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ESTIMATION OF THE MICROFILARIA LOAD IN A HOST USING THE MICROFILARIA COUNT IN A SKIN- SNIP SAMPLE TAKEN FROM ANY OTHER PART OF THE BODY OF THE HOST BELOW THE ILLIAC CREST.

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ABSTRACT

Estimation of the microfilaria (M_f) load (of Onchocerca Volvulus) in a human host has always been the concern of the dermatologists. They have usually done this by taking Skin-snip samples from different regions of the host's body from where they extrapolate to estimate the microfilaria load in the entire body. In this paper however, I present a model in which a Single-skin-snip sample is required and taken from a particular part of the host's body other than the Iliac Crest but below it, from which we therefore estimate the entire body load of the microfilaria. A model showing the total daily microfilaria output was also developed. It shows the inhibiting effect of the presence of the worms on one another in the number of microfilaria they can release.

KEYWORDS: Onchocerca Volvulus, Microfilaria Load, Skin-Snip, Iliac Crest, Estimation

INTRODUCTION

Microfilariae are the little worms produced by the Onchocerca Volvulus in the human host due to the presence of the adult worms, CWRU (2002). The history of the worms , Onchocerca Volvulus have been extensively treated in the works of Duke (1968), Wyatt (1971), Akogun *et al* (1992). We shall therefore, concern ourselves primarily with the estimation of the number of the microfilaria produced by the worms in the body of the host, which we shall term the microfilaria load. These Microfilariae when produced are buried in the subcutaneous layers in the skin. They are not equally distributed in all parts of the host's body, Akoh (1988), Wyatt (1971) Albeiz (1983), Kershaw *et al* (1954). Particularly, Akoh (1988) gave a detailed study to support this by studying the distribution of the microfilaria in the patients in Central Nigeria.

It might be very important to state that an Onchocerca Volvulus worm can live for upwards of Sixteen years and be still producing microfilaria in the body of the host. However the peak of microfilaria production by any worm is within the sixth to eightieth year of the life of the worm. In all, we can have up to forty worms or more in a given host depending on the endemicity of the disease in the area as well as the size of the host. We also know that if an individual is infected by the Onchocerca Volvulus, he remains infected for life unless he is correctly treated. The disease is a debilitating one that does not necessarily kill very easily so that the patient can live for long even after contracting the disease. The density of the microfilaria in a host is again dependent on the age/exposure level of the host. It might be important to state here that this disease can not be transmitted from one host to another without an intermediate vector, the Similum Damnosum (Blackfly), Alley *et al* (2001)

Because of the uneven distribution of the microfilaria in the body of the host, certain parts of the body of the host are more reliable in the estimation of the microfilaria load. Akoh (1988) and Wyatt (1971) showed in detail various percentage distributions of the microfilaria in different parts of the body of the host for the Savanna and Forest strains of the Onchocerca Volvulus. The Iliac Crest is shown to contain the greatest load of the microfilaria. However, this part of the body is considered private and thus forbidden to a non-partner in most African countries. This behaviour usually led to faulty results in many research works as Skin-snips were not easily taken from this part. This attitude is one of the reasons for the decision to formulate a Mathematical model that can be used to estimate the entire microfilaria load in the body of the host by just taking a Skin-snip sample at any other part of the host's body other than the Iliac crest but below it. The decision to consider the part below the Iliac crest is that this region is more reliable and the strain of the Similum Damnosum of interest bites below the Iliac crest primarily and thus, the bulk of the worms are found in this region. Since women are the worst hit by this disease and going by the culture of the people, it then will be a relief to researchers if a Mathematical model can be built which will not need the exposure of the iliac crest by these women. Onchocerciasis disease is the second leading causes of blindness in the world, http://www.alerttnet...(2002) as the microfilaria can migrate up to the eye. Alley *et al* (2001) had considered Macrofilaricides and Ochocerciasis control by drawing mathematical models of the prospects for their elimination. The driving force for this model is the belief that with a high vector biting rate and poor coverage, a very effective macrofilaricide would appear to have a substantially higher potential for achieving elimination of the parasite than those invemectin used for the control.

