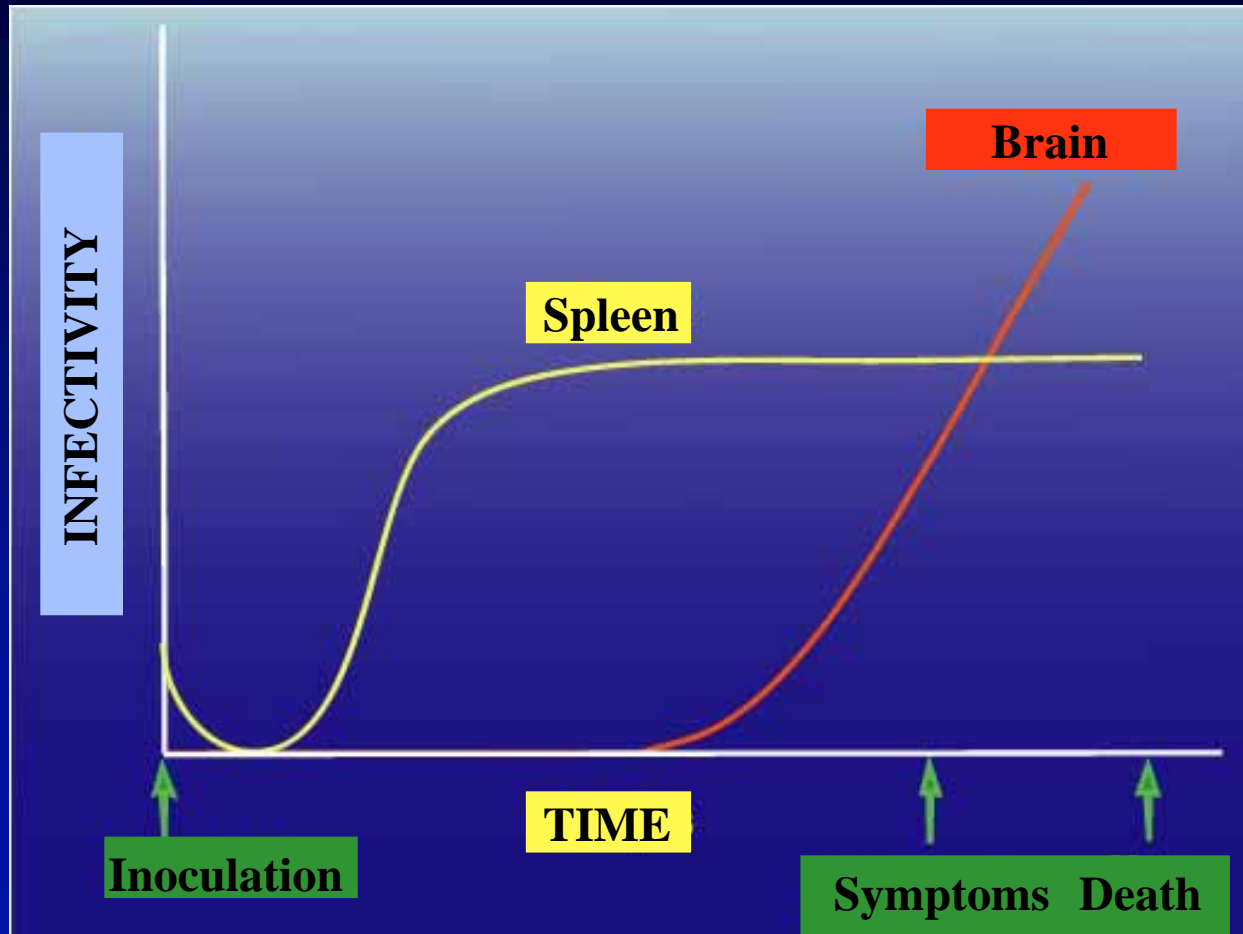
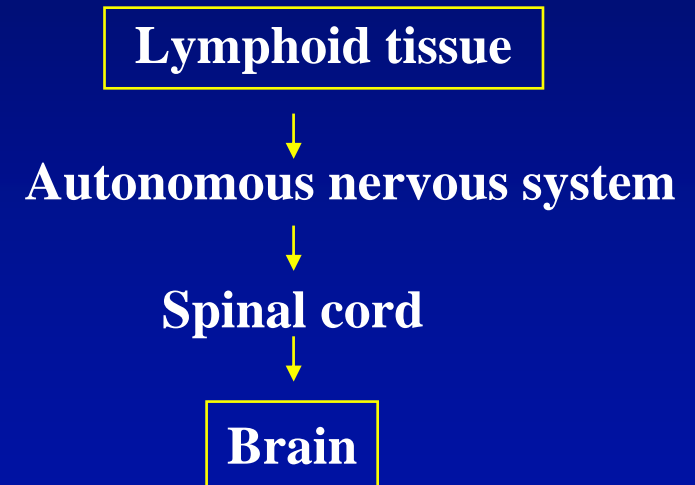


