Eurosurveillance scientific seminar

ESCAIDE 2012

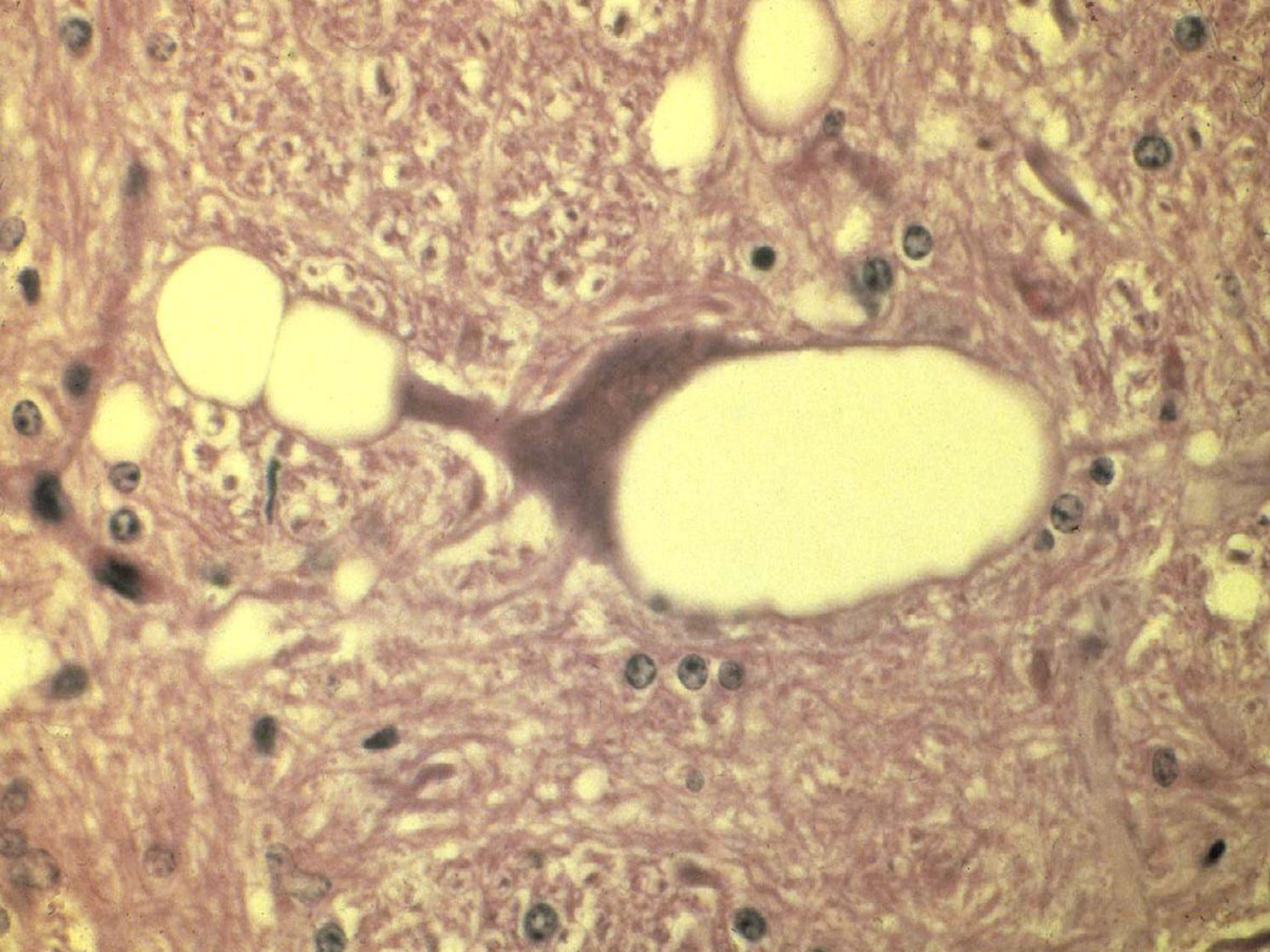
Prions, panic and pubic health

RG Will

National CJD Research and Surveillance Unit
University of Edinburgh
UK

CHARACTERISTICS OF PRION DISEASES

- Prolonged incubation periods.
- Uniformly fatal neurological diseases.
- Causal agents (prions) resistant to sterilisation.
- No serological test for infection.
- Infection may be present in tissues (LRS) during the incubation period.



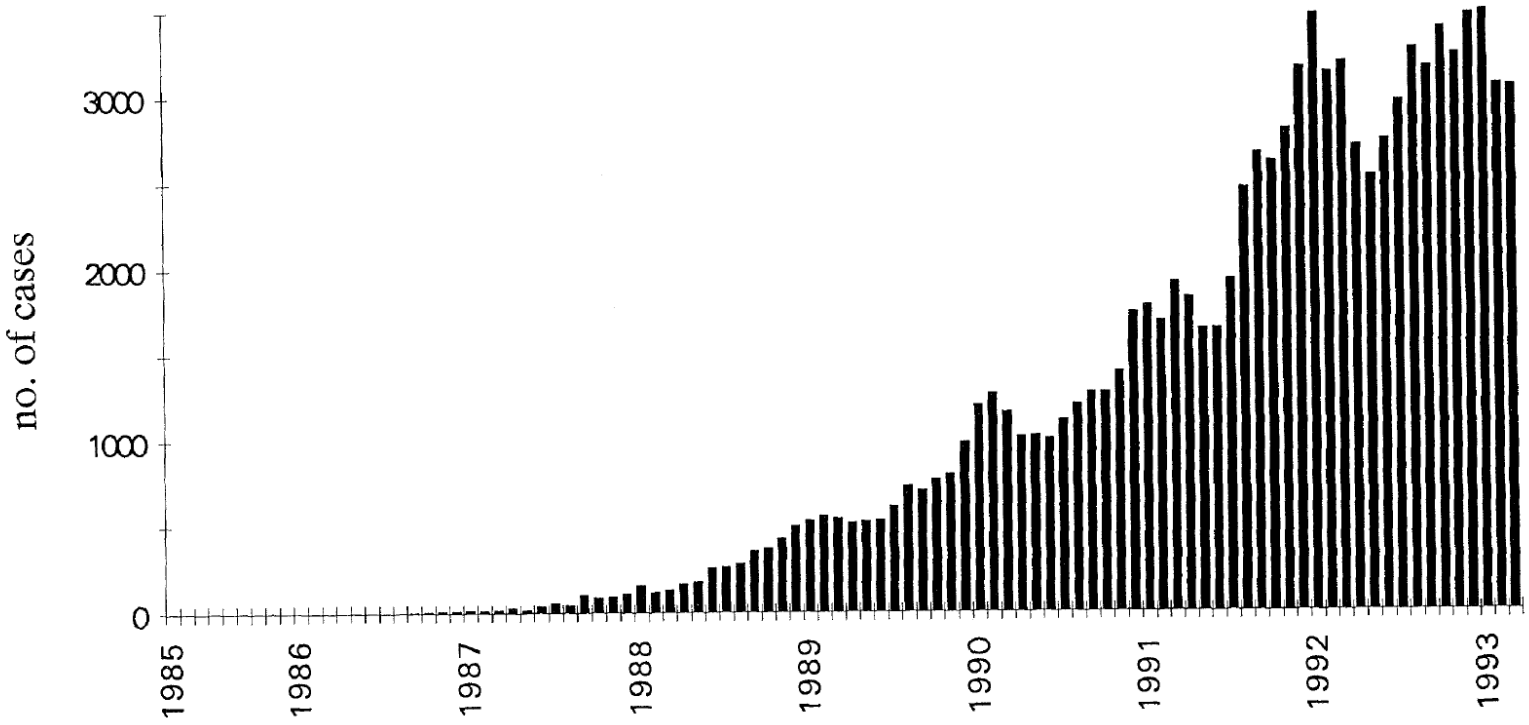
An epidemiologist's view of bovine spongiform encephalopathy

J. W. WILESMITH

Epidemiology Department, Central Veterinary Laboratory, New Haw, Addlestone, Surrey KT15 3NB, U.K.

Phil. Trans. R. Soc. Lond. B (1994) **343**, 357–361

Epidemic curve of cases by month and year of onset of clinical signs.



Phil. Trans. R. Soc. Lond. B (1994) **343**, 357–361

Veterinary Record

Veterinary Record 1988;**123**:638-644 doi:10.1136/vr.123.25.638

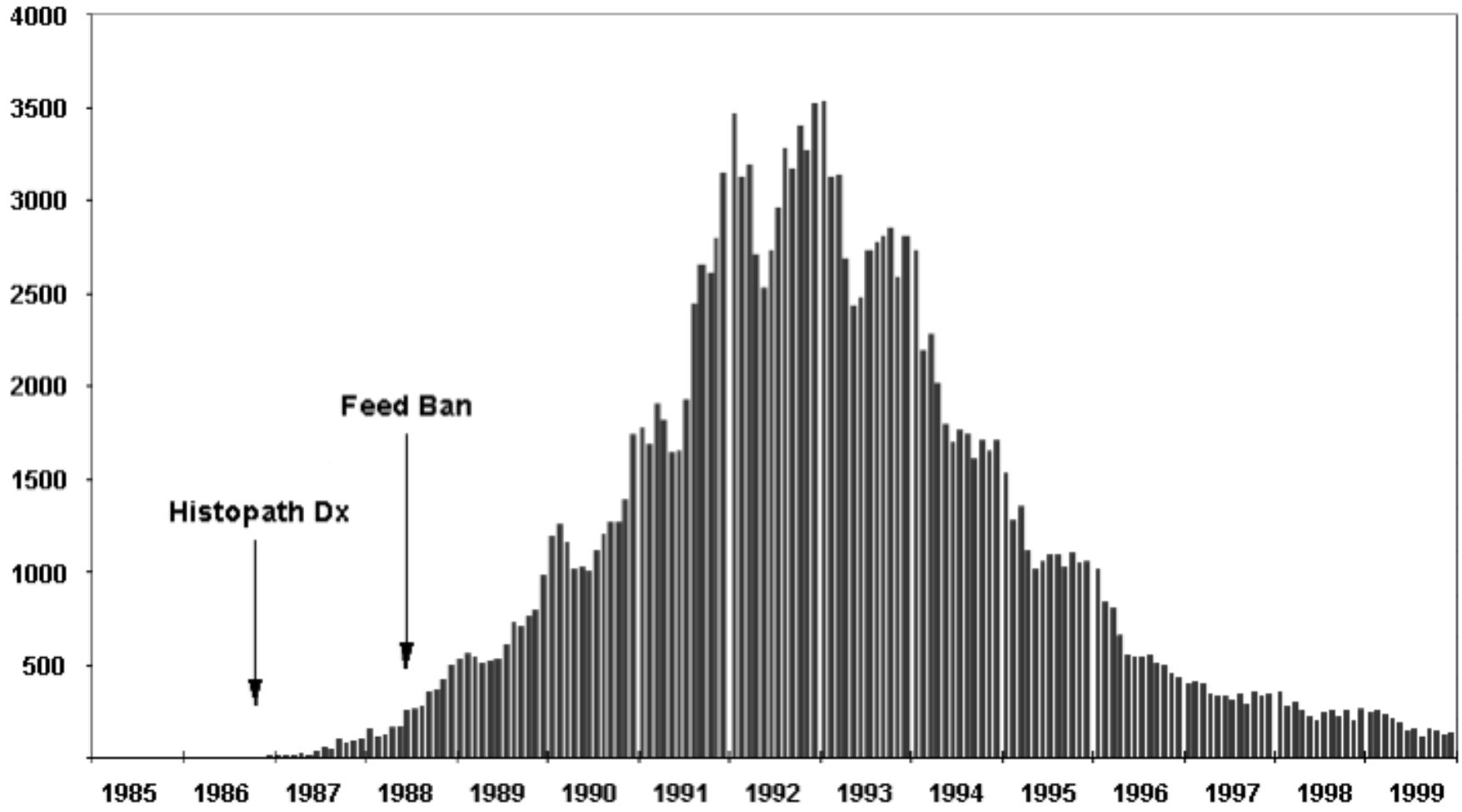
Bovine spongiform encephalopathy: epidemiological studies

