and Guillain-Barré syndrome had been diagnosed clinically.⁸

Effective therapy for Bickerstaff's brainstem encephalitis has yet to be established. As shown, Bickerstaff's brainstem encephalitis and Guillain-Barré syndrome are closely related; therefore, steroids should not be used to treat these disorders. Instead, the established treatments—plasmapheresis and intravenous immunoglobulins (IVIg)—should be used. Recent studies^{9,10} provide theoretical evidence that the removal of anti-GQ1b antibodies is reasonable and beneficial. Some patients with Bickerstaff's brainstem encephalitis respond favourably to plasmapheresis and IVIg.^{11,12} We recommend that no steroids, rather IVIg (or plasmapheresis), be used to treat Bickerstaff's brainstem encephalitis. Controlled clinical trials are needed to establish the efficacy of these procedures as therapy for this disease.

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Intravenous immunoglobulin causing reversible posterior leukoencephalopathy syndrome?

Turner and Willis describe a patient with the Miller Fisher syndrome treated with intravenous immunoglobulin (IVIg), who developed transient confusion and reversible blindness.¹ The authors state that the bilateral occipital lobe changes seen on brain MRI were secondary to cerebral infarction. They postulate that this may have occurred as a result of hyperviscosity, although at the time of the event the plasma viscosity was only marginally raised at 1.85 cP (normal range 1.5-1.72 cP). The images seem to show relative sparing of the cortex, which would be

rather unusual if the cause was indeed an arterial infarct as would be expected if the mechanism was hyperviscosity induced thromboembolism.² The authors do not specifically mention that they excluded a cerebral venous sinus thrombosis with appropriate imaging and although the pattern and clinical history would be slightly unusual, this is a possibility that needs to be considered.

We suspect, however, that this patient actually experienced the reversible posterior leukoencephalopathy syndrome (rPLES). This is a syndrome of reversible symptoms comprising any of altered mental function; headaches; visual loss; seizures; and weakness.^{3,4} The syndrome has been described with many underlying conditions^{3,4} and has previously been reported with IVIg use.^{5,6} The patient reported on¹ has many of the clinical and radiological features of rPLES, in particular the MRI changes are predominantly subcortical and the vision recovered well. A repeat MRI in this case would be useful and should show resolution of the abnormalities seen on T2 weighted imaging with little or no corresponding T1 weighted abnormality, showing that the brain had been oedematous rather than infarcted.

Reversible posterior leukoencephalopathy is an important syndromic diagnosis to make as it obviates the need for extensive stroke related investigations and has different implications for prognosis and future management.

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Turner and Willis reply:

We thank Maddison and Lewis for their considered comments. They suggest cerebral venous sinus thrombosis and reversible posterior leukoencephalopathy syndrome (rPLES) as two differential diagnoses for our reported case of IVIg associated with cerebral infarction.¹ Formal magnetic resonance venography was not performed on the patient; however, the major sinuses were patent on conventional MRI and the clinical picture was relatively short lived, making cerebral sinus thrombosis unlikely. The initial MR scan and a follow up scan 11 days later, after clinical improvement, demonstrated high signal changes on T2 and T1 weighted images in both the cortex and subcortical white matter indicative of irreversible cerebral damage,

most probably infarction. rPLES is a rapidly evolving neurological condition characterised by headache, nausea, and vomiting, visual field disturbances, altered mental status, decreased alertness, and seizures.² The leukoencephalopathy syndromes have a heterogeneous aetiology;³ reversible multifocal encephalopathy has been reported with IVIg,³ but as pointed out by Lewis⁴ the commonest association of rPLESs is hypertension. It has been suggested that in PLES, seizures are the causative factor and essential in the pathogenesis.⁵ Our patient had no evidence of epileptic activity or hypertension. Vasogenic oedema is hypothesised as the pathology of rPLES and explains its reversibility⁶ but clinical improvement is also recognised in thromboembolic pathology. The plasma viscosity was not greatly raised in our patient but there may be other contributing factors for IVIg to cause a thromboembolic phenomenon. It has been shown that IVIg preparations contain anticardiolipin and antiphospholipid antibodies, which may have a role in thromboembolism.⁶ The images shown in our paper¹ may not do justice to the radiological evidence but along with the raised plasma viscosity, the absence of hypertension and seizures we consider cerebral infarction the most likely pathology. Whatever the pathophysiology the lesson remains the same that in unwell patients IVIg should be used cautiously.

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Charles Bonnet syndrome: an example of cortical dissociation syndrome affecting vision?

Although Cole's article was published some time ago,¹ it was brought to our attention only recently during the weekly journal review by one of our senior house officers. Myself and my other neurological colleagues are left with little doubt that the symptoms of visual hallucinations experienced by Cole is due to the Charles Bonnet syndrome (CBS).

This syndrome comprises the triad of visual hallucinations, visual sensory deprivation, and preserved cognitive status. The visual hallucinations in CBS may persist on eye closure (unlike the visual hallucinations of hemianopia) and are often complex, vivid, and elaborate consisting of moving and colourful images. In epidemiological studies, two common factors for CBS were visual

sensory deprivation typically affecting the anterior visual pathway (due to cataract or senile macular degeneration) and advanced age (older than 60 years). As the hallucinatory symptoms in CBS occur with preserved insight, these are not true but pseudohallucinations.

