

inclusion bodies in the lung, liver, and gut (Ridaura-Sanz C: personal communication, 1979), suggest that CMV may be the causative agent in at least some patients. Third, our experience with CMV complement fixation antibody data, as now widely measured in the so-called TORCH screening method, is inconsistent. The unreliability of the method is well known, and our cases reinforce the lack of diagnostic accuracy of the test even in patients who are actively excreting virus.

Proof for the concept that CMV can cause slowly progressive CNS destruction is not yet available because the virus has not been isolated from brain tissue or CSF, nor have typical inclusion bodies been demonstrated in nervous tissue in these cases. Also, the pathogenesis of the changes is not clear. Whether they result from direct viral damage to brain tissue or are secondary to vasculitis or obstructive hydrocephalus due to inflammation and scarring of the aqueduct, basal cisterns, or surface pathways is unknown. The concept of an active and progressive infection is reinforced by Hanshaw's observation (Hanshaw JB: personal communication, 1979) that parents of children with perinatal CMV infections who were found to be partially deaf at school age reported that these children seemed to hear normally as infants.

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Cerebral Hemodynamics and Metabolism in Postoperative Cerebral Vasospasm and Treatment with Hypertensive Therapy

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A 24-year-old woman developed subarachnoid hemorrhage from an aneurysm at the bifurcation of the right internal carotid artery. Following successful clipping of the aneurysm she developed a left hemiplegia associated with focal cerebral vasospasm, which markedly improved when systemic blood pressure was raised with intravenous dopamine infusion. Regional cerebral blood flow and oxygen utilization were significantly depressed in both cerebral hemispheres, while blood volume was significantly elevated only on the side with vasospasm. Oxygen extraction was significantly elevated in *both* hemispheres, indicating a generalized impairment in oxygen delivery to the brain.

Montgomery EB Jr, Grubb RL Jr, Raichle ME:
Cerebral hemodynamics and metabolism in postoperative cerebral vasospasm and treatment with hypertensive therapy. *Ann Neurol* 9:502-506, 1981

Subarachnoid hemorrhage (SAH) from rupture of an intracranial aneurysm may produce severe focal and generalized disturbances in brain function by factors which include ischemia secondary to cerebral vasospasm as well as direct toxic effects of subarachnoid

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blood. Induced systemic hypertension has been used to treat cerebral ischemia from a variety of causes [3, 4], including cerebral vasospasm [1, 2, 4, 5, 8]. New quantitative metabolic and hemodynamic data reported here demonstrate that hypertensive therapy can effectively treat symptomatic cerebral ischemia associated with cerebral vasospasm after ligation of an intracranial aneurysm and also provide evidence of a generalized disturbance in oxygen delivery to the brain following SAH.

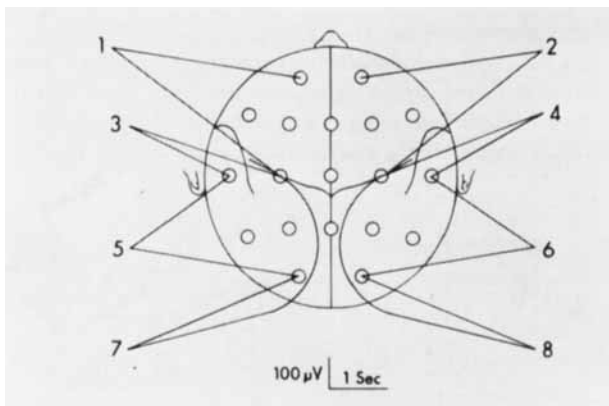
A 24-year-old right-handed woman suddenly developed severe headache and neck stiffness. On admission three days later her blood pressure was 178/88 mm Hg, and it had decreased to 110/70 by the next day. She was lethargic but oriented, with clear speech. Examination otherwise was normal. The cerebrospinal fluid (CSF) was bloody, xanthochromic, and under an opening pressure of 330 mm CSF. Angiography demonstrated an aneurysm at the bifurcation of the right internal carotid artery and no evidence of cerebral vasospasm. On the day prior to surgery a repeat lumbar puncture revealed an opening pressure of 250 mm CSF.

