A quantitative approach to the eradicability of onchocerciasis

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Schedule

• Filarial diseases & control programs
• Theoretical basis of persistence and eradicability: Transmission thresholds & breakpoints
• Density-dependent processes: Limitation & Facilitation
• The persistence graph
• How density-dependent processes influence the eradicability of an infection
• Quantitative considerations
• Conclusions
Introduction

Onchocerciasis: Vector control until 2002, successor program: mass drug administration of ivermectin

1975

Onchocerciasis Control Programme

African Programme for Onchocerciasis Control (APOCH)

2000

Global Program to Eliminate lymphatic filariasis (GPELF)

Lymphatic filariasis: Elimination intended by mass drug administration of ivermectin / DEC ...
Life-cycle of *Onchocerca volvulus*

- Adult parasite
- Vector
- Larvae

- L1
- L2
- L3
- L4

ATP (Annual Transmission Potential)

Definite host

Microfilariae
Density-dependent regulation in a host-parasite relationship

- **Facilitation** (positive feedback)
- **Limitation** (negative feedback)
- **No regulation**

No. of parasites in the vector: $n_4$

No. of parasites in the human host: $n_2$

Number of parasites of stage $x$: $n_x$

$n_{x+i}$
Comparing processes of density-dependent regulation

Common equilibrium parasite burden

No. of parasites in the human host

No. of parasites in the vector

$n_1$, $n_2$, $n_3$, $n_4$, $n_5$, $n_6$
### Equilibrium under limitation

<table>
<thead>
<tr>
<th>No. of parasites in the vector</th>
<th>No. of parasites in the human host</th>
</tr>
</thead>
<tbody>
<tr>
<td>$v$</td>
<td>$h(v)$</td>
</tr>
<tr>
<td>$v(h)$</td>
<td>$h(v)$</td>
</tr>
</tbody>
</table>

- **Equilibrium parasite density**: 
  - **Unstable zero**: 
  - Equilibrium parasite density

![Diagram showing the equilibrium under limitation](image-url)
Basics of persistence and eradicability

Transmission thresholds
... refer to a vector density below which the infection cannot persist

Threshold Biting Rate (TBR):
"If there are too few vector-host contacts, then, a parasite in the human host will die before the next one can establish"

Parasite burden

Force of infection
Equilibria under facilitation

- **h**: No. of parasites in the human host
- **v**: No. of parasites in the vector

Graphs showing:
- Stable equilibrium
- Unstable equilibrium
- Stable zero
Mating probability of dioecious parasites

\[ P(2\text{sex}) = 1 - P(\text{only male worms}) - P(\text{only female worms}) \]
\[ = 1 - 0.5^{\text{males}} - 0.5^{\text{females}} \]  \( // \) males == females = W
\[ = 1 - 0.5^{W-1} \]

\[ W \sim \text{NBD}(\bar{w}, k) : \]
\[ \phi(\bar{w}) = \sum_{W=1}^{\infty} \left(1 - 0.5^{W-1}\right) \bullet \text{NBD}(\bar{w}, k) \]
\[ = 1 + \left(\frac{k}{k + \bar{w}}\right)^k - 2^{k+1}\left(\frac{k}{2k + \bar{w}}\right)^k \]

Basics of persistence and eradicability

Transmission thresholds
... refer to a vector density below which the infection cannot persist

Threshold Biting Rate (TBR):
"If there are too few vector-host contacts, then, a parasite in the human host will die before the next one can establish"

Breakpoints
... refer to a parasite density below which the infection cannot persist

Mating process:
"If there are too few parasites in a host, then, mating is not possible and reproduction cannot occur"
Persistence graph of a filarial infection

- **Parasite density [parasites/host]**
- **Annual Biting Rate (ABR) [bloodmeals/year · host]**

The graph illustrates the persistence of a filarial infection based on the annual biting rate (ABR).

1. **Infection cannot persist**: The green area indicates conditions where the infection does not persist, and elimination is possible.
2. **Infection can persist, elimination is possible**: The blue area represents scenarios where infection can persist, but elimination is still feasible.
3. **Infection persists, elimination is difficult**: The red area shows situations where infection persists, making elimination challenging.

Points C1 and C2 on the graph indicate specific infection levels and biting rates that determine the persistence or elimination of the infection.
Model
(filarial parasites)

Acquisition & survival of adult parasites:
\[
\frac{dw}{dt} = \lambda(w, ATP) - (\sigma_w + \mu)w
\]
- Acquisition rate
- Mortality of adult worms + humans

Production & survival of microfilariae:
\[
\frac{dm}{dt} = \varphi(w) \beta(w) - (\sigma_m + \mu)m
\]
- Mating probability
- Rate of microfilarial production
- Mortality of adult worms + humans

Larval development in flies (assumed to be at equilibrium):
\[
l(m) = c_1 m / (1 + c_2 m)
\]

Annual Transmission Potential:
\[
ATP = \varepsilon ABR \cdot l/l^*
\]
- Annual Biting Rate
- Adjustment to provide comparable equilibriae
Density-dependent processes: Limitation & Facilitation

(a) "How many adult parasites result from a certain number of L3 transmitted?"

(b) "How many microfilariae in the skin result from adult female parasites?"

(c) "How many L3 per fly result from microfilariae ingested during a bloodmeal?"
Density-dependent processes modifying eradicability

Facilitation "facilitates" the eradicability of an infection, whereas limitation "limits" the prospects of eradication.
Eradicability & re-crudescence

Onchocerciasis: Vectorcontrol until 2002, successor program: mass drug administration of ivermectin

1975 2000

Onchocerciasis Control Programme
African Programme for Onchocerciasis Control (APOC)

Graph: Adult female parasites per host vs. ABR
Assumptions

concerning the degree of limitation with respect to the ATP

have most probably been over-optimistic
ABR - ATP relationship

62 pre-control villages from 9 OCP-countries: \( ATP \approx 0.02 \ ABR \)

Transmission threshold?
Conclusions

- The eradicability of a filarial infection is to a large extent determined by density-dependent processes.

- Facilitation processes "facilitate" the elimination of a parasite, whereas limitation processes "limit" the prospects of its elimination.

- Predictions of the success of intervention programs will be over-optimistic
  - if the degree of facilitation is overestimated or
  - if the degree of limitation is underestimated
... and vice versa.

- Former predictions most probably have been over-optimistic because the degree of limitation with respect to the ATP has been underestimated

- Outlook: further development/calibration of a deterministic transmission model
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