Chapter from the book *Novel Aspects on Cysticercosis and Neurocysticercosis*  
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1. Introduction

Neurocysticercosis (NCC) is still an endemic disease in most of the countries of Asia, Africa and Latin America, despite the important progress made in the development of effective tools for its prevention, diagnosis and treatment. Although the infection disappeared in many European countries during the nineteenth century, in some Eastern European countries control was not achieved until the beginning of the twentieth century, mainly due to the improvement of their political, social and economic status. Alarming recent reports show the persistence of the endemia in Africa [1-3](Table 1), as well as in the Americas [25](Table 2) and in Asia (Table 3). None of the endemic countries has been able to eradicate *Taenia solium*’s Taeniosis/Cysticercosis (T/C). Similarly, the frequency of human cases of NCC is increasing in some industrialized countries, such as the United States, Canada and Spain, due mostly to migrant workers, although some autochthonous cases have also occurred [92-97].

In this paper, we will try to understand the reasons behind such failures and propose strategies that can improve the control of the T/C.

2. Actual tools for diagnosis and treatment

It is clear that there are efficient tools for diagnosis and treatment, although investigations must surely go on and progress will be made.
| Country                  | Reference | Type of study | Subject included | Diagnosis based on | Seroprevalence Cysticercosis | Prevalence NCC |
|-------------------------|-----------|---------------|------------------|--------------------|-------------------------------|----------------|
| Burkina Faso            | [4]       | Population-based | 763              | Ag-ELISA           | 10,3%; 1.4%; 0%               |                |
|                         | [5]       | Population-based | 734              | Ag-ELISA           | 4.5%                          |                |
| Burundi                 | [6]       | Case-control   | 324 PWE 648 controls | Ab-ELISA           | 59.6 % PWE 31.5% controls    |                |
|                         | [7]       | PWE            | 250              | Ab-ELISA           | 61%                           |                |
| Burundi                 | [8]       | Case-control   | 303 PWE 606 Controls | Ab/Ag-ELISA        | Ab 58,7% ; Ag 38,3 PWE Ab 31, 4% Ag 20 % controls |
| Cameroon                | [9, 10]  | Population-based | 168              | Ab-ELISA           | 1,2%                          |                |
|                         | [11]      | Population-based | 500              | EITB               | 25,8%                         |                |
| Cameroon                | [12]      | Population-based | 137 Butchers 198 Controls | Ag-ELISA           | Butchers 3,6% Controls: 4,5% |
|                         | [13]      | Population-based | 504 PWE          | Ab/Ag ELISA        | 1,2% Ag 44,6% Ab             |                |
|                         | [14]      | Population-based | 4993             | Ag-ELISA CT scan   | 0,4% 1,0 % 3,0%              | 59,1% of sero+ |
|                         | [15]      | Population-based | 93 PWE 81Controls | Ab-ELISA           | 18,3% PWE 14,8% Controls     |                |
| Democratic Republic of Congo | [16] | Population-based | 943              | Ag-ELISA           | 21,6%                         |                |
| Madagascar              | [17]      | Population-based | 4375             | Ab-ELISA EITB      | 7-21%                         |                |
| Mozambique              | [18]      | US Peace Corps  | 73               | EITB               | 8,2%                          |                |
| Senegal                 | [19]      | Urban children  | 269              | Abs                | 20,8%                         |                |
| South Africa            | [21]      | PWE (Hospital)  | 92               | CT scan            | 37%                           |                |
| Tanzania                | [22, 23] | Hospital-based | 212 PWE          | CT scan            | 16.5%                         |                |
| Zambia                  | [24]      | Population-based | 708              | Ag-ELISA           | 5,8%                          |                |

Table 1. Prevalence (sero prevalence) of human neurocysticercosis in Africa. Only 2002-2012 articles were considered.

Improvement of neuroimaging techniques permits a sensitive and accurate diagnosis of NCC in the great majority of cases, the problem being its limited accessibility to the principal rural population. Immunodiagnosis based on serum antibody detection is an efficient marker of contact with the parasite, permitting the identification of endemic areas in which control and preventive measures must be intensified. Detection of parasite antigens in serum and cerebrospinal fluid permits a confident diagnosis of severe neurocysticercosis forms, allowing opportune and adequate treatment and reducing the morbidity [98]. Regarding NCC treatment, two cestocidal drugs (Praziquantel and
Albendazole) have been used for at least 30 years. Although different studies evaluating their efficacy have shown that these drugs are not efficient in all patients, they also revealed that they eliminate the parasites and diminish the symptomatology significantly more than placebo [99-101]. As a consequence, investigation in this area must continue.

