Elimination of Cysticercosis

Hugo García,
for the Cysticercosis Working Group in Peru

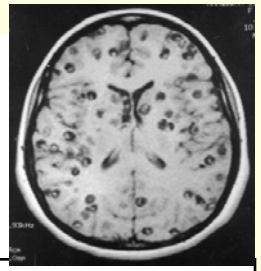
Taenia solium Cysticercosis

- Main cause of acquired epilepsy in developing countries, likely in the world
- Produces important economical losses to pig-raising peasants
- Endemic (hyperendemic?) in most Non-Muslim developing countries

Taenia solium

- Hum
- (Definitive Host)
- an

- Ingestion of infected pork,



- Ingestion of *T. solium* eggs
- by fecal contamination:
- **Human cysticercosis**

- P
- (Intermediate Host
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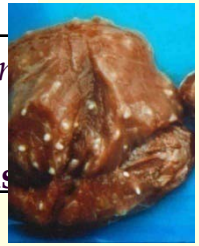
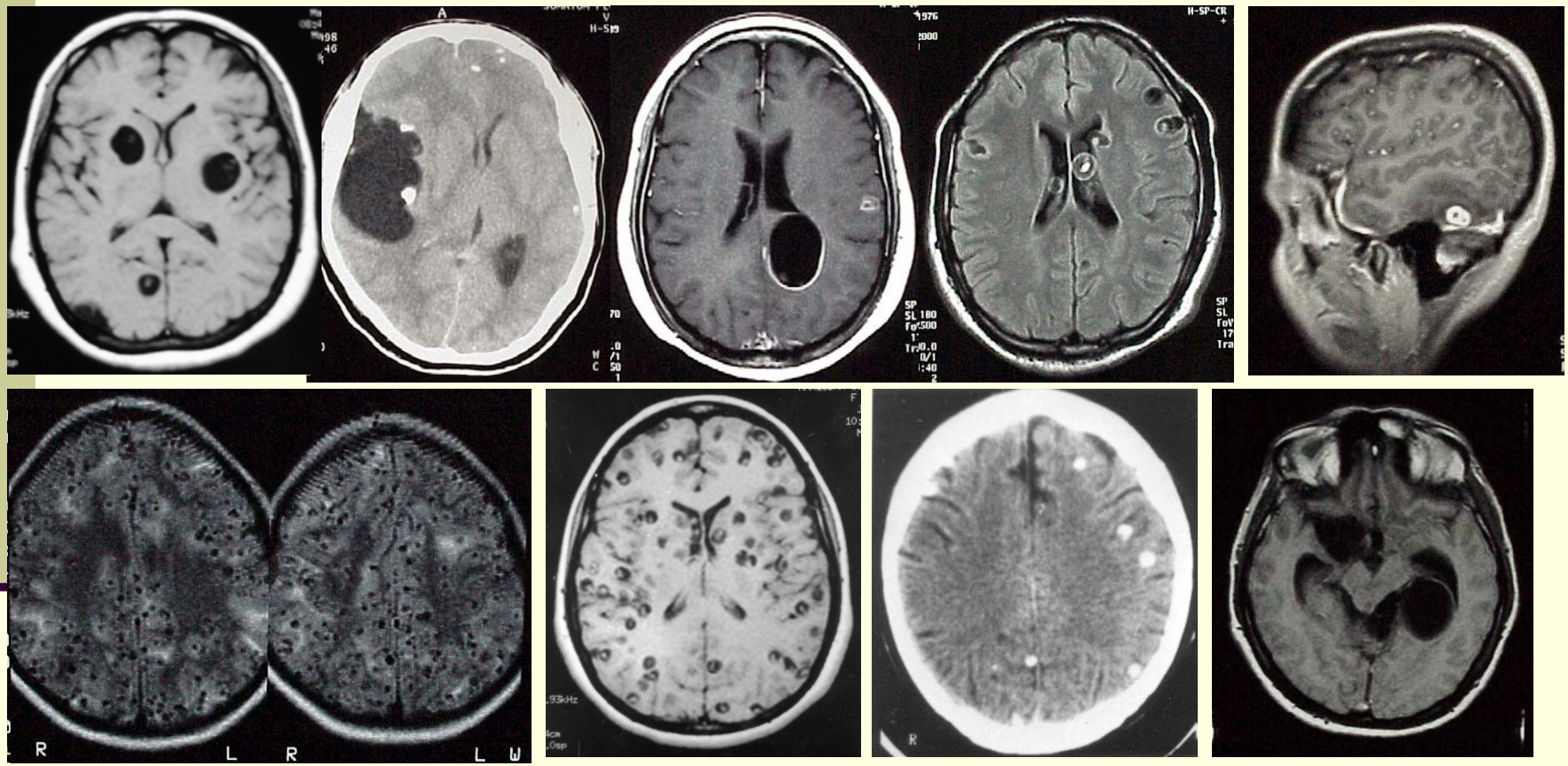
- Ingestion of *T. solium*
- eggs or proglottids:
- **Porcine cysticercosis**



The Neurocysticercoses



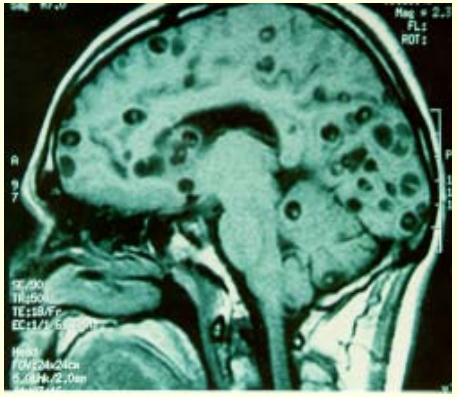
The Basics

- Complex, smart parasite
- Zoonotic
- Two hosts (two parasite populations)
- Enormous biotic potential
- Animal exposure derives from free or cheap feeding, which in survival economies is crucial to poor (all) families

Diagnosis of Taeniasis and NCC

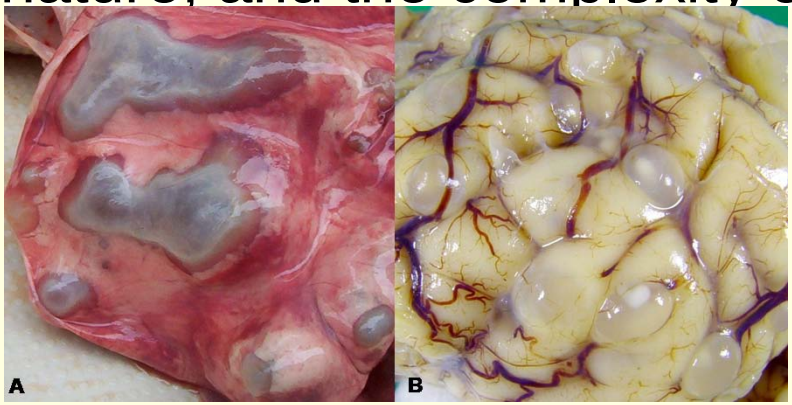
- **Taeniasis**
  - Stool microscopy - Quite available and cheap, poor diagnostic yield.
  - Coproantigen ELISA detection - Much more sensitive.

