食物鏈的詛咒：狂牛症之隱憂

牛隻海綿樣腦症與人類新型庫賈氏病

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11/06/2011

庫賈氏病與牛隻海綿樣腦症

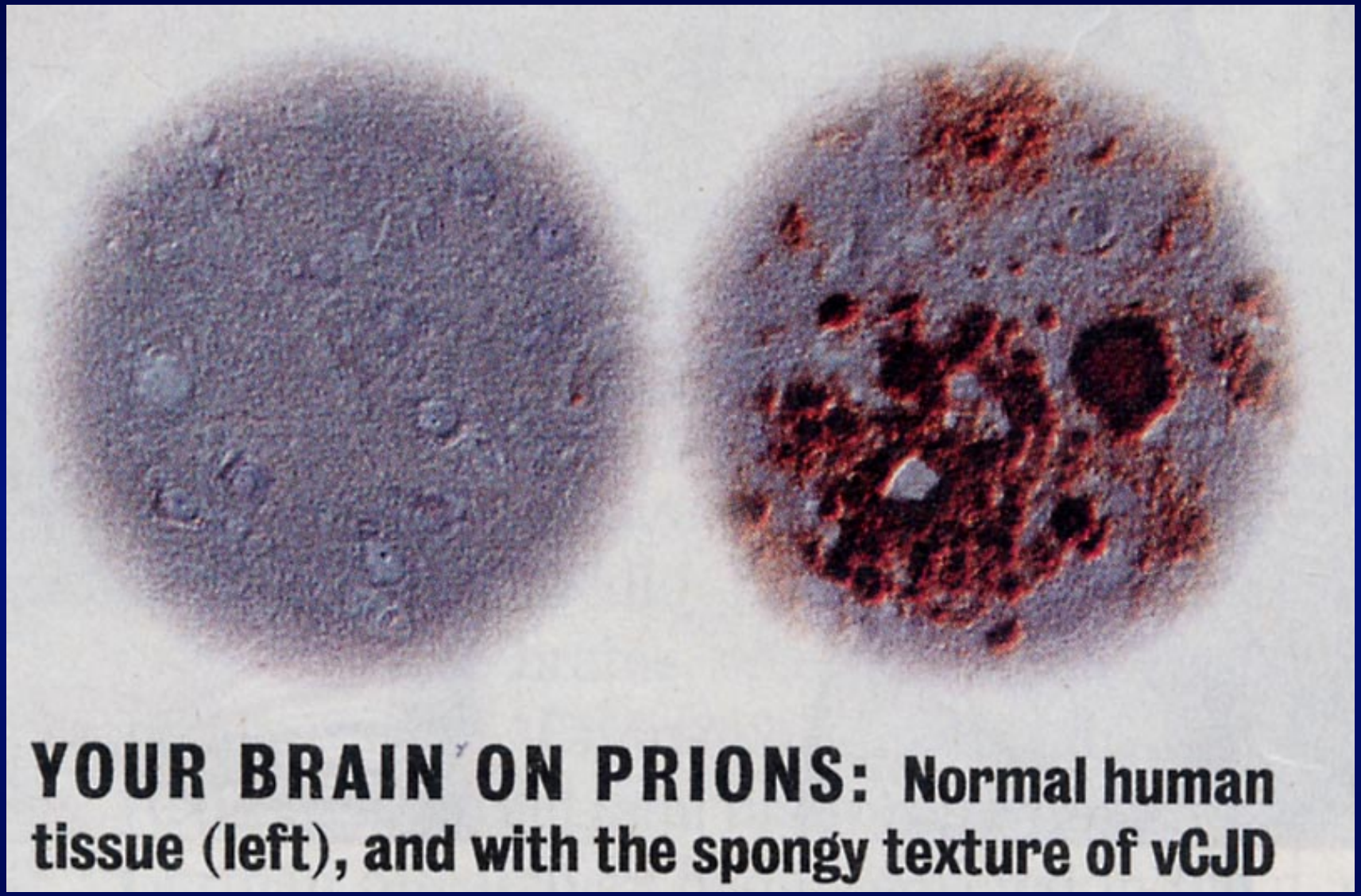
台灣庫賈氏病之現況與因應

長庚紀念醫院 - 高雄醫學中心

長庚大學醫學院

台灣神經學學會

陳順勝



YOUR BRAIN ON PRIONS: Normal human tissue (left), and with the spongy texture of vCJD

Newsweek, March 2, 2001

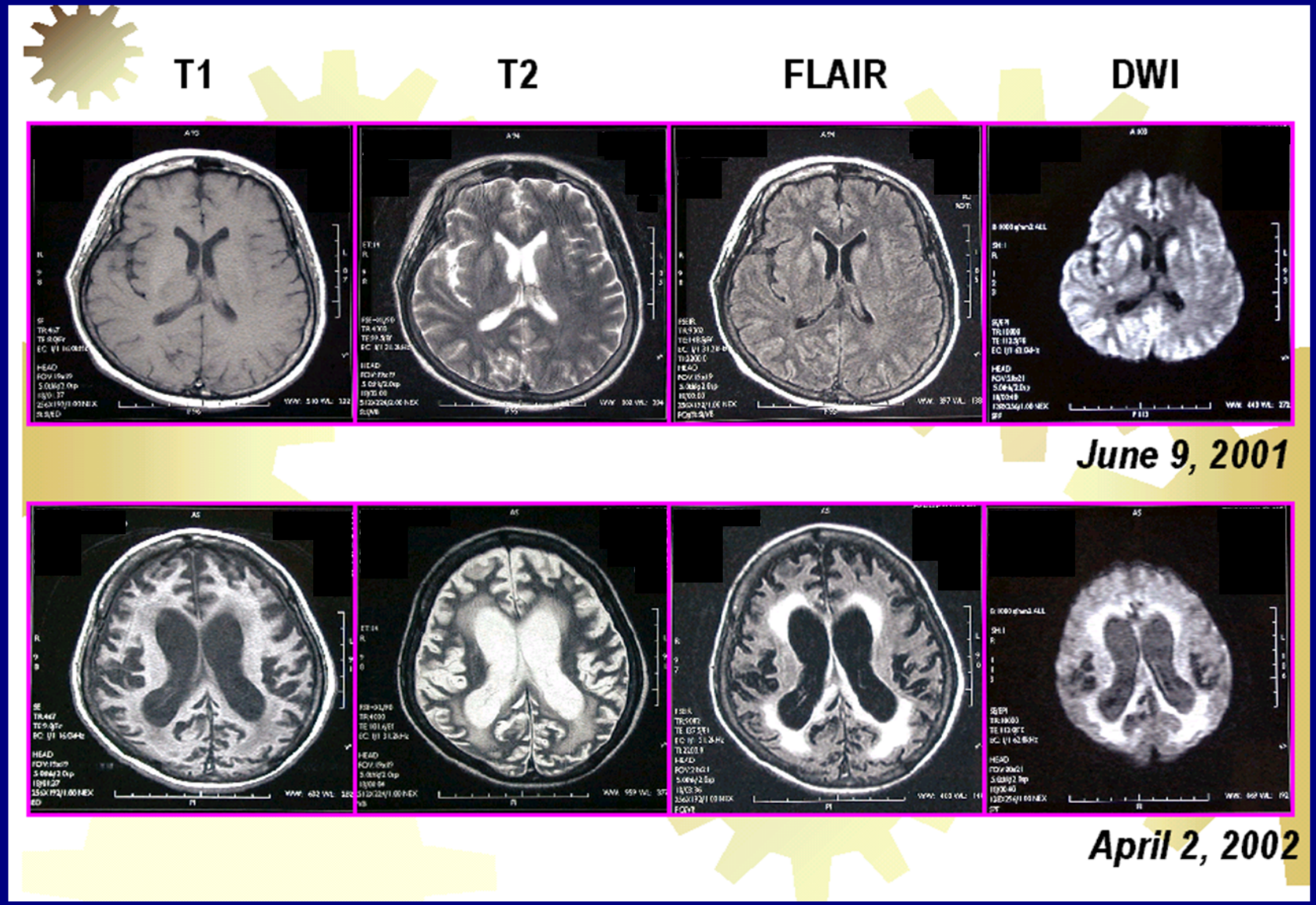
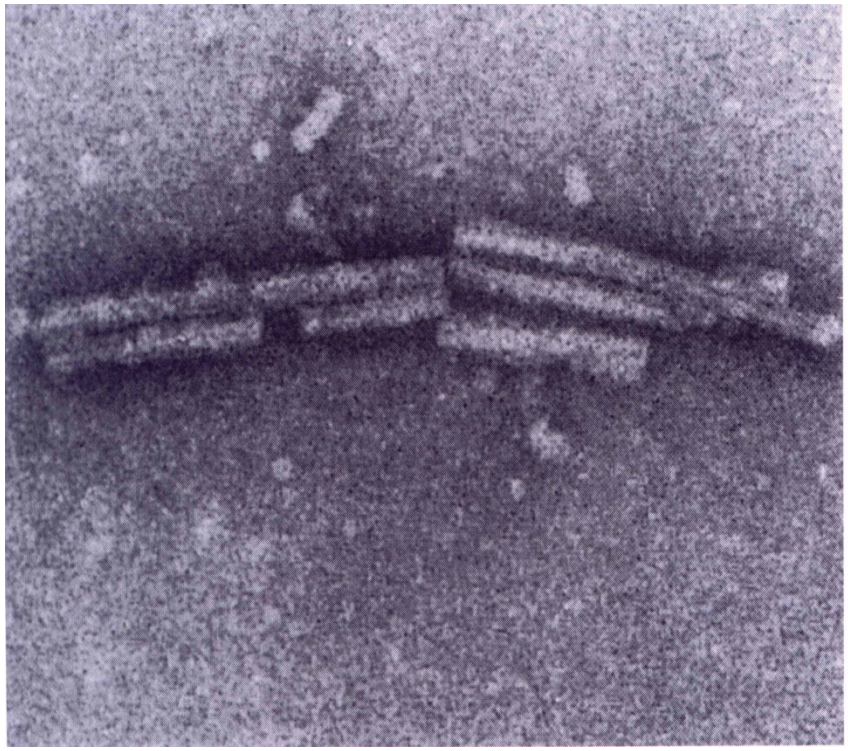
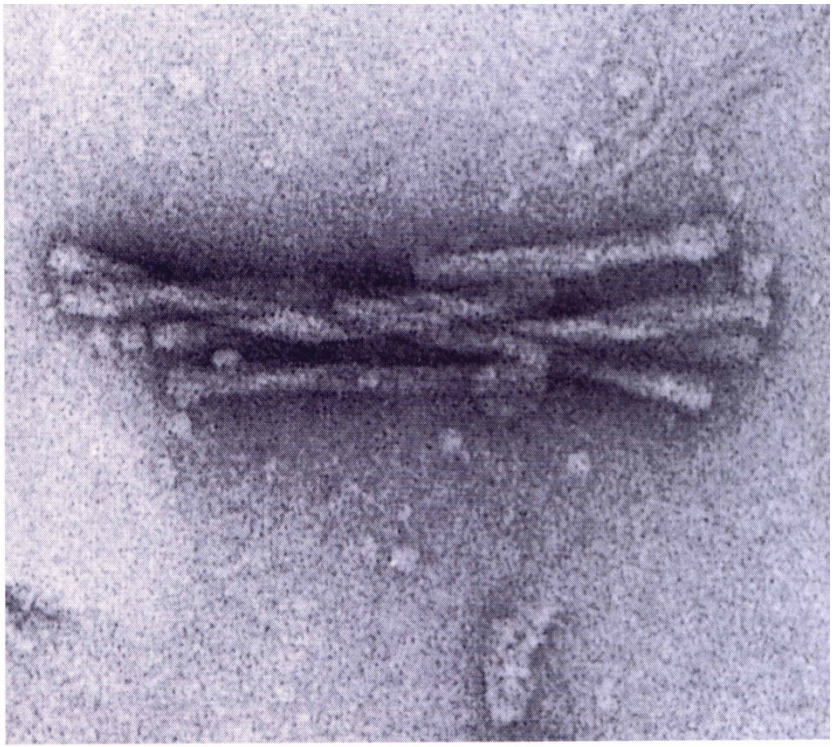


Fig 3. Serial T1, T2, FLAIR and DWI MRI findings of a CJD patient: upper – early stage; lower – late stage. FLAIR and DWI are more sensitive than traditional T1 and T2 MRI. FLAIR and DWI are more promise for detecting the lesion at early stage for the diagnosis of CJD. Usually findings are found in basal ganglion, thalamus, peri-aqueduct, cerebral cortex, especially at the parieto-occipital cortex and these are correlated well with the neurological findings and clinical severity.

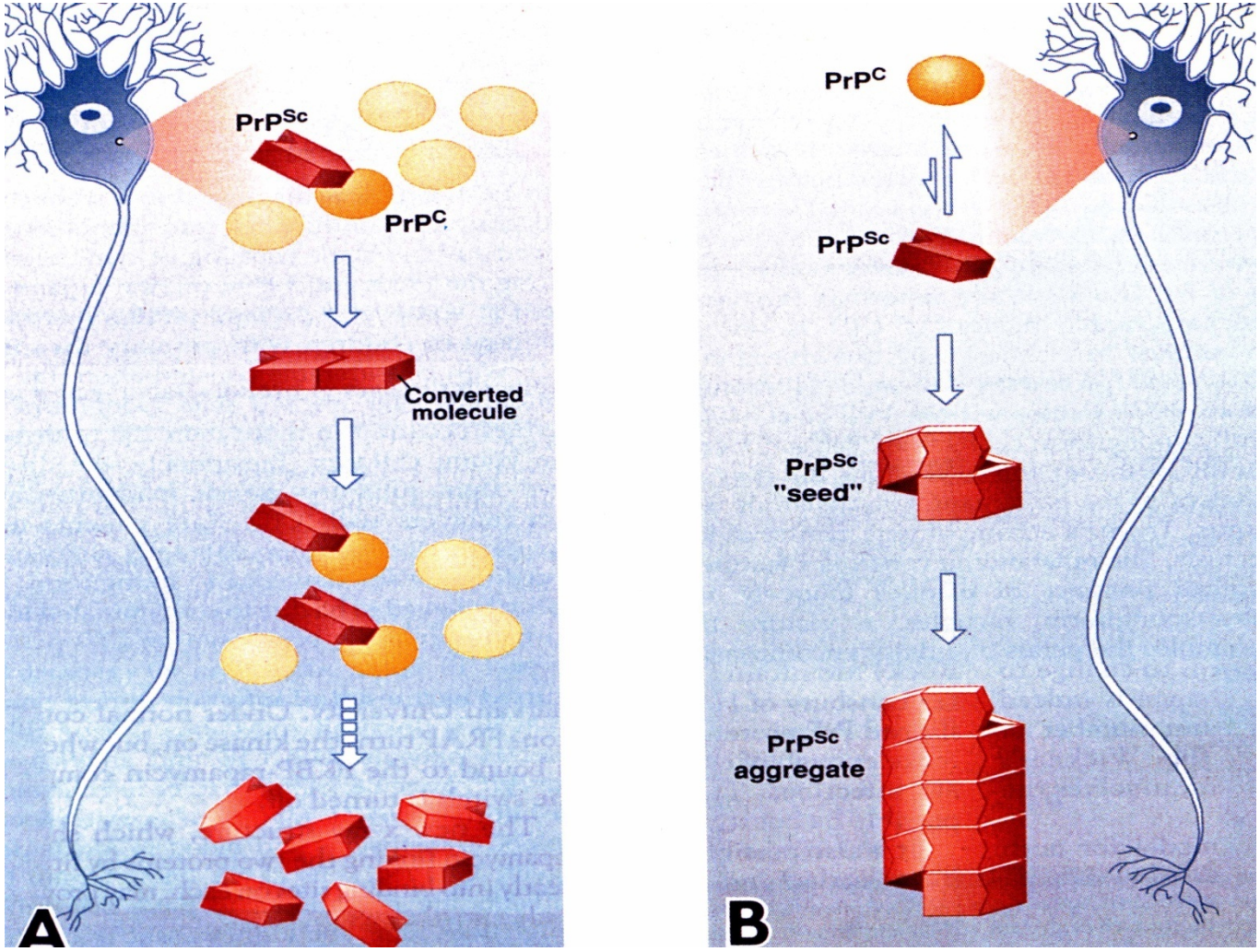
Purified prion protein rods from CJD under EM





(Prusiner 1997)

Hypothesis of infectious prions causing disease



(Prusiner 1997)

PrP^{c}與PrP^{sc}的不同
只是型態上的差異

普力昂疾病國內外歷史沿革

- 發現疾病及臨床觀察
- **Gajdusek** 與慢性感染學說
- **Prusiner** 與 **Prion**學說
- 致病機轉及觀念的改變:基因工程的進步
- 治療的現況

Creutzfeld and Jakob

庫賈氏病 (Creutzfeld Jakob Disease, CJD)，於1920年由 Hans Gerhard Creutzfeld發表第一個病例，隔年Alfons Maria Jakob 也發表四個類似的病例。

其中一名Jakob的病人所留下的腦部病理切片，經過後人一再的驗證後，認為這名病人有最典型的病理變化。

來自古老部落的怪病: Kuru

•Kuru是富雷土著的一句土話，是身體會顫抖的意思。得了Kuru症的病人，除了身體會出現這種不自主的顫抖之外，還會目光呆滯，並有走路不穩，手腳動作不靈活等情況，病況會逐漸加重而終致死亡。

•Kuru, 原本被認為是存在該部落的遺傳性或營養性疾病

•Gajdusek從高度的家族性相關，及家族中病患的死亡年紀相近，因而高度懷疑kuru症是遺傳因素所造成。

•這個不能圓滿地解釋kuru症的特殊的年齡及性別的分布:如果是小孩的病患，則男女比例差不多；如果是大人生病，幾乎都是女性。

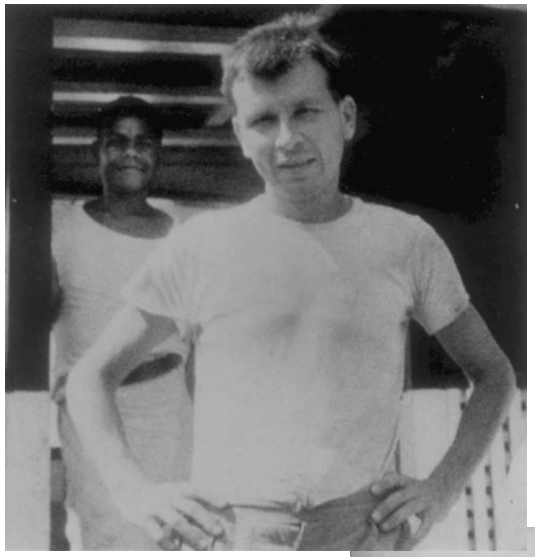
Gajdusek 研究Kuru

•Gajdusek 自1956 年開始研究Kuru, 當時年紀比蘇東坡自稱老夫的年紀還小四歲; 據說他不僅口才極佳,而且可以六種語言向人解試釋他的觀點

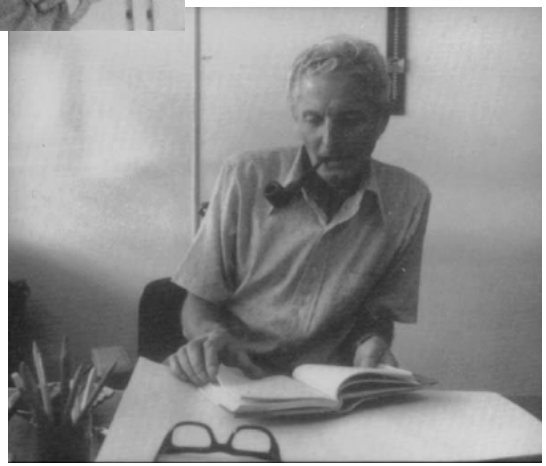
•他是一位美國小兒科醫師, 也是一位病毒學家;之所以對kuru產生興趣, 是因為有一回到澳洲旅遊時, 聽到kuru病的傳說