| Country | Reference | Type of study | Subject included | Diagnosis based on | Seroprevalence Cysticercosis (%) | Prevalence NCC |
|---------|-----------|---------------|------------------|--------------------|----------------------------------|----------------|
| Bolivia | [26]      | Population-based | 10124 (124 PWE)  | EITB, CT-scan      | 27.4% PWE                        |                |
|         | [27]      | Blood donors    | 1133             | Ab-ELISA           | 5.6                              |                |
|         | [28]      | Population-based | 694              | EITB               | 1.6                              |                |
|         | [29]      | Hospital-based  | 36379            | CT-scan            | 0.20%                            |                |
|         | [30]      | Population-based | 110 PWE          | EITB, Ag-ELISA     | 8.2 (EITB) 3.6 (ELISA)           |                |
| Brazil  | [31]      | Hospital-based  | 5 105 259        | Admission          | 0.01%                            |                |
|         | [32]      | Population-based | 354              | Ab-ELISA, EITB     | 11.3                             |                |
|         | [33]      | Population-based | 84               | Ab-ELISA           | 5.9                              |                |
|         | [34]      | Population-based | Deaths Sao Paulo state | Death certificate | 0.55/1000,00 0**                  |                |
|         | [35]      | Hospital-based  | 1501             | Autopsies          | 4.80**                           |                |
|         | [36]      | Hospital-based  | 1009             | CT-scan            | 9.02                             |                |
|         | [37]      | Hospital-based  | 6500             | Autopsies          | 0.80                             |                |
| Colombia| [38]      | Hospital based  | Psychiatric patients with neurological signs (98) Primary psychiatric patients (153) Controls (246) | EITB | Group 1: 5.1 Group 2: 2.6 Group 3: 2 |
|         | [39]      | Population-based | 399              | Ab-ELISA           | 52.9                             |                |
|         | [40]      | Patients with neurological symptoms | 1890 sera 989 CSF 52 sera + CSF | Ab-ELISA CT-scan/MRI | 14.9 82.2                       |                |
|         | [41]      | Population-based | 157              | Ab-ELISA           | 28.7                             |                |
|         | [42]      | Pig-breeders    | 46               | EITB               | 8.7                              |                |
|         | [43]      | Population-based | 665              | Ab-ELISA           | 28.4                             |                |
|         | [44]      | PWE             | 111              | Ab-ELISA           | 17.1                             |                |
|         | [45]      | PWE             | 223              | Ab-ELISA           | 35.9                             |                |
|         | [46]      | Population-based | 29360            | Ab-ELISA           | 8.55                             |                |
|         | [47]      | Population-based | 4306             | Ag-ELISA           | 4.99                             |                |
| Ecuador | [48]      | Population-based | 2415 (24 PWE)    | CT scan            | 33% PWE                          |                |
## Table 2. Prevalence (sero prevalence) of human neurocysticercosis in Latin America.

Only 2002-2012 articles were considered.

| Country       | Reference | Type of study | Subject included | Diagnosis based on          | Seroprevalence Cysticercosis (%) | Prevalence NCC |
|---------------|-----------|---------------|------------------|-----------------------------|----------------------------------|----------------|
| Haiti         | [51]      | Medical visits | 216              | EITB                        | 2.8                              |                |
| Honduras      | [52]      | Population-based | 6473 (151 PWE)   | EITB CT scan               | 37 (PWE)                        |                |
|               | [53]      | Population-based | 5609 (33 PWE)    | EITB CT scan               | 13.9 (PWE)                      |                |
| Mexico        | [54]      | Population-based | 154              | CT scan                    | 9.1                              |                |
|               | [55]      | Population-based | 649              | CT scan                    | 9.1                              |                |
|               | [56]      | Psychiatric patients | 105      | Ab-ELISA EITB               | 7.6 (ELISA) 0.9 (EITB)          |                |
|               | [57]      | PWE (late-onset) | 455              | CT scan                    | 21.1                             |                |
| Nicaragua     | [59]      | PWE            | 88               | Ab-ELISA EITB              | 8.0 (ELISA) 14.8 (EITB)          |                |
| Peru          | [60]      | Population-based | 2583             | EITB                        | 13.9                            |                |
|               | [61]      | Population-based | 316              | EITB                        | 21                               |                |
|               | [62]      | Population-based | 903              | EITB (825) CT scan (150)   | 24.2                            | 27.3           |
|               | [63]      | Housemaids     | 1178             | EITB CT-scan               | 14.6                            | 50 (of sero+)  |
|               | [64]      | Population-based | 803              | EITB CT-scan               | 24.4                            | 3              |
|               | [65]      | Population-based | 817 (8 PWE)      | EITB CT-scan               | 50 (PWE)                        |                |
|               | [66]      | Population-based | 368              | Ab-ELISA, EITB             | 3.3                              |                |
| Venezuela     | [67]      | Population-based | 68               | Ag/Ab ELISA                | Ag: 64.7, Ab: 79                 |                |
|               | [68]      | Population-based | 1254             | Ag/Ab ELISA                | Ag: 9.1; 6.1; 5.7 Ab: 36.5;36.5; 4 |                |
|               | [69]      | Hospital-based | 158 psychiatric patients 127 controls | EITB | Patients:18.3 Controls:1.6 |                |