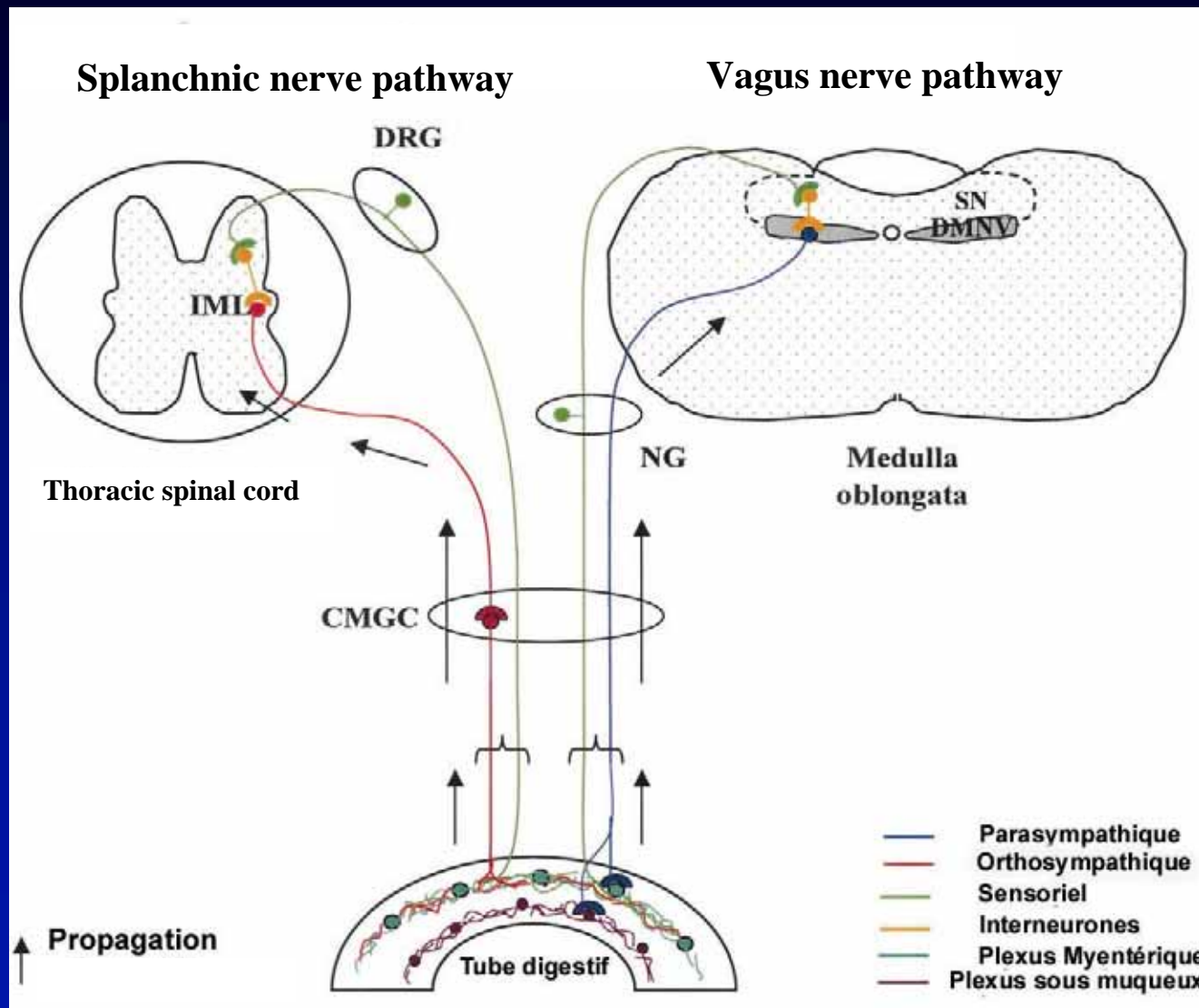
Propagation of prions after intraperitoneal infection



Neuroinvasion pathway :

