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# Studying the seasonality of scrapie transmission in an experimental flock

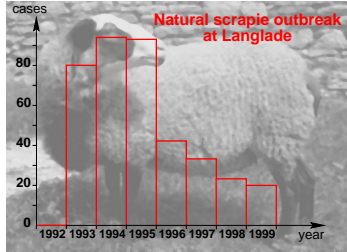
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## I. INTRODUCTION/OBJECTIVES

Presence of scrapie prions in the placenta suggests the possibility of **increased transmission during lambings**, an hypothesis we explore with a mathematical model focused on the disease transmission. The initial model was developed by Woolhouse's group [1] for several outbreaks in British sheep (e.g. [2]). We apply it here to the Langlade experimental flock in which a natural scrapie outbreak started in 1993 [3].

## II. METHODS



### II.1. DATA

- Experimental flock, INRA Toulouse; created 1971, closed 1979-96.
- Mostly Romanov breed (prolificity: 1-6, mean 3.1), size ca. 900.
- ➔ **Study flock:** Romanov, > 8 months, cohorts 83-95.

**Data available:** birth & death/removal, pedigree, scrapie histopathological diagnosis, PrP genotypes (10 from 4 alleles: VRQ, ARQ, AHQ, ARR).

### II.2. MODEL

**Dynamic system:** time  $t \geq 0$ , age  $0 \leq a \leq \Lambda$ , infection load  $0 \leq \theta \leq 1$ .

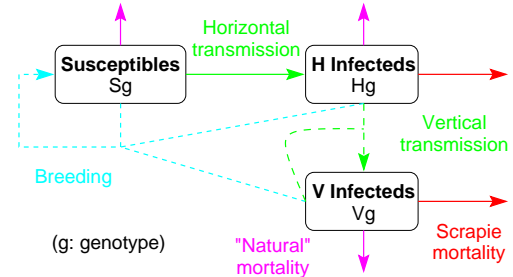
**Seasonal birth:** rate  $b(t, a') = b(t)$  if dam  $a'$  mature, = control / flock size  $\approx$  constant; + genetics: random mating  $G_{gg'}$ (t).

**Natural mortality:** truncated Weibull  $\mu(a)$ ,  $a < \Lambda$  (survival).

**Horizontal transmission  $g' \rightarrow g$ :** rate  $\beta_{gg'}(t, \theta') = k_h \sigma_g \theta' s(t)$ , genetic susceptibility  $\sigma_g$ , infectiousness  $\propto \theta'$ , season  $s(t)$ ; + variable initial load  $\theta_0$ : gamma distribution  $\Theta$ .

**Vertical transmission  $g' \rightarrow g$ :** rate  $\gamma_{gg'}(t, \theta') = k_v \sigma_g \theta'$ .

**Scrapie:** during incubation  $\frac{d\theta}{dt} = c_g \theta \rightarrow \theta = 1$ : clinical signs & death.



$$\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial a}\right) S_g(t, a) = -S_g \sum_{g'} \int_0^1 \beta_{gg'} [H_{g'} + V_{g'}] d\theta' da' - \mu S_g$$

$$S_g(t, 0) = \sum_{g'} G_{gg'} \int b \left( S_{g'} + \int (1 - \gamma_{gg'}) [H_{g'} + V_{g'}] d\theta' \right) da'$$

$$\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial a} + \frac{\partial c_g \theta}{\partial \theta}\right) H_g = \Theta S_g \sum_{g'} \int \beta_{gg'} [H_{g'} + V_{g'}] d\theta' da' - \mu H_g$$

$$H_g(t, 0, \theta) = 0 \quad H_g(t, a, 0) = 0$$

$$\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial a} + \frac{\partial c_g \theta}{\partial \theta}\right) V_g(t, a, \theta) = -\mu V_g$$

$$V_g(t, 0, \theta) = \Theta \sum_{g'} G_{gg'} \int \gamma_{gg'} [H_{g'} + V_{g'}] d\theta' da' \quad V_g(t, a, 0) = 0$$

## III. RESULTS

Outbreak simulation

### 1. Parameters

**From data:** lambing/transmission season, random mating  $G_{gg'}$ , natural mortality  $\mu$ , genetic susceptibility  $\sigma_g$  (VRQ-VRQ=0.78, VRQ-ARQ=0.57, ARQ-ARQ=0.48).

**Fitted:** transmission  $k_h, k_v$  and incubation  $\Theta, c_g$  (mean = 2 yrs).

**Outputs:** **incidence** = scrapie case distribution **with** seasonal transmission (= during lambings) or **without**; **prevalence** = proportion of infecteds **with** seasonal transmission.

### 2. Initial condition

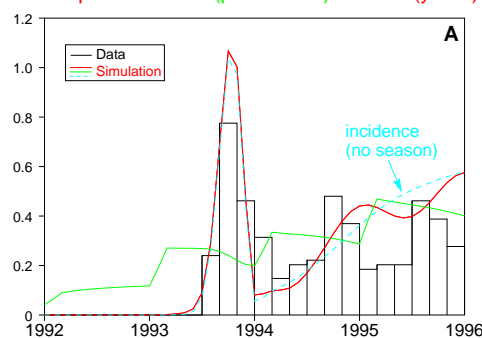
**From data:** susceptibles  $S_g(0, a)$  + scrapie infecteds  $H_g(0, a, \theta)$  from experimental\* batch, born end 1991 and 1st showing signs.

➔ **Horizon:** 1992-96 (same breeding practices).

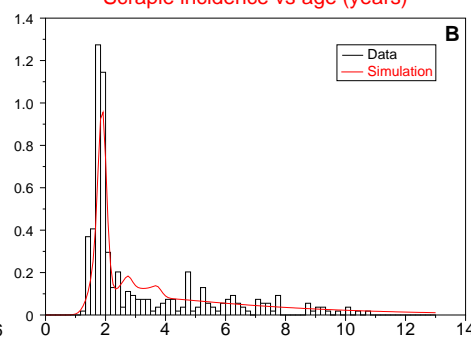
\* Experiment: genetic susceptibility to *Teladorsagia*, cf. [3].

### 3. Numerical method: Lax-Wendroff; Fortran code.

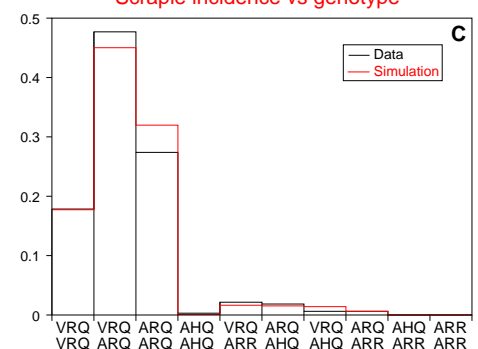
Scrapie incidence (prevalence) vs time (years)



Scrapie incidence vs age (years)



Scrapie incidence vs genotype



## IV. DISCUSSION

**A.** Oscillations appear with seasonal transmission, closer to data. 1st peak from initial condition.

**B.** No age dependent susceptibility implemented, still peak around 2 years because of exposure.

**B&C.** Both case distributions quite in accordance with the data.

## V. CONCLUSIONS

The seasonal transmission hypothesis seems consistent with the patterns we observe with our model.

**Further work:** • better fit for transmission;

• vertical → perinatal transmission.

### REFERENCES

- [1] Stringer et al. 1998, Math. Biosci. 153(2):79-98.  
[2] Matthews et al. 2001, Arch. Virol. 146(6):1173-1186.  
[3] Elsen et al. 1999, Arch. Virol. 155(3):431-445.