JW Wilesmith, **GA Wells**, **MP Cranwell** and **JB Ryan**

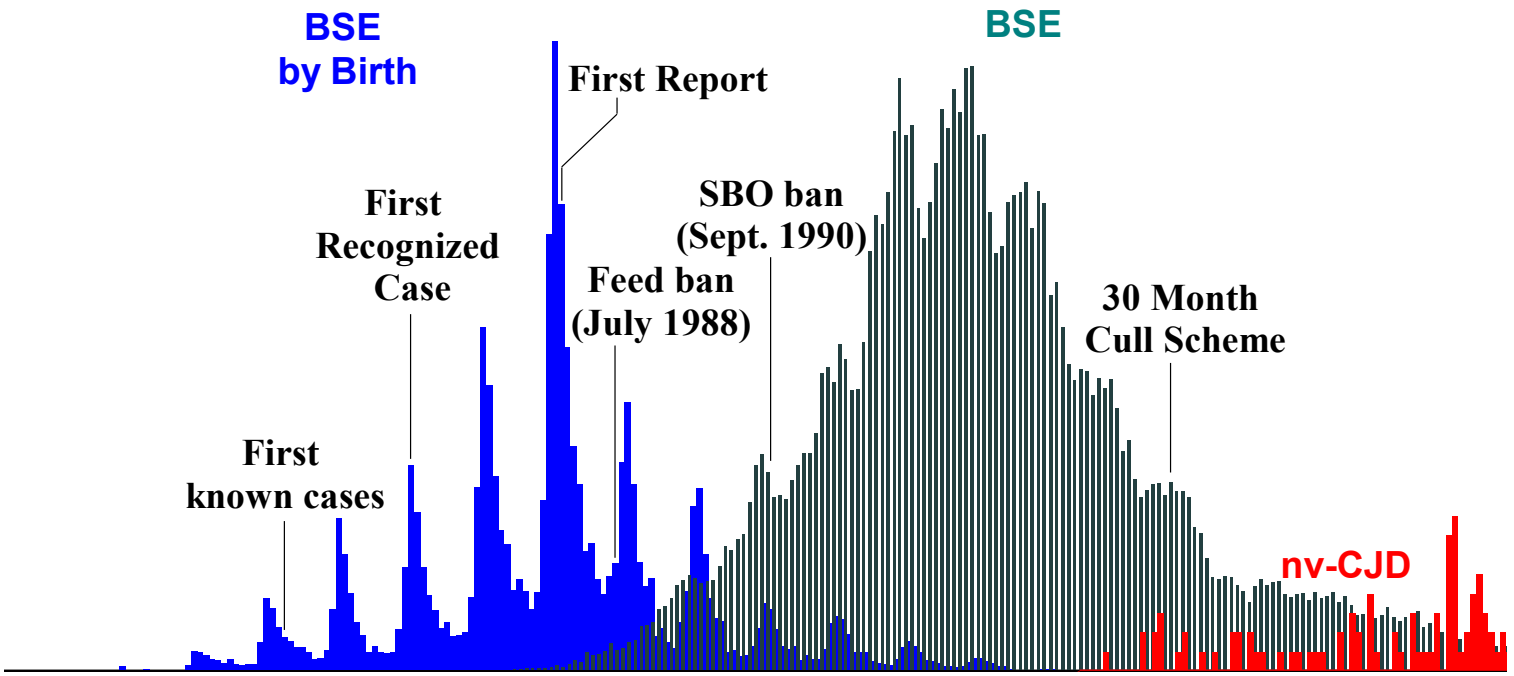
Abstract

This study, initiated in June 1987, describes the epidemiology of bovine spongiform encephalopathy (BSE), a recently described novel neurological disease of domestic cattle first identified in Great Britain in November 1986. Records suggested that the earliest suspected cases occurred in April 1985. There was variability in the presenting signs and the disease course, but the majority of cases developed behavioural disorders, gait ataxia, paresis and loss of bodyweight; pruritus was not a predominant sign. The form of the epidemic was typical of an extended common source in which all affected animals were index cases. The use of therapeutic or agricultural chemicals on affected farms presented no common factors. Specific genetic analyses eliminated BSE from being exclusively determined by simple mendelian inheritance. Neither was there any evidence that it was introduced into Great Britain by imported cattle or semen. The study supports previous evidence of aetiological similarities between BSE and scrapie of sheep. The findings were consistent with exposure of cattle to a scrapie-like agent, via cattle feedstuffs containing ruminant-derived protein. It is suggested that exposure began in 1981/82 and that the majority of affected animals became infected in calfhood.

BSE in Great Britain
(DEFRA)

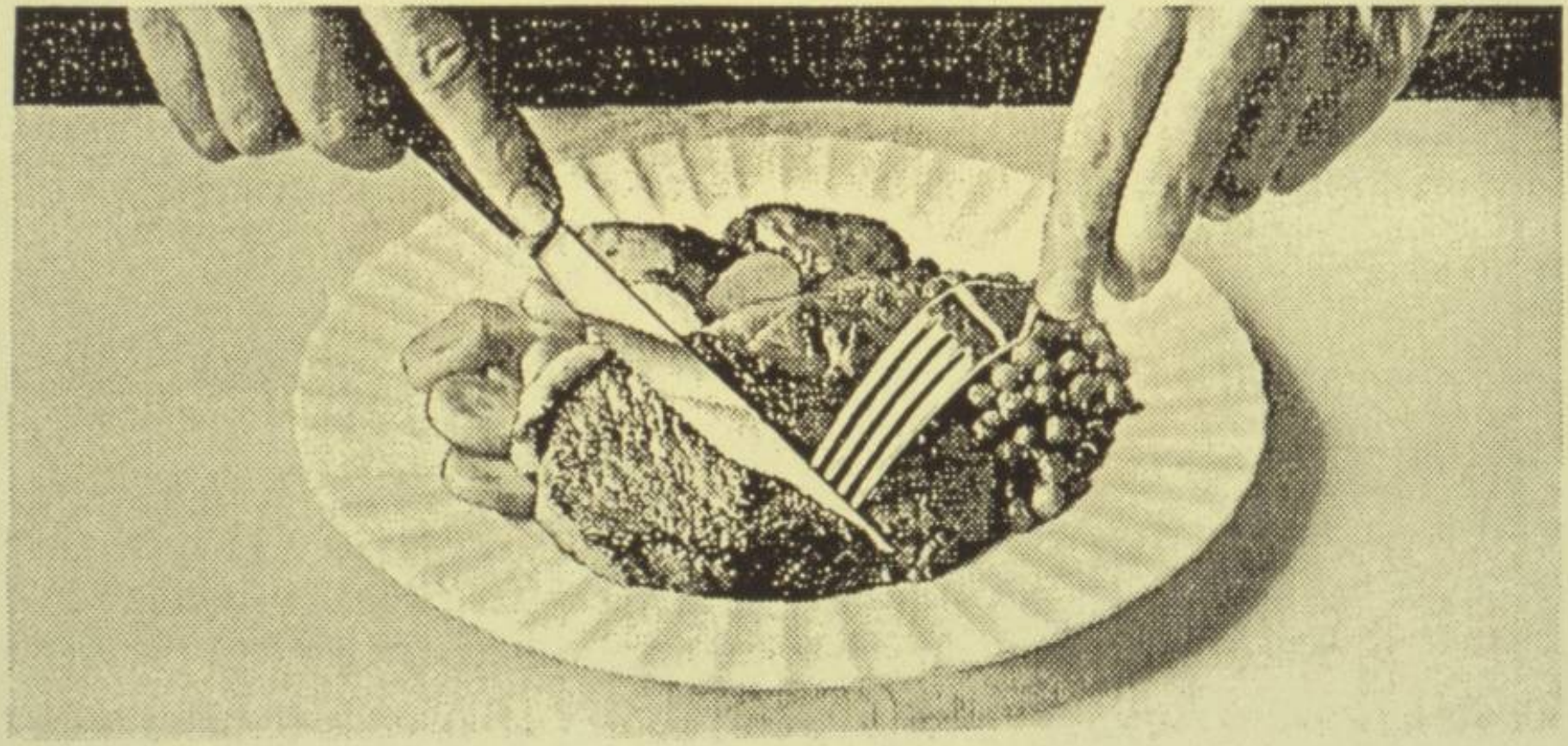


•WHO Consultation on
•Tissue Infectivity Distribution
•in Transmissible Spongiform Encephalopathies
•Geneva, September 14 – 16, 2005



by Robert G. Rohwer, Ph.D.
VA Medical Center
University of Maryland
Baltimore, MD

If an animal has mad cow disease, where does it go for surgery?



ANOTHER NEWS INVESTIGATION BY TODAY'S ALAN WATKINS INTO THE TRAGEDY OF CJD

The secret victims of killer brain disease

NEW evidence suggesting that the mysterious brain virus CJD has killed many previously unknown victims has been uncovered by scientists.

Experts attending a recent medical conference say news leaked out that British researchers have proof that Creutzfeldt-Jakob Disease — closely related to BSE (Mad Cow Disease) — is more common than

TODAY EXCLUSIVE

Toll is growing warn boffins

anyone realised. Scientists fear this also raises the possibility that the disease is on the increase without medical experts realising.

However, it is understood that the researchers are not suggesting any link with BSE, just reporting their findings.

The dramatic discovery was made in post mortems on hospital patients whose deaths would not normally have been investigated.

They showed that many of those registered as having died from other illness were suffering from CJD.

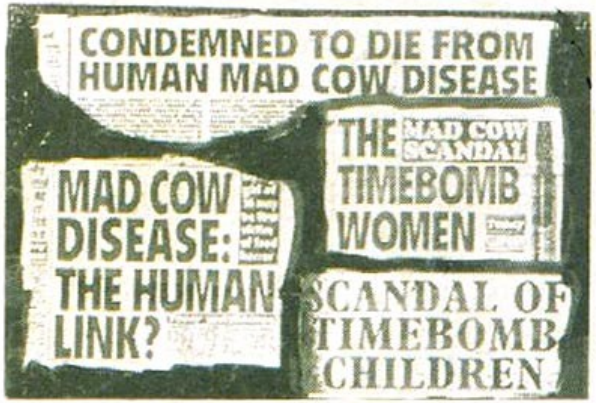
Delegates at the conference said telltale signs of the disease were found in a "significant percentage" of the brains examined.

Setback

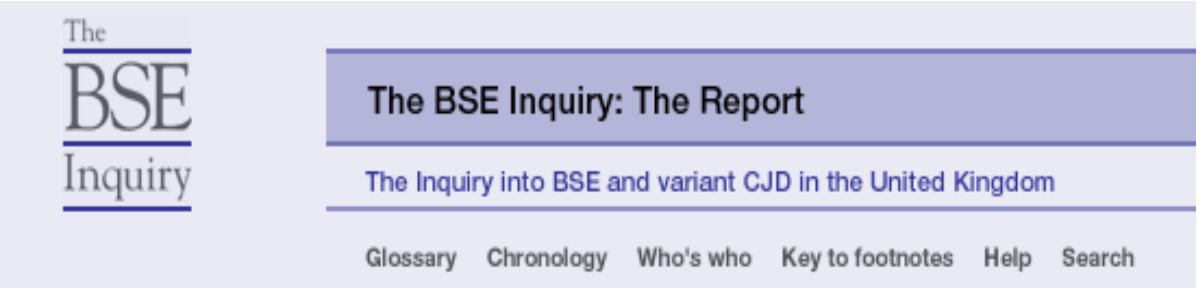
Independent experts researching whether the disease can transfer to humans from cattle.

It may be 10 years before any conclusion can be reached, if at all.

Some doctors have urged the Department of Health to make CJD a notifiable disease but the believes the Government



TODAY'S exclusive coverage of CJD and BSE



The Government introduced measures to guard against the risk that BSE might be a matter of life and death not merely for cattle but also for humans, but the possibility of a risk to humans was not communicated to the public or to those whose job it was to implement and enforce the precautionary measures.

The Government did not lie to the public about BSE. It believed that the risks posed by BSE to humans were remote. The Government was preoccupied with preventing an alarmist over-reaction to BSE because it believed that the risk was remote. It is now clear that this campaign of reassurance was a mistake. When on 20 March 1996 the Government announced that BSE had probably been transmitted to humans, the public felt that they had been betrayed. Confidence in government pronouncements about risk was a further casualty of BSE.