•Gajdusek到了澳洲和Zigas一起研究Kuru這個怪病，而於1957年11月4日發表了他們的第一篇報告，他們在報告中說：Kuru的病因仍未知。不過高度懷疑是遺傳因素所造成。

D. Carleton Gajdusek in New Guinea 1957



Vincent Zigas



重大的進展-羊搔癢症

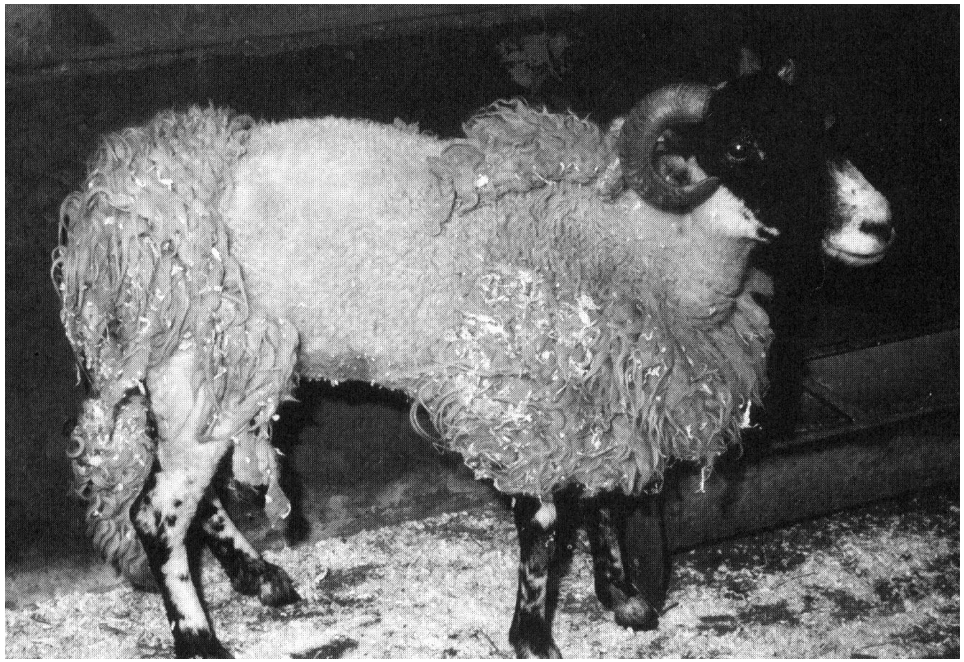
- 來自一個偶然的情況，這個偶然的情況與羊搔癢症有關。

Scrapie first recognized in England in 1732.

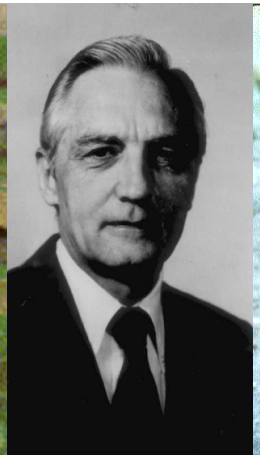
1888, neuronal vacuolation discovered in brains of scrapie-sick sheep

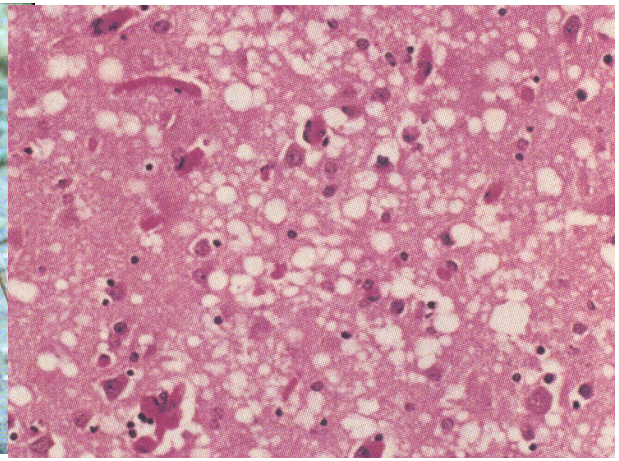
1918, contagious spread of scrapie in natural conditions suspected

1939, experimental transmission of scrapie from sheep to goat



Scrapie-kuru connection



有一位美國動物神經病理學者名為William Hadlow到倫敦進修, 在1959年6月28日一晚宴上遇到一位 Jellison, 當時 Jellison 告訴 Hadlow 去看個展覽; 5天後 Hadlow 真的去了…

Hadlow 看到 kuru 病人的腦組織病理圖, 和 scrapie 病羊的腦組織病理很像, 於是Hadlow 在 7 月18日寫一封信給Lancet, 也在7月21日寫一封信給Gajdusek; 不過Gajdusek 並不採信, 因為在病理檢查上並沒有發炎反應，而且他的接種實驗一直不成功…

The First Nobel Prize

Gajdusek於1956年在澳洲的巴布紐新幾內亞的土著部落開始研究Kuru症。

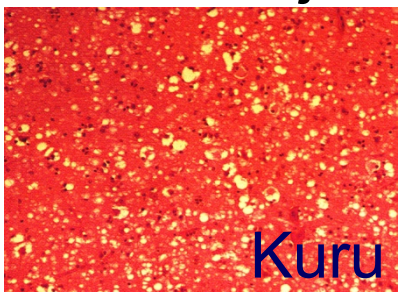
得了Kuru症的病人身體會不自主的顫抖、目光呆滯、走路不穩、手腳動作不靈活等症狀，而病人最後都會死亡，無一存活。

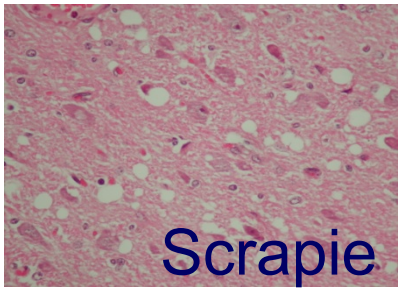
當時的Gajdusek認為其病因可能是當地營養不良或基因遺傳疾病，但卻無法圓滿合理地解釋Kuru症的特殊的年齡及性別分布(成人發病為女性居多，兒童則比例接近)。

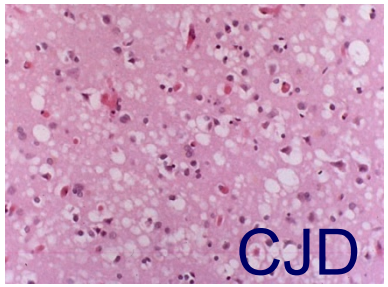
D. Carleton Gajdusek 1923-

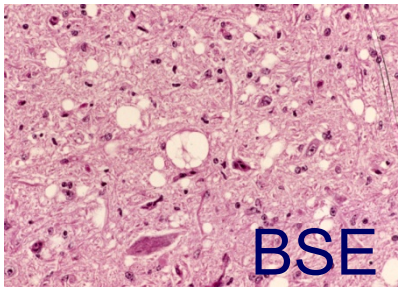
The First Nobel Prize

由於Gajdusek曾多次嘗試接種病源失敗，但此一瓶頸在一名獸醫師-William Hadlow看到Kuru症病人的腦切片後，有了重大突破。1959年，Hadlow發現Kuru症病人的腦切片與羊搔症病羊的腦切片極為相似後，他將此發現發表於Lancet，但對此發現，Gajdusek並不以為意。

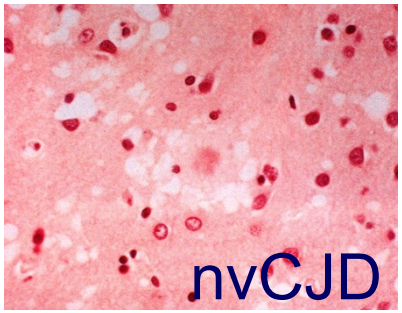






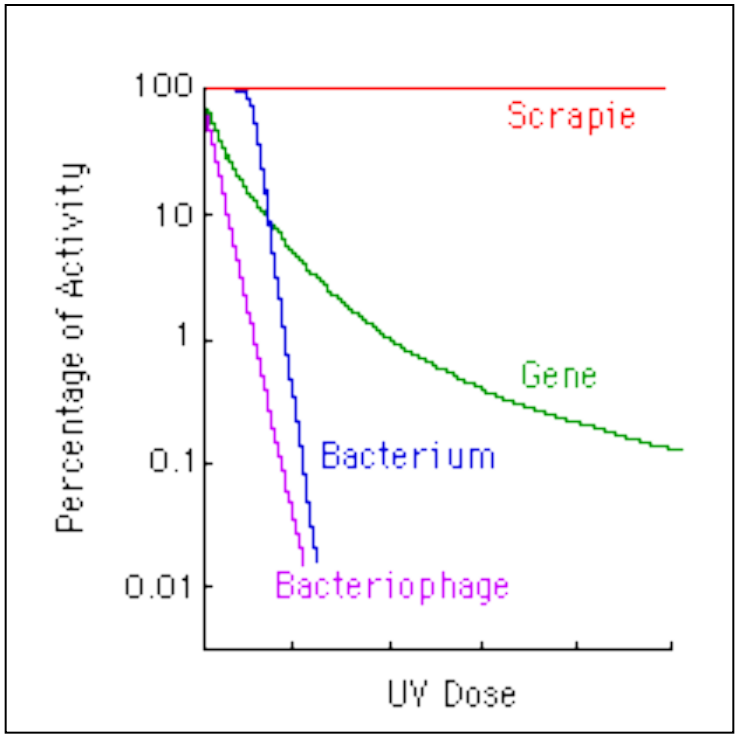


到了1965年，兩年前接受病童腦組織接種的黑猩猩開始發病，隔年Gajdusek將此結果發表後，1968年確定了Kuru症是一種慢性傳染的疾病。Gajdusek因此重大發現在1976年得到諾貝爾獎。



觀念從慢性病毒感染
轉為Prion 感染

Alper's report: 病原體的重要特性



What is it if the organism lacks DNA and RNA?

Tikvah Alper
Hammersmith Hospital, London

The exceptionally small size of the scrapie agent. Biochem Biophys Res Commun 1966; 22:278-284

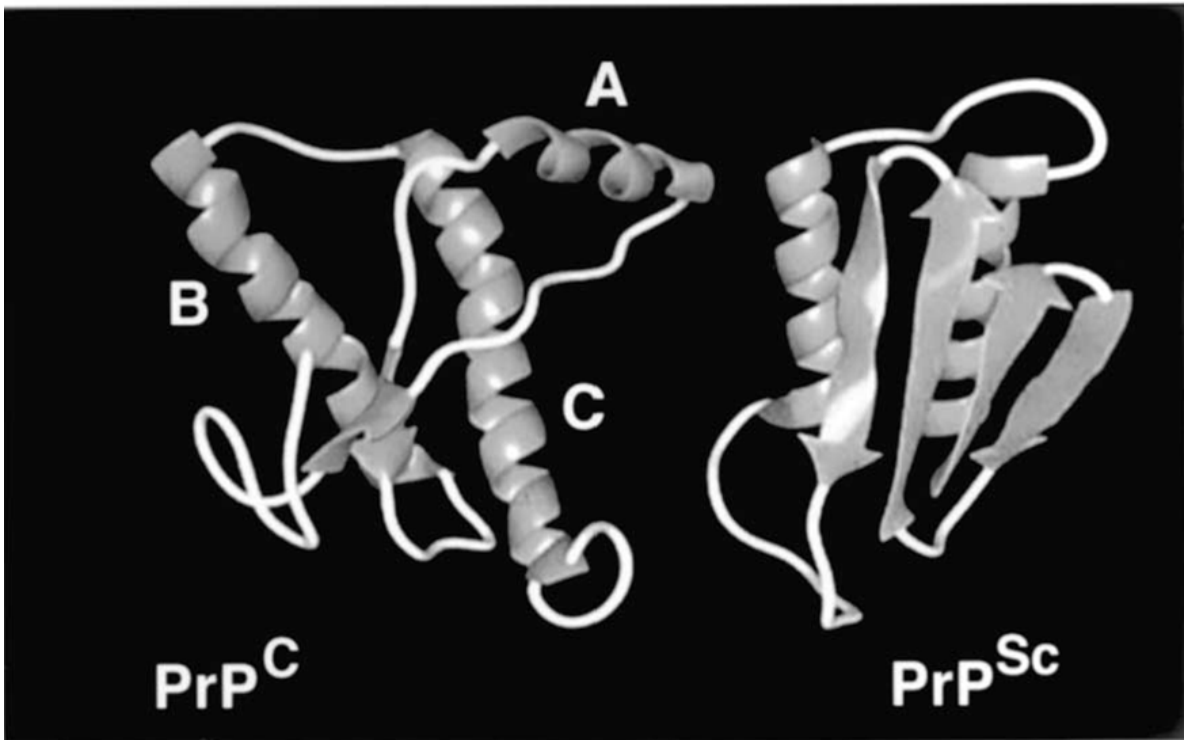
Does the agent of scrapie replicate without nucleic acid? Nature 1967; 214:764-766

Prion theory

- Dr. Stanley Prusiner, UCSF, Moffitt-Long Hospital
- 1972, 開始研究CJD,當時他年僅而立, 是UCSF的住院醫師; 是一位神經科醫師, 也是一位生物化學家
- 1982, 純化出 Prion; 文章發表在 Science: Novel proteinaceous particles cause scrapie.
- 55 歲得到Nobel Prize

The Second Nobel Prize

Prusiner在1982年純化出導致羊搔症的蛋白質PrP，並發現PrP有兩種型式：一種會致病(PrP^{sc})，另一種則不會(PrP^{c})，並且研究出PrP^{sc}的致病模型。Prusiner因此在1982年獲得諾貝爾獎。



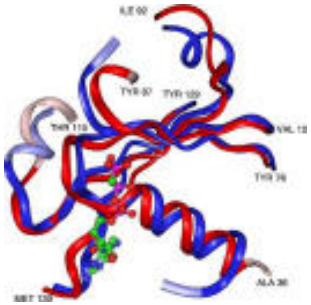
醫源性庫賈氏病

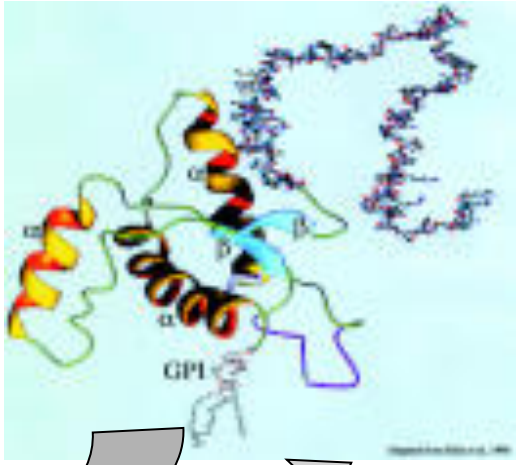
- Gajdusek的研究成果，讓人開始警覺到CJD是否會傳染，所以在1970年代開始，陸續有醫源性感染庫賈氏病的案例出現。
- First case occurred in 1971: a 55-year-old woman developed CJD 18 months after transplantation of a cadaveric corneal graft, which had been obtained from a 55-year-old man who had died of pathologically confirmed CJD (Duffy, DeVoe; reported in 1974).
- Brown在2000年的報告:267位iatrogenic CJD

  Corneal transplantation (3), stereotactic EEG (2), neurosurgery (5), dural matter graft (114), pituitary-derived hormone (139), gonadotropin (4)
- 小結論：這個病可以自成一類，可以有偶發型、遺傳型及感染型等數種型式。

Identification of PrP and gene

Purification and structural studies of a major scrapie prion protein. **Cell 1984; 38:127-134**





