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Elimination of *Taenia solium* Transmission in Northern Peru

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ORIGINAL ARTICLE

Elimination of *Taenia solium* Transmission in Northern Peru

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ABSTRACT

BACKGROUND

Taeniasis and cysticercosis are major causes of seizures and epilepsy. Infection by the causative parasite *Taenia solium* requires transmission between humans and pigs. The disease is considered to be eradicable, but data on attempts at regional elimination are lacking. We conducted a three-phase control program in Tumbes, Peru, to determine whether regional elimination would be feasible.

METHODS

We systematically tested and compared elimination strategies to show the feasibility of interrupting the transmission of *T. solium* infection in a region of highly endemic disease in Peru. In phase 1, we assessed the effectiveness and feasibility of six intervention strategies that involved screening of humans and pigs, antiparasitic treatment, prevention education, and pig replacement in 42 villages. In phase 2, we compared mass treatment with mass screening (each either with or without vaccination of pigs) in 17 villages. In phase 3, we implemented the final strategy of mass treatment of humans along with the mass treatment and vaccination of pigs in the entire rural region of Tumbes (107 villages comprising 81,170 people and 55,638 pigs). The effect of the intervention was measured after phases 2 and 3 with the use of detailed necropsy to detect pigs with live, nondegenerated cysts capable of causing new infection. The necropsy sampling was weighted in that we preferentially included more samples from seropositive pigs than from seronegative pigs.

RESULTS

Only two of the strategies implemented in phase 1 resulted in limited control over the transmission of *T. solium* infection, which highlighted the need to intensify the subsequent strategies. After the strategies in phase 2 were implemented, no cyst that was capable of further transmission of *T. solium* infection was found among 658 sampled pigs. One year later, without further intervention, 7 of 310 sampled pigs had live, nondegenerated cysts, but no infected pig was found in 11 of 17 villages, including all the villages in which mass antiparasitic treatment plus vaccination was implemented. After the final strategy was implemented in phase 3, a total of 3 of 342 pigs had live, nondegenerated cysts, but no infected pig was found in 105 of 107 villages.

CONCLUSIONS

We showed that the transmission of *T. solium* infection was interrupted on a regional scale in a highly endemic region in Peru. (Funded by the Bill and Melinda Gates Foundation and others.)

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Infection of the human brain by cystic larvae of the pork tapeworm species *Taenia solium* is the most frequent cause of late-onset seizures and epilepsy in the world.[1,2] Transmission is sustained in rural areas through a pig–human cycle in which humans harbor the adult intestinal tapeworm (taeniasis) and pigs carry the cystic larvae in their flesh (cysticercosis). In poor, rural villages, domestic pig husbandry and lack of sanitation allow pigs to become infected by consuming human feces containing tapeworm eggs. In turn, humans acquire taeniasis by consuming pork contaminated with larval cysts or acquire neurocysticercosis through incidental ingestion of tapeworm eggs.

A Quick Take is available at NEJM.org

In 1992, the International Task Force for Disease Eradication determined that *T. solium* was eradicable.[3,4] Over the ensuing decades, however, attempts to control transmission have been limited to studies targeting one or two villages; some of the attempts had no effect at all and most have had only transitory effects at best. Interventions have attempted to control taeniasis in the human population through targeted or mass human antiparasitic therapy[5-10] or to control cysticercosis in pigs through prevention education[9] and immunotherapy[11] and antiparasitic treatment[12,13] of pigs. The important advances that were made during this period, including the development of new diagnostic techniques, less-expensive and more-efficacious treatments, and a highly effective pig vaccine, suggested that regional elimination was feasible.[14-16] Our objective was to systematically test and compare elimination strategies to determine the feasibility of interrupting the transmission of *T. solium* infection in a highly endemic region in Peru.

