

Of pigs and people—WHO prepares to battle cysticercosis

Neurocysticercosis, the brain sequela of pork tapeworm disease, is the commonest cause of epilepsy in developing countries. Plans are underway to stamp out the infection. John Maurice reports.

What do pigs, people, and epilepsy have in common? Cysticercosis—a disease caused by the humble pork tapeworm *Taenia solium*—is the answer. Humble is perhaps the wrong epithet since the tapeworm's larvae can enter the brain and trigger severe epileptic seizures. Of the estimated 50 million people with epilepsy in the world today, 80% live in areas infested with *T solium*, and in about 30% of these people the worm is the cause of their epilepsy.

Neurocysticercosis, as this form of cysticercosis is called, has become the commonest cause of acquired epilepsy in developing countries, according to WHO estimates. The infection, which can also cause chronic headache, meningitis, hydrocephalus, dementia, blindness, and even death, is particularly prevalent in Latin America, sub-Saharan Africa, and southeast Asia. A recent ranking exercise, reported on July 1 by the UN's Food and Agriculture Organization, put *T solium* at the head of a list of top-ten food-borne parasites of "greatest global concern". Last month, WHO convened delegates from countries with endemic neurocysticercosis, tropical disease experts and pharmaceutical industry executives—about 50 people in all—to a meeting in its Geneva headquarters to work out how best to lower or even eliminate the burden of the infection.

Complex life cycle

"Neurocysticercosis can cause intense suffering in the resource-poor areas where it is most prevalent", says Bernadette Abela-Ridder, team leader of the zoonotic neglected diseases unit at WHO's Department of Neglected Tropical Diseases and organiser of the WHO meeting. "In these areas the epileptic seizures create fear and social

stigma. But the parasite also causes losses in the food chain value of pork meat and, as a result, a loss of income for many poor families. Moreover, the life cycle of the tapeworm is complex and the link between the disease and the consumption of undercooked pork is not easily or commonly understood."

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The life cycle of the tapeworm is indeed complex. Pigs scavenging for food ingest the parasite's eggs that people carrying the adult tapeworm have excreted. The eggs hatch and the newborn larvae penetrate the small intestine and travel in the bloodstream to various parts of the pig's body where they form cysts. A person eating the infected pork ingests the cysts, which enter the small intestine and develop over several weeks into an adult tapeworm with a segmented ribbon-like body 2–4 metres long. The disease at this stage is called taeniasis and usually produces few or no symptoms in the infected person. From time to time, the worm expels one or more segments of its body into the environment, each segment carrying from 30 000 to 50 000 infective eggs. When a person eats food infected with these eggs, the eggs hatch and the larvae travel to various parts of the body, including the brain, where they can cause epilepsy.

Control measures

No-one at the WHO meeting talked of eradicating *T solium* disease but the possibility has been mooted on several occasions over the past two decades. In 1993, the International Task Force

on Disease Eradication put the disease on its list of six potentially eradicable diseases. In 2012, WHO put *T solium* disease on its roadmap for controlling neglected tropical diseases.

Control of *T solium* disease means, essentially, breaking the life cycle that perpetuates it. Eric Fèvre, professor of veterinary infectious diseases at the Institute of Infection and Global Health, Liverpool University, UK, who chaired the WHO meeting, presented a landscape analysis of attempts by endemic countries to halt transmission of the disease. Examples included: encouraging pig farmers to keep their pigs penned or tethered to prevent them from scavenging for food that might be infected with *T solium* eggs; encouraging people living in endemic areas to cook their pork meat thoroughly and to avoid defecating in the open; improving meat inspection and sanitation in slaughterhouses; administering anthelmintic (anti-worm) drugs to whole communities or to all the pigs in a pig farm.

"When we looked at the effectiveness of these control programmes, whether implemented alone or in various combinations, we had to



Pigs foraging in areas infected with *Taenia solium* can ingest the parasite's eggs



Chris Stowers/Panos

Consumption of undercooked infected pork can lead to taeniasis

conclude that, overall, countries with endemic cysticercosis seem to have achieved little success in controlling the disease", Fèvre told *The Lancet*. "The good news though is that we now have new tools and that the countries represented in this meeting have pledged their firm commitment to using them to lower the burden of *T solium* disease."

Two highly effective tools have recently been developed, thanks largely to GALVmed, a public-private alliance funded by the Bill & Melinda Gates Foundation and the UK Government. One is a vaccine for pigs. Developed by a research team at the University of Melbourne, Australia, the vaccine completely eliminated transmission of *T solium* in a field trial in Cameroon. Marshall Lightowlers, who heads the team, says he is delighted at the vaccine's performance. "An exciting additional possibility", he told *The Lancet*, "would be to use the vaccine in people, since it would almost certainly prevent brain cysts in humans. It would not, however, affect transmission of the parasite, so vaccinating pigs would still be needed. The big problem, though, will be to find financial support to do clinical trials of the human vaccine." The second new tool is a drug, oxfendazole, which was originally developed in the 1990s and used successfully to clear pigs of the infection. It has recently become available in a formulation that

facilitates its administration to pigs but has not yet been registered for use in people. Early trials have found it to be 100% effective in clearing cysts from infected pigs (but not so effective in clearing the brain of cysts).

Meeting participants were impressed with the findings of a pilot project undertaken by a research team in a large rural area of northern Peru with a population of about 75 000 people and 20 000 pigs. The project used both of the new tools (plus mass treatment of the human population with niclosamide, a vermifuge) and completely cleared all evidence of the disease in almost all of the 100 or so rural villages participating in the project. Hugo Garcia, head of the Cysticercosis Unit at the Institute of Neurological Sciences and director of the Global Health Center at the

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Universidad Heredia in Lima, Peru, who headed the research team, could not hide his optimism. "Advances that have been made over the past two decades in the treatment of people and pigs and in the prevention of disease in pigs have clearly made it possible to speed up elimination of *T solium* disease", he told the meeting. He admits, though, that the project was seeking proof of concept and was not intended as a fully fledged control intervention. "We wanted simply to find out if transmission of the disease could be halted", he said.

In the discussion that followed his presentation, several participants pointed out that the Peru project had benefited from financial support from the Gates Foundation and it would be difficult, if not impossible,

to transpose to the resource-strapped areas where cysticercosis prevails.

Pig focus

Speaking to *The Lancet*, WHO's Abela-Ridder explained that interventions to control *T solium* disease in the past focused mainly on people. "The results of this approach were disappointing. We expect to see much more progress in the near future by concentrating more on the pig, as was the case in the Peru project."

Diagnosis, too, has had a face-lift. Immunodiagnostic assays have been developed that detect parasite antigens and are more sensitive and specific than the traditional microscopy of expelled tapeworm eggs in the faeces of people or palpating the underside of a pig's tongue for the presence of cysts, as many pig farmers still do before selling their animals.

Strong commitment

The meeting agreed to create a global network led by WHO to support efforts by endemic countries to control *T solium* disease and to ease the burden of the disease borne by people with epilepsy. Partners in the network will be players on the health and veterinary scenes as well as tropical disease researchers. The pharmaceutical industry will also participate but with observer status. WHO will work in close collaboration with the UN Food and Agricultural Organization and the World Organisation for Animal Health in assisting endemic countries. Brazil, China, Côte d'Ivoire, Madagascar, Peru, and Vietnam will be among the first countries to participate in the network.

"We have everything we need to bring this disease to its knees", Fèvre enthuses. "We have the tools and we have a strong commitment from the countries and from WHO. We know now that we can go beyond words and do something real on a big scale. The ball is rolling."

John Maurice