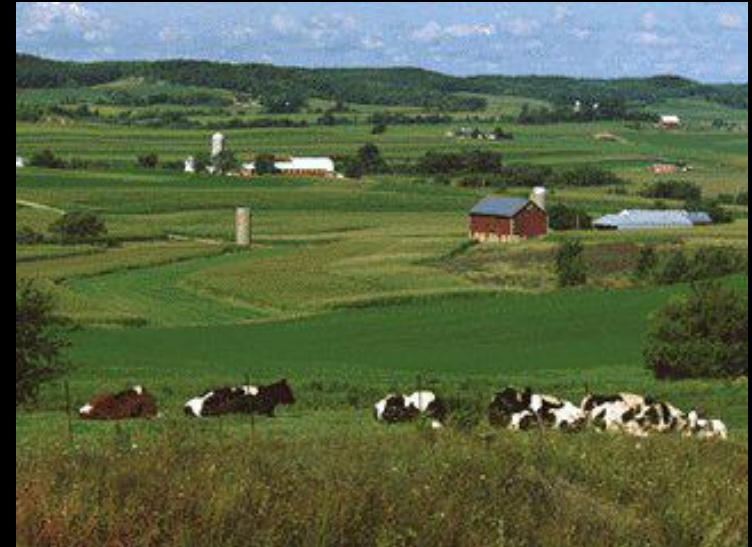
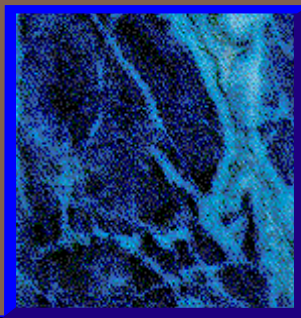


Bovine Spongiform Encephalopathy: An Update

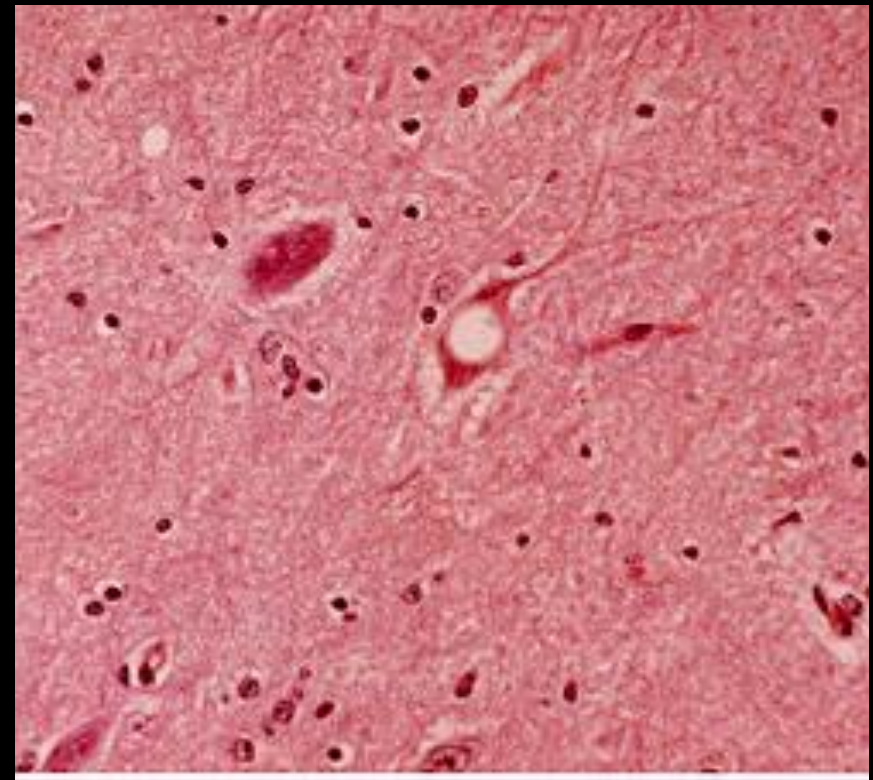
Linda A. Detwiler
Senior Staff Veterinarian
USDA, APHIS, VS

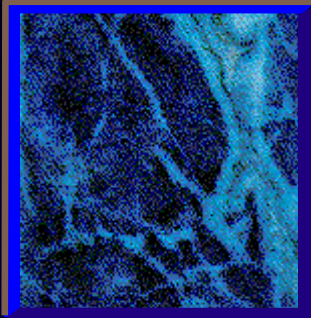




Transmissible Spongiform Encephalopathies

- ❑ prolonged incubation period
- ❑ progressive debilitating neurological illness
- ❑ pathological changes confined to CNS
- ❑ fatal

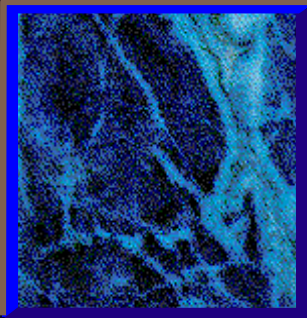




Transmissible Spongiform Encephalopathies

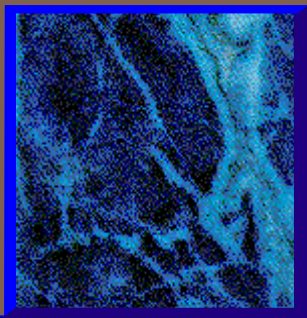
- ❑ Scrapie Associated Fibrils (SAF) - negative stain EM
- ❑ Transmissibility





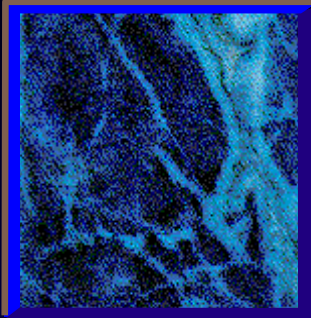
Transmissible Spongiform Encephalopathies: Etiology

- ❑ agent not fully characterized
- ❑ smaller than smallest known virus
- ❑ elicits no detectable immune or inflammatory response in the host
- ❑ resistant to most disinfectants and treatments which normally destroy nucleic acids



Transmissible Spongiform Encephalopathies: Agent Theories

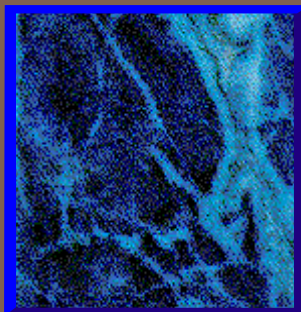
- ❑ **VIRUS** - unconventional, unusual biochemical and biophysical properties
- ❑ **VIRINO** - host-derived protein coat coupled to a small noncoding regulatory nucleic acid
- ❑ **PRION** - host-coded normal cellular protein becomes partially protease resistant through post translational conformation change



Transmissible Spongiform Encephalopathies: Human

- ❑ Creutzfeldt-Jakob Disease (CJD)
- ❑ Gerstmann-Straussler-Scheinker syndrome (GSS)
- ❑ fatal familial insomnia (FFI)
- ❑ Kuru
- ❑ variant CJD (vCJD)

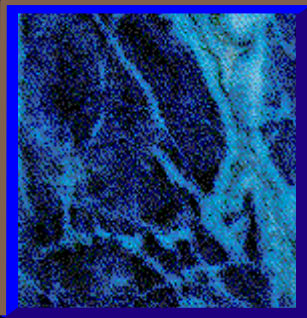




Transmissible Spongiform Encephalopathies: Scrapie

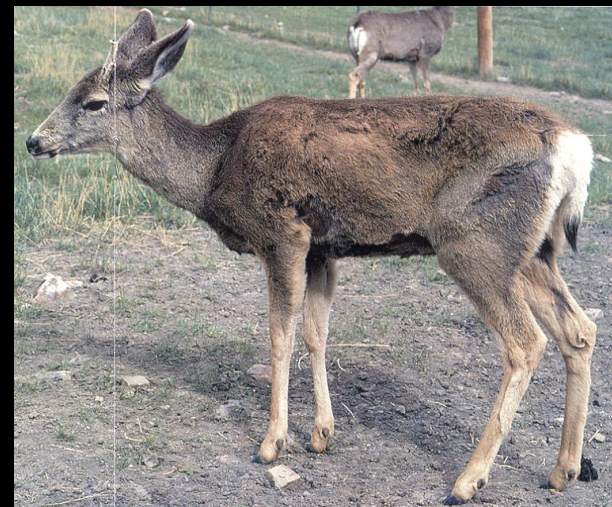
- ❑ Reported most sheep producing regions
- ❑ Known over 250 years
- ❑ Sheep, goats, moufflon

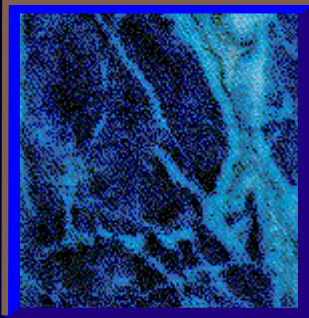




Transmissible Spongiform Encephalopathies: Chronic Wasting Disease

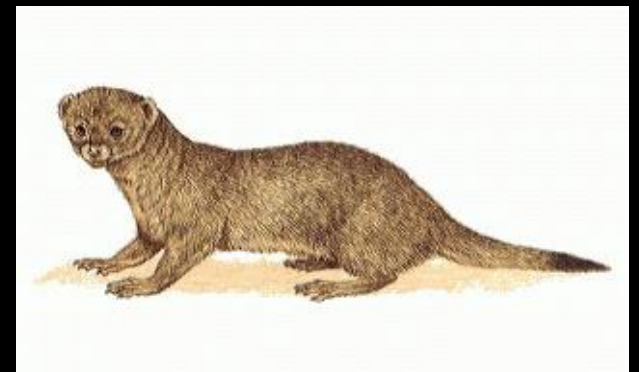
- ❑ First recognized as disease syndrome - 1967
- ❑ Colorado, Wyoming - endemic areas
- ❑ Farm raised elk

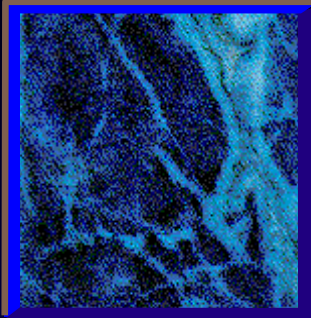




Transmissible Spongiform Encephalopathies: Transmissible Mink Encephalopathy

- ❑ Affects ranch raised mink
- ❑ First recognized in 1947
- ❑ Detected and documented in Canada, Finland, (East) Germany, Russia
- ❑ Associated with feed