Probe

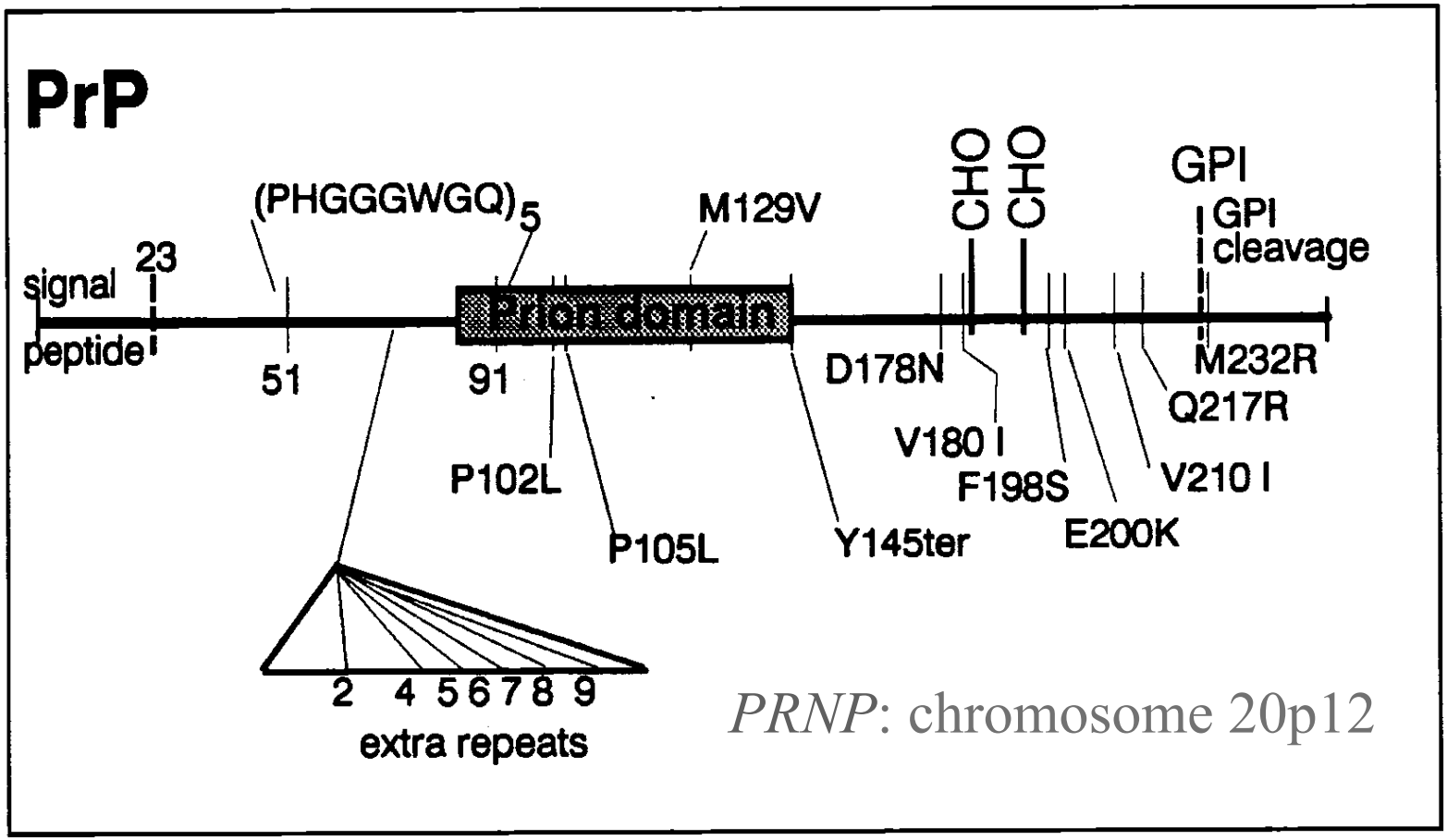
From hamster brain

- Prusiner與California Institute of Technology的Hood合作，辨認出位於PrP蛋白一端的15個胺基酸的序列，然後，根據這一段胺基酸序列做出一個probe

Point mutation in a patient with GSS

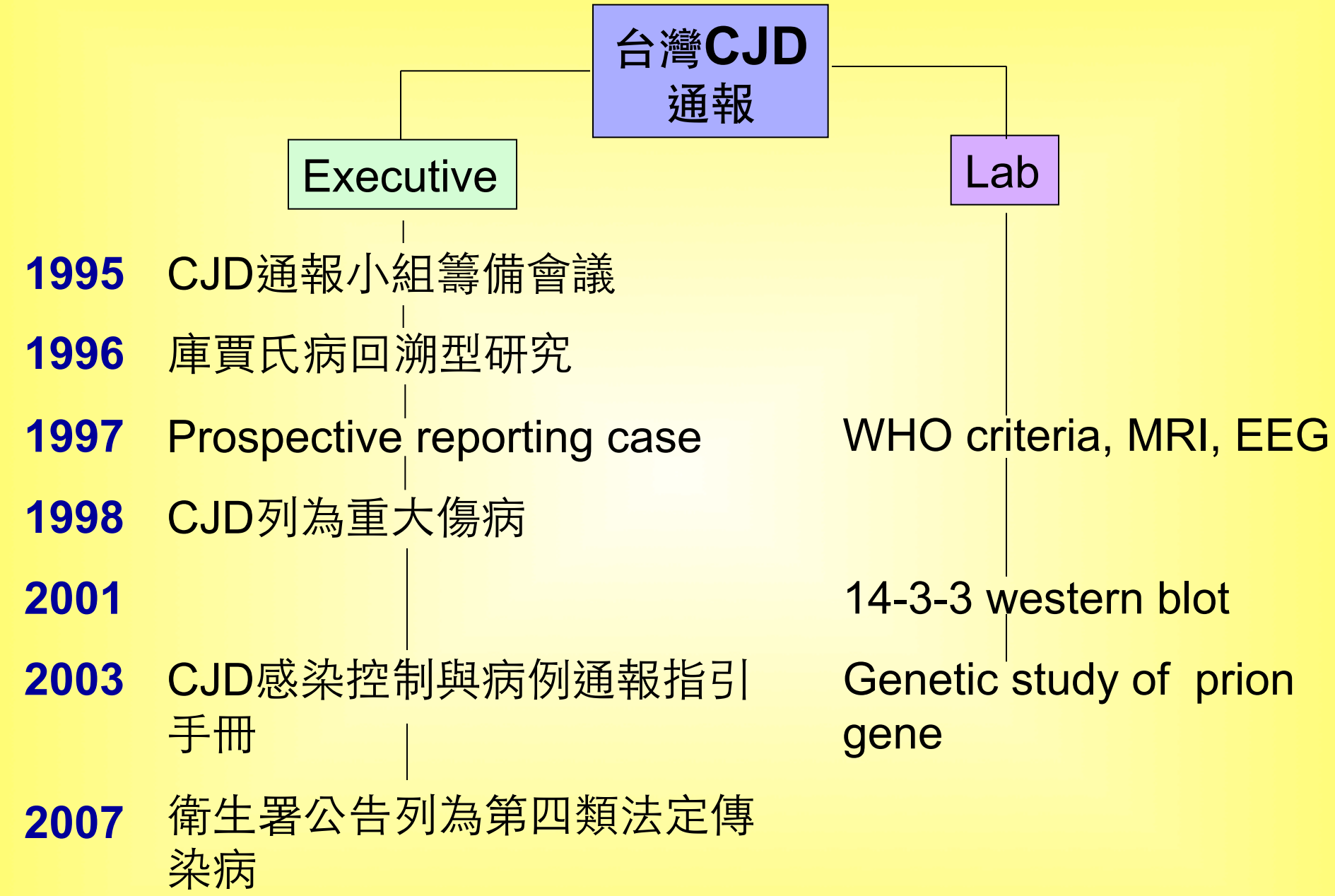
- 在1988年時，Prusiner和他實驗室中的同事Hsiao一起，從一個Gerstmann-Straussler-Scheink (GSS)症的病人身上clone出一段PrP的基因
- 然後和正常人的PrP基因做比較，相較之下，發現了一個點突變(point mutation)。
- 而這個點突變，會改變codon102的遺傳訊息，而將PrP蛋白質上的一個proline變成leucine。

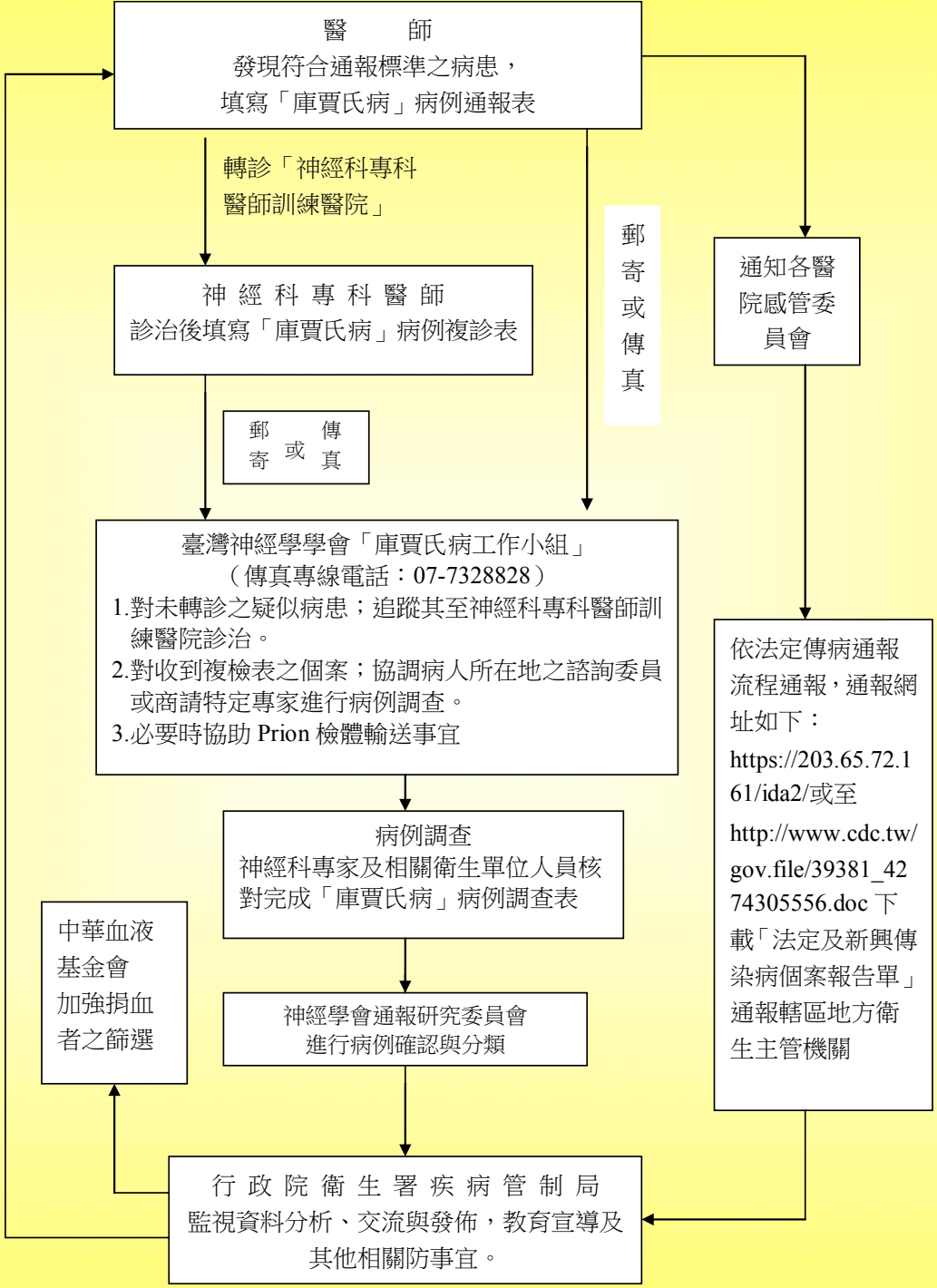
迄今至少有20個以上的突變



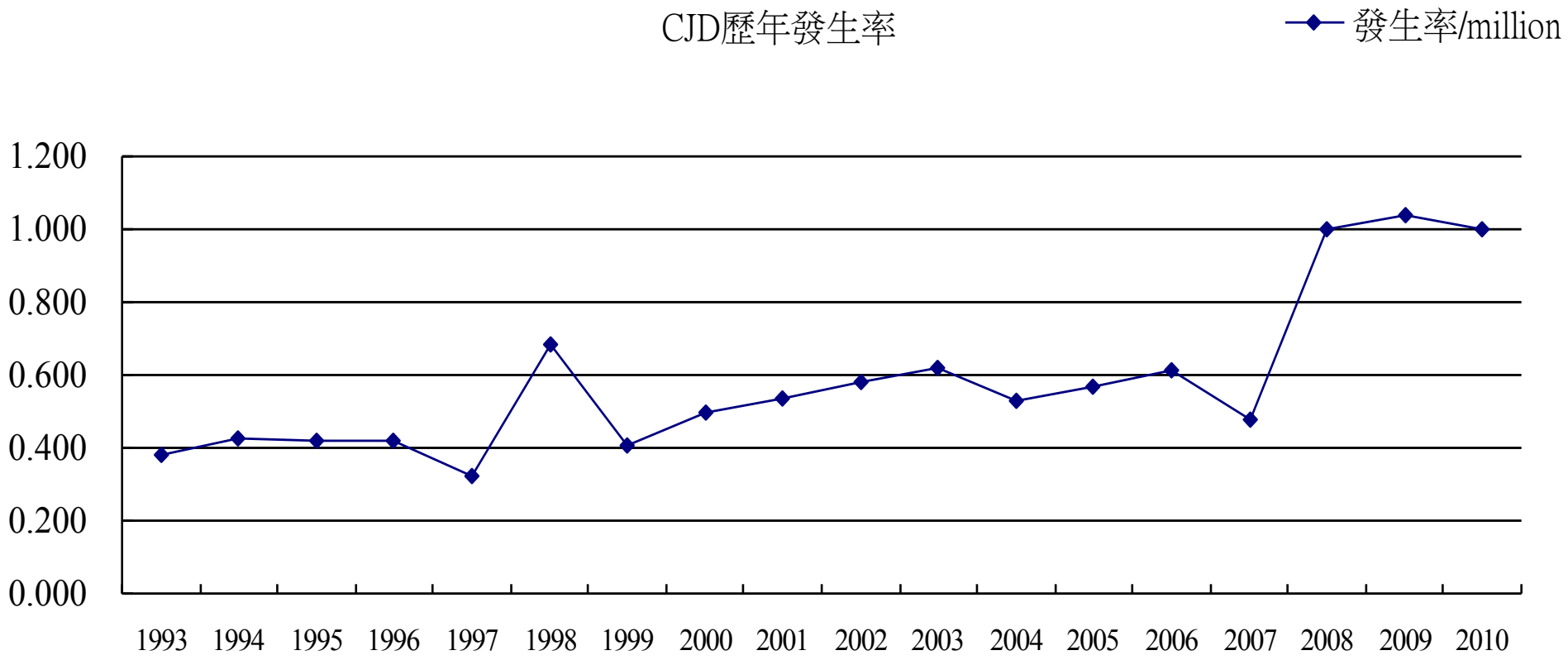
庫賈氏病的病因模式

- 偶發型(sporadic CJD, sCJD)：發病原因不明
- 遺傳型(familial CJD, fCJD)：部分家族顯性遺傳 (Cases in Taiwan)
- 醫源型(iatrogenic CJD, iCJD)：因醫療行為感染
- 新型(variant form CJD, vCJD)：英國於1996年首次於Lacent發表病例，並指出此病與狂牛症相關


台灣CJD
通報
Executive
Lab
1995
CJD通報小組籌備會議
1996
庫賈氏病回溯型研究
1997
Prospective reporting case
WHO criteria, MRI, EEG
1998
CJD列為重大傷病
2001
14-3-3 western blot
2003
CJD感染控制與病例通報指引手冊
Genetic study of prion gene
2007
衛生署公告列為第四類法定傳染病


醫　師
發現符合通報標準之病患，
填寫「庫賈氏病」病例通報表
轉診「神經科專科
醫師訓練醫院」
郵寄或傳真
通知各醫院感管委員會
神經科專科醫師
診治後填寫「庫賈氏病」病例複診表
郵寄或傳真
臺灣神經學學會「庫賈氏病工作小組」
（傳真專線電話：07-7328828）
1.對未轉診之疑似病患；追蹤其至神經科專科醫師訓練醫院診治。
2.對收到複檢表之個案；協調病人所在地之諮詢委員或商請特定專家進行病例調查。
3.必要時協助 Prion 檢體輸送事宜
依法定傳病通報流程通報，通報網址如下：
https://203.65.72.161/ida2/或至
http://www.cdc.tw/gov.file/39381_4274305556.doc 下載「法定及新興傳染病個案報告單」通報轄區地方衛生主管機關
病例調查
神經科專家及相關衛生單位人員核對完成「庫賈氏病」病例調查表
中華血液基金會
加強捐血者之篩選
神經學會通報研究委員會
進行病例確認與分類
行政院衛生署疾病管制局
監視資料分析、交流與發佈，教育宣導及其他相關防事宜。

