CESSARi
Research on
cystic echinococcosis
in sub-Saharan Africa

Thomas Romig
University of Hohenheim
Stuttgart, Germany

Funding source:
DFG (German Research Agency)
Program 'German-African cooperation projects in infectious diseases'

2009-2019
Total financial volume (9 years): 2.8 mio €
<table>
<thead>
<tr>
<th>The consortium: countries and institutions (phase 1-3)</th>
</tr>
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<tbody>
<tr>
<td><strong>Germany:</strong></td>
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<tr>
<td>University of Hohenheim (1-3)</td>
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<tr>
<td>Ulm University Hospital &amp; Medical Center (1-3)</td>
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<tr>
<td><strong>Sudan:</strong></td>
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<tr>
<td>Al-Neelain University, Khartoum (1-2)</td>
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<tr>
<td>Ministry of Livestock, Central Laboratories (1-3)</td>
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<tr>
<td>University of Gezira, Wad Medani (1-3)</td>
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<tr>
<td><strong>Ethiopia:</strong></td>
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<tr>
<td>Addis Ababa University, Addis Ababa (3)</td>
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<tr>
<td><strong>Kenya:</strong></td>
</tr>
<tr>
<td>African Medical and Research Foundation, Nairobi (1-2)</td>
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<tr>
<td>Kenya Medical Research Institute, Nairobi (1-3)</td>
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<td>Meru University of Science and Technology (1-3)</td>
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<td><strong>Uganda:</strong></td>
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<tr>
<td>Makerere University (1-2)</td>
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<td><strong>Zambia:</strong></td>
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<tr>
<td>University of Zambia, Lusaka (2-3)</td>
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<td><strong>Namibia:</strong></td>
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<tr>
<td>Ministry of the Environment, Windhoek (3)</td>
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<tr>
<td><strong>South Africa:</strong></td>
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<tr>
<td>University of the Witwatersrand, Johannesburg (1)</td>
</tr>
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</table>
Research objectives

1) Correlations of *Echinococcus* genotypes with geographical distribution, host preference and infectivity to humans

2) Identification of wildlife-based cycles and their interaction with 'domestic' echinococcosis cycles

3) Clinical manifestation

4) Impact on public health and economy

Other aims

Training, networking and capacity building

Study sites

- completed and ongoing
- postponed

[Map of study sites in Africa with marked locations.]
Activities depending on facilities present in each country:

Hospital records
Ultrasound screening surveys
Slaughterhouse surveys, feecal surveys of dogs
Wildlife surveys
Collection of isolates, molecular characterization
Estimate of public health and economic impact
**E. granulosus s.s.**  
dog-sheep  
wildlife  
G-Omo  
?

**E. felidis**  
wildlife

**E. equinus**  
dog – donkey  
wildlife

**E. ortleppi**  
dog-cattle/pig  
wildlife

**E. canadensis G6/7**  
dog – camel  
wildlife
Training and capacity building

Molecular biology in Hohenheim: 25 participants, 2-4 week courses

Abdominal ultrasound in Pavia: 20 participants

Abdominal ultrasound and percutaneous intervention in Ankara: 4 participants

Field ultrasound in Nairobi: 4 participants

Epidemiology in Ulm: 46 participants

Epidemiology in Johannesburg: 10 participants

Training and capacity building

41 academic theses completed or ongoing (BSc, MSc, PhD):

<table>
<thead>
<tr>
<th>Country</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudan</td>
<td>14</td>
</tr>
<tr>
<td>Kenya</td>
<td>8</td>
</tr>
<tr>
<td>Germany</td>
<td>10</td>
</tr>
<tr>
<td>Uganda</td>
<td>6</td>
</tr>
<tr>
<td>Namibia</td>
<td>2</td>
</tr>
<tr>
<td>Zambia</td>
<td>1</td>
</tr>
<tr>
<td>South Africa</td>
<td>1</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>1</td>
</tr>
</tbody>
</table>
Provided equipment

