Recent Advances in the Investigation and Management of Cerebrovascular Disease

By James Peter Murphy, M.D.

Cerebrovascular accidents represent the third most common cause of nontraumatic death in the United States of America. More patients are admitted to hospital wards with major brain stroke than with any other neurologic disorder. Fortunately, recent advances in our knowledge of the embryology, anatomy and physiology of the cerebral circulation are improving methods of diagnosis and treatment of cerebrovascular disease.

Embryology

Probably because of better recognition, cerebrovascular accidents due to rupture of congenital aneurysms of the circle of Willis or of arteriovenous malformations of the brain are far more numerous today than 20 years ago. In a series of 200 patients with cerebrovascular disorders analyzed by Brain, 16 per cent harbored aneurysms or congenital angiomas. Reinvestigation of the embryologic construction of the intracranial vascular circulation by Padget and others has disclosed the raison d'être of these developmental anomalies.

Faults in the media of arteries, particularly at the points of their bifurcation, failure of complete resorption of primitive vessels of phylogenetic but not ontogenetic importance, inadequate fusion or anastomosis of the carotid and vertebral circulations and incomplete splitting of the three vascular layers (cranial, meningeal and cerebral) of the embryonal head are largely responsible for the presence of intracranial circulatory malformations in adult life. Acquired factors such as arteriosclerotic weakening of the internal elastic lamina of arteries and focal necrosis of vessels during angiitis contribute to aneurysmal saculation and rupture which is manifest most often in maturity and not in infancy.

Anatomy

Collateral Arterial Circulation: Few vessels of the cerebrum and cerebellum are true end-arteries. Unfortunately, these lie in the critical fields of supply of the basal ganglia and internal capsule, pons and the tip of the temporal lobe. Collateral anastomoses are numerous, especially superficially, and increase numerically with age. At autopsy of elderly individuals, occlusion of major vessels such as the middle cerebral artery have been found without infarction, peripheral to the site of thrombosis. Anastomoses between the carotid and vertebral circulations are quite variable, a "normal" circle of Willis being found in only 50 per cent of brains examined. Only thus can hemiplegia, following unilateral carotid thrombosis in one patient, be reconciled with bilateral occlusion of both carotid arteries (verified by angiography) without clinical aftermath in others. External-internal carotid cross circulation is not a negligible factor in preserving intracranial circulation, as demonstrated by angiographic filling of the cerebral vessels via the ophthalmic artery after complete occlusion of the internal carotid.

From the Department of Neurological Surgery, George Washington University, Washington, D. C.
Microscopic Structure of Cerebral Arteries. The intracranial arteries are characterized by a relatively thin muscularis media. That cerebral arteriospasm may occur clinically nonetheless is evident in migraine with neurologic complications (for example, hemianopia). Sympathetic vasomotor fibers have been traced peripherally to arterioles of 50 micra caliber. The intact internal elastic lamella is of greater importance in maintaining arterial integrity than the thin medial coat and almost nonexistent adventitia. Only when the thick protective elastic membrane, deficient congenitally or weakened by sclerosing disease perforates, can cerebral hemorrhage occur.

Intracranial Veins and Dural Venous Sinuses. Intracranial venous anastomoses are numerous. Angiograms in cases of major cerebral venous occlusive disease disclose that the anastomotic vein of Labbé and the basal vein of Rosenthal are capable of conducting the principal aliquot of blood from one hemisphere to the ipsilateral transverse sinus. Gradual complete obliteration of the superior sagittal sinus or of one transverse sinus can be compensated for by collateral drainage. In a patient with probable sagittal sinus thrombosis and papilledema upon whom I performed a subtemporal decompression after normal ventriculography, the eye grounds and vision were perfect within six weeks. This is a not uncommon experience in the surgical treatment of "pseudotumor cerebri." Conversely, acute compression of the superior longitudinal (sagittal) sinus, by depressed fracture of the vertex of the skull, results in severely increased intracranial pressure.

The role of the vertebral venous plexus, anastomotic with the intracranial drainage through occipital and suboccipital emissary veins, is not negligible in compensating for venous thrombosis within the skull. Indeed, both internal and external jugular veins have been sacrificed during radical neck dissections for cancer with no more than temporary increase of intracranial pressure. The vertebral venous plexus conducts all blood from the head to the heart under these circumstances.

Physiology

The objective measurement by Kety and others of the rate and extent of cerebral flow of blood has been a great advance. Average normal cerebral blood flow is 54 to 65 cc. per minute per 100 Gm. of brain. The highest value recorded was 164 cc. per minute per 100 Gm. of brain in a patient with an arteriovenous anomaly; the lowest flow was 22 cc. per minute in a patient with polycythemia vera. With uncomplicated essential hypertension, cerebral blood flow and cerebral metabolic rate are normal; cerebrovascular resistance is increased. When hypertension and cerebral arteriosclerosis coexist, cerebral blood flow and brain metabolism are both reduced. Although carbon dioxide inhalation in patients with cerebral arteriosclerosis alone does not increase cerebral flow, when both hypertension and arteriosclerosis are present, an increase of almost 20 per cent in cerebral blood flow occurs during administration of carbon dioxide. Aging as such is associated with decreased cerebral blood flow and reduced oxygen uptake by the brain.

