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## Onchocerciasis: From Control to Possible Eradication

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### Abstract

Our understanding of onchocerciasis has evolved over the last one and a half centuries from a description of an annoying skin disease, called aptly enough “craw craw,” to an understanding of its transmission cycle and important role in blindness. Various control measures have been instituted as new tools have become available, and these have moved the field toward elimination and possible eradication. A review of the evolution of the program and the lessons learned along the way may be beneficial to other disease programs as they begin the “long march to elimination”—a journey that seems to speed up as the end draws near, but which is made difficult by last remaining cases and the enormous efforts these require to address.

### Introduction

The first lesson to learn in any war is to know the enemy. Onchocerciasis was first described in Ghana, where the intense itching and associated skin changes were given a local name of “craw craw” (Figure 4.1). O’Neil (1875) first described the presence of filaria in the skin of those infected. Robels (1917) described a similar disease in the Americas. The relationship with the black fly vector was demonstrated by Blacklock (1926), but the relationship to blindness was a bit more controversial. Hissette (1932) first described the effects of the microfilaria on the eye in the Belgian Congo, with Ridley (1945) fully describing the eye signs in what is now Ghana. As the basic disease pattern and method of transmission became better understood, it was clear that there were many variations. In Africa, there is a difference between the more blinding form of savannah onchocerciasis and its vectors and the forest form and its vectors (Duke and Anderson 1972; Duke and Garner 1976). In the Americas, the parasite is similar to the West African species and was probably brought over during slave trade (Zimmerman et al. 1994). However, the simulum vector is different, and it also differs between the various foci. In Africa the vectors



**Figure 4.1** Time line of efforts to eliminate onchocerciasis.

are again very different: some have potential long flight ranges while others are very short. Understanding vector movements as well as the disease foci is essential for the programs to succeed. However, understanding the disease (and its vectors) is not enough to begin a control/elimination program. This chapter reviews the evolution of the onchocerciasis program and the lessons learned along the way, which could be useful as other disease programs begin the long march to elimination or eradication where the last cases will take enormous efforts.

## Advocacy

Creating awareness of a disease among medical and public health authorities and the general public is an essential step toward control. When Sir John Wilson (founder of the British Empire Society for the Blind, now known as Sightsavers) visited Ghana with his wife, Jean, in 1946, they realized firsthand the impact of the disease, both as a public health and a personal problem. Stuck in their vehicle in a riverbed with all the windows closed to avoid simulium bites, Jean remarked to Sir John (Coles 2006:50):

You know, it’s no good calling this thing onchocerciasis. No one can pronounce it or spell it. You certainly can’t raise funds for it. Let’s call it “river blindness.”

Since its establishment in 1950, Sightsavers has conducted research into onchocerciasis to back up their advocacy and to advance control (Crisp 1956).

Advocacy is not a singular event to get a program going. As new tools become available, as new strategies develop, and as control changes to an elimination or eradication initiative, continuous feedback must be supplied to the political, funding, and scientific communities. The two major onchocerciasis programs—the Onchocerciasis Elimination Program for the Americas (OEPA) and the African Program for Onchocerciasis Control (APOC)—have been very effective in advocacy, publishing results and keeping in regular contact with their donors to inform them of progress. The former Onchocerciasis Control Program (OCP), which covered a large area of West Africa, was also very effective in generating support. In fact, some of the original funding partners of OCP, when it was launched in 1974, are still active.

## **Program Issues**

### **Develop Strategies Based on Wide-Ranging Scientific Disciplines**

Successful elimination/eradication programs require a full understanding of the basic science around the disease agent and its vector, as well as the strategies to be applied. The OCP strategy involved vector control: insecticides were deposited in rivers to target breeding sites. This strategy was first established in Kenya (Roberts et al. 1986), where the vector was relatively easy to control, before the danger of dumping harmful insecticides in the environment was fully understood. OCP control policy required regular deposition of an approved insecticide on breeding sites with close monitoring of insecticide resistance and possible adverse effects on the flora and fauna (Samba 1994; Boatin 2008). One interesting aspect of the program involves the public's perception of noninfected flies, which returned following the cessation of vector control; in some areas, the local population believed that the program failed because the flies returned. This highlights the importance of informing the population fully to ensure that they understand the process. Detailed social and anthropological surveys may be required to construct appropriate messages throughout the program.

