VASCULAR LESIONS

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ISCHEMIA AND INFARCTION

Cerebrovascular disease

- Injury to the brain as a consequence of altered blood flow
- Ischemic and hemorrhagic etiologies.
- 0.4% of emergency department visits in the US are for cerebrovascular disease
- 47% of patients visiting an emergency department are hypertensive.

Ischemia

- Pathogenesis:
- Hypoperfusion (global)
- Vessel occlusion (focal)
- Embolism most common cause of occlusion
- Mural thrombus (left atrium)
- Carotid plaque
- Aortic valve
- Atheromata
- Fat emboli (following long bone fracture) "shower" the cerebrum
-

Ischemia

- Fat emboli
- Manifest generalized cerebral dysfunction with disturbances of higher cortical function and consciousness, often without localizing signs.
- Widespread hemorrhagic lesions involving the white matter are characteristic of embolization of bone marrow after trauma

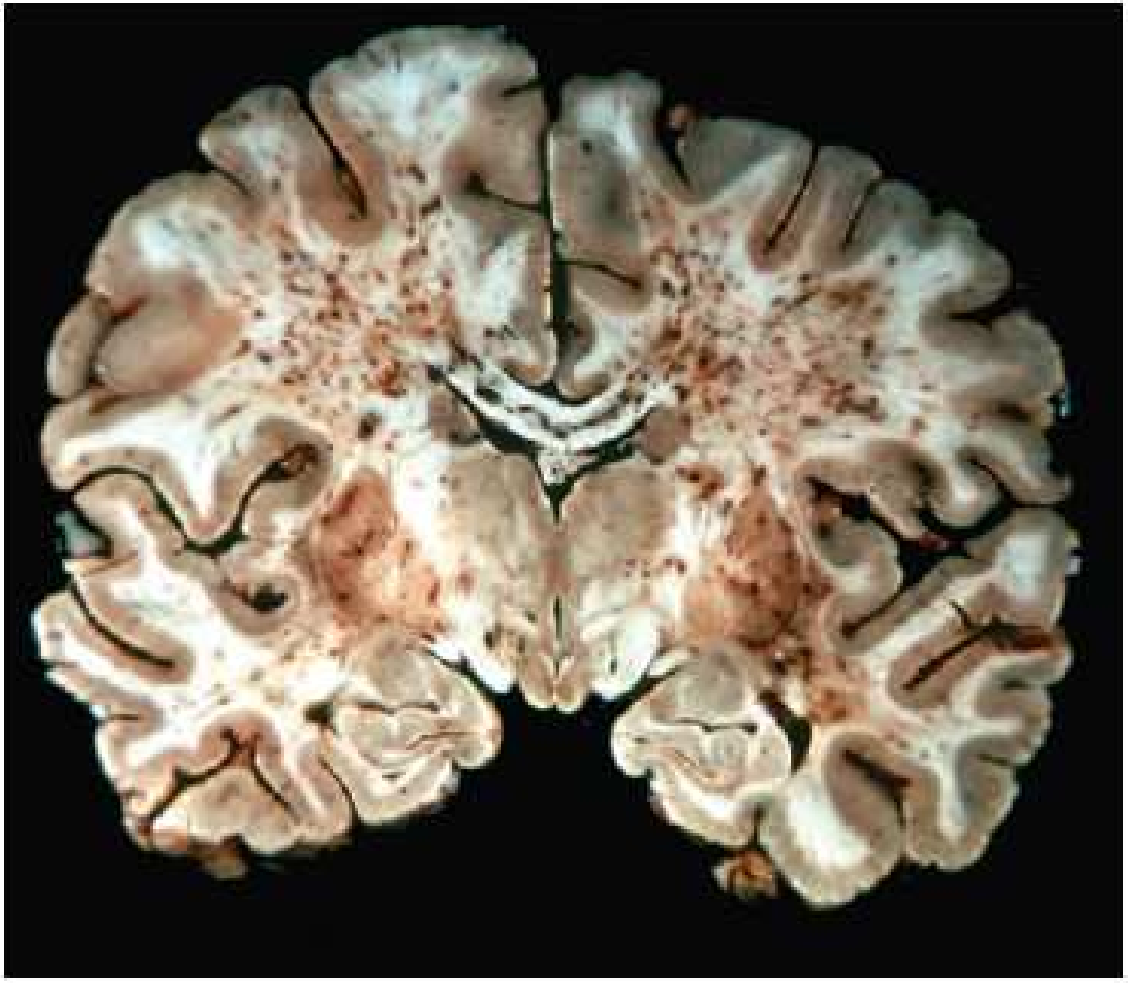


Figure 28-14 Widespread white-matter hemorrhages are characteristic of bone marrow embolization.

Ischemia

- Predisposing Factors:
- Myocardial infarction
- Aortic valve disease
- Atrial fibrillation
- Vasculitis
- Polyarteritis nodosa

Ischemia

- Gross pathology:
- The brain becomes edematous
- Gyri are widened and sulci narrowed in global injury
- Reduced cerebral perfusion
- Shock (may also lead to acute tubular necrosis)
- Cardiac arrest

Ischemia

- Cerebral O_2 stores lost within 20 seconds of the onset of cardiac arrest
- Glucose and ATP stores are lost by 5 minutes.
- <u>Areas most immediately threatened</u>
- Pyramidal cells in the Sommer sector (CA1) of the hippocampus
- Purkinje cells of the cerebellum
- Pyramidal cells of the cortex

Ischemia

- There is depletion of ATP and loss of the membrane potential that is essential for neuronal electrical activity.
- Accompanying this, there is elevation of cytoplasmic Ca^{2+} levels, which in turn activates a cascade of enzymatic processes that contribute to cellular injury.

