

Loiasis

“Jack Malahide, for instance, had a parasite in his blood which, according to local gossip, could only be caught on the rare occasions when it emerged to walk across his eyeball.”

--Julia O’Faolain, “The Religious Wars of 1944”

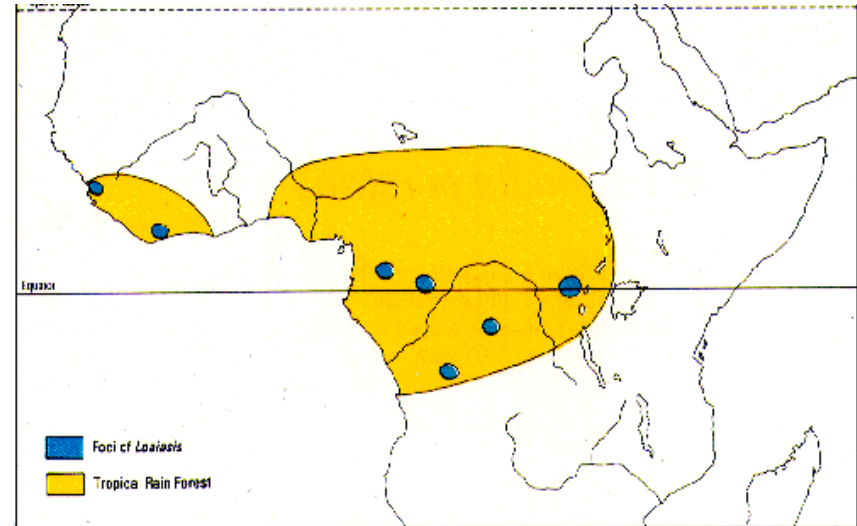
The New Yorker, May 23, 1944

Loiasis: Definition

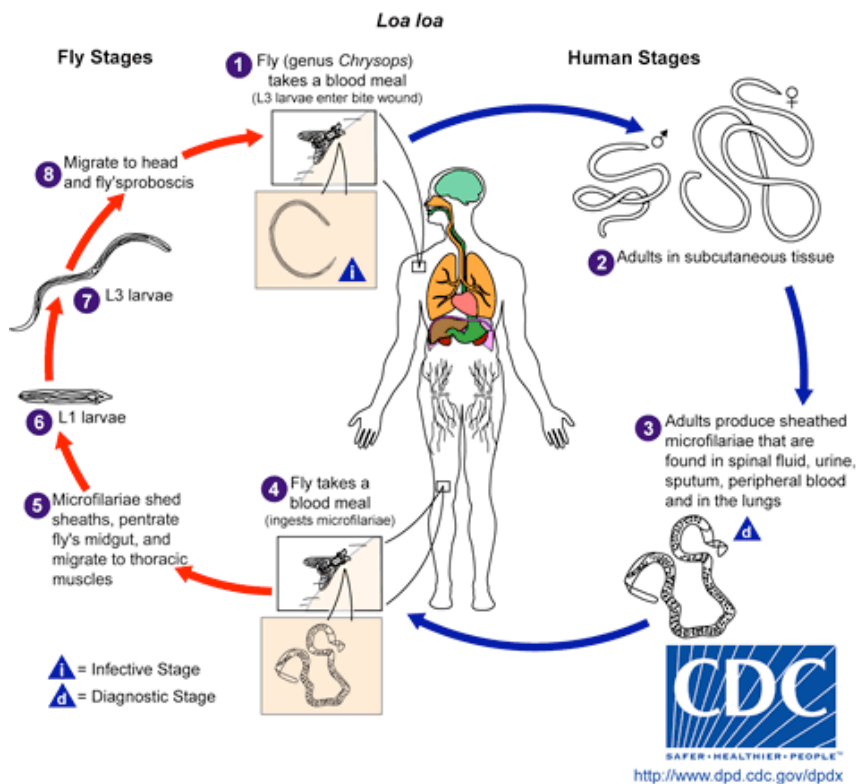
- Infection with the nematode *Loa loa*.
- Afflicts approximately 13 million people worldwide.
- Also known as the African eyeworm or the “loa” worm.

Geographical Distribution

- **Transitional savanna and rain forests of West and Central Africa.**
- **An emerging infection in areas where the establishment of rubber plantations have altered the rain forest ecology.**



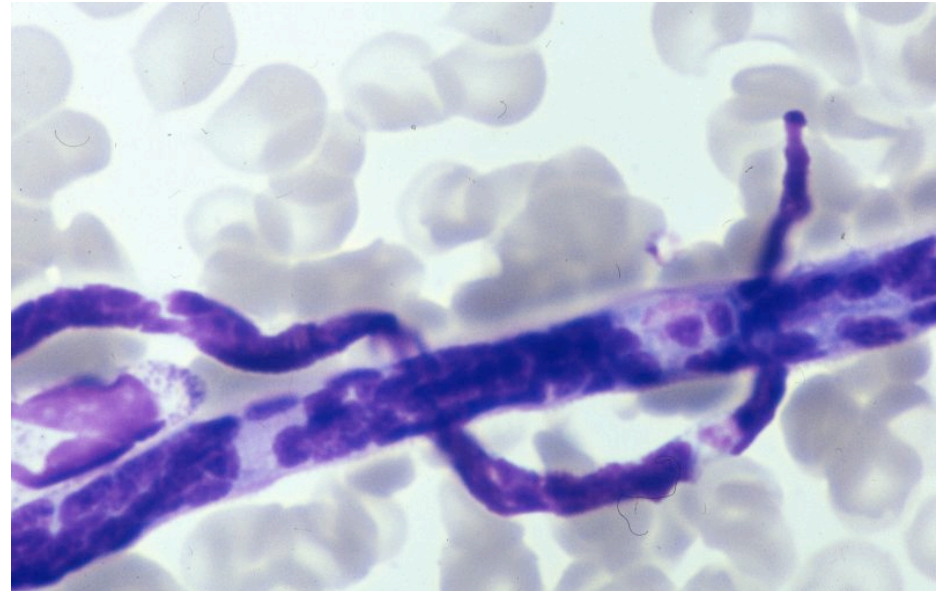
Loa loa Lifecycle



- Females 0.5 mm wide and 60 mm long.
- Males 0.4 mm wide and 32 mm long.
- Adults wander through subcutaneous tissue.
- Microfilaria enter the blood.

Loa loa: Adult Morphology

- **Similar to other filarial worms.**
- **Both genders have rounded elevations on the cuticle throughout their lengths called 'bosses.'**



***Loa loa* Lifecycle**



- **Microfilariae are present in the blood of humans during the day.**
- **Coincides with the mango fly (*Chrysops spp.*) feeding habits.**

Loiasis: Cellular and Molecular Pathogenesis

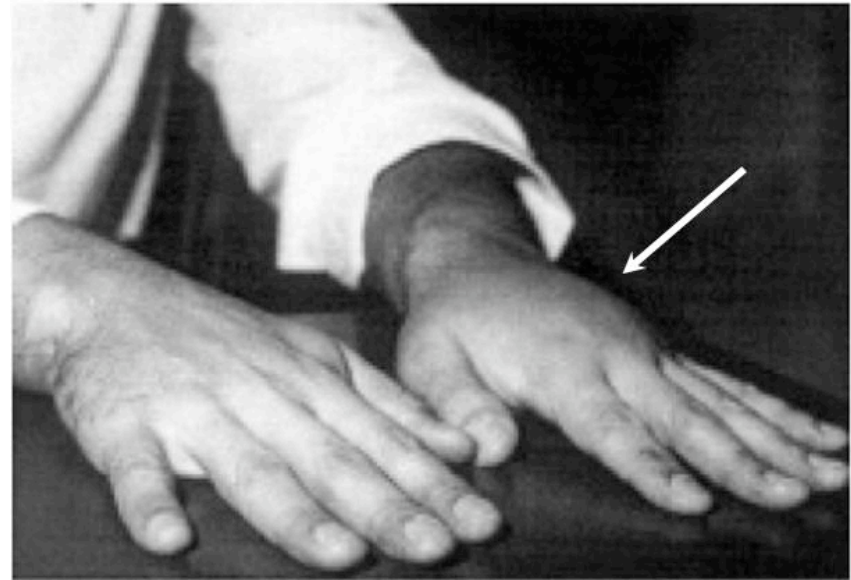
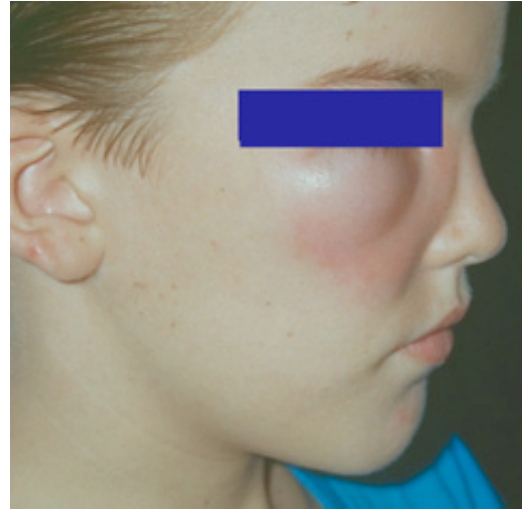
- Neither the adult worms in the subcutaneous tissues nor the microfilariae in the blood cause any direct changes.
- However, in some individuals the parasite can elicit a number of immune-mediated responses that have an **allergic** basis.

