at further risk from untreated imported material. We appreciate the possible risk to families or health-care attendants of exposure to these products but would regard these risks as very small when compared with the danger of concomitant blood exposure and would reinforce the need for extreme care during administration. The continued use of non-heated British concentrate will not compromise the aim of national self-sufficiency of factor VIII. All patients receiving heat-treated preparations must be thoroughly monitored for appearance of reactions and formation of factor VIII antibodies and results compared with those in the non-heat-treated cohort.

The urgency of the situation must not be allowed to obscure the need for a clearly defined policy for the future, formed on scientific evidence, and for management to be based on serological status. Hasty and ill-considered decisions may expose haemophiliacs to new and further risks and may foster complacency which could delay the implementation of measures required now to slow transmission of the virus and to protect the remaining vulnerable members of at-risk groups.

Regional Immunology Department; Public Health Laboratory Service; and Regional Blood Transfusion Service, Newcastle General Hospital; Newcastle upon Tyne NE4 6BE

A. G. BIRD
A. A. GOOD
A. COLLINS

SULPHADIAZINE DESENSITISATION IN AIDS PATIENTS

SIR,—Adverse reactions to sulphonamides in AIDS patients may become especially troublesome in the treatment of cerebral toxoplasmosis where regimens lacking sulphonamides are not effective. Successful desensitisation has been demonstrated in patients with inflammatory bowel disease but not, to our knowledge, in AIDS patients. We describe here successful desensitisation to sulphadiazine in three AIDS patients with cerebral toxoplasmosis who had severe sulphonamide reactions.

The patients, all male homosexuals, had AIDS diagnosed on the basis of biopsy-proven cerebral toxoplasmosis (one) and Pneumocystis carinii pneumonia (two). The latter two patients later had cerebral abscesses compatible with toxoplasmosis on computerised tomographic scanning which regressed completely on anti-toxoplasma therapy. All three patients had fever (more than 39.4°C), leucopenia (below 1500/μl), and a diffuse maculopapular rash during sulphonamide therapy for toxoplasmosis; two patients also had a right hemiparesis. One patient treated with pyrimethamine and clindamycin and one patient treated with pyrimethamine and streptomycin might have been reduced by nifedipine. Calcium antagonists had prophylactic value in other conditions suggest that calcium antagonists might be useful in moyamoya disease. For example, morbidity and mortality in patients with subarachnoid haemorrhage may have been reduced by nimodipine. Calcium antagonists had prophylactic value in treatment of migraine, and alternating hemiplegia in children has been reported to improve during therapy with flunarizine.

RESPONSE OF MOYAMOYA DISEASE TO VERAPAMIL

SIR,—Moyamoya disease is a vaso-occlusive disease of the intracranial circulation that is seldom seen in Western countries. The cause is unknown. The disease is characterised by occlusion of the intracranial internal carotid arteries and cerebral arteries, and it gets its name from the anastomotic networks seen on the angiogram (the Japanese word moyamoya means "puff of smoke"). The clinical course in children varies but often results in a chronic dependency. This gloomy outlook and the uncertain success of surgery justify the search for different treatments.

Clinical reports in other conditions suggest that calcium antagonists might be useful in moyamoya disease. For example, morbidity and mortality in patients with subarachnoid haemorrhage may have been reduced by nimodipine. Calcium antagonists had prophylactic value in treatment of migraine, and alternating hemiplegia in children has been reported to improve during therapy with flunarizine.

Case 1

This 6-year-old white girl with a history of seizures (with postictal stupor and right arm weakness) controlled by carbamazepine was admitted with progressive right hemiparesis and mutism. Angiography revealed transbasal and transtemporal anastomoses typical of moyamoya disease. After a left superficial temporal to middle cerebral artery graft and symphangiosis with a patch of dura and muscle her right arm remained slightly weak. At the age of 6 months she had a mental age of 2 years 7 months and was severely aphasic.

