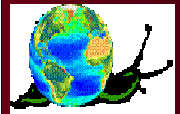


Modeling ecology and environment in schistosomiasis transmission and control for distributed heterogeneous populations

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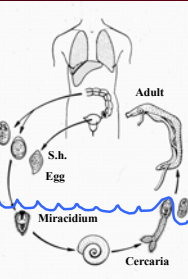


ABSTRACT

Three essential factors determine schistosomiasis transmission in endemic regions:
 • **environmental conditions** and water ecology that sustain intermediate host snails,
 • **human** populations and their **behavior**, contact-risk activities at potential transmission sites
 • **seasonal variability** that affects snail ecology and human behavior.
 Typically treatment alone can not eradicate the process of reinfection. So any design of a realistic and affordable control strategy (WHO, 2002) should account for both host environment and ecological factors.
 We outline an approach based on dynamic modeling of schistosomiasis transmission for heterogeneous populations in a environment, and develop suitable mathematical models and computer-based tools of analysis and prediction. They allow us to assess risk factors and design long-term control strategies that combine drug treatment with snail control. We outline some preliminary models and results that incorporate distributed human-snail populations, age-behavioral heterogeneities, and varying environmental features (geographic proximity of human and snail sites, and snail ecology). We apply these models to examine the long-term effects of chemotherapy, snail control or combined strategies, on chronic human morbidity, and identify optimal ones in terms of cost and efficacy.

BACKGROUND on Schistosomiasis

- Chronic parasitic trematode infection, that affects 200-300 million people worldwide
- Causes significant morbidity (esp. anemia) and premature mortality
- Parasite goes through complex life-cycle, that involves definitive human host and intermediate snail host,



- Cheap and efficient drugs are available, but treated patients get reinfected through exposure to infected snails.
- Complete eradication is out of reach
- **Control Strategies** include
 - Chemotherapy
 - Vector (snail) control
 - Vaccination
 - Environmental modification
- Optimal control strategies have not been established.

Epidemiology

- Transmission is highly focal
- Prevalence and intensity vary with age
- Morbidity varies with age
- Signs of early chronic disease correlated with greater intensity of infection

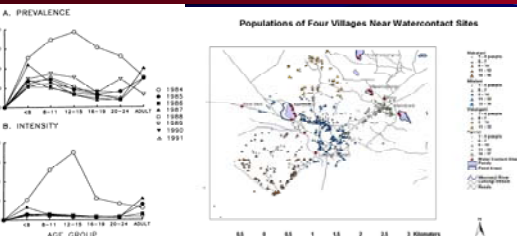


Fig. 1: Typical prevalence and worm burden distribution by age, based on longitudinal study of 9 villages 5 schools N = 7700

Fig. 2: Typical environment

MODELING

Long term Goals:

1. Develop transmission models for spatially distributed heterogeneous populations, that properly account for environmental factors, seasonal variability, snail ecology and human behavior
2. Identify the essential transmission/control parameters, and measures of morbidity
3. Develop model based control strategies: chemotherapy, snail control, landscape and behavior modification. Examine their efficacy, cost and produce, if possible optimal community-wide strategy for controlling disease.

Steps

1. Simple Ross-Macdonald model for single human/snail population!

Based on worm burden and (infected) snail prevalence variables: $w(t), y(t)$, that obey couple differential system:

$$(1) \begin{cases} \frac{dw}{dt} = Ay - \gamma w \\ \frac{dy}{dt} = Bw(1-y) - \mu y \end{cases} \quad \begin{matrix} A, B - \text{transmission rates, } \gamma, \mu - \\ \text{worm/snail mortalities} \end{matrix}$$

It predicts equilibrium (endemic) level, provided **Basic Reproduction Number (BRN)** $R_0 = AB/\gamma\mu > 1$. When subjected to chemotherapy at regular time intervals T , and efficacy $0 < f < 1$, the effective clearing rate γ increases by $-\ln(1-f)/T$. That changes R_0 and endemic levels in terms of control parameter T .

2. Distributed heterogeneous model (Gurarie-King²)

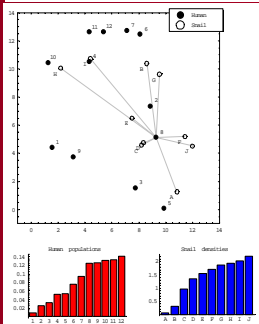


Fig. 3: Model environment consists of distributed human/snail clusters with specified densities, and the human populations stratified by age.

We parameterize environment by geographic locations of sites, human/snail densities and 'hurdle factors' that depend on distances $\{d_{ij}\}$ between i-human and j-snail sites.