Drug Therapy. Caffeine and aminophylline reduce cerebral blood flow measured by the nitrous oxide technic, paradoxically, in view of the common dependence upon morning coffee for wakefulness and the undoubted value of aminophylline in treatment of some patients with a recent stroke. Priscoline does not increase total cerebral blood circulation, whereas intravenous papaverine does. Histamine, nicotine acid and the nitrates are capable of enlarging the intracranial vascular bed, as verified by experimental observation, but only if the systemic blood pressure does not fall excessively.

Hypotension. The preceding observation applies particularly to the use of sympathetic ganglion blocking agents. Hexamethonium in particular is condemned in clinical practice; general hypotension results in marked reduction of cerebral blood flow and cerebral ischemia in elderly hypertensive patients. On the other hand, a hexamethonium-induced fall of blood pressure in animals results in dilatation of pial arteries, the "agonal phenomenon" of
Forbes. This may apply clinically to healthy young people in shock but not to the elderly, incapable of such a response.

Further investigation of induced hypotension assisting major surgery has revealed it to be a two-edged sword. If sclerosis of brain arteries exists, the procedure may be dangerous even though pressures in the brachial and carotid arteries have been found to be equal in the prone position. Unless compensatory mechanisms in the brain or its circulation accomplish increased extraction of oxygen from circulating blood, traumatic or artificial shock may become lethal, probably because of intracerebral hypostatic infarction. The electroencephalogram may be a sensitive indicator of disordered cerebral function occurring during surgical hypotension.

**Clinical Syndromes**

**Cerebral Vasospasm**

The concept of cerebral arteriospasm is controversial. It should be pointed out that every patient suffering from migraine who sustains transient hemianopia, aphasia or hemiplegia is probably experiencing temporary spasm of the posterior cerebral or middle cerebral arteries. Intracranial arteriospasm has been observed by neurologic surgeons operating upon the circle of Willis. Likewise, definite and persistent angiospasm, following embolization of cerebral arteries or induction of hypertension in experimental animals, has been observed through skull windows. The possible benefit of vasodilating drugs or of stellate block in patients with evanescent "strokes" should not be withheld.

**Cerebral Infarction**

Intracranial angiography and pathologic examinations have made it increasingly apparent that nonhemorrhagic and nonembolic cerebral accidents are not necessarily the result of true thrombosis, but are often the effect of infarction without thrombosis. In over 60 per cent of cerebral infarcts studied at autopsy, no intra-arterial thrombus can be found. Contrariwise, occluded arteries may be discovered without peripheral infarction. In the remainder of cases, thrombosis of a major vessel without adequate collateral circulation results in infarction of the brain.

**Infarction without Thrombosis:** Many nonhemorrhagic, nonembolic and nonthrombotic infarcts occur during sleep or when hypotension develops from another cause. Arteriosclerotic narrowing of the internal carotid or cerebral arteries and the absence of potentially functioning anastomoses are important contributory factors. Ecker has observed arteriospasm in 90 per cent of patients with stroke, hemorrhagic or otherwise. Anger or hostility may induce vascular spasm sufficient to occlude an already narrowed vessel.

**Cerebral Infarction in Heart Disease:** Heart failure is frequently an instigating or complicating factor in cerebral infarction. The simultaneous occurrence of infarcts in the heart (coronary occlusion) and brain is not uncommon. Brain damage in the cerebrocardiovascular syndrome is often nonthrombotic, although Scheink has reported the occurrence of true thrombosis of small cortical veins during chronic heart failure. This latter complication may be responsible for mental disturbance, hemiplegia or epileptic seizures in the decompensated cardiac patient.

The "Little Strokes:" Alvarez has stressed the clinical significance of a common finding in the routine autopsy examination of the brains of the elderly, long familiar to every neuropathologist, that is, multiple small cystic infarcts in the pons, mesencephalon, basal ganglia and thalami. These lesions are due to the combined effect of arteriosclerosis and brief but significant hypotension.

Diverse clinical syndromes, related in their fundamental pathologic substrate to "little strokes," are listed by Alvarez: (1) Episodes in chronic illness misdiagnosed as "nephritis," "abdominal upsets" and the like, in which "death keeps taking little bites" of the patient; (2) vague mental changes, particularly of memory; (3) loss of working ability; (4) premature aging, general "slowing-up" and carelessness; (5) fear of being alone; (6) loss of old interests and of joy in life; (7) poorly
localized but severe pains in the chest or abdomen; (8) “acute indigestion,” diarrhea or incontinence and (9) burning of the tongue or “bad taste in the mouth.” To these may be added (10) so-called “Menière’s syndrome” which is often a manifestation of infarction in the pons in the older patient, especially if there is loss of sensation of the face and (11) a group of disorders representing a cumulative effect, predominantly upon the motor system, of multiple and repeated infarcts in the brain stem—“arterio-sclerotic rigidity” of Foerster, pseudobulbar palsy, atypical Parkinsonism and the syndrome of “démarche à petit pas”.

