BASIC CONCEPTS OF CEREBRAL FLOW

Advancing technology has brought dramatic change to neurovascular surgery. Diagnostic methods now reveal detailed information never before available. Surgical techniques make procedures unheard of a decade ago readily applicable. The most dramatic changes, however, are conceptual; our ideas are changing. The clinical designations stroke and transient ischemic attack will probably be generally replaced by the more precise terms infarction and regional ischemia with specifications of location and qualification. Attention is being directed not only to the precise gross and microscopic pathology of the carotid bifurcation, but also to the circulation of the brain as a whole. This new terminology reflects a new precision in information. In many respects, these changes are reminiscent of those that occurred in cardiology and cardiac surgery more than a decade ago. "Myocardial infarction" has replaced "heart attack" just as "brain infarction" is now replacing "stroke."

The ischemic insult produces a three-dimensional lesion. The precise location, the structural composition, and the surrounding zones of ischemia constitute a spatial moiety that can be projected into the gross architecture of the brain. The position of such lesions often indicates the pathological mechanism, the clinical hazard, and the arterial branches involved. Angiography is necessary to identify precisely the blood supply to these branches. This is especially true of the posterior circulation, where the vascular tree is highly variable.

The spatial resolution attainable with the new generation of instruments, e.g., computed tomography (CT) and nuclear magnetic resonance (NMR) scanners, permits the identification of structural lesions and the quantitation of ischemia in the posterior fossa in a manner not previously possible. The advances in microvascular and vertebral artery surgery rest on such precise anatomical and hemodynamic data.

Access to the posterior fossa constitutes entry into the new world of sensation and perception. The sense organs, the cranial nerves, and the brain that integrates these components are also seats of new problems. First, sense-organ dysfunction must be distinguished from brain ischemia. Second, each medical specialty dealing with these problems has its own instrumentation, its own language, and its own perspective. Finally, the common language of brain hemodynamics and brain flow has not yet come into general usage.

There is increasing awareness of brain hemodynamics—the relationship of one vascular bed to another, of vessel flow in the neck to brain perfusion, and of system flow to brain function. The dynamic nature of blood flow to the brain and its alteration by mechanical and physiological factors make testing under static conditions or at only one site, e.g., the carotid bifurcation, incomplete. The progressive incorporation of stress into the neurovascular evaluation parallels the practices well established in cardiac diagnosis.

Current instrumentation has brought not only new kinds of information and new modes
of therapy but also confusion and turmoil with regard to objectives and the delivery of services. The role models of the specialties which worked a decade ago will no longer suffice. A new clinical algorithm is required to integrate diagnostic information with clinical application to yield maximum patient benefit in an environment that is increasingly cost-conscious and critical. The system approach to brain ischemia and blood flow attempts to integrate the multiple factors involved which are of clinical significance into a practical working theory. Moreover, this approach functions at different levels of expertise from the basic level, where the principles are established, to the advanced level, where technical detail is used and sophisticated judgment made.

**Critical Arterial Stenosis**

The existence of pressure gradient within an artery is usually considered evidence of significant arterial obstruction (Tindall et al., 1962; Wilkinson et al., 1964; Jawad et al., 1977). From this postulate evolved the concept of critical arterial stenosis. It is false that only atherosclerotic disease can produce significant obstructions, and that only the carotid bifurcation should be studied, that the determination of significance can exclude the intracranial vascular bed, or that the clinical decision can be based solely upon the angiogram.

Cardiac output, blood viscosity, the status of the arterial "runoff," the collateral capacity, the size of the vascular bed (Jawad et al., 1977), and the volume of blood flow may markedly modify the pressure gradient (Rodbard and Kikuchi, 1976). If the flow is low, severe obstruction may not produce a pressure gradient at all, but high flow will create a marked gradient with the same perfusion pressure (Young et al., 1977). Even a 50 percent arterial stenosis may become "critical" during low-pressure perfusion as encountered during cardiopulmonary bypass. Clinically, cardiac and vascular stress studies utilize high-blood-flow states to determine the significance of arterial obstruction. The hemodynamic consequences of obstruction, the functional disability, and the threat to life and to tissue are significant, and they should influence the interpretation of the angiogram.

The concept of critical arterial stenosis as it is applied to the highly collateralized cerebral vascular system falls short of the mark because it does not address critical issues: the impact on brain perfusion of total arterial occlusion (Nornes, 1973; Carney and Anderson, 1978b; Eikelboom, 1981; Prosenz et al., 1974) or of dynamic obstructions. Similarly, it cannot be applied to the obstruction of short length (Eikelboom et al., 1983), to the vertebral artery, or to vulnerable vascular beds. The angiogram of cervical arteries cannot predict the level of brain perfusion. Therefore, the significance of an obstruction of the carotid or vertebral artery should be determined by its impact on arterial flow (resting and reserve), brain perfusion, brain function, and brain structure.

When flow in both internal carotid arteries is studied simultaneously during the graded closure of one artery, the importance of the competitive increase of flow in the contralateral internal carotid artery and vertebral system immediately becomes apparent (Nornes, 1973; Nornes and Wikeby, 1977), the same way as the clamping of one aortocoronary graft will markedly affect the flow characteristics in the other (Reneman and Spencer, 1975).

**Criteria of Significant Arterial Obstruction**

An arterial obstruction is regarded as being significant when it compromises either brain perfusion, function, or structure. The obstruction may be static or dynamic. The dynamic obstruction induced by rotation or hyperextension of the head is characterized by its short length, duration, fluctuating severity, and fleeting pressure gradients. Acute catastrophic symptoms can be relieved by having the patient lie supine with the head in neutral position. Collateral channels do not develop in such situations.