METHODS

PROGRAM OVERVIEW

This program was a multi-institutional effort among two Peruvian universities (Universidad Peruana Cayetano Heredia and San Marcos University), Johns Hopkins Bloomberg School of Public Health, and the U.S. Centers for Disease Control and Prevention. To determine the feasibility of eliminating *T. solium* in rural regions of the study area (Tumbes Region, northern coast of Peru) (Fig. 1), we used a three-phase design to select the most effective and practical combination of human and animal interventions (Table 1). The outcomes of the three phases were measured in pigs, because the rapid turnover of this population allows for the timely assessment of overall transmission. Human disease was not measured as an outcome because neurocysticercosis may manifest years after infection, and the low prevalence of taeniasis (0.5 to 1.0%) makes it difficult to assess changes.

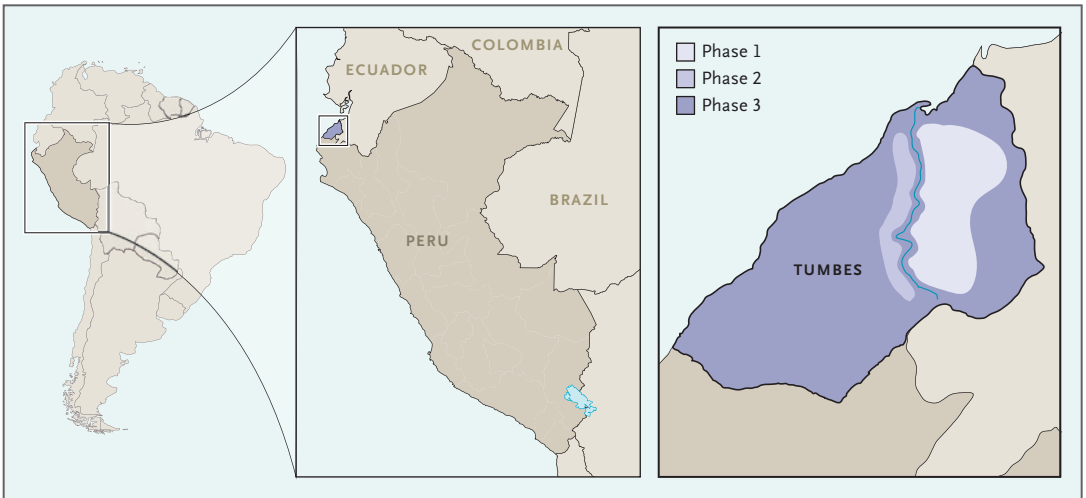

Figure 1. Regions of Tumbes, Peru, Covered during Each Phase of the Cysticercosis Elimination Demonstration Program.

Phase 3 covered the entire region of Tumbes, including those areas covered previously in phases 1 and 2.

Table 1. Timing of Interventions Applied in Humans and Pigs during Each Phase of the Cysticercosis Elimination Demonstration Program.

Intervention	Month of Intervention												
	0	1	2	3	4	5	6	7	8	9	10	11	12
Phase 1													
Mass treatment*													
Humans	—	NM	—	—	—	NM	—	—	—	NM	—	—	—
Pigs	OXF	—	—	OXF	—	—	OXF	—	—	OXF	—	—	OXF
Minimal mass treatment*													
Humans	—	NM	—	—	—	NM	—	—	—	—	—	—	—
Pigs	OXF	—	—	OXF	—	—	OXF	—	—	—	—	—	—
Strategic treatment*													
Humans	—	NM	—	—	—	—	—	—	—	—	—	—	—
Pigs	OXFc	OXFc	OXFc	OXFc	OXFc	OXFc	OXFc	OXFc	OXFc	OXFc	OXFc	OXFc	OXFc
Mass screening†													
Humans	—	SCR	—	—	—	SCR	—	—	—	—	—	—	—
Pigs	SCR	—	—	SCR	—	—	SCR	—	—	—	—	—	—
Prevention education‡													
Humans	EDU	EDU	EDU	EDU	EDU	EDU	EDU	EDU	EDU	EDU	EDU	EDU	EDU
Pigs	—	—	—	—	—	—	—	—	—	—	—	—	—
Pig replacement													
Humans	—	—	—	—	—	—	—	—	—	NM	—	—	—
Pigs§	—	—	—	—	—	—	—	—	—	CULL	—	—	—
Phase 2													
Mass treatment*													
Humans	—	NM	—	—	—	NM	—	—	—	NM	—	—	—
Pigs	OXF	—	OXF	—	OXF	—	OXF	—	OXF	—	—	—	—
Mass treatment with vaccine*													
Humans	—	NM	—	—	—	NM	—	—	—	NM	—	—	—
Pigs	OXF	—	OXF	—	OXF	VAC	OXF	—	OXF	—	—	—	—
Mass screening†													
Humans	—	SCR	—	—	—	SCR	—	—	—	—	—	—	—
Pigs	OXF	—	OXF	—	OXF	—	OXF	—	OXF	—	—	—	—
Mass screening with vaccine†													
Humans	—	SCR	—	—	—	SCR	—	—	—	—	—	—	—
Pigs	OXF	—	OXF	—	OXF	VAC	OXF	—	OXF	—	—	—	—
Phase 3: mass treatment with vaccine (final strategy)*													
Humans	—	NM	—	—	—	NM	—	—	—	NM	—	—	—
Pigs	OXF VAC	—	OXF	—	OXF	—	OXF VAC	—	OXF	—	OXF	—	—