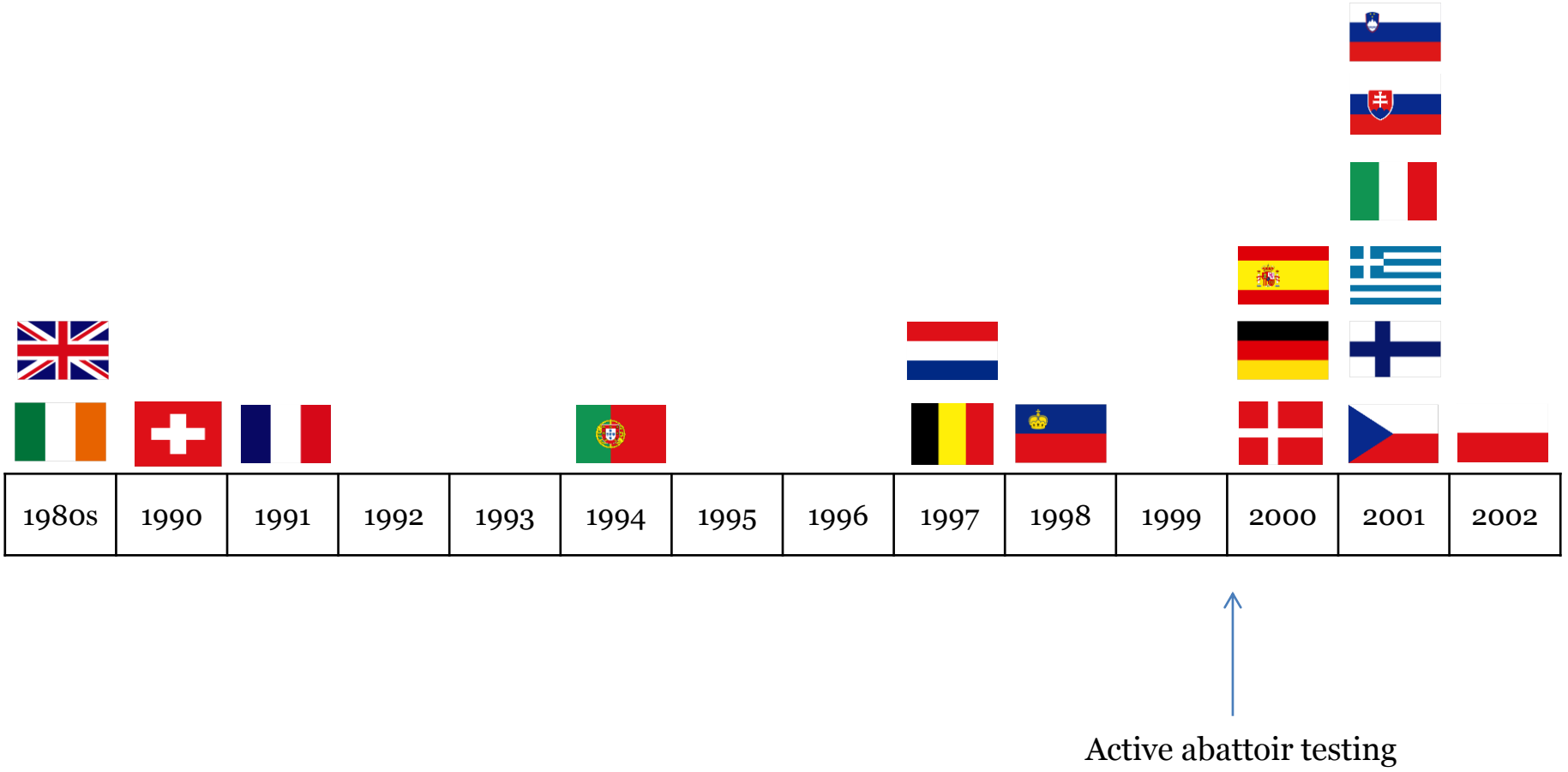
European Parliament BSE Inquiry report (1997)

All in all, since 1988 the UK authorities have introduced a considerable amount of legislation covering the various aspects of protection against possible BSE risks. The problem, therefore, lies not in any lack of appropriate legislative measures, but in the attitude of the government, which has failed to ensure the proper application of those measures and has not carried out the necessary checks.

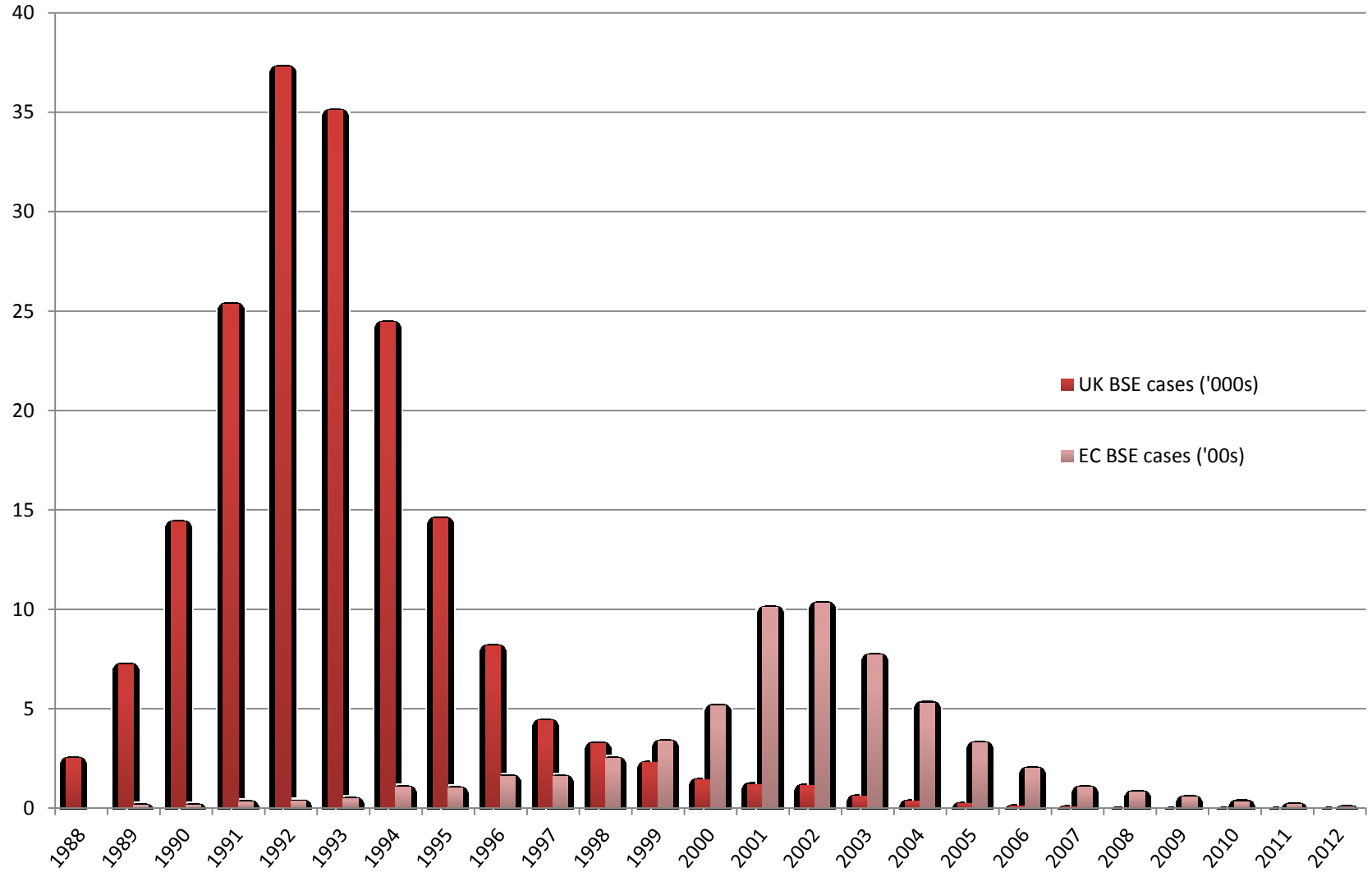
The crisis in 2000

Related in part to misplaced confidence in the absence of BSE in cattle populations in the context of inadequate surveillance

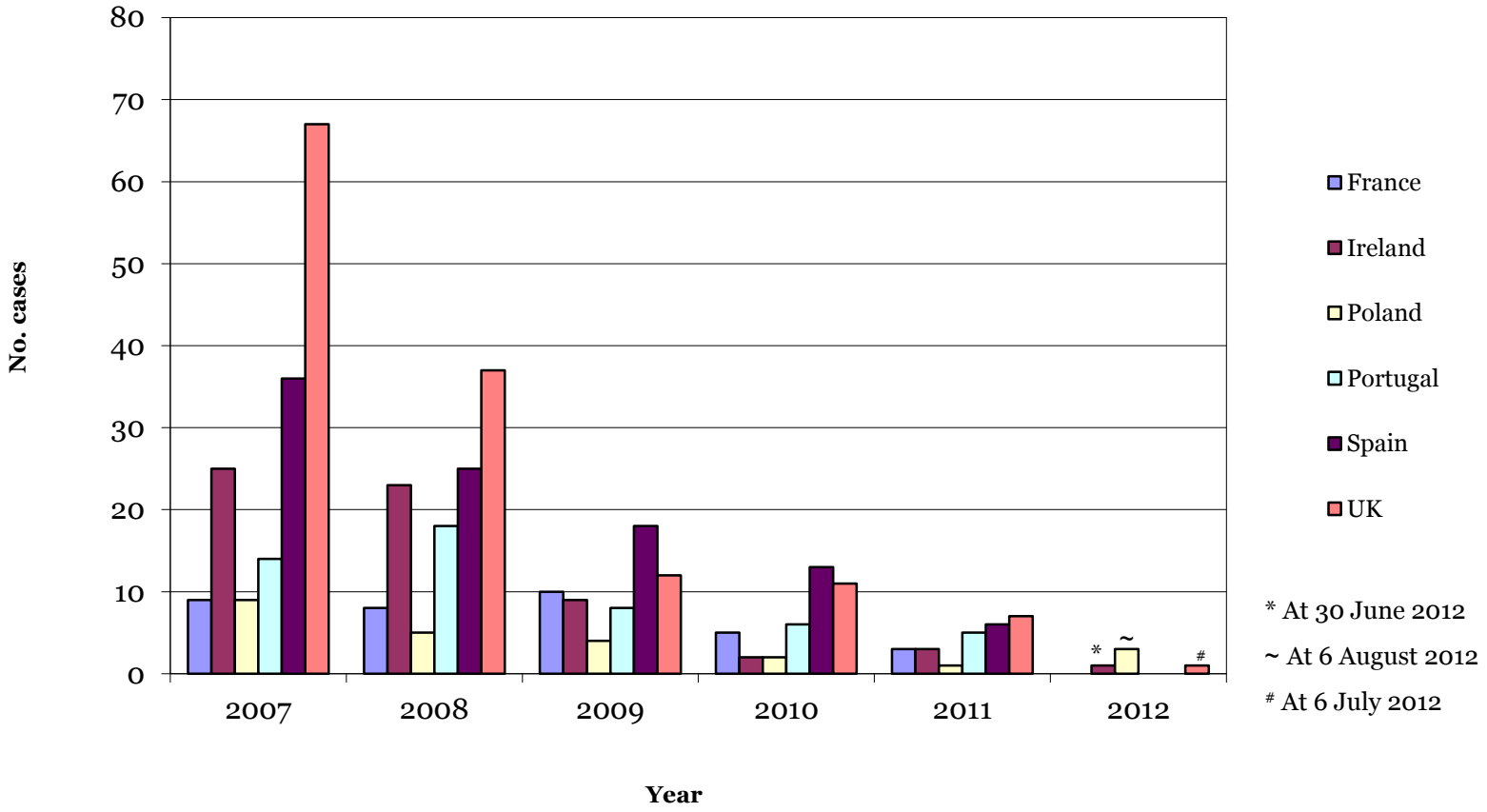
Year Indigenous BSE Identified in EU Countries