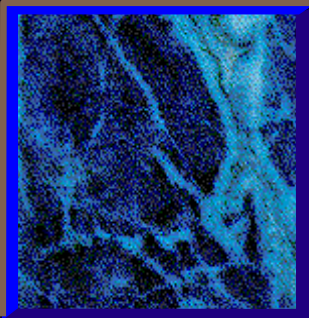




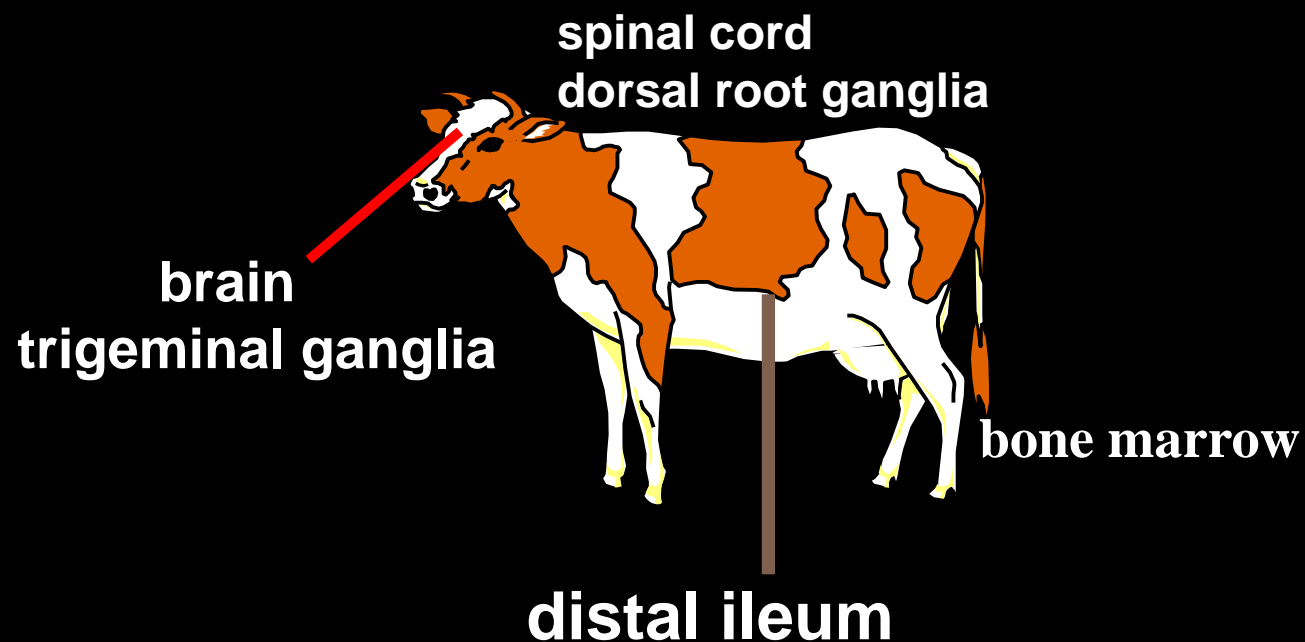
Transmissible Spongiform Encephalopathies: Animal

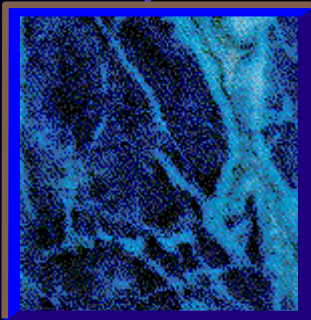
- ❑ Bovine Spongiform Encephalopathy
- ❑ Feline Spongiform Encephalopathy
- ❑ TSE of Exotic Ruminants





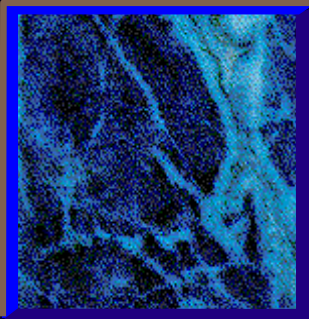
Distribution of Infectivity





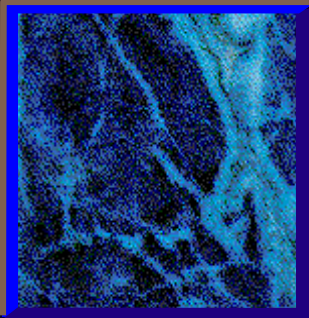
Transmission





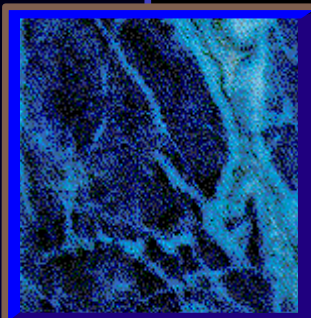
BSE Diagnostics

- ❑ No live animal test
- ❑ No preclinical test
- ❑ Need brain tissue
- ❑ Histology, IHC, WB, ELISA
- ❑ "Negatives" do not guarantee absence of infectivity



TSE Diagnostics: EU Approved

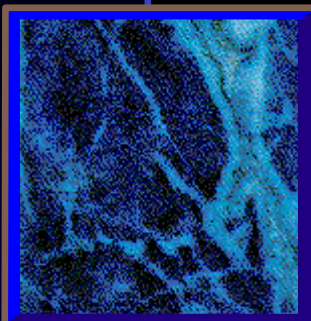
- ❑ Histology
- ❑ Standard IHC and Western Blot
- ❑ Prionics AG - modified Western Blot (8 hrs)
- ❑ Enfer Ltd. - High throughput chemiluminescence ELISA (3-4 hrs)
- ❑ CEA - Sandwich Immunoassay (3-4 hrs)
- ❑ all require brain/clinical cases



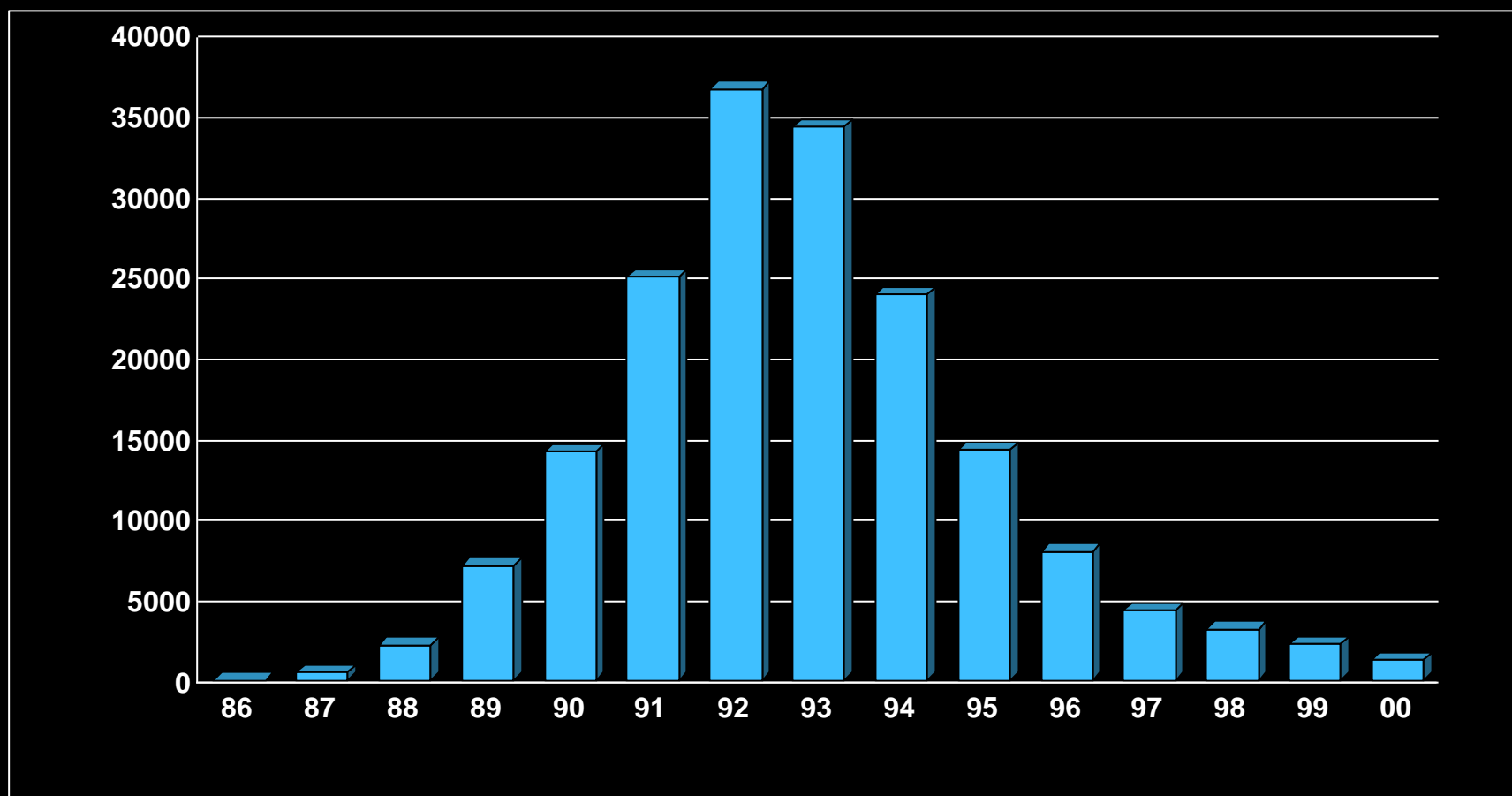
BSE STATISTICS for GREAT BRITAIN* (as of February 9, 2001)

Total number of confirmed cases:	177,717
Total number of affected herds:	35,150
Proportion of dairy herds affected:	61.3%
Proportion of beef suckler herds affected:	16.6%
Confirmed total herd incidence:	37.5%

* England, Scotland, Wales

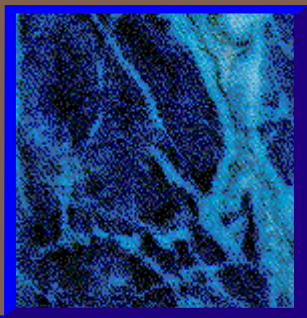


Confirmed cases of BSE in Great Britain by year of restriction (1986 - 1 December 2000)*



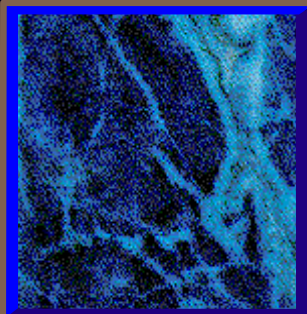
*Includes 46 cases not subject to official restriction and

identified by retrospective surveillance and other sources



UK MAFF Actions

- ❑ Mammalian to food animal feed ban
- ❑ Over thirty month scheme
- ❑ Selective Cull
- ❑ Offspring Cull
- ❑ SRM/SBO bans
- ❑ Beef on the bone prohibition - No longer in place



First cases of BSE

Total number of cases (3-12-01)

