Dynamics of Infected Snails and Mated Schistosoma Worms within the Human Host

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Abstract: Male and female worms are independently distributed within a human host each with a Poisson probability distribution mass function. Mating takes place immediately when partners are available. It was found that the mated worm function is non-linear near the origin and becomes almost linear as the worms increase. They increase with increase in the worm load due to aggregation of worms. This also increases the infection of snails which are secondary hosts. On the analysis of the model, three equilibrium states were found, two of which were stable and one unstable. A stable endemic equilibrium within a community is very much undesirable. So the main objective of the model was to have the point O(0,0) as the only equilibrium point. This is a situation where there are no worms within the human host and the environment is free of infected snails. A critical point, above which the disease would be chronic and below which the disease would be eradicated, was found and analyzed. The parameters indicated that to achieve a disease free environment, the death rate of worms within the human host should be much greater than the cercariae that penetrate the human. Also the death rate of infected snails should be much higher than the contact rate between the miracidia and the snails. It was concluded that de-worming and killing of snails should be emphasized for disease control and educating the masses on the modes of disease transmission is quite necessary for prevention of the disease.

INTRODUCTION

Schistosomiasis is caused by parasitic flat worms of the genus *Schistosoma*. Male and female mate within the human host and lay eggs in the blood vessels which line the bladder and intestine [1]. These eggs induce an immune reaction which causes the swelling of the spleen *hepatosplenic* and liver *liver fibrosis*. A portion of the eggs leave the body with the feaces or urine and find their way into the fresh water supply where they hatch into a free swimming ciliated larva called a miracidium of about 0.2mm long. If the miracidium reaches a fresh water snail of a suitable species, it penetrates and transforms into a sporocyst. The sporocyst begins an asexual phase of reproduction within the body of the snail producing thousands of daughter sporocysts.

Because of this, the disease is sometimes called snail fever since the snails serve as hosts for the transmission of the disease. The infected snails then release a second form of free swimming larva called a cercaria, of about 1mm long with a characteristic forked tail, into the water. The miracidia cannot infect a human being but the cercaria can. The cercaria eventually penetrate the skin of a human, loses its tail and enters the blood vessels as a *schistosomulum*. It grows to adult size, matures sexually and migrates to the liver where they cause *liver fluke*, or migrate to the intestines or the stomach where they cause schistosomiasis. After the mating of the male and female schistosomes and migration to a blood vessel, egg-laying starts and the life cycle of the parasite is closed, Fig.1. Each pair of *schistosomulae* produces hundreds to thousands of eggs per day. The eggs are spined and sieve through the tissues to the excretory tract. Most of the pathology associated with infection is due to immune responses to eggs that become trapped in the host tissues. The epidemiology of schistosomiasis to the human community is measured by the number of worms harbored by the infected human hosts and also the intensity of egg disposal through the excreta. The number of worms within the human host is termed as
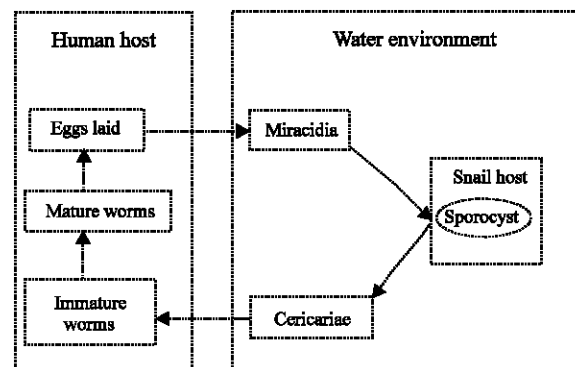

Fig. 1: A Flow Diagram of the Life Cycle of Schistosoma Parasites

the worm burden. The number of eggs disposed through the excreta depends on the number of mated parasites. Since the severity of schistosomiasis depends on these factors, we need to study the dynamics of the disease by considering the analysis of the worm burden within the human host. Also the transmission process involves snails as secondary hosts and so we shall consider the rate of infection of the snails since this is a function of the mated worms. Our main objective is to find a relation between mated worms and infected snails so as to establish parameters that could lead to a possible eradication of the disease.

