Risk of oral infection with BSE agent in Primates

What about muscle ?

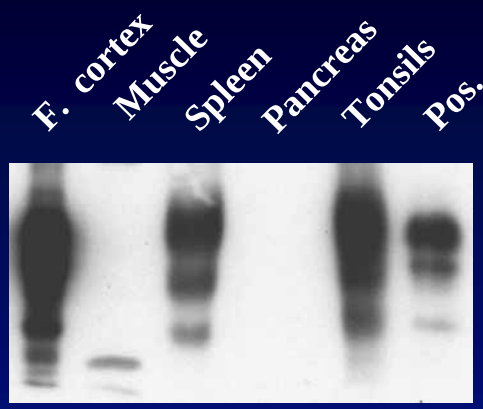
It is not a target tissue of prions.

Very low levels of infectivity (10 000 times less than in brain) have been detected by the most sensitive methods (intracerebral inoculation) in rodent models and in sheep.

Organ distribution of PrPres in vCJD

PrPres in peripheral tissues in vCJD and not sCJD

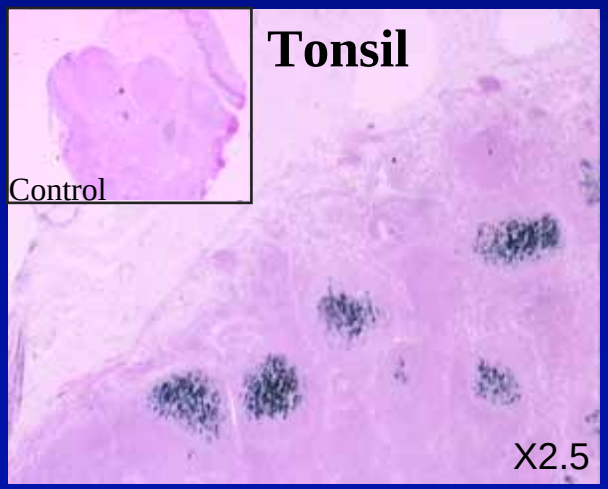
BSE 2P i.v.



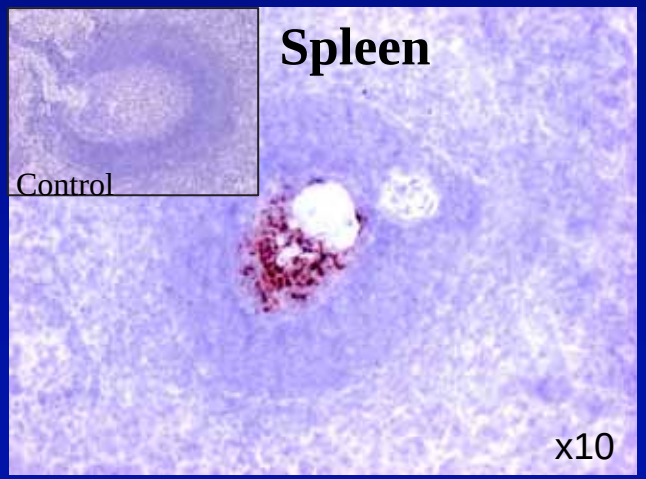
vCJD i.to.

BSE 2P oral

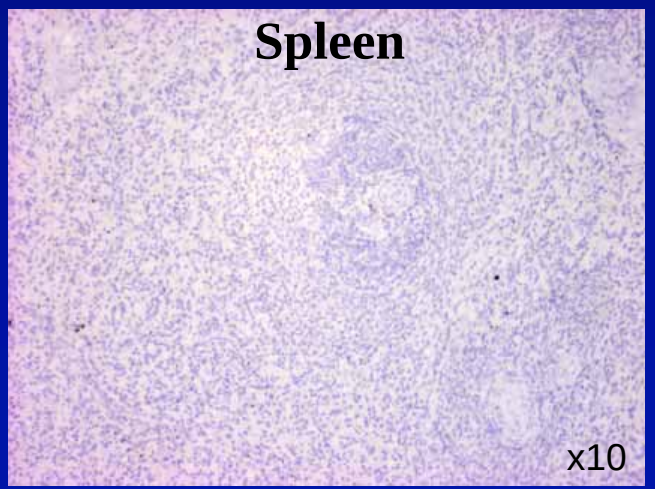
sCJD 2P i.c.+i.to.



PrP (SAF34) IHC



PrP (SAF34) IHC



PrP (SAF34) IHC

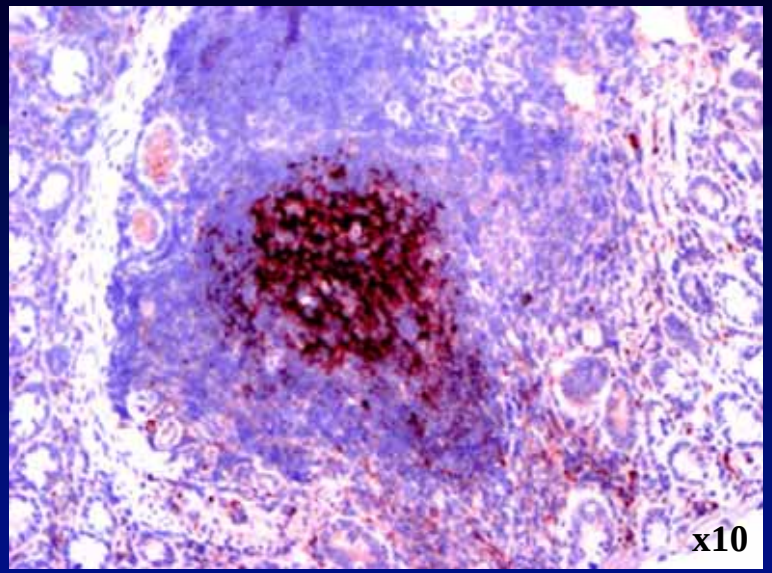
C. Lasmézas, Department of Infectology, Scripps Florida, USA