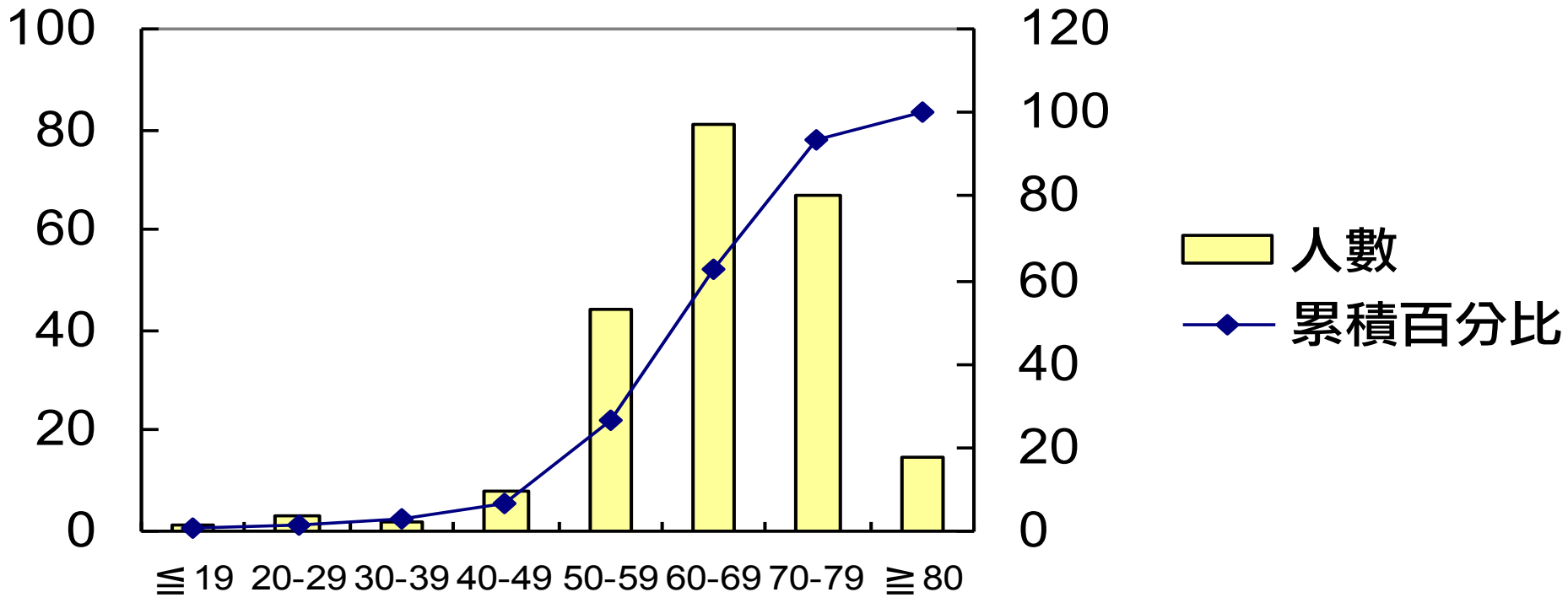
臺灣CJD歷年發生率

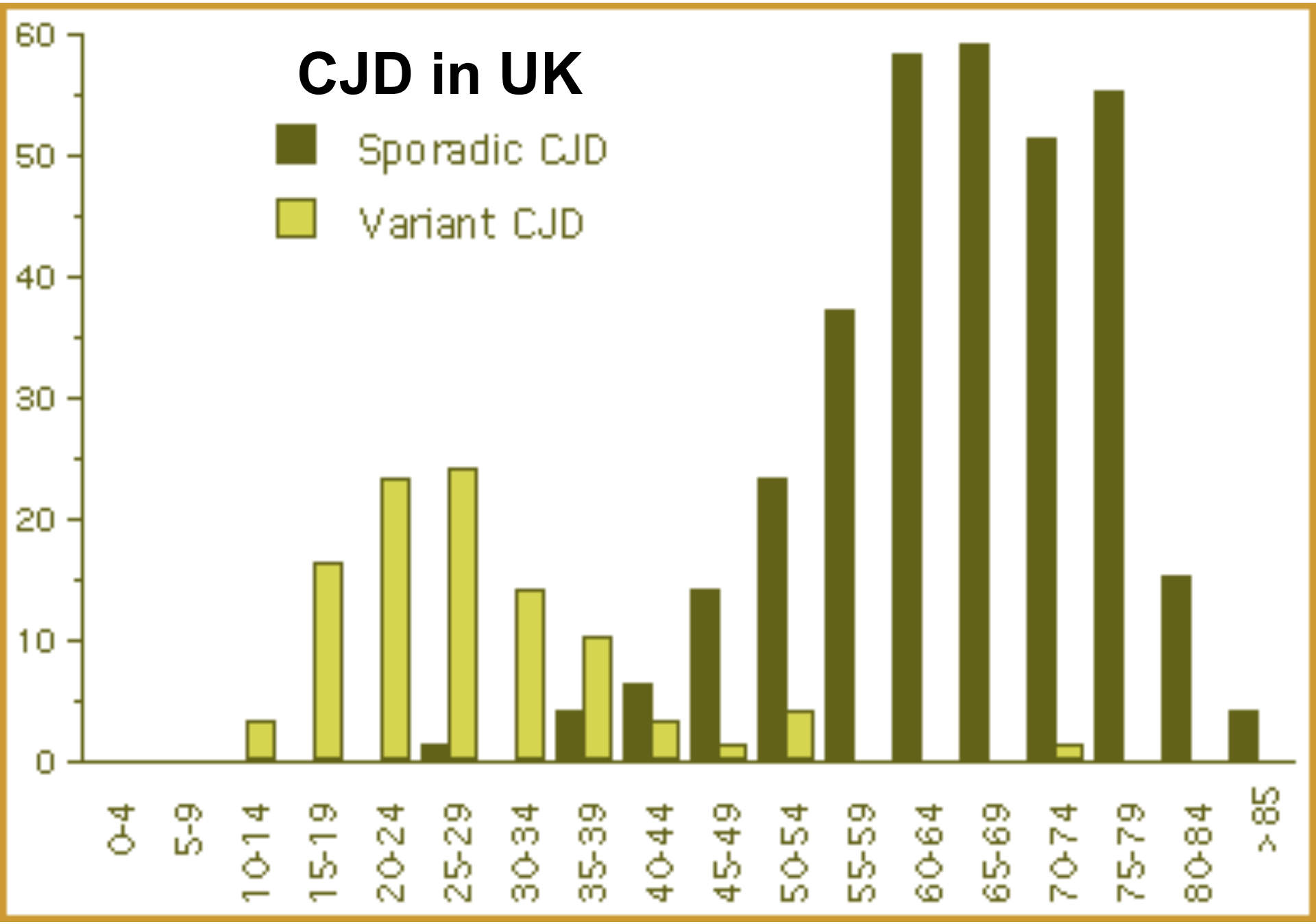


nv CJD in the world

	英國	法國	愛爾蘭共和國	義大利	美國	加拿大	沙烏地阿拉伯	日本	荷蘭	葡萄牙	西班牙*
Case No.	174	25	4	2	3	1	1	1	3	2	5

台灣庫賈氏病病人年齡分布



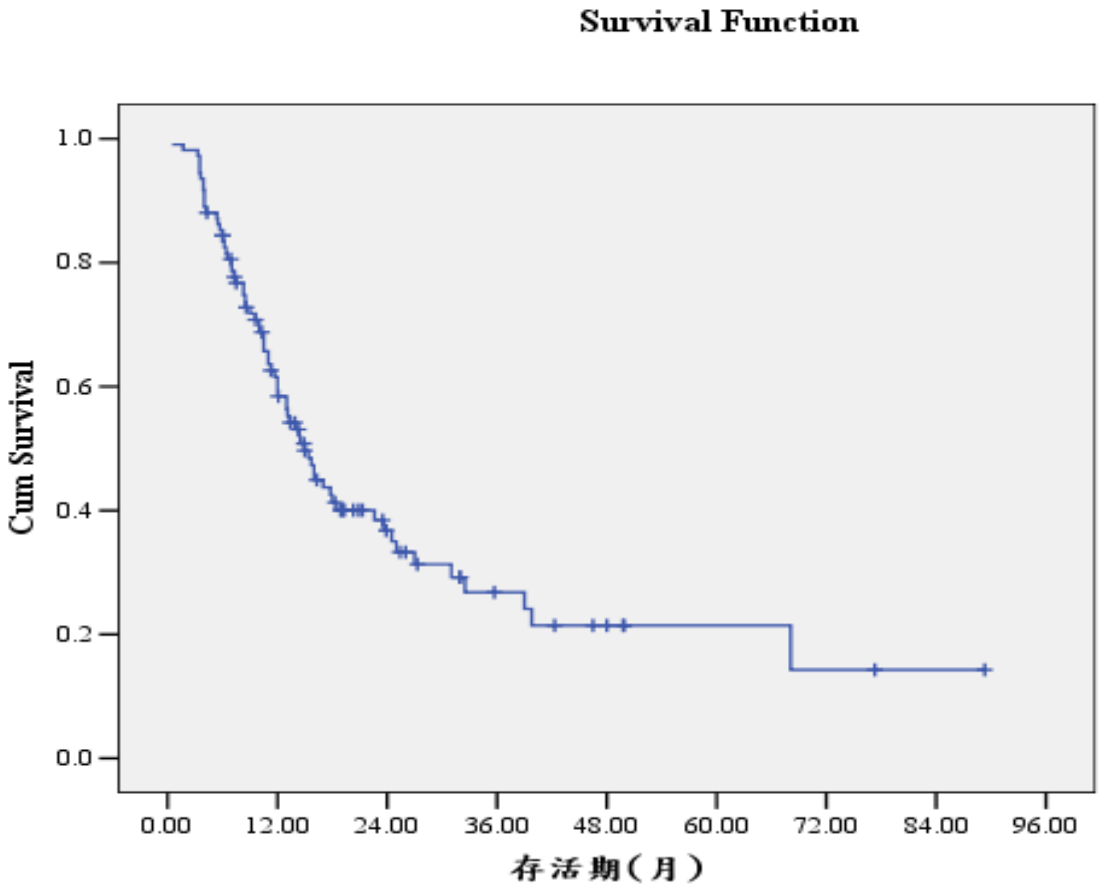

CJD in UK
Sporadic CJD
Variant CJD
60
50
40
30
20
10
0
0-4
5-9
10-14
15-19
20-24
25-29
30-34
35-39
40-44
45-49
50-54
55-59
60-64
65-69
70-74
75-79
80-84
>85

臺灣CJD疫情現況及研究成果-各國比較

國家別	平均年發生率/年別	平均年發生率/年別	平均年發生率/年別
奧地利	0.18（1969-1985）	0.67（1986-1994）	1.15（1995-2001）
法國	0.34（1968-1977）		1.52（1993-2001）
澳洲	0.66（1970-1980）		1.39（1997-2001）
美國	0.26（1973-1977）		1.1（1991-1998）
日本	0.45（1975-1977）		1.28（1979-2004）
臺灣		0.51（1995-2007）	0.97（2008-2009）

臺灣CJD疫情現況及研究成果

- 至98年，累計存活可達12月以上者僅達58.4%，累計存活達24月以上者僅達35.0%。較96年存活12月以上提升9.4%，存活24月以上增加15.1%。



Eur J Epidemiol
DOI 10.1007/s10654-010-9446-4

NEURO-EPIDEMIOLOGY

Incidence of Creutzfeldt-Jakob disease in Taiwan: a prospective 10-year surveillance

Chien-Jung Lu · Yu Sun · Shun-Sheng Chen

Received: 18 August 2009 / Accepted: 8 March 2010

Table 1 Annual incidence rate per 1,000,000 person year of CJD in Taiwan from 1998 to 2007

	Crude annual incidence in 2-year period					Total (1998–2007)		
	1998–1999	2000–2001	2002–2003	2004–2005	2006–2007	No. of CJD cases	Crude incidence (95% CI)	Age-adjusted incidence (95% CI)[a]
Men	0.44	0.48	0.70	0.61	0.39	60	0.52 (0.41–0.67)	0.51 (0.39–0.66)
Women	0.70	0.60	0.50	0.45	0.62	63	0.57 (0.45–0.73)	0.52 (0.40–0.68)
Total	0.57	0.54	0.60	0.53	0.50	123	0.55 (0.46–0.65)	0.52 (0.43–0.62)

[a] Age-adjusted annual incidences were calculated with the use of Taiwan census data in 2000

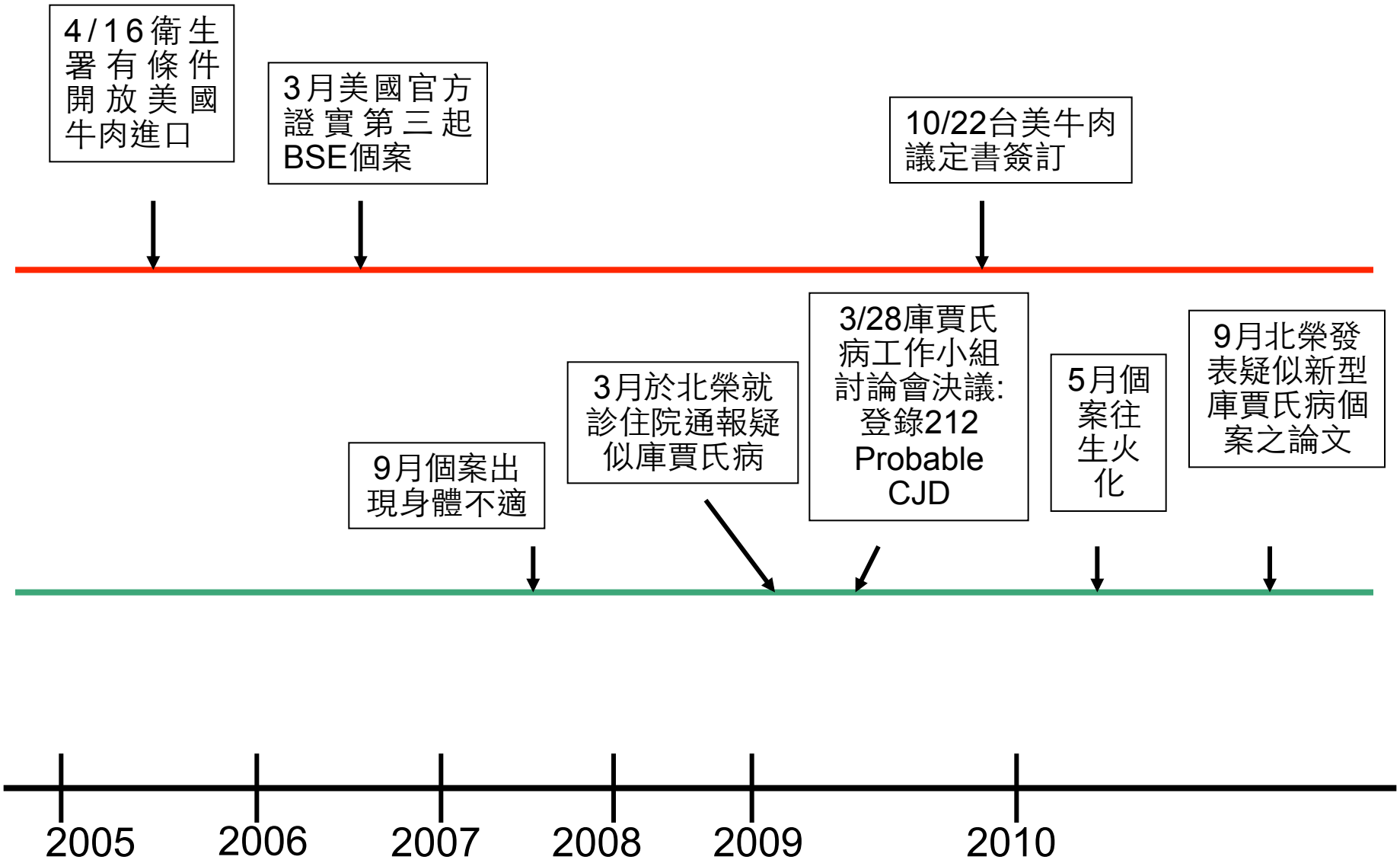
傳統庫賈氏病與新型庫賈氏病

特色	傳統庫賈氏病 CJD	新型庫賈氏病 nvCJD
死亡時的年齡中位數	68年	28年
患病期間中位數	4-5個月	13-14個月
臨床症狀和體徵	老年癡呆症，早期神經系統症狀	明顯精神病學/行為症狀；感覺異常dysesthesias ;延遲神經系統症狀
陣歇性腦電圖尖波	常有	經常無
高信號在尾狀核和殼核的擴散加權和FLAIR MRI	常有	經常無
枕葉雙邊高信號強度的FLAIR MRI檢查。此外後丘腦上矢狀T2序列	未報告	目前在> 75%的病例
免疫組織化學分析的腦組織	可變的積累。	標記積累蛋白酶抗朊蛋白
Presence of agent in lymphoid tissue	不容易發現	隨時檢測
Increased glycoform ratio on immunoblot analysis of protease-resistant prion protein	未報告	標記積累蛋白酶抗朊蛋白
澱粉樣蛋白斑在大腦組織	可能存在	可能存在

台灣首例新型庫賈氏病通報之回顧

此個案曾於1989年至1997年間留學英國，赴英國曼徹斯特讀書，適逢英國牛海綿狀腦病高峰期，且於2007年4月至2008年3月在澳洲進行機師訓練，但其機師訓練於97年7月中斷。於2008年9月開始出現身體不適，逐漸出現記憶障礙及嗜睡等狀況。因症狀未改善，2009年3月於台北某醫學中心就診住院，神經科醫師懷疑庫賈氏病，於2009/3/27通報至傳染病通報系統，同時採集CSF檢體。2009年3月28日召開庫賈氏病通報工作小組病例討論會，決議結果如下：病人的臨床症狀、神經學評估及MRI符合CJD典型症狀，EEG則不符合，14-3-3結果待驗，故依診斷標準將此病人列為庫賈氏病極可能個案，登錄為第212例庫賈氏病病人。因高度懷疑，為排除病人為新型庫賈氏病之可能，請主治醫師向家屬建議進行扁桃腺切片，並將其檢體除國內檢測外並送往美國及英國檢驗。並協請疾管局成立緊急應變小組安排後續事宜及相關因應措施。若在台灣進行檢驗窒礙難行，亦可考慮將病人直接送往英國進行進一步各項檢查及檢驗。2009年4月，14-3-3 protein檢驗結果為陰性。

美牛案 VS. 新型庫賈氏病個案



台灣首例新型庫賈氏病通報之回顧-專業責任與焦慮

說明一：通報後，全面啟動標準庫賈氏病感管措施，通報醫師告知家屬質疑診斷之可能性，通報醫師也承受相當大的壓力，小組建議未確診前宜低調小心處理，依英國通報小組未確診個案之經驗處理，並嚴守醫學隱私守密倫理。並建議疾管局專案直接介入關懷，設法說服切片確診之可能性，並按月討論追蹤病人病況。

說明二：病理切片場所、設備、專業人員、與prion研究之困難。

說明三：韓國、越南、與泰國曾有虛報新型庫賈氏病之國際笑話事件。

說明四：2009年有鑑於說服切片確診之困難，小組建議將本案寫成病例報告，投稿接受國際專家peer-review，以昭大信。原先通報醫師擬投稿台灣神經學學會，為求國內專家之迴避，小組建議投稿國際神經學刊物由國外專家認定，通報醫師接受。

2010年5月，個案往生，家屬拒絕接受病理解剖，大體已火化處理。2010年6月4日消基會來函疾管局，詢問是否有疑似新類型庫賈氏病病例通報相關資料案。2010年6月11日疾管局依通報小組記錄資料檔，回函表示目前尚無新類型庫賈氏病案例。2010年5月本小組刊登於歐洲流行病學雜誌亦尚未把本病例改判新型庫賈氏病，並獲國際傳染病學會ISID (International Society for Infectious Diseases)轉登。

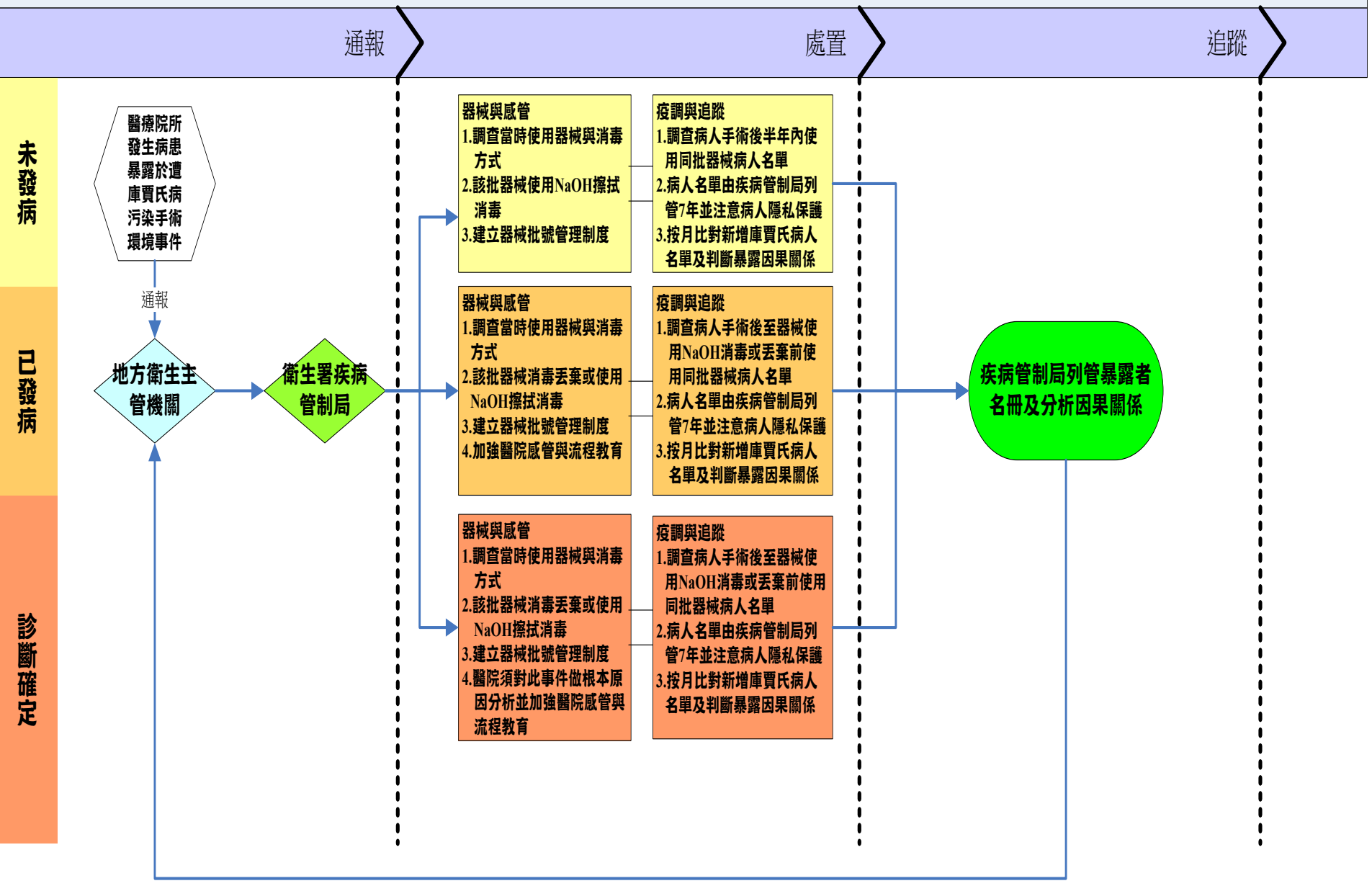
European Journal Epidemiology 2010; 25(5): 341-7
http://www.springerlink.com/content/150215ht76333700/。

