

Tapeworm cysts in the brain: can we prevent it happening?



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Imagine the consternation; you are a member of an orthodox Jewish family and you and another family member are diagnosed with larvae of a pork tapeworm in your brain. You have recurrent seizures as a result. Ridiculous? Not for members of a Jewish community in New York where a Mexican domestic worker harbouring a *Taenia solium* tapeworm had apparently contaminated the family's food with eggs from her tapeworm¹.

T. solium is a cestode parasite that is transmitted between pigs and people. Pigs may harbour the parasite's larval stage in their muscles (Figure 1). If we accidentally eat one of these larvae in poorly cooked pig meat, the adult tapeworm will develop in our small intestine. Humans are the only definitive host (the host in which the parasite undergoes sexual reproduction) for this species of tapeworm. A person with the tapeworm releases the parasite's eggs in their faeces, and the lifecycle is completed if foods contaminated with these eggs, or indeed the faeces themselves, are consumed by a pig. The disease is fully transmitted only where pigs roam freely and humans defecate in areas where the pigs are free roaming. This does not happen in New York. However, it does happen across large areas of central and South America, Africa and east and south-east Asia.

In former times *T. solium* and the human brain disease that the parasite causes, neurocysticercosis, were endemic throughout Europe and other parts of the current-day First World; however, improved public sanitation and hygienic standards for raising pigs have seen the disease in pigs eliminated without any efforts directed specifically to the disease. Likely the same will happen, in time, through economic development in those areas of the world where the disease remains endemic today. Unfortunately, this is unlikely to occur in our lifetimes. Meanwhile, those living in the *T. solium* endemic areas of the world continue to suffer epilepsy and death due to the presence of *T. solium* cysts in their brain. Keep in mind

that people from poor countries can travel anywhere with their intestinal residents and deliver their tapeworm eggs to you or me, just as happened in the New York community referred to above. No point turning vego. Consider this: I have a worm and I am not particularly hygienic when I go to the toilet. I make your salad; bingo – see you in the neurology clinic.

T. solium is not an obscure parasite. The Food and Agriculture Organization of the United Nations considers it to be the most important foodborne parasitic infection from a global perspective². *T. solium* is the most frequent preventable cause of seizure disorders, being associated with 29% of people with epilepsy³. The World Health Organization lists *T. solium* as one of 16 Neglected Tropical Diseases, and is actively promoting efforts to reduce the parasite's transmission⁴.

For those living in poor countries in which *T. solium* is endemic, help is at hand from, of all places, Australia. I say 'of all places' because the parasite is not, and has never been known to be, endemic here. Nevertheless, a research program at the University of Melbourne with an original genesis way back in the 1970s led eventually to the development of both the first effective non-living vaccine against a eukaryotic parasite and eventually also to a vaccine that can stop pigs being infected with *T. solium*. The vaccine uses a recombinant antigen known as TSOL18. Several independent experimental trials of TSOL18 have confirmed that it is extraordinarily effective⁵. A field trial of the vaccine was undertaken in which pairs of young piglets were distributed to families living in a *T. solium* endemic region of north-east Cameroon⁶. One animal from each pair was vaccinated and one acted as a control. When the animals were of normal eating-age (~12 months), they were recovered from the farmers and assessed for *T. solium* infection. About 20% of the controls were infected but not a single parasite was found in any of the 110 vaccinated animals.

So far, so good. However the field trial involved a single cohort of animals that was vaccinated. In a real life situation, new disease susceptible piglets are born into the community more-or-less every day. Difficulties arise when we try to work out a feasible and sustainable program to deliver vaccination regularly enough to prevent pigs becoming infected on an on-going basis. The 'standard' vaccination protocol calls for two immunizations about a month apart. It is difficult to give any veterinary care to pigs in the communities where *T. solium* is transmitted; however having to deliver two vaccines a month apart would be close to impossible.



Figure 1. (a) *Taenia solium* cysts (cysticerci) in the tongue of a naturally infected pig (Photo: M. Donadeu). (b) Cysticerci in the muscles of a heavily infected pig.

Using knowledge about the parasite's development in pigs and information from the successful Cameroonian field trial, various scenarios involving vaccination in pigs were compared for their predicted effectiveness to control *T. solium* transmission⁷. One scenario that appeared relatively practical was to vaccinate at 4-monthly intervals. While the scenario looked good theoretically, it could not be recommended because we had no information about whether the vaccine would raise a protective response if the interval between primary and secondary injections was longer than 4 weeks.

Recently we have completed an experiment in which pigs received their secondary immunization with TSOL18 at 4, 8, 12, 16 or 20 weeks after the first injection⁸. The results were very promising. Antibody responses to the vaccine generally increased beyond the 'standard' 4-week interval. Responses seen in the animals vaccinated at a 12 week interval were the best, and field evaluation of *T. solium* interventions are about to begin in several endemic regions of Africa that will involve vaccinations at 3 or 4 monthly intervals.

Despite the solid progress that has been made so far, much remains to be achieved before we would be likely to see pig vaccination

contribute to reducing the incidence of neurocysticercosis in people. One major difficulty with implementation of pig vaccination to prevent transmission of *T. solium* is that the owners of the animals often have little incentive to undertake control measures because the infection does not often directly cause illness or death in pigs. In the future, combination vaccines that include TSOL18 and also antigens that can provide protection against pig deaths caused by Classical Swine Fever (CSF) in the Americas, or African Swine Fever (ASF) in African countries, would improve the acceptability of pig vaccination by providing an economic incentive for the animal owners to vaccinate. While the potential for a combination with CSF is something that can be explored immediately because commercial vaccines already exist, there is yet to be a commercial vaccine for ASF.

As for the Jewish community in New York who use domestic staff sourced from *T. solium* endemic countries, and of course all the people who live permanently in those endemic countries, the risk of exposure to *T. solium* remains. Hopefully we will be able to overcome the practical difficulties around working with pigs in *T. solium* endemic areas so that implementation of pig vaccination can reduce *T. solium* transmission and decrease the incidence of human neurocysticercosis as a result.

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Biography

Marshall Lightowlers has been a full-time research scientist supported by medical research funding for more-or-less all of his working life. He currently holds appointments as Laureate Professor at The University of Melbourne's Faculty of Veterinary and Agricultural Sciences, and Principal Research Fellow with the NHMRC.