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SHORT CUTS TO DEVELOPMENT: METHODS TO CONTROL THE TRANSMISSION OF CYSTICERCOSIS IN DEVELOPING COUNTRIES

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MAGNITUDE OF THE PROBLEM

T. solium infection and the resulting disease neurocysticercosis, are highly endemic in all parts of the developing world where pigs are raised as a food source. Neurocysticercosis is present throughout Latin America, Indonesia, Africa, and parts of India. In rural areas of Latin America, between five and twenty percent of the population is infected with *T. solium*. In Mexico, Ecuador, and Brazil, the prevalence of neurocysticercosis found at autopsy exceeds 1%.[1,2] and both Mexico[3] and Peru,[4] 12% of acute neurological beds are occupied by patients with NCC. Neurocysticercosis was the fourth most common condition found at autopsy (ranking above tuberculosis) at the Santo Toribio Neurological Hospital of Lima, Peru. Over a 37 year period from 1950 to 1987, 136/2,200 (6%) of the autopsies performed at this hospital showed cysticercosis (L. Palomino, personal communication) reflecting the considerable mortality associated with this disease.

BIOLOGICAL BASIS OF DISEASE AND TRANSMISSION

Cysticercosis is a disease of pigs and people. The pig harbors the larval stage of *T. solium* and human beings acquire the adult tapeworm by eating under-cooked pork. Upon infestation, the larvae evaginate in the small intes-

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tine, mature over a period of months and produce gravid proglottids, each containing thousands of eggs. Disease occurs when humans become infected with the cysticerci, or larval stage through accidental ingestion of tapeworm eggs. Thus, humans can serve as both the definitive and the intermediate host. If ingested by a human or pig, the eggs hatch in the small intestine, and the larva travel through the small venules to muscle and brain tissue. Once there, the larvae develop over several months into mature larval cysts.[5]

From the standpoint of disease transmission to humans and maintenance of the cycle, only the tapeworm is of importance. Individuals who ingest the egg of the tapeworm and develop the larval (cystic) form do not pose a public health risk. They are a health concern because of their disease; but unless also infected with the tapeworm form of the disease have no part in maintaining the cycle of the parasite.

Developed countries, by improving sanitation and hygiene practices as well as moving to commercialization of nearly all piggeries have all but eradicated cysticercosis.[6] The practices of indoor plumbing and modern porcine husbandry largely dictate how free a region will be from *T. solium* transmission and consequently how much burden of disease from cysticercosis will occur. In developing countries the rates of cysticercosis are also low among individuals who live for most of their life in major urban centers for the same reasons: cities often have sewage, pork comes from commercialized piggeries or is inspected appropriately, and the meat is usually eaten after having been well cooked. Pigs in these areas are rarely bred in the houses and have little access to human feces. For example, in Lima, Peru, less than one percent of individuals born in the city have serological evidence of infection.[7]

Essentially, the *T. solium* cycle is transmitted mainly in rural areas where the lives of pigs and people are intimately intertwined. Pigs commonly have access to raw human sewage or feces, and *T. solium* infected meat is widely available. Unfortunately, these same regions are the last to develop adequate sanitation and to install widespread, safe animal husbandry practices. Thus, rural areas in where pigs are raised are by far the mainstay of *T. solium* transmission and the majority are highly endemic for neurocysticercosis.

CONTROL STRATEGIES

Intervention can occur by interrupting the human or pig steps of the cycle separately or both together. Human infection in endemic areas can be decreased either by detecting and treating just the tapeworm carriers or elimi-

nating the detection step and treating the whole population en mass.[8-11] Human infection can also be prevented by preventing the sale and consumption of *T. solium* infected meat.[6] The second control method targets porcine infection either by mass anthelminthic treatment[12-14] or in the future, if and when an effective vaccine becomes available, by immunization of the pig population.[15-20]

In the following discussion we will utilize information gathered from Peru, and other Latin American countries. We expect that the experience acquired in Latin America will be applicable with minor variations to other cysticercosis-endemic areas of the world.