該醫學中心醫師於2010年5月5日投稿極可能新型庫賈氏病個案論文一篇於Psychiatry and Clinical Neurosciences Journal，2010年8月13日依審查意見修稿，2010年9月9日期刊接受認定，決定刊此篇文章。2010年11月30日取得刊登之論文。2010年12月9日財訊雜誌獲得資訊報導此案。2010年12月6日已登錄在國際傳染病學會ISID (International Society for Infectious Diseases)。因本例已獲國際專家、國際期刊與相關學會之認定將在本月份例行月會討論改判。

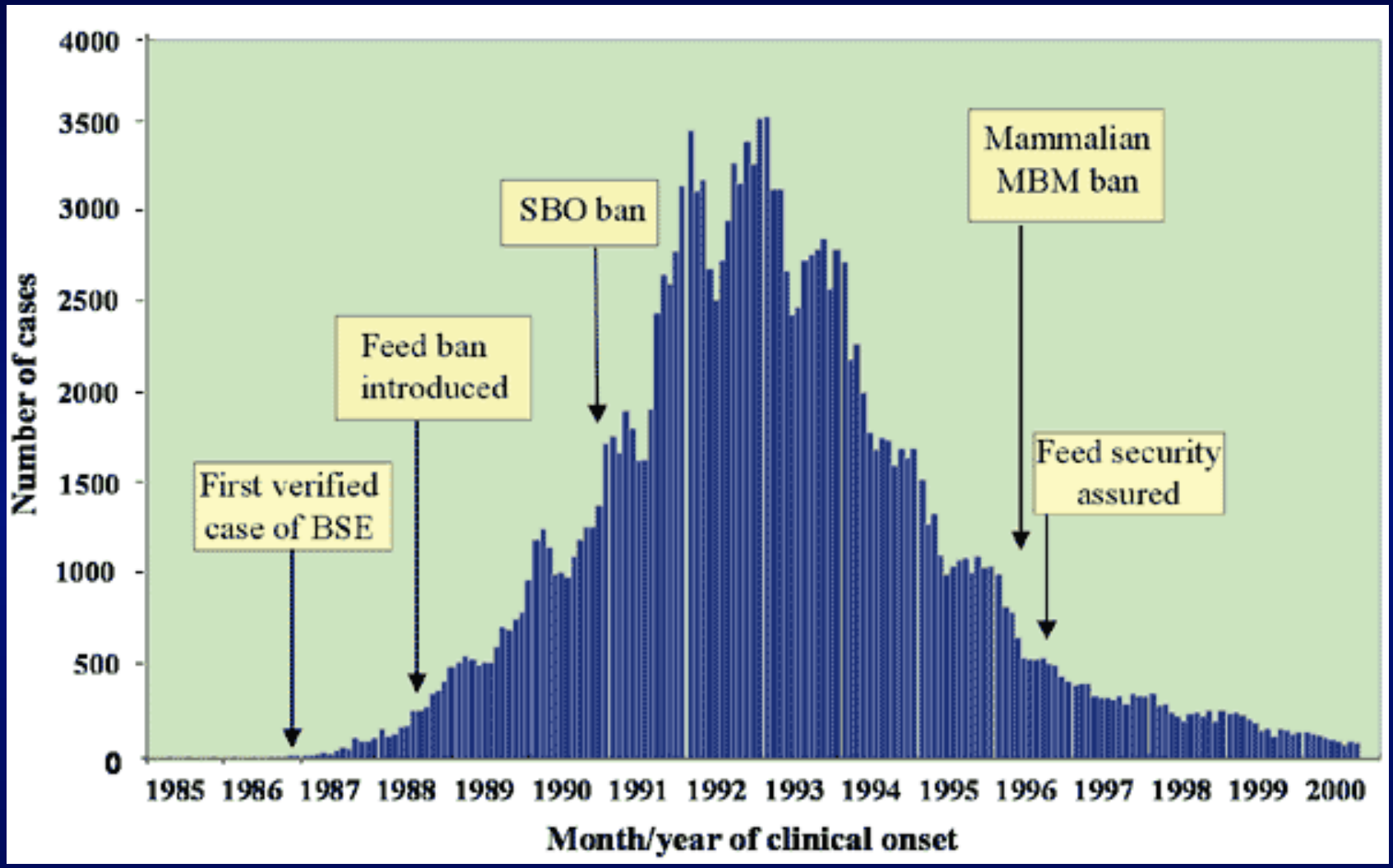
庫賈氏病人未感控管理意外手術之處置流程

器械與管理	意外手術種類	感管與疫調
1. 調查當時使用器械與消毒方式 2. 該批器械使用NaOH插拭消毒 3. 建立器械批號管理制度	未發病	1. 調查使用器械開刀病人名單半年 2. 病人名單由疾病管制局列管併注意隱私保護 3. 按月比對新庫賈氏病人判定暴露因果關析 4. 追蹤七年
1. 調查當時使用器械與消毒方式 2. 該批器械消毒丟棄或NaOH插拭消毒 3. 建立器械批號管理制度 4. 加強醫院感管與其流程教育訓練	已發病	1. 調查使用相同器械開刀病人名單直至器械NOH消毒或丟棄 2. 病人名單由疾病管制局列管併注意隱私保護 3. 按月比對新庫賈氏病人判定暴露因果關析 4. 追蹤七年
1. 調查當時使用器械與消毒方式，將該批器械消毒丟棄或 NaOH插拭消毒 2. 建立器械批號管理制度 3. 醫院須對此事件做根本原因分析(RCA)，提會討論併加強感管流程教育訓練	診斷確定	1. 調查使用器械開刀病人名單直至器械NaOH消毒或丟棄 2. 病人名單由疾病管制局列管併注意隱私保護 3. 按月比對新庫賈氏病人判定暴露因果關析，提會 討論 4. 追蹤七年

醫療院所病患暴露於遭庫賈氏病致病原污染手術環境之處置流程草案



人畜共通的流病經驗



British BSE & the Occurrence of nCJD Cases
from UK Surveillace Unit Homepage

Is Taiwan Potentially Risk for BSE and then vCJD??

BAD FEED FOR SALE

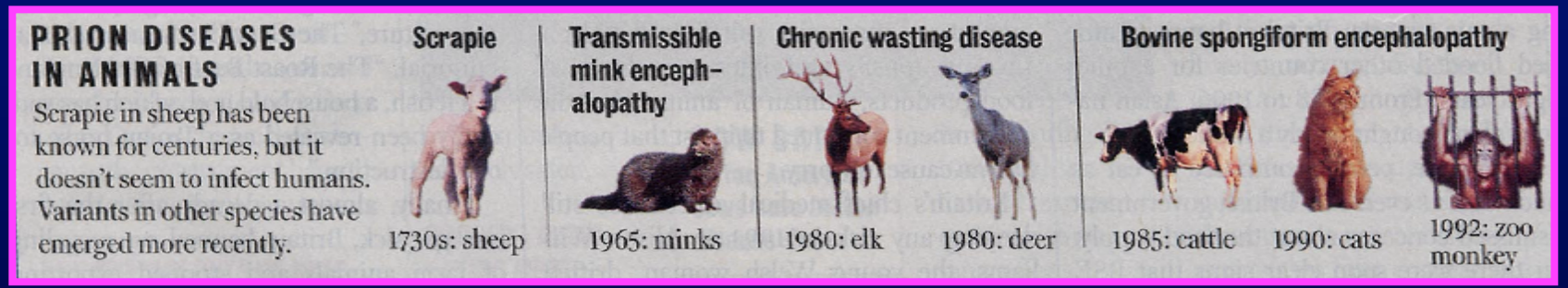
Official British figures show that more than 80 countries imported cattle feed that was probably infected. A partial list of deliveries, 1980–1996:

Imports, in metric tons

Indonesia	600,000
Thailand	185,000
Taiwan	45,000
Philippines	20,000

Newsweek, March, 2, 2001

Zoo spongiform encephalopathy



Newsweek, March 2, 2001

Transmissible Spongiform Encephalopathies (TSEs)

Animal Prion Diseases

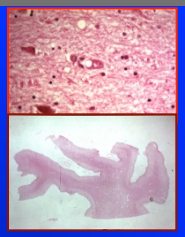
- Scrapie**(SC)**
- Bovine spongiform encephalopathy **(BSE)**

- Transmissible mink encephalopathy **(TME)**

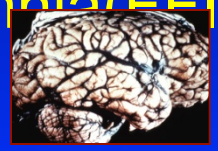
- Feline spongiform encephalopathy **(FSE)**

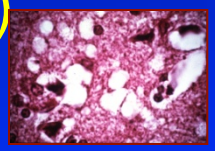
- Chronic wasting disease **(CWD)**

Human Prion Diseases



- Creutzfeldt-Jakob disease(CJD)
- New variant of CJD (nvCJD)
- Gerstamann-Straussler-Scheinker disease (GSS)
- Fatal familial insomnia(FFI)





- Kuru

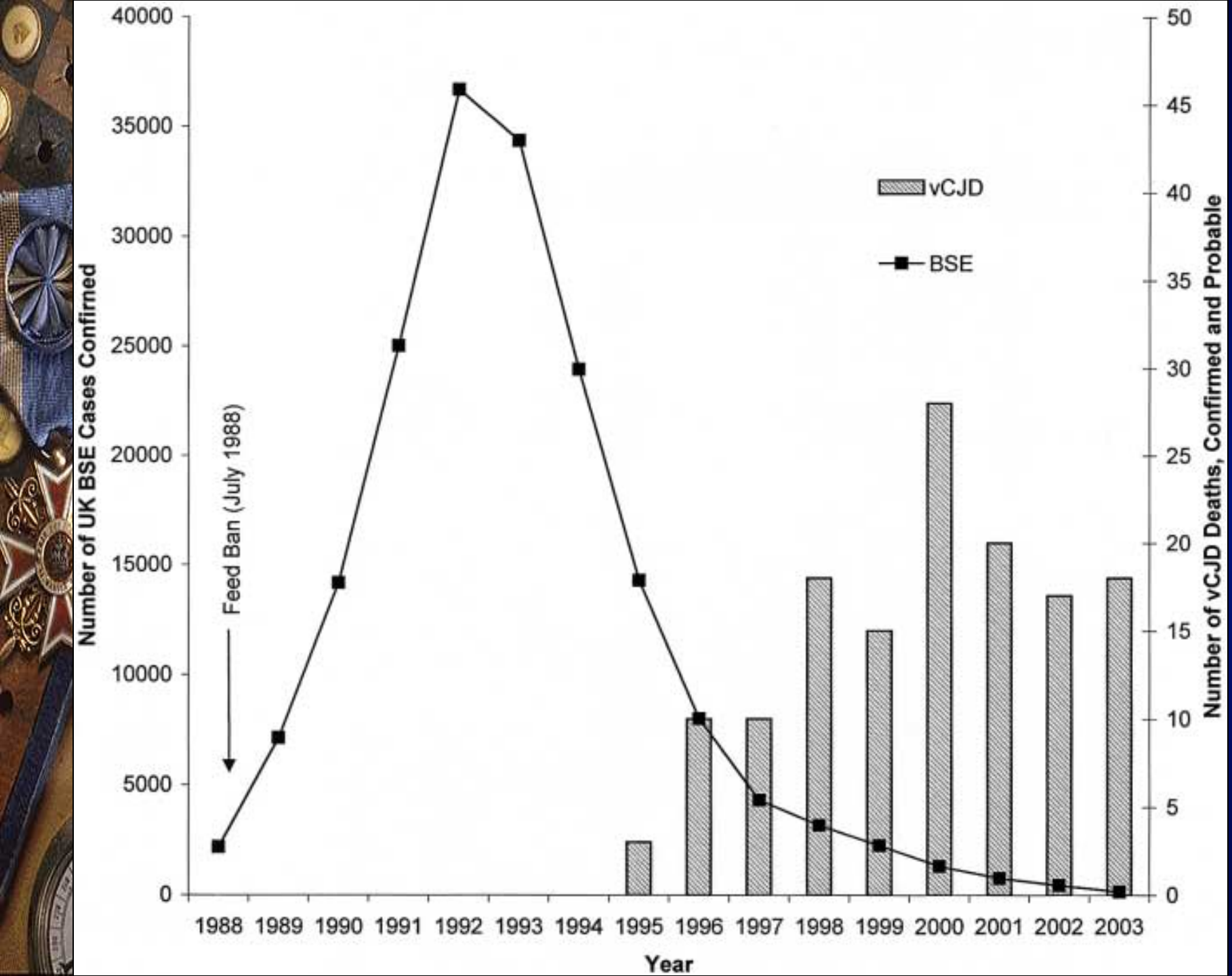

Number of UK BSE Cases Confirmed
Number of vCJD Deaths, Confirmed and Probable
Year
vCJD
BSE
Feed Ban (July 1988)
40000
35000
30000
25000
20000
15000
10000
5000
0
50
45
40
35
30
25
20
15
10
5
0
1988 1989 1990 1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003

Figure 3 Age-specific mortality rates from sporadic CJD in the UK 1970-2007

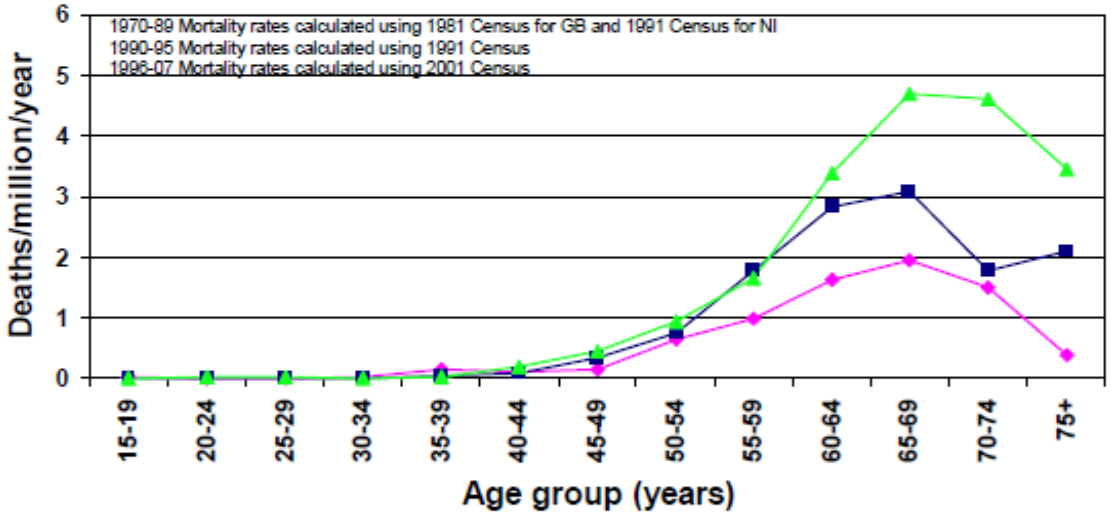
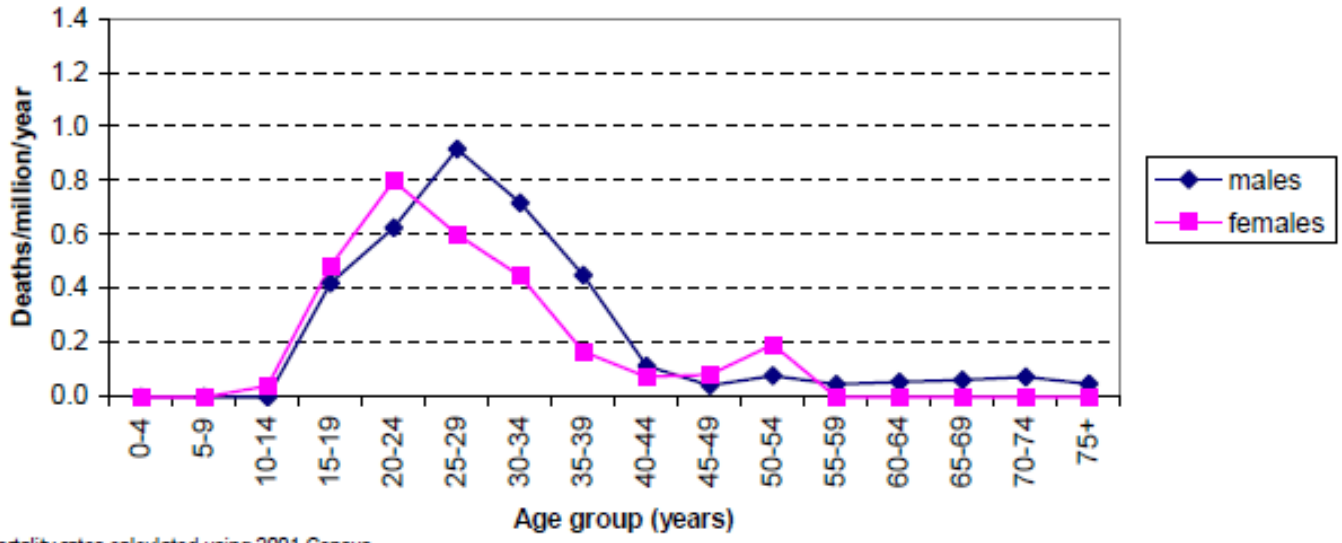


Figure 6 Age- and sex-specific mortality rates from vCJD in the UK
1 May 1995 - 31st December 2007



Mortality rates calculated using 2001 Census

Lancet 1996; 347: 921- 25

A new variant of Creutzfeldt-Jakob disease in the UK

R G Will, J W Ironside, M Zeidler, S N Cousens, K Estibeiro, A Alperovitch, S Poser, M Pocchiari, A Hofman, P G Smith

Summary

Background Epidemiological surveillance of Creutzfeldt-Jakob disease (CJD) was reinstituted in the UK in 1990 to identify any changes in the occurrence of this disease after the epidemic of bovine spongiform encephalopathy (BSE) in cattle.