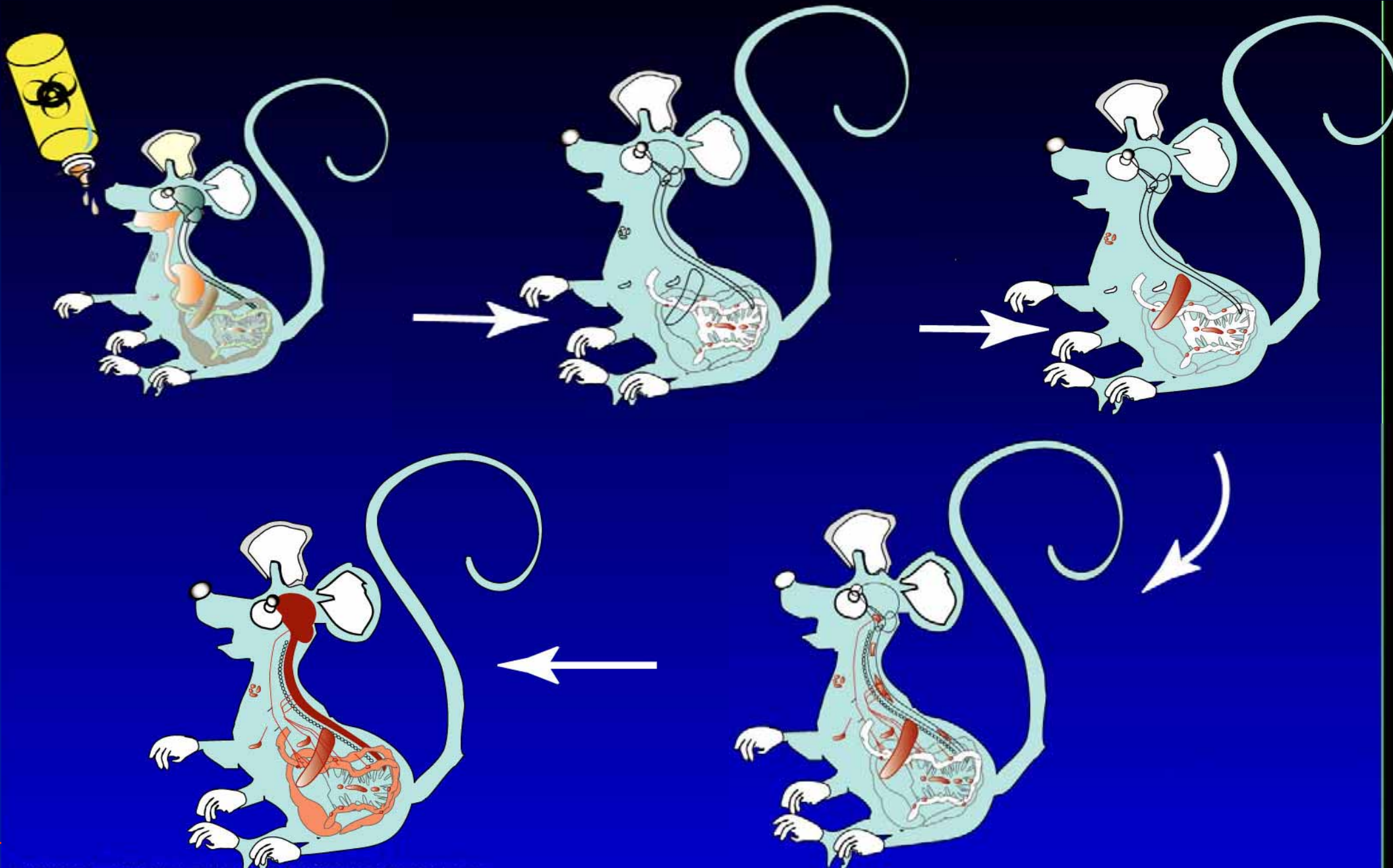


Propagation of TSE agents in hamsters after oral contamination



Beekes et al., 2001

Propagation of TSE agents after oral contamination



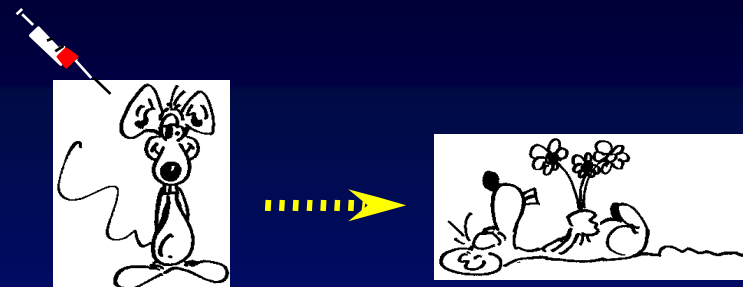
Strains of TSE agents



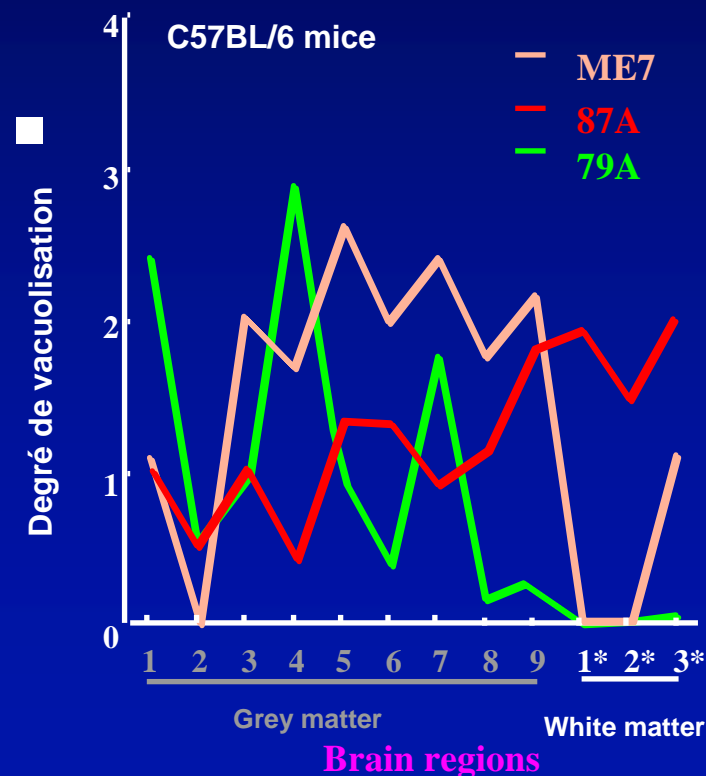
