

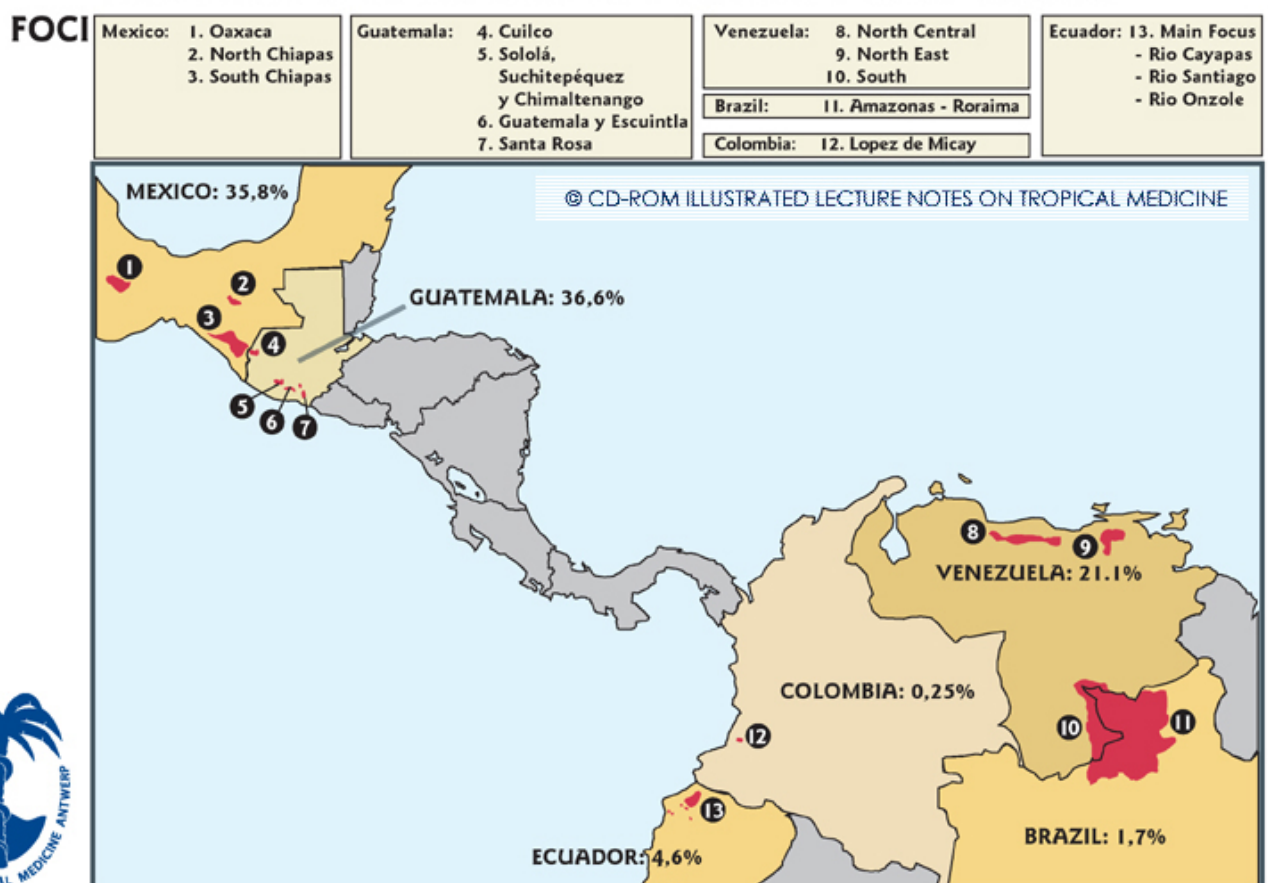
Onchocerciasis

Introduction

Onchocerciasis (syn. onchocercosis) is a disease resulting from infection by the nematode *Onchocerca volvulus*. The principal characteristics of the condition are pruritic dermatitis, subcutaneous nodules and ocular lesions. It is also known as “river blindness” because the blackfly vector breeds near fast-flowing streams and rivers.

