Assessing Exposure to BSE Infectivity: the impact of the over thirty month rule in the UK

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Overview

• The Over Thirty Month Rule (OTMR)
• Infectivity of Bovine Tissues
• Routes of Exposure
• Results
• Conclusions
The Over Thirty Month Rule

- Introduced in 1966 in order to reduce exposure of population to the BSE agent
- Meat from cattle older than 30 months not allowed to be used for food
- When dairy cows or beef suckler cows reach the end of their useful life and are *fit for human consumption*, sold into OTMS
  - Animals slaughtered in approved abattoir
  - Complete carcase, including all SRM and offal, sent for rendering
  - Resulting MBM subsequently incinerated
- Scheme costs about £400 million per annum
The Over Thirty Month Rule Review

• UK Food Standards Agency initiated a review of the Over Thirty Month Rule (OTMR) in 2002
• 2 groups set up to advise on changes:
  ➢ Risk Assessment Group (RAG): to advise on changes to risk of exposure
  ➢ Stakeholder Group: to advise on whether the rule can be varied without unacceptable risk to consumers
• RAG acted as steering group for projects to
  ➢ assess expected numbers of infected animals slaughtered for food
  ➢ Assess exposure to infectivity if infected animal slaughtered for food
Infectivity of tissues from animal with BSE

- Infectivity of CNS (Brain & Spinal cord)
- Infectivity of other tissues
- Development of infectivity through incubation period
- Species Barrier
Infectivity of CNS tissues – Oral Exposure

• Whole brain (VLA attack rate 1 - complete)
  ➢ 10/10 at 3 x 100g
  ➢ 10/10 at 100g
  ➢ 7/9 at 10g
  ➢ 7/10 at 1g

• Whole brain (VLA attack rate 2 - ongoing)
  ➢ 3/15 at 0.1g
  ➢ 1/15 at 0.01g
  ➢ 0/15 at 0.001g

• CNS tissues (whole brain) - SSC opinion
  ➢ 50 bovine oral ID$_{50}$/g (range 10 - 1000)
Infectivity of CNS tissues – Oral Exposure

- For Risk Assessments we have proposed a log-normal distribution with mean of 90 bovine oral ID$_{50}$/g and standard deviation of 150 (median value ~ 50)
- Present results from attack rate study indicates that infectivity unlikely to be greater than 10 bovine oral ID$_{50}$/g (range uncertain 1 – 100?)
Development of Infectivity through Incubation

Doubling Time = 2 months  4 months

32 months p.i  CNS positive

26 months p.i  CNS negative
# Infectivity from Clinical Case

Known infective tissues from pathogenesis experiment – bovine oral ID$_{50}$ units

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Weight</th>
<th>Infectivity</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>kg/animal</td>
<td>ID50/g</td>
<td>ID50/animal</td>
</tr>
<tr>
<td>Brain</td>
<td>0.5</td>
<td>50</td>
<td>25000</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>0.2</td>
<td>50</td>
<td>10000</td>
</tr>
<tr>
<td>Dorsal root ganglia</td>
<td>0.03</td>
<td>50</td>
<td>1500</td>
</tr>
<tr>
<td>Trigeminal ganglia</td>
<td>0.02</td>
<td>50</td>
<td>1000</td>
</tr>
<tr>
<td>Tonsil</td>
<td>0.05</td>
<td>0.005</td>
<td>0.25</td>
</tr>
<tr>
<td>Distal ileum</td>
<td>0.8</td>
<td>5</td>
<td>4000</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>1.6</strong></td>
<td></td>
<td><strong>41500</strong></td>
</tr>
</tbody>
</table>
Species Barrier – Cattle to Human

• With TSEs it normally requires more material to infect a different species
• Cattle to mouse species barrier shown to be ~ 500
• Cattle to Human species barrier is not known
• SSC proposed range from 1 to 10,000
• Some new insights from this work…..
Infective tissues and routes of exposure

- **Brain**
  - emboli in blood
  - contamination of head meat (tongue)
  - Direct consumption
- **Spinal cord**
  - contamination of carcase meat
  - MRM
  - Use in meat products?
- **Dorsal Root Ganglia**
  - bone in meat
  - MRM
- **Tonsil**
  - contamination of tongue
- **Trigeminal Ganglia**
- **Distal Ileum**
Brain Embolism - key assumptions