Sites of predilection for trauma to the carotid artery are at the base of the skull and the atlas (Batzdorf et al., 1979; Crissey and Bernstein, 1974; Sullivan et al., 1973). Although entrapment usually occurs around peritonsillar inflammatory scars and lymph nodes (Wernick et al., 1974), it may also be caused by anomalous muscle fibers (McMurtry and Yahr, 1966) or by the hypoglossal nerve (Mauersberger, 1974; Scotti et al., 1978) [See also Chapter 14]. Compression of the vertebral artery may occur at the base of the skull (Bell, 1969), but is seen more often at the level of the second cervical vertebra. Compression by osteophytes may also occur within the cervical spine. Sympathetic fibers may also mechanically interfere with vertebral flow, usually at the level of the sixth cervical vertebra.
Head motion may also cause arterial occlusion by compression or stretching and can affect both the carotid and the vertebral arteries in adults and children. Under normal conditions, the circle of Willis compensates for such vascular occlusion which may occur at the skull base. This has been demonstrated by postmortem angiography which revealed occlusion after rotation (Brown and Tatlow, 1963) and after head hyperextension. This phenomenon is also well documented in vivo (Bauer, 1984b; Bell, 1969; Hope et al, 1983). It has also been shown that sensitivity to head position is exaggerated in the presence of carotid occlusion (Bougousslavsky and Regli, 1983).

THE SYSTEM APPROACH TO BRAIN PERFUSION

Our fundamental concern in studying the circulation to the brain involves not only the blood flow through arteries and the brain tissues but also all those factors affecting the flow. The concepts of McDonald and Brain are extended to include the brain and the cardiovascular system. The objective of this approach is to provide a guide to the diagnosis and treatment of patients that will be most useful to the astute clinician.

Life is dynamic and full of stress. Walking erect, turning the head, and trauma are stresses commonly encountered. But there is a tendency to forget the stress owing to surgery and to disease. Cardiopulmonary bypass, anesthesia, blood loss, induced hypotension, and clamping of the carotid artery constitute formidable stress. The loss of cerebral "autoregulation" may make even the upright position extremely hazardous. Brain-stem ischemia does cause respiratory arrest and myocardial infarction does decompense brain flow (see Figure 5–1).

Forebrain-Hindbrain Division

Just as in the case of the heart, brain anatomy is constant but the demand and supply of blood is variable. Although according to traditional anatomy the brain is divided into the supratentorial cerebral hemispheres and the infratentorial brain stem and cerebellum, according to vascular territory it is divided into the anterior and posterior circulation. The commonly used clinical designations "cerebral insufficiency" and "vertebral-basilar insufficiency" are not only confusing and inconsistent, but also impractical because symptoms are primarily related to the vascular tree. According to the latter, forebrain includes the territories of the anterior and middle cerebral arteries, and the hindbrain includes the territories of the posterior cerebral arteries and the branches of the vertebral and basilar arteries. Specifically, the frontal and parietal lobes constitute the forebrain, whereas the occipital and temporal lobes, the cerebellum, the pons, and the brain stem constitute the hindbrain.

Identifying regional ischemia establishes the organic nature of the problem. The localization suggests the pathological mechanism and the arteries involved, but it cannot by itself indicate either the side of arterial obstruction, the mechanism of flow reduction, or the most suitable method of revascularization. In addition, decision-making requires precise knowledge of the specific vascular tree of the head and neck defined by angiography, the hemodynamics involved (Carney et al, 1981), and the functional disability of the patient.

Kramer (1912) repeated Willis's classic experiments by injecting methylene blue into the carotid and vertebral arteries in 50 dogs and three monkeys, killing the animals and observing the distribution of dye within the brain. "The results," Kramer reported, "were surprisingly constant." Specifically, injection of the carotid artery, when all other vessels were unobstructed, resulted in staining of the brain in the distribution of anterior and mid-
dle cerebral arteries, the anterior choroidal, and the posterior communicating artery. In the dog, only the posterior aspect of the occipital lobe lying on the tentorium remained unstained, but in the monkey, the posterior two thirds of the occipital lobes were stained.

Beside anatomical appearance and blood supply, the brain can also be divided according to the senses, because sensations, perceptions, and sense-organ functions are not vested in a single anatomical site. Small lesions of the brain can produce disability from apnea, sleep disorders, disequilibrium, deafness, and blindness. Vision involves the eye as well as multiple areas of the brain, each with a different blood supply. Up to this time, distinguishing brain ischemia from dysfunction of the end-organ has depended either upon end-organ testing or on demonstrating structural lesions in the cerebral hemisphere. The loss of balance, for example, may reflect either dysfunction of the normally perfused end-organ (the vestibular apparatus), dysfunction of the ischemic end-organ, regional brain-stem ischemia, or generalized brain ischemia.

Many medical specialties touch some aspect of a sense organ, cranial nerve, or the brain stem. Each has its own customs, its own terminology, and its own perception. The technical languages of the neurosciences separate one specialty from another. Some specialists quantify disability in traditional terms of end-organ dysfunction (American Medical Association, 1977) and not in terms of brain ischemia. The measurement of brain perfusion and vessel flow now introduces a common language of hemodynamics, which is necessary to integrate these disciplines.

**Normal Systems**

McDonald and Potter (1951), following in Kramer's footsteps, found a similar and distinct pattern of blood-flow distribution to the brain in unobstructed vessels. In this regard, McDonald postulated that the definition for the circle of Willis must be extended to include the vertebral and basilar arteries and the four intracranial anastomotic sites: the two posterior communicating arteries, the anterior communicating artery, and the basilar artery. When flow is balanced, i.e., when the pressures are balanced, the point of no flow is termed the *dead point*. The dead point is, in fact, a floating point that rapidly moves with changing conditions to the point of lowest pressure.

Furthermore, McDonald demonstrated the division of flow within the basilar artery: blood from one vertebral artery will perfuse the ipsilateral side of the brain stem through the segmental branches of the basilar artery. Obstruction of one vertebral artery increases the flow from the other side and moves the dead point toward the side of obstruction. Increasing the flow and pressure in one vertebral artery moves the dead point in the direction of low flow.

