SURVEILLANCE FOR *TAENIA SOLIUM* PARASITIC INFECTION IN OREGON

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ABSTRACT

Introduction

Neurocysticercosis (NCC) is parasitic central nervous system infection by *Taenia solium* larval cysts. The epidemiology in Oregon is poorly understood and the public health role is unclear.

Objectives

We conducted population surveillance in Oregon to determine the incidence of NCC, and to pilot targeted screening for tapeworms among affected households.

Methods

We examined hospital billing codes and medical charts for NCC diagnosed between January 1, 2006 and December 31, 2009. We collected stool and blood from household members in a subset of recent cases to screen for *T. solium* tapeworms and cysticercosis.

Results

We identified 87 incident cases for an annual incidence of 5.8/100,000 population among Hispanics. In 22 household investigations we found 2 additional NCC cases, but no evidence of current tapeworm infection.

Conclusion

Taenia solium infection is an important clinical and public health disease in Oregon, particularly among Hispanics. Public health intervention should focus on family members of identified cases, as household investigations can identify additional *T. solium* infection.

CHAPTER 1 – BACKGROUND ON *TAENIA SOLIUM* INFECTION

Introduction

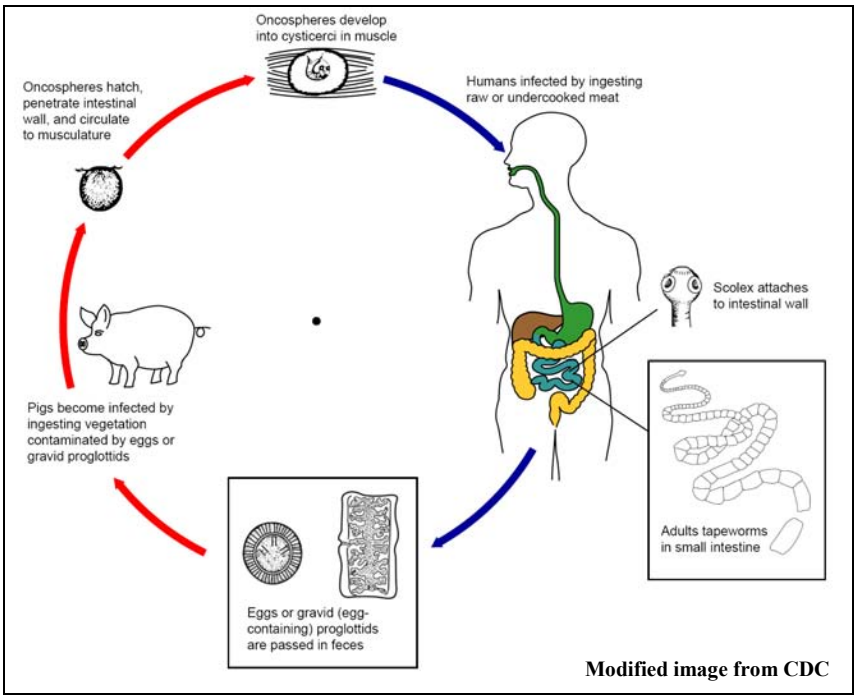
Neurocysticercosis (NCC) is a parasitic disease caused by central nervous system (CNS) infection of *Taenia solium* larval cysts. It is the most common parasitic infection of the CNS and the leading cause of acquired epilepsy in Latin America, Southeast Asia and Central Africa.[1,2] In endemic countries, NCC is responsible for 30-50% of all seizure cases.[3,4,5] It is also increasingly recognized as an important clinical and public health disease in the United States, primarily affecting immigrants and travelers from endemic regions. Worldwide it is a common disease, with over 50 million people affected.[6] NCC is potentially preventable by interruption of the fecal-oral route of transmission.

Etiology and transmission

The zoonotic lifecycle of *T. solium* cestode parasite is complex, involving both humans and pigs (Figure 1). Humans are the only definitive host capable of harboring an adult intestinal tapeworm, which reproduces by shedding infective eggs in the host feces. In the parasitic lifecycle, foraging pigs consume these eggs; the eggs develop into oncospheres, invade the intestinal wall and disseminate via the bloodstream to form larval cysts throughout the pig's body. The cycle completes when a human ingests poorly-cooked infected pork. After ingestion, the cyst evaginates and the protoscolex contained within attaches to the small bowel mucosa. Within 2-3 months, the immature tapeworm has

developed into a hermaphroditic adult capable of producing 50,000 to 200,000 eggs each day over a lifespan thought to average several years.[7] This complete lifecycle occurs primarily in regions where sanitation is poor and where pigs are allowed to roam free with access to raw sewage.

Figure 1. Lifecycle of *Taenia solium*

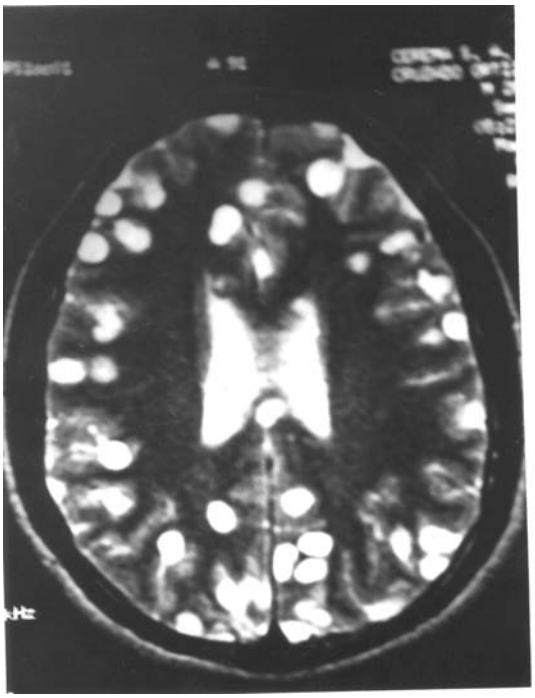


Clinical manifestations of infection

Cysticercosis is the condition that results from fecal-oral transmission of tapeworm eggs shed by a tapeworm carrier. Although cysts can form in most body tissues, they typically only cause symptoms when they develop in the central nervous system (CNS), a condition known as neurocysticercosis (NCC) (Figure 2). Seizures and headache are the most commonly recognized

symptoms, although cognitive dysfunction, visual complaints, focal neurologic deficits and psychiatric disturbances also occur.[8] Although rare, hydrocephalus and death may result if ventricular cysts obstruct the flow of cerebrospinal fluid. Infection with the adult intestinal tapeworm (taeniasis) is rarely symptomatic, although patients occasionally note the passage of gravid proglottids (tapeworm segments) in the stool.

Figure 2. Computerized tomography (CT scan) of neurocysticercosis, showing scattered fluid-filled spherical cysts in white.



Epidemiology of *Taenia solium* infection in the United States

Neurocysticercosis and its associated clinical and public health burden have been increasingly documented in the United States.[9,10,11,12,13,14] Population-based data have arisen primarily from states where *T. solium* infection is reportable to

public health authorities. California became the first state to require reporting in 1989; 112 cases of cysticercosis were reported in the first year, representing a crude annual incidence of 0.02 per 100,000 overall population, or 1.5 per 100,000 among Hispanics.[14] Separate data from Los Angeles County were similar, with an annual incidence of 1.6 per 100,000 among Hispanics.[13] A retrospective case-series from Oregon based on hospital discharge diagnoses estimated an annual incidence of 3.1 per 100,000 Hispanics.[11] Interestingly, these figures are higher than the incidence reported from Mexico City (0.8 per 100,000), although this probably represents more robust domestic surveillance with higher case ascertainment.[1]

Two seroprevalence studies have been conducted in the United States, demonstrating persistence of circulating antibodies against *T. solium* cysts among Hispanics in the United States. A study of adult migrant farmworkers in California, for example, showed 2.8% seroprevalence of antibodies specific to cysticercosis.[15] An earlier study among migrant Hispanics in North Carolina documented 10% with circulating antibodies, although the assay used was less specific than the Western Blot which is the current gold-standard.[16] Population-based seroprevalence studies can be difficult to interpret however, as the proportion of positives representing active infection versus remote endemic exposure versus ongoing exposure cannot be determined. Seroprevalence in Mexico ranges from 4% to 12%.[17]

With a couple of notable exceptions, few studies have attempted to document the public health impact of *T. solium* infection in the United States. In Los Angeles County, approximately 10% of all emergency room visits for seizures were attributed to NCC.[18] At the Ben Taub General Hospital in Houston, 2% of all outpatient neurology appointments were related to NCC, and 16% of seizures among Hispanics were attributable to NCC.[12] Severe forms of NCC, including ventricular and subarachnoid disease, are likely under-detected causes of premature mortality among Hispanics.[19]

Domestic transmission

Most cases of NCC presenting within the United States are likely acquired prior to emigration from an endemic country, as the interval between infection and symptom onset can range from years to decades. A study of British soldiers serving in India suggested a median incubation period of 3.5 years, with cases presenting as long as 40 years after the last known exposure.[20] However, domestic transmission from tapeworm carriers residing in the United States is known to occur. Multiple case reports document NCC among US-born people who had never traveled to an endemic area.[21] A recent report described an infant with seizures and NCC in New Jersey, whose mother emigrated from El Salvador 2 years prior and was shown to harbor a tapeworm.[22] A well-known investigation in New York described four unrelated cases of NCC in an Orthodox Jewish community. Foreign-born housekeepers were identified as the most likely source;

one housekeeper had an active tapeworm infection and another had antibodies suggesting prior infection.[23]

Population-based studies also suggest the occurrence of domestic transmission. Surveillance data from Los Angeles revealed that 7% of NCC cases had no exposure to endemic regions.[13] The hospital discharge study from Oregon had similar results; 9% of NCC cases were born in the United States and had not traveled to an endemic country.[11] Domestic transmission is probably underestimated in these studies, as some foreign-born individuals may have acquired their infection within the United States.