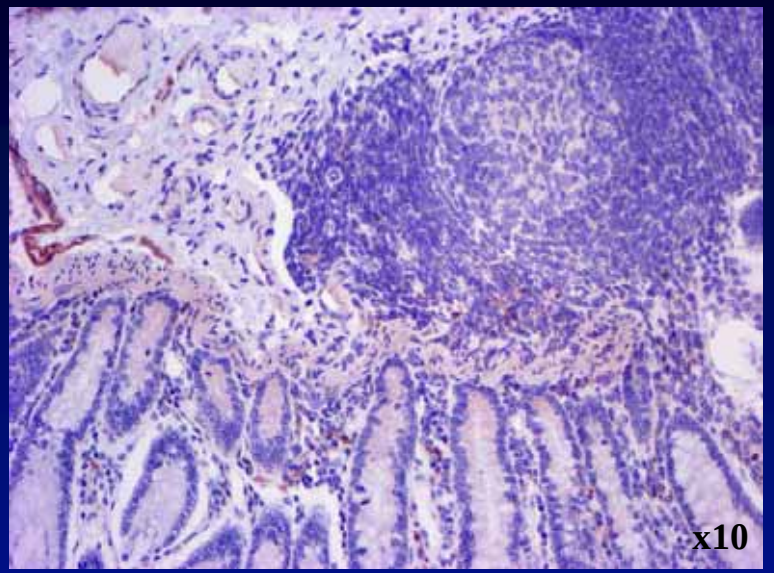
PrPres detection in the lymphoid tissue of the intestine

