The risk and dynamics of onchocerciasis recrudescence after cessation of vector control

A.P. Plaisier,¹ G.J. van Oortmarssen,² J. Remme,³ E.S. Alley,⁴ & J.D.F. Habbema⁵

Using a computer simulation study, we have investigated the risk and dynamics of onchocerciasis recrudescence after stopping vector control, in order to provide guidelines for operational decision-making in the Onchocerciasis Control Programme in West Africa (OCP). For this purpose, we used the micro-simulation model ONCHOSIM to predict for periods of 9–15 years of vector control the ensuing risk and dynamics of recrudescence in an onchocerciasis focus.

The model was quantified and validated using OCP evaluation and field research data. A range of plausible values was determined for important confounding parameters, i.e., vector biting rate, variation in exposure between individuals, parasite life span, and the relation between skin microfilarial load and vector infection. Different model quantifications were used in order to take account of the possible confounding effect of these parameters on the prediction of recrudescence.

In the absence of immigration of infected humans or invasion by infected flies, the model predicts that 14 years of full-scale vector control are required to reduce the risk of recrudescence to less than 1%. The risk depends, in particular, on the vector biting rate, and this has implications for the planning of post-larviciding surveillance. Recrudescence will be a relatively slow process, and its rate will depend on the duration of vector control. Even if vector control were stopped too early, i.e., after 12–13 years in a highly endemic area, it would take more than 20 years before the intensity of infection in the community would reach levels of public health importance.

Introduction

The objective of the Onchocerciasis Control Programme in West Africa (OCP) is to control onchocerciasis as a disease of public health and socioeconomic importance and to ensure that there will be no recrudescence thereafter (1). The strategy has been to interrupt transmission by vector control through larviciding, and this has been very successful. After 8–10 years of control operations, onchocerciasis was no longer a public health problem in more than 90% of the original OCP area (2), and after 12–14 years the prevalence of infection had fallen to very low levels or zero in most of this area (3, 4). Because of the major decline in the parasite reservoir and the high costs of aerial larviciding, it was important to determine how many years of successful vector control were needed before the operations could be discontinued, and the vector allowed to return, without running an unacceptable risk of onchocerciasis recrudescence thereafter.

The risk of recrudescence depends on the interaction between many factors. This made it necessary to use an epidemiological model to study the required duration of vector control. The computer simulation model ONCHOSIM (5), which has been developed to analyse epidemiological trends and to evaluate prospectively alternative control strategies, simulates the transmission of onchocerciasis and the effects of vector control and chemotherapy (6, 7). Using this model, we have investigated the risk and dynamics of recrudescence after different periods of vector control in an onchocerciasis focus. Reported is the impact of the major confounding model parameters on recrudescence and on the recommendations about the required duration of vector control.

Materials and methods

Simulation of recrudescence

The ONCHOSIM model uses the technique of microsimulation; this involves the simultaneous simulation of the life-histories of individual persons and of individual female and male parasites in the
human host (5). Collectively, the simulated persons constitute the population of a hypothetical endemic focus. One of the most important outputs of the simulation is the microfilarial load in skin-snips for each member of the population. In order to facilitate detailed comparison with observed data, the results of the simulation are presented in the same statistical format that is used for the epidemiological evaluation of vector control in the OCP.

Fig. 1 illustrates the results obtained with ONCHOSIM for the simulation of a period of vector control and recrudescence thereafter. Soon after the start of control, the community microfilarial load (CMFL), i.e., the geometric mean number of microfilariae per skin-snip (mf/s) in adults (8), starts to decrease, followed by the mf prevalence. When vector control is interrupted after 11 years, new inoculated worms become productive after a delay of several years, and the trends reverse; the mf prevalence starts rising first, followed by the CMFL much later.

**Confounding model parameters**

The transmission and control of onchocerciasis are governed by many parameters, most of which also influence the risk and dynamics of recrudescence. The following parameters are very important in this respect: the pre- and postcontrol level of exposure to the bites of *Simulium* spp. and the exposure variation in a community; the life span of the *Onchocerca volvulus* worm and possible variations in this; and the infection level of biting flies as a function of the human skin mf density. Estimates for these important confounding parameters are discussed below. They are based on epidemiological data collected by the OCP, especially the frequency distributions of skin-snip counts obtained at various intervals since the start of control, and on experimental results.