Eradication strategies which have functioned in developed countries are usually not suitable for most developing countries. In the past, the World Health Organization suggested that control programs would be successful if inspection of pig carcasses in slaughterhouses were rigorously enforced.[6] This strategy has failed miserably in most developing countries, however, for two interrelated reasons: First, instituting a policy in which pigs that are detected to have cysticercosis are confiscated without payment to the pigs owner leads to the establishment of a clandestine market for pigs that may be infected with *T. solium*. In Peru, if porcine cysticercosis is detected, the pig is confiscated and no payment is given to the peasant: In Peru, it is estimated that 55% of all pigs are illegally slaughtered,[21] and this figure is close to 100% in many rural areas. For instance, in Huancayo, Peru, only 30 of an estimated 35,000 pigs were killed at the slaughterhouse even though nearly all pigs were killed within their first year of life.[21] Secondly, targeting slaughterhouses as the primary intervention fails to influence the animal husbandry practices which occur before the pigs are brought to market. The policy of slaughterhouse inspection is effective only in non endemic areas or from commercial piggeries both situations where the vast majority of pigs are free of *T. solium* infection. Farmers will use the slaughter house under these conditions since there is a low risk of infection and thus confiscation. Small slaughter houses in outlying regions in order to attract business from the area's piggeries are not likely to practice control and confiscation. The rates of infection among pigs killed at these slaughterhouses may be as high as 30%.[21]

Thus, the inspection and condemnation measures supported by present policy[6] encourage high rates of infection with *T. solium* by targeting the slaughter house only and by failing to provide financial market incentives to reimburse the farmer and or slaughter house for infected pigs that are taken out of circulation or made safe for consumption by processing the meat after boiling.

ALTERNATIVE STRATEGIES

Draconian measures, such as killing all infected pigs and reintroducing uninfected pigs are neither culturally or economically acceptable for several reasons. Economically, the peasants and entire community could not absorb the loss of 25% of their pigs. Such a measure would also not be feasible due to the necessary massive investment in resources and trained personnel required to monitor the project. Finally, and perhaps most importantly, widespread killing of infected pigs fails to treat the human and environmental sources of infection. Therefore, it is unlikely that the introduced infection free pigs will stay free of infection for long. Gamma radiation has also been suggested as a control measure by the International Atomic Energy Commission in Vienna. This method of control does not take into account that the cost of machine apparatus and their maintenance is well beyond what is achievable for most rural slaughterhouses or even most developing nations.

Several alternative interventions exist. The alternative control strategy (or strategies) most likely to succeed are those which take into account the major impediments to control. A successful strategy will address all of the following issues: (1) present economic disincentives at the local level associated with controlling porcine cysticercosis; (2) lack of knowledge of the cycle, namely among rural communities, food preparers, and policy makers; (3) failure of central and local governments to consider it an important cause of disability and economic loss to the nation; (4) lack of intervention sustainability due to reintroduction of infection from an external source or failure to treat a portion of the reservoir either human or porcine effectively; and, (5) the continued maintenance of unhygienic practices (poor sanitation and negligent animal husbandry practices) that will permit the cycle to continue uninterrupted over time.

1. Economic obstacles.- It is worth emphasizing that policies and programs failing to recognize the economic significance of the pig trade in peasant communities will fail in their efforts to reduce the incidence of cysticercosis. In many rural economies, pigs serve as one of the main financial assets of the farmer. The possession of a pig is one of the few assets available to the farmer that can be quickly and easily converted into cash. A pig can be fed at little cost by permitting him to range free in villages or on free farm land and in this way obtain a variety of foods which supplement his diet, including human and other animals feces. Corn or grains allocated to feed pigs can then be used for other purposes. Permitting pigs to range freely also has a secondary

economic advantage in that pigs are utilized to maintain villages free from garbage, small vermin and animal and human feces. In fact, in many areas of Peru they are called the "village police" because of these activities.

Interruption of these gratis benefits to the pig owner and his community requires either the means to obtain a more attractive economic asset or strict village prohibition activities which penalize peasants for feeding pigs sewage and for allowing them to range freely. An illustrative example of community control occurred in a village which discovered its pigs eating rice from an adjoining field. Rapid and unified village (tethering the pigs) action was taken to prevent this from continuing.[22]

Finally, before leaving the issue of economics, it is important to address how a successful control program must take into account the financial incentives of the other party involved in the pig trade - the purchasing parties. Sustainable programs must aim to decrease the supply of infected meat to purchasers. Currently, diseased meat needs to be sold clandestinely and disguised by mixing it with uninfected pork. To the purchaser diseased meat has the advantage of a cheap price but the disadvantage of being illegal.[21] Control efforts need to purchase diseased meat at the market price and process it in a safe manner. This process would have several advantages: it would tend to replace the clandestine market. Diseased meat could be processed so all cysts are killed and then sold for sausage or other processed meats albeit at reduced prices. Thus the farmer would receive a higher price for a clean pig but would still bring his infected pig to the slaughter house since he would gain the same profit as he would at a clandestine market and without risk. Diseased pork would be made safe for consumption. Overtime since a higher price is given for clean pigs, market forces would be expected to push farmers to produce clean pigs either on an individual basis or by forming commercial piggeries.