FORMULATION OF THE EQUATIONS FOR THE MODEL

The following variables are considered:

* N_1 is the total number of snails
* N_2 is the total number of human hosts
* I_1 is the number of infected snails
* I_2 is the number of infected persons
* $W(t)$ is the number of worms within the human body at time
* $\psi(W)$ is the number of mated parasites within the human host
* q is the number of cercariae released by the infected snails.

The following are the parameters in the model:

* β_1 is the contact rate of the susceptible human population with the cercariae, q
* β_2 is the rate at which snail susceptibles get infected
* μ_4 is the death rate of the infected snails
* μ_5 is the death rate of mature worms.
* v_4 is the proportion of cercariae that eventually penetrate the human skin
* λ is the rate at which the worms distribute themselves into the human host.
* κ is the contact rate between the miracidia and the snails.

Schistosomiasis involves the mating of male and female parasites. The penetration of the males and females into the human host are independent of one another. The rate of infection of the snails is proportional to the number of paired worms $\psi(W)$ and also the rate of increase of worms in the human host depends on the number of cercariae q released by the infected snails.

The main interest is to find the number of worms W infecting each human host and the number of infected snails I_1 within the community. From this biological and epidemiological background of the disease, we get the rate of change of the infected snails as

$$\frac{dI_1}{dt} = \kappa \psi(W) \beta_2 (N_1 - I_1) - \mu_4 I_1 \qquad (1)$$

and the rate of change of the worm burden as

$$\frac{dW}{dt} = v q I_1 - \mu_5 W \qquad (2)$$

Equations (1) and (2) form a basic model for our discussion.

PROBABILITY DISTRIBUTION OF WORMS

In order to analyze equations (1) and (2), we need to get the expression for the mated parasites $\psi(W)$ and the distribution of worms W within the human host. Let us consider the penetration of the cercariae into the human host as an immigration process since the mated females never produce other mature worms directly inside the human host. This is a correct assumption since the worms join the human host as immigrants. To get the probability distribution, we make the following assumptions.

Assumptions on the Distribution of Worms: We now consider the following assumptions [3]:

* It is assumed that the worm enters and moves to a region in a human host independent of the number of worms in any other non overlapping region.
* The probability distribution for the number of worms in any region is the same for all regions.
* The regions are so small that we expect only one worm to occupy a single region. And the probability that exactly one worm occupies a particular region is approximately proportional to that region. This means that two worms cannot enter the human host at the same time and through the same entry point.
* Since the region is so small, the probability of having more than one worm in a single region is very negligible in comparison to the probability of one worm in that region. Because worms enter through different points of the skin, they occupy different areas before mating takes place.

Probability Mass Function for the Worm Burden: Let $p_n(z)$ be the probability that n worms occupy a region of size z. Let λ be the rate at which the worms establish themselves into these regions. From assumptions (c) and (d) we get the following equations:

$$p_1(h) = \lambda h + 0(h) \text{ for some } \lambda > 0 \qquad (3)$$

$$\sum_{k=2}^{\infty} p_k(h) = o(h) \qquad (4)$$

This means that the probability of finding two or more worms in a small region h is very negligible. Since the regions are independent, then

$$p_0(z+h) = p_0(z)p_0(h) \qquad (5)$$

and we then find that

$$p_0(z) = e^{-\lambda z} \qquad (6)$$

Using Assumptions in Sub-section 3.1, we can now determine $p_n(z)$ in the same way by solving the following equation recursively.

$$p_n(z+h) = p_n(z)p_0(h) + p_{n-1}(z)p_1(h) \\ + p_{n-2}(z)p_2(h) + \ldots p_0(z)p_n(h) \qquad (7)$$

From this we get

$$p_n(z+h) = p_n(z)p_0(h) + p_{n-1}(z)p_1(h) + 0(h) \qquad (8)$$

Continuing in this way we inductively get

$$p_n'(z) + \lambda p_n(z) = \lambda p_{n-1}(z) \qquad (9)$$

whose solution is

$$p_n(z) = \frac{(\lambda z)}{n!} e^{-\lambda z}, \text{ n = 1, 2, ...} \qquad (10)$$

which is a Poisson probability distribution mass function. Considering a whole human host to constitute a size of unit 1, we expect the number of worms in each human host to be λ.