**Exposure level (relative biting rate) and exposure heterogeneity**

After a given period of vector control, communities with a high precontrol endemicity level, and hence a high biting rate per person, have a higher risk of recrudescence than communities in less endemic areas. Analysis of the risk and dynamics of recrudescence for different endemic situations is, however, difficult because the real average biting rate per person in a village is not known. Reported values of the annual biting rate (ABR) apply to passive collection of flies close to the breeding sites (9). Although the ABRs are valuable for assessing the potential endemicity of an area and for monitoring the effects of vector control, the actual ABR experienced by villagers may be quite different. In the OCP area it has therefore not been possible to establish a direct relation between the average skin-snip count of a village and the precontrol ABR.

We have therefore defined a scale parameter (the relative biting rate (rbr)) to assess the biting rate relative to the skin-snip counts. A value of rbr = 1.0 corresponds to a biting rate in a village where the individuals are equally exposed and the mean mf/s is 100.

The risk of recrudescence is also influenced by the heterogeneity of exposure among members of a community. When the heterogeneity is high, infection will be concentrated in a few extremely highly exposed individuals, who will act as frequently bitten, highly infective sources of transmission. Exposure heterogeneity is quantified by the variation coefficient of the biting rate.

Estimates of the rbr and of the exposure variation coefficients for a village are based on the goodness-of-fit between observed and simulated skin-snip distributions. The estimates are not unique; using the procedure reported by Plaisier et al. (10), a good fit (with \( \chi^2_{0.05} \) as the critical point) can be obtained for a range of values of rbr and the coefficient of variation. Here, we analyse the recrudescence for two different quantifications of rbr and the variation coefficient in each of the villages of Tiercoura and Folonzo, Burkina Faso. The standard quantifications for both villages are shown in Table 1 as models 1 and 3, respectively. Models 2 and 4 represent quantifications that are among the most unfavourable from the point of view of recrudescence risk, but are nevertheless still compatible with the observed data for the two villages. Table 2 shows the observed precontrol CMFL and the precontrol mf/s distribution in the villages. Also, the simulated
The estimation of the risk and dynamics of recrudescence after cessation of vector control

Table 1: Model quantifications used for the determination of the risk and dynamics of recrudescence in the villages of Tiercoura and Folonzo, Burkina Faso

<table>
<thead>
<tr>
<th>Model number and designation</th>
<th>Relative biting rate</th>
<th>95th percentile life span (years)</th>
<th>L1-uptake curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (standard Tiercoura)</td>
<td>1.10 (0.36)*</td>
<td>13.7</td>
<td>I</td>
</tr>
<tr>
<td>2 (high-risk Tiercoura)</td>
<td>1.16 (0.52)</td>
<td>13.7</td>
<td>I</td>
</tr>
<tr>
<td>3 (standard Folonzo)</td>
<td>0.61 (0.52)</td>
<td>13.7</td>
<td>I</td>
</tr>
<tr>
<td>4 (high-risk Folonzo)</td>
<td>0.67 (0.68)</td>
<td>13.7</td>
<td>I</td>
</tr>
<tr>
<td>5 (low-risk life span)</td>
<td>1.10 (0.36)</td>
<td>12.8</td>
<td>I</td>
</tr>
<tr>
<td>6 (high-risk life span)</td>
<td>1.10 (0.36)</td>
<td>14.8</td>
<td>I</td>
</tr>
<tr>
<td>7 (high-risk L1-uptake)</td>
<td>1.10 (0.36)</td>
<td>13.7</td>
<td>II</td>
</tr>
</tbody>
</table>

* Figures in parentheses are the coefficients of variation.