UK >180,000

Belgium - 23

Ireland - 653

Spain - 32

Italy - 4

Portugal - 528

Netherlands - 13

Switzerland - 370

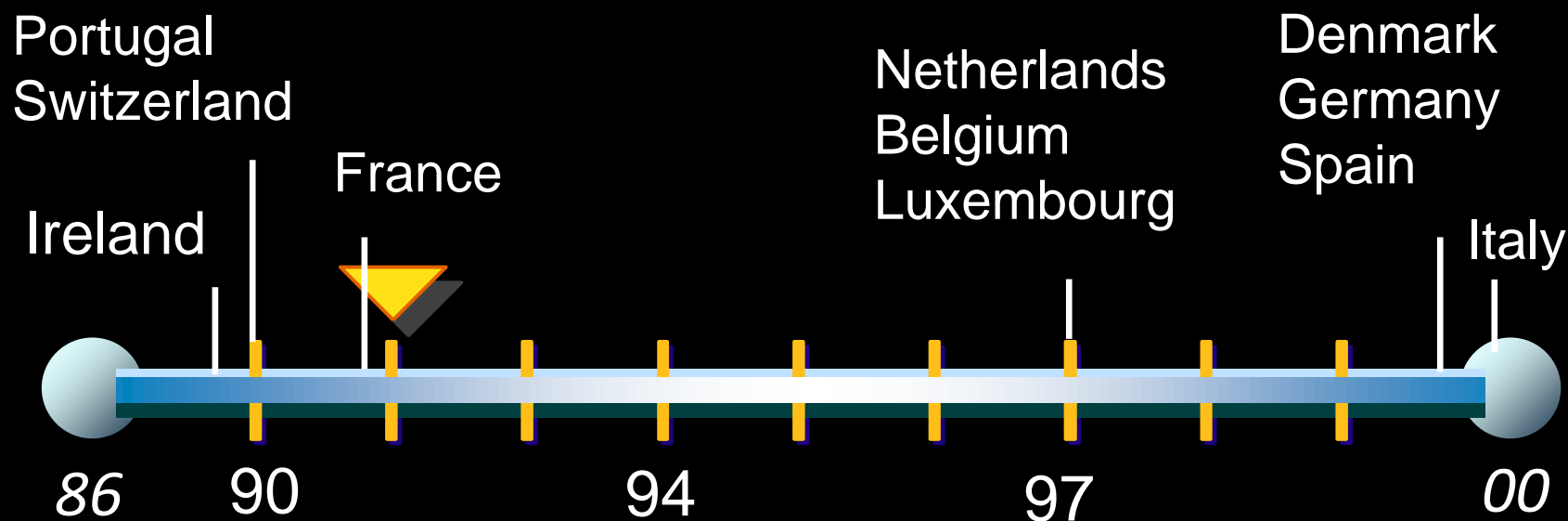
Liechtenstein - 2

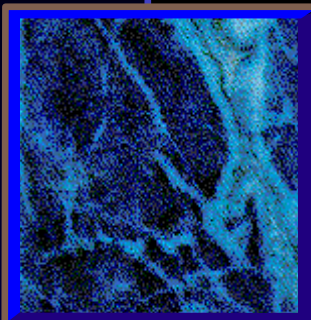
France - 279

Denmark - 2

Germany - 44

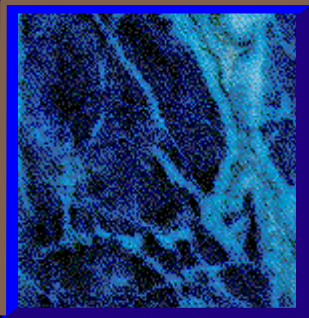
Luxembourg - 1





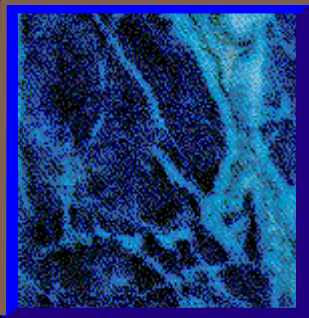
BSE Incidence Rate (per million cattle > 2 yrs)

	<u>98</u>	<u>99</u>
United Kingdom	596	422
Portugal	147	236
Switzerland	16	53
Ireland	22	27
France	2	3
Belgium	4	2
Netherlands	1	1



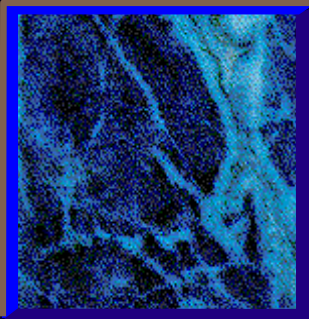
BSE: Control Measures in EU

- ❑ SRM bans on sheep, goats, cattle (Oct 2000)
- ❑ Prohibit feeding of most processed animal proteins (excluded fish meal) to farmed animal (Jan 2001)
- ❑ test of all cattle >30months at slaughter (if cannot test destroy) (Jan 2001)



EU BSE Surveillance

- ❑ CNS cases
- ❑ Fallen stock and emergency slaughter
- ❑ herd mates of positive cases in some countries
- ❑ all bovines to slaughter > 30 months of age or older
- ❑ Negative doesn't guarantee lack of infectivity



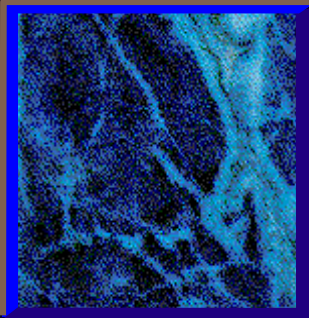
BSE: Comparison of surveillance

□ France

- 450,000 > 30 mos tested - 10 pos (1-01 to 3-01)
- 54,000 fallen stock tested - 68 pos (summer 2000 to 3-01)

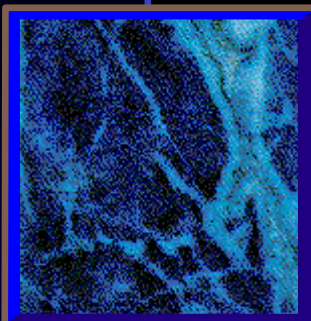
□ Switzerland

- 14,900 normal slaughter - (3 pos 99; 0 pos 00)
- 22,900 fallen and ES - (22 pos 99; 16 pos 00)



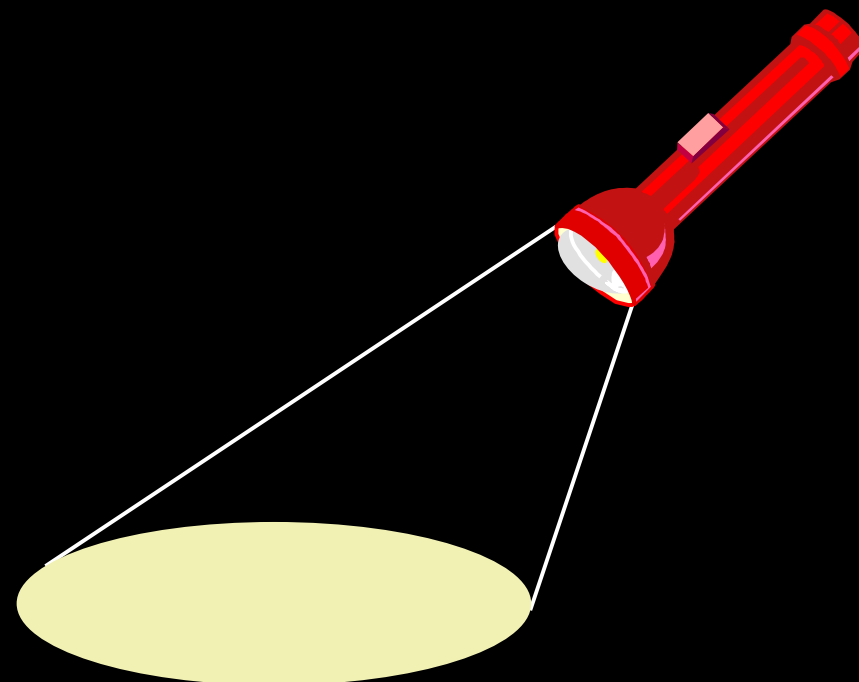
Fallout from BSE (Nov-Feb)

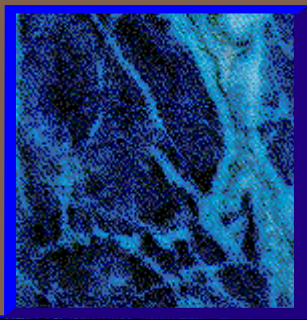
- ❑ Meat sales drop dramatically
- ❑ Loss of consumer confidence
- ❑ Politicians resign or lose jobs
- ❑ Disposal Problems (carcasses/MBM)
- ❑ Logistical test problems



EU Geographical BSE Risk

- ❑ 25+ countries evaluated
- ❑ Member states
- ❑ Non member states
- ❑ Examined:
 - ❑ Challenges
 - ❑ Stability of system





EU Geographical BSE Risk

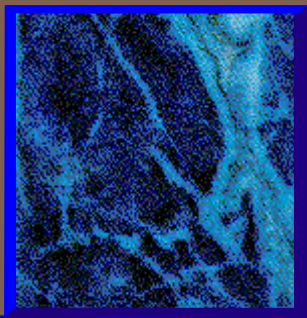
□ Challenges

□ External

- cattle
- MBM

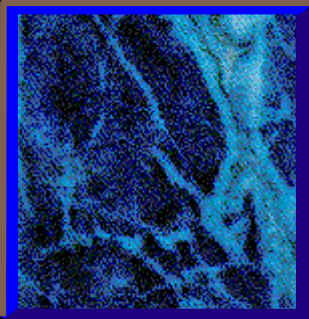
□ Internal

- cattle
- MBM



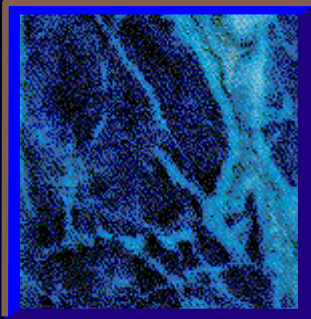
EU Geographical BSE Risk (*continued*)

- Stability
 - Feed bans
 - Rendering
 - Time
 - Temperature
 - Pressure
 - SRM bans



EU Categories of Risk

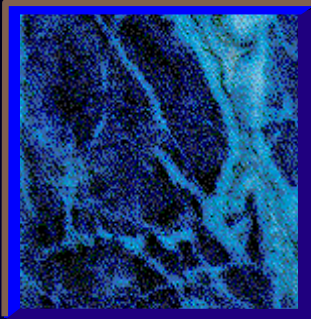
- I - Highly Unlikely
- II - Unlikely but Cannot be excluded
- III -
 - Likely but not confirmed
 - BSE confirmed at a lower level
- IV - BSE confirmed at a higher level



Category I

- ❑ Argentina
- ❑ Australia
- ❑ Chile
- ❑ New Zealand
- ❑ Norway
- ❑ Paraguay
- ❑ Uruguay
- ❑ Botswana
- ❑ Namibia
- ❑ Nicaragua,
- ❑ Swaziland

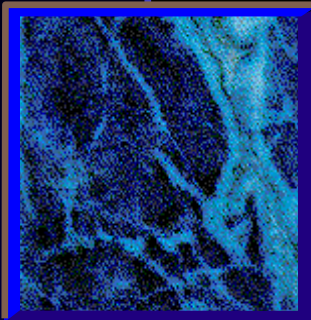




Category II

- ☐ Austria
- ☐ Finland
- ☐ Sweden
- ☐ Canada
- ☐ United States

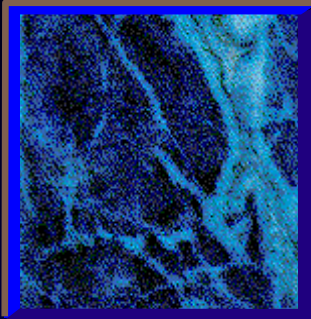




Category III

- ☐ Germany
- ☐ Italy
- ☐ Spain
- ☐ Lithuania
 - ☐ Belgium
 - ☐ Denmark
 - ☐ France
 - ☐ Ireland
 - ☐ Luxembourg
 - ☐ Netherlands
 - ☐ Switzerland

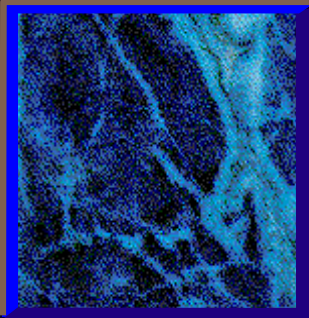




Category IV

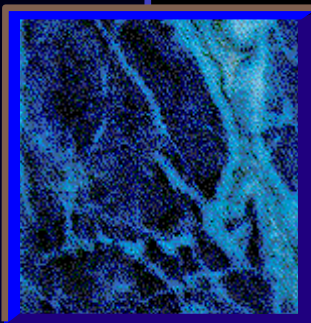
- ❑ United Kingdom
- ❑ Portugal





CJD vs. vCJD

- sporadic, genetic, iatrogenic
- 55-75 yrs of age
- ≤ 6 mos clinical course
- memory loss, myoclonus, dementia
- no plaques in brain
- food contaminated with BSE infected CNS
- 28 yrs. median
- avg 14 mos clinical course
- psychiatric followed by neuro
- florid plaques



vCJD Cases

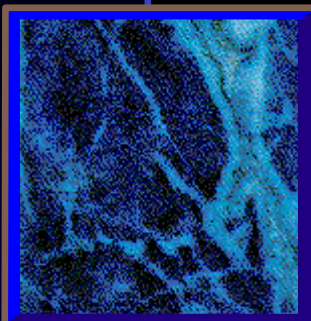
(as of April 2001)