• Embolism occurs in 4% of slaughters using Captive Bolt stunner
• 1 - 10g of brain tissue enters blood stream
• 1- 10% of emboli pass through lung and are left in muscle meat
• Remainder trapped in heart, lung or remain in blood
Head Meat

- Head meat removed from most carcases
- Significant potential for contamination with brain tissue from stun wound at time of slaughter or during transport to head boner
- Cooper & Bird (2002) made estimates of amounts of brain material recovered with each bovine head (g)

<table>
<thead>
<tr>
<th>Period</th>
<th>Mean</th>
<th>Median</th>
<th>95% Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before November 1980</td>
<td>1.65</td>
<td>1.46</td>
<td>0.38 3.99</td>
</tr>
<tr>
<td>November 1989 - May 1990</td>
<td>1.83</td>
<td>1.50</td>
<td>0.38 5.15</td>
</tr>
<tr>
<td>June 1990 - February 1992</td>
<td>1.32</td>
<td>1.16</td>
<td>0.35 3.10</td>
</tr>
<tr>
<td>February 1992 - March 1996</td>
<td>1.28</td>
<td>1.15</td>
<td>0.35 2.93</td>
</tr>
</tbody>
</table>
Contamination with brain tissue

- About 1.3 g brain tissue (0.3 - 5g) discharged from stun wound and contaminates cheek meat (Cooper & Bird)
- Assume: 10% of this material contaminates the tongue during removal

Contamination with tonsil

- Some tonsillar tissue present on tongues as trimmed for human consumption
- Typical weight of bovine tonsil is 50g
- Infectivity very low
- Assume 10% of infectivity in tonsil remains with tongue
Brain

- LFRA Ruminant Products Audit (1997) found that about 9% of independent butchers sold bovine brain directly for human consumption.
- Estimated that 200,000 brains sold in 1980, reducing to 100,000 in 1989.
- Brains not used in meat products
- Brains not collected from abattoirs handling cull cows
- Likely that brains would only have been collected from prime beef animals (assume 99%)
- If animal reaches late stage infection within 2.5 years relatively high chance (6%) that brain is used
Contamination due to carcass splitting

- 50mg of CNS material transferred to medial carcass surfaces following splitting with band saw
- Assume 1% of this transferred to meat; handling, transfer on cutting surfaces, etc.
- Less chance for contamination in larger abattoirs where meat is cut from the carcase whilst still hanging
Failure of SRM Controls

- 1998-2000 12,000 abattoir inspections; ~ 10 per plant/yr
- These represent about 4% of total animals slaughtered
- 7 unsatisfactory reports – one involving spinal cord
- Failure frequency = 1 in 240,000 (4% of number slaughtered)
- Assume 5% of total spinal cord (~10cm) left
- Assume 10% of infectivity enters food chain
- Potential exposure to infectivity if animal had clinical BSE = 50 bovine oral ID$_{50}$ units
What are Dorsal Root Ganglia?

Swellings in the nerve bundles, close to where they join the spinal cord

Located within the vertebral column

30 pairs @ 0.5g = 30g per carcase

Would not be removed with the spinal cord
DRG in Food

- **Meat Sold off the bone**
  - Limited trials suggest that the DRG would not be removed from the bone during normal deboning (part of 1 DRG removed from 4 carcases deboned - 1 in 240 - 0.4%)
  - For retail butcher assume 1% cut away with the meat

- **Meat Sold on the Bone**
  - Fraction of the DRG consumed will be highly variable
  - 1997 UK study assumed 5% as base case - but no data
  - Model as distribution with 95 percent range from 5% to 95%

- **Cooking**
  - No effect on infectivity
MRM

- MRM produced from up to 20% of carcases (1987)
- Vertebral column would normally be included
  - Potential contamination with DRG and spinal cord
- DRG: assume 90% of remaining DRG extracted into MRM
- Spinal cord: estimated amount (g) per carcase
  (Cooper & Bird, 2002)