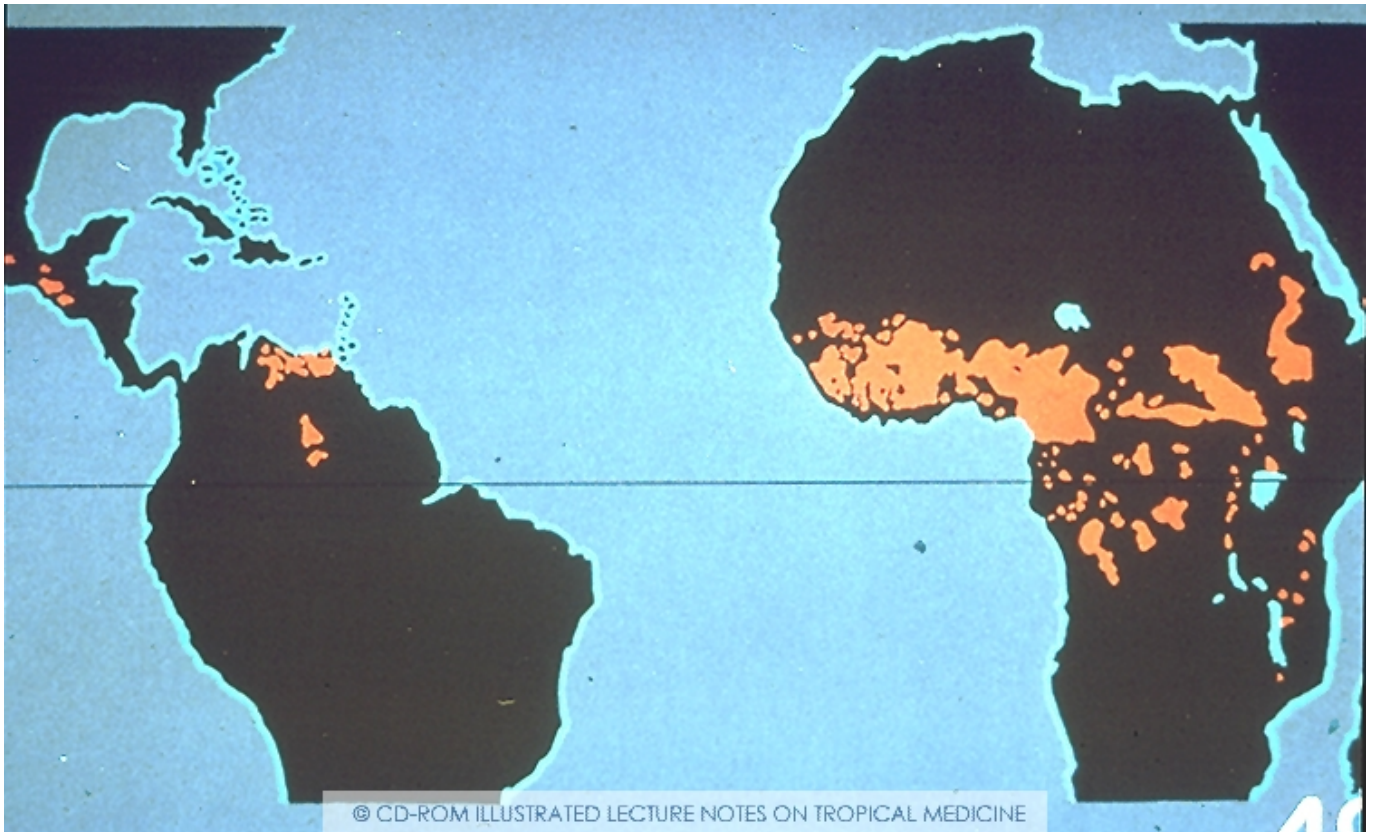
Distribution

ONCHOCERCIASIS IN LATIN AMERICA



Map of onchocerciasis endemic area in Latin America. Adapted from publication of ‘Programa para la Eliminación de la Oncocercosis en las American – OEPA’, with special thanks to Dr Juan

Martin Moreira.



Map of endemic onchocerciasis areas.

The disease occurs principally in large parts of Africa, especially West and Central Africa (including both Congos and Angola), but also in Sudan, Ethiopia, the north of Uganda and even Tanzania. About 99% of the cases are now limited to Africa, the remaining being observed in a few foci in Latin America (disease about to be eliminated there).

Vector

The infective larvae are transmitted by *Simulium* mosquitoes (“blackflies”). They reproduce in rocky rivers with fast stream and can cover large distances. The fact that the insects are good fliers makes vector control difficult. Sometimes there are only a few ecologically very suitable places, where thousands of eggs are then laid. This can lead to the sudden

simultaneous appearance of massive numbers of adult insects when the environmental conditions are right.

Only female insects suck blood (from humans as well as animals). This happens during the day in the open at well-defined times. The bite is painful.

