Neglected Parasitic Infections in the United States: Cysticercosis

Paul T. Cantey,* Christina M. Coyle, Frank J. Sorvillo, Patricia P. Wilkins, Michelle C. Starr, and Theodore E. Nash
Division of Parasitic Diseases and Malaria, Centers for Disease Control and Prevention, Atlanta, Georgia; Department of Medicine, Albert Einstein College of Medicine, Bronx, New York; Department of Pediatrics, University of Washington, Seattle, Washington; Department of Epidemiology, School of Public Health, University of California–Los Angeles, Los Angeles, California; Gastrointestinal Parasites Section, Laboratory of Parasitic Diseases, National Institutes of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland

Abstract. Cysticercosis is a potentially fatal and preventable neglected parasitic infection caused by the larval form of Taenia solium. Patients with symptomatic disease usually have signs and symptoms of neurocysticercosis, which commonly manifest as seizures or increased intracranial pressure. Although there are many persons living in the United States who emigrated from highly disease-endemic countries and there are foci of autochthonous transmission of the parasite in the United States, little is known about burden and epidemiology of the disease in this country. In addition, despite advances in the diagnosis and management of neurocysticercosis, there remain many unanswered questions. Improving our understanding and management of neurocysticercosis in the United States will require improved surveillance or focused prospective studies in appropriate areas and allocation of resources towards answering some of the key questions discussed in this report.

INTRODUCTION

Cysticercosis is a neglected parasitic infection caused by the larval form of the pork tapeworm Taenia solium. Neurocysticercosis, the most serious clinical manifestation of cysticercosis, is the leading cause of acquired epilepsy in disease-endemic countries, accounting for 29% of persons with epilepsy; this number may approach 50% in some disease-endemic areas.2–4 It has been increasingly recognized as a cause of severe and preventable neurologic disease in the United States,5 with up to 2% of emergency department visits for seizures being caused by the disease.6 Despite its importance much remains unknown about the impact of neurocysticercosis on human health in the United States.

THE DISEASE

Parasite life cycle. Humans with taeniasis are infected with the adult form of T. solium, which resides in the human intestine. The adult tapeworm excretes eggs, which are passed in the stool and can contaminate food, water, or soil. Once ingested by humans or pigs, T. solium eggs develop into embryos that penetrate the intestinal wall and disseminate hematogenously to various tissues. The parasite matures into the larval stage in the tissue and encysts into a cysticercus. No further development occurs until the tissue cysticercus is ingested. The parasite completes its life cycle when humans ingest raw or undercooked pork products contaminated with cysticerci. Larvae are released from the cysticerci and attach to the small bowel to develop into the adult form of the tapeworm. Pigs perpetuate the life cycle by serving as intermediate hosts and the source of cysts, which develop into tapeworms in humans (taeniasis). Cysticercosis occurs only after ingestion of eggs from a person with taeniasis. Transmission is fecal-oral; this includes transmission through person-to-person contact, through autoinfection, or through contaminated food.7 A visual representation of the life cycle can be found at http://www.cdc.gov/parasites/cysticercosis/biology.html.

Clinical disease. The cysts of cysticercosis may occur anywhere in the body but commonly develop in the muscles, subcutaneous tissues, or brain.8 Symptomatic human cysticercosis almost always presents as neurocysticercosis. Seizures are the most common manifestation of neurocysticercosis, although headaches, hydrocephalus, or focal neurologic signs are other common manifestations.5,9 Symptoms of neurocysticercosis are caused by either the inflammatory response of the host or mass effect and may present months or years after initial infection. Cyst location, stage (e.g., viable or degenerating), number, mass effect, and accompanying inflammation are the major determinants of symptomology, and extraparenchymal neurocysticercosis produces more serious disease.10–12 Cerebral calcifications are the most common radiologic finding of neurocysticercosis and are frequently the only finding in populations in disease-endemic areas.13 Although only a small subset of patients with calcifications have seizures or epilepsy, most persons with seizures only have calcifications.13 Edema develops around the calcification(s) and incites seizures in half of those patients with symptomatic calcifications.14 These patients with perilesional edema are often unnecessarily treated with anthelminthics because calcified lesions contain no living parasites.15

