CHAPTER 26
Cerebral Hemispheres: Neuropathology and Clinical Correlation I. Vascular Syndromes

The course and nature of some of the more common diseases affecting the cerebral hemispheres are already familiar to the student on the basis of those case histories presented in the previous chapter on cortical localization. We will refer back to some of those case histories. However, we will not limit our discussion simply to the neocortex but will discuss the cerebral hemispheres in a more general sense. It will also be convenient at this point to consider several broad categories of diseases, not previously discussed, which do not necessarily restrict themselves to the cerebral hemispheres.

Diseases affecting the cerebral hemispheres account for the largest proportion of central nervous system diseases encountered in medical practice. These diseases may be focal or diffuse in nature. There is also a third or intermediate category of multifocal (that is, comprised of many focal events). Our major concern in this chapter will be with focal vascular disease.

VASCULAR DISEASES OF THE CEREBRAL HEMISPHERE

Vascular problems account for the largest category of diseases affecting the cerebral hemispheres. Cerebrovascular disease remains the third leading cause of death in the United States. The annual incidence is close to 300,000. Approximately 261,000 fall into the ischemic/occlusive/category and 36,000 into the category of intracerebral and subarachnoid hemorrhage. The overall mortality due to this cause has been falling due to: (1) better control of hypertension; (2) better control of cardiac arrhythmias; (3) decreased incidence of rheumatic heart disease; (4) decreased incidence of meningovascular syphilis. Several types must be considered: (1) atherosclerosis with ischemia due to stenosis and occlusion (2) small infarcts (Lacunar infarcts) due to hypertension, (3) embolism, (4) intracerebral hemorrhage, and (5) subarachnoid hemorrhage. These various categories are not mutually exclusive. Thus occlusive vascular disease usually occurs in relation to the process of atherosclerosis - the deposition of fatty material (cholesterol) in the walls of arteries. However, emboli produce their effect essentially by occlusion of cerebral arteries. Such emboli generally originate in relation to clots within the chambers of the heart. At times, however, such embolic material has originated at an area of occlusive disease when atheromatous material or an overlying thrombus (clot) has broken loose to be carried into the more distal circulation. There is, on the other hand, an overlap between ischemic occlusive disease and intracerebral hemorrhage. Thus certain areas of tissue damage resulting from ischemia may become hemorrhagic secondarily. The symptoms and signs, which then evolve, may resemble those of intracerebral hemorrhage. The use of angiography, CT scan, and MRI have allowed a more precise delineation of infarct vs hemorrhage but have left a large group of patients where a specific cause of the infarct remains uncertain.

ISCHEMIC-OCCLUSIVE DISEASE:

Within this category the subtypes indicated in Table 26-1 may be specified (based on Kistler, 2000, Sacco et al 1989, and Wolf et al. 1987.

Earlier clinical and autopsy studies suggested a higher incidence of large or small vessel disease compared to embolic disease. (See Adams et al 1997).

Atherosclerosis involves the large- and medium-sized extracranial and intracranial portions of the cerebral arteries. With increasing deposition of fatty material at points of bifurcation or angulation, a progressive narrowing (stenosis) of the lumen occurs *(Fig. 26-1)*. Eventually, at approximately 70-75% stenosis, a

E. M. Marcus et al., *Integrated Neuroscience*
© Kluwer Academic Publishers 2003

decrease in cerebral blood flow through this point of narrowing in the vessel will occur (the actual relationship may be calculated according to Bernoulli's principle). The area supplied by this vessel may then at some point receive less than the required amount of blood (oxygen, glucose, and so forth). When this occurs, we may speak of cerebral ischemia. Kalimo et al (1997) outline the effects of decreased perfusion as follows: with a blood flow>40% of the normal value, normal spontaneous and evoked activities of nerve cells is still present. Between 30-40% of normal flow, neurons are unable to produce sufficient energy to continue transmission of impulses. At < 30 % of perfusion, transmission by the neuron no longer occurs although the neuron is still viable. When perfusion falls below 15% of normal, membrane failure begins to occur. The transmembrane ion gradients are no longer maintained and extracellular potassium rises. Unless perfusion and energy production are restored, irreversible nerve cell damage will occur. Note that there is a zone adjacent to this focal area of damage referred to as the penumbra where total failure has not yet occurred. This area represents tissue that could be saved by therapeutic measures.

TABLE 26-1 TYPES OF ISCHEMIC-OCCLUSIVE DISEASE

Cause of Ischemic-Occlusive Disease	Percent of Total Cases
1. Large vessel atherosclerosis:	15 % (internal carotid artery constitutes 9% of all ischemic)
2. Small vessel (lacunar)	9%
3. Embolic	Overall 60%(secondary to atrial fibrillation constitutes 15% of all ischemic)
4. Dissection and other causes	3%

The clinical correlates of this sequence of focal ischemia are as follows. A dysfunction of the involved ischemic area occurs with focal symptoms of weakness, numbness, and the like. This dysfunction may be only temporary

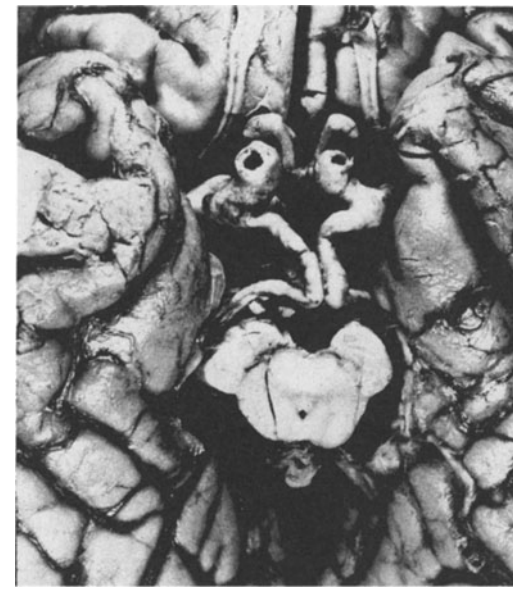

Figure 26-1. Atherosclerosis of arteries in the circle of Willis at the base of the brain. (Courtesy of Drs. John Hills and Jose Segarra).

in nature or it may be prolonged with actual tissue death (infarction) and residual neurological deficit. As progressive narrowing of the lumen occurs, eventually a point of total occlusion is reached. The narrowing of the lumen is moreover accentuated by several additional processes: (a) thrombus formation - the formation of a clot of platelets, fibrin, and blood cells due to stasis, change in intimal surface, and so forth, (b) ulceration of the intimal surface at the locus of the atherosclerotic surface at the locus of the atherosclerotic plaque, and (c) subintimal hemorrhage in relation to this area of deposition. The process of ulceration of the intimal wall may produce an originating site for emboli composed of the atheromatous material. Such an ulcerated intimal wall is a likely site of thrombus formation producing additional stenosis. The study of Eliasziw et al (1994) confirmed that plaque ulceration more than doubles the risk of stroke at higher degrees of stenosis. Fragments of the clot may also travel as emboli into the distal circulation.

We have used the joint term, atherosclerotic ischemic occlusive vascular disease, since there is no one-to-one relationship between actual occlusion of a vessel and tissue death

(infarction or encephalomalacia) in the region supplied by that artery. Thus, total occlusion of a vessel may occur with or without the development of significant neurological symptoms and signs. There may be at times persistent symptoms and signs correlated with significant tissue destruction. At other times, with stenosis, there may be only episodes of transient symptomatology without actual tissue destruction. These transient episodes, related to vascular insufficiency, are referred to as transient ischemic attacks.

The several factors which account for this lack of close correspondence between the state of a particular artery and the vascular status of the region supplied by that vessel have already been covered in the earlier discussion of basilar vertebral ischemic/occlusive disease. (Refer also to figure 26-7 below)

1. There are significant variations in the capacity of the circle of Willis to provide collateral circulation.

2. There are significant leptomeningeal anastomoses over the surface of the cerebral cortex between the anterior, middle, and posterior cerebral arteries of a given hemisphere. With regard to each cerebral artery one may then speak of its area of central supply and its area of peripheral supply. This latter peripheral area usually receives also the peripheral supply of adjacent vessels and is in a sense a border zone or watershed.

3. To a variable degree, anastomoses are present between the external and internal carotid arteries.

4. Finally, a considerable variability occurs because of certain general systemic and metabolic factors. Thus a narrowed vessel may still deliver sufficient blood when the systemic blood pressure is 190/100 but fails to do so when the blood pressure falls to 120/70 during sleep, on sudden standing after a long period of recumbency, and in relation to antihypertensive medications. Similarly, stenotic blood vessels may deliver a sufficient blood flow when metabolic conditions such as temperature serum sodium and glucose are normal but this blood flow may fail to meet essential requirements when metabolic conditions have changed.

Infarction (encephalomalacia): It is appropriate at this point to briefly summarize the gross and microscopic changes, which occur when ischemia has been of a sufficient degree to produce tissue death. The neuropathologist generally distinguishes between pale and hemorrhagic infarction. Most infarcts following ischemia are "pale" and are not complicated by hemorrhage at a gross level. During the first 4 to 6 hours no gross or microscopic changes are apparent. Between 8 and 48 hours swelling of gray and white matter is noted; the white matter may appear somewhat granular. After 48 hours the infarcted area feels soft and mushy; the descriptive term necrosis may be used. This state may be generally recognized by visual inspection. Over the next 10 days a decrease in swelling occurs. Through enzymatic processes, liquefaction occurs. By 3 weeks, in larger lesions a gross cavity begins to appear. Within a period of several months, all of the necrotic tissue is replaced by a fluid-filled cavity.

Advances in imaging studies have allowed for earlier detection of ischemia and infarction. Refer to Shaeblitz and Fisher, 1999. Perfusion imaging MRI studies will demonstrate decreased perfusion and presumably ischemia within 15 seconds.This ischemia may be reversible. This is similar to the older neurophysiologic test; the electroencephalogram which when employed in the operating room during carotid endarterectomy will begin to detect the changes of ischemia within 10-15 seconds. Diffusion weighted MRI studies may demonstrated differences between normal and ischemic presumably infarcted tissue within minutes to one hour.* Standard MRI will detect the increased water content of infarcted tissue at 6-12 hours. CT scans may also begin to detect early subtle changes related to

**The dicrepancy between perfusion imaging and diffusion weighted imaging may allow the identification of the ischemic not yet infarcted penumbra around an infarct.*

changes in water content (some effacement of sulci and gyri) at 3-4 hours although the clear cut appearance of infarction is usually delayed until 18-24 hours (Warach & Edelman, 1993, Kalimo et al, 1997).

From the microscopic standpoint indistinct staining of the neurons (which are more sensitive to anoxia than other elements, e.g., capillaries, and glia) may be noted as early as 12 hours. Within 1 to 3 days, swelling or shrinkage or alteration in the distribution of Nissl substance (chromatolysis) may be noted. Within 2 to 4 days disintegration of cells occurs. As these neuronal changes are developing, alterations are also occurring in the appearance of axons (swelling of myelin sheaths, poor staining, and disintegration) and of glial cells (swelling of astrocytes with fragmentation of processes).

While this process of necrosis is underway, various histological responses to the infarction are also taking place. Within 24 to 36 hours, the area of infarction is infiltrated by neutrophilic polymorphic leukocytes (the acute response cells). Within 24 hours of infarction, phagocytic cells (macrophages) begin to appear. These macrophages arise from various sources: microglia, blood vessel walls, circulating blood cells. By 48 hours of infarction, macrophages, filled with fatty debris (from myelin and cell breakdown), are noted. These cells remain the predominant repair cell from the period 5 days to 30 days *(Fig. 26-2)*. Some of these cells may be found years later at the edge of the infarct. If some hemorrhagic component has also been present, products from the breakdown of the blood may also be present in these cells. This removal of debris by the macrophages will eventually result in the appearance of the cavity that may be seen grossly.

At the same time that macrophages are removing the debris, the capillaries and astrocytes are beginning to engage in repair processes. Within several days to weeks after the infarct, new capillaries are noted at the edge of the lesion. There is also a thickening of the capillary walls with increased cellularity and the

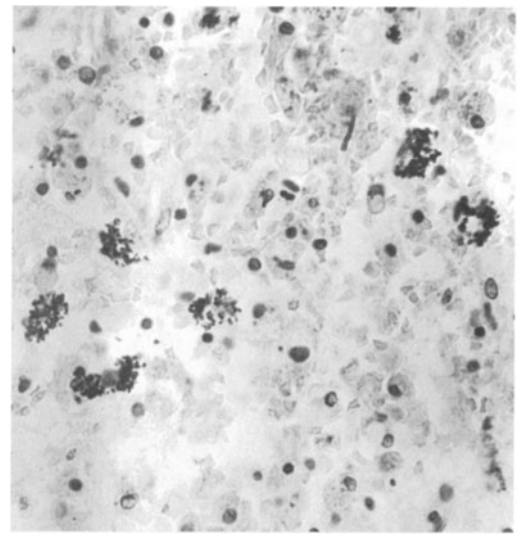

Figure 26-2. Macrophage stage of reaction in an area of necrosis. Approximately 28 days after a hemorrhagic infarct of the brain stem. Many macrophages are filled with heme pigment. (H & E x 400). (Courtesy of Dr. John Hills).

appearance of mesodermal fibrils in the adjacent tissue. There also occurs in this adjacent tissue a proliferation of astrocytes (first noted at 3 days) with the formation of reaction astrocytes containing large amounts of pink cytoplasm in H & E stains. There is a correlated proliferation of astroglial fibers. By 4 to 5 weeks a meshwork wall has been formed about the cavity by these mesodermal and glial fibers.

Hemorrhagic infarcts occur in 18-48 % of autopsy studies. Infarcts due to emboli are more likely to be hemorrhagic (51-71 % compared to non embolic infarcts, 2-21%). Venous infarcts are often hemorrhagic.

The syndromes associated with ischemic-occlusive disease of each of the arteries supplying the cerebral hemispheres will now be considered in greater detail[1]. The student, however, should interpret this material keeping in

[1]*At present most cerebral vascular disease involves the arterial circulation. Disease of the venous circulation is now less common. In the pre-antibiotic era, infectious processes involving the face , paranasal sinuses the mastoid and middle ear could secondarily involve the venous sinuses and cortical veins.*

mind those limitations of correlation that have been indicated above.

INTERNAL CAROTID ARTERY

The carotid artery may be involved by atherosclerosis in its extracranial or intracranial portions. The most common location for stenosis in this system is at the origin of the vessel at the bifurcation of the common carotid artery into the internal and external carotid branches *(Fig. 2-27)*. Another favorite location is at the carotid siphon. The branches of the internal carotid artery are in order as follows: the ophthalmic, posterior communicating, anterior choroidal, anterior cerebral, and middle cerebral. With stenosis of the internal carotid artery, a variable symptomatology and anatomical pattern of ischemia and infarction may develop *(Fig. 26-3)*. The pattern and time course of the syndrome are dependent on the availability of collateral circulation. One may distinguish transient ischemic attacks (TIAs) which last less than 24 hours with total recovery[2], progressing strokes, incomplete or partial strokes and completed total territory strokes. Transient ischemic attacks may be retinal or hemispheric and may be related to alteration in perfusion or to microemboli originating at the carotid bifurcation. This discussion will emphasize the perfusion etiology.

