example of brain stem involvement of hypertensive encephalopathy in the absence of peripheral cerebral lesions.

In patients with such pontine T2 hyperintensities, DWI is useful for two reasons. First, it is helpful in refining the differential diagnosis because hyperintensity on DWIs might favor other processes, such as acute ischemia or acute CPM (we have seen two such autopsy-proven cases of CPM), although it may still be possible in severe cases of PRES. Although in the majority of cases the lesions of PRES can be assumed to be reversible with treatment, we have seen a small number of severe cases with ischemic complications heralded by restriction of fluid movement on ADC maps. The use of DWI in these cases also provides prognostic information regarding the likelihood of reversibility.

As we learn more about PRES, we recognize the wider spectrum of imaging appearances of this condition. This spectrum has already been reported in the uremic encephalopathies, a group of conditions including hemolytic-uremic syndrome, hepatorenal syndrome, and thrombotic thrombocytopenic purpura. Some reports have demonstrated bilateral lesions in the parieto-occipital regions identical in appearance to those seen in PRES, whereas other reports have demonstrated predominant involvement of relatively central structures, such as the basal ganglia or the brain stem. It now appears that the uremic encephalopathies represent additional etiologies of PRES, which, for reasons unknown, have a greater tendency for central distribution.

Future research on PRES should be directed at perfusion imaging. To date, there have been a number of conflicting reports using perfusion imaging in these entities, with some reporting hyperperfusion and others reporting hypoperfusion. It is likely that these results depend on the time of imaging relative to the onset of therapy in patients with PRES. Present data tends to favor the theory that the condition begins with hyperperfusion, resulting in failure of autoregulation, and breakthrough accumulation of vasogenic edema. We believe that overly aggressive antihypertensive therapy, in the setting of disturbed cerebral blood flow autoregulation, can result in hypoperfusion, even with apparently normal blood pressures. In some severe cases, this can lead to infarction predominantly in the posterior border zones. Ischemia may also result from status epilepticus and hypoxic complications. Over the years, this mix of transient hyperperfusion and the infrequent ischemic complication has created much confusion in our attempt to elucidate the pathophysiologic mechanisms contributing to the various etiologies of PRES. Given the dynamic nature of brain perfusion in PRES, it may be useful to perform perfusion imaging in selected patients who are responding poorly to therapy as a guide for a more ''personalized'' titration of antihypertensive therapy.

In conclusion, it is important for neuroradiologists to become aware of the spectrum of imaging findings in the acute presentation of PRES. The diagnosis of PRES is one of the more satisfying diagnoses made in our practice, as it is often unsuspected by clinicians, and relatively dramatic changes on MR imaging can be predicted to be predominantly, if not completely, reversible. The neuroradiologist will often be the first physician to suggest the appropriate diagnosis in the hope of averting unnecessary biopsies and initiating appropriate therapy. Clinicians also need to become more familiar with this syndrome and the treatment issues in order to minimize underlying risk factors and to avoid potential ischemic complications.

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References

1. Hinchey J, Chaves C, Appignani B, et al. **A reversible posterior leukocephalopathy syndrome.** *N Engl J Med* 1996;334:494–500
2. Fryer JP, Fortier MV, Metrakos P, et al. **Central pontine myelinolysis and cyclosporin neurotoxicity following liver transplantation.** *Transplantation* 1996;61:658–61

Radiographic Screening for Orbital Foreign Bodies Prior to MR Imaging: Is It Worth It?

The article by Seidenwurm et al in this issue of the *AJNR* (page 426) addresses questions that are faced daily by any radiologist who performs MR imaging. These are: Does a patient have intraorbital metal that would be a contraindication for having an MR examination? Which patients should be screened radiographically? When is radiographic screening cost-effective? Because these are common dilemmas, the impact of any recommendations based on this study is potentially important. It is therefore imperative that a cost-effectiveness analysis (CEA) be rigorous and complete.

Guidelines have indeed been developed for conducting and evaluating CEAs (1). We reviewed Seidenwurm et al's article based on 10 points that all readers should consider when evaluating such studies (Table, page 246).

Cost-effectiveness can be determined by comparing the resources consumed by a given strategy (the costs) with the improvement in health that results from that strategy (the consequences). The consequences are measured in units most relevant to the strategy under study. This results in ratios such as ''dollars per year of life gained.''