Although previously believed to be uncommon, two recent retrospective reviews of patients who came to U.S. medical centers found almost one-third of the patients had extraparenchymal involvement.16,17 Clinical manifestations of extraparenchymal disease include headache, signs resulting from hydrocephalus, basilar arachnoiditis, and cerebrovascular complications.18 Subarachnoid involvement of the spinal cord is common in patients with basilar subarachnoid disease but is usually clinically silent at presentation.19

Diagnostic tests. The diagnosis of neurocysticercosis relies on neuroradiologic imaging and laboratory testing. Computed tomographic scans and magnetic resonance imaging can provide vital prognostic information and may be diagnostic if a scolex (anterior end of a tapeworm where the suckers or hooks are localized) is visualized. The advantages and disadvantages of computed tomographic scans and magnetic resonance imaging as part of the evaluation of persons with...
suspected neurocysticercosis have been discussed in more detail elsewhere. Serologic tests can assist in making the diagnosis in instances when a scolex is not visualized. The enzyme-linked immunoelectrotransfer blot (EITB) is currently the best tool for diagnosis because it has a specificity of 100% and a sensitivity of 94–100%. However, the sensitivity of EITB is lower in the presence of a single cyst (approximately 50%) or calcified cysts (approximately 75%). Currently, a number of tests that detect the circulating parasite antigen in the blood and cerebrospinal fluid have been developed and are undergoing validation. Preliminary results indicate that these tests may be useful for assessing the success of antihelminthic therapy in patients with extraparenchymal disease.

Taeniasis is diagnosed by microscopic identification of eggs and proglottids (segment of a tapeworm that contains the sexual organs) in feces. Examination of three stool samples collected on different days increases the sensitivity of the test for detecting eggs. Eggs of Taenia spp. cannot be differentiated, but a species determination may be possible if mature, gravid proglottids or the scolex are present. Recently developed coproantigen and molecular assays are more sensitive than stool examination, but neither is widely available. Serologic methods, which are available only in research settings, may be used to identify T. solium tapeworm carriers; however, because antibody persists for an unknown period after treatment, serologic testing may produce false-positive results if a patient has been treated for taeniasis in the recent past.

Management. The treatment of neurocysticercosis is complex and readers are referred elsewhere for more complete discussion of its intricacies. The focus of management should be to control seizures, mass effect, inflammation that may induce infarct, and intracranial hypertension. Therapy may include anticonvulsants, corticosteroids, or neurosurgical intervention to control acute neurologic complications. Therapy directed at the parasite should be used only when appropriate. Albendazole (the drug of choice) or praziquantel (second-line therapy) should be accompanied by corticosteroids to control the perilesional edema that develops as the parasites die and are recognized by the immune system. Shunts are frequently required to manage extraparenchymal disease. Minimally invasive endoscopic excision of intraventricular cysts is replacing standard microsurgical procedures in many instances. Because persons only develop neurocysticercosis in the United States and their close contacts should be screened for taeniasis.

BURDEN OF DISEASE IN THE UNITED STATES

Historically, neurocysticercosis in the United States has been believed to mainly affect immigrants from Latin America, where the disease is endemic. However, there have been case reports of disease acquired within the United States and by U.S. travelers who have visited disease-endemic countries. Despite the increasing recognition of the importance of neurocysticercosis in this country, essential data on the burden are lacking. Our limited understanding of the burden of neurocysticercosis is caused by multiple factors, including that the disease is only reportable in Arizona, California, New Mexico, Oregon, and Texas, and that under-reporting exists even in those jurisdictions where it is reportable. In addition, the available population-based survey data cannot be combined to derive population-level estimates because of the differing methods used (e.g., statewide discharge data versus theoretical catchment area).

