







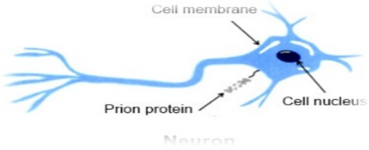
強化牛海綿狀腦病（BSE）國家監測
屠宰場獸醫師之關鍵職責與實務

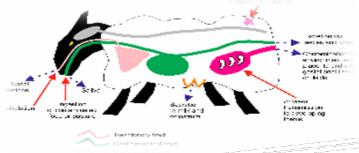
李淑慧博士

國立臺灣大學生物資源暨農學院

/兼任助理教授







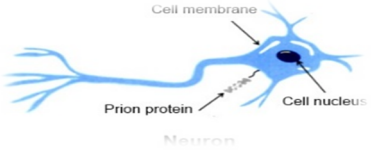



大綱

- 傳播性海綿狀腦病之相關文獻介紹
- BSE之傳統與最新檢測方法
- 2023年新版WOAH BSE 監測方法
- 防檢署 BSE 病例調查紀錄表解析
- BSE 疑似病例的檢測與確診
- BSE 疫病防控與國際規範
- 台灣申請 WOAH BSE風險可忽略國家應該要準備的相關申請文件及數據?









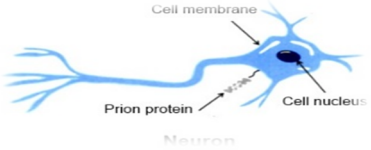


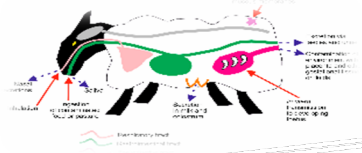


問題

- 請簡述牛海綿狀腦病(BSE)之實驗室診斷流程及其診斷上學理之依據?
- 請簡述人類感染變異庫賈氏症 (VCJD) 之致病機轉?
- 目前沒有BSE非疫國之稱呼,請簡述目前世界動物衛生組織(WOAH)對各國BSE現況之分類及要求?
- 台灣申請 WOAH BSE風險可忽略國家應該要準備的相關申請文件及數據?









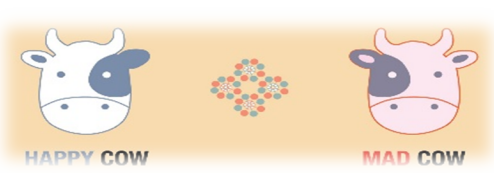


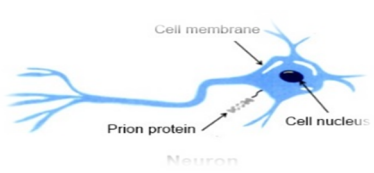
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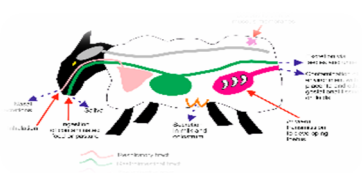
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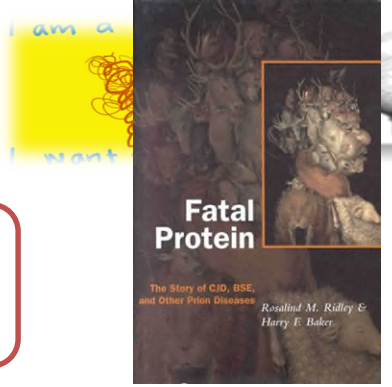


主題	文章/文件	年份	重點內容
綜論	Bovine spongiform encephalopathy: A review of current knowledge and future perspectives（期刊 review）[1]	2025	臨床、診斷技術、致病機轉、公共衛生風險綜整
臨床與診斷概述	MSD Veterinary Manual: Bovine Spongiform Encephalopathy[2]	2022 更新	臨床表現、診斷步驟與實驗室方法，實務導向
臨床分型與監測	WOAH Guidelines for Targeted BSE Surveillance（PDF）[9]	2023	臨床選案標準、目標性監測策略、案例決策樹
診斷方法綜整	Conventional and state-of-the-art detection methods of BSE（IJMS review，PDF）[18]	2023	IHC、WB、ELISA、PMCA、RT-QuIC 等方法優缺點與敏感度
標準實驗室診斷	WOAH Terrestrial Manual – BSE 章節（PDF）[15][16]	最新版約 2022–2023	標準樣本、IHC/WB 流程、品質管制
Prion 結構與機轉	The ultrastructure of infectious L-type BSE prions（PLOS 病毒學）[5]	2021	L-type BSE prion 超微結構、聚集型態與致病意義
Prion 結構綜述	Structure, Function and Stability of the BSE Prion（PDF 報告）[19]	2023	PrPSc 結構、生物物理特性與穩定性分析
全球風險與政策	EFSA topic page on BSE[3]	2026 更新	歐盟 BSE 風險管理、食品安全政策與科學意見連結
歐盟監測	EFSA EU summary report on TSEs 2023[10]	2024 發表	2023 年 EU/UK/其他國家 BSE 檢測數據與病例
歐盟 2024 監測	EU TSE surveillance 2024 summary（EFSA/EC 文件）[4][23]	2025	2024 年檢測數與 atypical 病例分布
WOAH 疫學與標準	WOAH disease page: BSE[11]	2025 更新	臨床概要、流行病學、風險地位分類連結
WOAH 標準更新	WOAH slide: Updates on TSE activities（PDF）[7]	2024	2023/2025 BSE 標準與官方風險地位更新
國家監測案例	UK atypical BSE case in Scotland 2024 epidemiology report[21]	2025	19 歲牛 atypical BSE 個案調查，說明自發性案例特徵
北美監測	US APHIS NVAP BSE reference guide[8]	2023	美國 BSE 監測策略與防範措施概要
加拿大監測	加拿大 National BSE Surveillance Program data[20]	2025 更新	1992–2025 各年檢測頭數與病例統計









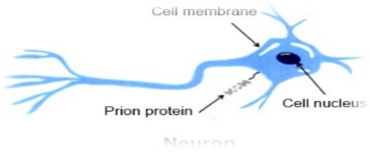


傳播性海綿狀腦病之相關文獻介紹

- Brief introduction of TSEs
- What is a prion?
- Prions infect animals and humans
- Pathogenesis of TSE







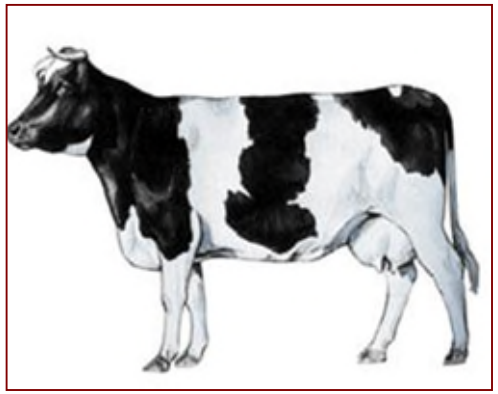
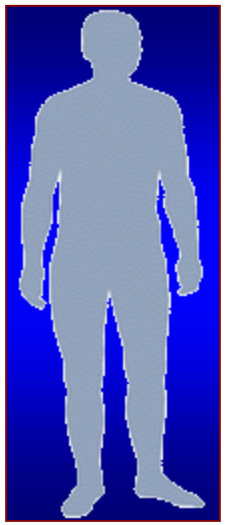






Prions infect animals and humans

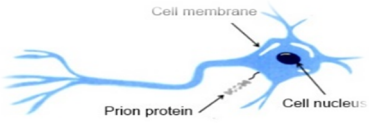
- Scrapie in sheep was first described during the18th century. feedstuff.

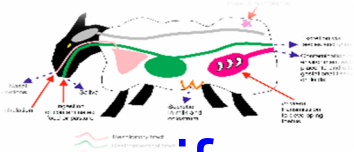




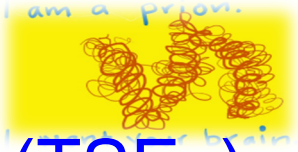


Cattle at a trough, and a buck deer in the wild. (Courtesy Ermias Belay)










Transmissible spongiform encephalopathies(TSEs)

Animal Prion Diseases

- Scrapie**(SC)**



- Bovine spongiform encephalopathy **(BSE)**



- Transmissible mink encephalopathy **(TME)**



- Feline spongiform encephalopathy **(FSE)**

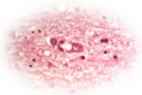


- Chronic wasting disease **(CWD)**



Human Prion Diseases

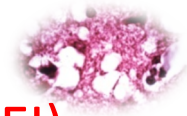
- Creutzfeldt-Jakob disease(CJD)



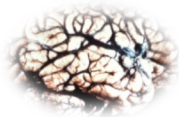
- Variant of CJD (vCJD)



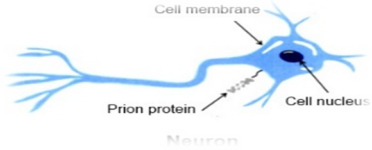
- Gerstamann-Straussler-Scheinker disease (GSS)



- Fatal familial insomnia(FFI)
- Kuru







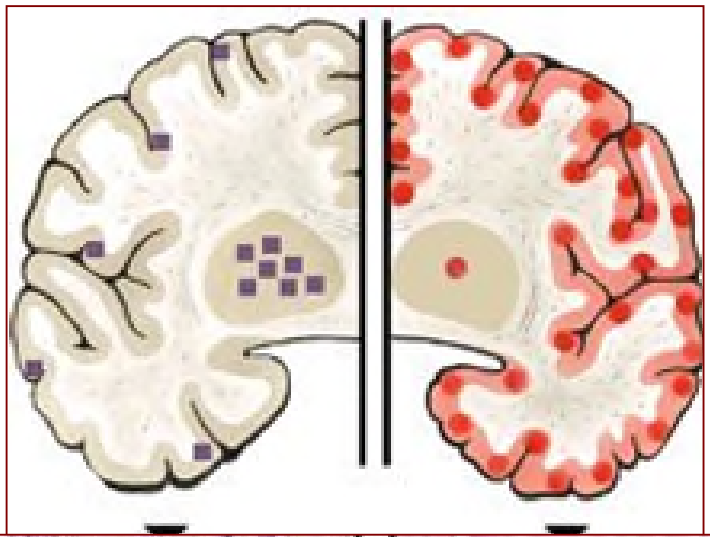


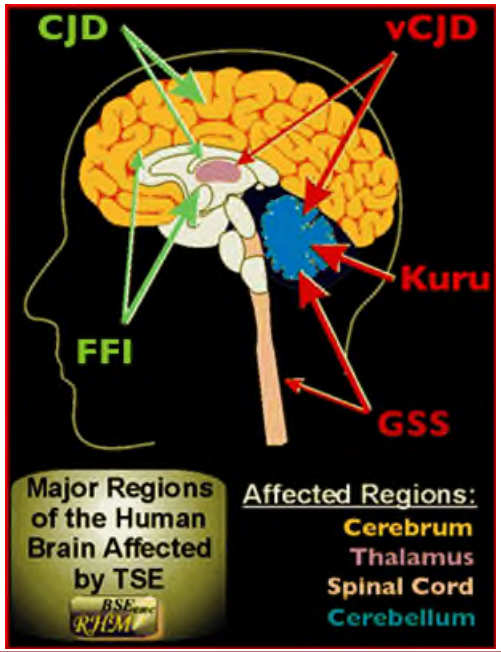


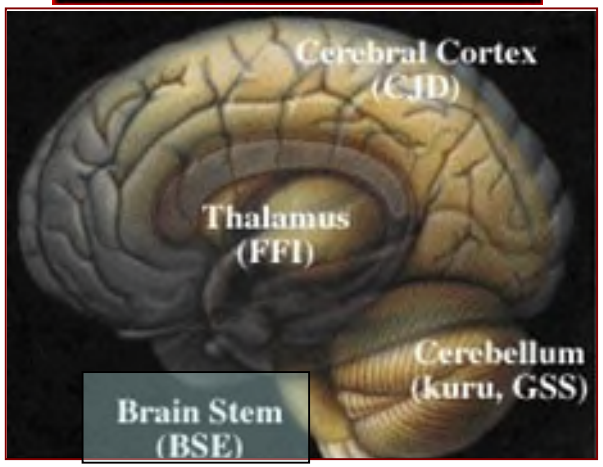




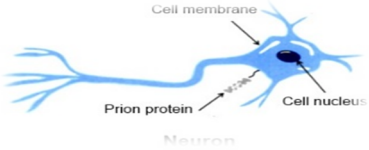
Different prions affect different regions of the brain











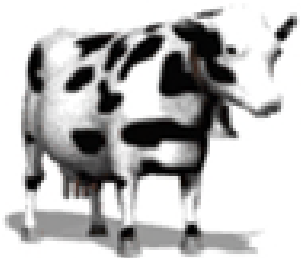


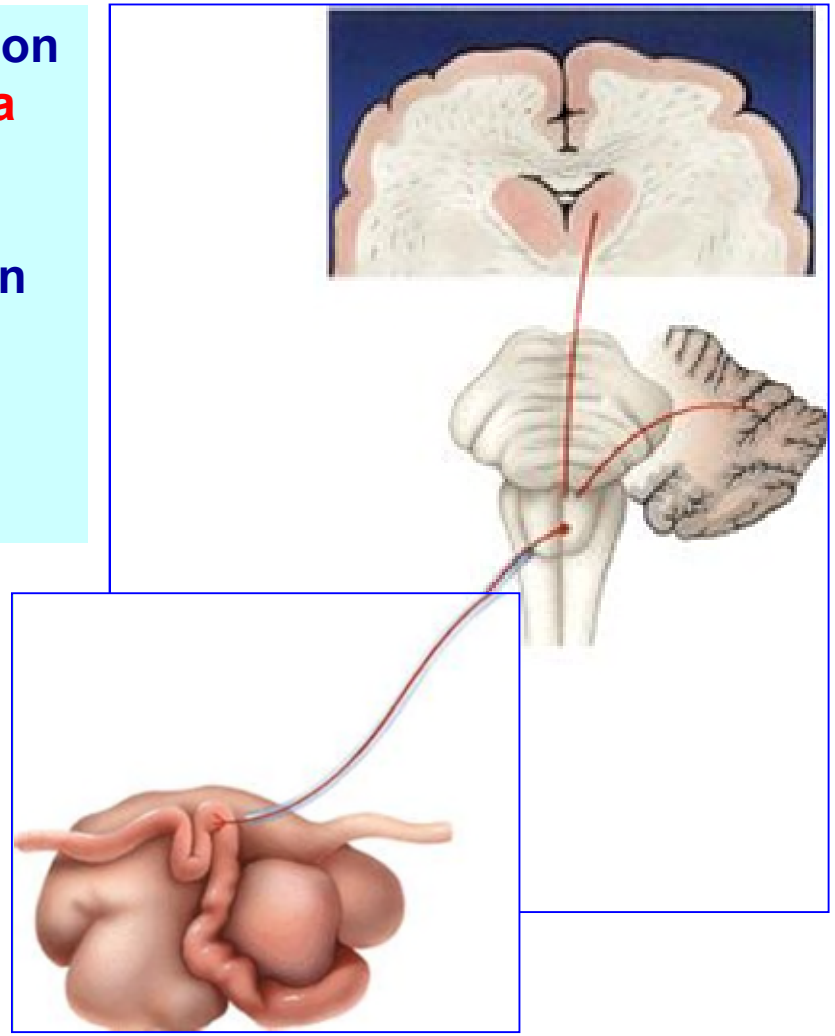




Prion diseases arise in three different ways

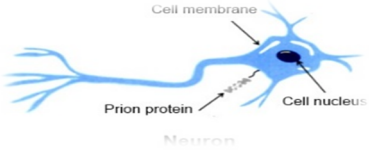
1. horizontal transmission from e.g. a sheep to a cow (BSE).
2. In inherited forms, mutations in the prion gene are transmitted from parent to child.
3. They can arise spontaneously.

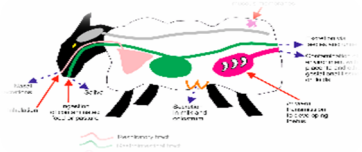










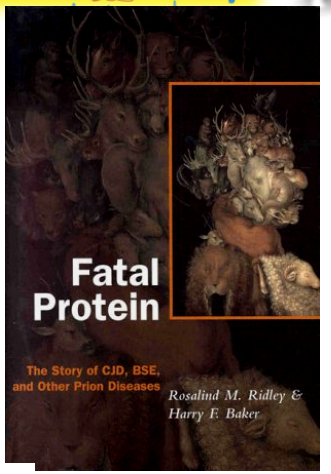


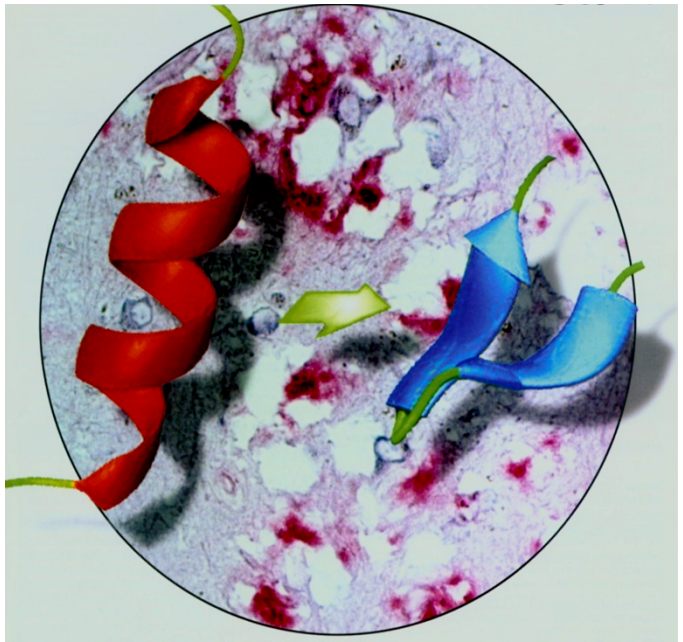






What is a prion?

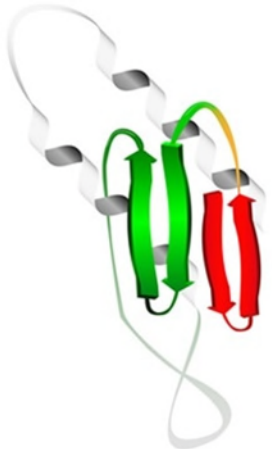




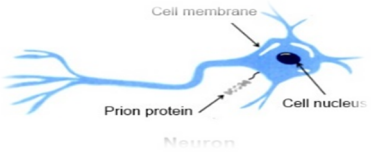
PrP^{C}
is a normal protein



PrP^{Sc}
the disease-causing form of the prion protein













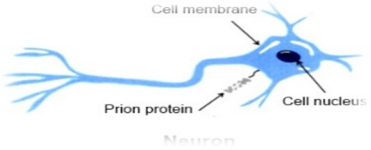

Stanley Prusiner

Nobel prize, 1997

Several lines of evidence support protein only model of infection

- Nucleic acid is not necessary for infectivity
- PrP^{Sc} is associated with scrapie infectivity
- Susceptibility of a host to prion infection is codetermined by the prion inoculum and the PrP gene
- Mutated gene can cause susceptibility to disease without apparent infection





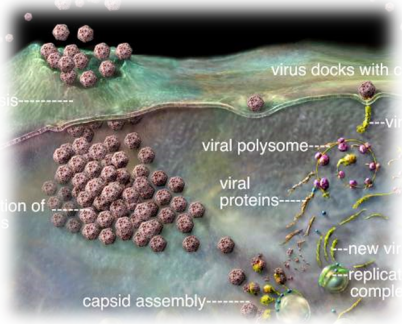




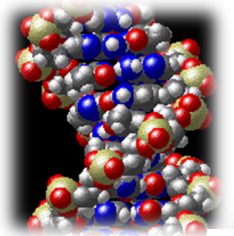


What is a prion?

Virus ?



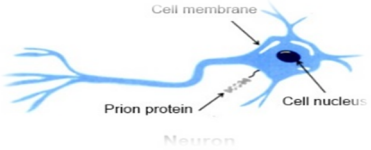
Nucleic acid?



Protein ?











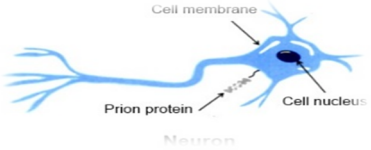


英國BSE二十年醜聞



1、這部影片主題是關於「狂牛症（BSE）醜聞」的長期隱瞞與制度失靈。
2、一場長達數十年的「科學、政策與信任崩壞」案例。











英國BSE

1 疾病起源與擴散

- BSE（牛海綿狀腦病）源於：
  - **反芻動物蛋白（肉骨粉，MBM）回餵牛隻**
- prion（普里昂）具有：
  - 極高抗性（耐熱、耐消毒）
  - 可跨物種（→ 人類vCJD）
- 關鍵一句

「飼料鏈失控，是這場災難的起點。」

2 政府與產業的早期忽視

- 初期警訊已存在，但：
  - 被低估為「動物疾病」
  - 未即時採取嚴格管制
- 政府與產業：
  - 傾向維持市場穩定
  - **延遲公開風險**

風險評估被「經濟考量」壓過科學判斷

3 「20年的謊言」—資訊隱瞞

- 長期對外宣稱：
  - 「對人體無害」
  - 「風險極低」
- 但內部：
  - 已知可能傳染人類（vCJD）
  - 有跨物種證據(貓、老虎)

公開訊息 ≠ 內部科學認知

4 公共衛生危機爆發

- 人類病例（vCJD）出現
- 社會恐慌擴大
- 牛肉市場崩盤

影響層面：

- 食品安全信任崩解
- 國際貿易受阻
- 政府公信力受創

5 科學與制度的補救

之後才逐步建立：

- 禁止MBM餵飼反芻動物
- 移除SRM（特定風險物質）
- 強化監測系統
- 改善屠宰與檢驗流程

這些措施，其實就是今天WOAH標準的基礎

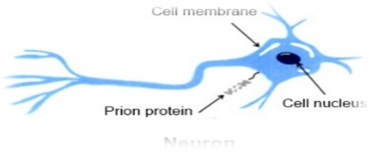
台灣目前需關注執行的事：

- 全面禁止反芻動物蛋白回餵
- SRM管理制度
- 飼料分流與查核
- BSE風險分級申請（Negligible Risk）

需警惕：

- 飼料交叉污染
- 制度落實與查核強度
- 長期監測的「疲乏效應」


HAPPY COW
MAD COW


Cell membrane
Prion protein
Cell nucleus
Neuron

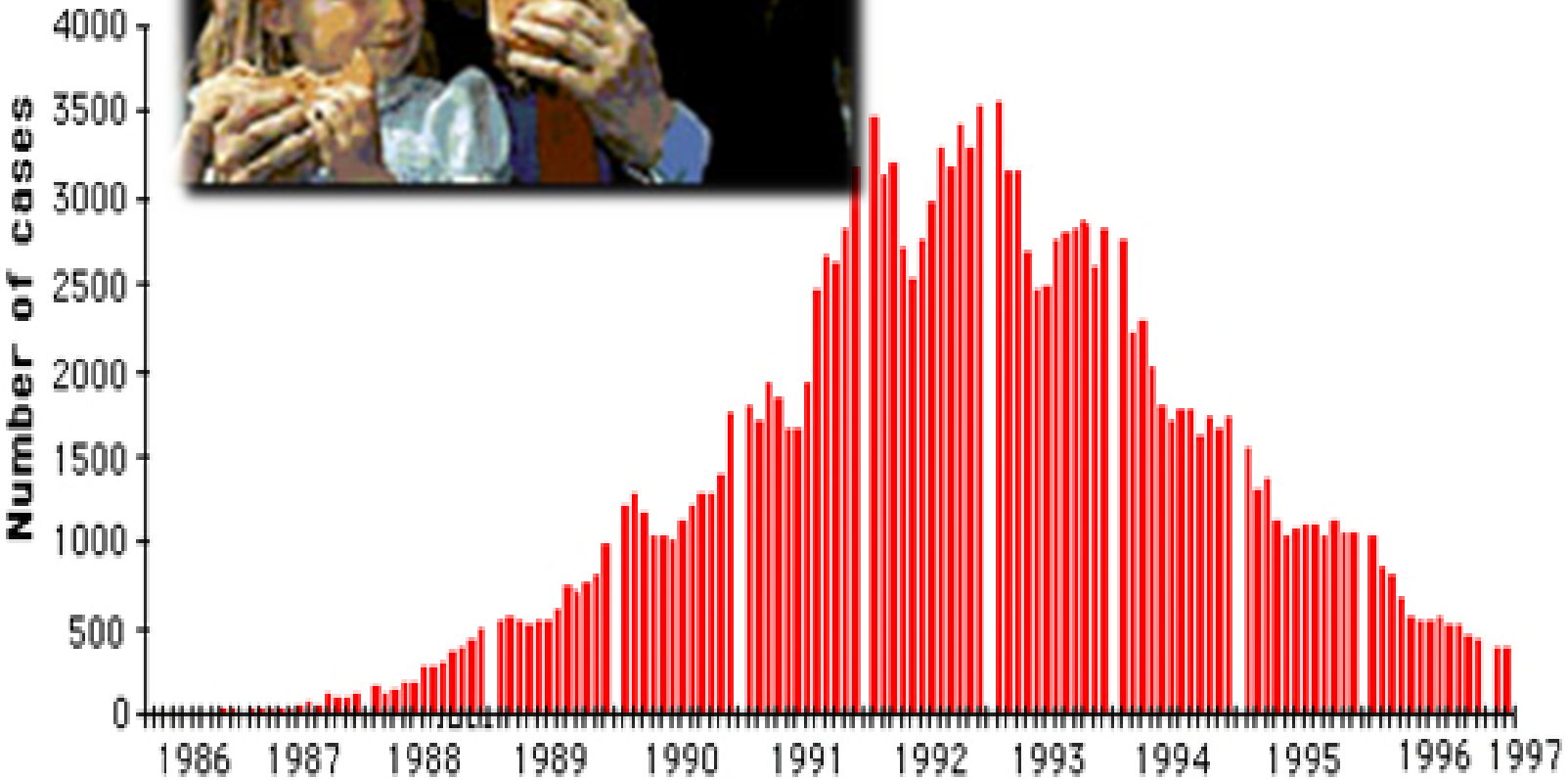




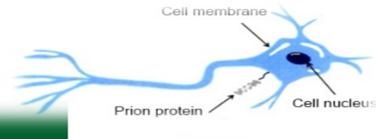

I am a prion.
I want your brain

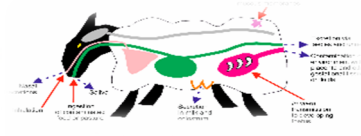





Number of cases
4000
3500
3000
2500
2000
1500
1000
500
0
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997











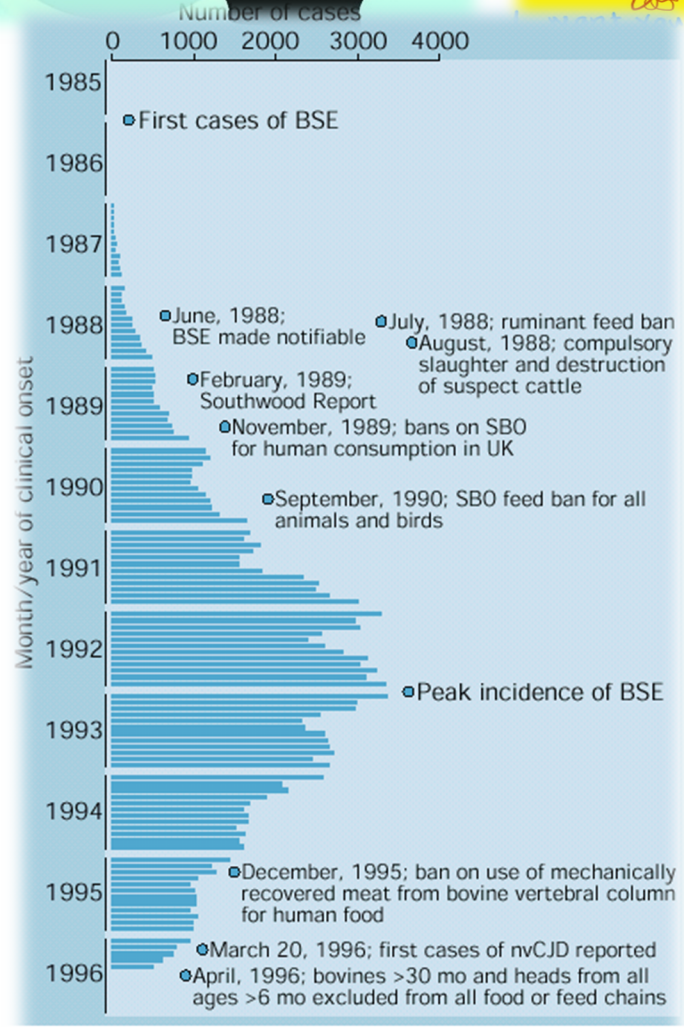


BSE Inquiry Report

The BSE Inquiry

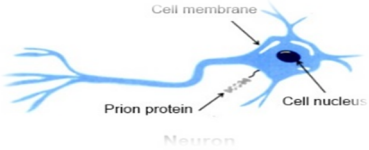
Volume 1

Findings and Conclusions



igure 1: **Confirmed cases of BSE by month and year of clinica**
nset in Great Britain, 1986 to May, 1996
ourtesy of MAFF.











Volume 1: Findings and conclusions

Volume 2: Science

Volume 3: The Early Years, 1986-88

Volume 4: The Southwood Working Party, 1988-89

Volume 5: Animal Health, 1989-96

Volume 6: Human Health, 1989-96

Volume 7: Medicines and Cosmetics

Volume 8: Variant CJD (vCJD)

Volume 9: Wales, Scotland and Northern Ireland

Volume 10: Economic Impact and International Trade

Volume 11 Scientists after Southwood

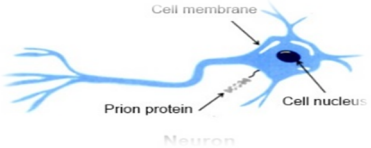
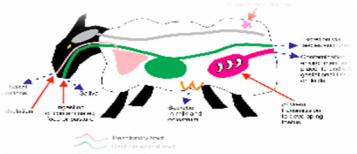
Volume 12: Livestock Farming

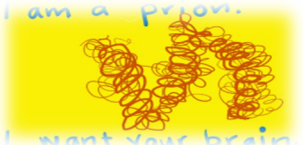
Volume 13: Industry Processes and Controls

Volume 14: Responsibilities for Human and Animal Health

Volume 15: Government and Public Administration

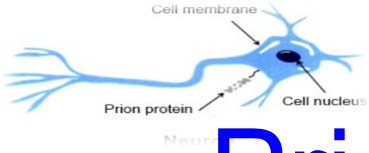
Volume 16: Reference Material


HAPPY COW
MAD COW

Cell membrane
Prion protein
Cell nucleus
Neuron



I am a prion.
I want your brain


Prion 特性



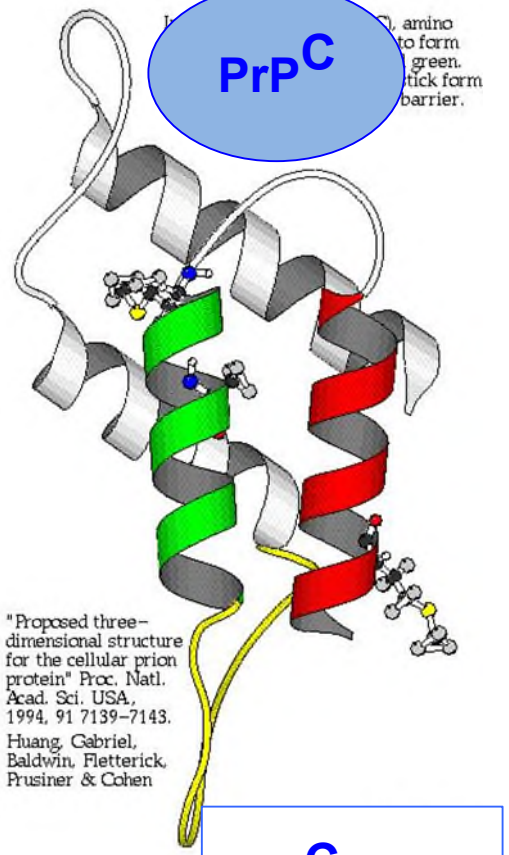




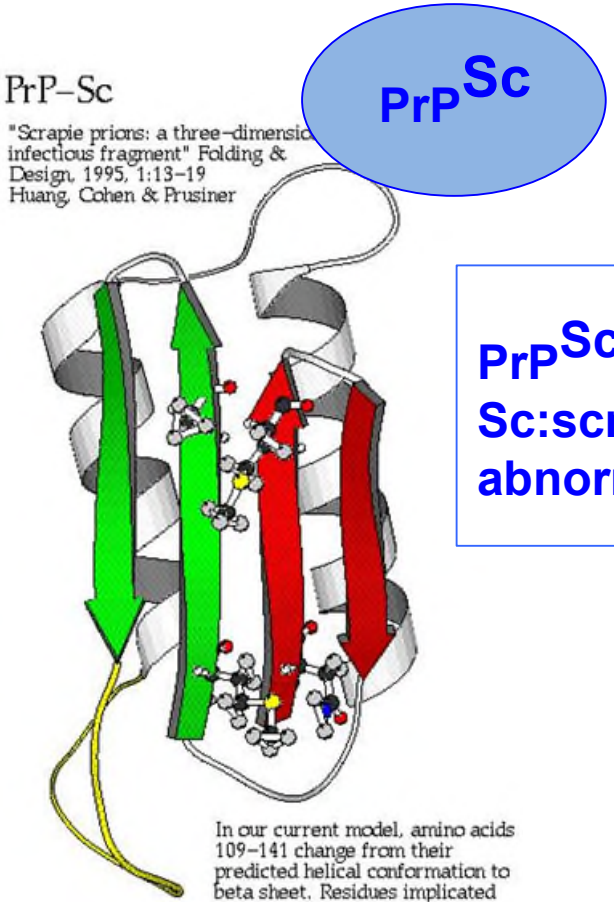




Prion protein



PrP^C
C: cellular normal



PrP^{Sc}
Sc:scrapie abnormal isoform

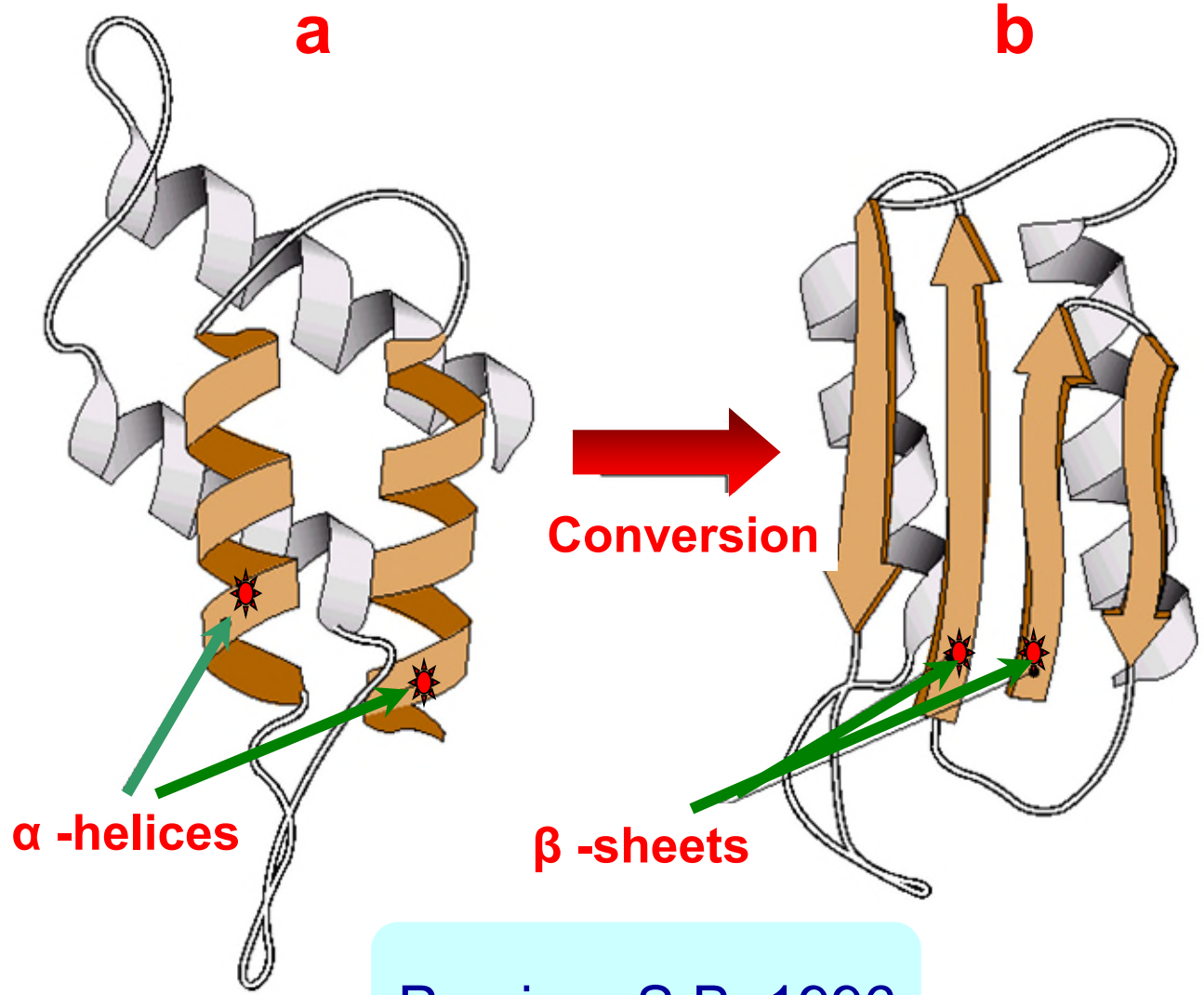
Prusiner S.B. 1996





a

b



Prusiner S.B. 1996



PrP mRNA

PrP Polypeptide

CHO CHO GPI

S—S

modification

PrP^C

209 amino acids

conversion

mature PrP^C 209a.a

PrP^{Sc}

209 amino acids

PrP^{Sc} 209a.a

PrP 27-30

Proteinase K

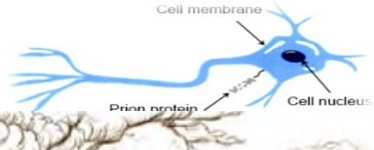
142 amino acids

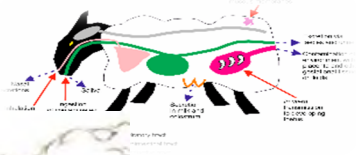
at least 142a.a

Codon

1 23 50 94 131 188 231 254



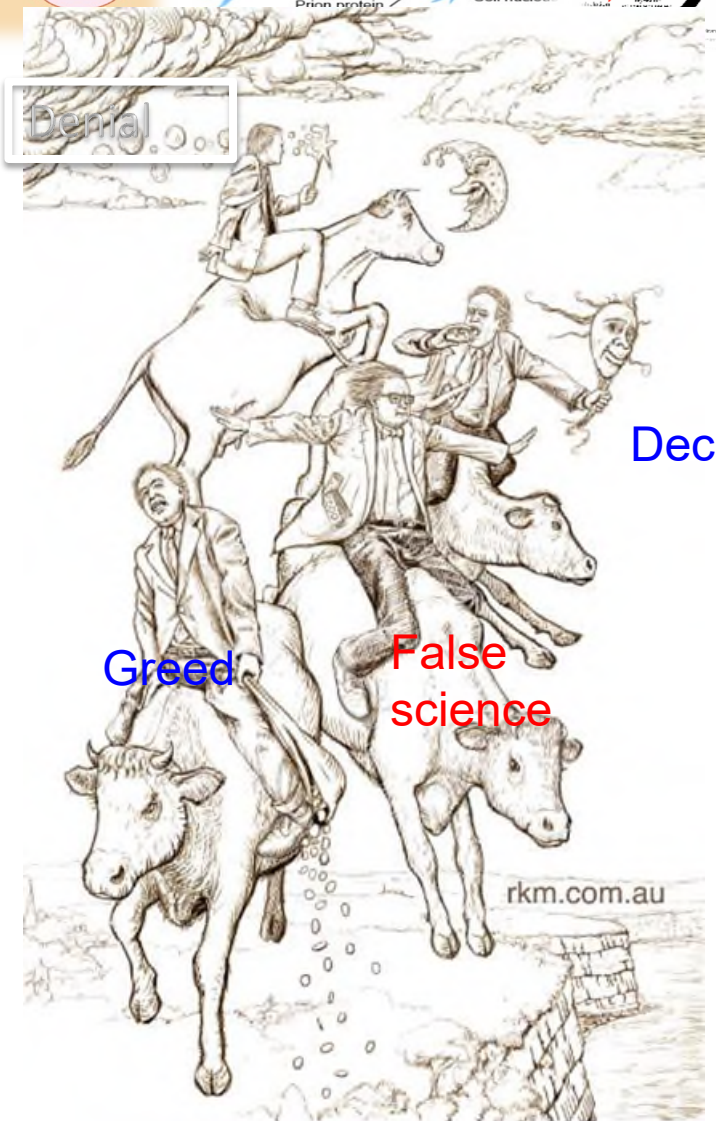






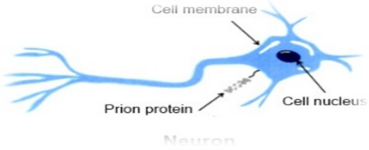


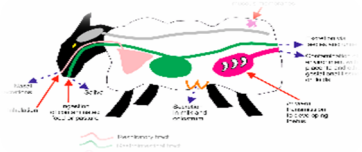
The four mad cow boys of the Apocalypse



- Denial: surrounded by fairy tales and clouds
- Deceit:hid has countenance behind a smiling mask and urged the people to eat the taint beast
- False science: we are not like unto the beasts of the fields, his foot became a cloven hoof unto the cow, he became continuous with the beasts.
- Greed:





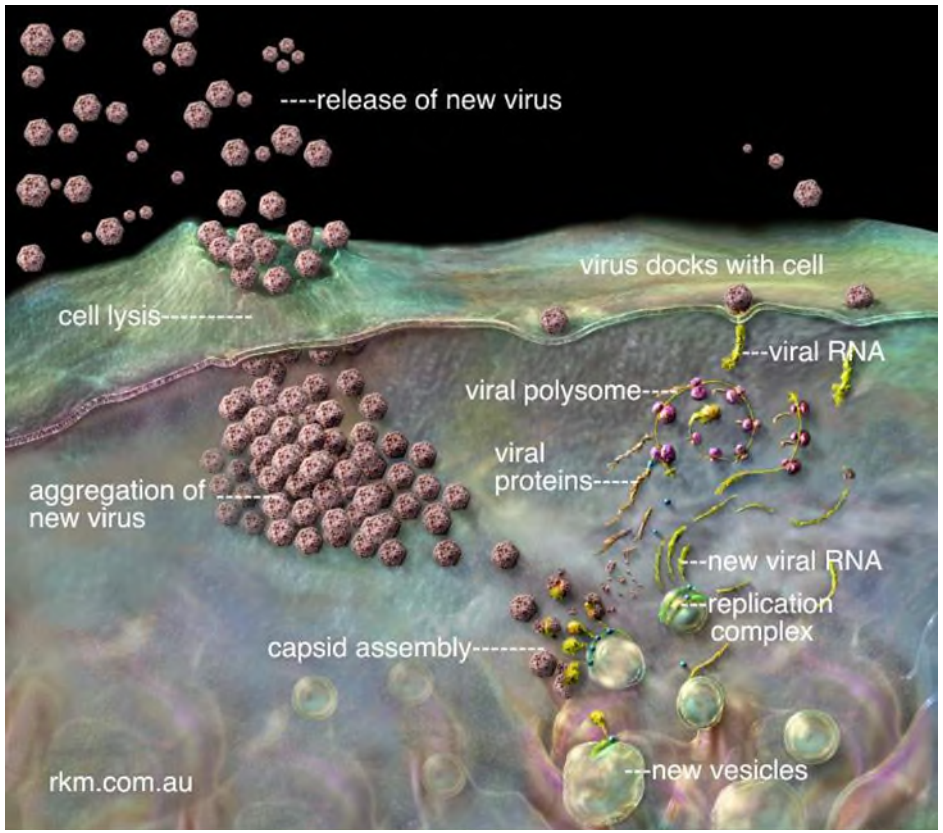








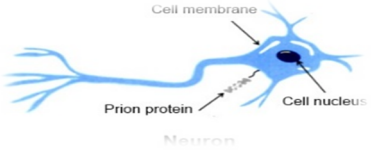
Foot and Mouth Disease Virus
Fast spread



Prion silent spread









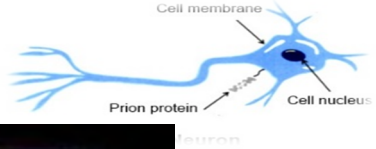



The Human Form of Mad Cow Disease Linked to Tooth Decay



May 18th, 2011
By Dental Health Magazine staff












CDC Warns Against Exposure to 'Mad Cow'-Like Brain Diseases

Travel to certain countries, hunting, eating wild deer meat raises risks, experts say

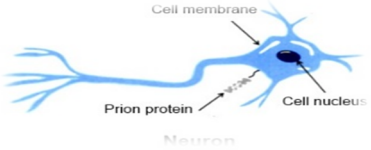
By Mary Elizabeth Dallas
Monday, May 23, 2011

1010 *J. Med. Chem.* **2011,** *54,* 1010–1021
DOI: 10.1021/jm101250y

Journal of Medicinal Chemistry Article

2-Aminothiazoles as Therapeutic Leads for Prion Diseases



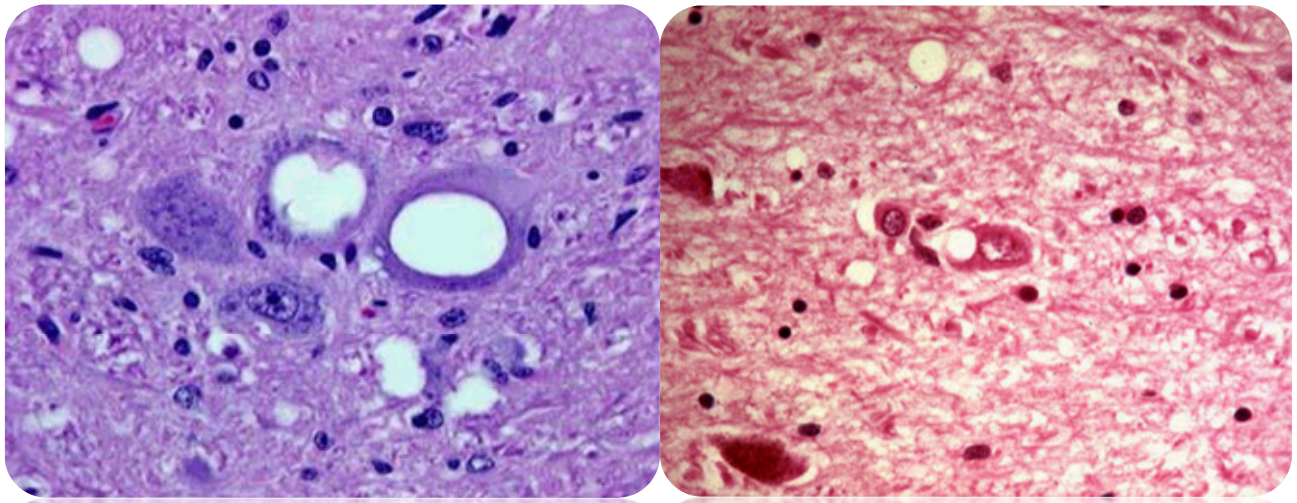






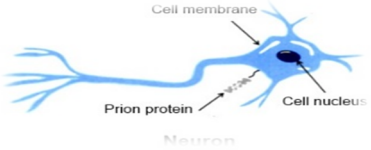


Prion Diseases



Spongiform Encephalopathies Brain with Large Vacuoles in the Cortex and Cerebellum