Criteria for evaluating a cost-effectiveness article

10 Criteria According to Drummond (1)	How Well Seidenwurm et al Fulfilled Criteria
1. Was a well-defined question posed in an answerable form?	Yes
2. Were all the important and relevant costs and consequences for each alternative identified?	Probably
3. Were costs and consequences measured accurately in appropriate physical units?	Partially
4. Was a comprehensive description of the competing alternatives given?	Partially
5. Was there evidence that the program's effectiveness had been established?	Yes
6. Were costs and consequences valued credibly?	Cannot tell
7. Were costs and consequences adjusted for differential timing?	Partially
8. Was an incremental analysis of costs and consequences of alternatives performed?	Yes
9. Was a sensitivity analysis performed?	Yes
10. Did presentation and discussion of study results include all issues of concern to users?	Yes

Most researchers think that, in general, quality of life should be incorporated into these analyses. Seidenwurm et al chose to use utilities, which are the most widely accepted measures of quality of life. Utilities refer to preferences for a particular level of health status. These preferences may be those of either an individual or society for a particular health outcome, and they result in a ''quality weighting'' factor. The denominator of a cost-utility analysis is therefore quality adjusted life years (QALY), rather than simply life years.

This is the type of analysis that Seidenwurm et al have performed. The first and most important step in the design of any study is the formation of a focused, answerable question. This question must describe the alternatives being compared as well as the viewpoint of the analysis. Seidenwurm et al do an admirable job by clearly stating that the purpose of their study was to compare the cost-effectiveness of clinical versus radiologic screening for orbital foreign bodies. They describe the clinical screening in adequate detail, but they could have provided more information for the radiologic screening, such as the number of views obtained. To their credit, the authors unambiguously declare that the analysis is from the societal viewpoint. This viewpoint takes into account the widest possible range of costs and consequences and is most appropriate for policy decision making.

Seidenwurm et al are somewhat unconventional in their identification of costs and consequences and in how they organize their economic model. Economists generally categorize costs as direct and indirect. The costs of organizing and operating a service are the direct costs, and they include health professionals' time, supplies, equipment, power, capital costs, and out-of-pocket expenses for the patient. Time lost from work is an indirect cost. In their classic paper on cost-effectiveness analysis, Weinstein and Stason (2) present the following equation for determining the net healthcare costs of an intervention:

$$\Delta C = \Delta C_{Rx} + \Delta C_{SE} — \Delta C_{Morb} + \Delta C_{Rx\ \Delta LE}$$

where ΔC_{Rx} includes all direct medical and healthcare costs, ΔC_{SE} are the costs associated with adverse effects of the intervention, ΔC_{Morb} are the savings due to prevention or alleviation of disease, and $\Delta C_{Rx\ \Delta LE}$ are the costs of treating diseases that would not have occurred if the patient had not lived longer because of the intervention. Because length of life is probably not affected significantly by the intervention (orbital screening), $\Delta C_{Rx\ \Delta LE}$ can be ignored. Similarly, there are probably no adverse effects of orbital screening, so this term can be ignored as well. ΔC_{Morb} needs to be estimated because this is the cost benefit of screening. The authors account for this with their variables A and M, both of which they assume to be $0 in their base case. Although one can question this base-case assumption, their sensitivity analysis demonstrated that these were not influential variables. The authors ignore direct out-of-pocket costs, and while it is difficult to be certain that these are insignificant, assuming they are negligible is conservative.

Seidenwurm et al chose to measure consequences in terms of QALY, which is the most appropriate measure for a cost-utility analysis. Drummond identifies two other categories of consequences: 1) changes in functional status (physical, social, and emotional functioning); and 2) changes in future resource use. Neither of these categories is addressed by Seidenwurm et al's article, but this is true of many economic analyses.

The authors state that the cost of screening was ''culled from the medical literature on screening for orbital foreign body, Medicare fee schedules for various examinations, and usual, customary and reasonable charges fee schedules for various examinations.'' Using Medicare fee schedules is probably appropriate in this setting, because they reflect a resource-based relative-value scale. Nevertheless, the authors remain vague as to how exactly they arrived at their base-case estimate of $173, an amount they indicate represents the charge of the examination rather than a true cost. Numerous authors have emphasized why it is important to distinguish between costs and charges, with a recent example being an editorial by Picus in *Radiology* (3). Seidenwurm et al state in their discussion that the Medicare allowable fee for a single view screening examination is $25. How do they account for the difference between this amount and their base case? They state that $25 does not cover the costs of radiography. This may be true, but needs justification. After all, their analysis demonstrated that the cost of the radiographic screening was a critical variable, and if the cost was as low as $25, then screening might be cost-effective.

