Onchocerciasis

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Onchocerciasis

- A progressive inflammatory eye and skin disease
- “River blindness”
- 18 million people infected of which 770,000 already have impaired vision with 250,000 blind (estimates for 2003)
- Caused by infection with the filarial nematode *Onchocerca volvulus*
Global burden of Onchocerciasis

Countries with onchocerciasis (river blindness)
Geographic Distribution of Onchocerciasis in the Americas

MEXICO:
1. Oaxaca Focus
2. Northern Chiapas Focus
3. Southern Chiapas Focus

GUATEMALA:
4. Cuilco Focus (Huehuetenango)
5. Central Focus: - Sololá, - Suchitepéquez - Chimaltenango
6. Escuintla, Guatemala Focus
7. Santa Rosa Focus

ECUADOR:
13. Esmeraldas/ Pichincha Focus - Cayapas River - Santiago River - Onzole River - Satellite Foci:

COLOMBIA:
12. López de Micay Focus

VENEZUELA:
8. North-central Focus
9. North-eastern Focus
10. Southern Focus (Amazonas/Bolivar)

BRAZIL:
11. Amazonas-Roraima Focus (YANOMAMI Area)
Causes of 45 million cases of blindness (<3/60)

- Cataract
- Refractive Error
- Glaucoma
- Diabetes Retinopathy
- Corneal Scar
- Anterior Refraction (AR)
- Childhood Blindness
- Trachoma
- Onchocerciasis
- Others

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Two-thirds of blind people are women and girls
History of Onchocerciasis (1)

1875 - Microfilariae of *O. volvulus* first observed by the Irish naval surgeon John O'Neill when examining skin snips from patients with *craw* in Ghana.

1890 - Adult worms discovered and identified by Patrick Manson, Scottish medical scientist.

1890 - Parasitologist Emile Brumpt recognizes that the infection occurs most commonly along river banks, and that the microfilariae in the skin come from deeper cutaneous nodules where adult filariae reside.
History of Onchocerciasis (2)

1915 - Rodolfo Robles, a Guatemalan physician, sheds light on the life cycle and transmission of the parasite. Using case studies of coffee plantation workers in Guatemala.

1890 - Role of the microfilariae in causing the skin lesions is established by Jean Montpellier and A. Lacroix.

1890 – Role of blackflies in the transmission of onchocerciasis is proven by the Scottish parasitologist Breadalbane Blacklock in Sierra Leone.
Onchocerciasis vector: black fly
The black fly story

- Black flies (*Simulium* spec., especially *S. damnosum*)
- Small diptera with a fly like habitus (but they are Nematocerca (closer related to mosquitoes)) and only the females bite)
- Larvae and pupae are aquatic filter feeders, living in fast flowing oxygen rich waters
Life cycle of Onchocerca volvulus

1. Blackfly (genus Simulium) takes a blood meal (L3 larvae enter bite wound)
2. Subcutaneous tissues
3. Adults in subcutaneous nodule
4. Adults produce unsheathed microfilariae that typically are found in skin and in lymphatics of connective tissues, but also occasionally in peripheral blood, urine, and sputum.
5. Blackfly takes a blood meal (juveniles, microfilariae)
6. Microfilariae penetrate blackfly’s midgut and migrate to thoracic muscles
7. L1 larvae
8. L3 larvae
9. Migrate to head and blackfly’s proboscis

= Infective Stage
= Diagnostic Stage
Onchocerciasis

- Adult worms live for 20 years
- Produce 1,000 mfs. each day
- Microfilariae live for 2 years
- Infected early in life - anergy
- Disease due to reaction of dead mfs.
### Illustrative numbers in onchocerciasis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females per nodule</td>
<td>2–50 worms&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Males per nodule (constantly exchanging)</td>
<td>1–10 worms&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Microfilariae produced per day</td>
<td></td>
</tr>
<tr>
<td>per adult female</td>
<td>1600&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Total body daily microfilariae turnover (steady state)</td>
<td>10,000–300,000&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Total body loads</td>
<td>As high as 150 million microfilariae&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Females remain incarcerated in nodules [9].

<sup>b</sup> Males move in and out of nodules throughout lifespan [9].

<sup>c</sup> From [11].

<sup>d</sup> From [10, 12].
Onchocercosis in the skin

- Adult worms (*macrofilaria*) live in nodules under the skin of the human host.
- The female is ovoviviparous and releases L1 (microfilaria).
- Microfilaria migrate through the cutis.
- **Black flies** take up microfilaria through the blood meal, the worms settle in the fly thorax muscle and develop into infectious L3.
Onchocerciasis: Skin manifestations (1)

- Skin is the principal site of infection
- Manifestations due to reaction to *O. volvulus* antigens

Swoda: dark, thick, itchy

Erysipela “de la costa”
Onchocerciasis: Skin manifestations (2)

Acute papular onchodermatitis (APOD)

Lichenified Onchodermatitis (LOD)
Onchocerciasis: SQ nodules

The adult worms form nodules in the cutis which are enclosed by the host with a fibrotic granuloma (onchocercoma). Onchocercomas are easily spotted especially when over bone or strong muscle. Present in 30% of cases – develop over 18 month period
Onchocerciasis in the eye