Humans might be infected by prions in 2 ways

- Acquired infection

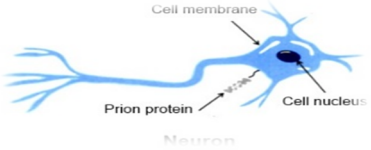
  diet, iatrogenic



- Apparently hereditary

both infectious and hereditary





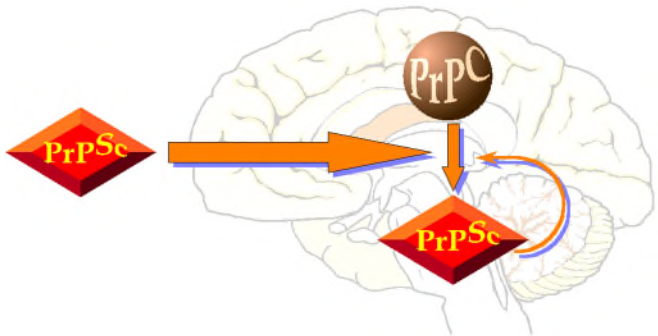






Pathogenesis of TSE





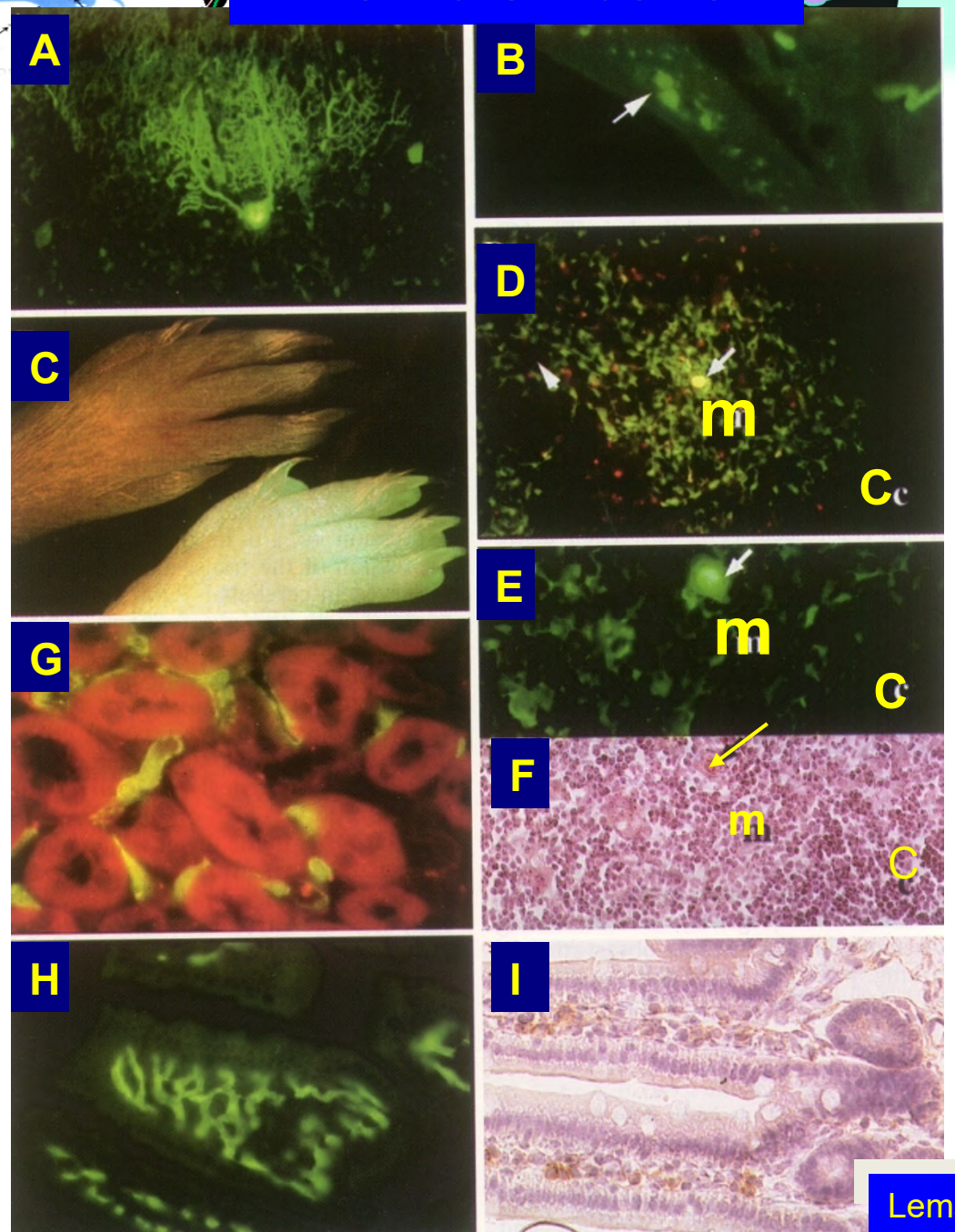
Prion distribution

FA Cerebellum cortex , Purkinje cells (Tg)

gfp , foot

FA renal cortex endothelial cells

Small intestine **gfp**



FA Intestine, ganglion cells

FA Thymus epithelial cells of medulla

FA Thymus epithelial cells of medulla

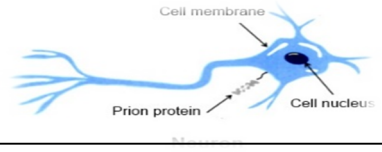
H&E Thymus

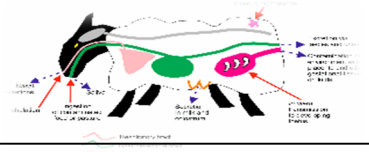
IHC Small intestine

Anti-Prp8G8

Lemaire-Vieille C. *et al.*,2000

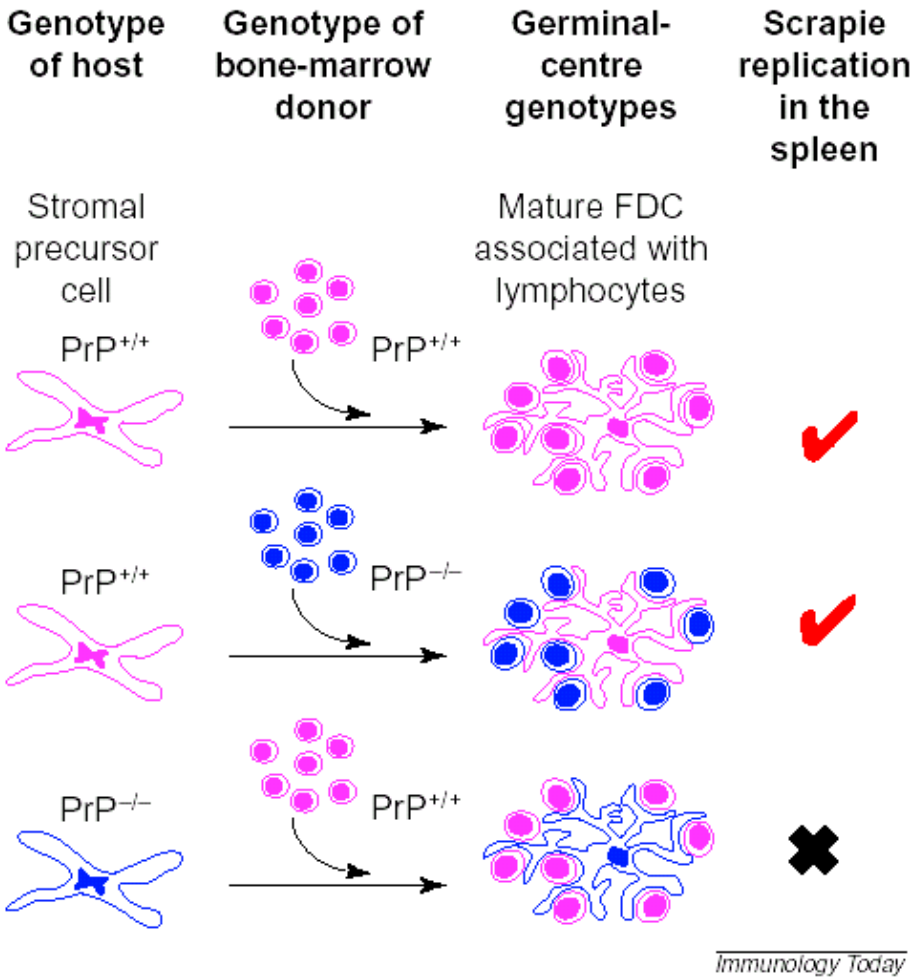


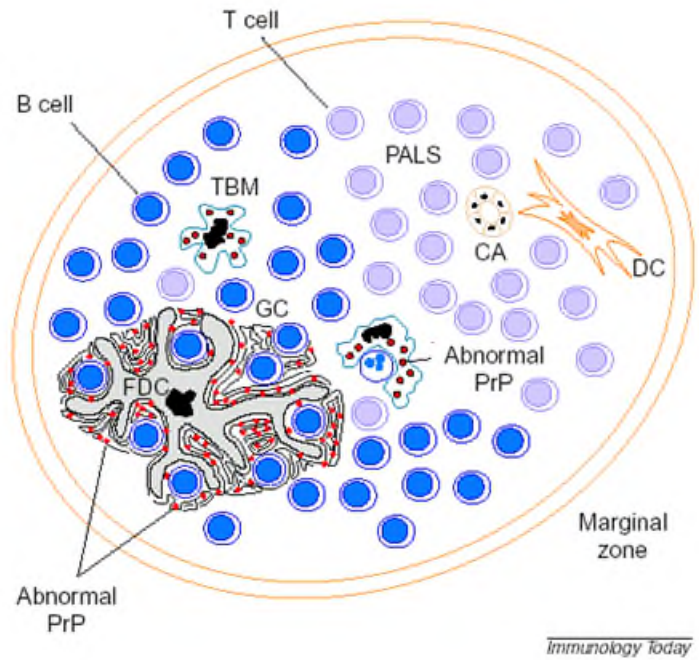






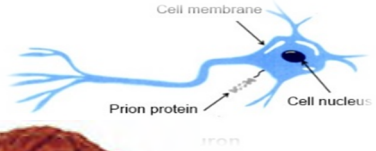

Follicular dendritic cells in TSE pathogenesis





Moira E. *et al;* 2000



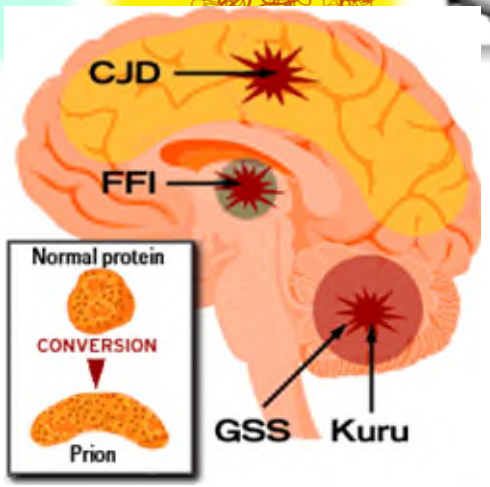







Kuru



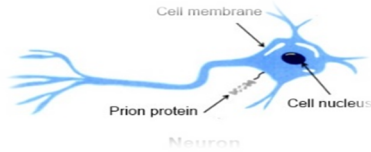


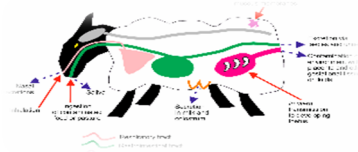
- Epidemic in fore population in New Guinea in 1957
- Transmitted by ritual cannibalism
- Incubation period from 4 to 20 years
- Progressive cerebellar ataxia,dementia

















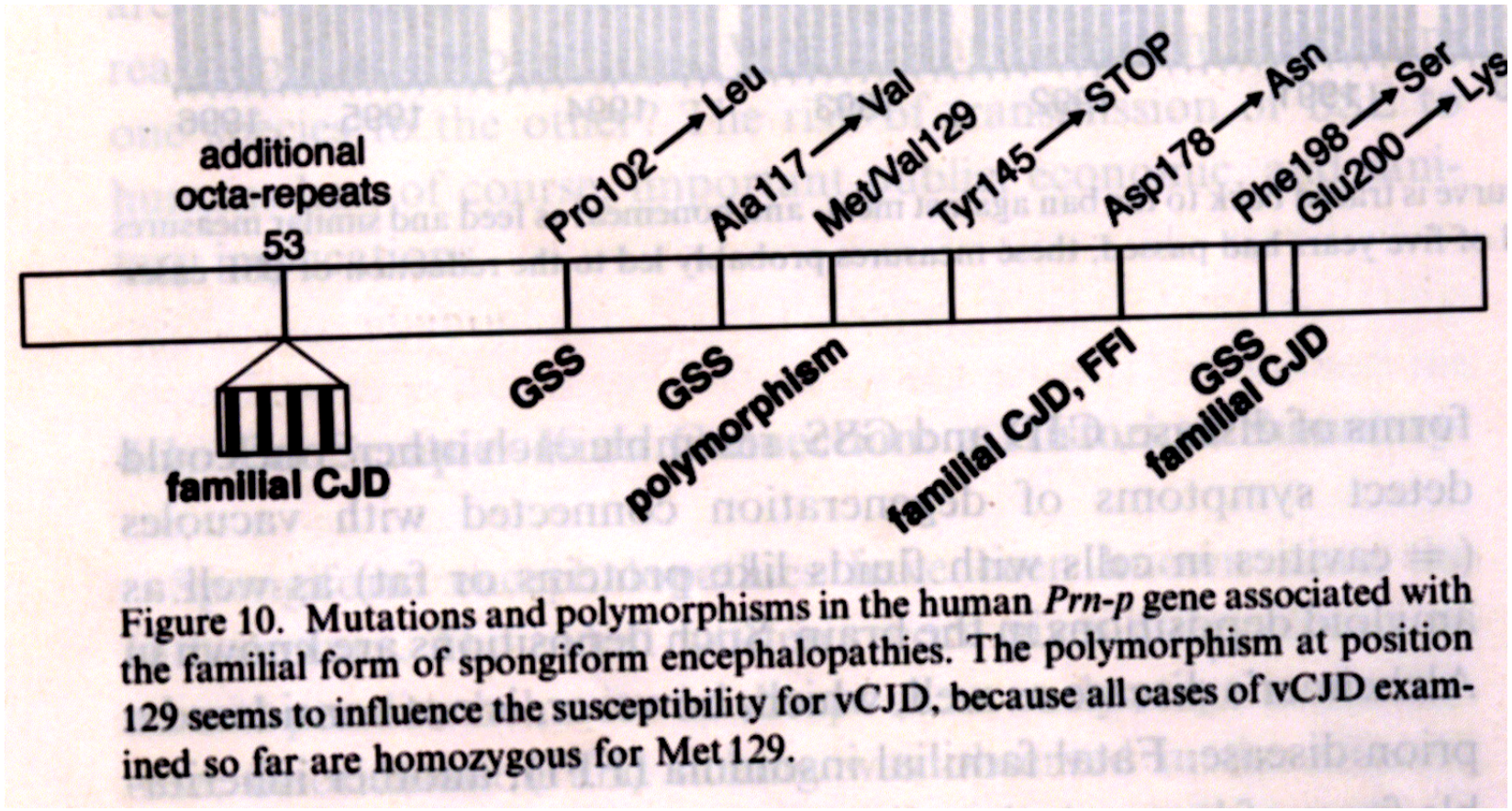


Figure 10. Mutations and polymorphisms in the human *Prn-p* gene associated with the familial form of spongiform encephalopathies. The polymorphism at position 129 seems to influence the susceptibility for vCJD, because all cases of vCJD examined so far are homozygous for Met 129.









摩弗倫羊

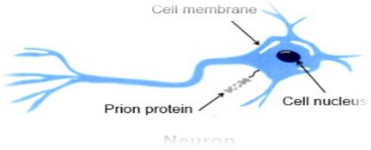
恆河猴

Panel 1: **Chronology of naturally occurring TSEs of man and animals**

Host	Disease	First reported
Man	Kuru	1957
	CJD and variants	1920/1928-92
	nvCJD	1995-96
Sheep	Scrapie	1730
Goats		1872
Moufflon*		1992
Mule deer	Chronic wasting disease	1967
Elk		
Ranch-bred mink	Transmissible mink encephalopathy	1965
Cattle	BSE	1986
Exotic ungulates (in zoos)	SE in captive nyala, gemsbok,* Arabian oryx,* scimitar-horned oryx,* greater kudu, eland,* ankole*	1986-95
Domestic cats	Feline SE	1990
Big cats (*Felidae*) (in zoos)*	SE affecting pumas, cheetahs, ocelots, tiger	1992-96
Macaque	SE	1996

*Transmissibility not formally established in these species.
SE=spongiform encephalopathy.



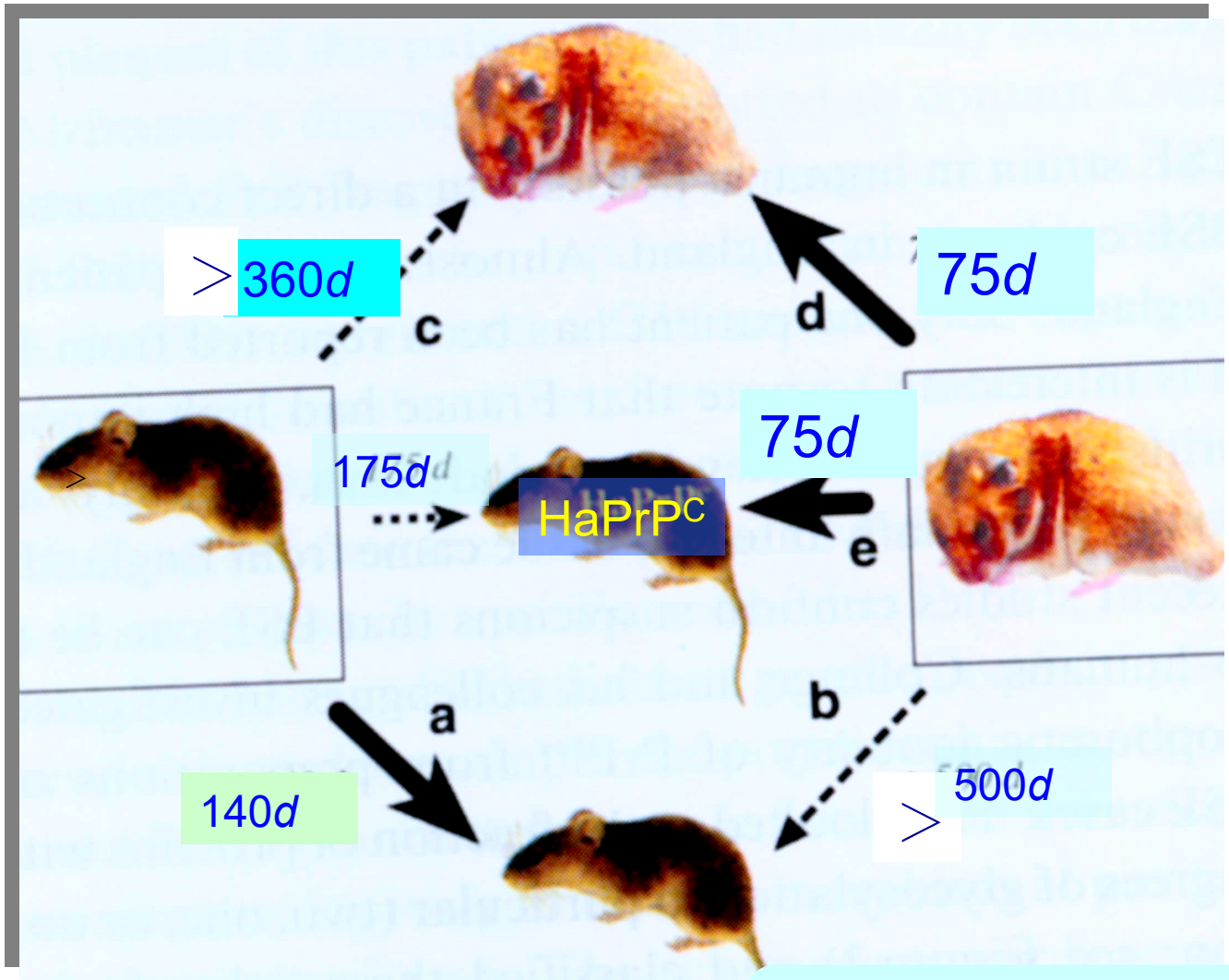






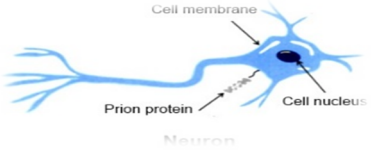


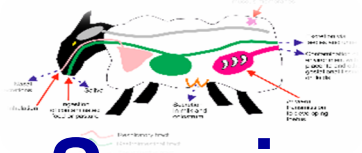
Species-barrier



Weissmann C. *et al.*, 1991



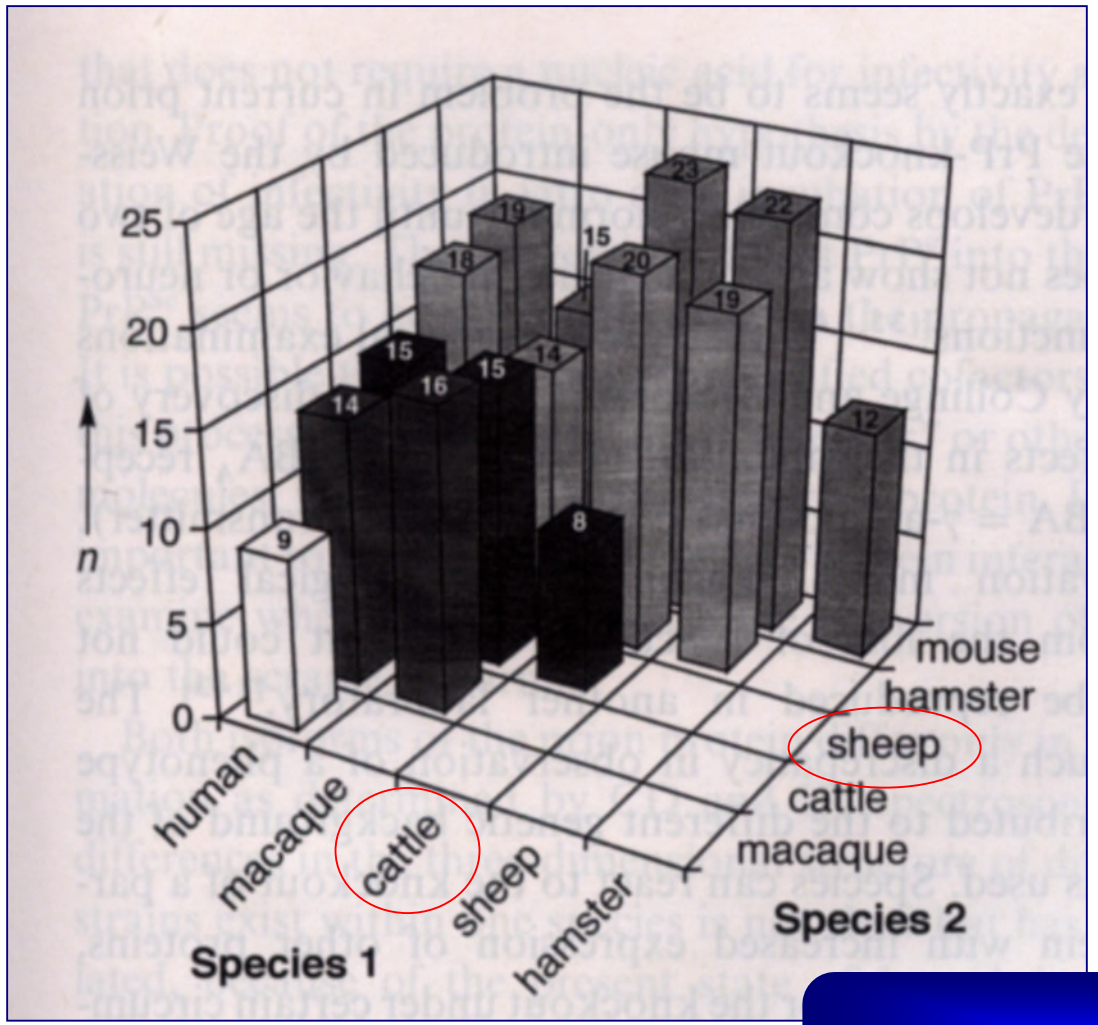






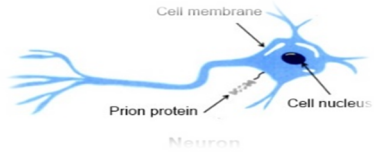


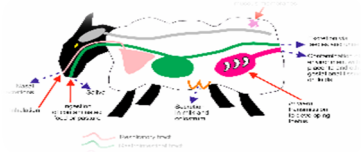
Species-barrier



Schatzl H.M. *et al.*, 1995


HAPPY COW
MAD COW

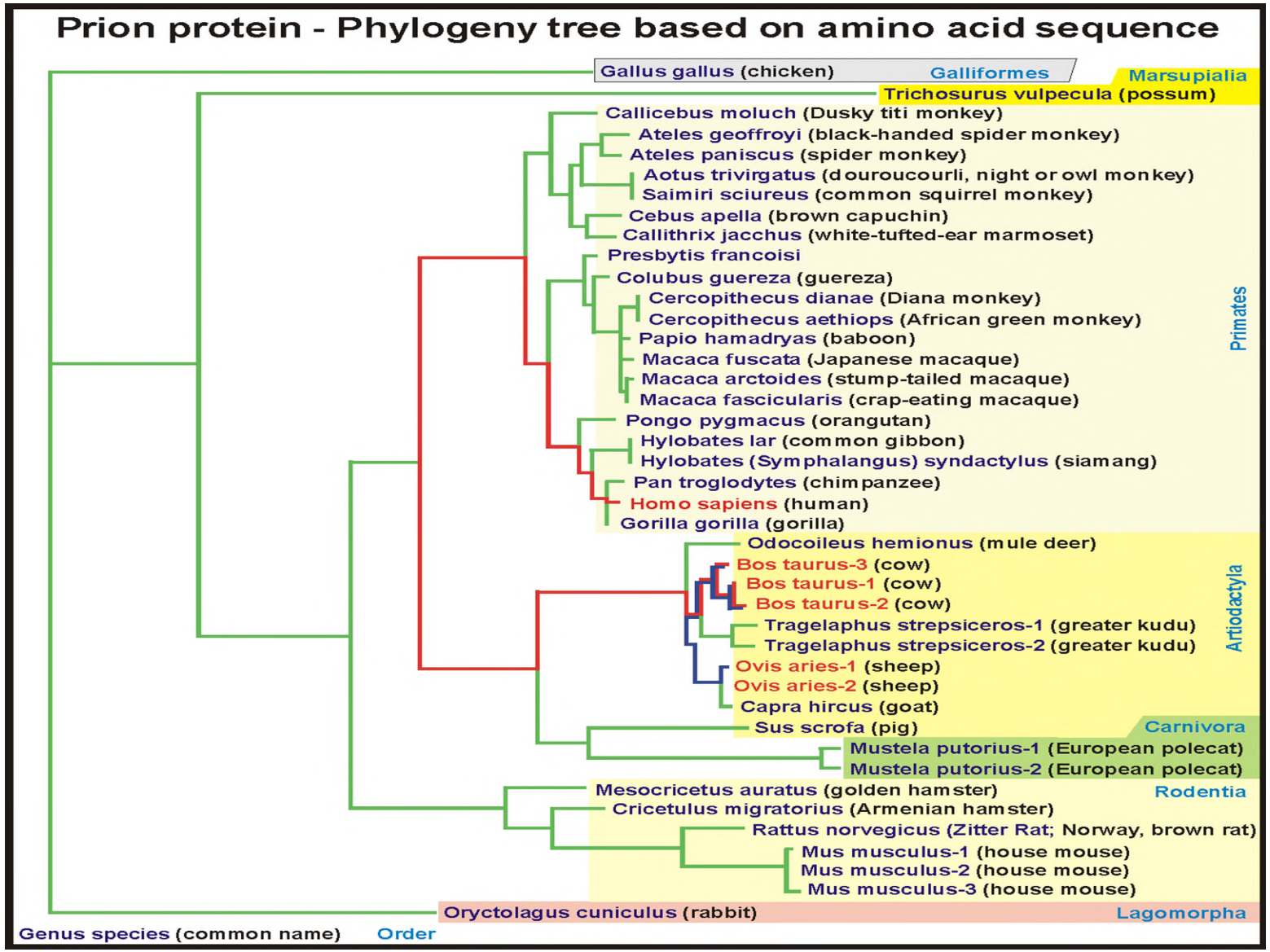

Cell membrane
Prion protein
Cell nucleus
Neuron



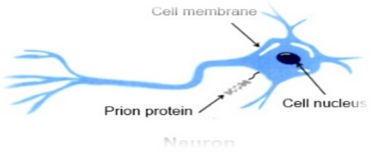


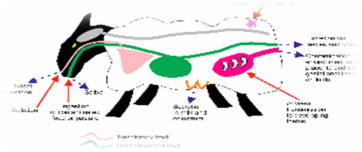

I am a prion.
I want your brain




Prion protein - Phylogeny tree based on amino acid sequence
Gallus gallus (chicken)
Galliformes
Marsupialia
Trichosurus vulpecula (possum)
Callicebus moluch (Dusky titi monkey)
Ateles geoffroyi (black-handed spider monkey)
Ateles paniscus (spider monkey)
Aotus trivirgatus (douroucourli, night or owl monkey)
Saimiri sciureus (common squirrel monkey)
Cebus apella (brown capuchin)
Callithrix jacchus (white-tufted-ear marmoset)
Presbytis francoisi
Colubus guereza (guereza)
Cercopithecus dianae (Diana monkey)
Cercopithecus aethiops (African green monkey)
Papio hamadryas (baboon)
Macaca fuscata (Japanese macaque)
Macaca arctoides (stump-tailed macaque)
Macaca fascicularis (crap-eating macaque)
Pongo pygmacus (orangutan)
Hylobates lar (common gibbon)
Hylobates (Symphalangus) syndactylus (siamang)
Pan troglodytes (chimpanzee)
Homo sapiens (human)
Gorilla gorilla (gorilla)
Primates
Odocoileus hemionus (mule deer)
Bos taurus-3 (cow)
Bos taurus-1 (cow)
Bos taurus-2 (cow)
Tragelaphus strepsiceros-1 (greater kudu)
Tragelaphus strepsiceros-2 (greater kudu)
Ovis aries-1 (sheep)
Ovis aries-2 (sheep)
Capra hircus (goat)
Artiodactyla
Sus scrofa (pig)
Carnivora
Mustela putorius-1 (European polecat)
Mustela putorius-2 (European polecat)
Mesocricetus auratus (golden hamster)
Cricetulus migratorius (Armenian hamster)
Rattus norvegicus (Zitter Rat; Norway, brown rat)
Mus musculus-1 (house mouse)
Mus musculus-2 (house mouse)
Mus musculus-3 (house mouse)
Rodentia
Oryctolagus cuniculus (rabbit)
Lagomorpha
Genus species (common name)
Order









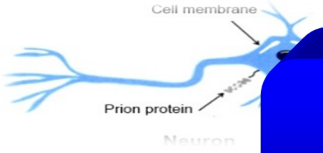


Prion infection impairs the cellular response to oxidative stress

- Prion infection results in an alteration of the molecular mechansims promoting cellular resistance to reactive oxygen species.(ROS)

Milhavet O. *et al.*,2000









PrP^{C} conversion into PrP^{Sc}

(1)

(2)

(3)

Cu metabolism

Activation of glial and microglial cells

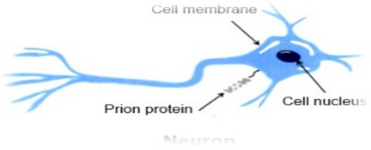
ROS

Protein and/or transcriptional regulation

Neuronal cell death

Milhavet O. *et al* 2000







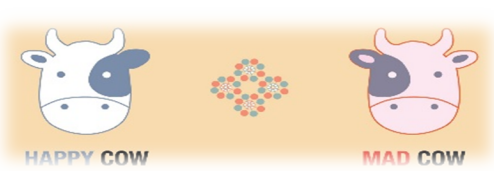




Accumulation of protease-resistant prion protein(PrP) and apoptosis of cerebellar granule cells in transgenic mice expressing a PrP insertional mutation

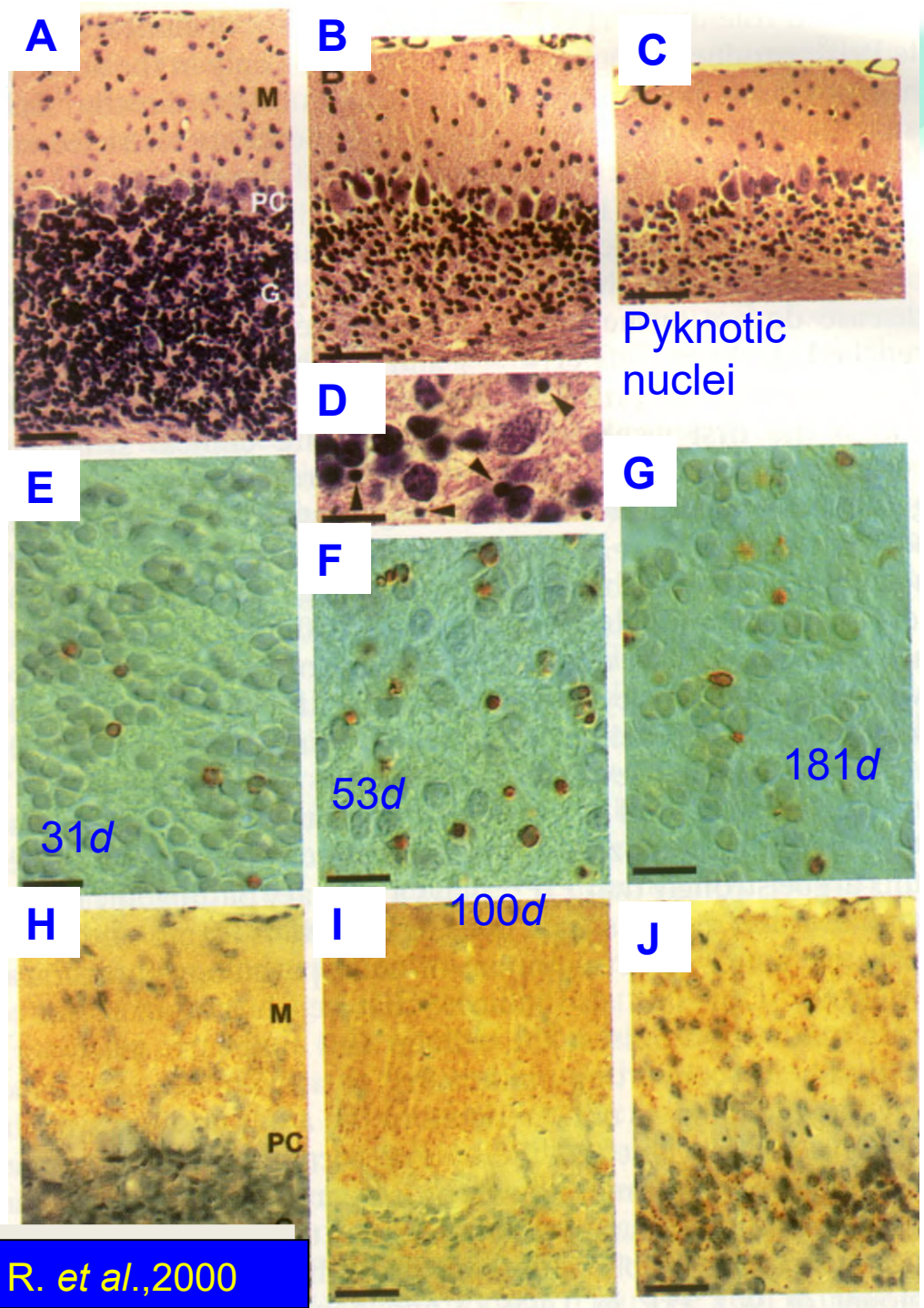
PrP accumulates, there is massive apoptosis of granule cells in the cerebellum

Chiesa R. *et al.*,2000





H &E
22days



Chiesa R. *et al.*,2000

Neuropathological changes in the cerebella of Tg mice

B;D H &E 100days

C: H &E 183days

E,F,G: ISEL(in situ)

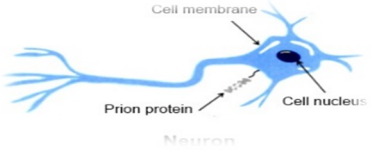
granule cell layer

H,I,J:IHC;
cerebellar cortex

PrP

J;181*d*









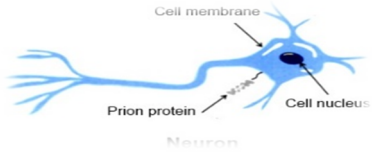


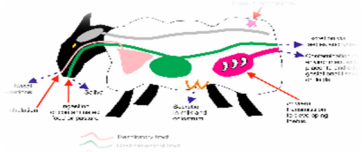
The role of prion peptide structure and aggregation in toxicity and membrane binding

β -sheets and amyloid structure of the prion peptides give rise to their toxicity and membrane binding affinities, especially in cholesterol-rich environments, may be related to toxicity.

Rymer D. L. *et al*., 2000





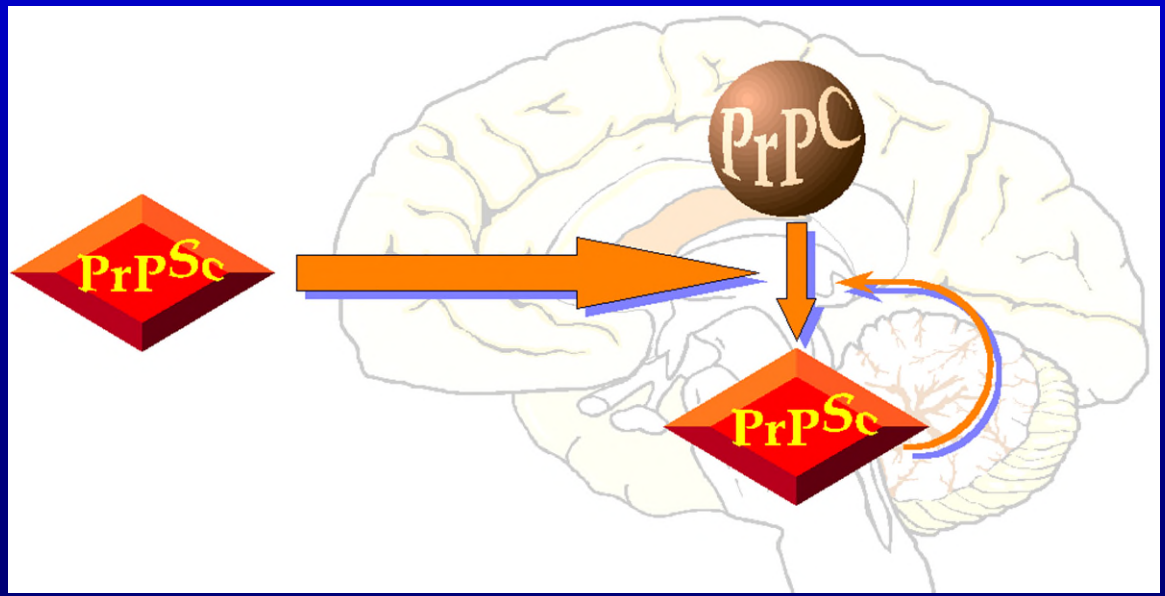




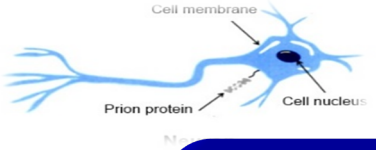


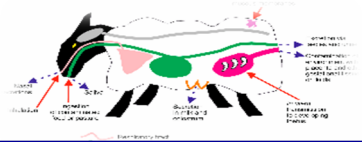
Pathogenesis

- Compare the biology of BSE with that of other TSE's













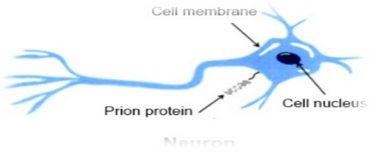
Prion disease and BSE crisis

There is now considerable concern that bovine prions may have been passed to humans, resulting in a new form of CJD

Stanley B. Prusiner

Science 1997









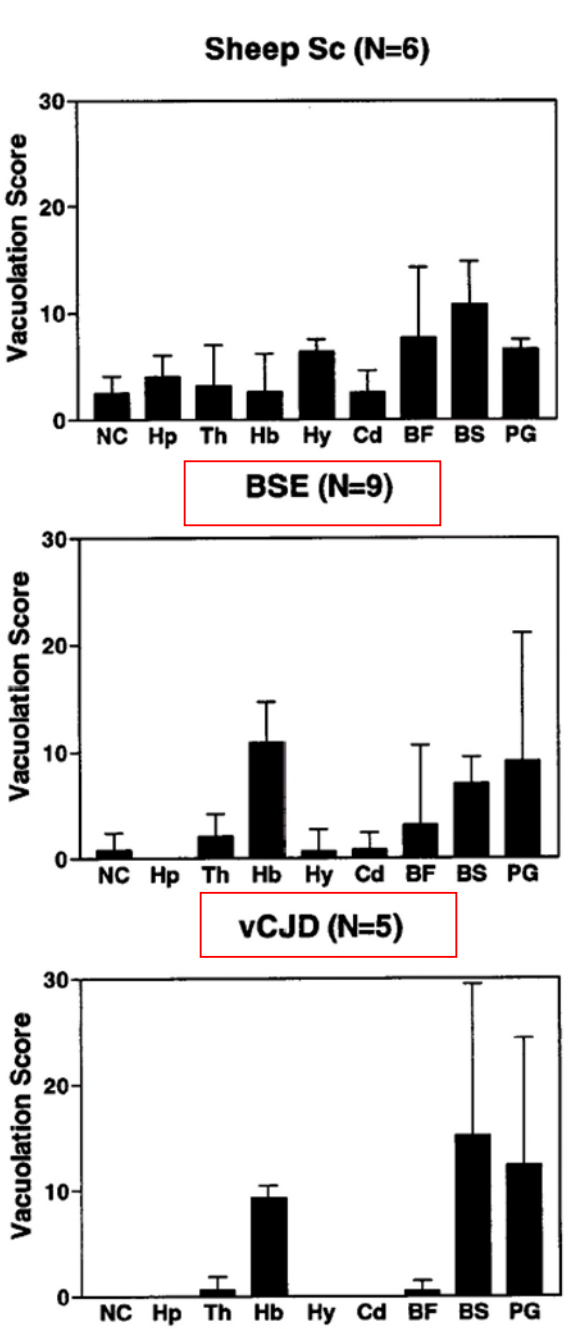


Compelling transgenetic evidence for transmission of bovine spongiform encephalopathy prions to humans

