A diagnostic and therapeutic scheme for a solitary cysticercus granuloma

G. Singh, DM
V. Rajshekhar, MCh
J.M.K. Murthy, DM
S. Prabhakar, DM
M. Modi, DM
N. Khandelwal, MD
H.H. Garcia, MD

Address correspondence and reprint requests to Dr. Gagandeep Singh, Department of Neurology, Dayanand Medical College, Ludhiana, 141001, Punjab, India
gagandeep_si@yahoo.co.uk

ABSTRACT

Background: Solitary cysticercus granuloma (SCG) is one of the most common forms of presentation of neurocysticercosis (NCC). The diagnostic workup and management approach to this condition remain uncertain and controversial.

Objective: To review evidence and develop a consensus approach to the diagnosis and treatment of SCG.

Methods: A multidisciplinary expert group meeting was convened in order to review and discuss various aspects of management of patients with SCG. Evidence reviewed was classified and a consensus was evolved according to standard protocols.

Results: SCG is commonly recognized on CT as an enhancing lesion measuring <20 mm. Further evaluation with MRI does not add much information. The use of antihelminthic agents (specifically, albendazole in combination with corticosteroids) and corticosteroids alone have been shown to improve radiologic resolution and seizure outcome in patients with SCG. However, the sizes of the effects are modest. By convention, all patients with SCG presenting with seizures are initiated on antiepileptic drugs (AEDs). Available evidence suggests that withdrawal of AEDs after complete resolution of the SCG is safe. There is a high risk of seizure relapse after AED withdrawal in patients with calcific residue following resolution of the SCG. The duration of AED prophylaxis in these individuals is unclear.

Conclusions: It is desirable to have large, multicenter trials with sufficiently long follow-up, comparing outcomes with the use of antihelminthics with or without corticosteroids and corticosteroids alone in order to dissect out the benefits accrued due to each of these classes of drugs.

Neurology® 2010;75:2236-2245

GLOSSARY

AED = antiepileptic drug; **CI** = confidence interval; **EITB** = enzyme-linked immunoelectrotransfer blot; **NCC** = neurocysticercosis; **OR** = odds ratio; **RCT** = randomized controlled trial; **SCG** = solitary cysticercus granuloma.

Neurocysticercosis (NCC) refers to infection of the human brain by the larval stage of the helminth *Taenia solium*. The disease is widely prevalent, especially in several low- and middle-income countries of the world, including India, China, sub-Saharan Africa, and Central and South America.^{1,2} In addition, NCC is of emerging importance in many high-income countries (e.g., United States) with high volumes of immigration traffic from *T solium*-endemic regions of the world.^{3,4}

The clinical and radiologic manifestations of NCC are pleomorphic.^{5,6} Several varieties of NCC have been recognized depending upon the number, location, and evolutionary stage of the cysticerci in the human brain.⁷⁻¹² At a previous consensus meeting, experts agreed that no single treatment approach could be advocated and that management options varied according to the type of clinical presentation.¹³ A common presenting form of NCC is the solitary

Supplemental data at
www.neurology.org

From the Department of Neurology (G.S.), Dayanand Medical College, Ludhiana; Department of Neurological Sciences (V.R.), Christian Medical College, Vellore; Department of Neurology (J.M.K.M.), CARE Hospitals, Hyderabad; Departments of Neurology (S.P., M.M.) and Radiodiagnosis (N.K.), Postgraduate Institute of Medical Education and Research, Chandigarh, India; and Department of Microbiology (H.H.G.), Universidad Peruana Cayetano Heredia, Lima, Peru, Cysticercosis Unit, Instituto de Ciencias Neurologicas, Lima, Peru.

Study funding: The meeting was partially supported by a grant from Zydus-Cadilla, India Ltd., which had no role in the organization and proceedings of the meeting and in the formulation of the recommendations and the decision to publish.

Disclosure: Author disclosures are provided at the end of the article.

cysticercus granuloma (SCG), which represents a single, degenerating parenchymal cysticercus cyst.^{14,15} This form of presentation is more frequently reported from India and the United States.^{4,16} It has also been reported in Latin American series, albeit with a somewhat lesser frequency.^{1,7,14,16,17} Treatment approach to SCG has not been optimally defined. While treatment with albendazole has been shown to improve outcome in live, cystic parenchymal cysticercosis, the benefits of antihelminthic treatment in patients with SCG remain uncertain despite several randomized trials.¹⁸⁻²⁵ Likewise, controversy exists regarding the use of corticosteroids, alone or in combination with antihelminthic drugs, and the optimal duration of antiepileptic drug (AED) therapy.²⁶⁻³² We report the outcome of an expert group meeting held in order to define the optimal management approach to SCG.

METHODS Eighteen experts with published research experience in cysticercosis (mostly neurologists but also a neurosurgeon, pediatrician, general physician, parasitologist, infectious disease specialist, and neuroradiologist) were invited to the meeting. They reviewed and presented evidence regarding the following: 1) role of imaging and serology in the diagnosis of SCG; 2) benefit of (or lack thereof) antihelminthic treatment (albendazole, praziquantel, or combined albendazole and praziquantel) alone or in combination with corticosteroids and corticosteroids alone (without antihelminthic drugs) on seizure outcome and radiologic resolution in SCG; 3) the optimal choice of and duration of AED treatment; and 4) the appropriate timing and modality for follow-up imaging.