Ischemia

- The metabolic depletion of energy associated with ischemia can result in inappropriate release of excitatory amino acid neurotransmitters such as glutamate
- Allow excessive influx of calcium ions through N-methyl-D-aspartate (NMDA)- type glutamate receptors.
- In the region of transition between necrotic tissue and the normal brain, there is an area of “at-risk” tissue, referred to as the penumbra.

Infarction

- The size, location, and shape of the infarct and the extent of tissue damage that results are influenced by the duration of the ischemia and the adequacy of collateral flow.
- The major source of collateral flow is the circle of Willis
- Supplemented by the external carotid-ophthalmic pathway.

Infarction

- Partial and inconstant reinforcement is available over the surface of the brain for the distal branches of the anterior, middle, and posterior cerebral arteries through cortical-leptomeningeal anastomoses.
- There is little if any collateral flow for the deep penetrating vessels supplying structures such as the thalamus, basal ganglia, and deep white matter.

Infarction

- Gross pathology:
- The first 6 hours
- There is little change in appearance
- By 48 hours
- The brain is pale, soft, and swollen
- Indistinct corticomedullary junction
- In a hemorrhagic infarction, blood is present
- Both ischemic and hemorrhagic infarcts follow similar temporal evolution.

Infarction

- From 2 to 10 days
- The brain becomes gelatinous and friable
- The boundary between normal and infarcted tissue becomes more distinct (edema resolves in the viable adjacent tissue).
- From 10 days to 3 weeks
- The infarcted area liquefies
- Fluid filled cavity that expands until damage cleared

Healing and repair

- Damage is largely irreversible after 12 hours
- Histopathology:
- First 12 hours
- Microvacuolization of neurons followed by eosinophilia of neuronal cytoplasm (“Red neurons”)
- Pyknosis and loss of nucleolus follow
- Neuronal bodies shrink
- Changes are seen somewhat later in astrocytes and oligodendrocytes.
- Myelinated fibers begin to disintegrate.

Healing and repair

- After 24 hours
- Infiltration with neutrophils
- Necrosis.
- Up to 48 hours
- Neutrophilic infiltration progressively increases and then falls off.
- Phagocytic cells are evident at 48 hours
- Derived from circulating monocytes and activated microglia
- Become the predominant cell type over time and may persist in the lesion for months or years
- Macrophages are filled with the products of myelin breakdown or blood

Healing and repair

- At 1 week after the insult
- Astrocytes at the edges of the lesion progressively enlarge, divide, and develop a prominent network of cytoplasmic extensions.
- After several months
- The astrocytic response recedes
- Left is a dense meshwork of glial fibers admixed with new capillaries and some perivascular connective tissue.
- In the cerebral cortex, the cavity is separated from the meninges and subarachnoid space by a gliotic layer of tissue derived from the molecular layer of the cortex. The pia and arachnoid are not affected.

Healing and repair

- After several months
- Subacute or chronic change
- Vascularization
- Gliosis
- Functionally related groups of neurons affected
- Loss of normally organized tissue
- Neuronal loss and gliosis lead to an uneven destruction in the cortex and produces a pattern of pseudolaminar necrosis.

Healing and repair

- Reactive and reparative stages proceed from the edges inward
- Not all areas of a lesion show the same features

- Hemorrhagic infarction
- blood extravasation and resorption are present

Ischemia and infarct

- In individuals receiving anticoagulant treatment, hemorrhagic infarcts may be associated with extensive intracerebral hematomas.
- Venous infarcts are often hemorrhagic
- May occur after thrombotic occlusion of the superior sagittal sinus or other sinuses
- May occur after occlusion of the deep cerebral veins