Available screening tools

Laboratory screening for *T. solium* tapeworm infection is accomplished by examining either stool or serum. Light microscopy for ova and parasites in stool is the most widely available method, but has poor sensitivity for *Taenia* species (~30%) due to the intermittent excretion of eggs. In addition, this method cannot distinguish between the eggs of *T. solium* and the relatively benign *T. saginata* (beef tapeworm), which are frequently co-endemic. An enzyme-linked immunosorbent assay (ELISA), commonly known as the coproantigen test, can detect tapeworm antigens in stool with a sensitivity of 99%, but is currently available only by special request from the Centers for Disease Control and Prevention (CDC).[24] This method is 99% specific for *Taenia* genus but does not differentiate *T. solium* from *T. saginata*.[25] Limitations of stool methods in general

include the logistical difficulty in collection, lack of cultural acceptability, and risk of infections for patients and laboratory staff when handling potentially infectious samples.

Serologic assays using enzyme-linked immunoelectrotransfer blot (EITB) are available to detect antibodies against *T. solium* tapeworms or cysts. A commercial EITB kit used to detect antibodies against cysts is widely available, and is offered by most reference laboratories to aid in clinical diagnosis of cysticercosis.[26] The CDC has developed an EITB assay which detects antibodies against *T. solium* tapeworms, is specific to *T. solium* taeniasis, and can be prepared from either natural or recombinant antigens.[27] This assay has not been approved for clinical use in the United Stated and is available only under experimental protocol. Although highly sensitive (98%) and specific (99%), this method is also limited in that it cannot distinguish past from current infection.

Targeted screening for Taenia solium tapeworms

Identifying and treating human tapeworm carriers is a logical target for prevention of additional cases of NCC. However, this proves challenging due to the low community prevalence of tapeworms, the asymptomatic nature of intestinal infection, and the poor sensitivity of routinely available screening tools. Even in hyperendemic regions of Latin America, the prevalence of *T. solium* tapeworm infection rarely exceeds 1-2%.[28] The prevalence of *T. solium* tapeworm infection in the United States is likely much lower; seroprevalence, reflecting both current

and remote infection, was 1.1% in a cross-sectional study of California migrant workers.[15] Increasing the pretest-probability of infection through targeted screening would likely be necessary for any screening program to be practical.

Studies from endemic regions have shown that co-infection with a tapeworm and living with a tapeworm carrier are both strong risk factors for NCC.[29] Although these associations have not been verified in non-endemic settings, the fecal-oral nature of transmission and the potential migration of tapeworm carriers suggests biologic plausibility. Household screening for *T. solium* tapeworms, including both the NCC case and close contacts, may therefore increase the probability of detection of *T. solium* tapeworms. Los Angeles County instituted this strategy in the late 1980s with some success; tapeworm carriers were found in 7% of investigated NCC cases, or 1.7% (6/247) of total contacts screened.[13] Contacts of NCC cases born in the United States appeared more likely to harbor a tapeworm than those of foreign-born NCC cases (OR 5.4, 95% CI 0.7-41.4).[13] This prevention strategy requires a robust surveillance system with efficient and timely identification of NCC cases to ensure thorough contact investigations.

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Ongoing *Taenia solium* surveillance in Oregon

In 2002, cysticercosis and taeniasis became reportable diseases in the state of Oregon. Clinicians and laboratories that diagnose *T. solium* infection are required to report the case to public health authorities within one working day. Because tapeworms are largely asymptomatic and the prevalence is low, *T. solium*

infection is rarely diagnosed in a laboratory. Passive surveillance therefore relies primarily on spontaneous clinician reporting of NCC cases. In the first five years of surveillance only seven cases of NCC were spontaneously reported. This low incidence conflicts with the findings of the hospital discharge database study that found 43 new cases of NCC in the preceding five years.[11] In addition, an increasing proportion of Oregonians are thought to be at risk for acquiring NCC. In 2008, 11% of all Oregonians were Hispanic, compared to 8% in the year 2000.[30] Approximately 170,000 Oregon Hispanics were born in Latin America where the disease is endemic.[31] In the context of an increasing population at risk, the small number of passively reported cases likely reflects an inadequate surveillance system rather than a true decrease in incident cases.

Thesis objective and aims

The overall objective of this thesis is to conduct and evaluate surveillance for *T. solium* infection in Oregon. Specific aims include:

1. To describe the epidemiology of *T. solium* infection in Oregon;
2. To explore predictors of *T. solium* infection among household members of people with known neurocysticercosis;
3. To apply Centers for Disease Control and Prevention (CDC) guidelines for evaluating public health surveillance systems; and,
4. To make recommendations regarding reporting, surveillance and investigation of *T. solium* infection in Oregon.

CHAPTER 2 – RESEARCH PROBLEM, METHODS AND RESULTS

Introduction to research problem

Neurocysticercosis (NCC) is a parasitic disease caused by central nervous system (CNS) infection of *Taenia solium* larval cysts. It is the most common parasitic infection of the CNS and the leading cause of acquired epilepsy in Latin America, Southeast Asia and Central Africa.[1,2] It is also increasingly recognized as an important clinical and public health disease in the United States, primarily affecting immigrants and travelers from endemic regions.[21]

Cysticercosis is a fecal-oral disease, acquired by ingestion of tapeworm eggs shed in the feces of a human tapeworm carrier. Ingested eggs develop into oncospheres, which invade the intestinal mucosa and disseminate throughout the body to form larval cysts. NCC occurs when cysts develop in the CNS, and is the primary source of morbidity and mortality.[8] The complete lifecycle occurs in regions with poor sanitary infrastructure, where foraging pigs have access to human feces. Most NCC cases seen in the US were likely acquired in endemic areas by immigrants or travelers, who entered the US already infected with cysts.[9] However, immigrants and travelers can also harbor tapeworms, and domestic transmission of NCC does occur.[22,23]

Few states require reporting of cysticercosis, therefore, population-based epidemiologic data in the US is limited. Even in jurisdictions that require

reporting, the clinical nature of NCC diagnosis complicates surveillance efforts. Laboratory surveillance does not capture NCC cases, as there are no routine laboratory tests to establish the diagnosis. Reporting therefore relies on clinician or institutional reporting. California became the first state to require reporting in 1989; 112 cases of cysticercosis were reported in the first year, representing a crude annual incidence of 0.02 per 100,000 overall population, or 1.5 per 100,000 among Hispanics.[14] A retrospective case-series from Oregon based on hospital discharge diagnoses estimated an annual incidence of 3.1 per 100,000 Hispanics.[11].

Oregon adopted administrative rules for *T. solium* reporting in 2002, after coroner examination implicated hydrocephalus secondary to obstructing ventricular cysts in two unexplained deaths. A subsequent retrospective study of hospital discharge diagnoses found 43 incident NCC cases between 1995 and 2000.[11] Five cases had no documented exposure to an endemic area, suggesting the possibility of local transmission. However, there were no efforts to stimulate passive reporting or to actively find unreported cases. As a result, only seven cases of NCC were reported to public health officials during the first 5 years of reporting. Oregon has a rapidly growing Hispanic population, currently representing 11% of the total population.[30] Approximately half of all Oregon Hispanics report birth outside the US.[31] In the context of an increasing population at risk, the small number of passively reported cases suggest inadequate surveillance.

Identification and treatment of tapeworm carriers in the US could prevent additional cases of NCC. However, tapeworm infection produces few symptoms, and the prevalence is typically less than 1-2% even in endemic regions.[28] Los Angeles County adopted a program of targeted screening for tapeworm carriers in the 1980s with some success. By screening household members of NCC cases using light microscopy on stool samples, LA County was able to identify an intestinal tapeworm in 7% of their investigations.[13] Improved screening methods have been developed in the interim, including an enzyme-linked immunosorbent assay (ELISA) for *Taenia* species coproantigens in stool and an enzyme-linked immunoelectrotransfer blot (EITB) for serum antibodies against *T. solium* tapeworm.[24,27] Serologic methods are promising, as they are specific to *T. solium* intestinal infection, highly sensitive (99%), and avoid the collection and processing of potentially infectious stool.[27]

Our objective was to evaluate the utility of public health surveillance for *T. solium* infection in Oregon. We implemented population-based active surveillance to determine the incidence of cysticercosis. We also piloted targeted screening for additional *T. solium* infection among affected households, using a combination of symptom screening, laboratory analysis of stool and serum, and radiographic imaging.