During surgery the aneurysm rebled but was successfully clipped. Immediately afterward the patient developed

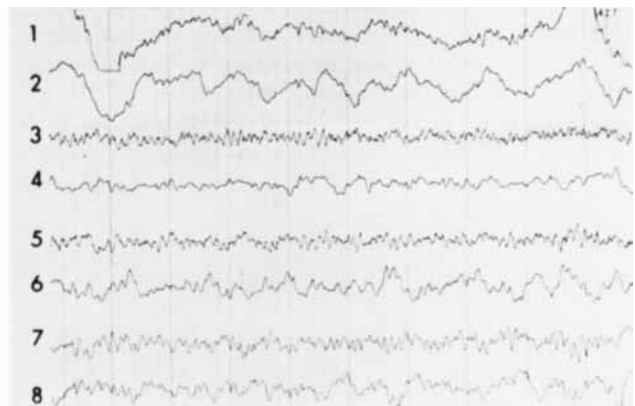
complete paralysis of the left side of the face and left arm; the remainder of the examination was unremarkable. Her blood pressure was 120/79 mm Hg. Within hours a constant intravenous infusion of dopamine was begun to maintain her systolic blood pressure at 140 to 150 mm Hg. The left-sided paralysis improved within minutes, leaving only moderate weakness of the left arm. By the second postoperative day there was only minimal weakness of her left hand and arm.

Postoperatively the patient experienced several episodes when her blood pressure fell below 135/95 mm Hg. Each time her mild left hemiparesis increased, often to the point of complete paralysis. In each instance the paralysis resolved promptly when her blood pressure rose with

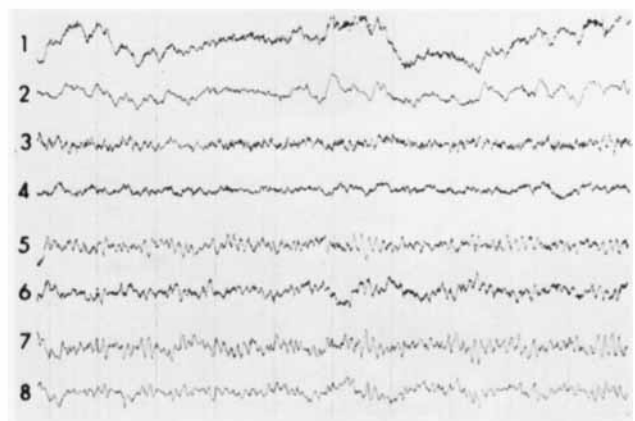
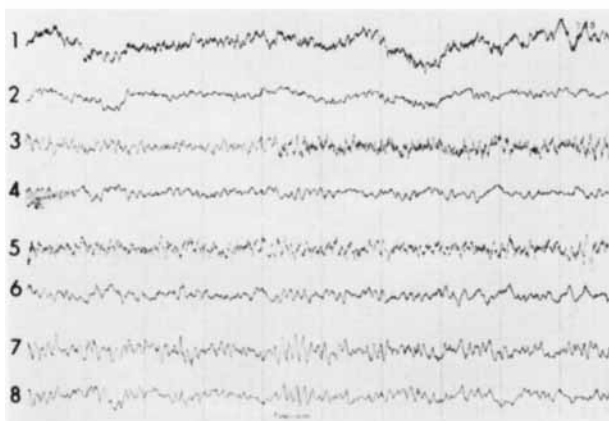
Fig 1. Continuous EEG recording made during an attempt to taper the dopamine infusion. A shows the EEG montage. B shows the baseline EEG while blood pressure was being maintained at 140/90 mm Hg. C shows the EEG when blood pressure was reduced to 100/70 mm Hg as dopamine infusion was tapered, associated with marked worsening of the left face and arm weakness. D shows return of the EEG to baseline as blood pressure was restored by increased dopamine infusion, associated with return of the left face and arm to baseline strength.



A



C



increased dopamine infusion. A critical blood pressure threshold of 135 mm Hg systolic became apparent.

On the seventh postoperative day an attempt was made to taper the dopamine while continuously monitoring the electroencephalogram (EEG). As the rate of dopamine infusion was decreased, the patient's blood pressure fell and the EEG from the right cerebral hemisphere slowed while that from the left hemisphere remained slightly slow and did not change (Fig 1). Simultaneously the previously mild left arm weakness increased markedly, so that at a blood pressure of 85/55 mm Hg the patient could not move her left fingers or arm. An increased rate of dopamine infusion restored her blood pressure to 140/90 mm Hg, improved the EEG, and returned left arm strength to baseline.

