Onchocerciasis
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“Do you want to hear about a case of eyeworm?”

• March 2012 email from local vet
• 8 yr old Boxer dog from Tarzana
• Ulcers in corneas both eyes
  – Surgery to patch ulcers
  – Also removed 1/2 cm “incidental” painless mass stuck to side of right eyeball
  • Mass sent to Univ of Wisconsin for histopathology
  • Filled with worms
  • Some species of “Onchocerca”
Onchocerca?  
What is that?  

Time to crack open the books...

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**Onchocerciasis aka “River Blindness”**

- Caused by filarial worm- *Onchocerca volvulus*
  - Distantly related to heartworm parasite of dogs and cats *Dirofilaria immitis*
  - Both contain endosymbiont bacteria *Wolbachia*
- 2nd leading cause of infectious blindness worldwide
- Vector: Black flies (*Simulium* spp)
  - Breed in rivers and streams
- Humans are the definitive host
  - Reservoir and victim

(Merck Manual)
Epidemiology and Control of River Blindness

- Endemic in Africa and Latin America, and in Yemen
  - 40 million infected (99% in Africa)
  - Worst hit villages - 1/3 of adults blinded
- Control Programs
  - 1974 – WHO’s Onchocerciasis Control Program (OCP)
    - first large scale control effort in W Africa: Vector control for first decade - partial success
    - 1987 - Drug company began free donations of ivermectin: mass distribution - much greater success
  - 1992 Onchocerciasis Elimination Program for the Americas (OEPA)
  - 1995 African Programme for Onchocerciasis Control (APOC)

(Rodriguez-Perez et al. 2011, Resnikoff et al. 2008, Adler et al 2010)

River Blindness endemic in 36 countries

http://www.stanford.edu/class/humbio103/ParaSites2006/Onchocerciasis/Epidemiology.html
**Onchocerca volvulus** Life Cycle

- Bite from infected black fly introduces L3 larvae into skin
- Larvae develop into adult worms in 12 to 18 months
- Adults live ~15 years
  - Females: ~50 cm
  - Males: ~5 cm
- Adults gather in painless nodules under skin and elsewhere in body
- Mature female worms produce microfilariae (mff)
  - Many 1000s per day
- Mff migrate over whole body through the skin and lymph system, invade eyes
- Dying adults or mff release *Wolbachia* bacteria, trigger inflammatory reaction from host.

(Merck Manual)
Diagnosis of River Blindness

- Palpate for nodules
  - remove surgically and examine for adult worms
- Skin Snip
  - Cut 3-5 grams of skin, place in saline or culture media for 4 hours, examine for mff coming out visually or by PCR. Estimate parasite load.
- Slit Lamp Eye Exam
  - Look for mff floating in eye
- Mazzotti Test or DEC patch test
  - Give dose of drug DEC which kills mff.
  - Intense itching in 2 hours if lots of mff dying
- ELISA blood test for antibodies against *Onchocerca*
  - Can’t tell difference betw current and past infection

[http://www.stanford.edu/class/humbio103/ParaSites2006/Onchocerciasis/Diagnosis.html](http://www.stanford.edu/class/humbio103/ParaSites2006/Onchocerciasis/Diagnosis.html)

Symptoms and Treatment of River Blindness

**Symptoms**
- Severity depends upon # of parasites in the body
- Painless nodules under skin packed full of adult worms. Usually over skull, ribs, ankles.
- *Microfilariae* (mff) migrate through skin all over body.
- Skin: thickening, scaly, itchy, patches of depigmentation, premature aging
- Eyes: mff migrate through cornea, dying mff trigger severe inflammation in eye.

**Treatment**
- First 100 years: Only surgical removal of adult worms
- Since 1988: ivermectin to kill mff stops parasite life cycle

Rodriguez-Perez et al, 2011
Nodules formed by adult worms

(Zerah Eye Centre)

(USAF - PH Source)

(Pugh Parasitology Collection)

10/11/2012

12

Skin rash from migrating and dying microfilariae

(Christoffel-Blinden Mission, Nigeria, in Resnikoff et al, 2008)

Opacification of corneas and blindness
Vector: Black Flies

Black Flies and *Onchocerca volvulus*

- 1926 First proven as vector for onchocerciasis
- No *Simulium* species feeds exclusively on humans
- In Africa
  - *Simulium damnosum* spp complex
  - High affinity for humans
  - Best known vector for onchocerciasis
- Central, South America:
  - *S. ochraceum*, *S. metallicum* and *S. exiguum* spp complexes

(Adler et al 2010, Rodríguez-Pérez et al 2011, Service 2012, Riley & Johanssen 1915)
Black Flies

- 3 Genera, 2000+ species
  - Among top 4 most important arthropod vectors
  - Vector for 28 pathogens
  - *Simulium* spp most medically important
- Males and females consume plant juices
- Females take blood meals before oviposition.
- Attack in daytime
- Mouth parts inflict cuts that lacerate capillaries (ouch!).
- Oozing blood sucked up
  - *Onchocerca* mff ooze from skin, ingested.