METHODS

Case definition and surveillance period

Cysticercosis cases were classified as confirmed or suspect based on published consensus diagnostic criteria.[2] We defined incident cases as those with initial diagnosis occurring in a four-year period, between January 1, 2006 and December 31, 2009. Non-Oregon resident cases were excluded.

Case ascertainment

During the 2009 calendar year, we requested quarterly reports of ICD-9 billing codes for cysticercosis (123.1) from all Oregon hospital systems. The first request included identification of historical cases going back to January 1, 2006; subsequent reports only included cases for the current quarter. All hospitals reported inpatient admissions, and those with integrated electronic medical records systems reported outpatient visits as well. To identify additional cases, we queried the CDC parasitology diagnostics laboratory and the main regional reference laboratory for Oregon cysticercosis serology. We also searched Oregon vital statistics data for deaths related to cysticercosis, both by diagnosis code and by keyword ("cysticercosis"," neurocysticercosis", and "taenia"). We obtained medical charts for all reported cases to verify the diagnosis and to extract clinical and epidemiologic data.

To stimulate passive reporting, we sent letters to clinicians likely to diagnose NCC, including migrant health providers, radiologists, pathologists, neurologists, neurosurgeons, as well as infectious disease and emergency department

physicians. We also distributed a newsletter regarding *T. solium* infection and reporting requirements to all licensed Oregon physicians.

Household investigations

Confirmed cases with incidence of new diagnosis occurring after July 1, 2008 were eligible for household investigation. After obtaining informed consent from the case and all household contacts, the study physician used a standard interview tool to gather demographic, clinical and epidemiologic data. From each participant, we collected a stool sample preserved in 10% formalin, as well as a fingerstick blood sample on quantifiable filter paper preserved in StabilZyme Select (SurModics; Eden Prairie, MN) stabilizer. We offered non-contrast computerized tomography (CT) of the head to any household contact with clinical history of seizures or severe/chronic headaches, or with any positive laboratory finding.

Laboratory methods

Laboratory processing was conducted at the CDC Parasitology Diagnostics Laboratory in Atlanta, Georgia. Fecal samples were examined by light microscopy for presence of *Taenia* species eggs or proglottids, and by ELISA for presence of *Taenia* species coproantigens. Serum samples were analyzed by enzyme-linked immunoelectrotransfer blots for presence of antibodies against *T. solium* cysts (EITB LLGP) and against *T. solium* adult tapeworms (rEITB).The EITB LLGP assay uses a semi-purified fraction of homogenized *T. solium* cysts

containing seven *T. solium* glycoprotein antigens. The rEITB for taeniasis is based on baculovirus expression-purified recombinant antigen rES33.

Data analysis

Annual incidence rates were expressed as the number of incident cases per 100,000 population, with denominator estimates obtained from American Community Survey yearly estimates. Data were analyzed using STATA 10 (StataCorp; College Station, TX). Continuous variables were assessed using either Kruskal-Wallis or Mann-Whitney tests for differences among/between groups of interest. Fisher's Exact test was used to compare distributions of proportions or to examine association between pairs of categorical measures. All tests are two-sided, with significance set at 0.05. We separately fit binomial and beta-binomial regression models to assess factors associated with additional household *T. solium* infection. Using the beta-binomial model, we calculated the intra-class correlation coefficient to measure variation in the probability of *T. solium* infection among members of a household.

RESULTS

There were 143 unique reports with diagnosis code 123.1 for Oregon residents during our surveillance period. Fifty-six reports were excluded; insufficient chart information was available to verify diagnosis or incidence year in 18 (12.6%), and 38 (26.6%) were diagnosed prior to 2006. Of the remaining 87 cases, 77 (88.5%) were identified through active surveillance, including 75 (86.2%) via hospital

queries, two (2.3%) via laboratory queries and two (2.3%) during household investigations. Eight cases (9.2%) were spontaneously reported by clinicians, of which six (75%) were from a single infectious disease clinician in a tertiary hospital setting.

Of the 87 cases, 72 (83%) were classified as confirmed and 15 (17%) were classified as suspect. All cases had radiographic imaging of the head; 83 (95.4%) had CT scan of the head; 52 (59.8%) had an MRI of the brain (Table S1). Confirmed cases were 8.5 times as likely to have received an MRI compared to suspect cases (OR 8.5, 95% CI 2.0-50.2). Birth country and travel history were not recorded for 12 of the suspect cases; an epidemiologic link to an endemic area would have changed the classification to confirmed in all 12. The other three suspect cases had radiologic evidence suggestive of cysticercosis, links to an endemic area, but their symptoms could have been explained by other diagnoses. Clinical and demographic characteristics are presented in Table 1. Suspect cases were more likely to be female (p=0.04), older (p<0.01), and more likely to have calcified lesions (p<0.01) compared to confirmed cases.

Of the 72 confirmed cases, 41 (57%) were hospitalized at the time of diagnosis (Table 2). The median inpatient stay was 4 days (IQR 3-9), accounting for a total of 292 hospital days during initial presentation only. Of these 41 hospitalizations, intensive care was involved in 16 (39%). Suspect cases were less likely to receive treatment with antiparasitics (p=0.03) or corticosteroids (p=0.03);

otherwise, there was no difference in hospitalization or treatment compared with confirmed cases. There were no deaths in which cysticercosis was listed as a contributing factor.

Suspect cases were excluded from incidence calculations (Table 3). Sixty-nine (95.8%) cases were Hispanic. Including the 12 suspect cases for which epidemiologic data was unavailable would increase the estimated mean annual incidence to 0.6 per 100,000 overall population and 6.7 per 100,000 Hispanic population. Although the number of cases reported was highest during the active study year (2009), there was no statistical difference compared to prior years (p=0.16).

Country of birth was documented in the medical chart for 55 cases (Table 4). Three cases were US-born (5.5%), all of whom were Hispanic. One was a 49 year old male who denied any international travel; he had a single obstructing 4th ventricular cyst confirmed by surgical pathology. Another US-born case was a 24 year old male with new-onset seizures, a single cystic parenchymal lesion on MRI, and positive serology for *T. solium* cysts. His only international travel included a single week in Mexico 17 years prior to diagnosis. Travel history was not available for the final US-born case, a 57 year old male with multiple parenchymal calcifications, seizures, and psychosis.

There were 32 confirmed cases of NCC with initial diagnosis after July 1, 2008, and therefore eligible for household investigation. We conducted household investigations in 22 (68.8%) cases; of these, 6 (27.3%) were definitive and 16 (72.7%) were probable (Table 5). Of the 10 cases in which no investigation took place, seven could not be located with contact information available in the chart, two were identified in other household investigations, and one was unable to provide informed consent due to psychosis. There was no significant difference between the 22 cases we investigated and the 10 we did not, with respect to demographic or clinical characteristics. Nor was there any significant difference between the 22 cases we investigated and the 40 confirmed cases which were diagnosed prior to July 1, 2008. The median time from immigration to the US in investigated cases was 10 years (IQR 6-14), with a median of 5 years (IQR 2-10) from last international travel to an endemic country.

The median household size was 6 people (IQR 4-7). Of the 111 total contacts, 79 (71.1%) were foreign-born and 41(36.9%) reported international travel within the last 2 years. All stool samples were negative by light microscopy and by ELISA for coproantigen. Two household contacts (1.5%) from separate investigations had serum antibodies against *T. solium* tapeworms. Nine cases (40.1%) and one household contact (0.9%) had circulating antibodies against *T. solium* cysts. The beta-binomial regression model, which includes an additional parameter for dispersion, fit the observed data better than the regular binomial model (Table 6). This model suggests the overall probability of *T. solium* infection among family

members of a confirmed case is 4% (95% CI: 1–14%), which is somewhat lower than the estimated 6% probability derived from a standard binomial model. This lower estimated infection probability is accompanied by increased variation, with the intraclass correlation coefficient from the beta-binomial estimated to be ρ=0.12 (90% CI: 0.011–0.49). Not counting the index case, the variability in the number of infected family members increases by 12% for a family of two, increases by 61.5% for a family of six, and practically doubles for a family of nine.

We offered head CT to 11 household contacts, three based on positive serology and eight based on clinical history. Of nine who accepted, two (22.2%) had parenchymal calcifications consistent with NCC. One was a 7 year old Burmese child who resettled with his family to Oregon one year earlier. He had a 3-year history of recurrent untreated generalized seizures which had not been reported to his physician. His mother was the household index case; she presented initially with severe headache and new-onset seizure, positive serology for *T. solium* cysts, and greater than 20 parenchymal cystic lesions. The boy's father had serum antibodies against *T. solium* tapeworm infection with negative stool studies. The other NCC case was an adult male from Mexico City with an occipital parenchymal calcification and chronic headaches; he had immigrated 21 years earlier and denied international travel since immigration. There was no other evidence of *T. solium* infection in his household other than the original case.

DISCUSSION

Cysticercosis is an important cause of morbidity in Oregon, particularly among the Hispanic population which maintains ongoing contact to endemic Latin America through immigration and travel. The observed mean annual incidence among Hispanics of 5.8/100,000 population is the highest documented rate within the United States, 4 times the estimates from California in the mid 1980's, and 2 times the prior estimate for Oregon.[11,13,14] Although we documented no deaths directly resulting from cysticercosis, the morbidity and public health burden are high. Hospitalization at time of diagnosis was common, requiring intensive care in over one third of hospitalizations. Our study did not quantify the burden related to treatment and follow-up of cases, but surgical complications, shunt failure, and side-effects from prolonged steroid use were noted.