* In the mass-treatment and strategic-treatment groups, humans received mass treatment with niclosamide (NM); in phases 1 and 2, post-treatment stool samples were obtained for analysis by microscopy and enzyme-linked immunosorbent assay (ELISA) for coproantigen detection. People with persistent taeniasis were retreated and followed until cured. In phase 3, post-treatment stool samples were obtained only after the first round of mass treatment with niclosamide. In phases 1 and 2, pigs in the mass-treatment and minimal-mass-treatment groups were administered oxfendazole (OXF) and those in the strategic-treatment group were administered OXF at baseline, with longitudinal treatment of pigs born into or entering the study villages (OXFc). One group of pigs in phase 2 and all pigs in phase 3 were administered OXF in addition to vaccination (VAC) with the TSOL18 pig vaccine (vaccine was administered in two doses spaced 3 weeks apart).

† In phases 1 and 2, humans were screened by both ELISA for coproantigen detection and light microscopy of stool; niclosamide was administered only in those with evidence of taeniasis. Pig serum samples were screened by enzyme-linked immunoelectrotransfer blot assay, which uses lentil lectin-bound glycoproteins; OXF was administered only in those pigs that were seropositive.

‡ Prevention education (EDU) was the reference strategy in phase 1.

§ The pig replacement strategy involved removing pigs from the community and replacing them with noninfected pigs (CULL).

STUDY OVERSIGHT

The study was reviewed and approved by the main institutional review board at Universidad Peruana Cayetano Heredia, by the Ethical Committee of Animal Welfare of the School of Veterinary Medicine, San Marcos University, and by the Peruvian Institute of Health — all in Lima, Peru. All the authors vouch for the completeness and accuracy of the data and analyses and for the fidelity of the study to the protocol, which is available with the full text of this article at NEJM.org.

PHASE 1

In phase 1, we compared the effectiveness and feasibility of six intervention strategies in 42 villages along the eastern margin of the Tumbes River (Fig. 1 and Table 1). The strategies included mass treatment, minimal mass treatment, mass screening, strategic treatment, prevention education, and pig replacement. Mass treatment involved mass administration of niclosamide for human taeniasis and oxfendazole for porcine cysticercosis; minimal mass treatment involved fewer rounds of the same drugs applied over a shorter period. Strategic treatment involved administration of oxfendazole only to pigs born into or entering the study villages (details of the intervention strategies are provided in the Supplementary Appendix, available at NEJM.org). All medicines (niclosamide for humans and oxfendazole for pigs) and tests, as well as the porcine vaccine TSOL18, were acquired for the study and provided to villagers at no cost (our program purchased the medicines and sent funds to the University of Melbourne for the production of the vaccine, which was produced with the assistance of one of the authors). The main outcome was the incidence of antibodies against *T. solium* cysticercosis in all pigs as measured by serologic testing every 3 months; prevention education was the reference strategy. Phase 1 interventions began in December 2004 and continued for 1 year.