- **Cysticercosis**
  - Primarily Imaging (CT/MRI)
  - Supported by specific serology in western blot



ZOONOTIC LARVAL CESTODE INFECTIONS: NEGLECTED, NEGLECTED TROPICAL DISEASES? Christine M. Budke[1], A. Clinton White Jr.[2], Hector H. Garcia[3, 4*] (PLoS NTDs, 2008)

- Despite gross underreporting and underestimation … available burden estimations indicate that that these infections represent **at least** a similar socio-economic impact to many of the conditions officially listed as neglected tropical diseases (NTDs) by various organizations and sites.
- …this is especially true given their impact on both human health and livestock production, their difficulty in diagnosis, their chronic nature, and the complexity of treatment and control.



Cysticercosis Control

- Key is separation of pigs from (infected) feces.
- Control has been achieved in developed countries through sanitation and good pig husbandry.

- In the majority of developing countries – due to population increase, decrease in finances and failures of management – sanitation and good pig husbandry are unlikely to occur.

Taeniasis / Cysticercosis, Eradicable Disease

1 – Humans as sole definitive host.

2 – Main reservoir (pig) is a domestic animal.

3 – No wild reservoirs nor vectors.

4 – Effective treatments available for tapeworm infections

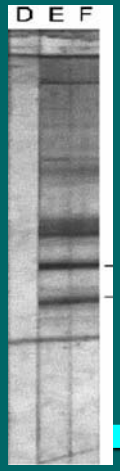
Changes in the Landscape

- Advances in the past two decades made it more likely that we can speed up eradication using means other than sanitation and good pig husbandry.
- Tools for detecting tapeworms effectively.
- We can also treat pigs and people effectively.
- We now have an effective pig vaccine.

Tools

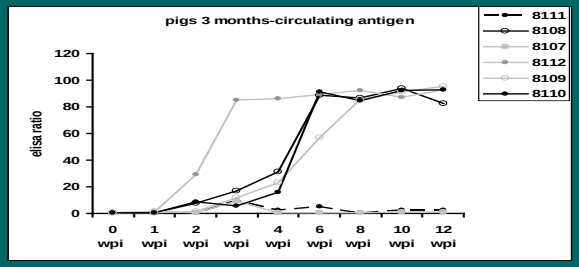
- Stool antigen detection

- Tapeworm stage-specific immuno-diagnosis

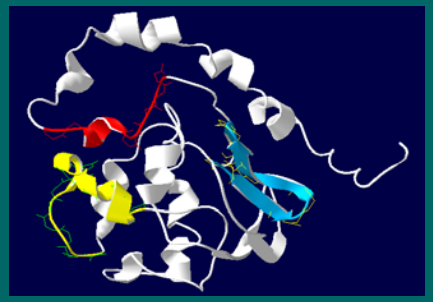


- Oxfendazole treatment of infected pigs

- Antigen-detection assays



- Pig vaccines



- Improved treatments for tapeworms, GIS/GPS spatial data, mathematical modeling, etc

The Remaining of This Talk
Part II of II

- Our program in Tumbes - Base thinking
- Initial round
- Changes to interventions
- Second round
- Evidences of efficacy
- Region (Tumbes) - wide scaling
- Monitoring of scaling
- Current scenario

Base Thinking

- Unlke CHD, we have the tools but don’t know how to use them most effectively.
- We need systematic studies of control that compare one method with the other.
- Once we find an optimum method we then need to determine its feasibility and long term sustainability. Including finding donors to fund control.

Control, the ultimate goal

A demonstration project to

Eliminate Cysticercosis in Peru

and thus develop a model by which the disease may be eradicated in other parts of the world