6 laboratories for basic molecular work (Sudan, Kenya, Uganda, Ghana)

4 sets of mobile ultrasound equipment (Sudan, Kenya, Uganda, Zambia)
Main difficulties / obstacles

War-related insecurity in South Sudan

Procedures to obtain research permits

International exchange of samples

Movement of equipment between institutions
The international impact of HERACLES collaborative project

Adriano Casalli
On behalf of HERACLES consortium

- WHO Collaborating Centre for the Epidemiology, Detection and Control of Cystic and Alveolar Echinococcosis;
- European Union Reference Laboratory for Parasites (EURLP), Department of Infectious Diseases, Istituto Superiore di Sanità (Rome, Italy)

Human cystic Echinoccosis ReseArch in CentraL and Eastern Societies

Research based, human focused

Timing: 1st October 2013 - 2018
Total costs: € 3,922,487.76
Beyond the Consortium: HERACLES extended network

CORE ACHIEVEMENTS

• Biggest research-based cross-sectional ultrasound-based population study (≈ 25,000)
• Creation of the European Register (ERCE) (≈ 2,000)
• Registered Echino-BioBank (≈ 5,000)
• Patent on anti-parasitic soluble drugs (Salts of benimidazoles)
• First proteomic description of parasite exosomes in echinococcal cyst and…
• …identification of biomarker candidates in exosome plasma by quantitative proteomic analysis
• Bring the importance of CE to the attention of health authorities encouraging the implementation of public health policies;
• Support biological, epidemiological and clinical research on CE.

European Register of Cystic Echinococcosis
(Prospective, observational, multilingual, multicentre, online Register)

• > 2,000 patients
• 44 affiliated centres
• EU standard for biobanking (1716/2011)
• official Biobank-collection (ISCIII register n. C0003432)

EchinoBiobank

- Human samples
- Animal samples
- Clinical data

open resources to foster systematic studies on CE

≈ 5,000 samples received
**The genetic diversity of *E. granulosus* from human hosts**

- Cyst collected: 742
- Countries involved: 31
- Species: *E. granulosus* G1, G3 (and G5, G6/7)
- Target genes: COX1 (1674bp), ND1 (894bp)

**Quantitative proteomic in human plasma**

(WP3)

A) First time demonstration of the presence of parasite and host derived exosomes in HF

B.1) Method to separate exosomes from human plasma samples and identify potential CE biomarkers

B.2) The analysis of human proteins identified in exosomes suggests different immune modulation patterns; pathways inducing such polarizations seem centred on Lyn/CDC148 regulation in the presence of Active CE cysts (skewed Th2 and regulatory) and on Rac/Cdc-42 stable activation in patients with Inactive CE (skewed Th1 and wound healing)

B.3) Identifed several parasite proteins which seem present differently in plasma from patients with Active or Inactive cysts (focus of future validation in WB using recombinant proteins and Phage derived mAb)

Isolation of exosomes from plasma pools (AP, IP, Ctr)

Mass spectrometry & Bioinformatics analysis

- Lyn/Src, TGFβ1 network in APhs
- Cdc42/Rac network in IPhs

A number of *E. granulosus* proteins also identified specifically in APs or IPs
“SALTS of compounds having BENZIMIDALIC structure”

• This invention consists of water-soluble BMZ salts as a racemic mixture as well as enantiopure forms.

Solubility at physiological pH (7.4):

- RBZ-Na = 14.49 mg/mL⁻¹ (versus 0.06 mg mL⁻¹ unsalified form)
- TCBZ-SO-Na = 19.30 mg/mL⁻¹ (versus <0.005 mg mL⁻¹ unsalified form)

Efficacy of RBZ-Na and its enantiomers

• Animal model with secondary infection of E. granulosus s.s.