PHASE 2

The two most effective strategies from phase 1 — minimal mass treatment and mass screening — were selected and modified (increasing the number of treatment rounds and shortening the interval between treatments) for head-to-head comparison. A total of 17 larger villages along the western margin of the Tumbes River were assigned to one of four study groups (mass treatment or mass screening, each either with or without vaccination of pigs) (Table 1). The mass screening strategy was modified, for logistic reasons, by replacing pig screening with mass chemotherapy in pigs, although screening for taeniasis in humans was still performed. We administered the TSOL18 vaccine[14,15] in two subgroups to assess the additional effect of pig vaccination. Because of the high background seropositivity rate noted in the pigs with negative findings on necropsy in phase 1, we changed our outcome measure to the prevalence of pigs with live, nondegenerated cysts on necropsy (Fig. 2).

Phase 2 interventions began in January 2007. Within 1 month after the last round of treatment, we attempted to purchase all seropositive pigs (despite our efforts, not all pigs were able to be purchased), as well as a random 5% sample of seronegative pigs, for necropsy. One year after the completion of the interventions, we performed a second round of necropsies using the same sampling strategy we used in the first round, although fewer seronegative pigs were included because infection was rare in seronegative animals.

PHASE 3

A final elimination strategy of mass chemotherapy with niclosamide in humans and with oxfendazole in pigs, in combination with pig vaccination (final mass treatment with vaccine), was implemented in all 107 rural villages in Tumbes Region over a period of 1 year (Fig. 1 and Table 1). The outcome measure was the prevalence of pigs with live, nondegenerated cysts on necropsy. Because of the greatly expanded scale of the intervention, the sampling strategy was changed to limit the number of necropsies, while increasing the likelihood of detecting infected pigs. We systematically sampled all pigs between the ages of 6 and 8 months because these pigs were born during the intervention period and were old enough to have a reduced likelihood of persistent maternal antibodies.[17] We attempted to purchase all seropositive pigs that had three or more reactive bands on Western blot analysis for necropsy, because prior necropsies showed that the most viable infections occurred in this group.[18] We also included a random 10% sample of seropositive

pigs that had one or two reactive bands on Western blot analysis.

STATISTICAL ANALYSIS

Additional details of the outcome measures, such as incidence rate ratios and prevalences, are provided in the final statistical analysis plan (available with the protocol at NEJM.org). All incidence rates according to intervention group and 95% confidence intervals were computed with the use of Poisson regression. The estimates of the incidence rate ratios and associated 95% confidence intervals were compared among the intervention groups with the use of Poisson regression, with the "prevention education" group as the reference group. The estimates were assessed for potential confounding (e.g., the average age of the pigs in different intervention groups), but no confounding effect was found. The outcome measures for the villages that received only the phase 3 intervention were compared with those of villages that had received a previous intervention to determine any carryover effect. An exact 95% binomial confidence interval was computed for the percentage of humans who were still infected after receiving treatment with niclosamide. Descriptive statistics, such as counts and prevalences, were used in the evaluation of the final intervention strategy that was selected.

RESULTS

PHASE 1

The baseline characteristics of villages participating in the elimination program across all phases are summarized in Table 2. Phase 1 interventions were performed in an area that covered 10,753 humans and 17,102 pigs. Mass screening and minimal mass treatment were the only strategies to show significant reductions in incidence (as assessed by serologic testing), as compared with the reference intervention of prevention education, although the effects were small (incidence rate ratios, 0.78 [95% confidence interval {CI}, 0.64 to 0.95] and 0.79 [95% CI, 0.65 to 0.97], respectively). These strategies were selected for modification and further evaluation in phase 2. The incidence rate ratios for the other strategies were 0.93 for strategic treatment and 0.96 for mass treatment (Table S1 in the Supplementary Appendix). Participation in pig replacement was deemed to be insufficient to achieve elimination because we were able to purchase only 326 of the 464 pigs (70%) in the pig-replacement group; thus, incidence among pigs (as measured by serologic testing) was not monitored in these villages.