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From the work of Akoh *et al* (1988), Wyatt (1971) and Kershaw *et al* (1954) there appears to be a correlation between the points of bite of the vector and or the point of domicile of the worms and the concentration of the microfilaria. Hence, we need some analysis on the surface area of the different parts of the body of the host. For a normal sized person (not Obese, dwarf or unequal growth), about fifty percent (50%) of the body surface area is found from the iliac crest downwards. Schulz-Key (1990) stated that microfilaria density in a given host stabilizes at about the age of twenty years if the host has been in the environment since birth and has had good exposure level. For a seventy kilogram man, the surface area of his body is about $1.8M^2$ and usually sustains about $8 - 12 \times 10^6$ microfilaria if the microfilaria density is about 7.1 microfilaria/mm^2 in the entire body or 14.7 microfilaria/mm^2 in the iliac crest. Going by the percentage stated above, it means that the surface area of the body of the host from the iliac crest downward is $0.9M^2$. Based on these and the work of Akoh (1988), Wyatt (1971) , Kershaw *et al* (1954), Guderin (1988) and Schulz-key (1990) we have the detailed analysis of the surface area of the different parts of the host's body from the iliac crest downwards as shown in Table 1.

The microfilaria distribution in these body areas using the Skin-snip samples taken from them according to the researchers listed above are shown as in Table 2.

Using our region of interest, we get another table showing the microfilaria (m_f) distribution in the most popular parts used by researchers in the determination of the m_f load in a patient's body. The percentage distribution as related to the m_f load in the skin-snip in this region is also given and we thus have it shown as in Table 3.

From Table 2, we can see that about 84.17% of the entire m_f load in the body, which is about 673,360,000 – 1, 010,040,000 are found at iliac crest and below.

Table 1

Part of the body	% Surface area	Actual body surface area (M^2)
Iliac Crest	32.14	0.28926
Iliac crest – knee	42.86	0.38574
Knee – Ankle (Calf/Shin)	22.5	0.2025
Foot	2.5	0.0225

Table 2

Part of the body	Microfilarial count in Skin –snip Sample	% distribution in the body
Head	12 (estimated)	4.6
Chest	24	9.27
Abdomen	5	1.95
Iliac crest	100	38.61
Thigh/Knee	56	21.62
Shin/Calf	58	22.39
Lower Leg/Ankle	4	1.54

Table 3

Part of the region	m_f count in Skin-snip	% distribution in the region
Iliac crest	100	45.87
Thigh/Knee	56	25.69
Shin/Calf	58	26.61
Ankle	4	01.83

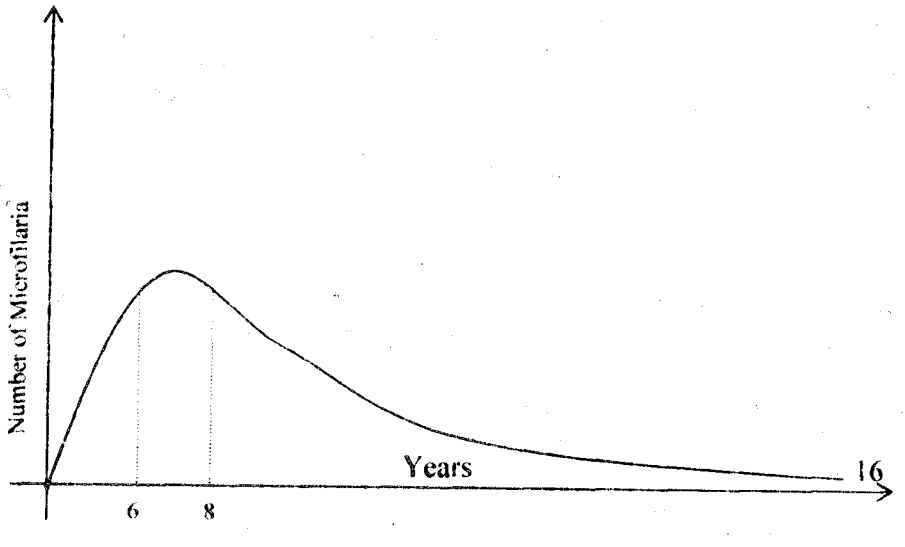
The Models

We shall consider this in two major parts. One of the models will be that showing the daily microfilaria output by the available Onchocerca worms in the host body while the next will be the model estimating the total microfilaria load in the body of the host. Thus, we have:

Model on Daily Microfilarial Output

To be able to get this, we shall get or know the worm load in the host, the level of immunity of the host and the microfilaria load already in the host that is below the threshold level. Also important here are the ages of these worms. However, if the host have been in the area for quite a long time, it is expected that the usual age distribution of the worms must have been established. From the works on the history of the worms as presented by Schulz-key (1990),), Schulz-key and Karam (1984), Schulz-key and Karam (1986), Karam *et al* (1987) and Schulz-key (1988), the bulk of the reproduction of the microfilaria comes from the worms in their 6^{th} – 8^{th} year followed by the aging ones (that is, above 8 years) and finally the new ones (that is, below 6 years). Also it is known from the work of Schulz-key (1988) that each worm has a reproduction cycle which is between 2 – 4 months. Thus, our model here reflects the microfilaria released by the worms at those periods of the cycle when it will be able to produce the microfilaria. New worms are only allowed to develop by the host's defense system when the microfilaria load in the body is below the established threshold level according to the body size of the host. The reduction in the threshold level is as a result of the aging of the Onchocerca Volvulus worms. Thus, to get the total daily output by the worm, we shall first consider a single worm and then extrapolate to the entire worm load in the body of the host.

For a particular worm, factors that play important role in the daily output are the age of the worm, the size of the host, the threshold level of the worm in the host, and probably the host's immune system. One other very important factor is the presence of other worms, their ages and even their daily output. The daily output of a particular worm from day of inoculation to death even though they are cyclic, can be shown pictorially as below for the period that the worm releases microfilaria.



For the model that represents such daily output to be built, let us make the following representations:
w_i = the definition of the particular worm of interest as i
x = age of the worm
s = surface area (size) of the host measured in M^2
D_0 = daily output by the particular worm
Using these variables, we develop the model as:

$$D_0 = axe^{-bx^3} \qquad 1.0$$

where a and b are constants to be determined. Using the information in the reproductive biology of Onchocerca Volvulus made by Schulz-key (1990) where he stated that daily reproductive range of the worms is 700 – 1500 microfilaria, we can estimate the constants a and b so that our model becomes on the average of 1200 daily as:

$$D_0 = 250xe^{-0.001x^3} \quad \text{for a = 250 and b = 0.001} \qquad 2.0$$

From this model for a particular worm, we can get the general daily output by the worms in the host's system. Since the presence of the worms affect the daily output of other worms, we have the model representing the total daily output of the worms as:

$$D_{T_0} = \sum_i^n \eta_i w_i \sum_i^n w_i D_{0i} \quad \text{for } i \neq j \qquad 3.0$$

where $\eta_i w_i$ stands for the inhibiting effect of w_i on the reproductive capacity of worm w_i and D_0 , represents the daily output of worm (w_i) as given by equation (2.0) and D_{T0} is the total daily output. Having got this daily total microfilaria output by Onchocerca worms in the host, let us now estimate the microfilaria load in the entire system of the host.

Model on the Microfilarial load in the host

This model shall be for a patient who had resided in an endemic area of this disease for a period that enabled the proper establishment of the required threshold levels of both the worm and the microfilaria. As such, the principal factors of interest are the surface

area of the host's part from where the skin-snip was taken, the microfilaria number in the skin-snip sample, the host's immune system and the total daily output by the worms in the host. We shall consider all these factors in relation to what obtains in our standard indicated in Table 3.

Now, let us make the following representations:

D_i = total microfilaria load in the part of the host
D_r = Total microfilaria load in the region below and including the iliac crest
D_b = total microfilaria load in the entire body of the host
m_f = number of microfilaria in the skin-snip taken below the iliac crest
m_p = number of microfilaria in the corresponding part as in m_f as in Table 3
A_e = estimated surface area of this part from where the skin-snip was taken
A_c = Corresponding surface area of this part as given in Table 3
p_p = Percentage microfilaria distribution in this part as in Table 3
p_r = Remaining percentage microfilaria distribution in other parts of the host's body Below and including the iliac crest.

