The 86th Meeting of the Society of British Neurological Surgeons was held in conjunction with the American Academy of Neurological Surgery in Bermuda from 6–9 November 1974

SUCCESSFUL TREATMENT OF DELAYED ARTERIAL SPASM IN THE RHESUS MONKEY AFTER SUBARACHNOID HAEMORRHAGE

CHRISTOPHER W. NORWOOD, G. JOSEPH POOLE, DIXON MOODY, and EBEN ALEXANDER, JR (Winston-Salem) noted that a successful treatment for delayed cerebral vasospasm after subarachnoid haemorrhage had been reported. In their Rhesus monkey population subjected to subarachnoid haemorrhage 62.5% developed delayed cerebral vasospasm. Seven were treated with a beta-adrenergic drug alone, and five of the seven responded to the drug, representing a 71% response rate. Four other monkeys with delayed cerebral vasospasm were treated with a combination of a phosphodiesterase inhibitor and a beta-adrenergic stimulator. One hundred per cent of these animals responded with complete relief of the delayed cerebral vasospasm. When the two groups of monkeys were treated as one group, nine of 11 animals with delayed cerebral vasospasm had relief of the vasospasm, representing an 81% response rate. The pharmacology of beta-adrenergic stimulators and phosphodiesterase inhibitors was discussed and a rationale for their synergistic effect was postulated.

STUDY OF CEREBRAL ARTERIAL SPASM. IN VITRO CONTRACTILE ACTIVITY OF VARIOUS VASOACTIVE AGENTS ON THE HUMAN BASILAR AND ANTERIOR CEREBRAL ARTERIES

GEORGE S. ALLEN, SHELLEY N. CHOU, and L. A. FRENCH (Minneapolis) had previously reported in vitro experiments in which a small volume chamber was used to determine the contractile activity of various vasoactive agents on canine basilar and middle cerebral arteries. They described similar experiments carried out on human basilar and anterior cerebral arteries. Segments of these vessels were removed within one hour of death from patients dying of a variety of causes, including subarachnoid haemorrhage from aneurysms. Cumulative dose-response curves were obtained from most of the agents tested, including serotonin, noradrenaline, and F₂ prostaglandin. These human arterial segments reacted to these agents in concentrations which were sometimes as low as $1 \times 10^{-15}$ molar. Serotonin produced a 90% maximal contraction of these arterial segments at a concentration 10–30 times less than that known to be present in blood. The cumulative dose-response curves for the human arteries were similar to those for the canine arteries. The canine cerebral artery must therefore be a good experimental model for the study of the aetiology of cerebral arterial spasm.

INFLUENCE ON THE HYPOTHALAMUS OF INTRACRANIAL ARTERIAL SPASM

ROBERT H. WILKINS (Temple, Texas) postulated that hypothalamic injury plays a role in the development of arterial spasm associated with ruptured intracranial aneurysms in humans. The evidence for this hypothesis was, firstly, that cerebral vasospasm in humans did not have the characteristics that might be expected if it were solely due to the exposure of the arteries to blood, as in animal models. There was, for example, a delay varying from hours to days after subarachnoid haemorrhage before spasm develops, even though the arteries at the base of the brain were immediately surrounded by extravasated blood. Not all patients developed vasospasm and, when it did occur, it seemed to follow preferentially rupture of aneurysms near the hypothalamus and involving vessels which supplied the hypothalamus. Secondly, there was postmortem evidence that patients with ruptured aneurysms had destructive lesions in the anterior hypothalamic area where they might be expected to cause overactivity of the sympathetic nervous system, an effect that had been shown by electrophysiography and other investigations to occur. This sympathetic overactivity seemed to occur in the same time sequence as did intracranial arterial spasm. Thirdly, a study of postoperative and post-traumatic cerebral vasospasm had provided analogous and supporting data. At least three mechanisms might be involved in the relationship between hypothalamic injury and the development of intracranial arterial spasm.
1. Sympathetic impulses from the posterior hypothalamus might descend through the brain-stem and spinal cord to the stellate and cervical ganglia and back to the cerebral vessels causing a constrictive effect which was not balanced by corresponding parasympathetic impulses.

