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Management of Cysticercosis Cerebri

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Infestation of the central nervous system (CNS) with the parasitic larval form of the cestode *Taenia solium, Cysticercosis Cerebri* represents an endemic problem in much of the underdeveloped world. In such areas, up to 4% of the population may be affected by neurocysticercosis, and it accounts for up to 11% of neurosurgical procedures performed in selected centers. The disease remains endemic in Central and South America, Mexico, Eastern Europe, and Asia. With an increasing immigrant influx, however, more cases of this enigmatic entity will be presenting to neurosurgeons in developed nations; therefore maintaining a high index of suspicion in persons of appropriate ethnic background, and recognizing the potential disease spectrum is paramount for all neurosurgeons.

Epidemiology

Humans are the usual definitive hosts of the adult parasite; and when they become the inadvertent intermediate hosts for the parasite (usually porcine), nervous system involvement may occur. Infestation with the larval form may occur with poor hygiene resulting in fecal-oral contamination, eating of contaminated foods, or presumably with reverse bowel peristalsis permitting ingestion of ova released by resident adult intestinal forms. The ingested oncospheres may then traverse the gastric or upper intestinal mucosa, and by subsequent hematogenous spread, infest the CNS by lodging in small arterioles at the gray/white interface.

In addition to the CNS, the larval form has a propensity to metastasize to subcutaneous tissue, both cardiac and skeletal musculature, and intraocular locations.

Diagnosis of Cysticercosis Cerebri

The diagnosis of intracranial infestation is secured in most cases by a constellation of epidemiologic, symptomatic, serologic, and radiographic features consistent with the disease. In our experience, the radiographic evaluation, especially computed tomography (CT) and more recently magnetic resonance imaging (MRI), offers the most specific diagnostic information. Other diagnostic studies, such as long bone radiographs to reveal soft tissue or muscle calcification, may be helpful, if only variably present. Examination of the stool for ova is routinely performed, but the presence of ova is not pathognomonic for determining intracranial involvement. CSF or serum eosinophilia is indicative of a parasitic infection but is neither specific nor sensitive. CSF or serum serological assays are known to be of limited diagnostic value, and are only positive in up to 60% of previously reported series of cysticercosis cerebri. In addition, the delay in obtaining results offers little advantage in the symptomatic patient. Newer serological methodologies show promise for increased diagnostic accuracy. A recently published series from Mexico reports an 87% sensitivity with CSF serology utilizing the Enzyme-Linked Immunoadsorbant Assay (ELISA).

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Spectrum of the Disease

With hematogenous spread the larvae may infest the cerebral parenchyma; by presumptive choroid plexus seeding, the larvae may access the CSF and then (directed by bulk flow) lodge in the ventricles and basilar cisterns. With infection in these locations, ependymitis, basilar arachnoiditis, and vasculitis may manifest either singularly or in combination. With vasculitic involvement, focal ischemia and cranial neuropathies may occur. The resultant clinical presentation is therefore dependent on: 1) the locale of infection, 2) larval load, 3) potential presence of attendant hydrocephalus with intraventricular or basilar infection, and 4) the host immune response.

In consideration of the above, the clinical manifestations of the infection are protean.

The live intraventricular cysts, having accessed the CSF pathways, are often noted throughout the ventricular system, suggesting a migratory lifestyle. Cysts harboring viable parasites may at various stages of volume development migrate through the ventricular system, occluding vital communication conduits and initiating frank acute hydrocephalus or impacting on neural elements and producing focal deficits. Indeed, this has been our experi-

Category: Infection

Key Words: Cysticercosis cerebri • Parenchymal cyst • Basilar cisternal cyst • intraventricular cyst