Infarction

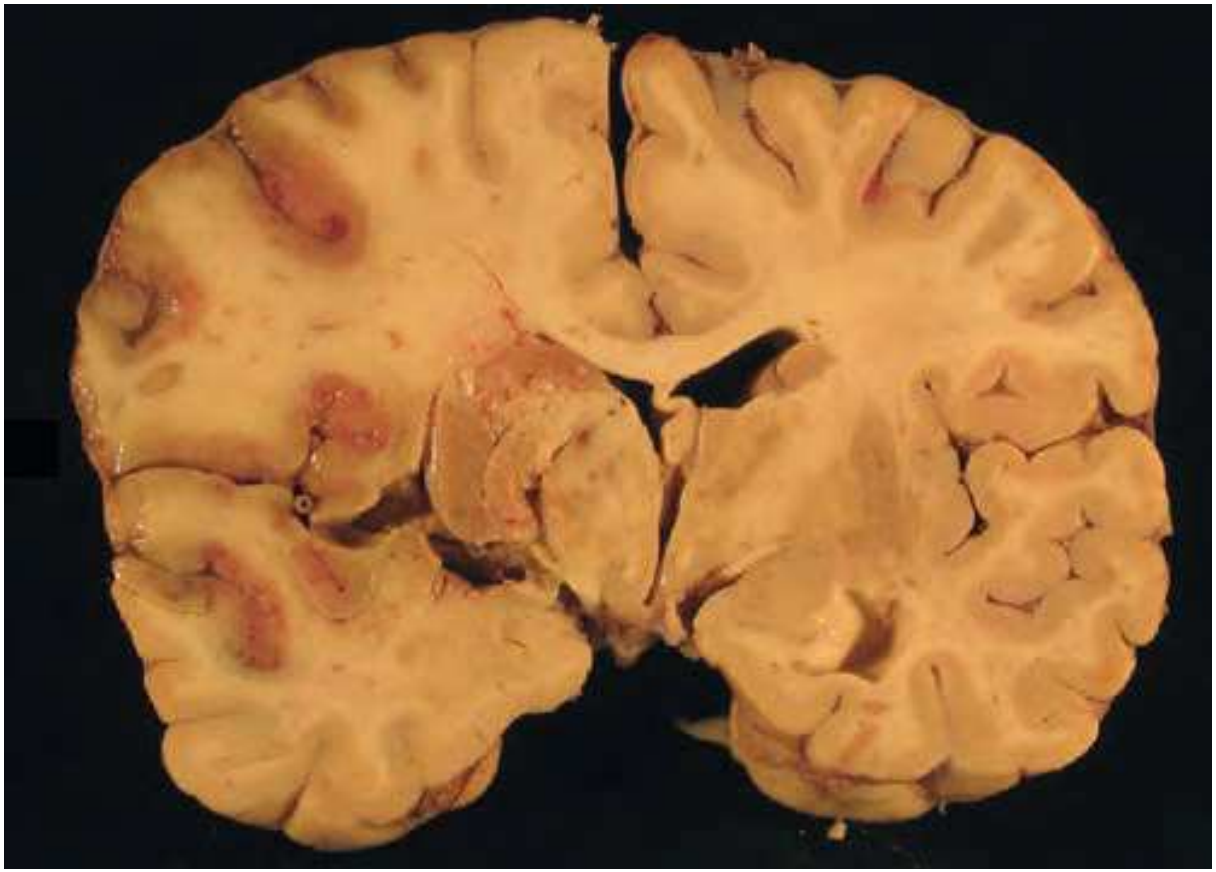
- Border zone (watershed) infarcts generally follow hypoperfusion
- Occur in watershed areas that are at the farthest distance from the arterial supply
- In the cerebral hemispheres, the border zone between the anterior and the middle cerebral artery distributions is at greatest risk.
- Damage to this region produces a sickle-shaped band of necrosis over the cerebral convexity a few centimeters lateral to the interhemispheric fissure.

Infarction

- Spinal cord infarction may be seen in the setting of hypoperfusion or as a consequence of traumatic interruption of the feeding tributaries derived from the aorta.
- Rarely, the cause is occlusion of the anterior spinal artery as a result of an embolus or vasculitis.

Hemorrhagic infarct

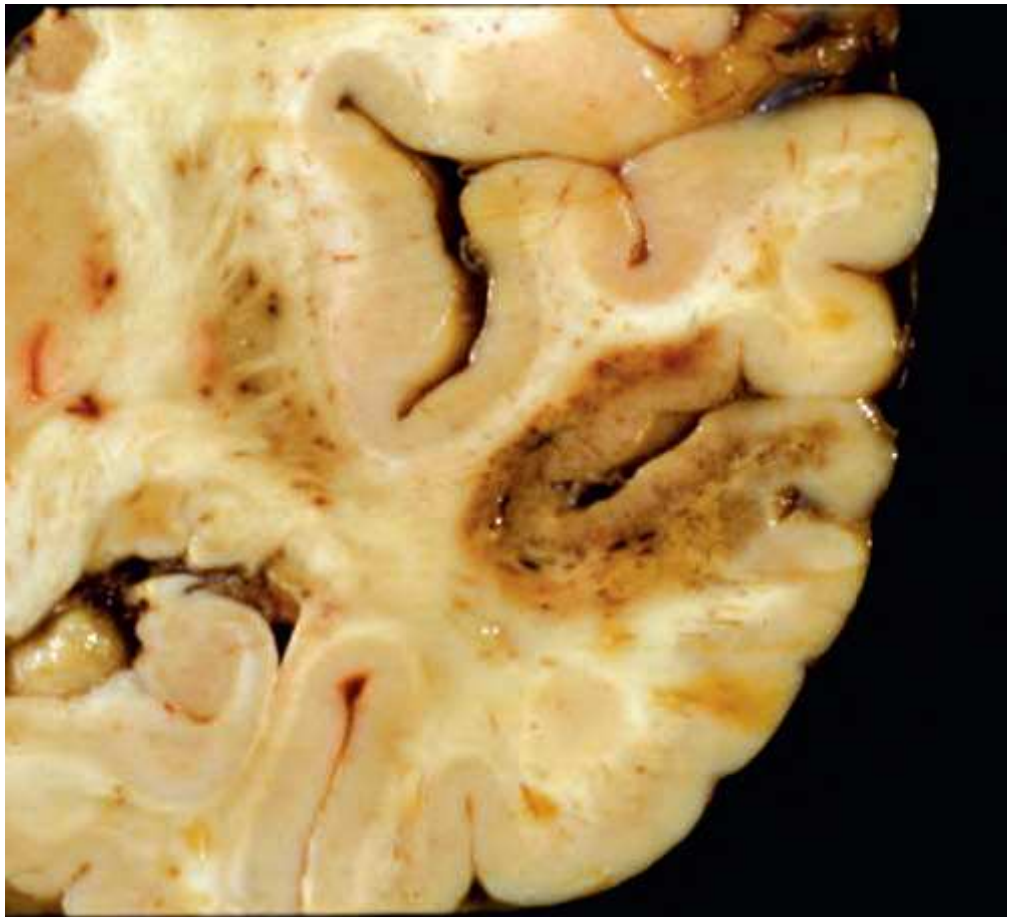
An ischemic infarction that involves the territory of the middle cerebral artery, including the striatum of the left side of this brain.



