The predicted and observed decline in onchocerciasis infection during 14 years of successful control of *Simulium* spp. in West Africa

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In 55 villages from the well-protected central area of the Onchocerciasis Control Programme in West Africa (OCP), skin snip surveys have been carried out at regular intervals since the programme started, and the latest round of surveys was undertaken after 12–14 years of successful vector control. The observed trends in the prevalence and intensity of onchocerciasis infection in cohorts of adults were compared with the trends predicted using a host–parasite model. After 12–14 years of control the community microfilarial load (CMFL) was close to zero in all villages. During the last few years of control, the prevalence of infection declined at an accelerated rate, and this was predicted by the model. There was generally good agreement between observed and predicted trends. The predictions were based on an estimated average duration of infection of 10.4 years, which corresponds to a mean reproductive lifespan for *Onchocerca volvulus* of 9–9.5 years, and an upper limit of 15 years for 95% of the infections. Differences between the observed and predicted data included the trend in CMFL between the first and second surveys, which in 18 villages did not show the predicted decline. Furthermore, the observed final decline in prevalence was faster than predicted in the north-eastern part of the central OCP area. After 14 years of vector control, the level of onchocerciasis has fallen to such a low level that consideration is being given to ending larviciding.

Introduction

Since it began in 1975, the strategy of the Onchocerciasis Control Programme in West Africa (OCP) has been to reduce transmission of the parasite *Onchocerca volvulus* to insignificant levels by means of vector control, and to maintain these levels for sufficiently long to allow the initial reservoir of the parasite to fall so low that vector control can be safely interrupted (1).

The period of successful vector control required depends primarily on the duration of onchocerciasis infection, which is a function of the reproductive lifespan of the adult *O. volvulus* and the longevity of their microfilariae. In 1975, little was known about the duration of onchocerciasis infection. The only relevant information was from East Africa, where cross-sectional skin snip surveys in three foci showed that active onchocerciasis infection still persisted 9–11 years after the elimination of the vector, while there was no active infection in another focus 18 years after interruption of transmission (2). As a result, vector control in the OCP area was originally planned to last for a period of 20 years (3).

Since 1975, epidemiological follow-up surveys have been undertaken in selected indicator villages from all the major river basins in the OCP area. The objective of these surveys was to evaluate the impact of vector control on transmission and on disease, and to document the decline in infection levels in the human population. For long-term planning and funding of OCP, it was important to arrive at accurate estimates of the reproductive lifespan of *O. volvulus* and to predict how many years of vector control were still needed before the parasite reservoir would fall to an insignificant level. Epidemiological modelling was used to evaluate the data. The first step was the development of a force-of-infection model for onchocerciasis (4) that facilitated a better understanding of age-specific epidemiological trends and resulted in new statistical methods for the comparative analysis of the epidemiological data. The use of this model led also to a preliminary estimate of 11 years for the average duration of onchocerciasis infection.

The force-of-infection model was based on certain simplifications, notably the assumption that the duration of onchocerciasis infection was constant, which made it inappropriate for the prediction of the final decline in the parasite reservoir. A more sophisticated model, based on the simulation of individual life-histories of human hosts and adult female worms,

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was therefore developed. The first predictions with this host–parasite model were made in 1985, and these indicate that onchocerciasis infection should be virtually eliminated 15 years after interruption of transmission. Since then, the model has been used to analyse and evaluate various epidemiological trends (5–7).

From December 1988 to February 1989, OCP carried out epidemiological evaluations in indicator villages from the original programme area, which had been under vector control for 12–14 years. Because of the predictions made by the host–parasite model, it was expected that the results would provide important information on the impact of vector control on the parasite reservoir and on the reproductive lifespan of *O. volvulus*. Here, we report the trends observed for the intensity and prevalence of infection during 12–14 years of successful vector control and compare them with the predictions that were made in 1985 using the host–parasite model.

**Materials and methods**

**Skin snip surveys**

In all epidemiological surveys in the OCP area, two skin snips are taken from the iliac crest of each person covered. The snips are incubated in distilled water for 30 minutes, subsequently examined microscopically for the presence of *O. volvulus* microfilariae (mf), and the numbers of microfilariae per snip (mf/s) are counted (8). The results are recorded on standard forms.