The resulting 'burden -prevalence' model (1) becomes large differential system in variables $\{w_{i,a}\}$ (i-site, a-age), and $\{y_j\}$ (prevalence at j site).

$$(2) \begin{cases} \frac{d\hat{w}}{dt} = A \cdot \hat{N}y - (\Gamma + G)\hat{w}; \\ \frac{d\hat{y}}{dt} = (1-\hat{y})B \cdot \hat{H}w - \mu\hat{y}; \end{cases}$$

Here G - (Leslie-type) aging matrix, Γ - worm attrition, matrices A, B depend on the important **transmission** parameters:

- (Age dependent) water contact rates $\{\omega_a\}$, weighted by geographic **hurdle factors**
- Contamination rates $\{\beta_a\}$
- Worm establishment rates $\{a_a\}$

The role of Ross-Macdonald BRN is played now by the **Basic Reproduction Matrix** R^0 , introduced and studied in ². There we assumed **independence** of environmental and behavioral factors (in terms of site/age population distribution, contact rates, etc), which allowed us to separate their contribution to worm burden endemicity (used as a proxy for acute morbidity). Our analysis has several implications, one of them - an explicit (computational) form of equilibrium **community mean burden**

$$(3) \quad \bar{w} = \sigma f(\rho)$$

expressed through **Basic Reproduction Scalars** ρ, σ (BRS) that encode age-behavioral factors, like contact rates, and **infection potential** f (that encodes environmental factors - snail distribution, and prevalences, along with geographic hurdles).

Different control strategies can be analyzed and computed in such formulation: in particular **age-targeted** chemotherapy (across the entire region) or **focal control** of high risk sites, e.g. site 4, close to high density snail sites I,H. Therapy control enters system (2) through an augmented attrition matrix (or matrices) $\Gamma \rightarrow \Gamma + \text{diag}(1/T_a)$, where T_a are (age dependent) treatment periods. They enter explicitly into functions ρ, σ , and thus allow to estimate the effect of any particular treatment regiment, or to search for an optimal one (in terms of cost) to minimize the community-wide burden.

We implemented such numeric algorithms in Wolfram Mathematica 5.

RESULTS

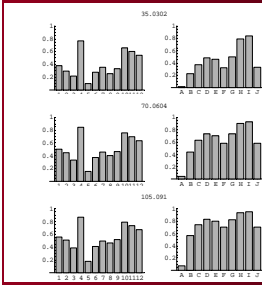


Fig.4: Community burden distribution (left) and snail prevalences (right) for model environment Fig.3, at several increasing values of BRS ρ . Site 4 clearly exhibits high risk area.

Age targeted therapy

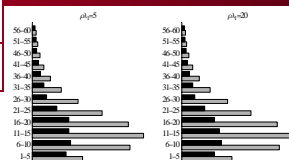


Fig. 5: Comparison of age distributed equilibrium worm burdens without treatment (gray) and with optimal frequency age-specific treatment (black), at allocated/full treatment-cost ratio: $C0/C0 = .2$, for two values of basic reproduction scalar (B.R.S.), (low), and (high)

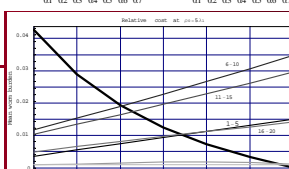


Fig.7: Effect of optimized treatment on community mean worm burden (solid black). The optimal therapy frequencies for the 6 youngest age groups are shown as functions of the ratio (allocated cost/cost of total population coverage) $\xi = C0/C0$, shown on the ordinate. In the setting where only 50% or fewer can be covered, then annual treatment of 6-15 yr age groups ($t = 1$), combined with treatment every 4-10 years for younger and older age groups ($t = 0.25$ to 0.1), provides the maximal possible reduction in community worm burdens.

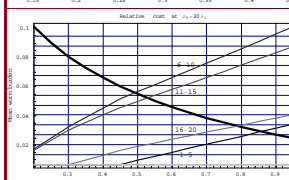


Fig. 8: Community mean worm burden as function of the BRS ρ in two cases: untreated population (black), and intense focal treatment of site 4 through complete eradication (gray). The dashed curve shows the relative gain in overall community worm burden between two cases. It falls rapidly with ρ , so the targeted treatment of site 4 alone gives less than 10% reduction for moderate values of ρ .

Site specific therapy

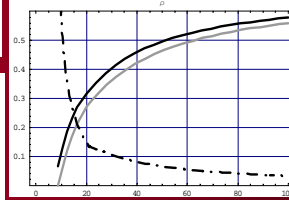


Fig. 9: Site distribution of worm burden for pretreatment human populations (gray), and the effect of extreme treatment for sites 4, 10 and 11 on the remaining untreated sites (dark bars). Left and right panels indicates overall impact under low/high transmission potential respectively. In either case the overall impact on the untreated sites is insignificant.

SUMMARY AND REFERENCES

We studied potential impact of area-wide control strategies on spatially-distributed endemic schistosome infection, using a distributed Macdonald-type model. An optimal age-targeted strategy was determined for a range of values ρ . Focal control fails to achieve the desired impact, due to linked environment.
 Future work (in progress) will extend the above models to include immunity, chronic morbidity, and seasonally varying snail ecology.

1. Macdonald, G. (1965). *Trans R Soc Trop Med Hyg* **59**, 489-506.
2. D. Gurarie, C. King, *Parasitology*, 2005 (to appear)