Loiasis: Cellular and Molecular Pathogenesis

- **Three different groups of individuals/symptoms:**
 - **Asymptomatic individuals have diminished anti-Loa allergic responses.**
 - **High levels of microfilariae.**
 - **Pronounced immunopathology with characteristic Calabar swellings**
 - **Elevated IgE and up-regulated IL-5.**
 - **Individuals who have neither Calabar swellings nor circulating microfilariae.**
 - **Live in hyperendemic regions.**

Loiasis: Calabar Swelling

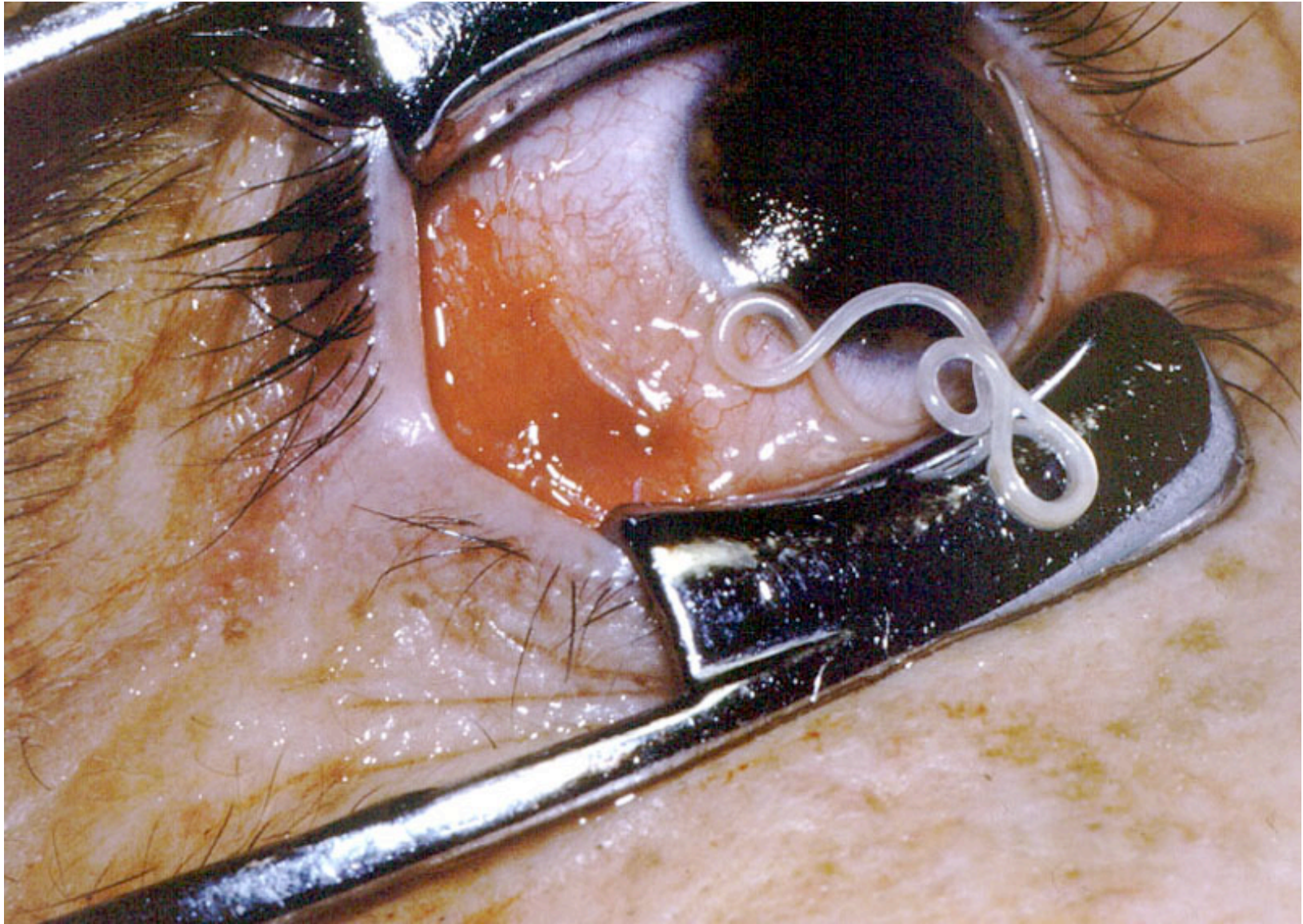
- **Characterized by itching, erythema and edema.**
- **Most commonly on the limbs and face.**
- **Sudden onset, and regress over a period of several hours.**
- **Recur at the same site most of the time.**



Loiasis: Eyeworm



- **Unique among human filariae in that the adults sometimes move across the eye.**
- **May cause swelling of the lids, congestions, itching, and pain.**
- **They may blind if they penetrate into the anterior chamber.**



***Loa loa*:Diagnosis**

- **Patients returning from West or Central Africa with localized angioedema or a worm beneath the conjunctiva should be suspected of having loiasis.**
- **Identification of microfilariae in the a thin blood smear (diurnal periodicity).**
- **ELISA-based assay against recombinant protein L1-SXP-1.**
- **PCR**

***Loa loa*: Treatment**

- **Diethylcarbamazine (DEC) destroys both adult worms and microfilariae.**
 - Administered in increments.
- **Done to reduce the likelihood of treatment-associated complications, including encephalopathy, that occur as a consequence of mass destruction of microfilariae.**
 - Anti-inflammatories.
- **Eye worms must be removed surgically.**

***Loa loa*:Control**

- **In hyperendemic regions of central Africa, 95% of the population have antibodies to *L. loa* antigen by age of two years.**
- **Mass targeted chemotherapy with DEC* may reduce transmission.**
- **Insecticide spraying of mango groves**

Onchocerciasis

(Onchocerca volvulus)

***The poor, and maimed, and the
halt, and the blind.***

Luke 14:21

Synonyms

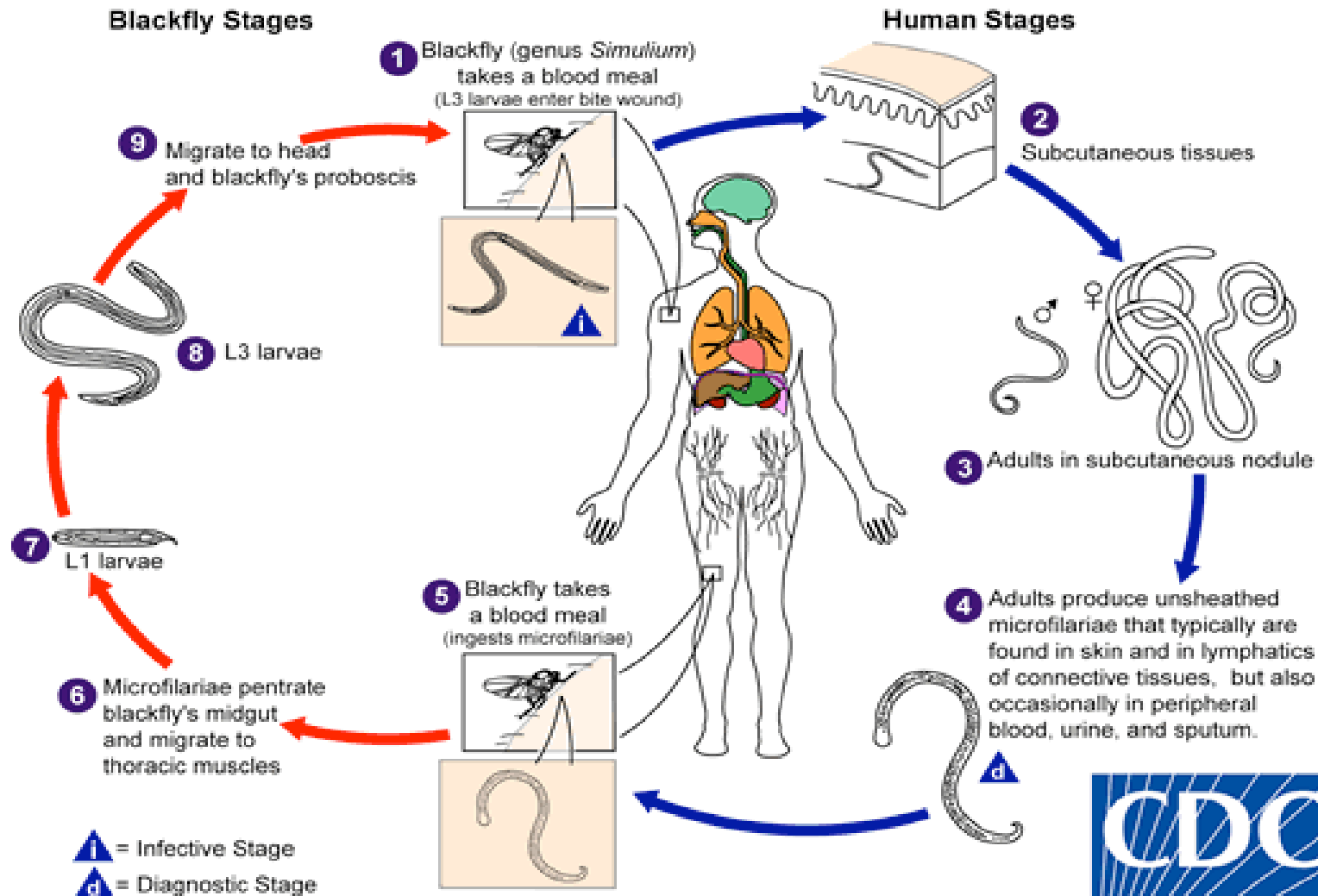
- **River blindness**
- **Blinding filarial disease**
- **White-water disease**
- **Enfermedad de Robles**
- **Mal marado**
- **Craw-craw**
- **Erisipela de la costa**
- **Cegura de los rios**
- **Gâl filarienne**