Frosch, MP, Anthony, DC, De Girolami, U, "The Central Nervous System," in Kumar, V, Abbas, AK, Aster, JC, (eds), Robbins and Cotran Pathologic Basis of Disease (9th ed.), Elsevier. Philadelphia. (2015) Fig. 28-9A Accessed 10/25/2019

Hemorrhagic infarct

A bland infarct with punctate hemorrhages, consistent with ischemia-reperfusion injury, is present in the temporal lobe.



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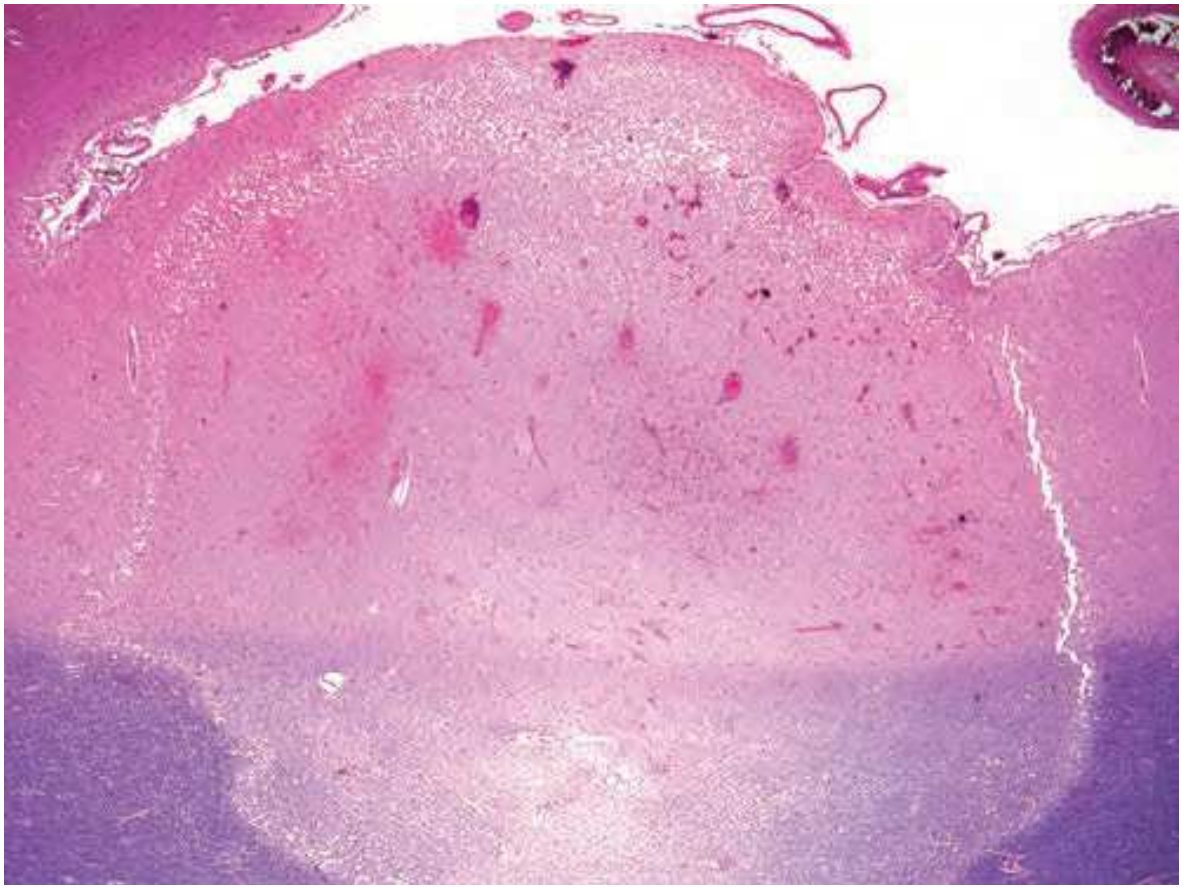
Cerebral infarction

At low magnification it is possible to see the demarcated areas of an acute infarction. In the underlying white matter, the areas of infarction are well shown by the myelin stain



