Bovine Spongiform Encephalopathy (BSE)

Yvonne Spencer
Head of Pathology Department, APHA-Weybridge

EU TSE Reference Laboratory Pathology Consultant
What are TSEs?

Scrapie - BSE - vCJD

Surveillance data
What are TSEs?

• Transmissible, progressive, fatal, neurological diseases in animals and humans

• BSE, Scrapie, CWD, FSE, TME, vCJD, Kuru, GSS, FFI…

• Infectious and sporadic forms, and experimental models
• TSE agent cannot be isolated - caused by proteinaceous infectious particles – prions
  – Misfolding of physiological protein PrP, from α-helix PrPc to disease-associated β-sheet PrPd
  – Existence of multiple protein conformations may explain different strains
  – PrP gene sequence may influence susceptibility to disease

• **PrPd in infected tissues is a consistent marker**
  – We depend upon PrP detection and characterisation in infected tissues for diagnosis and research
Classical Scrapie – the first TSE?

• Known to occur in sheep flocks for at least 350 years, and probably before
• Well characterised:
  – Clinical signs
  – Pathology
• Not considered zoonotic

Atypical scrapie

• First identified in 1998 (hence Nor-98)
• Retrospective cases to 1987 and 1989
• Epidemiology? Clinical signs? Pathology? – all different
• Almost always detected by active surveillance
• Zoonotic??
Clinical signs - Scrapie

Classical scrapie
- Age at onset ~2yrs
- Ataxia
- Pruritis, rubbing, wool loss
- Ill thrift
- Charging of fences, dogs etc.
- Scratch test – nibbling/curling lips, wagging tail
- Restlessness
- Dry wool and rough skin
- Teeth grinding
- Muscle twitching
- Convulsions

Atypical scrapie
- Age at onset ~6yrs
- Reduced menace response
- Ataxia
- Circling
- NOT – itching, rubbing, wool loss
Ataxia: classical vs atypical

Classical scrapie
(hindlimb ataxia)

Atypical scrapie
(circling/hypermetria)

Note that animals are alert, and not showing any pain or discomfort
Classical BSE

• First identified in cattle in 1986
• Considered ‘scrapie-like’, therefore not zoonotic
• 1980’s/90’s cases with similar brain pathology:
  – Exotic ungulates – gemsbok, eland, moufflon etc.
  – Felines – domestic cat, captive wild cats

• Cases geographically separated -> transmission via contaminated feed (MBM)
Clinical signs - BSE

• Changes in mental status, behaviour and activity:
  – Apprehension, fear, nervousness

• Sensation:
  – Over-reactivity to external stimuli, e.g. flash test
  – L- type – reduced reactivity

• Posture and movements:
  – Ataxia, tremor, wide-based stance,

• Non-specific signs:
  – Loss of body weight/condition
  – Reduced milk yield
  – Bradycardia
  – Decreased rumination
vCJD

- In 1996 first cases of vCJD published
- Unique and consistent phenotype:
  - clinical signs, neuropathology, epidemiology
- Total cases 177 within the UK*
  - 51 outside the UK (27 in France)
    - 6 linked to UK residency
Huge public concern – disproportionate?
Greatest risk may be iatrogenic

- Three secondary cases have been attributed to blood transfusion from cases which were pre-clinical at the time of donation
- Research shows PrP/infectivity almost impossible to remove completely from surgical steel
Abnormal prion accumulation was detected within the follicular dendritic cells of **16/32,411** suitable appendices.

None of the positive appendices have come from the known vCJD cases in the UK, because none of these cases had a history of appendectomy.

Final overall prevalence estimate, **493 per million** (95% (CI): 282 to 801 per million), remains statistically consistent with results from an earlier appendix survey.*

All under control?