Table 2: Characteristics of the reference villages of Tiercoura and Folonzo (for comparison, the simulated skin-snip count distributions of models 1–4 are shown)

| Village | River basin | 1975 census population* | Initial CMFL (mf/s)* | % of adults with an initial skin-snip count (mf/s) of:*
<table>
<thead>
<tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Tiercoura</td>
<td>Leraba</td>
<td>160 (66)</td>
<td>71</td>
<td>3.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<td>Model 3</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Model 4</td>
</tr>
</tbody>
</table>

* The first figure shown is the total population, while the figure in parentheses is the number of adults.
* mf/s = microfilariae per skin-snip.

mf/s distributions for models 1–4 are shown. It should be noted that, although in Tiercoura the observed CMFL (a geometric mean) is 71 mf/s, a large number of persons have a skin-snip count of > 128 mf/s; this is reflected in a relative biting rate of 1.10 in the standard quantification for Tiercoura.

Parasite life span

The estimation of the parasite’s reproductive life span has been reported in detail by Plaisier et al. (10). In the West African savanna, *O. volvulus* is estimated to live 9–11 years on average, while the variability is such that 95% of the parasites die before the age of 13–14 years. Especially the extreme longevity, as measured by the 95th percentile of the life span distribution, is important for recrudescence. For a mean life span of 10 years, the best fit for the 95th percentile is 13.7 years, and this value is used here as a standard quantification. The 95% confidence interval is estimated to be 12.8–14.8 years, and the risk and dynamics of recrudescence are analysed for the boundaries of this interval (models 5 and 6, respectively, in Table 1).

Skin microfilarial density, microfilarial uptake, and larval load of blackflies

The relationship between skin microfilarial density and the microfilarial uptake by biting flies is an important factor in the transmission of onchocerciasis. A number of studies have reported that the uptake increases with microfilarial density, but that saturation occurs at high densities (II). Infection levels of blackflies from the West African savanna suggest that, probably also because of the excess mortality of flies with very high larval loads, this saturation level is about 1.2 larvae per biting fly, and 2–3 larvae per infective fly, since, in general, the proportion of flies that engorge microfilariae does not exceed 50%, and most first-stage (L1) larvae

survive to the infective stage. However, if the parasite reservoir has been reduced by a long period of vector control, then in view of recrudescence, the capability of flies to engorge microfilariae at low skin densities rather than the saturation level, is important. This capability determines the degree of danger of the residual parasite reservoir for renewed transmission. Recently in the OCP area, a series of experiments has been conducted to determine the relationship between fly infection and skin microfilarial density. Volunteers with a known skin-snip count were exposed to blackflies, and the microfilarial load of the flies was then determined. Especially important are microfilariae that avoid encapsulation by the fly's peritrophic membrane and which can be considered to be the potentially infective larvae.

For the model, the relationship between the microfilarial density in human skin and the resulting number of L1 larvae in biting flies needs to be quantified (resulting in the L1-uptake curve). Based on experimental results, and using the procedure outlined in the Annex, a maximum likelihood estimate (MLE) was obtained for this relationship. The MLE determined for the saturation level of the larval load was 1.8 L1 larvae per fly (3.6 per infective fly). However, since the flies were dissected shortly after the blood-meal, excess mortality as a result of high larval loads could not be taken account of. Therefore, for the standard relationship in the simulations we set the saturation level at 1.2 L1 larvae per fly. Imposition of this restriction upon the relationship gives an MLE shown as curve I in Fig. 2. In the analysis, we tested also the impact of a relationship with the same initial slope as curve I, but with a saturation level of 0.8 L1 larvae per fly (1.6 larvae per infective fly, shown as curve II in Fig. 2; see also Table 1, model 7).

**Assessment of the risk and dynamics of recrudescence**

The analysis reports the risks and dynamics of recrudescence for the model quantifications shown in Table 1. For each of these models the recrudescence is analysed for several periods of vector control, ranging from 9 years to 15 years. To determine the risk for a given model and a given duration of control, we carried out 50 simulations. Because of the stochastic microsimulation approach, the outcomes for these 50 simulations are different, reflecting the chance character of the underlying processes. If 50 years after the end of vector control the simulated CMFL is still less than 10 mf/s, the given simulation is termed a “non-recrudescence” case. The risk of recrudescence was taken to be the fraction of the 50 simulations that lead to recrudescence. Logistic regression was used to smooth the risk as a function of the duration of control and to estimate the required duration of control needed to arrive at risk values of 50%, 5%, and 1% (see Fig. 3).