Medline and Cochrane Central Register for Controlled Clinical Trials were searched using the terms “solitary cysticercus granuloma” or “single lesion” and “neurocysticercosis.” A similar search was later undertaken using the LILACs, from which no articles could be retrieved using the search strategy. The primary search was further refined using appropriate search terms by each of the reviewers according to their assigned topics (appendices e-1 and e-3 on the *Neurology*[®] Web site at www.neurology.org). Bibliographies of retrieved articles were hand-searched for additional primary studies. In addition, inquiries were made from all invited experts to identify unpublished treatment trials for SCG. The retrieved studies were appraised and assessed regarding method of treatment assignment (randomization), control of selection bias (intention-to-treat vs per-protocol analysis and reporting of loss to follow-up), blinding, and method of outcome assessment. Available evidence for and against various therapeutic interventions and investigations were classified according to criteria given in appendix e-2 (tables e-1 and e-2).^{33,34} Where evidence regarding the study question was not available or was conflicting, attempt was made to generate consensus by discussion. Finally, the strength of recommendations made thereof were graded according to criteria outlined in appendix e-2 (table e-3).³⁵

Figure 1

Contrast CT appearance of single enhancing lesion with an eccentric nodule representing the scolex in the left frontal region

RESULTS **Definition of SCG.** The working definition of SCG for the purpose of formulating the diagnostic and therapeutic scheme was based on previously validated clinical and CT criteria (figure 1).^{15,36} These criteria were expanded and revised through consensus in order to include MRI features of SCG (figure 2, A–D, and table 1).

Natural history of SCG. The natural history of SCG was studied under 2 aspects: 1) radiologic resolution and 2) seizure outcome.

Radiologic resolution. To assess the natural resolution dynamics of SCG, only those studies that included patients soon after their first seizure were analyzed. Review of these observational studies suggested that the natural history of SCG could take one of the following paths: 1) the lesion could completely resolve or 2) the lesion could resolve by leaving a punctuate calcific residue.³⁷⁻³⁹ In one prospective study of 210 patients with SCG followed up after their first seizure, the estimated resolution rates on follow-up CT were 19% at 3 months, 36% at 6 months, and 63% at 1 year.³⁷

Seizure outcome. Seizure outcome in individuals with SCG was dichotomized into 1) those seizures that recurred while the granuloma was actively degenerating and 2) those that recurred following resolution of the granuloma. The natural history of seizure outcome was determined from data of control arms of the several controlled trials (no intervention other than AEDs) in SCG. These data refer to the inci-

Figure 2 MRI appearances of solitary cysticercus granuloma (SCG)

Coronal fluid-attenuated inversion recovery (A) and T1 unenhanced (B) both showing an eccentric scolex, and gadolinium-enhanced T1-weighted (C) and T2-weighted (D) images of an SCG in the right frontal location.

dence of seizure recurrence while the granuloma was actively degenerating and suggested that seizures could recur in 13%–48% of the individuals while on AEDs alone for 6–15 months (table 2).^{22,26,27,31,32} On the other hand, in a prospective, observational study evaluating the incidence of seizure recurrence following resolution of the granuloma and withdrawal of AEDs (mean follow-up period 66 months) in a referral hospital-based cohort of individuals, 15% of the individuals had seizures.³⁸

Statement. The majority of SCGs resolve by 1 year. The natural history of SCG may take one of the following paths: 1) the lesion may completely resolve or 2) the lesion may resolve by leaving behind a punctuate calcific residue. The risk of seizure recurrence remains high as long as the granuloma is visible on imaging as an enhancing lesion (level of evidence: Class IV) (table 2).^{22,26,27,31,32} Seizure outcome im-

proves following resolution of SCG (level of evidence: Class IV).

Investigative workup of SCG. Imaging. The initial imaging evaluation of SCG may be either contrast CT or MRI (figures 1 and 2, A–D). Two head-to-head comparison studies of CT and MRI in the characterization of SCG were available; however, these studies were performed on highly selected populations and the MRI techniques used were suboptimal.^{21,40} In these studies, MRI was not found to be superior to CT in the diagnosis of SCG (level of evidence: Class II).

Recommendation. Once CT demonstrates a single enhancing lesion consistent with a diagnosis of SCG (see table 1), further evaluation with MRI may not be required (strength of recommendation: C).

Immunologic tests. Although several serologic assays for cysticercosis are available, currently the enzyme-

Table 1 Clinical and radiologic features consistent with a diagnosis of SCG

A. Clinical features that are supportive of a diagnosis of SCG	
	Focal seizures with or without secondary generalization
	Note: Seizures may be new-onset or of longer duration; may be generalized at onset; may occur in clusters (2 or more seizures over 2–3 days); may be followed by unilateral or diffuse headaches lasting for a few hours to days; or may be followed by transient and mild postictal neurologic deficits
B. Clinical features that make a diagnosis of SCG unlikely	
	Persistent and severe neurologic deficit
	Clinical evidence of intracranial hypertension
	Evidence of neurologic disorder, other systemic disease (e.g., systemic infection such as AIDS) that can account for imaging findings
	Age <2 years and >60 years
C. CT features compatible with a diagnosis of SCG (see figure 1)	
	Single, small (<20 mm), well-defined
	Contrast-enhancing (closed ring, disc, or nodular type)
	With or without surrounding edema
	Associated with minimal mass effect and no midline shift
D. MRI features compatible with a diagnosis of SCG (see figure 2, A–D)	
	Single, small (<20 mm) lesion with fluid contents
	T1 sequence: intensity slightly greater than or isointense to CSF
	T2 sequence: hyperintense or isohypointense with central hyperintensity
	Ring or nodular type enhancement after contrast
	Scolex may or may not be visible as an eccentric nodule within the fluid cyst contents (T1 isointense and T2 iso/hypointense)
	Mild to moderate surrounding edema but no midline shift

Abbreviation: SCG = solitary cysticercus granuloma.

linked immunoelectrotransfer blot (EITB) assay is the standard of serologic diagnostic evaluation.⁴¹ It is highly sensitive and specific as a screening test for cysticercosis and detects exposure to the parasite. In multiple NCC, the EITB was found to be 100% sensitive and 99% specific when performed on serum. In hospital-based series of SCG, however, the yield of the EITB was considerably lower, i.e., 20%–80%^{42–44} (level of evidence: III). No published studies of the performance of the EITB in the CSF in cases of SCG are available. A practical limitation is

that the EITB is not widely available in many parts of the world where cysticercosis is endemic.