2. Knowledge of the parasite life cycle.- In Mexico, Knowledge, Attitude and Practice studies (KAP) studies have demonstrated that a minority of villagers understand the role of *T. solium* infection in pigs and the *T. solium* larvae's relationship to neurocysticercosis or epilepsy. Efforts to educate villagers at schools, village meetings, and on an individual basis have been highly successful. Villagers were able to describe how *T. solium* infection was transmitted, how it could be prevented and understanding the connection between infected pigs and the development of cysticercosis in people. The knowledge acquired however did not result in dramatic changes in corralling of pigs or limiting their access to feces.[23]

Again, an understanding of the role economic incentives play in behavioral change at the local level is essential to the development of health education control components. The major driving force behind raising pigs is economic. The health risk of transmitting and getting cysticercosis is not an immediate risk. Thus even though knowledge is present it does not weight actions as strongly as does the immediate economic advantage of maintaining pigs in a cheap but unhealthy manner.

3. Failure of governments to consider cysticercosis an important disease.- Cysticercosis is a reportable disease in many endemic countries in Latin America, but besides Mexico, where active surveillance is mandated in a recent legal norm, there are no official interventional control programs. To date, all interventions in the control of cysticercosis[8-11,16,23] have resulted from individual initiatives more than government programs.

Recently gathered information has demonstrated the endemicity of cysticercosis and its impact in morbidity and mortality in many developing countries[24] and a change in the perception of the subject by policy makers is expectable.

Items ***4, lack of sustainability***, and ***5, maintenance of unhygienic practices***, are closely related. As discussed below, the ultimate success of any action in controlling cysticercosis will depend on both the potential for the intervention be continued for several years after the first initial efforts, and the coverage of most -if not all- endemic zones to avoid reintroduction of infection from a remaining foci. Costs and cultural acceptability will therefore determine the future of any proposed intervention.

Based on this information and understanding of the current systems shortcomings, the remainder of this article will seek to evaluate the key alternative strategies; mass treatment of humans, concurrent treatment of pigs and humans, and recent vaccination efforts.

MASS TREATMENT OF HUMANS (BOTH INFECTED AND NON INFECTED).

Mass treatment refers to efforts to clear humans of *T. solium* tapeworms, and leave the porcine reservoir untouched. Eggs of *T. solium* are extremely durable; however, and can survive for years in the environment. Thus, this approach ignores a continuing source of infection to both pigs and people.

Several attempts to utilize mass treatment as a control measure have oc-

curred in Mexico, Ecuador, Brazil, and Guatemala. These programs produce substantial short term results, yet demonstrate little to no reduction in porcine or human infection when examined several years later. Incomplete interruption of the cycle may in fact permit transmission of infection to occur at levels greater than those present at pre-intervention.[9] This increase in transmission occurs presumably through the loss of immunity which accompanies mass treatment.[25] It would appear that conducting mass treatment of human tapeworm carriers in isolation of other activities results in temporal benefits only, since new cases will replace the treated ones.

COMBINED MASS THERAPY OF PIGS AND PEOPLE

Mass treatment of humans and pigs in combination, however, interrupts the life cycle at two points concurrently. Targeting treatment to tapeworm carriers (humans) or infected pigs requires cheap and simple detection. Methods are available for detection but they are expensive and difficult to apply to large population groups. A mass chemotherapy sacrifices specificity, but is simple, relatively cheap and feasible. Medicines for both pig and human are available and are relatively cheap: Praziquantel for humans costs approximately $0.25 and oxfendazole for pigs costs approximately $1.00 per dose. Both drugs can be given as single doses and both have a low rate of adverse effects. On rare occasions, a villager with cerebral cysticercosis may experience a seizure precipitated by praziquantel treatment if he or she may absorb enough to cause inflammation around a cyst.[26] Niclosamide is a highly effective, nonabsorbable alternative; however, this taenicidal drug is not used for mass campaigns because of it s high cost.