There are few data on the prevalence of taeniasis, or adult tapeworm infection, in the United States. However, persons with taeniasis are the source of autochthonous transmission of cysticercosis. The two published population-based studies of taeniasis suggest that the prevalence may be 0.5–3% in select populations. Data on the seroprevalence of cysticercosis in the United States are also limited. A small serosurvey in California, which examined a mixture of migrants and local residents, reported an overall seroprevalence by EITB of 1.8%, with a seroprevalence of 2.0% in migrants and 1.7% in residents. A serosurvey of members of an Orthodox Jewish Community in New York City that was performed in 1992–1993 in response to an earlier outbreak found a seroprevalence of 1.3% by EITB.

Burden of neurocysticercosis. A recent literature review of all case series in the United States with at least 20 patients during 1980–2004 identified 1,494 patients with neurocysticercosis. The authors noted that 76 infections (5.1%) were likely acquired within the United States. Another case-series published since this the review confirmed that the burden of disease remains significant, although neither report can be used to determine prevalence or incidence of symptomatic infection.

Some disease burden data can be gleaned from state-specific, surveillance-based epidemiologic studies in California and Oregon. These studies have determined that the incidence or incidence of hospitalization for neurocysticercosis ranges from 0.2–1.1/100,000 persons in the general population and 1.5–5.5/100,000 persons in the Hispanic population. The studies found that 5.4–18% of the hospitalized patients were born in the United States. The death rate ranged from 2% to 9.8%. Although these studies from Oregon and California represent the only population-based estimates of hospitalization for neurocysticercosis, it is likely that they underestimate the incidence of disease.

There has been one prospective study of the prevalence of neurocysticercosis in U.S. patients who came to emergency departments with seizures. This survey was conducted in the emergency departments of 11 institutions throughout the United States and found that 2.1% of a cohort of 1,801 patients with seizure disorders had neurocysticercosis, with a range of 0–10% by institution. The prevalence of neurocysticercosis among Hispanic patients with seizures in the study ranged from 9% to 13.5%; the overall prevalence was 9%. Five (21%) of the patients with neurocysticercosis were born in the United States. Previous retrospective studies found similar frequencies of seizure disorders attributable to neurocysticercosis.

Hospital-based data from several centers in California indicate that neurocysticercosis consumes significant health resources in the state. In one study, which included nearly 4,000 hospitalizations over more than 10 years, the total charge of hospitalization was $136.2 million, and the average annual charge was $7.9 million. The average hospital charge was $37,000 per hospitalization. In a later study, which included 304 hospitalizations for neurocysticercosis in a single
year, hospital charges totaled $17 million, and the average charge was $57,800.37

Data from the National Center for Health Statistics have been used by investigators to calculate a national estimate of mortality caused by neurocysticercosis.33 The investigators reported 221 neurocysticercosis-related deaths during 1990–2002, which represented an annual age-adjusted mortality rate of 0.06 per million population. Most deaths were reported in Hispanics (84.6%), with at least one neurocysticercosis death reported from 20 states; California accounted for 57% (126 deaths) of the total. Notably, 15% of all neurocysticercosis deaths were in U.S.-born patients.

Sources of the burden of infection. Much of the burden of cysticercosis in the United States is caused by the high burden of imported disease. Most immigrants with cysticercosis are from disease-endemic areas of Mexico and Latin America, but infected persons emigrate from areas in Asia and sub-Saharan Africa that also have high burdens of infection.33,52 Few studies to provide accurate estimates have been conducted among populations from areas that are highly endemic for this disease. However, based on studies in California53 and of populations of resettled refugees,55 taeniasis prevalence estimates in the range of 1–2% and serologic evidence of cysticercosis in the range of 5–20% are reasonable. It is important to note that because the disease is focal and typically less prevalent in urban areas, the numbers mentioned in the previous sentence should not be extrapolated to all patient populations.