Thrombosis of the Posterior Inferior Cerebellar Artery. The Wallenberg syndrome, the result of occlusion of the posterior inferior cerebellar artery or of the anterior inferior cerebellar artery (Foix) is selected for special comment from a host of specific intracranial arterial syndromes. It appears to be increasing in incidence among the younger age group. Angiographic studies reveal that the parent vertebral artery at the base of the skull may be thrombosed instead of the cerebellar vessels.20 When the syndrome appears in a 20 to 30 year old patient, hypoplasia of one posterior inferior cerebellar artery may be responsible for occlusion rather than arteriosclerosis. It is interesting that when thrombosis has actually occurred in the vertebral artery, the brain stem is capable of withstanding more ischemia than thought possible, since most patients with the Wallenberg syndrome recover fairly promptly, although not necessarily completely.

Carotid Thrombosis. Thrombosis in the cervical carotid artery with consequent intracerebral infarction is a subject of current clinical interest. The discovered incidence of cervical carotid thrombosis in angiograms, performed on patients with cerebrovascular disorder, is one to two per cent.10 The clinical significance of this observation is tempered by the observation that cerebral infarcts occur in only one-third of patients with carotid thrombosis,10 owing to adequate collateral supply of the ipsilateral cerebral hemisphere through the circle of Willis or via external-internal carotid anastomoses.

When impairment of brain function does occur, three clinical syndromes are possible18: (1) transient attacks of hemiplegia, (2) slow progression of hemiparesis, aphasia, etc., featured by severe headache and convulsions or (3) sudden, catastrophic infarction with coma, hemiplegia and loss of speech. Diagnosis is often difficult on clinical grounds alone. Angiography proves the existence of thrombosis of the common carotid artery below the carotid sinus or of the internal carotid artery just above the carotid bifurcation or in the carotid siphon. Without angiography, the diagnosis may be suspected or established by inability to palpate the pulse of the internal carotid normally felt in the posterolateral pharynx, or by the induction of immediate unconsciousness when the opposite carotid is occluded by manual pressure on the neck.

The treatment of carotid thrombosis is unsatisfactory by any means. Fortunately, spontaneous recovery is frequent, due to development of collateral circulation to the cerebral hemisphere deprived of blood, assisted by vasodilator drugs. Restitution of function is usually not complete.

Cerebral Embolism

After major embolism of the brain, neurologic disability is severe and rapid, compared with the more gradual development of spontaneous cerebral infarction. Valvular or myocardial heart disease as the source of emboli is almost always present. A problem complicating mitral valvulotomy is embolism from atrial thrombi. Temporary compression of the innominate and common carotid arteries during surgery is recommended in prevention. Hemiplegia, due to cerebral embolism from a myocardial mural thrombus, may be the first clinical sign of an otherwise silent coronary artery occlusion. The middle cerebral arteries, particularly the left, are often blocked by large embolic masses. The prognosis for recovery after major cerebral embolism in rheumatic heart disease is guarded.6

Other Types of Cerebral Embolism. Fragmentation of clots deposited on the interior of the carotid sinus was recognized as a cause of cerebral embolism by Chiari in 1905. Air embolism has occurred frequently in patients
undergoing neurosurgical procedures in the sitting position. Fat embolism not uncommonly accompanies severe head injury, especially when an automobile accident has resulted in multiple fractures and soft tissue contusions, and can account for decerebrate rigidity and hyperpyrexia. The vertebral venous plexus, readily influenced in direction of flow by sudden changes in intracavitary pressure, is a cardiac “by-pass” allowing metastasis of suppuration or malignancy from the lung to the brain.

**Cerebral Hemorrhage**

The frequency of hemorrhage into the brain as compared with the infrequency of apoplectic hemorrhage into other viscera remains unexplained. Anatomic peculiarities of the intracranial circulation are significant. The great importance of the internal elastic lamella in the walls of the cerebral arteries as contrasted with the lesser relative importance of this membrane in arteries elsewhere is undoubtedly a factor, as is the poverty of intra cranial vascular adventitia.

The implication by Charcot and Bouchard (1868) of miliary aneurysms on small intrinsic arteries as a cause of cerebral hemorrhage is substantiated by modern embryologic and anatomic research which has disclosed the frequency of developmental aberrance of the circle of Willis and branches, particularly in the critical zone of the basal ganglia and internal capsule. Zimmermann has emphasized the occurrence of dissecting aneurysms due to intramural rupture of a vasa vasorum in a sclerosed artery, which then perforates causing intracerebral hemorrhage. The hitherto unsuspected frequency of minute arteriovenous malformations in the basal forebrain circulation is a newly recognized cause of intracerebral hemorrhage in the young. The theory of Globus and Strauss, based upon a previous opinion of Rouxhous (1844) that perivascular encephalomalia surrounds an artery which is, therefore, more easily ruptured by increased intravascular tension, tends to be supported by experimental investigations.