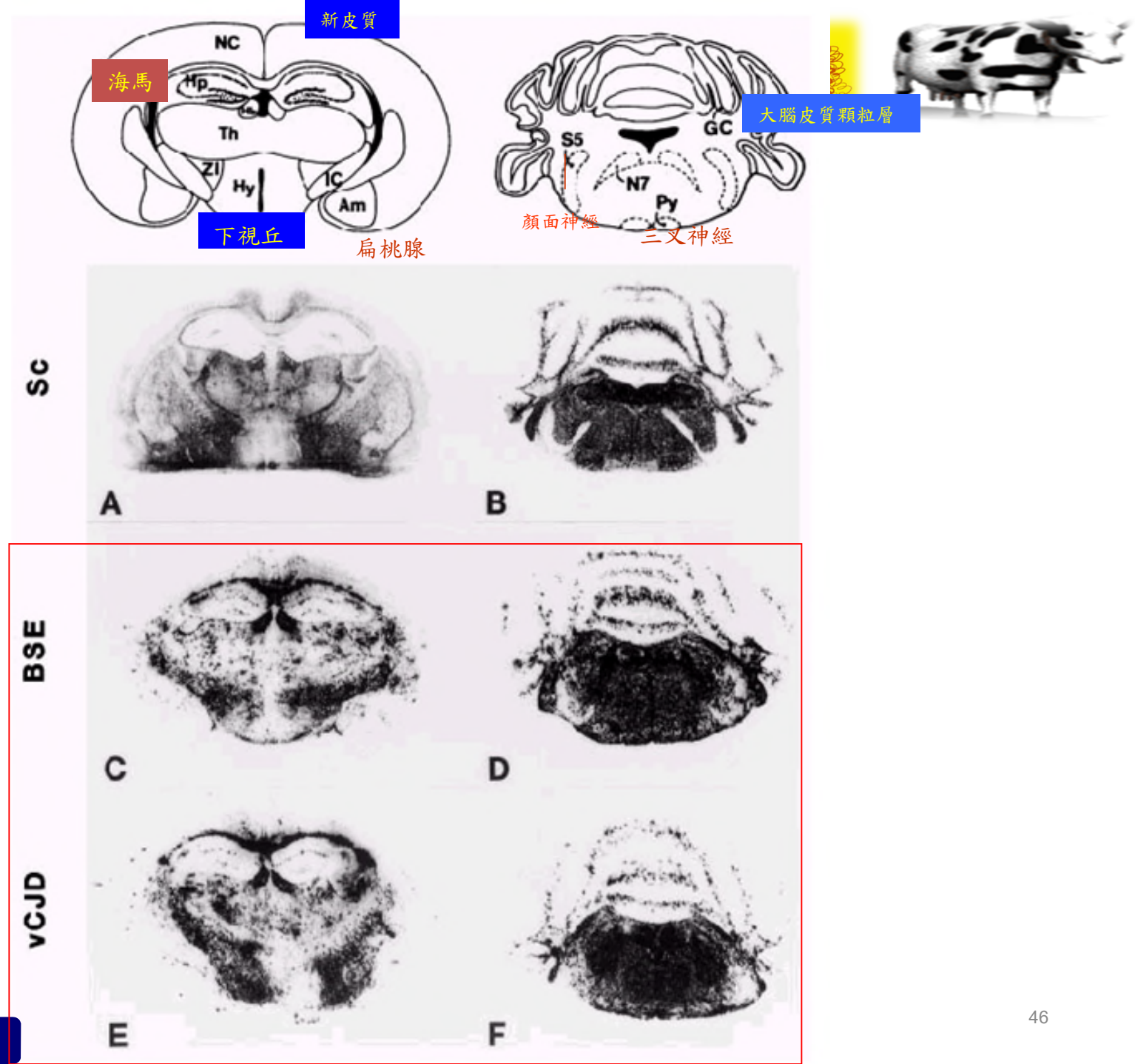
Michael R. Scott, Robert Will , James Ironside § , Hoang-Oanh B. Nguyen, Patrick Tremblay, Stephen J. DeArmond,

and Stanley B. Prusiner

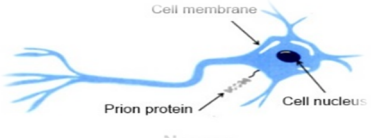
1999

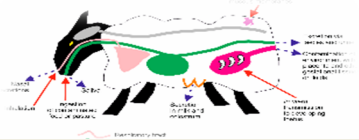


Scott M. R. *et al.*, 1999





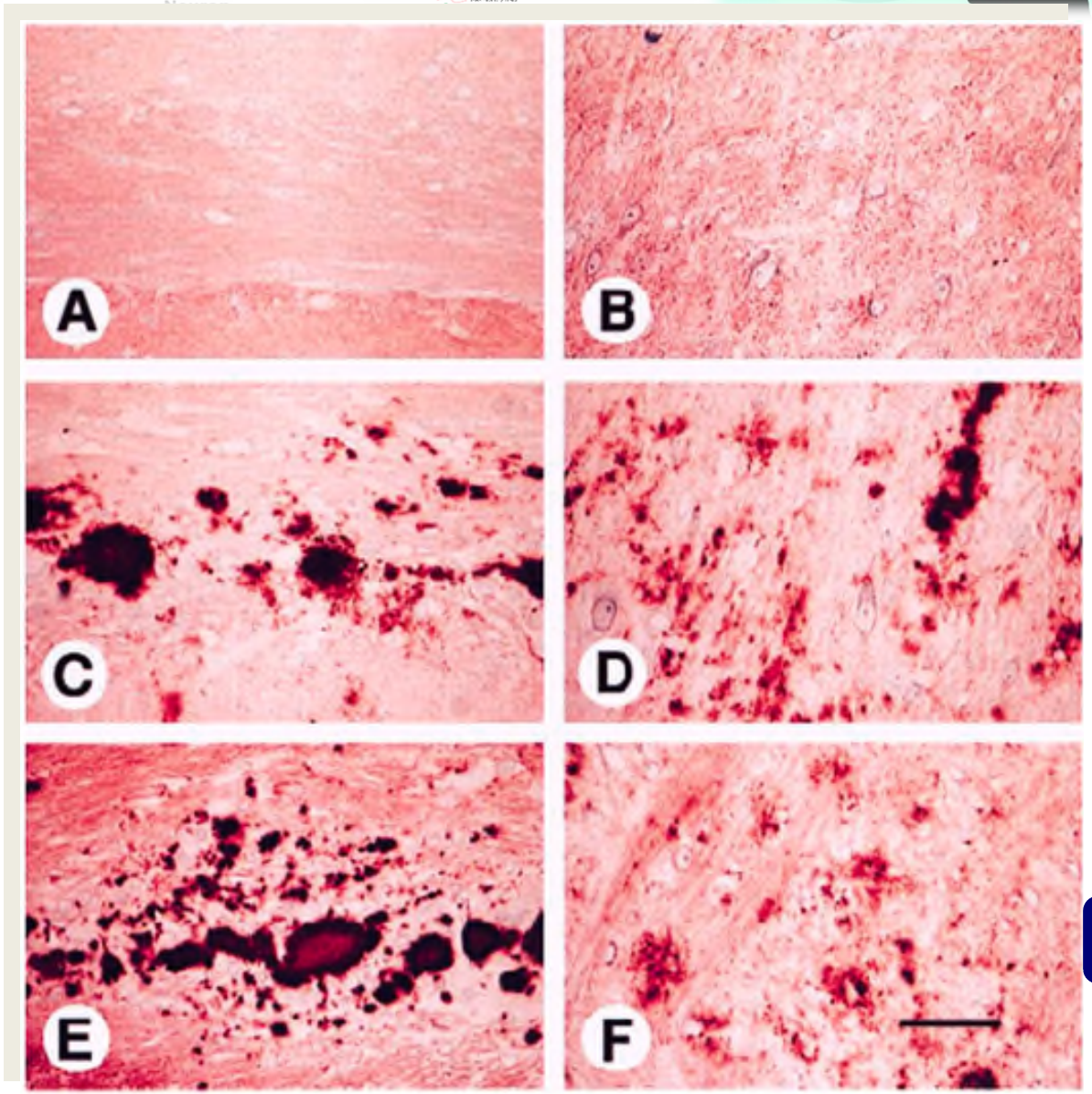












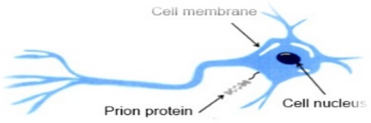
Control

BSE

nvCJD

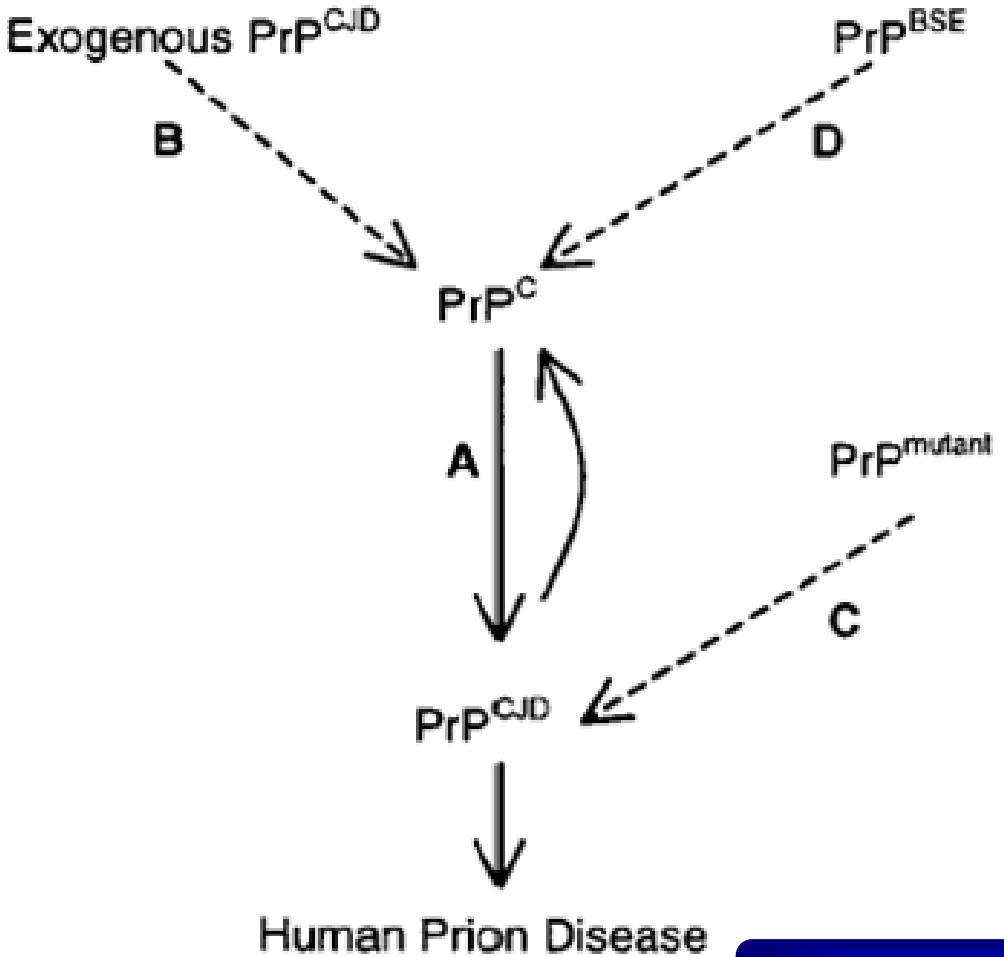
Scott M. R. *et al.*, 1999





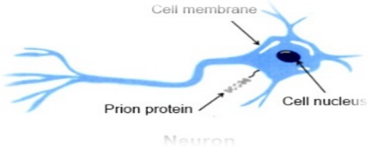




Scott M. R. *et al.*, 1999


HAPPY COW
MAD COW


Cell membrane
Prion protein
Cell nucleus
Neuron

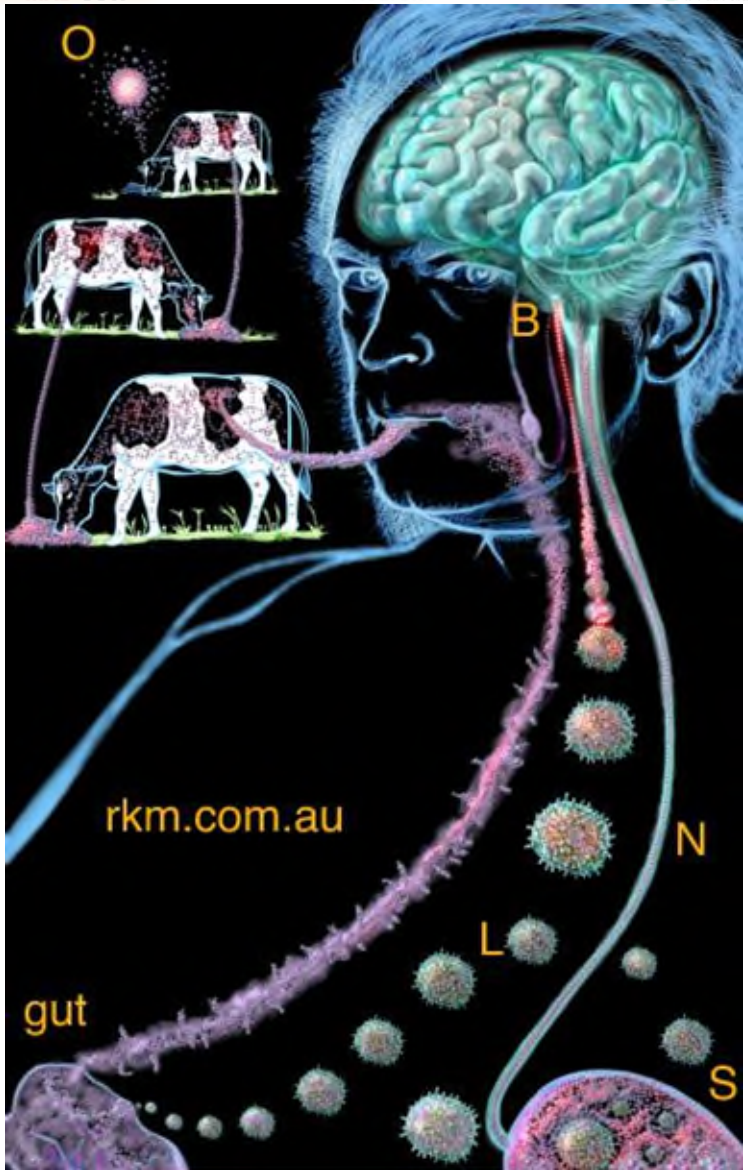


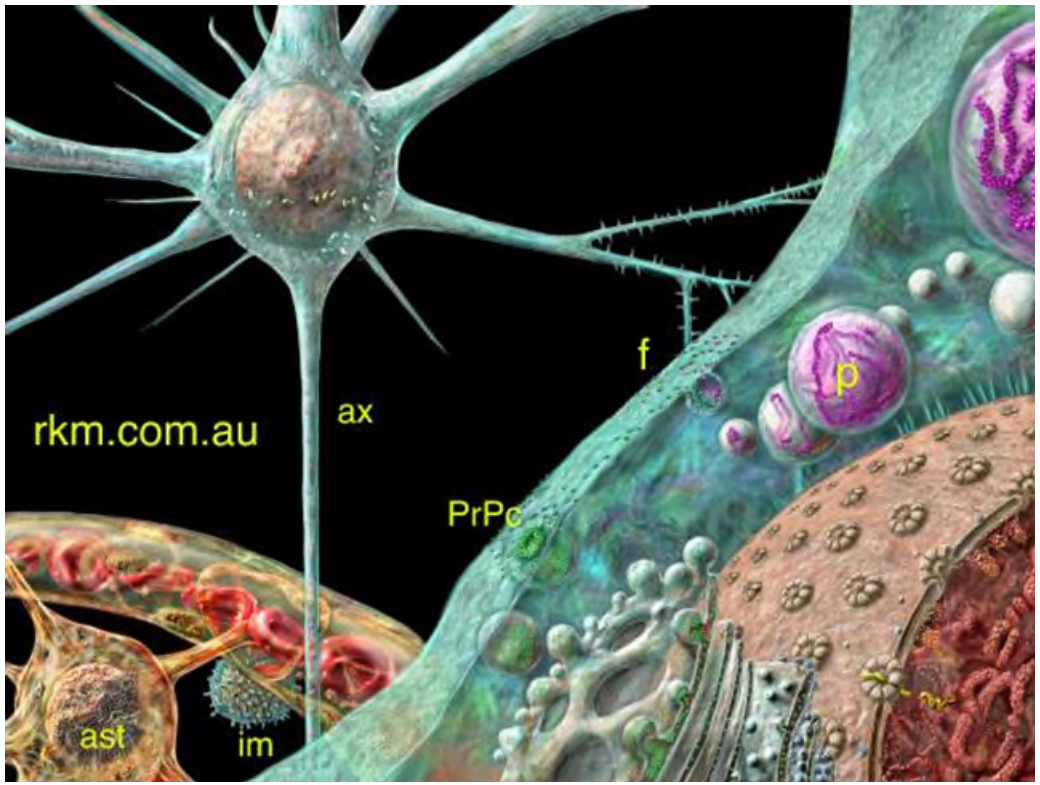



I am a prion.
I want your brain

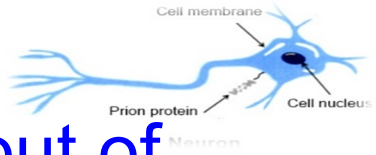


VCJD致病機轉-1


O
B
rkm.com.au
N
L
gut
S


rkm.com.au
ax
f
p
PrPc
ast
im










VCJD致病機轉-2

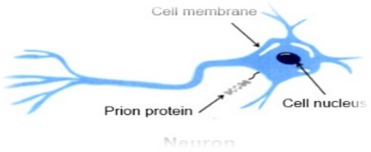
rout of prion uptake

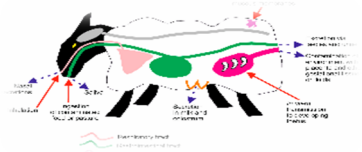
first site Prion replication

oral → Peyer's patches → FDC → Peripheral nerve → CNS

i.p. → Spleen → FDC → B





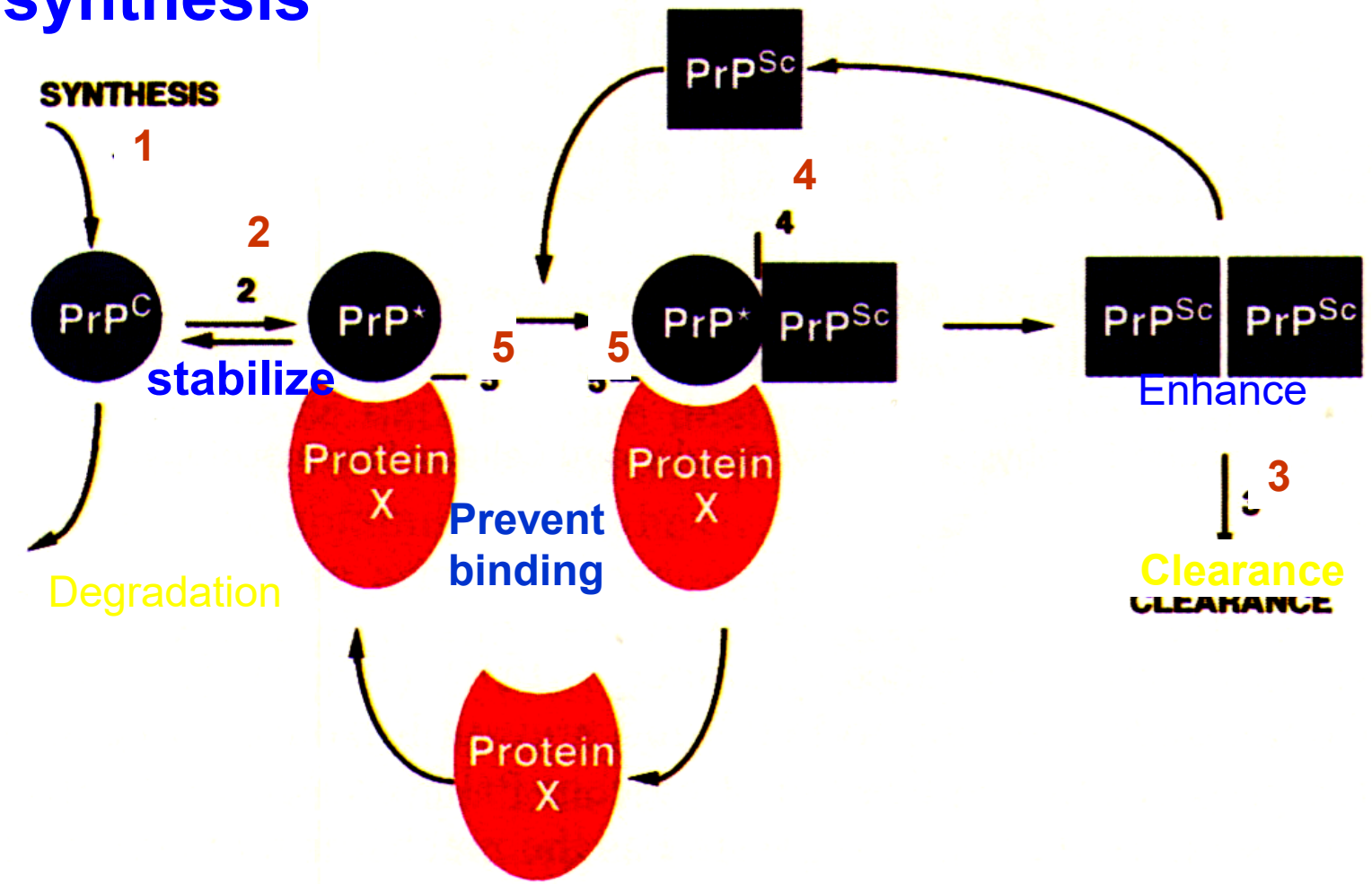




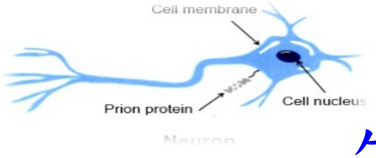


In search of cure for CJD

Block PrP^c synthesis











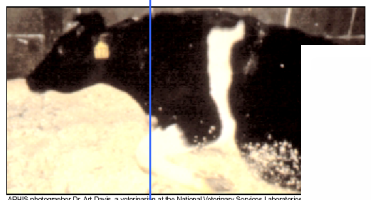


牛 海 綿 狀 腦 病

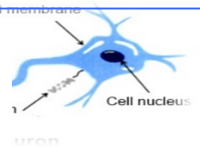
(Bovine Spongiform Encephalopathy)

- 狂牛病 (mad cow disease)
- 牛致死性神經變性疾病
- 世界上已有25個國家出現病例
- 人類 v-CJD 的發生與曾食入該病原有關
- 本病的發生對畜牧產業造成衝擊
- 人民對食品安全產生疑懼與恐慌



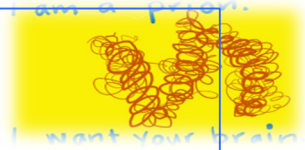


APHIS photographer Dr. Art Davis, a veterinarian at the National Veterinary Services Laboratories
Cattle affected by BSE experience progressive degeneratio
the nervous system. Changes in temperament (e.g., nervo
or aggression), abnormal posture, incoordination and diffic
rising, decreased milk production, and/or loss of weight de
continued appetite are followed by death.



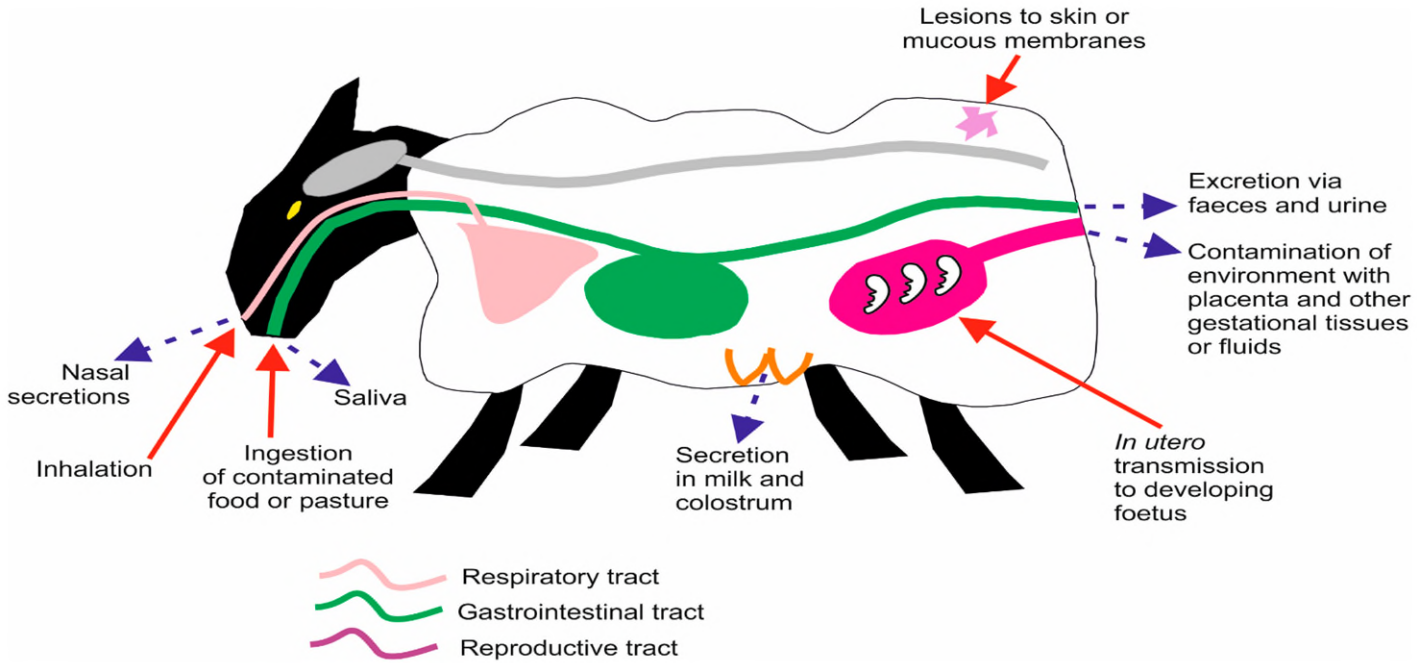






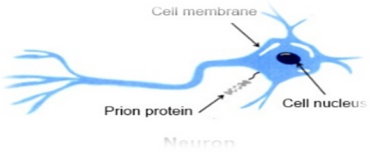


BSE引發消費者疑慮-如何吃得安心？



Safe to eat – On the basis of current knowledge, scientists agree that some bovine products are safe, regardless of the BSE status within a given country. Bovine products considered safe to eat or use include milk and milk products, gelatin prepared exclusively from hides and skins, and collagen prepared exclusively from hides and skins. Infectivity has never been detected in skeletal muscle tissues, from which most quality meat is derived. A number of scientists believe that skeletal muscle meat is as safe to consume as milk and milk products, provided that such meat has not been contaminated during slaughterhouse procedures.



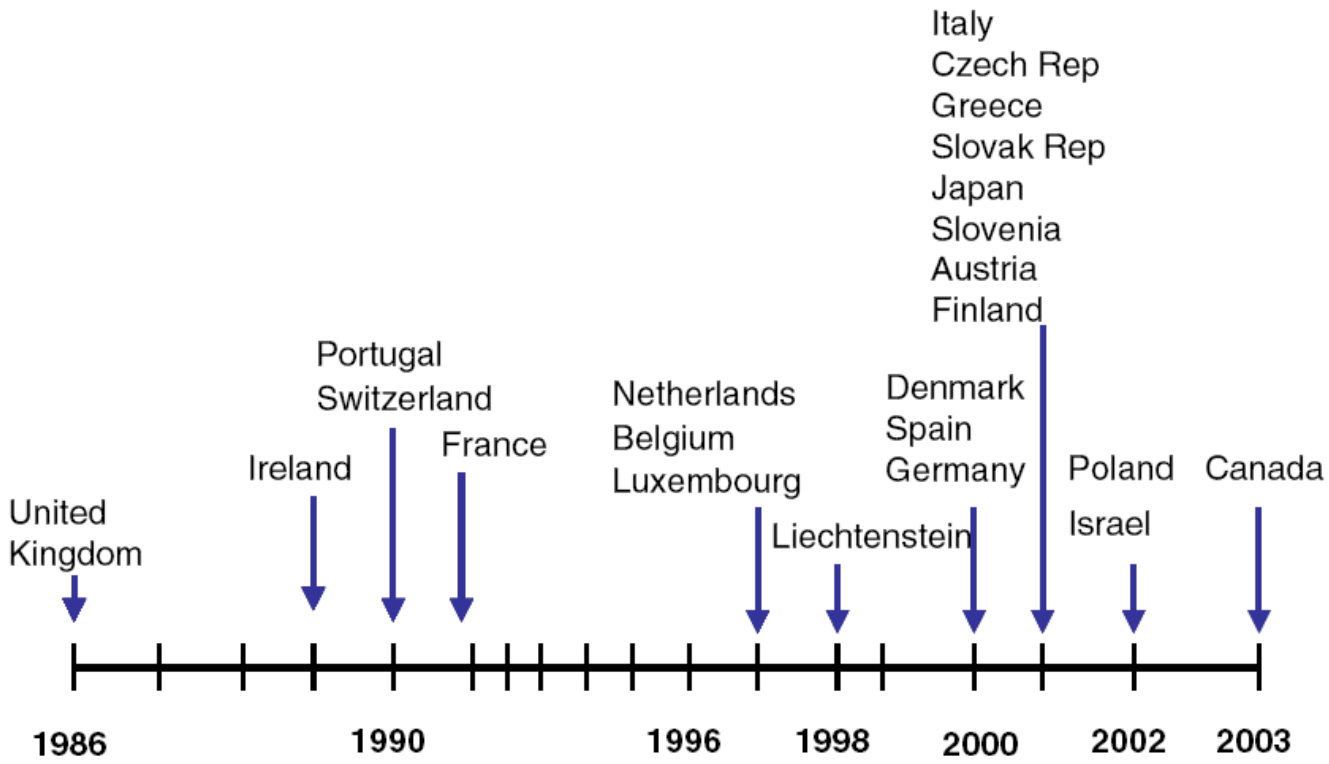







The future of BSE from the global perspective

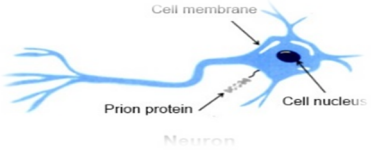
- BSE in the world: what we know today



Year of first reporting of indigenous BSE cases.

Meat Science 70 (2005) 555–562









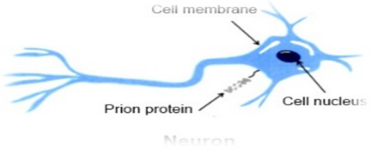


BSE clinical features include the following

- Changes in temperament such as nervousness or apprehensiveness
- Aggression towards other cattle or humans
- Kicking when being milked
- Reluctance to cross concrete, turn corners, and enter yards or doorways
- Head shyness with head held low
- Abnormal posture
- High-stepping gait, particularly of hind legs
- Incoordination
- Difficulty in rising or walking
- Skin tremors
- Decreased milk production
- Weight loss despite good appetite

The incubation period for BSE ranges from 2-8 years. Most cases in the United Kingdom have occurred in dairy cows aged 3-6 years.





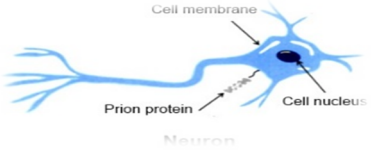





牛海綿狀腦病(BSE)

- 狂牛病(Mad Cow Disease)
  - 首例於1986年在英國被發現。
  - 牛海綿狀腦病(Bovine spongiform encephalopathy, BSE)的俗稱。
  - 臨床症狀：神經質且具攻擊性、站立及肌肉協調困難、姿勢異常、乳汁分泌減少、體重減輕，最後導致死亡。
  - 致病原：為普里昂(prion) 變性蛋白。
  - 傳播途徑：使用罹病牛隻之非供人食用廢棄部位製成肉骨粉，再轉為餵養牛隻的高蛋白質飼料，經由飼料感染。









續

牛 海 綿 狀 腦 病 (BSE)

- 曾發生狂牛病的國家有：

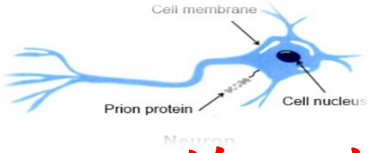
  歐洲：英國、愛爾蘭、法國、瑞士、葡萄牙、荷蘭、比利時、盧森堡、列支敦斯基、丹麥、西班牙、德國、義大利、捷克、希臘、斯洛伐克、斯洛維尼亞、芬蘭、奧地利、波蘭

  美洲：美國、加拿大

  亞洲：日本、以色列

- 全球狂牛病例，主要發生於英國(96.85%) 。
- 嚴格執行飼料禁令，並落實良好監測計畫，找出可疑病牛，現今狂牛病例已大幅下降。





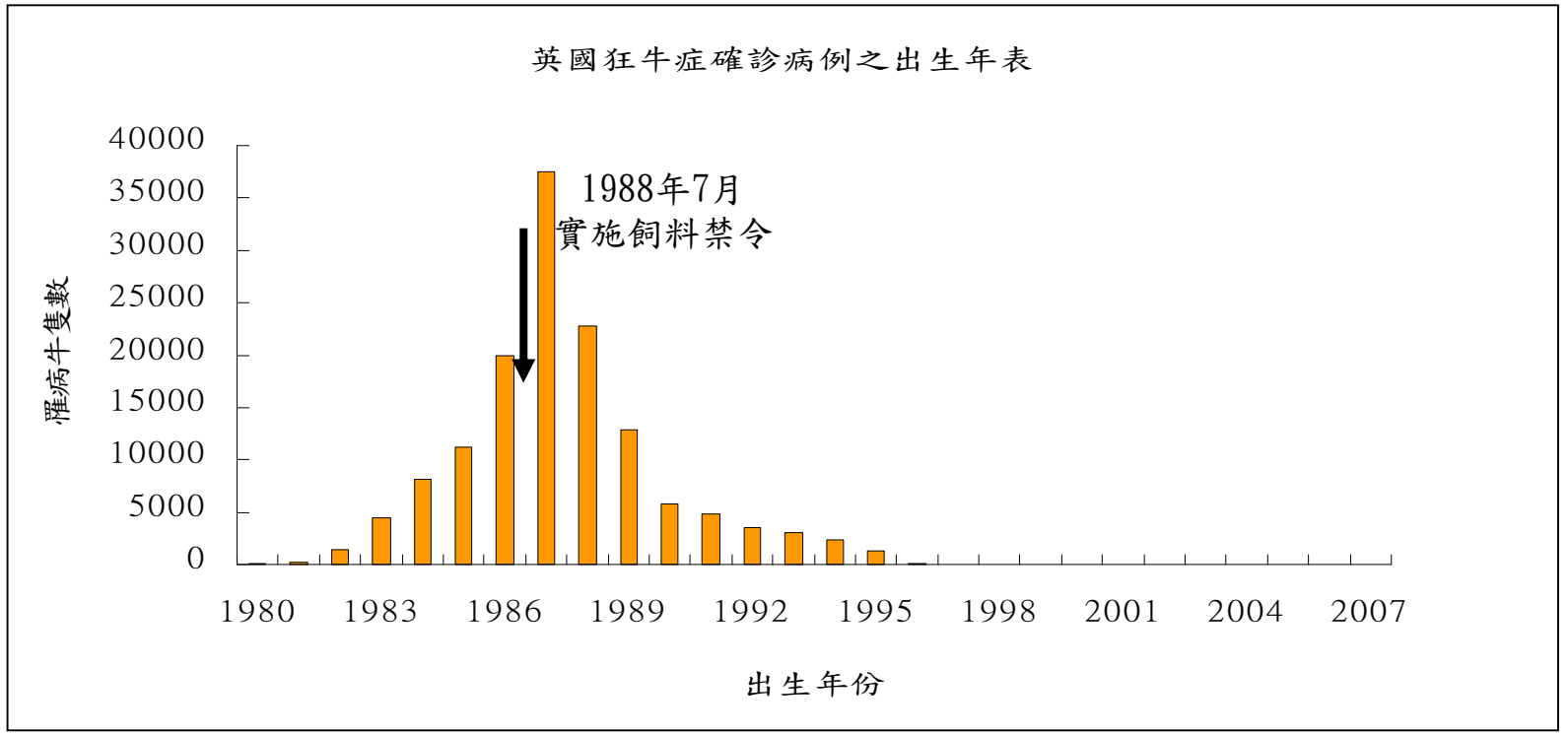




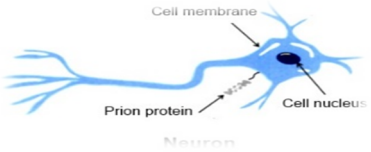


防 範 牛 海 綿 狀 腦 病 的 措施

- 嚴格執行飼料禁令
- 落實執行監測計畫，找出可疑病牛
- 改良傳統屠宰方式
- 各國採取有效防範措施，全球BSE案例發生急遽下降。









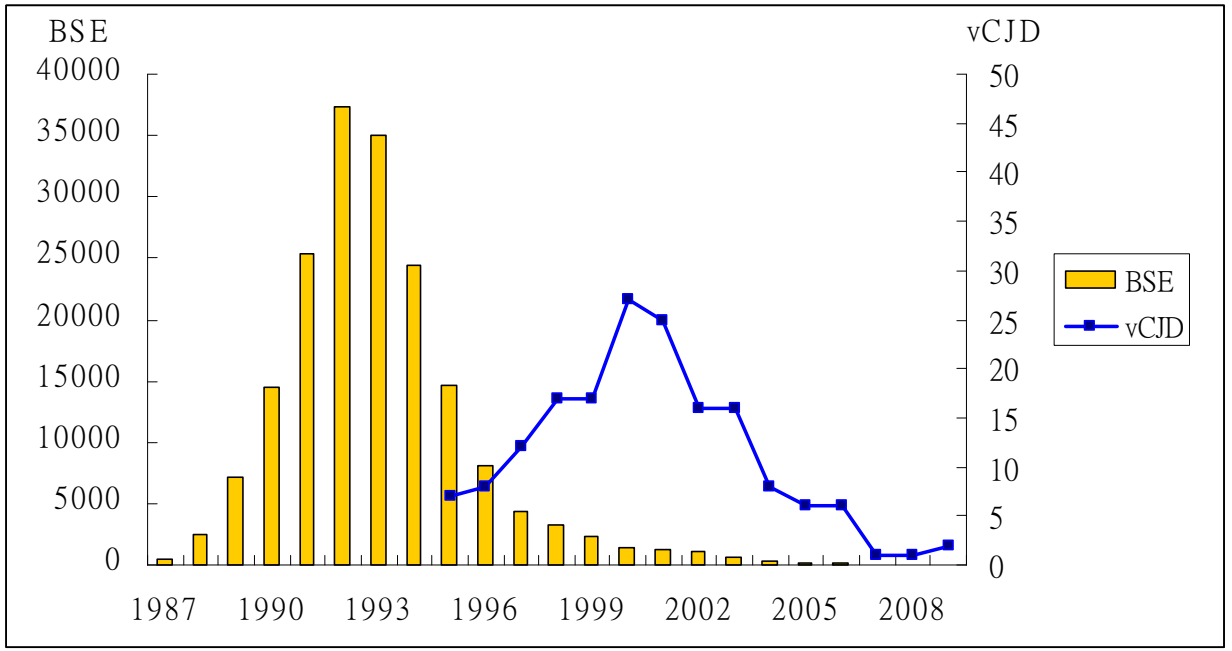




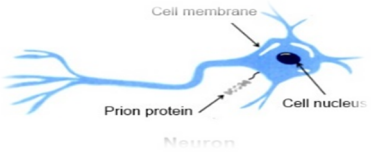
牛海綿狀腦病(BSE)及人類新型庫賈氏病(vCJD)

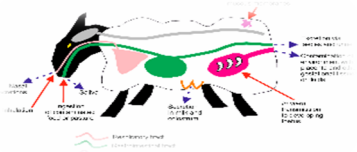
- 牛海綿狀腦病(BSE)全球全球超過 187,535例，英國佔96.9%。
- 人類新型庫賈氏病(vCJD)全球共226例，英國共計174例，佔76.9%。 **Worldwide total number of cases, as of January 2015 Source: EuroCJD**

英國牛海綿狀腦病 (BSE) & 新型庫賈氏病(vCJD)的分布圖













⚠️ 人類感染與風險

在英國，已有數起vCJD透過輸血或血漿輸注傳播的案例，儘管主要感染途徑仍為攝食受污染牛肉（McManus 等，2022）。

值得注意的是，器官移植與硬腦膜移植亦曾導致人類傳播庫賈氏症（CJD）（Heath 等，2006）。

然而，由於該疾病潛伏期極長，因此即使是長期素食者，也無法完全排除風險來源（Davanipour 等，2014）。

🧬 宿主範圍（Host range）

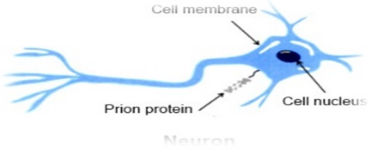
透過顱內接種（intracerebral inoculation）實驗，許多物種已被證實對BSE具有感受性，包括：

- 大鼠
- 綿羊
- 山羊
- 貂
- 貓
- 狨猴
- 馬

此外，倉鼠、牛、綿羊、山羊、嚙齒類與貂亦可透過口服感染（Tamgüney 等，2009）。

豬則曾透過顱內接種被實驗性感染，但尚未觀察到自然傳播的證據（Moore 等，2011）。










除了圈養的野生反芻動物外，BSE亦曾感染其他物種，例如：

- 家貓
- 動物園中的大型貓科動物

例如在英國，已有約81隻家貓與1隻獵豹感染的報告（OIE，2003）。

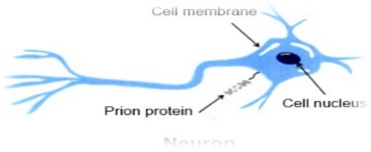
此外，在挪威、北愛爾蘭與列支敦斯登各有1例家牛感染非典型BSE（L-BSE）的案例。

據此推測，受污染飼料的攝食為此類物種感染BSE的主要途徑（EFSA 等，2017）。已有研究報告指出，大型貓科動物、羚羊、狐猴、長頸鹿，以及部分外來貓科動物（Orge 等，2021）均曾感染。

目前認為，此現象亦與屠宰場副產品（specifically offal）暴露有關。

有學者提出，在屠宰場副產品禁令（Specified Offal Ban, SOB）於1989年實施前，接觸BSE可能曾發生（在英國估計約有31例），其中包括德國1例（CJD（human disease）1998年）及法國1例（Sanchez-Juan 等，2007）。最終皆與攝食可能傳播BSE的腦、脊髓及其他組織相關。











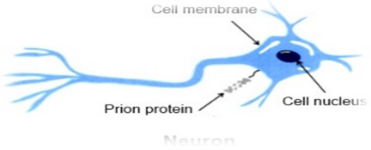
⚠️ 風險因子（Risk factors）

- 動物之間不會彼此傳播BSE，也不屬於接觸性疾病。此外，牛奶與乳製品亦不含BSE病原。
- 然而，根據研究，來自BSE感染牛的肉骨粉（MBM）是此疾病已知的唯一風險來源（Islam 等，2022）。
- 特定風險物質（Specified Risk Materials, SRMs）係指最可能含有並傳播BSE的組織，包括：
- 頭部、腦、脊髓、眼睛、脾臟、扁桃腺、顱骨、遠端迴腸（distal ileum）（WOAH，2008）
- 加工過程無法完全消除BSE prion，且其對熱與消毒具有高度抗性（Giles 等，2008）。

🧬 公共衛生重要性（Public health importance）

- 已有強而有力的證據顯示，BSE與人類vCJD之間存在關聯，因而引起全球關注。
- 英國研究人員推測，因受害者年齡較輕且臨床表現相似，vCJD可能源自於食用受污染牛肉產品（Ritchie 等，2021）。
- 病例顯示，BSE約於感染後9年發展為vCJD，與UK vCJD於1996年被報導的時間相符（ZJD與Gambetti，2009）。
- BSE與vCJD之間的因果關係，部分來自於其他國家缺乏類似病例（在監測系統完善的國家中）。
- 人類感染vCJD的案例，主要來自於攝食含有中樞神經組織的牛肉產品（Maheshwari 等，2015）。











人與人傳播（Human-to-human transmission）

- 在英國已有4例透過輸血或血漿輸注傳播vCJD的案例報告，儘管大多數病例仍源於攝食受污染牛肉（McManus 等，2022）。
- 研究估計，在英國疫情期間，每4,000名暴露者中約有1人可能成為無症狀帶原者（Gill 等，2020）。
- 然而，目前尚無證據顯示vCJD可透過體液（如血液、神經組織）自然傳播（Brown，2001）。

流行病學概況（Epidemiology）

在1996年11月至2004年11月間，英國共記錄151例vCJD病例（Ritchie 等，2021）。
此外，法國、愛爾蘭及美國亦有病例，患者多曾居住於英國（Baron 等，2012）。
截至2012年12月，歐洲共報告227例vCJD，其中多數（176例）發生於英國（Watson 等，2021）。







VARIANT CJD CASES WORLDWIDE

COUNTRY	TOTAL NUMBER OF PRIMARY CASES (NUMBER ALIVE)	TOTAL NUMBER OF SECONDARY CASES: BLOOD TRANSFUSION (NUMBER ALIVE)	RESIDENCE IN UK > 6 MONTHS DURING PERIOD 1980-1996
UK	175 (0)	3 (0)	178§
France	28 (0)	-	1
Republic of Ireland	4 (0)	-	2
Italy	3 (0)	-	0
USA	4† (0)	-	2
Canada	2 (0)	-	1
Saudi Arabia	1 (0)	-	0
Japan	1* (0)	-	0
Netherlands	3 (0)	-	0
Portugal	2 (0)	-	0
Spain	5 (0)	-	0
Taiwan	1 (0)	-	1

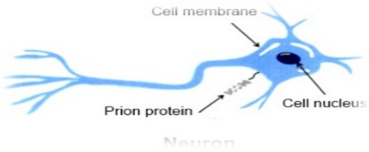
† The third US patient with vCJD was born and raised in Saudi Arabia and has lived permanently in the United States since late 2005. According to the US case-report, the patient was most likely infected as a child when living in Saudi Arabia. The completed investigation of the fourth US patient did not support the patient's having had extended travel to European countries, including the United Kingdom or travel to Saudi Arabia. It confirmed that the case was in a US citizen born outside the Americas and indicated that his infection occurred before he moved to the United States; the patient had resided in Kuwait, Russia and Lebanon (see http://wwwnc.cdc.gov/eid/article/21/5/pdfs/14-2017.pdf

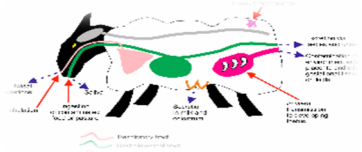
* The case from Japan had resided in the UK for 24 days in the period 1980-1996.