**Study population**

**Selection of villages.** The epidemiological follow-up surveys that were carried out from December 1988 to February 1989 in the original OCP area covered 90 villages. In the present analysis, only villages in well-protected areas were included; excluded were those from the eastern and western border area that have been reinvaded by infective *Simulium* spp. from outside the OCP area (5). Also excluded were villages from foci where there had been a relapse in transmission during the control period and those from areas where vector control had been incomplete. Furthermore, only villages that had had at least four follow-up surveys during the control period were included. This left a total of 55 villages, which represented all the major river basins from the well-protected central OCP area (see Fig. 1). Eighteen of these villages are located in the Phase I area, where vector control started in 1975 and has been continued since then. Eleven villages are in the Phase II area, where control started in 1976; and 26 villages from the Phase III area, which officially came under control in 1977. The duration of control in the villages in the Phase III area of the Koulpeolgo river valley in Burkina Faso was taken as 13 years, because larviciding along the White Volta in 1976 resulted in the complete protection of the neighbouring Koulpeolgo basin (9).

**Cohort populations.** Here, we describe the decline in onchocerciasis infection after interruption of transmission, with reference to the reproductive lifespan of *O. volvulus*. The approach used was to analyse the trend in the prevalence and intensity of onchocerciasis infection in cohorts of adults aged 20 years or more at the precontrol survey (4). Only adults who had undergone a skin snip examination at each survey were included in the analysis. Since most indicator villages were small and some villages had been surveyed as many as seven times, this selection criterion occasionally resulted in small cohorts. A total of 1536 adults were included in the analysis, and the average cohort size was 28 (range, 9–89).

**Host–parasite model**

The host–parasite model was developed specifically to analyse the impact of vector control on the parasite reservoir in human populations. This approach uses the technique of microsimulation (10), which allows great flexibility in modelling the dynamics of onchocerciasis infection. The parameters concerned with the initial endemicity level, exposure heterogeneity, longevity, and the level of microfilariae produced by adult female parasites are first specified, and the model is then used to obtain trends in microfilarial loads in human populations (expressed as the distribution and summary statistics of microfilarial counts in skin snips). Furthermore, the model also provides information about the distribution of adult female parasites, distinguishing between alive and dead, and calcified and non-calcified worms. The model is described in more detail in the Annex.

The model was quantified using literature data and by fitting it to the observed epidemiological results for the first 8–9 years of control in the OCP area from 1975 to 1984. The quantification outlined below was obtained and has been used since 1985 to predict the epidemiological trends during the vector control period. The mean longevity of infection was estimated to be 11 years for non-calcifying and 8 years for calcifying worms. In accordance with the

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results of nodulectomy surveys (9), it was assumed that 20% of the adult worms would eventually calcify. The estimated variability of the longevity on infection was such that 95% of longevities were less than 15 years. After a prepatent period of 1 year, the average contribution of a female worm to the skin snip count remained constant at 5.2 microfilariae until the worm was 8 years of age. Subsequently, the microfilariae contribution was decreased annually by 0.4 microfilariae per adult female worm in order to simulate the observed reduction in productivity of aged female worms (9). The standard deviation for the human exposure index was 0.86 and the coefficient of variation for the dispersal of microfilariae in skin snip counts was 0.84.

Data analysis
The skin snip data were analysed on personal computers using routine programs developed by OCP. The precontrol endemicity level of a village is characterized by the community microfilarial load (CMFL), which is the geometric mean number of microfilariae per snip in adults aged at least 20 years (4). The CMFL was also used to describe the intensity of onchocerciasis infection in cohort populations during the control period. The observed proportion of positive skin snips in a cohort during the last survey was compared with the proportion predicted for villages with the same precontrol endemicity level and duration of control. The goodness-of-fit between observed and predicted proportions was tested using a $\chi^2$ test with Yates' correction for continuity. In villages that exhibited a major increase in CMFL between the first and second survey, the CMFL for the second survey was taken as the basis for determining the endemicity level and the prediction of the epidemiological trends during the remaining control period.
Results

Predicted trends in onchocerciasis infection in cohorts of adults

The predicted trends in the CMFL for different initial endemicity levels are shown in Fig. 2. These predictions are the result of simulations in which the precontrol force-of-infection was taken to be 0.18, 0.51, 1.45, 2.75, and 3.95 infections per person per year, respectively. The results indicate that after a delay equal to the prepatent period, the CMFL should fall almost linearly during the first 8 years of control and tail off to values close to zero after 12–14 years. The absolute decline in the CMFL depends on the initial endemicity level.