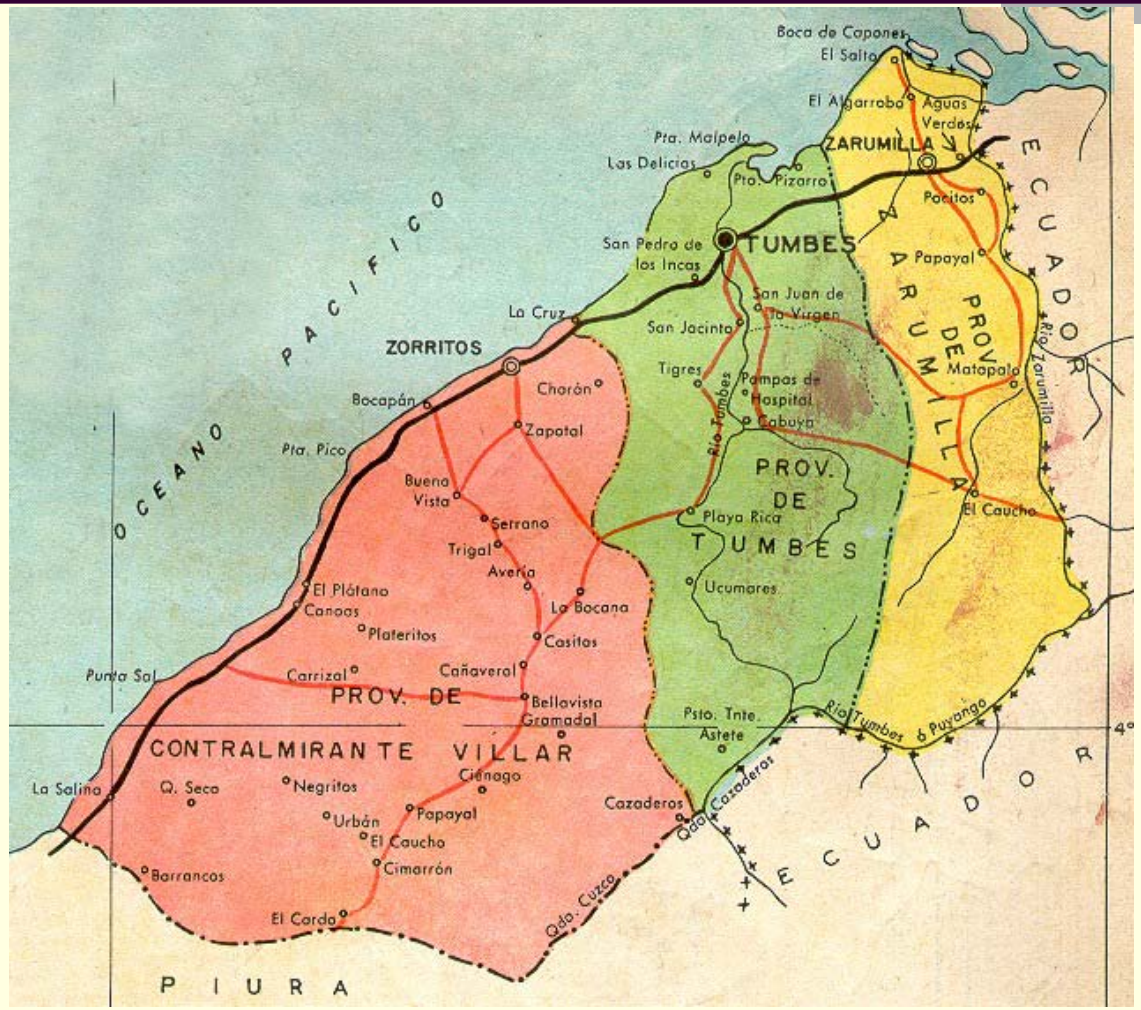
Prepared for

The Bill & Melinda Gates Foundation

Project Organization

- The project leadership, comprised of researchers from the Centers for Disease Control and Prevention, Johns Hopkins University, the Peruvian Ministry of Health, Universidad Peruana Cayetano Heredia, and the Universidad Nacional Mayor de San Marcos, is confident that the disease can be eliminated from a major disease-endemic area of Peru within seven years.

Tumbes


Boca de Capones
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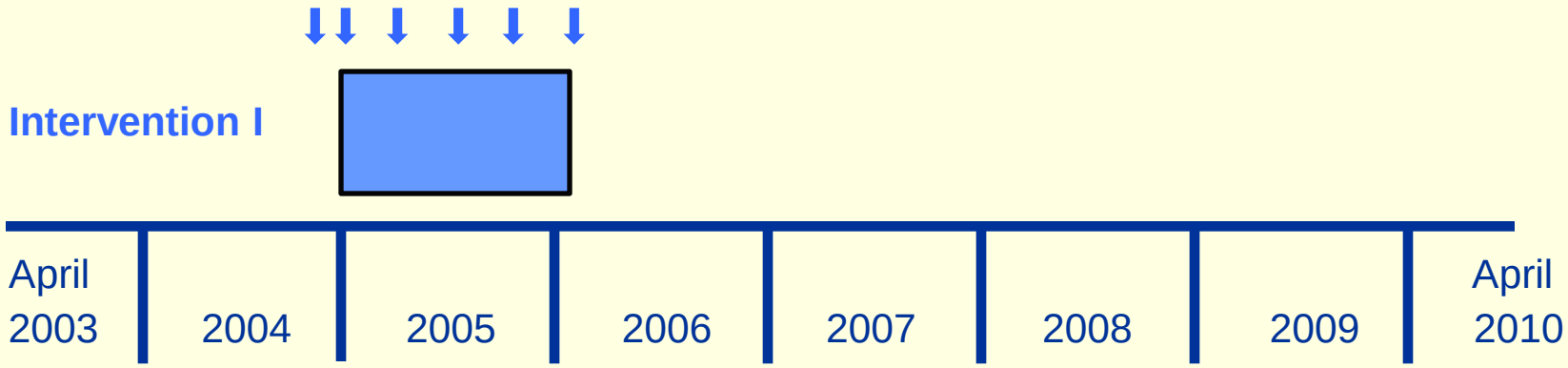
El Algarrobo
Aguas Verdes
ZARUMILLA
Pta. Malpelo
Las Delicias
Pto. Pizarro
Pocitos
ECUADOR
San Pedro de los Incas
TUMBES
Papayal
San Juan de la Virgen
La Cruz
San Jacinto
PROV. DE ZARUMILLA
Río Zarumilla
ZORRITOS
Tigres
Pampas de Hospital
Matapalo
Río Tumbes
Bocapán
Chorán
Cabuya
Zapotal
Pta. Pico
OCEANO PACIFICO
Buena Vista
PROV. DE TUMBES
Playa Rica
El Caucho
Serrano
Trigal
Avería
Ucumares
El Plátano
Canoas
La Bocana
Plateritos
Casitas
Punta Sal
Carrizal
Cañaveral
PROV. DE
Bellavista
Gramadal
Psto. Tnte. Astete
Río Tumbes & Puyango
CONTRALMIRANTE VILLAR
Cienago
La Salina
Q. Seco
Negritos
Cazaderos
Papayal
Urbán
El Caucho
Cimarrón
Barrancos
El Cardo
Qda. Cuzco
PIURA