The major change in onchocerciasis control occurred in 1987, when Merck and Co., Inc. announced the donation of Mectizan® (ivermectin) to as many people as needed it for as long as it was required. This was the first effort to attack the parasite itself. However, while fully effective against the larva (microfilaria), Mectizan® is only partially effective against the adult worm. Initially, it was given to communities in a very controlled manner and to individuals under treatment by physicians. Strategies changed as knowledge grew about the safety and efficacy of Mectizan®. By the early 1990s, many of the worst affected communities were already receiving mass treatment, and it was understood that treatment would be required for some years. Initially, ten years was the timeframe thought to be sufficient; however, as experience increased,

computer modeling indicated that twenty years would be more realistic, depending on initial prevalence and drug coverage. At the initial stages of the control program, it was noted that hypoendemic communities did not suffer much from either blindness or skin problems and were thus excluded; only more severely affected communities received treatment. Mobilizing communities for a 20-year control program required not only a good mechanism to determine which communities should be treated, but also methods to work with these communities to maintain momentum. The social sciences proved to be an essential part of ongoing program development. Now as strategies are turning toward elimination, some of those early decisions may need to be reconsidered. Because transmission is ongoing in some hypoendemic areas, treatment areas are being redefined as “transmission zones.” Some areas which have achieved good coverage seem now to be clear of the disease with current treatment. In-country human capacity must be developed to clarify the epidemiological status and to maintain surveillance. Problem areas (e.g., co-endemic areas with loiasis and onchocerciasis) become increasingly important when the goal is elimination/eradication. Different or modified strategies may be required (i.e., twice yearly rather than annual treatment with Mectizan®). As control shifts to elimination, ongoing research in a variety of disciplines is imperative so that the best strategies can be developed.

### **Develop Broad-Based Partnerships**

The impetus for an eradication program may initially come from a few committed scientists, but moving to the implementation phase requires a broad-based partnership, including representatives of the various scientific disciplines involved, public health experts, social scientists, and funding organizations. Nongovernmental organizations also play a crucial role by partnering with Ministries of Health to implement different control or eradication strategies. Partnerships require nurturing. When different partners are committed to the same overall objective, distinct priorities can be harmonized and everyone will benefit from the various insights each partner brings to the table. The success of the APOC program was highlighted during the annual Joint Action Forum in December 2010 (World Bank/APOC 2010):

APOC, established in 1995, brings together 19 African countries affected by river blindness in an effort to control and where possible, eliminate, this neglected tropical disease (NTD). APOC is led by the World Health Organization through technical and managerial support from program headquarters in Burkina Faso. As the longest running public-private partnership for health in Africa, APOC is unique in the involvement of a broad range of financial, scientific and operational partners. With strong leadership from African ministries of health and support from 146,000 local communities and some 15 international non-governmental organizations, APOC provided nearly 70 million people with treatment for river blindness in 2009.

### **Involve the Communities in the Process**

All elimination programs target communities, yet the level of community involvement has been highly variable. Some programs regard the public as passive recipients of what is deemed to be “good for them” by those who know. When the community does not want to be treated in such a way, this has sometimes been met with surprise.

To inform the community and mobilize the population for implementation, many programs use volunteers from the community. In some programs, volunteers are well paid for the few days’ work that must be completed for each treatment cycle. Although paying volunteers may be useful for quick interventions, it is clearly not a viable option for onchocerciasis control because Mectizan® must be distributed over a period of many years.

Various community approaches have been attempted with increasing responsibility given to the community. Research by APOC with the Special Programme for Research & Training in Tropical Diseases (TDR) shows that communities fully empowered to take their own initiatives are completely able to carry out Mectizan® distribution at the community level. This has led to the development of community-directed treatment with ivermectin or CDTI (Homeida et al. 2002; APOC 2009). The CDTI approach has been extended to other health interventions and, for some mass interventions, community-directed interventions (CDIs) have proved to be highly effective in terms of coverage as well as sustainability (WHO/TDR 2008).

### **Integrate with the Health System**

Some purely vertical targeted, short-term programs may be effective, but most eradication programs move from a control phase to an eradication initiative over a period of time, as have the onchocerciasis control programs. As initiatives progress over a longer timeframe, the specific strategies of an eradication program need to be integrated into the primary health care system at all levels, most importantly at the peripheral level.

The health care workers in charge of health centers are the key coordinators and the interface between the health system and the community. Some onchocerciasis control programs have run almost parallel programs, which becomes a problem when complications arise or where programs are not getting optimal results. Peripheral health workers are also responsible for the early reporting of cases.