Fig. 3 shows the predicted trends in the prevalence of infection in cohorts of adults—the higher the initial endemicity level, the longer it takes before the prevalence begins to fall but the more rapid is the rate of final descent. The host-parasite model predicts that onchocerciasis will have virtually died out after 15 years of control, when only very few positive skin snips should be found, mainly in villages with the highest precontrol endemicity levels.

Observed trends in CMFL in cohorts of adults

Fig. 4 shows the observed trends in CMFL in cohorts of adults in all 55 indicator villages. Comparison with the predictions shown in Fig. 2 indicates that the overall trend is quite similar, and that after 12–14 years of control the observed CMFL was almost zero in all the villages. Since it is difficult to use Fig. 4 to assess the relative trends in CMFL, the villages were subdivided into the following groups according to their initial endemicity level: 30–90 mf/s, 10–30 mf/s, and 3.3–10 mf/s. In addition, there was one hypo-endemic village with a pretreatment CMFL of 0.2 mf/s and a prevalence in adults of only 20%.

The observed trends in CMFL are shown in Fig. 5 for each of these three endemicity groups. Overall, the trend was very much as predicted for each of the three groups and the relative trend was the same for all endemicity levels. However, there were differences between the predicted and observed trends for several villages. The most striking differences concerned the change in CMFL between the first and second survey. In each group there were several villages for which the CMFL hardly changed, or even increased, between the first and the second survey. This was observed for 18 villages. In all but three of these villages the CMFL followed the predicted trend from the second survey onwards; for these three villages, however, the CMFL level did not change until the
third survey (after 7–8 years of control), but this was followed by a subsequent rapid decline. These 18 villages are marked in Fig. 1, and were found in most river basins in the central OCP area; no clear geographical pattern emerges, although the proportion of such villages was high in the extreme north-eastern focus in Niger.

**Observed trends in the prevalence of microfilariae in cohorts of adults**

The observed trends in the prevalence of microfilariae in cohorts of adults is shown in Fig. 6, for the same precontrol CMFL endemicity levels as in Fig. 5. The predicted accelerated fall in prevalence was observed in all villages, and the rate of decline depended markedly on the initial endemicity level. Most remarkable was the sudden drop in prevalence for the group of villages with a precontrol CMFL >30 mf/s (Fig. 6(a)). The decrease in prevalence was never significantly slower than predicted and the decline was faster in several villages. The difference between the observed and predicted number of positive skin snips at the last survey was statistically
significant for three of the most northern villages in the Phase II area \((P < 0.001\) for one village and \(P < 0.05\) for two villages) and for nine villages in the Phase III east area in Burkina Faso and northern Togo \((P < 0.01\) for six villages and \(P < 0.05\) for three villages). There were no significant differences for the 18 villages in the Phase I area, where the observed trends followed the predictions most closely. However, the predicted prevalences for the last survey in the Phase I area, which had been under vector control for 14 years, might have been too low to detect a significant difference. The predicted and observed prevalences were therefore also compared for the penultimate survey, which was undertaken after 10–12 years of control in 15 of the 18 villages, and after 8 years of control in the remaining three villages. No statistically significant differences were found.

**Discussion**

The epidemiological follow-up surveys that were undertaken after 12–14 years of successful vector control in the well-protected central OCP area provided valuable information on the impact of the control on the human reservoir of *O. volvulus*. The intensity of infection in the community, as indicated by the CMFL, was close to zero in all 55 villages surveyed. In noncontrolled endemic areas, the severity of ocular manifestations of onchocerciasis in the community is directly related to the CMFL (11). The extremely low CMFLs after 12–14 years of control therefore leave no doubt that onchocerciasis has been eliminated as a problem of public health importance from the central OCP area (5).