• Aim: Quantify parasite mass reduction, and damage to the parasite

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Medium</th>
<th>Efficacy % (µC – µT) / µC × 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABZ</td>
<td>DMSO</td>
<td>36.4*</td>
</tr>
<tr>
<td>RBZ-Na</td>
<td>PBS</td>
<td>41.0*</td>
</tr>
<tr>
<td>(R)-(+)-RBZ-Na</td>
<td>PBS</td>
<td>56.2*</td>
</tr>
<tr>
<td>(S)-(−)-RBZ-Na</td>
<td>PBS</td>
<td>13.3* Inactive</td>
</tr>
<tr>
<td>Control</td>
<td>DMSO</td>
<td>-------</td>
</tr>
</tbody>
</table>

Efficacy of the treatment

• Statistical significance (P<0.05 ANOVA)

Results suggest a therapeutic application of enantiopure forms of sulfoxides

To be finalized!
Biggest cross-sectional study research-based (ultrasound population surveys)

Aiming to: estimate %, cyst stage distribution, N of infected individuals

First original research ever published by “THE LANCET Infectious Diseases” on echinococcosis

AREA, SAMPLE SELECTION and CASE DEFINITION

- Districts selected with mid-range average annual hospital incidence of CE;
- US by convenience sampling;
- Consensus protocol & case definition/cyst staging (WHO-IWGE);
- US lesions assessed by 2 sonographers during screening;
- Re-evaluation by a core team.
Abdominal US screenings on **24,693** people in a total of **50** villages and **15** districts/provinces of Bulgaria, Romania, and Turkey.

US survey sessions, hosted in **community public structures** (community hall, primary health-care centres, schools, mosques)
General information about CE and HERACLES was provided to local authorities and the general population.

PUBLIC HEALTH EDUCATION CAMPAIGNS to 25,000 people and TRAINING to general practitioners and specialist physicians were provided during the US survey sessions.
Demographic characteristics of the study sample vs reference population

<table>
<thead>
<tr>
<th>Sample</th>
<th>Women</th>
<th>Men</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulgaria</td>
<td>&lt;20 years</td>
<td>927 (15.4%)</td>
<td>832 (29.0%)</td>
</tr>
<tr>
<td></td>
<td>20-29 years</td>
<td>372 (6.5%)</td>
<td>190 (6.5%)</td>
</tr>
<tr>
<td></td>
<td>30-39 years</td>
<td>774 (13.7%)</td>
<td>301 (10.3%)</td>
</tr>
<tr>
<td></td>
<td>40-49 years</td>
<td>163 (2.9%)</td>
<td>331 (11.7%)</td>
</tr>
<tr>
<td></td>
<td>50-59 years</td>
<td>574 (10.3%)</td>
<td>404 (13.6%)</td>
</tr>
<tr>
<td></td>
<td>60-74 years</td>
<td>1320 (23.5%)</td>
<td>727 (25.3%)</td>
</tr>
<tr>
<td>Total</td>
<td>5742 (100%)</td>
<td>2960 (100%)</td>
<td>8702 (100%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reference rural population, 2012</th>
<th>Women</th>
<th>Men</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulgaria</td>
<td>&lt;20 years</td>
<td>165 (27.4%)</td>
<td>126 (36.4%)</td>
</tr>
<tr>
<td></td>
<td>20-29 years</td>
<td>92 (16.9%)</td>
<td>186 (57.6%)</td>
</tr>
<tr>
<td></td>
<td>30-39 years</td>
<td>350 (10.1%)</td>
<td>321 (42.5%)</td>
</tr>
<tr>
<td></td>
<td>40-49 years</td>
<td>313 (10.7%)</td>
<td>133 (44.0%)</td>
</tr>
<tr>
<td></td>
<td>50-59 years</td>
<td>123 (12.2%)</td>
<td>56 (17.5%)</td>
</tr>
<tr>
<td></td>
<td>60-74 years</td>
<td>371 (53.2%)</td>
<td>209 (28.5%)</td>
</tr>
<tr>
<td>Total</td>
<td>960 (77.4%)</td>
<td>597 (73.2%)</td>
<td>1557 (73.7%)</td>
</tr>
</tbody>
</table>

Establishment of a prospective case retrieval system

Distribution of CE cyst stages by sex and age groups.