Expression for the Mated Parasites $\psi(W)$: It is noted that the number of mated worms depends on whether there exists worms of different sexes. We now let $F_m(t)$ be the number of mated females at time t, $M_m(t)$ be the number of mated males at time t, $F_s(t)$ be the number of single females at time t and $M_s(t)$ be the number of single males at time t. Since the number of mated females and mated males and their common value is equal to the minimum number of females $F(t)$ and the number of males $M(t)$, then we obtain the following relations:

$$W(t) = F(t) + M(t) \qquad (11)$$

$$F(t) = F_s(t) + F_m(t) \qquad (12)$$

$$M(t) = M_s(t) + M_m(t) \qquad (13)$$

$$\frac{W(t)}{2} = \min\{F(t), M(t)\} \qquad (14)$$

where $W(t)$ are the number of parasites harbored by the infected human host. So we expect the numbers of females and males to be each $W(t)/2$. Then

$$P(p \text{ males}) = e^{-W/2} \frac{1}{p!} \left(\frac{W}{2}\right)^p \qquad (15)$$

$$P(q \text{ females}) = e^{-W/2} \frac{1}{q!} \left(\frac{W}{2}\right)^q \qquad (16)$$

$$P(p \text{ males}, q \text{ females}) = e^{-W} \frac{1}{p!q!} \left(\frac{W}{2}\right)^{p+q} \qquad (17)$$

From probability theory, the expected number of paired parasites is given by:

$$E(W(t)) = \sum_{q=0}^{\infty} \sum_{p=0}^{\infty} 2 \min(p, q) e^{-W} \frac{1}{p!q!} \left(\frac{W}{2}\right)^{p+q} \qquad (18)$$
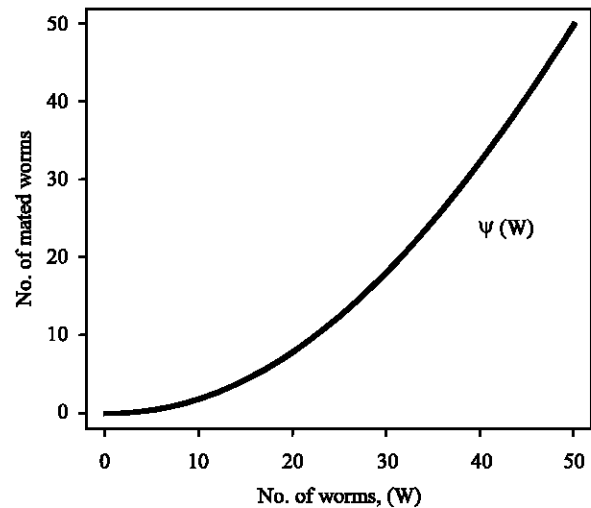
Fig. 2: The Relationship between the Total Number of Worms and the Mated ones within the Human Host

By making use of Bessel functions [4] and their properties as outlined in the appendix, we find that the expected number of mated parasites, $\psi(W(t))$ is given by $\psi(W) = W\{1 - e^{-W}[I_0(W) + I_1(W)]\}$ The function is $\psi(W)$ non-linear in W which is in conformity with the sexual behavior of the schistosomes biologically [5]. On applying the Bessel functions [4] and expanding the exponential function, we find that as $W \quad 0$

$$\frac{\psi(W)}{W} \approx \frac{W}{2} \tag{19}$$

and as W ,

$$\frac{\psi(W)}{W} \cong \left(1 - \left[\sqrt{\frac{2}{W\pi}}\right]\right) \tag{20}$$

From this analysis, we find that for big numbers of worms, the number of mated worms increases linearly and is non-linear when the worms are few as shown by the curve in Fig. 2. Equation (19) shows that as the number of worms decrease, the proportion of paired parasites almost becomes a linear function of W with gradient 1/2. And equation (20) shows that as the number of parasites increase, the proportion of paired parasites tends to 1 asymptotically. This is due to the fact that by nature these worms tend to aggregate within the human host and thus increasing the chances of mating.

