Regulatory mechanisms in the host-parasite relationship of human onchocerciasis in West Africa

18.12.2003
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Schedule

1. Intro
   • Biology and transmission cycle of onchocerciasis

2. Summary of previous work:
   • Formation of onchocercomata (nodules)
   • Parasite establishment in immunosuppressed hosts

3. Regulatory mechanisms within the human host
   • How many L3 manage to develop into an adult worm?
   • How many microfilariae are produced by adult worms?

4. Conclusions and further work
Transmission cycle of *O. volvulus*
Annual Transmission Potential: number of infectious larvae (L3) a human host is potentially exposed to per year
Four steps between \textit{IN} and \textit{OUT}

1. How many L3 are released from a fly during a bloodmeal?

2. How many L3 manage to develop into an adult worm?

3. How many microfilariae are produced by adult worms?

4. How many Mf are ingested by a fly during a bloodmeal?
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Formation of onchocercomata (nodules)

- $N=1$: The number of nodules follows a binomial distribution $p \times q$

- $N=2$: $p^3$, $3 \times p^2q$, $2 \times pq^2$, $pq^2$

- $N=3$: $q^3$

$p$: probability that the larva forms a new nodule

$q$: probability that the larva enters an existing nodule

→ The number of nodules follows a binomial distribution
Formation of onchocercal nodules

Assume that $q$ varies between hosts ($q \sim \text{beta} (\alpha, \beta)$):

Observations can be fitted by a beta-binomial distribution.
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Parasite establishment in immunosuppressed hosts

Immunity against infectious larvae (concomitant immunity)

Immunosuppression by adult parasites or microfilariae
Parasite establishment in immunosuppressed hosts

Problem:

- Nodulectomy data are rare
- How does parasite establishment depend on the ATP?
- Estimates refer to the number of parasites found by nodulectomy

To try:

- Estimate parasite establishment from palpation data which have been collected more frequently
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How many L3 manage to develop into an adult worm?

Establishment rate \( \lambda_{\text{True}} \)

\[ \frac{\text{Worms}}{\text{year}} \]

Worms

\[ W_{\text{True}} \]

Nodules

\[ K_{\text{True}} \]

\[ K_{\text{OP}} \]

\[ K_{\text{Palp}} \]

\[ = \text{Data} \]

\[ \sim \text{Binomial} (W_{\text{OP}} \mid W_{\text{True}}, 0.5) \]

\[ \sim \text{Binomial} (K_{\text{OP}} \mid K_{\text{True}}, 0.5) \]

\[ \sim \text{Binomial} (K_{\text{Palp}} \mid K_{\text{OP}}, 0.6) \]

\[ \sim \text{betaBinomial} (K_{\text{OP}} \mid W_{\text{OP}}, \alpha, \beta) \]

Data found by surgery

Data found by palpation

Simulation

Estimation

Data found by surgery situation

known

backcalculated

assumed

simulated
of 4 villages in Liberia

Palpation data and fits

Estimated establishment functions
Palpation data of 7 villages in the area of OCP

Estimated establishment functions:
Establishment function

ATP dependence of $\lambda_{\text{min}}$

Estimates

Liberia

OCP villages
The probability that an infectious larva develops into an adult worm

\[ P(L3 \rightarrow \text{adult worm}) \]

Dietz (1982)

Plaisier (1996)

regulation

no regulation

regulation
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The relationship between the number of adult worms and the microfilarial density

In the savannah and the forest data, the microfilarial density increases with the age of the human host.

Density-dependent in savannah data (Burkina Faso)

Almost linear in forest data (Liberia)

immunological tolerance rather than protective immunity
The probability that an L3 develops into an adult worm may decline with the ATP, pointing at regulatory process.

The microfilarial density depends on the burden of adult worms in the savannah but not in the forest data.
Summary

Empirical evidence has shown that the eradicability of onchocerciasis may be far more difficult as assumed.

As stated at the Conference on the eradicability of Onchocerciasis (January 2002), the model predictions of onchosim have been too optimistic and, therefore, it is recommended to recalibrate this model (or develop new ones).

The regulatory processes in the human are rudimentarily investigated.

Density-dependent microfilarial densities may be one of the reasons for overoptimistic predictions of onchosim (which assumes linearity).

The probability that a L3 develops into an adult parasite is still not known. Due to the relevance of this parameter, it must be asked: How reliably can we predict control programmes in the current state of knowledge?
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