**Human toxocariasis**

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**Introduction**

- **Human toxocariasis**: helminthic zoonosis caused by infection with *Toxocara* spp. L2 larvae:
  - *Toxocara canis* (mostly in canids)
  - *Toxocara cati* (mostly in felids)


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**Epidemiology**

Toxocariasis in the definitive host

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**Life cycle of Toxocara canis**

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**Prevalence of Toxocara canis in dogs**

- **Africa**
  - Egypt: 80.6%
  - RSA: 32

- **Australasia**
  - Australia: 38
  - Japan: 21.5

- **North America**
  - Canada: 34
  - USA: 13 - 49

- **Europe**
  - Austria: 16.5%
  - Germany: 11
  - France: 25
  - GB: 21
  - Italy: 34

- **South America**
  - Argentina: 28
  - Chile: 13.5
Prevalence of *Toxocara cati* in cats

- **Europe**
  - Germany 9.5%
  - Eire 42
  - Slovakia from 66% (urban) to 76% (rural)

Soil contamination by *Toxocara spp.* eggs

- **Africa**
  - Egypt 10%

- **Australasia**
  - Australia 1

- **North America**
  - Canada 2.3 – 18
  - USA 5.7 – 15

- **West Indies**
  - Guadeloupe 15.6

- **Europe**
  - Austria 5.7%
  - Germany 10
  - France 77
  - GB 75
  - Italy 24 – 52.7

- **South America**
  - Argentina 13.2 – 35.1

Mode of contamination

- Ingesting *Toxocara spp.* propagulae:
  - Embryonated eggs
  - Live L2 larvae (foodborne route)

  - Sturchler D, Weiss N and Gassner M. *J Infect Dis* 1990;162:571

Epidemiology

Toxocariasis in the human paratenic host

Classical risk factors (1)

- Eating raw vegetables grown in contaminated kitchen gardens

- Eating raw or underdone liver:

Classical risk factors (2)

- Rural dwelling

- Children

- Pica

- Contact with puppies
  - Keegan JD and Holland CV. *J Helminthol* 2013;87:78-84
Prevalence of anti-*T. canis* IgG
(as detected by ELISA)

- **Australia**
  - Australia 7%
- **North America**
  - Canada 4.5
  - USA 1–24
- **South America**
  - Argentina 39
  - Brazil 39
- **Africa**
  - Sudan 5%
- **Asia**
  - Japan 4
  - Iran 25.6
- **Europe**
  - Italia 4.2
  - GB 2.6
  - Switzerland 10–37

Région Midi – Pyrénées, France
(as detected by WB)

- 4.8%
- 14.6%
- 37%

Tropical Islands

- **Santa Lucia (B.W.I)**
  - 86% among children

- **La Réunion (French Indian Ocean)**
  - 92.8% among adults (by western-blot)

Pathophysiology

Immune evasion

- Exclusively larval parasitism
- Continuous renewal of the outer epicuticular layer
  - Shedding of the surface coat
  - Impeding the killer role of eosinophil cells

- Association with allergy

  - Release of glycoproteic excretory-secretory Ag (ES Ag) containing an allergenic fraction
  - Allergy symptoms

Clinical picture
Generalized vs compartmentalized forms

Generalized forms (1)

Major syndrome: visceral larva migrans (VLM)
- Fever
- Weight loss
- Chronic cough
- Wheezing
- Enlarged liver


- Loeffler’s infiltrates
- Hyperleucocytosis
- Hypereosinophilia
- Hypereosinophilia
- Elevated anti-A/B level

Generalized forms (2)

Minor syndrome: common toxocariasis
- Chronic weakness
- Allergy signs (resp., ORL, cut., opht.)
- Digestive disorders
- Mild blood eosinophilia
- Elevated level of serum total IgE


Generalized forms (3)

Minor syndrome: covert toxocariasis
- Anorexia, headache, abdominal pain, nausea, vomiting, lethargy, sleep and behavior disorders, pharyngitis, pneumonia, cough, wheeze, limb pains, cervical lymphadenitis and hepatomegaly
- 27% of the patients displayed no blood eosinophilia.


Compartmentalized forms (1)

Ocular toxocariasis
- Peripheral or / and posterior granuloma
- Nematode endophtalmitis
- Children < 12 years: 50%
- Vision loss: 85%
- Blood eosinophilia often lacking
- Immunodiagnosis (serum) often negative

Diffuse Unilateral Subacute Neuroretinitis

* by courtesy of Bascom Palmer Eye Institute, Miami, USA

Compartmentalized forms (2)

Neurological toxocariasis

- Less than twenty cases reported from 1950 to the present

- Non specific clinical signs = underdiagnosed?

Non-specific tests

- Blood count: eosinophilia (depending on the form)
- CSF eosinophilia in neurological forms
- Total serum IgE levels

Laboratory diagnosis

Direct optical diagnosis (1)

Larva or larval sections or debris in organs, biopsies, cerebrospinal, ocular or other fluids


Direct optical diagnosis (2)

Liver granuloma (here in a Macacus monkey)

Larva displaying characteristic lateral alae

By courtesy of L.T. Glickman, Philadelphia, PA

Hyalitis & retinal traction band

Compartmentalized forms

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By courtesy of L.T. Glickman, Philadelphia, PA
**Immunodiagnosis (1)**

At the beginning (1960s & early 1970s)

- Ag $\leftarrow$ *Toxocara canis* adult worms
- Lack of sensitivity and specificity


**Immunodiagnosis (2)**

First improvements

- Ag $\leftarrow$ *T. canis* embryonated eggs
- Ag $\leftarrow$ *Ascaris suum* uteri