- Chronic microfilaremia in the eye leads to sclerotizing ceratitis (a hardening inflammation of the clear front part of the eye)
- The cornea becomes opaque resulting in gradual loss of sight
- Nodules directly on the head seem to result in higher mf burden for the eyes and fast progression to blindness even in children
## Diagnostic tests described recently

<table>
<thead>
<tr>
<th>Study, diagnostic test</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ayong et al. [35]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine antigen dipstick assay</td>
<td>100</td>
<td>100</td>
<td>Not yet available commercially</td>
</tr>
<tr>
<td>Tear antigen dipstick assay</td>
<td>92</td>
<td>100</td>
<td>...</td>
</tr>
<tr>
<td>Vincent et al. [36]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum antigen immunoblot</td>
<td>100(^a)</td>
<td>100(^a)</td>
<td>...</td>
</tr>
<tr>
<td>Skin-snip PCR ELISA</td>
<td>90(^a)</td>
<td>100(^a)</td>
<td>...</td>
</tr>
<tr>
<td>Serum IgG4 (OC3.6gst) ELISA</td>
<td>78(^a)</td>
<td>100(^a)</td>
<td>...</td>
</tr>
<tr>
<td>Serum IgG4 (OC3.6gst and OC9.3gst) ELISA</td>
<td>97(^a)</td>
<td>100(^a)</td>
<td>...</td>
</tr>
<tr>
<td>Zhang et al. [37]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin-snip PCR PCHA</td>
<td>88</td>
<td>100</td>
<td>...</td>
</tr>
<tr>
<td>Skin-snip PCR AGE</td>
<td>84</td>
<td>100</td>
<td>...</td>
</tr>
<tr>
<td>Skin-snip PCR ELISA</td>
<td>91</td>
<td>100</td>
<td>...</td>
</tr>
<tr>
<td>Weil et al. [45]: serum antibody card test</td>
<td>91(^a)</td>
<td>95–100(^a)</td>
<td>...</td>
</tr>
<tr>
<td>Guzmán et al. [38]: serum antibody dot blot assay</td>
<td>99</td>
<td>90</td>
<td>Field-use friendly.</td>
</tr>
<tr>
<td>Nde et al. [47]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum antibody ELISA (hybrid recombinant antigen OvH2)</td>
<td>98.5</td>
<td>97.7</td>
<td>...</td>
</tr>
<tr>
<td>Serum antibody ELISA (hybrid recombinant antigen OvH3)</td>
<td>98.5</td>
<td>95.35</td>
<td>...</td>
</tr>
<tr>
<td>Boatin et al. [42]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin-snip microscopy</td>
<td>19–50(^a)</td>
<td>100(^b)</td>
<td>...</td>
</tr>
<tr>
<td>DEC skin patch test</td>
<td>36–83(^a)</td>
<td>99(^a)</td>
<td>...</td>
</tr>
<tr>
<td>PCR ELISA</td>
<td>50–88(^a)</td>
<td>96(^a)</td>
<td>...</td>
</tr>
</tbody>
</table>

**NOTE.** AGE, agarose gel electrophoresis; DEC, diethyl carbamazine; PCHA, paper chromatography hybridization assay

\(^a\) Interpreted from text.

\(^b\) Stated as benchmark in text.
Other clues to diagnosis

- Eosinophilia (rarely)
- High IgE level inconstant
- **Mazzotti Test:**
  - 50 mg of DEC (diethylcarbamazine)
  - Within 3 hrs.: pruritus and erythema
  - Caution to be used in highly infected patient
Treatment of Onchocerciasis

- **Diethylcarbamazine DEC** (kills microfilaria and in some species macrofilaria slowly with unknown mechanism)
- Sudden death of many MF can lead to severe inflammatory reaction of skin and eye
- **Ivermectin** (paralysis of worms by interfering with neural ion channels), does not kill macrofiliaria but dramatically reduce MF number and has milder side effects than DEC
- Pretreatment with steroids can reduce side effects
Treatment of Onchocerciasis

- Ivermectin causes diminution of microfilaria without inflammation
  

- Ivermectin treatment does not cause optic neuritis
  

- Ivermectin causes diminution of the burden of infection
  

Treatment has had a major effect on ocular morbidity although elimination of the disease has yet to be achieved.
Ivermectin effectiveness

- Single dose of 150 mcg/kg every 6-12 months
- Microfilaria elimination within 2 weeks
- Production of microfilaria averted for 6 months
- 11 dose therapy resulted in 32% elimination of adult worms
- Treatment span ~ 10 years
Nodulectomy

- Adult worms can be removed surgically to reduce microfilarial load to alleviate symptoms
- Good therapy for few or single superficial nodules
Prevention

• No vaccine, no chemoprophylaxis
• Protective immunity does not appear to develop in humans
• Mosquito protection using repellents
• Vector control in West Africa: weekly treatment of rivers and aerial insecticides
• Mass Ivermectin to break transmission cycle in 10-15 years
Trends in Causes of Blindness
1995 - 2002

- **Trachoma**
  - 1995: 1.9
  - 2002: 5.9

- **Corneal Scar**
  - 1995: 1.8
  - 2002: 4.1

- **Oncho**
  - 1995: 0.4
  - 2002: 0.9

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The success of the onchocerciasis control programme and its philosophy of community directed distribution has led to USAID, Gates Foundation, DFID, and other major donor interest in the Neglected Tropical Disease initiative.