Cerebral hemorrhage occurs almost exclusively in the hypertensive patient, barring the occasional intracerebral rupture of a large arterial aneurysm or small arteriovenous malformation in the normotensive individual. The most frequent site is the internal capsule. Sclerosing changes, accompanying but not necessarily due to the progress of hypertensive disease, destroy the internal elastic lamella of a small, intrinsic artery, perhaps congenitally weak at a point of bifurcation or of aneurysmal anomaly. When a sudden increase of already heightened intravascular tension occurs as during an emotional crisis, a dissecting aneurysm forms in the arteriosclerotic wall or a direct mural break ensues. Focal necrotic changes due to angitis may be contributory. As arterial blood escapes into the surrounding brain, it tears a path along tissue planes in an anteroposterior direction. Veins are torn, contributing venous to arterial hemorrhage.

These events progress with lightning-like rapidity. The involved part of the brain swells rapidly, forcing the medial inferior aspect of the ipsilateral temporal lobe (hippocampal area) down through the incisura of the tentorium, compressing the midbrain against the opposite tentorial ridge. Secondary hemorrhages result in the midbrain and pons because of acute tamponade of the basal vein of Rosenthal and allied small vessels. Consequent mesencephalic damage accounts for the familiar pattern of decerebrate rigidity prior to death. Transection of the midbrain or perforation of hemorrhage into the ventricular system are the immediate causes of exitus. Hematemesis or gastromalacia are terminal events. Cerebral hemorrhage is never as immediately fatal as is lethal subarachnoid hemorrhage.

**Subarachnoid Hemorrhage: Intracranial Aneurysm**

The distinction between “cerebral hemorrhage” and “subarachnoid hemorrhage” is important clinically. “Cerebral hemorrhage” implies rupture of an artery not essentially aneurysmal in character directly into the substance of the brain, in a patient who is afflicted with hypertension and/or arteriosclerosis. “Subarachnoid hemorrhage” is the term applied generally to perforation of a congenital arterial aneurysm of the circle of Willis pri-
arily into the subarachnoid cisterns surrounding the base of the brain. Blood from a direct intracerebral hemorrhage can reach the ventricular or subarachnoid spaces almost as rapidly as that from hemorrhage into the basal cisterns. The initial degree of interior brain damage, revealed by hemiplegia or coma, may permit an etiologic distinction of the source of bleeding. To further confuse differential diagnosis, it is apparent statistically that patients, harboring congenital aneurysms of the circle of Willis, are subject to premature cerebral arteriosclerosis and hypertension and that an intracerebral clot frequently surrounds an aneurysmal sac that has ruptured. Moreover, aneurysms may rupture into the brains of the elderly, just as in the middle-aged or juvenile patients.

Therefore, the only logical approach to differential diagnosis of the intracranial hemorrhagic disorders is one based upon strict adherence to all etiologic and pathogenetic rules. The importance of such accuracy of diagnosis is practical therapeutically.

**Pathologic Considerations.** The researches of Padget, Forbus, Bremer and others emphasize the role of embryologic aberrancy or failure in the development of intracranial aneurysms. That the average time of rupture of aneurysms of the circle of Willis is in the mid-forties emphasizes the contributory effect of other disease processes. The destructive action of arteriosclerosis or of focal angiitis is immediately responsible for perforation of aneurysms.

Postmortem investigations of patients dying from subarachnoid hemorrhage have revealed: (1) The high incidence of multiple cerebral arterial aneurysms; (2) the frequency of associated vascular dysplasia (cerebral arteriovenous malformation, coarctation of the aorta, polycystic kidneys); (3) the premature development of cerebral arteriosclerosis; (4) a significant combination with cardiac disorders; (5) evidence of repeated bleeding episodes prior to death; (6) cerebral parenchymatous lesions in 50 per cent of fatal cases and (7) an almost invariably anomalous circle of Willis.37

**Clinical Observations.** It is remarkable how often massive subarachnoid hemorrhage in the elderly may not result in classical signs of meningeal irritation. Concerning medicolegal aspects of this disorder, a reply to a “Letter to the Editor”, in the *Journal of the American Medical Association*, Jan. 29, 1955, states: “It may be postulated that if a person who had an intracranial aneurysm were to perform heavy physical exercise and possibly strain severely . . . enough alteration in intracranial tension to affect the thinned-out portion of an aneurysm might occur; rupture in this way might be associated with such activities. However, an exact cause-and-effect relationship would be very difficult to establish.”

**Prognosis.** Subarachnoid hemorrhage accounts for 5 per cent of all cases of sudden death and is responsible for 25 per cent of fatalities due to disease of the nervous system. The mortality rate in first serious attacks varies from 30 to 50 per cent in different reported series and second significant ruptures are said to have a fatal incidence of 75 per cent. On the other hand, Hyland37 declares that patients surviving an initial episode of subarachnoid bleeding have an 80 per cent chance of living indefinitely thereafter without fear of recurrence. Discrepancy in such prognostic predictions necessitates further statistical research. Mount,31 collating the experience from many neurologic centers found that the mortality rate from subarachnoid hemorrhage was 48 per cent in patients treated medically and only 14 per cent in patients treated surgically, a strong argument for surgical intervention when possible.

