Figure 1 Gross appearance of brain showing large subarachnoid haematoma over right convexity.

right cerebral hemisphere appeared larger than the left. A large patch of dense subarachnoid haemorrhage was seen over the right convexity. Patches of subarachnoid blood were also seen diffusely over the left cerebral convexity (figure 1). No other remarkable feature was evident. Serial coronal slices of the cerebral hemisphere showed an extra-cerebral haematoma in the subarachnoid space, measuring 5 cm by 4 cm, compressing the right cerebral hemisphere (figure 2). The right lateral ventricle was distorted, and there was a shift of the midline structures to the left. The blood vessels were normal. The source of the bleeding could not be clearly identified. The spinal cord and entire spine were normal. Histopathological examination did not reveal any evidence of hypersensitivity reaction.

The pathogenesis of intracranial subarachnoid haematoma in this case remains obscure as no bleeding point, aberrant vessels, or aneurysm could be identified at postmortem. There was no history of previous cardiac disease, headaches, seizures, or focal neurological deficit. The haematological picture was normal. Blood pressure recordings

before and after the procedure were within normal physiological limits. The bleeding was probably related to the lumbar myelography as it occurred within 12 hours after the procedure. Either the lumbar puncture or the dye used for myelography could have been the cause, the latter being only a remote possibility as iohexol has relatively low toxicity compared with other radiographic contrast media. Post-myelographic adverse reactions may be due to CNS irritation caused by the contrast medium used.¹

Iohexol has been observed to cause less post-myelographic detrimental effects than metrizamide (Amipaque, Nyco)²⁻⁷ or iophendylate (Myodil, Glaxo, UK). Headache and febrile episodes may occur after myelography and convulsions have been occasionally reported. Instances of anaphylactic reactions to the iodide compounds used have also been reported. Smith *et al* reported a case of severe cerebral vasospasm after iophendylate myelography.⁸ Bed rest after myelography is a common practice,⁹ although some believe that this does not influence the incidence of adverse reactions.¹⁰ An instance of haemorrhage occurred after cervical puncture in a patient with leukaemia and coagulation disorder leading to quadriplegia¹¹ and in a haematologically normal patient who underwent cervical myelography.¹² Acute subdural haematoma filling the upper cervical spinal canal and virtually the entire posterior cranial fossa leading to death has been reported after lateral cervical puncture.¹³ This followed accidental puncture of an anomalous intraspinal vertebral artery. Subarachnoid haematoma has occurred after lumbar puncture, causing cauda equina compression,¹⁴ and Llewellyn reported intracranial subdural haematoma complicating myelography.¹⁵ Multiple subcortical haemorrhages after lumbar metrizamide myelography have also been reported.¹⁶ In all these cases definite causes which caused the haemorrhage could be identified.

There are instances of intracranial haemorrhages after myelography with iodide contrast media in which no definite cause could be found. Dan reported a case of intracranial subdural haematoma after metrizamide myelography,¹⁷ and a similar case, with convulsions, subarachnoid haemorrhage and death after myelography with meglumine iothalamate, was reported by Bagchi in 1976.¹⁸

No definite cause for the intracranial bleeding in our patient was discovered. The clinical presentation, however, occurred 12 hours after myelography. In the absence of evidence for any other precipitating factor the possibility of association between the procedure and bleeding in this case cannot be ruled out.

ABHAY R SATOSKAR
Department of Pathology

ATUL GOEL
Department of Neurosurgery

ANAND P DESAI
Department of Pathology

TOSHA A USGAONKAR
Department of Surgery

K E M Hospital and Seth G S Medical College,
Parel, Bombay 400 012, India

Correspondence to: Dr Satoskar, 3 Asst Dean's
Qrts, K E M Hospital, Parel, Bombay 400 012, India

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Comments by Dr H P Bohn of Nycomed AS:

We, the manufacturers of the radiographic contrast media (CM) iohexol and metrizamide, believe that cerebral haemorrhage after myelography is more likely caused by the spinal puncture than by the CM itself. Our attention was first drawn to the subject by Professor RG Grainger of Sheffield who two years ago asked for information on the subject after the post-myelographic death of a 48 year old woman. This made us look for further cases, and since then another six (unpublished) cases have been identified by our pharmacovigilance unit. They have been reported from world wide sources; five are related to iohexol and one to metrizamide.