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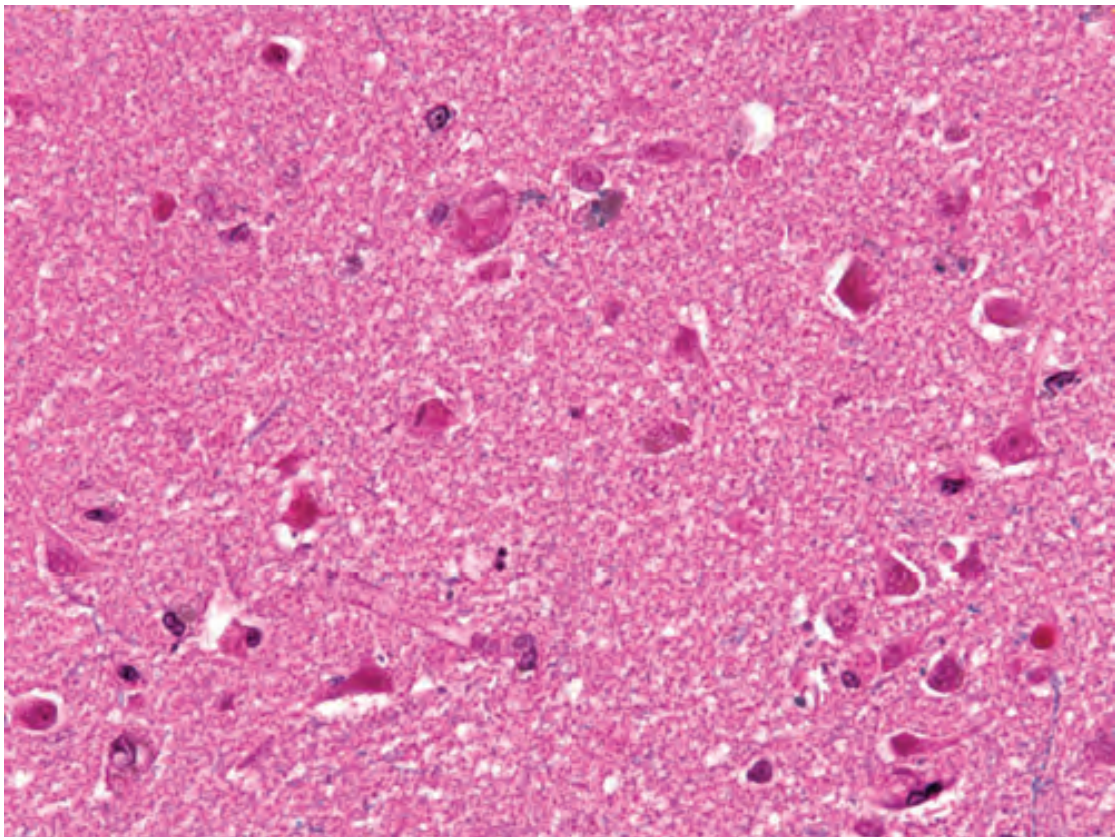
Cerebral infarction

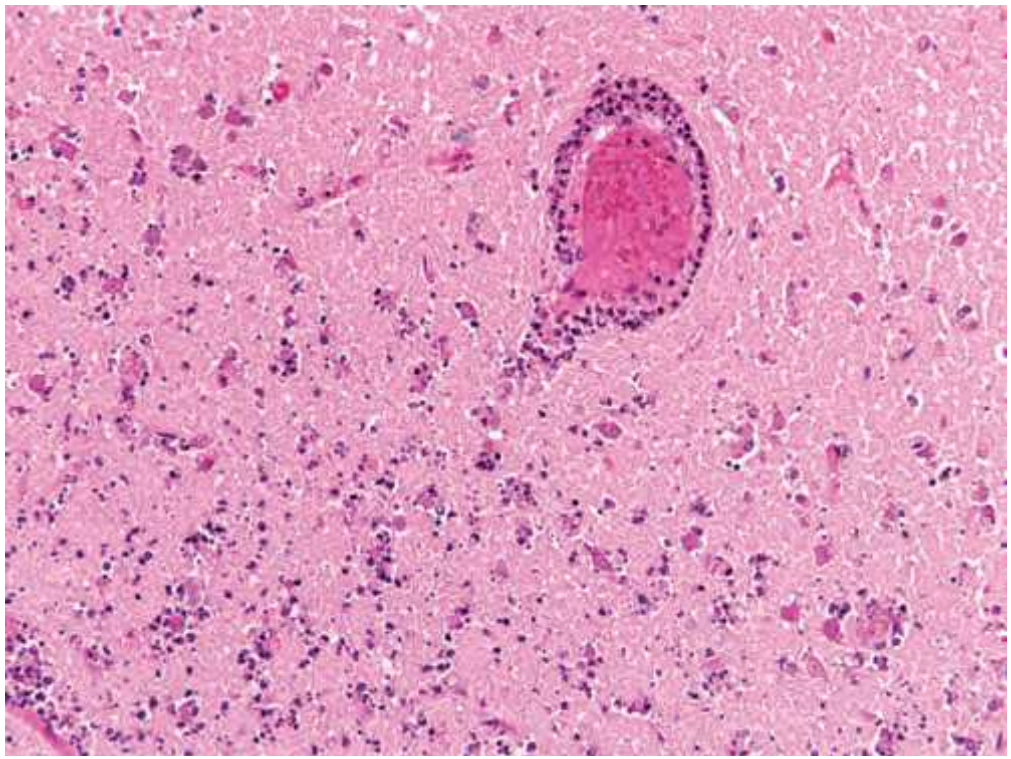
Acute ischemic injury causes diffuse eosinophilia of neurons, which are beginning to shrink.



