Cysticercosis Control: Bringing Advances to the Field

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ABSTRACT

Progress towards *Taenia solium* control is evident in the development of new technologies and in increasing regional coordination, yet disease eradication remains unlikely in the near future. In the meantime, translation of research advances into functioning control programs is necessary to address the ongoing disease burden in endemic areas. Multiple screening assays, effective treatments for both human and porcine infection, and vaccines blocking transmission to pigs are currently available. Strategies based on identification and treatment of *T. solium* adult tapeworms, as well as interventions that block cysticercosis acquisition in pigs have temporarily reduced transmission. Building on these successes with controlled community trials in varying endemic scenarios will drive progress towards regional elimination.

Key words: Control, Cysticercosis, Elimination, Eradication neurocysticercosis, *Taenia solium*

INTRODUCTION

Cysticercosis is an emerging zoonosis causing debilitating brain lesions in humans, widespread compromises in food safety and important economic losses from contaminated pork. It is caused by the pork tapeworm, *Taenia solium*, which infects both humans and pigs. As the most common helminthic infection of the central nervous system, *T. solium* is a leading cause of late-onset epilepsy in Latin America, Asia and sub-Saharan Africa;[1] in Latin America alone over 400,000 people have symptomatic disease.[2]

The International Task Force for Disease Eradication targeted cysticercosis as a potentially eradicable disease in 1992.[3] Yet despite the availability of multiple screening tools, effective treatment for humans and pigs, development of candidate pig vaccines and increased knowledge of local transmission dynamics, translation into operating control projects has been limited. Effective, affordable and sustainable interventions on local and regional levels are urgently needed to reduce the immediate burden of the disease.

Access this article online	
Quick Response Code:	Website: www.jgid.org
	DOI: 10.4103/0974-777X.81693

ETIOLOGY AND TRANSMISSION

Cysticercosis is a parasitic tissue infection by the larval form of the pork tapeworm, *T. solium*. Humans and pigs acquire cysticercosis by ingesting *T. solium* eggs shed in the feces of a human infected with the adult intestinal tapeworm. Once ingested, these eggs release onchospheres, which invade the intestinal wall and disseminate to form cysts throughout the body. Neurocysticercosis occurs when onchospheres invade the central nervous system. The natural lifecycle completes when a human consumes pork contaminated by *T. solium* larval cysts, as these may then develop into adult egg-producing intestinal tapeworms. While both pigs and humans can acquire cysticercosis, only humans can harbor a *T. solium* tapeworm. This endemic lifecycle occurs in regions where sanitation is poor and where pigs can access raw sewage. Small landowners in impoverished areas are therefore the most affected, although migrants and travelers in developed nations are also increasingly at risk.[4-7] Worldwide cysticercosis is a common disease, with over 50 million people affected.[1]

CONSEQUENCES OF ENDEMIC TRANSMISSION

Neurocysticercosis is a leading cause of preventable epilepsy responsible for 30% of adult onset epilepsy in endemic regions.[9-12] In these regions, 10–20% of the general population can have brain lesions consistent with

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neurocysticercosis on CT scans.[10,13-15] Seizures, precipitated by inflammation around degenerating or calcified cysts, occur in up to 70% of symptomatic diagnoses.[16] Young adults are frequently afflicted contributing to decreased productivity and unemployment among primary household wage-earners.[17] The stigma associated with epilepsy, along with direct healthcare costs related to diagnosis and management compound the problem by contributing to delayed diagnosis and undertreatment.[18] Chronic headaches, stroke syndromes, cognitive impairment and death also occur, but the associated health and economic burden remains unknown.

Porcine cysticercosis also harms local economies where domestically raised pigs provide an important source of cash or protein. Small landowners allow their pigs to roam free through villages to scavenge on waste, thereby reducing the amount of feed purchased before slaughter. However, when *T. solium* eggs are present in the environment, scavenging pigs become infected resulting in reduced sale price or confiscation of these animals. On a regional scale these losses can be significant. In China, 200,000,000 kg of contaminated pork meat is destroyed each year representing $120,000,000 USD in losses.[19] *T. solium* thus perpetuates conditions for continued transmission by further impoverishing those affected.