These numbers of reports are low compared with the estimated number of myelographies performed with iohexol and metrizamide throughout the years which amount to several million. The cases reported to us were, strangely enough, all women ($p=0.0078$) aged from 41 to 66 years. None had any relevant pre-existing disease and all were admitted for myelography by the lumbar route for low back pain, disc disease, or radicular symptoms. Most had more than

Figure 2 Coronal slices of brain showing subarachnoid haematoma on right side.

- Sykes RHD, Wasenaar W, Clark P. Incidence of adverse effects following metrizamide myelography in non-ambulatory and ambulatory patients. *Radiology* 1981;138:625-7.

usual headache or nausea or both after the procedure. The suspected onset time of intracranial haemorrhage varied from two to seven days after myelography. The site of bleeding varied greatly and was in many cases suspected to be multifocal: intracerebral/parietal and subarachnoid; intracerebral into basal ganglia; multifocal cortical; subarachnoid; intracerebral or frontal and parietal and temporal; and intracerebral or parietal were all reported. Two of the cases were associated with brain stem herniation.

The high number of such reports led us to investigate the literature for additional information. We found that cases of intracranial haemorrhage associated with myelography had been reported previously and one¹ may be added to the reference list of Dr Satoskar *et al.* Interestingly, we also found that intracranial haemorrhage after spinal puncture without use of CM (for example diagnostic LP or spinal anaesthesia) was not unknown.^{2,3} Schubbs and Raskin made reference to another 14 cases in their presentation already in 1936.⁴

At this stage one may only speculate on the possible mechanism for the haemorrhagic incidents: a drop in intracranial pressure associated with CSF leakage may well increase the pressure gradient across fragile venules and capillaries. This in itself may increase the risk of bleeding in predisposed patients. CSF support of the brain may also be affected leading to "sagging" and shearing forces. Heavy vomiting may perhaps pre-

cipitate bleeding in some cases. The possible role of the CM is uncertain and harder to explain. At this stage, however, it is important to keep an open mind and to keep looking for explanations. We are grateful to Dr Satoskar *et al.* for publishing their case. Hopefully this will contribute to a renewed interest in this serious but extremely rare complication to the myelographic procedure. I am personally convinced that the problem has been under-reported as it apparently may occur after a considerable delay thereby hiding the possible association with myelography. A renewed interest may lead to an increased recognition and reporting, thus providing us with a better understanding of incidence, avoidable risk factors, and mechanisms in the future.

HP BØHN

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- 4 Schubbs P, Raskin N. Cerebral haemorrhage following lumbar spinal puncture. *J Nerve Ment Dis* 1936;84:636-59.
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Plasma infusion in childhood Guillain-Barré syndrome

Guillain-Barré syndrome (GBS) is probably the most common cause of acute motor paralysis in children. Although many patients with GBS make a good recovery, there is a mortality of 3-5%, 10-20% require artificial respiration, and 10-22% remain disabled.¹ Severity and outcome in adults and children are similar.² Several studies have shown the usefulness of plasmapheresis in severely affected adults in a specialised setting.^{3,4} Technical difficulties and haemodynamic complications have precluded the routine use of conventional plasmapheresis in children. We report four children with GBS and two with chronic inflammatory polyneuropathy who responded well to treatment with plasma infusions.