Neurocysticercosis may be locally acquired. A recent review of all published U.S. data on locally acquired infection during 1954–2005 identified 78 cases reported from 12 states.50 Some of these infections had been linked to individual tapeworm carriers from disease-endemic countries30–40 although others could not identify such a link.39,57 Some infections among U.S.-born persons may reflect exposure to T. solium during travel to disease-endemic areas rather than local acquisition. Travel-associated cysticercosis has been described usually after trips to Mexico or other Latin American countries that have endemic disease.39,49 However, acquisition of neurocysticercosis during travel is not common and is more likely in long-term travelers.58

GAPS

There are many gaps in our understanding of the epidemiology of cysticercosis in the United States. Data on the prevalence of infection, the incidence of hospitalization, and the disease burden are incomplete and need to be improved. Mandatory reporting of the diagnosis or the creation of an integrated national medical database would enable a more complete understanding of the burden, particularly the burden of long-term care of non-hospitalized patients, although underreporting and missed diagnoses would likely be common until U.S. clinicians have a better understanding of the disease. In the absence of these factors, the Nationwide Inpatient Sample (http://www.hcup-us.ahrq.gov/nisoverview.jsp), a 20% sample of hospital discharges from acute care hospitals in the United States, may be of value in better defining the burden of symptomatic neurocysticercosis. Otherwise, we will continue to be dependent on data collected in the few areas of the country that have taken an active interest in this parasitic infection of neglected people. Of particular concern is the consistent finding of U.S.-born persons with taeniasis or autochthonously acquired cysticercosis. Although their infections may be primarily explained by exposure to persons from disease-endemic countries, focal areas of where the complete transmission cycle is maintained (i.e., there are infected pigs and humans) are possible. Characterization of these foci of transmission will require systematic investigation by using a standardized approach to assess symptoms, sensitive and specific serologic and stool testing, and appropriate neuroimaging. Finally, there are no prospective data on the risk of dying from neurocysticercosis.

Laboratory diagnostics for neurocysticercosis improved greatly with the development of the EITB. However, we need to better understand the dynamics of the test, particularly the decay of antibody after treatment. Preliminary data suggest that antigen testing can differentiate active from inactive disease in subarachnoid and ventricular neurocysticercosis and possibly parenchymal neurocysticercosis,25,59,60 but additional studies are need to confirm these findings. Antigen detection may prove to be most promising in following the response to therapy and defining treatment endpoints.55 A good serologic test for active taeniasis would simplify the search for human carriers who might infect others.

Although there is some consensus about the management of parenchymal disease and calcified lesions, many questions remain about the optimal treatment regimen for neurocysticercosis, the utility of corticosteroid-sparing adjunctive therapy (e.g., methotrexate), and the optimal management of subarachnoid disease.12,29,52 Randomized trials are needed to address several disease management priorities. One priority is to develop a better understanding of the contribution of perilesional edema to symptomatic neurocysticercosis and to determine when edema needs to be treated. Another priority is to demonstrate the benefit of medical management of subarachnoid disease. The best regimens for corticosteroids and steroid-sparing agents remain unclear and algorithms for radiologic or serologic monitoring of therapy need to be developed and tested. Randomized trials of the minimally invasive surgical therapy for intraventricular disease are needed to guide surgical practice.

CONCLUSIONS

Although there remain many uncertainties about the burden, optimal medical management, and most effective preventive and screening programs for neurocysticercosis, it is certain that there are patients with symptomatic infection who remain undiagnosed and patients with the diagnosis who receive suboptimal treatment. Improving our understanding of the epidemiology of the disease in the United States and its management will require consistent prioritization of efforts to close the identified gaps. These scientific endeavors need to be accompanied by increased awareness among health care providers and better public health outreach to affected populations, including populations that are difficult to reach with educational messages (e.g., undocumented immigrants or refugees).

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