The results from the pig-replacement group, however, had important implications for measuring the effects of the interventions in subsequent

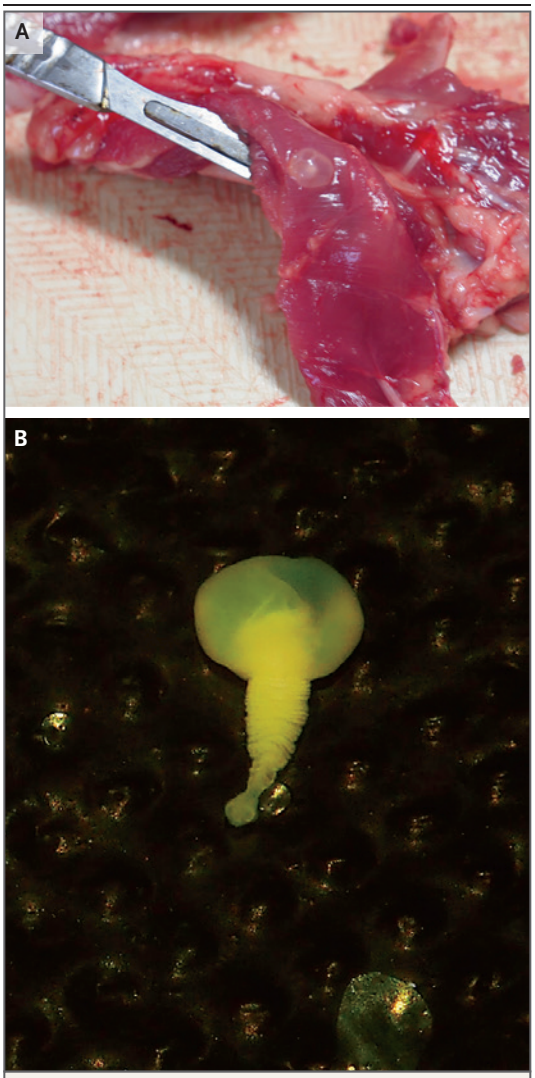

Figure 2. A Live, Nondegenerated Cyst and Evagination of the Cysticerci.

Panel A shows a live, nondegenerated cyst filled with clear fluid, with a central scolex visible within. In our study, necropsy samples of pig muscle or brain tissue were examined for this finding. Panel B shows the evagination of the tapeworm when the cyst was placed in a warm bile solution to confirm viability.

Table 2. Characteristics of Human and Pig Populations during Each Phase of the Cysticercosis Elimination Demonstration Program.*

Characteristic	Phase 1						Phase 2			Phase 3
	Mass Treatment	Minimal Mass Treatment	Strategic Treatment	Mass Screening	Prevention Education	Pig Replacement	Mass Treatment with Vaccine	Mass Treatment without Vaccine	Mass Screening with Vaccine	Mass Screening without Vaccine	Mass Treatment with Vaccine
Villages — no.	7	7	7	7	8	6	3	6	3	5	107
Humans — no.	2651	2127	2285	1660	1554	476	3418	2323	1756	2883	81,170
Male sex — %	51.3	52.6	53.8	51.8	53.0	52.7	51.1	54.6	50.2	51.1	51.4
Median age (IQR) — yr	27 (13–44)	26 (13–42)	25 (13–44)	27 (13–44)	26 (13–45)	24 (10–43)	26 (14–43)	27 (15–46)	28 (14–44)	28 (15–48)	25 (12–42)
Pigs — no.	3557	2909	3478	3441	3253	464	3255	3485	2874	3874	55,638
Male sex — %	42.7	45.7	44.7	46.2	46.4	42.2	44.9	43.4	42.3	43.9	NA
Median age (IQR) — mo	6 (2–12)	6 (3–12)	6 (3–12)	6 (3–12)	5 (2–12)	7 (3–18)	6 (3–10)	6 (3–10)	6 (3–10)	6 (3–10)	NA
Baseline prevalence of cysticercosis — %†	44.6	34.7	45.7	41.0	50.2	42.9	24.5	47.8	47.3	28.1	NA

* The groups differed significantly only with regard to antibody prevalence. NA denotes not assessed.
† Prevalence was assessed by enzyme-linked immunoelectrotransfer blot antibody testing.