RESULTS

Equilibrium States for Equations (1) and (2): Formulation of the model was based on theoretical work by several authors; [1-3]. The method used is analytic which is the best approach to solving theoretical models. We start by finding the equilibrium states for equations (1) and (2) by putting

$$\frac{dI_1}{dt} = 0 \quad \text{and} \quad \frac{dW}{dt} = 0 \tag{21}$$

We respectively find that

$$I_1^* = \frac{k\psi(W^*)\beta_2}{\mu_4 + k\psi(W^*)\beta_2} N_1 \tag{22}$$

and

$$I_1^* = \frac{\mu_5}{v_4 q} W^* \tag{23}$$

We observe that from expressions (19) and (20),
$\psi(W) \sim W^2/2$ as W 0 and also $\psi(W) \sim W$ as W .
From equation (23), we note that $W^* = (v_4 q / \mu_5)I_1^*$ and since $0 \le I_1 \le N_1$, then W^* cannot be greater than $W^* = (v_4 q / \mu_5)N_1$ So we now study the system in the rectangle $R[0 \le W \le (v_4 q N_1 / \mu_5), \ 0 \le I_1 \le N_1]$ On considering the case when W 0 such that $\psi(W) \sim W^2/2$ and if we substitute this value for $\psi(W)$ into equation (22) and taking $\kappa\beta_2 W^2$ to be very small compared to $2\mu_4$, we find that

$$I_1^* = \frac{k\psi(W^*)\beta_2}{\mu_4 + k\psi(W^*)\beta_2} N_1 \sim \frac{\kappa\beta_2 W^2}{2\mu_4} N_1 \tag{24}$$

Equating (23}) with (24) we get

$$\frac{\mu_5}{v_4 q} W^* = \frac{\kappa\beta_2 W^{*2}}{2\mu_4} N_1 \tag{25}$$

and on solving for W^*, we get two solutions

$$(W^*, I_1^*) = (0,0) \tag{26}$$

and

$$(W^*, I_1^*) = \left[\frac{2\mu_5\mu_4}{v_4 q \kappa\beta_2 N_1}, 2\left(\frac{\mu_5}{v_4 q}\right)^2 \frac{\mu_4}{\kappa\beta_2}\right] \tag{27}$$

near the origin but within the region R. On considering the case when $W \to \infty$ such that $\psi(W) \sim W$ and substitute this value for $\psi(W)$ into equation (22), we get

$$I_1^{**} = \frac{kW^{**}\beta_2}{\mu_4 + kW^{**}\beta_2} N_1 \tag{28}$$

Equating (23) and (28) and solving for W^{**}, we find

$$W^{**} = \frac{v_4 q N_1}{\mu_5} - \frac{\mu_4}{\kappa\beta_2} < \frac{v_4 q}{\mu_5} N_1 \tag{29}$$

Using (29) and substituting for W^{**} in (23) we find that

$$I_1^{**} = N_1 - \frac{\mu_4\mu_5}{v_4 q \kappa\beta_2} < N_1 \tag{30}$$

Thus the third point of intersection for the nullclines is

$$(W^{**}, I_1^{**}) = \left(\frac{v_4 q N_1}{\mu_5} - \frac{\mu_4}{\kappa\beta_2}, N_1 - \frac{\mu_4\mu_5}{v_4 q \kappa\beta_2}\right) \tag{31}$$