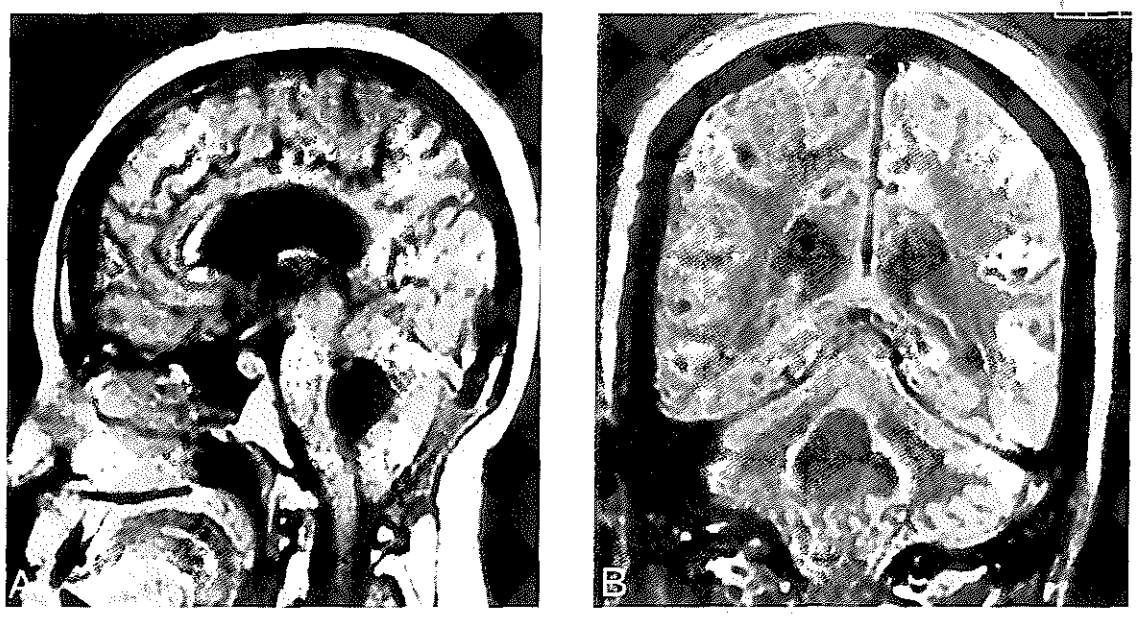

Figure 1. MRI showing multiple intracranial infestations, isointense with CSF on T1 images.

ence, having witnessed cysts in all ventricles. Intraventricular cysts may prove to be particularly hazardous, considering the potential for acute excursions of intracranial pressure. With larval death and changes in cyst wall permeability, focal or generalized ependymitis may occur, with the potential for occlusion of ventricular outlets by this same mechanism.

It is a well recognized phenomenon that ventricular migration proceeds toward the fourth ventricle, either by gravity or bulk flow, thus supporting the epidemiological observation that symptomatic intraventricular cysts occur most commonly in this location. Hydrocephalus (with headache of variable periods of time prior to presentation) is a common clinical manifestation of intraventricular cysts. Third ventricular cysts are thus particularly ominous, offering the substrate for acute neurological deterioration with aqueductal occlusion.

Parenchymal disease, usually considered the benign end of the symptomatic spectrum, occurs with hematogenous spread of the larvae. The usual *Cysticercosis cellulosae* cysts in the brain parenchyma commonly range in size from 3 to 18 mm, but occasionally these lesions may reach symptomatic space-occupying proportions. The cysts contain a discreet marginal larvae or scolex which may be visualized on high-resolution CT or MRI. Small asymptomatic lesions or those presenting with only seizure activity are usually managed expectantly in our institution if the epidemiologic, clinical, and radiographic characteristics corroborate the diagnosis of cysticercosis cerebri. These cysts usually become symptomatic during death of the larvae. During this stage, the dying parasite releases inflammatory toxins. These in turn cause inflammation of the surrounding parenchyma with subsequent inbibition (intake) of fluid secondary to loss of osmotic regulation, thereby enlarging the cyst. The most common single presentation with parenchymal disease is that of focal seizure activity. This has occurred in 92% of cases in some series, and up to 30 years after the original parasitic infestation. In instances of large symptomatic masses, however, surgical drainage or extirpation may be necessary.

In contrast to the parenchymal form of the disease, with CSF spread of the infestation, multiple cysts may form in grape-like clusters in the basilar cisterns, invoking hydrocephalus, basilar arachnoiditis, and cranial neuropathies. These cysts do not contain a viable scolex. It is unknown whether or not this represents a successful immunological response by the host. These aptly named *Cysticercal racemosus* cysts portend a much more ominous prognosis; symptomatology is produced directly by local mass effect in cases of large cysts, indirectly by the distortion of CSF conduits, or by vasculitic involvement.

