

Neurocysticercosis Cysticercal Epilepsy: Understanding the Complex Relationship Between Tapeworm Cysts and Seizures

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ABSTRACT

Infection with the swine tapeworm (*Taenia solium*) causes a significant global burden of disease, not only in terms of human health, but also in terms of economic hardship on smallholder pig farmers due to pig cysticercosis infection. In most underdeveloped nations, neurocysticercosis accounts for around 30% of all epilepsy cases. The primary strategy for immune-diagnosis should thus be to determine whether the serological results are aligned with the imaging-based diagnosis. In an enzyme-linked immune-electro transfer blot format, antibodies are detected using lentil lectin-purified parasite antigens, whilst antigens are detected using a monoclonal antibody-based enzyme-linked immunosorbent assay (ELISA). *Taenia solium*'s life cycle, parasitology, and immunology is complicated. The 73rd World Health Assembly in November 2020 accepted the Organization's neglected tropical diseases plan for 2021-2030.

History:

Human infection with the cystic larvae (cysticerci) of the pig tapeworm *Taenia solium* and neurological illness has been documented since the 16th century, when Rumler in 1558 and Panarolus in 1652 observed vesicles in epileptic patients' dura mater and corpus callosum. Only two centuries later, in Germany, Kuchenmeister revealed that ingestion of cysticerci resulted in intestinal taeniasis (seen in the necropsy of an executed prisoner 72 hours after feeding him cysts), effectively ending the parasite life cycle [1, 4]. The immune diagnosis of cysticercosis is complicated and heavily impacted by the course of infection, disease burden, cyst location, and the host's immunological response [2]. *Taenia solium* was widespread in most of Europe until the early 1900s and remains so in many regions of the world, including most of Latin America, Sub-Saharan Africa, Southeast Asia, the Indian subcontinent, and portions of China [3, 5]. In these areas, cysticerci infection of the human brain (neurocysticercosis) accounts for almost one-third of all instances of epilepsy. Even in nonendemic locations such as the United States and Europe/United Kingdom, travel and immigration make NCC a health burden [6].

INTRODUCTION:

Cysticercosis is a tissue infection in which larvae of tapeworm infect human tissues and they grow and complete their lifecycle inside tissues. Tapeworms are parasites and they need to live in different animal hosts to survive and grow [7]. A form of Cysticercosis is Neurocysticercosis (NCC) which is also the common cause of adult epilepsy [8, 9]. It is a parasitic disease caused by the pig tapeworm *Taenia solium* in the human brain. Humans are their primary host where they reach their adult stage but pigs and, in some cases, cows are their secondary/intermediate host [10]. Cysticercal epilepsy is a potentially fatal medical problem that affects people across the world by causing seizures [11]. These tapeworm eggs and larvae can attach to any tissue in the body once they enter our blood stream, but if they pass on to our brain then they cause neurocysticercosis [12]. Tapeworm reaches the intestine through uncooked meat [13]. *Taenia solium* infection occurs when someone eats improperly cooked pork [14]. This pig tapeworm is found in virtually every developing country where pigs are reared. The coexistence of domestic pig rearing and poor sanitary conditions allows the parasite life cycle to be established, in which pigs become infected with the larval cystic stage (cysticercus) by ingesting infective *Taenia* eggs excreted in the stools of a human carrying the adult intestinal tapeworm [15]. Humans can also host the larval stage and become infected with cysticercosis through fecal-oral exposure [16]. While most cysts are asymptomatic and go unnoticed, cysts in the nervous system (NCC) are a major cause of neurological morbidities in endemic areas [17]. *Taenia solium*, a zoonotic cestode, poses a significant public health and economic concern. *T. solium* is the foodborne parasite infection that causes the most disability-adjusted life-years (DALYs) worldwide, with an estimated 2.78 million DALYs in 2010 [18]. When humans consume *T. solium* eggs, cysticerci (human cysticercosis, or HCC) develops in the central nervous system, resulting in neurocysticercosis (NCC). The greatest health burden associated with *T. solium* causes roughly one-third of epilepsy/seizure disorders in endemic environments [19].

CASE STUDY:

A case study published in the new England journal of Medicine talks about a man who went to the hospital after having seizure at 4am. The doctors then saw him having a 2-minute-long seizure where he lost consciousness. They started to investigate his medical history and his general health. Everything seemed fine and healthy. He didn't smoke and he drank only occasionally, and he had been perfectly fine in the days leading up to the seizures. After performing a CT scan of his brain, the doctors realized that he had something called Neurocysticercosis. NCC is extremely common in Asia and Central America. In this case study the 38 years old man who had seizures had lived in rural Guatemala before moving to the U.S. So, the doctors were able to see his history and narrow down the cause of his seizures to NCC. He was put on anti-parasitic, anti-seizure and anti-inflammatory drugs and he was discharged five days later [20].