Methods Case ascertainment of CJD was mostly by direct referral from neurologists and neuropathologists. Death certificates on which CJD was mentioned were also obtained. Clinical details were obtained for all referred cases, and information on potential risk factors for CJD was obtained by a standard questionnaire administered to patients' relatives. Neuropathological examination was carried out on approximately 70% of suspect cases. Epidemiological studies of CJD using similar methodology to the UK study have been carried out in France, Germany, Italy, and the Netherlands between 1993 and 1995.

Findings Ten cases of CJD have been identified in the UK in recent months with a new neuropathological profile. Other consistent features that are unusual include the young age of the cases, clinical findings, and the absence of the electroencephalogram features typical for CJD. Similar cases have not been identified in other countries in the European surveillance system.

Interpretatlon These cases appear to represent a new variant of CJD, which may be unique to the UK. This raises the possibility that they are causally linked to BSE. Although this may be the most plausible explanation for this cluster of cases, a link with BSE cannot be confirmed on the basis of this evidence alone. It is essential to obtain further information on the current and past clinical and neuropathological profiles of CJD in the UK and elsewhere.

National CJD Surveillance Unit, Western General Hospital, Edinburgh EH4 2XU, UK (R G Will FRCP, J W Ironside MRCPath, M Zeidler MRCP, K Estibeiro BSc**); Department of Epidemiology and Population Science, London School of Hygiene and Tropical Medicine, London, UK (**S N Cousens Dip Math Stat, Prof P G Smith DSC); **INSEAM, Hopital de la Salpetrlere, Paris, France** (A Alperovitch MD); **Klinik und Poliklinik fur Neurologie, GeorgAugust- Universitat, Gottingen, Germany (**S Poser MD); **Laboratorio di Virologia, Istituto Superiore di Sanita, Rome, Italy (**M Pocchiari MD); **Erasmus University, Rotterdam, The Netherlands** (Prof A Hofman MD) **Correspondence to: Dr R G Will**

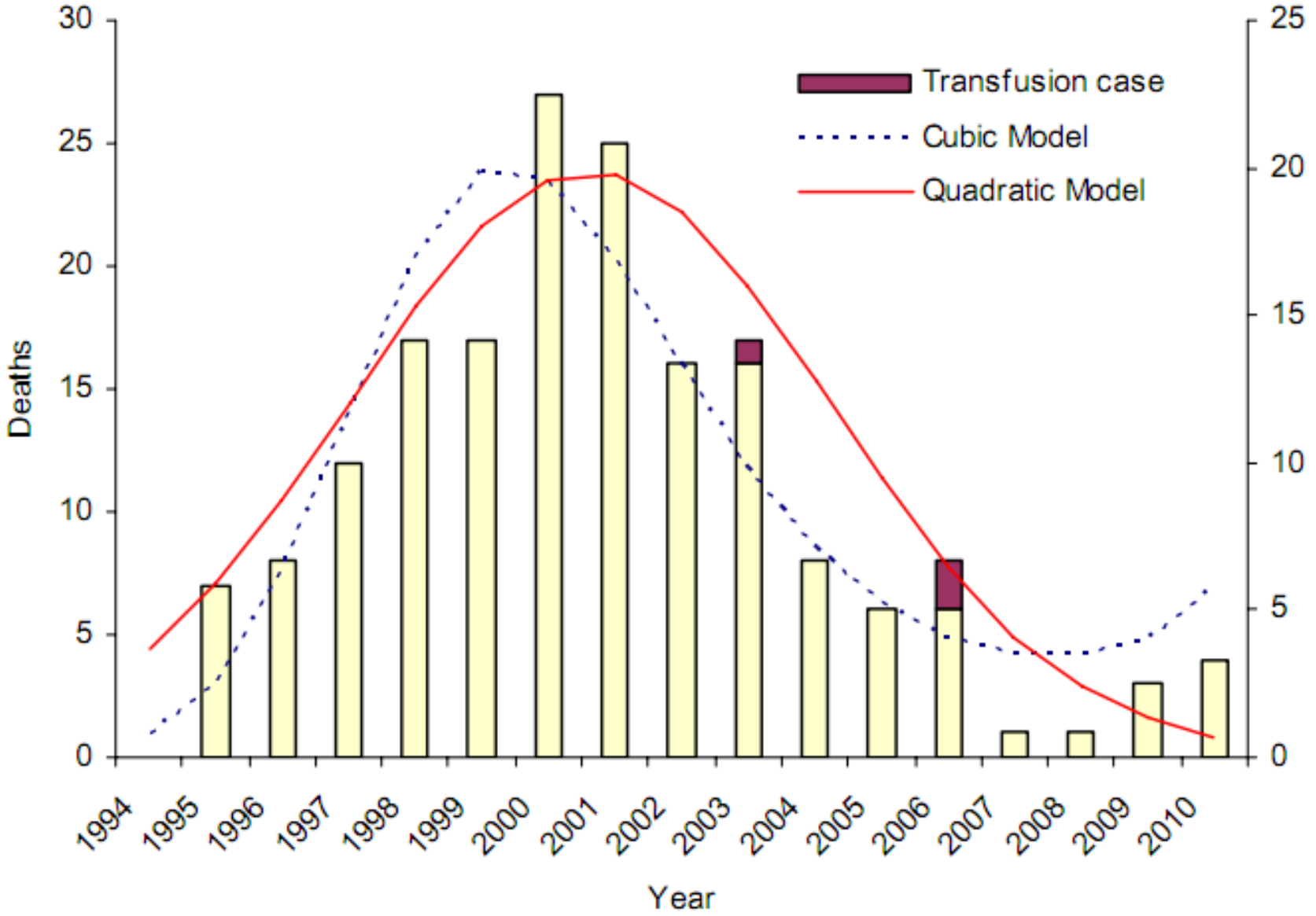
Table 2. Annual cases by onset, notification, diagnosis and death (including median age at death by year of death).

Year	Onset	Notification	Diagnosis	Death	Median age at death
1994	8	0	0	0	-
1995	10	8	7	3	-
1996	11	9	8	10	30
1997	14	13	12	10	26
1998	17	20	17	18	25.5
1999	29	16	17	15	29
2000	24	29	27	28	25.5
2001	17^	21	25	20	28
2002	14	15	16	17	29
2003	5^	16	16	18*	28
2004	9	6	8	9	26
2005	5	7	6	5	34
2006	3	5	6	5*	30
2007	2	1	1	5*	24
2008	3^	2	1	1	-
2009	3^	4	3	3	-
2010	0	2	4	3	-
Total	174	174	174	170	28

* Three cases have arisen to date who had a blood transfusion from earlier cases. These cases, who were all male, died (were diagnosed) in 2003 (2003), 2006 (2006) and 2007 (2006). These cases are included in the analyses although are likely to part of secondary spread.

^ This indicates the year of onset for the four living cases.

Figure 1: vCJD diagnoses by year with fitted quadratic and cubic trend lines



VARIANT CREUTZFELDT-JAKOB DISEASE

CURRENT DATA (AUGUST 2011)

COUNTRY	TOTAL NUMBER OF PRIMARY CASES (NUMBER ALIVE)	TOTAL NUMBER OF SECONDARY CASES: BLOOD TRANSFUSION (NUMBER ALIVE)	CUMULATIVE RESIDENCE IN UK > 6 MONTHS DURING PERIOD 1980-1996
UK	172 (3)	3 (0)	175
France	25 (0)	-	1
Republic of Ireland	4 (0)	-	2
Italy	2 (0)	-	0
USA	3† (0)	-	2
Canada	2 (1)	-	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 case from Japan had resided in the UK for 24 days in the period 1980-1996.

土壤中感染性普利昂蛋白質的風險與解決方法

Risk and Solution of Prion Protein in the Soil

資料來源 **Data Sources**
搜尋引擎 **Search Engine:** Pubmed
關鍵字 **Keyword:** Prion Protein, Soil
文獻數目: 24
文獻: Environ Sci Technol. 2009 Oct 15;43(20):7728-33.
PLoS One. 2009 Oct 21;4(10):e7518.
Prion. 2009 Jul;3(3):171-83.
Epub 2009 Jul 14.

土壤中感染性普利昂蛋白質的風險
Risk of Prion Protein in Soil

- The prions that produce scrapie disease in sheep remain bioavailble and infectious for at least 16 years in natural environments 造成羊搔病的感染性普利昂蛋白質在天然環境中保持生體利用和傳染性至少**16**年(Georgasson G, 2006)
- Binding of PrP^{TSE} by soil particles may maintain prions near the soil surface, thereby increasing animal exposure 土壤顆粒結合的感染性普利昂蛋白質可維持在土壤表面，從而提高動物接觸的機會(Johnson et al., 2006; Cookeet al., 2007; Ma et al., 2007)
- Prion sorption to some types of soil particles enhances oral TSE transmission 普利昂蛋白質吸附在某些類型的土壤顆粒，會增強經口傳染普利昂腦病變 (Johnson et al., 2007)

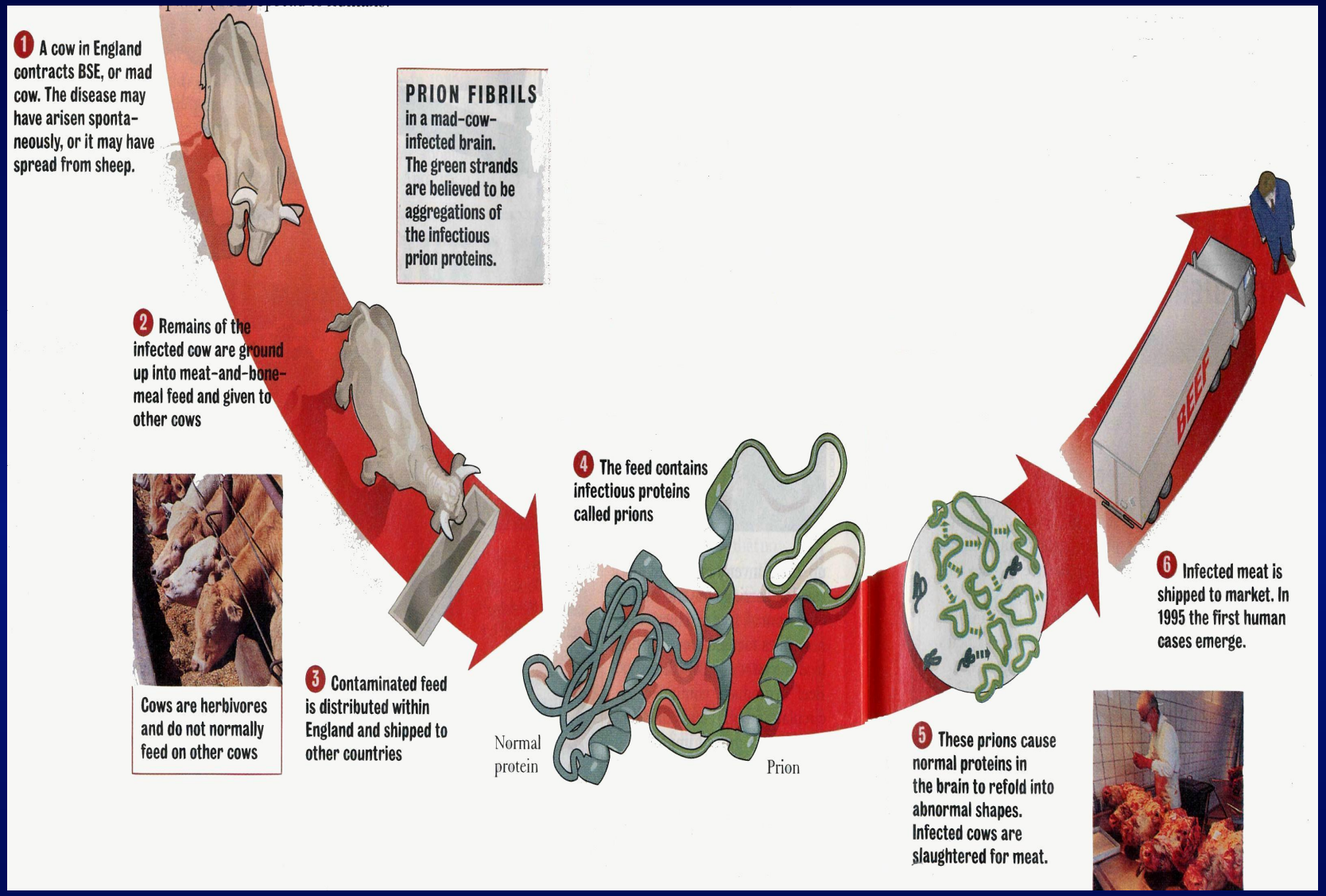
土壤與感染性普利昂蛋白質的互動關係與解決方法

- Manganese enhances prion protein survival in Model soils and increases prion infectivity to cell 錳增強了普利昂蛋白在模式土壤生存的機會，並增加細胞被傳染的機會 (Paul Davies, 2009)
- Do Ag/Ba/Sr piezoelectric crystals represent the transmissible pathogenic agent in TSEs? 銀/鋇/鉿等動能轉變電能晶體可以代表普利昂蛋白質腦病之傳染物質嗎？ (High Barn Farm, 2004)
- Pathogenic prion protein is degraded by a manganese oxide mineral found in soils 土壤中的氧化錳礦可以降低普利昂蛋白質之致病活性(Fabio Russo, 2009)
- Quantitative measurement of the efficacy of protein removal by cleaning formulations; comparative evaluation of prion-directed cleaning chemistries. 可以評估各種清潔處方清除普利昂蛋白質效性並可客觀定量比較 (Ungurs M, 2010)

牛隻與人類新型庫賈氏病關係如何?

CJD & BSE

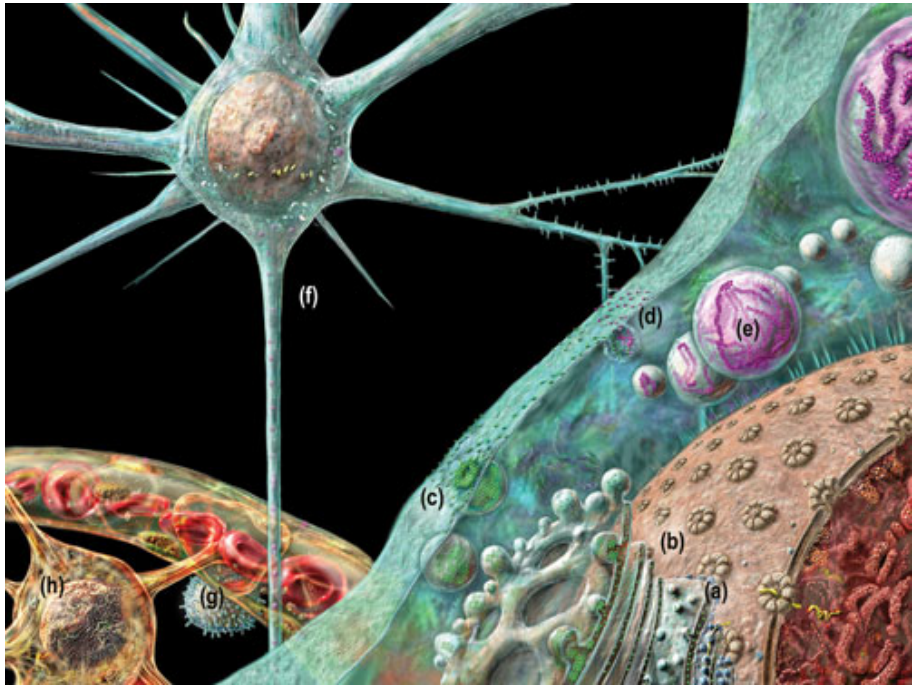
- 2002年Prusiner在美國國科會雜誌證明患有Prion疾病動物的肌肉含有高含量的Prion蛋白
- 2003年歐洲溫乳分子生物協學會證實Prusiner的說法
- 同年，新英格蘭雜誌發表32名CJD患者肌肉樣本中，有8個樣本含有傳染致死性的Prion蛋白



Newsweek, March 2, 2001

The Transmission of Prion Disease

Prion變性蛋白在人體內的感染路徑，由口而入的變性蛋白應會先在扁桃腺增生，然後隨著免疫系統的B細胞來到淋巴結和脾臟，再進入周邊神經，最後感染腦細胞



狂牛症病毒人體之感染途徑

繪圖：美術中心新聞組 徐振坤
資料來源：陳順勝醫師

1 感染狂牛症病毒之牛群

2 含變性普利昂蛋白的肉牛製品

3 牛肉被吃進人體

4 變性普利昂蛋白在扁桃腺增生
→至淋巴結及脾臟
→至周邊神經
→感染腦細胞

腦

神經

脾臟

淋巴結

此外，新型庫賈氏病患者的腦波多呈緩狀性波，腦脊髓液少見大量14-3-3蛋白（一種原存於腦細胞內的蛋白質），腦切片則可見空洞海綿樣變化。

國外證實 牛肉也可能含病源

衛生署一再宣示「在國內不曾出現狂牛症雙的前提下，直接出現新型庫賈氏症個案的機會微乎其微。」陳順勝表示，這句話用在本土個案有其信度，因為全世界有新型庫賈氏病個案的國家，都是在該國出現狂牛症約7年左右（vCJD潛伏期約7至10年），才出現第一個本土病例。但他強調，台灣仍應慎防「境外移入」個案的發生。

他說，變性普利昂蛋白有累積性，換言之，在病牛發病前，其體內很可能已有變性蛋白，此時，人類若在不知情下長時間持續攝取，還是有感染新型庫賈氏病的風險。

另對國際間牛肉進出口，目前仍僅將狂牛症病牛的SRM（腦、眼睛、脊髓、脊椎或背根神經節等）列為特定風險物質。陳順勝說，此舉可能低估了牛肉的風險，撇開牛隻屠宰過程中，牛肉部分可能遭汙染不談，國外知名學者的實驗也已證明，牛肉中同樣也會含有變性普利昂蛋白。

至於變性普利昂蛋白在人體內的感染路徑，中國醫藥大學附設醫院神經內科主治徐偉成表示，依相關動物實驗推論，由口而入的變性蛋白會先在扁桃腺增生，然後隨著免疫細統的B細胞來到淋巴結和脾臟，再進入周邊神經，最後感染腦細胞。