Onchocerciasis

- Transmitted from person to person by blackflies of the genus *Simulium*.
- Disease directly related to the infection dose.
- Clinical features dominated by one or more of three cardinal manifestations:
 - A persistent, itching dermatitis.
 - Cutaneous and subcutaneous nodules
 - Progressive ocular dermatitis.

O. volvulus Life Cycle

Onchocerca volvulus



<http://www.dpd.cdc.gov/dpdx>

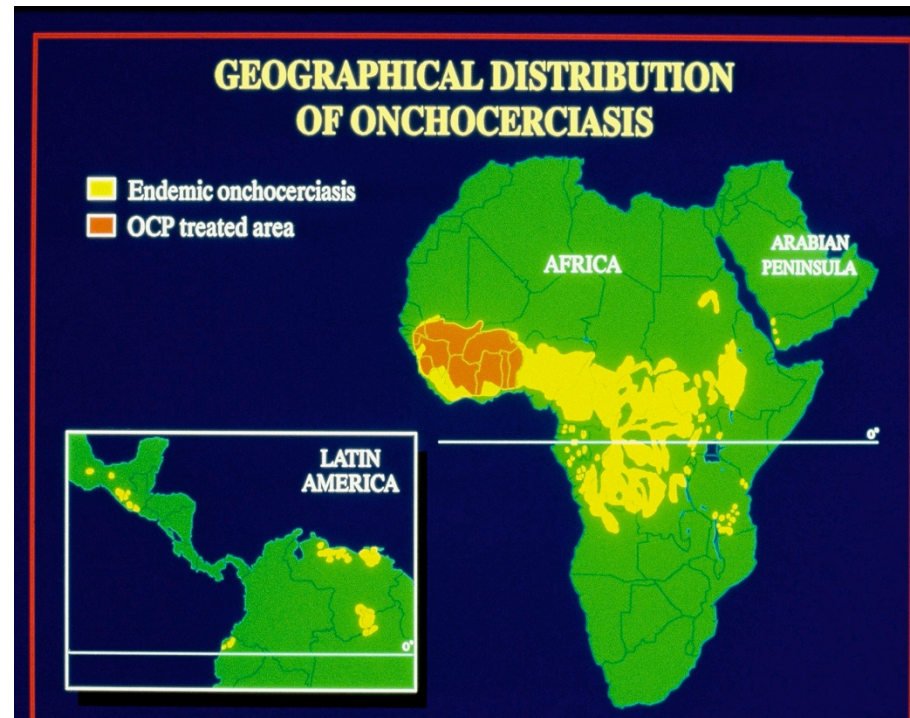
Historical Overview

- **Prior to WWII, onchocerciasis was barely known in the western world.**
- **Believed to be an infection occurring in remote places by a few benign parasitic nodules in the skin.**



Historical Overview

- Current estimates indicate that 18 million people remain infected worldwide, with 99% living in Sub-Saharan Africa, Yemen, and small foci in Latin America.
- Plans to treat 75 million people/year by 2010.
- **Eradicate by 2025.**
- **Kenya: onchocerciasis has been eradicated by controlling and eliminating the vector flies.**



Geographic Distribution

- **Four features that define Endemic areas:**
 - Tropical setting.
 - Turbulent stream.
 - Why?
 - Vegetation trailing in the stream.
 - Why?
 - Humans harboring the reservoir parasites.
- **Blackfly vector:**
 - Africa: *Simulium damnosum*
 - Central and South America: *S. exiguum*, *S. guianense*, *S. metallicum*, *S. oyapockense*, *S. quadrivittatum*, and ***S. ochraceum***.

Geographic Distribution

- Four features that define Endemic areas:
 - Tropical setting.
 - Turbulent stream.
 - Larvae that survive are those in water with high oxygen content.
 - Vegetation trailing in the stream.
 - Larvae attachment site. →
 - Humans harboring the reservoir parasites.
- Blackfly vector:
 - Africa: *Simulium damnosum*.
 - Central and South America: *S. exiguum*, *S. guianense*, *S. metallicum*, *S. oyapockense*, *S. quadrivittatum*, and *S. ochraceum*.



Historical Overview

- O'Neill J. On the presence of a filaria in 'craw craw.' *Lancet*. 1875. 1:265-266.
 - **craw-craw (kraw´kraw)** a name for *onchocerciasis* with chronic skin changes in West Africa.
 - **First described filarial dermatitis in natives of the Gold Coast (Ghana), and the technique he used to identify microfilariae survives as the standard diagnostic test—that is the skin snip.**

Historical Overview

- Major George M. Barnley, government entomologist in Uganda performing a skin snip in **1962**.
- Trained in armaments during WWII, he strung steel drums of insecticide across the Victoria Nile.



Historical Overview



- He exploded the drums simultaneously, instantly dosing the breadth of the river. The insecticide killed *Simulium* larvae for about 50 miles downstream.
- 10 years later, even though *Simulium* flies had repopulated the mouths of some of the small tributaries, **all people 10 years of age and younger were free of onchocerciasis.**

Control Programs

- Guatemala began a program to reduce onchocerciasis in the 1930s.
- The focus of the program was nodulectomy.
- Nodules were stored in 5 gal. pickle jars on shelves that lined the office of the then director of the program.
- Visiting scientists were welcome to handful.

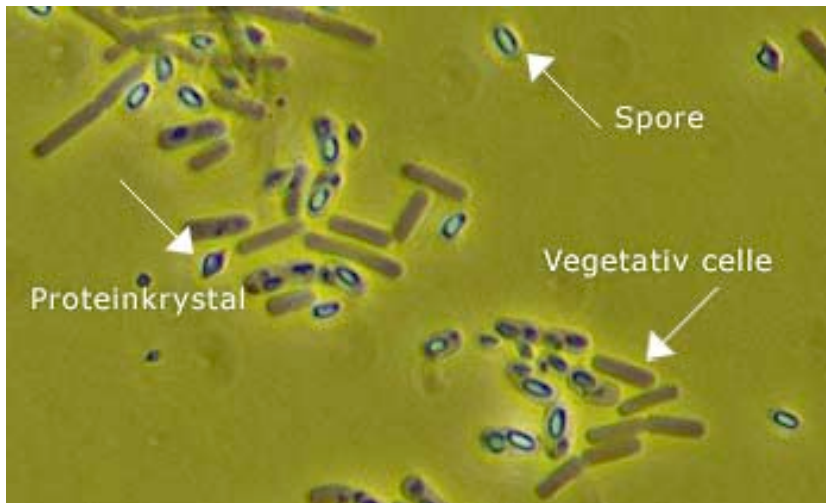
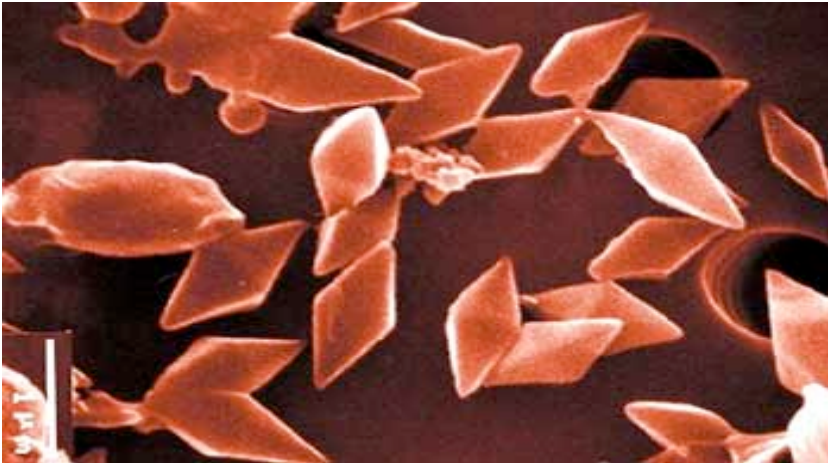