The most significant finding in the present study was the accelerated decline in the prevalence of onchocerciasis infection, which fell in accordance with the predictions made in 1985 using the host-parasite model. Particularly satisfying was the marked reduction in the prevalence in those villages that had the highest level of endemicity during the precontrol period. The observed trends suggest strongly that vector control has practically interrupted transmission throughout the central OCP area and that the parasite reservoir has been virtually eliminated. These trends are not inconsistent with the observations made by Roberts et al. in East Africa (2), but they indicate that the required duration of successful vector control is significantly less than the 20 years originally planned for OCP (3). In this connection it should be recalled that these results refer exclusively to cohorts of adults, who were the most exposed and infected section of the population before the start of the programme. The prevalence of onchocerciasis in the total population was always lower, especially during the last surveys, because children born since the start of control were free of infection and hardly any positive skin snips were obtained from individuals below 25 years of age.

The host–parasite model is an important improvement over the force-of-infection model (4), because it includes the variability in the reproductive lifespan of the adult female worms and consequently simulates much more realistically the later years of control. The good agreement between the predicted and observed trends supports the basic assumptions that underlie the model, including the hypothesis that the reproductive lifespan of the adult female worm is the main determinant of the epidemiological trends for onchocerciasis during a period of vector control. Furthermore, it indicates that the quantification of the model was based on realistic estimates of the most important parasitological parameters. The estimated duration of infection between inoculation and the disappearance of the last microfilariae from the skin was 10.4 years on average, while the variability factor indicated that 95% of all infections had a duration of less than 15 years. This corresponds to an average reproductive lifespan for *O. volvulus* of 9–9.5 years, based on the assumption that the average microfilarial longevity is 1–1.5 years (12). It should be noted that these estimates represent only one possible quantification of the model; detailed sensitivity analysis is at present being undertaken to determine the complete range of parameter values that are consistent with the observed epidemiological trends.

There were certain differences between the observed and predicted trends which merit further discussion. For example, in 18 of the 55 villages surveyed there was no decrease in CMFL between the first and second survey, although the model predicts an almost linear decline after an initial delay of about 1 year, corresponding to the prepatent period. These differences may be due to random variations in the CMFLs, in particular among the smaller cohorts, or to an underestimation of skin microfilarial loads during the baseline surveys, when many technicians were still inexperienced. However, some discrepancies may reflect precontrol variations in transmission that were not taken into account in the model predictions, which were based on the assumption of an equilibrium situation with a constant force-of-infection during the precontrol period. In reality however, there may be considerable annual differences in the intensity of transmission as a result of variations in hydrological conditions, which determine the availability and productivity of *Simulium* breeding sites (13). A relatively high intensity of transmission for a period of 1–2 years before the start

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\(^{2}\) See footnote a, p 332.
of control could explain the increase in CMFL between the first and second survey, because most of the infections acquired during the last precontrol years might still have been prepatent when the first survey was carried out.

In several villages in the Phase III east area and in the northern half of the Phase II area the observed epidemiological trends showed a significantly faster decline than predicted. Entomological data for 1975 (3) suggest that larviciding in the Phase I area may have had an important effect on transmission in the Phase II area by eliminating populations of S. damnosum s.l. that would otherwise have been important sources of reinvasion. Similarly, control in the Phase II area may have reduced biting rates and transmission in the Phase III east area. Also, the drought in the early 1970s may have had an additional effect by severely limiting vector breeding in many of the most northern foci in the OCP area (9). The combination of these factors could have been responsible for a more rapid decline in the parasite reservoir in large parts of the Phase II and Phase III areas. Alternatively, vector control in the Phase I area and in the southern half of the Phase II area may not have interrupted transmission sufficiently during the first year of larviciding operations, with the result that successful control was only achieved during subsequent years. This would imply that the model overestimates the duration of infection.