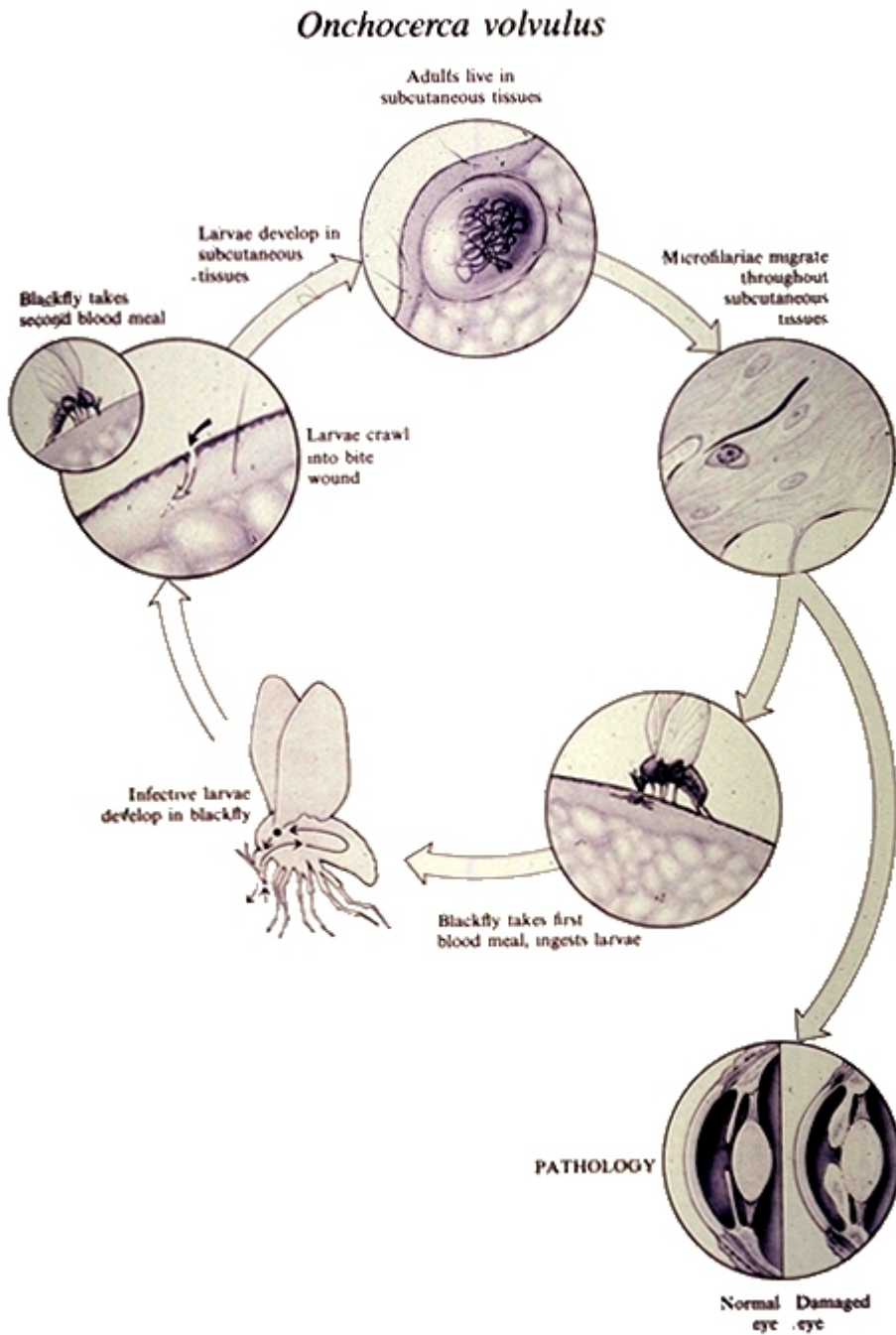
Life cycle

There is no significant animal reservoir. *Onchocerca volvulus* microfilariae are more tissue parasites than blood parasites.

The more insect bites someone suffers over the course of the years, the greater the worm load. After a bite from an infected insect, the infective larvae develop in humans to become adult worms (=macrofilariae) that live subcutaneously. The prepatent period (time between infection and detection of microfilariae) is 3 to 15 months.

The macrofilariae lie coiled subcutaneously in nodules and can live for up to 15 years. These nodules are predominantly located on the scalp and upper body in people living in Central and South America but occur more on the pelvis and legs in Africans. This has to do with the biting habits of the vector.

