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# *Scrapie – an overview; policy issues and potential eradication measures*

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# Objectives

- Current concerns relating to scrapie in sheep (not goats)
- The difficult choices for governments and the European Commission
- Limited options
- Where next - forward or backward?

# The dilemma

Why now? After all, scrapie has been recognised for 250 years.

# What if it is BSE and not scrapie?

- Can we discriminate between BSE and scrapie?
- Can we protect consumers in the meantime – “the precautionary principle rules”?
- Can we actually eradicate if we need to – all previous attempts have struggled?

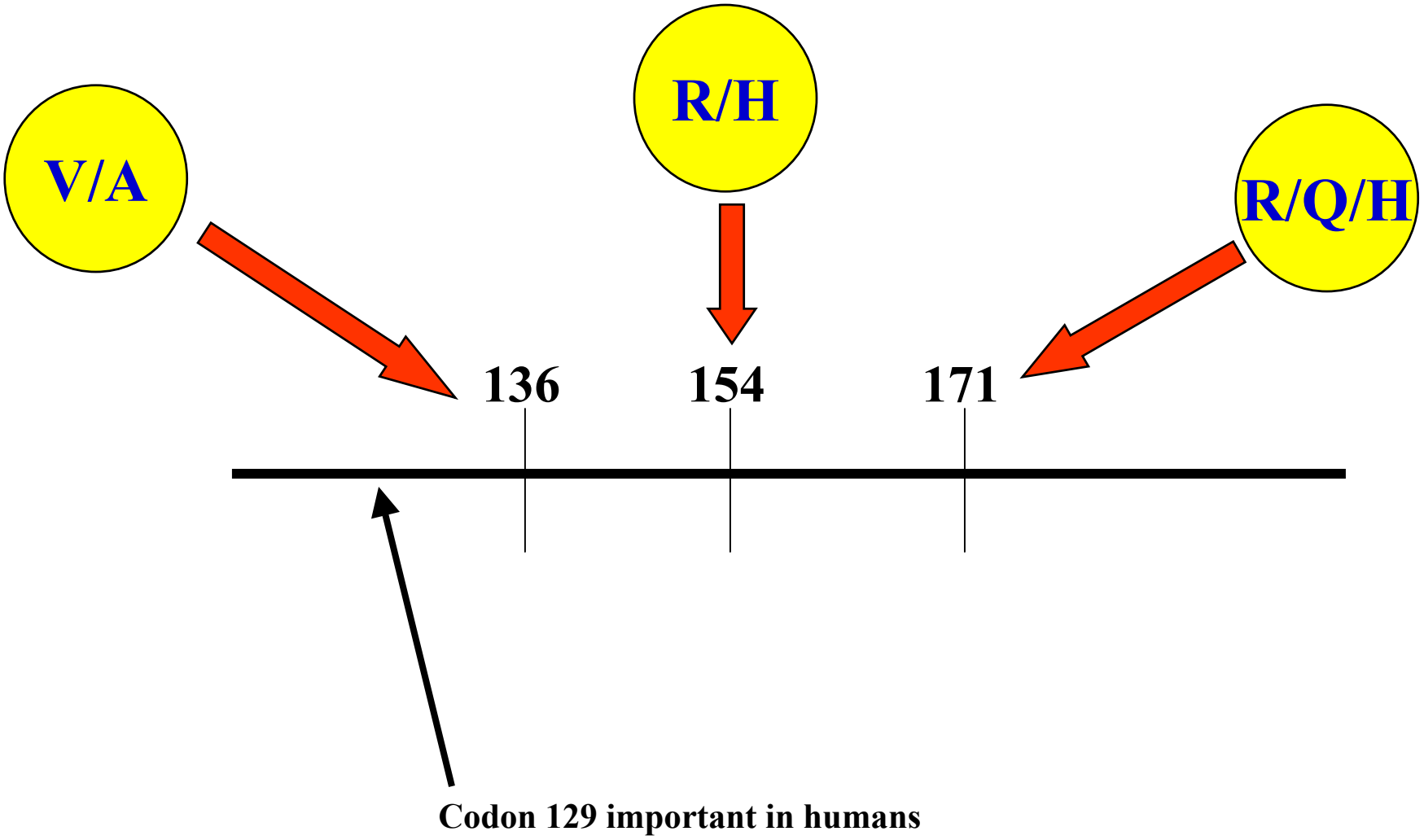
# Scrapie, prions and genes

- Long standing appreciation of an interplay between scrapie in sheep and inheritance
- Scrapie was in fact thought to be a genetic disease, especially in studies carried out by Parry in the Suffolk breed in the United Kingdom
- BUT there was also evidence of transmissibility
- Generally recognised now as one of the prion diseases – BSE, CJD, vCJD, CWD etc.

# Prions and genes

- Studies in sheep and mice gradually indicated:_
  - Not a genetic disease in sheep
  - Genetic influence on susceptibility however – one or more genes
- PrP (protease resistant protein) gene, or *PRNP* identified as major, but possibly not sole, influence

# The sheep PrP gene



# Polymorphisms in sheep

- Codon 171 is critical – no clinically affected scrapie sheep in world literature with RR at codon 171 (with one exception)
- If QQ present at codon 171, or QR, then other codons come into play in determining whether a sheep will become infected with scrapie (or BSE)
- But the response varies with breed, and with strain of scrapie

# PrP Genotype of clinical cases

**> 85% of cases occur in 3 genotypes**

| Genotype | 2002 | | 2003 | | |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Unknown | 80 | 19.85% | 17 | 4.47% | |