BSE cases 1998-2012 in the UK & EC

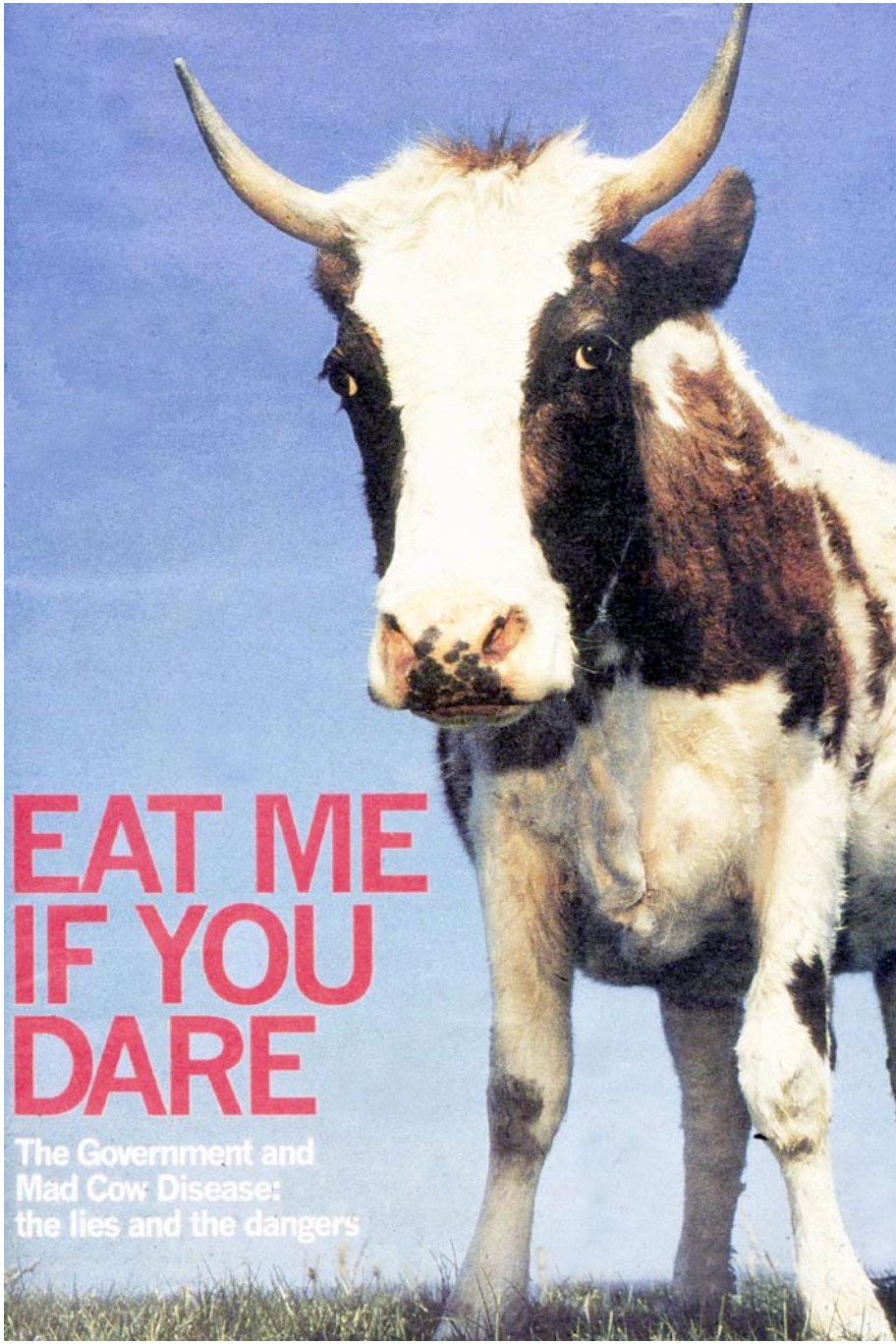


Number of reported cases of BSE
2007-2012

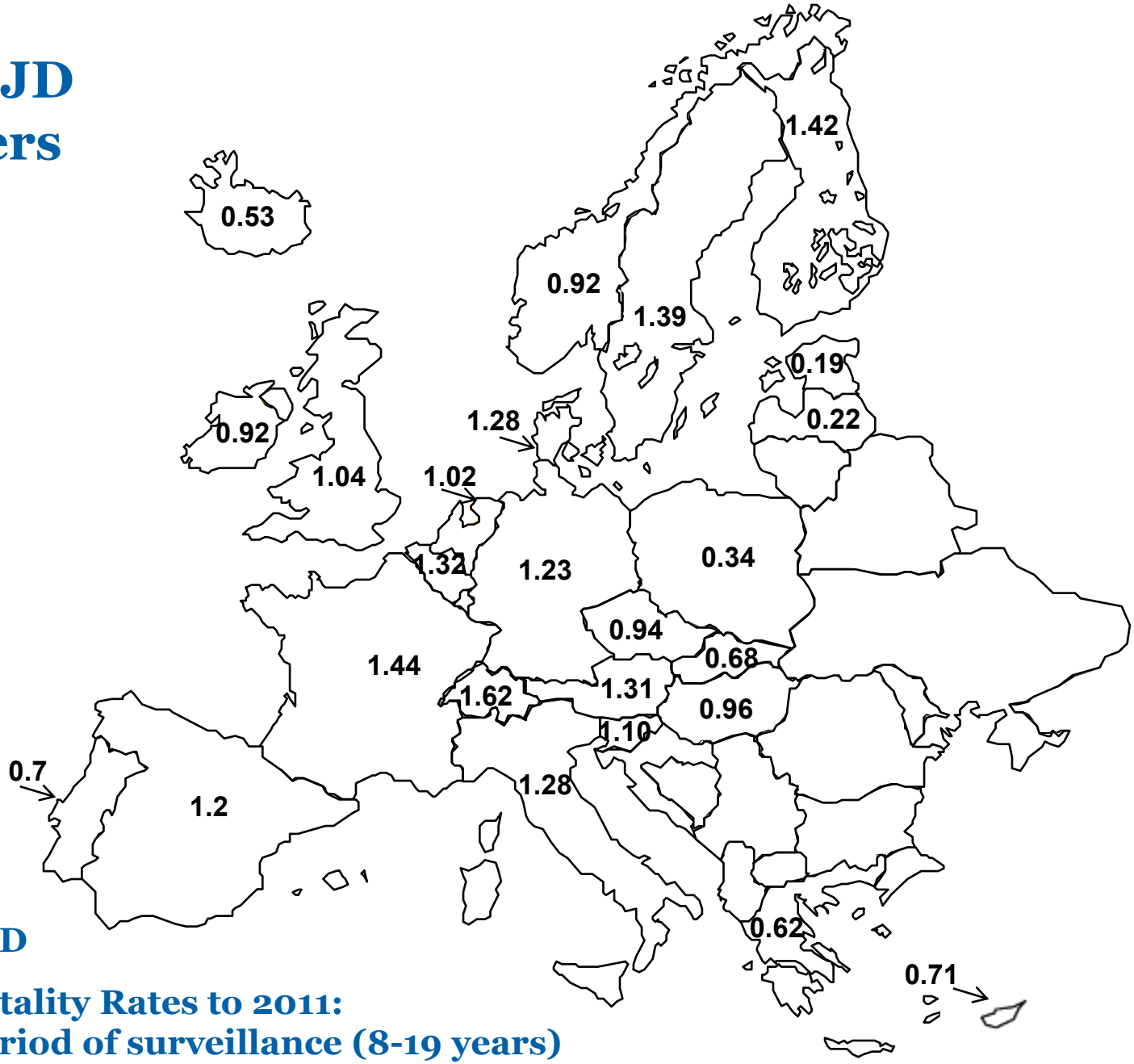


1989: Tyrrell Committee recommends reinstitution of national CJD surveillance

1st May 1990: National CJD Surveillance Unit established in Edinburgh



EUROCJD Members



Sporadic CJD

Annual Mortality Rates to 2011: Mean for period of surveillance (8-19 years)

Articles

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.

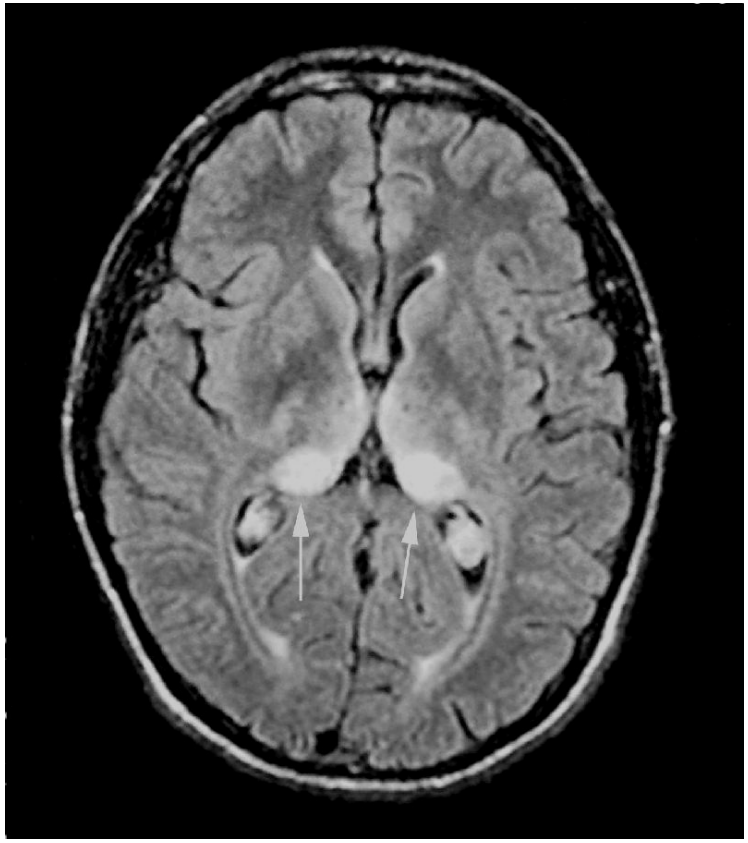
Introduction

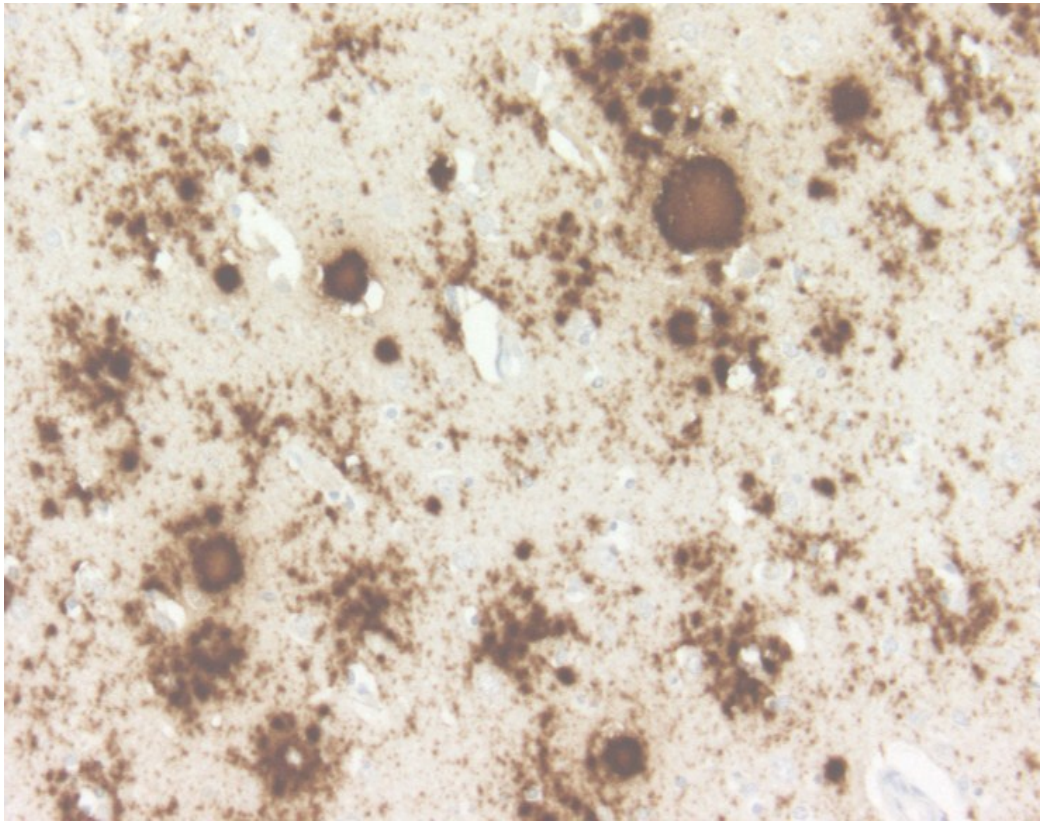
Because of the epidemic of bovine spongiform encephalopathy (BSE) in cattle, surveillance of Creutzfeldt-Jakob disease (CJD) in the UK was reinstituted in May, 1990. The purpose of the surveillance is to identify changes in the pattern of CJD which might indicate an association with BSE. We report ten cases of CJD in the UK with clinical onset of disease in 1994 and 1995. These cases all have neuropathological changes which, to our knowledge, have not been previously reported. They are also unusual in that they occurred in relatively young people, and the clinical course was not typical of cases of sporadic CJD in the UK.

