NOTES AND RECOMMENDATIONS FOR THE ESTABLISHMENT OF CONTROL PROGRAMS FOR *Taeniasis/cysticercosis* IN PERU

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ABSTRACT

Neurocysticercosis is the infection of the nervous system by the larvae (cysticerci) of the pork tapeworm *Taenia solium*. Neurocysticercosis is the major cause of acquired epilepsy worldwide and as such, it represents a global health problem. On the other hand, *T. solium* taeniasis/cysticercosis is one of very few infectious diseases considered to be potentially eradicable. Recently, a large-scale elimination program in Tumbes, Peru, demonstrated the feasibility of interrupting *T. solium* transmission. On the basis of these advances, the authors propose an initial series of actions to provide the foundations for regional and national programs for the control of taeniasis/cysticercosis, from simple and feasible interventions at the local level.

Keywords: Cysticercosis; Neurocysticercosis; Taeniasis; Taenia solium; Epidemiology; Communicable disease control (source: MeSH NLM).

APUNTES Y RECOMENDACIONES PARA EL ESTABLECIMIENTO DE PROGRAMAS DE CONTROL DE LA TENIASIS / CISTICERCOSIS POR *Taenia solium* EN EL PERÚ

RESUMEN

La neurocisticercosis es la infección del sistema nervioso por la larva (cisticerco) de la tenia del cerdo (*Taenia solium*). La neurocisticercosis es la mayor causa de epilepsia adquirida a nivel mundial y por ende un problema de salud pública global. De otro lado, la teniasis/cisticercosis por *T. solium* es una de las pocas infecciones consideradas potencialmente erradicables. Recientemente, un programa de eliminación de transmisión a gran escala en Tumbes, Perú, demostró la factibilidad de interrumpir la transmisión. Sobre la base de estos avances, se proponen una serie de lineamientos iniciales para poner las bases de programas de control regionales y nacionales de la teniasis/cisticercosis, partiendo de intervenciones simples y factibles a nivel local.

Palabras clave: Cisticercosis; Neurocisticercosis; Teniasis, Taenia solium; Epidemiología; Control de enfermedades transmisibles; Perú (fuente: DeCS BIREME).

INTRODUCTION

Neurocysticercosis (NCC), an infection of the human nervous system caused by the *Taenia solium* larvae (cysticerci), is an important cause of epilepsy in Peru and in most developing countries [(1)]. It also occurs frequently in developed countries due to migration from endemic regions and is considered a global public health concern [(2)]. Taeniasis/cysticercosis (T/C) by *T. solium* is one of the few infections considered to be potentially eradicable [(3)], which highlights the importance of searching for efficacious and plausible control interventions.

Design and application of control measures for this disease require knowledge of parasite transmission dynamics and of contributing factors. To better understand the epidemiology

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of taeniasis and cysticercosis by *T. solium*, it is essential to separate two markedly different scenarios: one occurring in endemic regions [4] where transmission is rampant and many people and swine are exposed to this parasite; and what is occurring in non-endemic regions, where the occurrence of cases is less frequent and is related to immigration or tourism [5].

T. solium is endemic across much of Peru (including the Northern coast, all the Andean region and the Upper jungle) [6]. In these areas, *T. solium* exposure is so frequent that in many rural communities, over half of the swine population present antibodies to the parasite. However, viable cysts in the carcass are only detected in some of them (5% to 10% of the total) [4]. Another group of animals is likely to have infections with very few cysts, undetectable at necropsy (most of the pigs with viable infections have less than five cysts in the whole carcass) [7]. The remaining group of seropositive animals may have had infections that resolved spontaneously.

The situation among human populations in endemic areas is similar, with the presence of many seropositive individuals (5-20%) and a significant proportion of infected individuals. The few epidemiological studies involving computerized axial tomography have shown that 10-20% of the human population develops NCC [8-10]. Most of these individuals have residual brain calcifications and apparently do not present with neurological symptoms. At the population level, the proportion of individuals with epilepsy is small (under 2%) and NCC represents 30 to 40% of these cases [11]. However, when that small fraction of individuals with symptomatic NCC is applied to the population denominator, it results in a substantial number of cases that seek medical care in hospitals and specialized centers. When you look at the clinical information available at these types of centers, the proportion of individuals with brain infections with viable cysts or degenerating cysts increases markedly [12-14].

