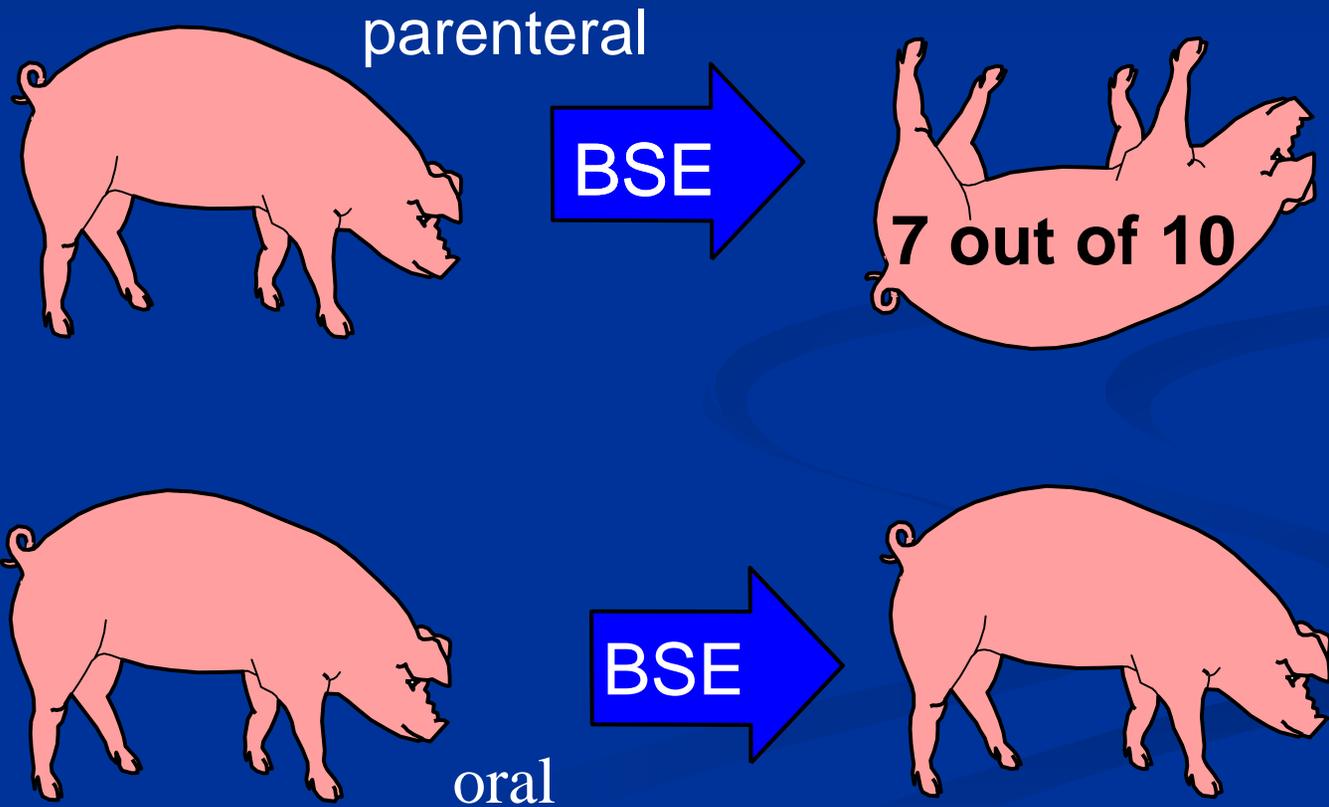
BSE in Sheep: European Situation

- Exposure to contaminated MBM
- Surveillance for TSE in sheep
- Must differentiate from scrapie - mouse bioassay system (2-3 yrs)
- None to date - limited number assessed
- Public Health Protection - SRM ban on sheep and goat tissues