Recommendation. Where available, the EITB may be performed on serum in order to establish exposure to *T solium* parasite in individuals with SCG (strength of recommendation: C).

Antihelminthic treatment of SCG. Overview of randomized controlled trials and meta-analysis. Several randomized trials attempted to clarify the effect of antihelminthic treatment in SCG. However, data from these trials were conflicting (table 3).^{22–25} Subsequently, a meta-analysis of randomized trials of albendazole in individuals with 1–2 parenchymal granuloma was undertaken.⁴⁵ Following this meta-analysis, more randomized controlled and pseudo-randomized trials comparing albendazole alone or with corticosteroids with corticosteroids alone or with a combination of albendazole, praziquantel, and corticosteroids were performed.^{20,28,46,47} A summary of these trials with the 2 main outcome measures, i.e., radiologic resolution and seizure outcome, is presented in tables 3 and 4.

The meta-analysis revealed a trend toward early resolution of 1–2 brain cysticercus granulomas with the administration of albendazole (odds ratio [OR] 1.18; 95% confidence interval [95% CI] 0.82–1.71).⁴⁵ However, a recalculation done after excluding one trial with an outlier OR showed that albendazole significantly improved resolution of the granuloma (OR 1.93; 95% CI 1.21–3.08). The meta-analysis also demonstrated a significant benefit of intervention in preventing seizure recurrence (OR 0.36; 95% CI 0.21–0.62).^{22,23,25,45}

Dose, duration, and side effects. All available trials used albendazole in a universally accepted dose of 15 mg/kg/day in 2–3 divided doses. However, the duration of treatment was quite variable (1–4 weeks).^{22–25} An uncontrolled study of subjects with SCG treated with albendazole reported adverse effects in 35%.⁴⁸ In one study, treatment was associated with a trend

Table 2 Natural history (complete resolution on follow-up CT) and seizure outcome derived from control arms (no treatment apart from antiepileptic drugs) of various controlled trials in SCG

Reference	No.	Complete resolution at 1 month	Complete resolution at 2–3 months	Complete resolution at 6 months	Seizure-free over 6 months	Seizure-free over 9 months	Seizure-free over 12 months
27	48	11 (22.9%)	NA	25 (52.8%)	35 (72.9%)	NA	NA
26	30	NA	NA	14 (46.7%)	16 (53.3%)	NA	NA
31	27	NA	5 (18.5%)	NA	NA	18 (66.7%)	NA
32	45	NA	24 (53.3%)	NA	NA	NA	33 (73.3%)
22	27	NA	NA	9 (33.3%)	22 (81.5%)	NA	NA

Abbreviations: NA = data not available; SCG = solitary cysticercus granuloma.

Table 3 Randomized controlled trials of treatment in SCG

Reference	Intervention, duration, days	Follow-up period for seizure outcome assessment, months	Time to assessment of radiologic outcome, months	Control group, n (%)			Treated group, n (%)		
				No.	Radiologic resolution	No. of subjects with seizures on follow-up	No.	Radiologic resolution	No. of subjects with seizures on follow-up
Randomized controlled trials of antihelminthic treatment of SCG									
21	Albendazole, 28	6	6	58	11 (19.5)	5 (8.6)	65	15 (22.6)	7 (10.8)
22	Albendazole, 28	6	6	27	9 (33.3)	5 (18.5)	24	11 (45.8)	3 (12.5)
23	Albendazole, 28 + dexamethasone, 5	6	3	62	53 (85.5)	17 (27.4)	61	47 (77.0)	5 (8.2)
24	Albendazole, 7	—	3	35	33 ^a (94.3)	NA	40	35 ^a (87.5)	NA
25	Albendazole, 28	At least 15	3	37	12 (32.4)	11 (29.7)	35	20 (57.1)	4 ^b (11.4)
Randomized controlled trials of corticosteroids in SCG									
26	Prednisolone 1 mg/kg, 10	9	6	30	16 (53.3)	14 (46.7)	30	14 (46.7)	4 (13.3)
27	Prednisolone 1 mg/kg, 10	6	6	48	25 (52.1)	13 (27.1)	49	43 (87.7)	3 (6.1)
31	Methylprednisolone 1 g/d, 5	9	2	27	5 (18.5)	9 (33.3)	25	15 (60.0)	4 (16.0)
32	Prednisolone 1 mg/kg, 7 d	12	2–3	50	24 (48.0)	12 (24.0)	50	32 (64.0)	5 (10.0)
49	Prednisolone 1 mg/kg, 14 d	9	6	75	21 (28.0)	19 (25.3)	73	28 (38.4)	16 (21.9)

Abbreviations: NA = data not available; SCG = solitary cysticercus granuloma.

^a Includes resolution with and without calcification.