- Active cysts were found in people of all ages, including children, and in all investigated provinces.
The crude % of CE infection was adjusted with direct standardisation by sex and age group by the 2015 country’s rural population.

<table>
<thead>
<tr>
<th>Cystic echinococcosis by imaging</th>
<th>Bulgari**</th>
<th>Romania**</th>
<th>Turkey***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal cystic echinococcosis detected/ participants screened</td>
<td>31/6602</td>
<td>35/656</td>
<td>51/8618</td>
</tr>
<tr>
<td>Crude prevalence</td>
<td>0.43% (0.26 - 0.59)</td>
<td>0.47% (0.20 - 0.75)</td>
<td>0.63% (0.20 - 1.85)</td>
</tr>
<tr>
<td>Standardised prevalence</td>
<td><strong>Reference Bulgarian rural population, 2015</strong></td>
<td><strong>Reference Romanian rural population, 2015</strong></td>
<td><strong>Reference Turkish rural population, 2015</strong></td>
</tr>
<tr>
<td></td>
<td>0.43% (0.26 - 0.55)</td>
<td>0.41% (0.25 - 0.65)</td>
<td>0.59% (0.25 - 1.85)</td>
</tr>
<tr>
<td></td>
<td><strong>Reference European population, 2013</strong></td>
<td><strong>Reference European population, 2013</strong></td>
<td><strong>Reference European population, 2013</strong></td>
</tr>
<tr>
<td></td>
<td>0.39% (0.28 - 0.51)</td>
<td>0.42% (0.27 - 0.67)</td>
<td>0.67% (0.31 - 1.33)</td>
</tr>
</tbody>
</table>

Conservative estimate of number of individuals* that may be affected with (abdominal) CE (in the rural population)

<table>
<thead>
<tr>
<th><strong>BULGARIA</strong></th>
<th><strong>ROMANIA</strong></th>
<th><strong>TURKEY</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Active cysts</strong></td>
<td>7,872 (5,520 - 11,220)</td>
<td>37,229 (23,405 - 59,166)</td>
</tr>
<tr>
<td>Inactive cysts</td>
<td>4,498 (2,395 - 8,439)</td>
<td>22,225 (11,180 - 44,132)</td>
</tr>
</tbody>
</table>

* estimated by multiplying the adjusted prevalence by the 2015 rural population;
TOP-DOWN dissemination (Bulgarian, Romanian, Turkish, English, Spanish, Italian)

http://www.who.int/neglected_diseases/en/
• “With the aim of improving surveillance of CE, we encourage international agencies (eg, EFSA, ECDC, and WHO) to lobby the European Commission to champion new health policies for the notification of human and animal CE”.

Funding is much appreciated but…
…real value lies in colleagues, friends and all the people contributing!
The state of the European Register of Cystic Echinococcosis
5 years after its inception

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WHO Collaborating Centre for the Epidemiology, Detection and Control of Cystic and Alveolar Echinococcosis Foodborne and Neglected Parasitic Diseases Unit
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28th World Congress on Echinococcosis
Lima, Peru, 29-31 October, 2019

Once upon a time...
UNDERREPORTING/ MISREPORTING

- Heterogeneous notification (incl. within Europe)
- Missing data of patients managed as outpatients
- Problems with data duplication
- No distinction between CE and AE
- No collection of clinical data

Objectives

- To indicate the burden of CE in Europe
- To bring the importance of CE to the attention of health authorities
- To encourage the planning and implementation of public health policies toward its management and control
- To support biological, epidemiological and clinical research on CE

Questions

- How many CE patients are seen in ERCE network centres?
- Where do they come from?
- How are they managed? (appropriateness and cost)
- What is the natural and post-treatment evolution of cysts

Data collected

- ERCE code
- Demographic info
- History
- Follow-up
- Cysts uniquely identified
On March 31st 2019

44 affiliated centres (1 more from Afghanistan in the meantime)
34 having registered at least 1 patient (map)
15 Countries (7 extra-european)

CUMULATIVE NUMBER OF AFFILIATED CENTRES

- never entered data
- affiliated but data entered by a national coordinating centre
- at least 1 patients recorded but no activity <18 months
- activity in <18 months
40% in Italian centres
6% from HERACLES screenings in Bulgaria, Romania and Turkey
20% immigrants (i.e. from country different from that of registration)
Recorded by 28 centres (84.5%) at least for 1 cyst in at least 1 visit for 1643 patients (78.3%) – not constant within centres and visits!