which lies within the rectangle $R[0 \le W \le (v_4 q N_1/\mu_5), \ 0 \le I_1 \le N_1]$ So we have found that all the nullclines intersect at three points within the rectangle R. On investigating the rates of change in various regions of the rectangle R, we get the phase diagram for equations (1) and (2) as shown in Fig. 3. All trajectories which start inside the rectangle R always move inside R and can never go beyond the boundaries of R. This shows that R is an invariant convex set. The trajectories indicate that there are two stable equilibrium points, one at the origin and another one at W^{**}. The equilibrium point at W^* is unstable.
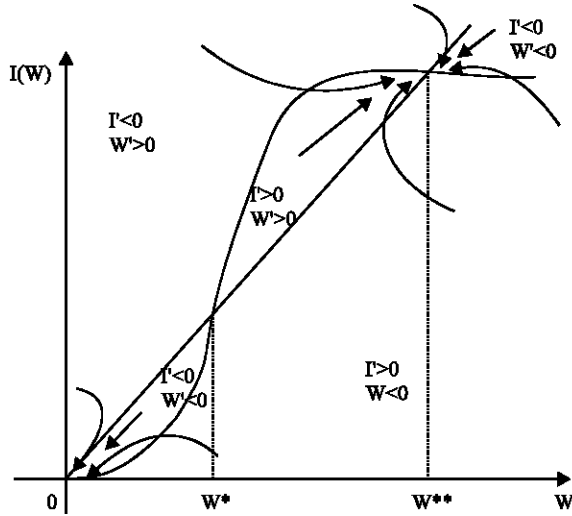
Fig. 3: The (I_1, W) Phase Diagram Showing the Nullclines for the Rate of Change of the Worm Burden within the Human Host and the Rate of Change of the Numbers of Infected Snails
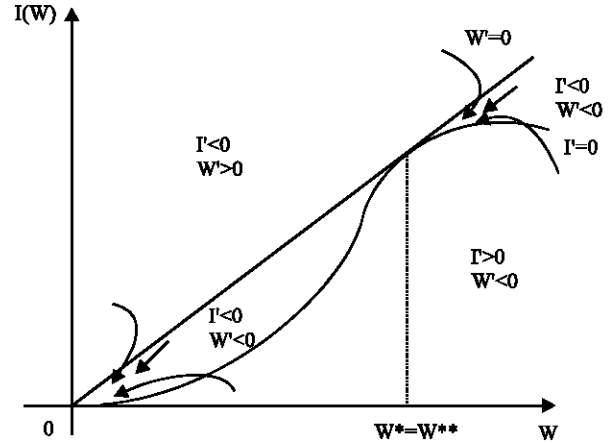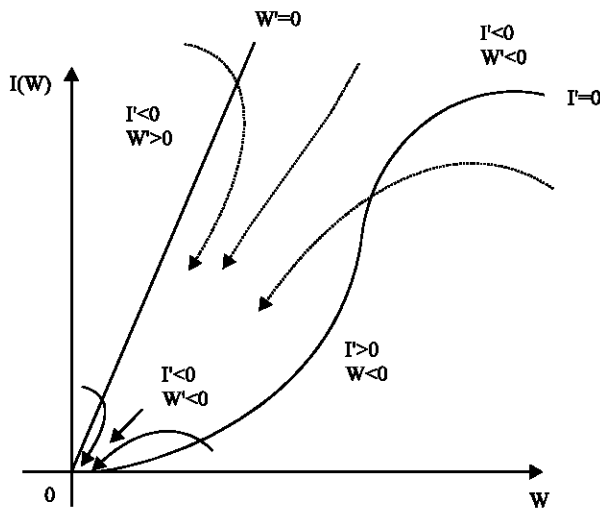

Fig. 4: The (I_1, W) Phase Diagram Showing that if the two Null Clines do not Intersect Inside the Rectangle R, then the only Equilibrium Point would be at the Point (0,0)

The Critical Point: There exists a point when $W^* = W^{**}$ as shown in Fig. 5. This is a critical point at which the disease is either maintained or eradicated from the community. The values of the parameters which satisfy such a condition play a vital role in public health as far as disease eradication is concerned.