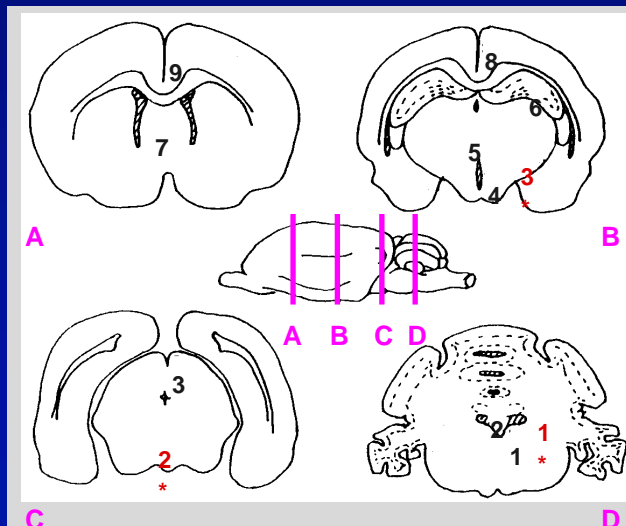
Strains of TSE agents

Each different strain can be identified in mice

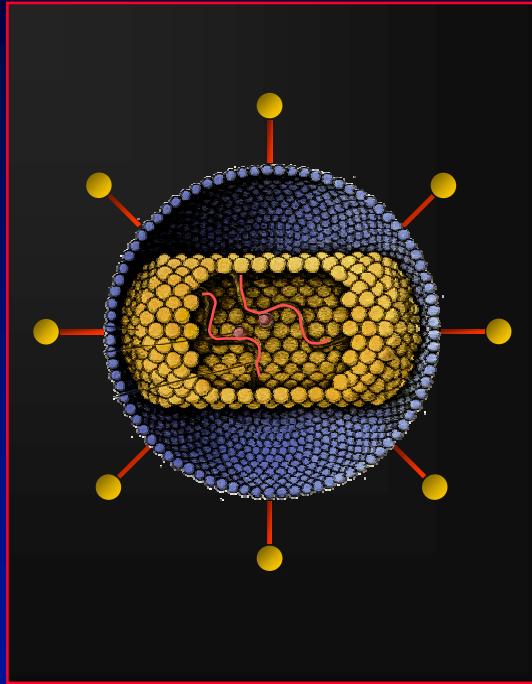
- Incubation period (route, dose)
- Lesion profile



Distribution of vacuoles

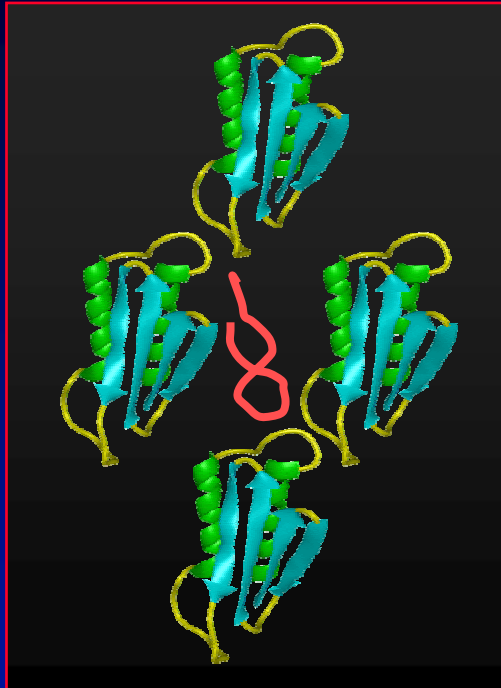


Nature of the infectious agent ?



