Advances in the Management and Surgical Treatment of Intracranial Aneurysms* **

THORALF M. SUNDT, JR., M.D.

Associate Professor of Neurosurgery, Mayo Medical School, University of Minnesota, Rochester

Introduction. Patients who have sustained a spontaneous subarachnoid hemorrhage are victims of a very serious illness. Not only are they subject at all times to the potentially catastrophic results of a recurrent bleed, but they are faced with the manifestations of the irritative effects of blood in the subarachnoid space where the blood may function as a poison to the vessel wall. These acutely ill individuals may suffer a composite of secondary effects from a bleed which may include a communicating hydrocephalus, cerebral edema (ischemic or chemically induced), sterile meningitis, inappropriate ADH syndrome (osmotic effects of blood in the cerebrospinal fluid), spasm, and the likelihood of a recurrent bleed.

Physiology and Pathogenesis. Both the physiology and the anatomy of the cerebral blood vessels differ from those of comparable size elsewhere in the body (1). Unlike most organs and muscles, the brain maintains a relatively constant blood flow throughout a wide range of cardiac output and activity. The flow is approximately 700–900 milliliters per minute, whether the cardiac output is five liters per minute, as during rest, or four or five times that volume, as in strenuous exercise (2). Cerebral blood flow apparently is not directly sensitive to circulating epinephrine or norepinephrine, as these catecholamines do not cross the intact blood-brain barrier (3). Furthermore, it is common knowledge that these catecholamines in physiological doses do not produce marked vasoconstriction, even when applied topically to relatively normal cortical vessels. The cerebral circulation seems to be governed by its own autoregulation, a mechanism at present poorly understood (4). In health, this mechanism is not directly sensitive to the peripheral blood pressure within reasonable extremes. In cases of acute head injury, subarachnoid hemorrhage or cerebral ischemia, however, the autoregulatory mechanism is no longer functional and cerebral circulation becomes pressure and volume dependent (5).

The presence of a great abundance of autonomic nerves in the conducting vessels in the subarachnoid space has been the subject of recent intensive investigation directed toward identifying a physiological role for this system. Because conflicting data are reported from a variety of highly respected groups, one might maintain almost any role for this system today and find laboratory data to substantiate his position. It is our judgment that the autonomic nervous system provides a modulating and buffer action for the conducting vessels in the subarachnoid space, and we will direct our attention to this aspect of the problem a little later in this discussion.

Intracranial vessels have a characteristic and unique design (1). Perhaps this is because vessels inside the head are protected by a rigid skull and are not subject to the moving stresses and angulations of vessels in the body. They have a thin intima and adventitia. The media is also quite thin and not heavily endowed with elastic tissue. There is, however, a thick internal elastic membrane of considerable importance in providing the wall with strength. Defects in the media occur so frequently that they can hardly be termed pathological.

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Quite different, however, is the occurrence of defects in the internal elastic membrane. When this membrane fragments and bulges through a defect in the media, an aneurysm forms. Controversy continues over the cause of this fragmentation—whether it is congenital or degenerative—and also over the importance of a preexisting medial defect. The point of importance concerning the necessity and technique for repair is that the elastic lamella ceases to exist in the aneurysm itself. Furthermore, as the aneurysm grows in size, although there is no increase in the pressure per unit of area, the total force on the aneurysm increases. This subjects the base of the aneurysm to increased tension and tends to cause progressive growth of the lesion.

The weakest points in an aneurysm are usually in the dome itself or at its base where it arises from the vessel. The wall consists of collagenous tissue, which is continuous with the adventitia and intima of the parent vessel. There is a marked difference in the thickness from one aneurysm to another. Frequently through the operating microscope one can actually see the blood swirling in eddying currents through the walls of a thin aneurysm. In other instances, the aneurysmal wall does not seem different in consistency or thickness from the parent vessel; in the special case of giant aneurysms, the wall is quite thick. There is, of course, no way to predict from arteriography alone what the case is in each patient. In those patients who survive a subarachnoid hemorrhage from an aneurysm, a blood clot forms around the aneurysmal membrane, and along with the surrounding arachnoid, seals the vessel temporarily.

Surgery of Aneurysms. Most surgery for aneurysms today is performed through the operating microscope. A description of the procedure for repair of an aneurysm might be of interest to those of you who are not surgeons.

We will discuss four aneurysms, two internal carotid artery aneurysms and two anterior communicating artery aneurysms, the location of most aneurysms upon which we operate. Space does not permit us to cover middle cerebral and basilar aneurysms; their appearance is not greatly different.