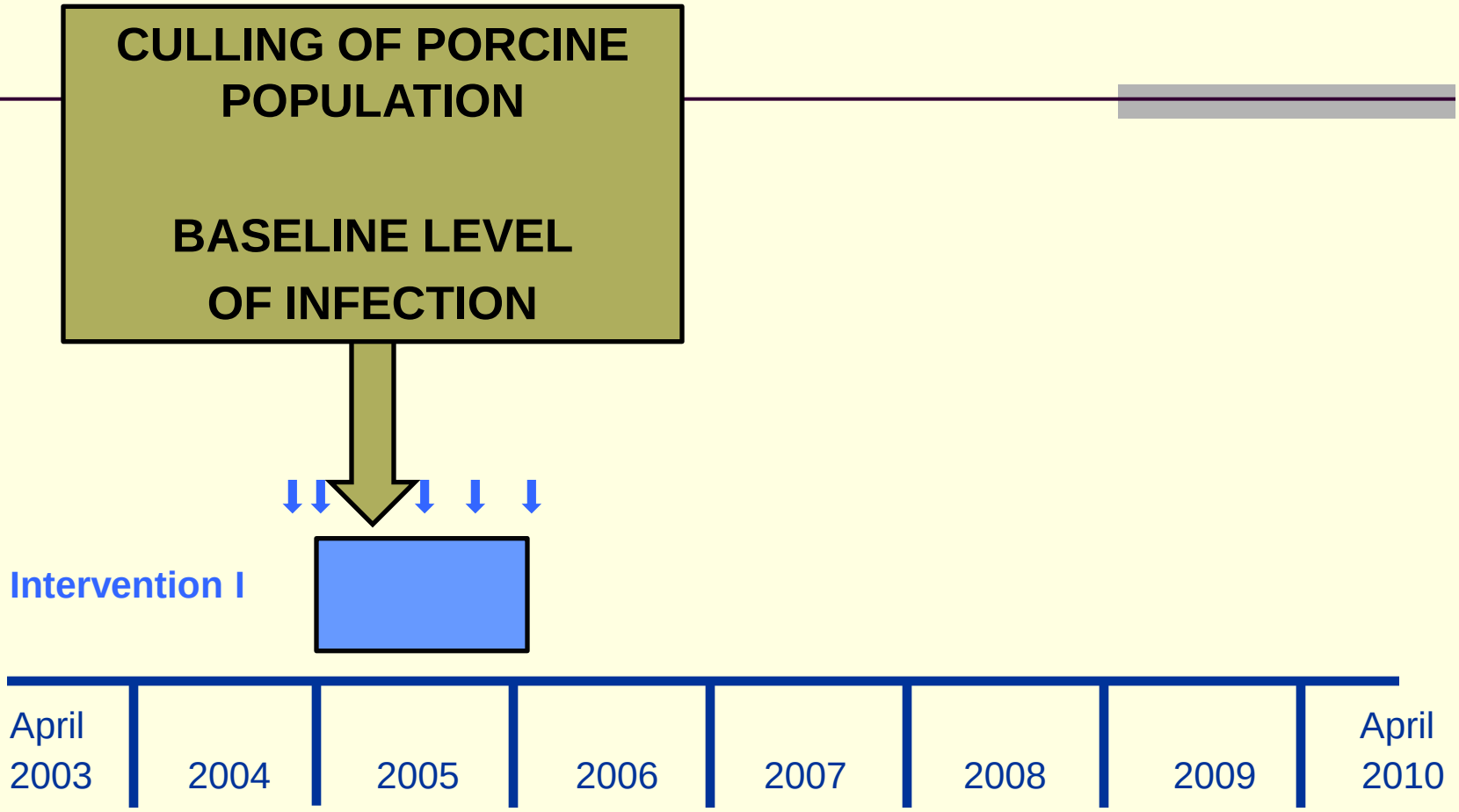

SOMATOM
Emotion

Initial Round

- These control strategies include the following (initially tested in 42 villages for a total population of 12,000 humans and 6,000 pigs)
  - Mass treatment of humans and pigs (2 regimes)
  - Targeted treatment of humans and pigs
  - Treatment of 3-month old pigs
  - Education
  - Pig culling and replacement

Initial Round




CULLING OF PORCINE POPULATION
BASELINE LEVEL OF INFECTION
Intervention I
April 2003
2004
2005
2006
2007
2008
2009
April 2010

Baseline Infection Levels

- Population 389 pigs
- Bought & culled 326 pigs

Seronegative	139
Weak seropositive	108
Moderate	73
Strong	6

Baseline Infection Levels

- Population 389 pigs; bought & culled 326 pigs

		w/live cysts
Seronegative	139	0 (0%)
Weak seropositive	108	2 (2%)
Moderate	73	12 (20%)
Strong	6	4 (67%)

- Extrapolated to total porcine population: 6% pigs with cysts.
- Numbers of cysts 1 to 2,698; mean 177

Initial Round

- Serological monitoring of incidence showed a decrease of ~20-30% of incidence in two interventions but elimination was apparently not achieved

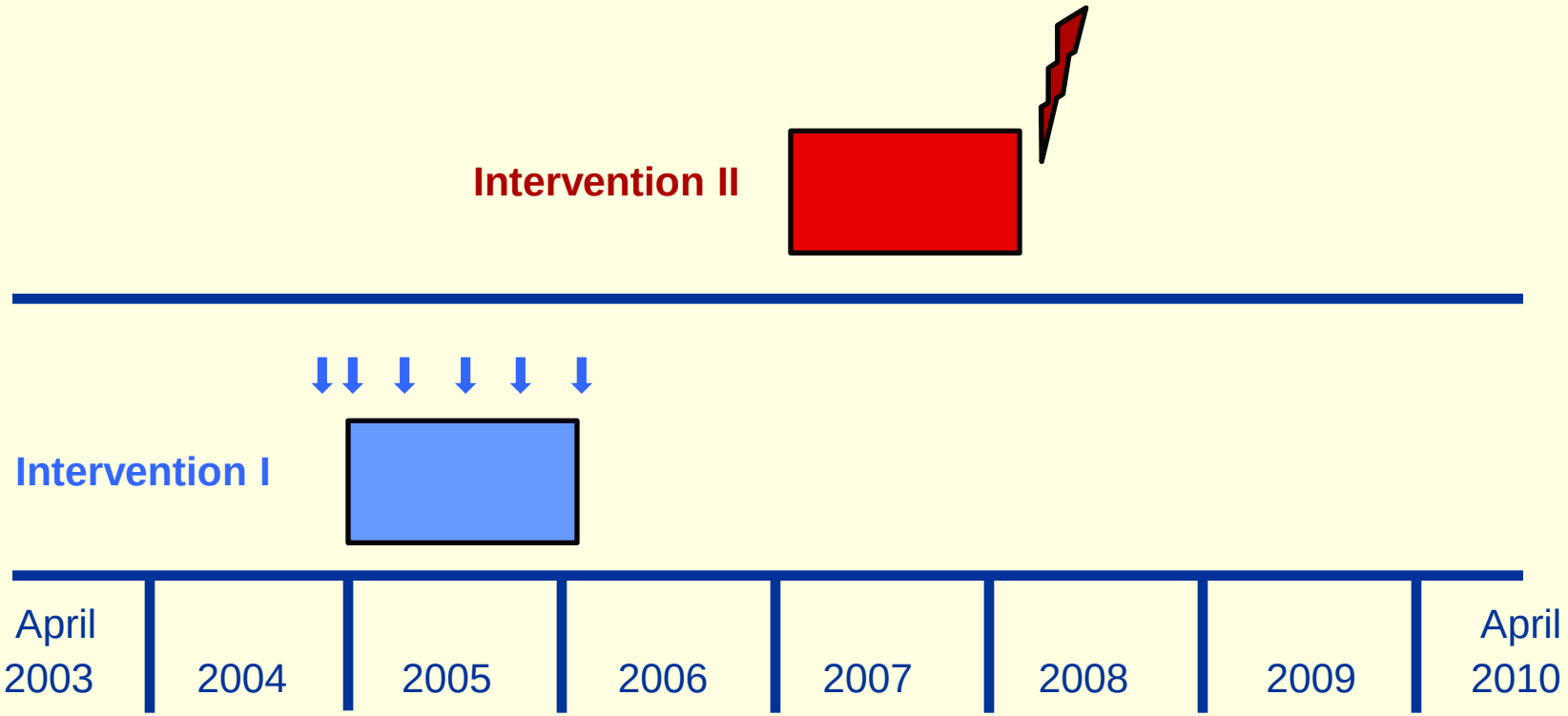
- We decided to:
  - Increase pressure
  - Add vaccine (already available)
  - Monitor with necropsy of seropositive pigs

