Echinococcus granulosus and E. multilocularis: epidemiology and VPH aspects in Europe

Peter Deplazes
Echinococcoses in Europe:

*Echinococcus granulosus s.l.*
Cystic Echinococcosis (CE)
hydatid disease

*Echinococcus multilocularis*
(Alveococcus multilocularis)
Alveolar Echinococcosis (AE)
Echinococcus granulosus
Cystic Echinococcosis (CE)
*Echinococcus granulosus*: larval stages mainly in the liver and lung

Brood capsules → fertil cyst
E. granulosus: Histology of the larval stage

Host tissue
Laminated layer
Germinal layer
Brood capsule
Protoscolices
Cyst with cyst fluid

Laminated layer
Global burden of cystic echinococcosis

- US $ 4.1 billion (adjusted for underreporting)
- 54% Human costs
- 46% Animal health costs

The overall economic loss attributable to CE in humans and animals in 2005 was estimated at € 148’964’534 (95% CI: 21’980’446–394’012’706). Human-associated losses were estimated at € 133’416’601 (95% CI: 6’658’738–379’273’434) and animal-associated losses at € 15’532’242 (95% CI: 13’447’378–17’789’491).
Approximate Geographical Distribution of *Echinococcus granulosus* s.l. (Status: 1999)

Sources: Schantz et al. (1995), Craig et al. (1996), Eckert et al. (2000)

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J. Eckert, F. Grimm

F: Free  PF: Provisionally Free
Echinococcosis in Serbia: An Issue for the 21st Century?

Branko Bobić, Aleksandra Nikolić, Sofija Katić Radivojević, Ivana Klun, and Olgica Djurković-Djaković

ECHINOCOCCOSIS IN SERBIA

Table 1. Characteristics of Patients Included in Clinical Studies of Cystic Echinococcosis (CE) Published Between 2000 and 2010

<table>
<thead>
<tr>
<th>Reference</th>
<th>Inclusion criteria</th>
<th>Study period</th>
<th>No. of cases</th>
<th>Age (years)</th>
<th>Female/male (%)</th>
<th>Rural/urban (%)</th>
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<tbody>
<tr>
<td>Basarić, 2007</td>
<td>Liver CE</td>
<td>1963–2006</td>
<td>1016</td>
<td>19–61</td>
<td>60/40</td>
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<tr>
<td></td>
<td></td>
<td>1998–2005a</td>
<td>315</td>
<td></td>
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<tr>
<td>Ćulafić et al., 2007</td>
<td>Liver CE</td>
<td>2006</td>
<td>30</td>
<td>15–75</td>
<td>60/40</td>
<td>56/44</td>
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<td>Ćulafić et al., 2010</td>
<td>Spleen CE</td>
<td>2000–2006</td>
<td>20</td>
<td>19–75</td>
<td>55/45</td>
<td>60/40</td>
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<tr>
<td>Djuricić et al., 2010</td>
<td>CE in children</td>
<td>1990–2006</td>
<td>149</td>
<td>2–18</td>
<td>57/43</td>
<td>54/46</td>
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<tr>
<td></td>
<td></td>
<td>1998–2006a</td>
<td>51</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Jevtić et al., 2008</td>
<td>CE treatment with albendazole</td>
<td>1998–2008</td>
<td>42</td>
<td>11–67</td>
<td>43/57</td>
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<td>Otašević et al., 2010</td>
<td>Liver/lung CE</td>
<td>1988–2009</td>
<td>570</td>
<td></td>
<td>67/33</td>
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<td></td>
<td>Adults</td>
<td>1999–2009a</td>
<td>289</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Children</td>
<td>1999–2009a</td>
<td>21</td>
<td>&lt;14</td>
<td></td>
<td></td>
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<tr>
<td>Alempijević et al., 2011</td>
<td>Liver CE</td>
<td>2008</td>
<td>52</td>
<td>17–76</td>
<td>69/31</td>
<td></td>
</tr>
</tbody>
</table>

*Years within the study period (1998–2010).*
Echinococcosis in Serbia: An Issue for the 21st Century?