The first case is of a left internal carotid artery aneurysm. Looking through the microscope, you expose the operative field, revealing the white structure of the optic nerve. Initially, with the point of an eleven blade knife, the arachnoid overlying the optic nerve is severed and the dissection is carried laterally to identify the internal carotid artery, the aneurysm arising and projecting laterally from that structure. (We prefer the tip of an eleven blade knife to a predesigned surgical instrument for this purpose; we have used the latter and found that they dull all too rapidly; the #11 blade can easily be replaced with a new, sharp blade.) There is a noticeable difference in the texture of the wall of the aneurysm and the carotid artery. The carotid artery is whitish by comparison to the aneurysm. A careful look at the aneurysm should permit you to see that the blood is swirling in eddying currents through the very thin-walled lesion. The clip we would use to repair this aneurysm is known as a clip-graft; in this case it would be applied with a right angle applier and the clip would circumferentially surround the internal carotid artery and seal the aneurysm at its base. We prefer this type of clip for repair of carotid artery aneurysms, because these aneurysms arise from a relatively wide portion in a relatively large vessel and repair with a straight clip does not reinforce the base or prevent the redevelopment of an aneurysm in the future, and furthermore, should the base tear with application, the clip seals the vessel. This is in direct contrast to middle cerebral aneurysms, for instance, in which ordinarily speaking one is able to find a relatively thick base in the aneurysm to accept a straight clip.

The second case is also an internal carotid artery aneurysm, but this aneurysm arises not only from the internal carotid artery but from the posterior communicating artery as well, which in the individual served as the sole source of blood supply to the posterior cerebral artery on the side of surgery. We could not use a clip-graft for fear of occlusion of the posterior communicating artery; the aneurysm must, therefore, be repaired with a Scoville clip, a type of straight spring clip. Following clipping of this aneurysm, a search made anteriorly to be certain of the patency of the posterior communicating artery showed it to be patent in this patient, and he made an uncomplicated postoperative recovery.

The third case is that of an anterior communicating artery aneurysm. Viewed through the operating microscope in an approach along the floor of the frontal fossa, the optic nerve would initially be identified and the dissection would be carried medially to the location of the anterior communicating artery and the aneurysm. Examination of the angiograms prior to surgery revealed that this aneurysm projected anteriorly, and comforted by this knowledge, the arachnoid overlying this lesion could be dissected

from between the two frontal lobes at their base, just anterior to the anatomical site of the vessel. Initially, the aneurysm would be difficult to see, being surrounded by some thick fibrinous material, which in turn was overlayed by arachnoid; these structures served to seal the aneurysm when it bled. The aneurysm having been dissected anteriorly away from the knee of the A-1 segment of the right anterior cerebral artery and the anterior communicating artery, a clip would be placed tangentially at this point, and following clipping, a search would be made posteriorly to be certain of patency of the major vessels.

The final case relates to an anterior communicating artery aneurysm repaired with a clip-graft. Both anterior cerebral arteries filled from the right A-1 segment—a not uncommon configuration in this type of aneurysm; that is, all too frequently both anterior cerebral arteries derive their blood supply from one side or the other through an enlarged A-1 segment. Therefore in this instance it would be particularly important to be certain that the anterior communicating artery remained patent, and therefore, the clip-graft would be placed with the right angle clip holder circumferentially around the anterior communicating artery sealing the small aneurysm projecting posteriorly at its base. The small aneurysms are often much more treacherous than the large aneurysms, because they do not offer a large enough sac to accept dissection and occlusion by a straight clip should they bleed.

Clinical Features and Diagnosis of Ruptured Aneurysms. The sudden onset of an excruciating headache, with or without the loss of consciousness, indicates a subarachnoid hemorrhage until proven otherwise. The patient describes an "explosion" in the head or a feeling of being struck behind the head with a hammer. Some patients complain of pain on one side, but more commonly the headache is primarily suboccipital in nature.

Often, the patient will have a seizure with his first hemorrhage, but repeated seizures thereafter are infrequent and anticonvulsants are usually not necessary. Patients may vary in their level of consciousness from alert to comatose following recovery of the bleed.

Most patients appear acutely ill and in pain. They complain chiefly of headache and commonly of nuchal rigidity, which incidentally increases after 24–48 hours. Blood pressure is commonly elevated. The patients who have suffered more severe hemorrhages are confused, stuporous, semicomatosed, or even comatosed. In this group, lateralizing signs such as hemiplegia, hemiparesis, or aphasia may be present. On the basis of the neurological symptomatology, Botterell (6) described a system of classification from grades I through V based upon the presence or absence of findings indicated above. A grade I patient is one with only minimal symptomatology, primarily headache; a grade V patient is preterminal and seldom considered a surgical candidate. Between grades I and V the classification is based upon a level of consciousness and the presence or absence of focal findings. This grading classification has proved to be of immense help in considering results of both operative and conservative management.