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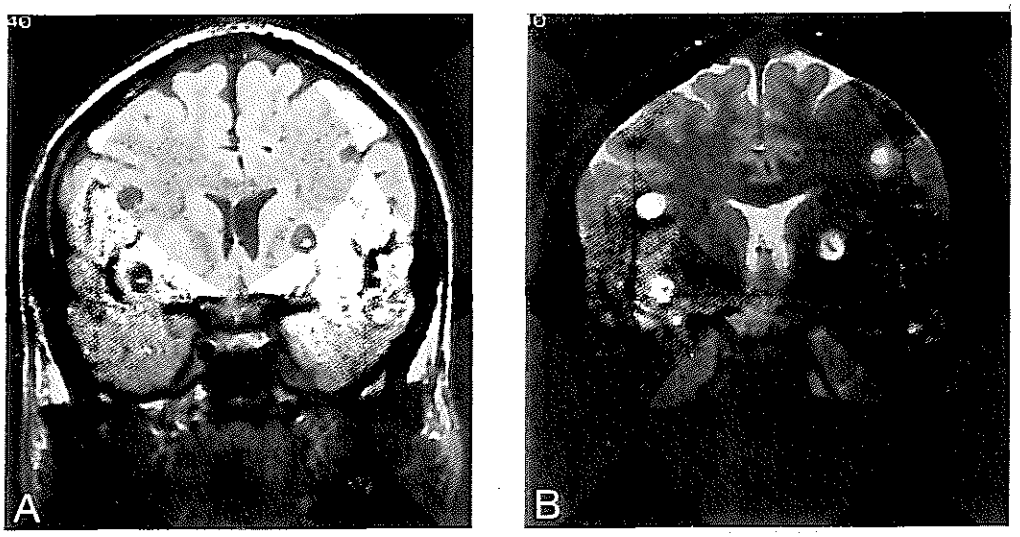

Figure 2. MRI showing multiple discreet marginal intracranial lesions (scoleces).

Radiographic Evaluation

The presence of ventriculomegaly in the patient suspected of having intracranial infestation with cysticercosis is highly suggestive of intraventricular cystic lesions. These lesions are usually isodense with CSF on CT scans, and, as such, usually are not discernable without the administration of a non-ionic contrast agent in the ventricular chamber. In the patient with a ventricular catheter placed for hydrocephalus, we routinely instill 2 to 3 cc of contrast media to adequately outline any intraventricular lesions, which exclude the contrast. In the clinically stable patient, MRI is the preferred study to visualize the lesions, which may also be isointense with CSF on routine T1 images (Figure 1). In this instance, proton density imaging may enhance visualization. T2-weighted MRI or intravenous contrast-enhanced CT images may demonstrate associated ependymitis with intraventricular disease.

Parenchymal cysticercosis cysts may be classified into three evolutionary stages: FIRST STAGE, *live parenchymal cysts:* A clearly defined cyst may be identified on CT or MR images. The very thin capsule cannot be visualized. Cyst fluid is isodense/isointense with CSF. The discreet marginal scolex may be identified (Figure 2). SECOND STAGE, *dying parenchymal cysts:* The capsule thickens and becomes identifiable on T1-weighted MRI. Cyst fluid becomes turbid and may be distinguished from CSF. Such changes may obscure resolution of the scolex. Enhancement of the cyst wall on CT is evident, as with gadolinium-DTPA on MRI, and may be an indication of an inflammatory response. THIRD STAGE, *dead cysts*: The dead larvae involute and calcify with time. CT appears to be superior to MRI in demonstrating the calcified scoleces.

In cisternal cysts, large lesions may manifest as space-occupying lesions that are usually isodense/isointense with CSF (Figure 3). Plain CT scans, while not optimal for their evaluation, may be augmented with the instillation of a non-ionic contrast agent into the subarachnoid space. As with intraventricular disease, proton density and T1-weighted MRIs are superior to T2-weighted images for the evaluation of cisternal cysts; however, T2-weighted images are useful for demonstrating any attendant arachnoiditis and tissue reaction.

Surgical Options

There are a wide variety of surgical options available. These are listed in Table 1.

Intraventricular cysts. Intraventricular cysts are harbored by some 15 to 20% of patients with neural compartment infestation. One important feature noted in our experience has been the high incidence (38%) of rapid

Intraventricular Cysts:

Lateral and Third Ventricular
- *1. Stereotactic Aspiration
- 2. Craniotomy
  - transcallosal
  - transcortical
- 3. CSF Diversion