| AHQ/AHQ | 0 | 0.00% | 1 | 0.28% | |
| AHQ/ARQ | 7 | 2.17% | 7 | 1.93% | |
| AHQ/VRQ | 1 | 0.31% | 0 | 0.00% | |
| ARH/ARH | 2 | 0.62% | 7 | 1.93% | |
| ARH/VRQ | 18 | 5.57% | 14 | 3.86% | |
| ARQ/ARH | 3 | 0.93% | 4 | 1.10% | |
| ARQ/ARQ | 84 | 26.01% | 93 | 25.62% | ← |
| ARQ/VRQ | 139 | 43.03% | 169 | 46.56% | ← |
| ARR/ARQ | 1 | 0.31% | 1 | 0.28% | |
| ARR/VRQ | 12 | 3.72% | 12 | 3.31% | |
| VRQ/VRQ | 56 | 17.34% | 55 | 15.15% | ← |
| Total general | 403 | | 380 | | |

# Possible precautionary approaches

- Remove high risk tissues – brain, spinal cord, spleen (specified risk materials)
- Improve live animal diagnostics to enable detection and eradication – works best in fully susceptible genotype, but there is no universally susceptible genotype
- Breed for resistance to TSEs (BSE and scrapie)

# Caveats

- Mechanisms of resistance not clear
- Total resistance to infection or is there a carrier state?
- Partial resistance, in the form of longer incubation period
- Influence on tissue distribution of infectivity
- Breed/strain differences - ARQ Suffolks vs Cheviot VRQ
- RR171 is the only route to resistance that appeared to be universal

# Conclusion

- Introduce limited SRM controls until such time as BSE is found in sheep – considered proportionate
- Take statutory action following diagnosis of scrapie
- Then breed for resistance – addressing all TSEs at once

# National scrapie plan PrP genotypes

| Genotype | NSP type | Susceptible/resistant |
|---|---|---|
| ARR/ARR | 1 | most resistant |
| ARR/ARQ | 2 | resistant |
| ARR/AHQ | | |
| ARR/ARH | | |
| ARQ/ARQ | 3 | little resistance |
| ARQ/AHQ | | |
| ARQ/ARH | | |
| AHQ/AHQ | | |
| AHQ/ARH | | |
| ARH/ARH | | |
| ARR/VRQ | 4 | susceptible |
| ARQ/VRQ | 5 | highly susceptible |
| AHQ/VRQ | | |
| ARH/VRQ | | |
| VRQ/VRQ | | |

