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# Spontaneously Arrested Transmission of Cysticercosis in a Highly Endemic Village with a Very Low Migration Rate

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*Abstract.* *Taenia solium* cysticercosis is difficult to eliminate without interventions or societal development. Atahualpa is a rural Ecuadorian village with documented low migration rate, where domestic pig raising is common and human cysticercosis is endemic. To assess neurocysticercosis (NCC) prevalence, 1,273 villagers aged ≥ 20 years underwent neuroimaging studies, which showed calcified lesions in 121 (9.5%) individuals, but no active disease. Likewise, positive reactions, apparently nonspecific, were found in only 3/200 subjects by the use of a monoclonal antibody-based enzyme-linked immunosorbent assay to detect *T. solium* antigens in urine. Only 2/418 pigs reacted to three antibody bands on serum western blot and none to more than three bands. This is the first time that spontaneously arrested *T. solium* transmission is documented in a known endemic village. Understanding why active transmission stopped could provide insights on potential targets for control interventions. Atahualpa could provide an optimal scenario for longitudinal studies on the consequences of calcified NCC.

Endemic areas for cysticercosis can be defined as places where all the interrelated steps needed for the completion of the life cycle of *Taenia solium* are present, including *Taenia* carriers harboring the adult parasite in the intestine, the practice of open-air defecation or improper disposal of human feces, the ability of free-roaming pigs to access human feces, and the consumption of undercooked pork.[1]

Once established in a given region, cysticercosis is difficult to eliminate. An historical example is the Enarotali region in Papua, which was free of cysticercosis until 1972, when Ekari people received a gift of infected pigs from the Indonesian government in Java. Soon thereafter, porcine cysticercosis and human taeniasis were diagnosed in the region, and an epidemic of human cysticercosis was observed among natives.[2] Nine years later, the disease spread to neighboring villages, and nowadays, it is still prevalent in the region.[3] In other cases, however, elimination has been possible through improved sanitation, pig corralling, and education. The clearest example is the almost complete elimination of cysticercosis from Western Europe during the first half of the twentieth century. More recently, the prevalence of human neurocysticercosis (NCC) also decreased in urban centers of developing countries, likely associated with development.[4,5] In addition, some other examples exist at rural levels in developing countries, where enduring public health campaigns helped to reduce the disease burden, as shown in Salamá (Honduras).[6] More recently, an intensive control program was conducted in Tumbes (Peru), involving several strategies directed to eliminate *T. solium* transmission. Results from this promising study provided robust evidence that transmission can be stopped in highly endemic villages after the combined implementation of several active interventions.[7]

A major subsequent problem in many of these settings has been the continuous movement of people from endemic areas. This is the case of Western Europe and the U.S., where migration of people with taeniasis still cause new cases of active cysticercosis in both natives and immigrants, and migration of individuals with NCC results in significant numbers of symptomatic NCC cases attending their health systems.[8,9] Spontaneously arrested transmission (in the absence of health education, improved sanitation, changes in lifestyles, or active control interventions) of this parasitic disease in an endemic population has not been ever documented.

Atahualpa is a rural village located in Coastal Ecuador, where domestic pig raising is common and human cysticercosis has proven to be endemic.[10] About 40% of pigs are not corralled and allowed to roam free in and around the houses and streets, being in close contact with humans (Figure 1). Atahualpa is remarkable for the homogeneous characteristics of its inhabitants regarding diet, socioeconomic status and living habits, the very low migration rate, and for the fact that pigs are born and raised in the village (and not purchased from other places).[11] According to our last door-to-door survey, about 20% of the houses still have open latrines for feces disposal, and evidence of open-air defecation still exists.

The village hosts a field research center from the Universidad Espiritu Santo, Ecuador, where multiple epidemiological studies have been performed in close collaboration with the local population. As part of several studies aimed to assess the prevalence of neurological diseases, including NCC, a total of 1,273 (84%) out of 1,512 eligible villagers aged ≥ 20 years received a noncontrasted head computed tomography (CT) scan, after signing the informed consent form.[12–14] CT showed lesions consistent with NCC in 121 cases (9.5%; 95% confidence interval: 8–11.3%). All of these individuals had calcified lesions in the brain parenchyma, but no other forms of NCC were seen on CT. In addition, none of these patients had previously received cysticidal agents in the past. As of August 2017, 494 participants, including 110 of the 121 individuals with NCC (91%) and 384 of 1,152 individuals without NCC on their CT scans (33%), also had a brain magnetic resonance imaging (MRI). MRIs did not detect any active cysticercotic lesion that might have been missed on CT (such as living or degenerating parenchymal, subarachnoid, or

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FIGURE 1. Free roaming pigs in Atahualpa's streets and house backyards and in close contact with humans (reproduced with permission from ref. 11). This figure appears in color at www.ajtmh.org.

ventricular cysts) and did not identify new NCC cases among those with a negative CT.