Cysticercal Epilepsy:

Cysticercal epilepsy is a neurological condition caused by an infection of *Taenia solium* larvae, the larvae of the pork tapeworm. This parasitic infection, known as cysticercosis, arises when people consume contaminated food or drink that contains tapeworm eggs. Once swallowed, these eggs can develop into cysts, these eggs or larvae calcify in tissues, most commonly in the muscles, eyes, and brain. The mere presence of cysts in the brain can cause seizures, which is the hallmark of cysticercal epilepsy [21].

Symptoms of Cystical Epilepsy:

- Seizures: The most noticeable symptom of cysticercal epilepsy is recurring seizures, which can vary in frequency and severity.
- Headaches: People with cysticercal epilepsy frequently feel intense headaches, which may be specific to the location where the cyst is growing.
- Cognitive Impairment: Cognitive processes such as memory and focus can be harmed when cysts press against brain structures.
- Neurological Deficits: Other neurological deficits such as weakness, vision problems, and speech difficulties may emerge depending on the size and location of the cysts.
- Nausea and Vomiting: As a result of increased intracranial pressure, some people may experience nausea and vomiting. Personality changes, mood fluctuations, and altered behavior patterns might also be seen.

Prevalence and geographical distribution:

Cysticercal epilepsy is more common in areas with inadequate sanitation and limited access to safe drinking water and waste disposal facilities. Several countries in Latin America, Sub-Saharan Africa, Southeast Asia, and parts of India are considered high-risk areas. In these areas, eating patterns and living conditions increase the danger of ingesting tapeworm eggs, which can develop to cysticercosis and, later, cysticercal epilepsy [22]. This condition's severity varies greatly between continents and even within various parts of the same country. Control and prevention efforts in endemic areas focus on improving sanitary conditions, health literacy, and access to healthcare, which can greatly lower the occurrence of cysticercal epilepsy [23].

The Tapeworm life cycle:

Taenia solium has a complicated life cycle that includes a typical intermediate host (pig) that hosts the parasitic larvae in its tissues and a single definitive host (human) that hosts the mature tapeworm in its intestinal tract [24]. The adult tapeworm normally excretes eggs or proglottids with the stool of the human final host, each egg carrying an infective hexacanth oncosphere (embryo) covered by a thick keratin embryophore [25, 26]. Free-roaming pigs have access to human excrement in regions with inadequate sanitation and eat on them, consuming tapeworm eggs [27]. The embryos are released from the eggshells, and they are activated by the action of gastric and intestinal juices, making use of their three sets of oncospherical hooks [28], stick to the epithelium of the intestine, and actively cross the intestinal mucosa, a process facilitated by parasite proteases secretion [29, 30]. The embryos enter the pig's circulatory system after passing the intestinal mucosa. Infective embryos are eventually transmitted through the bloodstream, where they establish themselves and mature into cystic, fluid-filled larvae or cysticerci, each having an invaginated scolex with a double crown of hooks along with four muscular suckers. *T. solium* taeniasis develops when humans consume undercooked pork harboring cysticerci. Following exposure to bile and intestinal juices, the scolex in the cyst evaginates, attaches to the intestinal mucosa via its suckers and double crown of hooks, and starts to produce proglottids at its neck region, making a strobila which develops into an adult tapeworm [30, 31].

Neurological impact of Tapeworm:

Neurocysticercosis is a disorder that occurs when tapeworm cysts form in the brain. Cysts can cause swelling, elevated intracranial pressure, and brain tissue damage [32, 33]. These cysts, depending on their size and location, can disrupt normal neurological activities, resulting in a variety of symptoms such as seizures, headaches, cognitive dysfunction, and neurological disorders. Cysts in the brain can cause seizures by irritating and inflaming brain tissue. Seizures can develop if cysts obstruct the flow of cerebrospinal fluid or injure blood vessels, further affecting brain function [34, 35].

Diagnosis:

- Cysticercal epilepsy is normally diagnosed using a combination of medical history, clinical evaluation, and diagnostic tests. Imaging examinations, such as CT scans or MRIs, are critical in finding brain cysts.
- Blood tests can occasionally aid in the detection of antibodies linked to the existence of tapeworm larvae in the body.
- A lumbar puncture (spinal tap) may be conducted to look for signs of infection or inflammation in the cerebrospinal fluid.