Fourth Ventricular
- *1. Suboccipital Craniectomy
- 2. CSF Diversion

Parenchymal Cysts:
- *1. Stereotactic Aspiration
- 2. Craniotomy

Basilar Cisternal Cysts:
- *1. Craniotomy
- 2. CSF Diversion

* preferred methodologies

Table 1. Surgical options

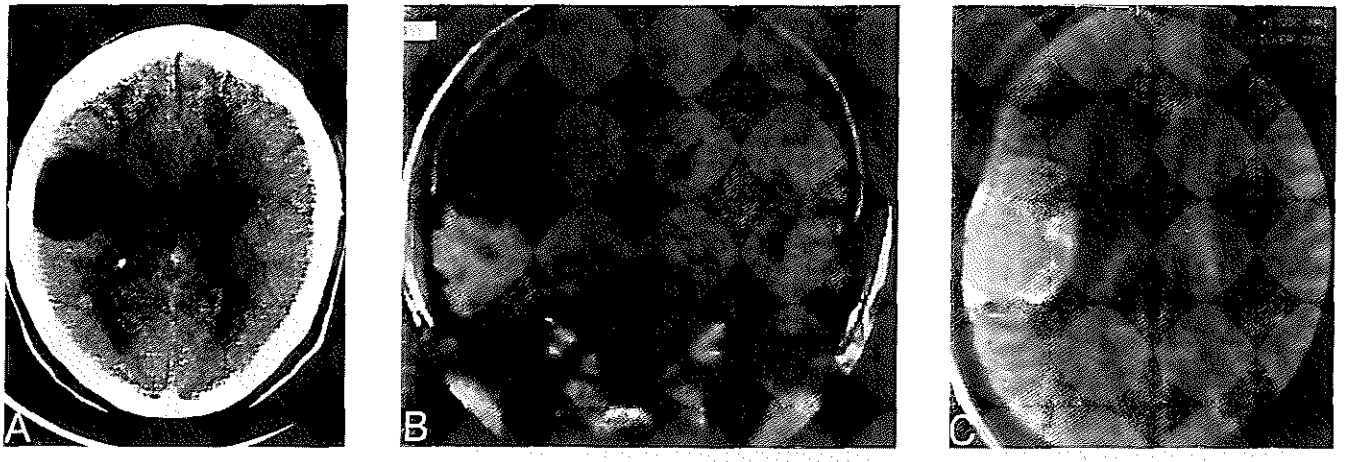

Figure 3. CT scan (*left*) and MRIs showing large space-occupying cystic intracranial lesion that is isodense/isointense with CSF.

clinical deterioration in this group of patients. In consideration of this deterioration, we advocate aggressive surgical intervention as a precautionary measure in this group.

In instances of intraventricular involvement, the two basic options are direct surgical attack on the cyst or a CSF diversion procedure to mitigate against impending hydrocephalus (Table 2). The potential for cyst migration must be assessed preoperatively as postural changes may cause possible frank migration between ventricular chambers.

In cases showing radiographic evidence of ependymitis or arachnoiditis on contrast enhanced CT or inflammation indicated on MRIs, we have found there may be some difficulty in excising intraventricular lesions. In this instance, strong consideration should be given to a primary CSF diversion procedure. In the *absence* of radiographic inflammation, direct surgical excision should be the optimum strategy with simple intraventricular cysts to decrease the risk of acute hydrocephalus while obviating the need for a shunting device.

Should the decision be made to attempt primary cyst excision, then the appropriate surgical approach must be determined. Cysts in the lateral and third ventricular chambers are well-suited to endoscopic aspiration utilizing specifically designed ventriculoscopic methodologies. These techniques have proven extremely useful; the contents of the cyst are aspirated under direct vision in the lateral and third ventricular chambers. In cases of intraventricular rupture, there have been no untoward effects. The concurrent use of high-potency glucocorticoids and generous ventricular irrigation with tepid lactated Ringer's solution are strongly recommended.

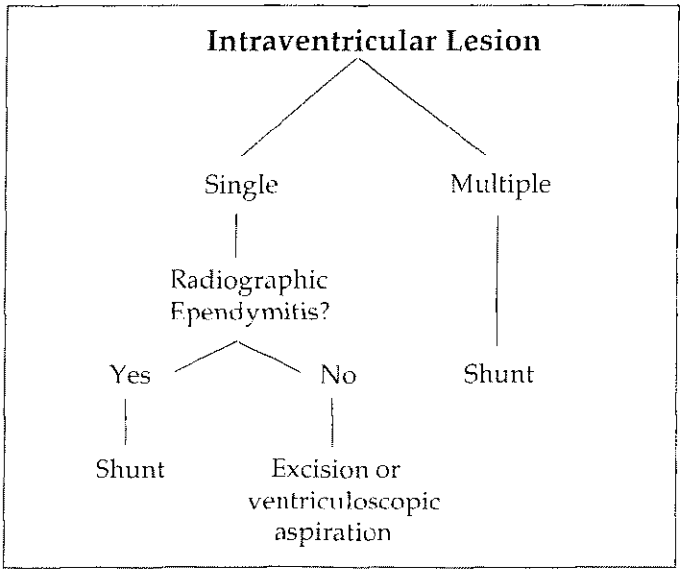

Table 2. Surgical options for intraventricular lesions.