**Arteriovenous Malformation**

The increasingly widespread use of angiography as a diagnostic technic has revealed a hitherto unsuspected frequency of arteriovenous malformation of the brain as an occasional cause of hydrocephalus in infancy, of stroke in childhood or adolescence and of epilepsy or of repeated minor or major subarachnoid hemorrhages at any age. Extensive studies have disclosed the prevalence in such patients of generalized angiomatosis, of which the Lindau-von Hippel disease is one type. Hemangiomatosis is transmitted as a mendelian
dominant gene, not sex-linked; it is one of few inherited neoplastic dyserythrias of man.\textsuperscript{20}

**Venous and Venous Sinus Disease**

Angiography has also disclosed that many cases of increased intracranial pressure or of obscure bleeding, particularly in the puerperium, are due to thrombosis or thrombophlebitis of the dural venous sinuses or of the cerebral veins. Stevens\textsuperscript{24} has pointed out the frequency with which cerebral venous occlusion causes puerperal hemiplegia, sometimes misdiagnosed as an eclamptic complication. He calls attention to the decreased blood clotting time in the last trimester of pregnancy and the increased incidence of thrombophlebitis elsewhere in the body at this time. Cerebral venograms have revealed extensive venous occlusions in such patients.\textsuperscript{21}

**Hypertensive Brain Disease**

Experimental malignant hypertension has been studied by Byrom.\textsuperscript{5} Cerebral attacks were precipitated in rats made hypertensive by the Goldblatt method when saline solution was substituted for drinking water. Pathologic examination revealed focal arterial necrosis, brain infarcts or hemorrhages in the majority of subjects. Cerebral water content was increased in encephalopathy but not in uncomplicated hypertension. Brain hydration was thought to be due to capillary leakage, secondary to the arterial spasm observed through skull windows. The point at which physiologic vasoconstriction as a response to heighted intravascular tension becomes uncontrolled focal spasm is said by Byrom to represent the dividing line between benign and malignant hypertension. Lowering of the blood pressure relieved intracranial angiospasm in his animals as it does in clinical patients, whereas cervical sympathectomy had no effect.

The concept of multiple “little strokes” as the explanation of chronic hypertensive cerebrovascular disease has been invoked by Hughes and co-workers.\textsuperscript{18} Whereas an automatic intrinsic mechanism of unknown type permits normal cerebral metabolism in uncomplicated hypertensive disease, despite a mean increase in cerebral vascular resistance of 75 per cent, the development of hypotension is not accompanied by persistence of adequate oxygen consumption, which decreases as the blood pressure falls. The necessity for caution in the induction of hypotension during surgery on the hypertensive patient is apparent.\textsuperscript{13}

**Cerebral Arteriosclerosis**

Extensive pathologic investigations of cerebral arteriosclerosis by Fisher\textsuperscript{41} reveal that: (1) cerebral arterial atheromatosis parallels that found elsewhere in the body; (2) atherosclerosis of the brain is a focal process and tends to occur where vessels enter the skull, loop, branch or bifurcate; (3) hypotensive vascular collapse, embolic phenomena or true thrombosis must also eventuate before cerebral arteriosclerosis can be responsible even in part for neurologic symptoms or signs; (4) collateral circulation may permit the occlusion of even large arteries without infarctive sequelae; (5) barring significant narrowing or thrombosis of one or both carotid arteries, arteriosclerosis per se is not a cause of senile dementia. Capillary fibrosis is found in 86 per cent of aged patients with normal mentality. Parkinsonism in old age cannot be explained as a result of arteriosclerosis alone.

“Cerebral Vascular Insufficiency.” Functional inadequacy of the intracranial circulation may account for transient neurologic episodes in the known or suspected presence of arterial disease. Hypotension or other unknown factors often are contributory. Arteriosclerotic insufficiency of circulation through the basilar artery is particularly common in the elderly patient. The numerous and tiny arterial derivatives supplying the all-important brain stem are easily deprived of blood, temporarily or permanently, with the familiar effects of “dizziness,” “fainting,” comatose attacks, transient or persistent tetraplegia or quadriplegia, “Menière’s syndrome,” diplopia or temporary blindness.

**Inflammatory Collagen Diseases**

Cerebral venous thrombophlebitis can develop in the young patient as a manifestation
of a rheumatic diathesis or as the result of transient bacteremia. The syndrome of preceding malaise, a sudden convulsive attack which is followed by fever, hemiplegia, aphasia or confusion is the characteristic clinical manifestation of thrombophlebitis of the brain. Spinal fluid examination reveals slightly increased pressure, excess of protein content and of cells. Venous rather than arterial involvement is suggested by the usually benign nature of the process.

Collagen vascular disease is accompanied by intracranial complications. One of the major causes of death from lupus erythematosus disseminatus is cerebral angiitis. Cerebral vascular involvement in serum disease and in supposedly benign temporal or cranial arteritis is not uncommon. Periarteritis nodosa involves the brain in 10 per cent of cases. In all these disorders small blood vessels are implicated.