PrP-mAb Bar 224

ILEO-CAECAL FOLD

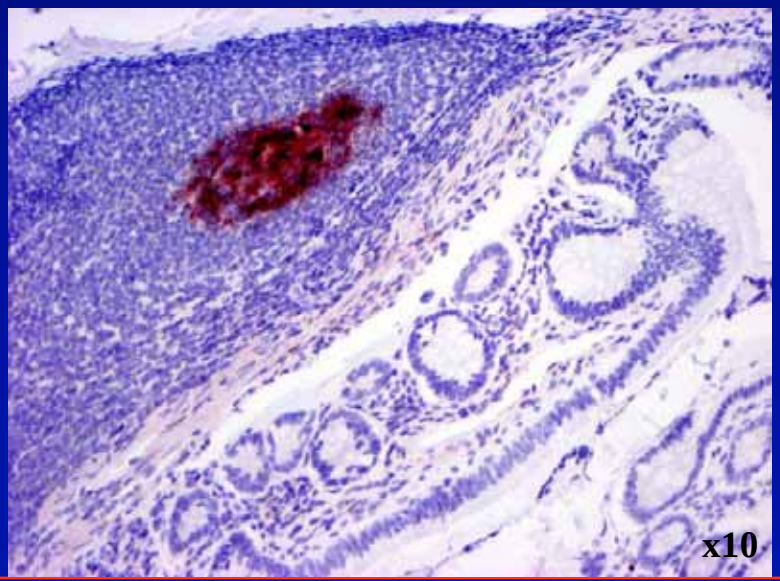
BSE intravenous

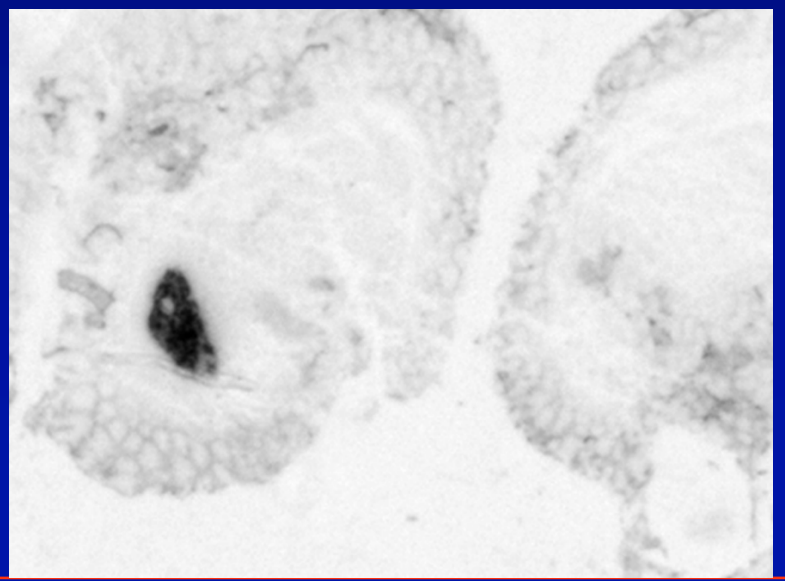




BSE oral

BSE oral





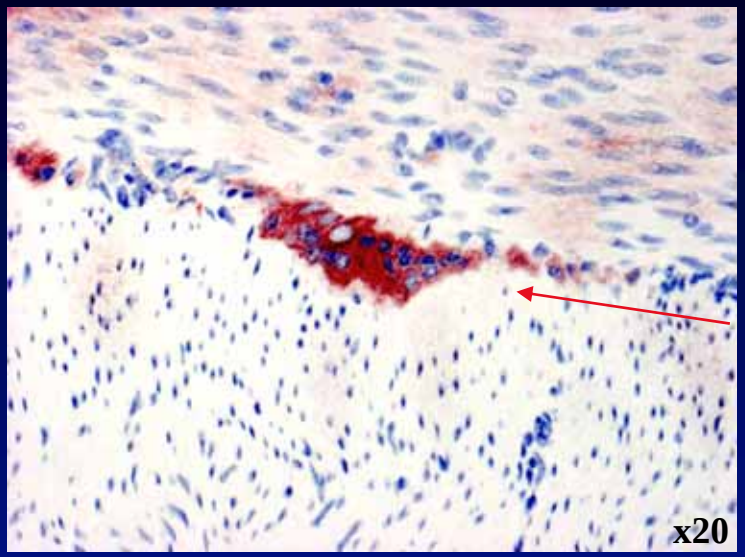
PET-Blot for PrPres

C. Lasmézas, Department of Infectology, Scripps Florida, USA

PrPres detection in the nervous tissue of the intestine

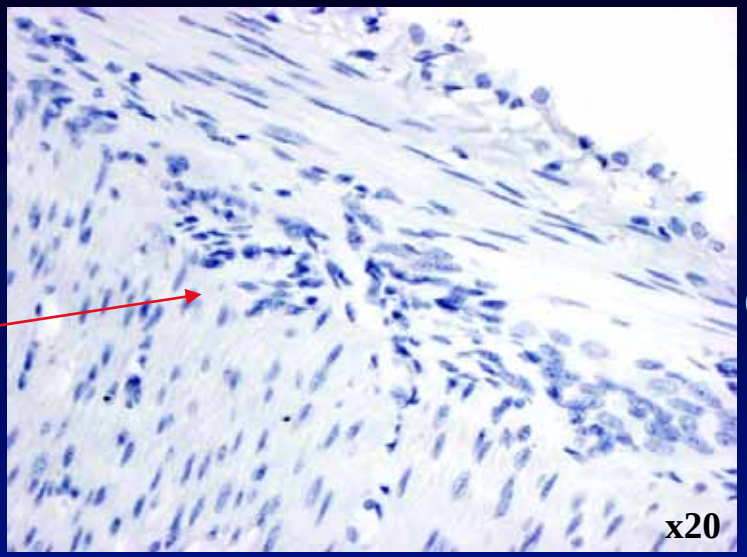