THE ECONOMIC ENGINE: DRIVING TRANSMISSION, LIMITING INTERVENTION

Local economic factors ultimately drive disease transmission and must be addressed in any successful control strategy.[17,20,21] Interventions which further impoverish small landowners may not be adopted or may create unintended consequences. For example, confiscation of infected pigs without compensation encourages bypass of official slaughterhouses, illicit sale of infected animals, and clandestine introduction of contaminated pork into the marketplace.[22] Illicit sale allows pig raisers to recoup some value from their infected animals, although typically only 25–50% from that of a clean pig.[22,23] Pig corralling to keep swine from consuming sewage is resisted, as it reduces profit margin by requiring owners to purchase feed for their animals. Similarly, while vaccines can break transmission to pigs, cost and acceptability of repeated immunization may limit uptake by villagers.[24-26] Vaccines against highly virulent classical swine fever are widely available but infrequently used in domestically raised pigs.[27]

TARGETING INTESTINAL TAPEWORMS

Adult intestinal tapeworms are the immediate source of both human and pig cysticercosis, thus treatment of intestinal tapeworm carriers is a key to control. However, identification is complicated by the typical asymptomatic clinical course, poor sensitivity of the widely available light microscopy, as well as the cost and limited accessibility of high-performance screening tests. Multiple screening tools are available which can be applied relative to local operating conditions [Table 1].

Single dose oral praziquantel and niclosamide are reported to be 90–95% efficacious for intestinal tapeworm treatment,[28]

Table 1: Screening methods and reported performance for *Taenia solium* adult intestinal infection

Substrate	Method		Sensitivity	Specificity	Comments
Symptoms	Self-report		Limited data available	Limited data available	Inexpensive, immediate interpretation, no lab required
Stool	Pros: Indicate current infection. Cons: Resistance to providing stool samples in general, infectious substrate samples in general. Infectious substrate.				
	Light microscopy	Eggs, proglottids, scolex[47]	~35%	100 (genus)	Inexpensive and widely available. Repeat samples necessary to increase sensitivity. Speciation possible for expelled proglottids or scolex.
	ELISA*	Multiple[47]	99	99 (genus)	Highly specific to *Taenia* genus but does not differentiate *T. solium* from *T. saginata*.
	ELISA*	Whole worm extract / ES antigen[48]	96	100	Specific to *T. solium* species, slight decrease in sensitivity compared to genus-specific coproantigen ELISA.
	Nested PCR†	Tso31[49]	97	100	Specific to *T. solium* species. Highly specialized laboratory.
	Multiplex PCR†	mt cox1[50]	Limited data available	Limited data available	Specific to *T. solium* species. Highly specialized laboratory.
Serum	Pros: Specific to antibodies against *T. solium* taeniasis. Fingerstick collection practical for field use. Cons: Unknown duration of antibody persistence. Positive results may not indicate active infection.				
	EITB‡	Native[51]	95	100	Limited supply of *T. solium* adult specimens for antigens.
		rES33[52]	97	100	Recombinant. No native antigen required. Improved reproducibility.
		rES38[52]	98	91	Same benefits as rES33. Slight gain in sensitivity with loss of specificity.
	MICT§	rES33[53]	95	96	Same recombinant benefits. Less technical expertise required, more rapid turnaround. Not field ready.