§ Case 178 from the UK was heterozygous at codon129 of the *PRNP* gene

Source: www.cjd.ed.ac.uk – data correct as at 03/05/2021











截至2022年5月，全球共報告233例新型庫賈氏病（vCJD）病例，分佈於12個國家：

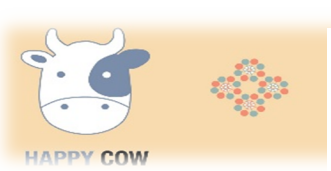
- 英國：178例
- 法國：29例
- 愛爾蘭：4例
- 美國：4例
- 加拿大：2例
- 義大利：3例
- 葡萄牙：2例
- 日本：1例
- 荷蘭：3例
- 沙烏地阿拉伯：1例
- 西班牙：5例
- 臺灣：1例

其中，法國（1例）、美國（2例）、加拿大（1例）、愛爾蘭（2例）及臺灣的病例，皆可能因在英國居住史而暴露於牛海綿狀腦病（BSE）致病原

疫情爆發及病例

變異型克雅氏症（vCJD）於1996年在英國出現病例後被發現。 1996年至2023年間，全球共通報了233例 vCJD死亡病例。絕大多數病例發生在英國。歐洲、亞洲、沙烏地阿拉伯、加拿大和美國也報告了病例。

美國已報告四例（vCJD）病例。據信所有患者均在其他國家感染。四名患者中有兩名在英國生活了數十年。第三名患者出生並成長於沙烏地阿拉伯，之後來到美國。目前尚不清楚第四名患者的感染途徑，但專家一致認為很可能是在美國境外。



THE UNIVERSITY of EDINBURGH

ecdc



Creutzfeldt-Jakob Disease International Surveillance Network

formerly EuroCJD

About Us Resources ▼ News

Data Tables

All Definite and Probable Cases +

All CJD (excluding vCJD): Annual Mortality Rates Per Million +

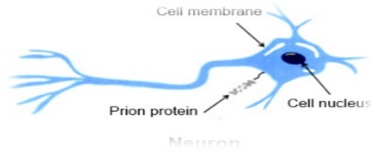
Sporadic CJD: Annual Mortality Rates Per Million +

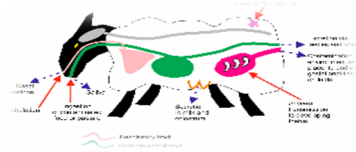
Sporadic CJD: Definite and Probable Cases +

vCJD Cases Worldwide -

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2
Canada								1	0	0	0	0	0	0	0	0	1	
France		1	0	0	0	1	1	3	0	2	6	6	3	0	2	0	0	(
Ireland					1	0	0	0	0	0	2	1						









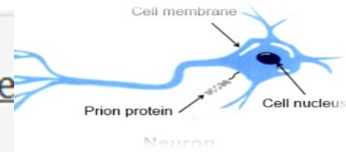


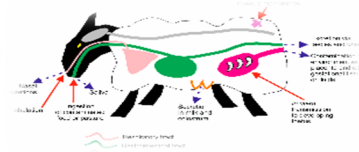
vCJD Cases Worldwide

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Canada								1	0	0	0	0	0	0	0	0	1
France		1	0	0	0	1	1	3	0	2	6	6	3	0	2	0	0
Ireland					1	0	0	0	0	0	2	1					
Italy									1	0	0	0	0	0	0	0	1
Japan										1							
Netherlands											1	1	0	1			
Portugal													1	0	1		
Saudi Arabia																1	
Spain											1	0	1	2	1		
Taiwan																1	
UK	3	10	10	18	15	28	20	17	18	9	5	5	5	2	3	3	5
USA										1		2					



vCJD Case





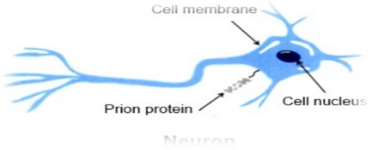






	3	2014	2015	2016	2017	2018	2019	2019	2020	2021	2022	2023	2024	Alive	Total
Canada															2
France		1	0	0	0	0	1	1							28
Ireland															4
Italy		0	0	1											3
Japan															1
Netherlands															3
Portugal															2
Saudi Arabia															1
Spain															5
Taiwan															1
UK		0	0	1											178
USA		1													4







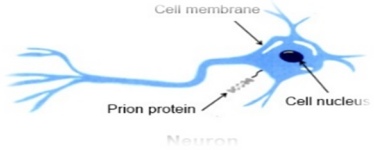




監測與高風險族群

- 高風險動物通常接受更嚴格檢測，例如出現神經症狀或無法站立的牛隻（EFSA 等，2018）。
- 多數國家僅針對高風險動物進行檢測。隨著疫情下降，許多國家已降低檢測標準（Olech，2023）。
- 當確認病例後，相關牧場通常會進行隔離檢疫，並調查感染來源（Simon 等，2008）。
- 同場出生或飼養的牛隻常被視為高風險族群，可能被撲殺或密集監測，因其暴露於高感染風險期（Kumagai 等，2019）。感染牛隻的後代亦可能具有較高風險。











國際風險分類（Risk classification）

由於BSE具有長潛伏期，病例數下降可能存在時間延遲。

世界動物衛生組織（WOAH）依據下列條件評估各國風險：

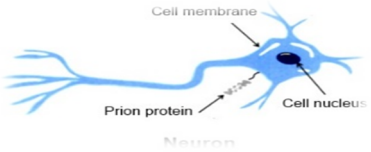
- 活牛進口
- 反芻動物蛋白輸入
- 飼料控制制度
- 實驗室與監測能力
- 病例數據

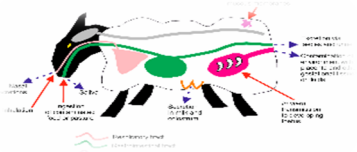
分類包括：

- **可控制風險（controlled risk）**
- **可忽略風險（negligible risk）**

部分國家亦被列為「未確定風險（undetermined risk）」





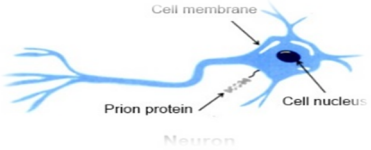






- 對於曾居住於BSE疫區國家的人員，限制其捐血已被證實能有效降低甚至阻斷BSE及其在人類中的變異型庫賈氏症（vCJD）之傳播（Brown 等，2016；Amin 等，2023）。
- 例如，巴西作為全球牛肉出口大國之一，近期因對BSE傳播的疑慮，已宣布減少對中國的牛肉出口（Global Times，2023）





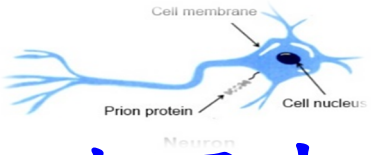





以牛肉的廚餘餵豬，會不會引起國內豬隻感染狂牛病（或稱「狂豬症」）？

- 科學資料顯示，牛和豬是不同種生物，基於風險分析之科學方法，衡量種別障礙、釋放風險及暴露風險等因子，並不會造成豬隻感染prion之疑慮。
- 狂牛病多發生在老牛，而衛生署開放的牛肉產品，是30月齡以下帶骨及不帶骨牛肉、內臟及絞肉，本來就不是特定風險物質，並不會造成豬隻感染疑慮。
- 1990年Dawson等人，將狂牛病牛的腦，經以餵食與體內接種方式，分別來感染牛、羊、豬及雞。結果豬以體內接種方式會發病，但餵食的豬不會發病。科學家認為，豬的腸管細胞沒有狂牛病變性蛋白的接受器，因此縱使豬吃到狂牛病的內臟廚餘，也絕對不會有「狂豬病」的出現。










我國申請認定BSE風險狀態案

一、第一次遞件申請：2005年10月

二、第二次遞件申請：2006年10月

三、依OIE要求補送資料：2006年12月

四、OIE回復審查意見：2007年2月

五、正式認可為風險已控制國家：
2007年5月OIE第76屆年會





Certificate

Bovine spongiform encephalopathy status of Taipei China

This is to certify that following a recommendation of the OIE Scientific Commission for Animal Diseases, the International Committee of the OIE approved on 25 May 2007 that Taipei China be classified by the OIE as a controlled risk country regarding bovine spongiform encephalopathy (BSE) status in accordance with the provisions of Article 2.3.13.4. of the OIE Terrestrial Animal Health Code.

This recognition is based on the documentation submitted to the OIE by the Official Veterinary Services of Taipei China. The Delegate of Taipei China to the OIE has the obligation to notify the OIE immediately if there is any significant epidemiological event relating to BSE in Taipei China and to confirm annually that the epidemiological situation has remained unchanged.

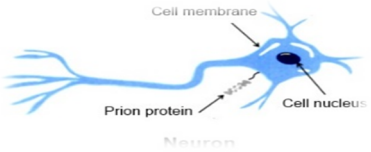
Paris, 25 May 2007

Barry O'Neil, President

Bernard Vallat, Director General

動植物防疫檢疫局動檢組高黃霖技正提供99年11月17日










OIE對於我國BSE風險狀態認定申請案之審查意見

一、病原釋出評估：自國外進口大量商品，且輸出國後來發生BSE，有「BSE病原可能已進入台灣」之風險。

二、暴露評估：持續於動物飼料中使用SRM、缺乏「化製過程中減少污染」之證據、某些生產線可能有交叉污染、為檢測交叉污染對飼料採樣之步驟其敏感度有限，如果BSE病原存在於國內牛群時，該病原有再循環與增幅之風險。

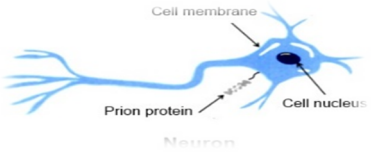
三、監測：台灣牛隻族群小，檢查頭數與分數符合2006年版法典之最低要求。

四、宣導計畫：符合2006年版法典之要求。

五、飼料禁令之控制與稽核：無法證明肉骨粉及油渣餵飼反芻獸之禁令已落實8年以上。

動植物防疫檢疫局動檢組高黃霖組長提供99年11月17日









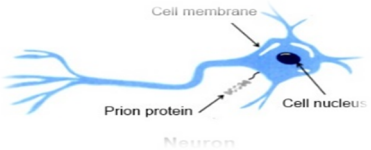


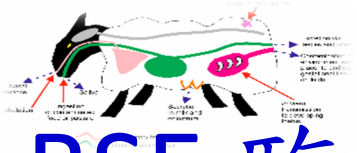
BSE 臨床症狀

- 行為異常
- 對刺激反應敏感
  光、聲音、觸覺
- 神經症狀
- 非神經症狀









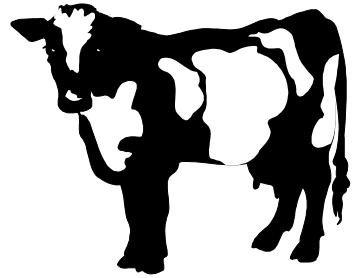




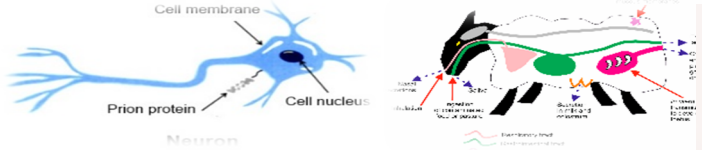
BSE 臨床症狀

經回溯性研究統計：

- 1/3 典型症狀
- 1/3 ± 神經症狀
- 1/3 無神經症狀
  - 泌乳量降低
  - 體重減輕
  - 乳房炎、蹄病、腹膜炎
  - 無法站立、側臥







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Bovine spongiform encephalopathy: A review of current knowledge and challenges

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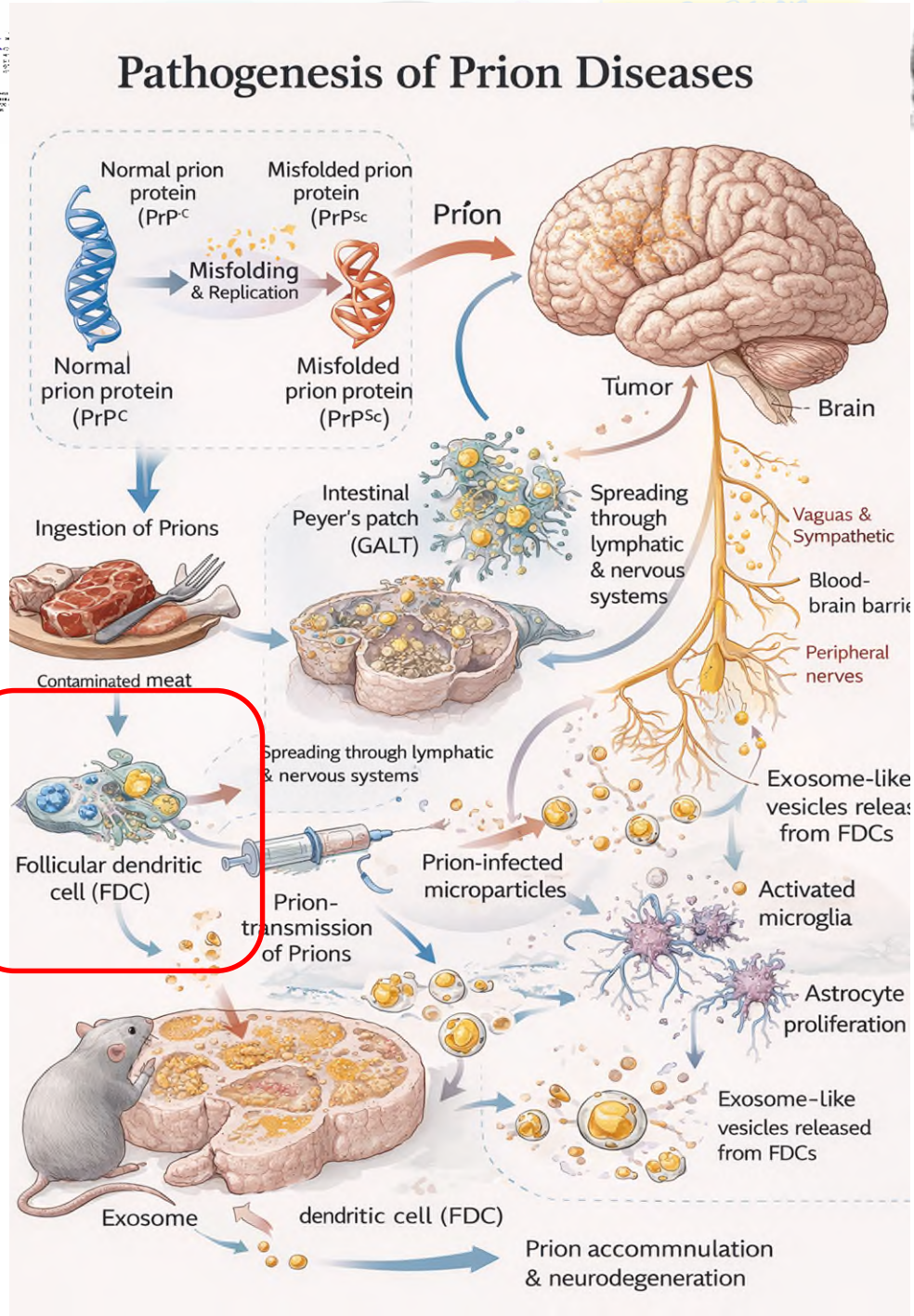
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ABSTRACT
Bovine spongiform encephalopathy (BSE), also referred to as mad cow disease, is a chronic degenerative disease that affects the central nervous system. BSE is caused by a misfolded isoform of the prion protein, a widely expressed glycoprotein. The illness is referred to as Variant Creutzfeldt-Jakob disease (vCJD) in humans. In the United Kingdom (UK), BSE in cattle was first discovered in 1986. Based on epidemiological data, it appears that animal feed containing tainted meat and bone meal (MBM) as a source of meat protein is the common cause of the BSE outbreak in the UK. Clinical indicators in cows include irregular body posture, incoordination, difficulty in standing, weight loss, and temperamental changes, including agitation and hostility. Feeding livestock MBM obtained from BSE-infected livestock contaminated with BSE prions is the only known risk factor for BSE development. Strong evidence linking BSE to human transmission and a variant type of CJD has brought the disease to the attention of many countries. Screening living animals for BSE is challenging. In most cases, suspected animals are usually killed. Typically, the central nervous system is examined for prions to diagnose this illness. There is currently no robust treatment for BSE. The prevention of BSE can be achieved by avoiding the feeding of susceptible animals with ruminant tissues that might carry prions.
Keywords: BSE, Cattle, Prion, Public health, vCJD.

Introduction

Bovine spongiform encephalopathy (BSE), also referred to as mad cow disease, is a chronic degenerative disease that affects the central nervous system (Haley and Richt, 2023). This is caused by a misfolded isoform of prion protein (PrPSc) that deviates from its normal cellular isoform, PrPC. The alternative form of BSE in humans is the variant Creutzfeldt-Jakob Disease (vCJD). BSE is a member of the transmissible spongiform encephalopathies (TSE) disease family (Brown and Abee, 2005; EFSA, 2022). The infectious agent of the disease is believed to be a misfolded protein known as a prion. The disease has a lengthy incubation period, spanning 30 months to

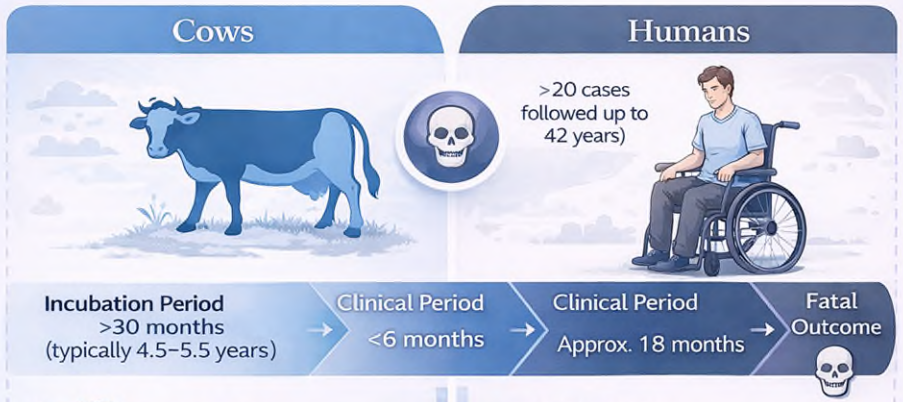
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Clinical Progression of Bovine Spongiform Encephalopathy (BSE)

Visualizing the Clinical Progression of Bovine Spongiform Encephalopathy (BSE)

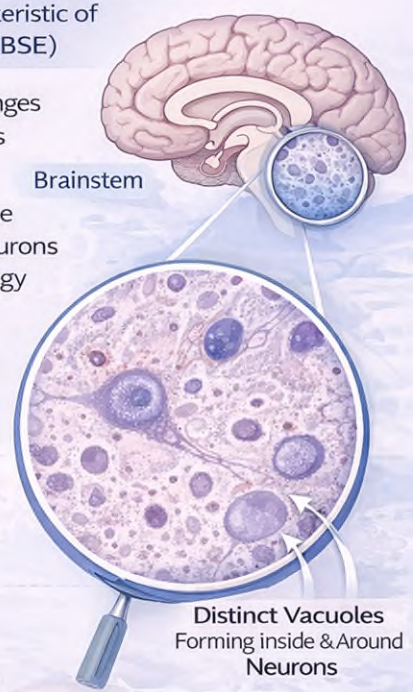




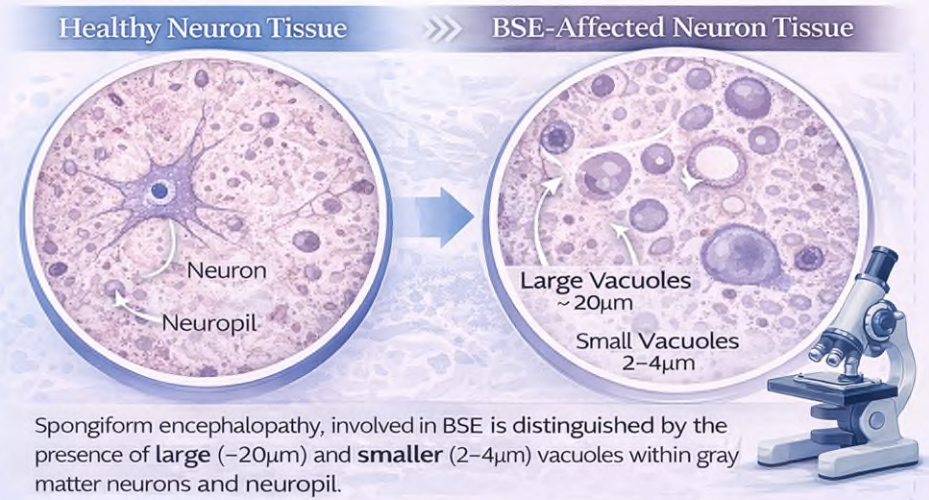
Spongiform Encephalopathy (BSE)

Microscopically Distinct Lesions Characteristic of Bovine Spongiform Encephalopathy (BSE)

- BSE leads to microscopically visible changes in the brainstem's gray matter, known as spongiform encephalopathy.
- Spongiform encephalopathy refers to the formation of **distinct vacuoles** within neurons or surrounding neuropil, creating a spongy appearance under the microscope.
- Most diagnostic BSE lesions feature vacuolation within gray matter neurons and neuropil.



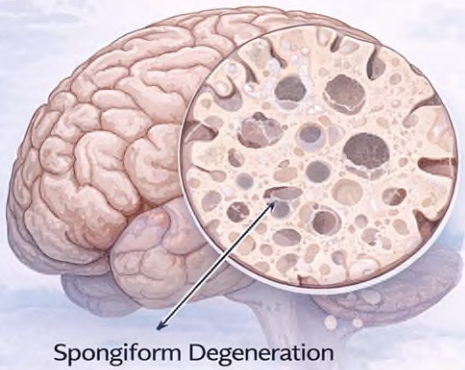
- BSE leads to microscopically visible changes in the brainstem's gray matter, known as spongiform encephalopathy.
- Spongiform encephalopathy refers to the formation of distinct vacuoles within neurons or surrounding neuropil,. creating a spongy appearance under the microscope.



Spongiform encephalopathy, involved in BSE is distinguished by the presence of **large** (~20μm) and **smaller** (2–4μm) vacuoles within gray matter neurons and neuropil.

Microscopic Pathology of Bovine Spongiform Encephalopathy (BSE)

Visualizing the Microscopic Pathology of Bovine Spongiform Encephalopathy (BSE)



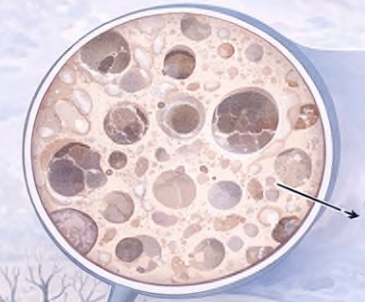
Spongiform Degeneration

Key Pathological Features of BSE:

- Neuron loss
- Astrocytosis (gliosis)
- Gray matter vacuolation and degeneration in multiple regions of the brainstem

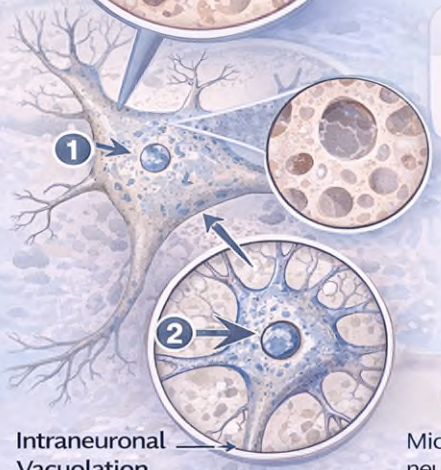
Two Primary Changes Within Neurons:

- Intraneuronal Vacuolation
- Perineuronal Vacuolation



"Spongiform Encephalopathy" describes the sponge-like appearance seen under the microscope due to widespread neuronal vacuolation **in the gray matter.**

Vacuoles appear as clear, bubble-like spaces



Intraneuronal Vacuolation

Two Primary Changes Within Neurons:

- Intraneuronal Vacuolation
- Perineuronal Vacuolation

A Key Diagnostic Indicator of BSE:

Microscopically, **vacuoles** form within gray matter neurons **(intraneuronal)** and in the **surrounding neuropil** (perineuronal).

A Key Diagnostic Indicator of BSE:

Microscopically, vacuoles form within gray matter neurons **(intraneuronal)** and in the **surrounding** neuropil **(perineuronal)**.

Transmission of BSE

- No evidence that BSE is transmitted between animals via non-feed routes.
- This contrasts with chronic wasting disease (CWD) and scrapie, whose prions can persist in the environment long-term (Gallardo & Delgado, 2021; Madsen-Bouterse *et al.*, 2016).





Saliva | Urine and Feces | Placental tissue | Milk

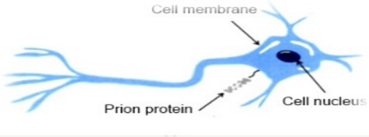
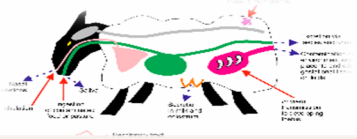
- CWD prions have been detected in saliva, urine, feces, placental tissue, and milk. No evidence that BSE prions are transmitted via these routes in these substrates (Anderson et al., 2019).

- No evidence that vCJD is transmitted naturally between humans (except via medical procedures like blood transfusions).

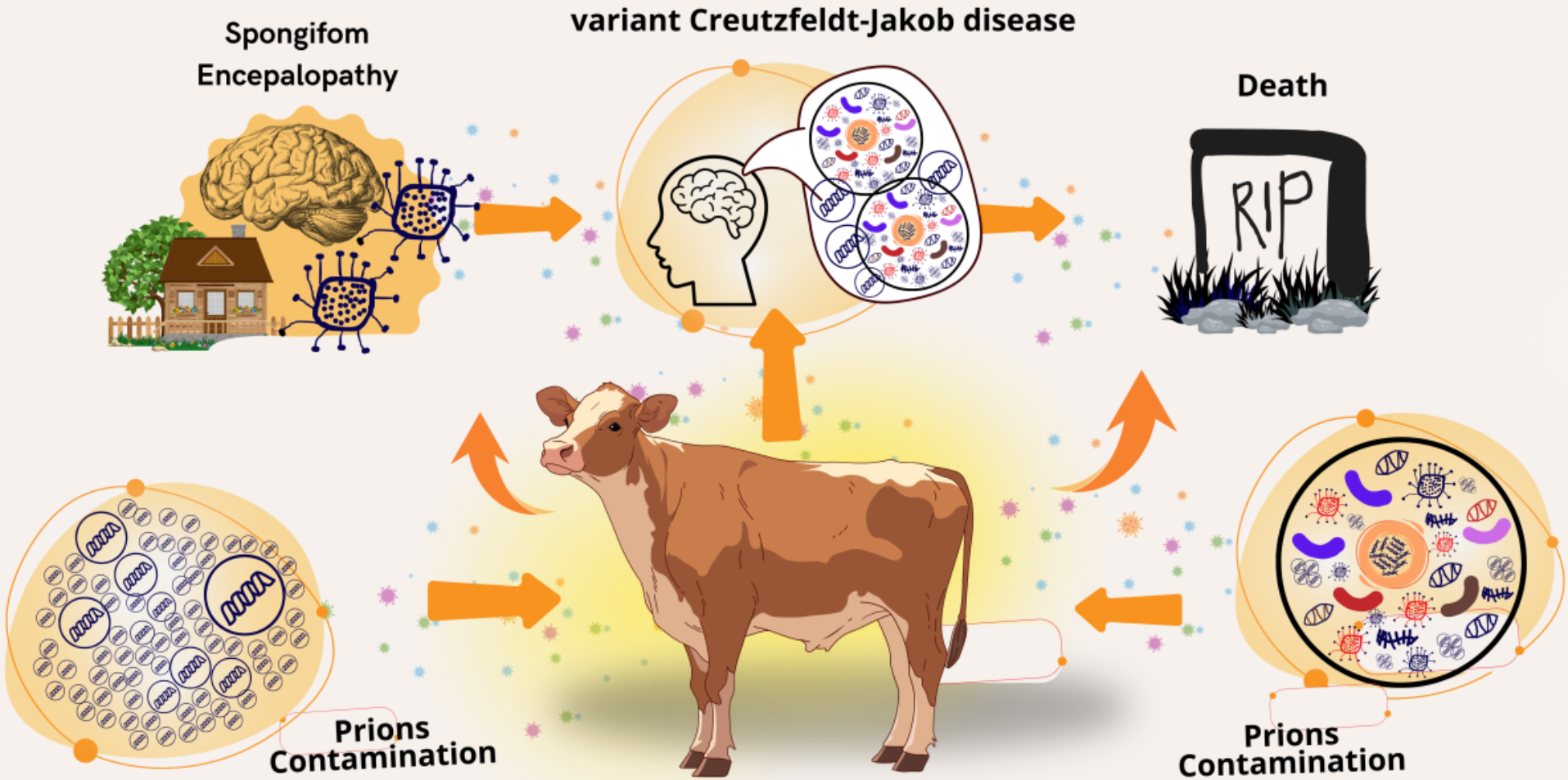
- ✅ Animals may ingest ~1 mg of infectious brain material to get infected.
- ✅ 5 g of infectious brain material injected into experimental monkeys was shown to cause BSE.
- ✅ Currently, human infectious dose remains unknown.

Lasmezas *et al.*, 2005

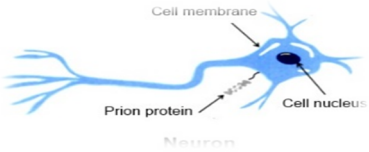


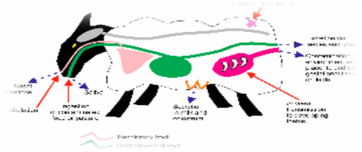

HAPPY COW

Cell membrane
Prion protein
Cell nucleus



I am a prion.



Spongifom
Encepalopathy
variant Creutzfeldt-Jakob disease
Death
RIP
Prions
Contamination
Prions
Contamination










牛感染BSE 致病機轉-1

2017

1、迴腸派氏斑為主要入口與早期增殖部位

“In cattle, the C-BSE agent primarily enters the gut-associated lymphatic tissue (GALT) of the ileum, namely the ileal Peyer’s patch (IPP), in which PrP^BSE and BSE infectivity are detectable from early after infection.”pmc.ncbi.nlm.nih “For the first time, BSE prions were detected in the IPP as early as 2 mpi… These data indicate that BSE prions propagate in the IPP of unweaned calves within 2 months of oral uptake of the agent.”pmc.ncbi.nlm.nih

2、由腸道經自主神經（內臟神經、迷走神經）上行至CNS

“Then, through mesenteric nerves, prion proteins accumulate in the cranial coeliaco-mesenteric ganglion complex, and then ascend to the thoracic spinal cord via the sympathetic nervous system (e.g. splanchnic nerves) and to the brainstem and the brain via the parasympathetic nervous system (e.g. vagus nerve) and nodose ganglion.”pmc.ncbi.nlm.nih “Our results demonstrate two routes involving the autonomic nervous system through which BSE prions spread by anterograde pathways from the gastrointestinal tract (GIT) to the central nervous system (CNS): (i) via the coeliac and mesenteric ganglion complex, splanchnic nerves and the lumbal/caudal thoracic spinal cord (representing the sympathetic GIT innervation); and (ii) via the Nervus vagus (parasympathetic GIT innervation).”pubmed.ncbi.nlm.nih

Ackermann et al. Vet Res (2017) 48:88
https://doi.org/10.1186/s13567-017-0495-5

VETERINARY RESEARCH

RESEARCH ARTICLE Open Access

Detection of PrP^{BSE} and prion infectivity in the ileal Peyer’s patch of young calves as early as 2 months after oral challenge with classical bovine spongiform encephalopathy

Ivett Ackermann[1], Anne Balkema-Buschmann[1], Reiner Ulrich[2], Kerstin Tauscher[2], James C. Shawulu[1], Markus Keller[1], Olanrewaju I. Fatola[1], Paul Brown[3] and Martin H. Groschup[1*]

Abstract

In classical bovine spongiform encephalopathy (C-BSE), an orally acquired prion disease of cattle, the ileal Peyer’s patch (IPP) represents the main entry port for the BSE agent. In earlier C-BSE pathogenesis studies, cattle at 4–6 months of age were orally challenged, while there are strong indications that the risk of infection is highest in young animals. In the present study, unweaned calves aged 4–6 weeks were orally challenged to determine the earliest time point at which newly formed PrP^{BSE} and BSE infectivity are detectable in the IPP. For this purpose, calves were culled 1 week as well as 2, 4, 6 and 8 months post-infection (mpi) and IPPs were examined for BSE infectivity using a bovine PrP transgenic mouse bioassay, and for PrP^{BSE} by immunohistochemistry (IHC) and protein misfolding cyclic amplification (PMCA) assays. For the first time, BSE prions were detected in the IPP as early as 2 mpi by transgenic mouse bioassay and PMCA and 4 mpi by IHC in the follicular dendritic cells (FDCs) of the IPP follicles. These data indicate that BSE prions propagate in the IPP of unweaned calves within 2 months of oral uptake of the agent.

Introduction

Transmissible spongiform encephalopathies (TSEs), or prion diseases, are fatal neurodegenerative disorders including scrapie, bovine spongiform encephalopathy (BSE) and chronic wasting disease (CWD) in animals and Creutzfeldt-Jakob disease (CJD) in humans. TSEs are characterised by the accumulation of an abnormal isoform of the prion protein (PrP^{TSE}), resulting from conversion of a host-encoded cellular membrane-bound glycoprotein (PrP^{C}) [1]. In classical bovine spongiform encephalopathy (C-BSE) of cattle, prions spread centripetally mainly via the autonomic nervous system from the gut to the central nervous system, primarily utilizing sympathetic and to a lesser extent parasympathetic structures, while the spinal cord constitutes an additional route [2]. Specified risk materials (SRM), which possibly contain BSE infectivity in incubating cattle, have been banned from manufacturing of food, health products and animal feedstuff, in order to minimize the BSE exposure risk for humans and cattle. Currently the list of SRM from bovines of all ages, as defined in the Regulation (EC) No 999/2001 (consolidated version as of 12.2016) includes the last four metres of the small intestine (distal ileum), the caecum, the mesentery and the tonsils in countries having a controlled BSE risk status, while no restrictions regarding the intestine apply for negligible risk countries.

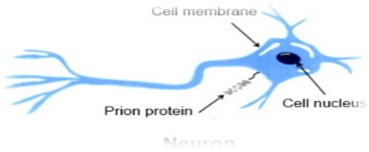
The ileal Peyer’s patch (IPP), representing the gut-associated lymphoid tissue (GALT) of the ileum, has been postulated to function as the primary site of entry for the BSE agent in cattle, as PrP^{BSE} and BSE infectivity have been detected from 4 mpi in this location [3–6]. The IPP is a packed lymphatic structure in young cattle with a maximal extension of about 4 m length at 12–18 months of age, which undergoes an involution that

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牛感染BSE 致病機轉-2

2021

3、CNS初始累積在DMNV與胸髓交感區

“Two preclinical animals killed at 36 and 48 MPI presented the earliest detectable and smallest deposition of immunolabelled PrPSc in the dorsal motor nucleus of the vagus nerve, the spinal trigeminal nucleus of the medulla oblongata at the obex region, and/or the intermediolateral nucleus of the 13th thoracic segment of the spinal cord.”pubmed.ncbi.nlm.nih

「牛隻經食入BSE變性普里昂蛋白後，病原首先在迴腸末端之迴腸派氏斑等腸相關淋巴組織增生，隨後經腸道自主神經系統，並沿交感之內臟神經及副交感之迷走神經，向上蔓延至胸腰段脊髓及延髓背側迷走神經核等中樞神經結構。」。



International Journal of *Molecular Sciences*

MDPI

Article

Prion Infectivity and PrP^{BSE} in the Peripheral and Central Nervous System of Cattle 8 Months Post Oral BSE Challenge

Ivett Ackermann [1], Reiner Ulrich [2], Kerstin Tauscher [3], Olanrewaju I. Fatola [1,4], Markus Keller [1], James C. Shawulu [1,5], Mark Arnold [6], Stefanie Czub [7], Martin H. Groschup [1] and Anne Balkema-Buschmann [1,*]

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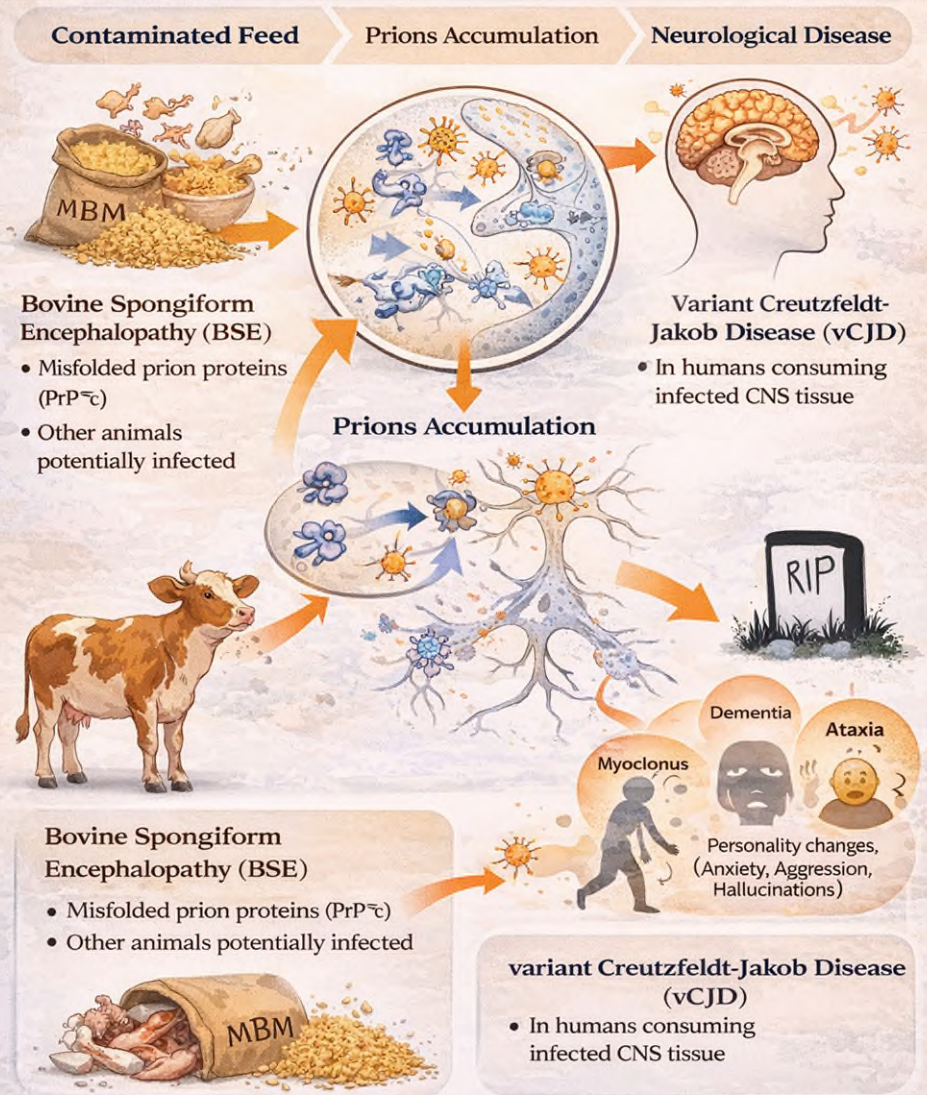
Abstract: After oral exposure of cattle with classical bovine spongiform encephalopathy (C-BSE), the infectious agent ascends from the gut to the central nervous system (CNS) primarily via the autonomic nervous system. However, the timeline of this progression has thus far remained widely undetermined. Previous studies were focused on later time points after oral exposure of animals that were already 4 to 6 months old when challenged. In contrast, in this present study, we have orally inoculated 4 to 6 weeks old unweaned calves with high doses of BSE to identify any possible BSE infectivity and/or PrP^{BSE} in peripheral nervous tissues during the first eight months post-inoculation (mpi). For the detection of BSE infectivity, we used a bovine PrP transgenic mouse bioassay, while PrP^{BSE} depositions were analyzed by immunohistochemistry (IHC) and by protein misfolding cyclic amplification (PMCA). We were able to show that as early as 8 mpi the thoracic spinal cord as well as the parasympathetic nodal ganglion of these animals contained PrP^{BSE} and BSE infectivity. This shows that the centripetal prion spread starts early after challenge at least in this age group, which represents an essential piece of information for the risk assessments for food, feed, and pharmaceutical products produced from young calves.

Keywords: prion protein; BSE; infectivity; PrP^{BSE}; cattle; peripheral and central nervous system; protein misfolding cyclic amplification (PMCA)

1. Introduction

Classical bovine spongiform encephalopathy (C-BSE) is a fatal neurodegenerative prion disease of cattle. Other prion diseases or transmissible spongiform encephalopathies (TSEs) include Creutzfeldt–Jakob disease (CJD) in humans, scrapie in small ruminants, as well as chronic wasting disease (CWD) in cervids. These disorders are caused by the conversion of a host-encoded cellular membrane-bound glycoprotein (PrP^{C}) into its abnormal isoform, the pathological prion protein (PrP^{TSE}) [1]. BSE is also a zoonotic disease, as the ingestion of BSE-contaminated food has been identified to cause the variant form of CJD [2,3].

Prion Pathogenesis:
From Prion Contamination to Neurological Disease



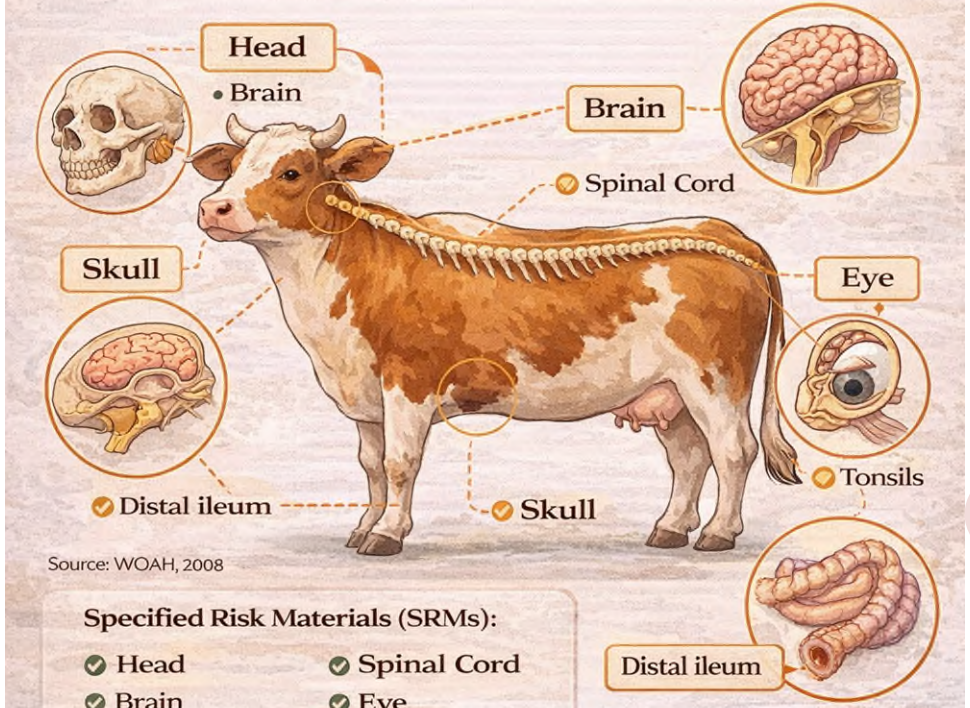
Comparison of BSE Laboratory Diagnostic Methods

	Brain TSE ELISA	Western Blot (WB)	Immuno-histochemistry	Bioassay
Method	PrP^{Sc}	PrP^{Sc}	PrP^{Sc}	Live animal response to BSE infection
Detection Target	Brain tissue homogenate	Brain tissue homogenate	Brain tissue sections	Brain inoculum injected into animals (e.g. transgenic mice)
Sensitivity	✓✓✓	✓✓✓	✓✓✓	✓✓✓✓+
Testing Time	<24 hours	Over 24 hours	Over 24 hours	Several months or longer
Live Animal Testing	No	No	No	Yes
Monitoring Purpose				✓✓
	• Surveillance • Rapid, widespread testing. • Screening large, numbers of samples	• Confirmation of BSE diagnosis • Distinction between BSE and scrapie	• Confirmatory of BSE diagnosis • Distinction between BSE and scrapie	• Highly sensitive • **Research** and strain characterization

Specified Risk Materials (SRMs)
in Bovine Spongiform Encephalopathy (BSE)

Specified Risk Materials (SRMs) contain tissues most likely to harbor and transmit BSE

⚠ **BSE prions** cannot be fully destroyed by heat and disinfectants.



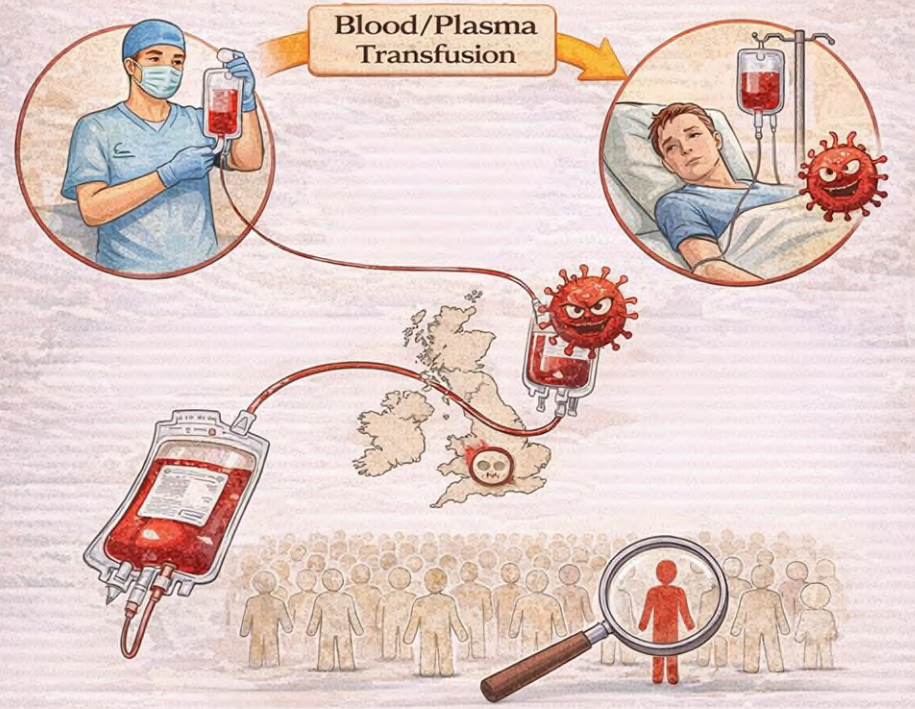
Source: WOAH, 2008

Specified Risk Materials (SRMs):

- Head
- Brain
- Spinal Cord
- Tonsils
- Skull
- Spinal Cord
- Eye
- Spleen
- Tonsils
- Distal ileum

⚠ BSE prions cannot be fully destroyed by heat and disinfectants.

Human-to-Human Transmission
of variant Creutzfeldt-Jakob Disease (vCJD)

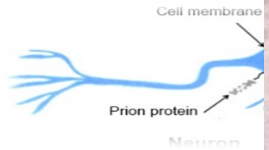


- **Four cases of** human-to-human transmission of vCJD in the UK via blood plasma transfusion (as of 2022).
- **Estimated during** UK outbreak: **1 in 4,000** exposed people may become asymptomatic carriers
- **No evidence** that vCJD spreads naturally through bodily fluids or tissues



Sources: McManus *et al.*, 2022; Gill *et al.*, 2020; Brown, 2001


HAPPY COW
MAD COW

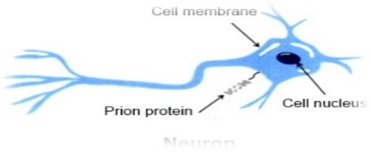

Cell membrane
Prion protein
Neuron

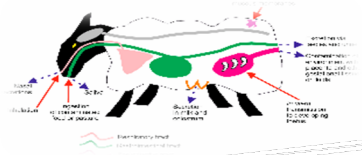

WOAH Bovine Spongiform Encephalopathy (BSE) Risk Classification Process
Does the country apply WOAH standards?
YES
WOAH will consider the following criteria:
Live cattle imports
Ruminant protein imports
Feed control measures
Surveillance capacity
Case data
NO
YES
Does evidence support negligible risk status?
NO
Negligible Risk
Country meets all criteria
Controled Risk
Undetermined Risk
Country has not fully met WOAH requirements to assess risk
WOAH: World Organisation for Animal Health


I am a prion.
I want your brain











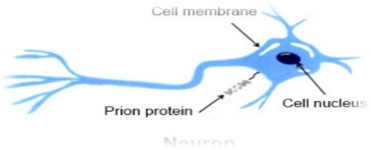


大綱

- 傳播性海綿狀腦病之相關文獻介紹
- BSE之傳統與最新檢測方法
- 2023年新版WOAH BSE 監測方法
- 防檢署 BSE 病例調查紀錄表解析
- BSE 疑似病例的檢測與確診
- BSE 疫病防控與國際規範
- 台灣申請 WOAH BSE風險可忽略國家應該要準備的相關申請文件及數據?













