Studying the seasonality of scrapie transmission in an experimental flock

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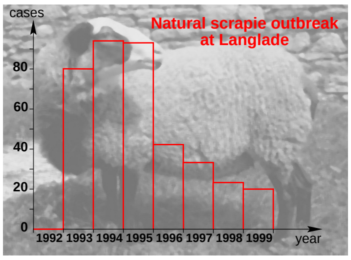
I. Introduction/Objectives

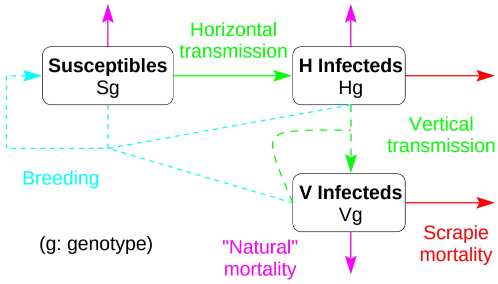
Presence of scrapie prions in the placenta suggests the possibility of ***increased transmission during lambings***, an hypothesis we explore with a mathematical model focused on the disease transmission. The initial model was developed by Woolhouse's group **[1]** for several outbreaks in British sheep (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.

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

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

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

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

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

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

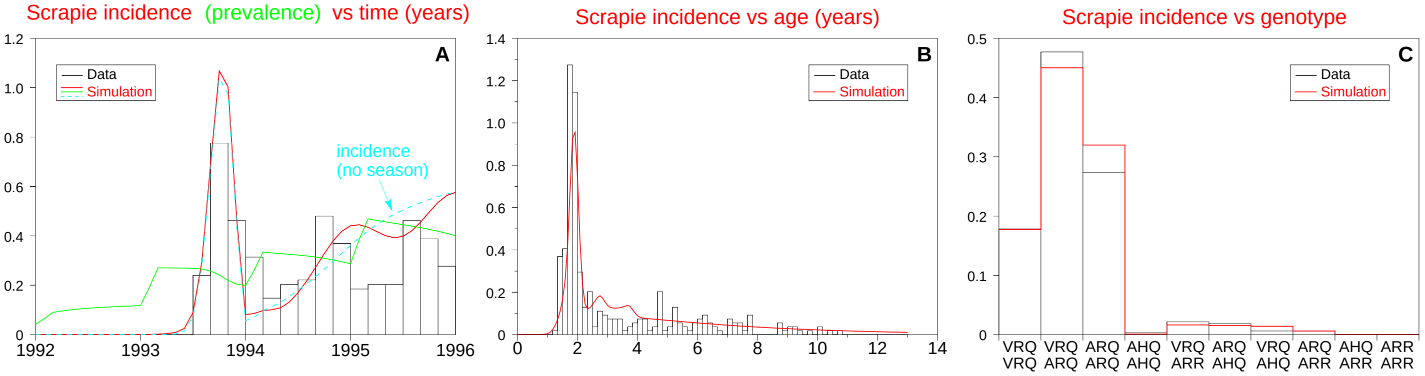
III. Results

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.