Using QALY as a metric for consequences implies accounting for preferences, either on the individual or societal level, for given health states. The authors estimate the degree of disability from monocular blindness using two separate sources. Both of these, however, probably use functional status and not preference-based measures, and thus are not true utilities. Nonetheless, their base-case estimate of the utility for monocular blindness being 0.24 is probably quite conservative. We recently collected a cohort of 142 patients who completed a time trade-off for monocular blindness, and the mean utility was 0.82.

It is impossible to tell from the authors' methods exactly how various types of disability were converted to QALYs. The authors include in their cost-effectiveness equation the variable ''D,'' which is the degree of disability associated with injury. They use disability rating guides to assess disability due to ocular injury, but do not provide essential details. QALYs describe a preference for a given health state, and not just the functional status within that health state.

The alternative to radiologic screening, clinical screening, is reasonably well described in their methods. Enough details are supplied so that a different provider could carry out the clinical screening. The radiologic screening is less thoroughly described, with no details provided as to whether one or more views were obtained, or if costs assumed digital or film-screen systems.

One of the most compelling aspects of the article is the last paragraph of the discussion section in which they describe their experience using the proposed screening protocol. Although limited to a single practice, this experience is a true measure of effectiveness (how a protocol performs in real life).

The authors appropriately use a range of discount rates for costs in their sensitivity analysis. They do not discount consequences. This is a somewhat controversial area, but for the most part, people agree that it should be done.

With respect to costs, the authors account for both the costs of radiologic screening, for which they use charges as a proxy, and the costs of clinical screening, which they argue are negligible. They also look at the incremental improvement in the detection of ocular foreign bodies and thus the incremental improvement in QALY of radiologic versus clinical screening.

Sensitivity analysis is a method to determine the degree of uncertainty associated with economic analyses. It is in many ways the equivalent of defining confidence intervals. A sensitivity analysis is performed by varying the value of a particular variable across a range of clinically relevant values. If large changes in the value of this variable do not substantially affect the cost-utility ratio, then the confidence in the original results is high. If certain variables do greatly affect the ratio, then greater precision is needed in defining the value of these variables. A one-way sensitivity analysis varies one variable at a time. Two-way and greater sensitivity analyses can be done, although the difficulty of interpreting the analysis increases as the number of variables increases.

The authors performed multiple one-way sensitivity analyses, and determined that cost of screening, expected life span, and prevalence of foreign bodies were all critical variables. This means that their model is not robust along a realistic range of values for these variables. The authors discount the importance of the cost of screening, asserting that the point at which screening becomes effective ($25) is so low as to be unrealistic. As I've stated, they need to justify that costs are significantly greater than $25. Similarly, if patients can be preselected to increase the prevalence of foreign bodies to 2.5%, then screening becomes cost-effective.

In their discussion, the authors touch on aspects of the analysis that required them to make critical assumptions, such as the average length of life, or the utility associated with blindness. One aspect of the decision-making process the authors do not address, but which may be the most critical variable, is the question of liability and the legal costs associated with ocular injury. This is an indirect cost, and therefore is not accounted for in their analysis. The fear of litigation, however, may be the driving force in current screening protocols.

As Drummond (1) states, the ''. . . intent in offering a checklist is not to create hypercritical users who will be satisfied only by superlative studies. . . [but rather to] help users of economic evaluations to identify quickly the strengths and weaknesses of studies.'' Although Seidenwurm et al fall somewhat short of the rigorous and complete standard set by Drummond, they have made a commendable effort, and their conclusions are probably correct.

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References

1. Drummond MF. ***Methods for the Economic Evaluation of Health Care Programmes*** 2nd ed. Oxford; New York: Oxford University Press; 1997 (Oxford medical publications)
2. Weinstein MC, Stason WB. **Foundations of cost-effectiveness analysis for health and medical practices.** *N Engl J Med* 1977; 296:716–721
3. Picus D. **Comparing competing medical procedures: costs or charges–what should it matter? [comment].** *Radiology* 1996; 199:623–624; discussion 624–625.