Methods

Since May, 1990, cases of CJD have been identified to the CJD Surveillance Unit, usually by direct referral from professional groups, which include neurologists and neuropathologists. All

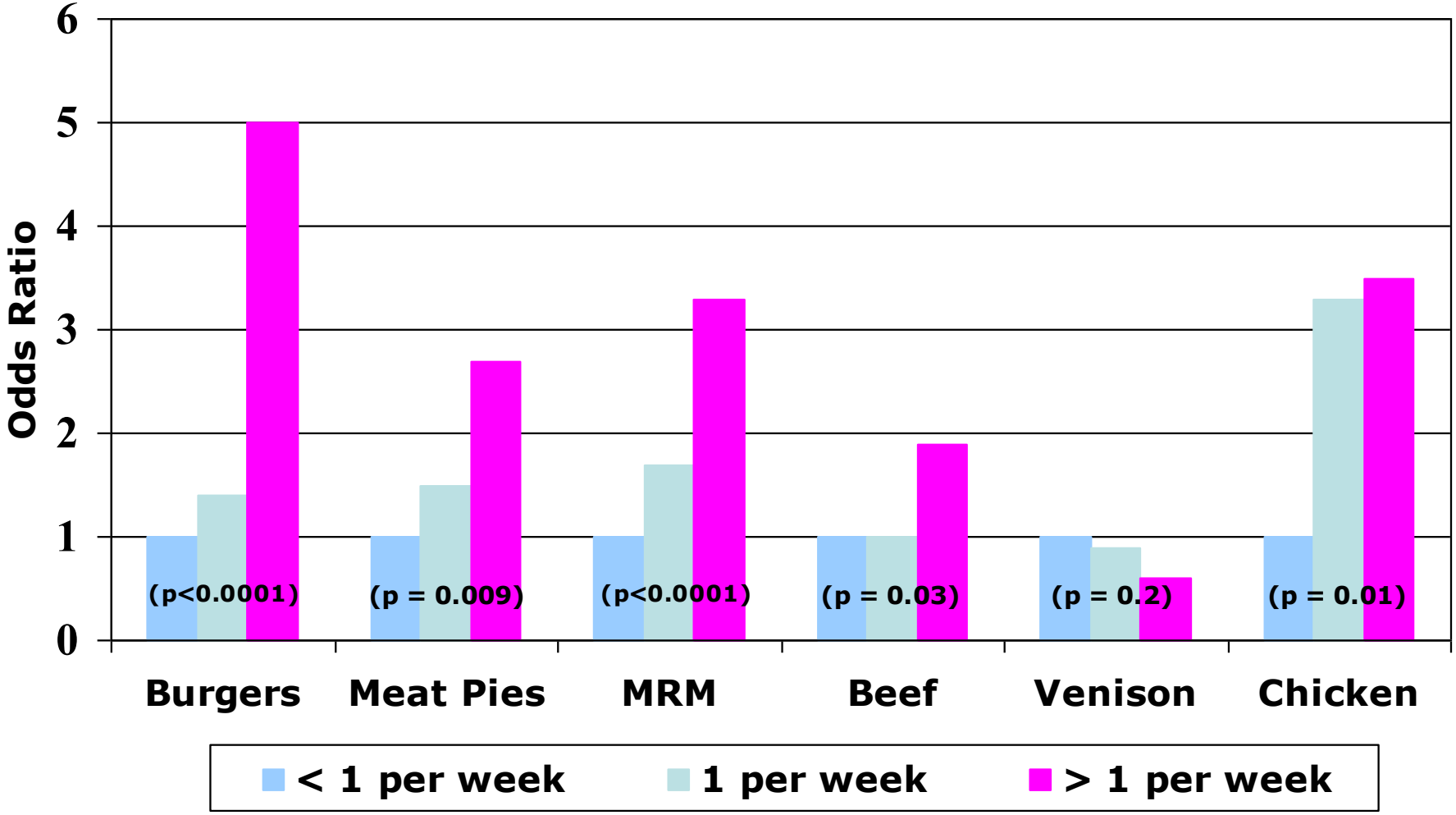
MRI scan and brain immunocytochemistry in variant CJD

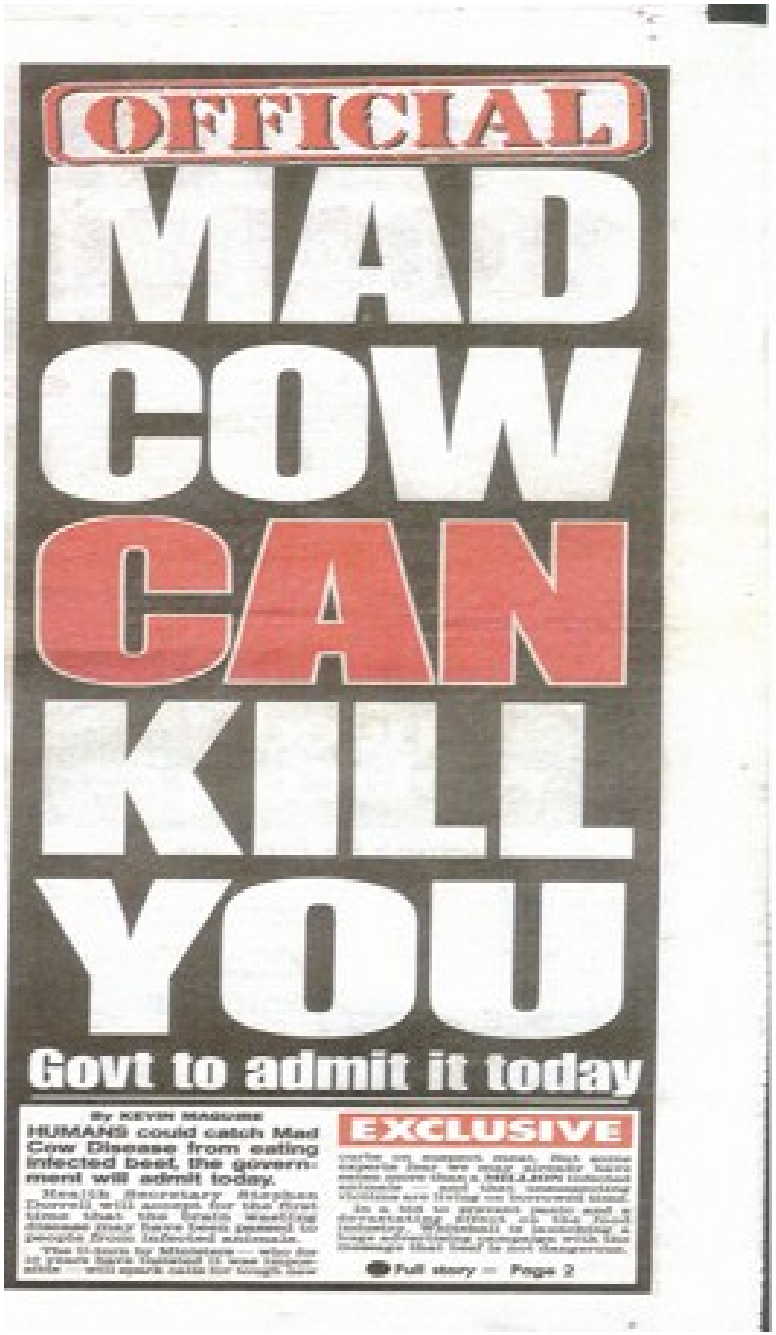




DIETARY RISK FACTORS
REPORTED AVERAGE FREQUENCY OF CONSUMPTION SINCE 1980 OF SELECTED FOOD ITEMS

Ward et al Ann Neurol 59; 111-120: 2006





OFFICIAL

MAD COW CAN KILL YOU

Govt to admit it today

By KEVIN MAGUIRE

HUMANS could catch Mad Cow Disease from eating infected beef, the government will admit today.

Health secretary Stephen Dorrell will accept for the first time that the brain wasting disease may have been passed to people from infected animals.

EXCLUSIVE

Full story — Page 2

March 20th
1996

The crisis in 1996

Les farines carnées ont circulé dans l'ensemble des pays de l'Union

Vache folle : toute l'Europe frappée

Bérengère Mathieu de Heaulme

Contrairement à ce que la majorité de nos partenaires européens affirme publiquement depuis deux semaines, la crise de la vache folle n'est pas seulement franco-britannique. Elle concerne l'ensemble de l'Union européenne : les quinze pays membres ont tous importé après 1996 des farines animales potentiellement contaminées par l'encéphalopathie spongiforme bovine (ESB).

Leurs populations sont donc toutes exposées à la nouvelle variante de la maladie de Creutzfeldt-Jakob (nv-MCJ). Voilà ce que prouvent les chiffres obtenus par *Le Figaro* auprès du syndicat des producteurs de farines animales (Sifco) qui les tient de l'European Renderers Association.

Le tableau des exportations et des importations de farines carnées en Europe permet de suivre à la trace le voyage du prion – cette protéine véhiculant l'ESB chez les bovins – sur le Vieux Continent. Ces chiffres ont été gardés sous silence depuis deux semaines, notamment par le service des douanes qui plaide la « *difficulté technique* » et « *les problèmes de catégories statistiques* ».

Patrick Colombier, vice-président du Sifco, confie : « *Je sais bien que ces chiffres ne feront pas plaisir à tout le monde. Mais il faut que les Français comprennent qu'il n'était pas nécessaire de frauder pour répandre dans toute l'Europe la maladie de la vache folle. Les lois étaient une porte ouverte à la contamination générale.* »

Ainsi, en 1999, les Allemands ont consommé 452 000 tonnes de farines de viande, dont 45 000 étaient importées. Les Belges, les Espagnols, les Français, les Italiens et les Néerlandais sont dans la même situation.

Suite page 9

WEST END FINAL

Evening Standard

LONDON, THURSDAY, 21 MARCH, 1996

INCORPORATING THE EVENING NEWS 30p

FRENCH BAN BRITISH BEEF

Germany calls for Europe boycott as Dorrell warns 11m cattle may have to die

by CHARLES REISS and PATRICK HENNESSY

CRISIS OVER BRITISH BEEF
Pages 2, 3, 4, 5 and 7
Leader comment: Page Nine

A BITTER cross-Channel dispute broke out today after France and Belgium slapped an instant ban on British beef amid mounting worries over mad cow disease.

With Germany calling for an EU-wide ban on British beef, the UK was facing growing isolation following yesterday's announcement that for the first time there was evidence to link mad cow disease to humans.

Health Secretary Stephen Dorrell today said that one consequence might be the slaughter of all 11 million cattle in Britain, should scientists advise that was necessary, with a possible £3 billion compensation cost.

According to the agriculture ministry, the final cost, taking into account loss of trade, the knock-on effects in food companies and the costs of importing beef, could be as high as £10billion.

Angry Agriculture Minister Douglas Hogg condemned the French decision as "quite unjustified" and "probably illegal". He called for urgent talks with Paris and the European Commission.

But his French counterpart, Philippe Vasseur, said the move was essential "to provide all necessary guarantees to French consumers".

With the future of Britain's £520 million annual beef exports to Europe facing a massive new threat, Mr Hogg went on the attack after a Cabinet meeting was interrupted to inform ministers of the French decision.

Within hours, the French were joined by the Belgians. A spokesman for farm minister Karel Pinxten described the measure as "conservative" and said it was taken ahead of "more definitive" measures expected after European Commission agriculture experts hold talks on Friday.

