TAENIASIS AND CYSTICERCOSIS IN MADAGASCAR

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National country coordinator of human cysticercosis

WHO informal Consultation on assembling a framework for control/elimination of Taenia solium and Neurocysticercosis
17 to 18 July 2014
WHO Headquarters, Geneva

Importance of human cysticercosis

- **Sero-epidemiological survey**
  - Prevalence range from 7 to 21% (highest prevalence in central highland) 2003 (Andriatsimahavandy et al, 2003)
  - Confirmed by Institut Pasteur report: 16% (in 7 regions)

- **Frequency of confirmed diagnostic at hospitals (Immunological diagnostic)**
  - 250 cases per year admitted at hospital in Antananarivo from 2004 to 2006
  - Patients with suspected clinical cysticercosis (2 mains hospitals): 42% and 43% of positive
  - Pediatric cases: 48.9% (+) in children (hospital pediatric of Tsaralalàna)
  - Free detection and treatment: 68% positive (625 patients examined and tested)

At Etablissement Universitaire de Soins et de Santé Publique of Analakely
Surveillance data: spatial distribution

Origins of patient treated in Hospital at the Capital in 2005 (33 Districts)

Reported suspected cases of cysticercosis from District an Municipality hospitals in 2013 (5891 cases)

Co-endemicity with some NTD

F: Lymphatic filariasis
S: Schistosomiasis
H: Soil transmitted helminthiasis
L: Leprosis
T: Taenia solium/Cysticercosis
R: Rabies
National control program

Goals:
To reduce human cysticercosis prevalency: 16% to under 10%
To eliminate human taeniasis

<table>
<thead>
<tr>
<th>Strategies</th>
<th>Components</th>
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<tbody>
<tr>
<td>Amelioration of diagnosis and treatment</td>
<td>- Simpler and standardized diagnostic tools</td>
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<tr>
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<td>- Creation of news Centers of diagnosis in other district</td>
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<td></td>
<td>- Gratis medicine treatment of neurocysticercosis</td>
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<tr>
<td>Intensification of prevention</td>
<td>- Preventive Chemotherapy of Taenia solium (Praziquantel)</td>
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<td>- Intensification of meat inspection</td>
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<td>- Promotion of Hand and Food sanitation/Lavatory</td>
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<td>- Public sensitization, health workers and decision makers</td>
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<tr>
<td>Developpement of operational research</td>
<td>- Scientific advanced of standardization diagnosis system</td>
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<td></td>
<td>- Prevalence and map of cysticercosis and taeniose in human and pig</td>
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<tr>
<td></td>
<td>- Economical impact</td>
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<tr>
<td></td>
<td>- Enhance surveillance and evaluation of intervention</td>
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<tr>
<td>Partnership and collaborating</td>
<td>- Veterinary services</td>
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<td></td>
<td>- NGO with sanitation project</td>
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<td></td>
<td>- Research center</td>
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Our achievements

<table>
<thead>
<tr>
<th>Activities</th>
<th>indicators</th>
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<tbody>
<tr>
<td>Preventive Chemotherapy</td>
<td>121,678 children treated</td>
</tr>
<tr>
<td>Training</td>
<td>2,000 documents</td>
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<tr>
<td></td>
<td>39 districts supervised</td>
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<tr>
<td></td>
<td>357 health workers</td>
</tr>
<tr>
<td></td>
<td>741 local decision makers</td>
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<tr>
<td>Social mobilization</td>
<td>5,000 posters</td>
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<tr>
<td></td>
<td>15,000 prospectus</td>
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<tr>
<td></td>
<td>2,000 books</td>
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<td>125 programs of radio-TV, 1 spot audio-visuel</td>
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<tr>
<td></td>
<td>with 87 diffusions</td>
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<td></td>
<td>40 mediatic shows in journal and magazine</td>
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<tr>
<td>Mapping with NTD</td>
<td>Integration with NTD in national plan</td>
</tr>
<tr>
<td>Pilot site</td>
<td>Planification of integrated intervention (on going)</td>
</tr>
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Our problems

- No financially support for activities
- Lack of Center for diagnostic in other town
- Diagnostic and treatment of cysticercosis are more expensive
- Medecine treatment of T. solium is not available in based health’s formation
- 12 distrits no endemic with Shistosomiase
- Diversity of information for public
- No meat inspection in some rural area
- Lack of data base
- Lack of coordination of activities
- Lack of management capacity

Our perspectives

- Research for understanding the global burden of *taenia solium* (in human and pig)
- Simpler diagnostic for humans and pig
- Standardization of diagnostic and treatment of human cysticercose
- Availability of medecine treatment of *taenia solium* in the Based health’s Centre
- Treatment’s Campaign of the larva form in pig and extended Treatment’s Campaign of adult form in human.
- System of surveillance in place and evaluated
- Cysticercosis map prevalency established
Our priorities