Migraine

The familiar scintillating scotomata and homonymous hemianopsia often precede or accompany an attack of unilateral headache and are probably due to spasm of the ophthalmic or posterior cerebral arteries which is usually reversible. Permanent brain damage may result, however, from migraine. In one of my patients, cerebral infarction was found at operation to be the effect of vasospasm during a severe migrainous seizure. Wolff and associates have observed spontaneous hematomas and effusions in the temporal muscles of certain migraine patients during episodes of headache. The frequency of abnormal electroencephalograms in this condition may be, in part, the aftermath of ischemic cerebral changes.

Diagnostic Studies

Spinal Puncture. The problem of whether or not blood withdrawn with spinal fluid via lumbar puncture is of previous origin or is due to trauma during spinal tap has recently been resolved by Matthews and Frommeyer. These investigators, studying blood in cerebrospinal fluid in vivo and in vitro have concluded that crenation of red blood cells occurs immediately in either media and is of no clinical assistance. Only the presence of "ghost cells" (envelopes of erythrocytes) and xanthochromia definitely prove the existence of subarachnoid or intraventricular hemorrhage prior to spinal puncture.

Intracranial Air Studies. The "small encephalogram" of Monrad-Krohn is much better tolerated by the patient with cerebrovascular disease than is total spinal fluid replacement. Adequate roentgenographic visualization of the ventricular system is often possible when only 25 to 30 cc. of air are injected through the spinal route, the patient sitting upright. Local anesthesia is sufficient, as the procedure is not painful. It is important to inject 10 to 15 cc. of air before spinal fluid is withdrawn; gas is more likely to be introduced into the ventricles in this manner and dangerous intracranial herniations are avoided. Ventriculography has been superseded largely by angiographic examination of patients with cerebrovascular disorders.

Intracranial Angiography. Cerebral angiography is the neuroradiologic technic suited most ideally to the differential diagnosis of intracranial vascular disease, since the blood vessels of the brain are visualized directly only when injected with a radiopaque contrast medium. The carotid and vertebral arteries may be cannulated either after surgical exposure of the vessels or better and most usually by the percutaneous method. Serial x-ray films taken during the progress of injection reveal first intracranial arteries and then veins; by rapid and multiple exposures, any phase of the cerebral vascular cycle may be demonstrated. Arterial aneurysms and arteriovenous malformations fill and are revealed in size, location and origin; displacement of arteries and veins from their normal positions denote intracranial mass lesions such as hematomas or areas of infarction. Poverty and angulation of arteries confirm an arteriosclerotic condition and failure of visualization of major vessels beyond points of occlusion proves the existence of intravascular thrombosis or embolism.

Many more carotid angiograms are performed than injections of the vertebral artery,
since the majority of accessible and treatable vascular lesions of the brain lie above the tentorium. Vertebral angiography is a more difficult and hazardous technic than is carotid angiography and the revelation of pathologic alteration of the blood vessels of the brain stem is often only of academic interest. Although principal diagnostic emphasis has been placed upon arteriography of the brain, an increasing number of reports concerning the value of venography is appearing in literature. One procedure described accomplishes filling of cerebral venous sinuses and veins via diploetic connections through the bone marrow of the skull. Injection of contrast medium into the exposed superior longitudinal sinus is the only method of proof of occlusion of this important vessel.

Thorotrast, a radioactive substance excellently radiopaque, has been abandoned for use in percutaneous cerebral angiography, since leakage of material from the site of injection results in a painful, disabling and even lethal granulomatosus cicatrix in the neck. Diodrast is the contrast medium universally employed at present; a 35 per cent concentration is the limit of tolerance by the cerebral vessels and even this strength is productive of an unpredictable degree of intracranial angiospasm. Iodine sensitivity should be ruled out beforehand and papaverine is administered intravenously, just before injection of diodrast, to prevent the arterial spasm which can and has caused hemiplegia or another untoward reaction.

Intracranial angiography is a procedure not to be undertaken lightly. It is indicated when possible surgery after subarachnoid hemorrhage requires a precise diagnosis, when the effects of arterial occlusion are otherwise indistinguishable from those of intracranial tumor and for exact localization of expansile intracranial lesions. Vascular contrast studies are precluded when differential distinction is only academic, when the patient is extremely old, is in an advanced state of arteriosclerosis or hypertension, in heart failure, uremia or has obviously had a recent severe infarctive stroke.

Electroencephalography. Although far from infallible, the electroencephalogram is of value in the differential diagnosis and management of vascular disorders of the brain and is an examination which is painless, convenient and may be readily repeated. Studying patients with hypertensive disease, Roberts and Walker2 found that the electroencephalogram was abnormal even without evidence of brain damage in over 50 per cent of cases. When neurologic signs other than epilepsy were present, the electroencephalograph test was abnormal in at least 80 per cent. When convulsive disorders resulted, all patients manifested significant electroencephalographic changes. Epilepsy is not a common aftermath of cerebrovascular accident.