**Abnormal Systems**

Like carotid compression, pressure injections during angiography disturb normal flow relationships. Yet both maneuvers are of clinical importance. Routine angiographic injections that visualize vascular patterns beyond those usually encountered should raise the question of reduced blood pressure or arterial obstruction in that particular area. On the other hand, inadequate visualization may be due to the inability of the pressure injection to overwhelm the high intravascular pressure.

In high-flow, low-resistance systems, as in arteriovenous malformations, the principle is the same. The dead point moves in the direction of the lowest pressure, i.e., the venous outflow tract. Despite high flow in the arteries, ischemia may result because an adequate tissue perfusion pressure cannot be maintained. In such a situation, the most severe ischemia may be either local or at a remote site.

Both Kramer and McDonald observed that the customary dye distribution was altered in the presence of multiple vessel occlusion. Ordinarily, because the pressure within the vascular bed of an occluded internal carotid artery is low, blood will flow to it from the higher-pressure carotid on the contralateral side through the anterior communicating artery. The dead point moves to the side of the obstruction, the side of lower pressure. Should this fail to occur, then either the remaining carotid is obstructed or significant flow is coming from the vertebral artery. Whenever a routine carotid injection fills the basilar artery, the pressure within the basilar artery is considered pathologically low and this merits explanation (see Figure 5-2).

**Divisions and Levels**

Brain (1957) recommended in the study of the nature of cerebral blood flow that we ac-
Figure 5-2. The circle of Willis and the vertebral arteries. The "dead" points (marked by bars) are the sites at which pressure is balanced between supplying arteries and where there is no flow. When the flow is balanced between the vertebral arteries, the dead point divides the stream within the basilar artery longitudinally. Obstruction of one artery causes shifting of the dead point in the direction of low pressure until balance is achieved.

cept McDonald and Potter's hypothesis that the basilar artery and the vertebral artery constitute a critical part of the circle of Willis. He argued that, because the circle of Willis is present in all species of mammals, its purpose is surely to guarantee blood flow to the brain when one or the other artery is blocked by the posture of the blood.

Furthermore, he pointed out that the posterior cerebral arteries, which normally arise from the vertebral system and supply one or both of the occipital and temporal lobes, must be considered distinct from the cerebral hemisphere supplied by the carotid artery. Brain concluded that collateral systems exist on three levels: (1) the level of supply, proximal to the circle of Willis, (2) the circle of Willis per se, and (3) the level of the vascular bed, distal to the circle of Willis, where the territories of end-arteries meet.

### Competitive Flow

Hardesty in 1960 demonstrated the reciprocal blood-flow relationship that exists between the two carotid arteries. When one is compromised, blood flow is increased in the contralateral vessel to maintain constant brain blood flow. Nornes (1973) showed that this relationship is not reciprocal but competitive and extends also to the vertebral artery. Toole and McGraw (1975) concluded that steal syndromes in reality constitute pressure-flow relationships between vascular trees, that "in some instances, the development of ischemic symptoms in the donor distribution led to false localization of the disease." Symptoms are the result of brain ischemia, the site of which may be remote from the site of arterial pathology. Furthermore, intrinsic brain pathology—tumors and arteriovenous malformations—may drastically alter the distribution of blood flow. Ischemic lesions in one hemisphere, e.g., cerebral infarction, may also cause ischemia in the contralateral hemisphere.

### Isotope Techniques

The vascular bed perfused by the carotid artery in living human beings may be delineated by continually infusing Krypton 81m directly into the vessel and scanning the head with a gamma camera. Krypton 81m has a short half-life of 13 seconds and will never reach equilibrium within the brain because of its rapid decay. Its distribution reflects the new arrival of tracer, therefore regional perfusion from the vessel injected. By 1980, tomographic assessment with a rotating gamma camera permitted higher resolution of blood-flow distribution, delineation of localized areas of reduced or increased perfusion, and the definition of collateral pathways.

Taki and co-workers (1984) studied the vertebral artery by the Krypton 81m method. Four basic perfusion patterns emerged: ipsilateral, contralateral, bilateral, and mosaic. These observations are consistent with the varied anatomy of the region and with the clinical presentations of patients. This technique combined with balloon occlusion of vessels may greatly aid our further understanding of the dynamics of hindbrain perfusion.

Scanning by position emission tomography (PET) has also supported this hemodynamic
approach to blood flow. PET data have shown that infarction in one site can alter the perfusion pattern in a nearby or remote site. Ischemia resulting from unilateral cerebral infarction has been shown to occur in both the contralateral hemisphere and the hindbrain.

From the foregoing, one may conclude that it is of practical importance to grasp the implications of the hemodynamic approach to the circulation of the brain and also to recognize the disadvantages and advantages of such an approach. For change, even from worse to better, is not made without inconvenience. It is not convenient to change from carotid stenosis and the angiogram to hemodynamics and perfusion. Observation and analysis are required. The carotid bifurcation becomes one tree in the forest. Brain perfusion, precise anatomy, and system hemodynamics must be understood, and new skills must be developed. Such endeavors alter our ways and our identity.

**PERFUSION AND THRESHOLDS OF FUNCTION**

In general, the function of the brain is directly related to perfusion. Progressive reduction of blood supply results in progressive deterioration, first of function and then of structure. Perfusion may decrease by two thirds of the normal before electrical dysfunction is noted. Metabolism is grossly disturbed when perfusion falls below 20 percent of the normal levels and cell death occurs shortly thereafter. What is notable is the wide range between optimal perfusion and cell death and the relatively narrow range between hypoperfusion and cell malfunction. The variables which may modify the course of these events include the metabolic activity of the cell, the particular function under consideration, the duration and type of stress, and the age of the individual. Both reduced perfusion and excessive perfusion are abnormal but they become pathological only if they compromise brain function, structure, growth or development (see Figure 5–3).