ILEUM

BSE oral



PrP-mAb Bar 224

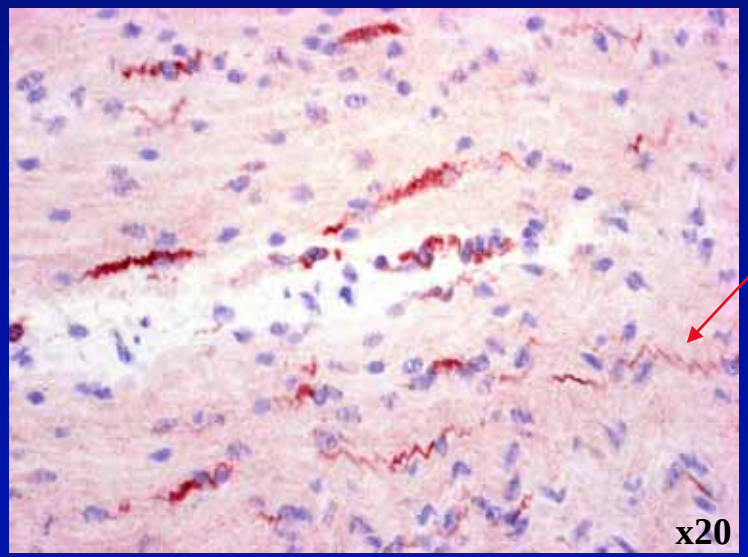
Myenteric plexus



PrP-mAb Bar 224

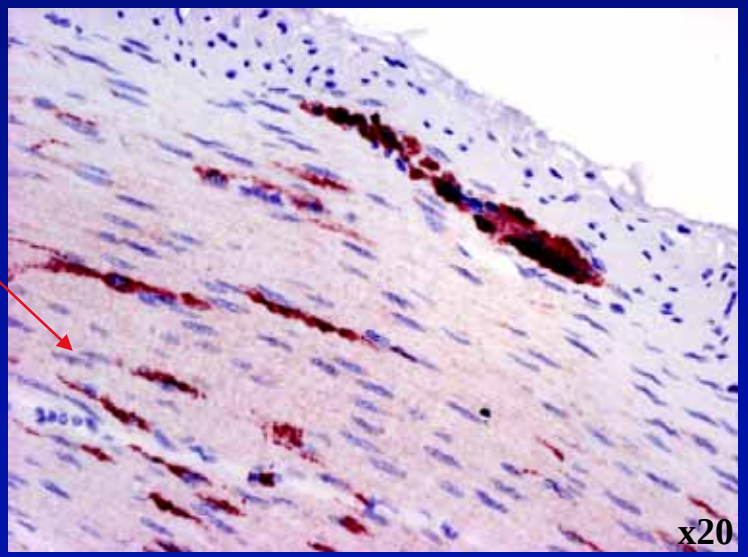
Control cynomolgus

BSE oral



PrP-mAb Bar 224

Inner circular layer



NSE-mAb

BSE oral

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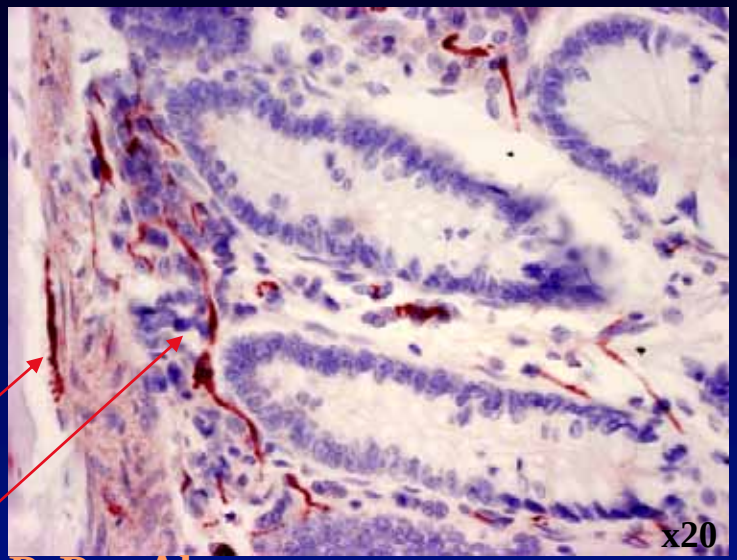
PrPres detection in the mucosa of the intestine