The relatively high incidence of cysticercosis in this study likely reflects increased case ascertainment rather than any increase in the underlying risk. Prior studies have relied primarily on hospital discharge databases for case finding, which do not capture emergency room visits that result in inpatient admission. By requesting quarterly reports based on hospital billing codes we were able to capture emergency department diagnoses. Many of these appear to have been less clinically severe, including uncomplicated new-onset seizures and headaches from calcified or non-obstructing cysts. In others we found subsequent inpatient stays for treatment complication or clinical deterioration.

Despite improved case ascertainment, the observed incidence in this study likely underestimates the true incidence of NCC in Oregon. First, we excluded suspect cases from incidence calculations. Although most suspect cases were clinically and demographically similar to confirmed cases, documentation of an epidemiologic link to an endemic area was not available in all medical charts. For the majority of suspect cases, epidemiologic evidence suggesting exposure to *T. solium* would have changed the classification to confirmed. Including these suspect cases increased the mean annual incidence to 6.7/100,000 among Hispanics. Second, although several hospital systems reported outpatient visits related to cysticercosis, most outpatient visits in the state were not captured. Because less clinically severe disease may be diagnosed and treated completely in the outpatient setting, we may have missed these cases. Finally, we suspect that under-diagnosis is common, particularly when the presenting symptom is headache related to intermittent inflammation around degenerating or calcified parenchymal cysts. There is often a high threshold for obtaining neuroimaging in the primary care setting for chronic or intermittent headaches. The population burden of headache related to NCC has not been characterized in endemic or non-endemic settings, but may generate significant use of outpatient resources.

Prevention opportunity within the US is primarily limited to identification and treatment of domestic *T. solium* tapeworm carriers. There are numerous reports of NCC among US-born people who have never traveled, implicating domestic exposure to *T. solium* eggs.[21,22,23] We found only one such case in our

surveillance period, although other population studies have described probable domestic transmission in 7-10% of NCC cases.[11,13] While most foreign-born cases were likely infected outside the US, it is possible that some foreign-born cases acquired their disease within the US. We documented frequent travel to and from endemic areas among NCC cases and their household members, suggesting that the risk of tapeworm acquisition is ongoing.

Despite using multiple highly-sensitive methods in both serum and stool, we were unable to detect current tapeworm infection by screening household members of NCC cases. There are several reasons why we may not have been able to replicate the prior success in LA County, where tapeworm carriers were identified in 7% of investigated households. First, our sample size in this pilot program was small, and chance alone could explain the difference. Second, incident cases in LA County were defined based on date of symptom onset rather than date of diagnosis. As symptom onset can substantially pre-date diagnosis, the cases we investigated may have been systematically biased towards a more remote exposure. We chose to define cases based on date of diagnosis, as exact symptom onset can be difficult to determine, particular for chronic or intermittent headaches. Third, there may be important underlying differences in both cases and household contacts between Oregon and LA County. With LA County's proximity to the border with Mexico, cases and household members may have more recent or more frequent international travel. In Oregon, the median time since immigration was 4 years greater compared to cases in the LA study.

Similarly, the surveillance or investigation results from each study may not be generalizable to other states or other non-endemic countries. Finally, *T. solium* control efforts have progressed in many areas of Latin America, and the underlying prevalence of tapeworm infection may have decreased in the twenty years since the LA program was implemented.

The strategy of routine screening for tapeworm carriers among household contacts of a symptomatic NCC case may be inherently limited due to the long latency between exposure to *T. solium* eggs and development of symptoms. We did find evidence of past tapeworm infection and possible transmission to other household members. Specific clinical or demographic characteristics of the NCC case may correlate with the presence of a tapeworm in the household, such as young age, remote endemic exposure, and viable or multiple lesions. Our sample size was too small to evaluate the effectiveness of limiting investigations based on these variables.

While the role of tapeworm screening for prevention of domestic transmission remains unclear, there are other important public health functions related to *T. solium* infection. Primary among these is a focus on the health of household members who are at increased risk of *T. solium* infection. Symptom screening identified household members with chronic headaches and/or seizures, and follow-up with head CT identified undiagnosed NCC in 22% of these. One was a 7 year old boy with untreated epilepsy who was subsequently referred to primary

care and treated with prophylactic antiepileptics. Similarly, early identification, referral and surgical treatment of chronic headache due to hydrocephalus and could also prevent serious complications. Education of household members is also important due to frequent travel to and from endemic areas. Recognition of the importance of avoiding consumption of undercooked pork, and of maintaining good hygiene at all times, may reduce infection among travelers. Finally, increasing clinician awareness about *T. solium* infection is an important public health function, particularly for clinicians that care for Hispanic and other immigrant populations.

CONCLUSIONS

Cysticercosis is an important clinical and public health disease in Oregon, particularly among Hispanics in which the incidence is at least 5.8/100,000 population. Public health intervention should focus on the health of household members, and on increasing awareness of the disease among affected families and among clinicians in general. Household investigations of NCC cases in Oregon identified additional cases of previously undiagnosed NCC and evidence of past intestinal tapeworm infection. Improved selection criteria for household investigations may increase the likelihood of detecting current tapeworm infection.

Table 1. Demographic and clinical characteristics of incident cysticercosis cases by diagnostic certainty, 2006-2009

	Confirmed n=72	Suspect n=15	*p**
Demographics:			
Male, n(%)	46 (63.9)	5 (33.3)	0.04
Age, median(IQR)	36 (28-43)	47 (35-66)	<0.01†
Foreign-born, n(%)	47 (94.0)	4 (100)	1.0
Presenting symptom: n(%)			
Seizures	29 (40.3)	4 (26.7)	0.07
Headache	27 (37.5)	3 (20.0)	--
Focal neuro deficit	5 (6.9)	1 (6.7)	--
Altered mental status	3 (4.2)	3 (20.0)	--
Trauma	2 (2.8)	2 (13.3)	--
Other	6 (8.3)	2 (12.3)	--
Number of lesions: n(%)			
1 lesion	22(30.6)	2 (13.3)	0.10
2-4 lesions	21 (29.2)	9 (60.0)	--
5+ lesions	29 (40.3)	4 (26.7)	--
Lesion location: n(%)			
Parenchymal	61 (84.7)	15 (100)	0.49
Extraparenchymal	3 (4.2)	0 (0)	--
Mixed	8 (11.1)	0 (0)	--
Lesion stage: n(%)			
Cystic only	22(30.6)	1 (6.7)	0.01
Calcified only	32 (44.4)	13 (86.6)	--
Mixed	18 (25.0)	1 (6.7)	--

* Fisher's exact test unless otherwise indicated
† Mann-Whitney test

IQR = interquartile range

Table 2. Hospitalization and treatment among confirmed incident cysticercosis cases, 2006-2009, n=72.

	Confirmed n(%)
Hospitalization	41 (56.9)
# of days, median (IQR)	4 (3-9)
ICU	16 (39.0)
Neurosurgery	8 (11.9)
Shunt placement	7 (10.5)
Anti-parasitics	21 (33.9)
Corticosteroids	22 (34.4)
Anti-epileptics	32 (52.5)

IQR = interquartile range

Table 3. Incidence of confirmed cysticercosis cases in Oregon by year, 2006-2009

	2006 n=14	2007 n=18	2008 n=14	2009 n=26[†]	All Yrs n=72
Hispanic, n(%)	13 (92.9)	18 (100)	14 (100)	24 (92.3)	69 (95.8)
Years since immigration, median (IQR)	8 (5-10)	6 (2-10)	10 (8-17)	10 (4-18)	9 (4-15)
Annual incidence, per 100,000 overall population	0.4	0.5	0.4	0.7	0.5
Annual incidence, per 100,000 Hispanic population	3.4	4.5	3.4	5.5	5.8

[†]Comparison of number of reported confirmed cases during the active study year (2009) versus prior years. (*p*=0.08, Fisher's exact test)

Table 4. Region and country of incident Oregon cysticercosis cases, 2006-2009

Region	n	(%)	Country
Central America / Caribbean	47	(85.5)	Mexico (40), Guatemala (5), Nicaragua (1), Cuba (1)
North America	3	(5.5)	United States (3)
Southeast Asia	2	(3.6)	Burma (1), Thailand (1)
South America	1	(1.8)	Ecuador (1)
Africa	1	(1.8)	Cameroon (1)
Europe	1	(1.8)	Germany (1)

Table 5. Demographics and clinical characteristics of investigated cases compared to non-investigated cases