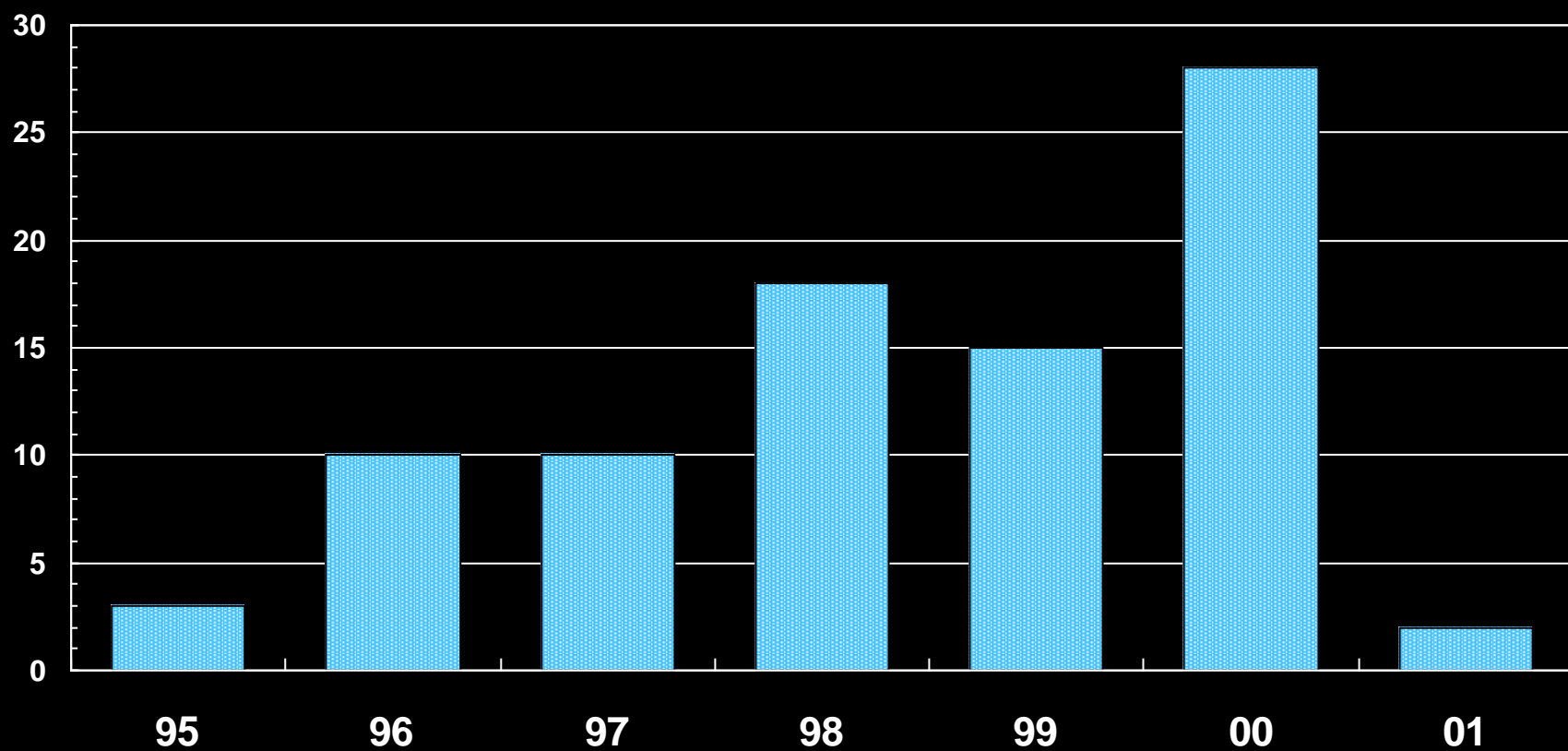
*** vCJD cases - 98 definite and probable**

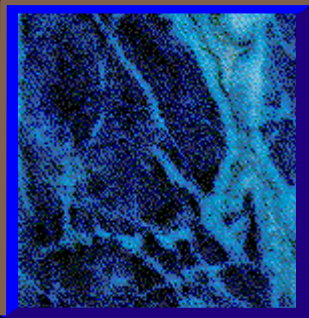


*** vCJD cases - 2 definite, 1 probable**

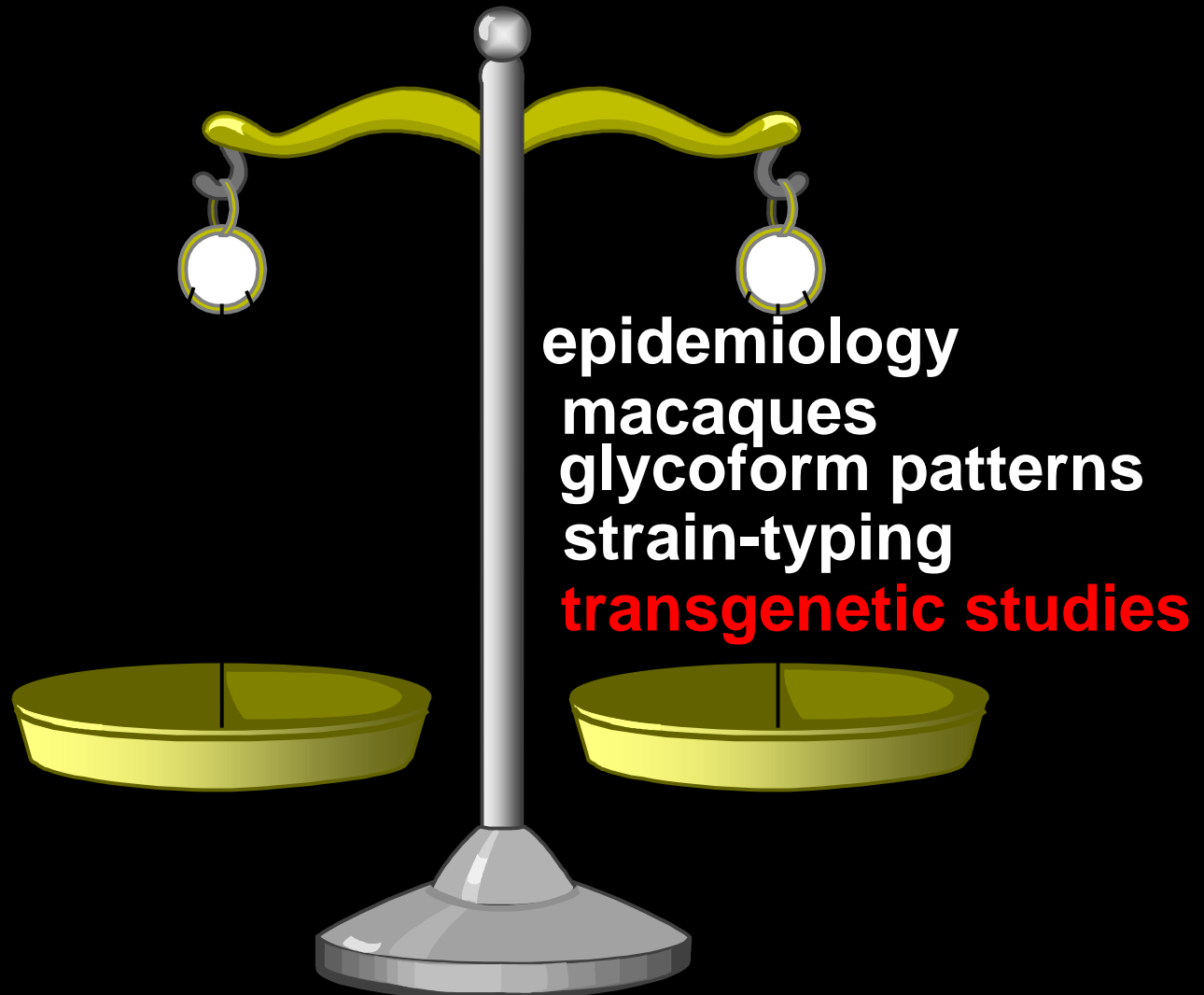


vCJD cases by Year

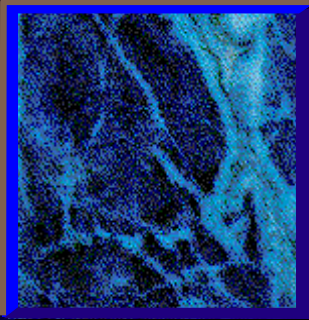




[?]
vCJD = BSE

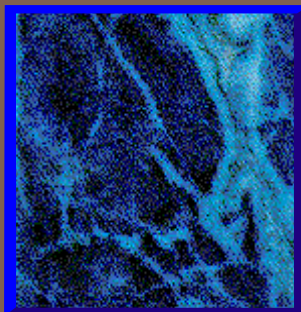


epidemiology
macaques
glycoform patterns
strain-typing
transgenic studies



vCJD: Distribution of Infectivity

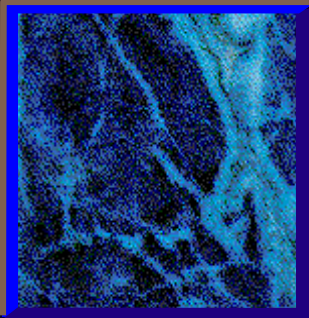
- ❑ Different than classical CJD
- ❑ Spleen, tonsil, appendix
- ❑ Retrospective study - 3000 samples - negative results
- ❑ leucodepletion of blood supply
- ❑ UK imports plasma and plasma products
- ❑ US and Canadian deferrals



USDA ACTIONS: Prevention and Surveillance

- ❑ Import Regulations
- ❑ Surveillance
- ❑ Formal Risk Assessments
- ❑ TSE Working Group

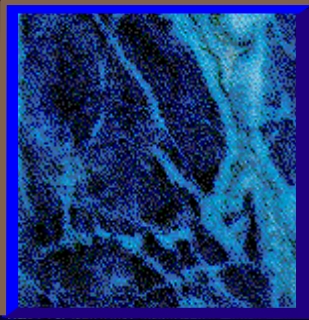




BSE - Prevention

- ❑ Import Restrictions - countries with BSE
 - ❑ July 1989 - live ruminants
 - ❑ November 1989 - ruminant products
 - ❑ 1991 - formal regulations
- ❑ Import Restrictions - Europe
 - ❑ December 1997
 - ❑ January 1998 - interim rule
 - ❑ all live ruminants and ruminant products