We need to find an expression under which $W^* = W^{**}$ in terms of model parameters. For the condition $W^* = W^{**}$ to exist, then this equation

$$\frac{v_4 q N_1}{\mu_5} - \frac{\mu_4}{\kappa\beta_2} = \frac{2\mu_4\mu_5}{v_4 q \kappa\beta_2} \qquad (32)$$

Fig. 5: The Phase Diagram Showing the Nullclines and the Trajectories when $W^* = W^{**}$

must be satisfied. To achieve disease eradication we try to find conditions under which inequality (33) can be satisfied:

$$\frac{v_4 q N_1}{\mu_5} \le \frac{\mu_4}{\kappa\beta_2}\left[1 + \frac{2\mu_5}{v_4 q}\right] \qquad (33)$$

In this case, we achieve a situation in Fig.4, where the line and the curve do not intersect in R. This means that the point O(0,0) would be the only solution to this inequality.

DISCUSSION AND CONCLUSION

The stability of the point (W^{**}, I_1^*) as indicated by the trajectories in Fig. 3 shows that if the number of worms are greater than W^* then the disease persists within the community and eventually becomes endemic. This situation is very much undesirable. We would desire to have (0,0) as the only stable equilibrium state within the community. In order to achieve the desired phase diagram in Fig. 4, we need to increase the death rate of worms μ_5 and to decrease the proportion of the cercariae qv_4 that eventually penetrate the human host as can be deduced from the linear relation $I_1^* = (\mu_5/v_4 q)W^*$ for the infected snails. Also from the parabolic relation $I_1 \sim \kappa\beta_2 W^{*2}/2\mu_4$ we need to decrease the contact rate, $\kappa\beta_2$ between the miracidia and the susceptible snails and increase the death rate of the snails. The public health sector can achieve this by constant de-worming of the human population in these endemic communities. Educating the community about good sanitary conditions is quite helpful. People should use latrines and should avoid as much as possible urinating and defecating in and around water reservoirs. This reduces the contact rate β_2 of the miracidia with the water snails. The death rate of the snails μ_4 can be increased by use of molluscicides to kill the snails, [2].

If these measures are considered, we get the point (0,0) as the only endemic equilibrium meaning that the disease would be eradicated from the community. This agrees with our results since we have found out that killing snails is one of the main factors that leads to disease eradication. With schistosomiasis, the disease progressively declines when the snail density falls to or below a critical level. If the density is above the critical level, an epidemic will ensue [7, 8].

Generally, from the analysis of inequality (33), we conclude that if the death rate of worms μ_5 within the human host is far much greater than the proportion of the cercariae qv_4 that penetrate the human host and/or if the death rate of snails μ_4 is far much greater than the contact rate $\kappa\beta_2$ between the miracidia and the snails then the disease is eventually eradicated.

The public health sector, having spotted focal endemic areas of schistosomiasis, should put more emphasis on disease control by chemotherapy and killing of the water snails by use of molluscicides. Although emphasis is put on the two control measures, need to educate the people on the modes of disease transmission is very much necessary for disease prevention.

ACKNOWLEDGEMENTS

APPENDIX

Expression for the Mated Parasites $\psi(W)$: It is noted that the number of mated worms depends on whether there exists worms of different sexes. We now let $F_m(t)$ be the number of mated females at time t, $M_m(t)$ be the number of mated males at time t, $F_s(t)$ be the number of single females at time t and $M_s(t)$ be the number of single males at time t. Since the number of mated females and mated males and their common value is equal to the minimum number of females $F(t)$ and the number of males $M(t)$, then we obtain the following relations:

$$W(t) = F(t) + M(t) \quad (34)$$

$$\min\{F(t), M(t)\} = F_m = M_m \quad (35)$$

$$F(t) = F_s(t) + F_m(t) \quad (36)$$

$$M(t) = M_s(t) + M_m(t) \quad (37)$$

$$\min\{F_s(t), M_s(t)\} = 0 \quad (38)$$

$$\frac{W(t)}{2} = \min\{F(t), M(t)\}$$

where $W(t)$ are the number of parasites harbored by the infected human host. So we expect the numbers of females and males to be each $W(t)/2$. The number of male parasites in a human host and the number of female parasites are assumed to be independently distributed each with a Poisson probability mass function. Then

$$P(p\ males) = e^{-W/2} \frac{1}{p!}\left(\frac{W}{2}\right)^p \quad (39)$$

$$P(q\ females) = e^{-W/2} \frac{1}{q!}\left(\frac{W}{2}\right)^q \quad (40)$$

$$P(p\ males, q\ females) = e^{-W} \frac{1}{p!q!}\left(\frac{W}{2}\right)^{p+q} \quad (41)$$