Control Programs

- Over the months and years, thousands of nodules were removed.
- Reduction in the serious complications of onchocerciasis were reduced but the disease not eliminated.
- **WHY?**



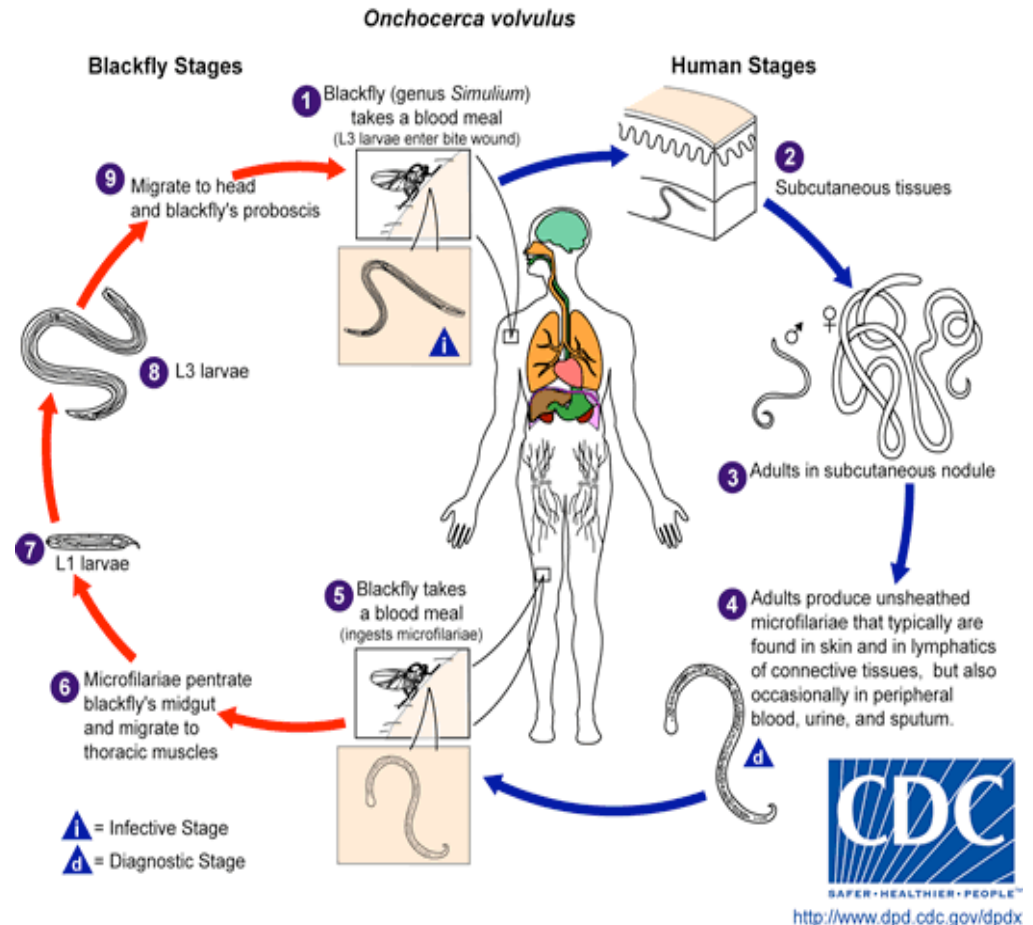
Control Programs



- In Africa:
 - Comprehensive eradication program began in 1975 by the International Bank for Reconstruction and Development and the WHO (Onchocerciasis Control Program-**OCP**).
 - Eradication by 2025.
 - Thrust of this program has been to spray the vector rivers.
 - Abate
 - *Bacillus thuringiensis*

Life Cycle

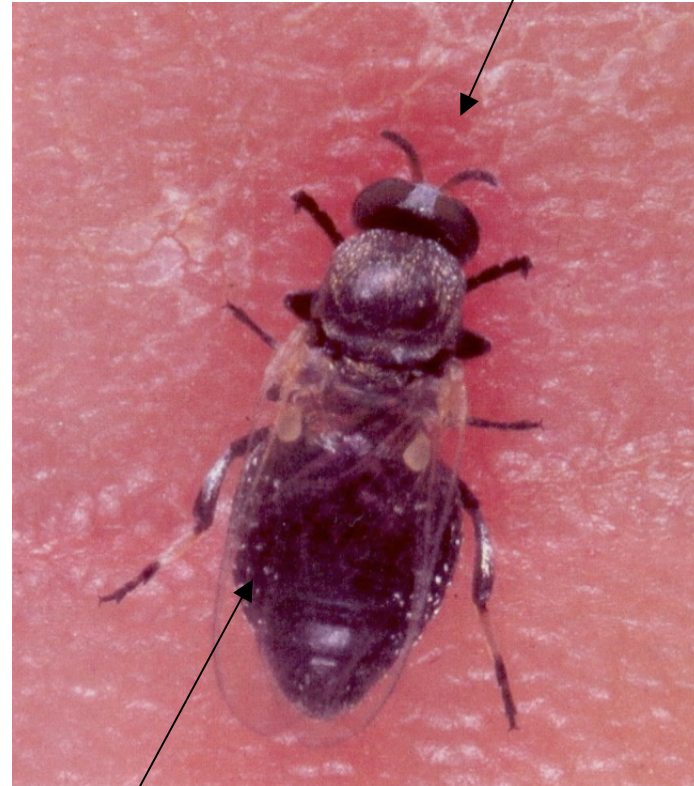
- **Black flies are tissue feeders, not blood suckers.**
 - **Observations by Brumpt, 1904.**
 - **Mosquito not the vector.**



Life Cycle

- **Coarse mouth parts.**
- **Rip and tear through the keratin and epidermis.**
- **Make a mulch out of keratin, cellular debris, tissue fluid and some serum and blood.**
- **Fly's saliva attracts microfilariae and acts as an anticoagulant.**