Body is 1.5 - 4mm long.


Black Fly Life Cycle

Sticky eggs
- Laid in moving water
- On submerged rocks or vegetation
- 100-900 per batch
- Hatch in 1-4 days

Mature larvae sticky pad of saliva
- Feed on microorganisms in water

Pupates in silken cocoon 2-6 days

Adults emerge en masse
- Float to surface in air bubbles; fly immediately
- 15-20 generations / year
- Large rivers: up to billion flies/km of river/day
- Parts of Amazon - black flies kill livestock, agriculture impossible

Photo: Pan American Health Organization
River Blindness in Latin America

- Latin America
  - *Simulium* vectors widespread
  - *Onchocerca volvulus* only known in 13 foci in 6 countries
    - Most heavily populated area at risk: Mexico-Guatemala border
      - 39 communities hyperendemic
  - Onchocerciasis Elimination Program for the Americas (OEPA)
    - Mass provision of ivermectin
    - Success in 8 of 13 foci controlled
      - Southern Mexico (Oaxaca, Chiapas):
        » 1995: 600,000 at risk
        » 2009: 150,000 at risk
      - population at risk reduced from almost 5 million to about 1/2 million

(Rodriguez-Perez et al 2011, Adler et al 2010)
Simulium ochraceum is not an efficient vector. Buccopharyngeal "teeth" lacerate the mff when ingested.

....BUT, it readily bites people, and currently feeds on a lot of infected people. ~1% of flies infected in endemic area.

2009: PAHO vows to reduce onchocerciasis to insignificant levels by 2015

Many areas in Amazon are "hyperendemic" - >60% infected.
Investigating Onchocerciasis in Los Angeles County Dogs

1. Is there a particular species of *Onchocerca* regularly found in dogs?
2. Have there been other cases in Southern California dogs?
3. Can the dog-infecting species of *Onchocerca* also infect people?

**Answers:** YES, YES, and….YES!

Onchocerciasis in Animals

**Horses**
- *O. cervicalis* in horses
  - Adult worm nodules: in nuchal ligament of neck
  - Vector: *Culicoides* spp (biting midges)
  - Present in US

**Cattle**
- *O. lienalis* and *O. gutterosa* in cattle
  - Adult worm nodules: in abdomen (*lienalis*) and nuchal ligament (*gutterosa*)
  - Vector: *Simulium* spp.
  - Present in US
Onchocerciasis in Animals

Dogs

-O. lupi
  - Adult worm nodules: anywhere inside eye socket
    - 0.5-2.5 cm
  - Vector: undetermined
  - Most common clinical signs (seen in dogs in Greece)
    - Swelling around eye, watery eye, discharge, eyeball and 3rd eyelid pushed out, pain, sensitivity to light, corneal lesions, granulomas
  - 1967 – first described as a parasite found in wolves in Russia
  - Many cases well-documented in Greece and Hungary.
  - In US? Yes! We’ll come back to that….

Can O. lupi infect people?

Case #1

- 18 year old girl in Turkey.
- Painful fly bite on upper eyelid
- 30 days later - painless redness in left eye
  - 5mm mass under conjunctiva of one eyeball.
- 28 d later, pain in eye, mass still there.
  - part of a female nematode extracted.
    - No mff in worm.
  - Identified morphologically and by PCR as O lupi.
- No other tx described.
- 5 months later – normal.
Can *O. lupi* infect people?

Case #2

- 26 yr old male in Turkey
- Lived in city, only travel had been a summer vacation of 10 days prior summer 2011. Dogs lived in patients home area. No fly bites reported.
- Irritation/itching of right eye progressing over 2 weeks. 5x5mm mass seen in conjunctiva.
  - CT scan of eye showed nothing else.
  - Tx 1 wk of topical steroid and antibiotic, plus oral antibiotic.
  - No improvement.
- Exploratory surgery found nematode tightly packed in mass. Parases stuck to tissue. Removed in pieces
  - Worm total length – 10 cm, female. No mff inside.
  - Identified morphologically and by PCR as *O. lupi*.

Otranto et al, 2012

Can *O. lupi* infect people?

Case #3

- 8 year old child in irrigated agricultural area of Tunisia. No travel. No fly bite reported.
- Dogs, cats, and lots of livestock in area.
- 4 weeks of pain in right eye.
- 8mm subconjunctival mass excised completely.
- Immature female worm coiled inside.
- Identified morphologically as *O. lupi*.

Otranto et al, 2012
Are there other Onchocerciasis cases in pets in the US?