**Transient Ischemic Attacks and Brain Infarction**

The terms stroke and transient ischemic attacks (TIAs) in neurology are analogous to cardiological definitions of “heart attacks” and “acute chest pain.” Precise information is replacing the latter terms with myocardial infarction and also supplies the location, such as “apex of the left ventricle” or “anteroseptal area.” The objective of TIA and stroke management is the preservation of brain function and rehabilitation, just as the objective of cardiac management is the preservation of left ventricular function and rehabilitation. Caplan (1984) succinctly states the case: “We cannot continue . . . the grouping of patients only by temporal description of their symptoms, an idea which has an unsatisfactory past and no future.”

In the past, the criteria for defining forebrain TIAs were generally agreed upon, though differences between observers were significant. Since the advent of the CT scan, the separation of focal ischemia from focal cerebral infarction with transient neurological findings has made conventional clinical diagnosis less certain. The distinction appears important, because TIA with brain infarction carries a worse prognosis. Moreover, patients may have a severe disturbance of the cerebral perfusion patterns for as long as six weeks without the occurrence of infarction. These recent developments raise the question of what exactly constitutes cerebral infarction?

**Selective Brain Cell Infarction**

In general, stroke implies a fixed and irreversible neurological deficit caused by infarction. There is, however, increasing recognition that neurological deficit may also be caused by hypoperfusion without infarction. A new type of brain lesion is now being recognized: ischemic insult to the brain under controlled hypotension. Ischemic hypoxia damages cells and structures in the order of decreasing metabolic activity. Gray matter is more vulnerable than white, and active cortical cells are damaged more easily and earlier than glial cells. The cortical cells of the occipital lobe are also more sensitive to insult than the Betz cells of the motor strip. This selective destruction of brain is more difficult to quantitate but is nonetheless increasingly important because function can be lost while gross structure is left intact (Lassen, 1982). CT, radioisotope, and NMR can now identify those ischemic lesions lacking the characteristics of infarction, thus making the analytical approach to treatment ever more relevant.
Acute Hindbrain Ischemia

Because of the difficulty in separating sense-organ dysfunction from brain-stem ischemia, there are really no defined criteria for the clinical diagnosis of hindbrain TIAs. There is also lack of agreement whether to include vertigo, visual disturbances, alterations of cognition, memory, etc. For this reason, hindbrain TIAs were excluded in the cooperative aspirin study (Bauer, 1984a). Although the value of CT scanning is limited within the posterior fossa because of the dense cortical bone, it can indeed measure focal brain-stem perfusion. On the other hand, NMR is unencumbered by bone and can identify small (2 to 5 mm) ischemic lesions in the brain-stem.

AUTOREGULATION

Autoregulation has been defined as the ability of the brain to maintain tissue perfusion at a relatively constant level, irrespective of changes in the circulation that may o

ing exercise or due to moderate ch

blood pressure. The loss of autoreg

to brain infarction, tumor, ischemia,

permits hypotension to cause profo-

ischemia and hypertension which

may result in hemorrhagic infarctic

The major difficulty in understan

regulation is that it does not relate i

ingful way to vascular anatomy, the distr

of the infarction, brain hemodynamics, or

arterial obstruction; thus, it is difficult to con

sider it in clinical decision-making. Some of

the specific situations where the pathology is

both hard to understand and difficult to han

dle are (1) the brain with abnormalities of the

circle of Willis that is vulnerable to infarction,

(2) the loss of autoregulation in a specific vas-

cular bed, and (3) the varying tolerance to ca-

rotid surgery. The explanation of these situa-

tions need not invoke a mystical mechanism

but should be based on pressure-flow relations-

ships, vascular configuration, and the local re-

sponse of the vascular bed.
Vulnerable Vascular Beds

Intracranial vascular patterns are associated with brain dysfunction, ischemia, and infarctions in a consistent fashion. The development of techniques for measuring brain perfusion and precisely localizing infarctions requires a working theory that provides an explanation of observed phenomena. This requires the integration of vascular patterns and vessel blood flow with regional perfusion and brain function. Vulnerability also varies with metabolic activity. The active gray matter, for example, is more vulnerable than white, cells of the occipital cortex are more sensitive than those of the motor strip, and the vestibular system is less protected than the auditory system.

The Watershed

The watershed is the interface of adjacent vascular beds. Cerebral vascular beds compose circulation to the brain just as segments join to form an orange. One of the watersheds is located within the forebrain between the anterior and middle cerebral arteries; another lies between forebrain and hindbrain, between the parietal and the occipital and temporal lobes (Torvik, 1984). Electroencephalographic abnormalities are common in temporal lobe ischemia, and some are considered diagnostic of ischemia (Maynard and Hughes, 1984). Decrease in blood flow to the watershed may be due to systemic hypotension (Adams et al., 1966; Torvik, 1984), hypertension, increased intracranial pressure (Overgaard and Tweed, 1983), or to multiple arterial stenoses. Reduced perfusion in the watershed areas in the presence of systemic hypotension is especially associated with a poor prognosis (Overgaard and Tweed, 1983).

Vascular beds, particularly vulnerable, include the collateral bed, the overextended vascular bed, the artery of small diameter or high resistance, the hypoplastic system, and the artery of modified resistance. Areas perfused by arteries of small diameter and great length are especially exposed to ischemic damage (Carney and Anderson, 1981b).

Brain Perfusion Versus Brachial Pressure

When the patient is in the supine position, the pressure in the brachial artery does not reflect blood pressure in the intracranial arteries as well as does the pressure of the ophthalmic artery (Gee, 1982; Borras et al., 1969). This discrepancy is the reason for using the ophthalmic artery pressure instead of the brachial blood pressure ratio to detect carotid obstruction. The upright or sitting position can also provoke intracranial arterial hypotension while the brachial blood pressure may remain normal (Carney et al., 1981; Caplan and Ser- gay, 1976). One should concentrate upon brain perfusion and dysfunction; undue reliance on the brachial blood pressure may be misleading.