Mr Hogg said: "We think France's decision is an unreasonable decision, quite unnecessary and probably illegal. It's a wholly disproportionate response and that, I think, raises very strong questions of illegality." Mr

Continued on Page 2 Col 6

Off menu at 10,000 schools

by DOROTA LEPKOWSKA
Education Correspondent

UP TO 10,000 schools have banned beef from dinner menus, and many more were joining the boycott today.

Birmingham and Nottingham announced that no more beef would be served in their schools. Buckinghamshire, Dorset and Cumbria are still serving beef but offering alternatives, and Cumbria Council is to reconsider its position on Monday.

Berkshire County Council announced today that after advice from its outside caterers, schools would not be serving beef from the beginning of the new school term in April. The Local Authority Caterers Association said that even before yesterday's announcement, a third of Britain's 30,000 schools no longer had beef on the menu as a result of BSE scares.

A spokesman for the Association of County Councils said: "We want the Government to provide more information. We welcome yesterday's statement but it should have been a lot sooner. There is a lot of concern amongst parents, teachers and children themselves."

TV & RADIO GUIDE 32, 41 & 42 BUSINESS DAY 33 FEATURES 21 EN

National news

BSE advisers see danger in European beef

Safety committee member will not eat French meat

James Meikle and **Jon Henley** in Paris

travelling abroad should, she said, "be made aware that it may well be British beef is

tation with our scientists."

France, which has refused to lift its ban on British beef and

International News

Millions at risk from CJD, say EU scientists

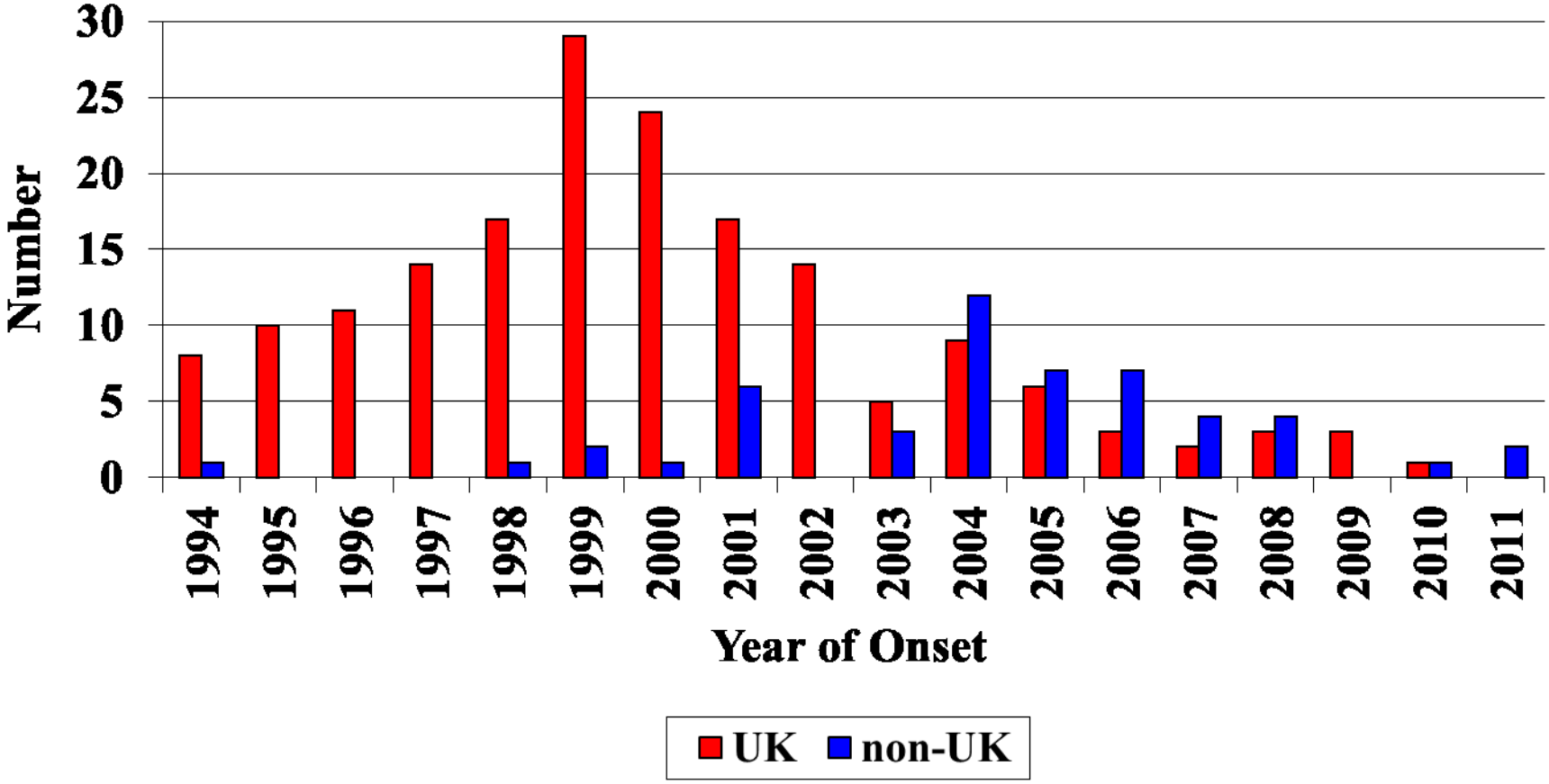
VARIANT CREUTZFELDT-JAKOB DISEASE
CURRENT DATA (NOVEMBER 2012)

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	173 (0)	3 (0)	176
France	27 (2)	-	1
R 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

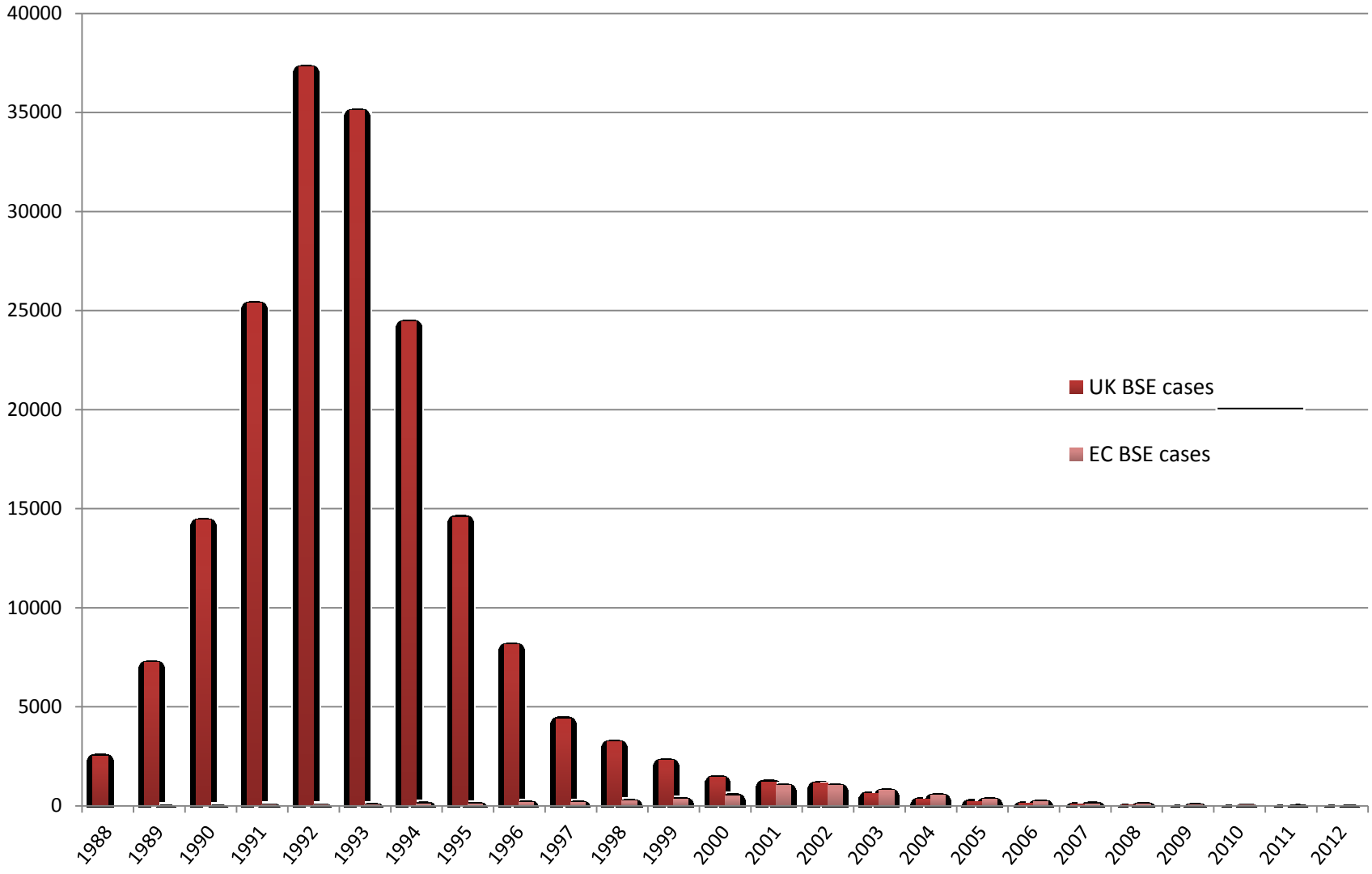
* the case from Japan had resided in the UK for 24 days in the period 1980-1996.

† 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.

