The control of human (neuro)cysticercosis: which way forward?

Dirk Engels a,*, Carlo Urbani b, Albino Belotto c, François Meslin a, Lorenzo Savioli a

a Department of Communicable Diseases Control, Prevention and Eradication, World Health Organization, Geneva, Switzerland
b Vector borne and other Parasitic Diseases, World Health Organization, Regional Office for the Western Pacific, Hanoi, Viet Nam
c Veterinary Public Health, World Health Organization, Regional Office for the Americas, Washington, DC, USA

Abstract

Taenia solium cysticercosis, and its public health and economic consequences, appears to be a growing problem in poor areas of Africa, Asia and Latin America where people eat pork and traditional pig husbandry is practiced (and expanding). Its burden is counted in terms of human disease (mainly neurocysticercosis related epilepsy) and economic losses, in a context of both commercial and traditional subsistence pig farming. Although substantial fragmentary information seems to be available from local settings, national and global burdens due to T. solium cysticercosis are still to be comprehensively assessed. With regard to control, several strategies have been checked out at a small or medium scale and have proven to be successful. Yet, no intervention programmes have been implemented so far at the national level with proven success. Although T. solium cysticercosis is considered to be a potentially eradicable disease, there is no evidence yet that it is feasible and recommendable to envisage this within a reasonable time frame. However, it appears realistic to aim for the rapid definition of a simple package of interventions, which can routinely be carried out by existing services and structures, and will give an optimal, long-term return in terms of burden relief. Also, a number of international initiatives and opportunities currently exist in which a more pro-active attitude towards the control of T. solium cysticercosis can be integrated and promoted. Commitment of both national and local authorities to control the disease needs to be convincingly solicited and, as for most zoonotic diseases, an interdisciplinary approach is essential.

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1. Introduction

Neurocysticercosis (NCC), an infection of the human brain by the larvae of the pork tapeworm Taenia solium, is considered to be the most important parasitic infection of the central nervous system. It occurs in large parts of Africa, Asia and Latin America where people eat pork and traditional pig husbandry is practiced. T. solium cysticercosis is a zoonotic parasitic disease, with domestic pigs as intermediate host of T. solium, and source of human taeniasis following consump-
tion of meat infected with cysticerci. However, human beings can also become intermediate hosts by directly ingesting *T. solium* eggs. These eggs then develop into cysticerci that migrate mostly into muscle or brain tissue. NCC is therefore a human-to-human infection acquired by the ingestion of *T. solium* eggs shed in the faeces of human carriers of the parasite. It therefore primarily occurs in poor areas with deficient sanitation. However, *T. solium* carriers are extremely potent sources of contagion, and human (neuro)cysticercosis can also occur in small outbreaks around immigrant carriers in Western countries (Roman et al., 2000). Cysticercosis is related to a few of the most burning problems in the world today: poverty in the marginal rural regions with subsistence animal husbandry, and migration from rural to urban areas or from developing to developed countries.

### 2. The burden due to *T. solium* cysticercosis

There are two major aspects in the burden due to *T. solium* cysticercosis. First of all, because of its localisation in the central nervous system, it is estimated to cause an important disease burden, particularly in terms of late-onset epilepsy. As the parasite also requires pigs as intermediate hosts to complete its life cycle, its consequences can also have a potentially large impact in terms of food safety and economical consequences.

The clinical relevance of *T. solium* cysticercosis in humans is related mainly to its central nervous system complications, particularly epilepsy. Although the majority of epilepsy cases belong to the idiopathic/cryptogenic type, a substantial portion of symptomatic epilepsy can be attributed to NCC in endemic areas. NCC is known to be a common cause of late-onset seizures in regions where *T. solium* is endemic, accounting for 30–50% of all cases. In Ecuador, approximately 10% of all epilepsy cases, and 25% of those attributable to a particular identifiable event, were due to NCC (Carpio and Hauser, 2002). This latter proportion can be as high as 50% in certain areas (Campbell and Farrell, 1987; Nsengiyumva G., personal communication). If NCC cases are subject to clustering, as has been demonstrated in Western countries (Schantz et al., 1992), the epilepsy related to it can result in a particular high socio-economic burden for affected families in the invariably poor—endemic areas.