Frosch, MP, Anthony, DC, De Girolami, U, “The Central Nervous System,” in Kumar, V, Abbas, AK, Aster, JC, (eds), Robbins and Cotran Pathologic Basis of Disease (9th ed.), Elsevier. Philadelphia. (2015) Fig. 28-13B Accessed 10/25/2019

Cerebral infarction

Neutrophil infiltration of infarct begins at edges of infarction where vascular supply has remained intact.



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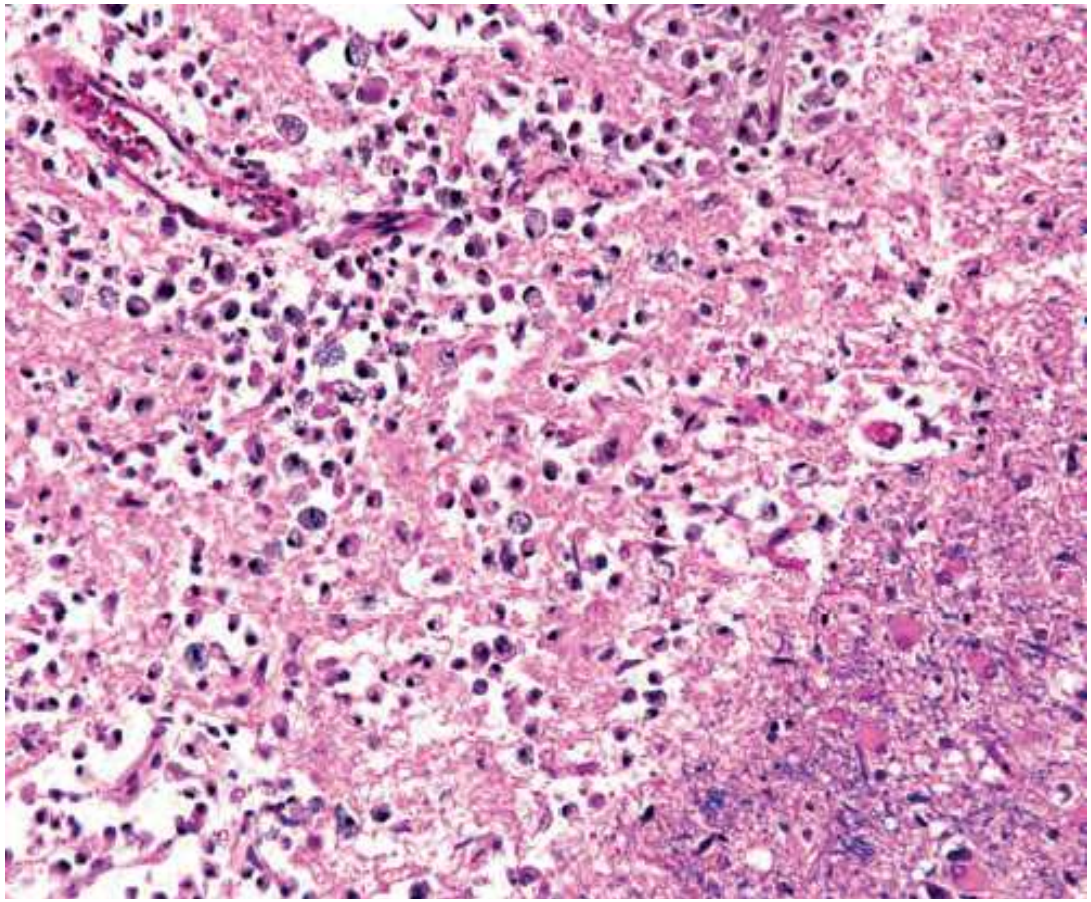
Cerebral infarction

After about 10 days, an area of infarction is characterized by the presence of macrophages and surrounding reactive gliosis.