According to a current study evaluating a mass treatment program of praziquantel (humans) and oxfendazole (pigs) in Peru, the approach is feasible and its related costs are within reason. Results are also able to be evaluated easily and cheaply by sampling pigs in treatment zones over time. Change in porcine infection over time is an excellent indicator of program success since porcine prevalence is higher, and a new cohort is yearly available for evaluation.

A successful program requires governmental involvement especially the health and agricultural ministries. How sustainable this type of program is, and how often it must be repeated to prevent the reproduction of *T. solium* is not known. Nor is it known how fast infection will recur once control is lifted. The most likely barrier to success is actually political, though. Achieving con-

sensus among all areas and levels of a diverse country to agree to a mass treatment program for both people and pigs as well as efforts to change sanitation and porcine husbandry clearly are difficult objectives to achieve in most third world countries. Whether such a program can be sustainable for more than several cycles is also questionable as politicians become disinterested.

In a country like Peru, the annual cost of a mass treatment program, excluding labor and transport costs, would be about 3 to 4 million dollars per cycle. This estimate is based on the following assumptions: Forty percent of the population is rural . Generally assuming that the number of pigs in the country is ten percent of the human population, approximately 900,000 pigs and nine million humans will require treatment in endemic areas of the country. The cost of oxfendazole ($1.00 per dose) and praziquantel ($0.25 per dose) brings the total to one million dollars for the treatment of pigs and about two and a quarter million dollars for humans for medicines alone. Additional costs of transport, gasoline, and staffing are not included. Given that some of these costs are fixed, one would expect a single cycle of treatment in a country like Peru could be accomplished for less than five million dollars.

VACCINE IMMUNIZATION THERAPY

A second strategy, the utilization of vaccines or immune therapy, is still in its infancy, but if effective, has a high potential. Immunity to cestode oncospheres plays a central role in the regulation of transmission of taeniid cestodes.[18] Gemmell[27,28] demonstrated that living oncospheres of *Taenia hydatigena* and *Taenia ovis* were required to stimulate a protective immune response in sheep. Rickard and Bell later demonstrated that the oncosphere itself and/or Excretory/Secretory antigens gave effective immunity against *T. ovis* infection.[29,30] A vaccine was produced against *T. ovis* infection using recombinant cDNA technology to produce commercial quantities of the protective Excretory/Secretory antigens.[31] These studies were the basis for the development of another successful cestode vaccine against *E. granulosus*.[32]

Preliminary evidence from pigs infected with gravid proglottid suggests that immunization with either crude or defined antigens prior to infection may be able to protect pigs from *T. solium* infection.[15-20] Such a porcine vaccine would have the potential of interrupting the cycle and over time should decrease the number of infected pigs and people. None the less, realistically, until a model is developed which can produce reliable and repeatable infection of *T. solium* and which can then be used to test the efficacy of different vac-

cine preparations, it is most likely that advances in vaccine development will proceed at best slowly.

Human vaccines. The role of vaccination of humans for the control of cysticercosis can be considered to have a low priority. The contributing reasons include: the high cost of developing such a vaccine, the lack of a suitable economic or governmental incentives for either the development or the marketing of a human vaccine, and the presence of a suitable low cost alternative control by effective taenicidal agents.

Porcine vaccines. Porcine vaccines are indeed attractive control measure possibilities. If a vaccine was available its cost would have to be quite low. Porcine cysticercosis is a disease uncommon to commercial piggeries, suggesting the clientele for this vaccine would be rural endemic villages. A high priced vaccine would undoubtedly be an effective impediment to the use of a vaccine strategy. The result might mirror the hog cholera vaccine which is effective and prevents a frequently fatal disease of pigs but is limited in most rural villages due to cost and inadequate distribution.

There are several reports of immunity to *T. solium* in pigs.[15-19] Pathak,[18] demonstrated a significant decrease in the number of cysts (94%, $p < 0.001$) vaccinating pigs with *T. solium* oncosphere excretory-secretory antigens. In another study in Mexico, there was a six-fold reduction in the mean number of cysts from 80 to 12 in five control versus six pigs immunized with a crude cyst antigen.[16]

New methods of obtaining oncosphere protective antigens that are present in other species of cestodes and are closely related to *T. solium* oncosphere proteins have recently been developed and will be tested as part of this proposal. Gauci *et al*[20] recently described a cDNA (TSOL-18) that encodes a protein with close homology to host protective oncosphere antigens from *T. ovis* and *T. saginata*. TSOL-18 was cloned from mRNA obtained from hatched and activated oncospheres of *T. solium*. The high level of predicted amino acid sequence homology among TSOL-18 and other host protective taeniid antigens suggests that the protein expressed by TSOL-18 may be used as a vaccine against *T. solium* infection in the pig.