Economic losses due to cysticercosis are mainly to be measured in terms of losses to the farmers or families resulting from loss of or depreciation in infected pig meat, and in terms of the impact of cysticercosis on pig productivity. In China, cysticercosis was among the target diseases of a national survey implemented in the late 1980s. The estimated number of cysticercosis patients was around 3 million (Zhou, personal communication). The discarded pork totals 0.2 billion kg in the whole country, causing a loss of one billion Chinese Yuan (US $121 million) per year (Ito et al., in press). In Burkina Faso, half of all carcasses discarded at the abattoir are condemned because of zoonotic diseases (Coulibaly and Yameogo, 2000).

However, two distinct situations have to be considered here: commercial pig farming—even at a small scale—and ‘subsistence’ pig farming in which a free-roaming pig does not cost anything to grow, has a well-defined role in keeping the family premises clean, and constitutes a sort of ‘savings account’ when sold on particular occasions. Especially in this latter situation, *T. solium* cysticercosis also constitutes a serious food safety hazard.

The currently published knowledge about the burden due to *T. solium* cysticercosis is fragmentary and substantially varies in nature. As for many other parasitic diseases, most available information relates to infection rates. Figures on morbidity or socio-economic consequences are more scarce. Geographically, it is generally considered that Latin America and the Far East are the most affected regions, but there is increasing evidence that also on the Indian subcontinent and in Eastern and Southern Africa, *T. solium* cysticercosis is a parasitic disease of public health concern. Especially in the latter area, increasing poverty and lack of grazing land for cattle, seems to contribute to the increasing popularity of subsistence pig farming. A global estimate of the burden due to *T. solium* cysticercosis is still lacking.
3. Control strategies and questions to be answered

There is substantial knowledge and expertise with case management of NCC cases in well equipped medical centres. The diagnosis of cysticercosis of the central nervous system involves the interpretation of non-specific clinical manifestations, often with characteristic findings on computed tomography or magnetic resonance imaging of the brain, and the use of specific serological tests. Its treatment can be associated with serious side-effects and usually requires hospitalisation.

Affected people in resource-poor areas therefore generally have limited access to adequate case management. There is also no consensus whether all cases of NCC do indeed benefit from cestocidal treatment and its associated sophisticated diagnostic assessment, or whether simple symptomatic treatment with anti-epileptic drugs alone can provide them the desired sustained comfort and quality of life. A recent Cochrane overview of drugs for treating NCC concluded that there is insufficient evidence to assess whether cestocidal therapy in NCC is associated with long-term beneficial effects (Salinas and Prasad, 2000). More evidence and consensus building is therefore needed in this area, in order to provide adequate care for those suffering from the disease at all health care levels. This is likely to generate the largest immediate relief in burden and social stigmatization, particularly for affected poor people.

With regard to the prevention of new cases of NCC in an affected community, there is small and medium scale evidence that a comprehensive control strategy—combining the treatment of T. solium carriers with improvements in hygiene, sanitation, pig husbandry and veterinary sanitary measures—is effective, to the extent that it is considered to be a potentially eradicable disease (Schantz et al., 1993; WHO, 1998). It has further been demonstrated that elimination of the (human) reservoir of T. solium infection is a key factor in control and/or eradication efforts (WHO, 1993).

From an operational standpoint, a few pragmatic research questions need to be further investigated before large scale action can be planned and promoted. Is there a role for active identification and treatment of T. solium carriers, when a treatment with praziquantel (at 5–10 mg/kg body weight) costs in the order of 0.05–0.10 US$ per person? Is mass treatment not more cost-effective? Is mass treatment of T. solium carriers with a 5–10 mg/kg dose of praziquantel effective and safe? How can it be implemented in areas where concurrent schistosomiasis needs to be treated with a dose of 40 mg/kg?