^b Excluded patients with seizures in the first month of follow-up.

toward increased risk of seizures for the period during which albendazole was administered.²⁵

Statement and recommendation. The meta-analysis and other studies suggest a possible beneficial effect of albendazole in subjects with SCG in the form of improved resolution rates of the granuloma and better seizure control (level of evidence: Class II). However, the size of these effects appears to be modest. Moreover, the component trials of the meta-analysis appear to have several limitations. Hence, in order to make definite conclusions regarding the effect of albendazole in SCG, larger multicentric trials with sound methodology are required. Until such evidence is available, a short course (1–2 weeks) of albendazole (with or without corticosteroids, de-

pending upon the judgment of the treating physician) may be prescribed soon after presentation, i.e., the first seizure (strength of recommendation: A).

Role of corticosteroids. The routine use of corticosteroids alone (without specific antihelminthic treatment) in the management of SCG was advocated by some authors. Four small published trials and one unpublished trial were available (table 3).^{26,27,31,32,49} Three of the published trials were from one center, thus essentially constituting a single-center experience.^{26,27,31} The study designs in some of these trials had limitations. All except the recent unpublished trial demonstrated both significantly better rates of radiologic resolution on follow-up CT scans and sig-

Table 4 Active comparator trials of antihelminthic drugs (albendazole and praziquantel) and corticosteroids in solitary cysticercus granuloma

Reference	Follow-up period, months	Radiologic outcome, months	Albendazole, n (%)			Albendazole/corticosteroid, n (%)			Corticosteroid, n (%)			Albendazole/praziquantel/corticosteroid		
			n	R	N	n	R	N	n	R	N	n	R	N
28	18	6	37	26 (59.5)	5 (14.3)	35	28 (62.9)	4 (10.8)	38	29 (52.6)	14 (36.8)	—	—	—
46	6	6	42	25 (59.5)	5 (11.9)	48	33 (68.8)	9 (18.8)	42	25 (59.5)	5 (11.8)			
20	6	6				50	26 (52.0)	3 (6.0)				53	38 (71.7)	3 (5.7)

Abbreviations: n = number of subjects in treatment arm; N = number of subjects with seizure recurrence during the follow-up period; R = number of subjects with radiologic resolution of solitary cysticercus granuloma on follow-up CT.

nificantly lesser incidence of seizure recurrence with corticosteroid treatment.^{26,27,31,32,49}

Statement and recommendation. While treating individuals with SCG, one can either prescribe a short course of corticosteroids alone (without specific antihelminthic treatment) or antihelminthic drugs (alone or with corticosteroids). The concept of prescribing a short course of corticosteroids alone is in conflict with the practice of administering antihelminthic drugs (alone or with corticosteroids) to individuals with SCG. Ideally, a large randomized, double-placebo-controlled trial comparing corticosteroids alone, albendazole alone, and albendazole with corticosteroids is required in order to dissect out the benefits accrued due to either agent. Until such evidence is available, definite recommendations regarding the use of corticosteroids alone in the management of SCG cannot be made (strength of recommendation: C).

Antiepileptic drug therapy. Duration of AED therapy. Three open-labeled trials compared administration of AEDs for short duration (6 months) vs longer duration (12–24 months) in individuals with SCG and seizures.^{29,30,50} The studies concluded that there was no additional benefit of the longer-duration AED administration in individuals in whom the SCG had resolved. However, pooled data from the 3 studies also suggested that the risk of seizure recurrence was greater (OR 1.29; 95% CI 0.70–2.35; $p = 0.42$) with short-duration AED treatment. This increased risk with early withdrawal of AEDs was largely due to an increased incidence of seizure recurrence in those individuals in whom the granuloma resolved leaving behind a calcific residue. The presence of a calcific residue increased the risk of seizure/second in the postresolution period (pooled OR 11.47; 95% CI 4.96–26.51; $p = 0.0001$).

Statement and recommendations. The risk of seizure recurrence in an individual with SCG is related to the persistence of the enhancing lesion (level of evidence: Class IV). The currently used AEDs effectively prevent seizure recurrence. It is appropriate to continue AEDs until such time that the lesion (granuloma) is actively degenerating (i.e., appears as an enhancing lesion on imaging studies). The AED may be withdrawn once complete resolution of the granuloma is demonstrated on follow-up imaging studies (strength of recommendation: C).

The long-term seizure outcome in patients with SCG is generally good (level of evidence: Class III). However, the risk of seizure recurrence remains high if the granuloma resolves leaving behind a calcific residue (level of evidence: Class II). In the case of resolution with calcification, longer duration of AED should be considered (strength of recom-

mendation: B). It is unclear how long AEDs should be administered to individuals with SCG that resolve with calcification.

Choice of AEDs. Apart from a single, small, open-labeled trial (clobazam vs phenytoin), there were no comparison studies of various AEDs in the management of seizures associated with SCG.⁵¹ Both phenytoin and carbamazepine were shown to increase the metabolism of praziquantel and albendazole, though the clinical significance of these interactions remained uncertain.^{52,53} Thus, these AEDs should ideally be avoided at least for the period of treatment with antihelminthic drugs in individuals with SCG. There is no reported experience with the newer AEDs in the treatment of seizures associated with SCG.

Recommendation. Any AED might be used for much of the period of treatment in individuals with SCG. A newer, non-enzyme-inducing AED might be considered for the period of time that antihelminthic treatment is administered (strength of recommendation: C).