	Eligible for household investigation			
	Investigated n=22	Not Investigated n=10	Not eligible n=40	*p**
Demographics:				
Male, n(%)	14(63.6)	9(90.0)	23(57.5)	0.16
Age, median(IQR)	31(28-37)	42(35-57)	35(25-43)	0.15†
Lesion number, n(%)				
Single lesion	6(27.3)	2(20.0)	14(35.0)	0.55
Multiple lesions	16(72.7)	8(80.0)	26(65.0)	--
Lesion location, n(%)				
Parenchymal	17(77.3)	9(90.0)	35(87.5)	0.21
Extraparenchymal	2(9.1)	1(10.0)	0(0)	--
Mixed	3(13.6)	0(0)	5(12.5)	--
Lesion stage, n(%)				
Cystic	6(27.3)	1(10.0)	15(37.5)	0.15
Calcified	8(36.4)	8(80.0)	16(40.0)	--
Mixed	8(36.4)	1(10.0)	9(22.5)	--
EITB-c positive, n(%)	9 (40.9)	--	--	

* Fisher's exact test unless otherwise indicated
† Kruskal-Wallis, χ^2

IQR = interquartile range

Table 6. Comparison of binomial and beta-binomial models of household T. solium infection to test for over-dispersion

	π	95% CI	Log likelihood	Test statistic	*p*
Binomial (intercept only)	0.06	0.03-0.13	-11.13	X_{21}^2=23.691	0.38
Beta-Binomial (intercept + dispersion)	0.04	0.01-0.14	-13.10	X_{20}^2=14.886	0.83
			Likelihood ratio test:	X_1^2=3.93	(*p*=0.024)

SUPPLEMENTARY TABLES

Table S1. Differences in cysticercosis diagnostic certainty by whether cerebral radiographic imaging was obtained

		Confirmed			
		Definitive	Probable	Suspect	
Head CT, n(%)	Yes	17(19.5)	52(59.9)	14(16.1)	p=0.54†
	No	2(2.3)	1(1.1)	1(1.1)	
MRI Brain, n(%)	Yes	16(18.4)	33(38.0)	3(3.4)	p<0.01†
	No	3(3.4)	20(23.0)	12(13.8)	

† Fisher's exact test for confirmed vs. suspect

Table S2. Cysticercosis lesion stage by number of lesions

	Single	Multiple	
Cystic only, n(%)	13(24.1)	9(16.7)	p=0.03†
Calcified only, n(%)	9(16.7)	23(42.5)	

† Fisher's exact test

Table S3. Cysticercosis lesion location by number of lesions

	Single	Multiple	
Parenchymal only, n(%)	21(32.8)	40(62.5)	p>0.99†
Extra-parenchymal only, n(%)	1(1.6)	2(3.1)	

† Fisher's exact test

CHAPTER 3 –EVALUATION OF SURVEILLANCE SYSTEM

Introduction

In 2001, the CDC published updated guidelines for the systematic evaluation of public health surveillance programs.[32] The standard stepwise procedures are applicable to periodic evaluation of long-standing systems, as well as to initial evaluation of pilot programs. The majority of the recommended evaluation components can be completed with regard to *T. solium* surveillance, and these are individually described in the sections below. Main components include defining the purpose of this evaluation and the stakeholders involved, defining the purpose, operation, and performance of the existing system, and providing recommendations for further action.

Purpose of evaluation

Taenia solium infection has been legally reportable in Oregon since 2002; clinicians or laboratories are required to report cases to public health authorities within one working day of diagnosis. The primary impetus for inclusion on the list of reportable diseases was the identification of *T. solium* as the cause of an initially unexplained death in a Hispanic teenager who had lived in Oregon since she was an infant.[11] She was found dead in her bed at home, and subsequent autopsy revealed the cause of death as obstructive hydrocephalus and brainstem herniation resulting from a 4th ventricular cyst. She had multiple primary care visits in the months preceding her death, and was being treated for “tension

headaches". Neuroimaging was not performed, although it would likely have revealed the true diagnosis and led to life-saving intervention. Her death revealed a lack of knowledge regarding the burden of *T. solium* infection in Oregon, and prompted a retrospective review of the hospital discharge database that estimated an annual incidence of 3.1/100,000 among Oregon Hispanics.[11] These experiences highlighted several important public health issues: 1) the estimated incidence of *T. solium* infection in Oregon is higher than expected; 2) considerable health resources are expended in diagnosis, treatment and follow-up of cases; 3) the Hispanic population is disproportionately affected; 4) clinician awareness is limited; 5) domestic transmission is likely occurring at some unknown rate; and 6) NCC is a disease of fecal-oral transmission and is therefore potentially preventable. Recognition of these issues, and the persistent lack of information regarding the epidemiology of *T. solium* infection in Oregon, prompted its inclusion among legally reportable diseases in the state.

However, there was no clear consensus at the time regarding the case definition or appropriate public health intervention. As a result, no additional efforts were made to stimulate reporting among clinicians, and investigative guidelines for local health departments were not finalized. Only seven cases were reported statewide over the next five years, which suggested that either the incidence had decreased in Oregon, or that the existing surveillance system was not capturing cases. Regardless, the primary health issues which prompted inclusion of *T. solium* as a reportable disease were not being addressed.

In January 2009, we began a period of active surveillance to attempt to bring these issues to the forefront. This included developing methods for active case finding, establishing case definitions and formalizing investigative guidelines with expected public health interventions. Results of this period of active surveillance, including targeted screening through household investigations are described separately in Chapter 2. The purpose of Chapter 3 is to review the performance and utility of the surveillance system itself, and to provide recommendations regarding its sustainability.

Identification of stakeholders

As a reportable disease, *T. solium* surveillance lies within the prevention and control program for the state of Oregon, and there multiple governmental and non-governmental stakeholders. On a federal level, the Emerging Infections Program (EIP) at the Centers for Disease Control and Prevention is involved as the primary funding source for the 2009 active surveillance project. Public health authority for intervention resides within the county health departments, whose nurses conduct public health investigations. Hospital systems across the state are involved through institutional reporting of cases. Clinicians are involved through patient care and through mandated reporting of cases. Specific clinical specialties are more likely to encounter cases, including infections disease practitioners, neurologists, neurosurgeons, emergency room physicians, and radiologists. Finally, the Oregon Hispanics experience the majority of the risk in

Oregon, and increased awareness in this community could lead to risk factor modification or early diagnosis. All of these stakeholders contribute to the function of the surveillance system and may benefit from information the system provides.

Surveillance objectives

While the ultimate goal of surveillance is to facilitate the promotion and protection of the public's health, the nature of information gathered will vary considerably based on the disease and population of interest, the level of existing knowledge and experience, the capacity of public health infrastructure, and the availability of resources. Very little is known regarding the epidemiology of *T. solium* infection in non-endemic settings, so surveillance is structured primarily to gather fundamental epidemiologic knowledge. The four main objectives of *T. solium* surveillance in Oregon are: 1) to measure the burden of infection within the state, including a baseline for comparison; 2) to monitor trends in diagnosis incidence over time; 3) to describe basic epidemiologic characteristics of *T. solium* infection in non-endemic settings, such as risk factors and populations at risk; and 4) to inform future surveillance and intervention programs.

Operation of the surveillance system

The surveillance system resides within the existing governmental public health infrastructure, with Oregon administrative rules (333-018-0000, 333-018-0015) providing legal authority for public health involvement. While cases on occasion

are reported directly to the local health departments, the majority are identified through quarterly requests of hospital system reporting based on ICD-9 billing codes. This institution-based reporting serves as the backbone of the surveillance system, accounting for the majority of reported cases. Requests are organized through the Acute and Communicable Disease Prevention (ACDP) program at the Oregon Department of Human Services.

Upon receipt of an institutional report, ACDP notifies the appropriate local health department (LHD) of pertinent reports, including case identifiers and any relevant clinical information contained in the report. The LHD and ACDP coordinate efforts to obtain medical charts from the reporting institution, to verify the diagnosis and date of incident diagnosis, and to further classify the case as Confirmed, Presumptive, or Suspect based on established diagnostic criteria (Appendix A). Confirmed and Presumptive cases are eligible for household investigation according to investigative guidelines developed by ACDP staff. Standardized forms are available to guide LHD and ACDP staff nurses in gathering relevant clinical and epidemiologic information (Appendix B). A web-based database managed by the ACDP is used to record relevant information; LHD nurses can access the system via the internet to enter data.

Dissemination of surveillance results

Information in the database is managed centrally by ACDP, which generates periodic reports to evaluate *T. solium* trends. These reports are disseminated

annually to the CDC EIP, as well as to individual LHD's with county and disease-specific information. Hospital institutions receive limited feedback with quarterly letters requesting reporting; typically, this consists of the number of additional cases and investigations directly resulting from institution reporting. The ACDP publishes a bi-weekly newsletter (the *CD Summary*), which is sent to all physicians within Oregon; this serves as a conduit for communicating surveillance results along with other important public health messages. Finally, ACDP staff conduct limited outreach to clinical and public health practitioners through presentations at local and regional conferences, and through visits to LHD's.

Resources required

The previous system of passive surveillance required essentially no resources as reporting was extremely rare. With active case finding, dedicated personnel became the primary resource required. During the 2009 active surveillance year, a preventive medicine resident paid by Oregon Health & Sciences University was primarily responsible for the role of the ACDP in *T. solium* surveillance, and was available to assist LHD nurses in their investigations. This is the primary position involved, requiring an ongoing commitment of approximately 0.5 FTE. The ultimate source of funding for the resident is federal, distributed though the Centers for Medicare and Medicaid Services. Additional ACDP staff and community physicians are occasionally involved, while local health department

nurses participate in case verification. Personnel resources are estimated to cost approximately $45,000 per year.