The criteria used for the diagnosis of GBS were those recommended by the National Institute of Neurological and Communicative Disorders. Irrespective of age, sex, and weight, 250 ml of fresh frozen plasma, tested negative for hepatitis B and HIV, were infused daily through an intravenous cannula

into a convenient limb vein for 10-14 days. The clinical progress was assessed in the early stages of the bedridden patient with the MRC sum score⁵: six muscles (deltoid, biceps brachii, extensor carpi, iliopsoas, quadriceps, tibialis anterior) were tested on both sides on the MRC scale to give a score ranging from 0 to 60. We also used the grading scale from the GBS study group³: grade 0—healthy; grade 1—minor symptoms or signs of neuropathy; grade 2—able to walk 5 m without assistance; grade 3—able to walk 5 m with assistance; grade 4—confined to bed or chairbound; grade 5—requiring assisted ventilation. None of the children were given steroids or other immunosuppressive drugs.

The nerve conduction velocities (NCV) of the median nerve and the compound muscle action potential (CMAP) from the abductor pollicis brevis were recorded on day one and day 14 of treatment. There were four girls and two boys (age range five to 11 years). Cases 1 to 4 presented acutely, case 5 presented with grade 3 weakness five months after onset, and case 6 was seen 40 days after a relapse. None required tracheostomy or assisted ventilation, though the vital capacity reached a

critical value of 300 ml in cases 3 and 4. All six showed a good response. The relapsing patient (case 6) improved dramatically from grade 4 to 2 in eight days. Response to plasma infusion is shown in the table. All children required less than 14 days (mean 10 days) to improve one grade. All, including the children with relapse and residual weakness, improved enough to walk unaided by the third week. The duration of hospital stay was reduced to 10-30 days. At the time of discharge from hospital all were ambulant without aid and had only a mild gait abnormality with some difficulty in getting up from a squatting position. NCV of the median nerve and the CMAP of the abductor pollicis brevis showed minor improvements in cases 1 to 4, but in the other two there was no measurable improvement after two weeks (table). No haemodynamic complications or allergic reactions were seen and plasma protein measurements twice a week did not show any significant change.

Whether the type of replacement fluid used has any beneficial effect is debatable.⁴ Improvement seen after high dose gammaglobulin infusion in chronic inflammatory polyneuropathies and in Guillain-Barré syndrome⁵ prompted us to use plasma infusions in children, in whom only small quantities may be required to produce beneficial results.

Although our study had no control group and consisted of only six patients, the impressive results are worth reporting. The children's length of hospital stay was clearly reduced to an impressive 10-30 days, much less than the average hospital stay of children managed conservatively, which is around 84 days.² None of the children required assisted ventilation, though the vital capacity fell to 300 ml in two patients. Possibly the early institution of treatment with plasma prevented their respiratory function deteriorating further. The time taken to improve one grade and the time taken to reach grade 2 were also remarkably shorter when compared with results from other series of conservative management and plasmapheresis.^{3,4} High dose gammaglobulin, which is very expensive, is not available in Sri Lanka and plasmapheresis cannot be done as the necessary equipment is not available. Therefore in a developing country like ours the only treatment we can offer these critically ill children is plasma infusion. A larger controlled study is planned.

JB PEIRIS
SB GUNATILAKE
PS RANASINGHE
AS THAVAKODIRASAH
*Institute of Neurology,
General Hospital, Colombo, Sri Lanka*

Correspondence to: Dr Gunatilake, 43 Fife Road, Colombo-5, Sri Lanka

Table Response to plasma infusion in six children with Guillain-Barré syndrome

Case number	Duration of illness before infusion (days)	Grade at infusion*	Time to improve one grade (days)	Time to reach grade two (days)	Duration of Hospital stay (days)	NCV**		CMAP***	
						At onset	Two wks	At onset	Two wks
1	10	4/3,0	10	20	30	24	30	2.7	4.6
2	7	4/3,2	10	13	27	40	51	2.4	4.5
3	4	4/2,0	12	14	28	34	50	0.3	0.9
4	11	4/2,1	9	13	28	39	52	1.2	2.4
5	150	3/4,3	10	10	10				
6	40	4/3,2	4	8	23				

*North American trial grading scale/MRC scale arm, leg.

**Nerve conduction velocity (normal for median nerve 51m/s).

***Compound muscle action potential (normal for wrist 10 mv).