Seizures recurred 11 months after surgery and she became mute with a right hemiparesis. She was brought to hospital with the right arm held flexed at the waist and the thumb in fist. She did not use the arm and walked clumsily. There was right hypotonia with a right hemiparesis. She was brought to hospital with the right arm held flexed at the waist and the thumb in fist. She did not use the arm and walked clumsily. There was right hypotonia with a right hemiparesis.

Cytomegalovirus retinitis was diagnosed in two patients 4 and 6 months after desensitisation. Whether this was promoted by the use of steroids is unclear, though no exacerbation of other opportunistic infections was noted. One patient remains alive 9 months after desensitisation with complete resolution of cerebral lesions and has tolerated a further reduction of dexamethasone to 1.5 mg daily. Two patients died, 1½ and 7 months after desensitisation, of unknown causes; the latter patient had resolution of cerebral abscesses documented by CT scan.

Sulphadiazine desensitisation seems feasible in AIDS patients experiencing severe sulphonamide reactions during therapy for toxoplasmosis. Although Luft et al were suggested that pyrimethamine, alone or with clindamycin or streptomycin, might be used in these patients, we noted progression of cerebral lesions in one patient treated with pyrimethamine and clindamycin and believe that sulphadiazine desensitisation may offer a useful alternative.

Section of Infectious Diseases,
Lenox Hill Hospital,
New York, NY 10021, USA

EVA T. BELL
MICHAEL L. TAPPER
ALAN A. POLLOCK

Note augmented filling of the transbasal collaterals and the increased verapamil, at high resolution to emphasise transbasal collaterals. Dimensions of anastomotic network (double asterisks), suggesting opacification of "new vessels". Calibre of posterior branch of middle cerebral artery is increased (double arrows), suggesting vasodilatation. Filling of left posterior cerebral vessel appeared to be increased in calibre (figure) before the most recent episode. During 18 months of oral therapy with verapamil (20 mg three times daily) no further neurological deficits have developed.

Case 2
This 3-year-old white boy had a history of focal seizures at age 11 months after which he uttered only grunts and switched to using his left hand. He had then been seizure-free for a year while taking phenobarbitone, and language improved. At the age of 2 he had an episode of lethargy and vomiting followed by focal right facial seizures. 16 months later he became fatigued over several weeks, vomited, and had tonic-clonic seizures followed by mutism and difficulty in swallowing. He switched back to right-handedness. A slight left facial and arm paresis persisted.

Common carotid injection of 5 ml of 60% meglumine indocyanate before and 10 min after intravenous administration of 10 mg verapamil. Some vessels in the region of the left basal ganglia and a posterior cerebral vessel appeared to be increased in calibre (figure) after verapamil. There were no complications and subsequently oral verapamil was started. The child did not improve beyond her condition before the most recent episode. During 18 months of oral therapy with verapamil (20 mg three times daily) no further neurological deficits have developed.

CSF CONCENTRATIONS OF RANITIDINE
Six—Cimetidine but not oxmetidine can be detected in the cerebrospinal fluid (CSF) in small amounts after a single intravenous dose1 and after one week of oral medication at therapeutic doses.2 Case-reports of mental confusion after treatment with ranitidine have been published3-6 so measurement of CSF ranitidine concentrations may be valuable.

Ten patients scheduled for diagnostic lumbar puncture volunteered to take 150 mg ranitidine twice daily for six days. On the morning of the seventh day 50 mg was given and lumbar puncture was done 2 h, 4 h, or 6 h later. Blood samples were taken before the morning dose on day 7 and at the same time as the lumbar puncture. Venous blood and CSF were analysed for ranitidine by an assay detecting 4 ng/ml or more.