On the eighth postoperative day, repeat angiography demonstrated severe, diffuse vasospasm involving the distal right internal carotid artery, the A₁ segment of the right anterior cerebral artery, and the right middle cerebral artery (Fig 2). During angiography the patient's blood pressure was maintained at a level of 140/80 mm Hg, and her neurological status remained stable.

Measurements of regional cerebral blood flow (rCBF), oxygen utilization (rCMRO₂), and blood volume (rCBV) were made in both cerebral hemispheres during angiography, with intracarotid injection of aliquots of the patient's blood tagged with radioactive ¹⁵O-labeled water, ¹⁵O-labeled carboxyhemoglobin, and ¹⁵O-labeled oxyhemoglobin using techniques described earlier [10]. Then *t* tests were used to compare differences in rCBF, rCMRO₂, and rCBV between the right and left cerebral hemispheres in the patient and to compare these results with previously determined normal values [10]. rCBF and rCMRO₂ were significantly depressed throughout both cerebral hemispheres, as shown in Figure 3, while a

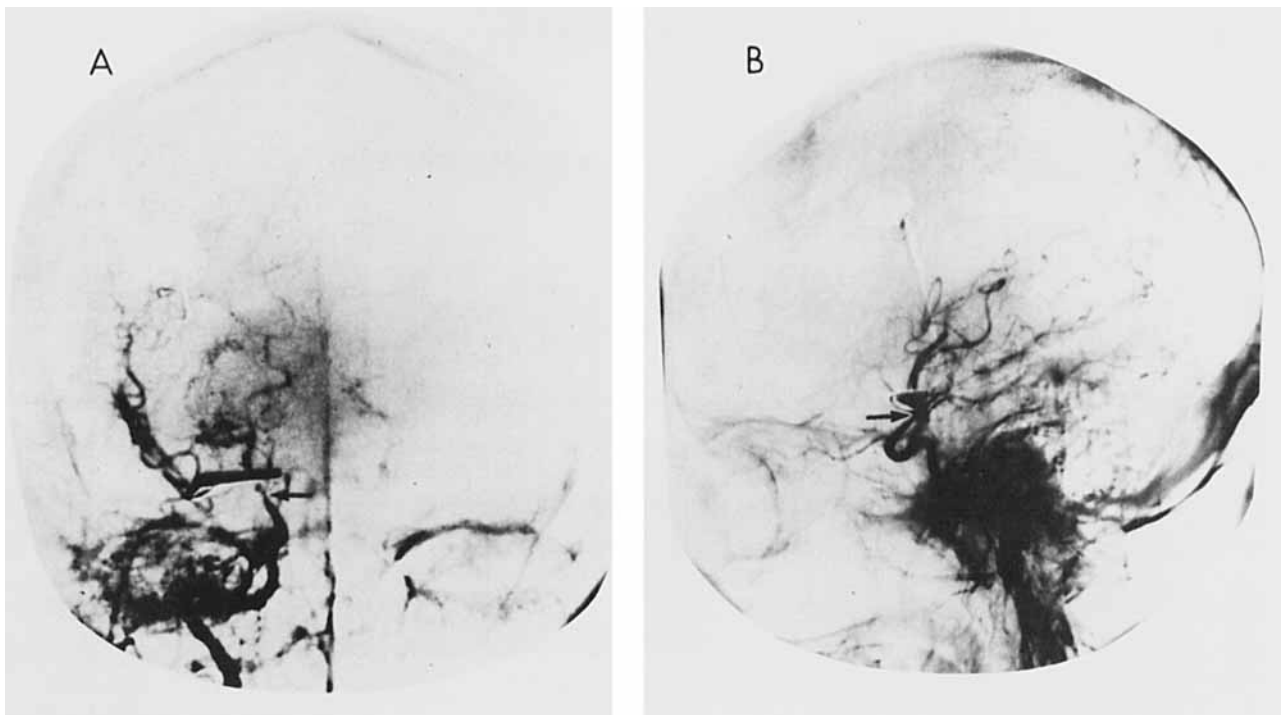
significant increase in rCBV was seen only in the right cerebral hemisphere. The depression of rCBF and rCMRO₂ was most marked in the right posterior frontal and parietal regions. Oxygen extraction, defined as the brain arteriovenous concentration difference for oxygen divided by the arterial oxygen concentration, was significantly increased ($p < 10^{-4}$) in both cerebral hemispheres.