徐偉成說，目前新型庫賈氏病與傳統庫賈氏病都沒有任何治療方式，國內外臨床曾嘗試開給患者藥物，最後都證實無法有效延緩或控制患者病程進展，多數患者仍會在發病1年半左右死亡。

狂牛病5大傳染途徑，擦保養品也會中獎！

查。可是開放
委會有獸醫，
類，不包括狂牛

養會致病

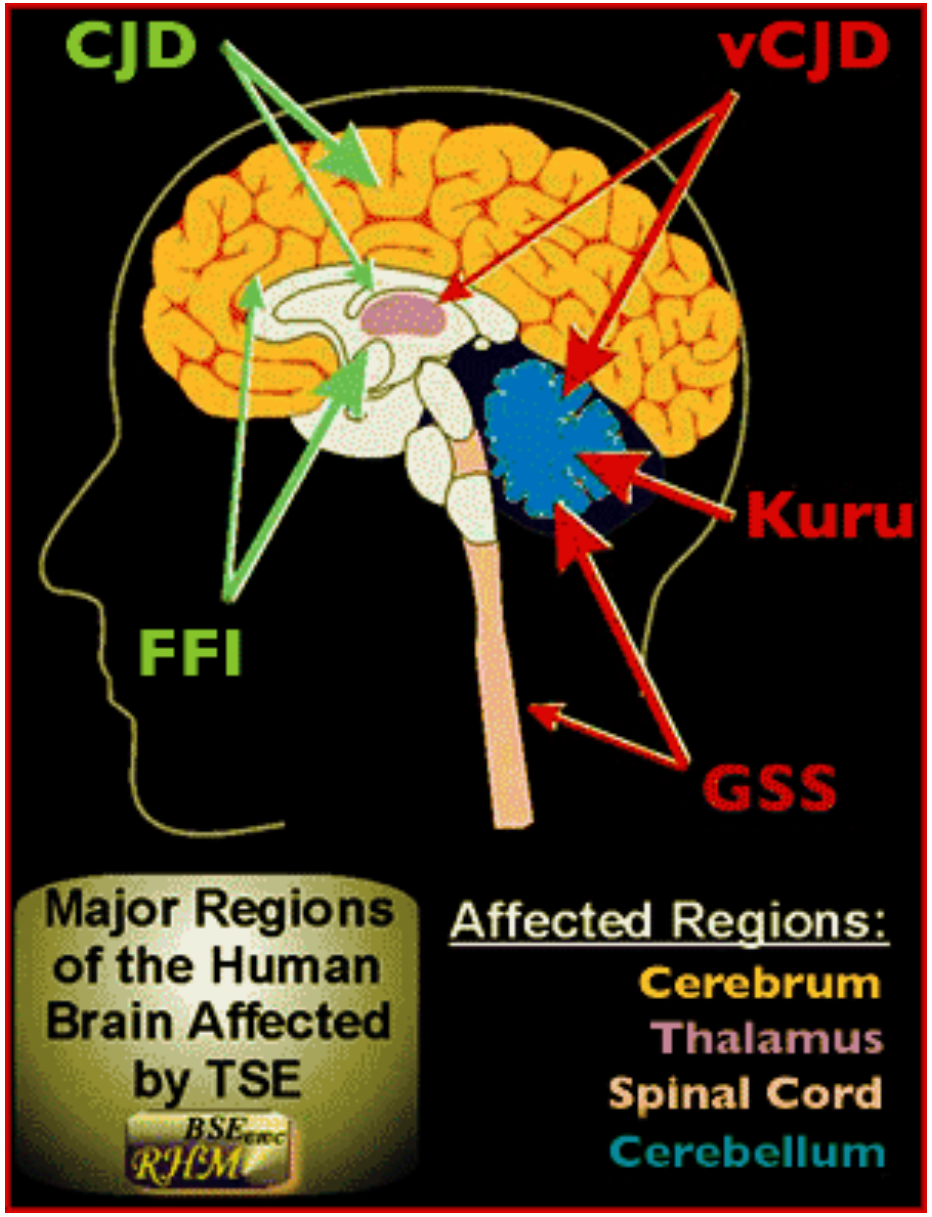
要原料，但牛
業結，可能混有
吃下受狂牛病感
即便是買一般
便進入泥土中，
人、牛、豬、

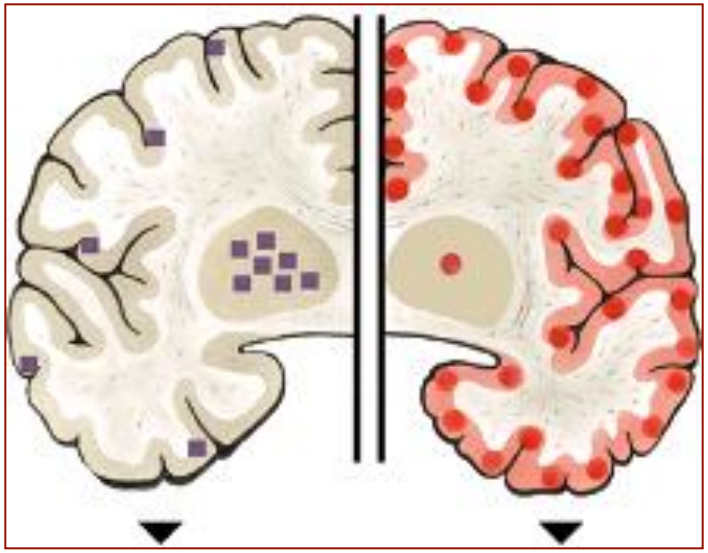
點的啃噬，慢慢纖維化後，就會變成像海綿一樣有很多空空洞洞而不自覺，直到發病、快速死亡，還可能被誤判是阿茲海默症、老人失智症。

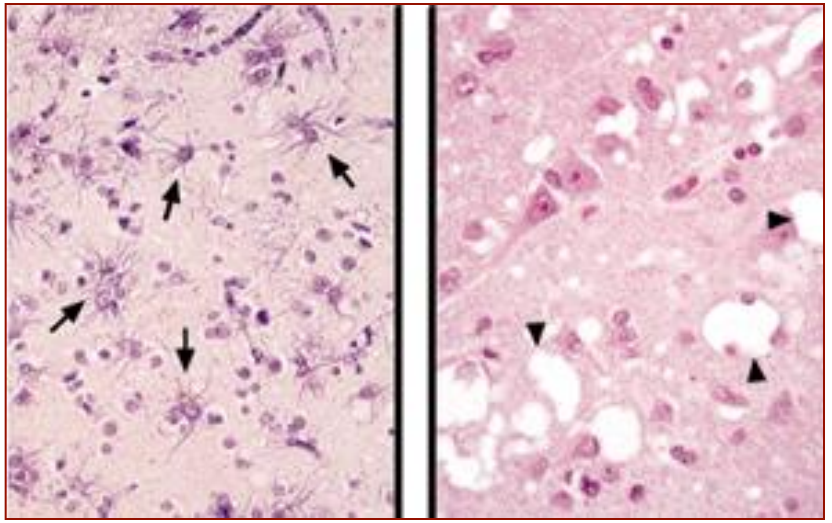
直接吃到受感染的牛肉、內臟，或間接吃到受感染的其他動物肉類和農作物蔬菜，都會把異常蛋白吃進體內，光這一點，就已經不是不吃美牛、把肉煮熟就沒事了，而是「連吃素的人都可能有事」。

雖有中西醫雙執照的署立台北醫院陳威達醫師說，「雖然機率不高，但遇到一次

整理：林敏秋







prion變性蛋白對傳統與新型庫賈氏病腦部侵犯部位的示意圖

Number of cases of bovine spongiform encephalopathy (BSE) reported in the United Kingdom

	Alderney	Great Britain	Guernsey (3)	Isle of Man (2)	Jersey	Northern Ireland	Total United Kingdom
1987 and before(4)	0	442	4	0	0	0	446
1988(4)	0	2 469	34	6	1	4	2 514
1989	0	7 137	52	6	4	29	7 228
1990	0	14 181	83	22	8	113	14 407
1991	0	25 032	75	67	15	170	25 359
1992	0	36 682	92	109	23	374	37 280
1993	0	34 370	115	111	35	459	35 090
1994	2	23 945	69	55	22	345	24 438
1995	0	14 302	44	33	10	173	14 562
1996	0	8 016	36	11	12	74	8 149
1997	0	4 312	44	9	5	23	4 393
1998	0	3 179	25	5	8	18	3 235
1999	0	2 274	11	3	6	7	2 301
2000	0	1 355	13	0	0	75	1 443
2001	0	1,113	2	0	0	87	1,202
2002	0	1,044	1	0	1	98	1,144
2003	0	549	0	0	0	62	611
2004	0	309	0	0	0	34	343
2005	0	203	0	0	0	22	225
2006	0	104	0	0	0	10	114
2007	0	53	0	0	0	14	67
2008	0	33	0	0	0	4	37
2009(5)	0	5	0	0	0	2	7

Annual incidence rate* of bovine spongiform encephalopathy (BSE) in OIE Member Countries that have reported cases, excluding the United Kingdom

Data updated on 27.05.2009

Country/Year	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Austria	0	0	0	0	0	0	0	0	0	0	0	0	0.96	0	0	0	2.114	2.114	1.076	0
Belgium	0	0	0	0	0	0	0	0	0.61	3.69	1.84	5.53	28.22	25.75	10.54	7.882	1.448	1.151	0	0
Canada	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.165	0.149	0.145	0.735	0.476	0.643
Czech Rep.	0	0	0	0	0	0	0	0	0	0	0	0	2.85	2.50	5.78	10.324	11.982	4.351	3.021	0
Denmark	0	0	0	0	0	0	0	0	0	0	0	1.14	6.77	3.35	2.39	1.296	1.289	0	0	0
Finland	0	0	0	0	0	0	0	0	0	0	0	0	2.39	0	0	0	0	0	0	0
France	0	0	0.45	0	0.09	0.27	0.27	1.09	0.54	1.64	2.82	14.73(a)	19.70	20.96	12.01	4.736	2.719	0.755	0,847	0,748
Germany	0	0	0	0	0	0	0	0	0	0	0	1.07	19.97	17.02	8.71	10.915	4.965	2.801	0.709	0.388
Greece	0	0	0	0	0	0	0	0	0	0	0	0	3.3	0	0	0	0	0	0	0
Ireland	4.41	4.12	5.00	5.14	4.57	5.43	4.57	20.28	21.39	20.79	22.83	38.17(a)	61.80(b)	88.39	57.81	43.327	23.996	14.572	9.170	8.437
Israel	0	0	0	0	0	0	0	0	0	0	0	0	0	6.25	0	0	0	0	0	0
Italy	0	0	0	0	0	0	0	0	0	0	0	0	14.1	10.60	9.86	2.348	2.396	2.097	0.727	0.329
Japan	0	0	0	0	0	0	0	0	0	0	0	0	1.44	0.97	1.96	2.491	3.575	5.018	1.540	0.525
Luxembourg	0	0	0	0	0	0	0	0	10	0	0	0	0	14.54	0	...	10.876	0	0	0
Netherlands	0	0	0	0	0	0	0	0	1	1.01	1.03	1.07	10.25	13.19	10.86	3.399	1.696	1.204	1.136	
Poland	0	0	0	0	0	0	0	0	0	0	0	0	0	1.28	1.49	3.578	...	...	2.507	1.472
Portugal	0	0	0	0	0	15.06	18.82	38.90	37.64	159.35	199.50	186.95	137.88	107.80	137.19	94.901	53.037	38.000	16.142	20.522
Slovakia	0	0	0	0	0	0	0	0	0	0	0	0	18.34	18.73	6.74	24.635	43.353	0	3,590	0
Slovenia	0	0	0	0	0	0	0	0	0	0	0	0	4.34	4.44	4.39	9.170	4.613	5.050	4,877	0
Spain	0	0	0	0	0	0	0	0	0	0	0	0.59	24.23	37.95	46.31	38.945	27.761	...	12,297	7,878
Sweden	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1.322	0	0
Switzerland	0	1	9.2	15.5	30.3	67.6	73.6	48.5	45.4	16	58.7	40.6	49.1	27.93	24.86	3.750	3.693	5.402	0	0
United Kingdom	See particular table																			
United States of America	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0.024	0.024	0	0

冷藏/冷凍牛肉進口統計資料

冷藏、冷凍數量 / 年度 / 國家	98年 1、2月	97年	96年	95年	94年	93年	92年	91年	90年
澳洲	0.22 3.71	1.44 25.30	1.50 28.35	1.71 26.76	2.67 27.59	2.36 24.69	1.18 30.54	1.38 31.85	1.66 27.10
加拿大	- 0.42	0.03 1.45	0.01 0.39	- -	- -	- -	0.12 1.93	0.2 3.40	0.20 2.80
紐西蘭	0.07 2.89	0.80 18.63	1.29 19.75	1.48 21.73	2.38 25.71	3.75 26.06	2.25 19.60	1.14 13.56	1.03 13.19
美國	0.93 1.76	6.78 15.79	5.36 12.90	3.67 15.63	3.32 3.72	0.07 0.58	3.26 12.86	2.90 10.26	2.70 8.16

資料來源:海關進出口資料整理統計　　量=千公噸

蕃薯藤-新聞-美國農業部瘋牛病檢測屢屢出錯,政府和農業出口面臨信譽質疑

路透社 2005-07-28 12:06

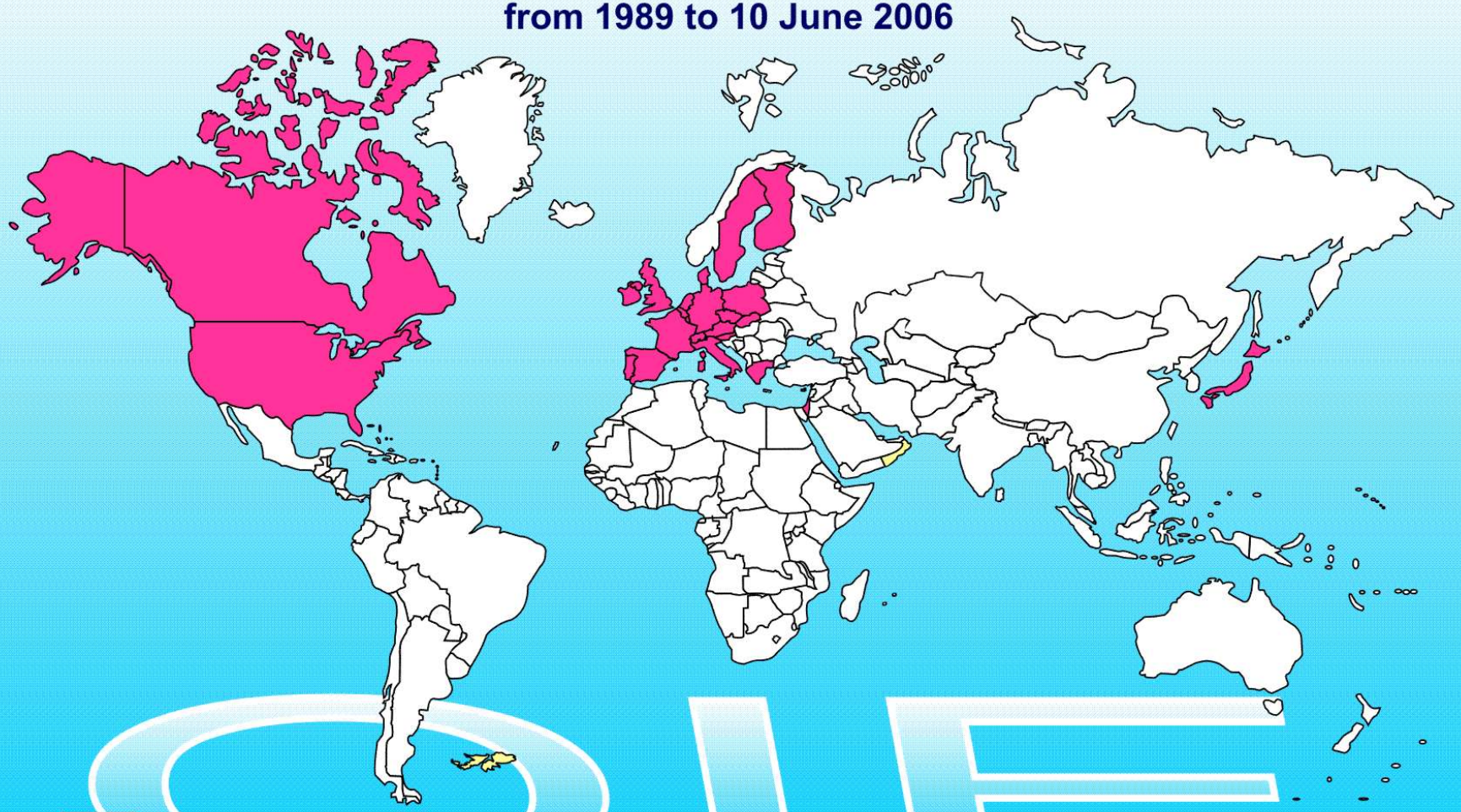
路透華盛頓電---行業及消費者團體周三表示，美國在瘋牛病檢測上屢次出錯和含糊不清，令人對政府可信度提出質疑，亦可能讓說服主要進口伙伴安心消費美國牛肉的努力打上折扣。