Puzzled by this complete absence of viable NCC infections in such a large proportion of a supposedly endemic population, we explored whether immunological evidence of viable infections could be found. A nested case–control study was thus conducted using a monoclonal antibody-based enzyme-linked immunosorbent assay to detect *T. solium* antigens in urine[15] in all individuals with calcified NCC as well as in a similar number of age- and sex-matched controls without evidence of NCC on CT. This method has been amply detailed elsewhere[16] and consists on the detection of *T. solium* antigens by the use of the B158C11 and B60H8 immunoglobulin G monoclonal antibodies of murine origin, which was originally described for use on serum samples, and then slightly modified for use on urine samples. Out of 200 samples analyzed (100 NCC patients and 100 healthy controls), only three individuals (two with calcified NCC and one control) had normalized ratios of optical densities greater than 2.5. Two of these three individuals had negative serum immunoblot tests for the detection of anticysticercal antibodies, and the remaining one had antibodies to two high molecular weight antigens only, suggesting that the positive antigen assay results represent nonspecific reactions.[17]

We then conducted a serological study of pigs aged $\geq 2$ months, regardless of whether they were corralled or not, to look for evidence of ongoing *T. solium* transmission in the pig population. After obtaining permission from pig owners, blood samples taken from the cranial vena cava and centrifuged in the field were obtained from 418 pigs and assessed with the enzyme-linked immunotransfer blot (EITB) assay using lentil-lectin purified glycoproteins for the detection of *T. solium* antibodies. Only two out of 418 pigs (0.5%) had three reactive bands, and no pig reacted to four or more antibody bands, again suggesting past infections only. According to previous necropsy studies, three bands is the best cut-off for defining pigs with viable infections, with sensitivity and specificity rates of about 77%.[18]

After confirming the absence of viable forms of NCC in humans and the almost nil prevalence of antibodies against *T. solium* cysticerci in pigs, we may conclude that active transmission of cysticercosis has stopped in Atahualpa. Although we did not test humans for taeniasis, the limited or nil evidence of egg exposure in humans and pigs suggests that transmission has been arrested in this community. As previously noticed, reduced transmission in other instances has always been attributed to development or to an applied health intervention.[4–7] At no time during our presence in Atahualpa have we conducted public health campaigns directed at prevention or control of cysticercosis, so it is unlikely that our presence influenced transmission.

As much as we know, this is the first time that interruption of *T. solium* transmission is documented in the absence of intervention or overall societal development. Proof-of-concept of spontaneous elimination of transmission is important not because it could be a recommendable option for endemic areas. Understanding why active transmission stopped in Atahualpa could provide insights into factors that could be targets for control interventions. If active transmission is still present in other villages in the region (currently under study), determining risk factors absent in Atahualpa may provide potential targets for specific interventions. It is possible, however, that interruption occurred as the result of natural fluctuations in transmission. A parasite population that relies on a relatively small, closed, and homogeneous host population may not be able to recover if the number of infected hosts drops below a critical threshold.

Because Atahualpa is a closed village with a very low migration rate, this community could provide an optimal scenario for longitudinal studies on the consequences of calcified NCC, given that no biases induced by new infections would be expected in the future. Calcified NCC has been associated with episodic perilesional edema in temporal relation with seizures or other neurological symptoms and also with an increased frequency of hippocampal atrophy and mesial temporal sclerosis.[19–21] Longitudinal studies, conducted in a population where about 10% of the adult population have calcified NCC and no new cases are expected, would be of great value to determine whether a causal relationship between calcified NCC and hippocampal atrophy really exists, to

characterize this association with the occurrence of epilepsy, and to determine whether neuroimaging features of hippocampal atrophy in patients with NCC resemble those of hippocampal atrophy from other etiologies.

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