**Immunodiagnosis (3)**

IEP with *A. suum* extracts showing specific type 1 line


**Immunodiagnosis (4)**

The turn point

- 1975: in vitro "cultivation" of *T. canis* larvae
- 1979: ELISA using *T. canis* ES Ag (TES-Ag)

**Immunodiagnosis (5)**

Production of TES Ag (Toulouse)

**Immunodiagnosis (6)**

TES-ELISA for IgG

- Reference test for immunodiagnosis
- Numerous commercial kits
- Sensitivity $\approx$ 91 %; specificity $\approx$ 86 %
- Possible issues in tropical countries
Immunodiagnosis (7)

Western-blots for specific IgG
- 2nd implementation in Infectious diseases
- Specific LWM 24 ↔ 35 kDa


Immunodiagnosis (8)

Elisa vs Western-blots (IgG)

<table>
<thead>
<tr>
<th></th>
<th>Elisa</th>
<th>Western-blots</th>
</tr>
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<tbody>
<tr>
<td>WB</td>
<td>26</td>
<td>5</td>
</tr>
<tr>
<td>Wb</td>
<td>35</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td>61</td>
<td>35</td>
</tr>
</tbody>
</table>

McNemar’s χ²: p < 0.001


Methods and strategies (1)

Generalized forms
- Long duration of detection of specific IgG
  - >2.7 y. as detected by TES-ELISA
  - At least 5 y. by WB
- Residual antibodies: high rates of seroprevalence
- Toxocariasis: exclusion diagnosis

Methods and strategies (2)

Ocular toxocariasis
- Test on serum usually negative:
  - parasite burden reduces to 1 larva
  - compartmentalized form
- Fluid testing coupled with serum testing:
  - on CSF
  - on aqueous fluid: anterior chamber paracentesis

Methods and strategies (3)

Post-treatment follow-up
- Using WB (IgG): impossible
  - Magnaval JF. Parasitology 1995;110 (Pt 5):529-533
- Using TES-ELISA (IgG): opinions differ
  - NO
  - YES

Diagnostic perspectives
Detection of current infections (1)

Dosage of the *eosinophil cationic protein (ECP)*

- ECP released from *activated* eosinophil cells
- Marker of *intratissular* eosinophilia


Detection of current infections (2)

Quantification of the *avidity* of specific IgG

Would be correlated with the disease duration


Improvement of specificity (1)

TES-ELISA for IgG3 / IgG4 subclasses

- Correlation with the infection duration
- Better specificity, lower sensitivity

Improvement of specificity (2)

Use of recombinant Ag

- rTES-Ag in the LMW range (24 – 35 kDa)
- High specificity, various results for sensitivity
- So far no assessment vs WB

Improvement of specificity (3)

TES-ELISA for IgE

- Specific IgE in patients with an *atopic status*
- Kinetics correlated with treatment efficacy

Molecular diagnosis

- Detection of the entire larvae
- Problem of the size of the inoculum
- Invasive sampling (biopsy)
- Identification of the larval structures
- Detection of circulating DNA: the future?
Provisional dead-ends

Detection of circulating Ag

- Lack of sensitivity (low larval burden)
- Poor specificity


The Toxocara cati problem (1)

- Certainly underestimated
  

- Many anecdotal reports:
  - IF, Ouchterlony, ELISA
  - Using extracts from adult worms or ES-Ag
- No published assessment of any method

The Toxocara cati problem (2)

- High degree of homology between the two species
  

- Further studies of specific fractions in T. cati ES Ag
  
- WB can’t discriminate between the two species

Efficient drugs

- Albendazole (ABZ)
  - 10 mg / kg / d for 15 days

- Diethylcarbamazine (DEC)
  - 4 mg / kg / d for 21 days

- Mebendazole (MBZ)
  - 25 mg/ kg/ d for 21 days

Magnaval JF. Parasitology 1995;110 (Pt 5):529-533

Other drugs

- Thiabendazole
  - Poor efficacy along with frequent side effects
  - Discontinued in Europe

  Magnaval JF and Charlet JP. Therapie 1997;42:541-544

- Ivermectine (a) & fluoromebendazole (b)
  - Probably ineffective (a)

  - Not absorbed in the digestive tract (b)
**Prophylaxis**

- **Collective**
  - Ousting dogs out of the playgrounds, sandpits, beaches ...

- **Individual**
  - Deworming dogs and cats 3 times a year with a broad-spectrum anthelmintic;
  - Fencing personal kitchen gardens;
  - Treating any pica;
  - Improving personal hygiene (careful hand-washing before any food intake, cigarette...);
  - No country salads and no raw or underdone liver.

**Indications**

- **No treatment**
  - Subject without any eosinophilia
  - Subject with eosinophilia but asymptomatic.

- **Treatment**
  - VLM;
  - Common toxocariasis ≥ 3 months;
  - Chronic eosinophilia along with inefficient prophylaxis;
  - Ocular toxocariasis (+/-).

**Ocular toxocariasis**

- **Prophylaxis**
  - First, corticosteroids: 1 mg/kg daily for 1 month
  - Then, ophthalmological check-up:
    - If cured: only ophthalmological follow-up;
    - If improved / worsened / stable: further corticosteroids then DEC

- Phototherapy: only for visible larva

- Surgery

**Neurological toxocariasis**

- **Prophylaxis**
  - Corticosteroids: 1 mg/kg day for 3 or 4 weeks

- Often sufficient; if, no anthelminthic use may be considered

**Conclusion**

- Environment highly contaminated
- High human seroprevalence
- Non specific clinical signs
- Laboratory diagnosis unable to detect active infection
- Therapeutic management based on physician experience

= Crucial role of prophylaxis