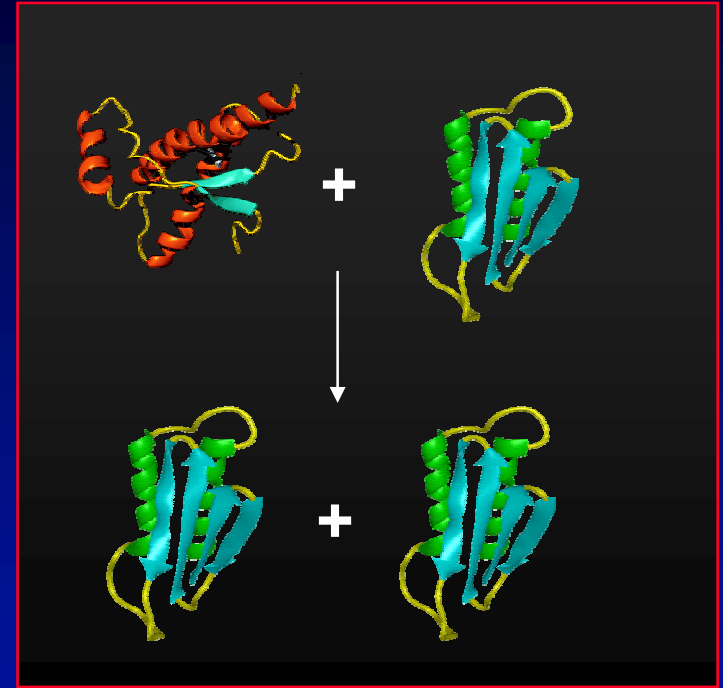
**Unidentified virus
(amyloidogenic)**

- exogenous genome encodes its own proteins
- PrPres = byproduct of the viral replication



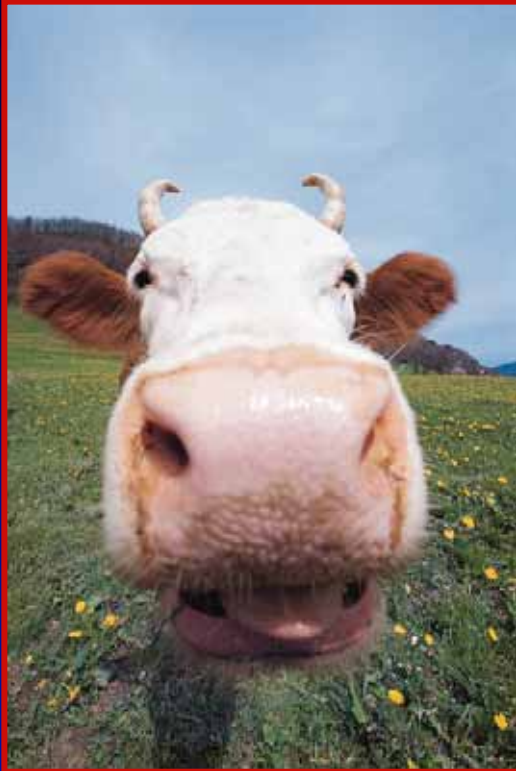
Virino

- little exogenous genome only for replication
- protective shell made of a host derived protein = PrPres



Prion

PrPc \rightarrow PrPres
+ protein X ?
+ chaperone ?



Bovine Spongiform Encephalopathy

■

and the species barrier

BSE numbers as to october 2005

Countries with cases in 1986 - 91

United Kingdom	184 281
Ireland Rep.	1531
Switzerland	458
Portugal	967
France	974
Netherlands	77
Belgium	130
Lichtenstein	2
Luxemburg	1

Countries with cases since 2000

Germany	389
Spain	589
Danemark	18

Countries with cases since 2001

■ Italy	133
Finland (1), Slovenia (6)	
Slovakia (20), Austria (2), Greece (1)	
Tchech Rep. (20), Poland (34)	
Israel (1), Japan (19)	