CAECUM

BSE intravenous

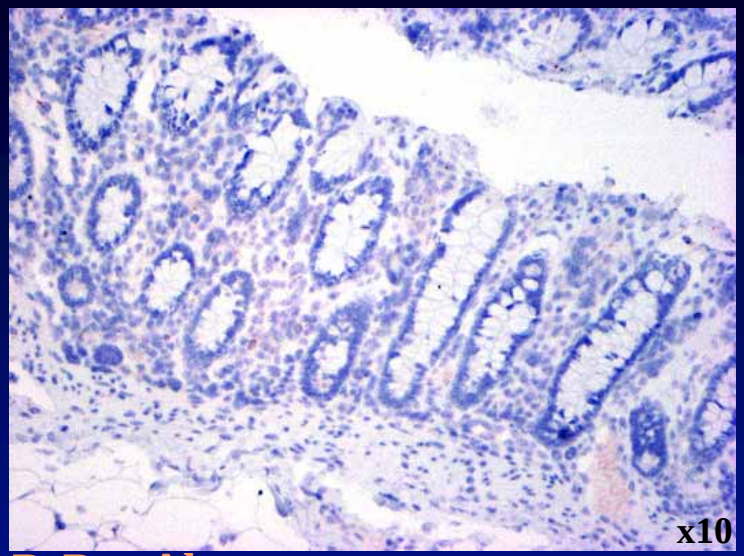
Submucosal plexus

Lamina propria



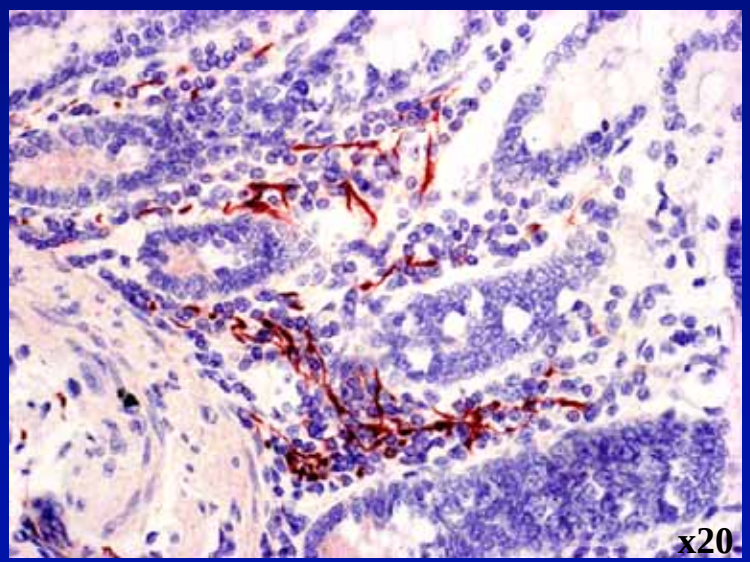
PrP-mAb Bar 224

Control cynomolgus



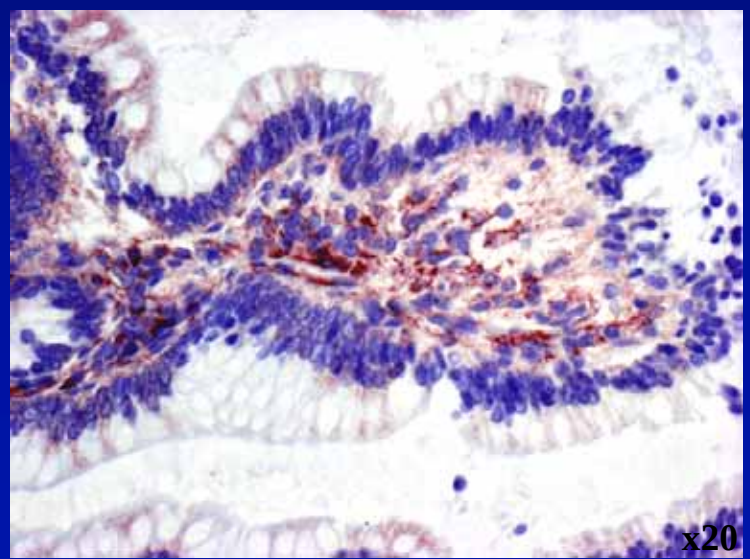
PrP-mAb Bar 224

BSE oral



PrP-mAb Bar 224

BSE oral

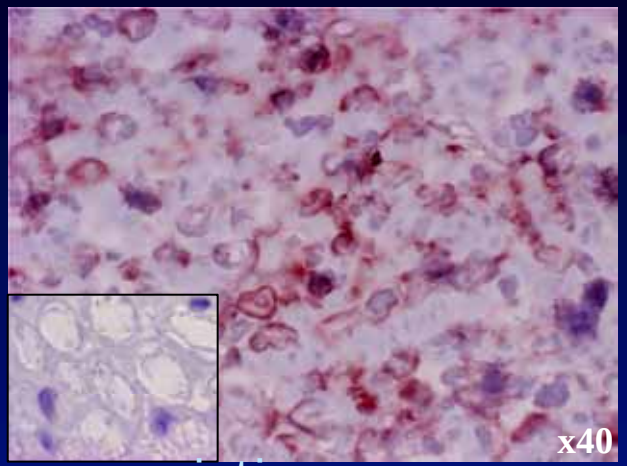


GAP43-mAb

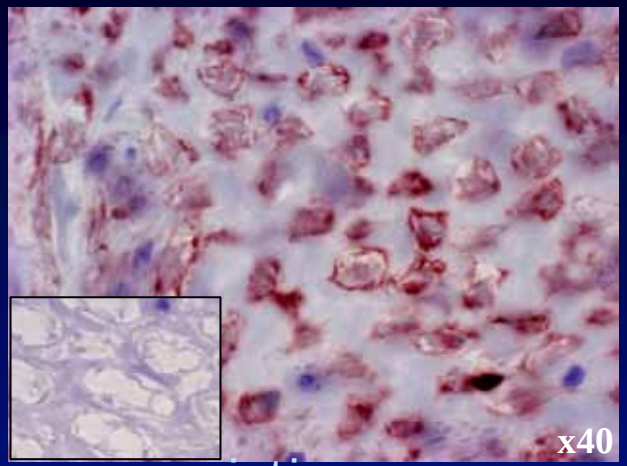
C. Lasmézas, Department of Infectology, Scripps Florida, USA