• The classical disease forms are now generally well controlled

• The most prevalent naturally-occurring TSE is now CWD in North America
  – The only form of disease that is increasing in prevalence
  – Only form of disease present in wild animal population
  – Very difficult to monitor or control as a result
  – Disease moving between free-living and captive cervids
  – Excreted in faeces/saliva
  – Surveillance and disease control both very difficult in wild populations/environments
  – No evidence of occupational risk to hunters
    ….. (yet?)
Underpinning surveillance
EU regulation 999/2001

- standardised EU-wide surveillance for TSE
- Provides increased confidence in the data
- Data used to inform policy decisions and review regulations
OIE stats for UK

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(1) Cases are shown by year of restriction.

(2) In the Isle of Man BSE is confirmed on the basis of a laboratory examination of tissues for the first case on a farm and thereafter by clinical signs only. However, all cases in animals born after the introduction of the feed ban have been subjected to histopathological/scrapie-associated fibrils analysis. To date, a total of 277 animals have been confirmed on clinical grounds only.

(3) In Guernsey BSE is generally confirmed on the basis of clinical signs only. To date, a total of 600 animals have been confirmed without laboratory examination.
What does this surveillance data tell us?

BSE is going away!

Chart B2: Evolution of the number of BSE positive cases in the 27 EU Member States since 2001 (EU annual report 2011)

Sources of data - OIE portal. EU annual reports, Ad hoc information from member states or referrals from third countries
Prevalence (log10 scale) of BSE in EU17* found by Active and Passive surveillance from 2001 and 2011

Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Slovenia, Spain, Sweden and the UK

European Food Safety Authority; Request for scientific and technical assistance on the minimum sample size to test should an annual BSE statistical testing regime be authorised in healthy slaughtered cattle. EFSA Journal 2012;10(10):2913. [90 pp.] doi:10.2903/j.efsa.2012.2913
Situation BSE in the world: 2008-2012

18 countries reported cases during this period:

14 countries in Europe (Austria, Czech Rep., Denmark, France, Germany, Ireland, Italy, Netherlands, Poland, Portugal, Slovakia, Spain, Switzerland and the UK)

4 elsewhere  USA, Canada, Brazil, Japan

- Only the UK, France, Ireland, Poland, Portugal and Spain reported cases every year during this period
- Decreasing trend in number of cases per year and annual incidence rate in countries reporting cases historically
- Two new countries that had never reported cases before: Czech Republic (2009), Denmark (2009)

Highest Annual incidence rate (Number of indigenous cases per million bovines aged over 24 months during the year): Portugal (from 20.5 in 2008 to 2.4 in 2012)
Atypical BSE

Atypical forms of disease now being identified (H-BSE; L-BSE)
- Differ from classical BSE and each other
- Only detected through active surveillance (to date), mostly older fallen stock. Small numbers – widely dispersed temporally and geographically
- New? Or just newly identified?
- Public health risk not yet established

EU BSE databases on 1 July 2014. By 2015, these data might be more comprehensive following a request from the European Commission to Member States for re-testing and retrospective classification of all positive bovine isolates in the EU in the years 2003–2009

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EFSA Journal 2014;12(7):3798
BSE - Recent cases (since 2012)

- One atypical case (H-BSE) in Norway 2015
- A second atypical case (H-BSE) in Brazil 2014
- Two atypical cases in Romania 2013, 2014
- One classical case in Canada 2015
- One classical case in UK in 2013
- Many EU countries (>20) are approaching ‘negligible risk’ as defined by the OIE
- If EU controls stay in place across the EU28, many countries are being compromised in terms of trade
Reviews of controls and regulations

• Surveillance targets have been changing in recent years
  – No screening of healthy slaughter population
  – Age threshold for fallen stock screening is rising. Was 30 months, now 48. Discussion about moving to 72

• Extensive discussion on whether it is appropriate, necessary or possible to attempt controls for atypical cases
  – Different (global) geographical distribution
  – Possibly spontaneous disease – no clear understanding of pathogenesis or risk factors
  – Very low prevalence

• Lots of pressure on the Commission to relax some control measures now that disease prevalence is so low
  – Specified risk material regulations are currently being reviewed, with proposals to delist some tissues completely
For further information on BSE and other animal TSEs refer to TSE EURL website

http://www.tse-lab-net.eu/

Director Dr Marion Simmons BVMS MVM PhD FRCPath MRCVS

Thank you!