The above features favor the development of a practical vaccine against *T. solium* in the intermediate host. It is presumed, but has not been demonstrated, that vaccination of the intermediate porcine host will reduce the prevalence of human cysticercosis. Vaccinations, in concert with other control measures, such as tapeworm detection and mass human or porcine chemo-

therapy, should be extremely effective in controlling cysticercosis.

Significant problems with porcine vaccination will need to be addressed prior to its use in the field. There is some evidence that pigs become infected with *T. solium* early in life.[33] If this is true, immunization must be performed at an early age. Pigs immunized at an early age may not be able to mount an effective protective immune response to a vaccine due to the immaturity of their immune system. Alternatively, vaccinating pigs later in life may not be effective: if pigs are infected early in life and then vaccinated, the ability of the vaccine to eliminate an already established infection is poor. We have previously shown that immunization of pigs after infection is not an effective means of combating porcine cysticercosis.[34] Also in young pigs, if maternal antibody is present it may inhibit an effective antibody response to *T. solium* vaccines.

The best route (oral versus systemic) to give a vaccine for porcine cysticercosis needs to be determined. An effective oral vaccine would block *T. solium* oncospheres from penetrating the intestinal barrier. Oral vaccines seem a better alternative because they would avoid spoilage of meat by vaccination, are easy to give, and can be applied multiple times by including it in feed. If it is not possible to develop an effective oral vaccine then systemic vaccination would need to be used but would be more difficult to apply since animals will need to be restrained for each application. Systemic vaccines would permit however the use of new vaccine technologies that are currently in development, that is new adjuvants and DNA vaccine strategies. Vaccine or immune therapy would be the most efficacious method for achieving control but it is unlikely that it will play a role in the next five to ten years.

PORCINE PARKS

Another suitable measure for the control of cysticercosis is the development of porcine parks. This option was originally designed for the management of organic garbage material in small cities, and involves the use of this material, previously processed, to feed the pigs, which are raised by their owners but in a closed place (park). This may be enforced by local authorities, since there is no economic prejudice to the peasants, and it is probable that a combination of this safe husbandry with veterinary control of slaughtering may be achieved.

Preliminary trials must confirm the acceptability of porcine parks by villagers, and the best way of processing the organic materials, and an adequate balance of dietary components to maximize the benefits in terms of meat.

GOVERNMENTAL AND FUNDING AGENCY SUPPORT

Until ten years ago, *T. solium* infection was not considered an important health issue. In the last decade, our ability to diagnose both infection and disease through serology and new imaging techniques such as the CT and MRI, and our increasing ability to treat neurocysticercosis more effectively with new anthelminthic agents, have demonstrated to governments the significance of this disease. Most countries have just began prevalence surveys. Only in Ecuador and Brasil have mass programs ever been instituted and none of these has remained sustainable.

Infection control efforts must focus on addressing the economics of the pig trade in order to increase government awareness and to stimulate both private and governmental action to increase the safety of animal husbandry practices. Development of porcine vaccines for control of *T. solium* infection need to be given a high priority by funding agencies. Mass treatment programs should be tried first as pilot programs and then on larger scale. Finally, while no successful measure is going to be easy to execute and enforce, the chance of controlling cysticercosis by treatment alone is limited as long as poverty and poor sanitation practices persist.

RECOMMENDATIONS FOR STAGED CONTROL PROGRAMS

We would recommend the following measures be considered:

Short run. In the short run an increase in commercial piggeries for supplying the majority of the meat market when ever possible. Village education especially in the schools concerning the importance of corralling pigs and the dangers of cysticercosis . In addition, slaughterhouse confiscation without payment needs to be stopped. Rather these animals should be bought and used after boiling for sausage or other prepared meats.

Midterm. A midterm strategy would be to put in place human and animal mass treatment in endemic areas. This could be best done using oxfendazole as a single dose for treating pigs in combination with mass treatment of villagers using either praziquantel or niclosamide. This midterm strategy has the following advantages: it can be applied nearly immediately once government support has been attained. Meat from *T. solium* infected pigs is suitable for marketing three months after oxfendazole is given. Distribution of drug is easy and can be performed both through the public and private sector. The problems with mass treatment of pigs with oxfendazole are that after treat-

ment cysts do not die immediately but can remain viable for a month or longer before dying. marketing of meat from these pigs will be delayed nearly three months from the time of treatment because this is the time it will take in order for cysts to completely resorb and appear normal to the consumer. The number of cycles of treatment of both pigs and humans needed before control can be established is still unknown.