Cyst staging used by 27 centres

At first registration, 30% of cysts did not have staging recorded

17 centres (51.5%) recorded at least 1 follow-up visit for at least 1 patient

435 patients have at least 1 follow-up visit recorded (1.6%-84.2% pt/centre)

* ANALYSIS BY "CYST STAGE – LOCATION – MANAGEMENT OBSERVATION"
(N= 523 patients, 726 cysts, 920 OBSERVATIONS)

§ n=11 treated by modified percutaneous treatment  ° n=4 treatment for other cysts

CAVEAT: no info about symptoms/complications or patient-specific conditions

1 Extra-European centre systematically no stage and all surgery (most w/o ABZ)
Conclusions

New centres constantly joining → interest

Somehow complementarity with hospital-derived data

Suitable starting platform for prospective data collection to overcome extreme difficulty of clinical trials

Voluntary adhesion and filling

Difficult to compare with official records

Variable, suboptimal (…) data completeness and quality (partly deriving from lack of knowledge of staging and stage-specific approach?)

28th World Congress on Echinococcosis
Lima, Peru, 29-31 October, 2019
"AWARNESS AIM"
- Only number of patients with CE and basic demographic data
- High number of centres, wide geographical distribution
- Little time and effort

"CLINICAL AIM"
- Individualisation of clinical questions and variables to address them
- Small number of highly committed centres
- Project-like commitment

Patrizia ROSSI, Francesca TAMAROZZI, Fabio GALATI, Okan AKHAN, Carmen M CRETU, Kamena VUTOVA, Mar SILES-LUCAS, Enrico BRUNETTI, Adriano CASULLI, on behalf of the ERCE network*

*In alphabetical order: Andrea ANGHEBEN, Nikolay BAGMET, Moncef BELHASSEN, Solange BRESSON-HADNI, Fabrizio BRUSCHI, Guido CALLERI, Barbara CASTIGLIONI, Cathy CHEMLA, Leonardo CHIANURA, Balazs DEZSENYI, Maria Teresa GIORDANI, Valbona GJONI, Levan GOGICHAISHVILI, Delia GOLETTI, Majid HARANDI, Gulziya ISMAILOVA, Fazal KARIM, Emma LAPINI, Felix LÖTSCH, Scilla MASTRANDREA, Guido MENOZZI, André PAUGAM, Alfonso RECORDARE, Malgorzata SULIMA, Antonella TEGGI, Carlo TORTI, Giustina VITALE, Martine WALLON, Lorenzo ZAMMARCHI

Funding from the European Commission Seventh Framework Programme (FP7/2007-2013) under the project HERACLES, grant agreement n°[602051] and PERITAS project under the framework of EU-LAC Health (http://eulachealth.eu/) and Ministries of Health of participating countries
The South American Initiative for the surveillance, control and prevention of Cystic Echinococcosis/Hidatidosis

Background

1999 – PAHO convenes a Working Group on “perspectives and possibilities for control and eradication of hydatid disease” in San Carlos de Bariloche, Argentina (International Congress of AIH/WAE). Among its main recommendations it’s included the elaboration of a Regional Project for control and elimination.

2001 – The Southern Cone Subregional Project for Control and Surveillance of Hydatidosis: Argentina, Brazil, Chile and Uruguay is part of the mandate that PAHO/WHO received from the Member States in the RIMSA XII, held in Sao Paulo, Brazil, in 2001.
Background

2013 – Coyhaique, Chile, the Subregional Project is transformed into a South American Initiative for the control and Surveillance of EQ, incorporating new countries and neotropical echinococcosis.