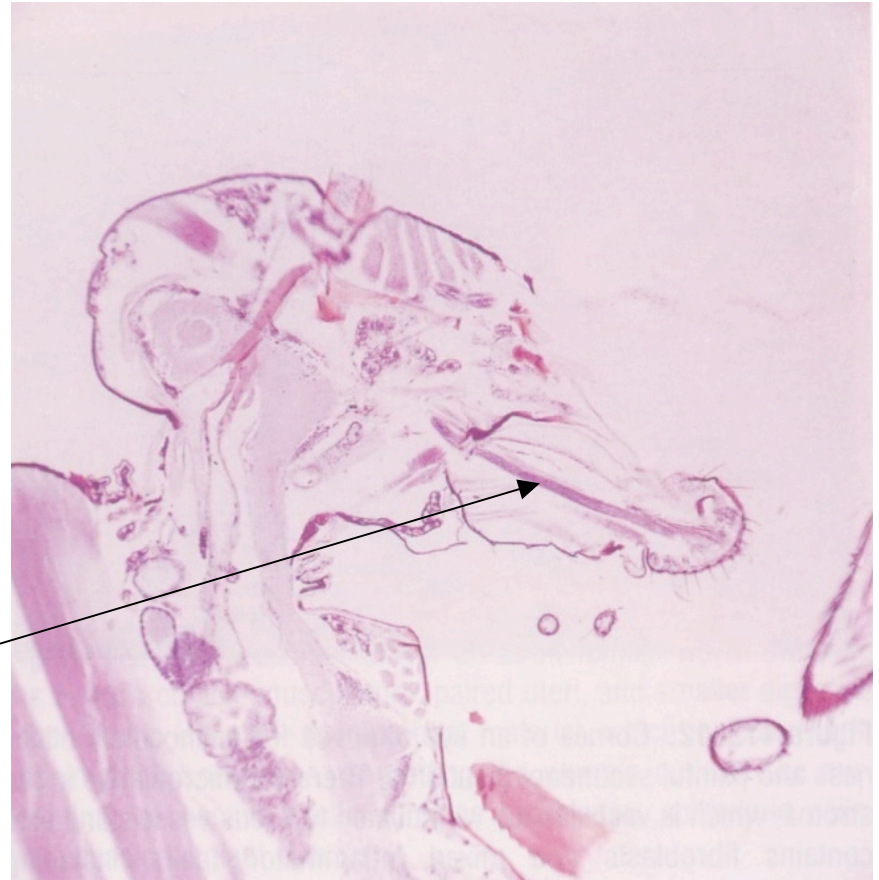
Erythema



Distended abdomen

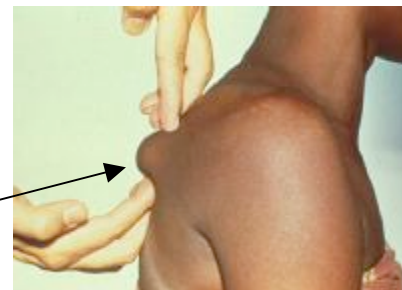
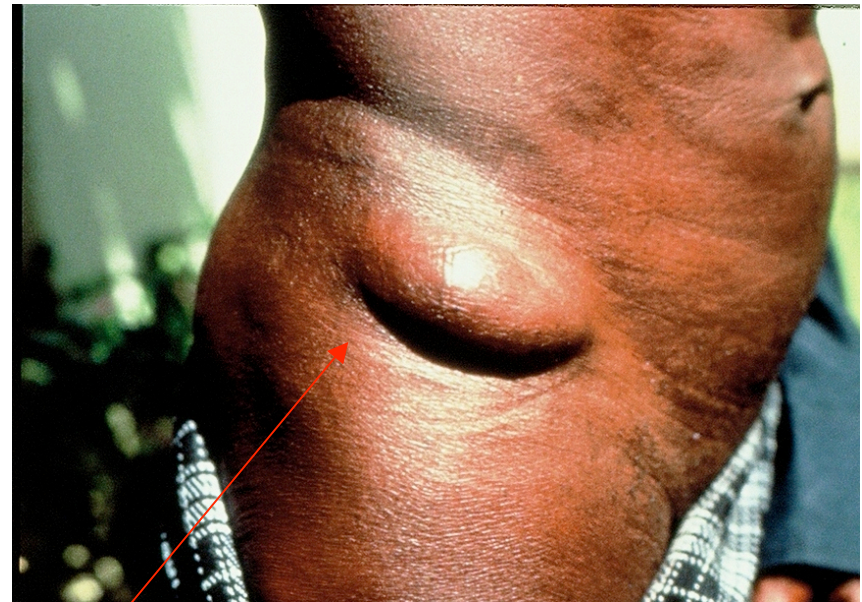
Life Cycle

- Once ingested by the fly, the microfilariae traverse the fly's intestine, migrate to the flight muscles, and mature to become infective larvae in 7-9 days.
- Infective larvae migrate to the mouth parts of the fly.
- **'Rodadores' and paralyzed flies.**



Life Cycle

- Once inside the human host, infective larvae develop into adult worms in the dermis and fascia, molting twice before maturing.
- Following copulation, the adult female worms produce microfilariae, completing the cycle.
- At some point (before or after copulation), the adult worms coil up and are surrounded by fibrous connective tissue.
 - Onchocercal nodule or onchocercomas.

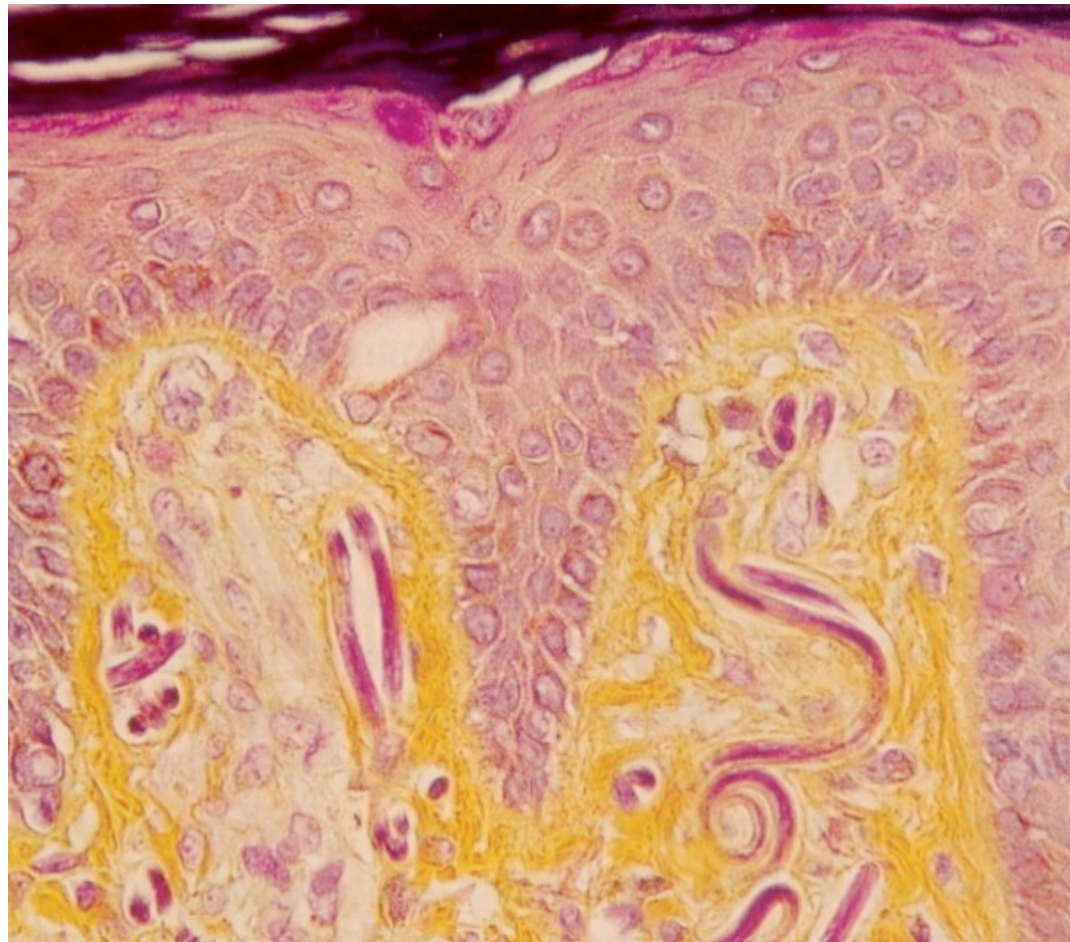


Life Cycle

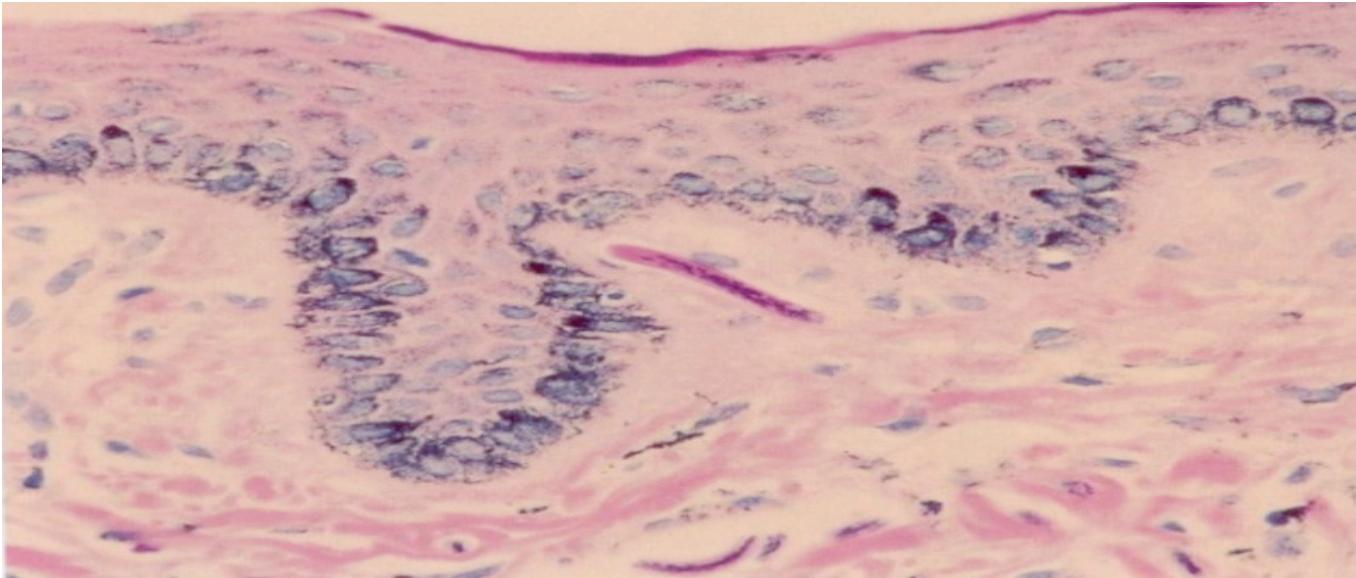
- **Adult worm pairs survive in humans for 15 years or more.**
- **Microfilariae may persist for up to 2 years after all adult worms have died.**