One syndrome involves the occurrence of repeated episodes of monocular blindness on the side of the involved carotid artery with or without the later development of hemispheric symptoms e.g. motor and sensory symptoms involving the contralateral extremities. The patient may describe a curtain descending over the field of vision of the involved eye. The episodes of monocular blindness are referred to as *amaurosis fugax*. In such cases, when symptoms are limited to monocular blindness we

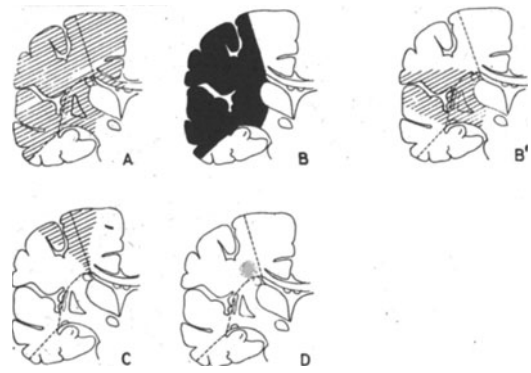

Figure 26-3. Various types of the 40 infarcts in 52 cases of occlusion of carotid artery at autopsy. A) Combined MCA and ACA Territories- 37.5%. B) Total MCA- 13%. B') Proximal MCA -21%. C) Watershed 19%. D) Terminal or deep border zone MCA/ACA- 5% (modified from Torvik, A., and Jorgensen, L.: J. Neurol. Sci., 3:415, 1966). MCA=middle cerebral artery territory, ACA=anterior cerebral artery territory.

may presume that there is ischemia predominantly in the ophthalmic artery distribution with the more distal carotid branches temporarily receiving adequate collateral supply from the posterior communicating and anterior communicating arteries and via leptomeningeal anastomosis over the cortical surface. With progression of the occlusive process even this collateral supply may become inadequate and additional symptoms develop.

One of the common patterns of carotid artery insufficiency is the carotid border zone syndrome *(Fig. 26-3, 26-4)*. With decreased perfusion by the carotid artery, symptoms will initially develop in the upper extremity, which corresponds to the cortical border zone between the middle and anterior cerebral arteries[3]. As such it receives some overlap supply from both the anterior and middle cerebral arteries. As perfusion pressure drops in the

[2]In reality, most TIAs are minutes in duration and rarely greater than one hour in duration. This has significance when the use of the thrombolytic agent recombinant tissue type plasminogen activator (t-PA) is considered requiring a more realistic definition (see below). This agent must be administered within three hours of stroke onset.

[3] For additional discussion refer to Bogousslavsky & Regli (1986). Note also that although the carotid (anterior border zone syndrome may be relatively common as an insufficiency syndrome, actual infarction limited to the border zone alone is less frequent (Mounier-Vehier, 1995)

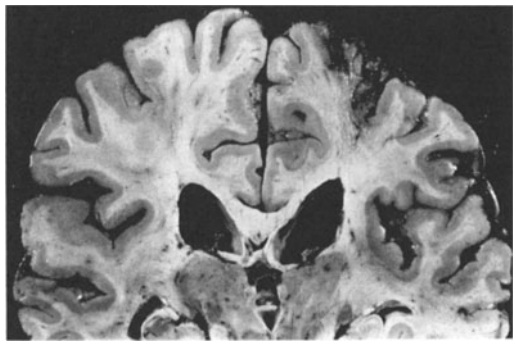

Figure 26-4. Left carotid stenosis with old infarction predominantly within the border zone between anterior and middle cerebral arteries. This 72-year-old male had a persistent paralysis of the right upper extremity with defective position sense at fingers. (Courtesy Drs. John Hills, and. Jose Segarra.)

carotid artery due to severe stenosis, this border zone will be first affected and the patient will experience numbness and weakness involving the arm and hand.

With increasing stenosis and increasing ischemia there will be involvement of the face with numbness and a supranuclear type weakness. If the ischemia involves the dominant hemisphere an expressive aphasia will develop due to involvement of Broca's motor speech area. These symptoms indicate the progression to involvement of the more central cortical supply area of the middle cerebral artery. As a general rule, one may assume that carotid ischemia and infarction will occur predominantly over the areas of cerebral cortex within the peripheral and central supply area of the middle cerebral artery *(Fig. 26-5)*. Involvement of the area supplied by the anterior cerebral artery is usually less marked since the anterior cerebral artery is more likely to receive a collateral supply via the anterior communicating artery and via leptomeningeal anastomosis over the corpus callosum from the opposite anterior cerebral artery. At times, however, both the middle and anterior cerebral areas will be involved and infarcted as in case 26-1. At times artery to artery embolization will occur involving primarily the middle cerebral artery *(Fig 26-14)*.

Case 26-1: This 23 year old right handed female on birth control pills, smoking one pack

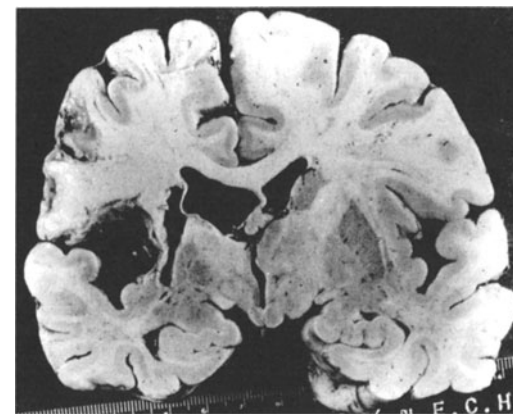

Figure 26-5. Total MCA territory infarct after left carotid clamping and excision 8 months prior to death in a 62 year old left handed male during a radical neck dissection. Patient progressed from a weakness of right hand grip, 8 hours after surgery to a complete right hemiparesis with right central facial weakness and a mixed aphasia. Subsequently recovery occurred in the lower extremity He wrote jargon with his left hand, could copy but was unable to comprehend. (Courtesy of Drs. John Hills and Dr. Jose Segarra.)

of cigarettes per day, on June 15, 1985 shortly after intranasal "snorting" of cocaine complained of gradually increasing right sided headache and then fell to the floor with a flaccid left hemiplegia with the head and eyes deviated to the right.

Neurological examination: *Mental status:* The patient denied any illness and could not explain why she was in the hospital. *Cranial nerves:* There was a left homonymous hemianopsia, deviation of head and eyes to the left and a left central facial weakness. *Motor system:* A flaccid left hemiparesis was present. *Reflexes:* deep tendon reflexes were initially depressed on the left side. Plantar responses were extensor bilaterally. *Sensory system:* a severe left hemisensory deficit, with a neglect of the left side of space and body was present.

Initial clinical diagnosis: Total right middle cerebral artery territory infarct.

Laboratory data: *Initial CT Scan* demonstrated hypodensity (infarction in right frontal and parietal areas). *Right carotid angiogram* demonstrated severe stenosis of the supraclinoid segment of the right internal carotid artery with severe stenosis of the M-1 segment of the right middle cerebral artery and multiple

areas of narrowing of the remainder of the right MCA. *Left carotid angiogram* indicated only limited cross filling of the distal right middle and anterior cerebral arteries.

On 6-21-85, 6 days after admission the previously alert patient suddenly developed a decreased level of consciousness and a fixed, dilated right pupil suggesting that tentorial herniation had been produced by severe edema or hemorrhagic transformation of the infarct. CT Scan now demonstrated massive infarction and edema-right anterior and middle cerebral artery territories plus-transtentorial and sub falx herniation *(Fig.26-6)*. With emergency management of the increased intracranial pressure- (monitor and osmotic agents) the patient became more alert and was transferred to a rehabilitation facility.

The following case histories indicate additional patterns of disease in patients with stenotic-occlusive disease of the carotid artery. In both cases the disease was in the extracranial portion of the vessel; thus an opportunity for surgical correction of the stenotic lesion was presented. Of course, similar symptoms could have occurred with disease of the intracranial portion of the carotid artery, e.g., with stenosis at the siphon. However, in evaluating patients presenting these symptoms, the student should remain alert to the possibility that surgically remedial disease is present. The aim should be recognition of such disease when insufficiency

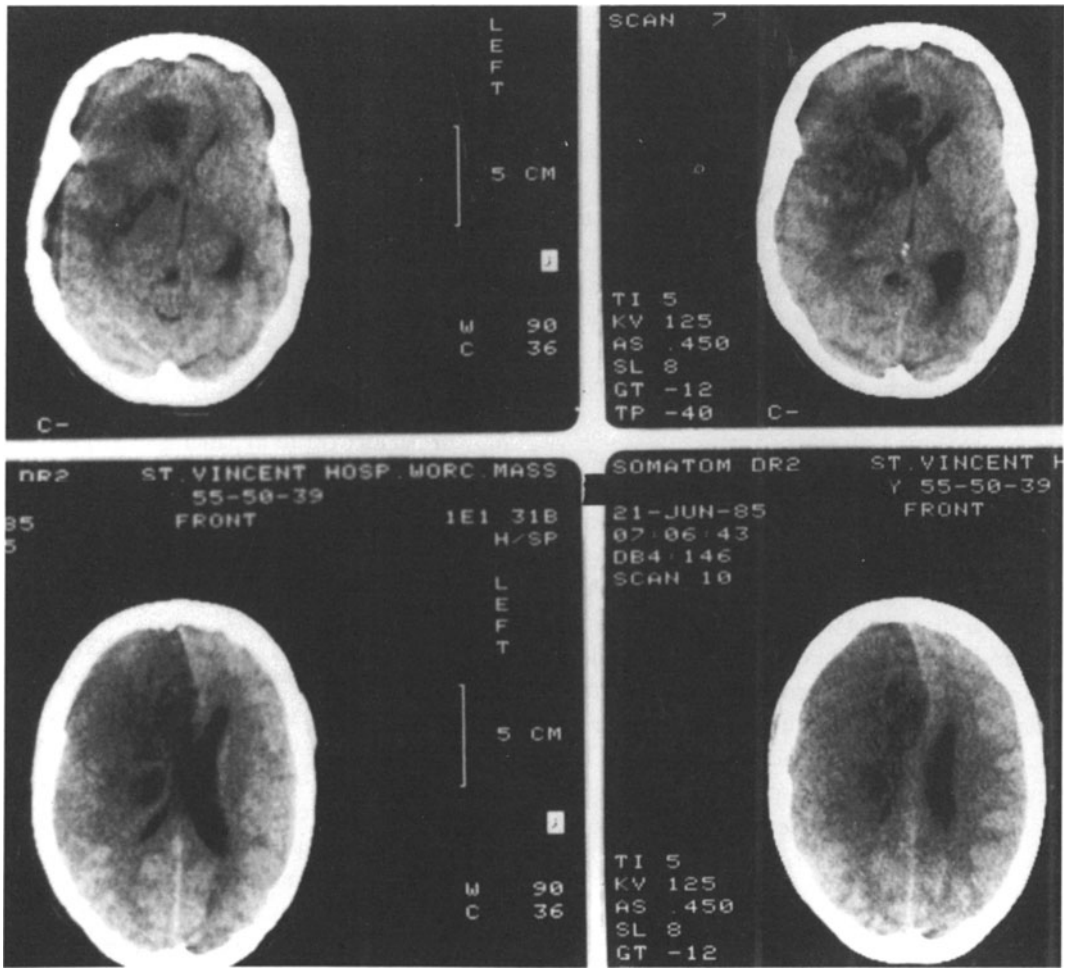

Figure 26-6. Combined infarction ACA and MCA territories related to severe stenosis of supraclinoid, internal carotid artery and proximal (M1) segment of MCA, with infarction territories of right anterior and middle cerebral arteries. CT scan. Case 26-1.Refer to text.

symptoms alone are present, that is, prior to the development of actual infarction. It also should be noted that in some cases no premonitory symptoms will be present but the patient will present with a completed stroke instead of a transient ischemic attack. A patient with carotid TIA's is presented in Case 26-2.

Case 26-2: This 54-year-old, right-handed, white male for 7 years had experienced twice per month intermittent 30-60 second episodes of blurring and blacking out of vision in the left eye. Ten days prior to admission, the patient had a 45-minute episode of minor weakness of the right face, arm, and leg plus numbness of the right side of the face accompanied a transient difficulty in speech (possibly dysarthria, possibly difficulty in word finding). The patient's mother died of a "stroke" at age 66 years, and his father, of heart disease at age 57.

General physical examination: Blood pressure elevated to 160/100 in both arms. Bruits (murmurs) were present over each carotid artery. The retinal artery pulsation was easily obliterated by pressure on the globe of the left eye. Peripheral pulses in the lower extremities were poor.

Neurological examination: Intact except for a minor right central facial weakness.

Laboratory data: Cholesterol was elevated to 284 mg%. *Arteriography (aortic arch study)* demonstrated a complete occlusion at the origin of the left internal carotid artery. A r*ight brachial arteriogram* demonstrated excellent collateral circulation with filling of the left anterior and middle cerebral arteries by cross flow through the anterior communicating artery from the right side. The intracranial portion of the left internal carotid artery filled from the left posterior communicating artery.

Subsequent course: A left carotid endarterectomy performed by Dr. Allan Callow restored blood flow following removal of the occlusive lesion (atherosclerosis with recent thrombosis) at the carotid bifurcation.

In general, carotid transient ischemic attacks (TIA) are more likely than vertebral-basilar TIA's to proceed to completed strokes. Patients with hemispheric attacks that present with hemiplegia are more likely to proceed to completed strokes than those patients with transient monocular blindness. In the study of Hurwitz et al (1985) cumulative risk for infarct after hemispheric carotid TIAs was 27% compared to 14% for monocular blindness-carotid TIAs. In general, most patients will experience the stroke after one or two transient ischemic attacks. Multiple TIA's over a long period of time are much less likely to result in completed strokes (Kase et al 1987).

Not all patients with carotid TIA's are found to have significant (>75%) stenosis or occlusion of the internal carotid artery. Pessin et al (1977) found that only 52% of 95 patients with carotid TIA's had significant stenosis (42% if hemispheric, 58% if transient monocular blindness and 80% if both types). The explanation for TIA's in patients with less than significant stenosis of the carotid artery is not certain. Emboli from ulcerated plaques; emboli from other sources such as the heart (or aortic arch) or micro platelet and fibrin emboli have all been suggested as possible explanations. (See also Ringelstein et al 1983 and Amarenco et al, 1992; Marshall 1971.)

The use of the antiplatelet agent aspirin has been effective in reducing both strokes and myocardial infarctions in patients with TIA's by 22%.

A current approach to the management of carotid TIAs is to promptly image the extracranial carotid arteries with ultrasound -doppler (Duplex scan)[4]. If significant stenosis (>70-75%) is found at the carotid bifurcation in the neck, then magnetic resonance angiography (MRA) or classical angiography followed by endarterectomy is undertaken. In many centers, the initial noninvasive study is the MRA eliminating the need for both the duplex scan and the angiography. The role of carotid endarterectomy in patients with severe carotid stenosis of 70-99% and TIA's or non disabling strokes was clearly established by the random-

[4]*Refer to Hennerici et al(1992) for a discussion of the technique.*

ized North American Symptomatic Carotid Endarterectomy Trial (1991), Kistler, et al (1991), Moore et al (1995) and emphasized by the long term follow up of these patients (Barnett et al 1998).