PrPres detection in the peripheral nervous system

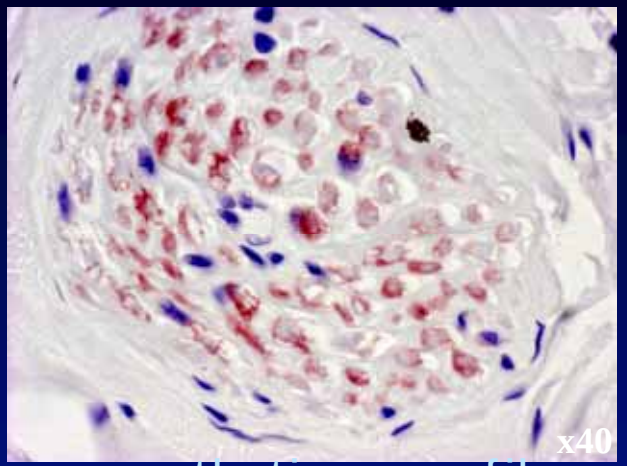
PrP-mAb Bar 224



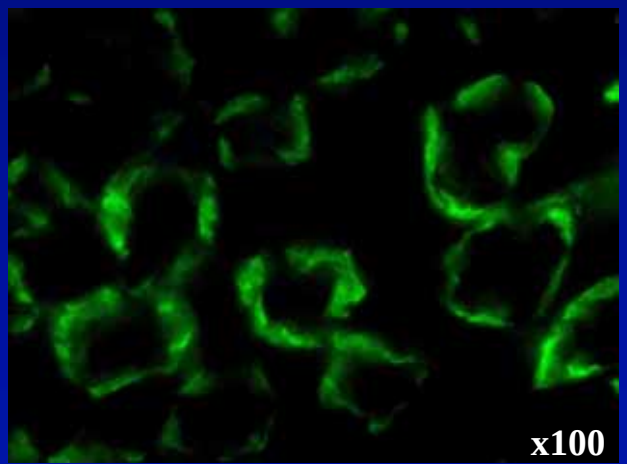
sciatic nerve
BSE intravenous



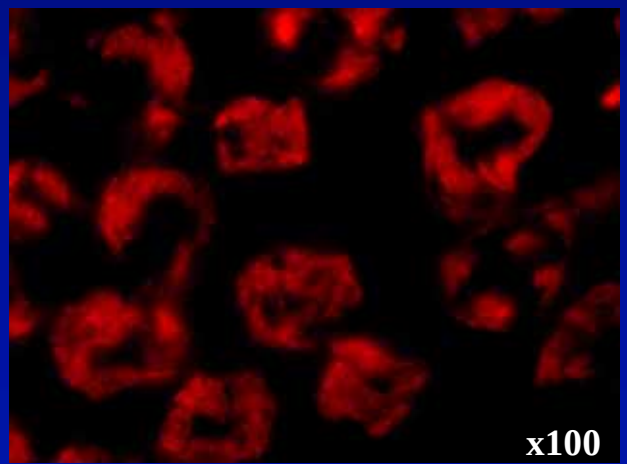
sciatic nerve
BSE oral



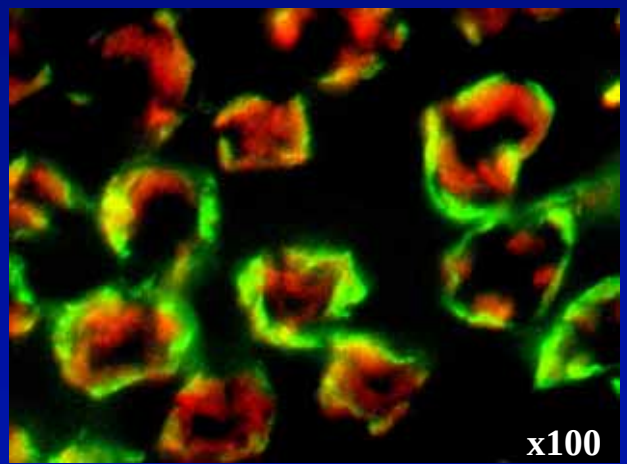
sympathetic nerve fibre
BSE oral



PrP



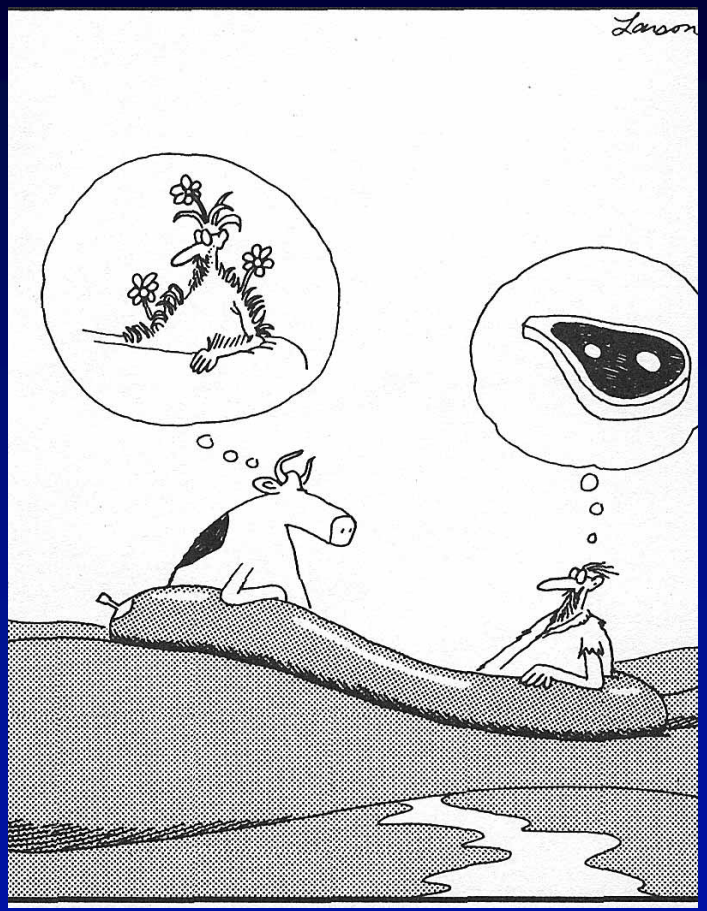
GFAP



PrP + GFAP

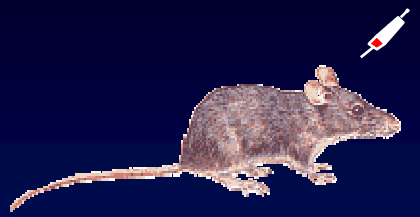
sciatic nerve, BSE intravenous

What is the species barrier ?



- **Prions are very difficult to transmit from one species to another**

Species barrier : linked to different host PrPs ?