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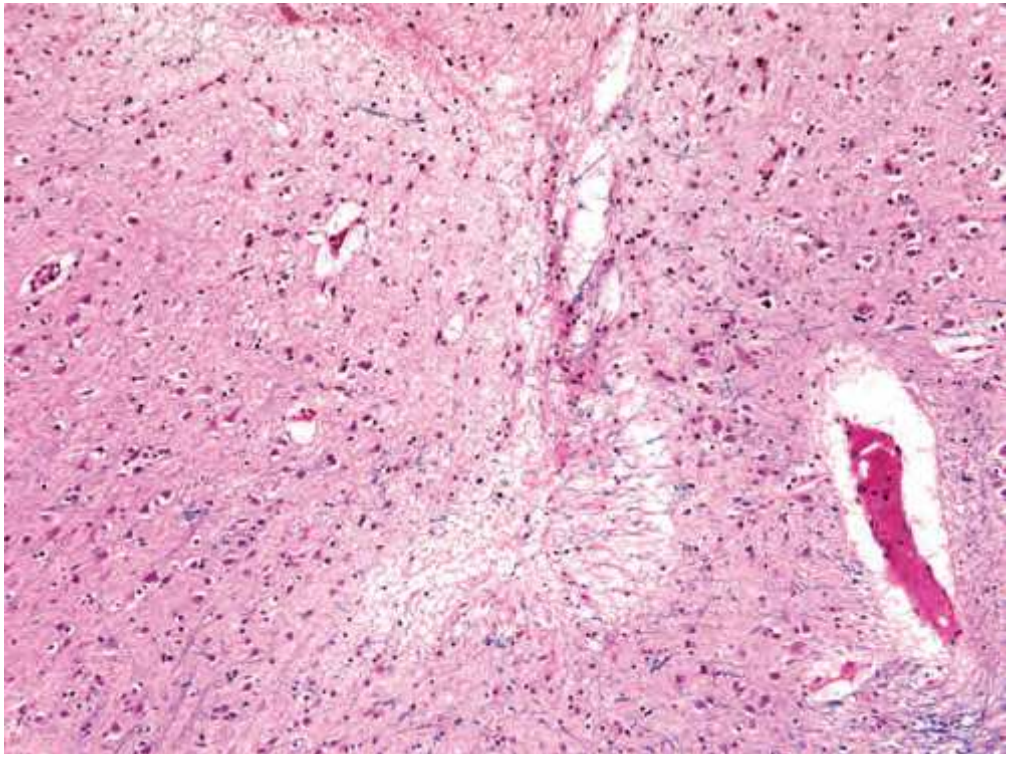
Cerebral infarction

Remote small intracortical infarcts are seen as areas of tissue loss with residual gliosis.



Frosch, MP, Anthony, DC, De Girolami, U, “The Central Nervous System,” in Kumar, V, Abbas, AK, Aster, JC, (eds), Robbins and Cotran Pathologic Basis of Disease (9th ed.), Elsevier. Philadelphia. (2015) Fig. 28-13D Accessed 10/25/2019

Infarction

- Hypertension accelerates arteriosclerotic changes in deep penetrating arteries and arterioles:
- The basal ganglia
- Hemispheric white matter
- Brainstem.
- These may occlude, producing single or multiple, small, cavitary infarcts (lacunae)
- Lacunar infarcts show tissue loss surrounded by gliosis and hemorrhages.

Lacunar infarcts

- These occur in (descending order of frequency):
- The lenticular nucleus
- Thalamus
- Internal capsule
- Deep white matter
- Caudate nucleus
- Pons

Infarction

- With rupture of the deep penetrating arteries and arterioles, small hemorrhages present.
- In time these hemorrhages resorb, leaving behind a slit-like cavity (slit hemorrhage) surrounded by brownish discoloration.
- On microscopic examination, slit hemorrhages show focal tissue destruction, pigment-laden macrophages, and gliosis.

Hypertensive encephalopathy

- Acute hypertensive encephalopathy is a clinicopathologic syndrome arising in the setting of malignant hypertension
- The most common clinical presentations of hypertensive emergencies are:
- Cerebral infarction (24.5%),
- Pulmonary edema (22.5%)
- Hypertensive encephalopathy (16.3%)
- Congestive heart failure(12%).

Hypertensive encephalopathy

- A patient with malignant hypertension always has retinal papilledema
- The pathologic hallmark of malignant hypertension is fibrinoid necrosis of the arterioles, which occurs systemically, but specifically in the kidneys.
- Patients with malignant hypertension have lower total cholesterol, LDL, and BMI values than do other hypertensives.
- However, the median estimated glomerular filtration rate is higher in the normotensive and hypertensive patients than in those with malignant hypertension.

Hypertensive emergency

- Hypertensive emergencies are characterized by severe hypertension (>180/120 mm Hg) in association with target organ dysfunction
- Median survival was 14 days for those with neurovascular emergencies and 50 days for those with cardiovascular emergencies
- The in-hospital and one-year mortality for those with hypertensive emergency are 13% and 39%, respectively.
- Those with preserved ejection fraction are treated differently than those with depressed ejection fraction

Multi-infarct dementia

- Vascular (multi-infarct) dementia, is caused by multifocal vascular disease of several types:
- (1) cerebral atherosclerosis
- (2) vessel thrombosis or embolization from carotid vessels or from the heart
- (3) cerebral arteriolar sclerosis from chronic hypertension.
- When the pattern of injury preferentially involves large areas of the subcortical white matter with myelin and axon loss, the disorder is referred to as Binswanger disease

Intracerebral bleeds

- Neurologic symptoms in hemorrhagic infarction increase gradually over minutes or a few hours.
- Subarachnoid hemorrhage develops in an instant.
- Focal brain dysfunction is less common and would suggest bleeding from an arteriovenous malformation.

Intracerebral bleeds

- Bleeding is usually derived from arterioles and small arteries.
- Bleeding is localized and spreads along white matter pathways.
- Hypertension accounts for >50% of clinically significant hemorrhages.
- 15% of chronic hypertensive deaths
- Putamen affected in up to 60% of cases.
- Thalamus and pons other common sites.
- Commonly designated “ganglionic hemorrhages”

Intracerebral bleeds

- The other major cause of bleeds in the basal ganglia is cerebral amyloid angiopathy.
- Most commonly associated with lobar hemorrhages (cerebral hemispheres)
- Associated with deposition of amyloid precursor proteins in the walls of medium and small-caliber meningeal and cortical vessels.
- Typically restricted to the leptomeningeal and cerebral cortical arterioles and capillaries, although involvement of the molecular layer of the cerebellum can be observed as well.