Long term. Long range strategy will depend on the presence of an effective porcine vaccine against *T. solium* and continued mass treatment of humans. Overtime this strategy should be able to eradicate cysticercosis from most endemic areas.

REFERENCES

1. Briceño CE, Biagi F, Martínez B. Cisticercosis. Observaciones sobre 97 casos de autopsia. *Prensa Médica de México* 1961; 26: 193-7.
2. Schenone H, Villarroel F, Rojas A, Ramirez R. Epidemiology of human cysticercosis in Latin America. In: Flisser A, Willms K, Laclette JP, Larralde C, Ridaura C, Beltran F. (Eds.) *Cysticercosis: present state of knowledge and perspectives.* New York: Academic Press, 1982: 25-38.
3. Flisser A. Neurocysticercosis in Mexico. *Parasitology Today* 1988; 4: 131-7.
4. García HH, Gilman R, Martinez M, Tsang VCW, Pilcher JB, Herrera G, *et al.* Cysticercosis as a major cause of epilepsy in Perú. *Lancet* 1993; 341: 197-200.
5. Nash TE, Neva FA. Recent advances in the diagnosis and treatment of cerebral cysticercosis. *New England Journal of Medicine* 1984; 311: 1492-6.
6. Gemmell M, Matyas Z, Pawlowsky Z, Soulsby EJL (Eds.) *Guidelines for surveillance and control of Taeniasis/Cysticercosis.* VPH/83.49. Geneva: World Health Organization; 1983: 1-207.
7. García HH, Martinez M, Gilman RH, Herrera G, Tsang VCW, Pilcher JB, *et al.* Diagnosis of cysticercosis in endemic regions. *Lancet* 1991; 338: 549-51.
8. Cruz M, Davis A, Dixon H, Pawlowski Z, Proaño J. Operational studies on the control of *Taenia solium* taeniasis/cysticercosis in Ecuador. *Bulletin of the World Health Organization* 1989; 67: 401-7.
9. Keilbach NM, de Aluja AS, Sarti-Gutierrez E. A programme to control taeniasis-cysticercosis (*T. solium*): experiences in a Mexican village. *Acta Leidensia* 1989; 57: 181-9.
10. Diaz-Camacho SP, Candil-Ruiz A, Suate V, Zazueta M, Felix M, Lozano R, *et al.* Epidemiologic study and control of *Taenia solium* infections with praziquantel in a rural village of Mexico. *American Journal of Tropical Medicine and Hygiene* 1991; 45: 522-31.
11. Camargo NJ. Strategies for the control of taeniasis-cysticercosis in the State of Parana,

Brazil. In: Garcia HH, Martinez SM (Eds.). *Teniasis/Cisticercosis por T. solium*. Lima: Ed. Universo; 1996: 341-6.