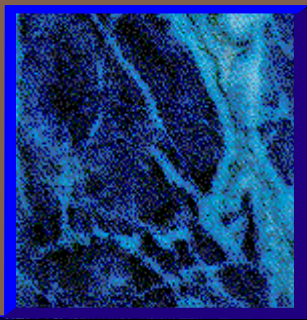




BSE - Prevention

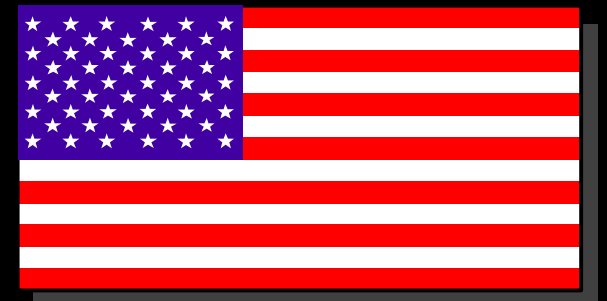
- ❑ Import Restrictions - Europe
 - ❑ December 6, 2000 - all MBM, etc. regardless of species
- ❑ Evaluations of other countries
 - ❑ South America underway
 - ❑ Central America
 - ❑ Asia

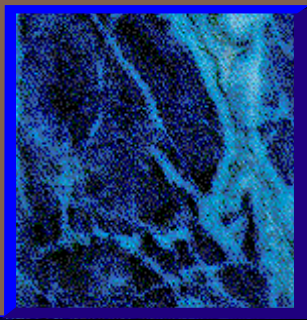




Import Policies and Regulations

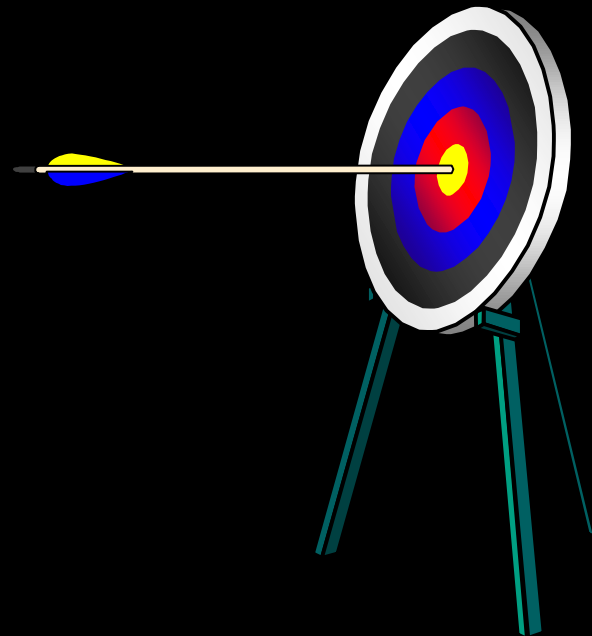
□ North American
Policy

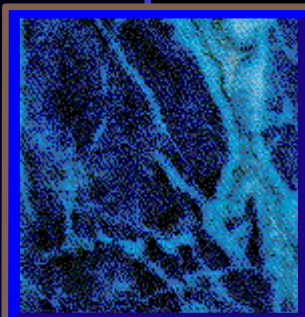




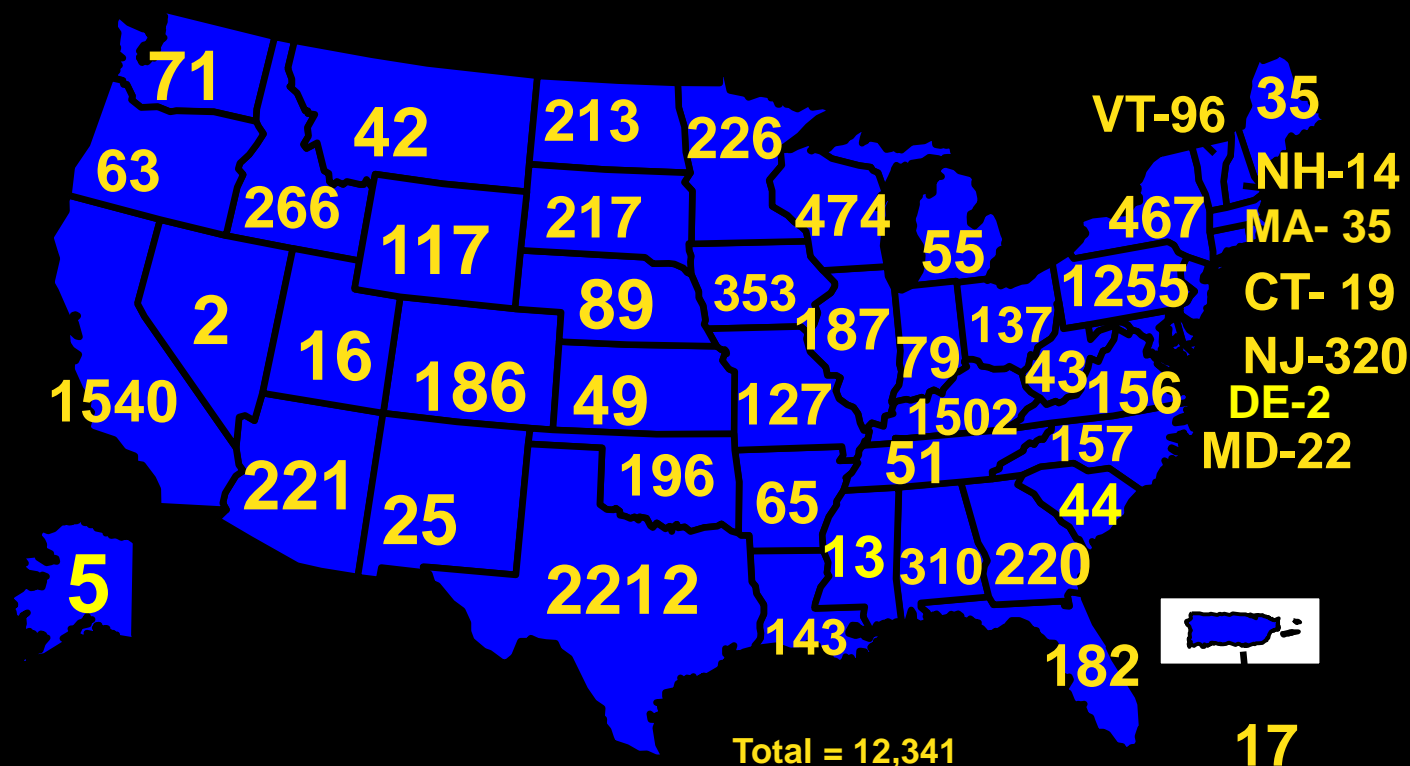
USDA ACTIONS: Surveillance

- ❑ Field CNS Cases
- ❑ VDL data
- ❑ CNS condemnns at slaughter
- ❑ "Downers"



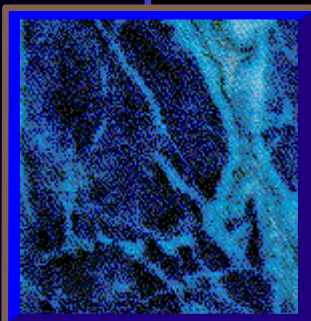


BSE Surveillance: Total Bovine Brain Submission by State May 10, 1990 thru March 31, 2001



Source: USDA, APHIS, NVSL

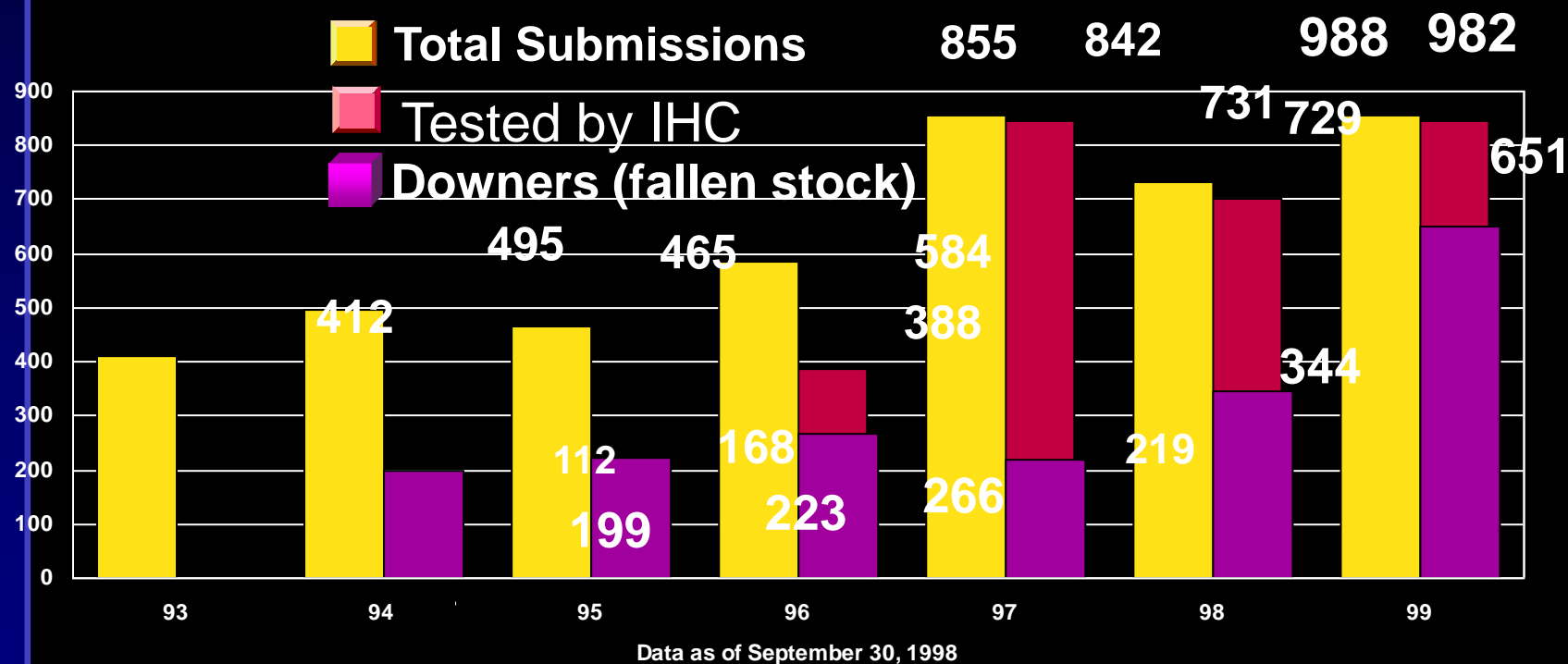
Note: None of the US Brain Submission Have Tested Positive for BSE

