Creation of a mathematical visceral leishmaniasis model

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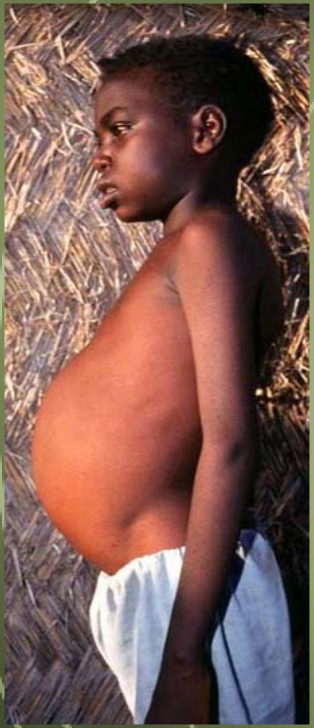


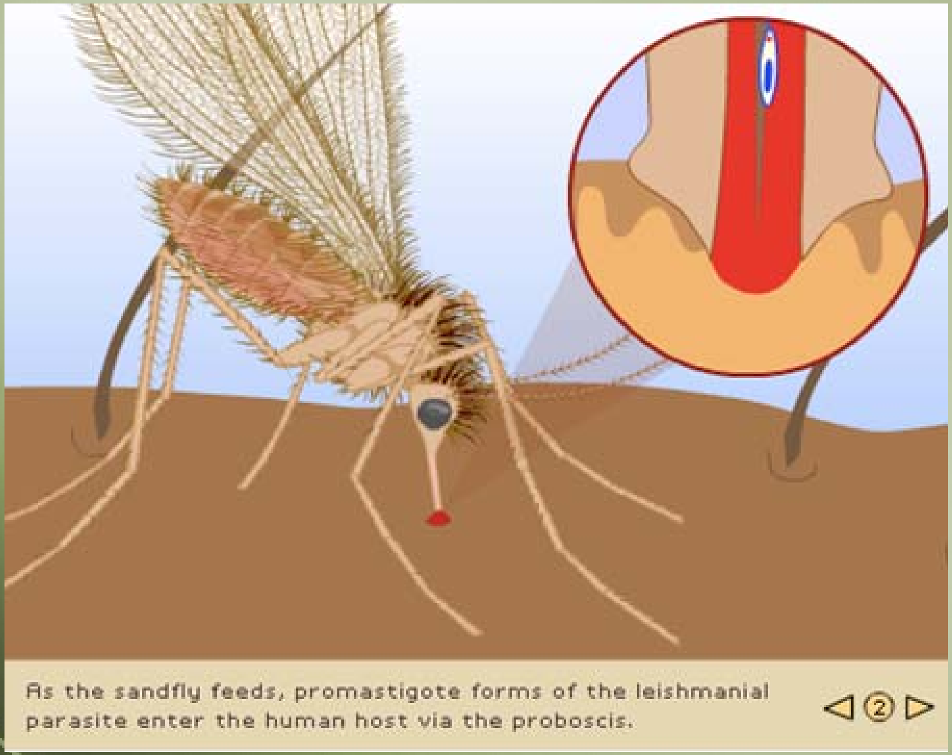
Background

- Leishmaniasis is caused by protozoa of the genus *Leishmania*.
- Transmission to humans and various animals occurs via phlebotomine sand fly bites.
- Infection by visceral leishmaniasis can result in weight-loss, fever, enlarged spleen and liver, and death if left untreated.
- The onset of the disease occurs in a matter of months.

Background Continued

- Currently visceral leishmaniasis is present in Europe, the Middle East, the Far East, Africa and Central and South America (WHO, 2008).
- The common vector of visceral leishmaniasis in Brazil is the sand fly *Lutzomyia longipalpis*.
- Domestic dogs are the main reservoir of *L. infantum* in many areas, including Brazil (Lainson & Rangel, 2005).

Life Cycle of Leishmania Video



(WHO, 2004)

Mathematical Model

- A mathematical model was developed to demonstrate how interactions between **sand flies, humans, and dogs** influence susceptible, infected, and removed populations and the basic reproduction ratios.
- Certain assumptions had to be made to make the model as biologically accurate as possible without being too complex to analyze.

Assumptions

- flies do not recover from infection due to their short life span
- flies bite each host at a general rate
- infected individuals are infectious
- there is no birth or death in the human population in this short amount of time
- animal and fly populations are constant (birth rate = death rate)

Assumptions Continued

- humans either become immune after infected or remain infected
- animals and humans are only infected after being bitten by infected flies
- animals leave the infected population to become susceptible again (no immunity)
- humans can infect flies (Costa, Stewart, Gomes, Garcez, Ramos, Bozza, *et. al*, 2002)
- animals and flies do not die from infection
- canines represent the animal population and a general recovery rate, birth or death rate, and probability of a bite leading to infection are used for the animal population

Table of Parameters Used in Model

Parameter	Definition	Parameter	Definition
S_x	susceptible x population where x={H (human), F (sand fly), A (animal)}	γ_x	recovery rate per capita of x from infection
I_x	infected x population	d_x	death rate per capita of x
R_H	immune human population	b_x	birth rate per capita of x
N_x	total x population	a	biting rate per capita
p_x	probability of bite leading to infection in x		