BSE in Sheep: Worse Case Scenario

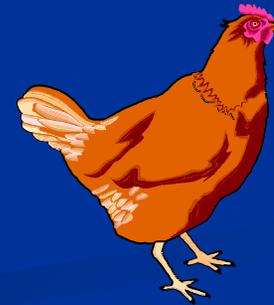
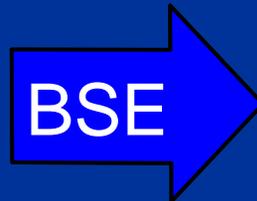
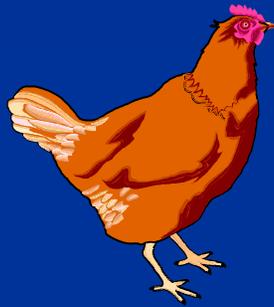
- Fatal zoonotic disease in a species with wide tissue distribution
- Disease spreads from one animal to another not solely by feed
- Disease clinically looks like common endemic disease, cannot be differentiated by validated rapid tests
- How does a country assure food safety?

BSE to Pigs: Research

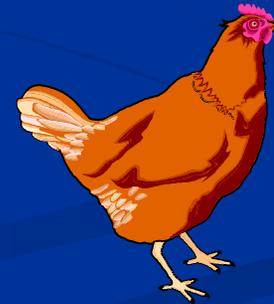
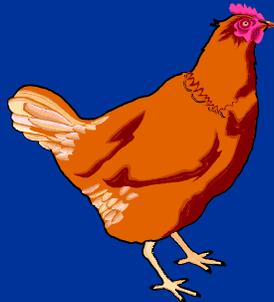


BSE to Chickens: Research

parenteral



oral



Expert Advice

- WHO
- Harvard
- International
Committee
- Other Scientists

Subclinical State: Pigs?

■ Neurobiology of Disease

Subclinical Bovine Spongiform Encephalopathy Infection in Transgenic Mice Expressing Porcine Prion Protein

Joaquín Castilla,¹ Alfonso Gutiérrez-Adán,² Alejandro Brun,¹ Deirdre Doyle,³ Belén Pintado,² Miguel A. Ramírez,² Francisco J. Salguero,¹ Beatriz Parra,¹ Fayna Díaz San Segundo,¹ José M. Sánchez-Vizcaíno,¹ Mark Rogers,³ and Juan M. Torres¹

¹Centro de Investigación en Sanidad Animal, Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria, Valdeolmos, 28130 Madrid, Spain, ²Departamento de Reproducción Animal y Conservación de Recursos Zoogenéticos, 28040 Madrid, Spain, and ³Department of Zoology and Conway Institute for Biomolecular and Biomedical Research, University College Dublin, Belfield, Dublin 4, Ireland

WHO

"No part or product of any animal which has shown signs of a TSE should enter any food chain (human or animal). In particular:

- All countries must ensure the killing and safe disposal of all parts or products of such animals so that TSE infectivity cannot enter any food chain.

Harvard

Implementation of a UK-style ban on specified risk material (*e.g.*, spinal cords, brains, vertebral columns) from both human food and animal feed reduces the predicted number of BSE cases in cattle by 80% and the potential human exposure by 95%.”

Experts

- International Committee
- Other scientists – have we asked them????

