Malaria

James Holland Jones
Department of Anthropology
Stanford University

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Global Burden of Malaria

- 300-500 million worldwide cases of acute malaria annually (see UN Millenium Project Report on Malaria)
- 1.1-2.7 million deaths annually, mostly to children < 5
- Sub-Saharan Africa carries 90% of the world’s malaria burden
- 20% of childhood deaths in Africa attributable to malaria
- Malaria slows economic growth in Africa by 1.3% (Gallup & Sachs 2001)
- Malaria hyperendemicity has cascading economic effects (Sachs & Malaney 2002)
The Malaria Vector

- $\sim 430$ *Anopheles* species
- $\sim 70$ malaria vectors
- 40 of major medical importance

- 3200 species of mosquito worldwide, belonging to 42 genera
- Only one genus, *Anopheles*, transmits human malaria
- *Anopheles* can transmit some arboviruses and filariasis, but these are more commonly transmitted by culicine mosquitoes
- *Anopheles* belongs to the subfamily *Anophelinae*, family *Culicidae*, order *Diptera*
Engorged *Anopheles* Mosquito
Primate Malarials

- *P. falciparum* sister to *P. reichenowi*, a malaria of chimpanzees

- This split corresponds with the human-chimp split

- *P. vivax* sister to *P. cynomolgi*, a malaria of SE Asian monkeys
\textit{P. vivax} Arose in SE Asia

- Despite earlier suggestions that \textit{P. vivax} has African origin, evidence suggests otherwise

- \textit{P. vivax} is sister group to \textit{P. cynomolgi}

- Phylogeny indicates the \textit{P. vivax} originated from a Plasmodium species related to species currently infecting SE Asian macaques

- \textit{P. vivax} diverged 45-81 Kya

\small{Cornejo & Escalante 2006; Escalante et al. 2005}
Haplotype Network for *P. vivax*

- Highest haplotype diversity in Asia
- Most frequent haplotypes in Asia
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• ∴ Malaria has spilled-over from a primate host multiple times
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- Otherwise, there is essentially no genetic diversity (e.g., there are virtually no synonymous substitutions)
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- A way to reconcile these results is that while *P. falciparum* rapidly expanded 6,000 years ago in Africa, other regional populations are more like 50-100 years old.
- This is precisely what Joy et al. (2003) find evidence for.
Conditions for an Epidemic
Figure 47.—DDT residual spraying in native quarters, using spray gun with power spray, vicinity of Ledo, Assam.
Malaria Control:
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• Treat Symptoms
Malaria Transmission Cycle

from Smith et al. (2007)
Vecotrial capacity ($C$) is a measure frequently used in malaria epidemiology.

It is very similar to $R_0$ in the sense that it assumes a completely susceptible human population.

Where it differs is that it does not consider transmissibility of the *Plasmodium*

$C$ measures the potential of an environment for malaria transmission neglecting both the state of the hosts and the transmissibility.
The Components of $C$

$C$ is the product of three quantities:

1. the emergence rate of mosquitoes per human per day
2. the squared number of mosquito bites on humans after mosquitoes become infectious
3. the probability of a mosquito surviving the *Plasmodium* incubation period

$$C \propto (\text{Emergence Rate}) \cdot (\text{Number of Bites})^2 \cdot (\text{Mosquito Survival})$$
Define the following quantities:

- $a$: Expected number of bites on humans per mosquito
- $m$: Equilibrium mosquito density per human
- $n$: Length of incubation period
- $p$: Daily survival probability of mosquitoes ($= e^{-g}$)

Vectorial capacity is then

$$C = mg \left( \frac{a}{g} \right)^2 e^{-gn} = \frac{ma^2 p^n}{-\log(p)}$$
Implications for Malaria Control

• Reducing adult mosquito survival ($p$) has the largest effect on $C$
• Reducing the biting rate ($a$) also has a strong effect, but it is considerably more shallow than reducing $p$
• This means that residual spraying (e.g., with DDT) will have a greater impact on outbreak control than employing bednets
Estimating $R_0$ From Data

- $R_0$ is difficult to estimate because some of the parameters are difficult to measure.
- It is much more common to find measurements of $C$ or $E$, the entomological inoculation rate.
- Fortunately, we can measure $R_0$ from the entomological inoculation rate.
The Entomological Inoculation Rate, $E$

- The Entomological Inoculation Rate, $E$ is the average number of infectious bites a person receives in a year.
- It is commonly measured.
- It is the product of three things:
  1. The human feeding rate $a$.
  2. The number of mosquitoes per person $m$.
  3. The sporozoite rate $Y$ (the fraction of mosquitoes that are infectious).

- At equilibrium, vectorial capacity ($C$) is related to $E$ by the following relationship:

$$C = \frac{E(1 + cSX)}{cX}$$

(1)

where $S = a/g$ is the expected number of bites a mosquito makes over its life (“the stability index”).
The formula for $R_0$ is:

$$R_0 = \frac{bc}{r}C \quad (2)$$

- Note the resemblance to the general formula for $R_0$
- It is the product of
  1. Transmissibility, $bc$, where transmissibility has two components: humans $\rightarrow$ mosquitoes and mosquitoes $\rightarrow$ humans
  2. The duration of infectiousness $1/r$
  3. The contact rate between infectious and susceptible individuals, $C$
Multi-Species Epidemic:

Complementary?
Or Inhibitory?

Exclusion

Persistence

$S_2$

$S_1$

$N_1$
Malaria Virulence Evolution

- *Plasmodium falciparum* only infects humans
- Yet we know that it once infected multiple species
- *P. falciparum* is also extremely virulent
- Is there a relationship between host species richness and the evolution of virulence?
- The simple answer is: yes
- The complicated answer is: it’s complicated
Evolution of Virulence in Multi-Host Infections

How Can Species Richness Decrease Epidemic Potential?

from Keesing, Holt & Ostfeld (2006)
Evolving Virulence: Conceptual Model I

Transmission Efficiency

\[ \mu \]

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Evolving Virulence: Conceptual Model II

Transmission Efficiency

$\beta(x^*)$

$\mu$

$\delta(x^*)$

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Evolution of Virulence in Multi-Host Infections

Evolving Virulence: Conceptual Model II

This increases virulence

Reduction in Species Richness Decreases Transmission Efficiency

\( \beta (x^*) \)

\( \beta (x^{**}) \)

\[ \mu \]

\[ \delta (x^*) \quad \delta (x^{**}) \]

Mortality

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