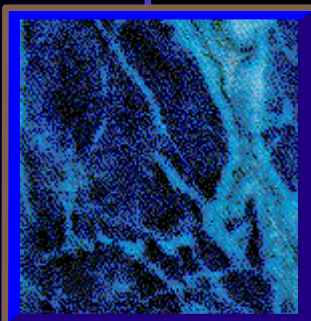


BSE Surveillance

NVSL Bovine Brain Submissions

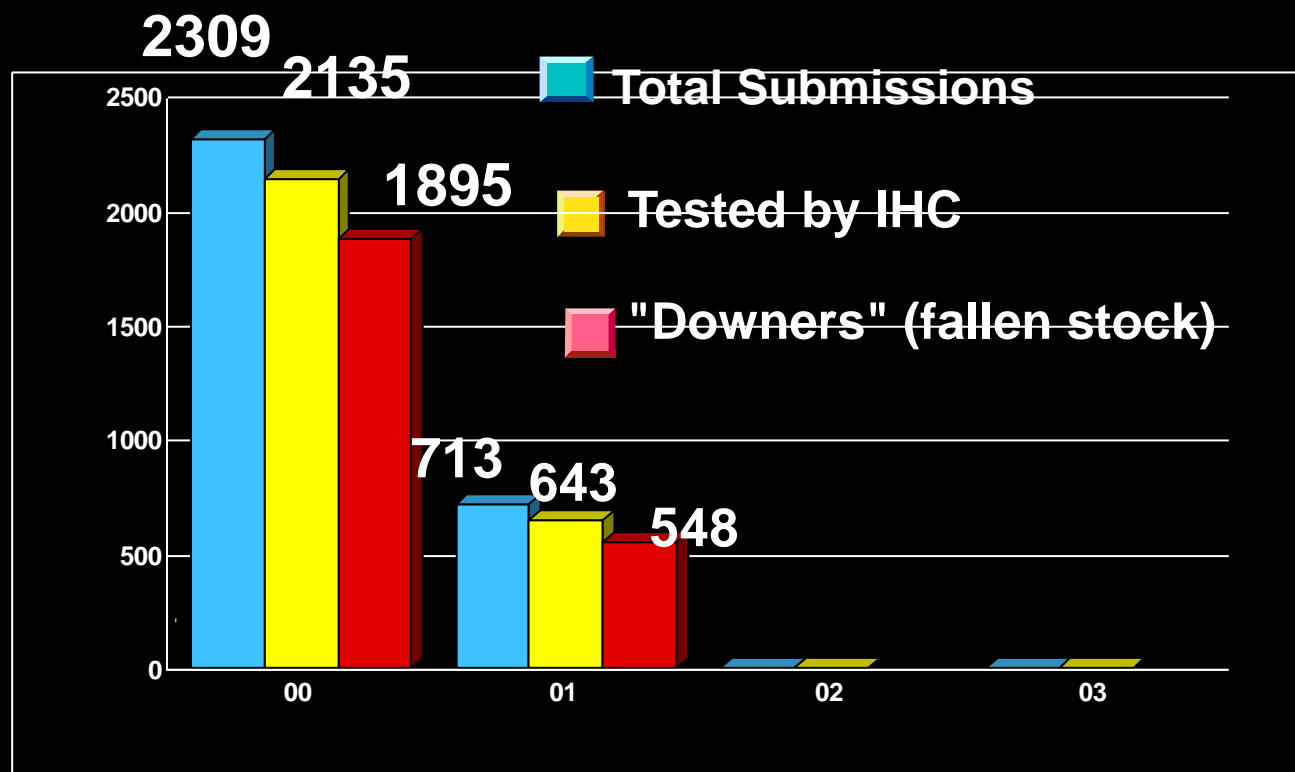
FY 93-99

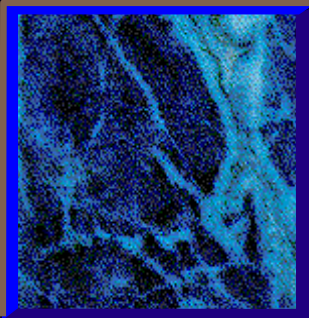




NVSL BSE Surveillance

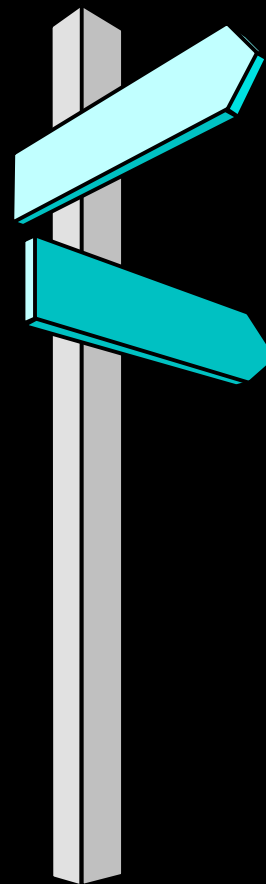
Bovine Brain Submissions FY 00-01 (as of 3-31-01)

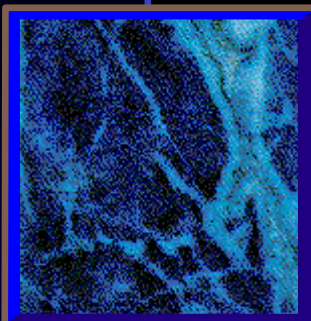




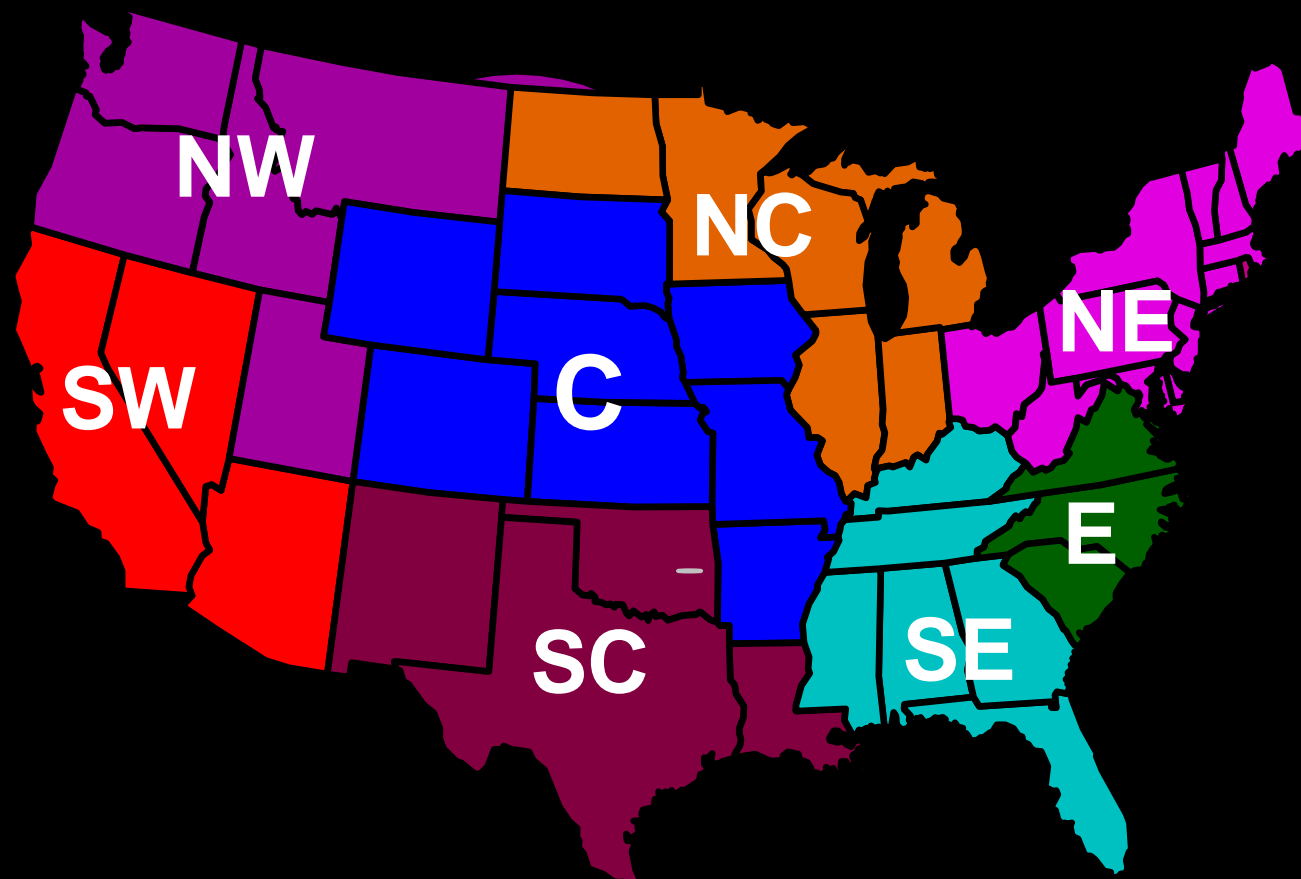
US Surveillance: Current Direction

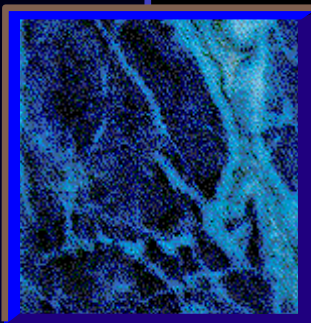
□ Regional Goals



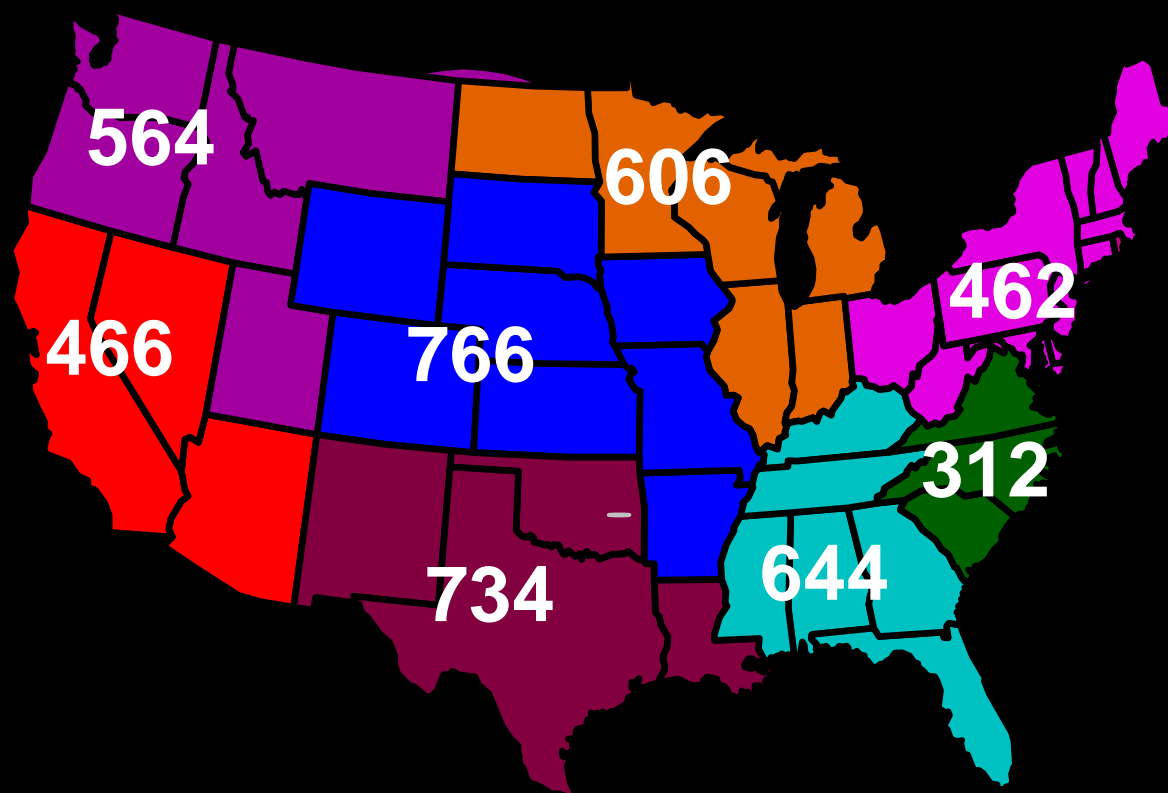


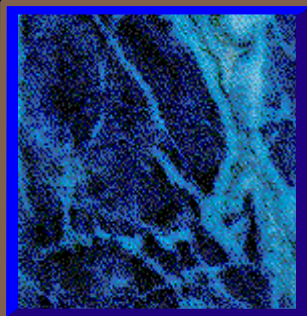
US Regions for BSE Surveillance





US Regional Goals for BSE Surveillance - FY 2001

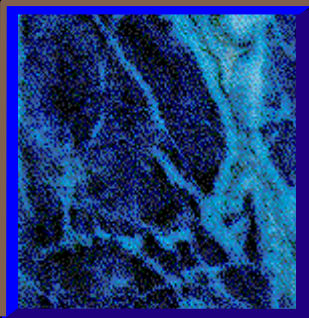




US Regional Goals for BSE Surveillance (2001)