• Preventive chemotherapy of taenia solium in 12 districts;

• Epidemiological survey Cysticercosis map prevalence established;

• Social mobilization, collaborating and partnership

• Training for provide global and regional leadership to promote and coordinate an integrate approach

• Availability of medecine treatment of taenia solium in the Based health’s Centre

• System of surveillance in place and evaluated

Thank you for your kind attention!
Pig farming and porcine cysticercosis in Madagascar

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² UMR SELMET, CIRAD Réunion Island

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Pig farming in Madagascar

- Pig population: **1,3 M heads in 500,000 pig farms** (*7th* in Africa)
- Average herd size: **2.4 animals**
- Two pig farming systems

Backyard

Closed

Closed

Closed

Pig population
Porcine cysticercosis: official data

- 336 cases/outbreaks reported in ten years
- Prevalence at slaughterhouses: 0.5 - 1%
- And many policies about pig farming
  - Live pig market
  - Scavenging

Pig trade sector and cysticercosis detection

Family slaughtering

Hidden sector for positive animals/carcasses
Porcine cysticercosis in real world

- Annual cost: EUR 360 M (96% for public health sector) (Andriamparany, 2012)
- 20 to 50% of income losses for farmers (1st position before ASF) (Rasamoelina-Andriamanivo, 2006)
- General misunderstanding: contamination pathways (ex: role of pig faeces), taeniasis vs cysticercosis and the link
- No official control program, Not yet defined as a priority disease
  ➔ Several studies done (and still on going) to get the real situation
    ➔ Surveillance in slaughterhouses
    ➔ Prevalence study at farm level

Surveillance in abattoirs

- One year daily monitoring (meat inspection) (march 2013-february 2014)
- Sample: 12 abattoirs/15 (Antananarivo centre)

  ➔ 59765 pigs slaughtered ➔ Overall prevalence: 4.7%

Results from logistic model with season, region, breed and abattoir

<table>
<thead>
<tr>
<th>Variable</th>
<th>Modalities</th>
<th>OR</th>
<th>p</th>
<th>CI</th>
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</thead>
<tbody>
<tr>
<td>Abattoir</td>
<td>Abattoir 1</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Abattoir 2</td>
<td>3.08</td>
<td>&lt;10-3</td>
<td>2.76-3.44</td>
</tr>
<tr>
<td>Breed</td>
<td>Exotic breed</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Local breed</td>
<td>5.53</td>
<td>&lt;10-3</td>
<td>4.79-6.38</td>
</tr>
<tr>
<td>Season</td>
<td>Dry and cold season</td>
<td>Ref</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Rainy season</td>
<td>1.75</td>
<td>&lt;10-3</td>
<td>1.61-1.91</td>
</tr>
<tr>
<td></td>
<td>Dry and hot season</td>
<td>1.12</td>
<td>0.04</td>
<td>1.01-1.25</td>
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Prevalence study

<table>
<thead>
<tr>
<th>Study site</th>
<th>Itasy (peri-urban area)</th>
<th>Moramanga (Rural area)</th>
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<tbody>
<tr>
<td>Farming system</td>
<td>Closed (medium scale)</td>
<td>Backyard and closed (small scale)</td>
</tr>
<tr>
<td>Type of study</td>
<td>Cross-sectional</td>
<td></td>
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<tr>
<td>Sample</td>
<td>66 farms and 268 pigs</td>
<td>117 farms and 266 pigs</td>
</tr>
<tr>
<td>Analysis</td>
<td>ELISA (Western blot on-going)</td>
<td>ELISA + Western blot</td>
</tr>
<tr>
<td>Data analysis</td>
<td>Mixed models</td>
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| Overall prevalence | 15%                            | 22%                           |
| Potential risk factors | Renting boar: OR=2.64 (p=0.05) | On-going                      |
|                      | Type of floor: wood/Clay OR=3.93 (p=0.02) |                                |

New challenge « Point of care » diagnostic tests

Dr Rahantamalala Anjanirina
Institut Pasteur de Madagascar

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Diagnostic Tools in Madagascar

- **Serological tests**
  - EITB, ELISA (CSF/Serum)
  - **Antigens from infected pork**
  - Availability of parasites
  - Laboratory-dependant preparation
  - Quantity insufficient for mass campaigns
  - Not suitable in Field

- **Tongue palpation/ Meat examination**
  - lack sensitivity

- **Brain CT-Scan**
  - Expensive, located in urban area

- **RT-PCR (CSF)**
  - Well organised labo, costly equipment

- **Serological tests (EITB, ELISA)**
  - Research projects

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Immuno-diagnostic in Madagascar