The connection between the specifics of a vertical approach and the need for a horizontal implementation approach has led to what is sometimes described as a diagonal approach (A. D. Hopkins 2009). When programs are not fully integrated into the health system, financial sustainability and technical and logistical support become difficult to maintain (Gyapong et al. 2010). Where programs are well integrated into primary health care, there is good evidence

to support the idea that health systems are strengthened from the “bottom up” (WHO/APOC 2007a). One way to help the process is to get the national health information systems to collect the data for whatever indicators are used. Peripheral health staff, who have to fill in a slot in their statistics sheets, are more likely to understand the importance of the activity.

### **Continue with Operational Research as Issues Arise**

As programs transform from control to eventual elimination or eradication, new issues require study to increase the effectiveness of the various activities. One aspect in all three major onchocerciasis control/elimination programs has been the operational research undertaken to resolve issues as they arise. With OCP, this was particularly related to the best use of insecticides for vector control, especially when resistance began to be an issue. It was operational research that developed the rapid mapping of the disease (Ngoumou and Wash 1993) and the CDTI approach for the APOC program, but it has also addressed other issues (e.g., various possibilities for co-implementation, new issues around transmission zones, and modalities of treatment in the pipeline).

Modeling the disease is an ongoing process that requires continual updating as more information becomes available. In the OEPA countries, smaller foci have enabled very detailed ophthalmological, parasitological, and entomological data to be collected regularly, and this has been the basis of all program decision making (Sauerbrey 2008).

As the program moves forward, some of the research topics that will need attention include changes in the criteria for treatment and improved diagnostics, particularly for knowing when to stop (WHO/APOC 2009).

### **Fix Targets but Be Flexible**

A 2003 conference concluded that onchocerciasis could be eliminated in the Americas but that elimination was unlikely to be achieved in Africa, apart from certain foci (Dadzie et al. 2003). A target was set to eliminate onchocerciasis by 2012 in the Americas. In Africa, the focus was put on building up to high, widespread coverage in meso- and hyperendemic areas to eliminate the disease “as a public health problem” (i.e., to control the worst effects of the disease in the most affected communities). From programs that had conducted longstanding ivermectin distribution in Africa, and as a result of studies which showed that transmission of the disease had been eliminated in some areas of West Africa (Diawara et al. 2009), questions surfaced as to “when treatment could be stopped.”

The APOC mandate is evolving from establishing sustainable ivermectin distribution systems in all meso- and hyperendemic areas by 2015 to eliminating onchocerciasis, where possible, within the same time period. At the APOC Joint Action Forum in December 2010, it was proposed that an extension of

APOC could result in the elimination of transmission in most African countries by 2020.

### **Final Stages Will Be More Difficult and Costly**

Control programs tend to begin in the easiest places to ensure that good results are accomplished. The APOC program began in areas where nongovernmental development organizations (NGDOs) had already been working and was thus able to be established on top of existing projects. This, together with the CDTI strategy, permitted a massive and effective scale-up in numbers of people under effective control.

However, repeated conflict in the D. R. Congo, southern Sudan, the Central African Republic, and Angola has hindered the scale-up of the APOC program in these conflict and post-conflict countries (WHO/APOC 2007a). The last places to be cleared of onchocerciasis will be those areas where work is most difficult, where the infrastructure has been destroyed, where qualified human resources are in scarce supply, and only limited national funding resources are available for the health system. These places will most likely pose some of the biggest difficulties to achieving the high coverage needed with ivermectin. As control moves to elimination, new strategies may be needed for these problem areas. As programs focus on the final remaining communities, which are usually in remote areas, follow-up will, once again, pose logistical difficulties and be comparatively very expensive to complete.

### **Keep Stakeholders Engaged**

The partners involved in APOC are often referred to as the “APOC family.” The World Bank, which is the fiscal agent for the trust fund, makes certain that all partners are kept informed, not just at the Joint Action Forum—when the whole “family” is convened—but also during the rest of the year (World Bank 2011a). The success of this engagement of partners contributing to the trust fund can be traced back to the OCP program in the 1970s; since then, many partners have contributed on a regular basis.

The APOC family depends on the major contribution of donated Mectizan®, without which there would be no APOC, government support and the involvement of NGDOs, which contribute up to 25%, and technical assistance where required (Haddad et al. 2008). This partnership requires transparency, openness, and a share in the successes. Like all families, disagreements arise from time to time over which strategies are best, but frank discussion and a steadfast commitment to the common final goal keeps the coalition strong and helps maintain progress.