Actuality including ARGENTINA, BRASIL, CHILE, PARAGUAY, PERU AND URUGUAY

Annual Meetings of the Initiative

- 2004 Montevideo, Uruguay
- 2005 Santiago, Chile
- 2006 Porto Alegre, Brasil
- 2007 Bariloche, Argentina
- 2008 Coyhaique, Chile
- 2009. Colonia, Uruguay
- 2010 Córdoba, Argentina
- 2013 Coyhaique, Chile
- 2014 Colonia, Uruguay
- 2014, Buenos Aires, Argentina
- 2015, Lima, Peru
- 2016, Rio de Janeiro, Brasil
- 2018, Buenos Aires, Argentina
- 2019, Lima, Peru
ACTIVITIES: Projects TCC


“Strengthening of international cooperation and technical exchange” Perú – Uruguay 2010”.

“Integrated Plan for prevention and control of cystic echinococcosis in the border area Brazil – Uruguay”.


“Plan for prevention and control of Hydatid disease in Tupiza, Bolivia” Bolivia - Uruguay.

ACTIVITIES . Surveillance (anual epi report)
ACTIVITIES: Laboratory

• Laboratory working group
  • Strengthening laboratory capacities
  • Training in INSP Chile (Peru; Argentina)
  • Ensure and maintain quality
  • Protocols evaluation/comparison
  • Communication and network
  • Collaboration

ACTIVITIES: Evaluation program (Uruguay)

• Held during September 2016
• International Experts; Government representatives; PAHO/PANAFTOSA
• Major conclusion: Successful program – Uruguay’s National Zoonosis Commission – Most Advanced
• CE/H is controlled in some specific areas
• For elimination some recommendations:
  • Assurance of the financial and human resources
  • Maintenance of the dosage lines
  • Intensification of US surveillance (kids 6-14)
  • Intensification of surveillance in dogs
  • Intensification of surveillance in the sheep
  • Information management robust database
  • Maintenance of the excellent component of education and health communication
- On line course on epidemiology and control of CE Duration 1 year (First 2014, Second 2016).

- More than 30 conferences of experts on different topics.

- Participation of 7 Universities of 4 countries: Argentina, Brazil, Peru and Uruguay.
Cystic echinococcosis in South America: a call for action

Carlos R. Portillo, Edmundo Larrieu, Eduardo A. Guzmán, Natalia Cisneros, Pilar Avendano, Carmen Felinto, Juan Segura, Caesar C. Casas, Estuardo Cadiz, Alejandra Larraíncea Zini Lee, Maudey Masena, Marco Ariz, Ana María Kawano, Marco A. M. Vigilato, Cintio Cosio, Marcos Espinola, and Victor J. Del Río Villas


Abstract: Cystic echinococcosis (CE) or hydatidosis is a parasitic disease caused by the larval stage of Echinococcus granulosus, a tapeworm that infects domestic and wild canines. The adult worm is found in the stomach and small intestine of ruminants, while the larval stage can develop in mammalian tissue. CE is a zoonotic disease that affects humans, animals, and vectors. The parasite is transmitted through the ingestion of infected intermediate hosts, typically dogs. The disease is endemic in various regions of South America, where it is considered a significant public health issue. The prevalence of CE in humans varies across countries, with some areas reporting high infection rates. Early diagnosis and treatment are crucial for managing the disease, but effective control strategies are still lacking. This review highlights the current status of CE in South America and discusses potential options for effective control and management of the disease.
ACTION PLAN. THE LAST EFFORT

PLAN DE ACCION PARA FORTALECER LA VIGILANCIA Y EL CONTROL DE LA HIDATIDOSIS / EQUINOCOCOSIS QUISTICA

2019/2023

ORGANIZACIÓN PANAMERICANA DE LA SALUD
CENTRO PANAMERICANO DE FIEBRE AFTOSA

- Grupo de puntos focales oficiales de los países, responsables por las decisiones referentes al Programa Regional