The Circle and the Postcircle

The configuration of the circle of Willis is variable (Wollschlaeger and Wollschlaeger, 1974; Krayenbuhl and Yasargil, 1968). Its functional capacity is best determined after one of the supplying vessels becomes occluded and the response of flow within the remaining arteries can be observed. Because a competitive relationship exists between the arteries supplying the circle, it might be expected that occlusion of one would result in increased flow in the rest (Nornes, 1973; Nornes and Wikeby, 1977). Compared with the arteries supplying the circle, the end-arteries to the brain have not received the attention that they deserve. Embolism and hypoperfusion are common in this segment, with vasospasm, aneurysm, dissection, and atherosclerosis assuming lesser roles (Spetzler et al., 1983). The detection of disease at this level can be best done using conventional selective angiography rather than intravenous digital subtraction techniques.

The middle cerebral artery has been studied extensively (Corston et al., 1984), primarily because of the interest in extracranial-intracranial bypass. The major cause of middle cerebral artery stenosis is embolism (Corston et al., 1984) from the proximal carotid artery. Total occlusion of the middle cerebral artery has been found to resolve on second angiogram six weeks later in 44 percent of the patients. Demonstration of hypoperfusion, with a pressure gradient, has been found useful in predicting...
surgical outcome (Spetzler et al., 1983). The anatomical complications that occur after superficial temporal to middle cerebral artery bypass are comparable to those after distal coronary bypass (Heros, 1984, Aldridge and Trimble, 1971).

Posterior cerebral artery occlusion is most often caused by emboli from the vertebral system. The emboli may lodge at the bifurcation and initiate the “top of the basilar” syndrome or enter the posterior cerebral artery and compromise the circulation to the occipital lobe.

Vascular Reserve Versus Collateral Flow

In the study of the coronary circulation, maximal capacity or the coronary vascular reserve may be measured by the increment of flow above resting level after transient coronary artery occlusion, exercise, or dilating agents. If the stimulus produces maximal dilation, then the increase in flow will also be maximal (Hoffman, 1984). Mosher and associates (1964), who studied coronary autoregulation, concluded that the pressure-flow diagram was the best way to illustrate the coronary vascular reserve. This reserve capacity may also be measured by cardiac stress testing.

When referring to the circulation to the brain, collateral flow should be distinguished from vascular reserve. Whereas the former is defined as that which takes place in the secondary vascular channels indirectly supplying the circle of Willis and which slowly increases to meet demand, the definition of the latter is the flow in excess of resting flow in primary channels directly supplying the circle of Willis. This can rapidly increase to accommodate demand. When the vascular reserve is exhausted and the efficiency of the circle of Willis decreases by the loss of flow from primary vessels, secondary flow through collateral channels may increase, but the reserve capacity will not improve.

The vascular reserve of either carotid artery can be tested by temporarily occluding the contralateral carotid (Eikelboom, 1981, Tada et al., 1975). If the vascular reserve is adequate, the blood flow through the patent carotid will increase and the perfusion pressure will be maintained in the vascular beds of both carotid and both ophthalmic arteries. If, however, the vascular reserve of the contralateral carotid is inadequate, ischemia of the brain will develop in one or both vascular beds. In either case, release of the temporary occlusion will result in increased flow above resting levels owing to reflex hyperemia.

Hyperperfusion

Sundt (1983) states that the primary cause for neurological complications after endarterectomy is ipsilateral hyperperfusion. In agreement with this, Schroeder and associates (1984) described a case of a 55-year-old man with an occluded right carotid who was operated upon for left carotid stenosis. Because clamping of the left carotid resulted in flattening and slowing of the electroencephalogram, a shunt was inserted. Marked bilateral hyperperfusion immediately followed endarterectomy, reaching 200 percent of the preoperative resting value. The patient became confused and developed a headache; his systolic blood pressure increased to 200 mm Hg from a preoperative value of 110 mm Hg. Decrease of blood pressure to normal levels was accomplished with medication, but it required a week for cortical perfusion to return.

In this case, the vascular reserve of the carotid was insufficient and only the reserve of the vertebral system remained able to directly supply the brain. Termination of one of the carotid arteries in ischemia in both hemispheres and in the brain stem as well. After carotid endarterectomy, the vascular reserve of the carotid increased markedly, and the flow increased in both carotid beds. Because ischemic autoregulation, reactive hyperperfusion in both hemisph

THE CONCEPT OF CEREBRAL FLC AND ITS REFLECTION TO DIAGNOSTIC APPROACHES

Since Egaz Moniz introduced cerebral angiography (Moniz, 1927), the method has been primarily structure-oriented, contributing much to our knowledge of vascular anatomy but less to brain perfusion.

Angiogram—Not the Gold Standard

The clinical value of the angiogram is coming increasingly under fire (Leeon et al., 1983). Recent correlations of surgical findings with angiographic findings tarnished this gold
standard. Thin-section, high resolution CT of the internal carotid artery now permits more accurate assessment of the extent of atherosclerotic plaque and the degree of luminal compromise (Comerota et al., 1981) than angiography. Similarly, real-time B-mode carotid imaging has also improved our understanding of the dynamic anatomy and pathology not appreciated by static imaging. The ability to determine precisely peak Doppler velocities now permits functional calculation of obstruction (Payen et al., 1982). As more brain perfusion studies become available, the limitations of angiography will be better appreciated.

Noninvasive Testing

In noninvasive testing, many reports have focused on the carotid bifurcation. As better methods of imaging of brain structure and determining brain perfusion are being utilized, noninvasive testing must also involve the brain itself. The blood velocity in the carotid arteries in the neck now can be related to cerebral perfusion (Risberg and Smith, 1980; Carney and Anderson, 1981a), and the combination of the range-gated Doppler and radioactive xenon perfusion studies of the brain has been used with success. The reduction of carotid velocity or significant asymmetry facilitates the selection of patients for further studies. Asymmetry of vertebral blood flow, however, is the rule, and its interpretation is more difficult.