Appropriate timing and modality of follow-up imaging. In an observational study of subjects with SCG and seizures followed up within 1 month of the first seizure, resolution of the granuloma on follow-up CT was demonstrated in 19% of cases at 3 months, 36% at 6 months, and 63% at 12 months.³⁷ The choice of follow-up imaging is between CT and MRI. Head-to-head comparison studies that might determine which of the 2 imaging modalities is superior for follow-up purposes have not been undertaken. An observational follow-up study based on magnetization transfer MRI demonstrated resolution with perilesional gliosis in a proportion of patients with SCG.⁵⁴ The authors of this study suggested that the occurrence of perilesional gliosis correlated with seizure recurrence in the follow-up period.

Recommendation. Follow-up imaging (either contrast-enhanced CT or MRI) should be undertaken at 6 months following initial symptomatic presentation in all individuals with SCG (strength of recommendation: C). However, earlier CT (e.g., at 3 months) might be useful in order to identify those lesions that enlarge or change morphology, hence suggesting an alternative etiology (e.g., neoplasm, tuberculoma, or fungal granuloma) (strength of recommendation: C).

DISCUSSION A logical first step in formulating the diagnostic and therapeutic scheme is to accurately define SCG. The SCG may be identified on either CT or MRI. The appearance on CT is commonly referred to as the single enhancing lesion (figure 1). The notion that these lesions represent solitary infes-

tation of the cerebral parenchyma by cysticercus is based on a single, small, highly selected series of stereotactic-guided biopsies from a referral hospital, which suggested a histologic diagnosis of cysticercosis in the majority (level of evidence: Class IV).⁵⁵ From a pathologic standpoint, the lesions might represent either the colloidal or granular-nodular stage in the evolutionary cycle of cysticerci as a clearcut differentiation between the 2 stages might not be possible upon imaging. In essence, the SCG represents a degenerating single cerebral cysticercus cyst. A scolex might or might not be identified upon imaging studies. In controlled follow-up studies of SCG, lesions with evidence of calcification upon imaging at presentation have mostly been excluded. Hence, the observation of a single, ring- or disc-enhancing lesion on CT is highly suggestive of a cysticercus granuloma, provided the size criterion of less than 20 mm is strictly met (level of evidence: Class IV) (table 1).⁵⁶ Lesions larger than 20 mm or conglomerate ring lesions might not denote SCG (level of evidence: Class IV).⁵⁷

Investigative workup of SCG. Imaging. Imaging and serologic studies are widely used in the diagnosis of NCC. Either CT or MRI may be used in the imaging evaluation of SCG (figures 1 and 2, A–D). Although MRI better characterizes the pathologic stage of the lesion (colloidal vs granular-nodular stage), identifies an eccentric nodule (or scolex), and may rarely reveal granulomas at sites that are obscured by bone artifacts (e.g., temporal location),¹⁴ it rarely provides additional information that might impact the management of SCG.^{21,40} In addition, there are limitations to performing MRI in resource-poor countries including the lack of widespread availability and the additional cost imposed. Hence, the expert group accepts by consensus that contrast-enhanced CT sufficiently establishes the radiologic diagnosis of SCG provided all criteria listed (table 1) are met (strength of recommendation: C). However, it may be cautioned here that in many resource-poor countries, the available CT scanners might be of the older generation and characterization of SCG on these scanners might be suboptimal.

Antihelminthic treatment of SCG. There are several problems with the published randomized trials of antihelminthic treatment in SCG. In most trials, sample size calculations have not been performed and many have not explicitly described the randomization procedures. Apparently, only some of the studies blinded the evaluators to outcome measures. Outcome measures and study designs relating to the assessment of seizure recurrence following therapeutic

intervention with antihelminthic agents have varied quite considerably between the various trials. For instance, some studies excluded seizures that occurred during the first month.²⁵ The period of follow-up in the trials also varied from 6 months to 15 months. Finally, all the randomized studies involved small numbers of subjects. Based on the results of the meta-analysis, it seems that albendazole provides modest benefit in the form of improved rates of radiologic resolution and a reduction in the incidence of seizure recurrence.⁴⁵ However, these effects have been evaluated only in the short term since the follow-up in the available trials is mostly less than 1 year.^{22–25}

Subgroup effects and covariates. It is possible that the effect of antihelminthic treatment on resolution of the lesion may vary among different subgroups of SCG. Examples of subgroups include colloidal vs granular-nodular morphology, the presence or absence of a demonstrable scolex on MRI, and disc vs ring pattern of enhancement on CT. None of the studies have analyzed subgroup effects on the outcome parameters, though it would be ideal to determine whether such effects exist in future trials. Likewise, the effect of timing of therapeutic intervention in relation to duration of symptoms on outcome has not been adequately studied. It is a matter of debate whether antihelminthic treatment should be instituted upon initial presentation following the first seizure or only if follow-up imaging shows persistence of granuloma.⁵⁸

Role of corticosteroids. Several trials regarding the use of a short course of corticosteroids alone (without specific antihelminthic treatment) are now available.^{26,27,31,32,49} One problem with the available trials is that they do not provide information on the timing of recurrent seizures in relation to the administration of corticosteroids. Thus, it is not clear if the benefits in seizure outcome due to corticosteroids are a result of the reduced likelihood of seizures during and immediately after corticosteroid administration owing to their anti-inflammatory action or due to a more sustained effect by altering the natural history of the granuloma.

Antiepileptic drug therapy. Carbamazepine and phenytoin are the most frequently used AEDs for prevention of seizure recurrence in individuals with SCG. The drugs are relatively cheap and easily available in most low- and middle-income countries. There is virtually no experience with the use of the newer AEDs in SCG. In addition, the newer AEDs may not be widely available and are more expensive.