If significant stenosis is not present, then the patient is treated with aspirin. If this is not effective, then anticoagulation with Warfarin derivatives may be considered (see Brust 1977, Whisnant et al 1978). Such therapy, however, is not without risks. The risk of bleeding complications with anticoagulation is greater than with the use of antiplatelet agents.

In Caucasians, most symptomatic lesions of the carotid artery occur at the bifurcation of the carotid artery in the neck. In non-Caucasians, intracranial lesions increase in frequency[5]. If attacks persist, angiography may be undertaken to document intracranial lesions before embarking on long-term anticoagulation.

In addition, the absence of a significant extracranial lesion should raise the possibility of a source of multiple emboli from cardiac or other sources (see below).

If total occlusion of the artery is demonstrated, several courses of action have been suggested:

a) Emergency removal of an acute thrombus; for example, if progression is occurring (see Walters et al 1987); This may be complicated by intracerebral hemorrhage particularly if infarction has already occurred and blood flow is restored into infarcted tissue (Piepgras et al 1988).

b) External carotid to internal carotid artery bypass. This has been found to be of little value (EC-IC Bypass Study Group, 1985).

Controversy exists as to the management of the patient with the asymptomatic carotid artery bruit or with asymptomatic carotid artery stenosis. In the past, many of these patients with no neurological symptoms or with symptoms unrelated to the specific carotid artery were unnecessarily subjected to carotid artery surgery with accompanying morbidity and mortality of that procedure (see Winslow et al 1988, Dyken, 1986, Hennerici et al, 1986, Levin et al, 1980, Bornstein and Norris, 1989). The study of Freischlag et al, 1992 does suggest a definite role for the procedure where the degree of stenosis is over 75% and where perioperative morbidity and mortality are low (<3%). The study of Chambers and Norris (1986) had previously demonstrated that asymptomatic patients with a stenosis of >75% had an ipsilateral stroke rate of more than 10% per year. The editorial of Kistler and Furie (2000) discusses the effects on both low flow and the formation of thrombus leading to embolic phenomena that follows upon stenosis. The results of randomized trials of patients with asymptomatic carotid artery stenosis suggest that severe stenosis (>90%) may benefit from surgery but leave unsettled the question of whether lesser degrees of stenosis (50-90%) may benefit (Barnett, 1993, Barnett & Haines 1993, The CASANOVA Study Group, 1991, Hobson, et al 1993, Mayberg & Winn, 1995).

The following case demonstrates a case in which the patient began with carotid TIAs progressed to a carotid border zone syndrome of infarction and then involved additionally all of the middle cerebral artery territory.

Case 26-3 (Patient of Dr. Thomas Mullins): This 72-year old right-handed white male had two episodes of right upper extremity weakness, each of two hours duration, beginning 2 days prior to admission. Following the first episode, the patient had transient slurring of speech, persistent left -right disorientation, dysgraphia, and could not understand what he had read.

Neurological examination: *The only findings related to language function:* speech was fluent with intact repetition, and object naming; however, reading comprehension, writing, and left-right orientation were all impaired. *Carotids:* a bruit was present on the left.

Clinical diagnosis: Carotid artery stenosis with TIA's reflecting decreased perfusion in

[5]*The effects of race and ethnicity on ischemic stroke are discussed by Zwefler et al (1995) and Selva & Chimowitz(1995).*

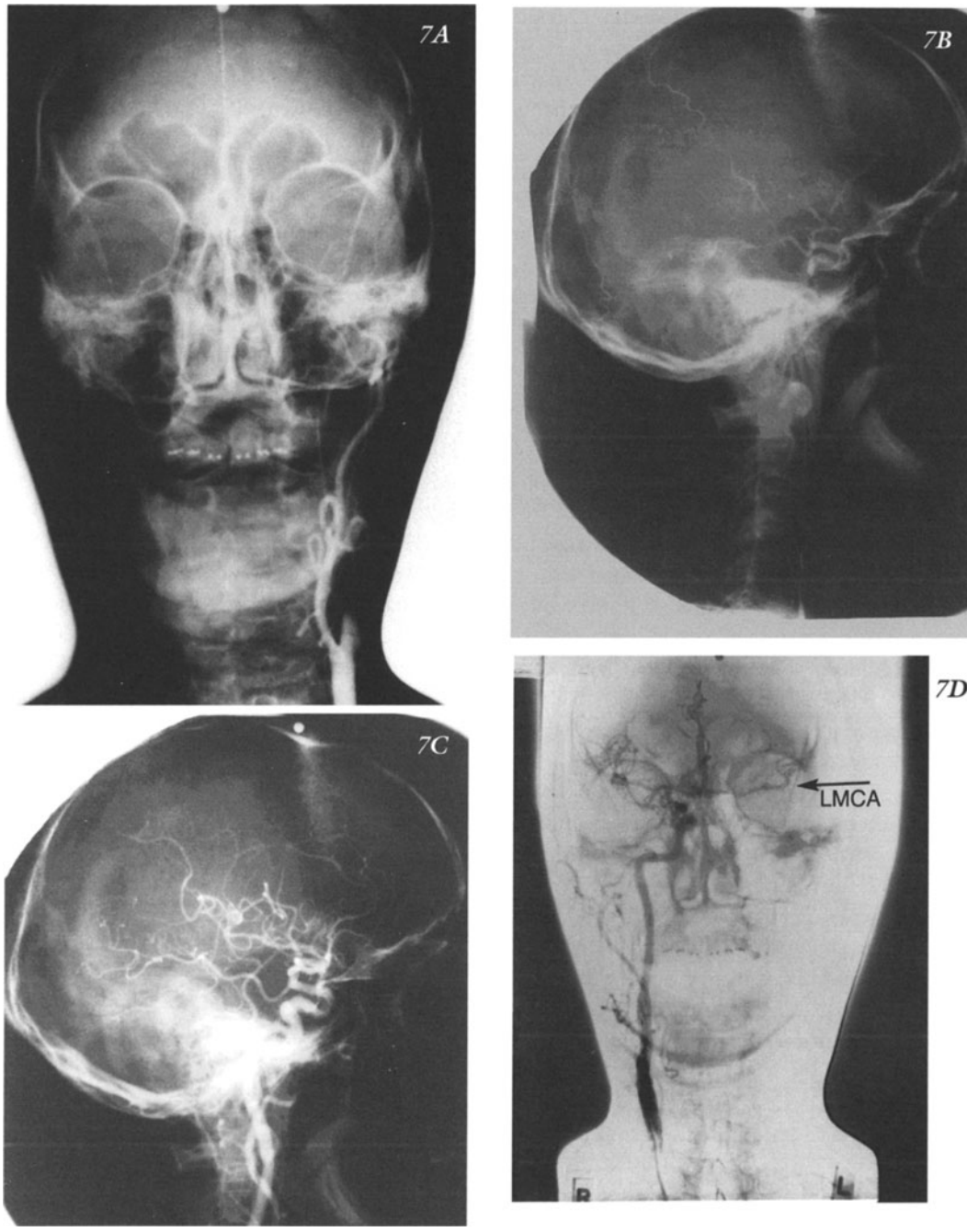

Figure 26-7. Internal carotid artery occlusion at the bifurcation. TIAs with subsequent infarction of middle and posterior cerebral artery territories. Case 26-3 (refer to text.) A and B) Left Carotid injection A)occlusion of left internal carotid just above the bifurcation. B) External carotid anastomotic branches (periorbital etc) allow late filling of the left internal carotid artery at the siphon and its branches. C and D) Right carotid injection C) Lateral view: posterior cerebral artery originates from carotid artery, D) AP view: cross filling of the left anterior cerebral artery and limited filling of the left middle cerebral artery (arrow).

the border zone followed by thrombosis and passage of emboli to the inferior division of the middle cerebral artery.

Laboratory data: *Arteriograms:* (a) the left internal carotid artery was completely occluded just above the bifurcation *(Fig. 26-*

7A). (b) The left external carotid artery filled the left internal carotid artery at the siphon through anastomosis about the orbit *(Fig. 26-7B).* However, there was a cutoff just below the siphon suggesting that the thrombus (clot) at the bifurcation had extended to this level. Moreover, the left middle and anterior cerebral arteries failed to fill in this manner. (c) The left posterior cerebral artery did originate from this segment of the otherwise occluded carotid siphon segment but with no retrograde filling into the basilar artery *(Fig. 26-7B).* (d) The right carotid artery filled not only the right middle cerebral and anterior cerebral artery but also was the source of the right posterior cerebral artery *(Fig. 26-7C).* (e) The right carotid system also supplied the left anterior cerebral artery and to a limited extent the left middle cerebral artery *(Fig. 26-7D).*

Subsequent course: On the day following admission, weakness in the right hand at wrist and finger extensors recurred. During the arteriogram, the patient was noted to have additional problems with speech. Weakness in the right upper extremity increased. Despite subsequent anticoagulation, additional progression occurred with total paralysis of the right upper extremity, aphasia and a right homonymous hemianopsia. The CT scan, which had been normal on admission now, 72 hours after these events, demonstrated acute infarction with severe edema involving the entire cortical and deep territory of the middle cerebral artery and the cortical territory of the posterior cerebral artery but with relative sparing of the anterior cerebral artery territory and most of the thalamic territory of the posterior cerebral artery (Fig. 26-8). Coma developed secondary to the herniation effects on the brainstem and the patient expired 8 days after admission.

Such massive swelling with herniation of temporal lobe through tentorium and secondary brainstem compression is the major acute cause of death in patients dying after acute carotid artery or massive middle cerebral artery infarctions (31%). Other causes of death are pneumonia (29%), cardiac arrest (17%), pulmonary embolus (13%) (Bounds et al, 1981).

Not all patients with acute carotid infarcts continue to progress. In the series of Jones and Milliken (1976), 39% of patients remained stable. Thirty-five percent had gradual improvement and 19% had a progressing deficit over 48 hours.

MIDDLE CEREBRAL ARTERY

The middle cerebral artery is the final branch and, in a sense the direct continuation of the internal carotid artery. One of the classic internal carotid artery syndromes is essentially a syndrome of the cortical branches of the middle cerebral artery.

Depending on the point of occlusion of the middle cerebral artery and its branches several syndromes are possible. Essentially these syndromes reflect disease of the lenticulostriate penetrating branches or the cortical branches. In some cases, the clinical picture reflects involvement of the territory of both penetrating and cortical branches due to occlusion at the stem or main trunk of the artery.

Syndrome of the Lenticulostriate penetrating branches: These branches supply the putamen, most of the caudate nucleus, the outer segments of the globus, pallidus, and most of the adjacent internal capsule (particularly the anterior half of the posterior limb). These vessels ascend with no anastomotic oops between adjacent branches. The classic clinical picture associated with occlusion of these branches is that of the pure motor syndrome, relatively rapid in onset, involving equally the face, arm, and leg in a spastic hemiplegia (so-called capsular hemiplegia). As discussed by Fisher and Curry (1965), there are often no sensory symptoms and no aphasia. These hemiplegic symptoms, reflecting capsular damage, tend to predominate initially over any symptoms related to the basal ganglia, although portions of the basal ganglia may also be infarcted. If the lesion is small (<1.5 cm.) termed a lacune, the patient may demonstrate a rapid improvement, so that within weeks or months, there is little if any residual motor disability. However with multiple lacunes, deficits may persist *(Fig. 26-*

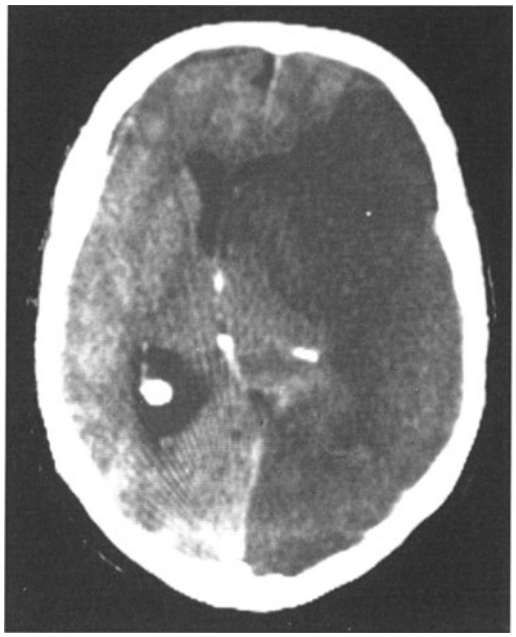

Figure 26-8: Case 26-3 as in figure 26-7. CT Scan obtained 72 hours after acute massive progression demonstrating infarction and massive edema of the left MCA territory and the cortical territory of the posterior cerebral artery, with sparing of ACA.

9). As indicated in *Fig. 26-10,* however, larger infarcts involving the lenticulostriate territory may result in a persistent spastic hemiplegia with considerable motor deficits and symptoms may include sensory and other features.

The basic pathological process has been termed segmental fibrinoid arterial degeneration (Fisher 1969). The walls of these small vessels become thickened and converted into a hyalinized material. Usually but not invariably, this occurs on a background of long-standing hypertension. At times, diabetes mellitus is present. The lenticulostriate branches rising as the initial branches of the middle cerebral artery are under relatively high pressure; not only may these vessels become occluded, they may be the site of small or large intracerebral hemorrhages also complicating the process of hypertension. We shall have cause to discuss these vessels again later in this chapter. However, not all patients with lacunar infarcts have hypertension or atherosclerosis or diabetes mellitus, and at autopsy not all patients demonstrate the specific changes in penetrating

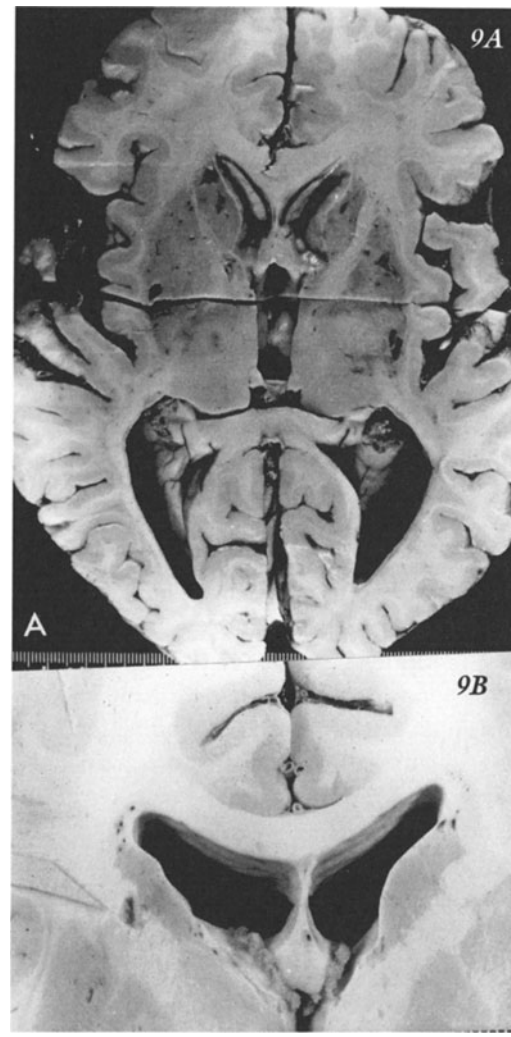

Figure 26-9. Lacunar Infarcts in MCA penetrating branch territories. A) Multiple small infarctions in a 71 year old hypertensive (210/116) who after multiple episodes of right hemiparesis and dysarthria and "dizzy spells" became wheelchair bound, with apraxia of lips, limbs and gait, pseudo bulbar, bilateral pyramidal and frontal release signs. B) Detail of a small lacunae from a 48-year-old white male, with severe hypertension (250/140). (Courtesy of Drs. John Hills and Dr. Jose Segarra.)

vessels noted by Fisher (1969). Other disease processes may certainly affect the penetrating vessels and these include: a) small emboli originating in the heart or arteries, b) the arteritis of meningovascular syphilis (Johns et al 1987); c) the arteritis of tuberculous meningitis; d) the vasculitis of autoimmune diseases such as polyarteritis, and lupus erythematosus (see

Millikan and Futrell 1990). Mast et al (1995) suggest that hypertension and diabetes are more related to multiple as opposed to single lacunar infarcts

Other types of penetrating branch infarct, so called "lacunar syndromes": A number of additional syndromes have been identified in the subsequent studies of Fisher and other investigators (Fisher 1982, Mohr 1982). These syndromes of penetrating branches of various blood vessels are outlined in Table 26-2.