phases. We performed a detailed necropsy in all 326 pigs we purchased to quantify the number of cysts to use as an estimate of the reservoir of infection among the pigs in the villages in which no intervention was implemented. Findings from the necropsies performed on these animals showed that 18 of the 326 pigs (5.5%) had live, nondegenerated cysts (range, 1 to 2698 cysts per animal) (Table 3). However, the majority — 180 of the 326 pigs (55.2%) — were seropositive for antibodies against cysticercosis, which suggested that serologic testing has poor predictive value for determining the size of the reservoir of infection among pigs. We tested 172 cysts from 11 pigs, and evidence of viability (i.e., the scolex evaginated and moved) was shown in 125 cysts (72.7%) from 7 pigs (63.6%).

PHASE 2

Phase 2 interventions were performed in an area that covered 10,380 humans and 13,488 pigs (Table 2). Immediately after the intervention, 658 pigs were culled from more than 4000 pigs for necropsy, and eight live, nondegenerated cysts were found in 6 pigs (Table 3). However, only four of these cysts from 3 pigs were confirmed to be true cysticerci, and the infectious capacity of these cysts appeared to be compromised. The three cysts that appeared to be the most healthy were tested for viability, and none evaginated. Histopathological analysis of the fourth cyst revealed a parasite cystic wall structure that did not contain a scolex. No pig with a live, nondegenerated cyst was found in 14 of 17 villages. We then conducted a second round of necropsy 12 months after the phase 2 interventions were completed and no further interventions had been implemented. We found live, nondegenerated cysts in 7 of 310 pigs culled from more than 3000 pigs for necropsy; however, viability testing was not performed in this round of necropsy. No pig with a live, nondegenerated cyst was found in 11 of 17 villages; 5 of the 6 villages with infected pigs had not received vaccine in phase 2.

PHASE 3

In phase 3, the final scaled-up intervention was implemented in 107 villages, covering 81,170 humans and 55,638 pigs (Table 2). Mass treatment with vaccine was chosen for the final scaled-up intervention because there was no difference between the two strategies in phase 2

Table 3. Results of Pig Necropsy According to Serologic Status at Each Phase of the Cysticercosis Elimination Demonstration Program.*

Phase and Serologic Status	Pig Blood Sample	Pig Necropsy Sample	Pigs with Live Nondegenerated Larval Cysts†
	number	*number (percentage)*	
Phase 1‡			
Seronegative	197	146 (74.1)	2 (1.4)
1–2 bands	186	128 (68.8)	4 (3.1)
3 bands	73	47 (64.4)	10 (21.3)
4–7 bands	8	5 (62.5)	2 (40.0)
Total	464	326 (70.3)	18 (5.5)
Phase 2, immediately after intervention			
Seronegative	3024	178 (5.9)	1 (0.6)
1–2 bands	556	184 (33.1)	0
3 bands	414	279 (67.4)	4 (1.4)
4–7 bands	25	17 (68.0)	1 (5.9)
Total	4019	658 (16.4)	6 (0.9)
Phase 2, 12 months after intervention			
Seronegative	2362	37 (1.6)	0
1–2 bands	505	143 (28.3)	2 (1.4)
3 bands	186	114 (61.3)	3 (2.6)
4–7 bands	20	16 (80.0)	2 (12.5)
Total	3073	310 (10.1)	7 (2.3)
Phase 3, immediately after intervention			
Seronegative	2532	—	—
1–2 bands	565	53 (9.4)	0
3 bands	365	235 (64.4)	1 (0.4)
4–7 bands	68	54 (79.4)	2 (3.7)
Total	3530	342 (9.7)	3 (0.9)

* Pig serum samples were assessed by enzyme-linked immunoelectrotransfer blot assay, which uses lentil lectin-bound glycoproteins. Serologic status was based on the number of reactive bands on Western blot analysis.
† Necropsy samples of pig muscle or brain tissue were examined for live, nondegenerated cysts filled with clear fluid. Necropsy samples covered most seropositive pigs to maximize the likelihood of detecting infections. Formal viability testing and histopathological analysis were performed in phase 2 only.
‡ Phase 1 necropsy was performed during a culling intervention in which the majority of pigs were removed from six geographically isolated villages in which no chemotherapy or vaccine had been applied previously.