The syndrome occurs as a result of the dissociation between visual perception and visual sensory input in psychologically normal aged people. Functional neuroimaging (fMRI) has shown that the hallucinations of colour, faces, textures, and objects in CBS correlate with the cerebral activity in the ventral extrastriate visual cortex whereas the contents of hallucinations reflect the functional specialisation of this region.² In our experience, carbamazepine has been partially effective in suppressing the visual pseudohallucinations of CBS, presumably because it might inhibit the increased ventral extrastriate neuronal activity in patients with CBS that persists between the attacks of hallucinatory symptoms.²

In Cole's case,¹ the occipital infarct in the dominant (left) hemisphere led to the dissociation between the visual sensory input (now limited to the right striate cortex) and the visual perception sense of the dominant extrastriate and the visual association cortex spared by the ischaemic event. Collicular vision ("blindsight") plays no part in the symptoms of visual hallucination. In the light of the recent fMRI data, CBS may be considered as a visual dissociation syndrome similar to the cortical dissociation syndromes well recognised in the Geschwind model of language function. Cole gives one of the finest clinical examples to illustrate this phenomenon. Why CBS should occur with visual sensory deprivation exclusively in elderly people and not in young people is unknown but it might reflect the nature of neural plasticity in the visual cortex as opposed to the other cortical functions.

We were, however, a little surprised that CBS did not feature even once in the otherwise erudite discussion of the case report.² Did Cole and the reviewers of the *Journal* not consider this common diagnostic possibility?

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Corticobasal ganglionic degeneration and/or frontotemporal dementia?

I read with interest the recent paper by Mathuranath *et al*¹ describing two patients with the pathology of corticobasal ganglionic degeneration (CBD), the first presenting with the syndrome of frontotemporal dementia and the second with a mixed picture dominated by progressive aphasia. The concept that CBD may present with clinical features distinct from the "perceptuomotor" syndrome widely recognised as "classic" of the disorder is not new. However, until recently it had generally been thought that these cases represented the minority and thus could be considered "atypical". However, knowledge about this disorder has evolved since our group and others reported the first

large series. I think that in 2000 it is not appropriate to quote our 1994 book chapter² stating that "Frank dementia or language dysfunctions are said to be rare and, if present, are mild, and typically occur late in the course of the disease," as current wisdom. Within 2 years of that book chapter ourselves and others were reporting alternative presentations for this pathology and most recently we have published the clinical-pathological experience of the Canadian Brain Tissue Bank in a paper that was presumably in press at the time that the paper of Mathuranath *et al* was being reviewed.³ In this study we found that of 13 patients proved pathologically to have CBD, nine presented with cognitive or language disturbances, only one failed to show dementia during the course of the illness and only four were diagnosed as having CBD in life. Since that time, a 14th patient has come to necropsy whose presentation was that of primary progressive aphasia.

There have also been patients reported in the literature by ourselves and others with alternative neuropathological disorders presenting with clinical features that were mistaken for the "classic" (but now it seems not the commonest) phenotype of CBD including progressive supranuclear palsy, Pick's disease, motor neuron inclusion body dementia, Alzheimer's disease, and familial frontotemporal dementia due to chromosome 17 mutations.

In summary, clinical and pathological experience at the turn of the century strongly supports the conclusions of Mathuranath *et al*. Clinical phenotypes have not proved to be restricted to specific pathological substrates and several different clinical phenotypes may be caused by the same underlying pathology, probably largely dependent on the anatomical distribution of greatest involvement. Where I mainly take issue with the authors is in their belief, which largely justifies their report, that a clear distinction between CBD and FTD is "currently accepted". The cumulative literature since our 1994 review, most recently culminating in a monograph on a topic,⁴ indicates that CBD is no longer thought of as a predominantly extrapyramidal disorder that is distinct and unrelated to frontotemporal dementia.

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Diagnostic criteria for corticobasal degeneration

The study of Mathuranath *et al*¹ of corticobasal degeneration (CBD) and its overlap with frontotemporal dementia (FTD) contributes interesting information to a controversial area of neurodegeneration. Unfortunately it also introduces a potentially confusing histopathological diagnostic error. The authors found oligodendroglial inclusions which they

considered to be glial cytoplasmic inclusions and claimed that these, diagnostic hallmark of multiple system atrophy, "have been described in other neurodegenerative diseases, including CBD". This is clearly not the case.

To support their view the authors refer to two papers^{2,3} reporting, among other cytoskeletal abnormalities, tau positive inclusions in oligodendroglial cells. A letter, published earlier in this *Journal*,⁴ but not quoted in the current paper,¹ has also claimed that glial cytoplasmic inclusions are not exclusive to multiple system atrophy. The evidence is now overwhelming that they are. What the authors of this¹ and the other papers²⁻⁴ have described are indeed tau positive oligodendroglial inclusions, but they are not the same as glial cytoplasmic inclusions.⁵ Oligodendroglial inclusions, chiefly coiled bodies, undoubtedly occur in various neurodegenerative diseases, including CBD, but their morphology and molecular pathology are different from those of glial cytoplasmic inclusions. Whereas glial cytoplasmic inclusions immunostain with α -synuclein⁶ and only with unphosphorylated tau antibodies,⁷ the oligodendroglial inclusions seen in CBD and other neurodegenerative diseases are α -synuclein negative and give positive reaction with both phosphorylated and unphosphorylated tau antibodies. This basic difference has been recognised by a new classification of neurodegenerative disorders: CBD is one of the tauopathies, whereas multiple system atrophy is an α -synucleinopathy. Thus glial cytoplasmic inclusions remain the most consistent and reliable diagnostic hallmarks of multiple system atrophy and do not occur in other neurodegenerative diseases.

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Xuereb and Hodges reply

The topic of how to apply the term "glial cytoplasmic inclusions" and their specificity to a particular disorder is clearly controversial and in a state of evolution. We used glial cytoplasmic inclusions in a non-specific way to indicate simply the presence of cytoplasmic inclusions in glial cells. We found these