The dynamics of recrudescence is characterized by the time to reach a given CMFL after stopping control measures. Especially the time needed to establish a CMFL of 10 mf/s is considered, since at this load onchocercal blindness starts to become an important public health problem in a stable endemic situation (12). This period of time is denoted the “recrudescence time”. For comparison, we also examined the times needed to produce CMFLs that correspond to 25% and 75%, respectively, of the precontrol value.

**Basic assumptions and starting points**

The following underlying assumptions were made for all the simulations:
- the force of infection during the years preceding control is stable;
- the larviciding-based vector control effectively interrupts transmission;
- there is no migration of infected persons into the area; and
- there is no invasion by infected flies and only a slight invasion by uninfected flies.

Because of this invasion, the flies can repopulate the breeding sites, and the precontrol biting rate

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See footnote a, p. 171.

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**Fig. 2.** The two curves used in the study for the relationship between skin microfilarial density (skin-snip count) and the resulting number of L1 larvae in biting flies (L1-uptake).
will be reached in a few months after the end of larviciding (13, 14). In the simulations, the precontrol village consisted of about 200 individuals and the annual rate of population increase was about 2.5%.

Results

Biting rate and exposure heterogeneity

Fig. 3 shows the probability of recrudescence for different durations of vector control for models 1–4, which differ in the values of biting rate and exposure heterogeneity, and which represent the standard and high-risk models for Tiercoura and Folonzo (see Table 1). From Fig. 3 it can be inferred that the specific circumstances in a village markedly influence the recrudescence risk. Although both villages are hyperendemic, the duration of vector control required to reduce the risk to acceptable levels in Folonzo is shorter than that in Tiercoura. If for both villages the model is used that gives the best fit with the observed skin-snip data (standard Tiercoura and standard Folonzo), the risk of recrudescence in Tiercoura is 1% if vector control is continued for about 13.5 years. In Folonzo vector control needs to be carried out for about 11.5 years (i.e., 2 years less)

Fig. 3. Probability of recrudescence as a function of the duration of vector control determined using four different model quantifications. Bars show the 95% confidence intervals. The vertical dashed lines indicate the vector control period after which the risk of recrudescence is reduced to 50%, 5%, and 1%.

Fig. 4. Average period (including 95% confidence intervals) after cessation of vector control before a community microfilarial load (CMFL) of 10 mfl/s is reached, as a function of the duration of vector control in Tiercoura and Folonzo (models 1–4, Table 1). Results are shown only when at least 3 simulations showed recrudescence.

to achieve the same risk of recrudescence.

In Folonzo, to arrive at a risk of 1%, the high-risk model predicts a vector control period of 13 years, i.e., 1.5 years more than the standard model. Similarly, in Tiercoura the high-risk model predicts 14 years, i.e., only 0.5 years longer than the standard model. The most plausible explanation for the different behaviour of the two high-risk models is that in a holoendemic village such as Tiercoura, the risk of recrudescence is mainly determined by the life span of *O. volvulus*, so that increasing the fly biting rate only causes a minimal increase in the risk. In Folonzo, however, because of the lower pre- and postcontrol infection loads of the human hosts, the risk of recrudescence is also determined by the mating chances and subsequent production of microfilariae by the few remaining parasites. Here, a slight increase in biting rate (which causes the overall worm load to increase) and exposure heterogeneity (which favours clustering of the worms, and hence increases the mating chances) has more impact on the risk of recrudescence.