Ranitidine was detected in the CSF in all ten patients (table). The CSF/plasma ratio was 0·08, 0·06, and 0·17 at 2, 4, or 6 h. The higher ratio in the 6 h samples can be ascribed to the lower plasma concentrations at that time. CSF/blood albumin ratios were used to define the status of the blood-brain barrier in each patient. One patient (a 75-year-old woman) had a defective blood-brain barrier but her ranitidine CSF/plasma ratio was 0·08, only slightly above the mean (0·06). No patient showed signs of mental confusion while taking ranitidine.7

The mental confusion seen in the occasional patient treated with cimetidine or ranitidine is unexplained. In two cases mental confusion developing in a patient on cimetidine did not recur when the patient took ranitidine.8 However, in one case7 ranitidine was given at a pharmacologically lower dose than cimetidine, though both drugs were given at doses higher than normally recommended. In the other case6 cimetidine was given in a high intravenous dose despite depressed renal function. When mental confusion appeared

Note augmented filling of the transbasal collaterals and the increased verapamil, at high resolution to emphasise transbasal collaterals. Dimensions of anastomotic network (double asterisks), suggesting opacification of "new vessels". Calibre of posterior branch of middle cerebral artery is increased (double arrows), suggesting vasodilatation. Filling of left posterior cerebral vessel appeared to be increased in calibre (figure) before the most recent episode. During 18 months of oral therapy with verapamil (20 mg three times daily) no further neurological deficits have developed.

Case 2
This 3-year-old white boy had a history of focal seizures at age 11 months after which he uttered only grunts and switched to using his left hand. He had then been seizure-free for a year while taking phenobarbitone, and language improved. At the age of 2 he had an episode of lethargy and vomiting followed by focal right facial seizures. 16 months later he became fatigued over several weeks, vomited, and had tonic-clonic seizures followed by mutism and difficulty in swallowing. He switched back to right-handedness. A slight left facial and arm paresis persisted.

Computerised tomography revealed right hemispheric loss of substance. The posterior cerebral and internal carotid arteries were occluded (with redirected flow) and transdural and transmeningeal anastomoses were noted. 3 months after bypass surgery (as in case 1) his vocabulary had increased but a mild left hemiparesis persisted and he reverted to left-handedness. At age 6½ he was admitted with a severe headache and left facial paresis. Shortly after intravenous administration of verapamil (10 mg over 5 min) the headache diminished, and by 60 min the facial paresis had resolved. 5 months later resolution of the acute deficit has persisted.

These two cases suggest that acute neurological deficits due to moyamoya disease may be improved by treatment with the calcium antagonist verapamil. In case 1 the deficits, progressive over one week, preceded by seizures, were consistent with a slow occlusive process. The increased perfusion through transbasal anastomoses (figure) suggested that verapamil acted by reversal of vasospasm. In case 2 the headache and facial paresis mimicked complicated migraine and could also be explained by vasospasm. Controlled studies, bearing in mind the possibility of adverse effects such as systemic hypotension with decreased cerebral perfusion and over-distension of abnormally fragile moyamoya blood vessels, are now needed. Clinicians in countries where moyamoya disease is more prevalent will be better placed to do these.

We thank Dr Dale Singer for her assistance with case 2, and Ms Debbra L. Neuviirth for secretarial help.

Departments of Neurology, Radiology (Division of Neuroradiology), Anesthesiology, and Pediatrics, and Communicable Disease (Division of Pediatric Neurology), University of Michigan Medical Center, Ann Arbor, Michigan 48109, USA

MICHAEL J. McLEAN
STEPHEN S. GEBARSKI
ABRAHAM F. L. VAN DER SPEK
GARY W. GOLDSTEIN


The mental confusion seen in the occasional patient treated with cimetidine or ranitidine is unexplained. In two cases mental confusion developing in a patient on cimetidine did not recur when the patient took ranitidine.7,8 However, in one case7 ranitidine was given at a pharmacologically lower dose than cimetidine, though both drugs were given at doses higher than normally recommended. In the other case6 cimetidine was given in a high intravenous dose despite depressed renal function. When mental confusion appeared