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Distribution of *E. granulosus* sensu lato in the Balkans

Modified after Bobic et al., 2012
E. granulosus (s. stricto), (G1,G2,G3)
Zoonotic!

(G7)

Pig strain

E. canadensis comp.
(can. E. intermedius)
Sources of *E. granulosus* in Lithuania

- High number of dogs in villages
- No anthelmintic treatment
- Home slaughtering
- Social conditions
- Habits

Cysts detected in 81 of 612 pigs (13.2% CI 10.7-16.2) from small family farms and in 4.1% (CI 0.8-11.5) from larger industrial farms.

- Older pigs (> 1 year) had a significantly higher prevalence

Pilot control experiment in Lithuania: Praziquantel treatment of dogs with baits (4x/year, autumn, winter, spring)
E. ortleppi G5
Echinococcus multilocularis: Biology
Echinococcus multilocularis: transmission biology

Definitive hosts: ecology, susceptibility and development

Egg: survival

Intermediate host: ecology, susceptibility

Metacestode: reproduction, survival

Adult stage: reproduction, survival
E. multilocularis: ways of transmission

Environment

Susceptibility?
(probably very low, but...)}
Diagnosis of alveolar echinococcosis

- imaging techniques (US, CT)
- serum antibody detection
- biopsy (not recommended)
- parasite structure, antigen, PCR after surgery
Course of alveolar echinococciosis

Incubation time 5-15 years

- Progressive growth and development of clinical symptoms
Alveolar Echinococcosis: Changes in survival over time

Life expectancy at age 54 years

Introduction of chemotherapy for treatment of AE

Torgerson et al., J Hepatol 2008
Costs of Alveolar Echinococcosis in Switzerland

Treatment costs per patient*
€ 103‘000 (CIs 90‘000-118‘000)

Loss of income per patient*
€ 78‘500 (45‘500-125‘500)

Total costs (minus not paid retirement pension)*
€ 108‘762 (48‘300-178‘500)

Total costs Switzerland
€ 2.0 Millionen (0.9-3.5 Million)

*Median, n = 155

Torgerson et al., J Hepatol 2008
Echinococcus multilocularis: Biology

Definitive host: fox

Intermediate host: voles
E. multilocularis reproduction in definitive hosts

Days post inoculation | dogs | cats | foxes | raccoon dogs |
--- | --- | --- | --- | --- |
1'563 | 57 | 134 | 67 |
899 | 28 | 331 |
2'466 | 642 | |

Worm burden

Estimated total egg excretion

279'910 | 573 | 346'473 | 335'361
E. multilocularis prevalences in dogs:
Germany, Switzerland, France:

Mean prevalences 0.2-0.3%
1‘000 infected dogs in CH
10‘000 in GER
Dyachenko et al. (2008), Deplazes et al. 2011)

Dogs with free access to
rodent habitats: 3-7%
Gottstein et al. (2001)
**Echinococcus multilocularis** distribution

New AE cases per year:
- Europe: 100-200
- Russia: 1100
- China: 17,000 (91%)

Torgerson et al., 2010

Number of alveolar echinococcosis cases reported in Kyrgyzstan, by patient sex, 1995–2011.

EID, Usubalieva et al., 2013
Siko et al. 2011, Parasitol. Research
Distribution of *E. multilocularis* in foxes

Urban situation
Fox in the city of Zürich
E. multilocularis egg contamination in the city of Zurich

Foxes infected with E. multilocularis at necropsy

Environmental contamination with eggs?
*E. multilocularis* detected (A) in fox faeces and (B) trapped voles (*A. terrestris*) in Zurich

Hofer et al. 2000, Parasitology

E. multilocularis infected *A. terrestris* 10 of 13 trapping areas (prevalences: 4.3%-20.9%)

Hofer et al. 2000, Parasitology
Factors affecting the urban cycle of *E. multilocularis* and the infection pressure with *E. multilocularis* eggs

- Forest
- Agriculture & recreational area
- Urban periphery
- Central urban area

**human population density and anthropogenic food supply**

**fox density**

**abundance of intermediate hosts**

**predation on rodents by foxes**

**environmental egg contamination**

**recreational and soil linked activities (farming, gardening, etc.)**

**free ranging dogs and cats**

**increased risk for AE?**

-> *evaluation of control strategy*

Deplazes et al., Trends in Parasitology, 2004
AE: A rare but emerging disease, hypothesis?