**UK data only**

# Key approaches to increasing resistance

- Reduce the frequency of susceptible, VRQ allele – EU minimum
- Increase the frequency of most resistant allele – ARR – basis of NSP
- Speed up by using resistant ewes too
- Cull affected flocks and restock with resistant, or selectively cull by genotype
- Rate of change dependent on breed frequencies

# PrP allele frequencies (%) in some purebred breeds

| Category | Breed | ARR | ARQ | ARH | AHQ | VRQ |
|---|---|---|---|---|---|---|
| | Scottish blackface | 31.1 | 58.9 | <0.1 | 7.6 | 2.4 |
| Hill breeds | Swaledale | 42.2 | 35.5 | <01 | 17.3 | 5 |
| | Welsh Mountain | 38.5 | 33.9 | 0.1 | 21.7 | 5.8 |
| | North Country Cheviot | 45.4 | 36.4 | 0.2 | 11.7 | 6.3 |
| Longwool | Bluefaced Leicester | 62.6 | 20.6 | <0.1 | 16.5 | 0.3 |
| | Border Leicester | 76.1 | 15.4 | <0.1 | 0.4 | 8.1 |
| | Suffolk | 76.5 | 22.1 | 1.1 | <0.1 | 0.3 |
| Terminal sire | Texel | 38.1 | 14.3 | 40.7 | 3.8 | 3.1 |
| | Charollais | 62 | 33.8 | 0.2 | 0.1 | 3.9 |

Data courtesy of Simon Gubbins, Institute for Animal Health and Janet Roden, University of Wales.

# Industry concerns

- Could breeding for resistance have other deleterious side effects?
- Anecdotal evidence in some flocks where it had been tried suggested not, but that scrapie was controlled quickly
- Research put in place to test side-effects of raising frequency of ARR allele

# Industry concerns

- Research into pedigree and commercial flocks – range of breeds, hill, lowland, longwool, terminal sires
- Measuring lamb growth, fat and muscle depth, survivability of lambs, maternal performance (milk/lambs)
- In the meantime also archive semen from rare breeds and susceptible rams

# And then came – active surveillance –

- One test in particular, Biorad TeSeE ELISA, identified cases that could not be confirmed by traditional methods
- Referred to frequently as “atypical scrapie” – of which Nor98 was the first to be described, but until then thought to be confined to Norway
- Clearly present throughout EU, and unlikely to have been detected before due to apparent absence of overt clinical disease

# Outcome of active surveillance in UK

| Year | Typical | Atypical |
|---|---|---|
| 2002 | 17 | 18 |
| 2003 | 43 | 52 |
| 2004 | 21 | 17 |
| 2005 | 3 | 4 |
| Total | 84 | 91 |

Note that clinical cases are excluded, and that the population sampled changed from year to year.

Data to 28 April 2005

# Genotype distribution first 91 atypical cases

| Genotype | Number* |
|---|---|
| ARR/ARR | 15 |
| AHQ/ARQ | 19 |
| ARR/AHQ | 19 |
| AHQ/AHQ | 12 |
| ARR/ARQ | 12 |
| ARQ/ARQ | 11 |
| ARR/ARH | 1 |
| ARQ/VRQ | 1 |
| AHQ/ARH | 1 |

As at 28 April 2005

# Where now with breeding programmes?

- Now shown to be transmissible to mice, at least in France
- Evidence suggests that they have always been present, undetected
- But may still represent a dead end and won't transmit to other sheep
- Pathogenesis still unknown

# Where now with breeding programmes?

- Carry on for now
- Atypicals and BSE are not identical – so ARR still protective for BSE
- Lower mortality due to scrapie also results in economic benefit to individual farmers

# No ewe turns yet

- Likely factors that might prompt a return to past practice would include:-
  - Proving the absence of BSE in the current small ruminant population
  - Or a recognition that residual risk is manageable at minimum cost
  - Or evidence that breeding for ARR does have serious deleterious effects.
- History will determine if policy will be applauded or criticised