Fig. 4 shows the recrudescence time, i.e., the period after cessation of vector control for the CMFL to reach 10 mfl/s. With all four models, the recrudescence time increases with the duration of vector control. Extending the duration of control therefore not only reduces the risk of recrudescence, but also reduces the rate at which the epidemiological indices increase. Furthermore, Fig. 4 indicates that for a given period of control the recrudescence time becomes shorter as the biting rate and exposure heterogeneity increase. Also the difference between the recrudescence times for the standard and high-risk models for Folonzo is greater than that for these
models in Tiercoura. In the high-risk Folonzo model the clustering of worms resulting in increased chances of mating and production of microfilariae had a greater impact than in the high-risk Tiercoura model.

With the standard model for Folonzo (model 3), 9 years of vector control, although not sufficient to prevent recrudescence, guarantee that for more than 25 years after the end of control activities the CMFL will still be below a dangerous level. For Tiercoura this recrudescence time is less than 10 years. For longer periods of control, the differences in recrudescence times between the various models remain virtually unchanged, notwithstanding the decreased recrudescence risk.

The times after control which elapses until 25% and 75% of the precontrol CMFLs are reached are shown in Fig. 5 for the standard models for Tiercoura and Folonzo. The clear differences between the two models demonstrate that not only the absolute recrudescence rate, but also the rate relative to the precontrol situation, is higher for villages with a higher endemicity. Since for both villages the plots for the 25% and 75% levels have the same slope, it can be concluded that if recrudescence exceeds 25% of the precontrol CMFL (which for Folonzo is still less than 10 mf/s), the rate of progression no longer depends on the duration of vector control.

**O. volvulus life span**

The effect of different values for the life span of *O. volvulus* on the results is shown in Table 3. As might be expected, the period of vector control needed to reduce the risk of recrudescence to acceptable levels increases with the value of the 95th percentile of the life span probability distribution. Using the most unfavourable assumption for the 95th percentile (5% of the worms reach an age of \(\geq 14.8\) years), we estimate that in a village such as Tiercoura vector control operations have to be continued for 14 years and 14.5 years, respectively, to reduce the recrudescence risk to 5% and 1%.

Also, the recrudescence time is a function of the *O. volvulus* life expectancy. After 12 years of control, the time to reach a CMFL of 10 mf/s increases from 16 years to 34 years when the 95th percentile of the life span decreases from 14.8 years to 12.8 years.

**L1-uptake**

Table 3 also shows the impact of two different assumptions about the L1-uptake of *Simulium* spp. as a function of the skin microfilarial density. For

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**Table 3:** Duration of vector control to reduce the risk of recrudescence to 50%, 5%, and 1%, and the recrudescence time after 12 years of vector control, for three different assumptions about the 95th percentile of the life span distribution of the adult worm, and two L1-uptake curves

<table>
<thead>
<tr>
<th>Duration of control (years) at a risk of recrudescence of:</th>
<th>50%</th>
<th>5%</th>
<th>1%</th>
<th>Recrudescence time (years)</th>
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</thead>
<tbody>
<tr>
<td><strong>95th percentile life span (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12.8</td>
<td>5</td>
<td>12.2</td>
<td>12.5</td>
<td>12.7</td>
</tr>
<tr>
<td>13.7</td>
<td>1</td>
<td>12.4</td>
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</tr>
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<td>14.8</td>
<td>6</td>
<td>13.3</td>
<td>14.0</td>
<td>14.5</td>
</tr>
<tr>
<td><strong>L1-uptake curve</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>1</td>
<td>12.4</td>
<td>13.0</td>
<td>13.4</td>
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<tr>
<td>II</td>
<td>7</td>
<td>12.8</td>
<td>13.4</td>
<td>13.8</td>
</tr>
</tbody>
</table>

* Figures in parentheses are 95% confidence intervals.
the curve with a low saturation level at high skin densities (curve II, Fig. 2), the risk of recrudescence is greater than that with the standard curve (curve I): about 6 months of additional vector control are required to produce recrudescence risks comparable with those obtained with the standard Tiercoura model. To reduce the risk to about 1%, approximately 14 years of vector control are required with the L1-uptake curve II. The high-risk characteristic of curve II arises because, to maintain a given precontrol endemicity level, the low saturation level must be balanced by higher values for other transmission parameters (e.g., the probability that infectious larvae transmitted by biting flies become a mature parasite). After vector control, before saturation has occurred, these higher values increase the recrudescence risk.