- Secretaria de Panaftosa

- Grupo consultivo y propositivo (Universidades, expertos)
Reforzar los sistemas de vigilancia epidemiológica
Caracterizar epidemiológicamente las ares endémicas de cada país. Definición de escenarios. Estimación de las poblaciones en riesgo por las autoridades nacionales de cada país
Definir flujos de información desde los niveles locales hasta su consolidación regional
Analizar la información. Producir informes epidemiológicos anuales consolidados desde PANAFTOSA/OPS/OMS
Desarrollar sistemas automatizados de información para la notificación de los países a PANAFTOSA/OPS/OMS
Desarrollar redes de laboratorio regional y de los países en base a los Laboratorios Nacionales Oficiales
Evaluación de técnicas disponibles. Ensayos Inter laboratorios coordinados por PANAFTOSA/OPS/OMS incluyendo laboratorios nacionales y de laboratorios de la red nacional
Armonizar técnicas seroepidemiológica en el diagnóstico de la hidatidosis humana y animal para facilitar la comparación y análisis de resultados

Evaluar el impacto y factibilidad de nuevas estrategias de control
Evaluar programas nacionales y regionales de hidatidosis
Mejorar las capacidades de diagnóstico precoz y tratamiento
Adecuar los programas de educación sanitaria
Propender a la cooperación técnica internacional.
Intercambios y capacitación de profesionales
Thank you! Gracias! Merci!
Development of New Diagnostic and Treatment Options for Helminthic Neglected Diseases

NDTND

Adriano Casulli

• WHO Collaborating Centre for the Epidemiology, Detection and Control of Cystic and Alveolar Echinococcosis;
• European Union Reference Laboratory for Parasites (EURLP), Department of Infectious Diseases, Istituto Superiore di Sanità (Rome, Italy)

4 countries involved:

• Facultad de Ciencias, UdelaR, URUGUAY: Estela Castillo, Uriel Koziol
• Facultades de Medicina, UNLP y UBA, ARGENTINA: Betina Córsico, Mara Rosenzvit (coordinator)
• University of Würzburg, GERMANY: Klaus Brehm
• Istituto Superiore di Sanita, ITALY: Adriano Casulli
• San Matteo Hospital Foundation, ITALY: Enrico Brunetti

Starting date: November, 2017
Ending date: November, 2020
Goals

- **Goal 1:** Evaluate fatty acid-binding proteins (FABPs) as drug targets for tapeworm diseases
- **Goal 2:** Evaluate miRNAs as therapeutic targets for tapeworm diseases
- **Goal 3:** Evaluate miRNAs and other small RNAs as biomarkers of CE and AE

NDTND project aims at developing new compounds that bind and inhibit essential and unique molecules of these parasites, and to find new detection tools to improve the status of both treatment and early diagnosis of helminthic NTDs (CE and AE).

Ultrasound screenings for cystic echinococcosis:

**ITALY**

- Provinces in Sardinia region: Nuoro and Oristano
  562 people screened by ultrasound

- Province in Calabria region: Catanzaro
  2,712 people screened by ultrasound
Ultrasound screenings for cystic echinococcosis:

ALBANIA

MAIN OBJECTIVES:
1. To generate data on the prevalence of CE in target rural areas of estimated mid-endemicity in Albania;
2. To estimate the number of people affected by CE in rural Albania.

Expected field work:
3 areas of mid-prevalence in the country, with a total of 4,500 people screened by ultrasound.