2. Injury to the hypothalamus might cause liberation of various vasoactive chemical agents into the cerebrospinal fluid.

3. Hypothalamic injury might stimulate widespread sympathetic discharge, especially affecting the adrenal medulla, increasing the levels of circulating catecholamines. This was the most likely mechanism. Subarachnoid haemorrhage, by damaging adrenergic nerve endings but not alpha adrenergic receptor sites, might cause denervation hypersensitivity of the intracranial arteries to catecholamine circulating in the blood or cerebrospinal fluid.

Any one of these mechanisms might serve as the initial stimulus to intracranial arterial spasm. The resulting biochemical and ultrastructural changes might outlast the duration of the stimulus by a number of days. Furthermore, such a stimulus probably acted in addition to, or synergistically with, the effects of blood in the intracranial subarachnoid space. Finally, since intracranial vasospasm was most marked in the anterior part of the circle of Willis, such spasm might itself cause further ischaemic injury to the hypothalamus, thus perpetuating the period of spasm.

TWENTY-FIVE YEARS' EXPERIENCE WITH MIDDLE CEREBRAL ANEURYSMS

JOHN GILLINGHAM (Edinburgh) considered that the real challenge today in endeavouring to prevent recurrent haemorrhage from middle cerebral aneurysms was the avoidance of serious morbidity. Important advances in management had been the recognition of the importance of small warning haemorrhages, careful timing of angiography, production of low intracranial pressure and moderately low arterial pressure during anaesthesia and dissection of the aneurysm sac, the use of magnification methods, and better techniques of clipping or investing. The neck of the sac was particularly vulnerable after recurrent haemorrhage and was sensitive to manipulations which would cause or aggravate vasospasm. The author preferred complete investment of the sac with fine mesh gauze cotton to clipping. Magnification might lead to more gentle dissection but the outcome of operation was likely to be poor if there were too much manipulation. The series under review consisted of 81 consecutive cases. Operation had been carried out on or about the seventh day if the patient’s condition were sufficiently satisfactory. The overall operation mortality was five out of the 81 cases and all of these were in patients placed in Botterell grades 3, 4, or 5. One patient died from recurrent haemorrhage 24 hours after operation, one had a thrombosed middle cerebral artery after fracture of an atheromatous plaque, one died from an unrelated cause, one had fatal cerebral ischaemia and swelling due to myocardial insufficiency five days after surgery, and one died of recurrent haemorrhage two months after operation. There was an early return to normal activities in 35 of the 41 grade 1 cases, in seven of the nine grade 2 cases, in seven of the 27 grade 3 cases, and in none of those placed in grades 4 and 5. The best results were in those who underwent surgery after only one haemorrhage. Patients without hypertension or vascular disease faired better than did those with these conditions. The four late deaths in the grade 1 cases were due to contralateral middle cerebral artery thrombosis in one patient and unrelated causes in three. The two late deaths in grade 2 patients were the results of unrelated illnesses. The one late death in a grade 3 patient who was severely hypertensive was due to recurrent haemorrhage from an aneurysm sac. The incidence of epilepsy was 13.7%. It was concluded that technical factors leading to morbidity and mortality were excessive manipulation during dissection leading to haemorrhage with or without spasm, kinking of a major arterial trunk or its branches by a clip, inadequate investment, fracture of an atheromatous plaque, recurrent arterial spasm and ischaemia, or extradural haematoma. Favourable prognostic features are the early referral of grade 1 patients, operation within 10 days of the first haemorrhage, and minimal interference during dissection of the aneurysm sac.

THE 'A' PRINCIPLE—A NEW APPROACH TO THE MANAGEMENT OF INTRACRANIAL ANEURYSMS

W. J. ATKINSON (Haywards Heath) drew attention to patients whose long-term follow-up after successful aneurysm surgery demonstrated subtle personality changes interfering with the life of the patient and his family. In the atherosclerotic patient the pulse wave was transmitted directly to the aneurysm and was not ‘taken up’ by the expansion of the arterial wall. It was suggested that efforts to prevent high systolic pressure reaching aneurysms would prevent subsequent haemorrhage, and that this could be done by causing the arterial wall proximal to the aneurysm to expand and so take up the systolic pressure. Clamps were placed on the internal carotid artery in the neck for periods varying from 15 to 60 minutes to contuse and break up the muscle and intimal layers of the arterial wall. Six patients had been treated in this way with one death. Damage to the wall of the internal carotid artery may produce a false aneurysm

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*J Neurol Neurosurg Psychiatry* 1975 38: 404-405

doi: 10.1136/jnnp.38.4.404-b