Furthermore, as revascularization procedures extend in the carotid and vertebral artery at skull base and extracranial-intracranial microvascular procedures are used, the focus of noninvasive testing must shift to accommodate this area. Some of the probes are not suitable for these areas, but modifications of these probes will allow their use in the operating room and permit the imaging of the intact vessels, thus reducing the need for angiography (See also Chapter 7 on noninvasive diagnosis).

Total Cerebral Blood Flow Versus Regional Perfusion

Severe disability owing to abnormal regional brain ischemia could coexist with normal total cerebral blood flow. Radioisotope techniques, first reported in 1961 (Lassen and Ingvar, 1961), lacked practical application until the advent of microvascular reconstruc-
enhancement by infusion aided in visualization of blood vessels, mass lesions of the brain and areas of “luxury perfusion.”

In 1977, pressure was brought to bear for more practical information regarding brain perfusion. This impetus came from two groups of surgeons: those performing superficial temporal-middle cerebral anastomoses and others performing vertebral artery surgery. The neurosurgeon sought to enhance flow to the middle cerebral artery by anastomosing it with the superficial temporal artery. Many questioned the value of this procedure. Surgeons responded by measuring brain perfusion in the territory of the middle cerebral artery with radioactive xenon and the critics by forming a study group to determine the efficacy of the procedure (ED/IC Bypass Study Group 1985). On the other hand, vertebral artery surgery was designed to enhance blood flow to the circle of Willis. Such an approach required a method to study brain perfusion in both the forebrain and the hindbrain (Carney and Anderson, 1978a). Reconstruction of the post-circle middle cerebral artery has been judged of limited value, reconstruction of the pre-circle vertebral artery still awaits evaluation.

Dynamic CT Scanning—Contrast Enhancement

By 1978, dynamic CT scans of the brain were being performed clinically, using iodinated contrast, a nondiffusible marker administered by bolus injection that is confined to the vessel lumen except in cases of disruption of the blood brain barrier, i.e., when luxury perfusion is not present. Contrast increases tissue density with the passage of the contrast bolus. Serial sections taken of the one level studied per injection permit the generation of a curve for each selected window. Interpretation is based on the mean transit time, which is qualitative, not quantitative.

One advantage of this technique is the larger number of scanners that could potentially perform the examination. The technique was applied clinically but drew little interest from radiologists who operated the scanners most often or from those studying brain perfusion who did not possess the scanners. Another advantage is the unique ability to penetrate the posterior fossa with high resolution for static imaging and dynamic scans.

Many radiologists, vascular surgeons, and clinicians came to accept angiography as the golden standard and carotid stenosis as the center of attention. Unexplained symptoms were attributed to embolism and treated as such, or labeled nonhemispheric and discounted. Discussion of critical arterial stenosis and the carotid bifurcation dominated medical and surgical meetings alike. Studies of brain perfusion would have changed this status quo but there was little interest in physiological evaluation and little was to be gained by change.

The 1970s saw an increasing number of clinicians entering diagnostic work because their need for physiological information exceeded that provided by existing services. Neurosurgeons have been by far the earliest and most active in the pursuit of applications of brain blood flow studies in clinical settings. It was a neurosurgeon who promoted the use of Xenon 133 for diagnosis and for use in the operating room. Its prime field of application was the accessible cerebral cortex, which correlated well with the electroencephalogram. Deep structures and the posterior fossa are not evaluated well by either technique.

Dynamic CT Scanning—Xenon Enhancement

In 1984, General Electric introduced the GE 9800 scanner, which had the ability to perform quantitative cerebral perfusion studies rapidly with low concentrations of stable xenon. Although there is significant experience with this technique, clinical experience with posterior fossa studies has yet to be reported. This was the first instrument to have commercially available software for this purpose. Stable xenon, which is administered by inhalation, is freely diffusible, and its solubility coefficient is utilized in calculating perfusion. It does not detect disruptions of the blood brain barrier but it does yield quantitative brain perfusion data.

Positron Emission Scanning

Positron emission tomography (PET) is a physiological instrument which has been used primarily in studies for metabolic problems and epilepsy. Time frames of study typically range in minutes. Stressing brain perfusion by dilating the vascular bed may require 30 to 40 minutes to achieve a steady state (Maziotta et al., 1984). The scanners can utilize both diffusible and nondiffusible markers and can dis-
tinguish disruption of blood brain barrier (lux-
ury perfusion) from focal hyperemia. Oxygen 
extraction is sometimes used as an index of 
tissue needs in low-flow areas. The assumption 
is that if oxygen extraction is high there is need 
for revascularization, and benefit would be de-

Nuclear Magnetic Resonance

Nuclear magnetic resonance (NMR) scan-
ers offer high-resolution image scans, unen-
cumbered by cortical bone, which can be dis-
played in the transverse, sagittal, and coronal 
planes. The visualization of small infarctions 
in the posterior fossa and of spinal cord abnor-
malities exceeds the potentials of any other 
technique. The measurement of linear blood 
flow with this technique has been demon-
Though the ability to quantitate tissue perfu-
sion is less likely, the estimation of regional 
magnitudes of flow appears possible. Interpreta-
tion of arterial obstruction may be difficult if 
the vessel is not imaged within a given section. 
Plaques are well visualized. Slowly flowing 
blood near the arterial wall is better visualized 
than high-velocity central flow. Turbulence 
increases the signal. The technical perform-
ance of NMR scanners is highly variable, even 
in scanners from the same manufacturer. Site 
preparation, maintenance, and personnel are 
key factors. Because the soft-tissue visualiza-
tion is so good, potential application is wide. 
The use of NMR will offer increasing opportu-
nities to clinicians.