YEAR OF ONSET OF vCJD SYMPTOMS



BSE cases 1998-2012 in the UK & EC

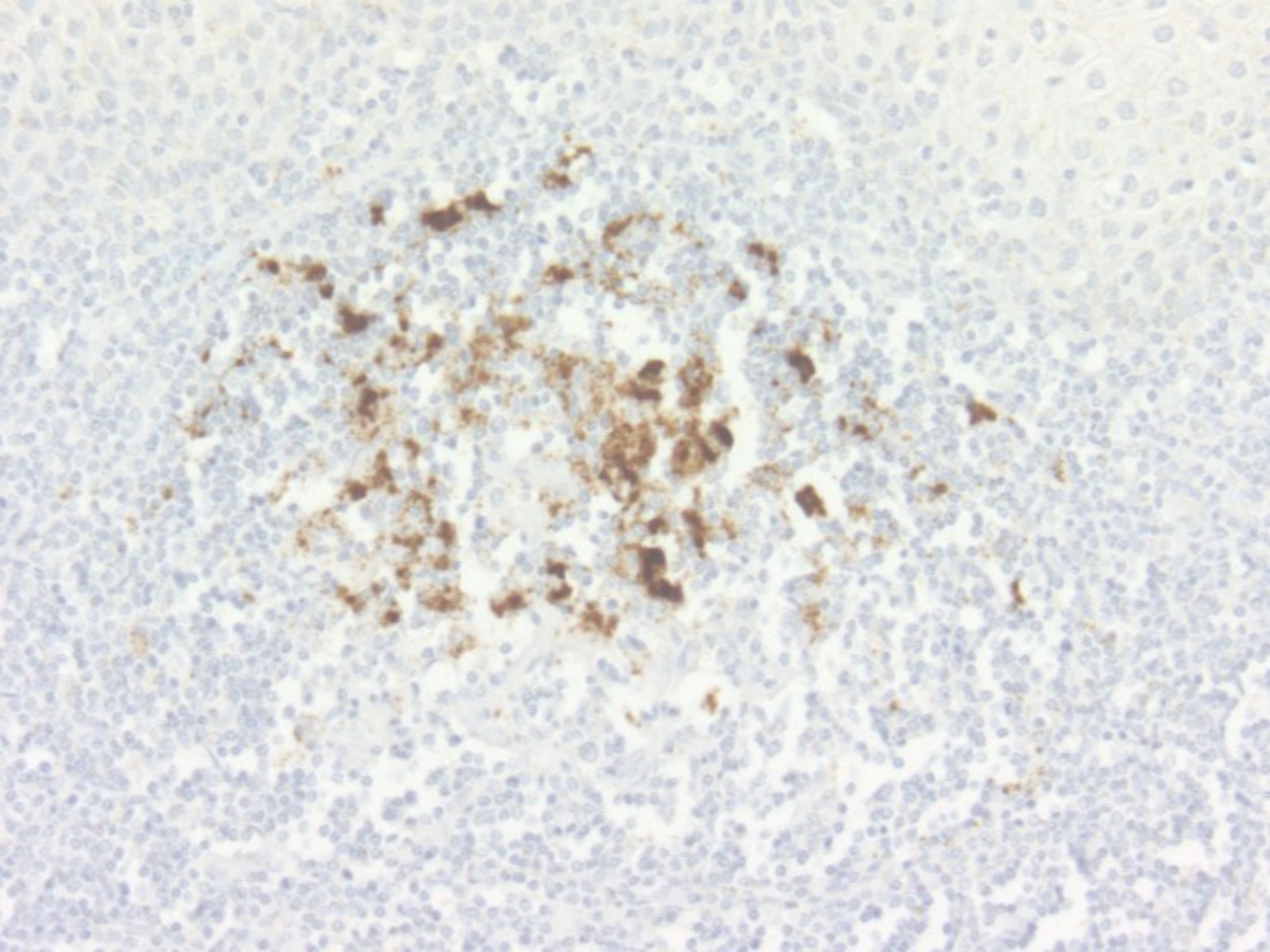


EMERGING
INFECTIOUS DISEASES

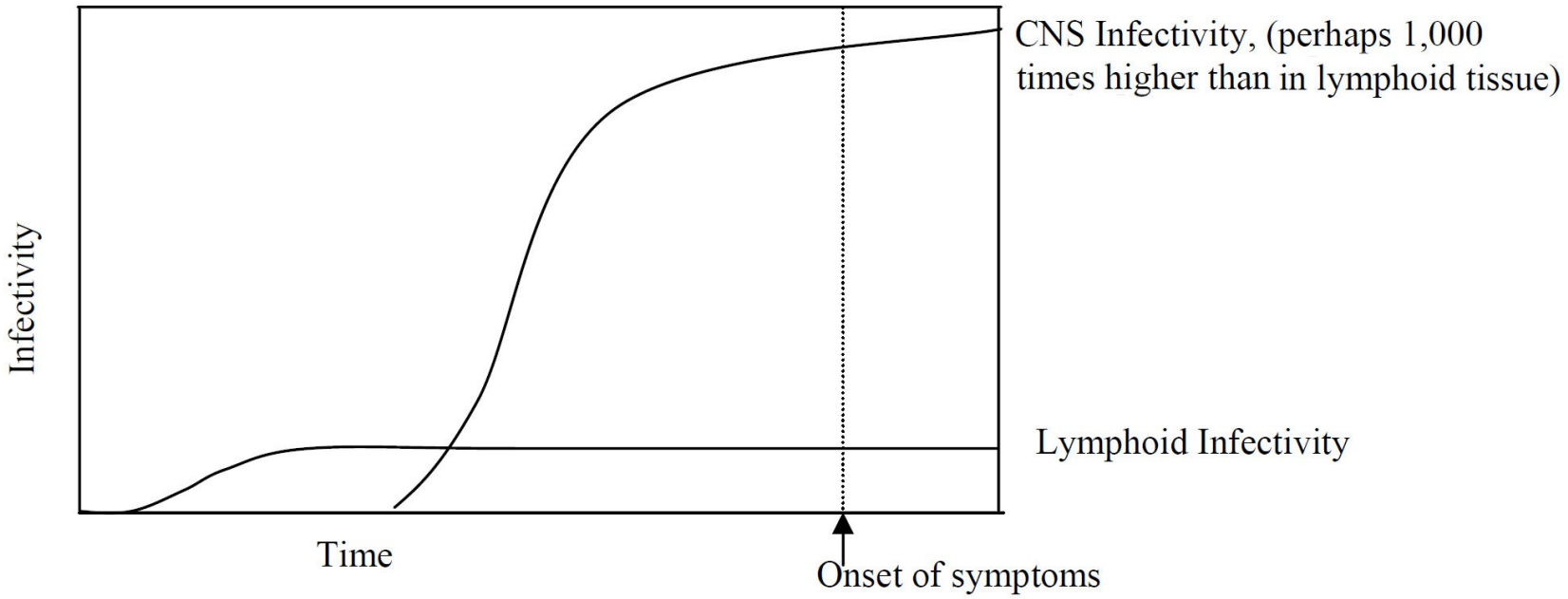
Source of Variant Creutzfeldt-Jakob Disease outside United Kingdom

Pascual Sanchez-Juan, Simon N. Cousens, Robert G. Will, and Cornelia M. van Duijn

This finding suggests that live bovine and/or carcass meat imports from the UK may have been an important source of exposure in at least some of the countries in which vCJD has been detected. These results are consistent with an analysis of data from France, which suggested that UK bovine imports were likely to have been a more important source of infection than indigenous BSE.



Probable pattern of tissue infectivity in variant CJD, based on scrapie models



Articles

Possible transmission of variant Creutzfeldt-Jakob disease by blood transfusion

C A Llewelyn, P E Hewitt, R S G Knight, K Amar, S Cousens, J Mackenzie, R G Will

Summary

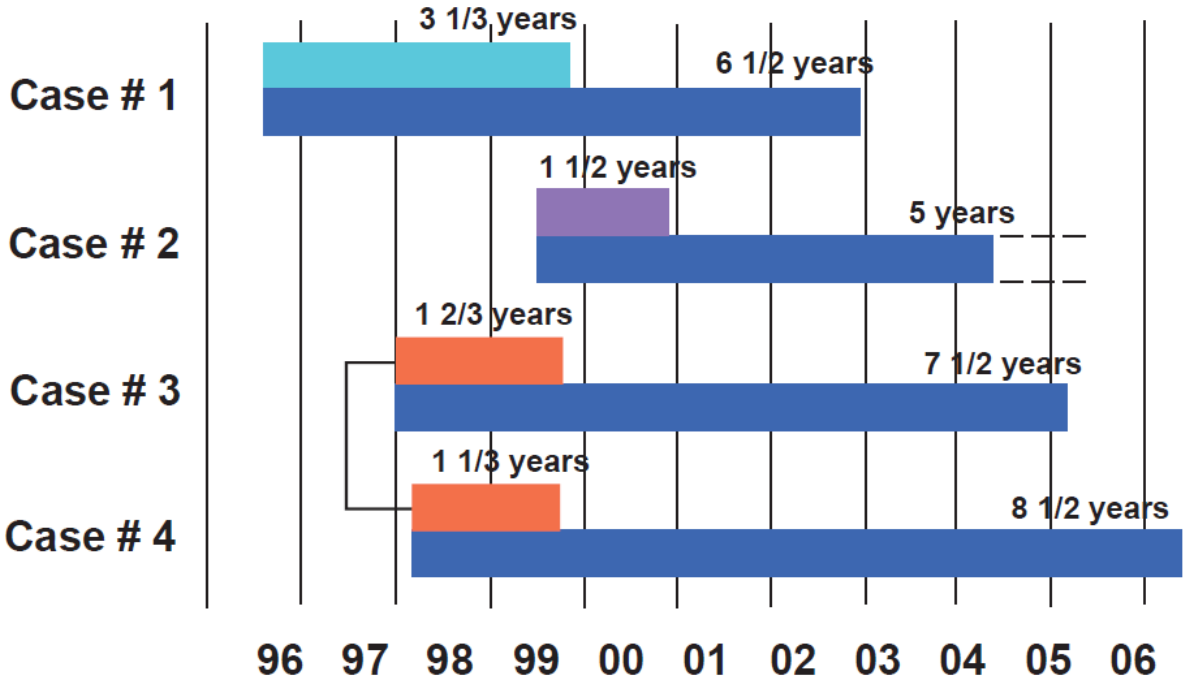
Background Variant Creutzfeldt-Jakob disease (vCJD) is a novel human prion disease caused by infection with the agent of bovine spongiform encephalopathy (BSE). Epidemiological evidence does not suggest that sporadic CJD is transmitted from person to person via blood transfusion, but this evidence may not apply to vCJD. We aimed to identify whether vCJD is transmissible through blood transfusion.

Introduction

Human prion diseases include sporadic Creutzfeldt-Jakob disease (CJD), which is of unknown cause; hereditary forms associated with mutations of the prion protein gene; variant CJD (vCJD), which has been causally linked to the bovine spongiform encephalopathy (BSE) agent; and iatrogenic cases transmitted via human pituitary hormones, human dura mater grafts, corneal grafts, and neurosurgical devices. All instances of iatrogenic transmission of CJD to date have been due to cross-

Journal of
INTERNAL MEDICINE

E. Norrby

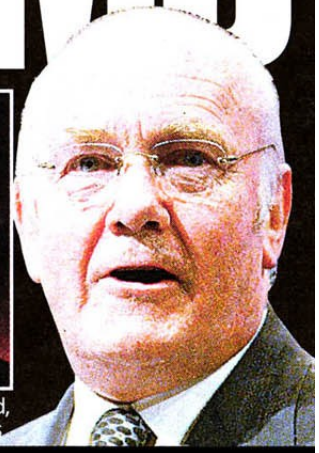


Four cases of variant Creutzfeldt-Jakob disease (vCJD) prion infection caused by blood transfusion. Cases 3 and 4 were infected by transfusion of blood from the same donor. In each case, the upper bar shows the time until the donor developed disease and the lower bar the time until disease appeared in the recipient or, as in case 2, vCJD prions were demonstrated in the tissues.

J Intern Med 2011; **270**:1–14.

CJD TIMEBOMB

Hundreds face nightmare wait to see if they were infected by blood



DEADLY: Donna-Marie died of CJD, which Reid, right, says could be passed on by blood donors

'WE'VE GOT A TERRIBL NIGHTMARE ON OUR HANDS'

Hundreds face 'Mad Cow Disease' timebomb over infected blood

TRAGEDY: Marie Walkden died after recei

Post mortem finding of asymptomatic variant Creutzfeldt-Jakob Disease (vCJD) abnormal prion protein in a UK resident with haemophilia

February 2009

The government introduced a number of measures from 1997 onwards to safeguard blood and plasma supplies.

- Since 1997 all cases of vCJD that are reported to the National CJD Surveillance Unit and diagnosed as having 'probable' vCJD, result in a search of the UK Blood Services blood donor records. If the patient has donated blood, any unused parts of that blood are immediately removed from stock. The fate of all used components of blood from the donor is traced, and surviving recipients informed of their risk.
- In July 1998, the Department of Health announced that plasma for the manufacture of blood products, such as clotting factors, would be obtained from non-UK sources.
- Since October 1999, white blood cells (which may carry the greatest risk of transmitting vCJD) have been removed from all blood used for transfusion.
- In August 2002 the Department of Health announced that fresh frozen plasma for treating babies and young children born after 1 January 1996 would be obtained from the USA, extended to all children under 16 years of age (Summer 2005).
- In December 2002, the Department of Health completed its purchase of the largest remaining independent US plasma collector, Life Resources Incorporated. This secures long-term supplies of non-UK blood plasma for the benefit of NHS patients.
- Since April 2004, blood donations have not been accepted from people who have themselves received a blood transfusion in the UK since 1980. This has been extended to include apheresis donors and donors who are unsure if they had previously had a blood transfusion (August 2004).
- Since late 2005, blood donations have not been accepted from donors whose blood was transfused to patients who later developed vCJD.
- The UK Blood Services continue to promote the appropriate use of blood and tissues and alternatives throughout the NHS.

Transfusion transmission of vCJD: a crisis avoided?