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<th>Median</th>
<th>95 % range</th>
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<tr>
<td>Before SBO legislation</td>
<td>3.3g</td>
<td>2.3g</td>
<td>0.2</td>
</tr>
<tr>
<td>After SBO legislation</td>
<td>1.5g</td>
<td>0.6g</td>
<td>0.02</td>
</tr>
</tbody>
</table>
MRM Production

From Cooper & Bird, 2002
Infectivity consumed from one infected bovine – 2001

<table>
<thead>
<tr>
<th></th>
<th>Bovine oral ID50</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
</tr>
<tr>
<td>DRG - proportion sold on bone</td>
<td>24</td>
</tr>
<tr>
<td>DRG - all sold off bone</td>
<td>16</td>
</tr>
<tr>
<td>Brain emboli</td>
<td>0.2</td>
</tr>
<tr>
<td>Carcase contamination - in meat</td>
<td>0.05</td>
</tr>
<tr>
<td>Tongue - contamination with brain</td>
<td>2.4</td>
</tr>
<tr>
<td>Tongue - contamination with tonsil</td>
<td>0.001</td>
</tr>
<tr>
<td>Failure of SRM controls</td>
<td>0.0007</td>
</tr>
<tr>
<td>Total - with some on bone</td>
<td>27</td>
</tr>
<tr>
<td>Total - with all off bone</td>
<td>19</td>
</tr>
</tbody>
</table>
Total Exposure to Infectivity 1980 - 2001

One fully infected bovine slaughtered for food


Log10 Bovine Oraql ID50

Year

SBO regs 1989
MRM ban
Beef on bone ban

95 Percentile range
Contributions to total exposure - Adult Beef

One fully infected bovine
Contributions to total exposure- Prime Beef

One fully infected bovine
Infectious Units Entering Food supply

- Estimates of infectivity from infected animal combined with estimates of numbers of infected animals slaughtered for food (by year and incubation stage)
- Estimates from Imperial College back calculation model (Ferguson & Donnelly, 2003)
- Assumes all animals > 30 months tested
- Base assumption that test 100% sensitive in last 3 months and all differential slaughter also in last 3 months
- Range of sensitivity options considered
Infectious Units Entering Food supply

54 million bovine oral ID50 units entered food supply from 1980 – 2001
>99% from animals older than 30 months

Base case with 3 months test sensitivity
Comparison with vCJD cases

- Estimate 54 million bovine oral ID50 units consumed from 1980 – 2001 (using stated assumptions for infectivity and test effectiveness)
- 122 cases of vCJD confirmed in UK (February 2003)
- Data now indicate a slow down in numbers of cases
- All cases tested (most) are homozygous for methionine at codon 129 of the PrP gene (~40% of population)
- Indicates species barrier for this population is about 4,000 (towards top end of range)
Contribution from Main Sources of Infectivity into food: 1980 - 2001

- Brain: 2.6%
- MRM: 42.3%
- Head meat: 29.8%
- DRG in meat: 24.8%
- Other: 0.5%

Percentage Contribution
# Estimated Exposure from Typical Meals

<table>
<thead>
<tr>
<th>Exposure per meal (Bovine oral ID50 units)</th>
<th>Close to onset</th>
<th>6 months before onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>250g burger with 10% MRM</td>
<td>6</td>
<td>0.8</td>
</tr>
<tr>
<td>250g burger with single DRG</td>
<td>25</td>
<td>3.0</td>
</tr>
<tr>
<td>250g burger with 50% head meat</td>
<td>5</td>
<td>0.6</td>
</tr>
<tr>
<td>250g bovine brain</td>
<td>12,500</td>
<td>1600.0</td>
</tr>
<tr>
<td>250g burger with 10% bovine brain</td>
<td>1,250</td>
<td>160.0</td>
</tr>
</tbody>
</table>
Conclusions

• Current exposure to BSE infectivity is very low
• Replacing OTMR by testing will increase risk, but additional exposure is negligible
• Total exposure to UK population (base case assumptions) estimated to be 54 million bovine ID50s
• Indicates very high species barrier
• MRM main contributor in total, but exposure very dispersed
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