Appropriate timing and modality of follow-up imaging. Based on limited data available, it is conventional practice to perform follow-up imaging 6 months after initial presentation of the SCG.³⁷ Either CT or MRI might be used for follow-up imaging. An argument in favor of CT is that it is thought to be superior to MRI in detecting calcific residues. However, modern MRI techniques (e.g., T2* imaging) are sufficiently sensitive for detecting minor calcifications.⁵⁹ Access to MRI may be restricted due to limited availability of MRI machines and also the cost involved. Hence, the choice of follow-up imaging between MRI and CT (or both) may be based on availability and cost considerations.

Several issues in the management of SCG need to be resolved in the future. The role of initial and follow-up investigations including CT and MRI needs to be determined in a larger controlled study. In addition, a carefully planned, double-blind, (double-) placebo-controlled randomized trial is desirable in order to define the role of various classes of therapeutic agents alone or in combination in individuals with SCG. The trial should incorporate quality of life measures and cost-benefit analyses especially in the economic conditions of the geographic regions in which SCG are commonly found.

AUTHOR CONTRIBUTIONS

The meeting was conceptualized and organized by G.S., S.P., and M.M.; V.R., J.M.K., and G.S. wrote the paper, which was reviewed by H.H.G. and S.P. All invited speakers reviewed the literature. Imaging illustrations were selected and provided by N.K.

COINVESTIGATORS

The following were the participants in the Expert Group Committee: J.S. Chopra, FRCP, PhD (Department of Neurology, Postgraduate Institute of Medical Education and Research, Chandigarh, India; Advisor, Expert Group Committee), R.S. Wadia, MD (Department of Neurology, BJ Medical College, Pune, India; Advisor, Expert Group Committee), Meena Gupta, MD, DM (Department of Neurology, GB Pant Hospital, New Delhi, India; Member, Expert Group Committee), M. Gourie Devi, MD, DM, DSc (Department of Neurology, Ganga Ram Hospital, New Delhi; Advisor, Expert Group Committee), M.V. Padma, MD, DM (Department of Neurology, All India Institute of Medical Science, New Delhi, India; Reviewer and Speaker, Expert Group Committee), Manjari Tripathi, MD, DM (Department of Neurology, All India Institute of Medical Science, New Delhi, India; Reviewer and Speaker, Expert Group Committee), Rakesh Shukla, MD, DM (Department of Neurology, Chhatrapati Shahuji Medical University, Lucknow, India; Reviewer and Speaker, Expert Group Committee), Gursaran Kour, MD (Sidhu Hospital Doraha, India; Resource General Practitioner, Expert Group), U.K. Misra, MD, DM (Department of Neurology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India; Reviewer and Speaker, Expert Group Committee), Kurupath Radhakrishnan, MD, DM (Department of Neurology, Shri Chitra Tirunal Institute of Medical Sciences and Technology, Trivandrum, Kerala, India; Reviewer and Speaker, Expert Group Committee), Pratibha Singhi, MD (Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh, India; Reviewer and Speaker, Expert Group Committee), Pratap Sanchee, MD, DM (Consultant Neurologist, Jodhpur, India; Member, Expert Group).

DISCLOSURE

Prof. Singh serves as an Associate Editor for *Neurology India*; has funding for travel from Janssen and Sanofi-Aventis; and has received research support from the Indian Council of Medical Research. Dr. Rajshekhar serves on the editorial boards of *Neurology India*, the *British Journal of Neurosurgery*, and *Stereotactic and Functional Neurosurgery*; and receives research support from the Indian Council of Medical Research and the Flemish InterUniversity Council. Dr. Murthy serves as Editor for *Neurology India* and on the editorial board of *Neurocritical Care*. Dr. Prabhakar has received research support from the Indian Council of Medical Research and Department of Biotechnology, India. Dr. Modi and Prof. Khandelwal report no disclosures. Dr. Garcia serves as an Associate Editor of *PLoS Neglected Tropical Diseases*, as an editorial consultant for *The Lancet*, and on the editorial boards of the *American Journal of Tropical Medicine and Hygiene*, *Experimental Parasitology*, the *World Journal of Gastroenterology*, *Annals of Neurosciences* (India), and the *Journal of Neuroparasitology*; and receives research support from the NIH (NINDS R01 NS054805 [PI] and TW001140 [PI]), the Gates Foundation, and The Wellcome Trust.

Received March 14, 2010. Accepted in final form August 23, 2010.