Conclusion:

To summarize, cysticercal epilepsy is a difficult medical disorder with major public health implications, particularly in areas with inadequate sanitation and insufficient access to treatment. Understanding the complex connection between seizures and tapeworm cysts and it is essential for developing effective preventative and treatment techniques. We can reduce the impact of this condition on afflicted individuals and communities by improving hygiene, applying control measures, sharing actual events, and furthering ongoing research. Greater awareness and research are essential for advancement in cysticercal epilepsy and, ultimately, improving the lives of those affected by this complicated condition.

References

- [1] Garcia, H. H., O'Neal, S. E., Noh, J., & Handali, S. (2018). Laboratory diagnosis of neurocysticercosis (*Taenia solium*). *Journal of clinical microbiology*, 56(9), 10-1128.
- [2] Garcia, Hector H., Armando E. Gonzalez, and Robert H. Gilman. "Taenia solium cysticercosis and its impact in neurological disease." *Clinical microbiology reviews* 33.3 (2020): 10-1128.
- [3] Dixon, Matthew A., et al. "Global Force-of-Infection Trends for Human Taenia solium Taeniasis/Cysticercosis." *medRxiv* (2022): 2022-02.
- [4] Nyangi, Chacha, et al. "Knowledge, attitudes and practices related to Taenia solium cysticercosis and taeniasis in Tanzania." *BMC Infectious Diseases* 22.1 (2022): 534.
- [5] Li, Taoying, et al. "High prevalence of taeniasis and Taenia solium cysticercosis in children in western Sichuan, China." *Acta Tropica* 199 (2019): 105133.
- [6] Prodjinotho, Ulrich Fabien, et al. "Host immune responses during Taenia solium Neurocysticercosis infection and treatment." *PLoS neglected tropical diseases* 14.4 (2020): e0008005.
- [7] Brunet, J., Benoild, A., Kremer, S., Dalvit, C., Lefebvre, N., Hansmann, Y., ... & Candolfi, E. (2015). First case of human cerebral Taenia martis cysticercosis. *Journal of clinical microbiology*, 53(8), 2756-2759. Dixon, Matthew A., et al. "Taenia solium taeniasis/cysticercosis: from parasite biology and immunology to diagnosis and control." *Advances in Parasitology* 112 (2021): 133-217.