Taken together, the observed and predicted trends indicate that the parasite reservoir should be virtually eliminated after 15 years of successful vector control, and in many areas even earlier. The question currently facing OCP is when can the expensive larviciding operations be stopped without running a serious risk of recrudescence of onchocerciasis. To answer this, priority has been given to investigations of blackfly feeding and transmission habits in order to determine the significance of low microfilarial loads, and to the further development of epidemiological models to predict the risk of recrudescence. Predictions of this type cannot be made using the host–parasite model, which does not address the transmission cycle of O. volvulus. Nevertheless, use of this model and the technique of microsimulation has led to the recent development of a comprehensive transmission model that allows the simultaneous simulation of populations of humans and parasites, the dynamics of the vector population, and of interventions based on larviciding or chemotherapy (14).

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Résumé

Le déclin de l'onchocercose pendant 14 ans de lutte réussie contre Simulium spp. en Afrique de l'Ouest: prévisions et observations

La stratégie du Programme de lutte contre l'onchocercose en Afrique de l'Ouest (OCP) a été d'amener la transmission d'Oncocerca volvulus à des niveaux insignifiants grâce à la lutte contre le vecteur et de prolonger cette lutte jusqu'à ce que le réservoir de parasites ait diminué au point que les mesures prises puissent être interrompues sans risque. Depuis le début du programme, des enquêtes de suivi épidémiologique ont été entreprises dans des villages indicateurs choisis pour évaluer l'impact de la lutte sur la transmission et sur la maladie, et pour attester le déclin des taux d'infestations dans la population humaine. Pour une planification et un financement à long terme, il était devenu de plus en plus important d'obtenir des estimations précises sur la durée de fécondité d'O. volvulus et de prédire combien d'années la lutte antivectorielle devait encore être poursuivie. Cela a nécessité l'emploi d'un modèle épidémiologique pour analyser les données de l'évaluation.

Un modèle hôte–parasite a été mis au point qui est basé sur une simulation des antécédents des hôtes humains et des vers femelles adultes. Le modèle a été quantifié en 1985 en utilisant des données publiées et les résultats épidémiologiques obtenus pendant les 8 à 9 premières années du programme de lutte. La longévité moyenne de l'infestation a été estimée à 11 ans pour les vers non calcifiants et 8 ans pour les 20% de vers qui se calcifiaient. La variabilité était telle que la longévité de l'infestation était de moins de 15 ans pour 95% des vers. Après soustraction de la longévité moyenne des microfilaries, cela correspond à une durée moyenne de fécondité de 9 à 9,5 ans pour O. volvulus. Ce chiffre a été utilisé depuis 1985 pour prédire les tendances épidémiologiques. La conclusion la plus importante était que l'onchocercose devrait être pratiquement éliminée après 15 années d'interruption de la transmission.
De décembre 1988 à janvier 1989, l'OCP a entrepris une autre série d'évaluations épidémiologiques dans 55 villages indicateurs de la région centrale bien protégée, soumise depuis 12 à 14 ans à une lutte antivectorielle réussie. Les tendances observées en ce qui concerne la prévalence et l'intensité de l'onchocercose dans des cohortes d'adultes de ces villages concordaient en général bien avec les prévisions.

L'intensité de l'infestation, mesurée par la charge microfilarienne communautaire, était proche de zéro dans les 55 villages. Cela confirme que l'onchocercose a été éliminée en tant que problème de santé publique important dans la région centrale de l'OCP. Le résultat le plus significatif était la réduction accélérée de la prévalence de l'infestation pendant les dernières années. Cette réduction était également prévue par le modèle et les tendances laissent à penser que la lutte antivectorielle a pratiquement interrompu la transmission dans l'ensemble de la région centrale de l'OCP et que le réservoir de parasites a été pratiquement éliminé.