CJD Surveillance
National Prion Disease
Pathology Surveillance Center

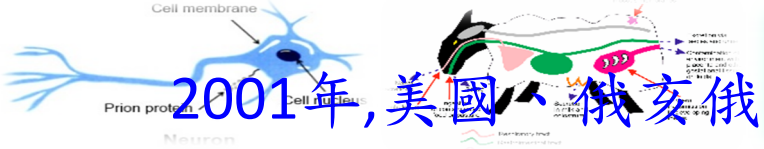
The Center is supported by the CDC and sponsored by the American Association of Neuropathologists



National Prion Disease Pathology Surveillance Center
Case Western Reserve University
2085 Adelbert Road, Room 419
Cleveland, Ohio 44106
Tel: 216-368-0587 / Fax: 216-368-4090
Email: cjdsurv@cwru.edu

2001年,美國、俄亥俄洲、克里夫蘭



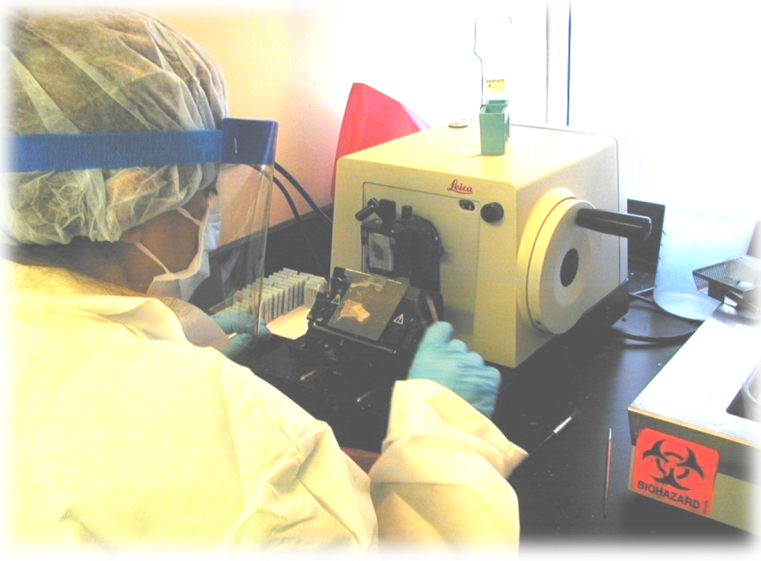




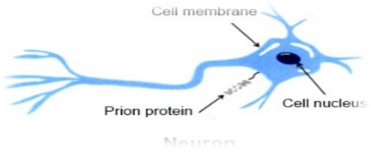


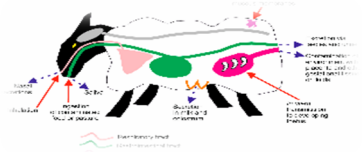

2001年,美國、俄亥俄洲、克里夫蘭




HAPPY COW
MAD COW


Cell membrane
Prion protein
Cell nucleus
Neuron

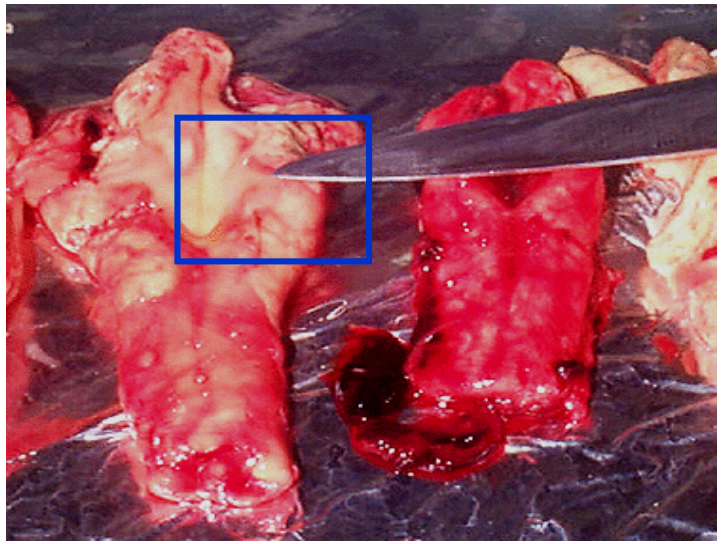


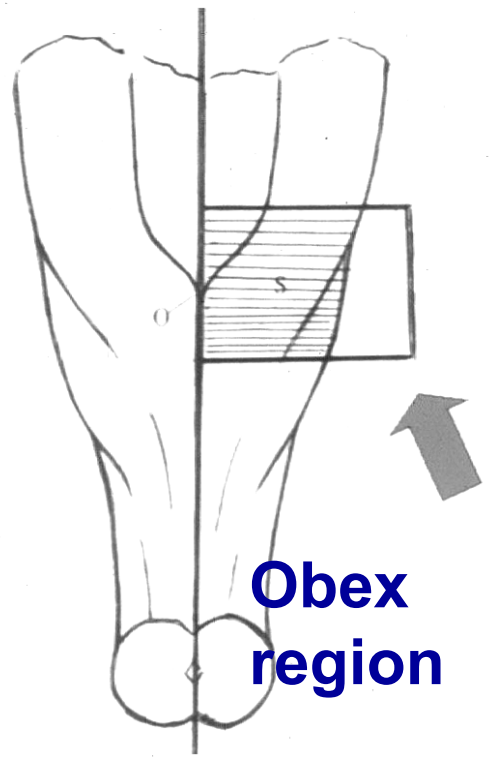












Obex region

BSE診斷流程





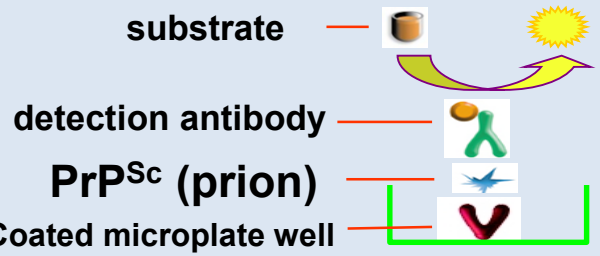
腦閂（Obex）

腦幹（延腦）

Primary test

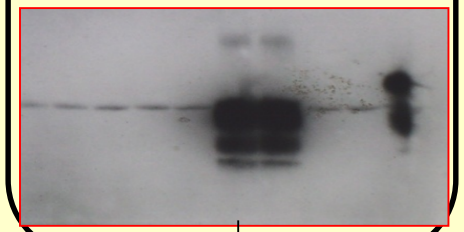
Confirmatory test

酵素連結免疫吸附法 (ELISA)

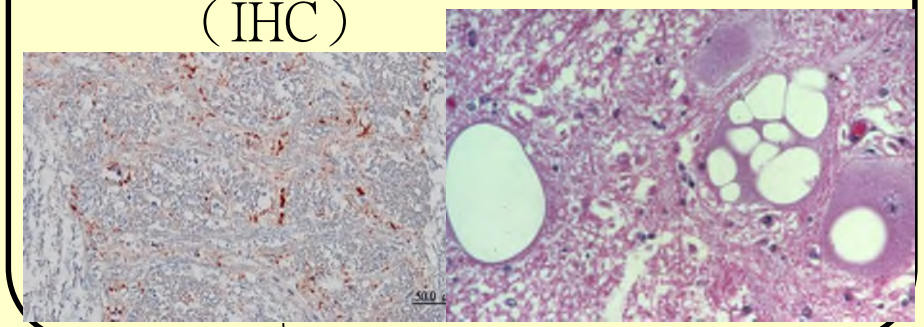


\+

西方免疫墨點法 (Western blot)



免疫組織化學染色（IHC）



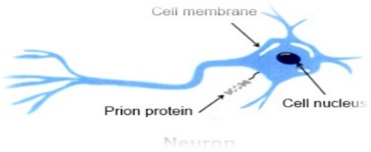
Final diagnosis：

\+ — BSE —

— \+

Final diagnosis：BSE +



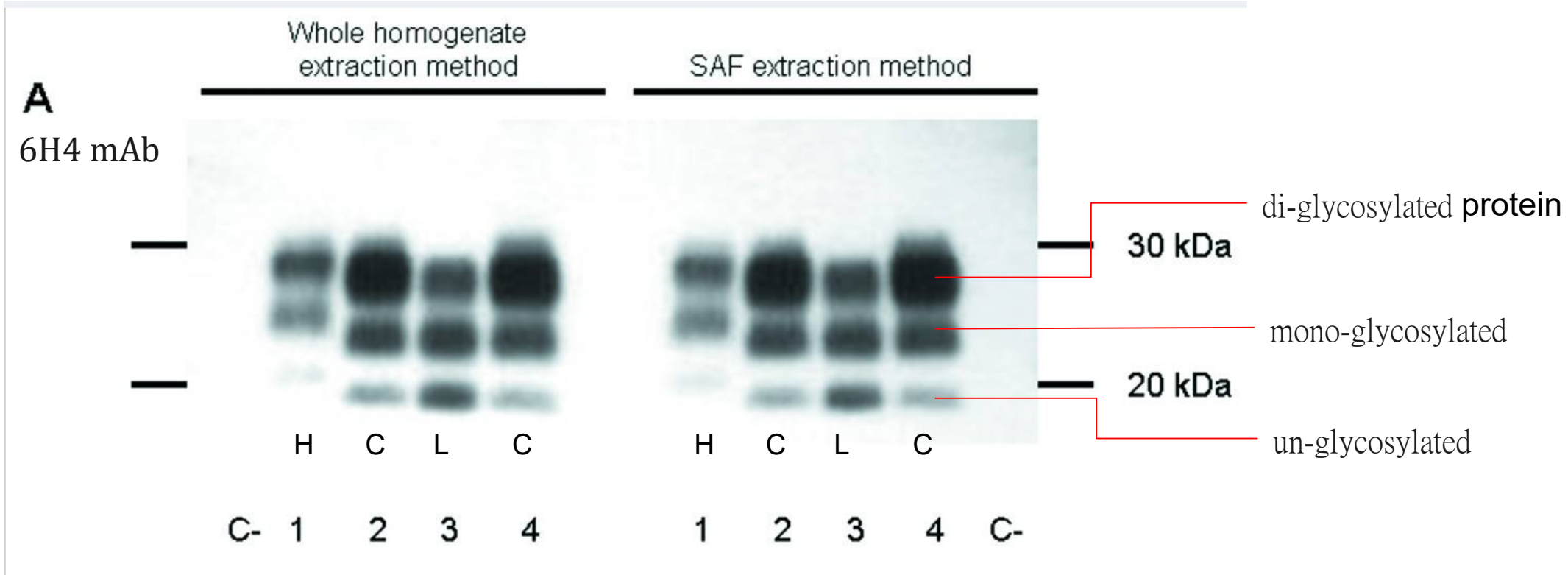








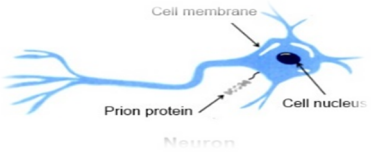
西方免疫墨點法

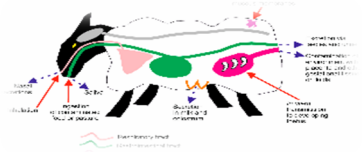


C-: negative control
1: U.S. H-type BSE
2: Italian C-type BSE
3: Italian L-type BSE
4: U.S. C-type BSE

Porcario *et. al.*, 2011
doi: 10.1186/1756-0500-4-376











WOAH BSE診斷

Table 1. Test methods available for the diagnosis of bovine spongiform encephalopathy and their purpose

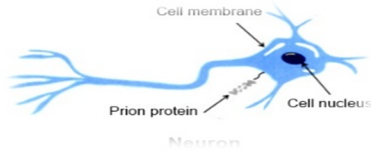
Method	Purpose					
	Population freedom from infection	Individual animal freedom from infection prior to movement	Contribute to eradication policies	Confirmation of clinical cases	Prevalence of infection – surveillance	Immune status in individual animals or populations post-vaccination
Detection of the agent[a]						
Immunohisto-chemistry	–	–	++	+++	++	–
Western immunoblot	–	–	++	+++	++	–
Rapid screening tests	–	–	+++	+	+++	–

Key: +++ = recommended for this purpose; ++ recommended but has limitations;
+ = suitable in very limited circumstances; – = not appropriate for this purpose.
[a] A combination of agent identification methods applied on the same clinical sample is recommended.

Rapid test methods:
- ELISA
- Lateral flow assays
- Rapid WB

WOAH Terrestrial Manual 2021, Chapter 3.4.5











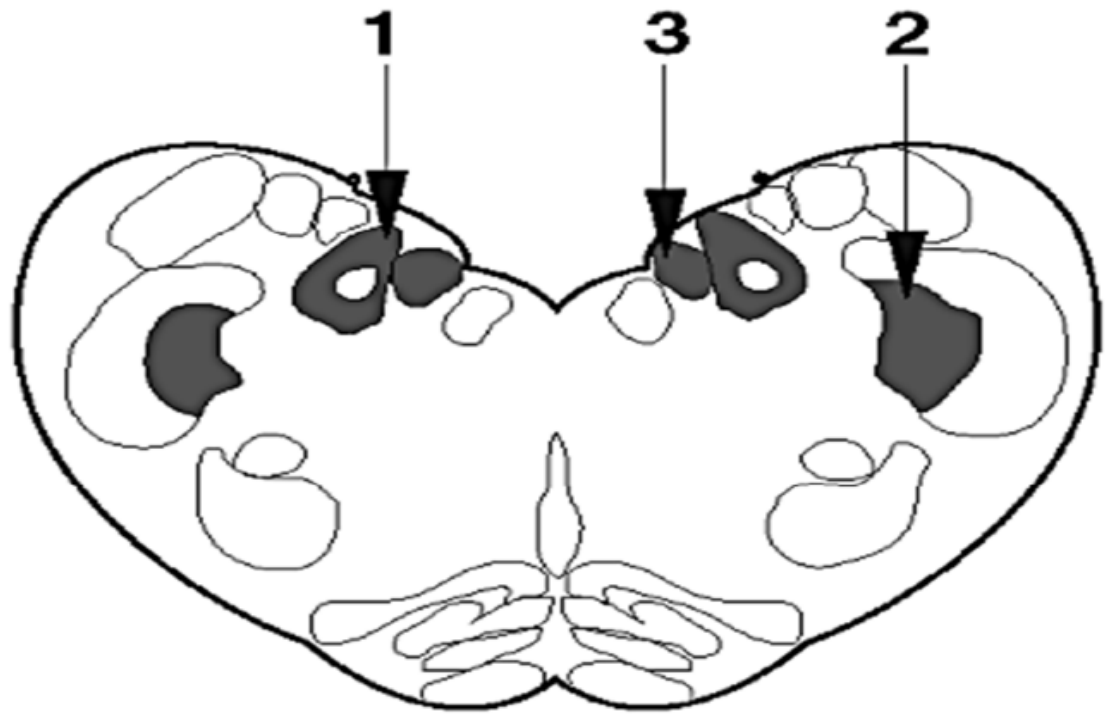
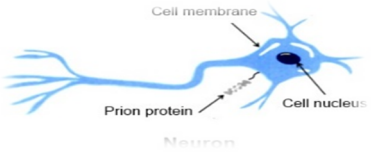


Figure 2. Cross-section of the bovine obex identifying the target sites for BSE diagnosis: (1) nucleus of the solitary tract; (2) nucleus of the trigeminal nerve; (3) dorsal motor nucleus of the vagus nerve. Reprinted from Ref. [17].

牛隻延腦（medulla oblongata）於閉孔（obex）水平之橫切面，顯示BSE診斷的目標區域：
(1)孤束核（nucleus of the solitary tract）
(2) 三叉神經核（nucleus of the trigeminal nerve）
(3) 迷走神經背側核（dorsal motor nucleus of the vagus nerve）











BSE Infection & Progression

Infection of calf in the first year of life

Clinic





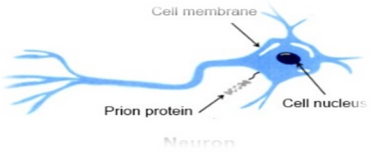
Incubation

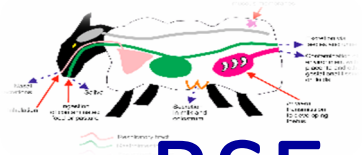
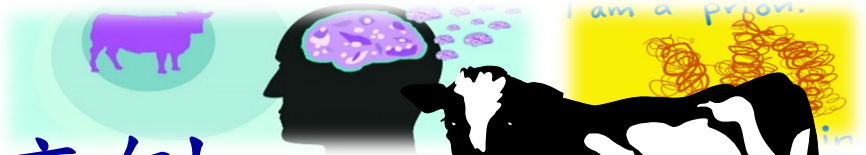
No evidence of BSE

Detection of PrP^{Sc} possible

Average age of clinical signs : 65 months





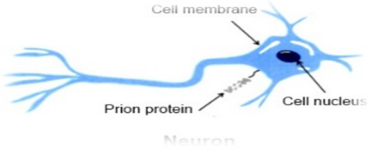



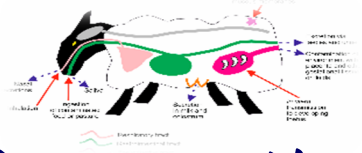

BSE 病例



- 發病年齡大多為 4 - 5 歲
- 年紀最小的病例為 20 月齡
- 年紀最大的病例為 19 歲
- 無品種或基因遺傳特異性







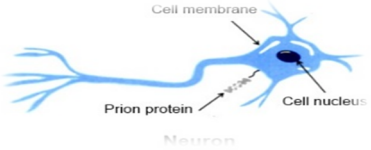




診　斷　困　難

- 潛伏期平均長達 5 年
- 目前可行的診斷法
  - –死亡動物
  - –腦組織
  - –潛伏期末 6 個月









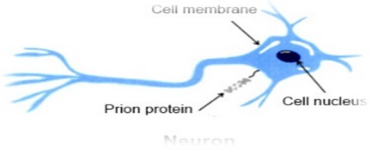


Methods of BSE Diagnosis

- **Clinical Symptoms**
- **Histology**
- **PrP^{sc}**
  - **Immunohistochemistry**
  - **SAF isolation**
  - **Western blot (Prionics® Check)**
  - **ELISA (BioRad®, Enfer®)**
- **Animal transmission**
  - **Transgenic animals**

~ Accepted by O. I. E.











BSE Clinical Signs

Retrospective evaluation

- **1/3 typical signs**
- **1/3 ± CNS signs**
- **1/3 no CNS signs**
  - **reduced milk yield**
  - **weight loss**
  - **mastitis, foot problems, peritonitis**
  - **recumbency**



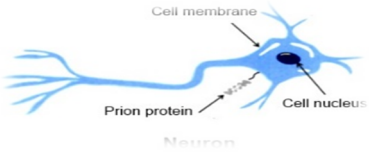


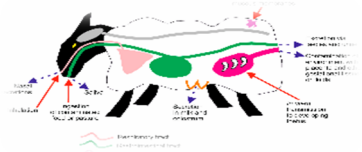
Differential diagnosis for BSE

- Listeriosis
- Non-suppurative encephalitis/ vasculitis
- Cerebrocortical necrosis/ polioencephalomalacia
- Brain edema
- Metabolic encephalopathy
- Tumors
- Others













《BSE之傳統與最新檢測方法》-1



International Journal of *Molecular Sciences*

MDPI

Review

Conventional and State-of-the-Art Detection Methods of Bovine Spongiform Encephalopathy (BSE)

Monika Olech

Department of Pathology, National Veterinary Research Institute, 24-100 Puławy, Poland; monika.olech@piwet.pulawy.pl

Abstract: Bovine spongiform encephalopathy (BSE) is a fatal neurodegenerative disease that belongs to a group of diseases known as transmissible spongiform encephalopathies (TSEs). It is believed that the infectious agent responsible for prion diseases is abnormally folded prion protein (PrP^{Sc}), which derives from a normal cellular protein (PrP^{C}), which is a cell surface glycoprotein predominantly expressed in neurons. There are three different types of BSE, the classical BSE (C-type) strain and two atypical strains (H-type and L-type). BSE is primarily a disease of cattle; however, sheep and goats also can be infected with BSE strains and develop a disease clinically and pathogenically indistinguishable from scrapie. Therefore, TSE cases in cattle and small ruminants require discriminatory testing to determine whether the TSE is BSE or scrapie and to discriminate classical BSE from the atypical H- or L-type strains. Many methods have been developed for the detection of BSE and have been reported in numerous studies. Detection of BSE is mainly based on the identification of characteristic lesions or detection of the PrP^{Sc} in the brain, often by use of their partial proteinase K resistance properties. The objective of this paper was to summarize the currently available methods, highlight their diagnostic performance, and emphasize the advantages and drawbacks of the application of individual tests.

Keywords: BSE; bovine spongiform encephalopathy; diagnosis; PrP; prion

check for updates

Citation: Olech, M. Conventional and State-of-the-Art Detection Methods of Bovine Spongiform Encephalopathy (BSE). *Int. J. Mol. Sci.* **2023**, *24*, 7135. https://doi.org/10.3390/ijms24087135

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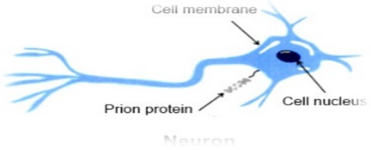
1. Introduction

Bovine spongiform encephalopathy (BSE) is a fatal neurodegenerative disease of cattle that belongs to a group of diseases known as transmissible spongiform encephalopathies (TSEs). The first huge epizootic of BSE was identified in Great Britain in 1986 and subsequently detected in cattle from many other countries worldwide. BSE has a long incubation period, between four to six years [1]. Clinical signs of the disease include behavioral abnormalities, hypersensitivity to touch and sound, gait abnormalities, weakness, and loss of body condition [2].

It is believed that the infectious agent responsible for prion diseases is abnormally folded prion protein (PrP^{Sc}), which derives from a cellular protein (PrP^{C}), which is a cell surface glycoprotein predominantly expressed in neurons. PrP^{C} is converted into the pathological form as a result of a conformational change, in which part of its α-helical structure is replaced by β-sheets [3,4]. The increase in the number of PrP^{Sc} conformers containing a high content of β-sheets motifs gives rise to hydrophobic PrP^{Sc} intracellular aggregates and form amyloid fibrils. PrP^{Sc} is toxic to cells of the central nervous system (CNS), and its formation is considered to be linked to the neurodegeneration of tissues within the CNS. Prions accumulate in high amounts in the brain, but low amounts of PrP^{Sc} are found in many tissues and biological fluids, even at the early stages of the presymptomatic period. PrP^{Sc} is partially proteinase kinase (PK)-resistant, resulting in the formation of an N-terminally truncated fragment known as PrP^{res} (res meaning resistant). This unique feature of this protein has been used to develop most of the testing methods currently used to detect of BSE. The clinical manifestations of the disease, although characteristic, are insufficient for a definitive diagnosis. The immune system is unable to produce a specific response to PrP^{Sc}

- BSE無疫苗、無治療 → 診斷就是防線
- 早期、快速、準確診斷 = 控制疫情關鍵
- 沒有單一完美方法診斷方法 → 必須多方法整合











《BSE之傳統與最新檢測方法》-2

🧠 二、診斷策略架構

🔄 標準流程（國際共識）

1️⃣ 篩檢（Rapid test / ELISA）

2️⃣ 確認（WB / IHC）

3️⃣ 分型（strain typing）

👉 重點：

- 快篩 ≠ 診斷
- 確診一定要看 PrP^Sc

三、傳統方法（已建立標準）

(1)組織病理學（Histopathology）

- ✔ 特異性高（看到空泡化）
- ❌ 敏感度低
- ❌ 受樣本品質影響大（自溶、假影）

👉 已逐漸被分子方法取代

(2)免疫組織化學（IHC）

✔ 偵測 PrP^Sc 沉積

✔ 提高敏感度

✔ 國際確認標準之一

👉 **關鍵角色：確診工具**

(3)Western blot（WB）

✔ 判讀 glycoform pattern

✔ 可做 strain typing

❌ 受 PK digestion 影響

👉 **確診＋分型雙功能**

(4)ELISA / Rapid tests

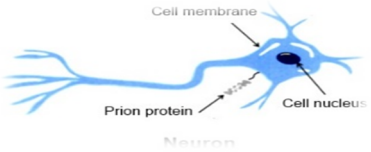
✔ 適合大規模篩檢

✔ 快速、自動化

❌ 假陽性可能

👉 **監測系統的第一道門**











《BSE之傳統與最新檢測方法》-3

⚙️ 四、新世代技術

🔥(1) PMCA（蛋白錯誤摺疊放大）

👉 核心概念：

- PrPˆSc = 種子（seed）
- 誘導 PrP^C → PrP^Sc
- 指數放大

👉 特點：

- **極高敏感度（接近生物測定）**
- 可偵測極低濃度（血液、體液）

👉 限制：

- 操作複雜
- 污染風險高
- 標準化困難

⚡(2) RT-QuIC（革命性技術）

👉 已逐漸取代 **PMCA**

核心優勢：

- 更快
- 更穩定
- 可即時偵測（real-time）
- 污染風險低

👉 敏感度：

- 比傳統快篩高 **10^4倍**

👉 可做到：

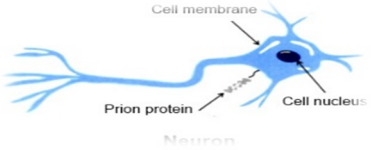
- 區分 C-BSE / H-BSE / L-BSE
- 檢測低濃度樣本

🧪 **(3)** 新整合技術（**A-FACCT**）

👉 PMCA + ELISA融合

👉 用於早期檢測（如**CWD**）











《BSE之傳統與最新檢測方法》-4

🧬 **五、關鍵影響因子（診斷成敗關鍵）**

⚠️**(1) 樣本品質**

- 自溶（autolysis）→ 降低診斷價值
- 冷凍/固定不當 → 偽陰性
- 👉 **實務重點：採樣品質 > 檢測技術**

⚠️**(2) PK digestion**

- 過強 → 訊號消失
- 過弱 → 偽陽性

👉 直接影響 WB / ELISA結果

⚠️**(3) 抗體選擇**

- 不同 epitope → 判讀差異
- 影響 strain typing

🧭 **六、未來發展方向（最關鍵 insight）**

👉 **未來趨勢：**

- 從「死後診斷」→「生前診斷」
- 從「檢出疾病」→「偵測無症狀感染」

👉 關鍵技術：

- PMCA
- RT-QuIC

👉 目標：

- 血液 / 體液檢測
- 群體監測

🧩 **七、整體結論**

🔹 **傳統方法**

- 穩定、標準化
- 用於確診

🔹 **新技術**

- 超高敏感度
- 可早期檢測

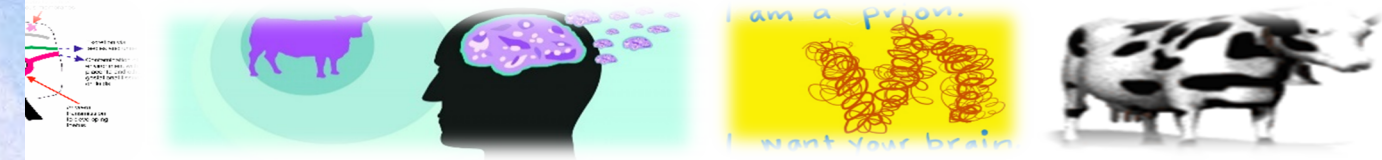
🔹 **最佳策略**

👉 **整合式診斷（multi-method approach）**

PET Blot vs IHC vs Western Blot

PET Blot	IHC	Western Blot
		
Paraffin-embedded tissue (PET Blot)	Immunohistochemistry (IHC)	Western Blot (WB)
Key Features • Tissue section affixed onto PVDF membrane • Uses paraffin-embedded tissue (formalin fixed) • Performs protease K digestion (full digestion of PrP^{Sc}) • Detects only the PrP^{Sc} left behind on the membrane	**Pros & Cons** • High sensitivity, superior for early PrP^{Sc} detection • Uses paraffin-embedded tissue (formalin fixed) • On slide, primary antibody labels PrP^{Sc} • Secondary antibody, plus chromogen or fluorescent marker	**Pros & Cons** • High sensitivity, mainly for confirmatory diagnosis • Time-consuming, requires subjective interpretation • Not suitable for large-scale typing • High specificity, separates PrP^{Sc} and PrP^{Sc} by size • Suitable for large-scale testing or research
Pros & Cons • High sensitivity, superior for early PrP^{Sc} detection • Provides qualitative evaluation of entire tissue section (macroscopic level)	**Pros & Cons** • High sensitivity, well-suited for PrP^{Sc} detection • Provides detailed cellular and subcellular localization • Can be used on autolyzed or frozen samples	**Pros & Cons** • High specificity, separates PrP^{Sc} and PrP^{Sc} by size • Suitable for large-scale testing or research • No cellular context, only shows molecular bands • Lower sensitivity, especially for early infections • Typically requires brain tissue sampling
Key Features • High sensitivity, superior for early PrP^{Sc} detection • Low throughput, mainly for confirmatory diagnosis		

- High sensitivity, superior for early PrP^{Sc} detection
- Provides qualitative evaluation of entire tissue section (macroscopic level)
- Limited PrP^{Sc} detection in lymphoid tissues
- Low throughput, mainly for confirmatory diagnosis
- Limited PrP^{Sc} detection in lymphoid tissues



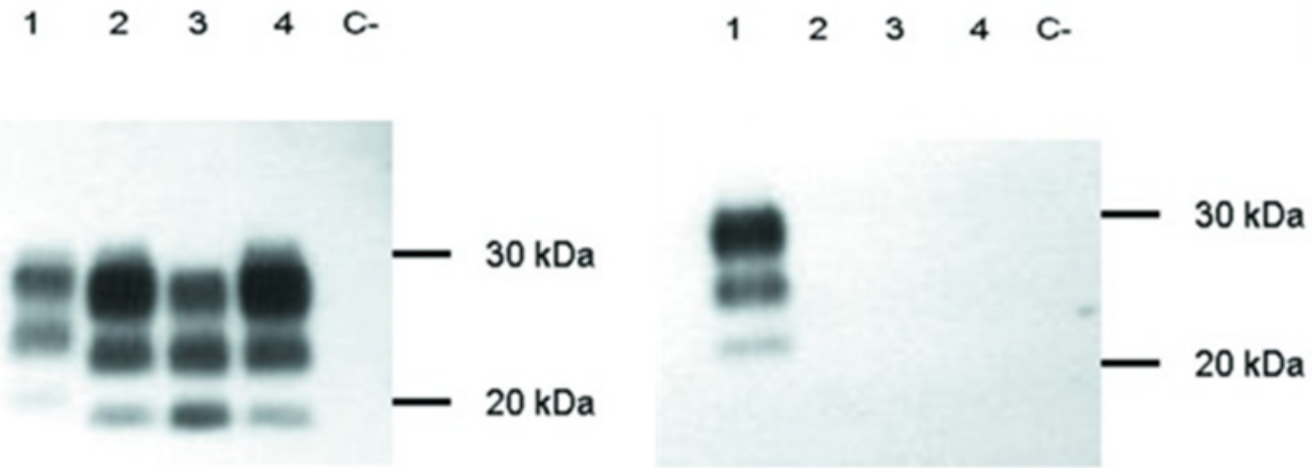


Figure 4. Western blot analysis. H-type BSE (1), C-type BSE (2), L-type BSE (3), and C-type BSE (4) samples and healthy bovine used as negative control (C-). mAbs 6H4 (a) and P4 (b) were used, respectively. Adapted from Ref. [35].

EU Diagnostic Workflow for TSE/BSE

1. SCREENING (Rapid Tests)

Applicable samples:
- Brainstem (obex region)
- Target populations (fallen stock, emergency slaughter, clinical suspects

Approved rapid tests:
- Bio-Rad TeSeE
- IDEXX HerdChek
- Prionics®-Check
- Others (EU–approved)



Critical Control Points
- Sample quality (brainstem preferred)
- PK digestion conditions (affects WB results)
- Antibody selection (epitope specificity)
- Use of reference laboratories (EURL validation)

Negative ✓ Report as negative

Positive / Inconclusive → Proceed to **confirmatory testing**

2. CONFIRMATORY TESTING

Reference methods:
- Western Blot (WB)
- Immunohistochemistry (IHC)

Detection target:
- PrP^{Sc} (protease-resistant or tissue deposition pattern)



→ ✓ *Wdtho r Llsl)* (prel pricing)

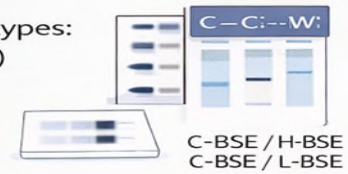
→ ✓ Proceed to typing

Not confirmed ✗ Negative (screening false positive)

Confirmed → Proceed to typing

3. TYPING (Strain Discrimination)

Purpose:
- Differentiate BSE types:
  - Classical (C-BSE)
  - Atypical:
    - H-type
    - L-type



Methods:
- Western blot glycoform profile
- Molecular weight shift
- Antibody binding pattern



Decision Logic (Simplified)

SCREENING
→ Positive / Inconclusive

CONFIRMATORY
→ (WB / IHC)
→ Confirmed TSE

TYPING
→ (C-BSE / H-BSE / L-BSE)

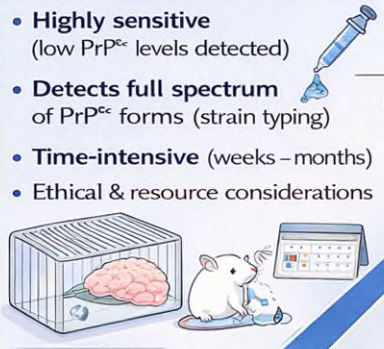
Source: EU TSE Regulations & EURL Guidance

In Vivo vs. In Vitro –

Diagnostic Performance Comparison for BSE/TSE

In Vivo Bioassay (Animal Models)

- **Highly sensitive** (low PrP^{Sc} levels detected)
- **Detects full spectrum** of PrP^{Sc} forms (strain typing)
- **Time-intensive** (weeks – months)
- Ethical & resource considerations



→ Highly sensitive

→ Detects full spectrum of PrP^{Sc} forms

→ Time-intensive (weeks – months)

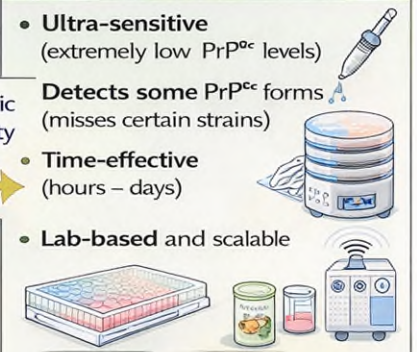
→ Ethical & resource considerations

Diagnostic Sensitivity Range

Time Efficiency

In Vitro PMCA (Protein Misfolding Cyclic Amplification)

- **Ultra-sensitive** (extremely low $PrP^{\alpha c}$ levels)
- **Detects some PrP^{Sc} forms** (misses certain strains)
- **Time-effective** (hours – days)
- **Lab-based** and scalable



- Ultra-sensitive (extremely high)
- Some PrP^{Sc} forms missed
- Lab-based and scalable

Lab-based and scalable

Strain Detection

	In Vivo	In Vitro
Sensitivity	++ (extremely high)	++ (+extremely high)
Scope	Full PrP^{Sc} spectrum (strain variation)	Full PrP^{Sc} spectrum (strain variation) Some PrP^{Sc} forms missed
Time Efficiency	Weeks – months	Hours – days
Scalability	Low throughput	High throughput (many samples)
Ethical Impact	Animal use	No animal use

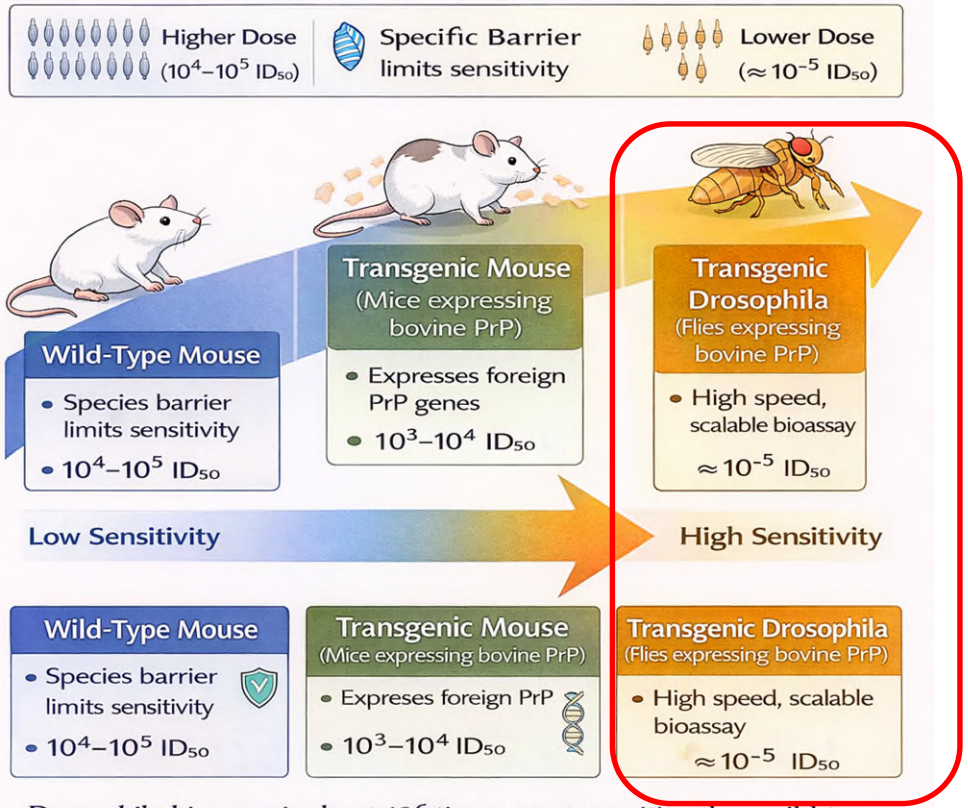
++ = extremely high — = extremely low

Conceptual Takeaway: The right method is not just about **salance** of speed, scale and ethical considerations.

*The right **method is not just about sensitivity; it's a balance of** speed, scale, and **ethical considerations.***

Animal Models for BSE/TSE Diagnostic Sensitivity

Diagnostic Sensitivity (Amount of PrP^{Sc} Required for Infection)

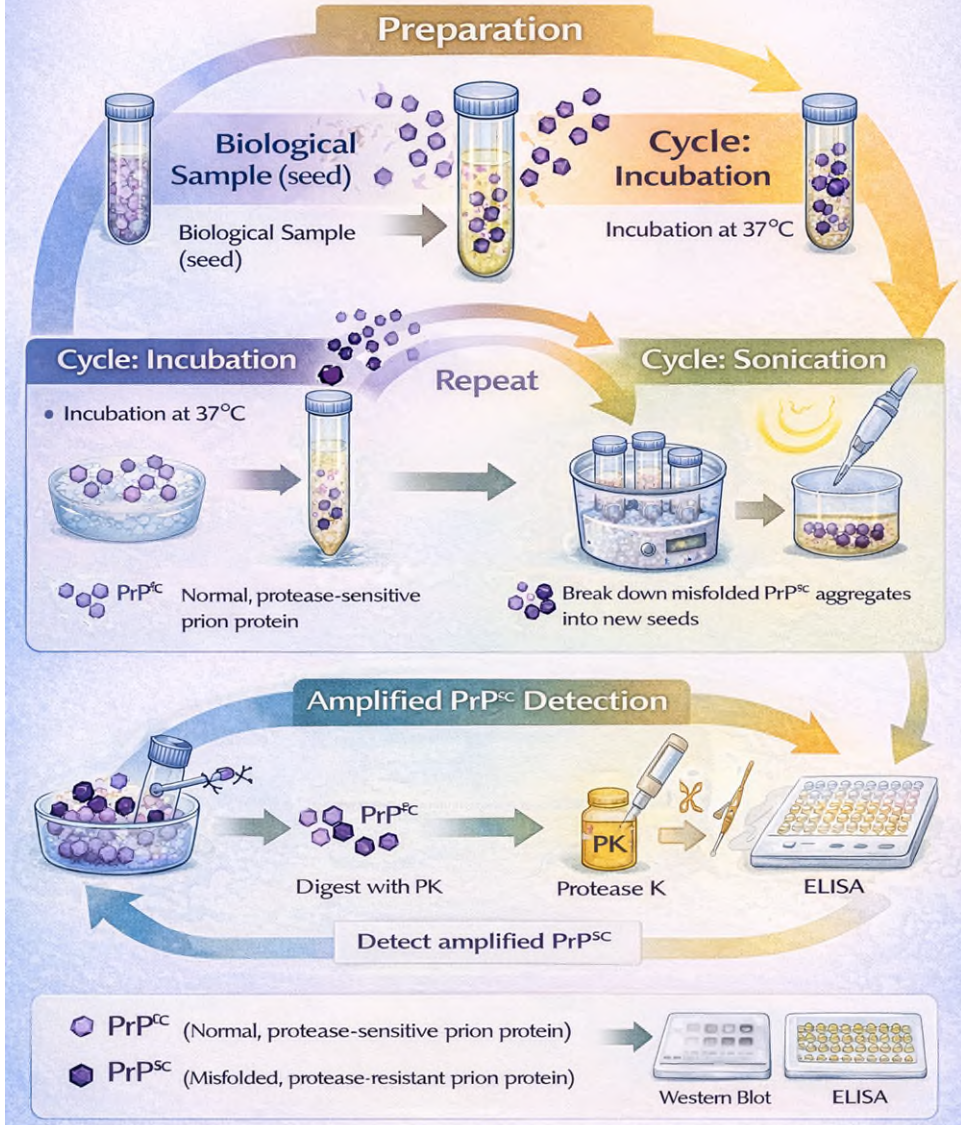


Drosophila bioassay is about 10^6 times more sensitive than wild-type mice for BSE/TSE detection.

Drosophila bioassay is about 10^6 times more sensitive than wild-type mice for BSE/TSE detection.

Protein Misfolding Cyclic Amplification (PMCA)

PMCA amplifies misfolded prion proteins (PrP^{C}) using a biological sample as a template to convert normal prion proteins (PrP^{C}) into misfolded forms through repeated incubation and sonication cycles.



Comparison of BSE/TSE Detection Methods

Sensitivity of Diagnostic Techniques

(based on 50% Infectious Dose, ID_{50})

PrP^{Sc} Detection Limit

10^{0} —

– 10^{-4}–10^{3}

– 10^{-4}–10^{5}

– 10^{-4}–10^{-5}

– 10^{-5}–10^{-6}

10^{-6}

– 10^{-5}–10^{-6}

10^{-6}

Western Blot (WB)

Detects PrP^{C} by protein separation, transfer, and antibody detection



Detection Limit: ≈10^{-4}–10^{3} ID_{50}

ELISA

Detects PrP^{Sc} using an enzyme-conjugated antibody in a plate-reader format



Detection Limit: ≈10^{-4}–10^{-5} ID_{50}

PMCA (Protein Misfolding Cyclic Amplification)

Amplifies trace amounts of PrP^{Sc} by converting PrP^{C} in a cyclical process



Detection Limit: ≈10^{-5}–10^{-6} ID_{50}

PMCA (Protein Misfolding Cyclic Amplification)

Amplifies trace amounts of PrP^{Sc} by converting PrP^{C} in a cyclical process

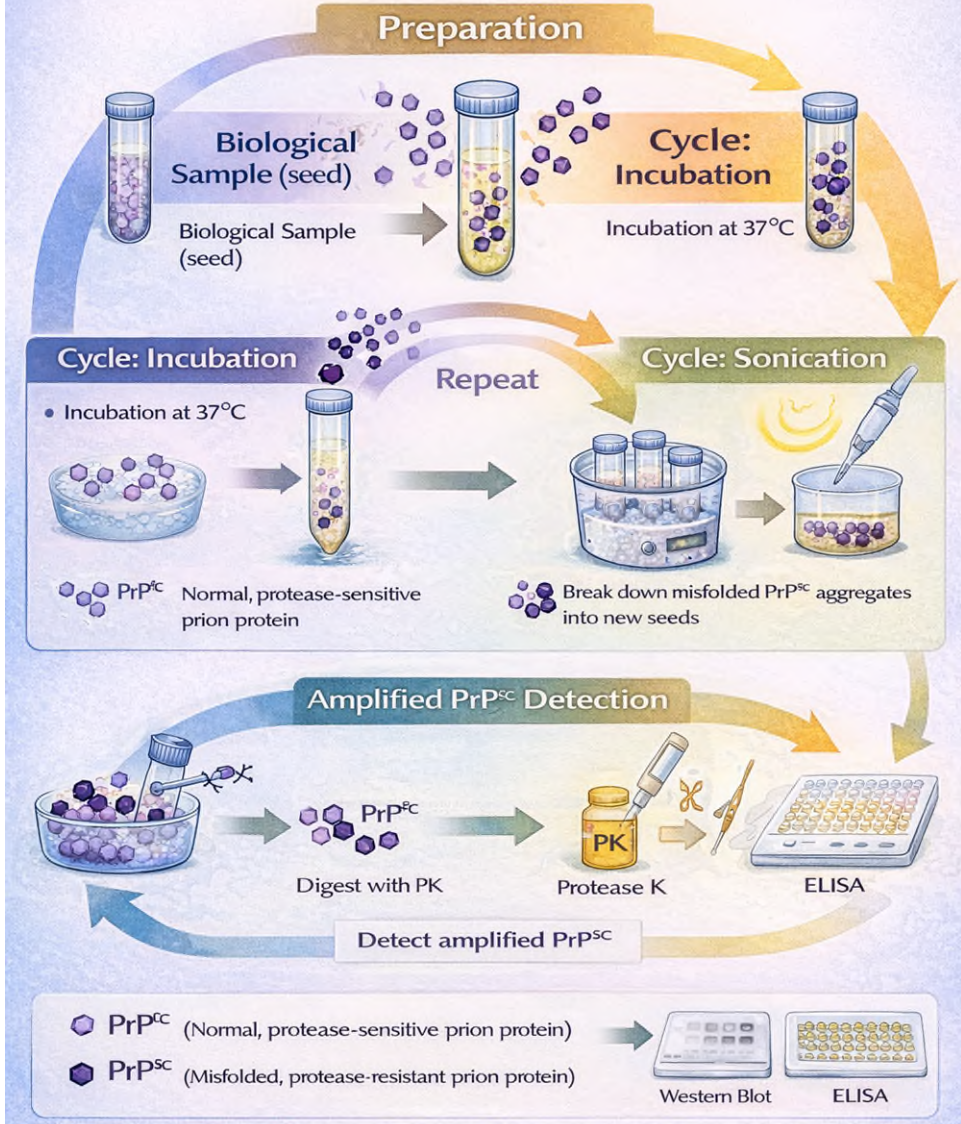


Detection Limit: ≈10^{-5}–10^{-6} ID_{50}

PMCA is up to 1,000 times more sensitive than these methods.

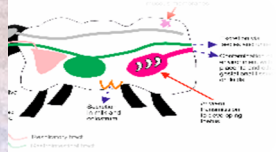
Protein Misfolding Cyclic Amplification (PMCA)

PMCA amplifies misfolded prion proteins (PrP^{Sc}) using a biological sample as a template to convert normal prion proteins (PrP^{C}) into misfolded forms through repeated incubation and sonication cycles.