Based on the significant increase of the infection pressure with *E. multilocularis* in rural and urban areas, an increase of the incidence of AE can be expected with a delay of 10-15 years!
Alveolar echinococcosis in animals

dog

Lemur catta

pig
Diagnosis of Echinococcus multilocularis and *E. granulosus* infection in definitive and intermediate or aberrant animal hosts
Diagnosis of intestinal *Echinococcus* infections

Macroscopic identification of worms: limit for *E. granulosus*, not feasible for *E. multilocularis* (very reduced in frozen material)

**Sedimentation and Counting Technique (SCT):** Gold Standard, Sensitivity of 96-100% (after freezing reduced), Specificity >98% (? During first time of prepatency)
Diagnosis of intestinal Echinococcus stages: post mortem

Intestinal scraping technique (IST):

SE 78% (compared with SCT); SP ≈100%.
Application at necropsy; laborious; polyspecific for intestinal helminths; semiquantitative,
Parasitological routine test at necropsy
Diagnosis in definitive hosts: intra vitam

**Arecoline purgation**

Specificity >98% (? In very early infections)

Sensitivity 38-78% *E. granulosus*, 20-30 *E. multilocularis*

Screening of dogs, but inefficient in up to 32% of the dogs

Arecoline hydrobromide is not approved for the use in dogs, serious adverse reactions.

Dog successfully purged of a large *Taenia* worm
Alternative intra vitam diagnosis of intestinal *Echinococcus* infection

**Copro-Antigens**

- Genus identification
  - ELISA

**Taeniid eggs**

- Species or strain identification
  - PCR / sequencing

**Copro-DNA**

- Species identification
  - PCR

Specific immune reactions

not reliable
Coproantigen - ELISA:
Sample collection and preparation

- Coproantigens are stable for at least 5 d at room temperature and for years at –20°C.
- Eggs of *Echinococcus* are inactivated by deep-freezing (-80°C for at least 2-4 days)

Home made tests required
Sensitivity of the *E. multilocularis* coproantigen ELISA in faecal samples of foxes

**Specificity:** 60-90%

*infection with non gravid worms only*
Diagnostic strategy: egg isolation

Faecal samples
Environmental samples

Sedimentation/Flotation
Sequential sieving

Microscopy
PCR with taeniid egg-positive samples only
Multiplex PCR for Taeniid identification

E. multilocularis

E. granulosus s.l. (all strains/species)

Taenia spp.

Trachsel et al., 2007, Parasitology, 134, 911
Strategy for diagnosis in definitive hosts

- cELISA
- coproscopy

**positive samples only**

DNA isolation from:
- isolated taeniid eggs
- faecal aliquot

**PCR**
Diagnosis in intermediate and aberrant hosts:

Post mortem: meat inspection and necropsy: Sensitivity high

Serology: sensitivity and specificity not determined for all endemic areas

In vivo: Ultrasound for liver infections only, sensitivity low
Diagnosis of alveolar echinococcosis in animals: Morphology, PCR, immunohistochemistry, specific antigen detection
Control of Cystic Echinococcosis

- long-term measures of public health education with primary health care
- veterinary public health activities, such as the improvement of slaughter hygiene and meat inspection, dog registration and sanitation measures

Experience from several countries has shown that this option alone may not be sufficient and too slow for effective *E. granulosus* control
Control of Cystic Echinococcosis
“attack phase”

- Elimination of definitive hosts (not feasible)
- Public health education of farmers
- Improvement of slaughter hygiene and meat inspection (especially private sector)
- Intensive praziquantel treatment of dogs
- Monitoring of the epidemiological situation
- Vaccination of sheep (new approach under investigation) (no vaccine for dogs available)
- Culling of infected (old) sheep
Control program in Cyprus