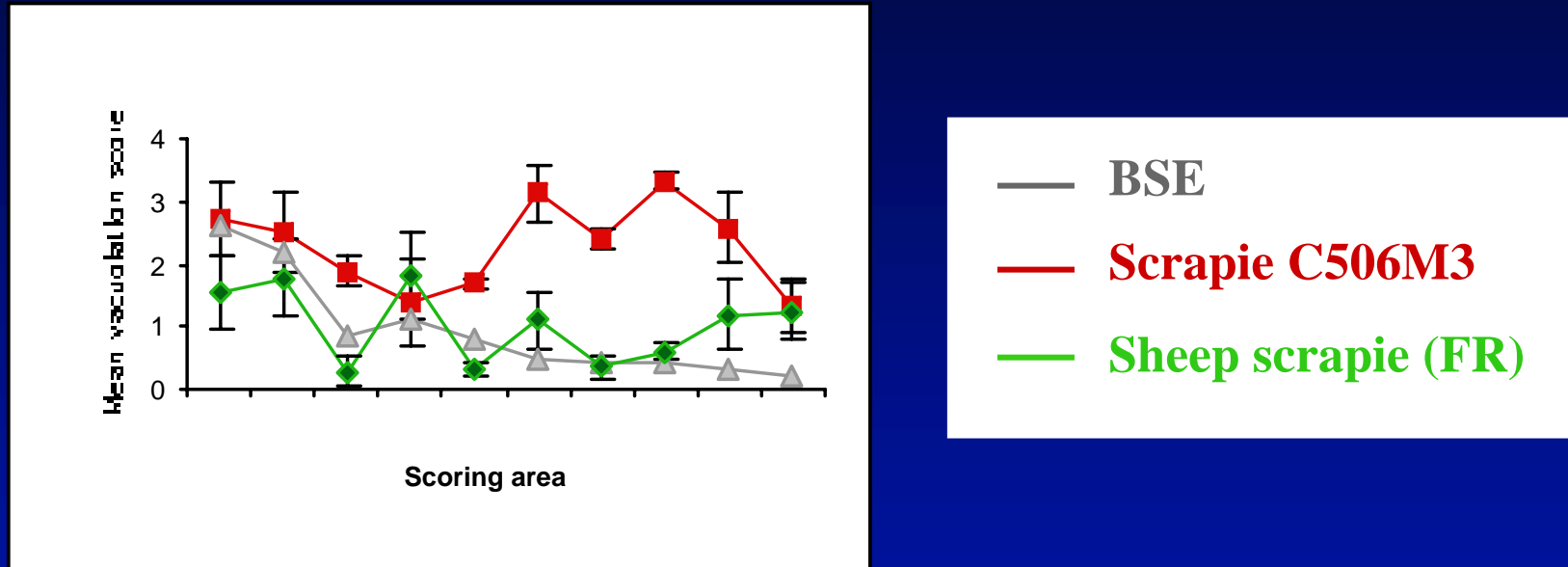
... since 2003

Canada (4)

... and since 2005

USA (1)

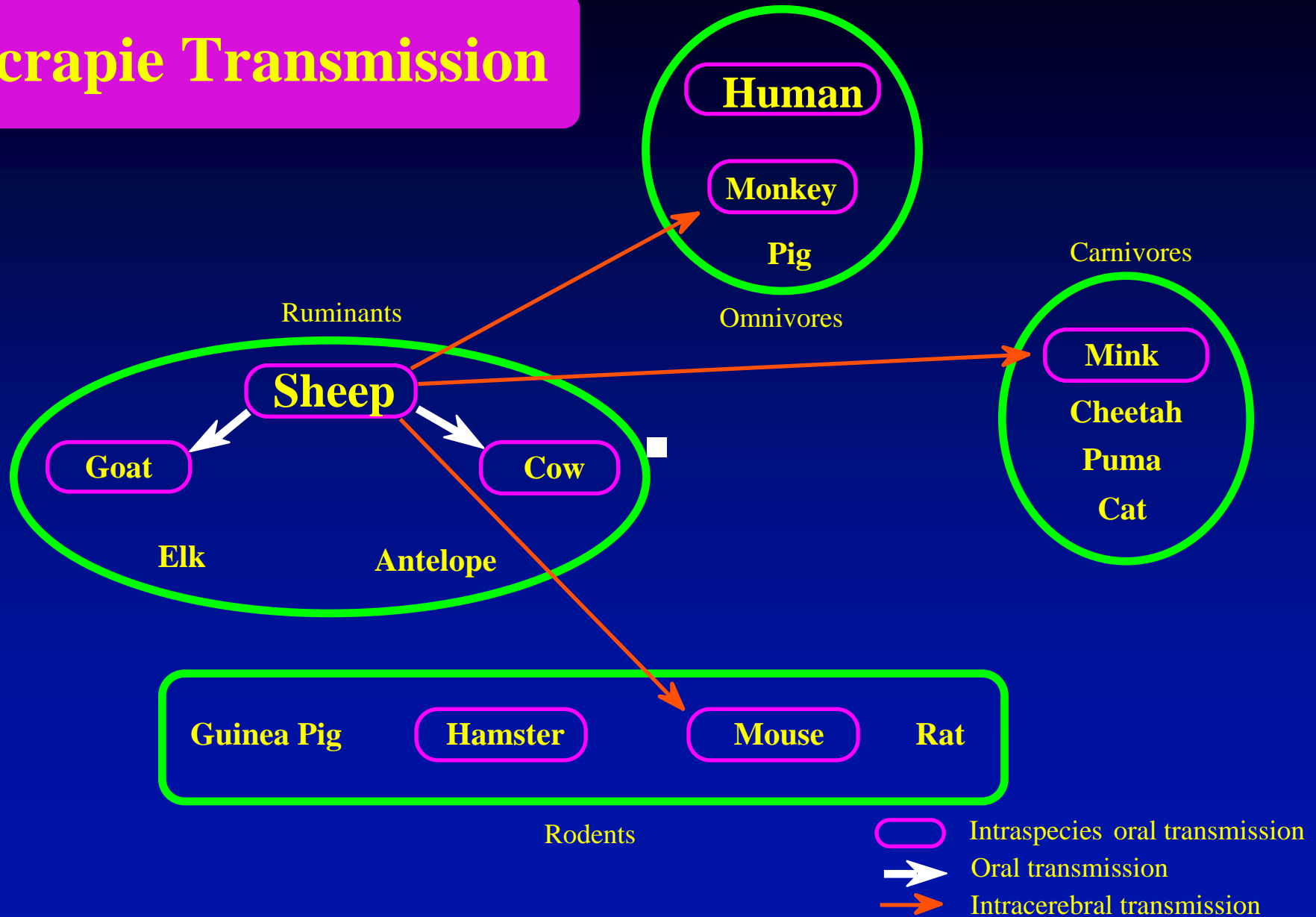
The BSE agent is a strain different from scrapie