- [8] Nguyen, David C., Ankita P. Desai, and Sree S. Cherian. "The Brief Case: the Boy Who Cried Worm." *Journal of Clinical Microbiology* 61.1 (2023): e00553-22.
- [9] Tappe, Dennis, et al. "Molecular identification of zoonotic tissue-invasive tapeworm larvae other than *Taenia solium* in suspected human cysticercosis cases." *Journal of clinical microbiology* 54.1 (2016): 172-174.
- [10] Veeravigrom, Montida, and Lunliya Thamprankul. "Neurocysticercosis in children." *Pediatric Clinics* 69.1 (2022): 115-127.
- [11] Nash, T. E., Del Brutto, O. H., Butman, J. A., Corona, T., Delgado-Escueta, A., Duron, R. M., ... & Garcia, H. H. (2004). Calcific neurocysticercosis and epileptogenesis. *Neurology*, 62(11), 1934-1938.
- [12] Garcia HH, Gonzalez AE, Evans CAW, Gilman RH, The Cysticercosis Working Group in Peru. *Taenia solium* cysticercosis. *Lancet* 2003;362: 547–556.
- [13] Schantz PM, Wilkins PP, Tsang VCW. Immigrants, imaging and immunoblots: the emergence of neurocysticercosis as a significant public health problem. In: Scheld WM, Craig WA, Hughes JM, eds. *Emerging infections* Washington: ASM Press, 1998;213–241.
- [14] White AC, Jr. Neurocysticercosis: a major cause of neurological disease worldwide. *Clin Infect Dis* 1997;24:101–113; quiz 114–115.
- [15] Del Brutto OH, Santibanez R, Noboa CA, Aguirre R, Diaz E, Alarcon TA. Epilepsy due to neurocysticercosis: analysis of 203 patients. *Neurology* 1992;42:389–392.
- [16] Flisser A. Taeniasis and cysticercosis due to *T. solium*. In: Sun T, ed. *Progress in clinical parasitology*. New York: CRC Press, Inc., 1994;77– 116.
- [17] Dixon, M. A., Winskill, P., Harrison, W. E., Whittaker, C., Schmidt, V., Flórez Sánchez, A. C., ... & Basañez, M. G. (2022). Global Force-of-Infection Trends for Human Taenia solium Taeniasis/Cysticercosis. *medRxiv*, 2022-02.
- [18] Dixon-Zegeye, M., Winskill, P., Harrison, W., Whittaker, C., Schmidt, V., Flórez Sánchez, A., ... & Basañez, M. G. Global force-of-infection trends for human taenia solium taeniasis/cysticercosis.
- [19] Holt HR, Inthavong P, Khamlome B, Blaszak K, Keokamphe C, Somoulay V, Phongmany A, Burr PA, Graham K, Allen J, Donnelly B, Blacksell SD, Unger F, Grace D, Alonso S, Gilbert J (2016) Endemicity of Zoonotic Diseases in Pigs and Humans in Lowland and Upland Lao PDR: Identification of Socio-cultural Risk Factors PLoS Neglected Tropical Diseases.
- [20] Yoshino K. Studies on the post-embryonal development of *Taenia solium*: III. On the development of *Cysticercus cellulosae* within the definitive intermediate host. *J Med Assoc Formosa* 1933;32:166–169.
- [21] Grove DI. 1990. A history of human helminthology. CABI, Wallingford, England.
- [22] Kean BH, Mott KE, Russell AJ. 1978. Tropical medicine and parasitology. Classic investigations, vol 2. Cornell University Press, Ithaca, NY.
- [23] Brizzi K, Pelden S, Tshokey T, Nirola DK, Diamond MB, Klein JP, Tshering L, Deki S, Nidup D, Bruno V, Dorny P, Garcia HH, Mateen FJ, Bhutan Epilepsy Project. 2016. Neurocysticercosis in Bhutan: a cross-sectional study in people with epilepsy. *Trans R Soc Trop Med Hyg* 110:517–526.
- [24] Debaqç G, Moyano LM, Garcia HH, Bomedienne F, Marin B, Ngoungou EB, Preux PM. 2017. Systematic review and meta-analysis estimating association of cysticercosis and neurocysticercosis with epilepsy. *PLoS Negl Trop Dis* 11:e0005153.
- [25] Melki J, Koffi E, Boka M, Toure A, Soumahoro MK, Jambou R. 2018. Taenia solium cysticercosis in West Africa: status update. *Parasite* 25:49.
- [26] Pawlowski, Z., Allan, J., & Sarti, E. (2005). Control of Taenia solium taeniasis/cysticercosis: from research towards implementation. *International journal for parasitology*, 35(11-12), 1221-1232.
- [27] Lightowers, M. W. (2013). Control of Taenia solium taeniasis/cysticercosis: past practices and new possibilities. *Parasitology*, 140(13), 1566-1577.
- [28] Wu, W., Qian, X., Huang, Y., & Hong, Q. (2012). A review of the control of clonorchiasis sinensis and Taenia solium taeniasis/cysticercosis in China. *Parasitology research*, 111, 1879-1884.
- [29] Rodriguez-Canul, R., Fraser, A., Allan, J. C., Dominguez-Alpizar, J. L., Arguez-Rodriguez, F., & Craig, P. S. (1999). Epidemiological study of Taenia solium taeniasis/cysticercosis in a rural village in Yucatan state, Mexico. *Annals of Tropical Medicine & Parasitology*, 93(1), 57-67.
- [30] Gabriël, S., Dorny, P., Mwape, K. E., Trevisan, C., Braae, U. C., Magnussen, P., ... & Johansen, M. V. (2017). Control of Taenia solium taeniasis/cysticercosis: The best way forward for sub-Saharan Africa?. *Acta tropica*, 165, 252-260.
- [31] Cruz, M., Davis, A., Dixon, H., Pawlowski, Z. S., & Proano, J. (1989). Operational studies on the control of Taenia solium taeniasis/cysticercosis in Ecuador. *Bulletin of the World Health Organization*, 67(4), 401.
- [32] Allan, J. C., Velasquez-Tohom, M., Garcia-Noval, J., Torres-Alvarez, R., Yurrita, P., Fletes, C., ... & Craig, P. S. (1996). Epidemiology of intestinal taeniasis in four, rural, Guatemalan communities. *Annals of Tropical Medicine & Parasitology*, 90(2), 157-165.
- [33] Garcia-Noval, J., Allan, J. C., Fletes, C., Moreno, E., DeMata, F., Torres-Alvarez, R., ... & Craig, P. S. (1996). Epidemiology of Taenia solium taeniasis and cysticercosis in two rural Guatemalan communities. *The American journal of tropical medicine and hygiene*, 55(3), 282-289.
- [34] Garcia-Noval, J., Sanchez, A. L., & Allan, J. C. (2002). 10 Taenia solium Taeniasis and Cysticercosis in Central America. *Taenia Solium Cysticercosis: From Basic to Clinical Science*, 91.