If vector control is stopped after 12 years (risk of recrudescence, about 100%), approximately 20 years are required to arrive at a CMFL of 10 mf/s; this is 5 years less than with the standard uptake curve I.

Discussion

The decision to stop vector control after many years of interruption of onchocerciasis transmission in the well-protected central OCP area is a difficult one to make. Premature interruption of vector control, when the residual parasite reservoir is still too large, may jeopardize all the achievements obtained so far and result in the recrudescence of onchocerciasis as a public health problem. On the other hand, aerial larviciding operations are very costly and any unnecessary continuation of them would prevent the use of funds where they are urgently needed, e.g., in the extension areas of the OCP where vector control has only recently been started.

A further complication is that there are no precedents that can serve as guidelines. The decision-making process, therefore, has to rely exclusively on the optimal use of epidemiological information and on current understanding of the dynamics of onchocerciasis transmission, infection, and about the disease itself. Epidemiological modelling has been helpful in this respect. The ONCHOSIM computer simulation model has been used to carry out an integral assessment of the relevant information and to provide objective predictions for the risk and dynamics of recrudescence after different periods of vector control.

Table 4 summarizes the recrudescence risks for the different models tested. The data indicate that in areas with the highest potential risk (such as Tiercoura) 14 years of vector control are required to reduce the risk of recrudescence to < 1% (estimated using the most plausible quantifications of the confounding parameters). Predictions for other quantifications for the confounding parameters, which are also compatible with the epidemiological data for the OCP, show that in the worst case after 14 years the risk of recrudescence is still greater than 1%, but less than 5%.

The simulations show that the risk of recrudescence is dependent on the local endemicity level and the associated relative vector biting rate. For the holoendemic village of Tiercoura the simulations indicate that the required duration of vector control is 14 years, while for the hyperendemic village of Folonzo they indicate 1.5–2 years less than this. The endemicity level in Folonzo (in terms of CMFL) was only half that in Tiercoura, where the precontrol CMFL of 70 mf/s made it one of the most endemic onchocerciasis villages in the original OCP area. The dependency of recrudescence on the biting rate also has implications for the epidemiological surveillance system that will be set up during the post-larviciding period to detect as early as possible eventual recrudescence. The biting rate varies greatly between villages and it is essential that the surveillance

<table>
<thead>
<tr>
<th>Model number and designation</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
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<tbody>
<tr>
<td>1 (standard Tiercoura)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>±</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2 (high-risk Tiercoura)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>3 (standard Folonzo)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>4 (high-risk Folonzo)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>5 (low-risk life span)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>6 (high-risk life span)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>±</td>
<td>–</td>
</tr>
<tr>
<td>7 (high-risk L1-uptake)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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</table>

* + = risk > 5%; ± = 1% < risk < 5%; – = risk < 1%.
will be carried out in villages where the vector biting rate per inhabitant is extremely high.

It has long been recognized that the required duration of blackfly control depends largely on the life span of *O. volvulus* (8, 15). Our findings confirm this and show that the remaining uncertainty about the upper limit of the life span distribution, which was estimated from longitudinal epidemiological skin-snip data from the OCP, has a significant effect on the predicted risk of recrudescence. Using the limits of the confidence interval for the age at which 95% of the worms have died, we calculated that the required duration of vector control was 12.7–14.5 years. In an earlier attempt to project the epidemiological trends after cessation of vector control, Dietz used a model in which he assumed an exponentially distributed life span for the worms with a mean of 8.3 years (16). From this assumption, which could not be verified against longitudinal data, it follows that 5% of the parasites lived for more than 25 years. Dietz's implausible assumption about the life span of *O. volvulus* therefore explains why he predicted recrudescence even after 20 years' interruption of transmission.