美國農業部正在就美國
行調查，對象是一頭至

當地獸醫4月對該疑似病牛做了腦體取樣，但直到上周農
釋說，該獸醫「忘記」提交樣本。

樣本被冷凍起來，這種做法是違反美國規定的，而且該獸
瘋牛病檢測方法受到限制。

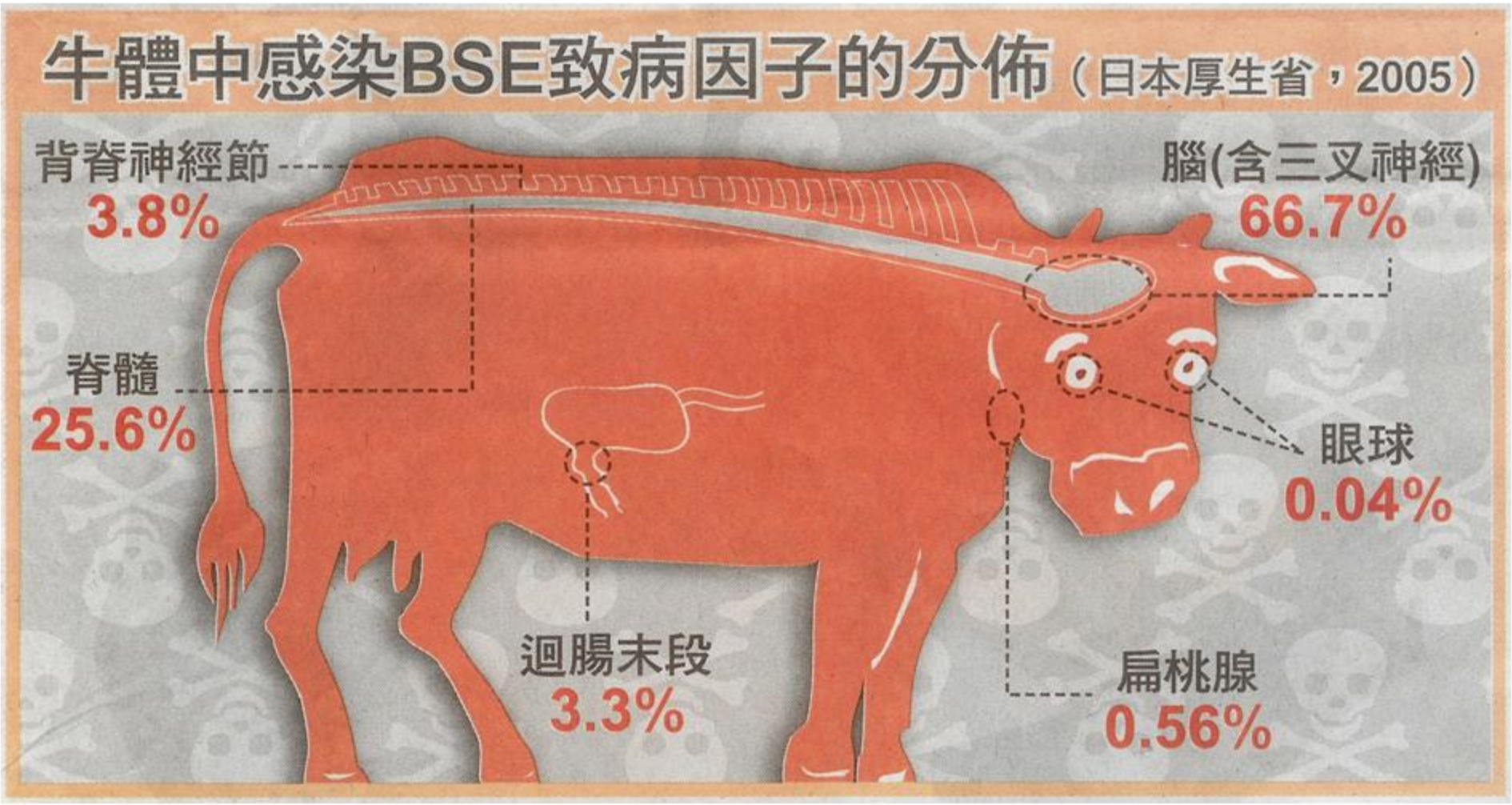
Geographical Distribution of Countries that Reported at least one BSE Confirmed Case from 1989 to 10 June 2006



Countries having reported BSE in indigenous animals

Countries/territories having reported BSE in imported animal(s) only

牛體中感染BSE致病因子的分佈（日本厚生省，2005）

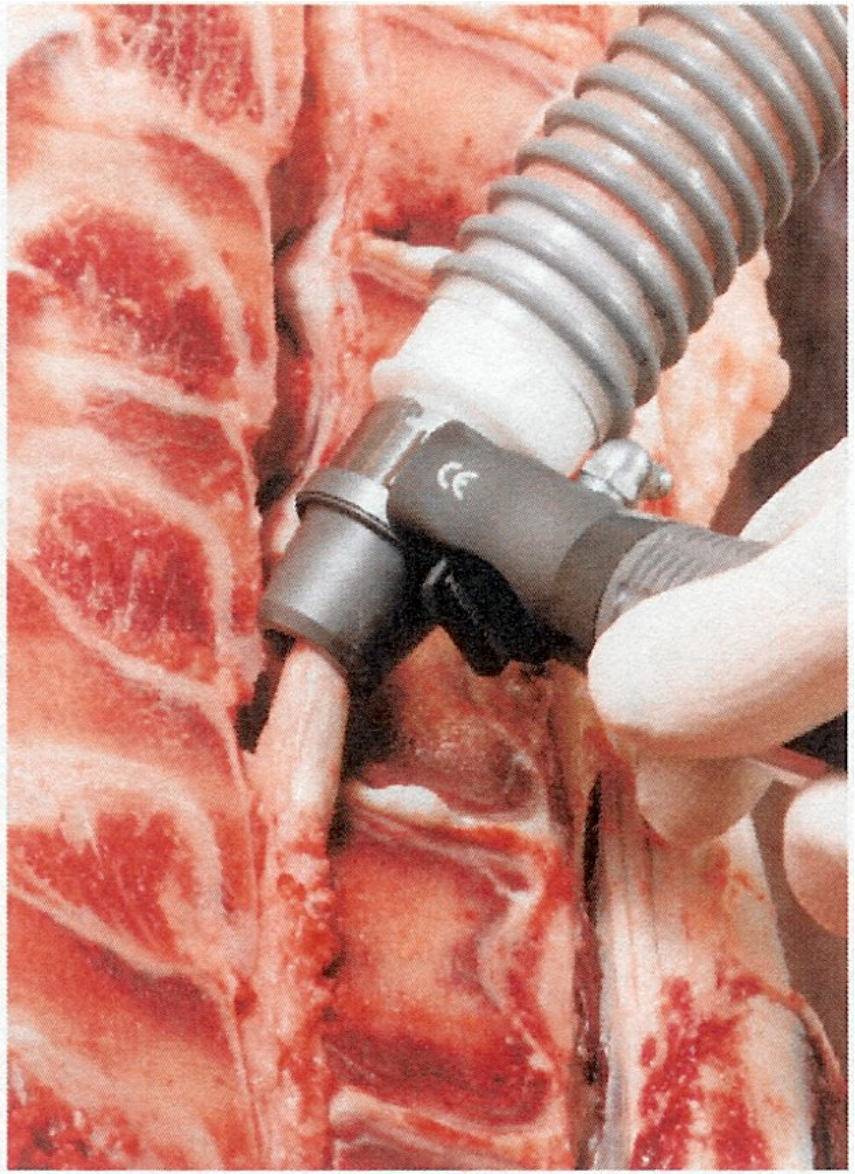


Removing risk

By Drs. Kerri Harris and Jeff Savell
meat&poultry@sosland.com

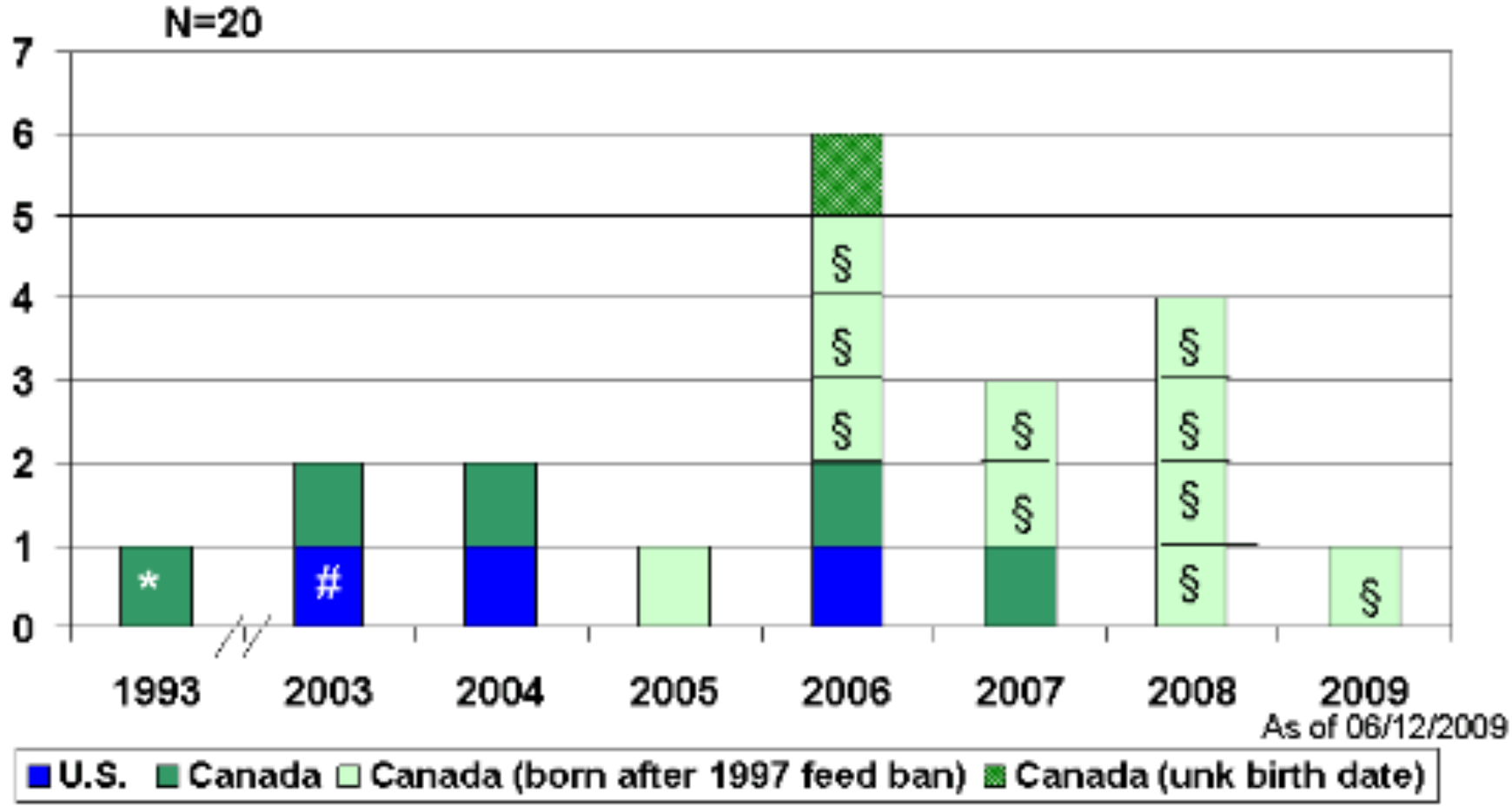
Developing best practices for the removal of S.R.M.'s

The cow that tested positive for bovine spongiform encephalopathy this past December triggered new regulatory requirements and many other changes in the U.S. beef industry. It appears most of the new regulatory requirements are designed as precautionary measures and many of the other changes are based on customer requirements. Regardless of the reasons, companies have reacted to the issue by implementing safeguards.



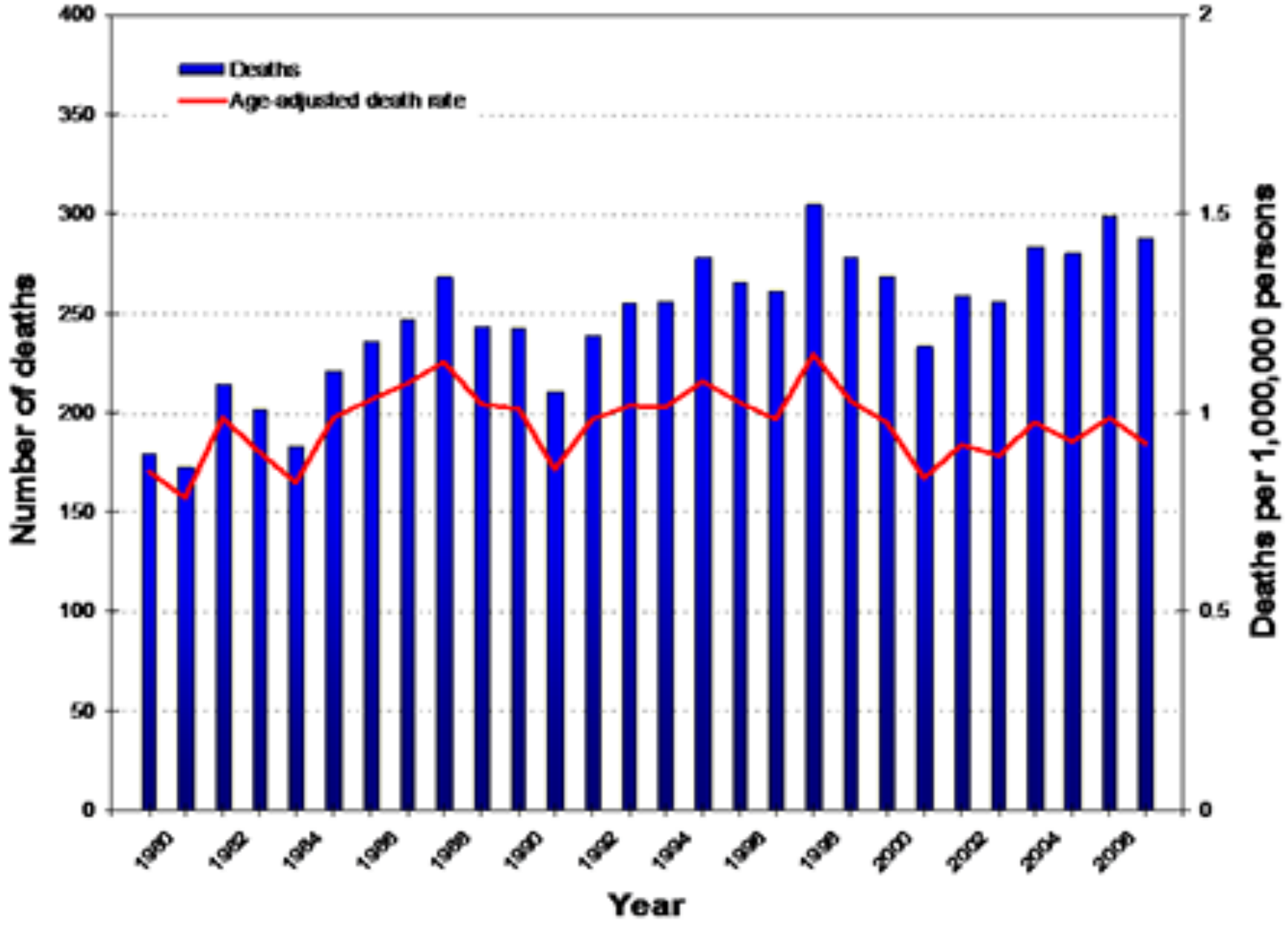
New regulations require the removal of the spinal cord from all animals that are 30 months or older. *Photo courtesy of: Bettcher Industries*

BSE Cases in North America, by Year and Country of Death, 1993-06/2009



* Imported from UK into Canada # Imported from Canada into US § Born after March 1, 1999

Creutzfeldt-Jakob disease deaths and age-adjusted death rate, United States, 1979-2006*



TRANSFUSION MEDICINE EPIDEMIOLOGY REVIEW (TMER)

TRANSFUSION MEDICINE EPIDEMIOLOGY REVIEW (TMER)

RESULTS

Thirty-one vCJD cases were reported to have been blood donors. Four additional cases who were not reported to have been blood donors were found to be registered with UKBTS. One of these cases was found to have been a blood donor while the other three cases were registered as donors but never made any donations. Twenty-four of the cases have been traced at blood centres including the four additional cases mentioned above. Components from 18 of these individuals were actually issued to hospitals. It has been established that 66 components were transfused to named recipients. Four instances of probable transfusion transmitted infection have been identified. The first recipient (Case 1) developed symptoms of vCJD 6?years after receiving a transfusion of red cells donated 3?years before the donor (Donor 1) developed symptoms of vCJD. The second recipient (Case 2) died from a non-neurological disorder 5 years after receiving blood from a donor (Donor 2) who subsequently developed vCJD; protease-resistant prion protein (PrP^{res}) was detected in the spleen but not in the brain. This is the first recorded of case in the UK of autopsy detection of presumed pre- or sub-clinical vCJD infection. The third recipient (Case 3) developed symptoms of vCJD 7 years, 10 months after receiving a

months before the donor (Donor 3) developed symptoms of vCJD. The fourth recipient (Case 4) who also received a transfusion from the same donor as Case 3, developed symptoms of vCJD 8 years, 4 months after receiving a transfusion of red cells donated about 17 months before this donor (Donor 3) developed symptoms of vCJD. (see publications). These findings strongly suggest that vCJD may be transmitted via blood transfusion. The identification of a third case of vCJD in this small cohort of known recipients of blood from persons incubating vCJD establishes beyond reasonable doubt that blood transfusion is a transmission route.

In the reverse study, 14 vCJD cases were reported to have received blood transfusions in the past. A further case received a blood transfusion after onset of illness. This case is excluded from the figures quoted. Checks revealed that of these 14 cases, one was not transfused, 4 had transfusions which pre-dated available records (pre 1980), and 9 had records of transfusion which could be traced

(

see vCJD cases who received blood transfusion(s) in the past). These 9 had received 207 donor exposures (with one patient given 103 components), which have been traced to 190 named donors (two of whom had vCJD as described above).

vCJD abnormal prion protein found in a patient with haemophilia at post mortem

17 February 2009

Evidence of infection with the agent (abnormal prion protein) that causes variant Creutzfeldt-Jakob Disease (vCJD) has been found at post mortem in the spleen of a person with haemophilia.

The patient, who was over 70 years old, died of a condition unrelated to vCJD and had shown no symptoms of vCJD or any other neurological condition prior to his death. The vCJD abnormal prion protein was only identified during post mortem research tests. The Health Protection Agency is working with the UK Haemophilia Centre Doctors Organisation to ensure all patients with bleeding disorders are made aware of this preliminary information which is being further investigated. This new finding will not change the way patients with haemophilia are cared for or treated.

A final view as to how vCJD abnormal prion protein was transmitted to this haemophilia patient has yet to be reached because investigations are continuing to determine the most likely route of transmission. It is known that the patient had been treated with several batches of UK sourced clotting factors before 1999, which is when measures to improve the safety of blood in relation to vCJD were introduced. The patient's treatment had included one batch of Factor VIII that was manufactured using plasma from a donor who went on to develop symptoms of vCJD six months after donating the plasma in 1996.

This is the first time that vCJD abnormal prion protein has been found in a patient with haemophilia, or any patient treated with plasma products. This new finding, however, does not change the public health vCJD 'at risk' status of patients with bleeding disorders.

衛　　生　　署

食　　品　　衛　　生　　處

農　　委　　會

海關檢疫

疾　　病　　管　　制　　局

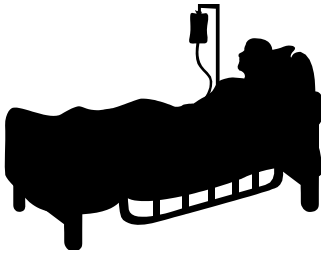
國內外牛隻畜牧

國內外牛隻屠宰

進口牛肉及國產牛肉之販售

國人食用PRPsc

國人食用受污染牛肉致病



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