TABLE 26-2: SYNDROMES OF PENETRATING BRANCHES OF CEREBRAL VESSELS:

PENETRATING ARTERY SYNDROME	LOCATION OF OCCLUSION
a) Pure motor syndrome of hemiplegia	Penetrating middle cerebral artery supply to internal capsule, less often basilar pontine paramedian arteries
b) Pure hemisensory	Posterior cerebral penetrating branches to ventral posterior lateral nucleus of thalamus or penetrating middle cerebral arteries to medial border of the posterior limb of the internal capsule
c) Dysarthria & Clumsy Hand Syndrome	Paramedian penetrating branches supplying the pons
d) Ataxic Hemiparesis:	Infarcts of the corona radiata and less often the posterior limb of the internal capsule-posterior limb (both middle cerebral artery penetrators) and to a minor degree, the pons (basilar-paramedian-penetrating)
e) Hypesthetic-ataxic hemiparesis	Infarction of the posterior limb (posterior medial segment) of the internal capsule and lateral thalamus (anterior choroidal artery). Less often the posterior cerebral artery penetrating branches are involved.
f) Hemichorea-hemiballism	Infarction of the subthalamus or thalamus penetrating branches post. cerebral artery, or lateral putamen of the striatum (penetrating branches of the middle cerebral artery (See chapter 19)
g) "Silent strokes"	Found on CT or MRI scan unrelated to clinical history.
h) Caudate infarcts producing slow apathetic (abulic) state or hyperactive restless state	Lesion in caudate with extension to anterior limb internal capsule - perforators proximal anterior or middle cerebral artery

Although many of these above lesions can be demonstrated on CT scans, MRI is the most effective technique for confirming localization *(Fig. 26-11)* (see Larson et al 1988, Rothcock et al 1987).

Lacunar State: Over time some patients have multiple infarcts involving multiple penetrating branches. The patient then begins to manifest a typical clinical syndrome that has been assigned the diagnosis of "lacunar state", based on the findings at the time of pathological examination of multiple small cavities *(Fig. 26-9, 26-11)*. The patient begins to manifest

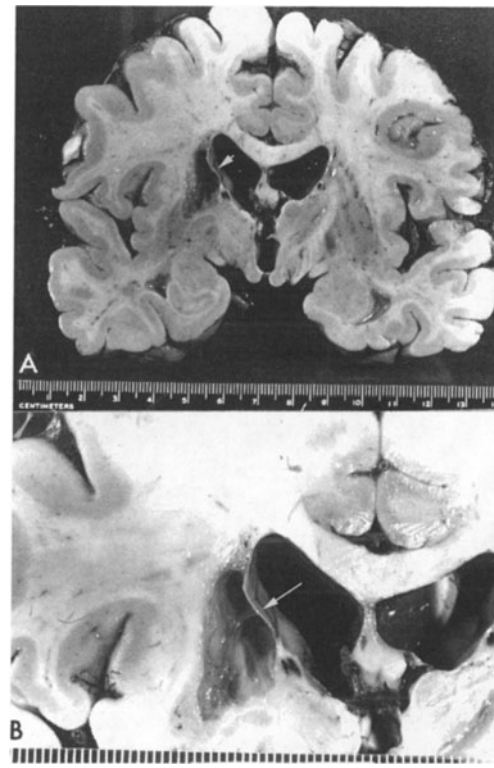

Figure 26-10. Lenticulostriate penetrating branches of the middle cerebral artery. This 73 year old hypertensive had at age 53 sustained a right hemiplegia with persistent and dense motor deficits involving the right central face, arm, and leg. A) Coronal section, B) close up of the cavity. (Courtesy of Drs. John Hills and Jose Segarra).

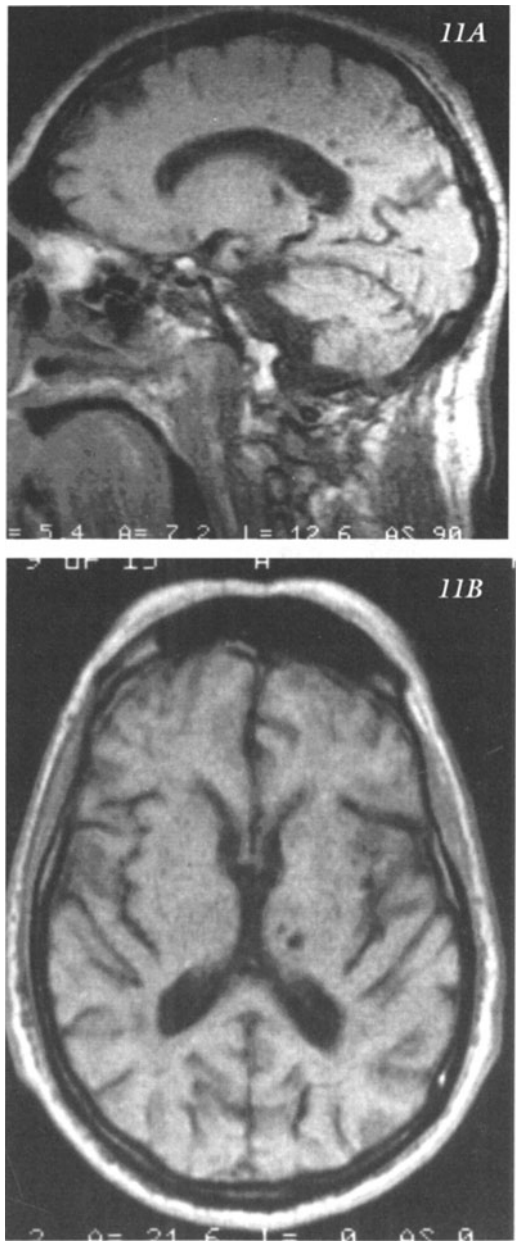

Figure 26-11. Multiple lacunar infarcts most prominent in penetrating branches left posterior cerebral artery: thalamus, posterior one third corpus callosum and adjacent white matter of left posterior cerebral hemisphere in a 70 year old right handed hypertensive male with multiple episodes of "collapse", possibly related to severe orthostatic changes. A) MRI - T1 weighted sagittal section- 12.6 mm left of midline) MRI-horizontal section.

an apraxia of gait, and a release of grasp reflex occurs as a result of damage to the descending fibers from the premotor areas. Clinical findings associated with disease of the basal ganglia may develop: rigidity and a slowness of movement and at times, a minor degree of tremor. These symptoms may reflect the damage to the putamen and globus pallidus or, perhaps, damage to the descending fibers from the premotor areas. This aspect of the syndrome has sometimes been designated as "arteriosclerotic Parkinson's disease" and can usually be distinguished from the classical Parkinson's disease (refer to chapters 18, &19). There may be a variable degree of cognitive dysfunction with considerable rigidity in problem solving, a loss of inhibition of emotional responses and impairment of executive function. Often the patients appear apathetic and are misdiagnosed as manifesting dementia or depression. Subcortical infarcts involving descending frontal systems are responsible (Wolfe et al 1990).

Syndromes of the Cortical Branches. (Figs. 26-12, 26-13). After providing a series of lenticulostriate branches, the main stem of the middle cerebral artery divides into two main cortical divisions: a superior division and an inferior division. At the point of division, the smaller

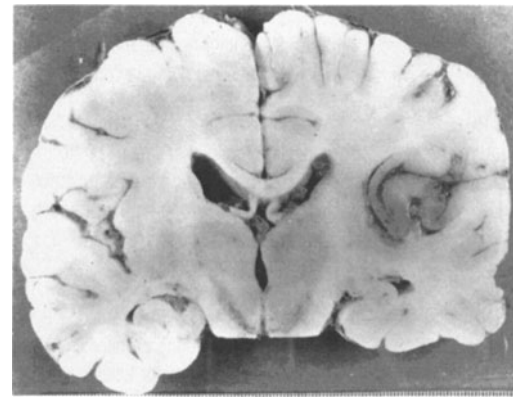

Figure 26-12. Acute hemorrhagic infarction of the central cortical territory of the MCA: calcific embolus occluded MCA following atheromatous occlusion of the carotid artery at the bifurcation. This 74-year-old, right-handed, white male, 5 days prior to death, had the sudden onset of pain in the left supraorbital region and lost consciousness. Upon regaining consciousness, the patient had a right central facial weakness, a right hemiparesis and was mute but was transiently able to follow commands. (Courtesy of Drs. John Hills and Jose Segarra.)

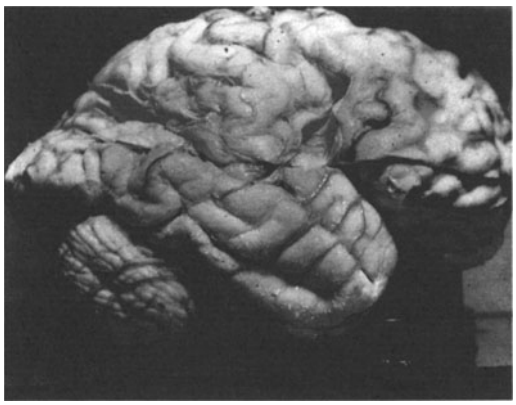

Figure 26-13. Cortical branches of the middle cerebral artery. Old infarcts involving much of the total cortical territory of the right middle cerebral artery. This 72-year-old, right-handed male with severe hypertension and auricular fibrillation expired after a 3 year history of least 4 episodes of left central facial weakness and left hemiplegia involving primarily the arm and a focal seizure involving the left arm. (Courtesy of Drs. John Hills and Jose Segarra.).

lateral orbital frontal and temporal polar arteries originate. The superior division has pre-Rolandic branches (to inferior frontal gyrus and premotor area including Broca's area in dominant hemisphere), Rolandic branches (to pre- and post-central gyri), and anterior parietal branches (to post-central gyrus). The inferior division includes anterior temporal, posterior parietal, angular and posterior temporal branches, named after the areas supplied. The syndrome that results from occlusion will depend on whether the main cortical stem, the superior or inferior division, or the branches thereof have been involved. In general the MCA cortical syndromes are assumed to be embolic in origin particularly in the Caucasian population. The stem, divisions and the cortical branches of the left middle cerebral artery are a frequent site for the lodgment of embolic material because there is a relatively direct vertical takeoff of the left common carotid artery from the arch of the aorta compared to the right carotid artery. In addition the middle cerebral artery is the direct continuation of the internal carotid artery; the cortical branches are the direct continuation of the main middle cerebral trunk.

As noted above, infarcts may occur due to carotid disease often due to artery-to-artery emboli.

Occlusion of the main cortical stem produces a mixed cortical motor -sensory syndrome involving the contralateral face (supranuclear) and arm; this is termed a faciobrachial paralysis. If this occurred in the dominant hemisphere a mixed type of aphasia would also be present with anterior (nonfluent) and posterior (fluent) components. Face and language involvement would be greater than hand involvement. The degree to which the hand is involved would depend on the degree of collateral circulation. Thus only the central cortical territory or the entire cortical territory of the middle cerebral artery could be involved.

Occlusion of the superior division in the dominant hemisphere would produce a mixed cortical motor- sensory syndrome involving again predominantly the face and hand plus an expressive Broca's type aphasia. This syndrome has already been illustrated in Chapter 24.

The less frequently encountered occlusion of the inferior division branches, producing dominant or non-dominant inferior parietal-post temporal syndromes including the syndromes of posterior type aphasias and parietal neglect already discussed in chapter 24. Refer also to Caplan et al, 1985, 1986 and Mohr et al, 1986.

Combined Syndrome: Total Occlusion of Initial Segment of Middle Cerebral Artery (Fig. 26-5). The resultant syndrome in this case will be the summation of the lenticulostriate and cortical branches syndrome. The following case history illustrates such an occlusion with massive infarction of the entire territory of the middle cerebral artery.

Case 26-4: This 61-year-old, right-handed hypertensive black housewife one week prior to admission, suddenly fell to the floor while taking a bath and lost consciousness. She was found by her son who noted that she was unable to move her left arm and leg. Her speech had been thick, but no aphasia had been present. No headache had been noted. Both parents had died of heart disease and

hypertension.

Physical examination: Blood pressure was 150/100 and pulse was regular at 84.

Neurological examination: *Mental status:* The patient was obtunded and slow to respond but grossly oriented to time, place, and person. *Cranial nerves:* Papilledema was present bilaterally particularly in the right fundus where a recent hemorrhage was present. The head and eyes were deviated to the right. The eyes did not move to the left on command but did move to the left on vestibular stimulation. The patient neglected stimuli in the left visual field. Pain sensation was decreased or neglected on the left side of the face. A marked left central facial weakness was present. *Motor system:* A complete flaccid paralysis of the left arm and leg was present. *Reflexes:* Deep tendon reflexes were increased on the left compared to the right. The left plantar response was extensor. *Sensory system:* All modalities of sensation were decreased on the left side of the body.

Clinical diagnosis: Acute occlusion of the stem of the middle cerebral artery, possibly embolic, although primary occlusions of intracranial arteries may occur in the non-Caucasian population. Hypertensive intracerebral hemorrhage was also possible.

Laboratory data: The EEG indicated severe focal damage with a relative absence of electrical activity in the right temporal area and focal 3 to 5 Hz slow waves most prominent in the right frontal area (Fig.2-23 and CD EEG atlas). Radioactive brain scan demonstrated a marked right hemisphere uptake of isotope (Hg^{197}) measuring 11x6x6 cm., extending from the right frontal area to the posterior parietal area extending from the surface to the deep midline *(Fig. 26-14)*. Right brachial arteriogram revealed a complete occlusion of the right middle cerebral artery at its origin *(Fig.26-15)*. Cerebrospinal fluid contained no significant cells.

Hospital course: The patient showed no significant improvement during a four-week hospital course.