Different quantifications of the relationship between L1-uptake and the skin microfilarial load of human hosts also affect the predicted risk and rate of recrudescence, although the effect was less than we expected. The L1-uptake curve with an early saturation point, and hence a high ratio between the initial slope and the saturation level (curve II), resulted in the greatest risk and the shortest recrudescence time. In view of the available experimental data, curves with a lower saturation point and a greater initial slope seem improbable (see Annex). However, it should be noted that in our simulations the levelling off of the L1-uptake curves at higher microfilarial loads is the most important density-dependent regulating mechanism in the transmission of onchocerciasis. Other regulation mechanisms may, however, exist (17) and could increase the risk of recrudescence. It can, therefore, be argued that the realism of curve II would increase if the L1-uptake curve in our model took other possible regulating mechanisms into account.

Our study has clarified several aspects of the dynamics of recrudescence of onchocerciasis. The recrudescence time, i.e., the time after cessation of control for the CMFL to reach 10 mf/s, depends on the duration of the preceding period of vector control: the longer the period of control, the longer it takes for the prevalence and intensity of infection to climb again to significant levels. The recrudescence time increases exponentially as the period of vector control approaches 14 years, and in this respect the last few years of vector control are the most cost-effective. After 10 years of vector control, recrudescence is relatively slow. Even in instances of recrudescence after 12–13 years of vector control, it would take more than 20 years for the CMFL to reach levels of public health importance.

These predictions for recrudescence apply only to situations where no other intervention is undertaken after cessation of vector control. However, it is important to note that ivermectin, an effective and well-tolerated macrofilaricide, has recently become available for the treatment of onchocerciasis, while research is continuing to develop a macrofilaricide (18). Although some studies suggest that the potential of ivermectin to control transmission in an endemic area is limited (7, 14), it may play an important role in controlling recrudescence.

Our conclusions depend on some basic assumptions, i.e., the existence of a stable endemic situation during the precontrol period, complete interruption of transmission during the vector control period, no reinvasion by infective flies, and no immigration of infected humans. There are, however, many situations where these assumptions do not hold. Variations in epidemiological trends during blackfly control have been attributed to major variations in transmission during precontrol years (4). Isolated foci have been identified where there has been a relapse in transmission (3), while the western and eastern flanks of the OCP area were reinvaded by infective flies (19). Immigration of infected individuals has not yet been proven to lead to problems (20), but more extensive field studies are currently being carried out, and computer simulation studies are planned to investigate the effects of immigration by infected persons and of reinvasion by infective flies.

There will be other situations where not all the assumptions made in the current analysis will hold true. However, these do not invalidate the above analysis, which is intended to provide general guidelines for operational decision-making on cessation of larviciding. For each situation the decision will have to be based on a critical analysis of the relevant epidemiological and entomological information using classical statistical methods, epidemiological modelling, and a large amount of common sense.

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Résumé
Risque et dynamique de la recrudescence de l’onchocercose après arrêt de la lutte antivectorielle

L’objectif du Programme de lutte contre l’onchocercose en Afrique de l’Ouest (OCP) est de combattre l’onchocercose en tant que maladie ayant d’importantes répercussions en santé publique et sur le plan socio-économique, et d’assurer l’absence de recrudescence. Le programme a pour stratégie d’interrompre la transmission par la lutte antivectorielle, au moyen d’épandage de larvicides. On a ainsi obtenu de très bons résultats, avec une très importante diminution du réservoir de parasites. En raison du coût élevé de l’épandage aérien de larvicides, il importe de déterminer au bout de combien d’années de lutte antivectorielle réussie les opérations peuvent être interrompues, et le vecteur reconstitué, sans que cela comporte un risque unacceptable de recrudescence de l’onchocercose.

Le but de la présente analyse est de fournir des directives pour la prise de décision dans la zone de l’OCP, en étudiant le risque et la dynamique de la recrudescence après arrêt de la lutte antivectorielle. Du fait du grand nombre de facteurs en cause, la construction d’un modèle épidémiologique est un bon moyen d’étude. Le modèle de microsimulation ONCHOSIM a été utilisé pour déterminer, pour des périodes de 9 à 15 ans de lutte antivectorielle, le risque et la dynamique de la recrudescence dans un foyer d’onchocercose.