***O. volvulus* in the dermal papillae**



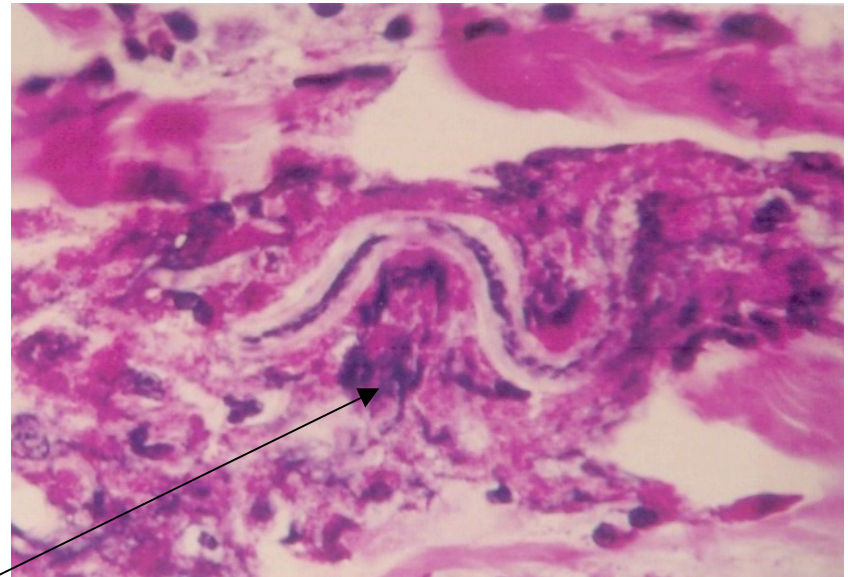
Microfilaria



- **Anterior clear space.**
- **Distinguish *O. volvulus* from *Mansonella strptocerca*, the other microfilaria that lives in human dermal collagen.**

Immunology

- Immune response to microfilaria varies between individuals from no response to severe extreme dermatitis ('sowda').
- When microfilaria degenerate (inflammatory rxn, **drugs, aging**) the microfilaria is surrounded almost immediately by eosinophils.



Immunology

- ***O. volvulus* drives a strong Th2 response.**
 - What cytokines involved?
- **Suppresses Th1-type immunity (e.g., PPD skin testing for tuberculosis, tetanus and other vaccinations.**
- **Increases susceptibility to lepromatous leprosy.**
- **Th2 response associated with keratitis in the cornea.**

Onchodermatitis

- **Inflammatory reaction to antigens released by degenerating microfilariae in the dermis and epidermis.**
- **Pruritus marks the early stage and may be the only manifestation of mild infections.**



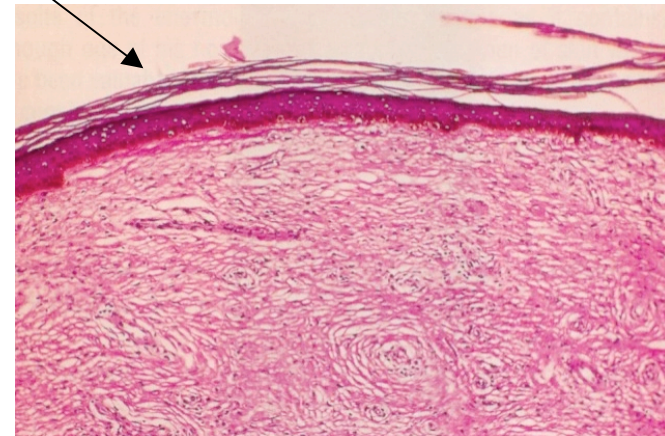
Onchodermatitis

- With progressive disease, itching is followed by altered pigmentation, edema, wrinkling and thickening of the dermis, depigmentation, spotty repigmentation, and atrophy and scaling of the epidermis.



Onchodermatitis

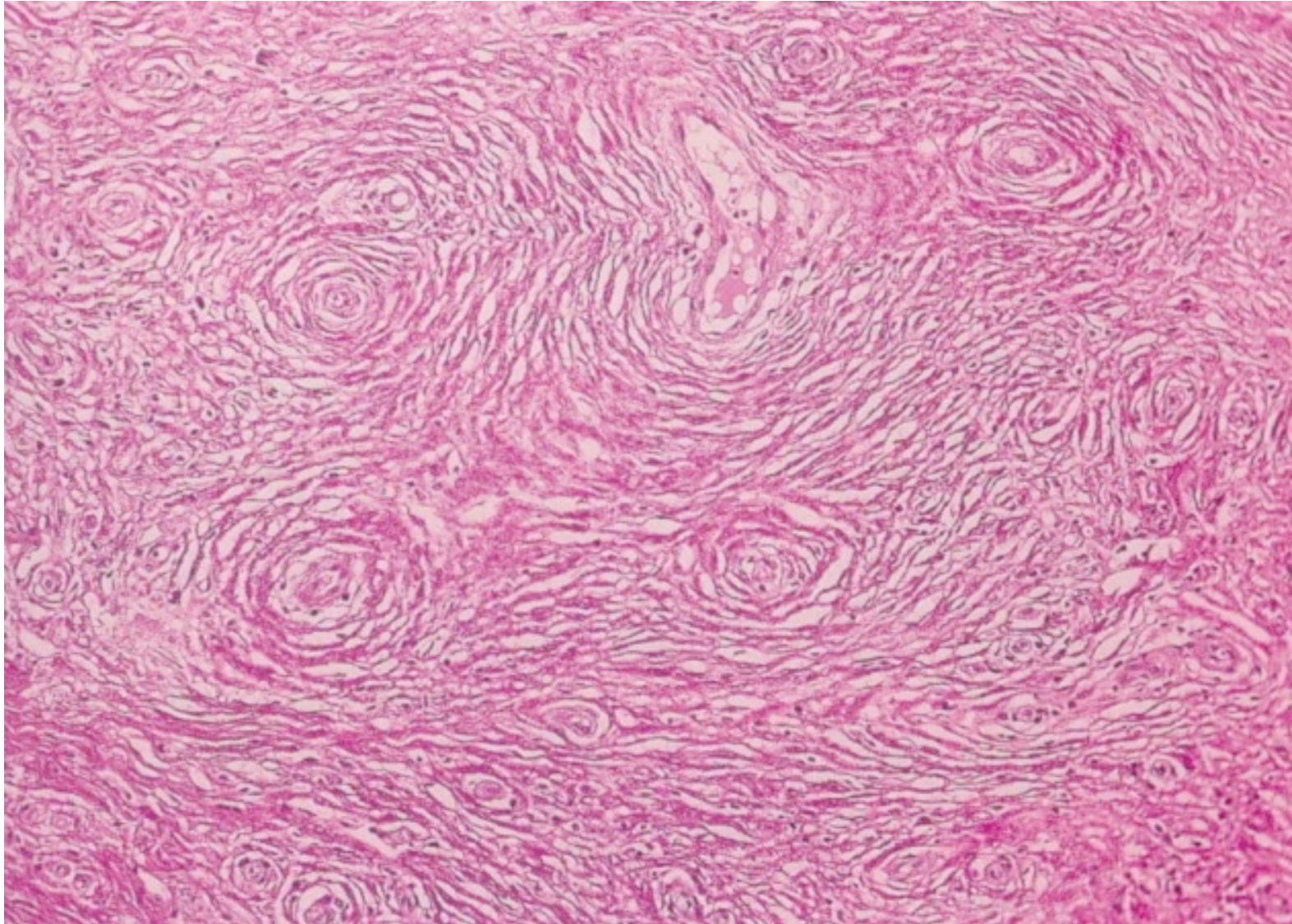
- Depigmentation with lymphedema of the lower limbs.
- ‘Parchment thin’ epidermis.
- Collagen replaced by scar tissue.



