ONCHOCERCIASIS: DIAGNOSTIC TARGET PRODUCT PROFILE

to support preventive chemotherapy

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Contents

1. Epidemiology

Onchocerciasis, also known as river blindness, affects an estimated 21 million people, with 99% of cases reported in 31 sub-Saharan countries (WHO, 2020a). The disease is caused by the filarial worm *Onchocerca volvulus*, which is transmitted by *Simulium* flies. Adult worms live in nodules, some of which are subcutaneous. Conversely, the embryos (microfilariae) can migrate through the skin, causing debilitating pruritus and skin disease, and to the eyes, leading to progressive and permanent blindness. Onchocerciasis is also hypothesized to lead to neurological disorders including epilepsy (Chesnais, 2020), nodding syndrome (Geelhand de Merxem, 2020) and stunted growth.

2. Public health response

Currently, at least 217.5 million people live in areas known to be endemic for onchocerciasis (WHO, 2019). Morbidity is controlled by annual mass drug administration (MDA) of ivermectin, with 157 million treatments delivered in 2018 (WHO, 2019). Ivermectin temporarily blocks transmission of infection by clearing microfilariae but does not kill the adult worms, which have a reproductive lifespan of about 10 years, requiring MDA to be continued for over a decade.

In 2010, based on progress towards the elimination of transmission of onchocerciasis in the Region of the Americas as well as in a few foci in sub-Saharan Africa, global targets were revised from the control of morbidity to elimination (interruption of transmission) (WHO, 2010). In 2020, following several rounds of public consultation, WHO published the draft road map for neglected tropical disease 2021–2030 (WHO, 2020b), which the Seventy-third World Health Assembly is expected to endorse. The road map identifies as a critical action the mapping of suspected onchocerciasis-endemic areas, with launch of MDA wherever indicated. It further identifies as critical the development of improved diagnostics to facilitate mapping and decision-making (WHO, 2020b; Fig. 12). The principal disease-specific target for onchocerciasis is to increase the number of countries verified as having interrupted transmission from four (12%)[1] in 2020 to 12 (31%) in 2030 (WHO, 2020b; Table).

This shift requires treatment to be expanded to include hypo-endemic settings which were previously excluded from MDA. Hypo-endemic areas are defined as having a palpable subcutaneous nodule prevalence < 20%, corresponding to a microfilariae prevalence of approximately < 35% (Zouré, 2014). Some of these hypo-endemic areas have been mapped, while others have not, and the maps are not necessarily current, leading to an uncertainty in the total number of people who must be reached. It is estimated that in 2011, 98 million people lived in areas in which the prevalence of palpable subcutaneous nodules was 0–4.9%, 77 million in areas of 5–20% nodule prevalence and 62 million in areas of > 20% nodule prevalence (Zouré, 2014).

3. Available diagnostic tools and their limitations

The main diagnostics for onchocerciasis fall into the following categories.

1. Analysis of skin biopsies, also known as skin snips, by microscopy or molecular techniques is considered to be definitive but is relatively insensitive, has low throughput and can be painful for the patient if appropriate equipment and techniques are not ensured. Populations are reluctant to participate in skin snipping, especially when onchocerciasis is not viewed by the locals as a problem and/or when children are involved.

[1] Colombia, Ecuador, Guatemala and Mexico.

2. Nodule palpation has been a main driver of the African Program for the Elimination of Onchocerciasis, being used for the rapid epidemiological assessment or rapid evaluation and monitoring of onchocerciasis. A prevalence of approximately 5% of people having palpable nodules of other etiologies makes this technique acceptable for meso- and hyper-endemic areas but insufficiently specific for hypo-endemic areas.
3. The DEC patch is a diethylcarbamazine-containing transdermal patch that kills microfilariae in the skin, triggering a reactive urticaria (the Mazzotti reaction) that can be visualized. The fact that it requires 2 days in the field[1] to monitor skin reactions is a limitation, and there are specificity issues in areas co-endemic with *L. loa* (Ozoh, 2007). "Ready-to-use" DEC patches (Awadzi, 2015) made under good manufacturing practice conditions by a manufacturer specialized in transdermal-delivery systems are available to health ministries requesting them from WHO (TDR contact: Dr A.C. Kuesel). Large-scale evaluation of the DEC patch has to date only occurred in populations that were skin snip negative (Diawara, 2009) and needs to be conducted in populations with different levels of skin microfilariae density to assess its performance and safety.
4. Ov16 serology is part of the current WHO criteria for stopping MDA, alongside entomological investigations (WHO, 2016). Identification of hypo-endemic areas is also under consideration. The third meeting of the WHO Onchocerciasis Technical Advisory Subgroup (Geneva, 26–28 February 2019) summarized the results of the evaluation of different Ov16 assays in a variety of programmatic contexts and identified differences in performance with different types of specimen and concerns of accuracy (WHO, 2020c). The enzyme-linked immunosorbent assay (ELISA) always requires dried-blood spots; a rapid diagnostic test performs better with dried-blood spots than with whole blood. One issue is the lack of standardization across different versions of these serological tests.
5. Entomological identification of ongoing transmission consists of detecting infective or infected *Simulium* flies by polymerase chain reaction (PCR). It requires trained personnel for laboratory work and field teams knowledgeable about methodologies for finding and capturing flies.

4. Diagnostic Technical Advisory Group

The WHO Department of Control of Neglected Tropical Diseases manages a diverse portfolio of 20 diseases and disease groups, each with its own unique epidemiological, diagnostic and control challenges. In 2019, WHO's Strategic and Technical Advisory Group for Neglected Tropical Diseases, the Organization's principal advisory group on neglected tropical diseases (NTDs), recommended the establishment of a Diagnostic Technical Advisory Group to help ensure a consistent approach to identifying and prioritizing diagnostic needs and to inform WHO strategies and guidance on the subject. The first meeting of the Group (Geneva, 30–31 October 2019) discussed priorities for the year ahead as well as