Human Populations

Rates of Change in Susceptible, Infected, and Recovered Human Populations:

$$S_H' = -\,a p_H (S_H / N_H)\, I_F$$

Human infection rate

$$I_H' = a p_H (S_H / N_H)\, I_F - \gamma_H I_H$$

Human infection rate — *Recovery rate*

$$R_H' = \gamma_H I_H$$

Recovery rate

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S_x	susceptible x population where x={H (human), F (sand fly), A (animal)}	γ_x	recovery rate per capita of x from infection
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Sand Fly Populations

Rates of Change in Susceptible/Recovered and Infected Sand Fly Populations:

$$S_F' = -a\,(p_{FA}\, I_A / N_A + p_{FH}\, I_H / N_H)\, s_F + b_F\, N_F - d_F\, S_F$$

Rate of flies infected — *Birth rate* — *Death rate*

$$I_F' = a\,(p_{FA}\, I_A / N_A + p_{FH}\, I_H / N_H)\, s_F - d_F\, I_F$$

Rate of flies infected — *Death rate*

Parameter	Definition	Parameter	Definition
S_x	susceptible x population where x={H (human), F (sand fly), A (animal)}	γ_x	recovery rate per capita of x from infection
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Animal Populations

Rates of Change in Susceptible/Recovered and Infected Animal Populations:

$$S_A' = -\,a p_A (S_A / N_A)\, I_F + b_A N_A - d_A S_A + \gamma_A I_A$$

Rate of animals infected · *Birth rate* · *Death rate* · *Recovery rate*

$$I_A' = a p_A (S_A / N_A)\, I_F - \gamma_A I_A - d_A I_A$$

Rate of animals infected · *Recovery rate* · *Death rate*

Parameter	Definition	Parameter	Definition
S_x	susceptible x population where x={H (human), F (sand fly), A (animal)}	γ_x	recovery rate per capita of x from infection
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Basic Reproduction Ratios

The **introduction of an infected animal** into completely susceptible populations of sand flies, humans, and animals **results in**

$$ap_{FA}N_F\,(1 \text{ infected} / N_A)\,[1 / (\gamma_A + d_A)] = ap_{FA}N_F \;/\; [N_A(\gamma_A + d_A)]$$

1 infected animal results in this many infected sand flies

$$ap_H(1/d_F)(N_H/N_H) = ap_H / d_F$$

Each infected sand fly results in this many infected humans

Thus,

$$\mathbf{R_{0A} = a^2 p_{FA} p_H N_F / [N_A d_F (\gamma_A + d_A)]}$$ ***total number of resulting human infections***

Parameter	Definition	Parameter	Definition
S_x	susceptible x population where x={H (human), F (sand fly), A (animal)}	γ_x	recovery rate per capita of x from infection
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R_H	immune human population	b_x	birth rate per capita of x
N_x	total x population	a	biting rate per capita
p_x	probability of bite leading to infection in x		

Basic Reproduction Ratios Continued

The **introduction of an infected human** into completely susceptible populations of sand flies, humans, and animals **results in**

$ap_{FH}N_F(1 \text{ infected} / N_H)(1/\gamma_H)$

1 infected human results in this many infected sand flies

$ap_H (1/ d_F)(N_H / N_H) = ap_H / d_F$

Each infected sand fly results in this many infected humans

Thus,

$\mathbf{R_{0H} = a^2 p_{FH} p_H N_F / [\ N_H d_F \gamma_H\ ]}$ ***total number of resulting human infections***

Parameter	Definition	Parameter	Definition
S_x	susceptible x population where x={H (human), F (sand fly), A (animal)}	γ_x	recovery rate per capita of x from infection
I_x	infected x population	d_x	death rate per capita of x
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Equilibrium Solutions

Trivial and Nontrivial Equilibrium Solutions

$I_H^* = 0$ $\quad$ $I_H^* = 0$

$I_F^* = 0$ $\quad$ $I_F^* = 0, [a^2 p_A p_{FA} N_F - d_F N_A(\gamma_A + d_A)] / [ap_A(ap_{FA} + d_F)]$

$I_A^* = 0$ $\quad$ $I_A^* = 0, [N_A - d_F N_A^2(\gamma_A + d_A) / [N_F a^2 p_A p_{FA}]] / [1 + N_A(\gamma_A + d_A) / (N_F a p_A)]$

The nontrivial equilibrium solutions are biologically realistic if I_F^* and I_A^* are greater than zero.

$N_F a^2 p_A p_{FA} / [d_F N_A(\gamma_A + d_A)] > 1$ $\quad$ if $p_H \geq p_A$, then

$N_F a^2 p_H p_{FA} / [d_F N_A(\gamma_A + d_A)] = R_{OA} > 1$

Thus, leishmaniasis remains endemic if and only if $R_{OA} > 1$ (Britton, 2003).

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Conclusion

- This summer I developed a mathematical model involving three interacting organisms: *Lutzomyia longipalpis*, animals/domestic dogs, and humans.
- This is **one of the first** visceral leishmaniasis models ever created.
- Often, models such as these only involve two organisms for simplicity, but by including all three which are very important in the spread of visceral leishmaniasis, this model may be **more biologically accurate**.

Future Directions

- I will continue working on this model in the fall.
- Sensitivity analysis will soon be performed.
- Great efforts are being made to discover efficient means of controlling the spread of Leishmaniasis, and after sensitivity analysis, this model may be used to **determine the most effective method of control**.
- In addition, published values for the model's parameters may be incorporated in order to evaluate R_{0A} and R_{0H}.
- The ultimate purpose for the model, however, is to **determine the effects of immigration and environmental change on** the basic reproductive ratios and, in doing so, observe their influence on **endemism**.

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