PrP^{Mo}

Susceptible to mouse prion infection

$PrP^{0/0}$

Not susceptible to mouse prion infection

Büeler et al. 1993

PrP^{Mo}

Not susceptible to **hamster** prion infection

PrP^{Ha}

Susceptible to **hamster** prion infection

Scott et al. 1989

Species barrier : linked to different host PrPs ?

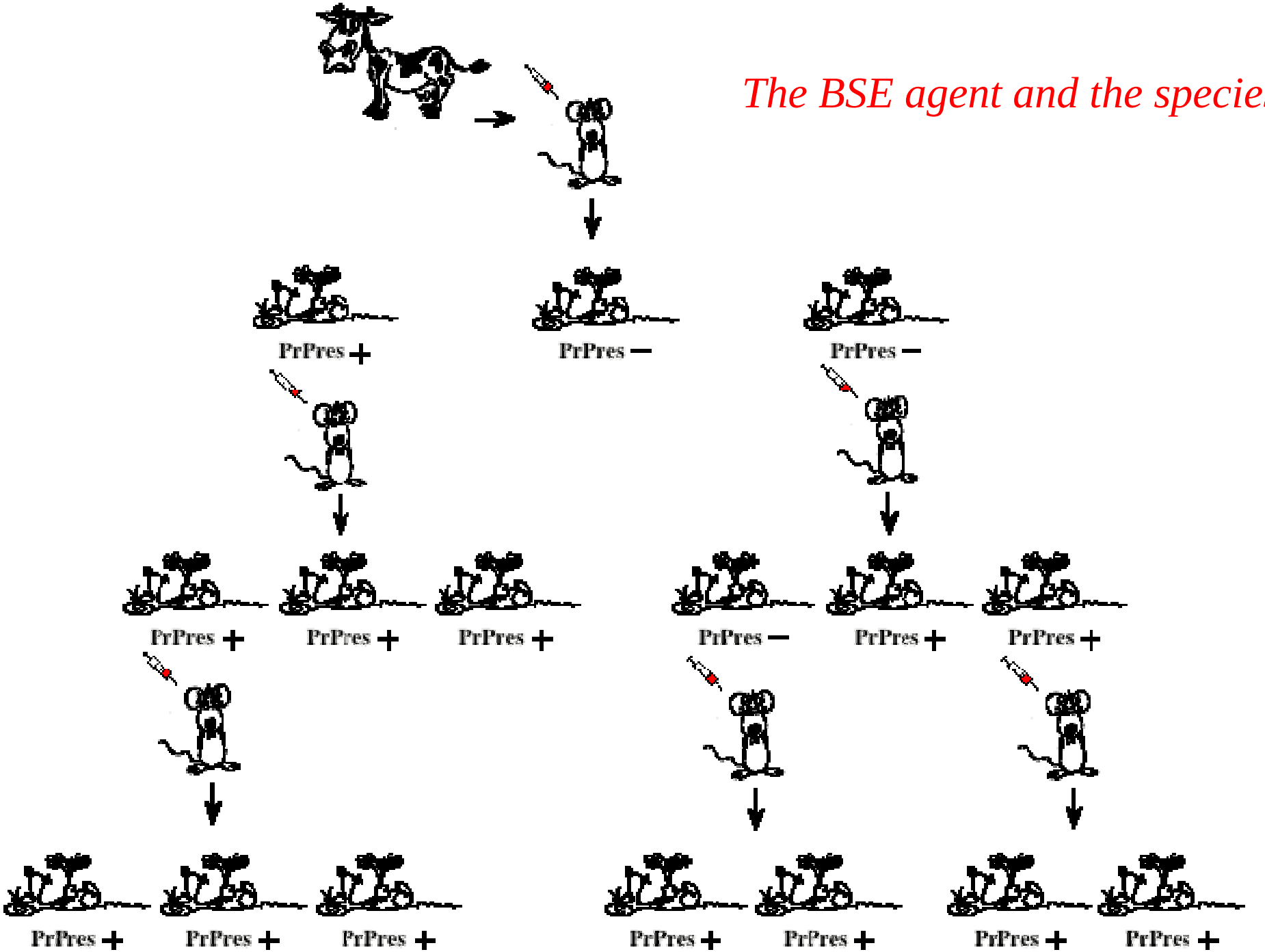
Sometimes transmission is possible :

Scrapie to mice, to hamsters
……. but not to humans

BSE to mice, to humans
…… but not to hamsters

What are the mechanisms ?

The BSE agent and the species barrier



BSE cow brain

100% transmission

Mouse

B1
368 days

Mean incubation :
540 days ± 79 (n=30)