Natural History of Subarachnoid Hemorrhage. Various studies in the epidemiology of subarachnoid hemorrhage from a ruptured intracranial aneurysm have indicated the catastrophic nature of this illness. If a patient remains moribund for more than 24 hours after his initial bleed, his likelihood of a one-year survival is 8% with rather a severe morbidity; if he recovers from the bleed with only minor symptoms present or a clouding of consciousness, his chances for a one-year survival are approximately 50% (7, 8). Furthermore, approximately 70% of the patients with an aneurysm demonstrated on angiography will have a second hemorrhage, the peak incidence of which is in the second or third week following the initial bleed (9). The second occurrence is usually more severe than the first, frequently leaving the patient in a state of unconsciousness or coma.

Timing of Surgery. Although it would seem optimal to operate on the patient within the first few days after the bleed in order to prevent a recurrent hemorrhage, experience in early surgery from a variety of outstanding institutions has indicated the high morbidity of such a course of action. Accordingly, almost all patients initially are managed conservatively.

Initial Management by Clinician. The most important step in the care of a subarachnoid hemorrhage is the early diagnosis of a warning bleed by the family physician. All too frequently the warning bleed is unrecognized and only after a subsequent and more severe bleed is the patient referred for definitive management. A sudden, excruciating headache with or without the loss of consciousness is a subarachnoid hemorrhage until proven otherwise. A careful atraumatic spinal puncture is necessary in the diagnosis of this illness.

As soon as the patient recovers from the insult of his first hemorrhage, he should be transported by ambulance or air ambulance to a center where such problems are handled in volume. These patients rarely represent acute surgical emergencies, and except in instances of an associated large intracerebral or subdural hematoma, benefit from conservative management for the first several days following hemorrhage. This period of bedrest is perhaps even better for the patient in the setting of the local facility than at the referral center. It is disquieting for the clinician to have a patient with a subarachnoid hemorrhage die prior to referral or prior to obtaining a neurological consultation, but he can be comforted to know that bedrest with light sedation and analgesic medication would have been recommended for the first four or five days or perhaps even longer at most major centers and little could have been done by others that was not done by himself.

One is tempted to lower the blood pressure moderately in such patients with the hope of preventing a recurrence of bleeding while awaiting surgery or diagnostic studies. There are currently conflicting reports, however, regarding the usefulness of this measure and certainly it is not without risk. As mentioned above, patients with a subarachnoid hemorrhage become pressure dependent for cerebral perfusion; if a significant degree of intracranial vasospasm is present, lowering the blood pressure can result in cerebral ischemia and even infarction. This is not to say that hypotensive treatment is not indicated in selected instances, but the criteria are so complex for hypotensive management that definite rules cannot be developed at present.

The use of dexamethasone or some other steroid has been advocated by many experienced workers in this field; others feel that the risk of a stress ulcer is aggravated by an unproven beneficial effect from this drug and have cautioned against its use as a routine procedure. My personal experience with the use of dexamethasone in this setting, in marked contrast to its dramatic effect on the edema of gliomas, has not been very encouraging.

Final data regarding the ability of ϵ-aminocaproic acid to prevent a rebleed is not available. My experience with this drug has not been good, but admittedly we have not used it in the large dosages currently recommended.

Patients who have had a subarachnoid hemorrhage are particularly vulnerable to develop a type of inappropriate antidiuretic hormone (ADH) syndrome; therefore, moderate restriction of fluids is recommended, so that the patient's total fluid intake is between 1500 and 2000 ml daily. Serum sodium should be drawn every 48 hours and if the patient has a fall in the serum sodium, indicating extracellular volume expansion, fluids should be restricted to 1000–1200 ml daily.

Spasm. Early surgery in this illness is risky primarily because it accentuates and aggravates a state of arterial spasm, a reaction to the vasoconstrictive effects of blood and its breakdown products in the subarachnoid space (10). It is a diagnosis based upon the caliber of intracranial vessels seen on angiography; it may be focal or generalized, minimal or severe, unilateral or bilateral. Symptomatically it may produce evidence of both generalized and focal cerebral ischemia, the former manifested by an alteration in the level of consciousness and confusion, the latter by a focal neurological deficit. Although blood related, its etiology and pathogenesis are far from being elucidated.

In general terms, the more severe and widespread the spasm, the worse the patient's clinical condition. Extrapolating from our cerebral blood flow data, it seems likely that spasm can be tolerated until a critical reduction in cerebral blood flow occurs—probably somewhere in the level of 20–30 ml/100 gm/min. Often, prior to this reduction in cerebral blood flow, an angiographic appearance of spasm will not be matched by the clinical appearance of the patient; some individuals look amazingly well considering the angiographic picture. The reverse is not true; patients who show the severe symptomatology of ischemia in this illness usually have angiographic correlation not only with evidence of focal vessel constriction but also of slowing of flow.

