Studying the seasonality of scrapie transmission in an experimental flock

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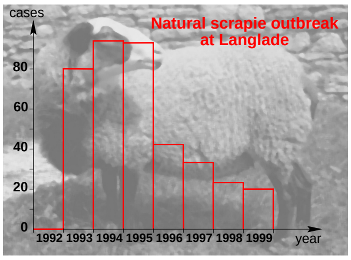
I. Introduction/Objectives

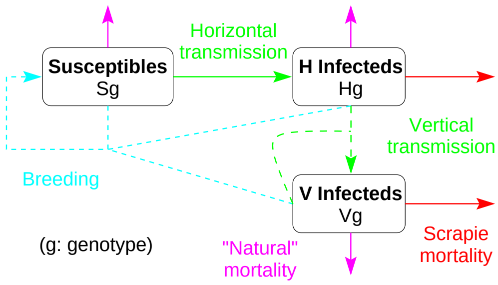
Presence of scrapie prions in the placenta suggests the possibility of ***increased transmission during lambings***, an hypothesis we explore with a mathematical model focused on the disease transmission. The initial model was developed by Woolhouse's group **[1]** for several outbreaks in British sheep (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** $t \geqslant 0$, **age** $0 \leqslant a \leqslant A$, **infection load** $0 \leqslant \theta \leqslant 1$.

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

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

Horizontal transmission $g' \to g$: rate $\beta_{gg'}(t,\theta') = k_h \sigma_g\, \theta' s(t)$,
genetic susceptibility σ_g, infectiousness $\propto \theta'$, season $s(t)$;
+ variable initial load θ_0: gamma distribution Θ.

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

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

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

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

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

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

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

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

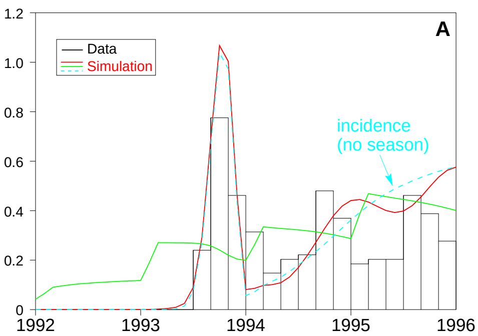
III. Results

Outbreak simulation

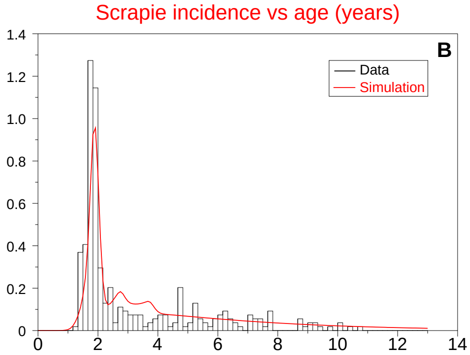
1. **Parameters**
   From data: lambing/transmission season, random mating $G_{gg'}$, natural mortality μ, genetic susceptibility σ_g (VRQ-VRQ=0.78, VRQ-ARQ=0.57, ARQ-ARQ=0.48).
   Fitted: transmission k_h, k_v and incubation Θ, c_g (mean = 2 yrs).
2. **Initial condition**
   From data: susceptibles $S_g(0,a)$ + 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.

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

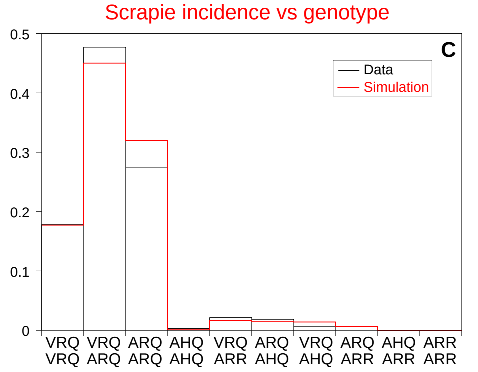
Scrapie incidence (prevalence) vs time (years)



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.

INRA