Simulium damnosum (Africa) tends to bite on the lower half of the body (98% of bites below the belt) and *Simulium ochraceum* (America) preferably bite on the upper part of the body. A female lays on average 1600 microfilariae per day. The microfilariae concentrate in the skin, eyes and lymph nodes. When the microfilariae die they cause a local inflammatory reaction.



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Life cycle of *Onchocerca volvulus*.

Onchocerca volvulus : Endosymbiont

Intracellular bacteria can be detected by electron microscopy in adult *Onchocerca volvulus* and also in the microfilariae. The bacteria belong to the genus *Wolbachia* of the Rickettsiales (Alphaproteobacteria) and are closely related to *Ehrlichia*, *Cowdria* and *Anaplasma*. The *Wolbachia* bacteria are transmitted transovarially, have a preference for oocytes and the lateral tissues (“lateral chords”) in the macrofilariae and have a development cycle that resembles that of the *Chlamydiae*. As for *Wuchereria* and *Brugyia* filariae, they have also become a new point of attack for therapy. It was possible to render the macrofilariae in onchocercomata bacteria-free by means of a 6-week treatment with doxycycline. At the same time parasitic embryogenesis was totally impaired. *Wolbachia* bacteria are also susceptible to rifampicin and this might become an option (like for lymphatic filariasis) for children less than 8 years and pregnant women. How far these findings are relevant for clinical practice has not been fully elucidated. *Wolbachia*-antigen released in the circulation contributes to the discomfort which is seen soon after administration of classic anti-filarial medication, but these symptoms do not seem to occur with tetracyclines.

Clinical aspects

Skin abnormalities

Pruritus occurs locally or systemically. There are scratch lesions often with bacterial superinfection. The chronic itching has given rise to the terms “gale filarienne” and “craw craw”. If untreated the dermatitis assumes the form of a pruritic papular dermatitis, progressing to a chronic rough, coarse, papular dermatitis, often with postinflammatory hyperpigmentation, followed by lichenification, atrophy and finally patchy depigmentation (leopard skin).

Pea- to plum-sized subcutaneous nodules are found predominantly over bony protuberances such as the hip, pelvis, ribs, shoulder blades and skull. These need to be distinguished from cysticerci.

Though not always found (in Africa in only 30 to 60% of positive people), enlargement of the inguinal nodes is sometimes also present, resulting in what is known as “hanging groin”.

Onchocerciasis causes localized elephantiasis (lymphoedema) in a number of cases.

Ocular lesions

Ocular lesions only occur after many years of severe infection and are therefore usually not present before the age of 30. They are more frequent in savanna regions than in the rainforest.

In onchocerciasis patients with heavy infections, microfilariae can be seen in the anterior chamber with a slit lamp. When microfilariae die, opaque fine 0.5 mm wide corneal lesions occur: **keratitis punctate**.

This is corneal inflammation with small spots on the cornea accompanied by redness of the conjunctiva. Sclerosing keratitis occurs later (hazy cornea with pannus formation) as well as iritis and uveitis, resulting in blindness (river blindness!). More rarely, there is involvement of the posterior part of the eye: chorioretinitis and optic nerve atrophy. Ocular lesions can be exacerbated by DEC therapy (**which is therefore formally contra-indicated**) but not by ivermectin.

There seems to exist an epidemiological link between onchocercosis and epilepsy, but more study on this subject is needed to confirm a causal relationship.

The world's leading causes of blindness are:

- cataract (clouding of the lens),
- trachoma (eye infection with the bacterium *Chlamydia trachomatis*),
- glaucoma (increased intra-ocular pressure with damage to the optic nerve),
- xerophthalmia (secondary to vitamin A deficiency with initial night blindness, followed by dry eyes and corneal softening),
- onchocerciasis,
- diabetes,
- leprosy,
- maculopathy and

- trauma.

Diagnosis

Detection of microfilariae in a skin snip

Various techniques may be used for detecting microfilariae in the skin. A skin snip is often used. A needle is used to raise the skin and a fine piece is shaved off with a razor blade. A standardised punch biopsy is also possible. The piece of tissue is placed in physiological saline. The specimen is then examined 15 minutes to 3 hours later to see whether or not microfilariae have emerged. In early infections (first 15 months) not enough microfilaria are present in the skin to be detected with a skin snip.

Detection of microfilariae in skin fluid.