Recently, we have employed a combination of isoproterenol (Isuprel®) and lidocaine hydrochloride (Xylocaine®) in the treatment of cerebral vasospasm (11). Isuprel® is given for its beta-adrenergic function and the Xylocaine® is used to counteract cardiac arrhythmias that might result from the intravenous administration of Isuprel®. All patients have had continuous EKG monitoring and special nursing care. Both drugs are administered intravenously on a continuous basis and should cardiac arrhythmias result, the Isuprel® is decreased in its strength and rate of administration or the Xylocaine® is increased in its strength and rate of administration.

There is a wealth of experimental evidence to indicate that the conducting vessels in the subarachnoid space have a rich adrenergic nerve supply which, after sympathectomy or subarachnoid hemorrhage, loses its fluorescence, indicating inactivation of the granulated vesicles at the nerve endings. These granulated vesicles are important not only for metabolism, production, storage, and release of norepinephrine but also for the control of function. In contrast with cholinergic endings in which an enzyme functions to destroy the freed acetylcholine, the limited duration of action of the adrenergic endings is thought to be related to the prompt reuptake of norepinephrine by the granulated vesicles. It is possible that some of the adverse effect of blood on a vessel is the result of this type of end-organ sympathectomy obliterating the function of the granulated vesicles and their buffer action. Alpha and beta sites are pharmacological concepts, not anatomical structures, and there is evidence that between various vasoconstrictive amines there is a competition for a type of membrane response. Isoproterenol is given not so much as a vasodilator but in an attempt to introduce a non-vasoconstrictive drug to compete at the end-organ for the membrane response and hopefully thereby to ameliorate the effects of vasoconstrictor substances such as serotonin. Our laboratory studies indicate that Isuprel® definitely does shorten the period of basilar artery constriction from the topical application of blood.

Table 1 illustrates the author's experience with the use of these drugs in operating on 159 patients over the past four years. This table is primarily intended to demonstrate the distribution of patients with this problem as a major complication and treated patients are identified in parentheses. The result columns indicate the final clinical state of the patient and not necessarily the response of the patient to the administration of these drugs. Most patients treated in the grade I and grade II categories were treated following surgery for the onset of a progressive neurological deficit. Most patients treated in the grade III and IV categories were treated prior to surgery in an attempt to arrest a progressive neurological deficit or improve their condition to a point where surgery could be tolerated. Patients who did not undergo surgery are not illustrated and not included.

TABLE 1

DISTRIBUTION OF TREATED* CASES AMONG ALL PATIENTS OPERATED ON ACCORDING TO GRADE AND FINAL CLINICAL RESULT

	Final Clinical Result			
Grade	Excellent	Good	Poor	Death
I	63 (7)	3		1
II	32 (6)	1 (1)	2	2 (1)
III	14 (5)	13 (3)	8 (2)	4
IV	2	1	8 (4)	5 (1)
Total	111	18	18	12

* No. of treated patients is in parentheses.

A retrospective analysis of the results of the use of these drugs indicates that no improvement has been noted, if the drugs have been used after a period of two hours from the time of the onset of the neurological deficit. Obviously, the more severe the deficit, the more important it is that therapy be instituted early. Although an occasional dramatic response has been noted, most commonly a progressive deficit is halted with a rather major recovery in the first 48 hours, and recovery thereafter related only to the predicted improvement and recovery pattern seen in patients with regions of focal ischemia. The drugs are, however, with careful monitoring, safe, and we have had no mortality from their use. It now remains for others to judge the merits and demerits of this program. Thirty patients treated in this group are shown; treatment was discontinued in another five because of arrhythmias.

In considering and analyzing the results of any medications, it is necessary that they be evaluated in properly selected patients. Spasm, as a major complication, was not uniformly seen in the patient group and although most morbidity and mortality is noted in the high-risk patients, grades III and IV, death and morbidity in these patients was not always a result of their preoperative state. Poor results and death in this group include one patient who bled in the hall prior to entering the operating room, one who bled during the induction of anesthesia, two who sustained a recurrent hemorrhage—the result of poor aneurysmal repair, and two who had occlusion of a major parent vessel from which a giant aneurysm arose. A permanent Korsakoff's syndrome accounted for a poor result in two patients (one of whom had a giant aneurysm and predated surgery). This syndrome, although occasionally the

result of spasm, is more commonly a complication of surgical trauma in the septal or preseptal area.

Conclusion. Improved neuroanesthesia and surgical techniques, especially including magnification of vision and an intense light source, have drastically lowered the operative mortality and morbidity in aneurysm surgery; however, because of a delay in surgery to avoid major vasospasm, many patients are lost from rebleeding. Until a solution to the complication of vasospasm is obtained, most major institutions still prefer to delay surgery. Isoproterenol and lidocaine seemingly ameliorate this dreaded complication but are certainly no panacea and we are still looking forward to a final miracle drug from one of our sister institutions (12).

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