Comparison of BSE Laboratory Diagnostic Methods

	Brain TSE ELISA	Western Blot (WB)	Immuno-histochemistry	Bioassay
Method	PrP^{Sc}	PrP^{Sc}	PrP^{Sc}	Live animal response to BSE infection
Detection Target	Brain tissue homogenate	Brain tissue homogenate	Brain tissue sections	Brain inoculum injected into animals (e.g. transgenic mice)
Sensitivity	✓✓✓	✓✓✓	✓✓✓	✓✓✓✓+
Testing Time	<24 hours	Over 24 hours	Over 24 hours	Several months or longer
Live Animal Testing	No	No	No	Yes
Monitoring Purpose				✓✓
	• Surveillance • Rapid, widespread testing. • Screening large, numbers of samples	• Confirmation of BSE diagnosis • Distinction between BSE and scrapie	• Confirmatory of BSE diagnosis • Distinction between BSE and scrapie	• Highly sensitive • **Research** and strain characterization









PMCA vs RT-QuIC 核心對比

特性	PMCA	RT-QuIC
放大方式	sonication	shaking
基質	brain homogenate	recombinant PrP
敏感度	極高	極高
速度	較慢	較快
污染風險	較高	較低
即時偵測	❌	✅
標準化	較困難	較佳

Evolution of Prion Amplification Technologies
PMCA → RT-QuIC Timeline

From Discovery to Real-Time Detection: Advancing Prion Diagnostics

Pre-2000 — PrP^{Sc} Detection Limitations



- Low sensitivity
- Bioassay (in vivo)
- PK digestion + WB

2001 — PMCA Invention



- Soto et al.
- Cyclic incubation + sonication
- First in vitro amplification

2005–2010 — PMCA Optimization



- DSP-PMCA
- Bead-PMCA (mb-PMCA)
- ePMCA (electric field)

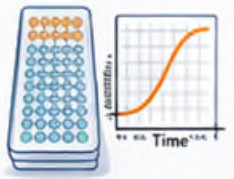
Sensitivity ↑ 10^4–10^5

2012–2015 — Serial PMCA (sPMCA)



- ✓ Serial rounds
- ✓ High sensitivity (97.2%) & specificity (100%) for BSE/scrapie

2016–2018 — Quantitative PMCA (qPMCA)



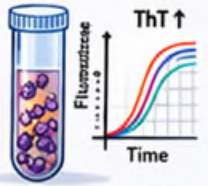
- ✓ Quantifies seeding activity (infectivity)
- ✓ Serial dilution & positive rate

2019–2022 — Limitations & Automation



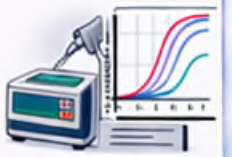
- ⚠ Sonication variability
- ⚠ Cross-contamination
- ⚠ Long assay time
- ✓ Need for real-time & standardized method

2013 — RT-QuIC Development



- Atarashi et al.
- Real-Time Quaking-Induced Conversion
- Recombinant PrP^C substrate

2018–2020 — RT-QuIC Clinical Breakthrough



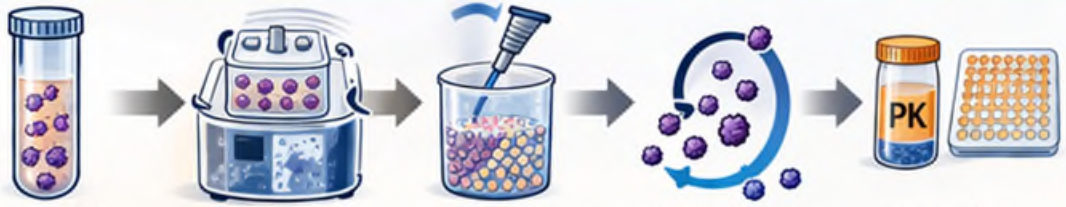
- ✓ Real-time detection (10–60 min)
- ✓ High sensitivity (10^{-6}–10^{-8} ID50)
- ✓ Blood, CSF, saliva applicable

2023–Now — Standardization & Integration



- Global RT-QuIC standard protocols
- PMCA & RT-QuIC complementary use
- Early diagnosis & surveillance

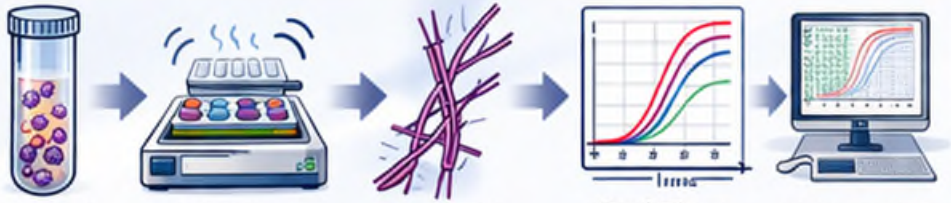
PMCA (Protein Misfolding Cyclic Amplification)



PrP^{Sc} Substrate → Incubation 37°C → Sonication (Disaggregation) → PrP^{Sc} Seeds Amplified → Detection (WB/ELISA)

High Sensitivity 10^4–10^6 | Time 15–48 h | Output Endpoint (WB/ELISA)

RT-QuIC (Real-Time Quaking-Induced Conversion)



Seeded PrP^{Sc} → Shaking (Quaking) → Amyloid Fibril Growth → Real-Time Fluorescence (ThT) → Automated Analysis

Ultra-High Sensitivity 10^{-6}–10^{-8} | Time 10–60 min | Output Real-Time Kinetics

Key Advantages of RT-QuIC

- Real-time monitoring
- Higher reproducibility
- Faster results
- Lower risk of contamination
- Field & clinical applicability

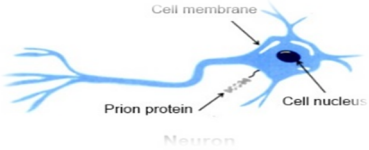




Table 3. *Cont.*

Method	Advantages	Disadvantages
IHC *	high specific and sensitive; fresh, frozen, and autolyzed samples can be used; paraffin-embedded and frozen tissue samples can be stored and accessed when required; allows cellular localization of protein; relatively inexpensive; widely used; it does not require any special equipment, results can be viewed using a conventional bright-field microscope; verify the results obtained by HA	semi-quantitative; multi-step procedure; variability depends on the fixation procedure, staining protocol, and antibody selection; particular areas of the brain are needed; requires specialized reagents and qualified personnel; subjective interpretation of results; low throughput; non-specific reactions can occur, time-consuming and laborious
PET-blot	highly sensitive and specific; can be used to discriminate TSE strains, macroscopic observation possible	not a rapid tool; not suitable for large-scale screening; time-consuming and laborious; requires paraffin-embedded tissues, specialized equipment, reagents, and qualified personnel; has lower microscopic resolution than IHC; multi-step procedure; it is not commonly used; lack of standardization
WB *	very sensitive and specific; fresh, frozen, and autolyzed samples can be used; widely used; provide valuable information about the biochemical properties of PrP^{Sc}; can be used to discriminate TSE strains; can be quantitative or qualitative; similar sensitivity to IHC	give no information on the neuroanatomical location of PrP^{Sc}; requires specialized equipment, reagents, and qualified personnel; multi-step procedure; non-specific reactions can occur; subjective interpretation of results; paraffin-embedded tissues cannot be used; sensitivity varies between methods and laboratories
Rapid tests *	highly sensitive and specific; rapid; suitable for large-scale screening; full automation is possible; based on WB, immunochromatography, and ELISA; does not need ultracentrifugation steeps needed to concentrate the PrP^{Sc}; can be quantitative or qualitative; fresh, frozen, and autolyzed samples can be used; can be used to discriminate TSE strains; most of them are commercially available	particular areas of the brain are needed; occasionally give false positive results; require specialized reagents and qualified personnel; some tests require specialized equipment; paraffin-embedded tissues cannot be used
IFA	cells or frozen tissue can be used; highly sensitive and specific; rapid,	expensive; requires specialized equipment (fluorescence or laser microscope), reagents, and qualified personnel; lack of standardization; frozen sections have poor morphology; non-specific results can occur; low throughput,
IFMA	extremely sensitive; allow simultaneous detection of multiple analytes; amenable to high-volume testing; can be used to discriminate TSE strains; automated	expensive; requires specialized equipment (cytometer), reagents, and qualified personnel; non-specific results can occur; rarely used; lack of standardization
SAF	highly specific; autolyzed sample can be used	results depend on the region used and sample purification scheme; labor-intensive; requires specialized equipment (electron microscope), reagents, and qualified personnel; less sensitive than WB; rarely used; only qualitative
Bioassay	the most sensitive and specific; provide information about PrP^{Sc} infectivity; strain-typing method	labor-intensive and time-consuming; not suitable for large-scale screening; have the highest sensitivity only when performed in homologous species
PMCA	extremely sensitive, can be used to understand the biology of prion proteins, can be quantitative or qualitative; can be automated; can be used for antemortem TSE diagnosis	requires specialized equipment (sonicator), reagents, and qualified personnel; no real-time detection; time-consuming; false-positive results may occur; lack of standardization; requires additional substrate purification step











典型與非典型 BSE 差異比較表

分類項目	典型 BSE（Classical BSE）	非典型 BSE（Atypical BSE）
首次發現時間	1986 年於英國	2003 年後陸續於全球發現（如法國、德國、美國等）
感染來源	通常與餵食含有感染性肉骨粉有關	被認為是自發性或偶發性突變（類似人類散發性 CJD）
年齡分布	多發於較年輕牛（4～6 歲）	多見於老齡牛（＞8 歲）
病理型態	一種明確的蛋白異常型態	分為兩型：H 型與 L 型
傳播性	高，曾造成全球性傳播風險	傳播性低，尚無大規模疫情記錄
對人類風險	可透過食物鏈傳播，導致 vCJD	對人類健康風險仍不明確，但可能性較低
監測與通報	列為 OIE/WOAH 強制通報疾病	仍需通報，但屬於偶發個案
主要影響地區	英國與歐洲多國	北美、歐洲、亞洲均有零星案例









Classical vs Atypical BSE

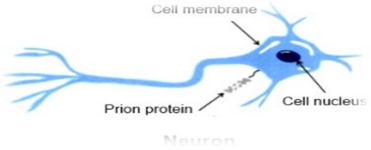
Classical BSE is often a "man-made epidemic," while atypical BSE is more like a "sporadic event in a natural setting."

Classical BSE (C-BSE)		Atypical BSE (H-BSE / L-BSE)
C-BSE		(H-BSE/L-BSE)
Strongly linked to consumption of contaminated meat and bone meal (MBM)	Epidemiological Pattern	Mostly sporadic or unknown source
Epidemic	Age of Occurrence	Sporadic
Approx. 4-6 years old	Molecular Characteristics	Mostly ≥8 years old
PrP^{Sc} grysecd for consistent	Pathological Distribution	PrP^{Sc} differs in molecular type (H-type / L-type)
Mainly in central nervous system	Transmission Risk	More variable, some types more widespread or different areas
High (via feed transmission)	Relationship to Humans	Low (no clear horizontal transmission evidence)
Confirmed closely linked to vCJD	Surveillance Cases	Still unclear (but has potential risk)
Identified after large-scale monitoring	Ile Ellance	Often found in fallen/emergency-slaughtered cattle

When we talk about classical BSE, we are actually examining "system failures", and when we see atypical BSE, we are handling "risks still unresolved in nature."

項目	典型 BSE（C-BSE）	非典型 BSE（H-BSE / L-BSE）
發生原因	與攝入受污染肉骨粉（MBM）**高度相關	多為自發性（sporadic）或未知來源
流行型態	流行性（epidemic）	散發性（sporadic）
好發年齡	約 4－6歲	多為 8歲以上老齡牛
分子特徵	PrP^Sc 糖基化型態固定	PrP^Sc 分子型態不同（H型 / L型
病理分布	主要在中樞神經系統	分布較變異，部分型態更廣泛或不同區域
傳播風險	高（經飼料傳播）	低（無明確水平傳播證據）
與人類關聯	✓ 已證實與 vCJD密切相關	❓ 關聯性尚不明確（但具潛在風險）
發現方式	疫情爆發後大量監測發現	多由主動監測（倒斃牛）發現
發生趨勢	已因管制措施大幅下降	持續零星出現
防疫意義	政策核心（飼料禁令）	監測與風險評估重點









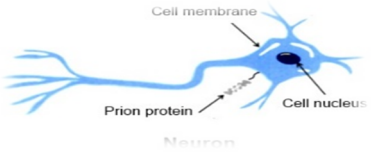


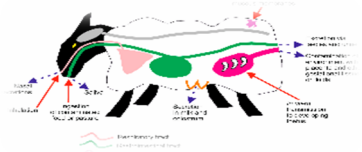
Atypical BSE

- different phenotype of BSE have been reported.
- At least two strain variants (H-type, and L-type) of atypical BSE have been recognized in:

♦ UK, Italy, France, Sweden, Germany, Poland, Denmark, Netherland, Belgium, Switzerland, USA, Canada, Japan





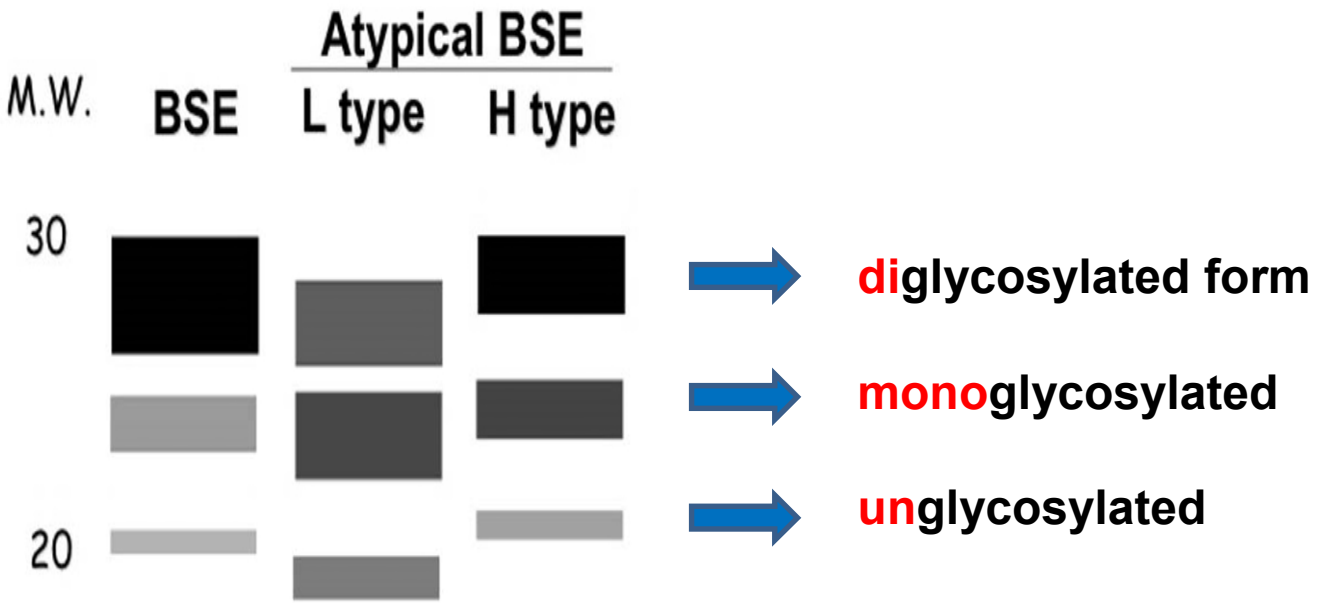




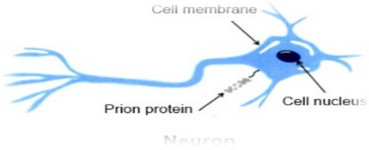


Atypical BSE

- initially identified by ELISA testing
- Follow up testing by western blot revealed different profiles BSE
- Origin of H and L types is unknown











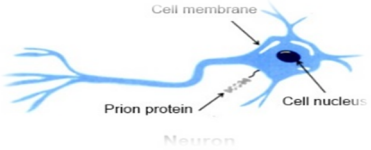


- transmission studies on Japanese L-BSE to bovinized transgenic mice, and cattle.
- ♦ As with the classical BSE prions, L-BSE prions accumulated in central and peripheral nerve tissues but not in lymphoid tissues.
- ♦ the current definition of specified risk materials is applicable to L-BSE cattle.

(Iwamaru Y. et al. 2010, Emerg Infect Dis 16(7): 1151-1154.)

- Atypical BSE: mostly among aged cows Sporadic BSE? Food borne contamination by a scrapie?
  - ♦ Ban on ruminant-derived feed to caw
  - ♦ BSE test for aged caw
  - ♦ Current BSE diagnostic procedure can detect atypical BSE
  - ♦ Need the risk analysis for the occurrence of atypical BSE Evaluate the risk from newly emerging prions.
- In order to prevent future outbreaks of atypical BSE, control programs should not be withdrawn without careful consideration!!










12 May 2011 Last updated at 17:00 GMT

Campaigners demand 'mad cow disease' criminal inquiry

By Dominic Blake BBC News

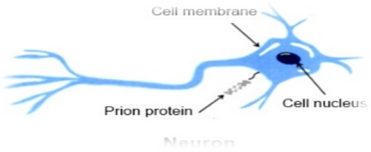


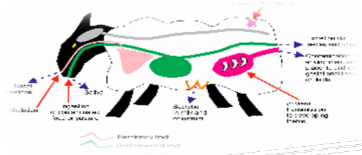




Christine Lord's son Andrew Black, 24, died of vCJD in 2007







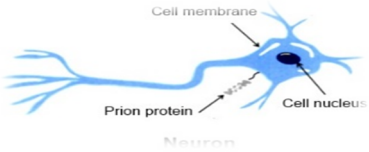


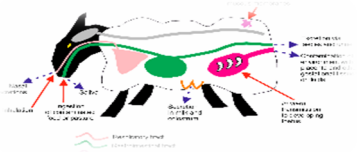

大綱

- 2023年新版WOAH BSE 監測方法
- BSE 疫病防控與國際規範
- 台灣申請 WOAH BSE風險可忽略國家應該要準備的相關申請文件及數據?













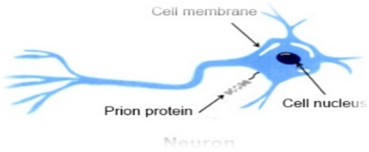
2023新BSE標準與舊版差異-1

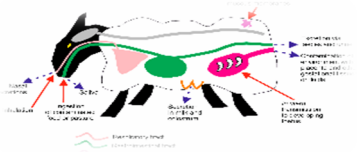
2023 年新版 BSE 標準（陸生動物衛生法典第 11.4 章）相較舊版，關鍵在「風險評估方式改變、監測系統簡化、非典型 BSE 角色調整」三大面向。[1][2][3]

一、整體理念與風險評估模式的改變

- 新版強調必須做「完整 BSE 風險評估」，明確要求包含 entry（輸入）、exposure（暴露）兩大評估，作為決定一國／一區 BSE 風險狀態的核心依據；舊版較著重結構化監測數據與管制作為主體。[3][1]
- 對「何時起可認定牛群內 BSE 再循環風險已可忽略」的時間點給了更清楚的技術框架，並要求在官方風險認定檔中明示該日期；舊版對這個日期的闡述較少、彈性較大。[4][3]









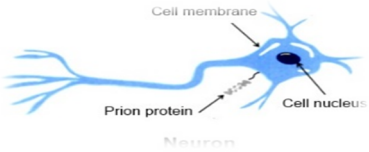


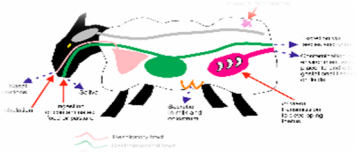
2023新BSE標準與舊版差異-2

二、BSE 監測與監控要求的重大調整

- 舊版採「分數制（point-based）監測系統」，要求各年齡／風險群別的檢測頭數達到一定積分，新版取消此制度，改為「目標性監測（targeted surveillance）」，搭配 2023 年新版《BSE 目標性監測指引》作為操作文件，使小牛群國家較易符合要求。[5][6][1]
- 新版監測強調與實際流行病學情境相符，可根據牛隻族群規模與結構調整監測設計，而不是一套硬性的積分模板；舊版對所有國家較一體適用。[1][5]









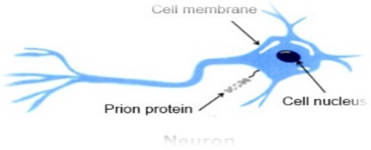


2023新BSE標準與舊版差異-3

三、疾病列管與「非典型 BSE」地位的改變

- 新版把「非典型 BSE」自 WOAH 列管疾病名單中移除，因此不再屬於必須「官方通報」的疾病；舊版將典型與非典型 BSE 一併列為需通報。[3][1]
- 目前僅「經典型 BSE」仍為 WOAH 列管並須通報的疾病，新版同時強調非典型 BSE 是「自發、極低率且對公衛與動物衛生影響有限」的事件；舊版在這一點的區分較不明確。[1][3]










2023新BSE標準與舊版差異-4

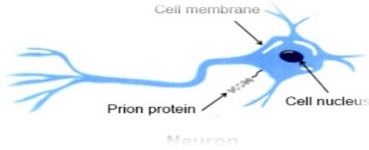
四、官方風險狀態認定與維持程序上的差異

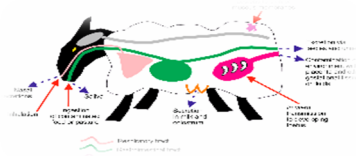
- 新版對既有「可忽略／受控 BSE 風險」會員進行了回溯評估，確認在新標準下仍然符合，特別是那些當初主要依「輸入風險可忽略」而非「暴露風險可忽略」取得地位的國家；舊版沒有這段過渡要求。[2][1]
- 新版配套了一套過渡期安排：2023 版標準於 2023 年 5 月總會通過後生效，但對官方風險申請／複確認程序給予約一年的準備期，讓會員國得以調整監測與管理措施；舊版當然沒有這項新過渡設計。[2]

五、貿易與風險溝通上的差異

- 新版更強調「當貨品依本章標準進口時，輸入國的 BSE 風險不受出口國風險狀態影響」的原則，以鼓勵在科學風險管理下避免過度貿易限制；舊版雖有相似精神，但文字與實務著墨較少。[4][1]
- 移除非典型 BSE 必通報義務，被視為減少不必要貿易限制的重要一環，避免因極少數非典型個案造成不成比例的貿易影響；舊版在實務上常引發這類爭議。[3][1]









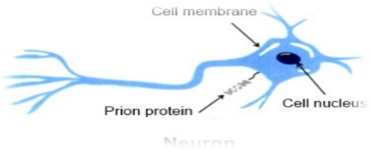


影片探討英國採用WOAH標準對抗牛海綿狀腦病的益處，強調國際科學共識提供了行動的合法性及信心，並增強了產業、消費者及政府官員的信任。

本段影片探討了在面對新興疾病時，缺乏共識的疾病控制標準所帶來的挑戰，並強調了建立標準的重要性。
- 影片提到在面對新興疾病時，研究人員需要努力理解病情的異常情況。}
- 強調目前缺乏一致的疾病控制標準，這使得應對新興疾病變得更加困難。}
- 人們尋求對疾病控制措施的信心和保證，顯示出標準化的重要性。}

本段影片探討了WOAH標準在英國對於牛海綿狀腦病（BSE）的重要性，強調國際間的協議與科學依據如何增強消費者及產業的信心。
- 成員國之間的協議對於應對BSE至關重要，因為這能夠確保行動的一致性。}
- BSE是一種新興疾病，相關標準的制定基於科學證據，這增強了國際接受度。}
- 這些標準不僅增強了產業和消費者的信心，也讓政府部門對於所採取的行動感到安心。}





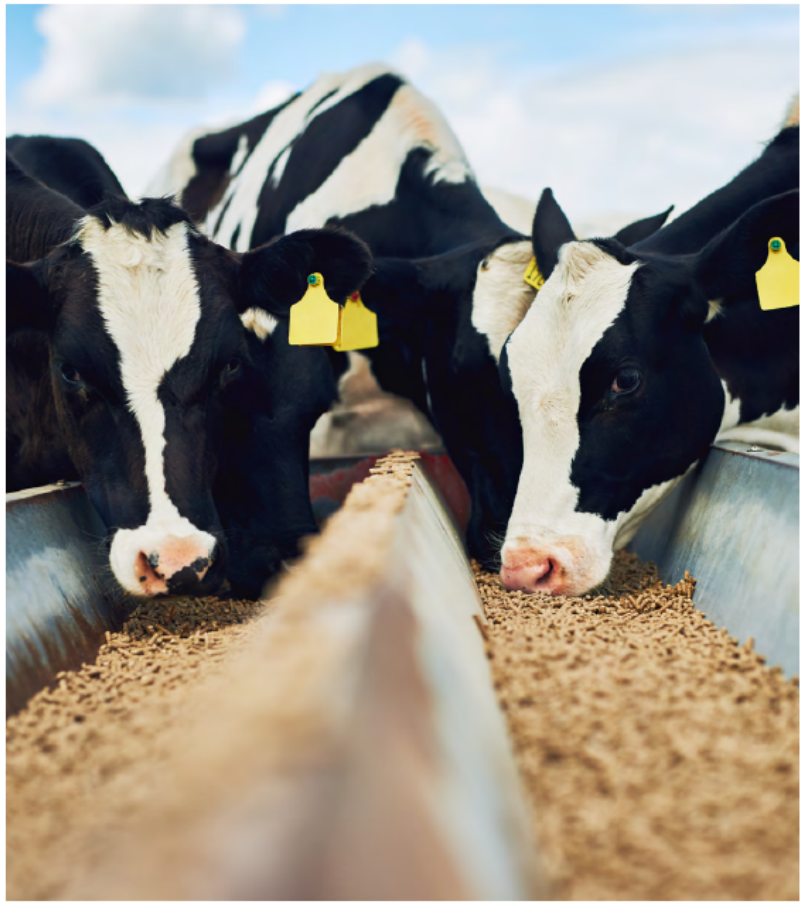






Guidelines for Targeted BSE Surveillance

July 2023



《Guidelines for Targeted BSE Surveillance》重點包括：

1. BSE監測目的

確保早期發現疑似BSE個案，以保護公共健康並維護出口市場信任。

2. 目標性監測對象

包括高風險族群，如：

1. 出現神經症狀的牛隻
2. 緊急屠宰牛（emergency slaughter animals）
3. 死亡牛（fallen stock）
4. 年齡超過一定標準的牛（依國家規範）

3. 採樣與實驗室檢測指引

1. 說明如何採集腦幹組織樣本（通常為延腦）
2. 標準檢測技術如快速試劑（rapid tests）、免疫組織化學染色、Western blot等

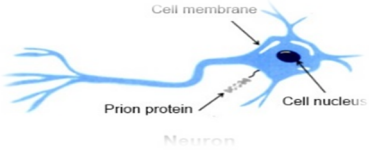
4. 資料紀錄與通報流程

建議的紀錄方式、報告格式與時效性要求。

5. 風險溝通與資訊透明

協助農民、業者與主管機關理解政策依據與回報機制，降低恐慌。



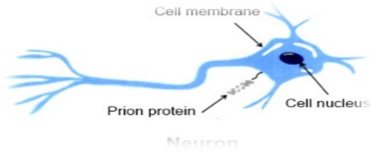


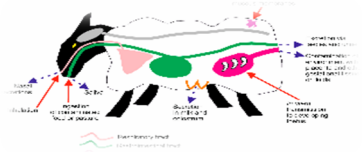





核心面向	舊版（OIE）	新版（WOAH 2023）	關鍵轉變
制度核心	Quantity-based surveillance	Risk-based surveillance	從「數量」→「風險」
監測方法	Points system（點數制度）	Targeted surveillance（目標族群）	從「統計」→「流行病學」
檢測策略	大量檢測（sample size）	高風險族群檢測	從「全面撒網」→「精準打擊」
目標動物	廣泛族群	臨床疑似、倒地牛、緊急屠宰、神經症狀牛	聚焦高風險
風險分類	靜態分類	動態風險評估（強調feed ban）	從「分類」→「系統運作」
官方認定	依賴檢測數量	系統性證據（監測＋飼料管理＋通報）	從「數據」→「制度」
貿易邏輯	國家風險主導	Safe commodities概念	從「國家」→「產品」
科學基礎	疫情高風險時代	疫情後期（post-epidemic）	反映全球風險下降
監測目標	證明無病存在	偵測殘存風險（residual risk）	思維轉換










2.

Targeting animals for BSE surveillance

(Article 11.4.20. Point 2 of the *Terrestrial Code*)

The objective of BSE surveillance is to detect the disease in the bovine population. Article 11.4.20 of the *Terrestrial Code* identifies those animals that should be reported and followed up with appropriate laboratory testing in accordance with the Terrestrial Manual to accurately confirm or rule out the presence of BSE. They are classified into four distinctive groups:

a. Bovines displaying progressive clinical signs suggestive of BSE.

b. Bovines showing behavioural or neurological signs at ante-mortem inspection at slaughterhouses or abattoirs.

c. Bovines presented as unable to rise or walk without assistance with an appropriate supporting clinical history (i.e. the presentation cannot be attributed to other common causes of recumbency).

d. Bovines found dead (fallen stock) with an appropriate supporting clinical history (i.e. the presentation cannot be attributed to other common causes of death).

These groups correspond to bovines that lie on the clinical spectrum of BSE, and have a higher probability of having BSE, if the disease was present in the country, compared to the general bovine population.

2.1 Bovines displaying progressive behavioural or neurological clinical signs suggestive of BSE

(Article 11.4.20. 2a of the *Terrestrial Code*)

Bovines displaying progressive clinical signs suggestive of BSE are those animals displaying progressive behavioural or neurological signs suggestive of BSE that are refractory to treatment. As part of the procedures and protocols in place covering all stages in the livestock production chain (Article 1.8.5.4 of the *Terrestrial Code*), an official veterinarian requires a detailed anamnesis to confirm that the bovine fits the criteria to be targeted for BSE surveillance, for example: 'an adult animal, the only one affected in the herd with a change in behaviour or temperament, sensation and/or posture/locomotion'.

A working knowledge of 'normal' bovine behaviour is required to know the range of normal behaviour, in particular in the early stages, where clear neurological abnormalities (e.g. incoordination) may not yet be manifest. If unsure and the welfare of the animal is not compromised (it is not recumbent or in obvious distress) it may be advisable to re-schedule another visit after 1-2 weeks to assess whether signs have progressed. This also enables the veterinarian to assess any effect of treatment or wait for blood test results to rule out other diseases if appropriate. It is important to note that BSE may be accompanied by other diseases (e.g. listeriosis and BSE or ketosis and BSE), although this is rare. The lack of response to treatment of any suspected disease and further disease progression may be indicative of BSE. The clinical signs should be documented, particularly if a re-visit is scheduled, using either a detailed clinical examination form (see Appendix 3 for an example) or a simple questionnaire with tick boxes for signs associated with BSE or conditions with similar signs, which is easier to analyse, to compare the frequency of signs with other conditions that may be confused with BSE (see Appendix 4 for an example).

BSE 監測之目標動物（Targeting animals for BSE surveillance）

（《陸生動物衛生法典》第11.4.20條 第2點）

BSE（牛海綿狀腦病）監測的目標，是在牛隻族群中偵測疾病的存在。

《陸生動物衛生法典》第11.4.20條指出，應通報並依據適當的實驗室檢測進行追蹤的動物，須能準確確認或排除BSE。這些動物可分為以下四類：

a. 出現進行性臨床症狀，且疑似為BSE之牛隻。

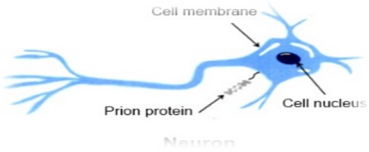
b. 在屠宰場於屠前檢查（ante-mortem inspection）時，出現行為或神經學異常之牛隻。

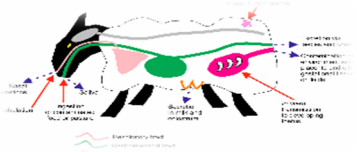
c. 無法自行站立或行走，且具相應臨床病史之牛隻（即其症狀無法歸因於其他常見倒臥原因）。

d. 發現死亡之牛隻（倒斃牛，fallen stock），且具相應臨床病史（即其死亡無法歸因於其他原因）。

上述族群代表處於BSE臨床表現範圍內之牛隻，相較於一般牛群，若該國存在BSE，其感染機率較高。











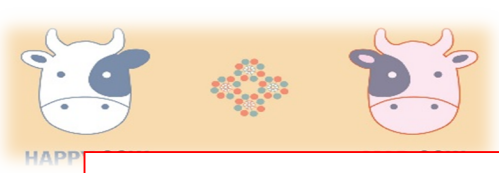
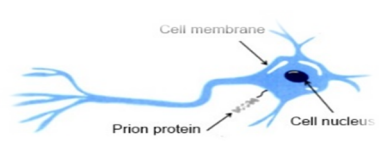
出現進行性行為或神經學症狀之牛隻（疑似BSE）

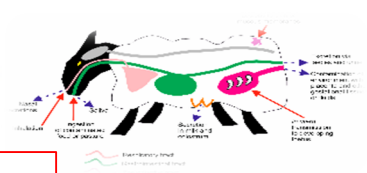
（《陸生動物衛生法典》第11.4.20條 2(a)）
出現進行性行為或神經學症狀，且對治療無反應之牛隻，即為疑似BSE病例。
依據畜牧生產鏈中之程序與規範（《陸生動物衛生法典》第11.8.54條），官方獸醫需進行詳細病史詢問（anamnesis），以確認該牛是否符合BSE監測目標。例如：
「一頭成年動物，僅個體受到影響，且出現行為、性情或姿勢／運動異常。」

對於「正常」牛隻行為的基本認識，是判斷異常的關鍵，尤其在疾病早期，明顯神經症狀（如運動失調）可能尚未出現。
若牛隻未處於衰弱或明顯壓力狀態（例如未倒臥），可安排於1－2週後再次訪視，以評估症狀是否持續進展。
此時亦可進行適當檢測（如血液檢查），以排除其他疾病。
需特別注意，BSE可能伴隨其他疾病（如李斯特菌症、BSE或酮症等），雖然此情況較為罕見。
對於疑似病例，若對治療無反應，且病程持續進展，均應詳細記錄。
特別是在安排複診時，建議使用：

- 詳細臨床檢查表（如附錄3），或
- 簡易問卷（勾選症狀）

以利後續分析、比較症狀出現頻率，並與其他可能與BSE混淆之疾病加以區分（參見附錄4）。







Appendix 3

Clinical examination forms with examples

Example 1

Animal No: 110110 654321 Farm: Owner:
Clinician:
Date:

- If normal: tick (✓)
- if abnormal: circle (◯ when listed) and describe in detail on following page if insufficient space in box
- if test not performed: cross out (X), and always indicate why if non-performance is due to the animal's reaction

ANIMAL FREE

Posture (head, neck, limbs, back)	Low head on occasions	
Walking (amount / willingness)	Stop and go	
Turning	✓	
Running (amount / willingness)	Trot: None	Gallop: None
OVERALL GAIT **Stiff/Lame** { (No) / Yes, describe: (No) / May be / Yes, describe: (No) / Yes, describe: **Neurological** **Other on gait**		
Slipping / Falling (describe if yes)	(No) / Yes _____	(No) / Yes _____
Obstacle (device: drain cover)	Hesitant to step over drain; sniffs a lot before crossing	
Acceptance of crush (going in)	Hesitant; needs to be pushed with force	

ANIMAL IN CRUSH

	Symmetry	Left	Right
Eye position (strabismus?)	✓		
Eyelid position (ptosis?)	✓		
Third eyelids (position)	✓		
Nose (sym. & movements to breath)	✓		
Menace response	Exaggerated (head toss)		
Ears (position and reaction to touch)	✓		
Blink (lateral & medial canthus)	✓		
Nose (reaction to touch)	✓		
Lips (sym. / reaction to touch: smile)	✓		
Eye movements	✓		
Sweat beads on muzzle	✓		
Salivation (✓, ↑, or ↑↑)	Increased after head tests		
Jaw position / Tongue tone	✓	✓	

臨床檢查表（含範例）

🟥 **範例 1**

動物編號：110110 654321
牧場：
飼主：
臨床檢查者：
日期：

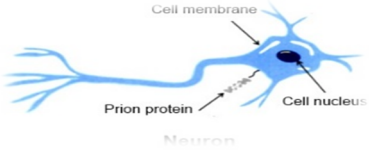
📌 **填寫說明**

- 若為正常：請勾選（✓）
- 若異常：請圈選（◯）（若有列出選項），並於空白處詳細描述（若空間不足請於下一頁補充）
- 若未執行該測試：請標示（✘），並說明原因（例如因動物反應無法進行）

🟦 動物自由活動觀察（ANIMAL FREE）

項目	結果
姿勢（頭部、頸部、四肢、背部）	偶爾低頭
行走（幅度／意願）	停走不定（走走停停）
轉彎	—
奔跑（幅度／意願）	小跑：無；疾跑：無







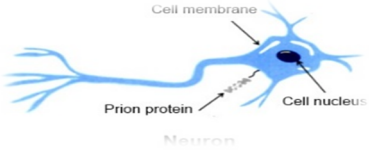



整體步態（OVERALL GAIT）

評估項目	結果
僵硬／跛行	無／有（請描述）
神經性異常	無／可能／有（請描述）
其他步態異常	無／有（請描述）

項目	結果
滑倒／跌倒（如有請描述）	無／有
跨越障礙（如排水溝）	猶豫跨越；跨越前頻繁嗅聞
驅趕反應（進入設施）	猶豫，需要強力驅趕







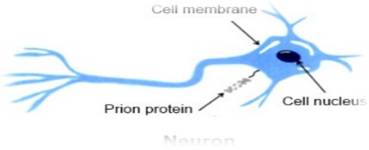




動物固定後檢查（ANIMAL IN CRUSH）

檢查項目	對稱性	左側	右側
眼球位置（斜視）	✓		
眼瞼下垂（ptosis）	✓		
第三眼瞼位置	✓		
鼻孔對稱性與呼吸動作	✓		
威嚇反應（menace response）	誇大（抬頭）		
耳朵（位置與觸覺反應）	✓		
眨眼反射與內眥反射	✓		
鼻部觸覺反應	✓		
唇部（觸覺反應／微笑反應）	✓		
眼球運動	✓		
出汗（正常／減少／增加）	✓		
流涎（正常／減少／增加）	頭部測試後增加		
下顎位置／舌張力	✓		✓











🟦 頭部固定檢查（HEAD RESTRAINED / HALTER）

檢查項目	對稱性	左側	右側
視神經／眼底（fundus）	未檢查（光線過亮）		
瞳孔光反射（直接與間接）	未檢查（光線過亮）		
角膜反射	✓		
皮膚軀幹反射（CT）與頸部針刺測試（NP）	CT：✓		NP：緊張（甩頭、發聲）
尾巴張力／肛門張力	✓		✓

HEAD RESTRAINED/ HALTER

	Symmetry	Left	Right
Optic nerve / fundus	Not examined (too bright)		
Light reaction (direct & consensual)	Not examined (too bright)		
Corneal reflex	✔		
Cutaneous trunci (CT) **& neck prick** (NP)	CT: ✔	NP: nervous (head toss), vocal	
Tail tone / anal tone	✔	✔	

OVERALL ASSESSMENT

Mental status ✔ (normal), dull, depressed, 'hyper', etc.	Hyper, seems very alert, constantly moving ears	
Behaviour & reactivity free ✔ (normal), excited, playful, fearful, nervous, friendly, boisterous, dangerous, 'hyper', active, quiet etc.	Nervous, startles frequently, e.g. when bird flew over, when sniffing crush	
Behaviour in crush ✔ (normal), quiet, restless, agitated, agitated 1st then settled down, never settled down, frantic, etc.	Head toss when approached from front; generally restless	
Behaviour Head restraint (HR) & Head tests (HT)	HR: Nervous, head tossing	HT: Nervous, head tossing
Clipboard test "	Body flinch 5x	
Bang test (BT) **/ Hand Clap** (HC)	BT: No reaction	HC: No reaction
Flash test	Not tested (too bright)	
Flexible stick test	Forceful kicking (only tried 2x)	
Tremors	No / Yes, describe: Fine head tremor when undisturbed in crush	
Scratch test	✔	

🟦 整體評估（OVERALL ASSESSMENT）

🧠 精神狀態（Mental status）

（正常、遲鈍、憂鬱、過度興奮等）

👉 過度興奮，警覺性高，耳朵持續活動

行為與反應（自由狀態）

（正常、興奮、活潑、恐懼、緊張、友善、躁動、危險、過動、安靜等）

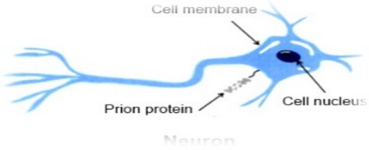
👉 緊張、易受驚嚇（例如鳥飛過、接近保定架時）

🧱 保定狀態下行為（Behaviour in crush）

（正常、安靜、不安、激動、對壓力反應強、無法安定、狂躁等）

👉 從前方接近時會甩頭；整體呈現不安











🔍 頭部限制與測試反應（Head restraint & tests）

項目	結果
HR（頭部固定）	緊張、甩頭
HT（頭部測試）	緊張、甩頭

🧪 行為測試（Behavioural tests）

測試項目	結果
櫃門測試（Clipboard test）	身體閃避 5 次
敲擊測試（Bang test）／拍手測試（Hand clap）	無反應
閃光測試（Flash test）	未執行（光線過亮）
柔性棒測試（Flexible stick test）	嘗試踢擊（2 次）

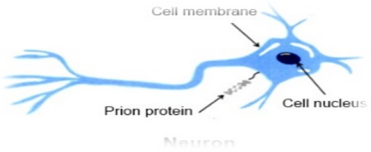
🌊 震顫與感覺（Neurological signs）

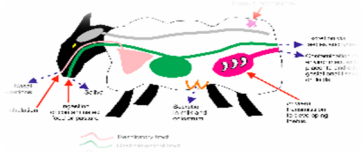
項目	結果
震顫（Tremors）	無／有（描述）：在保定狀態下出現輕微頭部顫抖
抓癢測試（Scratch test）	✓

「典型 BSE 神經行為異常組合」：

- 高警覺＋過度反應（hyperesthesia）
- 易受驚嚇（startle response ↑）
- 行為不穩定（restlessness）
- 頭部動作異常（head tossing）
- 輕微神經症狀（tremor）











Example 2

Animal No: 110110 654321 Date:

GENERAL EXAMINATION

Temperature: 38.7°C Mucous membranes: ✔

Heart rate: 56 bpm despite restlessness Lymph nodes: ✔

Ruminal Contractions: ✔ Body condition: Good (3)

Dehydrated? ✔

Additional/ extraneural findings: grazes on hind legs

Behaviour in pen prior to exam: very alert, following every move; separated from others as becoming aggressive towards other cows

Status: ( ) BSE not suspected
(✔) Maybe BSE
( ) BSE suspect

TO DO:

Action	Date completed	Result
Bloods taken: EDTA, Serum	01 July 2022	
Urine taken:		
Skin scraping (location):		
Video of (describe):	01 July 2022	Behaviour in pen
Still photograph of (describe):		
Other:		Reschedule visit in 14 days to check for clinical progression

🟦 範例 2（Example 2）

動物編號：110110 654321
日期：

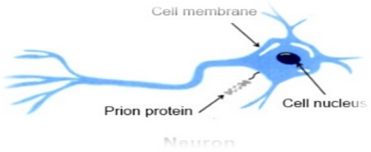
🟦 一般檢查（GENERAL EXAMINATION）

- **體溫**：38.7˚C
- **心跳速率**：56 bpm（在不安狀態下仍偏低）
- **瘤胃蠕動**：✓ 正常
- **脫水狀態**：✓ 無
- **黏膜**：✓ 正常
- **淋巴結**：✓ 正常
- **體況評分（BCS）**：良好（3分）

🟥 其他（非神經性）發現

👉 後肢有擦傷











🟦 待辦事項（TO DO）

🌱 臨床判讀亮點

👉 此案例呈現的是「早期或非典型 BSE 懷疑個案」：

- 無明顯全身性異常（體溫、瘤胃正常）
- 行為異常為主要線索（攻擊性＋過度警覺）
- 尚未進入明顯神經症狀期

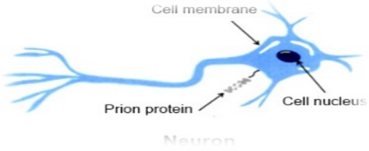
項目	完成日期	結果
血液採樣（EDTA、血清）	2022年7月1日	—
尿液採樣	—	—
皮膚刮取（部位）	—	—
影像紀錄（影片）	2022年7月1日	圍欄內行為
靜態照片（描述）	—	—
其他	—	14天後回診追蹤臨床進展

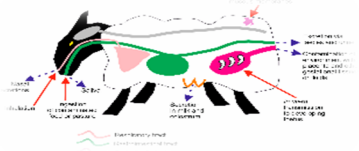
臨床判讀亮點（給您教學／演講用）

👉 此案例呈現的是「早期或非典型 BSE 懷疑個案」：

- 無明顯全身性異常（體溫、瘤胃正常）
- 行為異常為主要線索（攻擊性＋過度警覺）
- 尚未進入明顯神經症狀期











Appendix 4

Example of a questionnaire on the clinical presentation of reported suspect BSE cases

Clinical signs observed by veterinary officer.
(Please enter 'X' in appropriate box(es) if observed. If only reported by farmer and not observed by veterinary officer, enter 'R')

Disorders of behaviour and personality

Apprehension		Ear twitching		Kicking in parlour	
Hypersensitivity		Ear held at odd angles		Reluctance to go into parlouror through doorways	
Touch					
Sound					
'Maniacal'		Abnormal behaviour		Head pressing	
Panic striken		Head shyness		Head rubbing	
Temperament change		Licking of flank		Teeth grinding	
Abnormal head carriage		Licking of nose		Other	

Locomotor/Neurological signs

Blindness		Falling		Recumbency	
Circling		Paresis		Tremors	
Hindleg ataxia		Foreleg ataxia		Knuckling of fetlock	

General signs

	Decrease	No change	Increase	Not applicable
Weight				
Condition				
Milk yield				

Initial signs:

Clinical progression:

Other comments:

附錄 4

疑似 BSE 病例臨床表現問卷範例

臨床症狀紀錄說明

由獸醫師觀察到的臨床症狀：

- 若有觀察到，請於適當欄位填寫「X」
- 若僅由飼主回報但未經獸醫觀察，請填寫「R」

行為與性格異常（Disorders of behaviour and personality）

類別	症狀
焦慮／警覺（Apprehension）	耳朵抽動（ear twitching）、在擠奶室踢腿
過度敏感（Hypersensitivity）	耳朵異常姿勢、對觸覺敏感、對聲音敏感、拒絕進入擠奶室（特別是門口）
躁動（Maniacal）	異常行為
驚恐反應（Panic stricken）	頭部畏縮（head shyness）、頭部壓迫（head pressing）、頭部摩擦（head rubbing）
性情改變（Temperament change）	舔舐側腹、磨牙
異常頭部姿勢（Abnormal head carriage）	舔鼻、其他









這張圖清楚呈現了針對牛海綿狀腦病（BSE）的目標性監測從**動物出現異常→通報→檢測→確認或排除疾病**的完整流程。

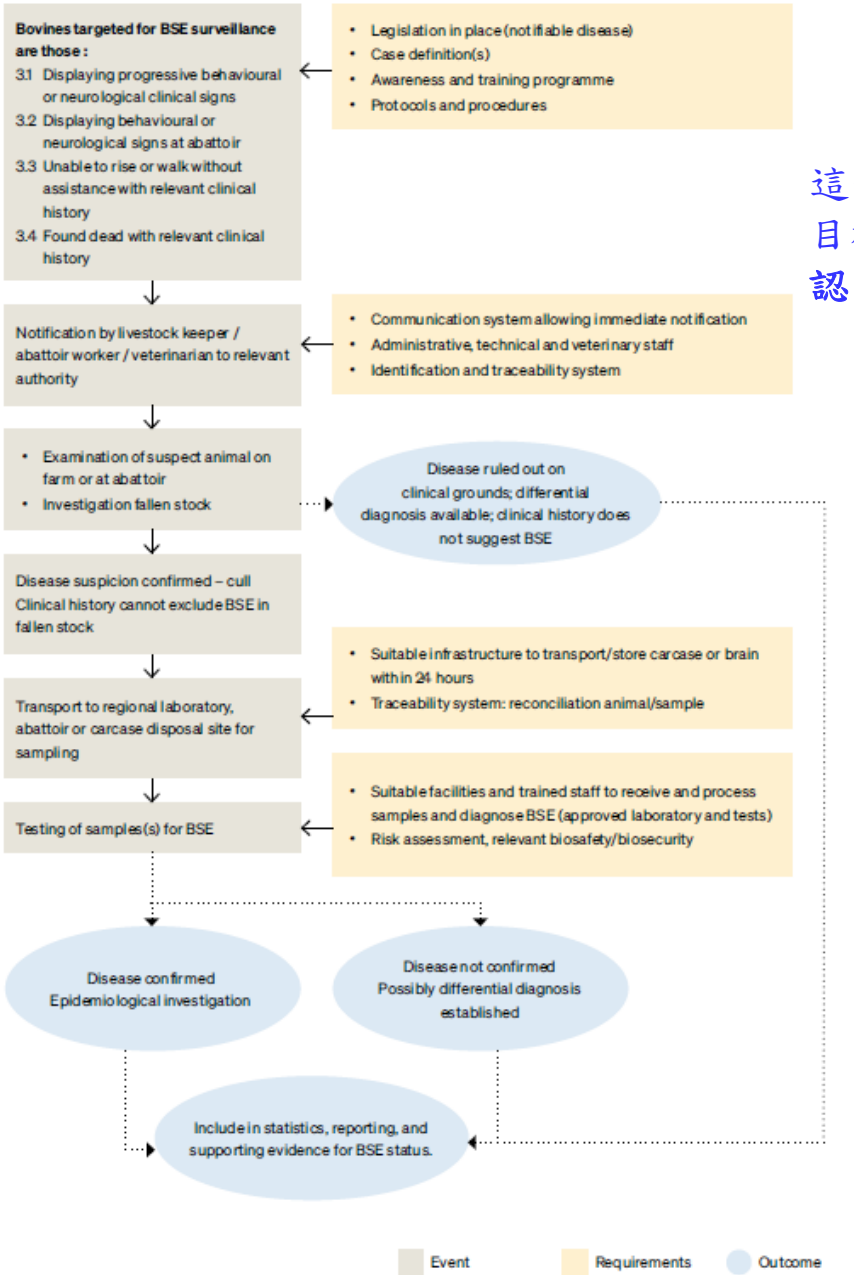
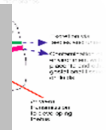
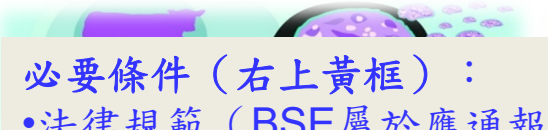