and because mass screening was considered to be logistically impractical at this scale. In the human population, niclosamide was administered in three rounds, with 84.7% of the entire population receiving at least one dose. Adverse reactions to niclosamide were rare; the most common adverse reactions were mild abdominal pain (0.4%), liquid stools (0.2%), and headache (0.1%). There were no severe adverse events associated with niclosamide. In the pig population, oxfendazole was administered every 2 months, and two vaccination campaigns, each of which included two rounds of vaccination, were also performed. At the end of the intervention, we screened 3530 pigs 6 to 8 months of age by serologic testing and performed necropsy on 342 seropositive pigs, including 289 of the 433 seropositive pigs that had three or more reactive bands on Western blot analysis (66.7%) and 53 of the 565 seropositive pigs that had 1 or 2 reac-

tive bands (9.4%) (Table 3). We found 3 pigs with live, nondegenerated cysts, 2 of which were heavily infected. These 3 pigs were not recorded in the rounds of intervention and may have been missed during the intervention or may have been imported into the pig population after the intervention. No pig with a live, nondegenerated cyst was found in 105 of the 107 villages.

DISCUSSION

Taeniasis and cysticercosis due to *T. solium* are among the few diseases that are considered to be potentially eradicable. The results of this program show that it is feasible to interrupt *T. solium* transmission on a regional scale, thereby preventing human and porcine cysticercosis. The reservoir of infection in the intermediate host was eliminated in 105 of 107 villages through a 1-year attack phase. Elimination persisted in most areas for at least 1 year without further intervention. However, this program was designed to show the feasibility of interrupting parasite transmission in a defined geographic region, not to maintain elimination. We expect that the effect will be temporary if it is not bolstered by additional activities.

As many previous studies have shown, *T. solium* is resistant to control.[5-10,12] Gains in control may disappear quickly if the parasite reservoir is not reduced beyond the point at which the parasite population can recover.[19,20] The small or null effect of the phase 1 interventions prompted us to intensify subsequent approaches by shortening the interval between rounds of mass treatment and by administering the TSOL18 vaccine in pigs.[14-16] The result of intensification was dramatic — the infectious larval stage reservoir almost completely disappeared in phase 2. The few cysts that were found did not appear to be capable of perpetuating the pig–human cycle. This critical finding allowed us to reproduce elimination in a much larger population during phase 3. Although we found three infected pigs at the end of phase 3, we were not able to determine whether these pigs were missed during the intervention or were imported after the intervention. It is also possible that we missed some infected pigs in our end-point sampling. However, the prevalence of pigs with viable cysts was reduced to minimal levels, thus decreasing the potential for further transmission from the pigs in most if not all villages. The results of the phase 3 intervention were similar in the villages that had received a previous intervention during phase 1 or phase 2 (two pigs with cysts were found) and the new villages that received only the phase 3 intervention (one pig with cysts was found), suggesting that a carryover effect in the villages that had received a previous intervention was not a major factor.

We evaluated the efficacy of our elimination strategies in pigs rather than in humans for multiple reasons. Although taeniasis is the immediate source of cysticercosis in pigs and humans, measuring changes in the prevalence or incidence of taeniasis requires mass collection and screening of stool samples, which is impractical in a large-scale elimination program.[21] We chose not to measure taeniasis as an outcome because of the logistic complexities and costs involved and the potentially detrimental effect that the need for stool collection could have had on the rate of participation among villagers. In retrospect, we recognize that stool collection and enzyme-linked immunosorbent assay (ELISA) for coproantigen detection at the end of phase 3 could have provided an additional gauge of the effect of the intervention. However, the attack on the reservoir of taeniasis was strong, with multiple rounds of chemotherapy. The phase 3 intervention against taeniasis included three rounds of mass treatment, in which 85% of the population received treatment at least once. Furthermore, we collected post-treatment stool samples in the first round of mass treatment and followed persons who had results that indicated that they had a tapeworm with the most sensitive test available to verify that the parasites were killed.[22]