Lessons

The potential risk of transfusion transmission of vCJD provides a useful model for decision-making in the presence of scientific uncertainty. The key lesson from this policy-making experience is that lack of definitive evidence should not preclude action for serious potential exposures.

www.thelancet.com ***Vol 364 August 7, 2004***

Prevalence studies of abnormal PrP

Courtesy of Dr Noel Gill HPA

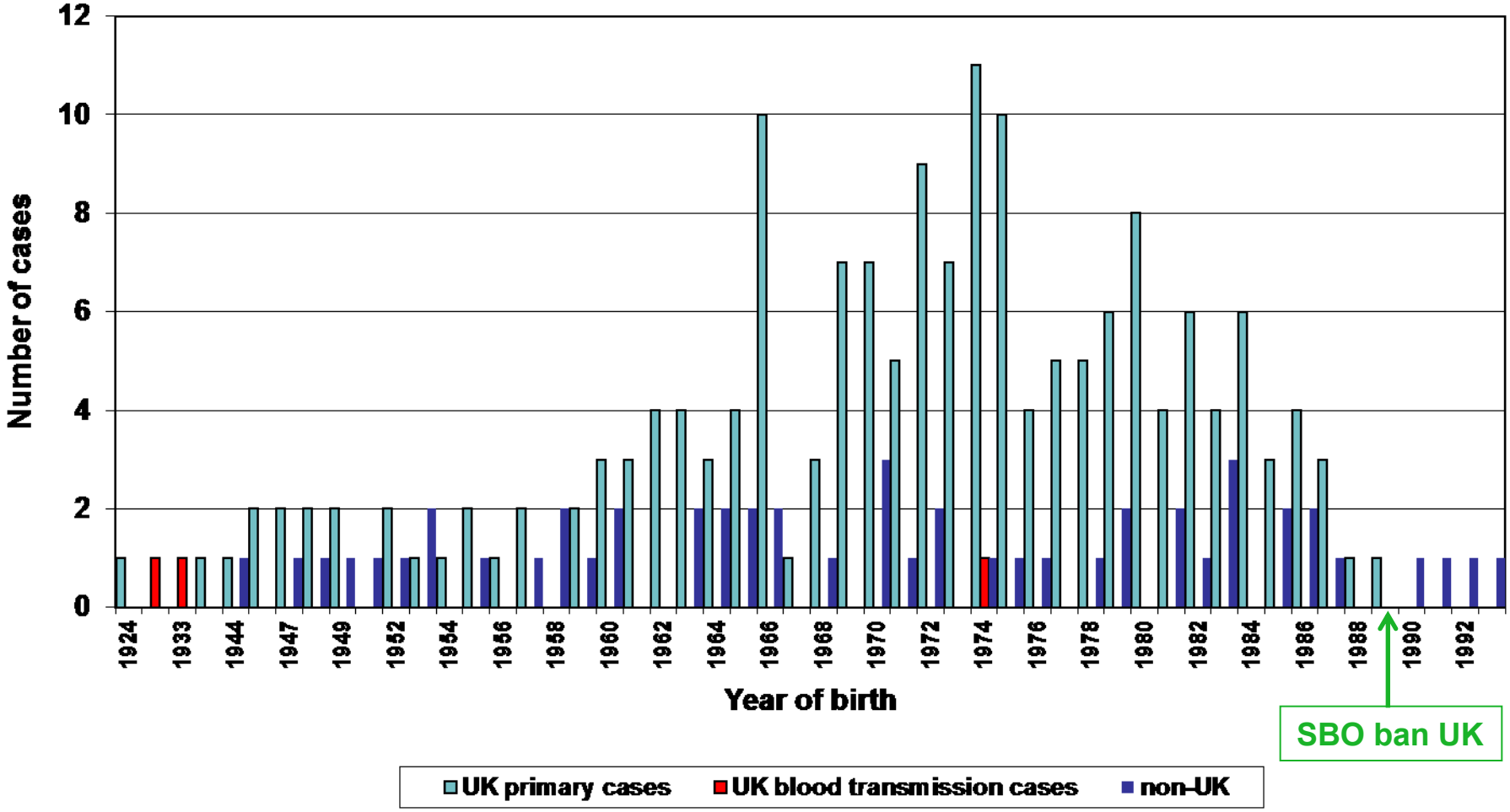
Year	Tissue	Positive/tested		Prevalence estimate/million
2004	Appendix	3/12,674		235 (49-692)
2004	Tonsil	0/2,000		
2011	Tonsil	1/10,075		99 (3-553)
2011	Appendix	4/13,878		288 (79-738)
2012	Appendix	16/ 32,441		493 (282-801)
1941-1960 Birth Cohort		2/3120	(2/4607)	733 (269-1596)
1961-1985 Birth Cohort		2/10,758	(5/48,676)	412 (198-758)

THE SUNDAY TIMES

60,000 may have human variant of mad cow disease

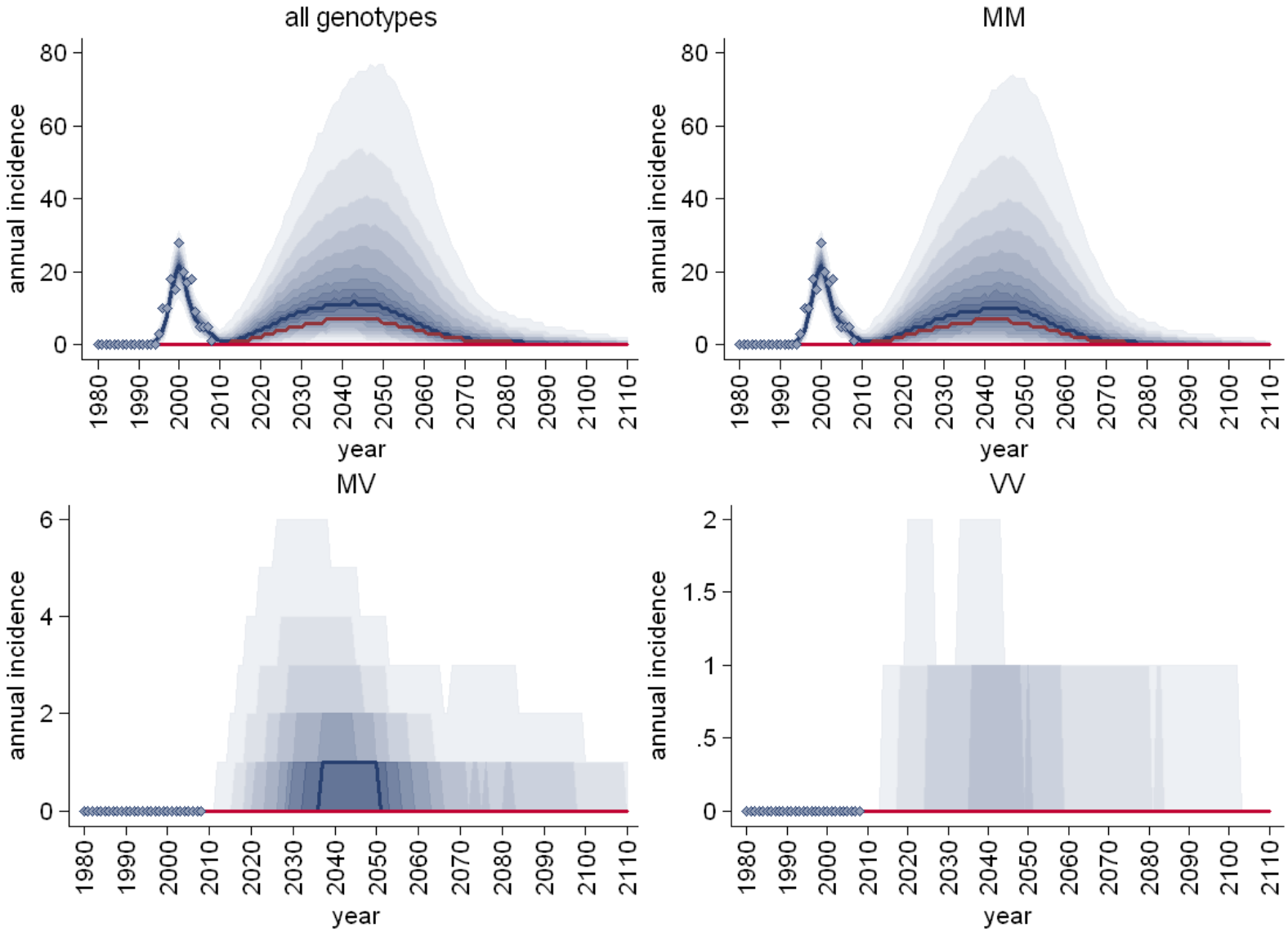
Sunday 18, September 2011

UK (n=176) AND NON-UK (n=51) CASES SHOWN BY YEAR OF BIRTH



epidemic time series

Courtesy of Tini Garske et al



Continuing public health concerns

- Prevalence of human BSE infection
- ?Surgical transmission of vCJD
- ?Vertical transmission of vCJD
- ?Novel forms of human BSE infection (MV/VV)
- Atypical BSE/scrapie
- Chronic wasting disease of deer (North America)
- Countries exposed to BSE with inadequate animal or human surveillance

The Guardian Tuesday December 5 1995

Mad scientist disease

The dangers of genetic engineering underline science's need to take moral responsibility for the results of its actions, **George Monbiot** argues

A COUPLE of months ago, a breakthrough was announced in Scotland. Scientists had inserted genes from a luminous jellyfish into crop plants, so that they would glow in the dark when they

plistic nonsense years ago. But there was nothing particularly surprising about the vacuous euphoria which greeted the development. Genetic engineering's usefulness is routinely exaggerated and its dangers downplayed. Part of the reason is that

money. As the disadvantaged of the world are the least able to pay, they are the least likely to be helped by this kind of science.

The second is naivity. Many researchers could fairly be described as idiot savants, brilliant specialists

Scientific terrorism

Vague talk of risk by experts can ruin an industry — but it boosts research

Just imagine. You have read about the Swissair disaster and are about to fly in a plane of the same make. As you leave for the airport, you read a report from a government scientist. He says that, in his opinion, there is "a very real risk" of the same fault occurring in other planes of the type. "If this distinct possibility is true," he goes on, "it would be an emergency."

What on earth do you do? Do you fly anyway, change your flight, or wait for the Government to ground every plane? After all, the man is an official scientist. He has gone public. He purports to know.

Those were the exact words that a member of the Government's bovine Spongiform Encephalopathy Advisory Committee (Seac), Professor Jeffrey Almond, used this week about lamb. You will recall that BSE led to one of the worst outbreaks of mad-politician disease in 1995-97. Nobody today should need warning to be cautious. The outbreak followed a tiny number of cases of human CJD, which had appears to have missed out on a full share of the research gusher unleashed on his "bovine" colleagues during the crisis. Obsessed with mad cows, we forgot about mad sheep, mad goats and other consumable and researchable quadrupeds.

After the BSE scare and as a precautionary measure, Britain (alone in Europe) has banned sheep tissue from the food chain. Seac scientists also checked for BSE in sheep, as distinct from the sheep version called scrapie, but found none. Even at the height of the scare, the risk of any Briton ever catching CJD from beef was put at between one in 50 million and one in a billion, surely the bottom of any Richter scale of danger. In which case, the risk now of catching

Simon

a time, if the test is treated as meaningless? There are 40 million sheep out there. Do we test them all, on so wild an off-chance? Mr Almond asks, suppose just 0.1 per cent of the nation's flock had BSE, it would represent thousands of animals. It would indeed, but this is the oldest of statistician's tricks. Grab from the air an apparently trivial percentage and then reveal it as a huge number. I might as well reply, suppose only 0.000000001 per cent had BSE, then what?

If BSE were to be found in sheep, incants Mr Almond in the face of all the evidence, "that could pose a risk to humans ... we could be facing a potential national emergency". We note the use of conditionals, "if ... could be ... potential". They are cho-

that £150 million has been paid by the Treasury to the same feed companies whose practices caused the BSE epidemic in the first place. These are vast sums by any reckoning.

In a book out this week called *Consiliance*, the American scientist Edward O.Wilson calls on his colleagues to seize the high ground from the humanities. Scientists must teach economists, politicians, philosophers, even musicians how to reason, he says. They must boast the new discoveries in behavioural psychology, cultural genetics and brain chemistry. Wilson offers a rollicking good read. But the boot is sometimes on the other foot. When scientists cross into politics they too can get in a terrible mess.

When a scientist peers over his glasses, lowers his voice an octave and intones "I have discovered a risk", how are we supposed to react? We all take risks, every hour of every day. How much risk does this man

Acknowledgements

- Neurologists and Neuropathologists throughout the UK
- All our collaborators in the UK and internationally
- All the staff at the NCJDRSU
- Patients and their families
- Funded by the Department of Health, the Scottish Government, the European Union

DH Department of Health

The Scottish Government

Why has the vCJD outbreak been relatively limited?

What is the incubation period in vCJD?

Why are the cases of vCJD relatively young?

Why is there a mismatch between estimated prevalence of infection and the observed number of cases?

Why are there not more transfusion related cases?