Cysticercosis Control

- The following phase examined only two interventions, selected mostly by efficacy but also on compliance and feasibility: mass versus targeted treatment of human taeniasis with niclosamide – both included mass treatment of pigs.

- In each of the above, half of the villages had their pigs vaccinated with TSOL18 (factorial design)

Second Round



What Happened

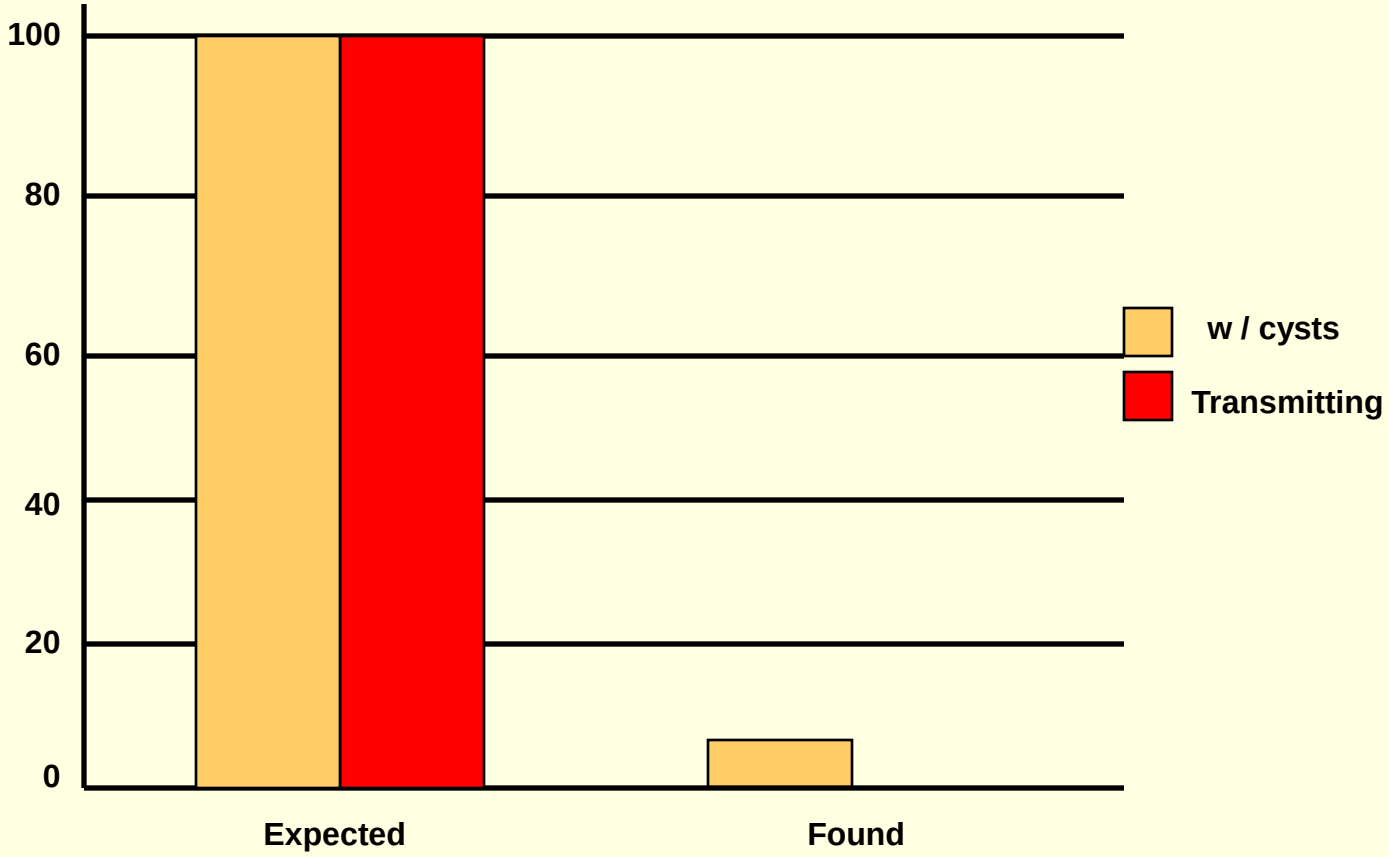
- At the end of the second round, we sampled all pigs and bought 658 including all pigs with strong serological responses and most of those with weak serology, plus some negatives

- In a population like this we would expect 10-20% of pigs with viable cysts, some with thousands of cysts.