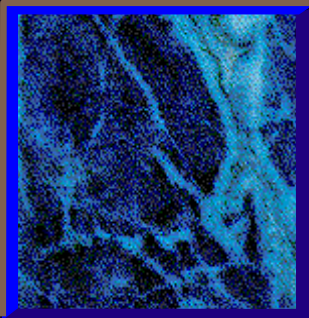
REGION	GOAL 2x OIE goals	FY 99	FY 2000	FY 2001*
NW	564	27	134	118
SW	466	256	226	68
C	766	159	120	60
SC	734	281	1094	250
NC	606	135	240	54
NE	462	331	461	122
E	312	26	30	16
SE	644	194	367	51

* as of March 31, 2001



Increase of submissions

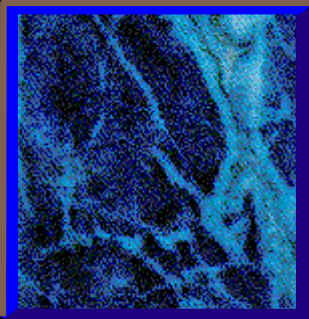
- ❑ Down cattle:
 - ❑ aged; dairy vs. beef
 - ❑ condemns at slaughter
 - ❑ 3D/4D
 - ❑ Renderers
- ❑ Remind VDLs to submit data



Surveillance Reminders

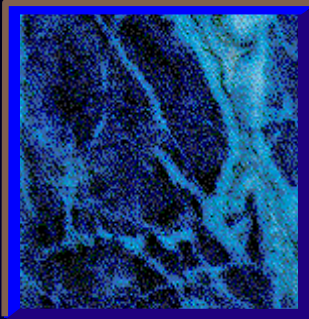
- ❑ Submissions need:
 - ❑ obex
 - ❑ age of bovine
 - ❑ ID
 - ❑ clinical signs (or down)
 - ❑ 10-4 & supplemental
 - ❑ plant number
- ❑ Questions call NVSL
(515-663-7521)



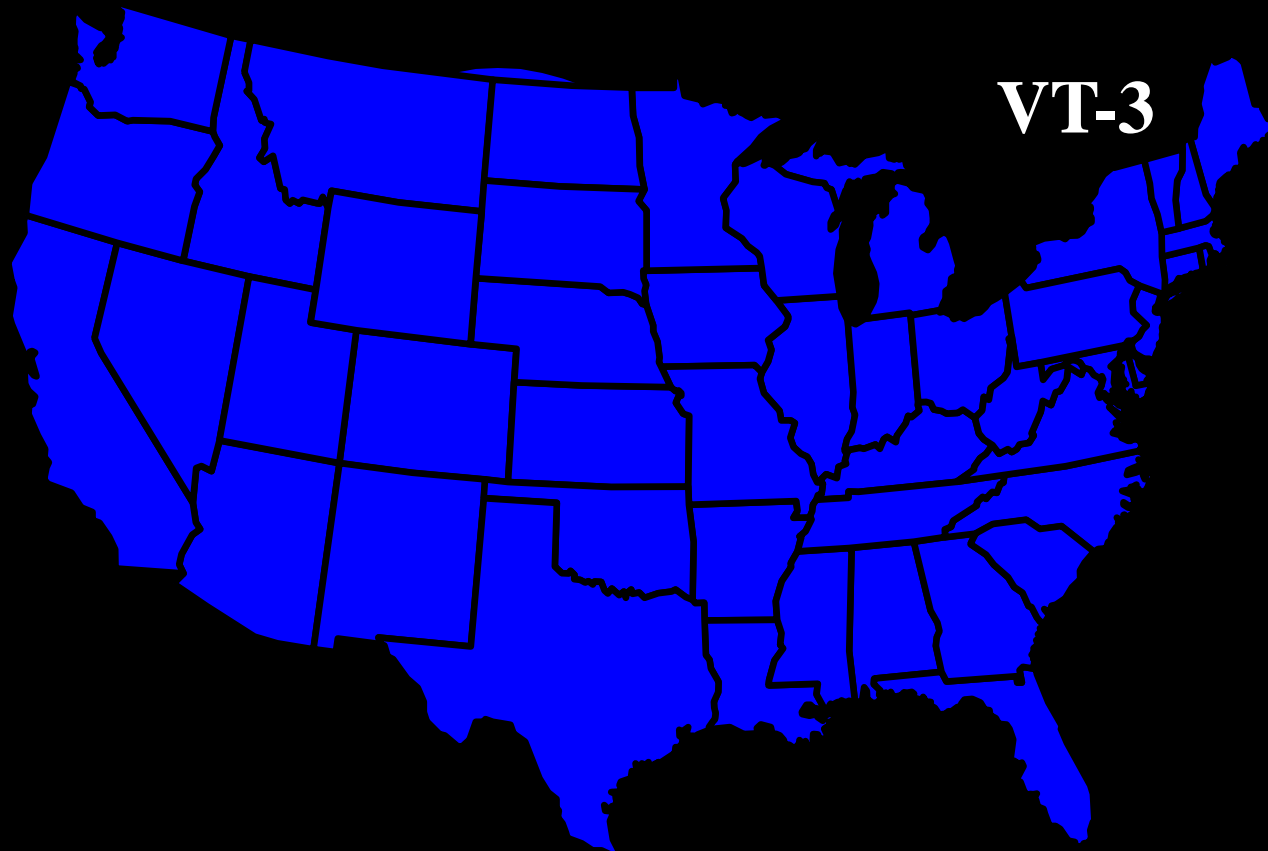


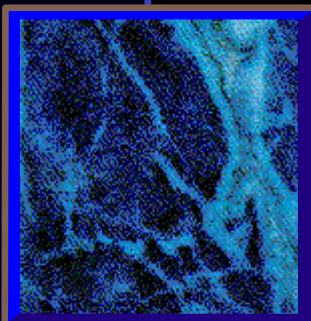
Test Methodology

- ❑ Histology
- ❑ Immunohistochemistry
- ❑ Western Blot
- ❑ New tests:
 - ❑ Enfer (High throughput chemiluminescent ELISA - 3-4 hrs)
 - ❑ Prionics (modified WB - 8 hrs)
 - ❑ Biorad (Sandwich Immunoassay (3-4 hrs)
- ❑ All need brain

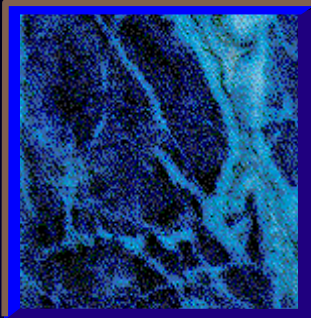


Status of Cattle Imported into the US from the United Kingdom and Ireland (as of May 2, 2001)





www.aphis.usda.gov/oa/bse

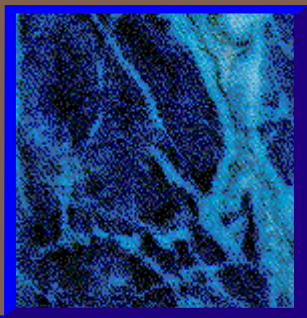


BSE Risk Assessment



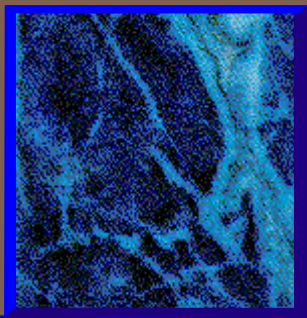
**Harvard School of
Public Health**

Tuskegee University



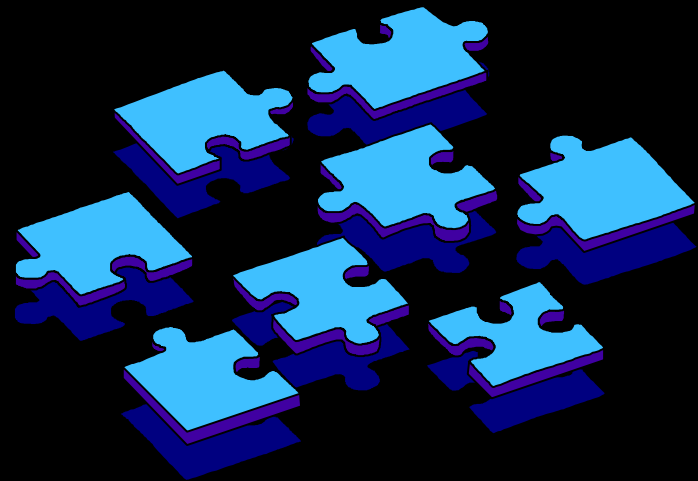
BSE Risk Assessment

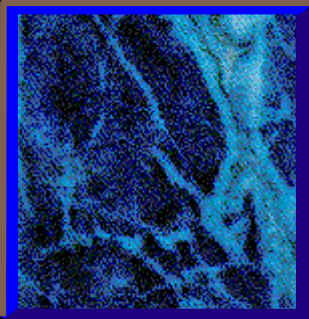
- ❑ Define scope
- ❑ Describe potential pathways BSE infectivity into national herd or food supply
- ❑ Characterize and quantify steps in pathways
- ❑ Identify key steps for research or risk management



BSE Response Plan

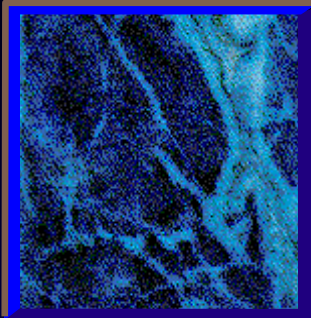
- ❑ First version early 1990's
- ❑ Slightly revisions early 1996
- ❑ Major revisions 1996-98