*Enzyme-linked immunosorbent assay; †Polymerase chain reaction; ‡Enzyme-linked immuno-electrotransfer blot; §Magnetic immunochromatographic test and have been used in mass treatment campaigns.[29-32] Niclosamide has the advantage that it is minimally absorbed from the intestinal tract and has no activity against *T. solium* cysts. Inadvertent damage to cysts during treatment with praziquantel can precipitate neurologic symptoms in people with undiagnosed NCC.[33,34]

MASS SCREENING AND CHEMOTHERAPY

Taken together, the low community prevalence and asymptomatic nature of adult tapeworm infection suggest a population-based strategy for screening and treatment. Mass human chemotherapy with niclosamide and praziquantel has been attempted in multiple countries.[30-32] While initial success is noted in decreased porcine cysticercosis and human taeniasis, these results are temporary if not sustained. Combined human and pig mass chemotherapy in Peru showed a return to baseline within 1–-2 years.[32] Persistence of underlying conditions for transmission, decreased herd immunity among pigs, and migration of adult tapeworm carriers all contribute to endemic stability.[35] A longitudinal program is therefore critical to sustain control benefits.

FOCI-CENTERED INTERVENTIONS

Alternatively, intervention may be directed towards identified foci where risk of adult tapeworm infection is increased. One potential strategy involves screening or presumptive treatment for intestinal tapeworms within geographic vicinity of infected pigs. Risk concentration around infected pigs has been demonstrated in Peru and Tanzania, although this pattern was not seen in a study in Mexico.[36-38] Using infected pigs to identify at-risk foci has potential operational advantages in that 1) heavily infected pigs can be identified by tongue examination, and 2) the short lifespan of pigs raised for slaughter indicates relatively recent exposure to tapeworm eggs.

Attempts to identify at-risk foci around human cysticercosis may be neither efficacious nor practical. Epilepsy does not appear to cluster around intestinal tapeworm carriers, likely due to long latency between exposure and symptom onset in neurocysticercosis.[39] And although human seroprevalence shows both familial and geographic clustering around intestinal tapeworm carriers, antibodies against cysts may indicate remote exposure.[40]

INCREASING LOCAL AWARENESS

Community education campaigns, alone or combined with other interventions, can contribute to control effectiveness.[41,42] In addition to basic information about transmission routes, hygiene and methods for raising healthy pigs, educational messages should focus on immediate and tangible benefits of changed behavior, such as the economic benefits of raising healthy pigs. Provision of tangible incentives and infrastructure improvement may facilitate behavior modification.[41]

MONITORING PROGRAM EFFECTIVENESS

Several tools are available to estimate short-tem trends in community transmission of *T. solium* infection, including serologic antibody and antigen assays, radio-imaging, meat inspection and tongue examination of swine. All have inherent limitations in practicality or performance, and a combination may be necessary for accurate assessment. Measurements in pigs may be the most time-sensitive, as rapid turnover creates successive cohorts of at-risk pigs, which can be monitored serially. Pig seroprevalence has been used to trend community *T. solium* transmission following mass treatment campaigns.[31,32] Monitoring of sentinel pigs can also indicate areas of persistent risk or re-introduction of intestinal tapeworms into previously cleared areas.[43] Surveillance for infected pigs followed by treatment with oxfendazole could have the additional benefit of reducing the flow of contaminated pork into the marketplace.[44-46] However, further research into the safety and acceptability of oxfendazole-treated pork is needed.

CONCLUSIONS

While widespread development of sanitary infrastructure and animal husbandry practices could ultimately eradicate *T. solium*, this is not a short-term reality in most rural endemic areas. In the meantime, effective, affordable and sustainable interventions on local and regional levels are urgently needed to reduce immediate burden of disease. Regional elimination remains an important objective, as disease transmission rapidly returns to baseline if control interventions lapse. Progress in regional coordination is evident through formation of regional Cysticercosis Working Groups and advances in diagnostics, modeling and treatment are expected. However, technical advances from all sources must be continually translated into operating control projects to address ongoing harm. The Cysticercosis Working Group in Peru provides an excellent model, as it continues to expand field operations and progress towards elimination in Northern Peru.

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How to cite this article: O’Neal S, Winthrop KL, Gonzalez AE. Cysticercosis control: Bringing advances to the field. J Global Infect Dis 2011;3:156-60.

Source of Support: Nil. **Conflict of Interest:** None declared.