Measurement of the changes in the prevalence or incidence of symptomatic neurocysticercosis among humans would provide the best indication of the effect of the intervention on human health, if it were not for the long latent period of the infection. In most cases, symptoms appear and persist years after infection.[23,24] However, we expect that our intervention will result in a decrease in the incidence of seizures and epilepsy over the next 5 to 10 years, similar to that observed in another control program in Honduras.[25] On the other hand, pigs provide a convenient and dynamic sample for measuring the effect of a control program. Approximately half the pig population is renewed every 4 to 6 months, so new cohorts of unexposed pigs are introduced continuously.[26] We measured the effect of our inter-

vention using detailed necropsy of seropositive pigs — an expensive and labor-intensive process. Detailed necropsy would not be feasible for large-scale programs, and therefore alternative markers for viable infection specific to *T. solium* cysticercosis are needed.

Our final strategy was based on performing multiple rounds of mass chemotherapy; we found that mass screening involved considerable operational challenges with no additional benefit with respect to the outcome. The acceptable safety profile of niclosamide allowed our approach; safety concerns may preclude the use of praziquantel as an alternate drug in areas endemic for *T. solium*.[27] Unfortunately, we found that the efficacy of niclosamide was substantially lower than the 90% reported previously[28]; among 38 humans with taeniasis who received niclosamide, 14 (36.8%; 95% CI, 21.8 to 54.0) were still infected 2 weeks after mass treatment in phase 1, as assessed by ELISA for coproantigen detection plus stool microscopy. The use of higher or repeated doses may increase efficacy but has not been evaluated for safety. Whether interruption of transmission in a population can occur in fewer rounds of intervention cannot be assessed from our data.

We also included the use of TSOL18 vaccine in our strategy to maintain herd immunity after elimination through chemotherapy. Others have argued that vaccination can contribute to the attack phase, suggesting that one round of oxfendazole in pigs plus sustained vaccination may suffice to eliminate transmission.[16] The efficacy of TSOL18 makes this a possibility.[14-16] However, unsolved issues with pig immunization remain. The current vaccine formulation requires two doses, which may be impractical in the field. Also, infections in pigs before an age at which they can feasibly be immunized presents challenges for vaccination,[29] although the combined use of vaccination plus oxfendazole may address this issue.[16]

The few infected pigs that we found at the end of phase 3 could reflect a reintroduction of the parasite. Once elimination zones have been established, it seems reasonable to expand them to surrounding populations to buffer against reintroduction. Immigration poses a constant threat of reintroduction, because people with taeniasis will migrate into disease-free areas. Infected pigs and pork could also be transported into disease-free areas and could give rise to new intestinal tapeworms. A functioning surveillance system is therefore paramount for efficient detection and mitigation of new cases before the parasite can reestablish itself in a region. It would make sense for surveillance to be operated at the community level with oversight and tangible support from the regional and national governments. A series of nonbiologic factors may need to be considered to ensure the success and sustainability of a control program, including community involvement, prevention education, and ongoing surveillance. Cysticercosis is a disease of poverty, and the economic effect of pig cysticercosis will be the most convincing argument for villager cooperation.

Substantial work remains for elimination programs to become a reality in endemic regions around the world. Controlled experiments are needed with respect to more-refined, less-intensive, and less-expensive strategies than those used previously. However, the basic tools are available, and costs could decrease substantially when these tools are produced in the quantities required for control programs. A new formulation of the TSOL18 vaccine produced in accordance with Good Manufacturing Practice standards in India is being tested for efficacy in Peru, and oxfendazole is currently produced and available commercially in Africa. A field version of the coproantigen test is currently available, and a more replicable version based on monoclonal antibodies is being tested. The elimination of *T. solium* requires a short-term attack phase, as compared with the sustained efforts over decades required to control filarial or hydatid disease.[30] Governments will need to ensure the availability of resources to expand control and sustain it for at least a few years. Our elimination agenda in Peru involves expanding the elimination area using less-expensive and simpler methods, providing cost estimates for elimination strategies based on these methods, and sharing the outcome data with the appropriate authorities.

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APPENDIX

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