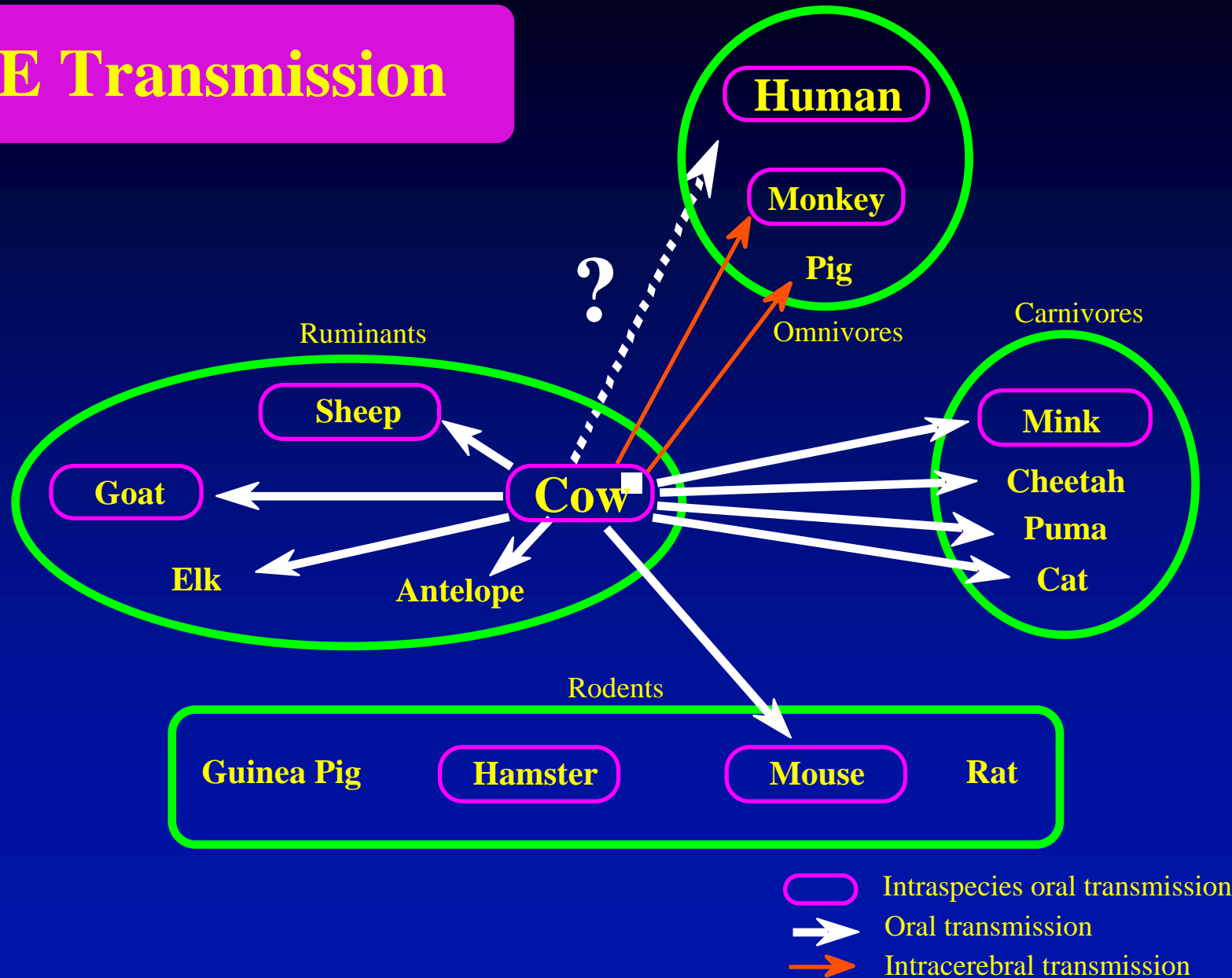
Lesion profiles in C57BL/6 mice

C. Lasmézas et al., PNAS, 2001

Scrapie Transmission



BSE Transmission



vCJD : a new human disease

- 10 cases in the United Kingdom in march 1996
- Mean age : 30 years.
- Similar symptoms and brain pathology
 - Severe lesions in the basal ganglia and thalamus
 - Characteristic « florid » plaques



Link with BSE ?