**GP- EITB:Tsang et al, 1989 : gold standard**

**GP extraction / purification EITB / ELISA:**
ONLY in Pasteur Institute of Madagascar

<table>
<thead>
<tr>
<th>CSF</th>
<th>Serum</th>
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<tr>
<td>50kDa</td>
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<tr>
<td>39-42kDa</td>
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<tr>
<td>24kDa</td>
<td></td>
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<tr>
<td>21kDa</td>
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<td>18kDa</td>
<td></td>
</tr>
<tr>
<td>14kDa</td>
<td></td>
</tr>
<tr>
<td>13kDa</td>
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<table>
<thead>
<tr>
<th>HUMAN</th>
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<tbody>
<tr>
<td>CSF</td>
</tr>
<tr>
<td>Serum</td>
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<tr>
<td>Neg</td>
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<table>
<thead>
<tr>
<th>SWINE</th>
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<tbody>
<tr>
<td>Serum</td>
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<tr>
<td>Neg</td>
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</table>

- **(Active Cysticercosis)**
- **13/14kDa**
- **18kDa**
- **21kDa**
- **24kDa**
- **42kDa**
- **50kDa**

- **12 000/year**
New challenge: “Point of care” diagnostic test RDTs development

GP Antigens
(Tsang et al., 1989)
8kDa, 14kDa, 18kDa, 50kDa

Cyst fluid (CF)
8 new identified: 20-40kDa (Patent application)

Recombinant (E. coli)

Serum
Pos.
Neg.

Anti-Tag (HIS)

8kDa-1 8kDa-2 18kDa 14kDa

CF1 CF6 CF7

RDTs: next steps?
Large-scale purification and production

Cloning

E. coli

Recombinant Antigens

RDTs
Control Test (Recombinant)

Blood

T- T+

US $ 1
LAMP: Isothermal amplification

Simple molecular-diagnostic of NCC

Reaction at 65°C Use of bath water not thermocycler

Enzyme Stable at RT (Theksoe et al., 2008)

6 primers: more specific

Positivity by simple coloration using dye

Diagnostic of NCC by LAMP: initial results (1)

Test of sensibility
Gene: Cox1
Cysticerci DNA

q-PCR and LAMP performance with *T. solium* cyst DNA

Titration on q-PCR

Titration by LAMP

Cyst DNA dilution

NTC 1 10^1 10^2 10^3 10^4

LAMP: 2h with hydroxynaphthol detection

LAMP and RT-PCR: similar sensibility (1pg ADN/ml vs 0.1pg ADN/ml)
Diagnostic of NCC by LAMP: initial results (2)

LCRs Assay
Gene: Cox1
CSFs DNA

LAMP - performance with CSF samples without DNA extraction

LAMP : confirmation of EITB/RT-PCR results

What control strategy for Madagascar?

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Strategy used for porcine cysticercosis

• Bases
  – Voluntary vs policy
  – Motivators: Better price for quality meat + Threat of disease
  – Intervention adapted to context

☐ Activities done or on-going
  ■ Multidisciplinary/multi-institutional and international team
  ■ Quantifying prevalence and risk factors
  ■ Community diagnosis (behavior) and training + Value chain analysis
  ■ Large communication (consumers, farmers, …)
  ■ Setting up a “meat cyst free” value chain
    ➢ Good husbandry practices
    ➢ Alternative to scavenging system (by using local free resources)
    ➢ Networking actors for supplying piglets
    ➢ Quantify/Qualify the need of the product (Supermarket, …)
    ➢ Control procedures (NEED of BETTER DIAGNOSTIC TOOLS)
    ➢ …

What are the limitations? And the opportunities?

• Limitations:
  ▪ Representativeness of study undertaken
  ▪ Financial limitation
  ▪ Research vs operational intervention
    ➤ Coordination of actions with ministry of health and veterinary services
  ▪ Integration of new tools: oxfendazole, vaccine
  ▪ Lack of evidence of effectiveness of some intervention / questions?
    ➢ Washing vegetables: how? With what?
    ➢ Cooking methods and effects on cyst?
    ➢ Viability of eggs in different environmental conditions?

• Opportunities
  ▪ This meeting
  ▪ Other sanitation project and the other NTD program
  ▪ Oxfendazole and vaccine ➤ Integration within the strategy
  ▪ Program of Epidemiology-surveillance with Indian Ocean Commission (“One health approach”)
What do we propose now?

1. Baseline (Survey and bibliography)
   - National Prevalence and variability among regions & associated risk factors
   - Determinant of behaviors
   - Effectiveness of sanitation project (popularization of lavatory)

2. Testing cost/effectiveness of some combination of interventions in pilot sites (Current strategy + New tools) (experiment and/or landscape analysis)

3. Up-scaling followed by surveillance and evaluation (indicators?)

WHO Coordination

Acknowledgments

- WHO, FAO and OIE
- All the team from the beginning till now: Ronan Jambou, IPM team, Vet students, MOH team, CIRAD
- Funder of on-going projects: FSP PARRUR (French Embassy)/ Swiss embassy, QUALIREG (Reunion region and CIRAD), IPM

Control of cysticercosis in Madagascar: beware of the pitfalls