With these representations, we obtain the model for the microfilarial load in a particular part of the body of the host where a skin-snip sample was taken as:

$$D_i \quad \alpha \quad \frac{m_f}{m_p} \times \frac{A_e}{A_c} \quad = \quad \lambda_i \times \frac{m_f}{m_p} \times \frac{A_e}{A_c} \qquad 4.0$$

where λ_i is a proportionality constant whose value depends on the particular part of interest.

For the total microfilaria load in the entire region below and including the iliac crest, we have that

$$D_r \quad = \quad D_i \times \frac{p_r}{p_p} \quad = \quad \lambda_i \times \frac{m_f}{m_p} \times \frac{A_e}{A_c} \times \frac{p_r}{p_p} \qquad 5.0$$

Now since the Microfilaria concentration in the iliac crest and below constitutes about 84.17% of those in the entire body, we then have the ratio of the microfilaria concentration in the entire body to that in this region as:

$$\frac{100}{84.17} = 1.188 \quad \Rightarrow \quad 1.188:1$$

Hence, the total microfilaria load or concentration in the entire body based on the estimated microfilaria load in this region is:

$$D_b = D_r \times 1.188 = 1.188 \quad \times \quad \lambda_i \times \frac{m_f}{m_p} \times \frac{A_e}{A_c} \times \frac{p_r}{p_p} \qquad 6.0$$

In equation (6.0), m_p, p_r, p_p and A_c are all relatively known constants. This is because once the required point for the sample test is chosen, then the values of these constants are known and explicit as indicated in Table 3. However, the only unknown variables are m_f and A_e, which can be quantitatively and experimentally measured. As estimated earlier, λ_i , though a constant, is not constant throughout the parts in the region. However, it is constant in a particular part irrespective of the body surface area or microfilaria count in a skin-snip from the area. Hence, λ_i must be estimated and known for the various areas of interest as will be shown later.

Analysis of Results

Equation (2.0) gives the expression for the estimate of the daily microfilaria output by a particular worm while equation (3.0) is the estimation of the total daily microfilaria output by the entire Onchocerca worms in the human host. The conditions for the validity of these equations had been given but one prime condition is that the human host must have lived long enough in the endemic area with proper exposure to ensure the attainment of the threshold levels of both the worm and the microfilaria. If however the human host does not satisfy this condition, then the equations may not properly apply and thus will need modifications. In equation (6.0) all the relatively known constants can be regarded as a single constant for a particular individual so that this equation can be re-written as:

$$D_b = \beta \lambda_i m_f \times \frac{p_r}{p_p} \qquad \text{where}$$

$$\beta = 1.188 \times \frac{A_e}{m_p A_c}$$

However, we shall use the expression for the total microfilaria load at the region to calculate the values for λ_i for the different parts. Thus, we have the values for λ_i as:

Part of the region	Value of λ_i
Iliac crest	7132603.0
Thigh/Knee	2909874.0
Shin/Calf	3051865.0
Ankle	157776.0

To arrive at these values for λ_i, we have assumed that the microfilaria load is the average of the range given and thus, 10×10^6. This shall therefore imply that if there is deviation in the range, which might result from the strain of the Blackfly, then the values for λ_i will change and need to be recomputed.

In conclusion. Once we are able to measure the microfilaria load in a given skin-snip sample taken below the iliac crest as well as the surface area of that particular part (e.g. the thigh/Knee), we can always estimate the microfilaria load in the entire body of the human host. We need not take samples from the various parts of the body. The advantages of this model over the method where skin-snip samples were taken from different parts of the body of the patient are many. The most important of these is that women in particular are saved from the humiliation and agony of asking them to expose their iliac crest (seen traditionally as a taboo in Africa) to a stranger. Secondly, it saves the scientists the pains and inaccuracies arising from having to take skin-snip samples from various parts of the body of the patient.

I therefore recommend that this model be used by our scientists in the estimation of the microfilaria load and the treatment of the disease in a patient.

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