EITB: Electro immune transfer blot; PWE: people with epilepsy. Ag: Circulating antigens of *T. solium* metacestodes, Ab: Antibodies anti-cysticercal. * Only patients diagnosed between 2000 and 2009 were included. ** Cases of cysticercosis in general were reported.
## Table 3. Prevalence (seroprevalence) of human neurocysticercosis in Asia only 2002-2012 articles were considered.

| Country     | Reference | Type of Study | Subject included | Diagnosis Based on | seroprevalence | Prevalence NCC |
|-------------|-----------|---------------|------------------|-------------------|----------------|----------------|
| China       | [70]      | Population-based | 202              | Ab-ELISA          | 2.97%          |                |
|             | [71]      | Population-based | 72               | CT-scan           | 26%            |                |
|             | [72]      | Hospital study  | 1026 PWE         | CT-scan           | 34.6%          |                |
|             | [73]      | Population-based | 1063             | EITB              | 15.9%          |                |
|             | [74]      | Population-based | 450              | Ab-ELISA          | 22.4%          |                |
|             | [75]      | Population-based | 595              | CT-scan           | 15.1%          |                |
|             | [76]      | Population-based | 141 PWE          | CT-scan           | 24.8%          |                |
|             | [77]      | Population-based | 1064 (sera)      | Ab / Ag-ELISA CT-scan | 15.9% (Ac) / 4.5% (Ag) |                |
| India       | [78]      | Neurological patients | 103              | Ac-ELISA          | 33 (32%)       |                |
|             | [79]      | Population-based | 1442 controls 91 suspected cases of NCC 100 healthy students | Indirect haemagglutination (IHA) | 6.1% controls 21.97% suspected cases 0% healthy students |                |
|             | [80]      | Blood donors    | 216              | Ab-ELISA / Ag-Co- agglutination | 14 (6.48 %) |                |
| Indonésia   | [81]      | Population-based (1539 people) | 1120 cases of burns, 293 PWE (Papua) / 74 PWE, 746 controls (Bali) | Ab-ELISA | 67% PWE, 65% SCN (Papua) 13.5% PWE 12.5% controls (Bali) |                |
|             | [82]      | Population-based | 17 PWE 32 SCN 47 control | Ab-ELISA | 70.6% PWE 62.5% SCN 25.5% control |                |
|             | [83]      | Population-based | 96               | Ab-ELISA          | 45.8%          |                |
|             | [84]      | Population-based | 311              | Ab-ELISA          | 0.3%           |                |
| Korea       | [85]      | Population-based | 74,448           | Ab-ELISA          | 8.3% (1993) 2.2% (2006) |                |
| Malasya     | [86]      | Population-based | 135              | Ab-ELISA          | 2.2%           |                |
| Nepal       | [87]      | Hospital study  | 300 PWE MRI      | Ab-ELISA          | 47%            |                |
| Philippines | [88]      | Population-based | 497              | Ab-ELISA          | 24.6%          |                |
| Thailand    | [89]      | Population-based | 159              | Ab-ELISA          | 5.70%          |                |
| Viet Nam    | [90]      | Population-based | 210              | Ab-ELISA          | 5.7%           |                |
|             | [91]      | Population-based | 707 (303 mountain, 175 coast 229 urban) | Ag-ELISA, CT scan | 5.3% (mountain) 0.6% (coast) 0% (urban) |                |

PWE: people with epilepsy / SCN: subcutaneous nodules
Regarding porcine cysticercosis, diagnosis based on tongue inspection has been conventionally used, but does not detect all affected pigs. Serology permits, although not with ideal sensibility and specificity, identification of the areas where the life-cycle of the parasite persists. Echography (ultrasound) has recently been introduced as a sensitive (95%) and specific (97%) method of diagnosis (Kappa coefficient of 90%) [102]. Treatment of cysticercotic pigs with oxfendazole has shown a good efficiency [103].