Mouse

2PB1
167 days ±2

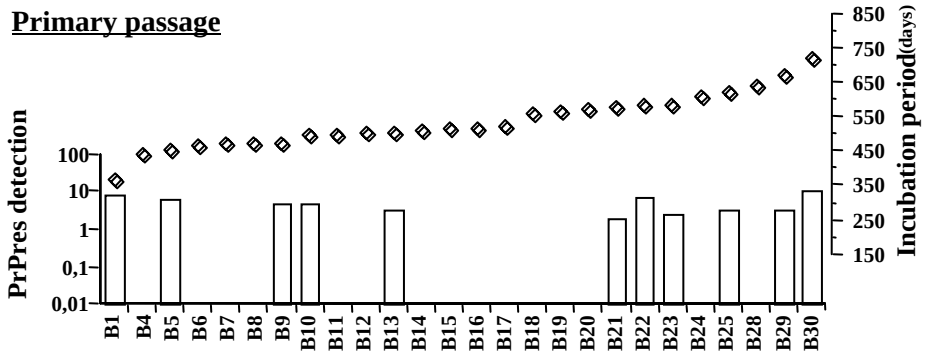
Mouse

3PB1
181 days ±4

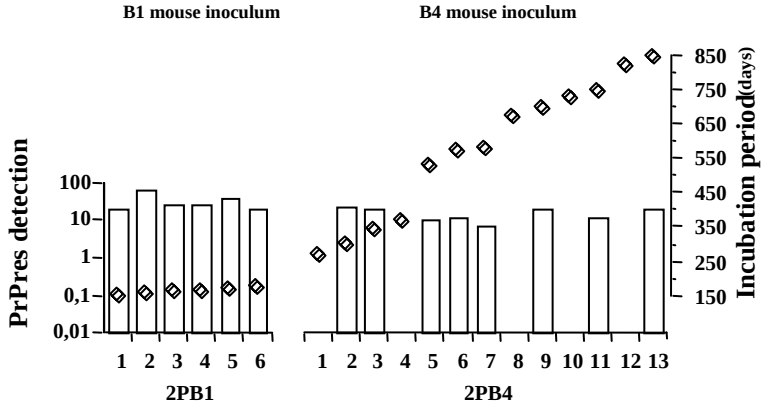
Mouse

6PB1
170 days ±4

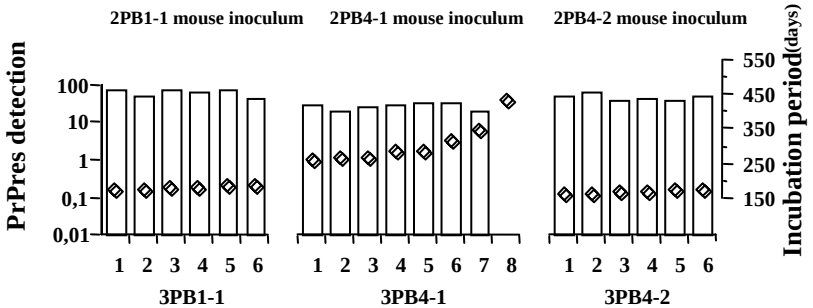
Primary passage



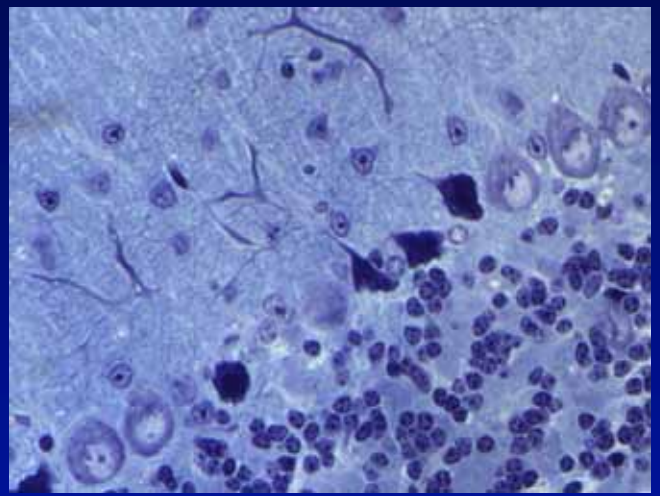
Second passage



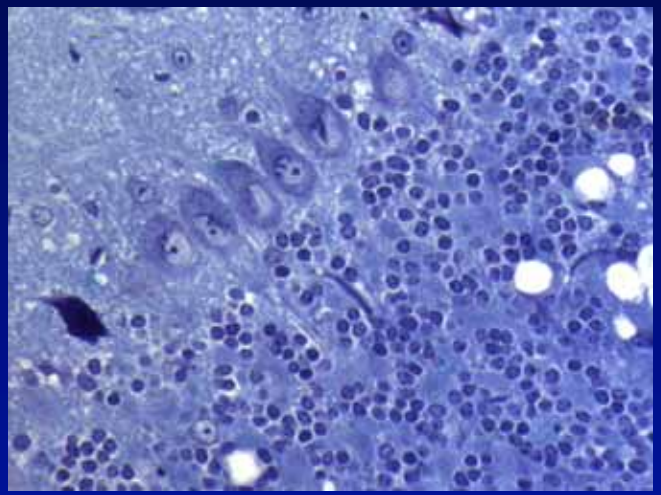
Third passage



Neuronal death without vacuolation in PrPres mice



PrPres- mouse



PrPres+ mouse

Molecular mechanisms of the species barrier

Lessons from BSE :

1. **The interspecies transmission can lead to the emergence of strains replicating with undetectable levels of PrPres.**

2. **PrPres « neg » phenotype is labile as PrPres « pos » strains are selected upon further passages.**

3. **Does the molecular mechanism of strain adaptation reside in the acquisition of the capacity by the infectious agent to convert the new host PrP into the pathogenic conformer ?**

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Thank you very much for your attention