From probability theory, the expected number of paired parasites is given by

$$E(W(t)) = \sum_{q=0}^{\infty} \sum_{p=0}^{\infty} 2\min(p, q)\ e^{-W} \frac{1}{p!q!}\left(\frac{W}{2}\right)^{p+q} \quad (42)$$

By making use of Bessel functions [4] and their properties, we find that the expected number of single females at time t is

$$E[F_s(t)] = \sum_{l=0}^{\infty} le^{-W(t)} I_l(W(t)) \quad (43)$$

$$= e^{-W(t)} \sum_{l=1}^{\infty} l I_l(W(t)) \quad (44)$$

where the functions $(I_l(t))$ are Bessel functions [4]. We then find that [6]

$$E[F_s(t)] = e^{-W(t)} \frac{W(t)}{2} \sum_{l=1}^{\infty} [I_{l-1}(W(t)) - I_{l+1}(W(t))] \quad (45)$$

$$E[F_s(t)] = e^{-W(t)} \frac{W(t)}{2} [I_0(W) - I_1(W(t))]$$

The total population is clearly composed of single and mated females and males. Thus $W(t)$ given by the following expression:

$$W(t) = F_s(t) + F_m(t) + M_s(t) + M_m(t) \qquad (46)$$

But the number of mated females is equal to the number of mated males. And the number of single males has the same expectation as the number of single females. Now the expected number of mated females is given by

$$E[F_m(t)] = \frac{1}{2} E[W(t)] - E[F_s(t)]$$

$$E[F_m(t)] = \frac{1}{2} W - \frac{1}{2} We^{-W(t)}[I_0(W) + I_1(W)] \qquad (47)$$

$$\Rightarrow \psi(W) = 2E[F_m(t)] \qquad (48)$$

where

$$\psi(W) = W\{1 - e^{-W(t)}[I_0(W) + I_1(W)]\} \qquad (49)$$

The function $\psi(W)$ is non-linear in W which is in conformity with the sexual behavior of the schistosomes biologically [5]. On applying the Bessel functions [4] and expanding the exponential function, we get

$$\psi(W) = W - (W - W^2 + \frac{W^3}{2!} + \cdots)$$
$$(1 + \frac{W}{2} + \left(\frac{W}{2}\right)^2 + \frac{1}{2!}\left(\frac{W}{2}\right)^3 + \cdots) \qquad (50)$$

As $W \to 0$ and using the Bessel functions and their properties and by Soni [6], we find that

$$I_0(W) + I_1(W) = \frac{2e^W}{\sqrt{2\pi W}} \qquad (51)$$

from which we then get

$$\psi(W) \sim W(1 - e^{-W}(\frac{2e^W}{\sqrt{2\pi W}}), \quad W \to \infty \qquad (52)$$

$$\psi(W) \sim W(1 - (\sqrt{\frac{2}{W\pi}}), \quad W \to \infty \qquad (53)$$

$$\frac{\psi(W)}{W} \sim (1 - (\sqrt{\frac{2}{W\pi}}), \quad W \to \infty \qquad (54)$$

This equation gives the proportion of paired parasites per human host. From this analysis, we find that for big numbers of worms, the number of mated worms increases linearly and is non-linear when the worms are few as shown by the curve in Fig. 2. Generally as $W \to 0$,

$$\frac{\psi(W)}{W} \sim \frac{W}{2} \qquad (55)$$

and as $W \to \infty$

$$\frac{\psi(W)}{W} \sim (1 - (\sqrt{\frac{2}{W\pi}}), \quad W \to \infty \qquad (56)$$

Equation (55) shows that as the number of worms decrease, the proportion of paired parasites almost becomes a linear function of W with gradient 1/2 and equation (56) shows that as the number of parasites increase, the proportion of paired parasites tends to 1 asymptotically. This is due to the fact that by nature these worms tend to aggregate within the human host and thus increasing the chances of mating.

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