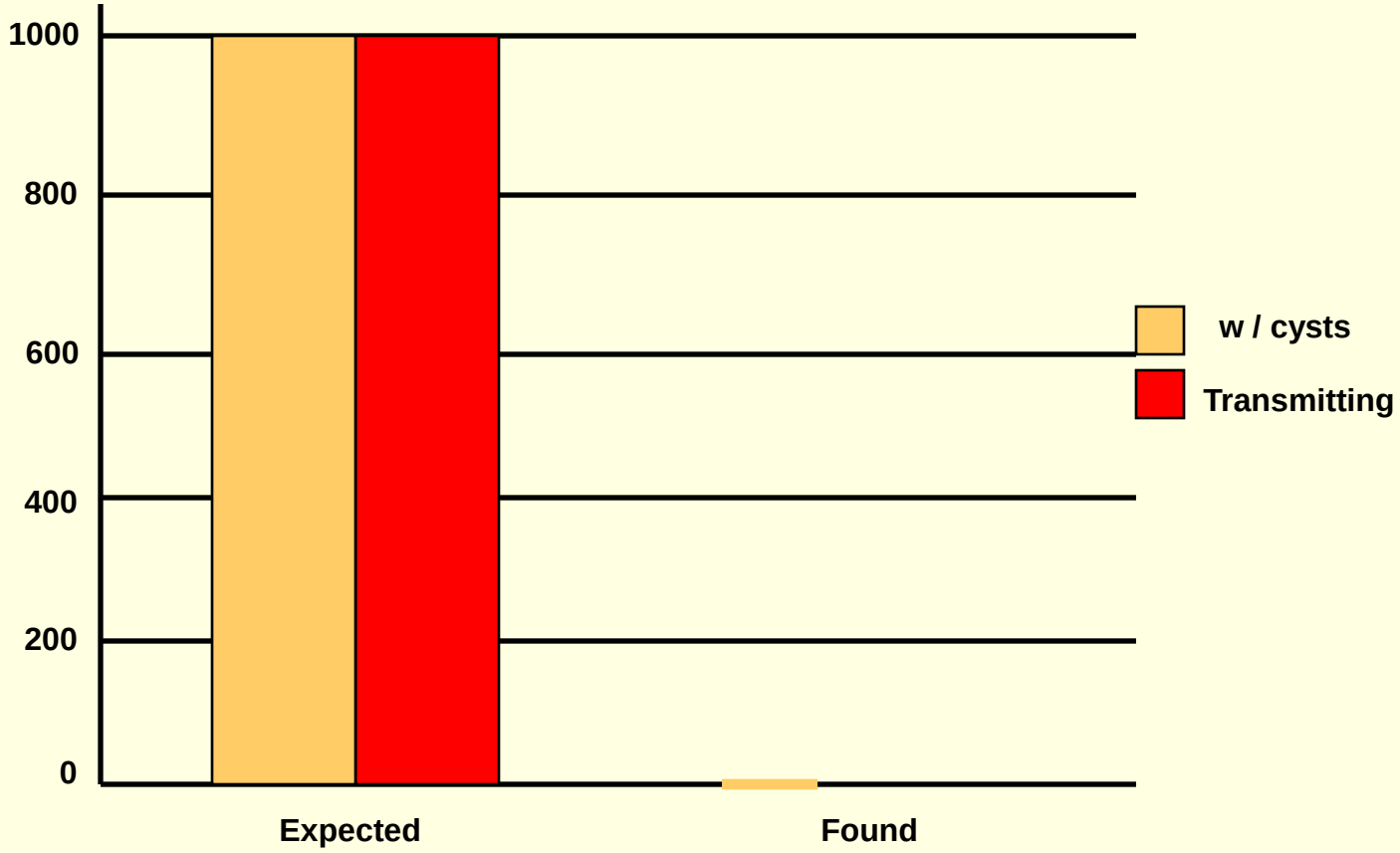
Pig Necropsies After Intervention II

- Population varied from 5000 to 6000 pigs
- Bought & culled 658 pigs, 411 of them seropositive.
- Apparently live cysts in 6 animals, total 8 cysts, 4 in brain