Outreach to clinical and public health practitioners included a mass mailing to 2000 target Oregon clinicians, distribution of a newsletter regarding cysticercosis to all licensed Oregon physicians, and travel expenses for health department visits and conference presentations. Additional expense was incurred in telephone, fax, and office supplies. Some federal programmatic support was provided by the CDC Emerging Infections Program, although these funds are primarily used to conduct household investigations rather than initial surveillance. State program operating budgets provide the remainder of these funds. Total cost for outreach and support is estimated at $6000 per year.

Surveillance performance

There are a many performance measures that can be used to determine the overall utility of the surveillance system with respect to its intended objectives. This following section describes several performance characteristics relevant to existing *T. solium* surveillance. The objectives are repeated for ease of reference.

a. System objectives

The four main objectives of *T. solium* surveillance in Oregon are: 1) to measure the burden of infection within the state, including a baseline for comparison; 2) to

monitor trends in infection incidence over time; 3) to describe basic epidemiologic characteristics of *T. solium* infection in non-endemic settings, such as risk factors and populations at risk; and 4) to inform future surveillance and intervention programs.

b. Simplicity/Flexibility

Simplicity of a surveillance system refers to the overall structure and ease of operation, and is closely related to flexibility (the ability to adapt to changing conditions such as case load, personnel, or available funding). Surveillance for cysticercosis is complicated by the necessity of active case finding, and by the diffuse nature of reporting through individual institutions. Quarterly letters were sent to contacts at 42 different institutions, each of whom was initially identified through a series of telephone calls and letters. Because organization structure varies, contacts are from multiple departments, primarily including Health Information Services, Billing, and Infection Control. Frequent turnover among health information or billing code staff meant that requests were often delayed, multiple reminders via telephone and fax were required, or new contacts needed to be established. The case definition based on clinical diagnostic criteria was also cumbersome and complicated, requiring intensive chart review to verify and classify the diagnosis. Local health department nurses frequently required assistance and consultation from ACDP in this process.

There were no major changes during the 2009 active surveillance period to evaluate specific issues regarding flexibility. However, some general observations can be made. First, the direct involvement of personnel from both state and local health departments accommodated fluctuations in case load and competing priorities. For example, announcement of a global influenza pandemic increased the work load dramatically for local health department nurses during the summer and fall of 2009. Assistance from the state ACDP accommodated this need to allow surveillance to continue. On the other hand, the system was personnel intensive at the level of the ACDP. This position was occupied by a preventive medicine resident from Oregon Health & Science University, who was able to dedicate considerable effort to this project. Residents may not be available in subsequent years, and any ACDP position would likely require additional funding support. In this respect, the system in its current form is highly inflexible, jeopardizing sustainability.

c. Acceptability

Acceptability refers to the willingness of individuals and/or institutions to participate in surveillance. The reasons for lack of reporting by clinicians are not completely clear. Some may reflect unwillingness to participate, such as a perceived time burden for reporting during a busy clinic day. Other reasons may be related more to a lack of awareness of reporting requirements rather than to overall acceptability. Communicable disease reporting has increasingly shifted toward laboratory reporting, which is not pertinent to cysticercosis diagnosis.

Clinicians may mistakenly expect the lab system to cover cysticercosis and other communicable disease reporting.

All hospital systems in Oregon participated in billing code reporting, although quarterly reports were frequently delayed or required a reminder notice. Informal conversations regarding the burden of generating reports revealed fairly uniform responses; once the code was generated for the initial report, subsequent reports were easily replicated. A low perceived burden on the part of the institutions likely contributed to excellent overall participation.

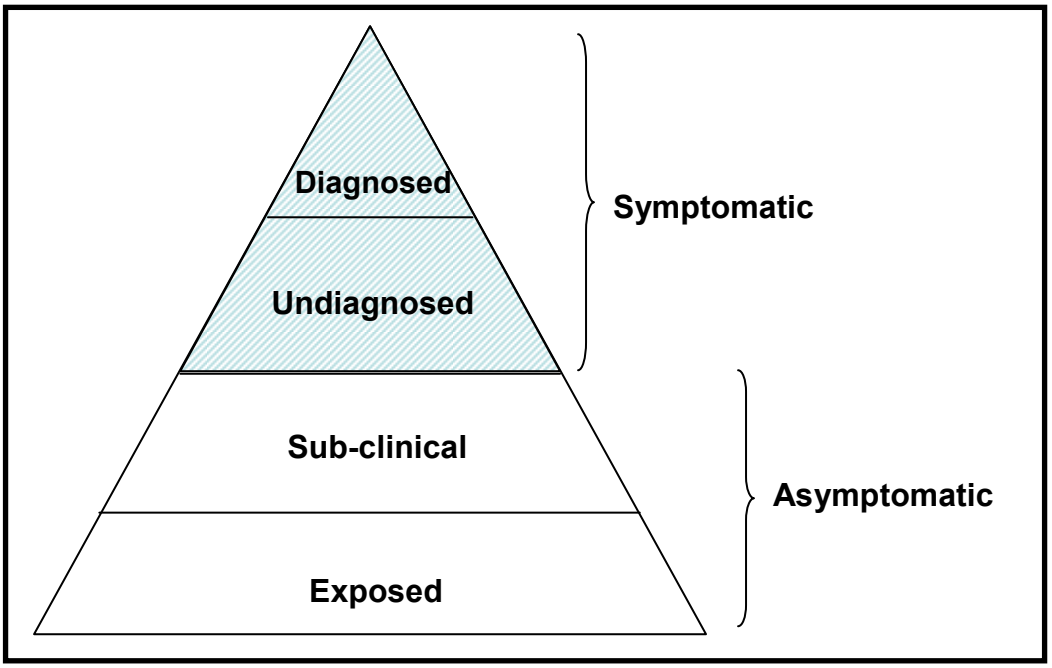
Local health department nurses expressed recognition of the public health importance of *T. solium* infection, as well as guarded interest in participating in surveillance and investigations; a lack of time and resources was frequently cited as a deterent. The 2009 period of active surveillance coincided with drastic budget cuts for most LHD's along with an influenza pandemic, and public health nurses in general were assuming increased work burden. In addition, several nurses opined that the case classification was cumbersome, involving detailed and time-consuming chart reviews.

d. Sensitivity

Sensitivity refers to the proportion of all incident cases in a given population under surveillance that are correctly identified as incident cases by the system. There is no gold standard for determining the true incidence of *T. solium*

cysticercosis. The system described here is perhaps help most comprehensive method described to date for non-endemic settings, and no other system is in place within Oregon for comparison. However, some qualitative assessment is possible. *Taenia solium* cysticercosis community burden is likely well-represented by a traditional pyramidal diagram, in which a large proportion of exposed people compromise the base of the pyramid, and a much smaller proportion of diagnosed cases form the peak (Figure 3). From a non-endemic public health perspective, diagnosed and undiagnosed-symptomatic cases (shaded areas) are perhaps the most relevant cases to capture, as they contribute all of the morbidity and mortality.

Figure 3. Diagramatic representation of the population burden of cysticercosis



With respect to diagnosed cases, our surveillance system likely captures most incident inpatient diagnoses. The hospital discharge database contains limited demographic identifiers for individual patients, which can be used to match cases reported directly by hospitals based on billing codes. Matching cases on discharge date, age, gender and facility for years 2006-2008, there was only a single case in the hospital discharge database that was not captured in our surveillance system. The converse is not true, as our surveillance system appeared to capture several inpatient admissions not included in the discharge database. Data from 2009 cases were not available for matching, as there is a significant delay in updating the hospital discharge diagnosis database. An important difference between the 2 sources of cases is that emergency department visits which do not result in inpatient admission are not included in the hospital discharge database. However, these visits are captured in our surveillance based on billing codes.

There is no information available to make comparisons regarding cysticercosis patients diagnosed and managed in the outpatient setting. Our system likely captures a small portion of these cases, as outpatient reporting is only available from a few institutions. Some of these cases may eventually be captured due to development of complications or adverse events related to treatment or natural disease progression. Others may never require emergency or inpatient evaluation. There is no data currently available to make informed estimates as to the number of cases in either of these groups in Oregon.

The second tier of undiagnosed-symptomatic cases likely represents the largest proportion of cases that are not captured by our system. Intermittent inflammation due to degenerating or calcified parenchymal cysts can cause chronic or recurrent headaches. Because diagnosis of NCC relies heavily on neuroimaging, and the threshold for obtaining these exams is high in primary care settings, many such cases likely go undiagnosed. There is no information available regarding the proportion of chronic/intermittent attributable to NCC.

e. Positive predictive value

Positive predictive value (PPV) refers to the proportion of reported cases which are in fact true cases. There were 143 total unique reports of cysticercosis in our 4-year surveillance period, of which 38 were excluded for incidence prior to 2006. These 38 were not completely evaluated using our diagnostic criteria and are therefore not included in calculation of the PPV. Of the remaining 105, there was insufficient chart information to verify the diagnosis in 18, another 15 were classified as suspect cases, and 72 were confirmed cases. Of the 15 suspect cases, 12 were likely true cases (missing travel and immigration history in the chart to establish an epidemiologic link) and are included as true cases in the PPV. If all 18 unverified cases are considered false-positives, then a conservative estimate of the PPV is 84/105 = 80%.

f. Timeliness

Timeliness refers to the ability of a surveillance system to identify cases early enough in the disease course to allow appropriate intervention or evaluation. With cysticercosis, the candidate control intervention involves screening for tapeworm carriers among household members of a newly diagnosed case. Because the latency between exposure and symptom development may be years (may even be greater than the lifespan of an intestinal tapeworm), this approach may not be effective. Minimizing the time from diagnosis to reporting is therefore important if this intervention is to be used. Clinician reporting at the time of diagnosis is therefore preferable, but has remained uncommon despite efforts to promote reporting. Reporting based on billing codes is a significant improvement over hospital discharge databases (which may be 1-2 years behind), but still incorporates some delay. Some hospitals reported this delay on occasion to be as great as 4-6 weeks. In comparison to the long latency between exposure and symptom onset, several weeks delay for reporting may not significantly alter the outcome of any resulting investigation.