If stereotactic drainage of the cyst is not possible, then the open surgical corridor should be chosen based primarily on the location of the cyst. Usually a transcortical microsurgical approach is utilized to access lateral ventricular cysts, and a transcallosal interfornicial corridor is the preferred approach to third ventricular lesions. In all cases, a generous fenestration of the septum pellucidum is done to ensure adequate bilateral drainage through a unilateral approach.

In the absence of overt radiographic evidence of inflammation, fourth ventricular cysts are easily extractable by suboccipital craniectomy, separation of the cerebellar tonsils, and gentle ventricular irrigation.

In cases of multiple intraventricular lesions or in cases with overt radiographic evidence of ependymitis or basilar arachnoiditis (often associated with racemose cysts), we advocate a primary CSF diversion procedure. Multiple conduits may be necessary in cases with a loculated ventricular system secondary to multiple cysts or attendant ependymitis. In this instance, there is a problem in maintaining patent shunt systems. There also exists the possibility of local expansion of the intraventricular lesions causing focal compression (especially in cases of third or fourth ventricular involvement) , which would require an additional direct drainage or excision.

Parenchymal cysts. Our experience with parenchymal space-occupying lesions shows 8.4% of patients with newly diagnosed cysticercosis cerebri manifesting symptomatology from large cisternal and parenchymal cysts. These cysts may arise anywhere in the cerebrum, most commonly at the level of the gray/white interface, and as such, they often defy easy surgical access.

With the potential for recurrence of the cyst in the

absence of total cyst excision, and with the realization that the life span of the larvae may be up to ten years, we manage all large parenchymal lesions primarily with stereotactic aspiration of the cyst, simultaneously implanting indwelling cyst catheter-reservoir systems. This enables repeat aspiration of the cyst in the event of symptomatic recurrence. Although craniotomy offers the potential advantage of open surgical excision of the entire cyst wall and scolex, which thus decreases the rate of cyst recurrence, it has been only of marginal efficacy in our experience. Attempted craniotomy with excision of the cyst has been associated with unacceptable morbidity and frequent cyst recurrence. Clinically, the cyst wall is often found to be tenacious in its adherence to surrounding neural and vascular elements, which may preclude total removal. In our series, the patients who were managed by primary craniotomy all required subsequent drainage procedures; this is in direct contrast to the patients who underwent an initial stereotactic procedure with placement of a cyst catheter-reservoir system. All of these patients were managed successfully by percutaneous aspiration of their reservoir with minimum morbidity. In comparison to other cystic lesions, the cysticercal walls are not difficult to puncture. This obviates the need to use excessively sharp probes, which may cause potential vascular injury. Therefore, we advocate the use of stereotactic methodologies in the initial management of all large intra-axial lesions.

Cisternal Cysts. Basilar cisternal cysts may reach large space-occupying proportions. They may cause symptoms by direct impact on surrounding neural elements or indirectly by obstructing CSF conduits. In contrast with intraparenchymal cysts, cisternal lesions may often be easily removed with gentle traction and irrigation. In the absence of overt radiographic evidence of surrounding arachnoiditis (e.g., CT contrast enhancement), we advocate open craniotomy and evacuation of these large lesions. Indeed, in the majority of cases, the removal of these cysts may be performed without violation of the cyst wall. This obviates the potential for chemical meningitis as reported by other authors. In our experience, with the concurrent use of high potency glucocorticoids, rupture of intraventricular or cisternal cysts has not been associated with inflammatory reactions as observed by others. Madrazo et al., having noted this complication with intraoperative rupture of only intraventricular cysts, have postulated that the contents of the dead cysticercus (*C. racemosus*) may be nontoxic as opposed to that of the live cysticercus (*C. cellulosae*).

Outcome

There is marked disparity in reported outcome of *Cysticercosis cerebri* in the literature. This represents the spectrum of clinical and pathophysiological consequences of infection. The literature also reflects a skewed sample of the disease populace. The outcome is primarily dependent on the location and extent of intracranial infestation. Dixon and Lipscomb, in following 450 patients with the disease, determined an overall case fatality of cerebral cysticercosis of 10.4% (in some cases over a period of 30 years).