Residual electroencephalographic abnormalities following cerebral infarction are common in the ipsilateral temporal area. Relatively constant production of irregular slow waves tends to distinguish infarction from infiltrative malignant neoplasm which usually produces high voltage delta activity in bursts. Minor irregular and slow spike activity from the anterior temporal leads is a frequent finding in elderly patients and is probably the result of small infarctions in the tip of the temporal lobe, the hippocampal portion of which is supplied by an end-artery.

Therapy

Cerebral Vasospasm. If one assumes that intracranial arteriospasm is responsible for certain cerebrovascular accidents or their complications and that sympathetic nervous influences may perpetrate deleterious angiospastic effects, it seems logical to suppose that stellate nerve block, with temporary paralysis of the intracranial autonomic sympathetic inflow would be of value in such cases. There is no subject of greater neurologic debate at present. At one extreme are enthusiastic adherents of the procedure who claim benefit in all types of nonhemorrhagic stroke after stellate block. At the other extreme are those who deny that intracranial arteriospasm ever occurs, who negate the possible operation of sympathetic innervation in regulation of cerebral blood flow under even emergency conditions and who even claim that the patient with an
infarctive brain lesion is made worse by the procedure.32

Stellate block can do no more than relieve vasospasm of major arteries or of small vessels on the periphery of a small infarctive lesion of the brain. This arterial spasm may be of unknown cause or be secondary to anoxia or endovascular stretch. Since collateral channels may be enhanced by vasodilation and since clinical experience indicates that temporarily anoxic neurones in border zones of ischemia are capable of revival, there is no reason to withhold stellate block from the patient with a recent nonhemorrhagic stroke. The fact that total cerebral blood flow is not increased by stellate block does not eliminate the possibility of improvement of local vascular irrigation. A safe but effective technic should be employed; the procedure is not to be relied upon to the exclusion of other therapeutic methods. Dramatic results are achieved in 3 to 5 per cent of patients, a moderate but definite response may be predicted in an additional 30 per cent and no effect is seen in 60 per cent or more (Naffziger and Adams).33

Cerebral Hemorrhage: A small but important group of patients are potential candidates for intracranial surgery after spontaneous cerebral hemorrhage. The clinical syndrome in these cases is: (1) initial verified brain hemorrhage with coma or stupor, (2) restoration of consciousness in the presence of lateralizing neurologic signs and (3) subsequent loss of alert behavior attended by other manifestations of increasing intracranial pressure. Lateral shift of the calcified pineal gland in plain x-ray films of the skull may be taken as adequate confirmatory diagnosis of intracerebral clot. Ventriculographic compression, in air-studies or displacement of the major cerebral arteries seen in angiograms, are better neuroradiologic localizing procedures. The results of surgery in such patients are good with respect to the episode; further complications of hypertensive cardiovascular disease usually appear subsequently. Operative intervention has nothing to offer the usual intraventricular flooding “hypertensive blow-out.”

Cerebral Embolism: Since most instances of cerebral embolism originate from intravascular clots elsewhere, especially in the chambers or on the valves of the heart, it is apparent that the principal measure of prevention of initial or recurrent cerebral embolization is anticoagulant therapy.39 The variability of blood coagulation in other types of brain stroke precludes routine use of such treatment except in the particular instances of suspected incipient thrombosis of the internal carotid or basilar arteries, extension of clotting from an arterial aneurysm treated by ligation of the main carotid vessel or migratory thrombophlebitis with intracranial involvement. The usually normal clotting time after cerebral infarction with or without thrombosis eliminates anticoagulant treatment as of any value in this condition and adds the possible danger of conversion of an anemic lesion into a hemorrhagic one.

Stellate block is the procedure of choice in initial therapy of the patient with sudden cerebral embolism, before anticoagulant drugs are administered. Persistent peripheral angiospasm has been proved to follow major cerebral arterial embolic occlusion. The effects of cerebral fat embolism may be counteracted by intravenous injection of calcium gluconate. During suspected air embolism the patient should be turned upon his left side immediately.

Cerebral Thrombosis, Infarction: Stellate block may be tried with possible benefit if angiospasm on the periphery of the lesion is significant. Polarographic study of the brain after experimental arterial occlusive lesions discloses a minimization of ischemia when pure oxygen is breathed.30 The importance of maintenance of a normal systemic blood pressure should be emphasized. Recent clinical experience suggests that the addition of 5 to 7 per cent carbon dioxide to inhaled oxygen may be an aid to the development of collateral cerebral circulation.

Cortisone or hydrocortisone aid recovery from hemiplegia after cerebral infarction. Nicotinic acid (300 mg. three times daily) seems to be particularly beneficial following occlusion of the posterior inferior cerebellar artery.