Prognosis for survival during the acute state of the first week depends on the degree of

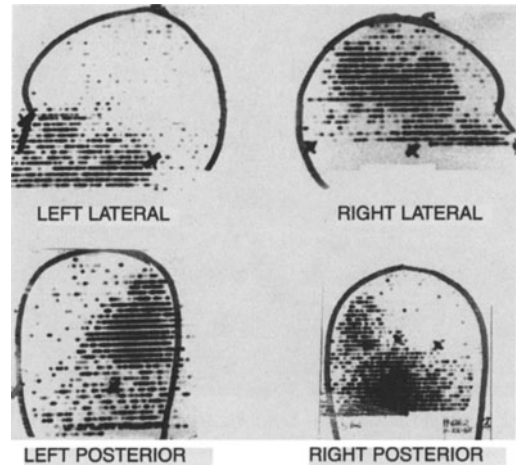

Figure 26-14. Right middle cerebral artery occlusion Case 26-4. Brain scan. A marked uptake of isotope (Hg197) is found throughout the territory of the right middle cerebral artery (22 days after the event). This is demonstrated in the posterior, anterior, and right lateral scans. (Courtesy of Dr. Bertram Selverstone).

edema. In patients with massive middle cerebral artery territory infarcts due to MCA occlusion who already had early CT scan evidence of brain swelling within 24 hours of the ictus, fifty five percent of these patients expired, over-

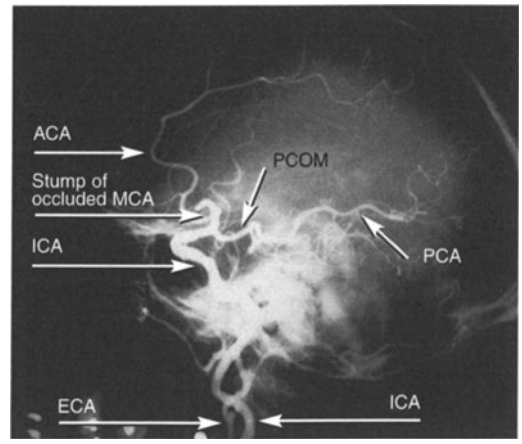

Figure 26-15. Right middle cerebral artery occlusion. Case 26-4. A) Selective common carotid injection reveals total right middle cerebral artery occlusion. (Courtesy of Dr. Samuel Wolpert). B) Reference diagram of the major branches of the internal carotid artery. ICA= internal carotid artery, ACA= anterior cerebral artery, PCA= posterior cerebral artery (supplied directly from the IC as a continuation of the PCOM posterior communicating artery), MCA= middle cerebral artery. (Refer to Fig. 26-7C and 2-27c for normal reference).

whelmingly of herniation effects. Patients older than 45 years had a poorer prognosis than younger patients. Infection of the lungs is a serious complication of large infarcts and a major cause of death during the second week. If the patient survives, prognosis for recovery is related to the size of infarct. Less than 3 cm. infarcts may be associated with a good recovery, greater than 3 cm. with severe disability (Olson, 1991).

ANTERIOR CEREBRAL ARTERY

In our clinical experience occlusive disease of the anterior cerebral artery is much less common than that involving the internal carotid or middle cerebral arteries accounting for approximately 1.8% of all ischemic infarcts - Bogousslavsky and Regli 1990). The anatomical explanation for this is evident. Each anterior cerebral receives collateral circulation from several possible sources: (a) leptomeningeal anastomotic end-to-end loops from the middle cerebral artery of the same side, (b) leptomeningeal anastomotic loops from the contralateral anterior cerebral artery over the corpus callosum, and (c) anterior communicating artery from the contralateral anterior cerebral artery. Finally, at postmortem examination atherosclerotic plaques are found less frequently in the anterior cerebral than in the larger internal carotid, middle cerebral, basilar, and vertebral arteries. In the series of Bogousslavsky and Regli (1990) 63% of the 27 patients had infarcts secondary to an embolus from the heart or carotid artery.

Penetrating and cortical branches may be distinguished. *The penetrating branches* including a larger vessel, the recurrent artery of Heubner supply the anterior limb of the internal capsule and the anterior head of the caudate nucleus. *The cortical branches:* orbital frontal, frontal polar, callosal marginal and pericallosal supply much of the corpus callosum (genu and body), and the orbital frontal cortex, the medial aspects of the frontal and parietal lobes including the sensory motor areas of the paracentral lobule and the supplementary motor cortex. Symptoms then when they occur will be most severe in the contralateral lower extremity with minor involvement of the contralateral supper extremity and minor or no involvement of the face. Most patients will have involvement of both the cortical and penetrating branch-subcortical territories. Infarcts limited to the penetrating branch territories may occur (Caplan et al, 1990). Note that not all vascular syndromes with predominant leg involvement are due to occlusion of the anterior cerebral artery. Occlusion of the superior sagittal sinus or basilar-vertebral disease affecting the brain stem may also produce predominant leg weakness (refer to Schneider &Gautier, 1994 for additional discussion).

At times both anterior cerebral arteries may be essentially branches of the same proximal segment. Occlusion of this proximal anterior cerebral artery segment will then result in infarction of the medial frontal-parietal areas of

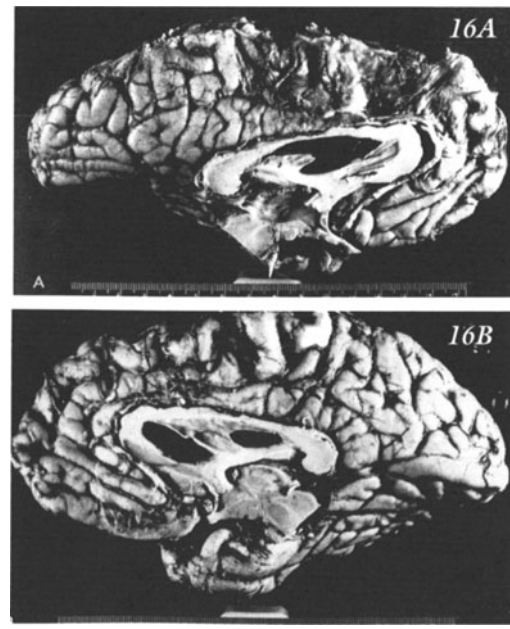

Figure 26-16. Anterior cerebral arteries: old bilateral infarcts with due to severe bilateral stenosis ACA (complete occlusion on right). Left hemisphere involvement was marked (A), with a lesser involvement of the right hemisphere (B). This 61-year-old, right-handed female 16 months prior to death developed difficulty in speech, right-sided weakness, apraxia of hand movements and progressed 2 days later to an akinetic mute state with urinary incontinence.(Courtesy of Drs. John Hills, and Jose Segarra.

both hemispheres *(Fig .26-16)*. The resultant syndrome will include a more prolonged change in personality and affect (due to involvement of the prefrontal and anterior cingulate areas), an akinetic and mute state (Freeman, 1971) (due to involvement of the prefrontal and premotor areas), urinary incontinence (due to involvement of the para- central lobule, medial premotor, and supplementary motor areas), and a sensory motor syndrome involving both lower extremities (due to involvement of paracentral lobule). There may also be a significant apraxia of the nondominant hand from damage to the corpus callosum depriving the premotor and motor areas in the nondominant motor hemisphere of information from the dominant hemisphere. A bilateral release of the grasp reflex is present because of the bilateral involvement of the premotor and supplementary motor areas. Many of these features may follow unilateral infarction in lesser degree. Transient mutism and transcortical motor aphasia are more prominent with dominant hemisphere infarcts, neglect syndromes with nondominant infarcts. Release of instinctive grasp is usually contralateral to the infarct. An example of infarction in the distribution of the anterior cerebral arteries complicating aneurysm surgery is provided in case 26-9.

ANTERIOR COMMUNICATING ARTERY

Penetrating branches from this vessel supply the anterior hypothalamus, the optic chiasm and the suprachiasmatic and paraolfactory areas.

ANTERIOR CHOROIDAL ARTERY

This is the only branch of the internal carotid artery that has not yet been discussed. This vessel supplies the inner portion of the globus pallidus, a small adjacent section of the posterior limb of the internal capsule (including the area occupied by the ansa and fasciculus lenticularis) and to a variable degree the adjacent sector of the ventral posterior lateral nucleus of the thalamus and of the lateral geniculate or geniculocalcarine tract. Various clinical results may follow occlusion of this vessel. There is no single characteristic syndrome. The initial surgical procedures of Cooper indicated that occlusion of this vessel in the patient with Parkinson's disease as discussed in chapter 19 resulted in a relief of tremor and rigidity in the contralateral limbs without the development of hemiparesis or other focal deficits. Foix in 1925 first described a triad of hemiplegia, hemianesthesia, and homonymous hemianopsia associated with infarction of the territory of the anterior choroidal artery (Bruno et. al. 1989 and Decroix et. al. 1986). With the development of CT scan and MRI scan, the syndrome is now more frequently recognized. Essentially this is a variable penetrating or lacunar syndrome ranging from a pure motor syndrome to the full-blown triad.

POSTERIOR CEREBRAL ARTERY

The posterior cerebral arteries usually originate as the direct continuation of the basilar artery following its bifurcation. At times, then, occlusive disease of the vertebral or basilar artery will be manifested by the development of symptoms within the posterior cerebral territory. At times, a mixture of brain stem and cerebral hemisphere symptoms will be present. At times, bilateral posterior cerebral artery symptoms will be present. Moreover, since the cortical and penetrating vessels of the posterior cerebral artery are the distal branches of the basilar vertebral circulation, they will at times be subject to embolization from extracerebral sources (cardiac) or from occlusive disease in the more proximal sections of the basilar or vertebral arteries. As demonstrated previously in some patients (25%), the cortical divisions of the posterior cerebral arteries may originate as a direct continuation of the posterior communicating artery.

Essentially two categories of posterior cerebral symptomatology may be recognized: (a) syndromes of the penetrating branches, and (b) syndromes of the cortical branches. With main trunk occlusions, a mixture of these two syndromes may be present.

Overall, posterior cerebral artery cortical

TABLE 26-3. COMPARISON OF SYNDROMES FROM PENETRATING VERSUS CORTICAL BRANCHES OF PCA.

VESSEL	SYNDROME
The Penetrating Branches. -supply the rostral portion of the midbrain and the thalamus (often involved in lacunar infarcts)	-Occlusion of penetrators to midbrain damages the cerebral peduncle, the third cranial nerve, and the red nucleus (Weber's or Benedikt's Syndrome -Occlusion of penetrators to subthalamus & VL nucleus of thalamus produces contralateral hemichorea or hemiballismus Damage to VPM/VPL of thalamus produces contralateral loss of sensation and possible pain syndrome (thalamogeniculate artery-thalamic syndrome).
The Cortical Branches (Fig. 26-17,26-18). -anterior temporal and posterior temporal branches to the inferior and medial surfaces of the temporal lobe, posterior cerebral artery then divides into a parieto-occipital branch and the calcarine artery to the visual (calcarine) cortex.	-In bilateral posterior cerebral disease impairment of recent memory may occur, accompanied by a significant degree of confusion and disorientation ±bilateral blindness -If the dominant temporal lobe is involved, a confusional state may follow unilateral posterior cerebral disease. -Ischemia or infarction within the calcarine artery territory produces a contralateral homonymous hemianopsia, often with sparing of the macular area due to collateral circulation from MCA (see above if bilateral) (See Chapter 23).

infarcts account for 5% of all infarcts. Usually the infarcts reflect embolic occlusion (see Fisher 1986, Pessin et al 1987, Koroshetz and Ropper 1987). Among the 54 cases presented by Kinkel et.al. (1984), 11% demonstrated total involvement of the cortical territory. Most had partial involvement primarily of calcarine and/or the posterior temporal artery territory. Nine percent had bilateral infarcts.

The following case history illustrates many aspects of ischemia within the cortical distribution of the posterior cerebral artery. This patient demonstrates the general rule that posterior cerebral cortical infarcts are usually embolic.

Case 26-5: This 55 year old ambidextrous married white female research coordinator at approximately 11:30 AM on the day of admission suddenly developed blurring of vision in her left visual field, possibly in her left eye and was found to have a left visual field defect. Shortly thereafter, she developed tingling paresthesias of the left face arm and leg. Hypertension was under treatment with hydrochlorothiazide and Lasix.

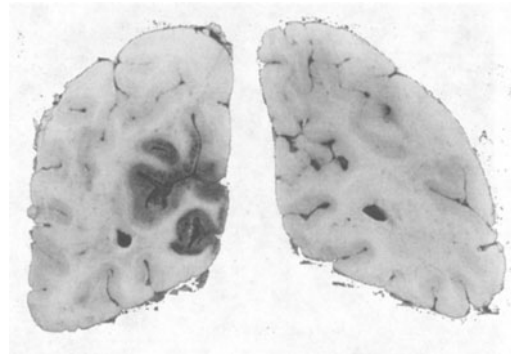

Figure 26-17. Posterior cerebral artery: acute hemorrhagic infarction predominantly within the distribution of the right calcarine branch. This 53-year-old male with a right frontal-anterior temporal glioma had tentorial herniation with compression of the right posterior cerebral artery (in addition to brain stem structures). (Courtesy of Drs. John Hills and Jose Segarra.)

Physical examination: Blood pressure was elevated to 160/70. Weight was elevated to 264 pounds. A small ecchymosis was present under the toenail of the left second digit.

Neurological examination, (3hours after onset): *Cranial nerves:* A non-congruous left homonymous hemianopsia was present greater in the left temporal field than the right nasal field. *Reflexes:* Deep tendon stretch reflexes were decreased in the lower extremities (patellar, 1+ and Achilles, 0). Plantar responses were equivocal, with the left probably extensor. *Sensory system:* pain and graphesthesia were decreased over the left foot.

Clinical diagnosis: Posterior cerebral artery ischemia and possible infarct, (possibly embolic), involving the right calcarine cortex and thalamus or a lacunar event involving the right thalamus.

Laboratory data: *MRI,* 4days after onset *(Fig.26-18)* demonstrated a small infarct in the right occipital visual cortex area in the distribu-

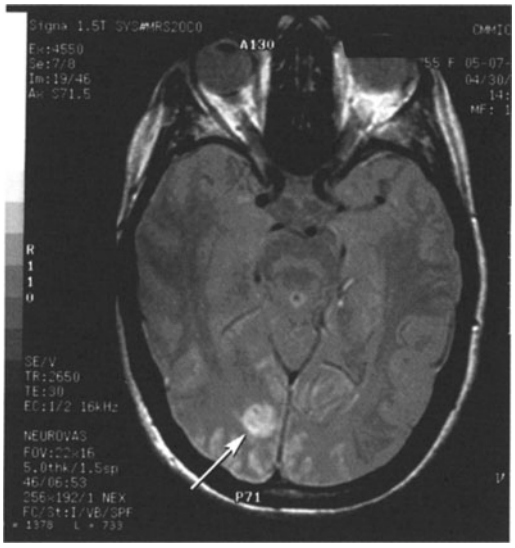

Figure 26-18. Infarct right occipital area ,calcarine artery branch territory (Embolus to posterior cerebral artery from heart). MRI. Case 26-5.