The dopamine infusion was gradually tapered over the next several days and was discontinued on the fifteenth postoperative day without any deterioration in the patient's neurological condition. Follow-up examination three months later showed no abnormalities except for mild impairment of fine finger movements of the left hand and moderate left central facial weakness.

Discussion

We have previously reported decreased rCBF and rCMRO₂ with increased rCBV in patients with SAH and severe vasospasm causing neurological deficits [7], as observed in this case. The large increase in rCBV can be interpreted as a reflection of massive dilation of radiographically inconspicuous intraparenchymal blood vessels (i.e., poststenotic dilatation). The increased oxygen extraction in the hemisphere affected by vasospasm represents failure of the vasculature to meet local metabolic demands. This is

Fig 2. Anteroposterior (A) and lateral (B) views of the postoperative angiogram demonstrating satisfactory clipping of the aneurysm. Severe, diffuse vasospasm involves the distal right internal carotid artery (arrows), the A₁ segment of the right anterior cerebral artery, and the right middle cerebral artery.



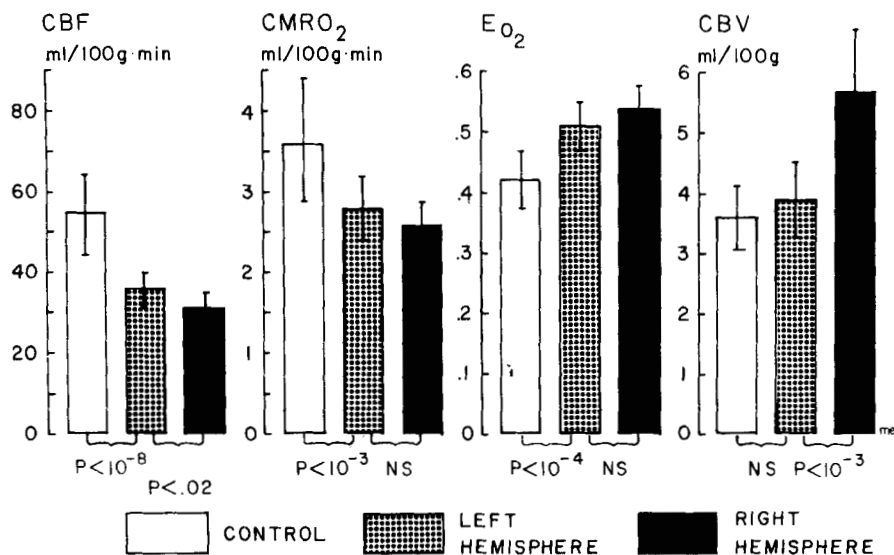


Fig 3. Measurements of cerebral blood flow (CBF), cerebral metabolic rate for oxygen (CMRO₂), cerebral oxygen extraction (E_{o2}), and cerebral blood volume (CBV) obtained at the time of the angiogram shown in Figure 2. Data from each cerebral hemisphere represent the mean (\pm SEM) of 13 regions. Control data were obtained in previous studies from our laboratory [12].

supported by the direct correlation between the patient's fluctuating neurological signs and the level of arterial blood pressure.

The results in this case demonstrated depressed blood flow and oxygen consumption coupled with increased oxygen extraction in the cerebral hemisphere not involved by vasospasm and functionally normal as judged by clinical examination and EEG. In our previous report [7] we did not have occasion to study the uninvolved and presumably normal cerebral hemisphere in a patient with SAH. Although finding depressed rCBF and rCMRO₂ was not surprising considering the presumed toxic effect of subarachnoid blood [9], the increased oxygen extraction was quite unexpected. Our tentative conclusion is that oxygen delivery to the hemisphere without evident vasospasm was also compromised. The mechanism and importance of this finding are uncertain.