REFERENCES

1. Rajshekhar V, Joshi DD, Doanh NQ, van De N, Xiaonong Z. *Taenia solium* taeniosis/cysticercosis in Asia: epidemiology, impact and issues. *Acta Trop* 2003;87:53–60.
2. Garcia HH, Gonzalez AE, Gilman RH. Diagnosis, treatment and control of *Taenia solium* cysticercosis. *Curr Opin Infect Dis* 2003;16:411–419.
3. Ong S, Talan DA, Moran GJ, et al. Neurocysticercosis in radiographically imaged seizure patients in U.S. emergency departments. *Emerg Infect Dis* 2002;8:608–613.
4. Wallin MT, Kurtzke JF. Neurocysticercosis in the United States: review of an important emerging infection. *Neurology* 2004;63:1559–1564.
5. McCormick GF, Zee CS, Heiden J. Cysticercosis cerebri. Review of 127 cases *Arch Neurol* 1982;39:534–539.
6. Garcia HH, Del Brutto OH. *Taenia solium* cysticercosis. *Infect Dis Clin North Am* 2000;14:97–119.
7. Del Brutto OH. Single parenchymal brain cysticercus in the acute encephalitic phase: definition of a distinct form of neurocysticercosis with a benign prognosis. *J Neurol Neurosurg Psychiatry* 1995;58:247–249.
8. Rajshekhar V. Solitary cerebral cysticercus granuloma. *Epilepsia* 2003;44(suppl 1):25–28.
9. Garcia HH, Del Brutto OH. Heavy nonencephalitic cerebral cysticercosis in tapeworm carriers: The Cysticercosis Working Group in Peru. *Neurology* 1999;53:1582–1584.
10. Del Brutto OH, Zenteno MA, Salgado P, Sotelo J. MR imaging in cysticercotic encephalitis. *AJNR Am J Neuroradiol* 1989;10:S18–S20.
11. Rangel R, Torres B, Del Brutto O, Sotelo J. Cysticercotic encephalitis: a severe form in young females. *Am J Trop Med Hyg* 1987;36:387–392.
12. Rio de la Loza LJ, Meza EL. Cysticercotic encephalitis: case report of miliary infestation in an encephalopathic fashion. *Arch Neurol* 2008;65:276–277.
13. Garcia HH, Evans CA, Nash TE, et al. Current consensus guidelines for treatment of neurocysticercosis. *Clin Microbiol Rev* 2002;15:747–756.
14. Singh G, Singh P, Singh I, Rani A, Kaushal S, Avasthi G. Epidemiologic classification of seizures associated with neurocysticercosis: observations from a sample of seizure disorders in neurologic care in India. *Acta Neurol Scand* 2006;113:233–240.

15. Rajshekhar V. Etiology and management of single small CT lesions in patients with seizures: understanding a controversy. *Acta Neurol Scand* 1991;84:465–470.
16. Mitchell WG, Crawford TO. Intraparenchymal cerebral cysticercosis in children: diagnosis and treatment. *Pediatrics* 1988;82:76–82.
17. Murthy JM, Yangala R. Etiological spectrum of symptomatic localization related epilepsies: a study from South India. *J Neurol Sci* 1998;158:65–70.
18. Garcia HH, Pretell EJ, Gilman RH, et al. A trial of antiparasitic treatment to reduce the rate of seizures due to cerebral cysticercosis. *N Engl J Med* 2004;350:249–258.
19. Carpio A, Kelvin EA, Bagiella E, et al. Effects of albendazole treatment on neurocysticercosis: a randomised controlled trial. *J Neurol Neurosurg Psychiatry* 2008;79:1050–1055.
20. Kaur S, Singhi P, Singhi S, Khandelwal N. Combination therapy with albendazole and praziquantel versus albendazole alone in children with seizures and single lesion neurocysticercosis: a randomized, placebo-controlled double blind trial. *Pediatr Infect Dis J* 2009;28:403–406.
21. de Souza A, Thennarasu K, Yeshraj G, Kovoor JM, Nalini A. Randomized controlled trial of albendazole in new onset epilepsy and MRI confirmed solitary cerebral cysticercal lesion: effect on long-term seizure outcome. *J Neurol Sci* 2009;276:108–114.
22. Gogia S, Talukdar B, Choudhury V, Arora BS. Neurocysticercosis in children: clinical findings and response to albendazole therapy in a randomized, double-blind, placebo-controlled trial in newly diagnosed cases. *Trans R Soc Trop Med Hyg* 2003;97:416–421.
23. Kalra V, Dua T, Kumar V. Efficacy of albendazole and short-course dexamethasone treatment in children with 1 or 2 ring-enhancing lesions of neurocysticercosis: a randomized controlled trial. *J Pediatr* 2003;143:111–114.
24. Padma MV, Behari M, Misra NK, Ahuja GK. Albendazole in single CT ring lesions in epilepsy. *Neurology* 1994;44:1344–1346.
25. Baranwal AK, Singhi PD, Khandelwal N, Singhi SC. Albendazole therapy in children with focal seizures and single small enhancing computerized tomographic lesions: a randomized, placebo-controlled, double blind trial. *Pediatr Infect Dis J* 1998;17:696–700.
26. Garg RK, Potluri N, Kar AM, et al. Short course of prednisolone in patients with solitary cysticercus granuloma: a double blind placebo controlled study. *J Infect* 2006;53:65–69.
27. Mall RK, Agarwal A, Garg RK, Kar AM, Shukla R. Short course of prednisolone in Indian patients with solitary cysticercus granuloma and new-onset seizures. *Epilepsia* 2003;44:1397–1401.
28. Singhi P, Jain V, Khandelwal N. Corticosteroids versus albendazole for treatment of single small enhancing computed tomographic lesions in children with neurocysticercosis. *J Child Neurol* 2004;19:323–327.
29. Verma A, Misra S. Outcome of short-term antiepileptic treatment in patients with solitary cerebral cysticercus granuloma. *Acta Neurol Scand* 2006;113:174–177.
30. Thussu A, Arora A, Prabhakar S, Lal V, Sawhney IM. Acute symptomatic seizures due to single CT lesions: how long to treat with antiepileptic drugs? *Neurol India* 2002;50:141–144.
31. Prakash S, Garg RK, Kar AM, et al. Intravenous methyl prednisolone in patients with solitary cysticercus granuloma: a random evaluation. *Seizure* 2006;15:328–332.
32. Kishore D, Misra S. Short course of oral prednisolone on disappearance of lesion and seizure recurrence in patients of solitary cysticercal granuloma with single small enhancing CT lesion: an open label randomized prospective study. *J Assoc Physicians India* 2007;55:419–424.
33. Riviello JJ, Jr., Ashwal S, Hirtz D, et al. Practice parameter: diagnostic assessment of the child with status epilepticus (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology* 2006;67:1542–1550.
34. French J, Gronseth G. Lost in a jungle of evidence: we need a compass. *Neurology* 2008;71:1634–1638.
35. Gronseth G, French J. Practice parameters and technology assessments: what they are, what they are not, and why you should care. *Neurology* 2008;71:1639–1643.
36. Rajshekhar V, Chandy MJ. Validation of diagnostic criteria for solitary cerebral cysticercus granuloma in patients presenting with seizures. *Acta Neurol Scand* 1997;96:76–81.
37. Rajshekhar V. Rate of spontaneous resolution of a solitary cysticercus granuloma in patients with seizures. *Neurology* 2001;57:2315–2317.
38. Rajshekhar V, Jeyaseelan L. Seizure outcome in patients with a solitary cerebral cysticercus granuloma. *Neurology* 2004;62:2236–2240.
39. Carpio A, Hauser WA. Prognosis for seizure recurrence in patients with newly diagnosed neurocysticercosis. *Neurology* 2002;59:1730–1734.
40. Rajshekhar V, Chandy MJ. Comparative study of CT and MRI in patients with seizures and a solitary cerebral cysticercus granuloma. *Neuroradiology* 1996;38:542–546.
41. Tsang VC, Brand JA, Boyer AE. An enzyme-linked immunoelectrotransfer blot assay and glycoprotein antigens for diagnosing human cysticercosis (*Taenia solium*). *J Infect Dis* 1989;159:50–59.
42. Prabhakaran V, Rajshekhar V, Murrell KD, Oommen A. Conformation-sensitive immunoassays improve the serodiagnosis of solitary cysticercus granuloma in Indian patients. *Trans R Soc Trop Med Hyg* 2007;101:570–577.
43. Singh G, Kaushal V, Ram S, Kaushal RK, Dhanuka AK, Khurana S. Cysticercus immunoblot assay in patients with single, small enhancing lesions and multilesional neurocysticercosis. *J Assoc Physicians India* 1999;47:476–479.
44. Rajshekhar V, Wilson M, Schantz PM. Cysticercus immunoblot assay in Indian patients with single small enhancing CT lesions. *J Neurol Neurosurg Psychiatry* 1991;54:561–562.
45. Del Brutto OH, Roos KL, Coffey CS, Garcia HH. Meta-analysis: cysticidal drugs for neurocysticercosis: albendazole and praziquantel. *Ann Intern Med* 2006;145:43–51.
46. Sharma SR AA, Kar AM, Shukla Rakesh, Garg RK. Evaluation of role of steroid alone and with albendazole in patients of epilepsy with single-small enhancing computerized tomography lesions. *Ann Indian Acad Neurol* 2007;10:39–43.
47. Thussu A, Chattopadhyay A, Sawhney IM, Khandelwal N. Albendazole therapy for single small enhancing CT lesions (SSECTL) in the brain in epilepsy. *J Neurol Neurosurg Psychiatry* 2008;79:272–275.
48. Rajshekhar V. Incidence and significance of adverse effects of albendazole therapy in patients with a persistent