Multi-centre study on *Echinococcus multilocularis* and *Echinococcus granulosus* s.l. in Europe: development and harmonization of diagnostic methods in the food chain (MEmE)

**MEmE:** Composition: 17 partners from Europe and Asia Timing: January 2020 - June 2022 Funding: 2,496,126 € for European partners

Project funded by the European Commission under One Health European Joint Programme (Horizon 2020)
PERITAS

“MOLECULAR EPIDEMIOLOGICAL STUDIES on PATHWAYS of TRANSMISSION and LONG LASTING CAPACITY BUILDING to PREVENT CYSTIC ECHINOCOCCOSIS INFECTION”

PARTNERS

• ITALY - Istituto Superiore di Sanità - Adriano Casulli (coordinator)
• SPAIN - Agencia Estatal Consejo Superior de Investigaciones Científicas - Mar Siles-Lucas
• SPAIN - Instituto de Salud Carlos III - María Jesús Perteguer Prieto
• CHILE - Universidad Austral de Chile - Gerardo Acosta
• ARGENTINA - National University of Rio Negro - Edmundo Larrieu (Leonardo Uchiumi)
• PERU - Universidad Peruana Cayetano Heredia - Saul Santivanez

5 countries; 6 Institutes; 3y duration; Total project cost: 1.083.580 €.
PERITAS
was Alexander the Great's favorite dog, who accompanied him during his military exploits.

New educational campaigns (with elucidated risk factors) aiming to prevent/control CE

Allocation of patients to TREATEMENT (FOLLOW-UP)

Focused Questionnaires

F.A.S.E. trainings Focused Assessment with Sonography for Echinococcosis

Identification of highly-endemic CLUSTERS

ULTRASOUND Screenings Argentina, Chile, Peru

HOSPITALS NETWORK Argentina, Chile, Italy

WP1

WP2

MOLECULAR EPIDEMIOLOGICAL STUDIES on PATHWAYS of TRANSMISSION

ENVIRONMENTAL SAMPLING of VILLAGES

WP2

WP3

Patients enrolled in E.R.C.E. (European Register of CE)

Creation of I.R.C.E. (International Register of CE)

SEROLOGICAL test for epidemiological studies

Validation of recombinant antigens

BIO-SAMPLES

ECHINO-BIOBANK

3rd year

2nd year

1st year

WP1

WP2

WP3
What is PERITAS:

- **STAGE_1: CROSS-SECTIONAL**
  Ultrasound-based population surveys for endemic CE cluster identification.

- **STAGE_2: CASE-CONTROL**
  Village-based study for environmental sampling.

**STAGE_3: Double blind MOLECULAR TESTS**

**STEP 1: ULTRASOUND POPULATION SCREENINGS**
**CROSS-SECTIONAL study (2019)**

- To individuate villages/areas with high prevalence of abdominal active CE.
- Administration of risk factors questionnaire targeting hand-to-mouth habits.

- **Chile** → 2,435 screened in Coquimbo
- **Argentina** → 581 screened in Rio Negro
- **Peru** → 790 screened in Junín
STEP 2: ENVIRONMENTAL SAMPLING of MATRICES
CASE-CONTROL study (2019-2020)

- To individuate and compare matrices contaminated by *E. granulosus s.l.* eggs in cases and controls households and in common areas

VILLAGE

HOUSEHOLDS
(5 CE positives and 15 negatives)
Judgmental sampling

COMMON AREAS
(3 sites per village)
(Town square; Main Park; Outdoor market)

- MATRICES:
  - Family shoes; Own dog faeces; Own dog fur;
  - Self-grown vegetables; Soil

- MATRICES:
  - Soil; Dispersed dog faecal samples; Market sold vegetables; Flies

STEP 3: MICROSCOPY and MOLECULAR ANALYSIS
DOUBLE-BLIND TESTS (2020-21)

MATRICES:
- Soil
- Shoes soles
- Dog’s feces
- Dog’s fur
- Lettuce
- Flies

PROCEDURES:
1. Protocols
2. Training
3. Recovery tests
4. Analysis
   - Sample enrichment;
   - Eggs isolation;
   - DNA extraction;
   - PCR amplification.
Main RESEARCH QUESTIONS to be answered:

- There is any correlation between environmental contamination and human infections?
- Which are the main matrices contaminated by *E. granulosus s.l.* eggs?
- Which are the at-risk behaviours/habits associated with odds of CE infection?