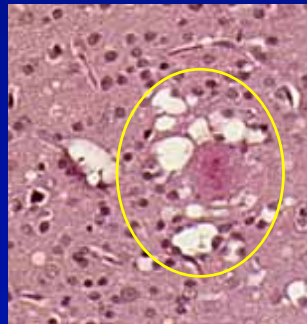
vCJD : a new human disease

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vCJD is BSE in Primates

*BSE in cynomolgus
macaques*

Lasmézas et al. Nature 1996



vCJD in humans

Will et al. Lancet 1996

Human exposure to the BSE agent

- 1980-1989/90 in the United Kingdom (1996 France, 2000 EU)

Brain and spinal cord can enter the food chain.

- 1990-1996 in the United Kingdom

Risk from vertebrae in mechanically recovered meat and from dorsal root ganglia.

- Non cattle BSE sources ?

Sheep have been fed with MBM and are susceptible to BSE.

Protection of the food chain

The Specified Risk Material (SRM) ban

UK : 1989 (Scotland & NI jan. 1990)

France : 1996

EU : 2000

USA : 2004

Japan : 2001

Bovine Skull (brain, eyes) > 12 m (UK 6 m, USA 30 m, Japan all ages)
Spinal cord > 12 m (UK 6 m, USA 30 m, Japan all ages)
Tonsils > 12 m (FR, USA and Japan all ages)
Intestine all ages (distal ileum USA and Japan)
UK, PT, FR : Thymus, Spleen > 6 m

Sheep Skull (brain, eyes) > 12 m (FR 6 m)
Spinal cord > 12 m (FR 6 m)
Tonsils > 12 m (FR all ages)
Spleen all ages

BSE and vCJD: risk for human health

- *PrPsc distribution (IHC)*

	Tonsils	Spleens	Lymph nodes	Appendices
vCJD	18/18	21/21	15/15	19/20
iCJD	All negative			
sCJD	All negative ■			

From J. Ironside

Pathogenesis of vCJD is different from sCJD



Risk of accidental interhuman transmission

vCJD : update of the number of cases (october 2005)

United Kingdom : 157

Republic of Ireland : 3

France : 15

Hong-Kong : 1 (2002)

Canada : 1 (2002) ■

USA : 1 (2002)

UK origin probable

Italy : 1 (2003)

Japan : 1 (2004)

Netherlands : 1 (2005)

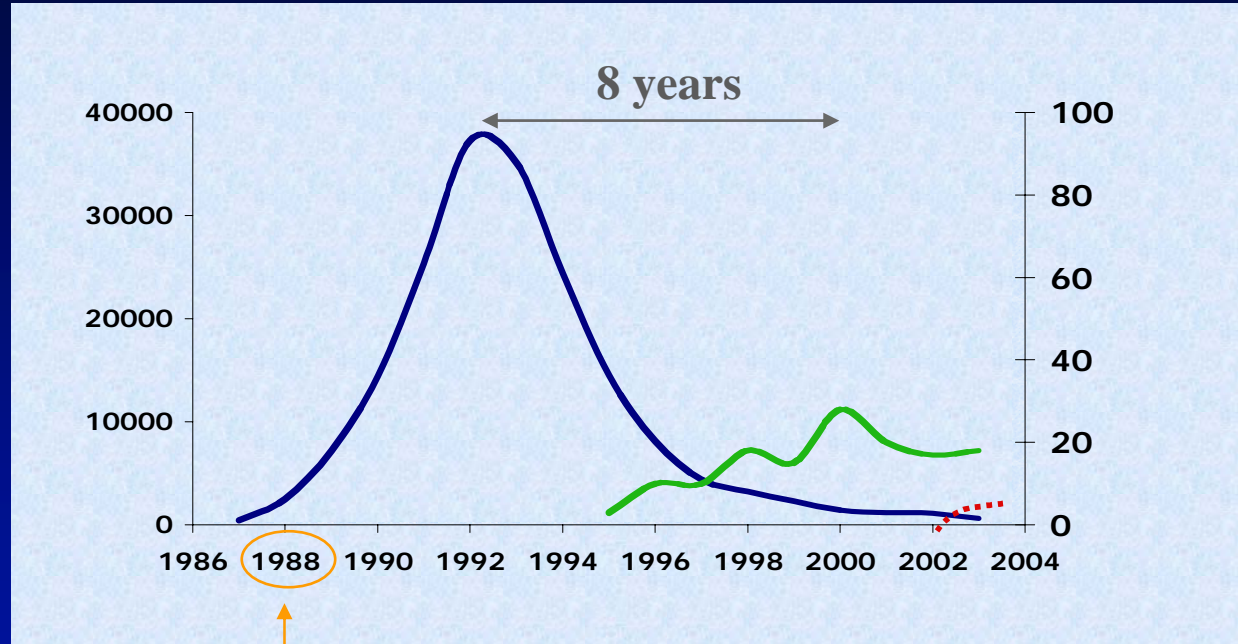
Portugal : 1 (2005)

Spain : 1 (2005)

BSE and vCJD in the United Kingdom

UK BSE cases/year

UK vCJD cases/year



UK iatrogenic vCJD cases

Ruminant Feed Ban

*« Real ban » : Mm proteins to all farmed animals
1996 UK, 2001 EU*