Pigs with Cysts

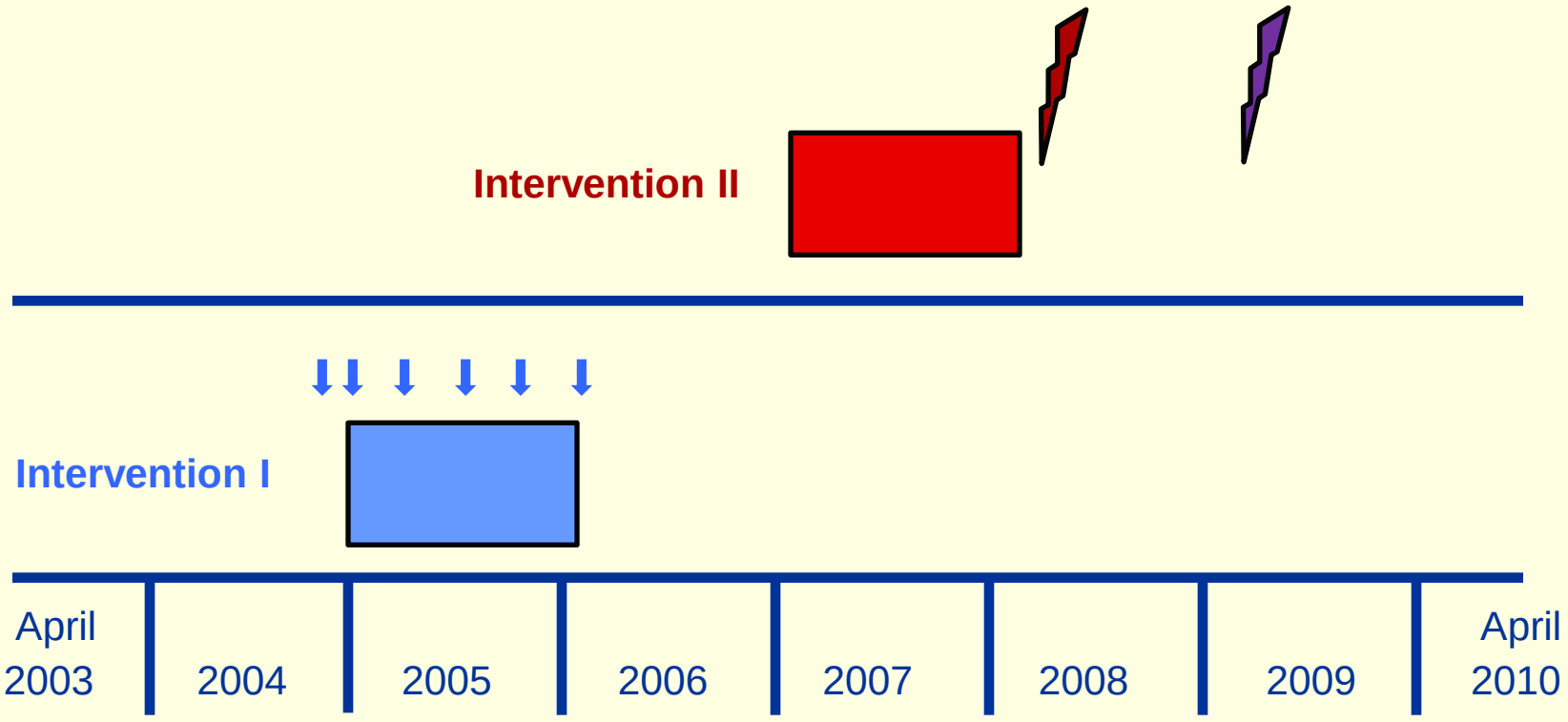


Cysts



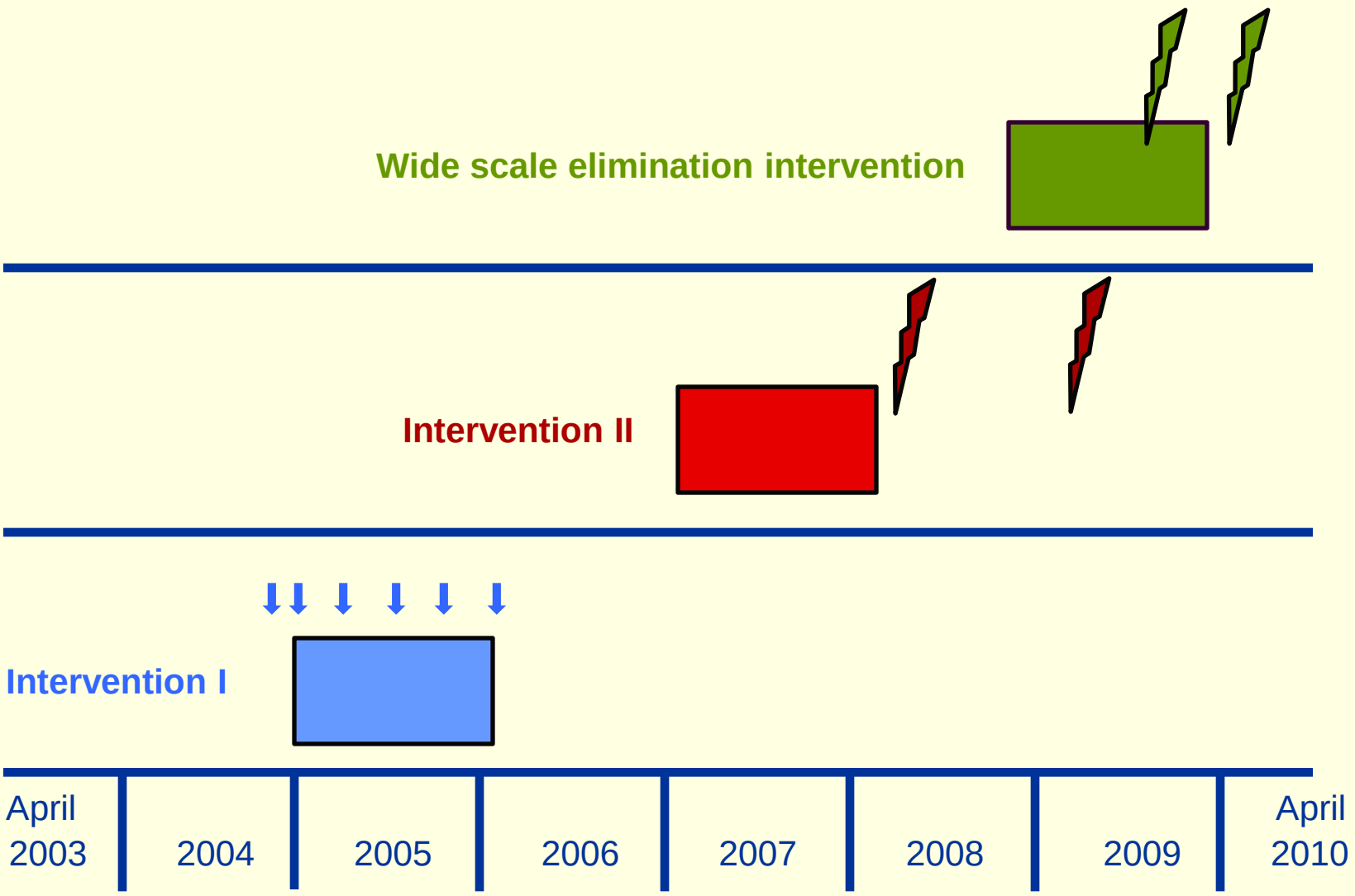
One Year Later

- We repeated the process



Pig Necropsies
One Year After Intervention II

- Bought & culled 310 pigs, 273 seropositive
- 7 pigs with viable cysts, 2 heavily infected
- Vaccine areas: Only 2 pigs in a cluster – non compliant families


Wide scale elimination intervention
Intervention II
Intervention I
April 2003
2004
2005
2006
2007
2008
2009
April 2010

Then

- The successful strategy was applied in 104 villages
- Same monitoring one year after – 300+ seropositive pigs

Pig Necropsies During Scaling

- Bought & culled 322 pigs from 107 villages

		w/viable cysts
Seronegative	0	-
Weak seropositive	46	0 (0%)
Moderate	209	4 (2%)
Strong	67	0 (0%)

Pig Necropsies at the End of Scaling

- Bought & culled 330 pigs from 104 villages

		w/viable cysts
Seronegative	0	-
Weak seropositive	51	0 (0%)
Moderate	227	1 (0.5%)
Strong	52	2 (4%)

Then

- 101villages clear
- 1 with one pig with one brain cyst
- 2 heavily infected pigs in a family who refuse to participate

So What?

- Well, we demonstrated that transmission can be interrupted and the interruption can be sustained
- A few infective pigs survived
  - Confirm that not enough to re-establish
  - Emphasis in monitoring
- Problem is not yet solved

The Final Scheme

- Oxfendazole in pigs, 5 times (0,2,4,6,8 months)
- Niclosamide in humans, 3 times (1, 5 and 9 months)
- Stool coproantigen after initial NSM treatment
- Pig vaccine at months 4 and 8

What To Do Now?