Diagrammatic representation of the BSE epidemic

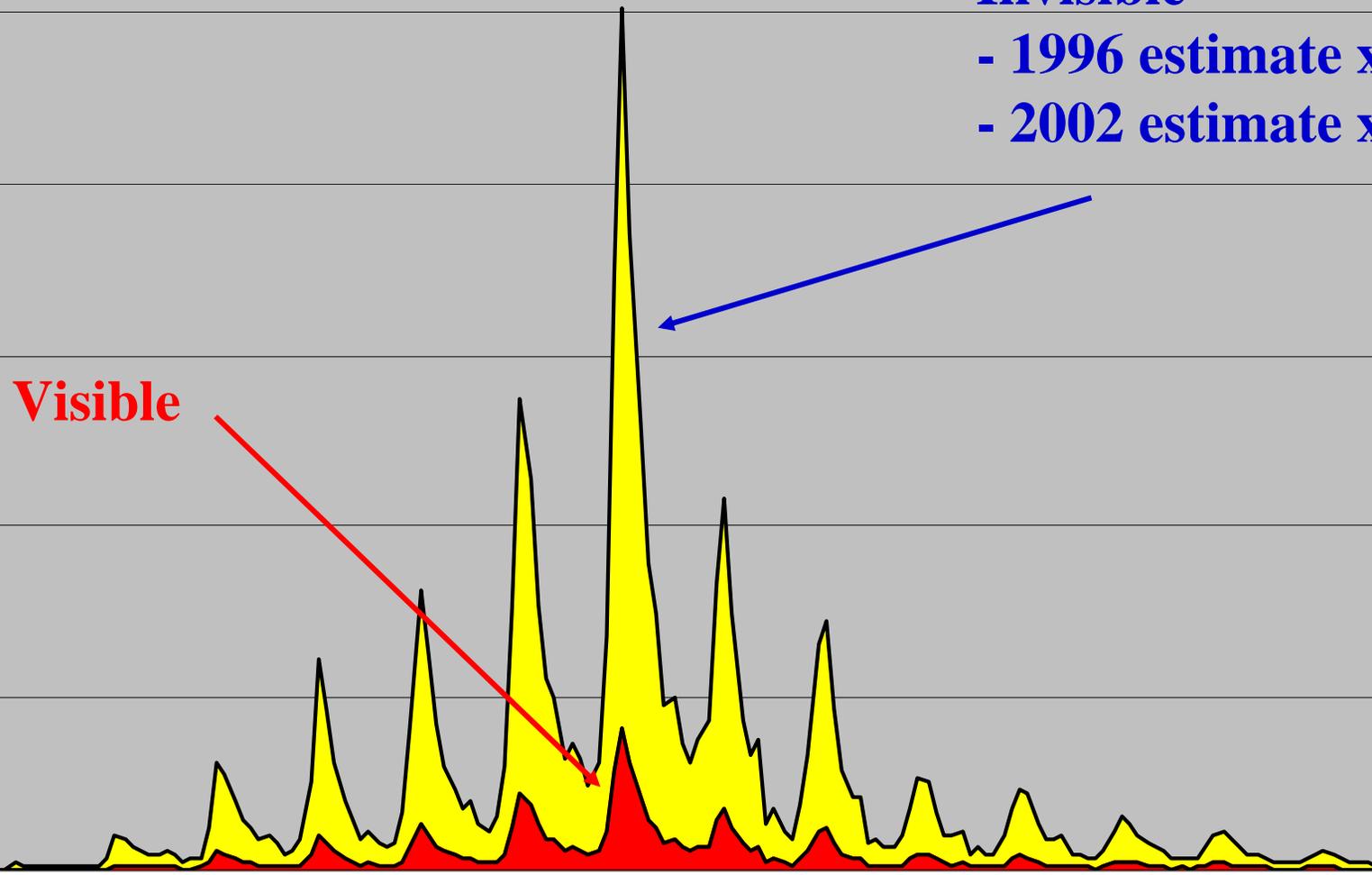
Plot is by date of birth

Invisible

- 1996 estimate x 5

- 2002 estimate x 15+

Visible



Harvard

- Harvard report: With the current protections in place if BSE were in the country the cases would be on the decline.
- The model predicts BSE would be gone in 20 years.
- Can we afford to wait 20 years???

Transmissible Spongiform Encephalopathies: Family

Long incubation diseases with limits to preclinical test

Think - if I knew disease would be here tomorrow, what should I have done yesterday



BSE Headlines:

WATCH THIS SPACE, MORE
EXCITING INFORMATION TO
COME.....