Figure 1. 可信賴BSE監測系統的流程總覽圖

Overview of the flow of the components of a credible surveillance system to detect BSE cases







1. 監測對象（左上灰色區塊）

監測對象的牛隻類型包括：

- **3.1** 有進行性行為或神經異常症狀的牛
- **3.2** 在屠宰場出現上述異常的牛
- **3.3** 無法站立或行走，且有相關臨床病史的牛
- **3.4** 有臨床病史的死亡牛

必要條件（右上黃框）：

- 法律規範（BSE屬於應通報疾病）
- 明確病例定義
- 教育訓練與通報程序

Bovines targeted for BSE surveillance are those :

3.1 Displaying progressive behavioural or neurological clinical signs

3.2 Displaying behavioural or neurological signs at abattoir

3.3 Unable to rise or walk without assistance with relevant clinical history

3.4 Found dead with relevant clinical history

- Legislation in place (notifiable disease)
- Case definition(s)
- Awareness and training programme
- Protocols and procedures

↓

Notification by livestock keeper / abattoir worker / veterinarian to relevant authority

- Communication system allowing immediate notification
- Administrative, technical and veterinary staff
- Identification and traceability system

↓

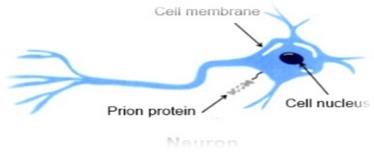
2. 疑似通報與初步檢查

- 畜牧業者、屠宰場員工或獸醫應通報給主管機關
- 執行現場檢查或對死亡動物進行調查

通報系統應具備：

- 即時通報機制
- 專業行政與獸醫團隊
- 個體識別與可追溯系統











- Examination of suspect animal on farm or at abattoir
- Investigation fallen stock

Disease ruled out on clinical grounds; differential diagnosis available; clinical history does not suggest BSE

Disease suspicion confirmed – cull
Clinical history cannot exclude BSE in fallen stock

Transport to regional laboratory, abattoir or carcase disposal site for sampling

- Suitable infrastructure to transport/store carcase or brain within 24 hours
- Traceability system: reconciliation animal/sample

Testing of samples(s) for BSE

- Suitable facilities and trained staff to receive and process samples and diagnose BSE (approved laboratory and tests)
- Risk assessment, relevant biosafety/biosecurity

Disease confirmed
Epidemiological investigation

Disease not confirmed
Possibly differential diagnosis established

🔍 **3. 初步診斷與樣本採集**

- 若無法排除BSE，確認為疑似病例，應**人道撲殺**
- 將屍體或腦部樣本**24小時內送達合格實驗室或處理場**

🟡 **必要基礎設施：**

- 可冷藏保存樣本/腦部的設備
- 動物樣本追蹤整合系統

🧪 **4. 實驗室檢測**

- 採用已認可實驗室與檢測法進行確認
- 符合生物安全與風險評估要求

🟡 **要求條件：**

- 具備訓練有素的人員與設施
- 落實生物安全與風險管理



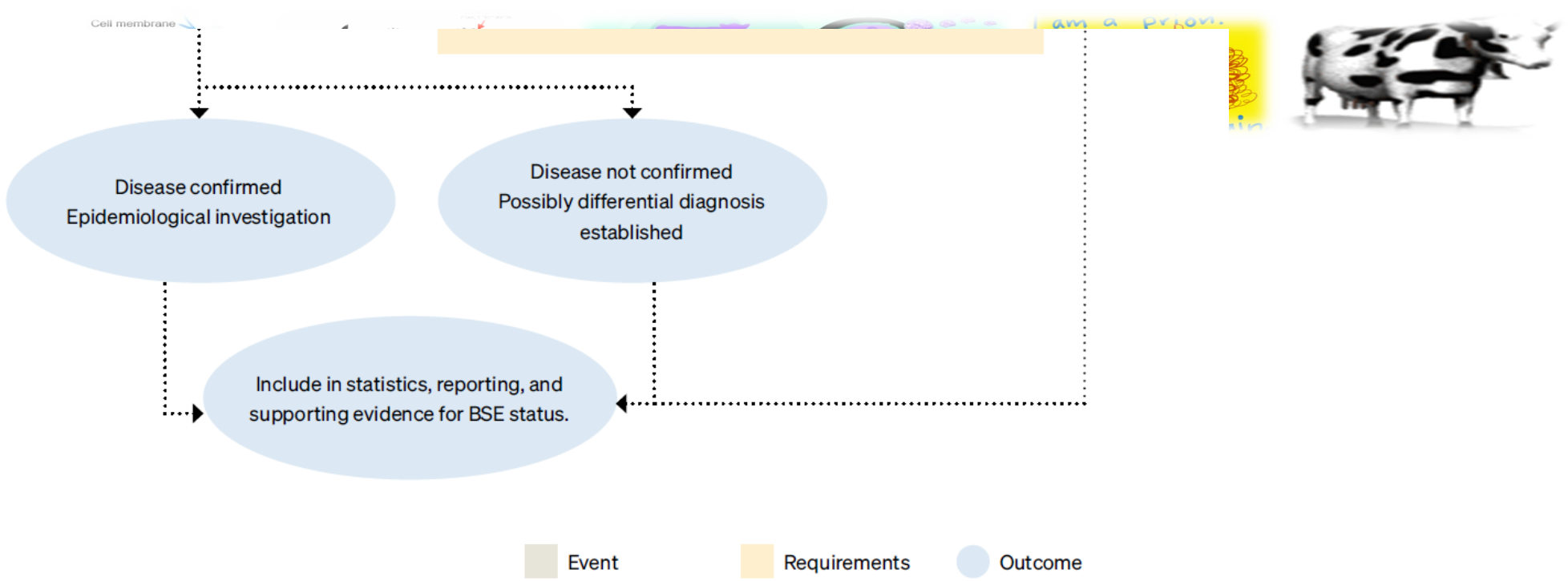
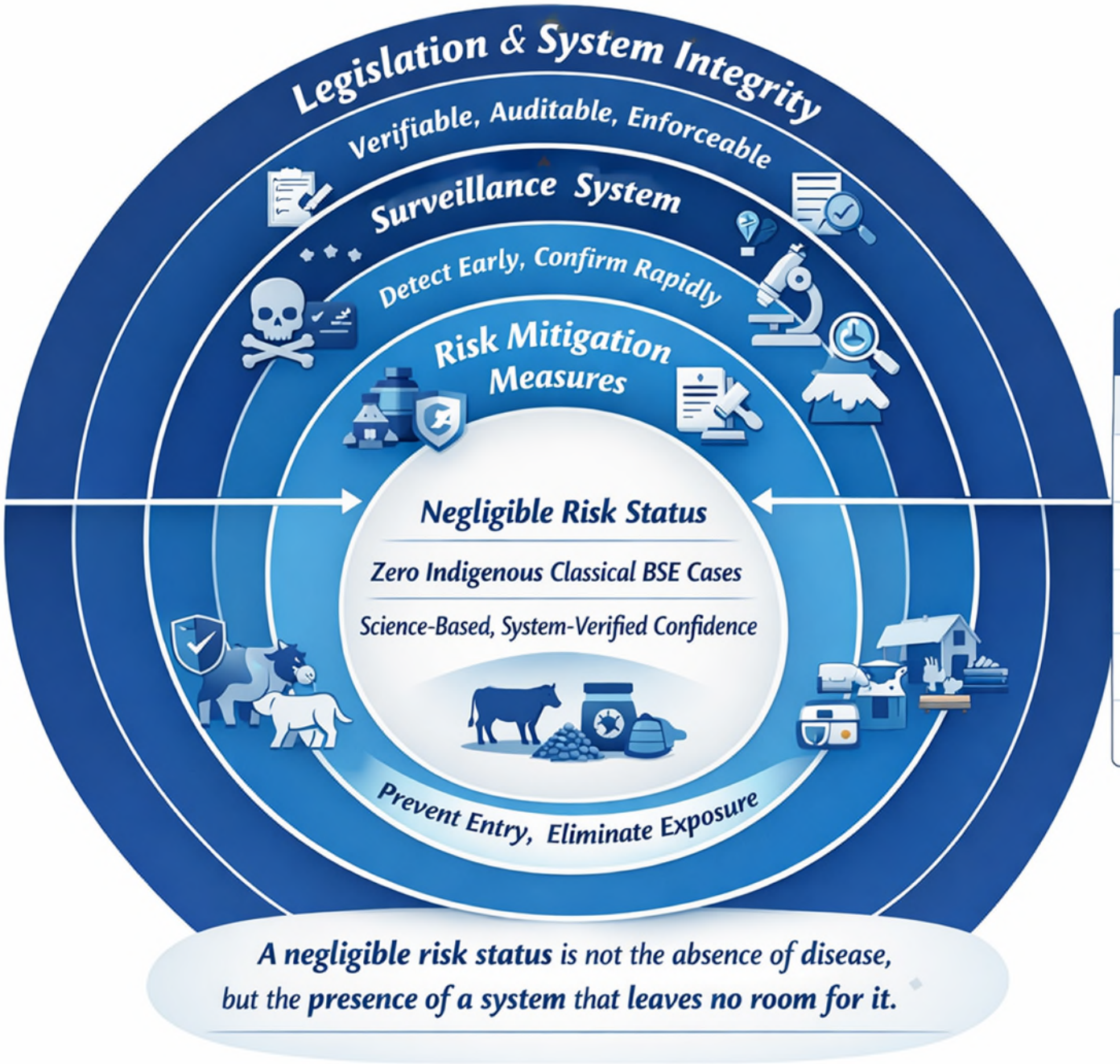


Figure 1.
Overview of the flow of the components of a credible surveillance system to detect BSE cases

✅ 5. 結果與後續處理（底部三個藍色圓形）

1. 若確認為BSE：
    1. 立即進行流行病學調查
2. 若未確認為BSE：
    1. 可考慮為其他差異性診斷（如神經性疾病等）
3. 所有結果：
    1. 都應納入統計、通報與提供國家BSE狀態佐證資料

顏色	代表內容
灰色區塊	流程步驟（事件）
黃色區塊	系統性要求
藍色橢圓形	結果與結論（Outcome）



WOAH 2023 Alignment	
WOAH Requirement	Taiwan Implementation
Entry Risk Assessment	Border Control System
Exposure Risk Assessment	Feed Ban & Segregation
Simplified Surveillance	Targeted Surveillance
SRM Control	Slaughterhouse Removal
Documentation	Integrated Traceability

台灣申請WOAH BSE風險可忽略國之管控策略圖

WOAH BSE 標準新舊版本實務對照表（舊版 vs 2023 新版 vs 台灣現況）-1					
參考依據：WOAH 陸生動物衛生法典第11.4章（2023版）｜BSE目標性監測指引（2023.07）｜WOAH Q&A（2023.04）					
項目類別	評估面向	舊版要求（2019年以前）	新版要求（2023版）	台灣現況說明	符合狀態
風險評估架構	整體評估架構	以「已具備管制措施＋監測資料」為核心，由WOAH依據申請文件判定風險狀態；未強制要求四步驟風險評估架構。	明確要求提交完整BSE風險評估，包含四大步驟： ①輸入風險（Entry） ②暴露風險（Exposure） ③後果評估（Consequence） ④風險整合（Risk Estimation）	目前台灣配合WOAH要求，已建立風險評估體系，歷年向WOAH申請維持「已控制BSE風險國」地位均有文件支持	⚠️ 需強化說明
	風險狀態起始日期	核定「可忽略/受控」的基準年沒有嚴格要求須明示；審查較具彈性。	必須在申請文件中明確標示「BSE再循環風險可忽略的起始日期」，並科學論證選定該日期的依據（連結飼料禁令、渲染改革等時間點）。	台灣應明確載明起始年份（例如1998年禁止反芻動物蛋白飼料生效年），並在申請文件中呈現。	⚠️ 需強化說明
監測系統	監測架構	採「積分制（Point-based）監測系統」： 依牛隻年齡與風險群（健康屠宰、臨死前屠宰、死亡、神經症狀）設定年度採樣積分目標，每頭採樣依年齡計算積分，達到門檻才算合格。	廢除積分制，改採「目標性監測（Targeted Surveillance）」： 以族群規模與流行病學情境為基礎，設計監測方案；採樣重點為「高風險群（神經症狀、臨死前屠宰、死廢牛）」。	台灣已依新版指引轉換為目標性監測架構，每年公告監測計畫並執行?	⚠️ 需強化說明
	採樣對象優先順序	高、中、低風險群均列入積分計算，即使健康屠宰牛亦需大量採樣才能累積積分達標。	明確要求以高風險群為優先： ①神經症狀牛 ②緊急屠宰/臨死前屠宰牛 ③死廢牛 健康屠宰牛優先順序最低。	台灣已調整監測程序，優先針對高風險群進行主動監測健康屠宰監測量相對減少，符合新版精神?。	⚠️ 需強化說明
	小牛群國家可行性	積分制對牛群規模小的國家（如台灣）造成極大壓力，需採大量樣本才能達標，造成執行困難。	目標性監測依族群規模彈性設計，小牛群國家只要高風險群監測完整，即可符合要求，無須強制大量採樣。	台灣牛隻族群規模相對小，新制對台灣較為有利，監測負擔顯著降低。	✅ 受益改變
	年度報告義務	每年提交監測結果報告至WOAH，用於複確認風險狀態。	維持每年複確認義務，但報告格式配合新版風險評估框架調整，需涵蓋：監測執行摘要、風險因素變化、新增病例調查（若有）。	台灣每年向WOAH提交複確認文件，農業部動植物防疫檢疫署主責。	✅ 已符合
資料來源：WOAH Terrestrial Code Ch.11.4（2023）｜BSE Targeted Surveillance Guidelines（2023.07）｜WOAH Q&A（2023.04） ｜製表日期：2026-04-08					
圖例說明：🟡 舊版要求（黃底） 🟢 新版要求（綠底） 🟠 台灣現況（橘底） ✅ 已符合 ⚠️ 需補充/強化					

WOAH BSE 標準新舊版本實務對照表（舊版 vs 2023 新版 vs 台灣現況）-2

參考依據：WOAH 陸生動物衛生法典第11.4章（2023版）｜BSE目標性監測指引（2023.07）｜WOAH Q&A（2023.04）

項目類別	評估面向	舊版要求（2019年以前）	新版要求（2023版）	台灣現況說明	符合狀態
疾病列管	非典型BSE通報義務	「典型BSE」與「非典型BSE（L型、H型）」均列為WOAH法定通報疾病；發現非典型病例須官方通報，實務上常引發貿易限制爭議。	非典型BSE自WOAH列管疾病名單中移除，不再需要官方通報；WOAH認定非典型BSE屬「自發性、極低率事件，對公衛與動物衛生影響有限」。	台灣依新版規範，非典型BSE無需通報；典型BSE仍為國內法定動物傳染病，須向WOAH通報	✅ 已符合
	典型BSE通報	發現任何BSE病例（典型/非典型）均需通報，並啟動疫情調查程序。	僅典型BSE仍為WOAH列管及通報疾病，發現本土新病例將影響風險狀態，須啟動完整流行病學調查。	台灣迄今無本土典型BSE確診案例，維持零案例紀錄是「可忽略風險」地位的重要基礎。	✅ 維持紀錄
飼料禁令	禁令範圍	要求「禁止反芻動物飼餵反芻動物來源蛋白（MBM）」，必須有法規明文規定且確實執行。	要求維持相同原則，並在Exposure assessment中說明： ①禁令法源與實施日期 ②執法機制（查核頻率、違規案件數） ③宣導成效（業者知悉程度）	台灣自1998年起明令禁止牛隻飼料添加反芻動物來源蛋白，農業部每年執行飼料稽核，無違規案件紀錄。	✅ 已符合
	交叉污染預防	有提及須防止交叉污染，但未要求在申請文件中詳細說明飼料廠的防控措施細節。	新版要求在Exposure assessment中詳細說明： ①飼料廠是否同線生產牛飼料與含MBM飼料 ②清洗/分線/排程預防交叉污染措施 ③官方稽核頻率與結果	台灣飼料廠管理納入《飼料管理法》飼料廠須標示原料成分，農業部定期稽查，但詳細交叉污染防控說明仍需補強於申請文件中	⚠️ 申請文件需補充
化製與高感染性組織	化製標準	要求化製達133°C、20分鐘、3 bar滅活條件，或等效替代程序。	維持相同技術標準，但新版在Exposure assessment中要求明確說明： ①化製廠採用之溫度/壓力/時間 ②是否有等效程序及依據 ③死廢牛進入渲染廠的管道與覆蓋率	台灣化製廠依規定需符合高溫高壓滅活條件，死廢牛回報與集中處理由縣市政府配合管理。	⚠️ 申請文件需補充

資料來源：WOAH Terrestrial Code Ch.11.4（2023）｜BSE Targeted Surveillance Guidelines（2023.07）｜WOAH Q&A（2023.04）　｜製表日期：2026-04-08

圖例說明：🟡 舊版要求（黃底）　🟢 新版要求（綠底）　🟠 台灣現況（橘底）　✅ 已符合　⚠️ 需補充/強化

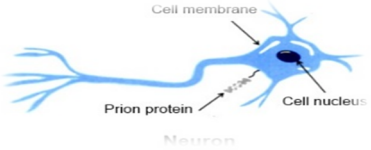
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項目類別	評估面向	舊版要求（2019年以前）	新版要求（2023版）	台灣現況說明	符合狀態
	特定危險組織（SRM）去除	要求將SRM（腦、脊髓、眼睛、扁桃腺、遠端迴腸）排除於食品/飼料鏈之外。	維持SRM排除要求，新版另要求在Consequence assessment中說明：若SRM意外進入飼料鏈，在現行管制下BSE擴散的可能性評估。	台灣未規定屠宰時須去除SRM，且禁止作為食品或飼料原料；執行面由屠宰衛生稽查負責。	⚠️ 申請文件需補充
輸入風險管理	活牛進口管理	要求說明進口牛隻的來源國風險狀態與頭數，但未強制要求8年時間框架。	Entry assessment要求回溯最近8年： ①進口牛隻頭數、來源國、用途（肥育/乳牛/屠宰） ②來源國BSE風險狀態 ③是否有SRM接觸史	台灣進口活牛極少主要來源國均為WOAH認可之低風險國（澳洲、紐西蘭）；相關紀錄完整，輸入風險極低	✅ 風險極低
	反芻動物蛋白粉進口	需說明是否禁止進口MBM及相關商品，但文件細節要求較少。	Entry assessment要求列明： ①近8年MBM進口量 ②用途（飼料/肥料） ③去向（直接施用/轉售給牛場） ④含MBM肥料施用於牧草地情形	台灣禁止進口含反芻動物蛋白的牛用飼料，含MBM肥料之使用限制需在申請文件中說明清楚	⚠️ 申請文件需補充肥料部分
貿易與風險溝通	貿易安全保障	有基本貿易安全原則，但對「貿易不應受進口國BSE狀態影響」的闡述較不清晰。	新版強調：依第11.4章規範的商品進口，輸入國的BSE風險不受出口國風險狀態左右；目的是減少以BSE為由的不合理貿易限制。	台灣進口牛肉依WOAH標準核可，2023年新版可作為台灣拓展牛肉貿易的科學依據。	✅ 利於台灣貿易
	非典型BSE對貿易影響	非典型BSE發現即需通報，實務上常引發對應國家採取進口禁令，損失重大。	非典型BSE不再通報，可大幅減少因極個案引發不必要貿易限制；維護出口國和進口國的貿易穩定性。	台灣目前無出口牛肉，此改變對台灣影響較小；但在引進牛肉進口評估時可適用此原則對出口國進行合理評估	✅ 適用性參考

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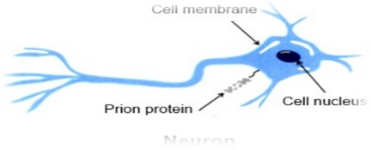






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過渡期安排	既有風險認定之效力	無過渡期特別規定。	WOAH確認：2023年前已取得官方風險認定的會員國，在新標準下其認定效力維持；但複確認文件需依新格式提交。	台灣「可控制BSE風險國」地位依然有效，惟後續年度複確認需符合2023版新格式，包含四步驟風險評估摘要	⚠️ 複確認格式需更新
資料來源：WOAH Terrestrial Code Ch.11.4（2023）｜BSE Targeted Surveillance Guidelines（2023.07）｜WOAH Q&A（2023.04） ｜製表日期：2026-04-08					
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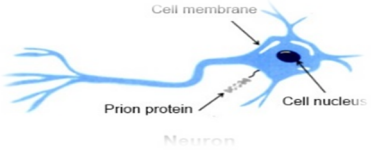


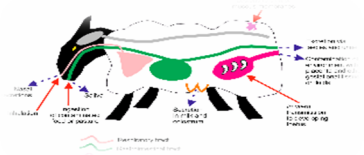


牛海綿狀腦病（BSE）_神經症狀_運動能力改變





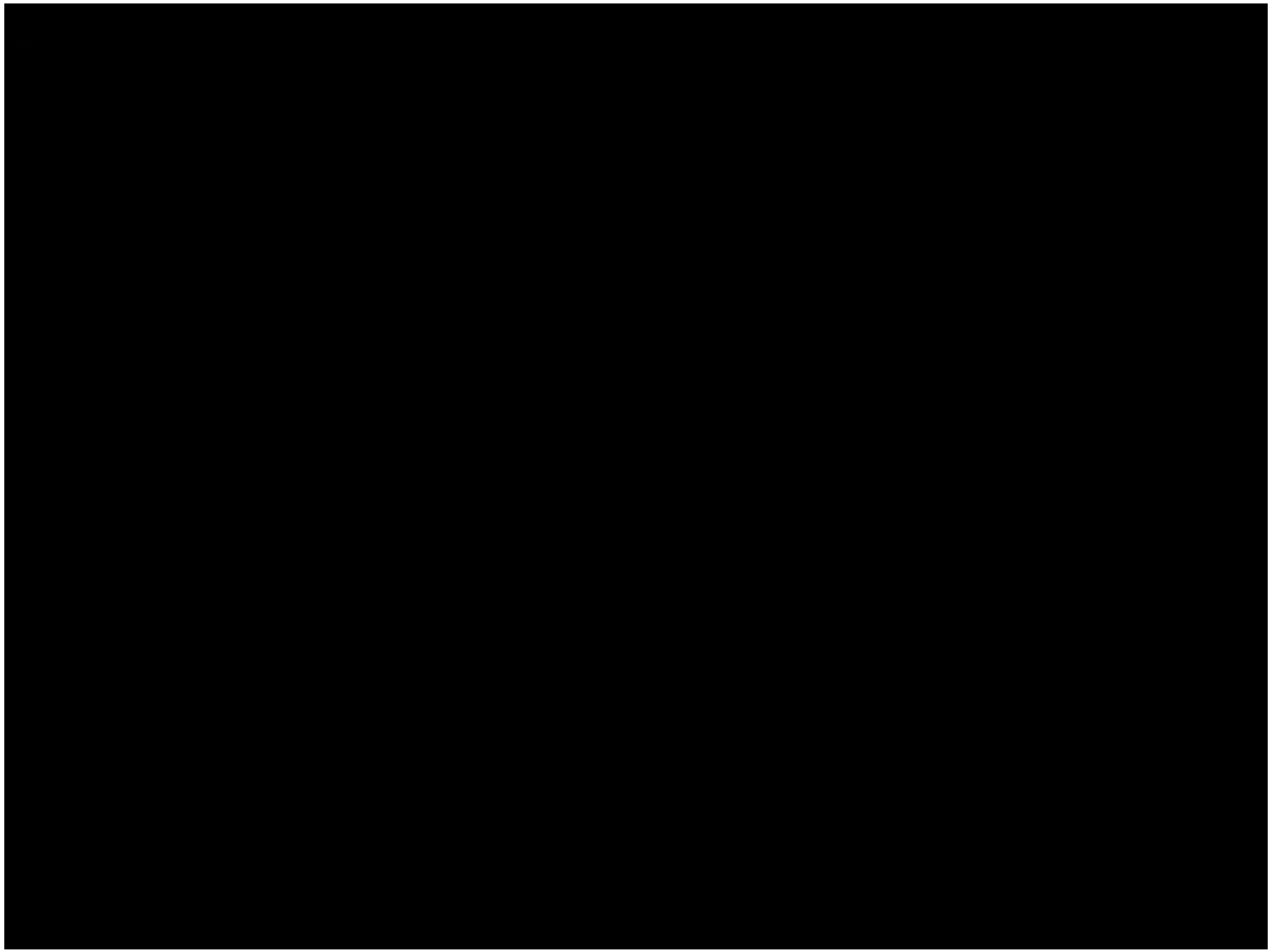




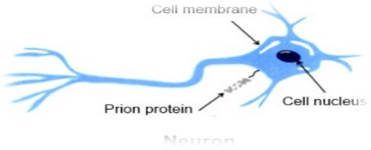




牛海綿狀腦病（BSE）神經症狀_行為改變





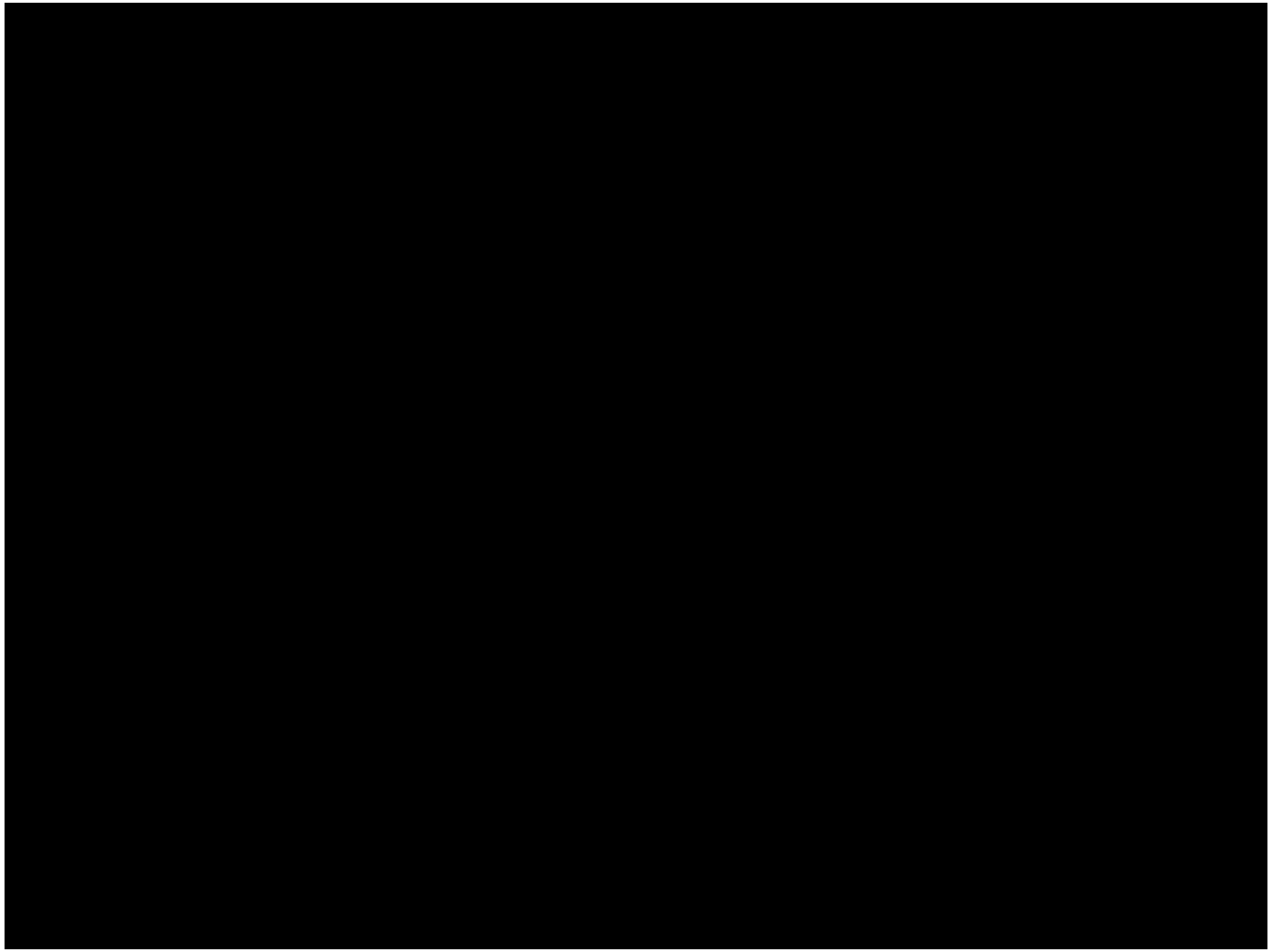




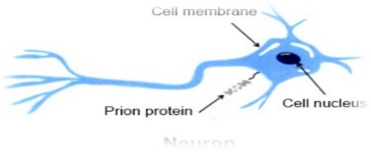


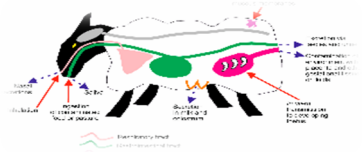


牛海綿狀腦病（BSE）神經症狀_感覺障礙





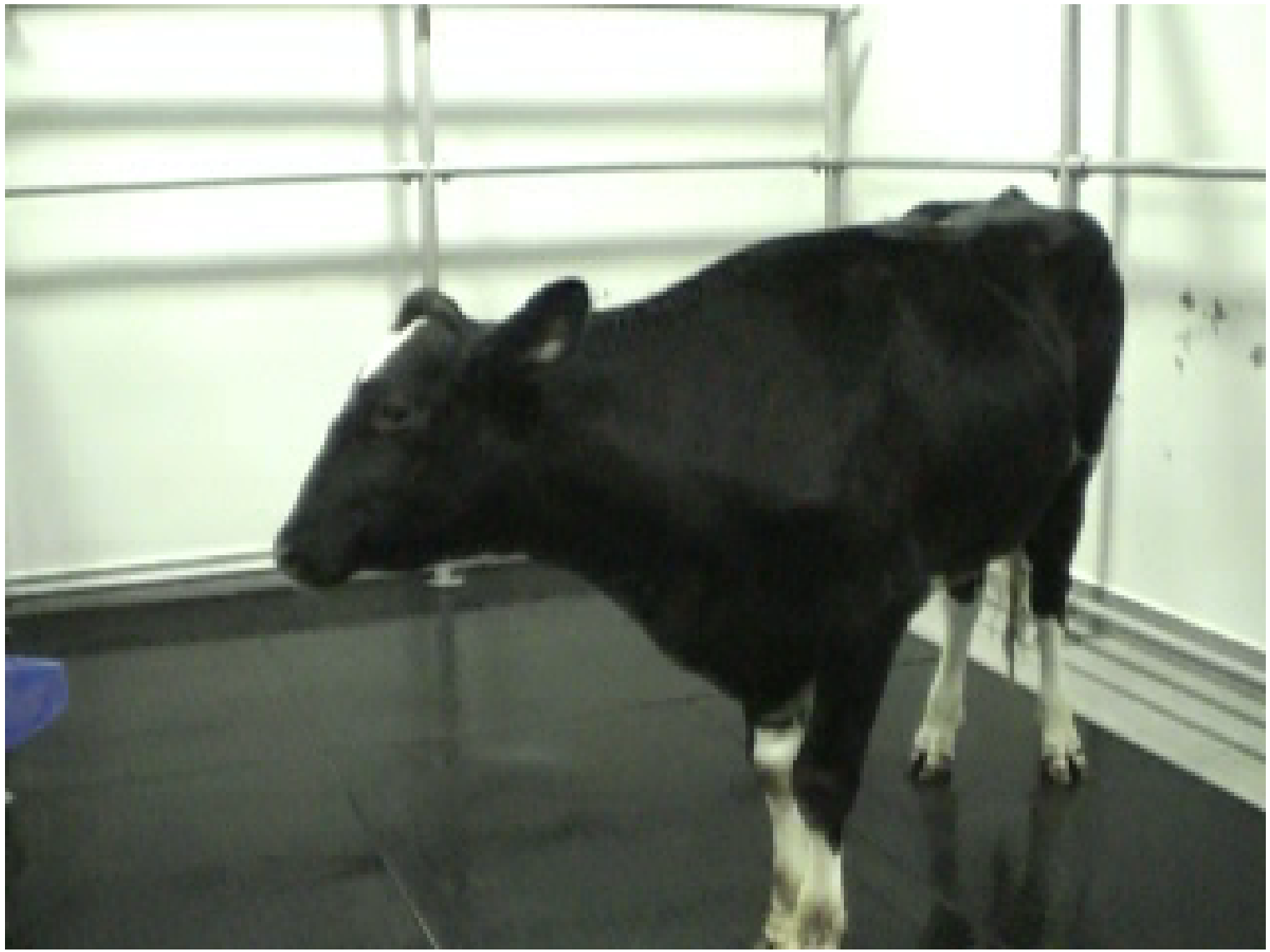






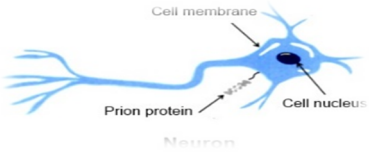


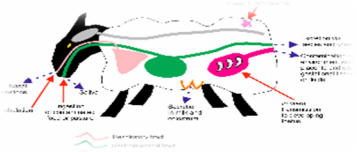
牛海綿狀腦病（BSE）神經症狀_日本



疾病分類	疾病名稱	行為與人格障礙	抽搐	視覺功能障礙	腦神經障礙	頭部傾斜或平衡異常	肌肉痙攣與破傷風症狀	昏迷與意識狀態改變	協調功能障礙	肢體無力或運動失調	止癢或自殘行為	來源
牛海綿狀腦病	牛海綿狀腦病 (BSE)	V	無	無	無	無	V	V	V	V	V	1
感染性	狂犬病 (Rabies)	V	V	無	V	無	無	V	無	無	V	1
佔位性病變	膿瘍 (Abscesses)	V	V	V	V	V	V	V	V	V	無	1
物理性	頭部外傷 (Head trauma)	V	V	V	V	V	V	V	V	無	無	1
營養性	維生素B1缺乏性腦皮質壞死 (Thiamine responsive CCN)	V	V	V	V	無	V	V	無	V	無	1
中毒	鉛中毒 (Lead poisoning)	V	V	V	V	無	V	V	無	V	無	1
家族與先天性	牛蠟樣質脂褐質沉積症 (Bovine ceroid lipofuscinosis)	V	V	V	無	無	無	V	無	V	無	1
家族與先天性	全身性糖原蓄積症 (Generalised glycogenosis)	V	V	V	無	無	無	V	無	V	無	1
代謝性	低鎂血症 (Hypomagnesemia)	V	V	無	無	無	V	V	無	V	無	1
感染性	李斯特菌症 (Listeriosis)	V	無	無	V	V	無	V	無	無	無	1
家族與先天性	甘露糖苷貯積症 (Mannosidosis)	V	無	無	無	無	無	無	無	無	無	1
家族與先天性	內斜視 (Convergent strabismus)	無	無	無	V	無	無	無	無	無	無	1











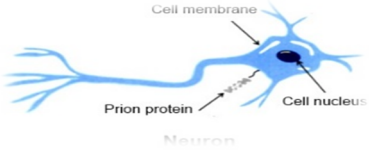
Guidelines for Targeted BSE Surveillance

附錄 2：與狂牛症 (BSE) 鑑別診斷相關的神經系統疾病

表一：神經系統異常之主要臨床症狀分類

症狀群組	包含之臨床症狀 (英文)	臨床症狀翻譯 (中文)
發作與痙攣	Seizures, Opisthotonos, Coma, muscle spasm, tetany, tremor	癲癇發作、角弓反張、昏迷、肌肉痙攣、強直性痙攣、震顫
腦神經與前庭視覺異常	Cranial nerve disorders (including strabismus and dysphagia), Head tilt, circling, nystagmus and other signs of vestibular dysfunction, Visual abnormalities	腦神經疾病（包含斜視與吞嚥困難）、頭部傾斜、轉圈、眼球震顫及其他前庭功能障礙徵兆、視覺異常
意識與行為感覺障礙	Disorders of consciousness, altered states of behaviour and personality, episodic diseases, licking, self-mutilation, Itching	意識障礙、行為與性格狀態改變、陣發性疾病、舔舐、自殘、搔癢
運動與協調功能障礙	Incoordination, Tetraparesis, paraparesis, ataxia, weakness of the limbs, cerebellar diseases	協調不良、四肢輕癱、下肢輕癱、共濟失調、四肢無力、小腦疾病



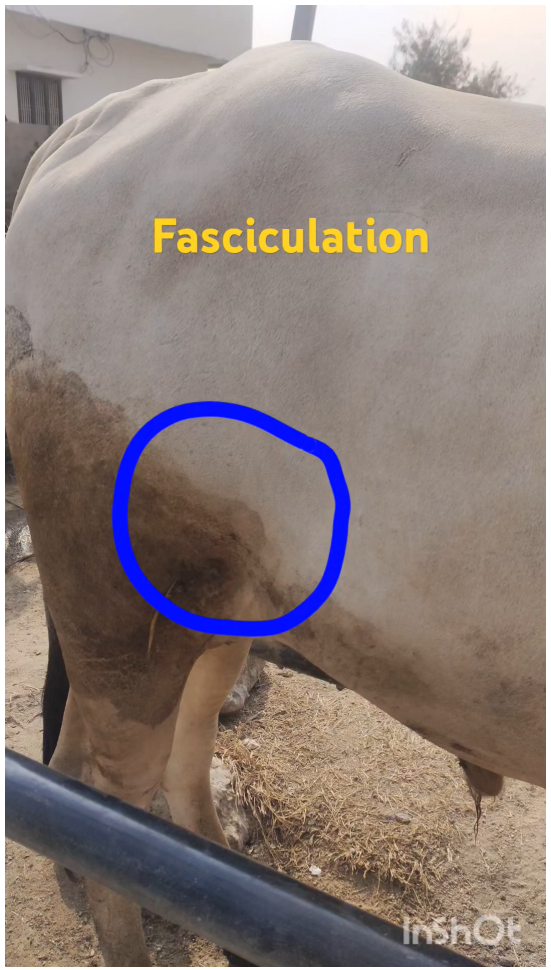


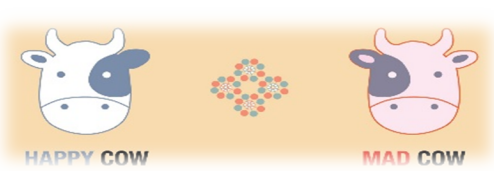






牛隻癲癇發作/癲癇/抽搐/抽搐！尚克·辛格醫生





二：需與狂牛症鑑別診斷之疾病分類列表-1

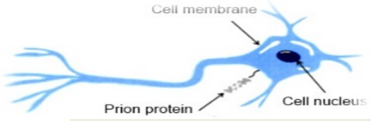
疾病類別	英文疾病名稱	中文翻譯
(疾病指標)	BSE	狂牛症（牛海綿狀腦病）
先天性 (Congenital)	Bovine ceroid lipofuscinosis	牛神經蠟樣脂褐質沉積症
	Generalised glycogenosis	全身性肝醣儲積症
	Mannosidosis	甘露糖苷貯積症
	Convergent strabismus	內斜視
	Congenital Exophthalmus	先天性眼球突出
	Spastic syndrome of adult bovines	成年牛痙攣症候群
	Familial epilepsy	家族性癲癇
	Cerebellar abiotrophy	小腦無生力/退化
	Familial Progressive ataxia of Charolais bovines	夏洛萊牛家族性進行性共濟失調
	Bovine progressive degenerative myeloencephalopathy ('weaver')	牛進行性退化性脊髓腦病 ('織布工')
	Kyphosis of Jersey bovines	娟珊牛脊柱後凸
	Multifocal symmetrical encephalopathy	多發性對稱性腦病



二：需與狂牛症鑑別診斷之疾病分類列表-2

疾病類別	英文疾病名稱	中文翻譯
（疾病指標）	BSE	狂牛症（牛海綿狀腦病）
物理性 (Physical)	Head trauma	頭部創傷
	Post-calving paralysis	產後癱瘓
	Spinal cord and vertebral trauma	脊髓與脊椎創傷
營養性 (Nutritional)	Thiamine responsive cerebrocortical necrosis	維生素B1反應性大腦皮質壞死
	Vitamin A deficiency	維生素A缺乏症
	Nutritional myodegeneration (white muscle disease)	營養性肌肉退化 (白肌病)
	Sodium deficiency	鈉缺乏症
	Hypomagnesemia	低血鎂症



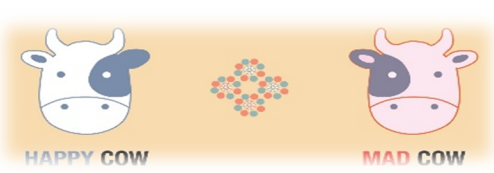







二：需與狂牛症鑑別診斷之疾病分類列表-3

疾病類別	英文疾病名稱	中文翻譯
（疾病指標）	BSE	狂牛症（牛海綿狀腦病）
代謝性 (Metabolic)	Ketosis	酮酸血症
	Hepatic encephalopathy	肝性腦病
	Hypocalcaemia	低血鈣症
	Metabolic encephalopathies	代謝性腦病



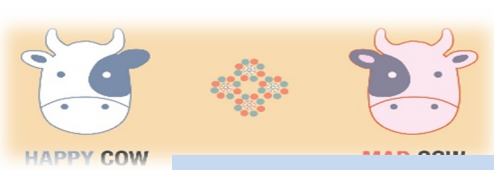
二：需與狂牛症鑑別診斷之疾病分類列表-4

感染性 (Infectious)	Bacterial meningitis and meningoventriculitis	細菌性腦膜炎與腦膜腦室炎
	Louping ill	跳躍病
	Thromboembolic meningoencephalitis (TEM)	血栓栓塞性腦膜腦炎
	Listeriosis	李斯特菌症
	Rabies	狂犬病
	Pseudorabies	偽狂犬病
	Verminous encephalitis	寄生蟲性腦炎
	Myelitis	脊髓炎
	Mycotic encephalitis	黴菌性腦炎



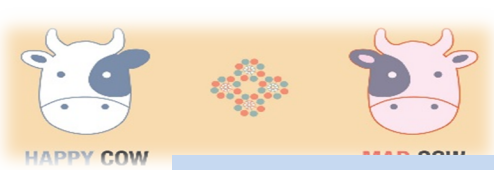
二：需與狂牛症鑑別診斷之疾病分類列表-5

疾病類別	英文疾病名稱	中文翻譯
（疾病指標）	BSE	狂牛症（牛海綿狀腦病）
感染性 (Infectious)	Babesia encephalitis	巴貝蟲腦炎
	Otitis media-interna	中內耳炎
	Sarcocystitis	肉孢子蟲症
	Clostridial polymyositis	梭狀芽孢桿菌多發性肌炎
	Theileriosis	泰勒蟲症
	Bovine trypanosomiasis	牛錐蟲病
	Bovine parasitic otitis	牛寄生蟲性耳炎
	Actinobacillosis, actinomycosis	放線桿菌病，放線菌病



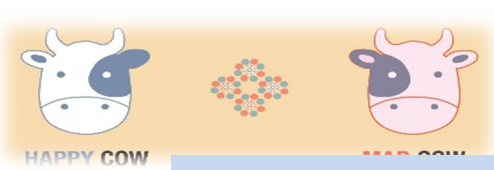
二：需與狂牛症鑑別診斷之疾病分類列表-6

疾病類別	英文疾病名稱	中文翻譯
（疾病指標）	BSE	狂牛症（牛海綿狀腦病）
特發性 (Idiopathic)	Nervous coccidiosis	神經性球蟲病
	Thoracolumbar spondylosis deformans and osteoarthrosis	胸腰椎變形性脊椎病與骨關節炎
空間佔位性病變 (Space occupying lesions)	Abscesses	膿瘍
	Neoplasia	腫瘤
	Granuloma	肉芽腫
	Cysts involving the central nervous system	涉及中樞神經系統的囊腫



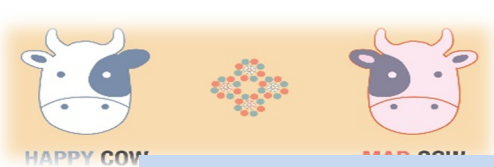
二：需與狂牛症鑑別診斷之疾病分類列表-7

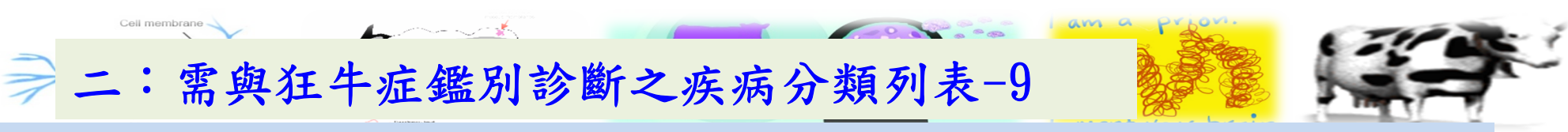
疾病類別	英文疾病名稱	中文翻譯
（疾病指標）	BSE	狂牛症（牛海綿狀腦病）
中毒性 (Toxic)	Lead poisoning	鉛中毒
	Metaldehyde toxicity	聚乙醛中毒
	Cyanide poisoning	氰化物中毒
	Salt and water intoxication	鹽與水中毒
	Organophosphates	有機磷中毒
	Ivermectin toxicosis	伊維菌素中毒
	Methyl bromide intoxication	溴甲烷中毒
	Ethylene glycol toxicosis	乙二醇中毒



二：需與狂牛症鑑別診斷之疾病分類列表-8

疾病類別	英文疾病名稱	中文翻譯
（疾病指標）	BSE	狂牛症（牛海綿狀腦病）
中毒性 (Toxic)	Chlorinated hydrocarbons	氯化碳氫化合物
	Urea-ammonia	尿素-氨中毒
	Strabismus	斜視 (註：原文將此列於毒性區塊)
	Thiamine responsive cerebrocortical necrosis	維生素B1反應性大腦皮質壞死 (註：原文重複列於此處)
	Organomercury toxicity	有機汞中毒
	Polyether antibiotics: monesin and lasalocid intoxication	聚醚類抗生素：莫能菌素與拉沙洛西中毒

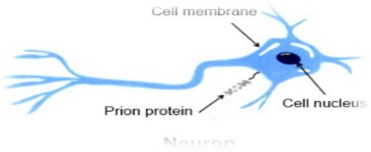


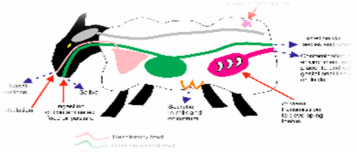


二：需與狂牛症鑑別診斷之疾病分類列表-9

疾病類別	英文疾病名稱	中文翻譯
（疾病指標）	BSE	狂牛症（牛海綿狀腦病）
中毒性 (Toxic)	Sorghum toxicity	高粱中毒
	Plant associated tremor syndromes	植物相關震顫症候群
	Miscellaneous toxic plants (e.g. locoweed)	雜項有毒植物（如瘋草）
	Plant induced mannosidosis	植物引起的甘露糖苷貯積症
	Nitrofurazone toxicosis	呋喃西林中毒
	Tick paralysis	壁蝨麻痺
	Kochia scoparia poisoning (Mexican fireweed)	地膚中毒（墨西哥火草）











Recognition of the Bovine Spongiform Encephalopathy Risk Status of Members
(Adopted by the World Assembly of Delegates on 29 May 2025 in view of an entry into force on 30 May 2025)

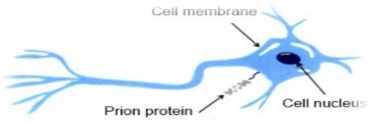
The Director General publish the following List of Members recognised as having a controlled BSE risk in accordance with Chapter 11.4. of the Terrestrial Code:

- Chinese Taipei：中華台北
- Ecuador：厄瓜多
- Greece：希臘
- Russia：俄羅斯

The Director General publish the following List of Members recognised as having a negligible BSE risk in accordance with Chapter 11.4. of the Terrestrial Code:

Argentina
Australia
Austria
Belgium
Bolivia
Brazil
Bulgaria
Canada
Chile
Colombia
Costa Rica
Croatia
Cyprus
Czech Republic
Denmark
Estonia
Finland[1]
France
Germany
Hungary
Iceland
India
Ireland
Israel
Italy
Japan
Korea (Rep. of)
Latvia
Liechtenstein
Lithuania
Luxembourg
Malta
Mexico
Namibia
New Zealand
Nicaragua
Norway
Panama
Paraguay
Peru
Poland
Portugal[2]
Romania
Serbia[3]
Singapore
Slovakia
Slovenia
Spain[4]
Sweden
Switzerland
The Netherlands
United States of America
Uruguay











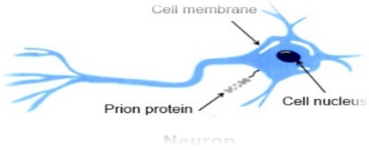
規劃與評估BSE監測的指標範例

Table 1.