On the other hand, in non-endemic regions, where free-roaming swine breeding is absent, NCC cases occur among migrant and less commonly among individuals with a history of travel to endemic areas [5]. In this scenario, there is practically no active transmission. Autochthonous cases are rare and are also related to a *Taenia* carrier, who is commonly an immigrant from an endemic region [15].

CONTROL OF *Taeniasis/Cysticercosis*

There is a long list of transmission and control studies conducted in isolated communities. In the Salama Study in Honduras, a broad health promotion and prevention intervention, emphasizing taeniasis/cysticercosis among other conditions, took place in a population of about 7,000 people [16]. This intervention resulted in a gradual decrease of transmission and epilepsy. In Peru, over the last 12 years, the Cysticercosis Working Group of Peru conducted a transmission elimination program in a population of 80,000 people in rural Tumbes. This program demonstrated that interrupting transmission was feasible and that the effect lasted one year or more [17].

Demonstrating that elimination is possible, in light of the results of the above-mentioned program, represents a milestone toward control, elimination, and eradication of *Taenia solium*. The design of future programs may benefit from important information such as the safety of large-scale niclosamide administration, case identification by means of copro-antigens, mass administration of oxfendazole and TSOL18 vaccine in the swine population, and achieving participation goals. On the other hand, the intervention scheme used was complex and involved several rounds of massive treatment to human and swine population, in addition to a vaccine for swine.

Clearly, the following actions are also required: appropriate coordination with local authorities, identification of population subgroups that may be reluctant to participate and remain as residual infection foci, as well as the design of post-intervention surveillance systems. Our perception of the future agenda is to simplify the program, provide robust and cheap tools, and adjust the intervention approach to different scenarios through pilot studies. It is very important not to jump into unplanned control interventions without appropriate effect measurement, as the result may otherwise be counter-productive. The failure of a control program leads to discouragement among the population and institutions in charge of decision-making.

Based on a concept of organization by regions, we would like to submit for consideration some guidelines that we hope will be useful. A summary is presented in Table 1 with a detailed description in the following pages.

BASELINE MEASURES

This first section presents a basic approach for the registration and management of transmission foci as well as for individual cases of taeniasis and cysticerosis. These systems should be implemented independently regardless of whether an organized program of control/elimination is in place. Depending on the type of action, a local installation needs to be identified, within the Ministries of Health or Agriculture (or a responsible committee), to take charge of the action and its registry. Reports must be centralized at regional and national level at the corresponding agencies and levels.

Confirmation of the presence of T/C / Identification of swine cysticercosis foci. The most important piece of information, not only for a control or elimination program for taeniasis/cysticercosis, but also for the primary management of transmission foci and infection cases, is to define if there

Table 1. Proposed objectives by region for the control of taeniasis/cysticercosis

Regional Objectives	Approach
Determine the presence of taeniasis/cysticercosis in the region, or in certain provinces in the region	Actions to confirm the presence of taeniasis/cysticercosis. Case definition of swine cysticercosis
Familiarize health personnel with the diagnosis and clinical manifestations of taeniasis	Case definitions for suspected and confirmed cases of taeniasis
Familiarize health personnel with level I management, referral and follow-up of taeniasis cases	Management of taeniasis by levels, referral criteria and counter-referral criteria, follow-up
Familiarize health personnel with the diagnosis and clinical manifestations of neurocysticercosis	Case definitions for suspected and confirmed cases of human neurocysticercosis
Familiarize health personnel with level I management, referral and follow up of neurocysticercosis cases	Management of neurocysticercosis by levels, referral criteria and counter-referral criteria, follow-up
Propose initial measures for infection control	Actions for the control of taeniasis/cysticercosis
Develop a budget plan based on results	Specification and definition of indicators of meeting the goals

is local transmission of T/C in each province or by districts in order to define endemic and non-endemic areas. This would allow for the definition of areas where time and effort need to be invested in implementing diagnosis and case management systems, while at the same time, defining areas that require active control/elimination programs. Exact determination of prevalence levels does not have any practical use and, in general, does not change the need for control activities [16,18].

Epidemiological evidence suggests that T/C establishes a usual level of endemicity, within a reasonable range of variation, to maintain its transmission [4,19]. In this sense, if the objective of the program is elimination, as it is in our opinion, the degree of endemicity (the exact prevalence level) is of little practical use, since what is being proposed is the elimination of transmission, expanding into geographic areas that are transmission-free. These areas must be defined at places farthest from migration and gradually expand to nearby areas in an concentric manner, independently of its endemicity degree [17].