Deux types de différences sont apparus entre les tendances observées et les tendances prévues. Dans un tiers des villages, il n'y a pas eu de diminution de la charge microfilarienne communautaire entre la période et la seconde enquête, bien que le modèle ait prévu un déclin à peu près linéaire après une période d'un an. Cela peut être dû à des variations aléatoires de la charge microfilarienne, à une sous-estimation des charges microfilariennes pendant les enquêtes préliminaires et à des variations de la transmission avant la période de lutte. De plus, dans divers villages du nord-est où la lutte a commencé un ou deux ans plus tard, les tendances observées étaient nettement plus rapides que celles qui avaient été prévues. Il est possible que la première année de mesures larvicides dans l'ouest ait eu un impact important sur la transmission dans le nord-est. Cependant, il est également possible que la première année de mesures larvicides n'ait pas suffisamment interrompu la transmission, auquel cas la durée de l'infestation a été surestimée par le modèle.

L'association des tendances observées et prévues montre que le réservoir de parasites devrait être pratiquement éliminé après 15 ans de lutte antivectorielle réussie, et même plus rapidement dans de nombreuses régions. Le problème qui se pose actuellement à l'OCP est de savoir quand les opérations larvicides cœuteuses peuvent être arrêtées sans qu'il y ait un risque sérieux de recrudescence de l'onchocercose. Pour permettre de répondre à cette question, les études de simulation dans la région de l'OCP ont récemment été étendues, avec la mise au point d'un modèle complet de transmission.

References

Annex

**Simulation of onchocerciasis infection in cohorts of adults using the host–parasite model**

**Structure of the host–parasite model.** The model describes the following aspects of onchocerciasis in a human population: new infections of individuals, with the possibility of multiple infections; the longevity of adult female parasites in human hosts; and the age-specific contribution of each adult female parasite to the microfilarial density in the skin. Here, only a fixed human cohort is considered, and apart from aging, all other human population dynamics (e.g., birth, death, and migration) are neglected.

**Infections.** The human population is heterogeneous with respect to the risk of becoming infected with onchocerciasis. Part of this heterogeneity is modelled explicitly by defining age- and subpopulation-specific exposure. Thus, \( E_{xa}(a, s) \) denotes the relative exposure for the \( i \)-th person in age-class \( a \) and subpopulation \( s \). Further individual variation is taken into account by using the exposure index, \( E_x \), which follows a continuous Weibull-type probability distribution with mean \( = 1.0 \) and standard deviation \( s_x \).

The force-of-infection (foi) denotes the rate at which a person with an average exposure acquires a new infection with onchocerciasis. Only successful infections are considered, i.e., the inoculation of a female parasite that succeeds in becoming a mature worm and produces microfilariae. For an individual, \( i \), the infection rate \( f_{oi} \) is given by:

\[
    f_{oi} = f_{oi} \cdot E_x \cdot E_{xa}(a, s)
\]

The foi needs to be specified and can vary for different time intervals. Typically, foi is assigned a constant value in a precontrol situation, and equals zero in the case of complete interruption of transmission as a result of vector control.

**Worm longevity and microfilarial offspring.** For each parasite in a human host the microfilarial production \( mo \) is a function of worm age \( w \), determined from the moment of inoculation. The prepatent period, the longevity of microfilariae, and the mating probability are not modelled explicitly, and should be taken into account in specifying the function \( mo(w) \).

A distinction is made between non-calcifying and calcifying parasites, and each is assigned a specific distribution of the longevity, \( Tl \). Dead worms can be identified for some time, \( Td \), which also depends on their state of calcification. Both \( Tl \) and \( Td \) are governed by a Weibull-type distribution, for which the mean and standard deviation should be specified.

For a human host with a given microfilarial load, skin snip counts show some variation because of the dispersal of microfilariae in the body and the variability that is inherent in the skin snipping and counting procedure. This variability is also modelled according to a Weibull-type distribution.

**Simulation.** The model is implemented using a computer program that is based on the technique of microsimulation \( (10) \), whereby individual life-histories of human hosts and adult parasites in each host are simulated. Events in the life-histories, e.g., human birth, human death, infection, and death of adult parasites, are generated by random selection from the corresponding probability distributions. Skin snip counts are simulated for each member of the human population at specified times, to give age-specific microfilarial load distributions and CMFL values.

In evaluations of the impact of vector control following a stable endemic situation, the initial force-of-infection is simulated for a period of at least \( Tl + Td \) years before the start of control, to obtain a stable parasite distribution in the human population.