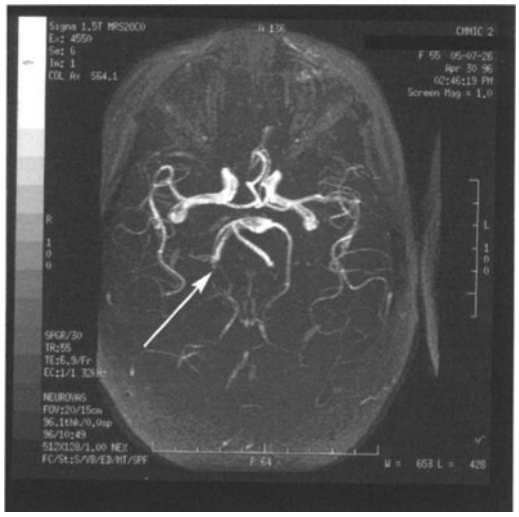

Figure 26-19. Occlusion of right posterior cerebral artery(arrow). MRA. Case 26-5 as above.

tion of the calcarine artery. *MRA (Fig.26-19)* demonstrated decreased flow in the right posterior cerebral artery. There was filling of more distal branches via anastomatic flow. *Holter monitoring* demonstrated multiple brief episodes of paroxysmal atrial fibrillation. The *transesophageal echocardiogram* demonstrated a definite patent foramen ovale with right to left shunting.

Subsequent course: Re-evaluation of the patient 22 hours after the onset of symptoms demonstrated clearing of all neurologic findings. When seen 2 weeks after the event her only complaint related to some problems in reading. This patient already been receiving aspirin at the time of the event and this was discontinued. She was begun on lifelong systemic anticoagulation with coumadin by the consultant cardiologist Dr. Filiberti since she had two conditions associated with embolization: paroxysmal atrial fibrillation and patent foramen ovale with right to left shunting. The patient did well over the subsequent 5 years.

Case 26-6 presented on CD ROM provides an example of a patient with bilateral posterior cerebral artery ischemia, manifested by acute onset of blindness and confusion.

CEREBRAL EMBOLISM

This topic has already been discussed and illustrated above in cases 26-3, 26-4, 26-5 and in the chapter on aphasia. The middle cerebral and posterior cerebral artery cortical branches are primary targets.

In general, cerebral embolism is a complication of cardiovascular disease. However, as we have indicated, artery to artery (the carotid, vertebral or basilar) embolization of thrombus or atheromatous material is also frequent. Rarely emboli may be composed of tumor cells or, following trauma, of fat or air (Jacobson et al, 1986; Knoppee et al, 1988). The embolus in most cases is a fragment of thrombus (clot, platelets, fibrin, and blood cells) that has become detached from a larger thrombus within the heart or proximal artery. The causes of such a thrombus within the heart are several:

a. A clot will often form in the left auricular appendage when atrial fibrillation is present. This is often the case when a relative stasis of blood in this area occurs as in mitral stenosis (Wolf et al, 1978, 1991, Peterson 1990).

b. A "mural thrombus" may form on the endocardium in relation to an area of myocardial infarction (Foster and Halperin, 1989, Konnrad, 1984).

c. Thrombus may collect on heart valves (so called valvular vegetations), usually the

mitral valve, when these valves are the subject of infection and inflammation as in bacterial endocarditis with embolic material breaking off and entering into the circulation at times of change in cardiac rhythm. (Hart et al 1990, Jones and Siekert, 1989, Salgado et al 1989).

d. The aorta may be a source of embolic material (Amarenco et al, 1994,Jones et al 1995, Kistler 1994)

e. In patients with a patent foramen ovale, within the heart, embolic material may originate in the veins of the legs or pelvis. Such patients may have both pulmonary and "paradoxical" cerebral emboli. (Lechat et. al. 1988, Jones et al, 1983).

Multiple small emboli of cardiac origin may occur to many cerebral vessels to produce a syndrome of multiple small vessel occlusions with a resultant clinical picture of dementia, alteration in personality, and so forth. Patients with multiple cerebral emboli also have embolization to extracerebral areas as well, such as the femoral artery, the kidney, the spleen, and the skin. Emboli to the kidney will often be detected following the sudden appearance of red blood cells in the urine (hematuria).

Differentiating embolic from non-embolic ischemic-occlusive disease. Several points should be considered: (see also Ramirez-Lassepas et al, 1987):

a. Perhaps most important is the fact that embolic occlusion of a vessel is sudden. In general there are no preceding transient ischemic events. At times, the event may be so sudden that the patient stops speaking in mid sentence with a complete loss of speech. On the other hand, infarction due to ischemic-occlusive disease is often preceded by one or more transient episodes of ischemia.

b. Since embolic occlusions are sudden, the event may be accompanied by a focal or generalized seizure.

c. Embolic occlusions may occur during any time of the day and often during periods of activity. Ischemic-occlusive infarctions tend to occur during sleep when blood pressure is relatively lower or shortly after arising in relation perhaps to transient falls in blood pressure.

d. Infarction due to embolic occlusion of a vessel is more likely to be hemorrhagic than a non-embolic infarction. This is related to reperfusion of an area of recent necrosis due to disintegration of the embolus or to the development of collateral (leptomeningeal anastomotic flow). (Fisher and Adams 1951, Okada, 1989, Ogata, et al, 1989.) In such an area, the walls of blood vessels have also been ischemic and recently damaged. Such vessels when again perfused under a normal head of pressure will then leak blood into the surrounding tissues. In the study of Honig et al (1993), MRI at 3 weeks demonstrated hemorrhagic transformation in 68% of cardioembolic infarcts but always without clinical deterioration.

e. Infarctions due to embolic occlusions are also often subject to rapid improvement because with the disintegration of embolic material, blood flow is restored.

Treatment is discussed below.

MANAGEMENT OF ISCHEMIC AND OF EMBOLIC DISEASE

As regards management of patients with atherosclerotic ischemic-occlusive disease the student should consult Biller & Love (2000) and Brott &Bogousslavsky (2000). For patients seen within 3 hours of an occlusion usually embolic of the middle cerebral artery, the use of intravenous t-PA may be considered if the CT scan does not demonstrate hemorrhage or more than one third of the middle cerebral artery territory involved by infarction. For patients seen within 6 hours direct intra-arterial thrombolysis may be considered. For most patients who have suffered infarcts, there are no specific curative therapies. Considerable recovery will occur in a supportive setting for many patients. Some patients with transient ischemic episodes or infarcts with minimal residual within the carotid distribution will have treatable extracranial vascular disease, which will benefit from surgical correction of the stenosis or occlusion. In addition to direct surgical carotid endarterectomy, the use of bal-

loon angioplasty with or without stents is being developed as for coronary artery disease. Many patients with transient ischemic attacks or with a prior stroke will have a significant reduction in stroke risk with antiplatelet therapy (aspirin). Anticoagulation has a significant role in the prevention of cerebral emboli in patients with atrial fibrillation of both rheumatic and non-rheumatic origin but has little value in other types of occlusive disease. The best treatment is prevention. The major factors which can be controlled are hypertension, the risk factors for cardiac disease including the prevention of rheumatic and coronary artery heart disease, cigarette smoking, diabetes mellitus, dietary factors and illicit drug use (Refer also to Bronner et al, 1995 and White et al, 2000, Inzitari et al, 2000). A major risk factor that unfortunately cannot be well controlled is the family predisposition for cerebrovascular or coronary artery disease (Graffagnino et al, 1994). For a discussion of ischemic-occlusive disease involving the basilar-vertebral circulation, the student should refer to the chapters on the brain stem and cerebellum.

INTRACRANIAL HEMORRHAGE:

There are two types of intracranial hemorrhage: *intracerebral hemorrhage and subarachnoid hemorrhage.* In the Framingham study (Sacco et al 1984), intracerebral hemorrhages constituted 5% of all strokes and subarachnoid hemorrhage; 9% of all strokes. Both have a high mortality. The young and middle age Black population in the United States has an increased risk of both intracranial and subarachnoid hemorrhage compared to the white population, (Broderick, et al 1992).

INTRACEREBRAL HEMORRHAGE

Intracerebral hemorrhage is primary in 83 % of cases and secondary in the remaining 15%. Hemorrhage into the brain may occur in patients receiving anticoagulants, Kase et al 1985, Franke et al 1990, or as a complication of various hematological problems which are characterized by bleeding disorders, e.g., leukemia (Fig. 26-20). Bleeding into the brain may also occur in relation to arteriovenous malformation or to intracranial tumors (such as glioblastomas or metastatic malignancy, Little et al, 1979) or as the complication of the rupture of a saccular aneurysm where there is extension of blood from the subarachnoid space into the substance of the cerebral hemisphere. In general, however, the term intracerebral hemorrhage is applied to those primary massive and medium-sized hemorrhages into the parenchyma of the brain. The major risk factor is hypertension. However in approximately 40% of patients, blood pressure is normal (Brott et al 1986). Other risk factors include excessive alcohol intake, and cerebral amyloid angiopathy with deposition of beta amyloid in cerebral blood vessels. The latter condition is associated with the presence of the e-2 and e-4 alleles of the apolipoprotein E gene. Recurrent hemorrhages may occur at different sites. Patients with intracerebral hemorrhages are seen less commonly on general neu-

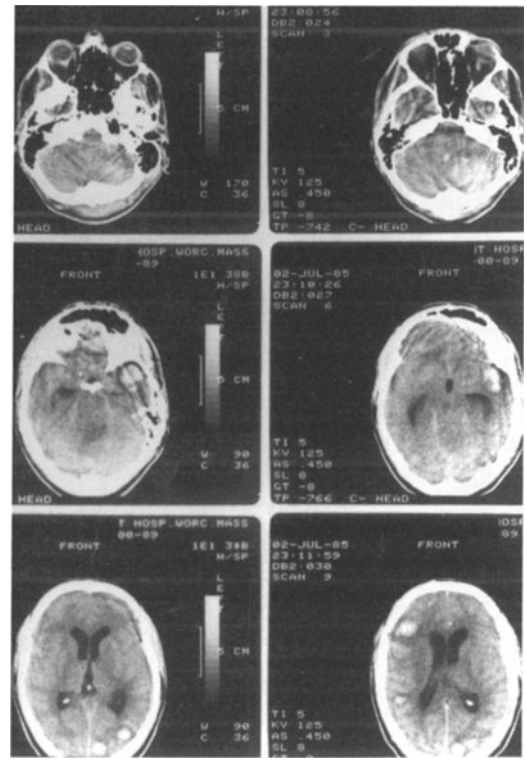

Figure 26-20. Multiple cerebral hemorrhages secondary to acute thrombocytopenia (platelet count of 17,000) with acute lymphatic leukemia.CT scan without contrast in a 24 year old with headache and acute onset of coma ,clinical brain death and a flat EEG.

TABLE 26-4. INTRACEREBRAL HEMORRHAGE

Location	Vessel	Frequency*/Figure	Clinical Manifestations
Putamen-lateral ganglionic mass-internal capsule	Lenticulostriate penetrators: middle cerebral artery	33-40% Fig.26-21, 26-22	Progressive headache, hemiparesis hemianesthesia, confusion ,herniation and coma
Temporal lobe stem and lobar (Lobar often secondary to amyloid angiopathy)	Superficial small and medium arteries	23% Fig. 2-29	Progressive temporal lobe or other cortical mass with focal seizures. Recurrent or multiple.
Thalamus	Penetrators: posterior cerebral artery	20% Fig. 26-24	Unilateral numbness, Hemianesthesia, and vertical gaze impairment
Pons	Paramedian penetrators of the basilar artery	7% Fig 13-26	Sudden quadriplegia, coma, respiratory impairment, death Small lateral tegmental lesions may survive.
Cerebellum	Branches posterior inferior or superiorcerebellar arteries	8% Fig. 20-13	Sudden headache, vomiting, vertigo, ataxia, then extra-ocular findings and coma

* Based on series of Hier et al, 1977,Kase et al, 1982,Kase and Caplan, 1986

rological and neurosurgical services than patients with occlusive vascular disease and those with subarachnoid hemorrhage. Patients with intracerebral hemorrhage are, however, relatively common when acute general medical admissions and autopsies are considered. There is certainly a predilection for certain areas of the brain as demonstrated in Table 26-4.

The basic pathogenesis involved in intracerebral hemorrhage is not certain. The fact that penetrating arteries such as the lenticulostriate arteries, are also involved in occlusion with lacunar infarction in hypertension has led to several hypotheses concerning the etiology of the hemorrhages:

a. The vessel wall may be weakened by this process and may dilate and rupture (the miliary aneurysm of Bouchard and Charcot).

b. The vessel may occlude with infarction. When collateral flow is then introduced into the acutely necrotic area, hemorrhage occurs.

c. Related to this hypothesis is the concept of fluctuations in blood pressure. Certainly such wide fluctuations may occur in some hypertensive patients. With a fall in blood pressure, infarctions would occur. With restoration of elevated blood pressure, these necrotic vessel walls would be unable to take the stress of the increased pressure and would bleed.

d. Another explanation suggests that in some cases venous occlusion may have occurred. Venous occlusions are usually hemorrhagic.

In both explanations (b) and (c) there is implied a concept of hemorrhagic infarction. In some cases of premonitory ischemia, symptoms will be noted.

e. It has been suggested that in younger patients when hypertension is not present. bleeding has occurred from an arteriovenous malformation, the evidence of which has been destroyed by the massive hemorrhage (Case 26-7 on CD).

f. The use of sympathomimetic drugs utilized in nasal decongestants and cough syrups in addition to amphetamines and the use of illicit street drugs such as "crack" cocaine have also been implicated in younger adults

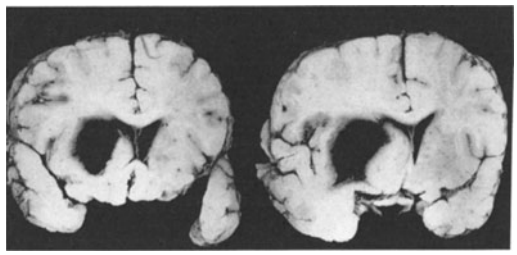

Figure 26-21. Intracerebral hemorrhage from the penetrating (lenticulostriate) branches of the right middle cerebral artery. into the putamen with displacement of adjacent structures, and ruptured into the lateral ventricle. This 46-year-old, black female with severe hypertension (230/130) had the sudden onset of left face, arm, leg paralysis,left visual field defect, and then 72 hours later tentorial herniation with progressive brain stem deterioration. (See Fig. 13-8) (Courtesy of Tufts Pathology Department.)

(Harrington et al 1983, Levine et al 1990).

g. In elderly patients when hypertension may or may not be present and when the location of the hemorrhage is lobar involving the superficial small and medium sized arteries rather than small deep penetrating branch vessel, a process of "amyloid angiopathy" has been identified. Deposits of amyloid occur in the media and adventitia of these vessels without the presence of systemic amyloidosis. (See discussion above and Finelli et al, 1984, Molinari, 1993).

The pathological features to be found with an intracerebral hemorrhage may be briefly summarized. The hematoma may continue to expand during the first three hours resulting in continued deterioration. Within a few hours of cessation of the hemorrhage, clotting occurs. In general with hypertensive hemorrhages, bleeding does not again occur into the same area. The blood is not quickly removed from the brain parenchyma. If this hemorrhage is actually a complication of infarction, then in the early stages, the changes of ischemic infarction will be noted with infiltration of adjacent ischemic tissue by polymorphonuclear leukocytes.

The actual clot of a hemorrhage will remain as a red or reddish black mass for a matter of several weeks. Macrophages that may have been already abundant in adjacent necrotic tissue begin to digest red blood cells at the periphery of the hemorrhage producing the yellow-brown iron pigment hemosiderin. At three weeks, this produces at the periphery, a rim of orange. The more central area of hemorrhage never undergoes phagocytosis but is converted to a semiliquid mass after several additional weeks or months.