This report emphasizes the efficacy of induced systemic hypertension in the treatment of cerebral ischemia due to postoperative vasospasm. The mechanism of improvement was probably improved rCBF due to increased perfusion pressure across large, stenotic blood vessels. During hypertensive therapy the central venous pressure should be maintained between 8 and 15 cm H₂O by infusions of whole blood, albumin, or low-molecular-weight dextran [5]. If these methods are unsuccessful, vasopressor agents may be necessary. Levarterenol and phenylephrine

are frequently used. This case report and one other [1] indicate that dopamine may be a better pressor agent because renal perfusion is more adequately maintained and tachycardia is less troublesome (particularly at doses less than 10 μ g/kg/min) [6]. Hypertensive therapy should be continued for several days, then slowly tapered.

The authors wish to thank Mr John Hood, Mrs Christa Cooper, and the staff of the Washington University School of Medicine cyclotron for their invaluable technical assistance in studying this patient.

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Preservation of the Phrenic Motoneurons in Werdnig-Hoffmann Disease

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A neuropathological study on spinal cords at the third, fourth, and fifth cervical levels in 4 patients with Werdnig-Hoffmann disease revealed marked, generalized loss of motoneurons except for a cluster of large or medium-sized ones in the most medial portion of the anteromedial cell group. These well-preserved neurons were regarded as the phrenic motoneurons because diaphragmatic movement was the only muscle activity that remained until the last stage of illness. Furthermore, in its location and its cytoarchitectonic and neuronal characteristics, this neuronal cluster coincides with the phrenic nucleus as previously localized in the spinal cords of patients with phrenicotomy.

Kuzuhara S, Chou SM: Preservation of the phrenic motoneurons in Werdnig-Hoffmann disease. *Ann Neurol* 9:506-510, 1981

Sparing of diaphragmatic movement until the latest stage of illness is characteristic of Werdnig-Hoffmann disease (WHD) [2, 3, 10, 12], although a few exceptional cases with initial muscle weakness confined to the diaphragm have been described [18]. Most of the previously reported postmortem examinations of infants with WHD have substantiated macroscopically and microscopically normal diaphragm despite severe atrophy of the other skeletal muscles secondary to degeneration and loss of motoneurons in the spinal cord and brainstem.

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Previous neuropathological studies on the spinal cord in WHD have paid little attention to the phrenic nucleus. This report describes the cervical cords of patients with WHD and focuses attention on the phrenic nucleus, localized to the anteromedial area of the anterior horns of the third, fourth, and fifth cervical segments, most prominently at C4 [14].

Materials and Methods

Cervical spinal cords obtained from 4 autopsy cases with a clinical history of progressive muscle weakness and wasting were included in this study. The patients had been diagnosed clinically as having WHD, and their diagnoses were confirmed by muscle biopsies and necropsies. Light and electron microscopic findings and morphometric analysis on the spinal roots of these patients were reported previously [14].

Physical examinations and chest roentgenograms revealed diaphragmatic contractions until the latest stage in all 4 patients, although they died of respiratory problems. A histological examination of the diaphragm performed in 1 patient revealed normal musculature. The spinal cords had been stored in phosphate-buffered neutral formalin for years after several segments were sampled for the previous studies. The C3, C4, and C5 segments, identified by counting the spinal roots, were sampled and embedded in paraffin. From each block more than ten serial transverse sections each of either 8 or 15 μ thickness were studied with hematoxylin and eosin, cresyl violet (Nissl), Klüver-Barrera, and Holzer stains.

For controls, the spinal cords from 3 patients of comparable age who died of nonneuromuscular diseases were examined in a similar manner. Clinical summaries of the 4 patients with WHD and 3 control cases are shown in the Table.

Results

In the control cases three major neuron groups were identified in the anterior horns of the cervical cord: the anteromedial, anterolateral, and posterolateral groups (Figs 1B, 2B). The first two groups were present at all the spinal levels examined, whereas the last was not apparent at the C3 level but was at C4, with a gradual increase in size caudally through the C4 and C5 levels.

In all 4 patients with WHD there was severe loss of large motoneurons with astrocytosis in the anterior horns, having the appearance of empty-cell beds (Figs 1A, 2A). The remainder of the motoneurons occasionally showed central chromatolysis. Although these pathological findings were seen throughout the anterior horn at each segment, a small cluster of well-preserved motoneurons was consistently noted in the most medial portion of the anteromedial area of the anterior horns from the C3 to C5 levels, most strikingly at C4 (Figs 1A, 2A).

This neuronal cluster was not readily delineated from other motoneurons in the anteromedial cell