Examples of indicators for planning and evaluating BSE surveillance.

Risk group	Examples of reference indicators
Bovines displaying progressive behavioural or neurological clinical signs suggestive of BSE	• List of diseases or conditions causing neurological signs in adult bovines that are present in the country • Expected prevalence of these diseases (if data available) • Percentage of notifications of bovines with neurological signs compatible with BSE in recent years • Number of adult bovines notified as BSE suspects
Bovines showing behavioural or neurological signs at ante-mortem inspection at slaughterhouses or abattoirs	• Most frequent causes of rejection at ante-mortem inspection at abattoirs or slaughterhouses • Percentage of adult bovines that did not pass the ante-mortem inspection at abattoirs or slaughterhouses
Bovines presented as unable to rise or walk without assistance	• List of diseases or conditions causing recumbency in adult bovines (over four years old) in the country • Percentage of adults unable to rise or walk without assistance, found on farm, relative to the adult bovine stock (over four years old) (if available, including suspect diagnosis)
Bovines found dead (fallen stock) with an appropriate supporting clinical history	• Percentage of adult bovines found dead in the field/on farm relative to adult bovine population • Percentage of adult bovines found dead in transport relative to transported adult bovine population. • Percentage of adult animals found dead at animal markets or abattoirs relative to the adult bovine population present at animal markets or abattoirs







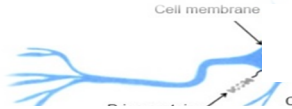




規劃與評估BSE監測的指標範例

高風險族群	參考指標範例
表現出逐漸惡化的行為或神經症狀的牛隻（疑似BSE）	• 國內造成牛隻神經症狀的疾病或病況清單 • 該類疾病的預期盛行率（若有資料） • 近年來具神經症狀並疑似BSE之通報牛隻的比例 • 被通報為BSE疑似病例的成年牛隻數量
屠宰前檢查時出現行為或神經症狀的牛隻	• 屠宰場進行屠宰前檢查時最常見的拒收原因 • 未通過屠宰前檢查的成年牛隻比例
無法站立或需協助行走的牛隻	• 國內造成成年牛隻（4歲以上）無法站立的疾病清單 • 發現於牧場中無法站立或需協助行走的成年牛隻比例（相對於4歲以上成年牛群，若有可疑診斷則納入）
死亡牛隻（倒斃個體），具適當臨床病史者	• 場內或野外發現死亡成年牛隻比例（相對於成年牛群） • 運輸過程中死亡成年牛隻比例（相對於運輸牛群） • 在市場或屠宰場發現死亡牛隻比例（相對於現場成年牛隻總數）





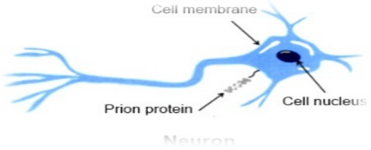
「牛隻神經行為異常的鑑別診斷分類表」





Metabolic					Nutritional				Physical			Familial and Congenital												
Metabolic encephalopathies	Hypocalcaemia	Hepatic encephalopathy	Ketosis	Hypomagnesemia	Sodium deficiency	Nutritional myodegeneration (white muscle disease)	Vitamin A deficiency	Thiamine responsive cerebrocortical necrosis	Spinal cord and vertebral trauma	Post-calving paralysis	Head trauma	Multifocal symmetrical encephalopathy	Kyphosis of Jersey bovines	Bovine progressive degenerative myeloencephalopathy ('weaver')	Progressive ataxia of Charolais bovines	Cerebellar abiotrophy	Familial epilepsy	Spastic syndrome of adult bovines	Exophthalmus	Convergent strabismus	Mannosidosis	Generalised glycogenosis	Bovine ceroid lipofuscinosis	BSE	Disease / Disorder
	×	×	×	×	×			×			×										×	×	×	×	Disorders of behaviour and personality
	×	×		×	×		×	×			×						×					×	×	×	Seizures
×					×		×	×			×											×	×		Visual dysfunction
								×			×								×	×					Cranial nerve disorders (including strabismus and dysphagia)
											×														Head tilt, circling, nystagmus and other signs of vestibular abnormalities
	×			×				×			×							×						×	Opisthotonos, tetany, tremor, muscle spasm
	×	×	×	×				×			×											×	×	×	Coma and altered states of consciousness
											×					×								×	Incoordination of the head and the limbs: cerebellar diseases
	×			×		×		×	×	×		×	×	×	×							×	×	×	Tetraparesis, paraparesis, ataxia of the limbs, and episodic weakness
			×		×																			×	Itching, licking, self-mutilation











牛隻神經異常臨床症狀的鑑別診斷對照表（二），但涵蓋的是更多屬於感染性（Infectious）、特發性（Idiopathic）、及佔位性病灶（Space occupying lesions）等病因。

英文	中文翻譯
Cysts involving the central nervous system	中樞神經系統囊腫
Neoplasia	腫瘤
Abscesses	膿瘍
Nervous coccidiosis	神經性球蟲病
Botulism	肉毒中毒
Listeriosis	李斯特菌感染
Rabies	狂犬病
Tetanus	破傷風
Thromboembolic meningo-encephalitis	血栓栓塞性腦膜腦炎

牛隻神經異常臨床症狀的鑑別診斷對照表（二），但涵蓋的是更多屬於感染性（Infectious）、特發性（Idiopathic）、及佔位性病灶（Space occupying lesions）等病因。

Disease / Disorder	Infectious																												Idiopathic		Space occupying lesions			
	Bacterial meningitis and meningoventriculitis	Louping ill	Thromboembolic meningoencephalitis (TEM)	Listeriosis	Rabies	Pseudorabies	Verminous encephalitis	Myelitis	Sporadic bovine encephalomyelitis (Buss disease) and other inflammatory meningoencephalomyelitides	Encephalitis of viral bovine rhinotracheitis	Malignant catarrhal fever (MCF)	Botulism	Tetanus	Mycotic encephalitis	Babesia encephalitis	Otitis media-interna	Sarcocystitis	Clostridial polymyositis	Theileriosis	Bovine trypanosomiasis	Bovine parasitic otitis	Actinobacillosis, actinomycosis	Nervous coccidiosis	Thoracolumbar spondylosis deformans and osteoarthrosis	Abscesses	Neoplasia	Granuloma	Cysts involving the central nervous system
Disorders of behaviour and personality	×	×	×	×	×	×	×	×	×	×	×	×	×	×	×	×						×	×		×	×	×	×
Seizures	×				×	×			×		×			×									×		×	×	×	×
Visual dysfunction	×		×			×				×	×			×									×		×	×	×	×
Cranial nerve disorders (including strabismus and dysphagia)	×		×	×	×		×		×	×		×		×									×		×	×	×	×
Head tilt, circling, nystagmus and other signs of vestibular abnormalities				×			×	×								×	×		×	×	×				×	×	×	×
Opisthotonos, tetany, tremor, muscle spasm	×												×										×		×	×	×	×
Coma and altered states of consciousness	×	×	×	×	×	×	×	×	×	×	×	×	×	×	×	×						×	×		×	×	×	×
Incoordination of the head and the limbs: cerebellar diseases	×						×	×								×									×	×	×	×
Tetraparesis, paraparesis, ataxia of the limbs, and episodic weakness		×	×					×	×	×		×	×	×	×		×	×						×	×	×	×	×
Itching, licking, self-mutilation					×	×																						







Disease / Disorder	Toxic																								
	Lead poisoning	Metaldehyde toxicity	Cyanide poisoning	Salt and water intoxication	Organophosphates	Ivermectin toxicosis	Methyl bromide intoxication	Ethylene glycol toxicosis	Chlorinated hydrocarbons	Urea-ammonia	Strabismus	Thiamine responsive cerebrocortical necrosis	Organomercury toxicity	Polyether antibiotics: monesin and lasalocid intoxication	*Sorghum toxicity*	Plant associated tremor syndromes	Miscellaneous toxic plants (e.g. locoweed)	Plant induced mannosidosis	Nitrofurazone toxicosis	Tick paralysis	*Kochia scoparia* poisoning (Mexican fireweed)
Disorders of behaviour and personality	×		×	×	×				×	×	×	×	×				×	×			×
Seizures	×	×	×	×	×				×	×		×				×	×				
Visual dysfunction	×			×						×		×	×				×				×
Cranial nerve disorders (including strabismus and dysphagia)	×			×	×							×									
Head tilt, circling, nystagmus and other signs of vestibular abnormalities																×					
Opisthotonos, tetany, tremor, muscle spasm	×	×	×	×	×				×							×			×		
Coma and altered states of consciousness	×		×	×	×				×	×	×	×	×				×	×			×
Incoordination of the head and the limbs: cerebellar diseases													×				×				
Tetraparesis, paraparesis, ataxia of the limbs, and episodic weakness	×				×	×	×	×					×	×	×		×			×	
Itching, licking, self-mutilation					×	×															



BSE鑑別診斷中神經症狀分類對照與說明

行為與性格異常（Disorders of behaviour and personality）

牛隻出現個性改變，例如變得焦躁、攻擊、反常膽怯，或表現出不尋常的反應與行為。

癲癇發作（Seizures）

不自主的抽搐、全身肌肉強直或間歇性痙攣，可能伴隨短暫意識喪失。

視覺功能障礙（Visual dysfunction）

牛隻可能出現視力模糊、對光無反應、碰撞障礙物或瞳孔反射異常等情形。

顱神經功能障礙（如斜視、眼球突出）（Cranial nerve dysfunction (including strabismus and exophthalmos))

表現如面部肌肉癱瘓、斜視、眼球突出、吞嚥困難或耳朵無法移動。

頭部傾斜、繞圈行走、步態異常（Head tilt, circling, abnormal gait）

牛頭部歪斜、一方向繞圈、不穩步態或協調性喪失，是前庭或神經損傷的典型徵象。

角弓反張、肌肉僵直、顫抖、痙攣（Opisthotonus, tetany, tremor, muscle spasm）

頭背過度後仰、全身僵硬、間歇性顫抖或肌肉不自主抽動。

昏迷或意識狀態改變（Coma and altered states of consciousness）

牛可能陷入昏迷或表現出遲鈍、恍惚、對環境無反應等意識障礙。

頭部或四肢麻痺/癱瘓（Paresis/paralysis of the head and/or limbs）

局部或全身肌肉無力、無法站立或移動，可能為神經損傷或中樞神經疾病所致。

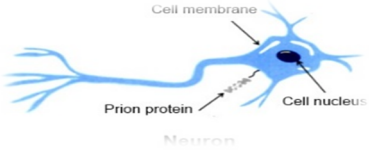
震顫、間歇性興奮狀態（Tremor, episodic states of excitement）

不明原因之顫抖、過度興奮、行為不穩定等週期性出現的異常狀態。

搔癢、舔咬、自殘（Itching, licking, self-mutilation）

牛持續舔咬身體、搔癢、撞牆或咬舌，常見於狂牛症初期。





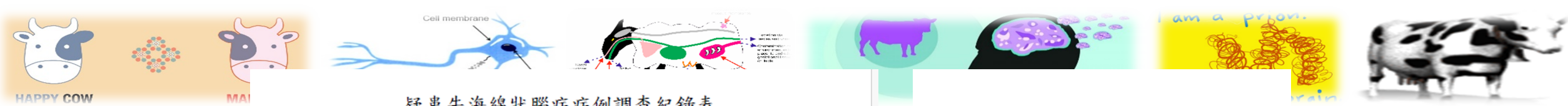






BSE鑑別診斷中樞神經症狀分類對照說明

中文名稱與說明	英文對照
行為與性格異常	Disorders of behaviour and personality
癲癇發作	Seizures
視覺功能障礙（可包括瞳孔放大、視覺消失、對光反應減弱、碰撞障礙物或瞳孔反射異常等情形）	Visual dysfunction
顱神經功能障礙（如斜視、眼球突出）	Cranial nerve dysfunction (including strabismus and exophthalmos)
頭部傾斜、繞圈行走、步態異常	Head tilt, circling, abnormal gait
角弓反張、肌肉僵直、顫抖、痙攣	Opisthotonus, tetany, tremor, muscle spasm
昏迷或意識狀態改變	Coma and altered states of consciousness
頭部或四肢麻痺／癱瘓	Paresis/paralysis of the head and/or limbs
震顫、間歇性興奮狀態	Tremor, episodic states of excitement
搔癢、舔吮、自殘	Itching, licking, self-mutilation



疑患牛海綿狀腦病病例調查紀錄表

壹、 基本資料

調查單位		調查日期	
填表人員名稱		填表人員職稱	
牛隻標號		來源場(飼主)	
牛隻種類[註1]		牛隻年齡	
調查後處置	□判定不為感染案例[註2]		□採樣後送檢

註1：牛隻種類請填種牛、肉牛或乳牛。

註2：需檢附詳細相關臨床病史敘述，以及排除感染牛海綿狀腦病之原因說明。

貳、 病例紀錄

一、表格填寫方式：確認請打勾；僅牧場回報請以三角形標記；無法判斷請以 N/A 標記。

二、 行為改變：

行為	勾選	行為	勾選
憂鬱(觀察臉部、眼神)		頭部姿勢異常	
觸覺過敏(刺激頸部、後肢)		觸碰頭部時表現不安或迴避	
聽覺過敏(敲擊金屬)		將頭部用力頂在牆壁	
發狂(具攻擊性、踢人)		頭部摩擦身體或物體	
恐慌(退縮、逃跑)		舔拭腹脅部	
不願意進入榨乳室、地磅等		舔舐鼻子	
在榨乳室出現踢腿的行為		耳痙攣	
磨牙		耳角度異常	

三、 運動/神經症狀

症狀	勾選	症狀	勾選	症狀	勾選
失明		跌倒或步伐異常		倒臥	
迴旋運動		輕癱		震顫	
後肢共濟失調		前肢共濟失調		球節彎曲	

四、 體態/產乳量變化

變化項目	減少	未改變	增加	無法判斷
體重				
體態				
產乳量				

參、 其他紀錄

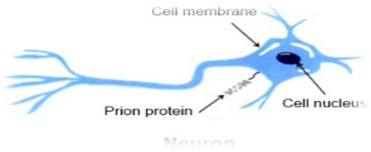
一、初始症狀：

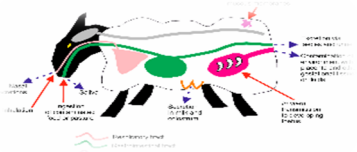
二、臨床進展：

三、來源場敘述：

四、補充說明：











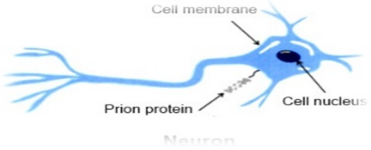
疑患牛海綿狀腦病病例調查紀錄表

壹、 基本資料

調查單位		調查日期	
填表人員名稱		填表人員職稱	
牛隻標號		來源場(飼主)	
牛隻種類註1		牛隻年齡	
調查後處置	□判定不為感染案例註2 □採樣後送檢		

註1：牛隻種類請填種牛、肉牛或乳牛。
註2：需檢附詳細相關臨床病史敘述，以及排除感染牛海綿狀腦病之原因說明。











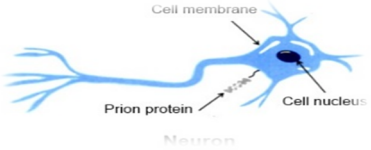
貳、 病例紀錄

一. 表格填寫方式：確認請打勾；僅牧場回報請以三角形標記；無法判斷請以N/A標記。

二. 行為改變：

行為	勾選	行為	勾選
憂鬱(觀察臉部、眼神)		頭部姿勢異常	
觸覺過敏(刺激頸部、後肢)		觸碰頭部時表現不安或迴避	
聽覺過敏(敲擊金屬)		將頭部用力頂在牆壁	
發狂(具攻擊性、踢人)		頭部摩擦身體或物體	
恐慌(退縮、逃跑)		舔拭腹脅部	
不願意進入榨乳室、地磅		舔舐鼻子	
在榨乳室出現踢腿的行為		耳痙攣	
磨牙		耳角度異常	











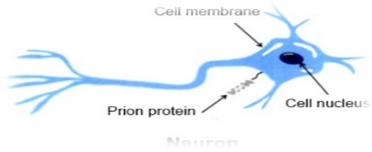
三、 運動/神經症狀

症狀	勾選	症狀	勾選	症狀	勾選
失明		跛行或步伐異常		倒臥	
迴旋運動		輕癱		震顫	
後肢共濟失調		前肢共濟失調		球節彎曲	

四、 體態/產乳量變化

變化項目	減少	未改變	增加	無法判斷
體重				
體態				
產乳量				











Prion不活化方法-1

一、經典物理與化學不活化（作為基準）

- 強鹼：1 N NaOH，室溫處理 1 小時，仍是許多指南的基準方法之一。
- 氧化性消毒劑：次氯酸鈉（含可用氯 20,000 ppm 以上）、過一硫酸氫鉀（potassium peroxymonosulfate）等，在表面或不鏽鋼載體上的人類CJD與CWD prion有良好不活化效果。
- 高溫高壓：預真空高壓蒸氣滅菌仍是耐熱器械首選；對prion需較長時間與高溫（例如 134°C 延長時間），常與鹼性洗滌結合。

核心認知（為何prion難以不活化）

•Prion為異常摺疊蛋白（PrP^Sc），**無核酸**

•對一般消毒方式高度抗性：

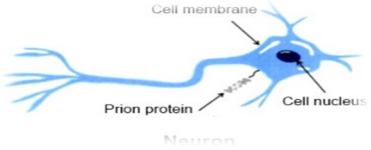
紫外線、γ射線、121°C高壓滅菌 → **無效**

•不同株（strain）抗性差異極大: BSE prion可比其他prion**高達10^6倍抗性**

代表性新文獻（基準消毒條件研究）

- 2024 PLOS One：「Sodium hypochlorite inactivation of human CJD prions」：在人類sCJD來源prion上比較不同濃度與接觸時間的漂白水，證實濃度與時間皆顯著影響不活化效果。
- 2024 mSphere：「Rapid and sensitive determination of residual prion infectivity」：整理指出NaOH、次氯酸鈉、酸性SDS、次氯酸、酚類製劑（如Environ LpH、Wexide-128）皆可不活化，但不同prion strain感受性差異大，需小心推論到新株。










Prion不活化方法-2

（1）經典實驗研究

1 Taylor DM, 1994（經典BSE不活化研究）

•Decontamination studies with the agents of bovine spongiform encephalopathy

•重點：

- 次氯酸鈉（≥20,000 ppm）→ 可完全消除感染力
- NaOH（1–2M）→ 有效但未完全
- 134–138°C高壓滅菌 → 仍可能殘存感染力

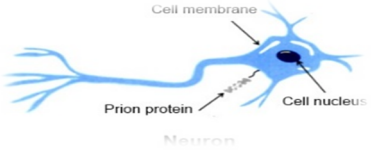
2 Giles et al., 2008（prion抗性比較）

•Resistance of BSE prions to inactivation

•發現：

- BSE prion比：
  - 小鼠prion → 高1000倍抗性
  - 倉鼠prion → 高10^6倍抗性











Prion不活化方法-3

🧪 **（2）WHO / CDC 指引基礎文獻**

3 Rutala & Weber / CDC Guidelines

•CDC Guideline for Disinfection and Sterilization in Healthcare Facilities

•建議方法：

- 1N NaOH（1 hr）
- 20,000 ppm NaOCl（1 hr）
  - 134˚C高壓滅菌

🔵 **（3）機制與方法回顧性研究**

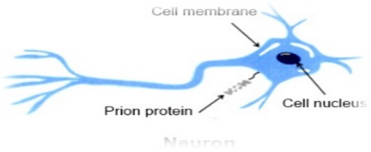
4 Sakudo et al., 2022（最新綜述）

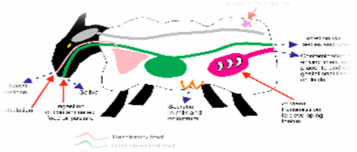
•Recent Advances in Prion Inactivation by Plasma Sterilizer

•重點：

- 傳統方法無效：
  - UV、γ射線、121˚C
- 有效策略：
  - NaOH
  - NaOCl
  - 延長高溫滅菌
  - 焚化 >1000˚C











Prion不活化方法-4

5 Sakudo et al., Inactivation Methods for Prions（綜合指南）

•Inactivation Methods for Prions

•建議實務流程：

- 清洗 → 鹼性洗劑 → 134°C autoclave
- H_2O_2 plasma（器械）
- 焚化（食品或高風險材料）

🌎 **（4）環境與持續性研究**

6 Eraña et al., 2020（評估方法）

•Evaluation of prion decontamination procedures

•強調：

- 必須用：
  - PMCA
  - bioassay

  才能確認「真正不活化」

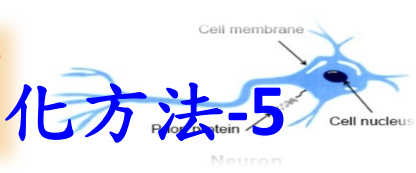
7 Mini-review：環境中prion不活化

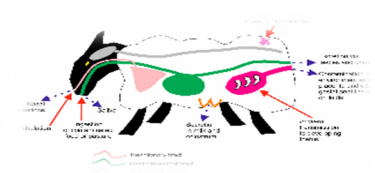
•Inactivation of infectious prions in the environment

•指出：

- prion可在土壤中長期存在
- 環境去除極困難










Prion不活化方法-5

代表性新文獻（基準消毒條件研究）

- 2024 PLOS One：「Sodium hypochlorite inactivation of human CJD prions」：在人類sCJD來源prion上比較不同濃度與接觸時間的漂白水，證實濃度與時間皆顯著影響不活化效果。
- 2024 mSphere：「Rapid and sensitive determination of residual prion infectivity」：整理指出NaOH、次氯酸鈉、酸性SDS、次氯酸、酚類製劑（如Environ LpH、Wexide-128）皆可不活化，但不同prion strain感受性差異大，需小心推論到新株。

二、低溫滅菌技術：過氧化氫／過氧乙酸氣化與等離子

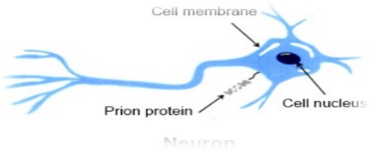
1. VHPPA（氫氧化物＋過氧乙酸氣化）

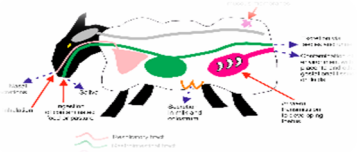
- 2020研究以混合氫過氧化物–過氧乙酸氣化（VHPPA）處理prion污染樣本，使用蛋白錯構循環放大（PMCA）與小鼠攻毒試驗評估。VHPPA處理後PrP^res條帶消失，小鼠存活時間明顯延長，顯示感染力大幅下降，適用於耐熱性較差的醫療器材。

2. 氫過氧化物氣體等離子（含臭氧輔助）

- 2022 review「Recent Advances in Prion Inactivation by Plasma Sterilizer」：系統整理使用氫過氧化物氣體與電漿技術不活化prion的研究。
- RENO-S130（氫過氧化物＋介電阻擋放電產生臭氧）對不鏽鋼線上的prion顯著延長小鼠存活，PMCA亦證實感染力降低。低壓感應耦合電漿（ICP，Ar或Ar/O_2）在不鏽鋼及絲線模型上有高效不活化效果，但可能伴隨顯著表面升溫，部分效果來自加熱。這些技術的意義在於：為「耐熱度有限的醫療器械」提供高效不活化選項，逐漸被列入實務指引建議之中。











Prion不活化方法-6

三、新一代清洗劑與「溫和」配方篩選

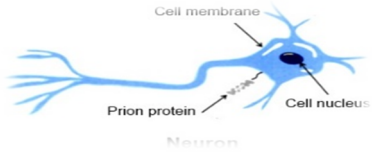
1. TFD Premium 及其他鹼性／氧化性配方

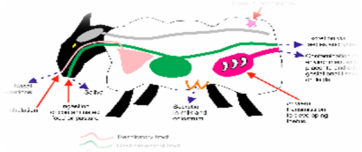
- 2025 J Hosp 感染相關研究：「Optimization and evaluation of new decontamination procedures inactivating human prions」：
  - 以人源prion（sCJD、vCJD）污染不鏽鋼載體，測試多種清洗劑與條件。
  - 新配方 TFD Premium 在室溫條件下，對人源prion的去污效果優於或至少不遜於WHO參考方法（1 N NaOH 1 h）。
  - 對不同prion株（如Tg650-sCJD-VV2 vs vCJD）感受性不同，Tg650-sCJD-VV2較具耐受性。

- 2024 PLOS One：「A screen of oxidative and alkaline prion decontaminants using real-time seed amplification assay (TESSA)」：
  - 建立TESSA（以不鏽鋼珠搭配RT-QuIC的高通量篩選平台），一次評估約70種市售與新配方清洗劑。
  - 找到：
    - 一種次氯酸鹽基底配方、
    - 兩種商用鹼性配方、
    - 一種手動鹼性預洗劑，在模擬自動洗滌消毒條件下對prion有高度不活化效果。

  - 在轉基因小鼠攻毒試驗中，這些配方可將不鏽鋼珠上的prion濃度降至檢出限以下。










Prion不活化方法-4

2. CWD與環境prion去污

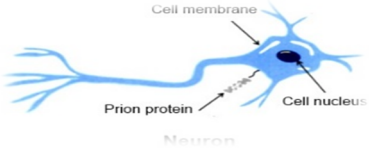
- 2025 Emerging Infectious Diseases：「Detection and Decontamination of Chronic Wasting Disease Prions on Surfaces」：
  - 示範使用表面採樣搭配PMCA檢測CWD prion殘留，並測試多種去污液。
  - 常用家用漂白水與過一硫酸氫鉀（potassium peroxymonosulfate）溶液在表面CWD prion不活化上效果良好。

四、新工具：RT-QuIC／PMCA（Protein Misfolding Cyclic Amplification）作為不活化效果評估平台

- 2022–2025間多篇研究指出，PMCA與RT-QuIC可作為替代動物試驗的高敏感評估工具：
  - 2024 以RT-QuIC加拭子法評估表面去污效果，並強調不同prion株對同一不活化方法感受性差異很大。
  - 2024–2025的PMCA相關研究顯示，表面採樣＋PMCA可用於實驗室房間與設備去污效果驗證，發現即使採用「核准方法」，高濃度prion仍可殘留，強調「必須實測」而不是只依賴程序設計。

這一類方法將未來prion不活化研究從「只有動物攻毒」轉向「高通量、可半定量」平台，有利於開發新清洗劑與流程。







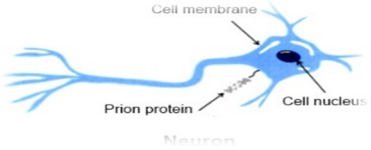



Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (BSE)

- Recommendations for safety precautions for handling BSE-infected material now assume that BSE is a zoonosis and a containment category 3 (with derogation) has been ascribed.
- Recommended physical inactivation is by porous load autoclaving at 134°C–138°C for 18 minutes at 30 lb/in2.
- Disinfection is carried out using sodium hypochlorite containing 2% available chlorine, or 2 N sodium hydroxide, applied for more than 1 hour at 20°C for surfaces, or overnight for equipment .

***Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2008* Part 2**
OIE Listed Diseases and Other Diseases of Importance to International Trade









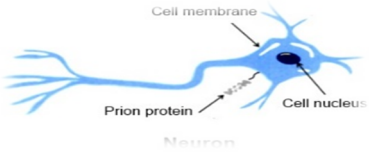


FIXATION, TISSUE PROCESSING, HISTOLOGY AND IMMUNOHISTOCHEMISTRY STAINING PROCEDURES FOR THE DIAGNOSIS OF BSE AND SCRAPIE

- Fixation
- Formic acid Decontamination
- Tissue processing
- Histological staining
- PrP immunostaining











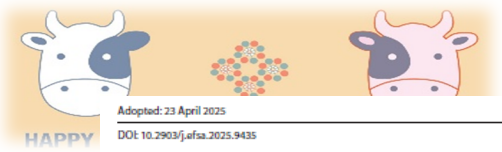

Prion不活化方法-5

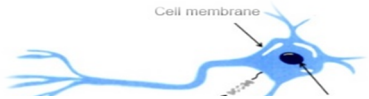
五、固定液與病理標本處理

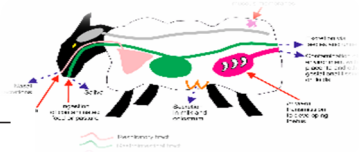
- 2025一篇關於甲酸處理對腦組織與prion檢出影響的研究指出，現行prion不活化常依賴「強酸、強鹼或長時間高壓蒸氣」，但這些對組織形態與免疫染色有明顯影響；文章系統評估甲酸處理對病理標本的影響，討論在兼顧形態與安全之間如何折衷。

甲酸(蟻酸)處理對腦組織prion的不活化影響

由於使用標準去污方法難以滅活prion，因此在臨床、診斷和研究環境中，從事prion研究的人員面臨重大風險。甲酸處理已被證明能有效去污感染性prion，並常用於生物安全實踐中以防止職業暴露。然而，甲酸處理方案對組織樣本形態的影響尚未被充分記錄。本研究旨在以表現出不同程度神經退化的小鼠腦半球組織為模型，探討甲酸處理對中樞神經系統組織的形態學影響。本研究包括正常、未患病的野生型組織和5xFAD模型（此模型可重現阿茲海默症（AD）的部分特徵）。此外，本研究還使用了一種患有慢性消耗性疾病（CWD，一種鹿和麋鹿的prion disease）的模型，以分析甲酸對具有海綿狀變性的組織的影響。將甲酸處理組和未處理的對照組的組織進行石蠟包埋、切片、染色和顯微成像。對解剖區域進行定量分析和評估，以確定各處理組間組織的寬度、面積和結構完整性。我們的研究結果表明，雖然甲酸先前已被報導能有效滅活prion，但它會破壞小鼠腦組織的形態。此外，甲酸的影響在腦組織的不同區域分佈不均。年齡與甲酸處理組的形態變化無關。值得注意的是，組織中神經退化性變的存在似乎並未加劇甲酸處理後的形態變化。這些結果強調了探索其他prion滅活方法的必要性，以確保在處理prion感染組織時安全可靠，同時不損害組織的完整性











Adopted: 23 April 2025
DOI: 10.2903/j.efsa.2025.9435

efsa JOURNAL

SCIENTIFIC OPINION

Effect of incineration, co-incineration and combustion on TSE hazards in category 1 animal by-products

EFSA Panel on Biological Hazards (BIOHAZ) | Ana Allende | Avelino Alvarez-Ordóñez | Valeria Bortolaia | Sara Bover-Cid | Alessandra De Cesare | Wietske Dohmen | Laurent Guillier | Lieve Maria Herman | Liesbeth Jacxsens | Lapo Mughini-Gras | Maarten Nauta | Jakob Ottoson | Luisa Peixe | Fernando Perez-Rodriguez | Panagiotis Skandamis | Elisabetta Suffredini | Olivier Andreoletti | Vincent Béringue | John Griffin | Marion Simmons | Kamela Kryemadhi | Barbara Lanfranchi | Angel Ortiz-Pelaez | Romolo Nonno

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The declarations of interest of all scientific experts active in EFSA's work are available at https://open.efsa.europa.eu/experts

Abstract

The European Commission requested EFSA to assess the effect of incineration, co-incineration and combustion of Category 1 animal by-products (ABP) on the BSE/TSE hazards in ash resulting from these treatments. The presence of residual TSE hazards is assessed by detection of prion infectivity or seeding activity. TSE agents or prions are challenging to inactivate completely using heat-based methods. Different TSE strains exhibit varying degrees of thermoresistance. Based on available studies at temperatures 120–134°C, the C-BSE strain is more thermoresistant than other evaluated strains. The vast majority of Category 1 ABP is rendered into 'meat and bone meal' prior to incineration/co-incineration/combustion. Scenarios involving co-incineration for cement production do not need to be considered because all ash is incorporated into the cement. It is not possible to generalise the time/temperature combinations to which Category 1 ABP are subjected across all processes. Due to the challenges in precisely measuring the temperature and residence time in industrial systems, and the wide range of system designs and operating conditions, it can only be assumed that Category 1 ABP are exposed to at least the legal requirements as determined by the conditions of the gas produced or injected into the process: 850°C for 2 s or 1100°C for 0.2 s. The limited sensitivity of the method used in a study involving C-BSE at 1000°C for 20 min prevented a conclusive exclusion of residual C-BSE prions.. Therefore, it is not possible to exclude – with high certainty (> 99%) – the presence of residual BSE/TSE hazards in ash produced from the incineration, co-incineration or combustion of Category 1 ABP. It is recommended to generate data on the actual reduction of infectivity in 'meat and bone meal' spiked with thermoresistant TSE field strains after treatment with the time/temperature combinations required by the legislation or specific industry processes.

KEYWORDS
ABP, animal by-products, ash, combustion, incineration, prions, TSE

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一、Prion不活化方法（核心研究）

🔹 1. 醫療器械與不活化驗證（最新關鍵文獻）

•Igel A. et al. (2024)

PMCA to demonstrate the efficacy of prion inactivation methods on reusable medical devices

Journal of Hospital Infection

👉 DOI: 10.1016/j.jhin.2024.07.020

📌 重點：

•使用 **PMCA（蛋白誤摺擴增技術）** 評估不活化效果

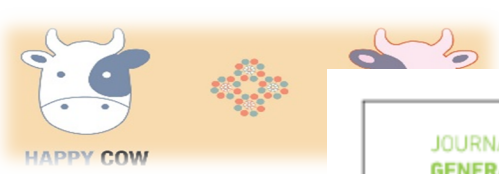
•比較：

- 高壓蒸氣（steam）
- NaOH
- 次氯酸鈉

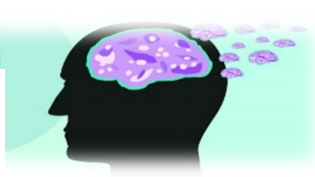
•發現：

👉 **PMCA結果與動物感染試驗高度一致**

👉 H_2O_2低溫滅菌（STERRAD）對多種prion有效











JOURNAL OF GENERAL VIROLOGY

RESEARCH ARTICLE

Matsuura et al., Journal of General Virology 2020;101:136–142
DOI 10.1099/jgv.0.001335

MICROBIOLOGY SOCIETY

Eliminating transmissibility of bovine spongiform encephalopathy by dry-heat treatment

Yuichi Matsuura[1], Yukiko Ishikawa[1]†, Yuichi Murayama[1]‡, Takashi Yokoyama[1], Robert A. Somerville[2], Tetsuyuki Kitamoto[3] and Shirou Mohri[1,3,*]

Abstract

Bovine spongiform encephalopathy (BSE) prion is more resistant to heat inactivation compared to other prions, but the effect of heat inactivation has been reported to differ depending on the BSE-contaminated tissue state or heating type. We aimed to evaluate the secure level of inactivation of original BSE transmissibility by dry-heating. Cattle tissues affected with BSE were subjected to dry-heat treatment for 20 min at various temperatures ranging from 150 to 1000 °C. To assess the inactivation effect, we conducted protein misfolding cyclic amplification (PMCA) and follicular dendritic cell (FDC) assays in transgenic mice expressing bovine prion protein genes. Under dry-heating at 600 °C or higher, BSE cattle tissues lost their transmissibility in transgenic mice. In contrast, transmissibility was detected in the cattle tissues treated at temperatures of 400 °C or lower through the FDC assay combined with PMCA. In this study, we confirmed that transmissibility was eliminated in BSE-affected cattle tissues by dry-heating at 600 °C or higher.

INTRODUCTION

Transmissible spongiform encephalopathy (TSE) includes bovine spongiform encephalopathy (BSE), Creutzfeldt–Jakob disease (CJD) in humans, scrapie in sheep and goats, and chronic wasting disease in deer and elk. These transmitted diseases are fatal and lead to major issues in animal and human health. Transmissibility of TSE is associated with prion that is mainly constituted of abnormal prion protein (PrP^{Sc}) converted from host-encoded normal prion protein (PrP^{C}) in TSE-affected animals [1, 2]. The distribution of PrP^{Sc} is not limited to neural tissues [3–6]. Moreover, prions are highly resistant to conventional physical and chemical procedures that inactivate or eliminate microbes [7]. Persistent BSE transmissibility during rendering of cattle tissues is likely the major contributory cause of epizootic diseases [8] and creates problems such as environmental contamination in sewage [9, 10], landfills [11] and soil [12, 13]. Previous studies in hamsters using the scrapie 263K strain have recommended dry-heating or incineration at 1000 °C for disinfecting medical and veterinary wastes [14].

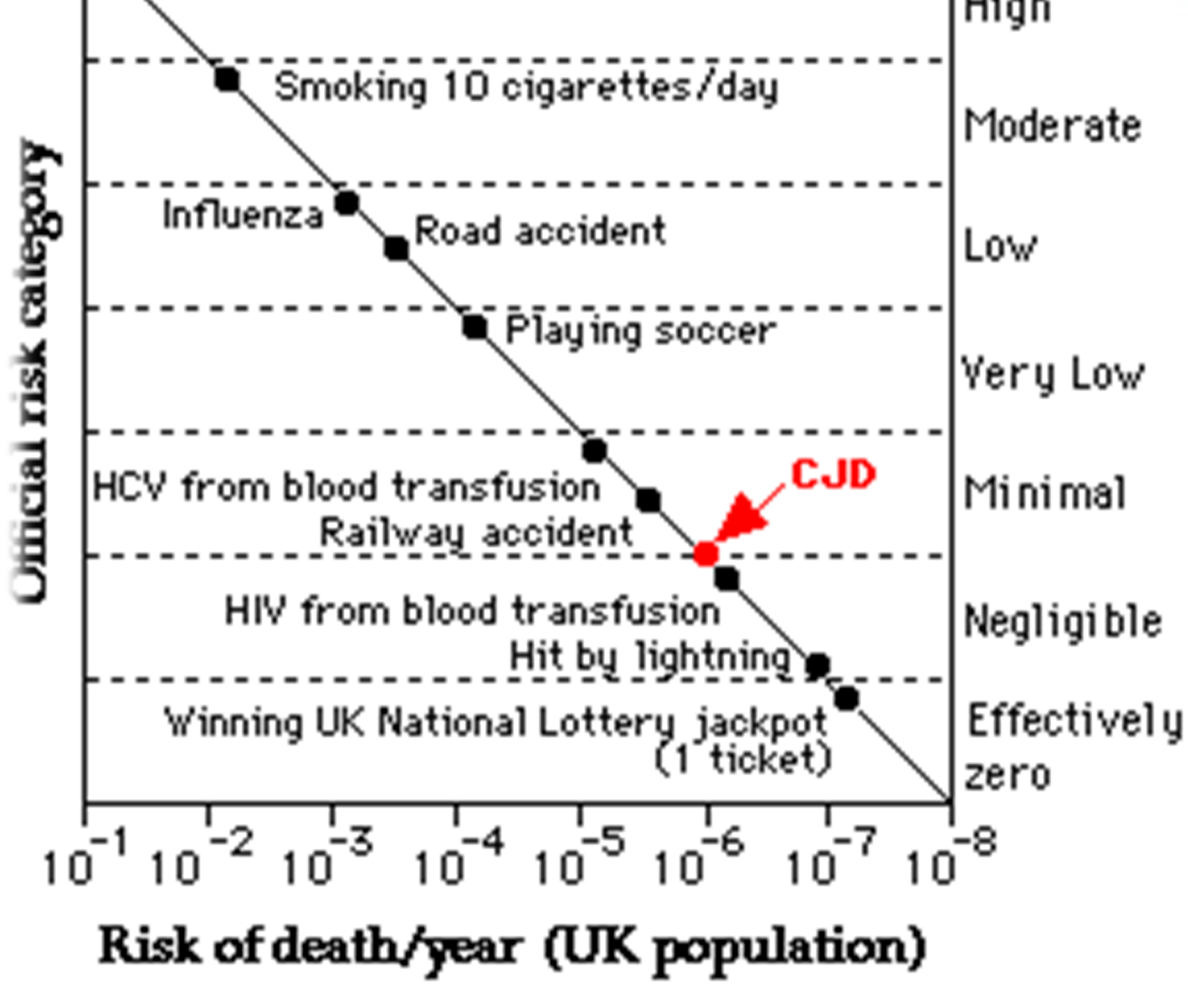
Inactivation of TSE prions varies depending on the tissue states; e.g. homogenate or macerate, type of heating; e.g. wet or dry, autoclave mechanism; e.g. gravity displacement or porous-load, and species of TSE [15–19]. BSE prion causing variant CJD in humans is more resistant to wet-heat inactivation than the other CJDs and scrapie prions [7, 20–23]. The transmissibility of BSE persists even after autoclave treatment at 133 °C for 20 min [20], 134 °C for up to 2 h [22, 23] or 150 °C for 20 min [24]. Heating in yellow grease at 180 °C for 1 h does not inactivate the BSE prion [25]. Additionally, tissue drying enhances the heat resistance of BSE prion over tissues containing high moisture levels [24].

This study was conducted to assess BSE inactivation by subjecting affected cattle tissues to dry-heat treatment. After treatment, inactivation of BSE prion was measured in two assays. Protein misfolding cyclic amplification (PMCA) was performed to monitor PrP^{Sc} seeding activity resulting in the conversion of normal PrP to proteinase K (PK) resistant form

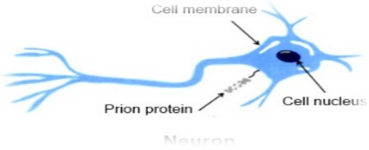
本研究首次報告了乾熱處理在牛組織中的BSE prion去活化效果，顯示600˚C及以上的處理能夠完全消除BSE的傳染性。這一結果對於牛隻屠宰廢物的安全處理具有重要意義，建議在適當的高溫下進行焚燒以防止潛在的傳染風險


HAPPY COW
MAD COW


Cell membrane


Official risk category
High
Moderate
Low
Very Low
Minimal
Negligible
Effectively zero
Smoking 10 cigarettes/day
Influenza
Road accident
Playing soccer
HCV from blood transfusion
Railway accident
CJD
HIV from blood transfusion
Hit by lightning
Winning UK National Lottery jackpot (1 ticket)
10-1 10-2 10-3 10-4 10-5 10-6 10-7 10-8
Risk of death/year (UK population)





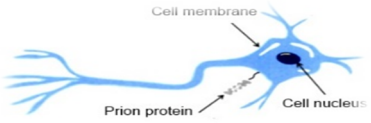


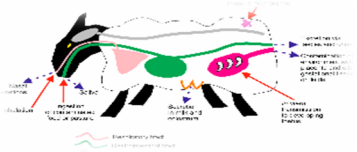



結論（Conclusion）

- BSE是一種可傳染的神經系統疾病，由錯誤摺疊的蛋白質所引起，主要影響牛隻。
- BSE最主要的傳播途徑為攝食受感染動物組織。該疾病透過食用含有感染性物質的肉骨粉（MBM）傳播。
- 此疾病對經濟與公共衛生具有重大影響。
- 人類感染BSE的主要途徑為食用受污染的牛肉產品，這些產品可能含有中樞神經組織。這些組織目前被稱為特定風險物質（SRMs）。
- 因此，應避免將可能含有prion的反芻動物組織餵飼給易感動物，以預防BSE。





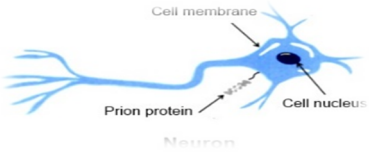





結論

- 狂牛症無法生前檢驗
- 狂牛症除採取腦組織外其他組織不易檢出Prion
- 進口內臟或絞肉_無法檢測出是否有prion之污染
- 要確保進口牛肉之食用衛生安全，一定要實施輸出國產地查核
- 檢驗生產履歷、飼料禁令是否落實
- 該輸出國BSE風險評估報告、屠宰場查廠
- 該輸出國獸醫師服務體系是否健全
- 一定要有屠檢獸醫師的檢核報告
- 回歸食品衛生檢查之基準

















謝謝聆聽!感恩! 12:51 休息一下