<table>
<thead>
<tr>
<th>Year</th>
<th>Location</th>
<th>Case Details</th>
<th>Citation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1991</td>
<td>San Gabriel Mts, LA County, CA</td>
<td>Grew masses in both eyes, both eyes removed. Gravid female worm(s) seen. Morphology compared to <em>O. lienalis</em>.</td>
<td>Orihel et al, 1991</td>
</tr>
<tr>
<td>1993</td>
<td>LA County, CA</td>
<td>Corneal lesion and mass on iris – eye removed. Adult male and gravid female worms embedded in sclera. Morphology compared to <em>O. volvulus</em> and <em>O. lienalis</em>.</td>
<td>Gardiner et al, 1993</td>
</tr>
<tr>
<td>2000</td>
<td>Lancaster, CA</td>
<td>Eye removed. Worm in large nodule behind eyeball. Gravid female worm(s) seen. Morphology compared to <em>O. lienalis</em>.</td>
<td>Eberhard et al, 2000</td>
</tr>
<tr>
<td>2000</td>
<td>Yuma, AZ</td>
<td>Worm living in corneal lesion. Gravid female worm(s) seen. Morphology compared to <em>O. lienalis</em>.</td>
<td>Eberhard et al, 2000</td>
</tr>
<tr>
<td>2005</td>
<td>California</td>
<td>Red eye that grew painful. Eye removed. Worm in 1.5 cm mass. Single female worm, not gravid. Morphology compared to <em>O. lienalis</em> and <em>O. lupi</em>.</td>
<td>Zarfoss et al, 2005</td>
</tr>
<tr>
<td>2012</td>
<td>New Mexico</td>
<td>½ cm mass removed from conjunctiva of eye. Gravid female worms seen. Compared to <em>O. lupi</em>.</td>
<td>Sanchez et al, 2012</td>
</tr>
</tbody>
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Ongoing research on *Onchocerca lupi* in the USA

- Dr. Richard Dubielzig, Univ of Wisconsin, College of Vet Med
  - Many PCR-confirmed *O. lupi* cases from around So Cal – to be published….

<table>
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<tr>
<th>Location</th>
<th># of cases confirmed in dogs by biopsy, 1994-2012 (most since 2004)</th>
</tr>
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<tbody>
<tr>
<td>San Diego County</td>
<td>7</td>
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<tr>
<td>Los Angeles County</td>
<td>5</td>
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<tr>
<td>San Luis Obispo County</td>
<td>1</td>
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<tr>
<td>Arizona</td>
<td>4</td>
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<tr>
<td>Also has individual cases from TX, OK, MN, UT</td>
<td></td>
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</tbody>
</table>

- Dr Amber Labelle, Univ of Illinois, College of Vet Med
  - Offered to perform PCR testing on fixed tissue samples from So Cal in Dr Dubielzig’s collection at request of LA County VPH

- GLACVCD agreed to collect black flies from the LA River
  - near the 2012 canine Tarzana case

- Dr. Thomas Unnasch of Univ of South Florida agreed to PCR test black flies collected by GLACVCD.
2012 LA County case

- 8 yr old Boxer dog from **Tarzana**
- Ulcers in corneas both eyes
  - Surgery to patch ulcers
  - Also removed 1/2 cm “incidental” painless mass stuck to side of right eyeball
    - Dr Dubielzig reported mass to contain **Onchocerca**
- Dr Nutman running PCR test on fixed tissue.

2006 LA County case

- Labrador Mix from **Los Angeles, 90068**
- Mass on Sclera of left eye.
- Surgery to remove mass – contained
- Dr. Nutman running PCR test on fixed tissue.
2004 LA County case

- Australian Shepherd from Juniper Hills
- Both eyes
- Conjunctival swelling.
- Right eye only
- Corneal degeneration
- Glaucoma.
- Small biopsy of conjunctival - only inflammation.
- Dx obtained after eye removed – worms seen
- No tissue available for PCR in 2012.

2012 San Diego County case

- 4 year old Pitbull Mix
- Two masses firmly adherent to sclera in one eye
  - 1 cm
  - 0.8 cm
- Surgically removed
- Diagnosed as Onchocerca spp on Biopsy by Dr. Dubielzig.
- **Confirmed by PCR as O. lupi by Dr Thomas Nutman. Very similar to O. lupi in Hungary.**
GLACVCD's Black Fly Control Program

- 1994 - infestation severe along 18 mile stretch of LA River S. vittatum primarily. Occasional S. virgatum, and S. piperi

- Control Plan:
  1. Monitor larval abundance
  2. Monitor black fly larvae abundance
  3. Apply Bti when larval #s above thresholds
  4. Monitor effectiveness of treatment

- Bti = *Bacillus thurigiensis israeliensis*
  - soil bacteria
  - safe to humans and wildlife
  - kills simulid and mosquito larvae when ingested
  - available as slow-release briquettes or powder that is mixed with water and sprayed on larval habitats
  - no multiplication of the bacteria - must repeat application


Questions?

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More Onchocerca lupi cases in Greece. Shared with permission, from Dr Anastasia Komnenou

Discharge, hair loss, redness, bulging eye and 3rd eyelid

Tumor-like mass

Surgery to remove nodule mass

Severe corneal ulcer and nodule

Consult with a Public Health Veterinarian!

213-989-7060
vet@ph.lacounty.gov
publichealth.lacounty.gov/vet
References

- Center for Genomics and Bioinformatics WIKI Collaboration Center. Accessed 10/8/12 from: https://wiki.cgb.indiana.edu/display/gap/GapOverview
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