When the brain is examined many months after a hemorrhage, there will be found a residual cleft or cavity with orange-stained walls. The staining is due to the persistence of hemosiderin-containing macrophages. The wall, in general, is similar to that surrounding the cavity, which results from an ischemic infarct. A proliferation of capillaries has occurred with the formation of connective tissue fibers. In adjacent tissue, proliferation of astrocytes has occurred with the formation of glial fibers.

The gross changes over time may be demonstrated with sequential MRI or CT scans *(Fig. 26-22, 26-23)*.

The clinical manifestations will depend on the location and size of the hemorrhage and are summarized in Table 26-4. In general with the most common variety - those into the putamen -there is the sudden onset of progressive headache, followed by progressive hemiparesis, and then within minutes to hours by hemianesthesia, confusion, and coma. The progression of symptoms is due to the progressive enlargement of the hematoma and to dissection of the hemorrhage along fiber pathways. Displacement of midline brain stem structures and tentorial herniation often occurs. With these brain stem complications and with extension of the hemorrhage into the ventricular system, a decerebrate state and a compromise of respiratory functions develop. Death occurs in a high percentage of such patients (75 per cent) within hours to days. Overall, 50% of patients with large hemorrhages expire. The prognosis for smaller hemorrhages is more favorable (21%). Prognosis is directly related to a) size of hematoma on CT scan and b) level of consciousness (Hier et al 1977,Broderick et al 1993). Patients with small hemorrhages may have only a minimal degree of disability since

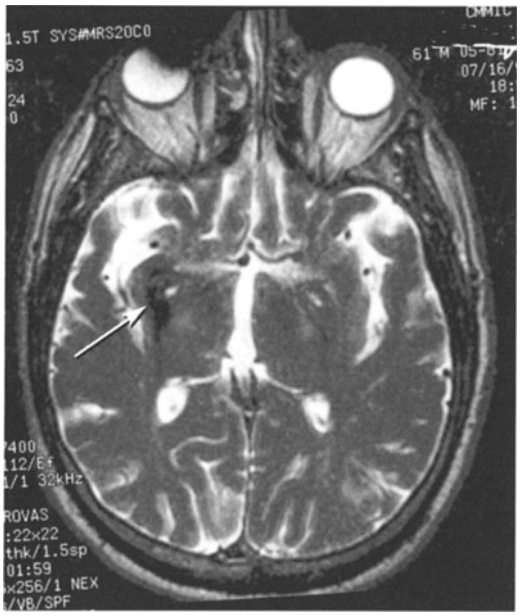

Figure 26-22. Resolving hematoma right putamen, hypodensity of a cystic cavity with residual hemosiderin and dystrophic calcification (arrow), on MRI T2, 16 months after the acute hemorrhage. This 61 year old right handed white male had the acute onset of a left hemiparesis, had an excellent recovery of leg function but continued to have severe spastic weakness in the left upper extremity with tonic neck effects, a hemiplegic gait, decreased pain sensation in left face and arm and a dressing apraxia left arm.

the hemorrhage displaces structures rather than destroying structures as in an infarct.

The diagnosis of intracerebral hemorrhage may be made on the basis of the sudden onset of symptoms. The onset occurs during a period of activity as opposed to the pattern for arteriosclerotic ischemic-occlusive disease where onset during sleep or shortly after awakening is more characteristic. Occasionally warning prodromal symptoms are present; such warning symptoms, however, are more characteristic of ischemic-occlusive disease.

In general, the cerebrospinal fluid is under increased pressure and usually but not invariably contains red blood cells. The number of such cells, however, is usually less than that found in subarachnoid hemorrhage.

At the present time, the major aids in diagnosis are the CT scan and the MRI scans. There is then no indication for lumbar puncture such a procedure in any case may be

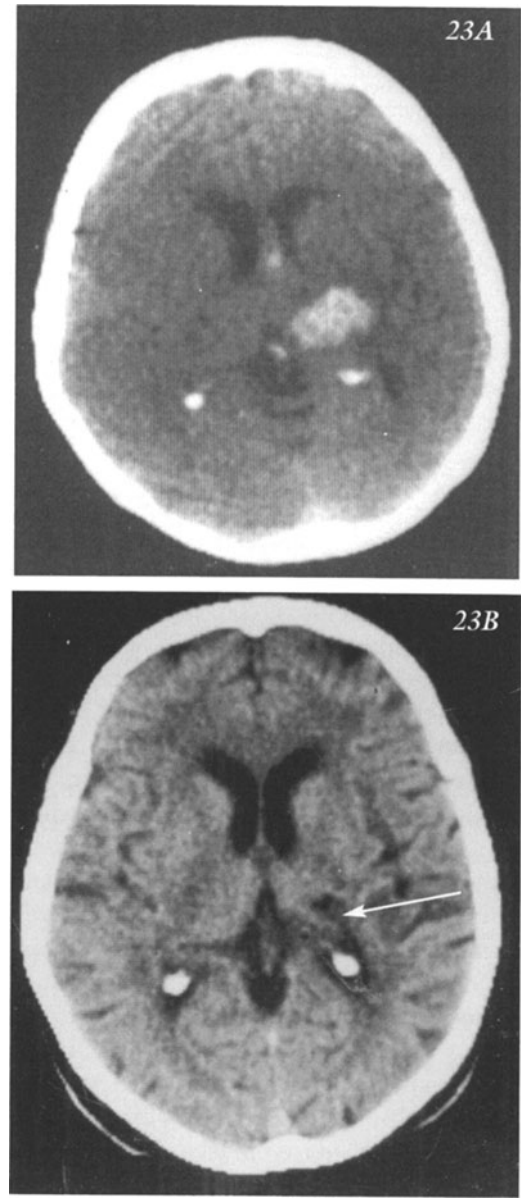

Figure 26-23. A) Acute hemorrhage left thalamus on CT Scan of a 72 year old woman with clinical findings of severe hypertension (210/130), dense right sided hemiparesis and sensory deficits plus fluent aphasia. B) Old cystic cavity (arrow) on CT Scan, 2.5 years later. She had significant sensory symptoms and cortical sensory deficits in right arm and leg, ataxia of gait, intention tremor of right hand and leg and occasional choreiform movements of the right hand.

dangerous when increased intracranial pressure is present.

As regards treatment, the deep location within the putamen, thalamus, and pons means

that surgical evacuation of these massive hemorrhages is not feasible. Moreover, with most large pontine hemorrhages, death rapidly ensues. With extension of hemorrhages of the putamen or thalamus into the ventricle, death usually occurs within a short time. However, expanding masses of more superficial lobar hematoma within temporal or parietal lobe, offer the possibility of surgical therapy. Cerebellar hematomas when diagnosed prior to brainstem compromise are often evacuated with a high degree of recovery. Qureshi et al (2001) have reviewed current approaches to management.

SUBARACHNOID HEMORRHAGE

The diagnosis of primary subarachnoid hemorrhage is made on the basis of gross blood present in the cerebrospinal fluid in the absence of primary intracerebral hemorrhage or trauma. Both of these conditions may have secondary leakage of some blood into the subarachnoid space. In 85% of cases of primary subarachnoid hemorrhage in the adult, the source of bleeding is a ruptured saccular aneurysm. (Refer to table 26-5). The basic pathology in the saccular or berry aneurysm is a defect in the media and internal elastic membrane of the vessel wall. Since the media of cerebral arteries develops in a multicentric manner, adjacent sections meet at arterial bifurcations where clefts or gaps in the media are common. These developmental defects in the media probably occur to some extent in all individuals. When later in life thinning or loss of the internal elastic membrane is superimposed at this point of defect, the thin layer of intima bulges out and is covered only by the loose connective tissue of the adventitia. The ballooned protrusion is referred to as a saccular aneurysm.

The unruptured saccular aneurysm is usually asymptomatic. Unruptured saccular aneurysms occur as an incidental finding in 1-2 percent of routine autopsies[6]. Most do not rupture and do not cause symptoms. Occasionally, however, symptoms may be noted prior to rupture. Thus, an enlarging aneurysm of the posterior communicating artery may compress the third nerve. At times an aneurysm of the cavernous portion of the carotid artery may invade the pituitary fossa or compress the optic chiasm (table 26-5) or rupture into the cavernous sinus. In general, the initial symptoms are those related to rupture. The usual symptoms are those of sudden severe headache, (the most severe ever experienced by the patient), vomiting, neck pain, and stiffness. The latter symptoms are due to meningeal irritation. Sudden straining, exercise, or sexual activity often precipitates the headache. In massive rupture, sudden onset of coma may occur. In a less severe bleed, consciousness is sometimes well preserved. Often no specific focal symptoms are present, and it may then be difficult to determine particularly in the comatose patient, on the basis of the clinical findings alone, the actual site of rupture. At times, the presence of minor focal signs will allow the localization of the aneurysm. Those cases where consciousness has been preserved and where few focal signs are present can of course be readily distinguished from cases of primary intracerebral hemorrhage. In intracerebral hemorrhage, secondary leakage of blood into the subarachnoid space may occur, but in the early stages although consciousness may be preserved or clouded well-developed focal signs are present, e.g., hemiparesis, hemianesthesia, hemianopsia, and quadriparesis.

At times in cases of ruptured aneurysm, significant focal or bilateral signs of cerebral involvement will be present. In some cases coma will be an early sign. In some of these cases extension of the hemorrhage into the substance of the cerebral hemisphere has

---

[6]*More recent large autopsy studies suggest an overall frequency of intracranial aneurysms of 5% with a population based incidence of subarachnoid hemorrhage secondary to aneurysms of 10 per 10,000 per year (see Phillips et al, 1980). Patients with autosomal dominant polycystic kidney disease or a family history are at increased risk for aneurysms and require noninvasive screening (Wiebers and Torres, 1992).*

TABLE 26-5: SUMMARY OF THE CAUSES OF SUBARACHNOID HEMORRHAGE (SAH), ANEURYSM LOCATION AND MANIFESTATIONS.

LOCATION OR TYPE	FREQUENCY ALL ANEURYSMS FIGURE #, CASE#	FREQUENCY AS CAUSE OF SAH	EARLY MANIFESTATIONS OR SYMPTOMS OF COMPRESSION PRIOR TO RUPTURE
I. ANEURYSMS		**85%**	**SUDDEN ONSET OF WORST EVER HEADACHE PLUS STIFF NECK**
Junction of post Communicating & internal carotid	30% Fig .26-24 Cases 12-1, 26-8 (On CD)		Third nerve paralysis since third cranial nerve runs close to and parallel to the posterior communicating artery
Bifurcation MCA	20% Fig.26-25 Case 26-9(CD)		Focal symptoms in MCA territory: focal weakness or seizure face, speech etc
Junction anterior communicating-anterior cerebral	30% Fig. 26-26, 26-27, 26-28 Case 26-10(CD)		Compression optic chiasm, or bilateral prefrontal or bilateral lower extremity or coma or mute state or if giant ,dementia. Often non localized SAH
Basilar vertebral system	5-10%		Variable
Multiple aneurysms	15%		Variable, usually only one is the site of SAH
II. OTHER SAH CAUSES		**15%**	
Perimesencephalic		10%	Non localized: worst headache, stiff neck, drowsiness (Fig. 26-29)
Other: AVM, mycotic aneurysms		5%	Variable depending on location (often distal cortical branches in mycotic). Seizures are frequent in both.

occurred. At times, rupture from the base of the brain into the third ventricle has occurred. At times, the vessel beyond the point of rupture has been deprived of blood, and infarction has occurred within its territory. Embolism from clot in the dome of the aneurysm may occur. At times, spasm of the artery distal to the point of aneurysm will occur, related perhaps to the presence of blood in the subarachnoid space. Such arterial spasm may produce sufficient vasoconstriction, apparently via adrenergic mechanisms, to result in ischemia and infarction.

Those red blood cells that have entered the subarachnoid space undergo a series of changes. Within a few hours, disruption of red blood cells has begun with a yellow discoloration (so called xanthochromia) of the spinal fluid. At this time oxyhemoglobin and methemoglobin may also be detected in the spinal fluid. After 48 hours, increasing amounts of bilirubin pigment may be noted with an increase in the degree of xanthochromia. The red blood cells have usually been completely disrupted by 10 days after the hemorrhage. The bilirubin product of this disruption disappears more slowly. The spinal fluid does not become colorless for 15 to 30 days after the hemorrhage. In tissues adjacent to the subarachnoid blood, hemosiderin-filled macrophages may be seen for several weeks after the acute episode of bleeding. Initially in the spinal fluid obtained by lumbar puncture, the ratio of white blood cells to red blood cells is the same as in the peripheral blood. With the passage of time, after the acute hemorrhage, as red blood cells are disrupted and as meningeal reaction occurs, a relative increase in white

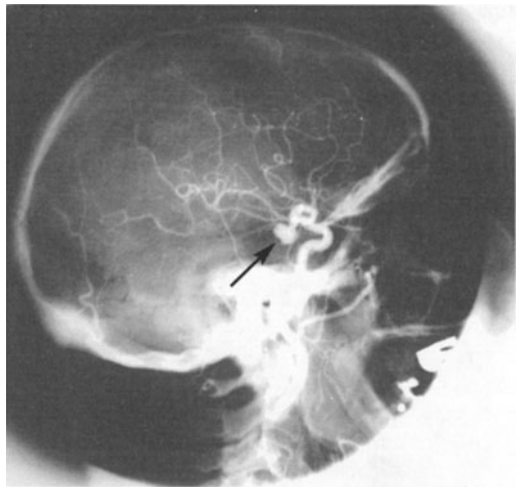

Figure 26-24. Saccular aneurysm, (arrow) arising from junction right internal carotid artery and posterior communicating artery demonstrated by right carotid arteriogram. This 70-year-old widow, 18 months previously, had the sudden onset of severe pain in the right eye and complete third nerve paralysis which had partially improved in the interim. (Courtesy of Dr. Samuel Wolpert.). (Compare to Fig. 26-7C and 2-27 for non-aneurysm reference).

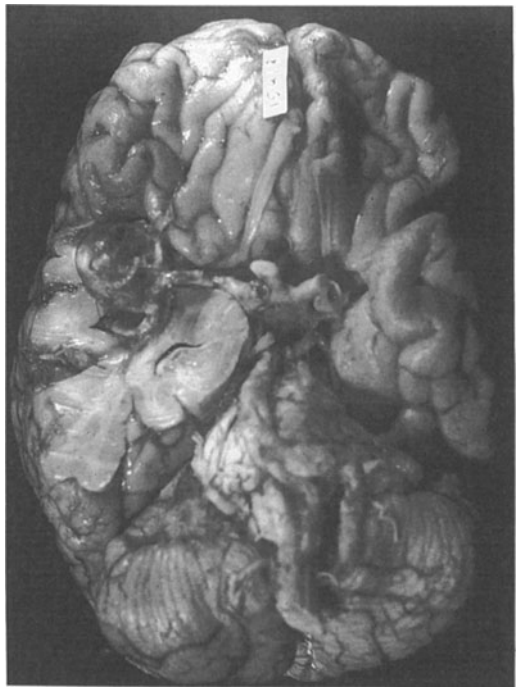

Figure 26-25. Giant aneurysm arising from the bifurcation of the right middle cerebral artery. (Courtesy of Dr. C. W. Watson.)

blood cells will be noted.