In addition to this, more information is needed on the impact of large scale praziquantel administration on taeniasis/cysticercosis epidemiology and neurological clinical manifestations. In an intervention study with mass treatment against taeniasis in a rural community in Mexico, a reduction of 56% in human taeniasis was seen 42 months after intervention, and late-onset general seizures were reported to have decreased by 70%. Anti-cysticeri antibodies in the human population were also reduced by 75% (Sarti et al., 2000). However there is no consensus that this strategy alone is able to control the source of (human) tapeworm infections, i.e. cysticercosis in pigs (Lightowlers, 1999). There is therefore an urgent need to replicate these interventions to confirm the impact on reduction of cysticercosis in highly endemic areas.

Apart from the treatment of T. solium carriers, is systematic treatment of pigs necessary or useful to interrupt transmission? Or is mass treatment of humans indeed sufficient to obtain this? What is the impact, and its duration, of human mass treatment on infection rates in piglets? How does this compare with the average life span of a piglet? As improved pig husbandry invariably implies more constraints and costs, what are the chances of acceptance of it by rural "subsistence" pig holders? Alternatively, is there a role for individual treatment of pigs—in view of their slaughter or sale—to improve household economics and/or ensure food safety? How easy is treatment of pigs and how accessible are the drugs?

It may also be that veterinary sanitary measures are the key factor in the control of taeniasis/cysticercosis. Cysticercosis virtually disappeared from Europe when the role of porcine cysticercosis became understood and meat inspection was
strictly applied as the single most effective method to prevent and control it. Effective, practical vaccines have been developed against cysticercosis in sheep and cattle and a recent trial has proved recombinant antigens to be effective against *T. solium* cysticercosis in pigs. A strategy for eradication of *T. solium* has been proposed, based on a combined approach of chemotherapy of human tapeworm carriers and vaccination of all pigs at risk of infection (Lightowlers, 1999). However, the cost of such a strategy could jeopardize its feasibility, particularly in poor areas where ‘subsistence’ pig farming is practiced.

Is there a specific role for the provision of clean water and sanitation in the control of cysticercosis, without tumbling into the pitfalls of geographically limited, not widely replicable pilot initiatives? Or should we rather aim for a general background improvement of living conditions that will eventually wipe out several poverty-related communicable diseases? And in the meantime simply make sure that we take away most of the burden that those diseases cause to people? Health education in itself did not seem to be effective in reducing transmission of the infection, as reported in Tasmania and New Zealand. In Mexico, sustained educational interventions, supported by actively enforced legislation, has proved to have an impact on transmission from humans to pigs (Sarti et al., 1997).

There is so far no evidence that it is feasible and recommendable to envisage eradication of *T. solium* cysticercosis within a reasonable time frame. Alternatively, it is important to define a simple package of interventions, which can be routinely carried out by existing services and structures, and will give an optimal, long-term return in terms of preserving people from an excessive burden.

4. Surveillance and reporting

In an attempt to step up the control of *T. solium* cysticercosis, it has recently been proposed to declare NCC an international reportable disease (Roman et al., 2000). However, taeniasis and cysticercosis do not lead to sudden large-scale international outbreaks of disease and therefore would not seem to constitute an appropriate subject for international notification. Nevertheless, national surveillance and reporting—as part of a routine system—is important.

From a human public health standpoint, surveillance of *T. solium* cysticercosis does logically take its origin in case records of its main clinical consequences, through a syndromic approach towards epilepsy and other common central nervous system consequences, or sub-cutaneous nodules where this manifestation is predominant. If carried out adequately, this type of surveillance will naturally lead to a more accurate understanding of the extent of the problem, to the identification of transmission foci, and a more active approach of public health decision makers towards prevention and control of the disease. However, a consensus has yet to be reached on standardized criteria that can adequately be used in resource-poor areas and be built in guidelines for early differential diagnosis of epilepsy in peripheral health care structures, and to deliver optimal treatment (specific and/or symptomatic) to people at that level, or refer them to a higher level of the health care system (Scott et al., 2001).