Conclusions

Cysticercosis is an important public health issues in Oregon, particularly among Hispanics who are disproportionately at risk. Benefits of the current system include use of hospital billing codes for case finding, which has greater sensitivity and timeliness compared to use of the hospital discharge diagnosis database. Acceptability is high among reporting institutions, with excellent participation, and the PPV of reported cases is reasonable.

There are several challenges to sustainability of the current system. The main limitation involves identification and support of personnel to continue active case finding, a necessary component as clinician participation in disease reporting remains low. The diffuse nature of institutional case reporting is personnel-intensive at the level of the ACDP, and is further complicated by a cumbersome case definition requiring intensive review of medical charts to verify the diagnosis. Although LHD nurses can assume the role of case verification, ACDP assistance will be required frequently. Apart from personnel requirements, the surveillance system consumes few resources.

Recommendations

Although mandated reporting began in 2002, effective surveillance for *T. solium* cysticercosis did not begin until 2009. The current system is structured to meet its intended objectives, but longitudinal surveillance is required. To enable continued surveillance, several improvements should be made:

1. **Improved integration:** While the surveillance system is currently housed within ACDP, the primary organizing position is currently filled by a temporary position with outside funding. While investigation activities could relatively easily be transferred to the current call structure within ACDP, active case finding requires dedicated FTE. Methods to decrease the potential work burden associated with case finding are described below.

2. **Streamlining institution reporting**: Institutional case reporting is a necessary component, and there are two potential options to relieve ACDP work load associated with organizing these reports. The first option is to approach institutions to formalize and automate the quarterly reporting, which will reduce ACDP work load related to report request and follow-up. The second option is to move toward centralized source when it becomes available. As part of ongoing health reform within Oregon, the state is requiring participation by all health care providers and insurers in an "all-claims / all-payers" database. This database system is currently under development, and is anticipated to be operational during the 2010 calendar year. There are efforts up-front to facilitate public health and communicable disease reporting through this database, which could serve as a central repository for relevant billing codes. The delay between patient visit and ability to access this information from the database is currently unknown.

3. **Simplifying case definitions:** There is substantial potential benefit in using established consensus criteria for verification of cases, which can set a standard for use in other jurisdictions which monitor *T. solium* incidence. One option is to simplify the verification and classification system, although this may introduce additional false positive cases. Such a classification system would have only Confirmed and Suspect cases (eliminate Presumptive), and could be limited to symptoms, radiography, serology and pathology consistent

with cysticercosis. Dropping epidemiologic criteria would simplify chart review, and may not dramatically increase false positives.

4. **Increasing clinician awareness:** Clinicians should continue to be educated with respect to underdiagnosis and underreporting. With respect to diagnosis, education should be targeted towards primary care clinicians likely to see Hispanic populations most at risk, with an emphasis on inclusion of NCC as a differential diagnosis for chronic or recurrent headaches. To improve reporting, specific physician groups should be targeted, specifically including infectious disease physicians, neurologists, and neurosurgeons. These specialists are consulted in most cases but rarely make reports. One possible way to improve reporting of these groups is to solicit assistance through their respective state professional societies. Endorsement of reporting by these societies could improve member reporting. In addition, regular outreach with surveillance and investigation results should be made through periodic letters and presentations.

5. **Interventions:** While surveillance can continue without control and prevention opportunities, an effective surveillance system provides a unique opportunity for testing interventions. Targeted household screening and treatment for tapeworm carriers is one potential method which has been effective in other areas. In our analysis of the Oregon pilot program, an insufficient number of investigations were available to make confident

conclusions regarding effectiveness of this intervention. Increased experience may allow discrimination of subsets of cases in which identification of tapeworms is more likely such as US-born cases or NCC in children. Although the pilot intervention was structured as public health research, continuation of this activity should be incorporated into routine public health practice.

APPENDIX A

3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

Case definitions for cysticercosis depend on combinations of diagnostic criteria outlined in the table below. If it seems complicated, it may be because it is. We didn't make this stuff up; these are time-honored classifications developed by experts that apparently work reasonably well in practice.

A. Confirmed case

Criterion Type	Finding
Absolute	Histologic identification of the parasite
	Visualization of the parasite by fundoscopic examination
	Evidence of cystic lesions showing the scolex on CT or MRI
Major	Evidence of lesions suggestive of neurocysticercosis on neuroimaging studies
	Detection of *T. solium* cysticercal antibodies
	Characteristic "cigar-shaped" calcifications in thigh and calf muscles on X-ray.
Minor	Presence of subcutaneous nodules (without histologic confirmation)
	Evidence of punctuate soft-tissue or intracranial calcifications on X-ray
	Clinical manifestations suggestive of neurocysticercosis
	Disappearance of intracranial lesions after treatment with anticysticercal drugs
Epidemiological	History of living in or frequent travel to a presumptively endemic area
	Close (e.g., household) contact with a tapeworm carrier

- 1 absolute criterion *or*
- 2 major criteria *or*
- 1 major *and* 2 minor *and* 1 epi criterion.

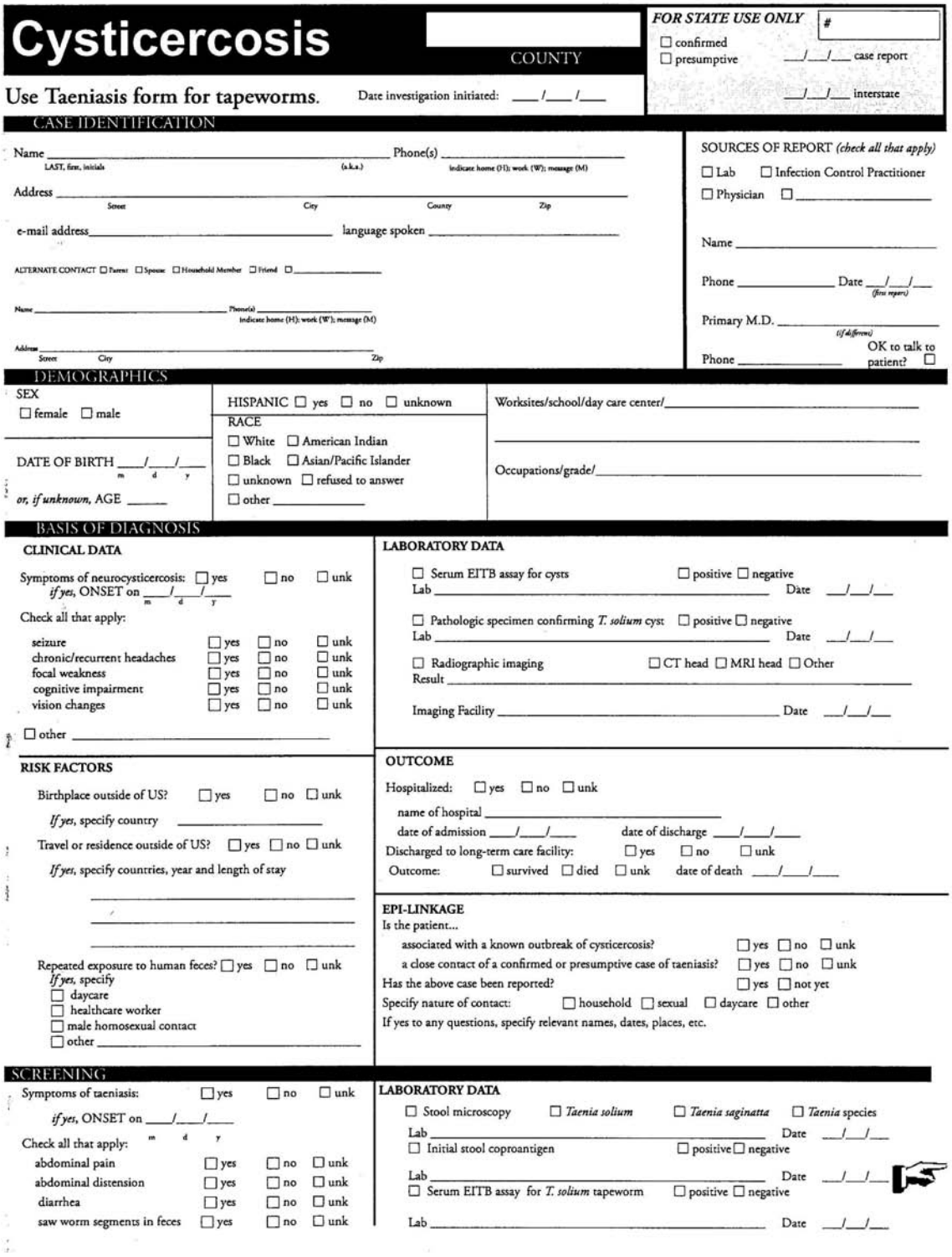
B. Presumptive case

- 1 major *and* 2 minor criteria *or*
- 1 major *and* 1 minor *and* 1 epi criterion *or*
- 3 minor *and* 1 epi criterion.