Diagnosis of the adult form of *T. solium* is perhaps the topic where more efforts must be made. Although a species-specific coproantigen ELISA was developed, reaching very good performance [104], further studies are required to evaluate it in field conditions. And this is not so easy, as prevalence of taeniosis seems to be much lower than that of cysticercosis, a fact understandable as one tapeworm carrier can infect hundreds of people and thousands of pigs. Treatment of taeniosis with niclosamide or praziquantel has shown to be very efficient [105].

In conclusion, although efforts must continue in some areas, today we have tools that allow the detection of endemic areas and the effective diagnosis and treatment of patients in most circumstances. This situation, adding to the existence of specific tools for prevention (vaccine), allows the design of extensive and effective preventive and control programs.

### 3. Strategies to eradicate the disease

Cysticercosis is considered a neglected “tools-ready disease” according to WHO [106] and as a potentially eradicable disease since 1993 [107]. This is feasible because there are no animal reservoirs besides humans and pigs, the only source of *T. solium* infection for pigs being humans (the definitive host), interrupting the parasite’s life cycle seems an easy task by intervention strategies acting upon different stages of the parasite’s development.

Different strategies have been proposed and tested, generally experimental and at small scale, to eradicate the (T/C) complex, the most notable being:

1. Massive cestocidal treatment to humans in order to reduce the number of tapeworm carriers [108-110].
2. Health education programs aiming to promote the understanding of the mechanisms of transmission of the parasite and to improve hygienic behavior, pig-management and sanitary conditions which fosters transmission [111-113].
3. Treatment of infected pigs [103, 114-116].
4. Vaccination of rural pigs: different vaccines have been tested in field conditions and have demonstrated their efficacy in preventing swine cysticercosis [117-120].
5. Combinations of different strategies: pig vaccination and treatment [121], massive human cestocidal treatment associated with pig vaccination and treatment [122,123].

Almost all these strategies have shown some degree of efficacy, this fact contrasting with the persistence of the parasite in all the endemic countries in the 1950’s. It should be noted that, to our knowledge, programs promoting letrinizaton of rural communities and construction
of pig housing have not been tested (probably due to economic and logistic costs) although it seems to be a very efficient strategy for many parasitic and infectious disease transmitted by faeces.

4. What must be done?

This is a truly kafkian situation: we are in the presence of a parasite that causes a potentially severe human disease, as well as important economic losses; paradoxically, it is clear that the disease is potentially eradicable and, in fact, scientists and health authorities know how to eradicate it and have strategies to reach this goal. Despite all these resources, and their demonstrated effectiveness, the signs of a decrease of the transmission rate in the endemic countries are inconclusive or doubtful and, worse yet, in some non-endemic countries, an increase in the number of neurocysticercosis cases is occurring.

Faced with this perspective, it becomes evident that we will not attain the eradication of *T. solium* without:

4.1. The intervention of the national and international health authorities in control programs

International initiatives have been concerned with the problem of cysticercosis for many years and several meetings were organised, the most important being: WHO Technical Consultation (Geneva, 1983), Pan American Health Organization (PAHO) Informal Consultation on Taeniasis/Cysticercosis (Porto Allegre, 1990), International Task Force for Disease Eradication (ITFDE, Atlanta, 1993), PAHO/WHO Informal Consultation on the Taeniasis/Cysticercosis Complex (Brasilia, 1995), North Atlantic Treaty Organization (NATO) Seminar on Emergent Helminth Zoonoses, (Pozna, 2000), Fifty-Fifth World Health Assembly, (Geneva, 2002), ITFDE II (Atlanta, 2003), WHO Expert Consultation on Foodborne Trematode Infections (Ventiane, 2009). In most of them, strategies for prevention and control of T/C were analyzed and recommendations were made. Since 2008, the WHO has included T/C in its Global Plan to combat Neglected Tropical diseases [124].

Regarding national health authorities, not much has been done. In very few countries, specific norms have been recommended. Such is the case of Latin America where only Mexico has an official norm for the vigilance, the prevention and the control of T/C in the first level of attention which was published in 1994 (modified in 2004) [125]. The Mexican norm includes the implementation of education and information programs, the identification and treatment of tapeworm carriers, the referral of subjects with suspected of NCC to a second level of attention, the confiscation of infected pigs, and the obligation to notify the diagnosed cases of NCC, taeniosis and swine cysticercosis to the corresponding authorities. The effort must be applauded, and has surely contributed to the awareness of the general population and of the medical personnel about the problem. Unfortunately, still, 15 years after its promulgation, cases of swine and human cysticercosis are still being diagnosed and not notified in Mexico. Probably, this is due to the fact that this norm did not
reach the rural zones where the life-cycle of *T. solium* is still active and notification is not equally honored by all professionals (or because there are no health facilities in these areas).