5. Opportunities to step up the control of *T. solium* cysticercosis

There are some international initiatives and opportunities in which a more pro-active attitude towards *T. solium* cysticercosis can be integrated and promoted. The Global Campaign against Epilepsy ‘Out of the Shadows’ is an international initiative aimed at alleviating the medical, social and economic burden due to epilepsy, and reducing its treatment gap (De Boer, 2002). The partnership for parasite control (PPC) was originally created to forge a reduction in the burden due to schistosomiasis and soil-transmitted helminth infections by the implementation of simple but lasting measures that field actors can easily build into their routine operations (Savioli et al., 2002). This type of strategy can be extended to other parasitic diseases for which the control objectives are similar. There is increasing international con-
cern about food safety (WHO, 2002) and combat-
ing poverty and a group of neglected diseases and ill conditions related to it (WHO, 2001).

Both the World Health Organization (WHO) and the Food and Agriculture Organization (FAO) are committed to collaborating with national governments in developing national or regional control programmes. During the last two decades, WHO has given increasing attention to the problem of taeniasis/cysticercosis complex. Research requirements were first defined in 1981 (FAO/UNEP/WHO, 1981). Guidelines for the surveillance, prevention and control of parasitic zoonoses were issued in 1983 (WHO, 1983). In 1995, an Informal Consultation on Taeniosis/Cysticercosis Complex was held in Brazil (PAHO/WHO, 1997). In 2002, the problem of NCC was brought to the attention of the 55th World Health Assembly, and the issue is expected to be debated in the near future.

WHO’s mandate is to assist Member States in the effort of defining the disease burden, and establishing simple evidence-based control measures, of which the cost-effectiveness and sustainability have clearly been evaluated. WHO is also in a position to contribute to networking, facilitate the exchange of experiences and information, co-ordinate initiatives and solicit interest of the donors community. The Agency can also pilot WHO scientific work in view of the development of a strategic approach, and attract—together with other international organizations such as FAO or OIE (Office International des Epizooties)—the attention of Ministries of Health and Agriculture on this emerging public health issue.

In the more technical field, Expert Committees and Informal Consultations can contribute to synthesizing all the available information, obtain a consensus on strategic approaches and issue recommendations. WHO’s network of collaborative centres constitutes a valuable source of expertise and information to this purpose.

6. Possible short term action to be taken

Prior to any planning of action, the public health and/or economic relevance of cysticercosis must be defined. Simple assessment tools have to be further developed in order to identify suspected areas—e.g. with simple questionnaire surveys. This type of ‘rapid epidemiological assessment’ could then be complemented by well-targeted serological investigations. Collection of data from hospital records and slaughterhouses (or traditional places of slaughtering) are also essential. The risk of disease should be mapped, and interventions prioritized.

At the present stage, no intervention programmes have been implemented at the national level with proven success. However, several strategies for control have been checked out at a smaller scale and have proven to be successful.

In terms of strategic approach, there are two options. On one hand there is the comprehensive approach, in which control is based on long-term interventions, involving appropriate legislation, health education, modernization of swine husbandry practices, more efficient and all-inclusive coverage of meat inspection, adequate sanitary facilities and measures to detect and treat human carriers. On the other hand there is the ‘focused’ approach, which aims to select those interventions that provide the most cost-effective return, and target them to areas most in need. This approach appears to favour mainly health education and systematic treatment, of humans and/or pigs.

Although the first approach has undoubtedly the best long-term perspectives, it is inherent to socio-economic development, development of adequate levels of infrastructure and general improvement of life. Focused interventions have a more limited impact, but are probably more immediately sustainable and can provide good short-term results in term of burden relief.

In conclusion, the problem appears to be considerable. A first step to short term action would be to document the public health and/or economic relevance of cysticercosis, and to convincingly bring it to the attention of decision makers. A series of simple cost-effective intervention tools appear to be available and capable of relieving most of the medical and economic burden caused by the disease. As for most zoonotic diseases, an interdisciplinary approach is needed, involving medical and veterinary workers, as well as munici-
palities and farmers’ organizations. Commitment of both national and local authorities to control the disease is essential, but may naturally happen if the burden is evident and the proposed solutions reasonable in the local public health and socio-economic context.

References