Evaluation and Management of the Patient with Subarachnoid Hemorrhage: Early recognition of subarachnoid hemorrhage is important since the overall mortality of ruptured aneurysms is at least 50% and the survivors have a significant morbidity. The recent reviews of Schievink (1997, and van Gijn & Rinkel (2001) are excellent sources of information. Prognostic factors include early recognition at the time of the initial hemorrhage, age, level of consciousness and neurological condition.

Patients presenting at the emergency room with the sudden onset of the worst headache ever should undergo an immediate CT scan searching for subarachnoid blood *(Fig. 26-29)*. The CT Scan will be negative in 5-10% of patients, usually those with a minor bleed and these patients should undergo a lumbar puncture searching for subarachnoid blood. If either of these studies demonstrates subarachnoid blood, then immediate angiography should be performed, followed by immediate surgery procedure designed to clip the aneurysm. Surgical therapy has as its primary objective the

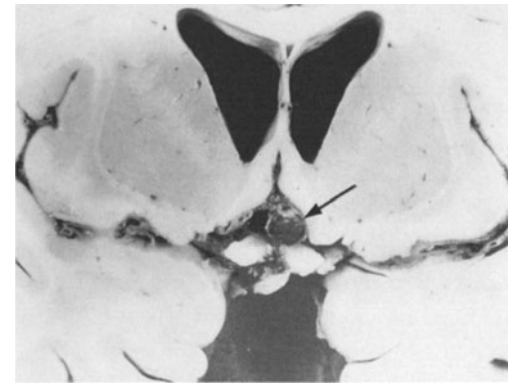

Figure 26-26. Saccular aneurysm at junction of anterior communicating and left anterior cerebral artery situated close to the optic chiasm. This 52-year-old, white male had the sudden onset one evening of headache, nausea, and vomiting. On examination, the next morning he was stuporous, inattentive, disoriented but could move all of his extremities, had bilateral Babinski sign and release of strong grasp reflexes plus. urinary and fecal incontinence. CSF had > 100,000 red blood cells per cu.mm; the supernatant fluid was xanthochromic. (Courtesy of Drs. John Hills, Dr. Jose Segarra)

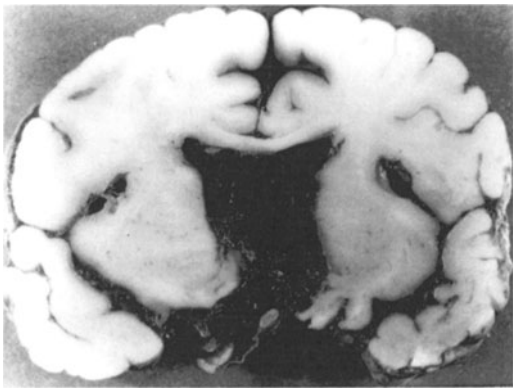

Figure 26-27. Saccular anterior communicating aneurysm with rupture into ventricular system. This 65-year-old white male, 14 days after a confirmed subarachnoid hemorrhage without definite localizing findings, had a generalized seizure followed by quadriplegia and coma. (Courtesy of Drs. John Hills, and Jose Segarra)

prevention of additional subarachnoid hemorrhage. Modern advances now under development include the use of spiral CT scan angiography or high resolution MRA. In some patients the direct clipping procedures are being replaced by endoscopic obliteration of the aneurysm. In patients who survive an initial bleed, a second bleed is associated with a very high mortality of 50%. Complications are summarized in Table 26-6.

In considering the matter of therapy, it is important to examine the mortality of the disease. In the study of Sacco et al 1984, one third of the 36 total cases were in coma at the onset and this group had a 30-day mortality of 83%. Two thirds were conscious at the onset with a 29% mortality at 30 days. Of this conscious group of 24 patients, 15 developed no deficits and 13 of 15 survived with a 30-day mortality of 13%. Of the 9 conscious patients who developed a delayed deficit, the mortality was 56%. The overall 30-day mortality was 47%.

Many patients (18%) die acutely and may never reach a neurosurgical center. In the Cooperative Study of Subarachnoid Hemorrhage (Locksley 1969), 27% of patients who reached a neurosurgical center died within the first week. Of patients dying within 72 hours, 90% had an associated intracerebral hemorrhage. Re-bleeding is a major cause of morbidity and mortality in these patients. Approximately 33% of patients re bleed in the first 30 days with a mortality of 42%. Most episodes of rebleeding occur within the first 14 days particularly between day 5 and day 9. However, rebleeding continues to occur even 10-20 years after the initial hemorrhage in patients not subjected to surgical therapy. In the series of Winn et al (1977), rebleeding in such patients was estimated at 3.5% per year during the first ten years with an associated mortality of 67%.

Although direct intracranial surgery was at one time attended by a considerable mortality and morbidity, major advances including microsurgery, neuroanesthesia with more effective control of blood pressure and

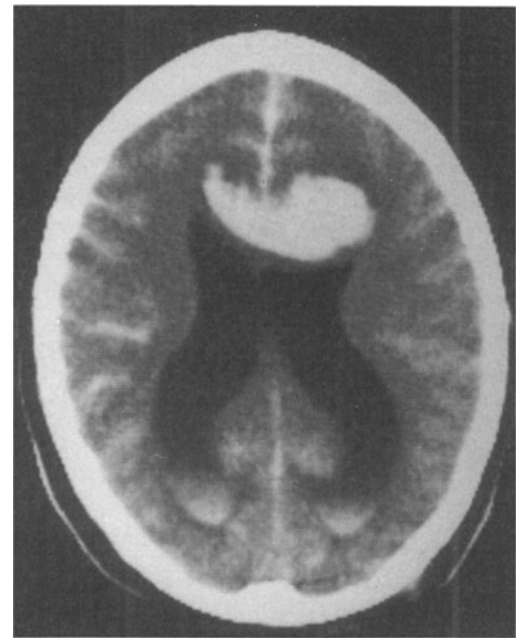

Figure 26-28. Aneurysm anterior communicating-anterior cerebral junction: Sub arachnoid and intracerebral hemorrhage with rupture into ventricular system and hydrocephalus. CT Scan (nonenhanced). This 51 year old male was found in a confused state and soon lapsed into unconsciousness with mild nuchal rigidity, miotic pupils, decerebrate movements on the left side, flaccidity on the right side and bilateral Babinski signs. He improved with osmotic shrinking agents (Mannitol), steroids, ventricular drainage, and subsequent clipping of the aneurysm, evacuation of clot and eventually a shunt procedure.

TABLE 26-6: COMPLICATIONS OF THE INITIAL HEMORRHAGE OR OF A SECOND HEMORRHAGE

COMPLICATION	PREVENTION OR TREATMENT
Recurrence of SAH	Prevent by immediate arteriography and clipping of aneurysm after initial SAH
Rupture into the ventricle with brain stem compression Massive SAH with tentorial and tonsillar herniation	Prognosis poor, coma then death, possible use of ventricular drainage and mannitol
Dissection into brain with hematoma formation	Evacuate hematoma and clip aneurysm to prevent herniation and rebleeding
Vasospasm secondary to aminergic substances in blood	Calcium channel blockers (Nimodipine) and increase blood pressure after clipping aneurysm to increase perfusion
Acute or chronic hydrocephalus due to blockage of cisterns, ventricles and subarachnoid space	For acute shunt after ventricular drainage For chronic shunt
Seizures	Treat with anticonvulsants: phenytoin or phenobarbital
Compressive effects of large and giant aneurysms	Clip and decompress aneurysm
Cardiac arrhythmias	Treat with pacemaker or appropriate anti-arrhythmia agents

intracranial pressure plus the use of CT scanning have resulted in a marked improvement in results (see Adams et al 1987, 1983, Biller et al 1988, Ohman and Heiskanen, 1989, Ropper and Zervas, 1984). The use of calcium channel blockers has decreased vasospasm-induced infarction.

Patient selection is of considerable importance and this is dependent on grading of the patient as regards level of consciousness and the presence or absence of focal neurological deficit. The Classification of Hunt and Hess, 1968, (Table 26-7) utilizes a 5-grade scale.

The World Federation of Neurological Surgeons grading scale is discussed by van Gijn and Rinkel (2001).

The Unruptured Intracranial Aneurysm: These aneurysms may be detected because of a) compression of cranial nerves, b) angiogram performed in patients with transient ischemic attacks, or ruptured aneurysm at another site c) the increasing use of CT and MRI scan (Ojemann, 1981, Wiebers et al 1981, and Zacks et al 1984). The most extensive study is the International Study of Unruptured Intracranial Aneurysms (Wiebers et al, 1998) demonstrating a clear-cut relationship of aneurysm size and risk of hemorrhage. Essentially those smaller than 10 mm in diameter on angiographic study at the time of diagnosis are unlikely to subsequently rupture, cumulative rate of rupture was less than 0.05 % per year. If the patient already had a repaired aneurysm at another site after subarachnoid hemorrhage the rate of rupture was 0.5% per year. For aneurysms of 10 mm or more in diameter, the rate of rupture approached 1.0 % per year for both types of patient the previously untreated and the previously treated at another site (about 20X-11 X the rate for the smaller aneurysms). The rate of rupture for giant aneurysms (> than 25mm in diameter) was 6% in the first year. Currently, MRI angiography can reliably detect unruptured aneurysms greater than 2-3 mm in diameter, although many earlier studies have utilized 5mm in diameter as the sensitivity cut off (see Wiebers and Torres). When two or more members of the same family have aneurysms, MRA of asymptomatic members should be considered.

NEUROLOGICCOMPLICATIONS OF BACTERIAL ENDOCARDITIS (see CD ROM for, case 26-11 and Figures 26-30, 26-31)

Osler in 1885 first recognized the neurological complications of endocarditis (association of fever, heart murmur and hemiplegia). The neurological effects of infections of the heart valves remain a major problem. Patients with rheumatic heart disease were once the

TABLE 26-7 HUNT AND HESS CLASSIFICATION-WITH CORRELATIONS

GRADE	DESCRIPTION	PROGNOSIS
1	Asymptomatic or minimal headache and slight nuchal rigidity	Excellent if early surgery
2	Moderate to severe headache and nuchal rigidity but no neurologic deficit	Excellent if early surgery
3	Drowsiness, confusion, or mild focal deficit	Excellent if early surgery
4	Stupor, moderate to severe hemiparesis, early decerebrate rigidity and vegetative disturbance	Poor unless on CT, treatable hydrocephalus or hematoma
5	Deep coma; decerebrate rigidity and moribund appearance.	Very poor unless as above

major patients at risk. At present, other major etiologic factors have emerged including intravenous drug addiction, prosthetic valves, and the use of various intravenous and intracardiac lines.

The streptococcus (particularly viridans) remains the predominant organism, although increasingly Staphylococcus aureus and fungi must also be considered. The overall incidence of neurological complication in large series from the Mass. General Hospital] amounts to 39% (Pruitt et al, 1978). In 16% of endocarditis patients, the neurological complication was the initial complaint. The development of neurological complications had a significant effect on prognosis. If neurological complications were present, mortality was 58%, if not present, 20%. The major neurological complications are summarized in table 26-8.

Durack (1995) discusses the prevention of infective endocarditis.

ARTERIOVENOUS MALFORMATIONS (Refer to CD ROM for Fig. 26-32, 26-33, 26-34 and case 26-12 in which a long standing seizure disorder was secondary to an AVM)

Included within this diagnostic category of vascular malformations are a variety of pathological entities, (based on frequency) such as 1) arteriovenous anomalies, 2) cavernous angiomas, 3) venous malformation, 4) telangiectasis 5) arteriovenous fistulas and 6) dual vascular malformations. All are congenital. (However, arteriovenous fistulas may occur with trauma e.g. carotid cavernous). In general these represent developmental (at times on a hereditary basis) tangles of abnormal vessels within the substance of the brain (less often involving meningeal vessels). These abnormal vessels provide arteriovenous shunting of blood. Since the vessels are abnormal with defects in their walls, bleeding into the substance of the brain (producing an intracerebral hematoma) or into the subarachnoid space

TABLE 26-8: NEUROLOGIC COMPLICATIONS OF BACTERIAL ENDOCARDITIS

COMPLICATION	FREQUENCY	MANIFESTATIONS
Cerebral embolism	17% (6-31%), 3% of all cerebral emboli	Usually MCA cortical territory or stem (see above)
Multiple micro-emboli	11%	Confusional state or personality change or seizures
Mycotic aneurysm	2-10% (2.5-6 % of all aneurysms)	Subarachnoid hemorrhage often more distal branches of the MCA
Intra cerebral hemorrhage	7-8%	Usually lenticulostriate
Meningitis	16%	In 50% of purulent usually staphylococ cus was identified
Brain abscess	Single large is not common	Usually multiple and microscopic- possible confusional state or seizure
Infection of vertebrae or disc space with compression syndromes	Not a common syndrome, although osteomyelitis may occur	Spinal cord or root compression

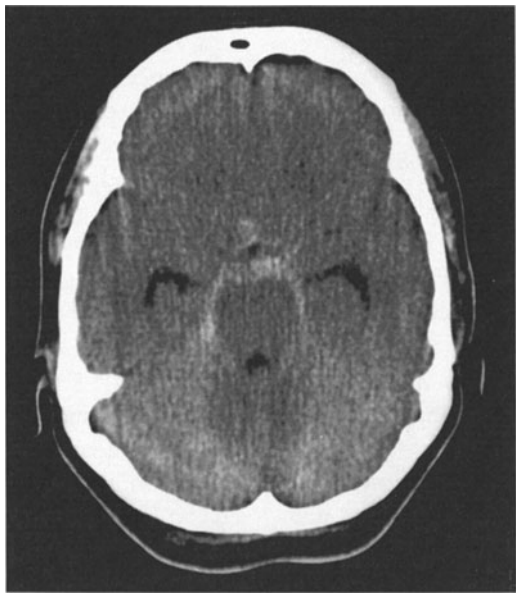

Figure 26-29. Perimesencephalic,unlocalized subarachnoid hemorrhage. Non enhanced CT scan demonstrating blood in the interpeduncular, prepontine, suprasellar and ambient cisterns. This 46 year old woman experienced the acute onset of "the worst headache in her life" lethargy and nuchal rigidity but had an otherwise normal neurological examination. Two series of angiograms and all hematologic studies were normal. She has done well over the subsequent 7 years.

may occur. Moreover, these abnormal vessels are also prone to occlusion with the development of local infarction of cerebral tissue .In general; these malformations produce symptoms earlier in life than do saccular aneurysms. They are moreover less often fatal. Thus several episodes of subarachnoid hemorrhage may occur without loss of life. The initial manifestations are as follows: seizures, often focal in 50%, intracerebral hemorrhage in 20 %, and subarachnoid hemorrhage in 20%. Although involving primarily the cerebral hemisphere, the brain stem, spinal cord or cerebellum may be involved.

DISORDERS OF VEINS AND SINUSES.

Cavernous sinus thrombosis or cortical vein thrombosis may occur in adults due to infection and has already been discussed. Occlusion of the superior sagittal and lateral and straight sinus is primarily a disease of the infant less than one month of age and reflects dehydration and other systemic and perinatal factors. Refer to the recent report of DeVeber et al (2001) for a more complete review.