Prevalence in humans: 1972: 5 / 100'000, 1983: <0.1 / 100'000

Echinococcus - Prevalence (%)
The mean number of protoscoleces observed in each age class of sheep (solid bars). The open bars show the fitted model results together with their 95% Credible Intervals.
Control strategies against *E. granulosus* (sheep strain) in continental areas (Torgerson et al. 2011)

- Combined anthelmintic treatment of dogs and vaccination of sheep
- Anthelmintic treatment of dogs
- Vaccination, anthelmintics and removal of old sheep

**prevalence in sheep**

**years**
Control of Alveolar Echinococcosis

- Deworm dogs
- Hygiene: wash / cook food, wash hands, avoid contact to foxes
- Control of intermediate hosts
- Control foxes hunting
- Limit food resources
- Deworm foxes
- Prevent dogs from predation on rodents
- Control intermediate hosts
Regulation of the fox population

- high number of offspring
- high natural mortality during the first year
- many animals without reproduction (social control in family groups)

- culling and high hunting pressure unsatisfactory for population control
- high acceptance in urban areas despite awareness of AE-transmission!
Baiting of foxes with praziquantel

Prof. Frank, Lucius, Romig et al., Universität Hohenheim, Stuttgart, D

Reduction of *E. multilocularis*-prevalences in foxes from 65% to 20% in an area of 3’400 km²

**Droncit-Bait** (50 mg Praziquantel), 20 baits/km², every 6 weeks
Faeces positive for *E. multilocularis* coproantigen in baited and in control areas (N=1205)
Cost benefit of a local baiting strategy

<table>
<thead>
<tr>
<th>factor</th>
<th>estimate</th>
<th>unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>area</td>
<td>92</td>
<td>km²</td>
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<tr>
<td>N inhabitants</td>
<td>350'000</td>
<td>pers.</td>
</tr>
<tr>
<td>incidence</td>
<td>0.26 *10⁻⁵</td>
<td></td>
</tr>
<tr>
<td>years with disease</td>
<td>30.75</td>
<td>y</td>
</tr>
<tr>
<td>total costs patient</td>
<td>108'762</td>
<td>€</td>
</tr>
<tr>
<td>cost per patient &amp; year</td>
<td>3'537</td>
<td>€</td>
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<td>incubation period</td>
<td>10.00</td>
<td>y</td>
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<td>cost per bait</td>
<td>0.75</td>
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<tr>
<td>bait intervals phase 1</td>
<td>12.00</td>
<td>x</td>
</tr>
<tr>
<td>bait density (per km²)</td>
<td>50.00</td>
<td>baits</td>
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<tr>
<td>portion of treated area</td>
<td>40</td>
<td>%</td>
</tr>
<tr>
<td>work hours per km²</td>
<td>3.00</td>
<td>h</td>
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<tr>
<td>work costs per hour</td>
<td>20.00</td>
<td>€</td>
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<tr>
<td>yearly campaign cost 1</td>
<td>43'056</td>
<td>€</td>
</tr>
<tr>
<td>duration phase 1</td>
<td>3.00</td>
<td>y</td>
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<tr>
<td>bait intervals phase 2</td>
<td>5.00</td>
<td>x</td>
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<td>yearly campaign cost 2</td>
<td>17'940</td>
<td>€</td>
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<td>N feacal sample control</td>
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<td>search time per sample</td>
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<td>labor cost per sample</td>
<td>10</td>
<td>€</td>
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<tr>
<td>yearly cost control</td>
<td>6000</td>
<td>€</td>
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</table>
ESCCAP Guidelines

ESCCAP (European Scientific Counsel Companion Animal Parasites) is an independent, non-profit making organization whose role is to develop guidelines for the prevention and control of parasites in pet animals. The guidelines are developed to promote the health of pets, enhance the safety of the public and preserve the bond between pets and people.

There is great diversity in the parasites and their importance across Europe.

- Provide vets and pet owners the best possible information for controlling pet parasite infections, infestations and zoonoses
- Create independent guidelines & educational materials for optimal pet parasite control
- National activities are focussed on local situations