## Monitoring, Evaluation, and Surveillance

The advantage of the onchocerciasis program can be found in the method of control: following a simple dosing regimen, mass drug administration (MDA) of a safe drug is used and there are few side effects. Because the drug is so safe, the trigger point for beginning a control treatment has been considerably simplified. As MDA for onchocerciasis is integrated into the preventive chemotherapy (PCT) program of WHO (2006c), as well as the integrated monitoring of PCT programs, care must be taken to ensure that the specifics of onchocerciasis eradication are not lost in a mass of tablet distribution.

### Baseline

REMO mapping (or rapid epidemiological mapping of onchocerciasis) is a tool used to determine where to treat. It is not, however, a full pretreatment epidemiological evaluation. As programs move toward the goal of eradication, it will be necessary to redefine these areas and collect solid epidemiological information on which to base decisions about stopping treatment. APOC countries will also need to train local national staff to carry out these parasitological and entomological surveys. In the lymphatic filariasis program, mapping using immunochromatography (ICT) cards has always been backed up by epidemiological surveys, which must be conducted before treatment can begin.

### Coverage Figures

To move from control to elimination requires a high level of MDA coverage. APOC's target is 80% of the total population, which equates to over 90% of the eligible population, because children under 5 years of age, women who are pregnant or lactating during the first post-delivery week, and those who are chronically ill are not eligible for treatment. MDA is done by community distributors who establish their own registers of the population. Independent monitoring does happen in projects from time to time, but there are no regular post-treatment coverage surveys to monitor the work of the distributors, although techniques are available (Schwarz et al. 1999). In Ghana, significant population growth in some areas has led to the formation of new communities or "sub-villages." Community distributors have only counted and treated the initial villages in their program, leaving these new communities without MDA, and not included in the coverage calculation leading to an artificially high coverage figure. The lymphatic filariasis program, in contrast, has a formalized annual reporting system. For NTDs, WHO has developed guidelines to help monitor treatment coverage (WHO 2010d).



## Diagnostic Tools

When the program goal was control, impact was measured in terms of morbidity, prevalence of visual impairment and blindness, and prevalence of debilitating skin disease. As the program evolves from control to elimination/eradication, more specific and sensitive diagnostic tools are required. One possibility with onchocerciasis is to test the flies, if these can be caught and analyzed easily. Using human flycatchers, however, is getting more difficult, both from a practical and ethical standpoint.

Populations are becoming more resistant to skin snips, which, although considered in some ways the “gold standard,” are actually not very sensitive when there is a low prevalence of the disease. APOC is using the DEC (diethylcarbamazine) patch test, which since the early trials has developed into a more practical tool, but still has problems of reliability. The OEPA uses the OV16 antibody test, which is only useful for patients who have never been infected and thus must be targeted toward children. At present, there is no ideal test, and it remains to be determined how much research should be done to ensure that there are no new infections.

## What Constitutes Eradication? What Number Is Zero?

The emphasis for onchocerciasis eradication has been the “elimination of transmission.” There is a point at which the disease is no longer able to reproduce itself. In onchocerciasis eradication models, this is termed the breakpoint and has led APOC to define “elimination” as follows:

Elimination occurs when:

- Interventions in a defined geographical area have reduced *Onchocerca volvulus* infection and transmission to a point where the parasite population is believed to be irreversibly moving to its demise or extinction (i.e., below the breakpoint).
- Interventions at that point have been stopped.
- Post-intervention surveillance for an appropriate period has demonstrated no recrudescence of transmission to a level suggesting recovery of the *O. volvulus* population.
- Additional surveillance is necessary for timely detection of reintroduced infection from other areas.

Eradication of onchocerciasis will only occur when all old cases are no longer infected. This will happen when transmission is interrupted for a long enough time, but will not fit into this definition initially.

In 2000, the WHO defined elimination of onchocerciasis using criteria of morbidity (defined as the absence of microfilariae in the anterior segment of the eye) and transmission criteria defined as:

- OCP standard of infective larvae (L3) in flies <0.05% (0.1% in parous flies),
- annual transmission potential lower than 5–20 L3 per season,
- absence of detectable infection in school children and an antibody prevalence of <0.1%, and finally
- no new infections in recent migrants.

These criteria, however, do not fit all circumstances due to differences in the vector and the epidemiology.

### **Conclusion**

Over the past half century, onchocerciasis control has progressed from the strategy of vector control to strategies based on mass drug administration. Success of the current strategies and the strong cooperation of affected communities have altered the vision from one of disease control to interruption of transmission within the next ten years and eventual eradication. The tasks ahead are to meet the current elimination goals and develop the surveillance, monitoring, and diagnostic tools that make it possible to certify that the disease has been eradicated.