- We may chose from several diferent view points
- We may claim to have ended the war. People may then jump to do control interventions
- What is wrong with it?

What is Wrong on Jumping Too Fast?

- Recipy is not yet ready
- Tools are somewhat expensive and not that available, treatment efficacy is suboptimal, required coverages are high
- Still, what is wrong with trying?

What is Wrong with Trying?

- Potential waste of effort and resources
- Worse, if programs fail, discouragement will seriously affect the future of control

Hydatidosis Control Reasons for Failure

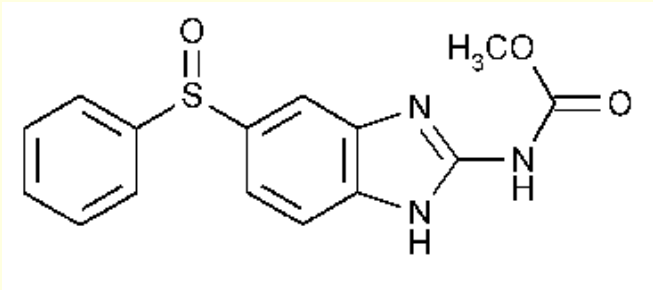
- A programme…had little effect over the first 20 years…too much reliance on rural owners to dose their own dogs, use of a purgative rather than a cestocidal drug, lack of local staff, insufficient funds,lack of baseline data, and political upheaval. Other control programmes failed for: (1) premature withdrawal of government funding (mid-Wales); (2) small and under-funded control authority (Turkana), with virtually no facilities; (3) poor management of stray dogs (Sardinia); and (4) political upheaval or security issues, or both (terrorism in Peru, social changes in the former Soviet Union) *(Craig et al, Lancet Inf Dis 2007)*

What To Do Then?

- Focused interventions, aimed to:
  - Improve existing tools
  - Make them handier and cheaper
  - Adapt them to local scenarios
- Identify potential weaknesses to avoid future failures
- Comprehensive elimination programs by now only in places with high likelihood of success

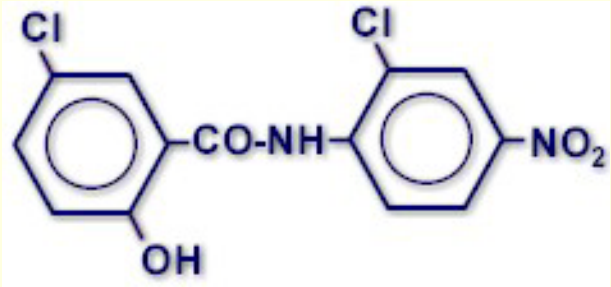
What about the tools?

- **Oxfendazole in pigs**
  - Locally produced
  - 22.5%
  - Withdrawal time and pharmacokinetics in pigs already determined



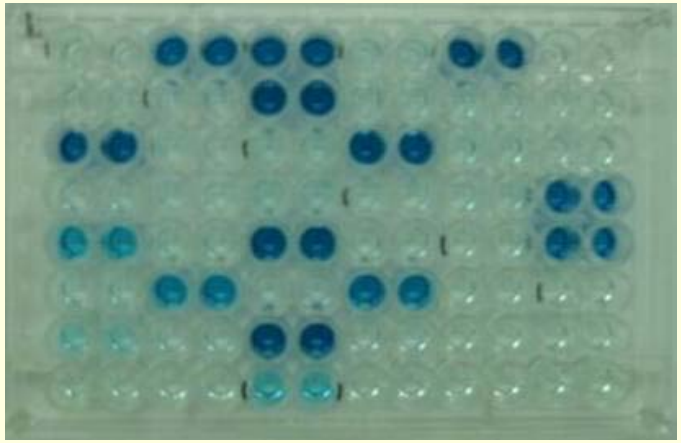
What about the tools?

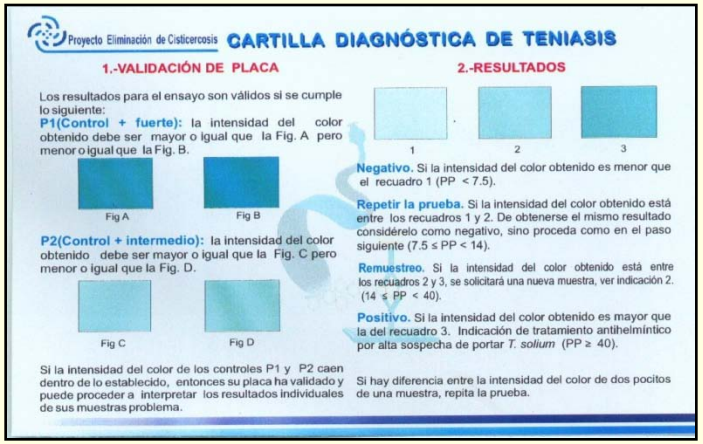
- **Niclosamide in humans**
  - Safe
  - Efficacy under 70%
  - Testing of low dose PZQ already ongoing
  - If PZQ causes neurological side effects we may need to try 3 g niclosamide (Phase I)



What about the tools?

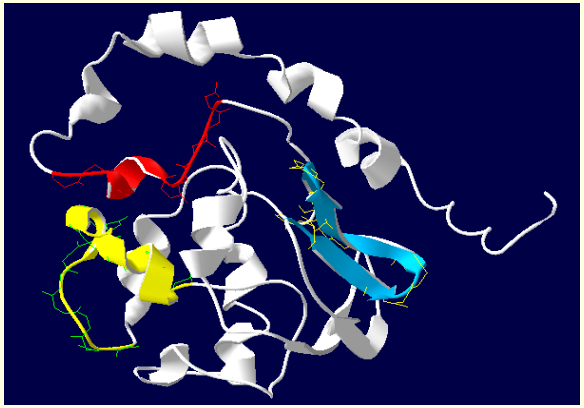
- **Coproantigen detection**
  - Robust, field applicable version already developed
  - Reagent storage at -20, bottled water, milk powder, visual reading





What about the tools?

- **Pig vaccine**
  - TSOL18, developed at the University of Melbourne, already produced at large scale under GMP
  - Field trials to begin soon



What more could be added?

- Point of care diagnostic assay for taeniasis. Cheap. Field-applicable. Useful for monitoring
- Alternative pig vaccines. Single dose if possible
- **Practical monitoring systems for control areas**

Muchas gracias