As seen in the foregoing, as high-resolution 
measurement of brain perfusion and detailed 
structural information become more readily 
available, the precise knowledge of anatomy 
and pathology and an understanding of the 
system and brain hemodynamics are becom-
ing practical necessities. Carotid surgery based 
upon angiography will give way to more ad-
vanced techniques of diagnosis and surgery.

HEMODILUTION

Increasing the intravascular blood volume 
with cell-free colloidal solutions, e.g., low-
molecular-weight dextran, improves the per-
fusion of ischemic brain (Wood et al., 1984). 
Hypervolemic hemodilution proved to be pro-
tective against cerebral infarction in experi-
mental ligation of the middle cerebral artery 
(Wood et al., 1984). It is believed that the he-
matocrit must decrease significantly to en-

The therapeutic application of this process 
has been widespread among neurosurgeons in 
the treatment of brain ischemia and for the 
purpose of brain protection during surgery. It 
has been applied in the course of graded occlu-
sion of the internal carotid artery and for initial 
treatment for acute neurological deficits (Van-
derArk and Pomerantz, 1973) as shown by the 

Intracranial Pressure

The technique of hemodilution differs in 
cardiac and neurovascular surgery. Noncolloi-
dal solutions used to prime the cardiopulmo-
nary bypass result in an increase of tissue in-
terstitial pressure and fluid retention, but the 
effects on intracranial pressure and cerebral 
edema are not known. While hypoosmolar 
solutions increase, hyperosmolar solutions, 
such as albumin, decrease edema, including 
cerebral edema (Little et al., 1981). Wood 
recommends the use of the hyperosmolar,
low-molecular-weight dextran; nevertheless, volume expansion increases intracranial pressure, possibly by increased cerebral blood volume (Wood et al., 1982b).

Brain ischemia by itself causes cerebral edema (Hossman et al., 1976), which in turn increases intracranial pressure and may further decrease brain perfusion. If the edema is marked and the perfusion pressure is low, deterioration of the cerebral circulation occurs, being first manifested in the watershed areas. Perfusion measured in these regions has been useful in detecting the development of ischemia and in predicting poor neurological prognosis (Overgaard and Tweed, 1983).

**Isovolemic Hemodilution**

Isovolemic hemodilution (Gejha, 1976) using albumin solution enhances brain perfusion and reduces cerebral edema during neurovascular surgery and in acute neurological deficits. In patients with high hematocrits the blood volume is first restored to normal. If the hematocrit remains high, phlebotomy is performed before surgery is undertaken. This approach has resulted in electroencephalographic stability during surgery and reduced the need for intraluminal shunting.

**Heart Disease**

Coronary artery disease almost triples the risk for stroke, and cardiac failure increases the risk five-fold (Kannel et al., 1983). Atrial fibrillation with or without valvular involvement (Sage and VanUitert, 1983) carries itself an inherent risk of embolism and stroke. Congenital cardiac anomalies and their correction also compromise brain perfusion (Adams et al., 1984). This raises several questions: Is neurological dysfunction a symptom? If the cause of brain ischemia is cardiac, should the heart be treated in the absence of specific cardiac complaints (Adams et al., 1984; Hertzer and Lees, 1981; Rokey et al., 1984)? The decrease in cardiac output and brain ischemia may be the result of either disease or even be the consequence of medication. Although the overzealous use of cardiac medications should be tempered, the use of physiologic pacemakers, volume expansion, and anticoagulant therapy should be utilized whenever necessary.

In conclusion, technical advances in diagnostic and therapeutic instrumentation have made possible a novel hemodynamic approach to understanding and measuring brain perfusion, including flow through the arteries of the neck. This, combined with increased resolution imaging, permits objective evaluation of the circulation of both the forebrain and of the posterior fossa. Furthermore, objective demonstration of neurological dysfunction and regional ischemia provides the tools to determine adequacy of vessel flow in general.

The dynamic physiological approach to brain blood flow permits a rational clinical evaluation of brain ischemia. System hemodynamics also assume increased importance in both surgical and medical management of the acute neurological deficit. Now, in a symbolic sense, the brain can be held in the hand and examined.

**REFERENCES**


Caplan, L.: Treatment of cerebral ischemia — where are we headed? 


Carney, A.L.: Vertebral artery surgery: historical development, basic concepts of brain hemodynamics, and clinical experience of 102 cases. 


Carney, A.L., and Anderson, E.M.: Collateral ophthalmic artery pressure (COAP) and the collateral ocular pulse (COP). In Diethrich, E.B. (ed.): 


Comerota, A.J.; Cranley, J.J.; and Cook, S.E.: Realtime B-mode carotid imaging in diagnosis of cerebrovascular disease. 


Crissley, M.M., and Bernstein, E.F.: Delayed presentation of carotid intimal tear following blunt cranio-metabolic trauma. 


EC/IC Bypass Study Group: Failure of extracranial-intracranial arterial bypass to reduce the risk of ischemic stroke. 

Uitgeversmaatschappij Huisartsenpers BV, Utrecht, 1981.


Eisenberg, S.: Cerebral circulatory effects of acutely induced hypervolemia in human subjects. 

Gee, W.: Carotid physiology with ocular pneumoplethysmography. 

Gejha, A.: Coronary and cardiovascular dynamics and oxygen availability during acute normovolemic anemia. 


Heros, R.C.: Thromboembolic complications after combined internal carotid ligation and extra- to intracranial bypass. 


Hope, E.E.; Bodensteiner, J.B.; and Barnes, P.: Cerebral infarction related to neck position in an adolescent. 


Hounsfield, G.N.: Computed transverse axial scanning (tomography). Description of system. 

Jawad, K.; Miller, J.D.; Wyper, D.J.; and Rowa, J.O.: Measurement of CBF and carotid artery pressure compared with angiography. 