Subarachnoid Hemorrhage: Intracranial
Aneurysm: Despite favorable reports of selected cases of ruptured intracranial aneurysm cured by intracranial clipping, the current mortality statistics in all patients with subarachnoid hemorrhage thus treated are cautionary. Proximal ligation of the cervical carotid artery is the procedure of choice in the control of aneurysms arising from the terminal intracranial carotid artery or its proximal branches, provided that preoperative occlusion demonstrates the ability of the brain to survive when inflow from one carotid has been sacrificed. Peripheral aneurysmal lesions may be dealt with directly as surgical judgment dictates. Since cervical carotid ligation reduces pressure in intracranial derivative vessels of small size almost as much as does clipping of the parent branch vessel, as to the logical method of approach is difficult.

One knows that an aneurysm obliterated under direct vision is cured; one assumes that reduction of arterial pressure-head by cervical carotid ligation causes local thrombosis of the aneurysm. Long-term follow-up in reported series indicates that the latter event does occur; surgical mortality statistics favor cervical ligation rather than craniotomy. Two patients upon whom I operated recently had exactly similar aneurysms of the Sylvian middle cerebral artery revealed by angiography. One was treated by ligation of the carotid in the neck, the other by direct intracranial clipping. Both are doing well; the patient who underwent craniotomy has a spastic arm which he did not have prior to surgery. His aneurysm is definitely cured. The other patient is only assumed to be cured but is completely free of neurologic disability.

Arteriovenous Malformations: Surgical treatment is becoming more effective as operative technics are perfected and are assisted by planned hypotension or hypothermia. Direct approach to the lesion when possible is advocated by most neurosurgeons. The opinion has been expressed that carotid ligation is not only valueless but may be dangerous. I treated a patient with a large arteriovenous malformation of the middle cerebral artery and vein of Trolard by ligation of the common carotid artery. He had been operated upon previously (craniotomy) some years before, and tense brain was bulging through a large cranial defect. Diplopia was extreme and the patient was in coma. Intended excision of the lesion after preliminary arterial ligation was abandoned when cardiac arrest occurred. Nonetheless, the decompression became soft, double vision disappeared; the patient is now fully employed.

Several more such patients are apparently controlled after carotid ligation ipsilaterally with large arteriovenous anomalies demonstrated to be fed preferentially from one carotid artery. It is evident that the disease is not eradicated and it is realized that sizeable intracranial vascular malformations are often supplied by more than one major artery. However, it is important to note that a symptomatic response may be obtained by an indirect surgical approach when actual removal of the abnormal blood vessels might paralyze, otherwise cripple permanently or kill. Epilepsy, often symptomatic of these lesions, is not eliminated by surgery of any kind.

Intracranial Thrombophlebitis, Venous Thrombosis. The use of anticoagulant therapy is ideally suited to this type of cerebrovascular disease. Antibiotic drugs are also indicated in large dosage and for many months, if the inflammatory features of the disorder are thought to be bacterial in origin. By such treatment, patients suffering from cavernous sinus thrombosis, formerly inevitably fatal, are now being saved. Therapy must be prolonged and may require surgical assistance, such as drainage of subdural hygroma.

Hypertensive Brain Disease. In the management of hypertensive encephalopathy, lowering the elevated blood pressure usually proves adequate to clear the sensorium, stop seizures and release vasoconstriction. Careful intravenous “titration” with various ganglion blocking agents is advised. Magnesium sulfate is used in the control of eclamptic convulsions. Antiepileptic drugs should be employed in the combined presence of chronic hypertensive brain disease, an abnormal electroencephalogram and paroxysmal neurologic symptoms.

Cerebral Arteriosclerosis. Alvarez advises the old method of medicinal therapy, intravenous
and oral iodides, although he is not very enthusiastic. Since there is no real proof that food causes arteriosclerosis, decision concerning the advantage of a low fat diet has not been reached. The vasodilating effect of histamine administered cautiously often helps to overcome the effects of “little strokes.” Sustained anticoagulant therapy has been suggested to prevent thrombosis when insufficiency of the basilar artery is suspected. Oral Metrazol is recommended for improvement in mood, orientation, industry and cooperation in patients with severe cerebral arteriosclerotic changes.31

General Management of the Patient. Contrary to previous misconception, physiologic saline solution given intravenously in the usual amount does not increase intracranial pressure. Intravenous glucose in water does result in rise of intracranial tension owing to blood hydration after the liver extracts sugar. With reference to intracranial pressure alone, the ideal parenteral solution is 2 to 5 per cent glucose in 0.42 per cent saline, this combination causes little disturbance of cerebrospinal fluid pressure and does not predispose to edema formation.2 On the other hand, if hypnoveratremia develops, saline solutions are to be withheld until serum sodium values return to normal.

Much has properly been made of the beneficial effect of physiotherapy in helping to restore the hemiplegic patient to normal, to a working level or simply to a stage of self-care. Even simple home exercises may have almost as much effect as the more elaborate group programs in departments of physical medicine, although the latter are ideal. Learning on both the parietal and nonparietal sides of the body occurs chiefly in the first two months after brain injury.35

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Recent Advances in the Investigation and Management of Cerebrovascular Disease
JAMES PETER MURPHY

Circulation. 1956;13:281-293
doi: 10.1161/01.CIR.13.2.281

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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