- solitary cysticercus granuloma. *Acta Neurol Scand* 1998;98:121–123.
49. Singla M. Short course of prednisolone in solitary cysticercus granuloma [postgraduate thesis]. Chandigarh, India: Postgraduate Institute of Medical Education and Research; 2009.
 50. Gupta M, Agarwal P, Khwaja GA, et al. Randomized prospective study of outcome of short term antiepileptic treatment in small single enhancing CT lesion in brain. *Neurol India* 2002;50:145–147.
 51. Kaushal S, Rani A, Chopra SC, Singh G. Safety and efficacy of clobazam versus phenytoin-sodium in the antiepileptic drug treatment of solitary cysticercus granulomas. *Neurol India* 2006;54:157–160.
 52. Bittencourt PR, Gracia CM, Martins R, Fernandes AG, Diekmann HW, Jung W. Phenytoin and carbamazepine decreased oral bioavailability of praziquantel. *Neurology* 1992;42:492–496.
 53. Lanchote VL, Garcia FS, Dreossi SA, Takayanagui OM. Pharmacokinetic interaction between albendazole sulfoxide enantiomers and antiepileptic drugs in patients with neurocysticercosis. *Ther Drug Monit* 2002;24:338–345.
 54. Pradhan S, Kathuria MK, Gupta RK. Perilesional gliosis and seizure outcome: a study based on magnetization transfer magnetic resonance imaging in patients with neurocysticercosis. *Ann Neurol* 2000;48:181–187.
 55. Chandy MJ, Rajshekhar V, Prakash S, et al. Cysticercosis causing single, small CT lesions in Indian patients with seizures. *Lancet* 1989;1:390–391.
 56. Rajshekhar V, Chacko G, Haran RP, Chandy MJ, Chandi SM. Clinicoradiological and pathological correlations in patients with solitary cysticercus granuloma and epilepsy: focus on presence of the parasite and oedema formation. *J Neurol Neurosurg Psychiatry* 1995;59:284–286.
 57. Rajshekhar V, Haran RP, Prakash GS, Chandy MJ. Differentiating solitary small cysticercus granulomas and tuberculomas in patients with epilepsy: clinical and computerized tomographic criteria. *J Neurosurg* 1993;78:402–407.
 58. Thussu A, Arora A, Lal V, Prabhakar S, Sawhney IM. Albendazole therapy for solitary persistent cysticercus granuloma. *Neurol India* 2001;49:95–97.
 59. Wu Z, Mittal S, Kish K, Yu Y, Hu J, Haacke EM. Identification of calcification with MRI using susceptibility-weighted imaging: a case study. *J Magn Reson Imaging* 2009;29:177–182.