On the other hand, it may be tempting to estimate the population prevalence of taeniasis, swine cysticercosis, or neurocysticercosis, in order to focalize control actions. This position assumes two concepts: a) that control measures to be proposed are not practical enough or low-cost enough to become implemented in all endemic sites (otherwise it would unnecessarily discriminate low endemicity districts, which still have T/C), and b) control measures do not target elimination (if you are targeting elimination, conducting the activities in non-neighboring areas makes little practical sense and it would encourage failure due to re-introduction from neighboring endemic areas. [17].

Even if one is favoring control over elimination, the relative value of baseline prevalence estimates is very limited.In this sense, we propose that initial actions to confirm the presence of T/C be focused on finding pigs with cysticercosis. In contrast to taeniasis, swine cysticercosis is very well known by the population, who calls it "triquina." Although finding a person with *Taenia solium* taeniasis confirms a transmission focus, cysticercosis in the swine population is an indicator present at higher prevalence levels, more dynamic because of rapid population renewal [18,20]. A system based on swine cysticercosis would be more sensitive to changes.

Districts with evidence of active T/C transmission must be identified and a regional and national map of endemic areas must be prepared. In this regard, we propose a definition of active transmission referring to the presence of swine cysticercosis cases in the year before. Swine cysticercosis can be initially defined based on verbal reports, using a previously-defined text to be used when questioning local health agents. In a second stage, cysts could be collected by district or by village for microscopic confirmation. A reporting system for swine cysticercosis must take into consideration health regulations that call for confiscation and incineration of infected carcasses, which, to be practical, annuls the possibility of case reporting on behalf of the farmers for fear of losing their meat. Below is a list of our proposed inclusive definitions:

SUSPECTED CASE OF PORCINE CYSTICERCOSIS

a. A pig in which nodules on the base of the tongue have been detected by palpation or by visual inspection.
b. A pig in which cysts suspicious for cysticercosis (small and whitish) have been detected after slaughter

CONFIRMED CASE OF PORCINE CYSTICERCOSIS

Diagnostic confirmation using microscopic examination of a cyst preserved in alcohol or formaldehyde.

In order to make this record feasible, the first thing to establish is an epidemiological information record (case report) based on the network of local health clinics and/or health promotors. The population must be informed that meat contaminated with cysticercosis should not be eaten, or else, that it should be fried in bite-size pieces. In a following stage, the population may be educated to bring small pieces of tissue with suspected cysts to the health clinic or to the agency responsible for veterinary care. Considering the normal reluctance of the population to report ill animals because of the risk of having their animals confiscated or facing punitive measures, an incentive program may be needed for the initial reports. If this were the case, one of the requirements for incentives must include confirmation of the place of origin of the infected pig.

Actions subsequent to the report of a swine cysticercosis case must be defined. The existing evidence, in addition to common sense, suggests clustering of swine cysticercosis around a human case with taeniasis [21-23]. Upon a report of a pig with cysticercosis, a basic intervention scheme would involve oxfendazole administration [24-26] to all the pigs in the house and a screening for taef in all the individuals who dwell in the house and possibly, the neighboring houses. This must include informing the population that animals treated with oxfendazole should not be killed for at least two weeks after treatment. During this two-week period anti-parasitic drug residues may persist in the meat [27]. Alternatively, treatment with niclosamide could also be administered to the individuals who dwell in the house. In this case, collecting a fecal sample immediately after treatment to identify infected individuals and to confirm that they have been cured, would be highly recommended. Application of biosafety measures in the treatment of individuals suspected of being *T. solium* carriers should be emphasized.

Definition of suspected case and confirmed case of taeniasis. *T. solium* taeniasis is rarely observed by patients, in contrast to *T. saginata* infections [28]. It is highly probable that a self-reporting system result in the detection of mostly *T. saginata* cases. The authors hereby propose the addition of suspected case and confirmed case definitions. This may originally be presumed, just like in the above-mentioned item, based on verbal reports, using pre-defined texts to be used in questions to local health personnel. It should match endemicity areas to swine cysticercosis. A second stage may ask for collection of fecal samples and/or parasite material for microscopic confirmation at a second level center. Since sensitivity of microscopic testing of feces for the diagnosis of *T. solium* taeniasis is rather poor, a negative result does not exclude parasitosis. Ideally, immunological diagnosis through coproantigen test should be available [29,30], at least at the head of each health network. Results from the coproantigen test must be interpreted in relation to the test cut-off point, with the understanding that weak positives often do not correlate with active taeniasis infection.