C. Suspect case

- 1 major *or*
- 2 minor *or*
- 1 minor *and* 1 epidemiologic criterion.

APPENDIX B



Cysticercosis

COUNTY

Use Taeniasis form for tapeworms. Date investigation initiated: ___/___/___

FOR STATE USE ONLY #

☐ confirmed ☐ presumptive ___/___/___ case report

___/___/___ interstate

CASE IDENTIFICATION

Name _____ (LAST, first, initials) (a.k.a.) Phone(s) _____ (indicate home (H); work (W); message (M))

Address _____ (Street) (City) (County) (Zip)

e-mail address _____ language spoken _____

ALTERNATE CONTACT ☐ Parent ☐ Spouse ☐ Household Member ☐ Friend ☐ _____

Name _____ Phone(s) _____ (indicate home (H); work (W); message (M))

Address _____ (Street) (City) (Zip)

SOURCES OF REPORT *(check all that apply)*

☐ Lab ☐ Infection Control Practitioner

☐ Physician ☐ _____

Name _____

Phone _____ Date ___/___/___ (first report)

Primary M.D. _____ (if different)

Phone _____ OK to talk to patient? ☐

DEMOGRAPHICS

SEX

☐ female ☐ male

DATE OF BIRTH ___/___/___ (m d y)

or, if unknown, AGE _____

HISPANIC ☐ yes ☐ no ☐ unknown

RACE

☐ White ☐ American Indian

☐ Black ☐ Asian/Pacific Islander

☐ unknown ☐ refused to answer

☐ other _____

Worksites/school/day care center/_____

Occupations/grade/_____

BASIS OF DIAGNOSIS

CLINICAL DATA

Symptoms of neurocysticercosis: ☐ yes ☐ no ☐ unk

if yes, ONSET on ___/___/___ (m d y)

Check all that apply:

seizure	☐ yes	☐ no	☐ unk
chronic/recurrent headaches	☐ yes	☐ no	☐ unk
focal weakness	☐ yes	☐ no	☐ unk
cognitive impairment	☐ yes	☐ no	☐ unk
vision changes	☐ yes	☐ no	☐ unk

☐ other _____

LABORATORY DATA

☐ Serum EITB assay for cysts ☐ positive ☐ negative

Lab _____ Date ___/___/___

☐ Pathologic specimen confirming *T. solium* cyst ☐ positive ☐ negative

Lab _____ Date ___/___/___

☐ Radiographic imaging ☐ CT head ☐ MRI head ☐ Other

Result _____

Imaging Facility _____ Date ___/___/___

RISK FACTORS

Birthplace outside of US? ☐ yes ☐ no ☐ unk

If yes, specify country _____

Travel or residence outside of US? ☐ yes ☐ no ☐ unk

If yes, specify countries, year and length of stay

_____

_____

_____

Repeated exposure to human feces? ☐ yes ☐ no ☐ unk

If yes, specify

☐ daycare

☐ healthcare worker

☐ male homosexual contact

☐ other _____

OUTCOME

Hospitalized: ☐ yes ☐ no ☐ unk

name of hospital _____

date of admission ___/___/___ date of discharge ___/___/___

Discharged to long-term care facility: ☐ yes ☐ no ☐ unk

Outcome: ☐ survived ☐ died ☐ unk date of death ___/___/___

EPI-LINKAGE

Is the patient...

associated with a known outbreak of cysticercosis? ☐ yes ☐ no ☐ unk

a close contact of a confirmed or presumptive case of taeniasis? ☐ yes ☐ no ☐ unk

Has the above case been reported? ☐ yes ☐ not yet

Specify nature of contact: ☐ household ☐ sexual ☐ daycare ☐ other

If yes to any questions, specify relevant names, dates, places, etc.

SCREENING

Symptoms of taeniasis: ☐ yes ☐ no ☐ unk

if yes, ONSET on ___/___/___ (m d y)

Check all that apply:

abdominal pain	☐ yes	☐ no	☐ unk
abdominal distension	☐ yes	☐ no	☐ unk
diarrhea	☐ yes	☐ no	☐ unk
saw worm segments in feces	☐ yes	☐ no	☐ unk

LABORATORY DATA

☐ Stool microscopy ☐ *Taenia solium* ☐ *Taenia saginatta* ☐ *Taenia* species

Lab _____ Date ___/___/___

☐ Initial stool coproantigen ☐ positive ☐ negative

Lab _____ Date ___/___/___

☐ Serum EITB assay for *T. solium* tapeworm ☐ positive ☐ negative

Lab _____ Date ___/___/___

PATIENT'S NAME

CASE-CONTACT MANAGEMENT AND FOLLOW-UP

Name | Age | Relation to Case | By proxy | Proxy name

☐ yes ☐ no

NEUROCYSTICERCOSIS SCREENING
if yes to any recommend medical evaluation of neurocysticercosis.

	yes	no	unk	date
seizure	☐	☐	☐	___/___/___
cognitive impairment	☐	☐	☐	___/___/___
chronic/recurrent headaches	☐	☐	☐	___/___/___
focal weakness	☐	☐	☐	___/___/___
vision changes	☐	☐	☐	___/___/___
unexplained neuro deficit	☐	☐	☐	___/___/___

TAENISIS SCREENING
Saw worm segments in feces ☐ yes ☐ no ___/___/___

Stool microscopy ☐ *Taenia solium* ☐ *Taenia saginatta* ☐ *Taenia* species
Lab _____ Date ___/___/___

Initial stool coproantigen ☐ positive ☐ negative
Lab _____ Date ___/___/___

Serum EITB assay for *T. solium* tapeworm ☐ positive ☐ negative
Lab _____ Date ___/___/___

Comments

Stool Sample Collected ☐ yes ☐ no ☐ unk
Medical Evaluation ☐ yes ☐ no ☐ unk
Education Provided ☐ yes ☐ no ☐ unk

Name | Age | Relation to Case | By proxy | Proxy name

☐ yes ☐ no

NEUROCYSTICERCOSIS SCREENING
if yes to any recommend medical evaluation of neurocysticercosis.

	yes	no	unk	date
seizure	☐	☐	☐	___/___/___
cognitive impairment	☐	☐	☐	___/___/___
chronic/recurrent headaches	☐	☐	☐	___/___/___
focal weakness	☐	☐	☐	___/___/___
vision changes	☐	☐	☐	___/___/___
unexplained neuro deficit	☐	☐	☐	___/___/___

TAENISIS SCREENING
Saw worm segments in feces ☐ yes ☐ no ___/___/___

Stool microscopy ☐ *Taenia solium* ☐ *Taenia saginatta* ☐ *Taenia* species
Lab _____ Date ___/___/___

Initial stool coproantigen ☐ positive ☐ negative
Lab _____ Date ___/___/___

Serum EITB assay for *T. solium* tapeworm ☐ positive ☐ negative
Lab _____ Date ___/___/___

Comments:

Stool Sample Collected ☐ yes ☐ no ☐ unk
Medical Evaluation ☐ yes ☐ no ☐ unk
Education Provided ☐ yes ☐ no ☐ unk

Name | Age | Relation to Case | By proxy | Proxy name

☐ yes ☐ no

NEUROCYSTICERCOSIS SCREENING
if yes to any recommend medical evaluation of neurocysticercosis.

	yes	no	unk	date
seizure	☐	☐	☐	___/___/___
cognitive impairment	☐	☐	☐	___/___/___
chronic/recurrent headaches	☐	☐	☐	___/___/___
focal weakness	☐	☐	☐	___/___/___
vision changes	☐	☐	☐	___/___/___
unexplained neuro deficit	☐	☐	☐	___/___/___

TAENISIS SCREENING
Saw worm segments in feces ☐ yes ☐ no ___/___/___

Stool microscopy ☐ *Taenia solium* ☐ *Taenia saginatta* ☐ *Taenia* species
Lab _____ Date ___/___/___

Initial stool coproantigen ☐ positive ☐ negative
Lab _____ Date ___/___/___

Serum EITB assay for *T. solium* tapeworm ☐ positive ☐ negative
Lab _____ Date ___/___/___

Comments:

Stool Sample Collected ☐ yes ☐ no ☐ unk
Medical Evaluation ☐ yes ☐ no ☐ unk
Education Provided ☐ yes ☐ no ☐ unk

ADMINISTRATION

Remember to copy patient's name to the top of this page.

Initial report sent to OHS on ___/___/___

Completed by _____ Date _____ Phone _____

Case investigation sent to OHS on ___/___/___

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