Onchocercal dermatitis

- **Long-standing infection of a middle aged patient (Uganda).**
- **The skin is shiny, caused by thinning of the epidermis.**
- **Wrinkling and edema, causing loose folds of skin.**





Onchocercal dermatitis

- **Scaling of the epidermis.**
- **Scaling was made worse by a test dose of diethylcarbamazine (DEC).**



Nodules

- **Contain adult worms.**
- **Round or flattened, firm, movable, located over boney prominences.**
- **Not tender or painful.**
- **Few millimeters to several centimeters across.**
- **Discrete or clustered.**



Nodules

- **In Africa, onchocercal nodules are concentrated on the lower half of the body.**
- **In Central and South America, onchocercal nodules are more common on the upper body—on the head, over scapular spines, and over the upper ribs.**

Nodules

- **In Africa, onchocercal nodules are concentrated on the lower half of the body.**
- **In Central and South America, onchocercal nodules are more common on the upper body—on the head, over scapular spines, and over the upper ribs.**
 - **Explained by the fact that the Central and South American flies tend to feed on the upper trunk and head.**

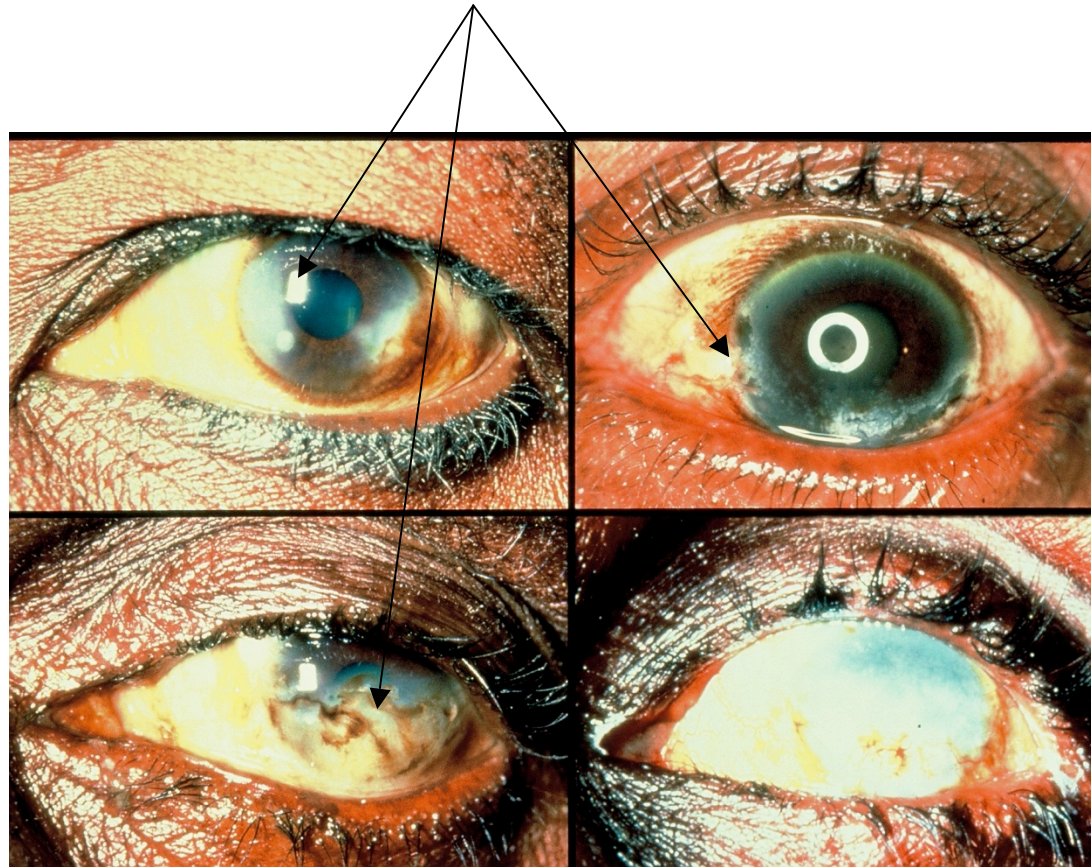
Eye lesions

- **Caused by microfilariae that penetrate and damage components of the anterior and posterior segments.**
- **Eye lesions common in endemic areas where nodules are located on the head and shoulder girdle.**