SUSPECTED CASE OF TAENIASIS

a. Individual reporting having excreted parasites or flat, whitish or yellowish parasite pieces.
b. Dwellers of a house where a pig was identified with live cysts upon slaughter.

CONFIRMED CASE OF TAENIASIS

Positive fecal test by microscopy and coproantigen detection.

According to the above description, actions suggested include collection of fecal samples from suspected cases, pre-processing (fixing in formalin phosphate buffered saline [PBS]) and shipping to a local confirmation center for microscopy and coproantigen test. If positive, adequate treatment must be coordinated as detailed below.

Management of taeniasis by level, criteria for referral and counter-referral, follow up. Treatment of taeniasis is extremely important for the prevention of swine cases and to help control the disease. Biosafety measures for health personnel, for the patient and the environment must be taken into consideration given the fact that manipulation of feces infected with *T. solium* may result in cysticercosis or neurocysticercosis. This process must be conducted under medical supervision to prevent or manage adverse effects of the purge or medication, and to avoid contamination by contact with infective eggs in feces [31].

The drug of choice is niclosamide. The use of praziquantel in the treatment of taeniasis may generate epileptic seizures in individuals who have asymptomatic NCC, so its use is not recommended unless NCC has been ruled out by neuroimages (computerized axial tomography or magnetic resonance) and serology [1].

The patient must adhere to a strictly soft diet for at least 2 days. In the morning of treatment day, a light purge will be administered. Once liquid feces are obtained, the appropriate dose of niclosamide must be given (2 gr orally for adults, 1 gr for children older than 6). Two hours after niclosamide intake, a second purge is administered [30,31]. The whole process must involve abundant oral hydration to avoid dehydration or electrolyte disorders, and to facilitate purge and elimination of the worm. After taeniasis diagnosis, all fecal samples must be collected in disposable containers and eliminated following biosafety guidelines, which implies defining and establishing a proper elimination system. It is recommended to refer patients to a level 2 health clinic or higher for treatment and observation for a few hours after purge.

Whenever possible, a new fecal sample must be collected 15 days after treatment and sent for coproantigen detection at a reference laboratory in order to confirm patient cure [17,30]. Confirmation of cure is very important, because in cases of

undetected therapeutic failure, all efforts undertaken would be entirely useless.

Clinical evaluation must be performed. Patients with taeniasis and a history of epileptic seizures and other neurologic symptoms must be referred to a level 3 clinic or higher, to be evaluated for neurocysticercosis.

Definition of suspected and confirmed cases of human neurocysticercosis. There are no operational definitions for cysticercosis cases at endemic population level. The following definition proposals represent the most frequent presentations associated with neurocysticercosis.

SUSPECTED CASE OF NEUROCYSTICERCOSIS

a. Individual with a history of episodes compatible with epileptic crises: loss of consciousness, involuntary movements of hands, arms or legs, light vision, etc., particularly if these episodes start after 15 years of age.
b. Individual with symptoms compatible with increased intracranial pressure: severe headache, dizziness, vomiting.
c. Individual with neurological symptoms and palpable subcutaneous nodules.

CONFIRMED CASE OF NEUROCYSTICERCOSIS

Individual with neurological symptoms and brain imaging (computerized axial tomography or magnetic resonance) showing lesions compatible with NCC, or showing neurological symptoms and a compatible Western blot positive result to cysticercosis antibodies [32].

Management of NCC by levels, referral and counter-referral criteria, follow up. In cases of suspected cases of NCC (epilepsy or intracranial hypertension in endemic areas), the health personal must follow the clinical practice guidelines for management of cysticercosis, published by the Instituto Nacional de Ciencias Neurologicas [33], both for the management of the condition by levels, and for referral, counter-referral and follow-up.

ACTIONS FOR CONTROL AND ELIMINATION OF TAENIASIS/ CYSTICERCOSIS

Initially, community control of T/C must be focused on detection and treatment of taeniasis cases, treatment with oxfendazole for suspected pigs and decreased risk behavior, such as not eating meat with cysticercosis, encouraging hand washing behavior and use of latrines.