Kramer, S.P.: Function of the circle of Willis. 


Lassen, N.A.: Incomplete cerebral infarction — focal incomplete tissue necrosis not leading to emoliciss. 

Lassen, N.A., and Christiansen, M.D.: Physiology of cerebral blood flow. 


Neurosurgery. 9:552–58, 1981.


Mauersberger, W.: Cerebral Durchblutungsstörungen und Parese des Nervus hypoplossus bei extremer Schlingebildung der Arteria carotis interna. 


Mazzotta, J.C., and Engel, J., Jr.: The use and impact of positron computed tomography scanning in epilepsy. 


Mills, C.M.; Brant-Zawadzki, M.; Crooks, L.E.; Kauf-
man, L.; Sheldon, P.; Norman, D.; Bank, W.; and New-
ton, T.H.: Nuclear magnetic resonance: principles of
blood flow imaging. Am. J. Radiol., 142(1):165–70,
1984.

Moniz, E.: L'encephalographie arterielle, son importance
Mosher, P.; Ross, J., Jr.; McFate, P.A.; and Shaw, R.F.;
Nornes H., and Wikeby, P.: Cerebral arterial blood flow
Overgaard, J., and Tweed, W.A.: Cerebral circulation after
Payen, D.M.; Levy, B.I.; Menegalli, D.J.; Lajat, Y.I.;
Proszenz, P.; Heiss, W.D.; Tschabitscher, H.; and Ehr
Reneman, R.S., and Spencer, M.P.: The functional state
of the coronary vascular system after aorto-coronary
bypass surgery. In Norman, J.C. (ed.): Coronary Artery
Medicine and Surgery. Appleton-Century-Crofts, New
York, 1975.

Risberg, J., and Smith, P.: Prediction of hemispheric
blood flow from carotid velocity measurements. A
Study with the Doppler and I33Xe Inhalation tech-
Rodbard, S., and Kikuchi, Y.: Arterial stenosis, pressure
1976.
Rokey, R.; Rolak, L.A.; Harati, Y.; Kutka, N.; and Verani,
M.S.: Coronary artery disease in patients with cerebro-
vascular disease; a prospective study. Ann. Neurol.,
Sage, J.L., and VanUttert, R.L.: Risk of recurrent stroke
with atrial fibrillation: differences between rheumatic
and atherosclerotic heart disease. Stroke, 14:537–40,
1983.
Schroeder, T.; Holstein, P.E.; and Engell, H.C.: Hyperper-
Scotti, G.; Melancon, D.; and Olivier, A.: Hypoglossal
paralysis due to compression by a tortuous internal ca-
rotid artery in the neck. Neuororadioloy, 14:263–65,
1978.
Spetzler, R.F.; Rostli, R.A.; and Zabramski, J.: Middle ce-
rebral artery perfusion pressure in cerebrovascular oc-

Sullivan, H.G.; Vines, F.S.; and Becker, D.P.: Sequelae of
indirect internal carotid injury. Radiology. 109:91–8,

Sundt, T.M., Jr.: The ischemic tolerance of neural tissue
and the need for monitoring and selective shunting dur-
ing carotid endarterectomy. Stroke, 14:93–8, 1983.
Sundt, T.M., and Waltz, A.G.: Hemodilution and anti-
cogulation: effect on the microvasculature and micro-
circulation of the cerebral cortex after arterial occlusion.
Sundt, T.M.; Sharbrough, F.W.; Anderson, R.E.; and
Michenfelder, J.D.: Cerebral blood flow measurements
and electroencephalograms during carotid endarterec-

Tada, K.; Nukada, T.; Yoneda, S.; Kuriyama, Y.; and
Abe, H.: Assessment of the capacity of the cerebral col-
lateral circulation using ultrasonic Doppler technique.
Taki, W.; Handa, H.; Higa, T.; Tanada, K.; Fukuyama,
H.; Fujita, T.; Yonekawa, Y.; Kameyama, M.; and Tor-
izuka, K.: Distribution of the blood flow supplied by the
vertebral artery in humans as assessed by emission CT.
Tindall, G.T.; Odom, G.L.; Cupp, H.B., Jr., and Dillon,
M.L.: Studies on carotid artery flow and pressure. J.

Torvik, A.: The pathogenesis of watershed infarcts in the
VanderArk, G.D., and Pomerantz, M.: Reversal of neuro-
logic signs by increasing the cardiac output. Surg.
Wernick, S.; Jerva, M.J.; and Guandique, M.A.: Extrinsic
compression of the internal carotid artery by enlarged
16, 1974.
Wilkinson, H.A.; Wright, R.L.; and Sweet, W.H.: Correla-
tion of reduction in pressure and angiographic cross
filling with tolerance of carotid occlusion. J. Neurosurg.,
Wollschaeger, G., and Wollschaeger, P.B.: The circle of
Willis. In Newton, T.H., and Potts, D.G.(eds.): Radiol-
y of the Skull and Brain. Vol. 2. C.V. Mosby, St.
Louis, Missouri, 1974.
Wood, J.H.; Simeone, F.A.; and Snyder, L.L.: Cortical
oxygen transport during hypervolemic hemodilutional
therapy for focal cerebral ischemia (abstr.). Neurosur-
gery, 10:781, 1982a.
Wood, J.H.; Simeone, F.A.; Fink, E.A.; and Golden,
M.A.: Correlative aspects of hypervolemic hemodilu-
tion. Low molecular weight dextran infusions after ex-
perimental cerebral artery occlusion. Neurology (Cleve-
eological aspects of experimental hypervolemic hemodi-
lution with low molecular weight dextran: relationships of cortical blood flow, cardiac output and in-
tracranial pressure to fresh blood viscosity and plasma
Young, D.F.; Cholvin, N.R.; Kirkeeide, R.L.; and Roth
A.C.: Hemodynamics of arterial stenosis at elevated