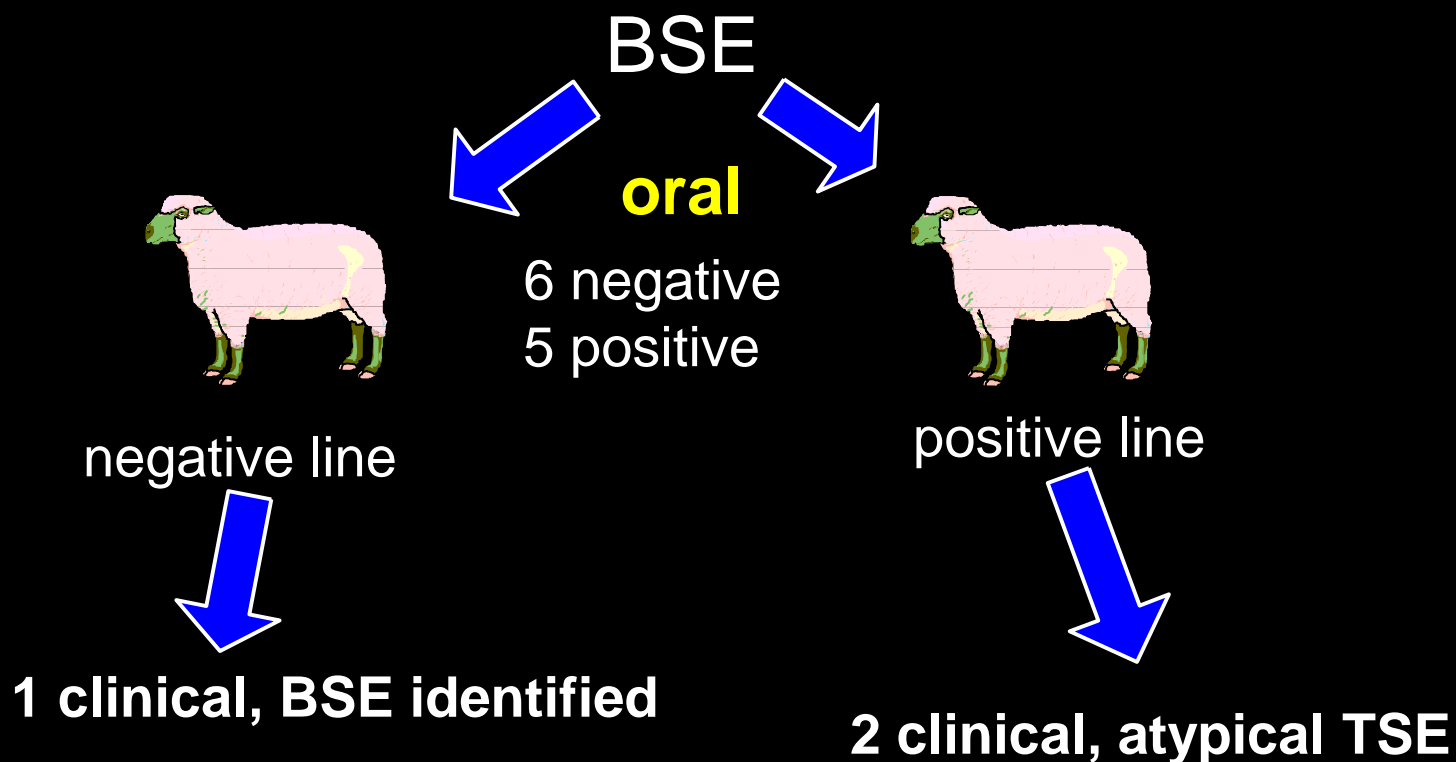


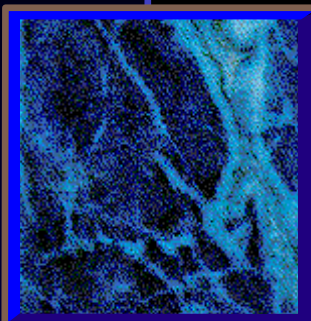
BSE Prevention: Feed Ban

- ❑ FDA Authority
- ❑ Prohibited to feed most mammalian proteins to ruminants
- ❑ Exceptions:
 - ❑ milk
 - ❑ blood
 - ❑ gelatin
 - ❑ plate waste
 - ❑ pure equine/pure porcine



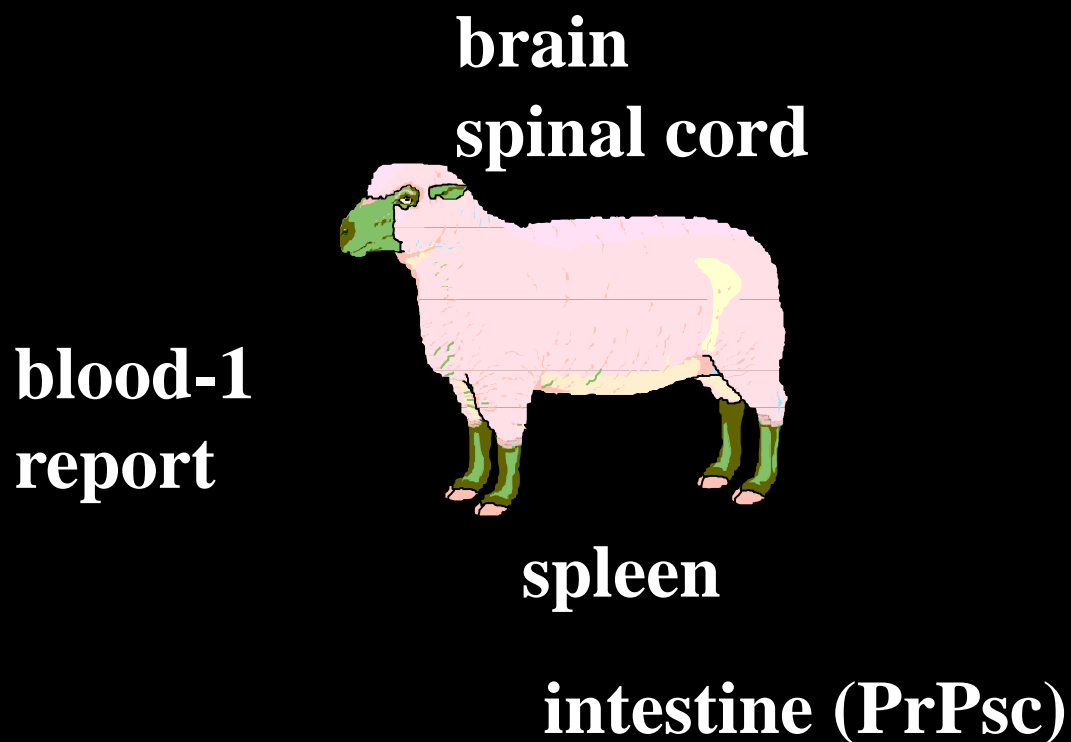
BSE in Sheep: Research (Foster et. al.)

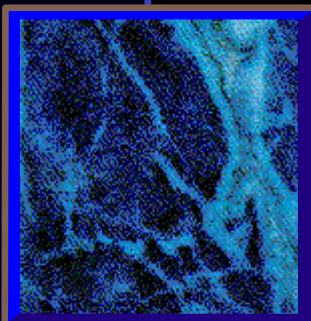




BSE in Sheep: Research

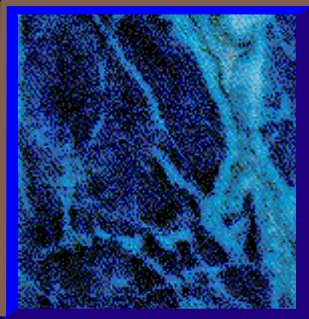
Distribution of Infectivity





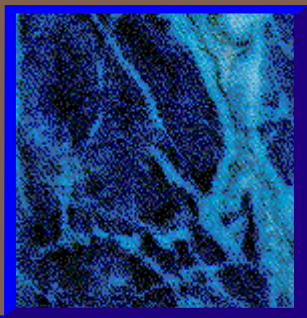
BSE in Sheep: European Situation

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



Imported Sheep in Vermont

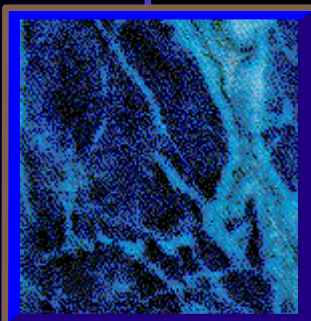
- ❑ Two shipments imported from Belgium and Netherlands
- ❑ August and November 1996
- ❑ 65 head total
- ❑ Distribution:
 - ❑ 52 - Vermont farm 1
 - ❑ 11 - Vermont farm 2
 - ❑ 2 rams - New York farm



Imported Sheep in Vermont

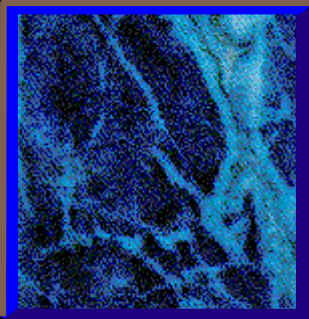
- ❑ Monitored since entry
- ❑ Quarantined since 10-98
- ❑ 9 progeny sold prior to quar.





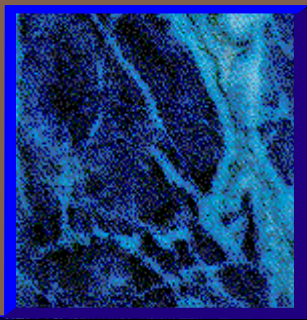
Imported Sheep in Vermont

- ❑ USDA bought culls, sick and picked up dead
- ❑ Sampled and incinerated
- ❑ Results:
 - ❑ Histology - vacuolated neurons, astrocytosis, neuronal degeneration
 - ❑ CE - blood positives
 - ❑ Western - 4 brain positives



Imported Sheep in Vermont

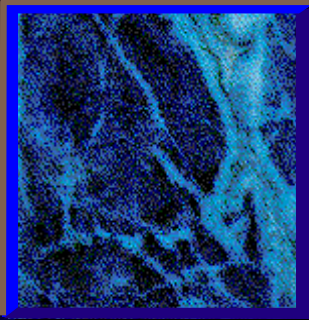
- ❑ Test cannot differentiate "strains" or variants of scrapie from BSE
- ❑ Mouse bioassay
- ❑ 2-3 years
- ❑ Named atypical (histology) TSE of foreign origin



Imported Sheep in Vermont

- ❑ Owners asked to voluntarily depopulate - one agreed
- ❑ Declaration of Extraordinary Emergency and Emergency declared on July 14, 2000
- ❑ Orders issued to seize sheep of 2 flocks

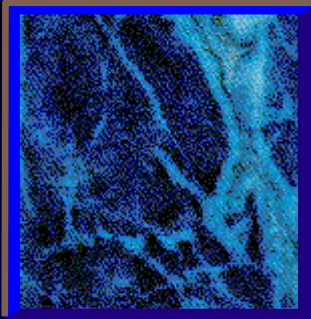




Imported Sheep in Vermont

- ❑ Two owners went to court for a temporary restraining order (TRO) - July 2000
- ❑ Judge ruled in USDA's favor and did not grant TRO
- ❑ Owners did not comply
- ❑ Motion for order to comply and rule on merits

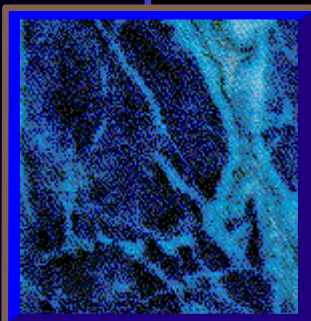




Imported Sheep in Vermont (*continued*)

- ❑ Feb. 6, 2001 - Judge denied plaintiffs motion for summary judgment
- ❑ Granted defendants motion for judgment and orders for compliance
- ❑ Plaintiffs ordered to comply with Secretary's Declaration forthwith
- ❑ Plaintiffs file motion for stay

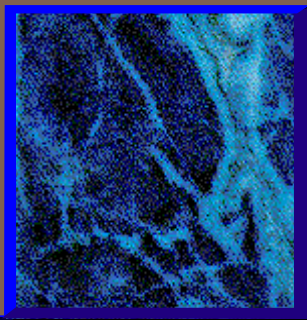




Imported Sheep in Vermont (*continued*)

- ❑ Federal District Court Judge denies motion for stay
- ❑ Plaintiffs file motion for stay with Second Circuit Court
- ❑ Motion denied
- ❑ Sheep removed from farms week of March 19, 2001

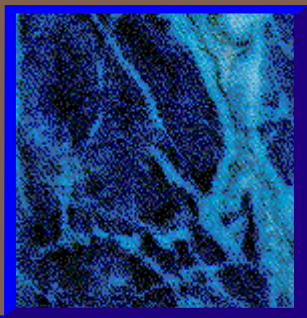




Imported Sheep in Vermont (*continued*)

- April 10, 2001 - Arguments in front of second circuit court
- April 20, 2001 - Court rules appeal is moot





CONCLUSIONS

- ❑ No BSE in US to date
- ❑ Continue conservative approach
- ❑ Continue and increase surveillance
- ❑ Adjust as science and policy dictates