This is done by means of scarification with a sterile razor blade. Preferably several sites are examined (often 4 sites are chosen). The fluid obtained can be collected on a glass slide and stained with Giemsa to allow identification.

Detection of microfilariae at other sites

Occasionally *O. volvulus* microfilariae are found in the blood and in the urine.

Nodulectomy

This is both diagnostic and curative if all the nodules are resected. However the palpable skin nodules are often outnumbered by deeper lying subcutaneous nodules. The macrofilariae are found in the nodule.

Slit lamp examination

This is a non-invasive test, but requires considerable experience. It is best to get the patient

to lay his/her head on his/her knees for at least 2 minutes before the examination to allow more microfilariae to come into the anterior eye chamber.

Mazzotti test

If the diagnosis is doubtful, the patient may be given 50 mg DEC orally. If microfilariae are present, a severe itching reaction will occur within 2 hours. This is caused by an allergic reaction to the proteins released after the rapid breakdown of microfilariae. Because this is very unpleasant, this test should be used only when strictly necessary. An alternative tool, a patch with DEC, is better used (if available) because it causes a localised reaction on the skin.

Serology

Serology cannot distinguish between the various species of filariae. The antigen used is usually extracted from a different worm: *Litosomoides sigmodontis*. It is useless for patient care in endemic settings.

Treatment

Ivermectin (Mectizan®, Stromectol®)

Ivermectin is a fast-acting, safe and effective microfilaricide. Ivermectin has a broad spectrum and is active against various worms and arthropods (ectoparasites). In onchocerciasis, it is active against the free microfilariae and those that are still in the uterus of the female.

It can be given in a single oral dose (4 tablets of 3 mg for an adult; 200 microg./kg in children). It must be given repeatedly. The ideal frequency of administration (once a year or more frequently) still remains to be determined. Ivermectin does not penetrate the aqueous humour. Consequently it does not cause intra-ocular inflammatory reactions that might exacerbate ocular lesions. It was initially thought that pregnancy constituted a contraindication to treatment with ivermectin but no increase in the incidence of abnormalities has been observed in neonates when the product has accidentally been taken by the mothers

during pregnancy. In areas of Loa loa a slight risk of neurological side-effects of ivermectin exists (see below). In 1987 the manufacturer of ivermectin (Merck Company) announced that the company would make the medication freely available to combat onchocerciasis.

Moxidectin

A promising new drug moxidectin, has been shown to have significant macrofilaricidal activity in animal studies and could be capable to interrupt transmission within six annual rounds of treatment. This drug might replace Ivermectin in the future.

Tetracyclines

Tetracyclines such as doxycycline and vibramycin can kill *Wolbachia* endosymbionts of macrofilariae.

According to initial findings, the subsequent suppression of embryogenesis by ivermectin lasts much longer (at least 18 months) and results eventually to the death of the adult worms (macrofilaricidal effect). A four-week course of doxycycline is very effective in killing macrofilariae and is increasingly used in non-endemic settings to avoid repeated annual treatment with ivermectin for many years. In endemic countries however annual administration of ivermectin is still preferred for its fast effect on microfilariae (the pathogenic form in onchocerciasis) and its simplicity of use (mass drug administration of a 4-week doxycycline treatment is unfeasible).

Nodulectomy

This involves the removal of superficial nodules and is (was) popular in Central America.

Prevention

In 1968, the WHO decided to start a large scale onchocerciasis control programme (OCP). The emphasis of the programme is on vector control in areas where the disease is often associated with blindness (savanna-type onchocerciasis). Initially it involved 7 West African

countries (Benin, Burkina Faso, Ivory Coast, Ghana, Mali, Niger and Togo).

After a few years of preparation, the vector control programme started in 1974. In 1978, and subsequently in 1986, the programme was extended to the west and south (including Guinea, Guinea-Bissau, Senegal and Sierra Leone) to a total of 11 countries. It covers an area of 1,235,000 km² with 50,000 km of river. Initially 30,000,000 people lived there. In view of the fact that an adult female worm lives on average 11 years, it was estimated that a minimum of 14 years of insect control would be necessary to eradicate the human reservoir of onchocerciasis. Later, after a successful (but costly) period of intensive vector control, activities focused on regular administration of ivermectin (after 1987 and the free access to this drug) through vertical programs and subsequently primary care settings in order to decrease both morbidity and transmission. At present interruption of transmission has been achieved in large areas and onchocerciasis no longer constitutes a public health problem there.

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