12. Gonzales AE, Garcia HH, Gilman RH, Gavidia CM, Tsang VCW, Bernal T, *et al.* Effective, single dose treatment of porcine cysticercosis with oxfendazole. *American Journal of Tropical Medicine and Hygiene* 1996; 54: 391-4.
13. Gonzalez AE, Falcon N, Gavidia C, Garcia HH, Tsang VCW, Bernal T, *et al.* Treatment of swine cysticercosis with oxfendazole: a dose-response trial. *Veterinary Record* 1997; 141: 420-2.
14. Gonzalez AE, Falcon N, Gavidia C, Garcia HH, Tsang VCW, Bernal T, *et al.* Time-response curve of oxfendazole in the treatment of swine cysticercosis. *American Journal of Tropical Medicine and Hygiene* 1998; 59: 832-6.
15. Nascimento E, Costa JO, Guimaraes MP, Tavares CAP. Effective immune protection of pigs against cysticercosis. *Veterinary Immunology and Immunopathology* 1995; 45: 127-37.
16. Molinari JL, Soto R, Tato D, Rodriguez D, Retana A, Sepulveda J, Palet A. Immunization against porcine cysticercosis in an endemic area in Mexico: a field and laboratory study. *American Journal of Tropical Medicine and Hygiene* 1993; 49: 502-12
17. Sciutto E, de Aluja A, Fragoso G, Rodarte LF, Hernández M, Villalobos N, *et al.* Immunization of pigs against *T. solium* cysticercosis: factors related to effective protection. *Veterinary Parasitology* 1995; 60: 53-67
18. Pathak KML, Gaur SMS. Immunization of pigs with culture antigens of *T. solium*. *Veterinary Parasitology* 1980; 34: 353-6.
19. Gauci CG, Flisser A, Lightowler MW. A *Taenia solium* oncosphere protein homologous to host -protective *Taenia ovis* and *T saginata* 18 kDa antigens. *International Journal for Parasitology* 1998; 28: 757-60.
20. Manoutcharian K, Rosas G, Hernandez M, Fragoso G, Aluja A, Villalobos N, *et al.* Cysticercosis: identification and cloning of protective recombinant antigens. *Journal of Parasitology* 1996; 82: 250-4.
21. Cysticercosis Working Group in Peru. The marketing of cysticercotic pigs in the sierra of Peru. *Bulletin of the World Health Organization* 1993; 71: 223-8.
22. Garcia HH, Cysticercosis Working Group in Peru. Epidemiology of *Taenia solium* infection in Peru. In Tada I, (Eds.) Proceedings of the IX International Congress of Parasitology, Chiba, Japan. Milan: Monduzzi Editore; 1998:
23. Sarti E, Flisser A, Schantz PM, Gleizer M, Loya M, Plancarte A, *et al.* Development and evaluation of a health education intervention against *Taenia solium* in a rural community in Mexico. *American Journal of Tropical Medicine and Hygiene* 1997; 56: 127-32.
24. Tsang VCW, Wilson M. *Taenia solium* cysticercosis is an under-recognized but serious public health problem. *Parasitology Today* 1995; 11: 124-6.
25. Gemmell MA. A critical approach to the concepts of control and eradication of echinococcosis/hydatidosis and taeniasis/cysticercosis. *International Journal for Parasitology* 1987; 17: 465-72.
26. Flisser A, Madrazo I, Plancarte A, Schantz P, Allan J, Craig P, *et al.* Neurological symptoms in occult neurocysticercosis after a single taeniacidal dose of praziquantel. *Lancet* 1993; 342: 748.

27. Gemmell MA, Blundell SK, Macnamara FN. Immunological responses of the mammalian host against tapeworm infections. VII. The effect of the time interval between artificial immunization and the ingestion of egg on the development of immunity by sheep to *Taenia hydatigena*. *Experimental Parasitology* 1968; 23: 83-7.
28. Blundell SK, Gemmell MA, Macnamara FN. Immunological responses of the mammalian host against tapeworm infections. VI. Demonstration of humoral immunity in sheep induced by the activated embryos of *Taenia hydatigena* and *T. ovis*. *Experimental Parasitology* 1968; 23: 79-82.
29. Rickard MD, Bell KJ. Successful vaccination of lambs against infection with *Taenia ovis* using antigens produced during in vitro cultivation of the larval stages. *Research in Veterinary Science* 1971; 12: 401-2.
30. Rickard MD, Adolph AJ. Vaccination of lambs against infection with *Taenia ovis* using antigens collected during short-term in vitro incubation of activated *T. ovis* oncospheres. *Parasitology* 1977; 75: 183-8.
31. Johnson KS, Harrison GBL, Lightowlers MW, O'Hoy KL, Cougle WG, Dempster RP, *et al.* Vaccination against ovine cysticercosis using a defined recombinant antigen. *Nature* 1989; 338: 585-7.
32. Lightowlers MW Lawrence SB, Gaucci CG, Young J, Ralston M, Maas D. Vaccination against hydatidosis using a defined recombinant antigen. *Parasite Immunology* 1996; 18: 457-62
33. De Aluja AS, Villalobos AN, Plancarte A, Rodarte LF, Hernandez M, Sciutto E. Experimental *Taenia solium* cysticercosis in pigs: characteristics of the infection and antibody response. *Veterinary Parasitology* 1996; 61: 49-59.
34. Evans CAW, Gonzalez AE, Gilman RH, Verastegui M, Garcia HH, Chavera A, *et al.* Immunotherapy for porcine cysticercosis: implications for prevention of human disease. *American Journal of Tropical Medicine and Hygiene* 1997; 56: 33-7.