Intraventricular disease, in the absence of attendant ependymitis or basilar cisternal involvement, is easily amenable to surgical intervention. The presence of isolated intraventricular involvement portends a satisfactory outcome in the majority of cases, managed either by primary cyst extraction or diversion. Unfortunately, as is often the case, patients may harbor the disease in multiple intracranial locations. Thus, the ultimate outcome is contingent on the possible presence of basilar involvement, which could adversely affect the prognosis of a patient who would otherwise remain clinically stable.

Our experience with parenchymatous disease indicates that this is a relatively benign infestation in the majority of cases. If the disease is limited to the parenchyma, and the presentation is one of focal neurological deficit or seizure, the prognosis is better than in the patient who presents with signs or symptoms of raised intracranial pressure. Even in the small percentage of patients who harbor sizeable lesions requiring surgical drainage, the ultimate outcome will be limited by the concomitant basilar involvement. In our series, the patients with lesions who were managed by the implantation of cyst catheter-reservoir systems all improved clinically. This was in direct contrast to those patients who underwent primary craniotomy, all of whom required an additional surgical intervention for cyst recurrence. It was necessary, however, to aspirate the cyst-reservoir percutaneously in this group on several occasions. Overall, the patients experienced an 88% improvement in the neurological deficit, and a 75% improvement in symptomatology in those cases managed surgically in our institution. The median follow-up for this group exceeded 36 months. There does exist a very small subgroup of patients with extensive parenchymal infection who may present with a clinical meningo-encephalitis and who may follow a much more malignant clinical course.

It is generally recognized that in the basal cisternal form of infestation *(C. racemosus)*, the prognosis is dependent on the presence of associated arachnoiditis and vasculitis, often reflected in a significant CSF pleocytosis. The disease process defies surgical cure, with vasculitis leading to cranial nerve palsies and ischemia. In these cases, the prognosis is guarded, often with a relentless deterioration in clinical course despite CSF diversion.

Medical Therapy

The anthelminthic agent Praziquantel (Biltricide, Miles Pharmaceuticals) has shown promise in the medical treatment of intracranial cysticercosis. This heterocyclic pyrazino-isoquinolone derivative has been demonstrated in preliminary studies to be effective against parenchymatous lesions. In our institution, all patients with symptomatic, multiple, active parenchymal lesions are treated with a two-week course of the drug. Should symptomatic progression occur despite medical therapy, surgery should

then be contemplated in the patient with large space-occupying cysts. Concurrent treatment with corticosteroids is recommended.

Another advantage in using this anthelminthic is sterilization of the intestinal tract where the adult form may be harbored, a potential source of reinfection with the ova. Patients with multiple, small, active lesions not amenable to surgical methodologies deserve a course of treatment. Its use as an adjuvant in large space-occupying parenchymal lesions has yet to be defined; however smaller attendant intracranial cysts resolved in patients treated with the agent.

Clinical trials have yet to prove beneficial outcome with ventricular lesions. The drug is likely to be of little benefit in cisternal disease, as the *C. racemosus* cysts contain no viable scolex.

As yet, we have no experience with the use of the newer anthelminthic agent albendazole.

Readings

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Answer questions on response card for volume 011, lesson 19

IMPORTANT: MARK ONLY ONE OVAL AND USE NUMBER 2 PENCIL ONLY

Response card must be mailed on or before December 6, 1989

1. The larval form of the cestode *Taenia solium* may infest the ventricular, parenchymal, cisternal, and spinal spaces.
   True or False?

2. The most common time for symptomatic manifestation of the parenchymal form of infection is with death of the larvae.
   True or False?

3. Parenchymal involvement is the most benign manifestation of intracranial infestation.
   True or False?

4. Intraventricular cysts are readily visualized on unenhanced CT scans.
   True or False?

5. Craniotomy is the preferred surgical treatment for intraparenchymal disease.
   True or False?

6. Craniotomy is the preferred surgical methodology for large cisternal lesions.
   True or False?

7. The absence of radiographically discernable intraventricular cysts eliminates the potential for the development of hydrocephalus.
   True or False?

8. All patients with intraventricular cysts are candidates for surgical removal of the lesion.
   True or False?

9. Craniotomy for excision of parenchymal lesions is associated with potential recurrence.
   True or False?

10. Praziquantel has been demonstrated to be efficacious in cisternal and intraventricular disease.
    True or False?