In spite of the fact that the feasibility of *T. solium* elimination has already been demonstrated [17, 30], there is still a long way to go. Areas for improvement include simplifying the program used in Tumbes, defining monitoring and post-intervention surveillance systems, adapting interventions and monitoring to different local realities, etc. There are ongoing evaluation programs for the control interventions used in Tumbes, particularly to simplify the approach and make tools available in endemic areas. These programs include mass treatment of the human population with niclosamide, mass treatment of the swine population with oxfendazole, and vaccination of the swine population. To date, there is not a defined strategy selected or tested for application at a large scale. In this context, and until an optimal program is defined, the above-mentioned control actions provide a first line of action until a regional or national program becomes available.

DEFINITION OF ACHIEVEMENT INDICATORS FOR LEVELS I AND II

It is essential to define appropriate indicators within the operational system of government organizations in order to operationalize actions against taeniasis/cysticercosis. Table 2 shows suggestions for each one of the items described in this manuscript.

The final aim of biomedical research is to improve health and living conditions throughout society. In pursuit of this aim, the role of research groups, such as ours, is to provide evidence and tools so that results of our research become health policies in appropriate instances. At the national level, the Ministry of Health and Ministry of Agriculture are responsible for actions toward control of taeniasis/cysticercosis, in collaboration with regional health directorates and academia. In order to meet the proposed goals, we need an organization at local, regional and national level that encompasses human and veterinary health, as well as education at the social level. This organization must be adequately funded, so that it may meet its operational requirements.

Establishing the above-described organization requires the corresponding decision making at central or at regional level. Neurocysticercosis is a major contributor to neurological diseases in Peru. We hope that the above concepts will serve as a tool for the implementation of activities, with baseline actions at the beginning, but eventually leading to regional or national control programs.

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Table 2. Actions, objectives and indicators of proposed achievements for levels I and II

Item	Action	Objectives	Achievements
1	Establishment of a registry system for swine cysticercosis reports	-Suspected case of swine cysticercosis -Confirmed case of swine cysticercosis	-Case registry -Report of microscopy results
	Treatment of swine cysticercosis	-Swine in at-risk households treated with oxfendazole	-Case registry
	Educational actions (presentations, educational videos; campaigns at schools; community participatory workshops)	-Educational activities at school -Educational activities at the community	-Report of activity (house visits and treatment) -Report of activity
2	Diagnosis of taeniasis (positive to microscopy or coproantigen)	-Taeniasis cases detected	-Report of surveillance (patient reporting expulsion of proglottids, or patient with fecal test positive to *Taenia* spp. eggs, or positive to coproantigen)
3	Treatment of taeniasis	-Cases of treated taeniasis -Cases of taeniasis with confirmed cure (negative coproantigen 15 days after treatment or later)	-Report of treatment -Laboratory result
4	Diagnosis of neurocysticercosis	-Suspected case of neurocysticercosis detected	-Report of surveillance (individual with episodes compatible with epileptic crises, symptoms compatible with intracranial pressure, or neurologic symptoms, and subcutaneous nodules)
		-Confirmed case of neurocysticercosis	-Report of surveillance (patient with neurological symptoms and diagnosis supported by a positive Western blot, computed tomography or magnetic resonance for cysticercosis)
5	Management of neurocysticercosis cases	-Case of NCC* epilepsy undergoing proper anti-epileptic treatment	-Surveillance report (patient on adequate doses of first line anti-epileptic drug: phenytoin, carbamazepine, valproic acid or phenobarbital)
		-Case of hydrocephalus or intracranial hypertension, treated with symptomatic drugs and stabilized for referral	-Case of stabilized hydrocephalus or intracranial hypertension. Stable vital signs, resolved or mild headache, no vomiting.
	Referral of neurocysticercosis to a higher level	-Case of NCC* epilepsy with viable parasites referred for anti-parasitic treatment at level 3 or higher	-Surveillance report (patient with epileptic crises and a positive antigen test or tomography or magnetic resonance showing viable cysts with or without inflammation)
		-Case of hydrocephalus or intracranial hypertension referred to level 3 for medical or surgical management	-Report of the referral system
6	Control of taeniasis/ cysticercosis	-Detection of taeniasis cases: screening at community level	-Report of activity
		-Treatment of taeniasis: mass chemotherapy with niclosamide	-Report of activity
		-Treatment of swine cysticercosis: mass chemotherapy with oxfendazole	-Report of activity

*Neurocysticercosis

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