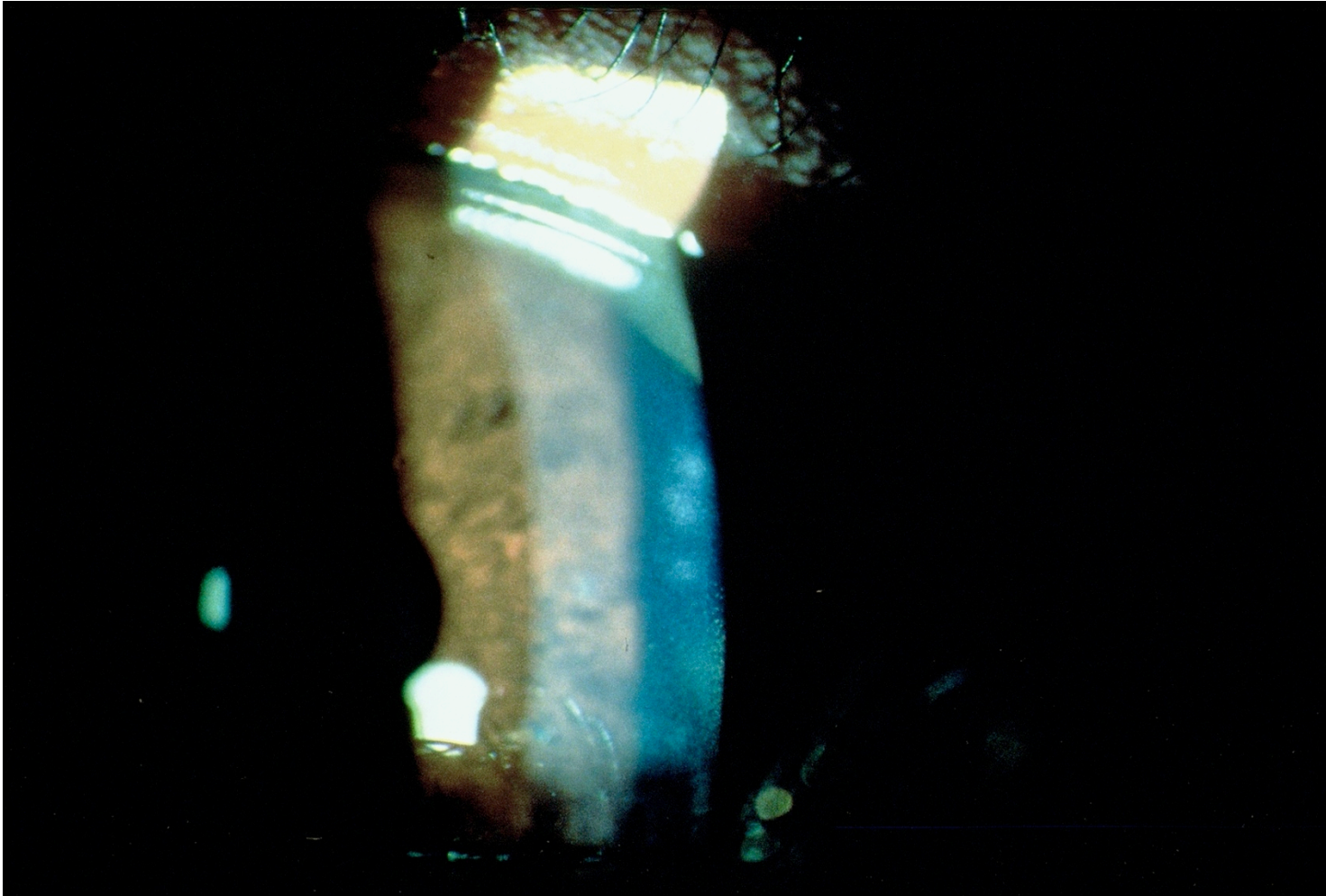
Sclerosing keratitis

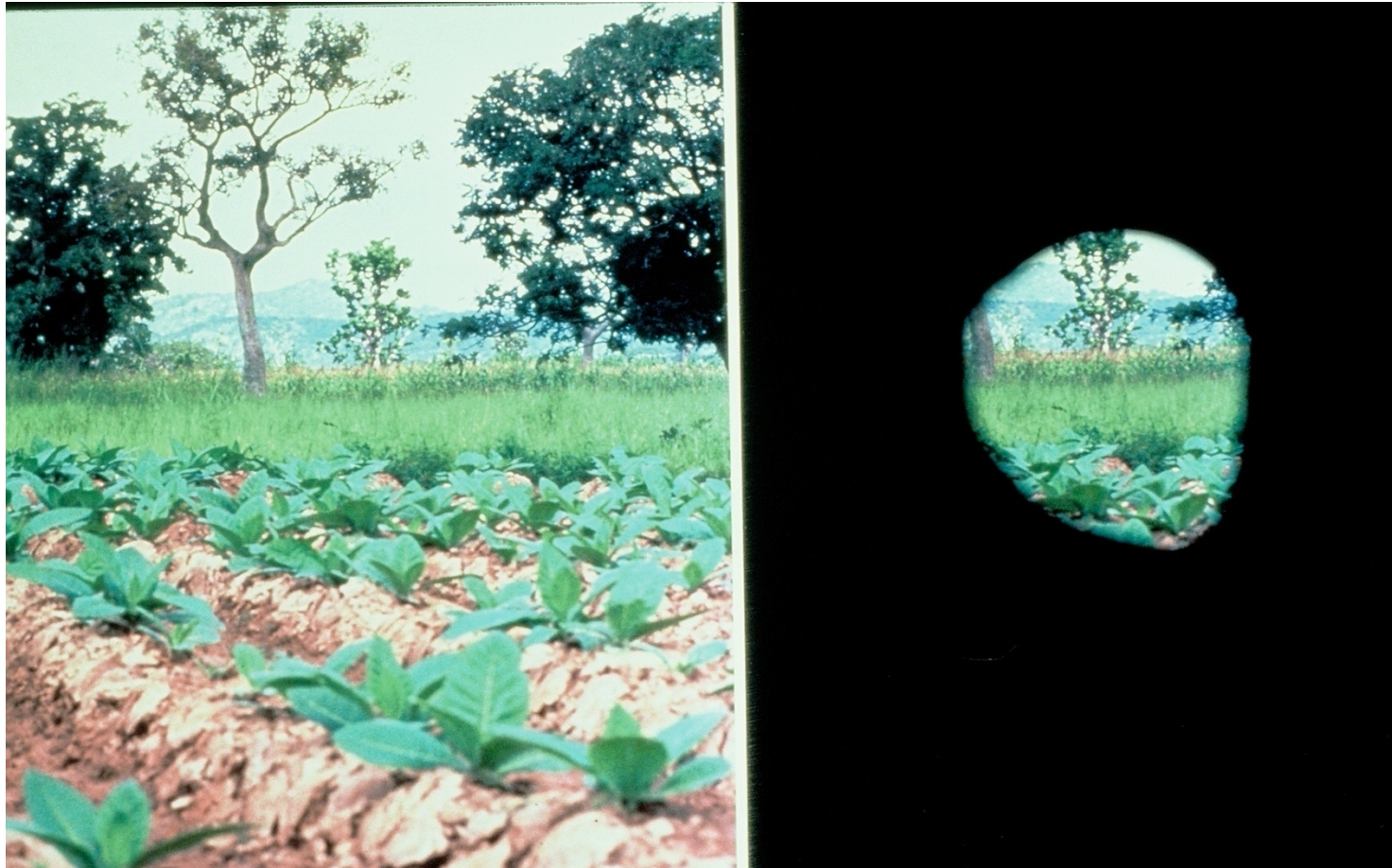
Sclerosing keratitis



Ocular lesions caused by both degenerating and living microfilariae.

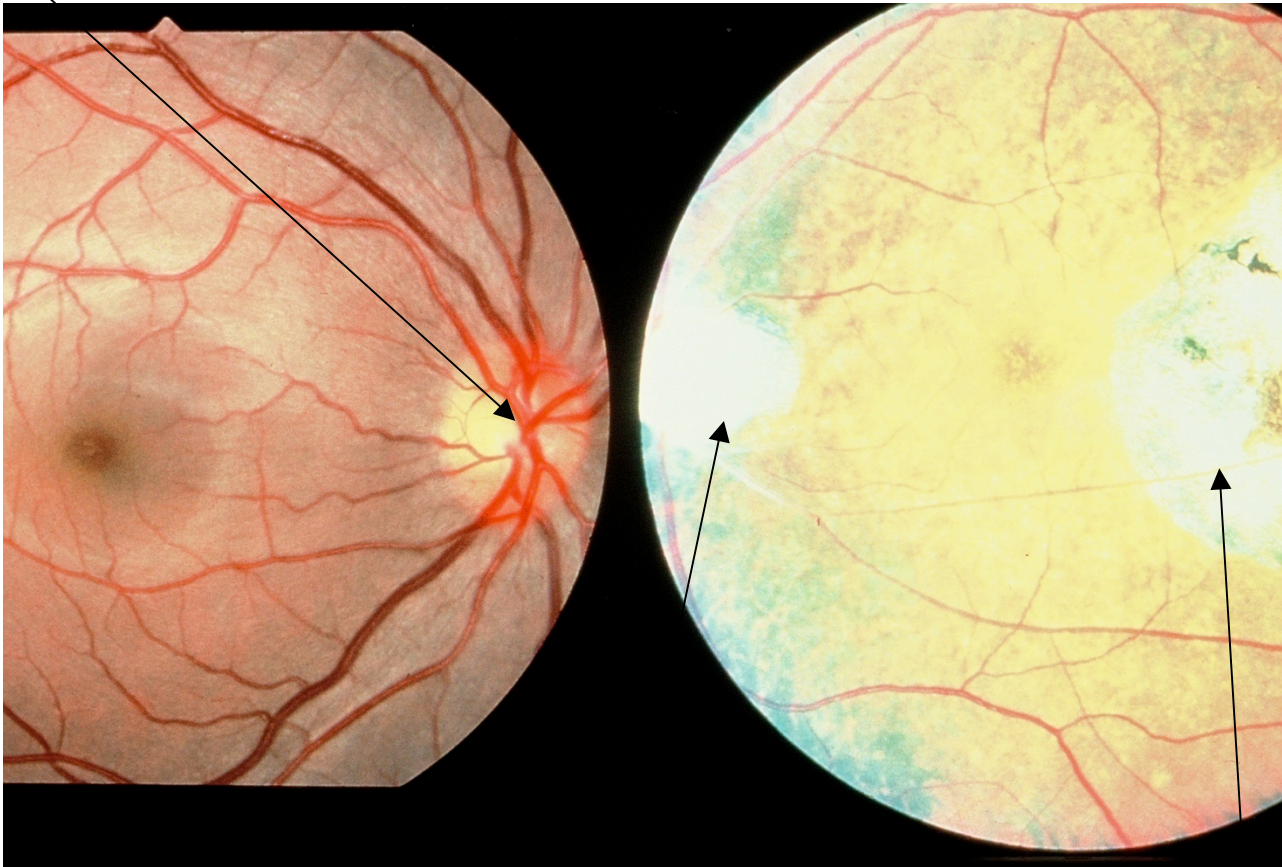
Snowflake' or 'cracked ice' opacities





At right; the view through the eyes of someone with severe disease at the back of the eye. 'Tunnel vision' caused by damage to the optic Nerve.

Normal optic disc



Optic atrophy

Choroido-retinal atrophy

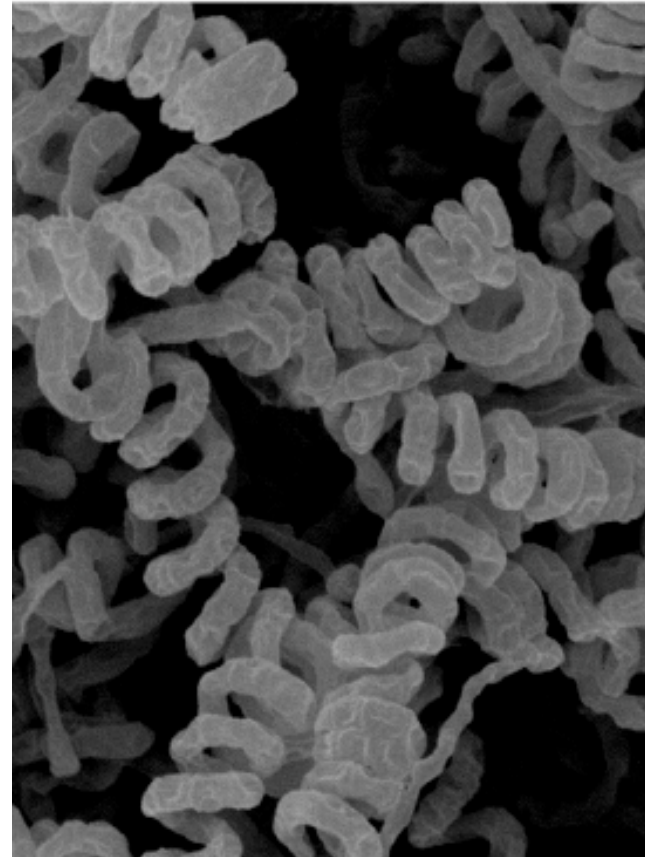
Treatment

- **Nodulectomy.**
 - **Difficult if nodules are embedded deeply in tissues.**



Treatment

- **DEC**
- **Albendazole**
- **Ivermectin**
 - **Single dose kills microfilariae in some of the uterine tubes.**
 - **Decrease concentration of microfilaria over time.**
 - **Reverses symptoms.**



Streptomyces avermitilis sp. nov.
Int J. Syst. Evol. Microbiol. 52: 2011-2014 (2002)

