

Evidence Against Rapid Emergence of Praziquantel Resistance in *Schistosoma haematobium*, Kenya

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Appendix

The following system of differential equations was used to model the level of schistosome infection and prevalence of resistant worms in the treated study population, where

σ is the number of sensitive schistosomes per host,

ρ is the number of resistant schistosomes per host, and

$\sigma + \rho = M$, the mean number of worms per host.

If p = the proportion of treated infections each year, and

h = the efficacy of one course of treatment, then

$c = -\ln(1 - ph)$ is the relative increase in the per capita death rate of sensitive worms due to treatment. The basic death rate for sensitive and resistant parasites is an aggregate function of parasite and host death rates, represented in the equations as

$$\gamma_r = \frac{1}{\text{resistant parasite lifespan}} + \frac{1}{\text{host lifespan}}$$

and

$$\gamma_s = \frac{1}{\text{sensitive parasite lifespan}} + \frac{1}{\text{host lifespan}}$$

R_0 represents the basic reproductive rate of the susceptible worm. If $\square =$ the relative loss of reproductive fitness of the resistant phenotype (with value from 0 to 1), then

$R_{0r} = R_0(1 - \square)$, represents the spontaneous mutation rate of resistant worms. To reflect the impact of obligate sexual mating and unequal distribution of worms among hosts, F is a fecundity expression where

$\psi =$ the mating probability,

$z =$ the density-dependent effect on worm fecundity, and

$k =$ the aggregation constant of the negative binomial distribution of worms,

$$F(\sigma + \rho) = \Psi \left[1 + (\sigma + \rho) \frac{(1-z)}{k} \right]^{-(k+1)}$$

such that

$$\frac{d\sigma}{dt} = \gamma_s \cdot \sigma \cdot [R_0 \cdot F(\sigma + \rho) - 1 - \frac{c}{\gamma_s}]$$

Then, along the lines of equation 17.5 of Anderson and May (29) for repeated treatment, and assuming resistant parasites to be completely unaffected by treatment,

For the numerical analysis of these equations, we used the ODE solver of MathCAD (MathSoft, Inc., Cambridge MA) based on the

$$\frac{d\rho}{dt} = \gamma_r \cdot \rho \cdot (R_{0r} \cdot F(\sigma + \rho) - 1) + \chi \cdot p \cdot \sigma$$

Runge-Kutta estimation with $\geq 1,000$ steps for a model time span of 20 years.

Initial variable estimates were taken from our field data (treatment coverage among total infected population, $p = .25$ to $.75$; treatment efficacy, $h = .65$ to $.95$; aggregation constant, $k = 0.067$; host lifespan = 50 years) or from previously published estimates for *S. haematobium* biology ($R_0 = 2$ to 4; parasite lifespan = 3 to 5 years; density effect on fecundity, $z = 0.96$ to 0.99) (29).

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