It is important to promote the confiscation of infected pigs, but who is going to pay the owners, and who will go to the endemic communities (for example >2500 municipalities in Mexico) and make the diagnosis in more than six million rural pigs that get renewed every year? Clearly, pig owners must be included in a control program, for the obvious reason that they are the most interested in not having infected pigs.

It is highly relevant to promote the notification of infected individuals, but who will make this notification? Hospitals with an efficient epidemiologic department are scarce and medical doctors in public institutions are generally over loaded by the clinical workload. The comparison of the official statistics and the statistics published from only one hospital center can demonstrate the problem: in 2004, in the Instituto Nacional de Neurología y Neurocirugía, located in Mexico City, an institution that treats only patients lacking social security, 120 new cases of NCC were diagnosed [58], while in the official statistics, in this same year, approximately 400 new NCC cases were reported throughout Mexico [126]. It is very improbable that a sole institution accounts for a quarter of all the Mexican NCC cases, and probably this is due to a significant under-reporting of cases. Faced with this undesirable practice, what actions can the governments take? It is probably necessary: 1) to maintain a continuing health education program available to the population and the medical personnel, insisting on their obligation to notify the cases and promoting the establishment of epidemiological departments and surveillance system in all the hospitals, 2) to actively lobby for the implementation of a National Control Program that could be started as a priority in the areas from where most cases are referred. In relation to this point, the critical question is, who can organize a preventive program? The scientists probably not, as the logistics of such programs require an established structure supported by a recognized local authority. Since 2009, in Mexico, an extensive pilot control program is under way, in certain areas of the poorest states, based on health and sanitary education and associated with vaccination of pigs. Local authorities are part of the efforts, helping with the identification of the endemic areas, by furnishing sera collected from the pigs, and by funding the program. The results so far are encouraging. People in the remote areas accept suggestions for improvement in their pig raising methods and for their personal hygiene, including the indispensable installation of latrines [127]. What has become clear is that programs must be of long duration, at least 5 years. It is of little use to visit communities, give talks, vaccinate pigs and leave. People in these “forgotten” areas need long-lasting help, advice and supervision. Therefore, without the active participation of the governments, failure of any control program is predictable because scientists cannot apply it at large enough scales and sufficient time. Finally, the presence of cysticercosis is an objective indicator of unacceptable conditions in a rural community, and their improvement will not only contribute to the eradication of cysticercosis, but will also bring collateral benefits, such as the control of other soil transmitted diseases and increased public awareness of respect for adequate simple public health measures.
4.2. Implementation of regional networks

As T. solium does not respect frontiers, it is necessary to organize multidisciplinary regional networks of specialists that must be the interlocutors of the local government and international organizations, and that must participate in the decision of where the preventive measures must be applied, and what type of measures are the most adequate regarding the individual characteristics of the country affected. Such efforts are currently established:

- In Asia, the Regional Network for Asian Schistosomiasis and other important zoonoses (RNAS+) was created in 2006 (extension of the RNA created in 2000) and since this date has published several papers and has maintained discussions on preventive measures to be applied to effectively combat zoonoses.

- In Africa: the Cysticercosis Working Group in Eastern and Southern Africa (CWGEASA) was established in 2002 to promote communication, collaboration and coordination of integrated research and control activities to combat cysticercosis.

- In Europe, The European Cysticercosis Working Group, inaugurated in 2008 and receiving organizational support from the World Health Organization (WHO)/Food and Agricultural Organization of the United Nations (FAO) Collaborating Centre for Parasitic Zoonoses in Denmark and the University of Edinburgh, Scotland, and aimed at finding ways to achieve a more effective, concerted approach to combat cysticercosis in Europe, as well as in the main cysticercosis-endemic areas of Africa, Asia, and Latin America [128].

- In Latin America, since 1987, the Cysticercosis Working Group in Peru has made several epidemiological, diagnostic and control studies in this country [129] and recently a new Ibero-Latinamerican network was created to promote the investigation and the implementation of preventive measures in the entire continent.

At the moment, although some objectives have been reached, their scope is still limited. To improve the situation, it is necessary: 1) to expand exchanges between the different networks; 2) to open ways of communication between these networks and the national and international authorities.

In conclusion, to reach the control of T. solium infections it is very important to open new ways of communication between the scientists, grouped in networks, and with the international and the national health authorities. Agreements must be made in which the role and responsibilities of each of them are clearly defined. If one of these conditions fails, we are afraid that in 50 years, today’s T/C epidemiological situation will persist.

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