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Control of *Taenia Solium* Transmission of Taeniosis and Cysticercosis in Endemic Countries: The Roles of Continental Networks of Specialists and of Local Health Authorities

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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%	
	[8]	Case-control	303 PWE 606 Controls	Ab/Ag - ELISA	Ab 58,7% ; Ag 38,3 PWE Ab 31,4% Ag 20 % controls	
	[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%	
	[18]	US Peace Corps	73	EITB	8,2%	
Mozambique	[19]	Urban children	269	Abs	20,8%	
Senegal	[20]	Population-based	403	Ag-ELISA EITB CT scan	11,9%	23,3% of sero+
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
Brazil	[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)	
	[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		0.55/1000,000**
	[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 CTscan/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	
Ecuador	[47]	Population-based	4306	Ag-ELISA	4.99	
	[48]	Population-based	2415 (24 PWE)	CT scan		33% PWE

Country	Reference	Type of study	Subject included	Diagnosis based on	Seroprevalence Cysticercosis (%)	Prevalence NCC
	[49]	Population-based	800	Ag-ELISA, EITB	2.25	
	[50]	Hospital-based	194 PWE (late-onset)	CT scan/MRI		19.6*
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
	[58]	All NC patients diagnosed at INNN in 2004	4706	CT scan/ MRI		2.5
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) CTscan (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 (3)	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 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	Prevalence NCC
China	[70]	Population-based	202	Ab-ELISA	2.97%.	
India	[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)	
	[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		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	Ag-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

Table 3. Prevalence (seroprevalence) of human neurocysticercosis in Asia only 2002-2012 articles were considered.

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 letrization 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 kaffian 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 (CWGESA) 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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