Le modèle a été quantifié et validé au moyen de données OCP provenant de l’évaluation et de la recherche sur le terrain. On a déterminé des éventails de valeurs plausibles pour divers paramètres confondants, à savoir le taux d’agressivité du vecteur, la variation de l’exposition d’un individu à l’autre, la durée de vie du parasite, et la relation entre la charge microfilarienne cutanée et le degré d’infestation du vecteur. On a obtenu les valeurs correspondant à ces paramètres en ajustant le modèle à la situation antérieure aux opérations de lutte et d’après les tendances observées au cours de la lutte antivectorielle dans un certain nombre de villages, dont Tiercoura (Burkina Faso), qui figurait parmi les villages de plus forte endémicité dans la région OCP d’origine. Différentes quantifications du modèle ont été utilisées pour prévoir la recrudescence, afin de tenir compte de l’effet confondant possible de tous ces paramètres.

Selon ce modèle, il est prévu qu’en l’absence d’immigration de sujets infestés ou d’invasion de mouches infestées, il faut 14 ans de lutte antivectorielle à grande échelle pour abaisser le risque de recrudescence à moins de 1%. Cette prévision s’applique à Tiercoura. Dans les localités de plus faible endémicité, c’est-à-dire avec un plus faible taux d’agressivité de Simulium, il est prévu que 12 ans de lutte environ suffiraient pour réduire le risque à moins de 1%. Le risque de recrudescence est également influencé par les hypothèses quant à l’âge auquel la plus grande partie des parasites atteignent la fin de leur période reproductive. En donnant à ce paramètre sa valeur la plus élevée (donc la moins favorable), il y aurait encore un risque de recrudescence d’environ 5% dans les villages de forte endémicité au bout de 14 ans de lutte. Comme le risque semble dépendre aussi en particulier du taux d’agressivité du vecteur, il faudrait spécialement poursuivre la surveillance post-lutte dans les villages où de forts taux d’agressivité sont prévisibles.

La recrudescence serait un processus relativement lent, son évolution dépendant de la durée de la lutte antivectorielle. Il est prévu que, même si cette lutte devait être arrêtée prématurément, c’est-à-dire au bout de 12 à 13 ans dans une zone de forte endémicité, il faudrait plus de 20 ans avant que l’intensité de l’infestation dans la communauté atteigne des taux préoccupants pour la santé publique. La recrudescence réapparaîtra toutefois plus rapidement, 5 à 9 ans plus tôt, si davantage de parasites survivent à la période de lutte antivectorielle ou si les simulies revenues dans la région sont davantage infestées au contact du réservoir humain résiduel.

References


Annex

To describe the mean L1-uptake of 50 flies (y) as a function of the skin-snip count (x), we use the following relationship:

\[ y = a(1 - e^{-bx}) (1 + e^{-cx}) \]

where \(a(1 - e^{-bx})\) describes a simple saturation curve with saturation level \(a\) and initial slope \(ab\), and \((1 + e^{-cx})\) permits adjustment of the initial slope. At a given skin load, \(x_i\), the uptake follows a negative binomial distribution with mean, \(y_i\), and parameter of aggregation, \(k\). It is further assumed that \(k\) is independent of \(x\).

Using a downhill simplex method (21), this model is fitted to the experimental data by maximizing the likelihood function (i.e., searching for the maximum likelihood estimation, MLE). The MLE gives values for \(a, b, c,\) and \(k\) of 1.82, 0.0096, 0.0677, and 8.0, respectively. Restricting the saturation level to 1.2 larvae per fly (2.4 per infective fly) in the above relationship, implies that \(a = 1.2\). The MLE for this restricted relationship gives values for \(b, c,\) and \(k\) of 0.0213, 0.0861, and 6.6, respectively.

For curve II the values for \(a, b,\) and \(c\) were fixed at 0.8, 0.044, and 0.1686, respectively. With this relationship the MLE gives a value for \(k\) of 4.4. A likelihood ratio test of curve II to curve I results in a P-value of slightly more than 0.05, so that curve II lies within a 95% confidence region of curve I.