Intracerebral bleeds

- The presence of either the ε2 or ε4 allele of the ApoE gene is associated with an increased risk of rebleeding.
- Autosomal dominant form is associated with mutation in $A\beta_{40}$ peptide.

Intracerebral bleeds

- Other causes are:
- Trauma
- Bleeding disorder
- Hemophilia
- Platelet counts <10,000 fmol
- Cocaine or methamphetamine use
- Vascular malformation

Intracerebral bleeds

- Charcot-Bouchard (micro) aneurysms occur in small vessels, are a result of chronic hypertension, and occur principally in the basal ganglia.

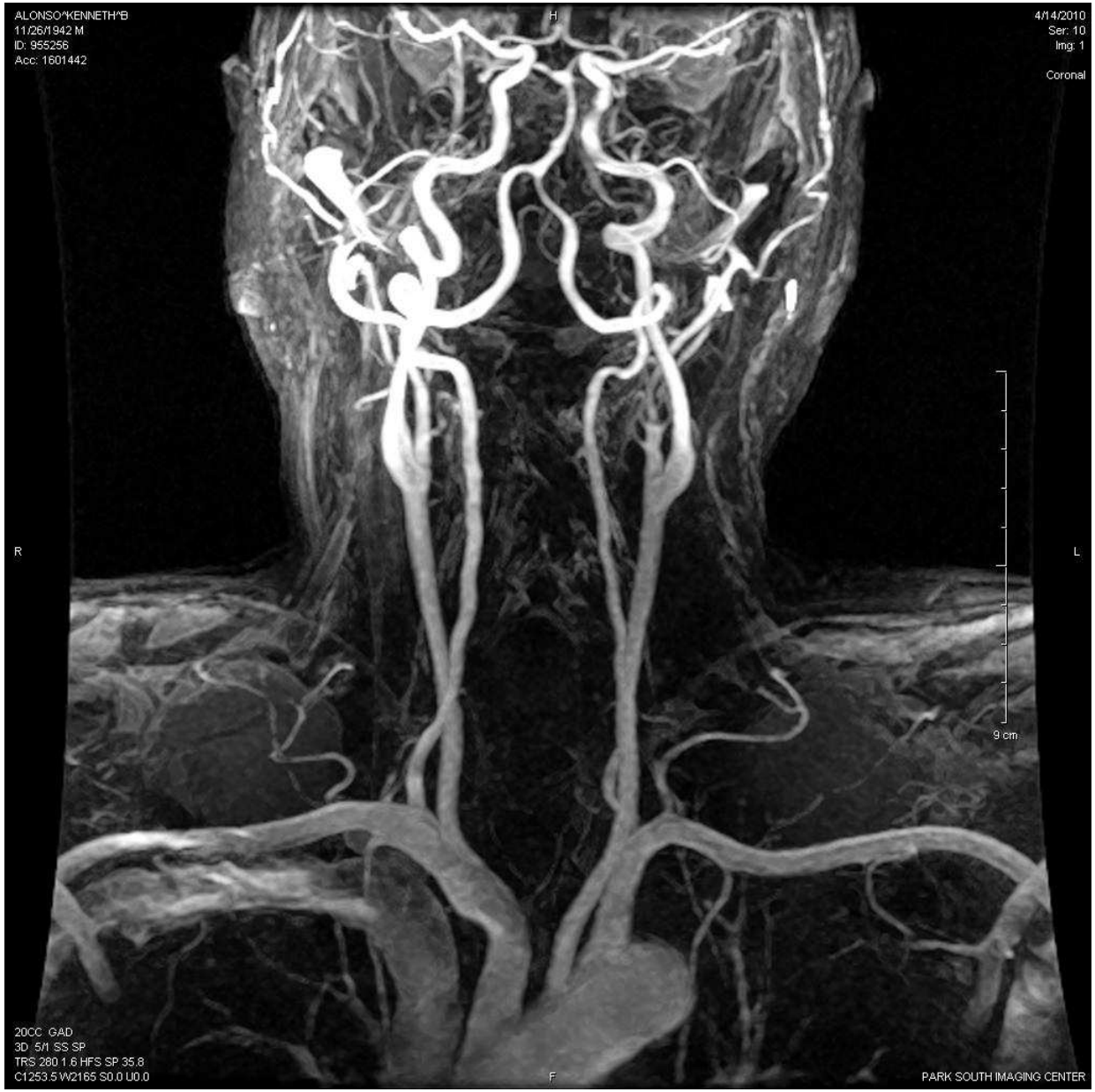
Intracerebral bleeds

- Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)
- Usual presentation at 35 years of age
- Involves leptomeningeal vessels and white matter
- Multiple infarcts
- Autosomal dominant disorder
- Concentric thickening of adventitia and media, loss of smooth muscle cells, and the presence of basophilic, PAS positive deposits (misfolded Notch 3 proteins).

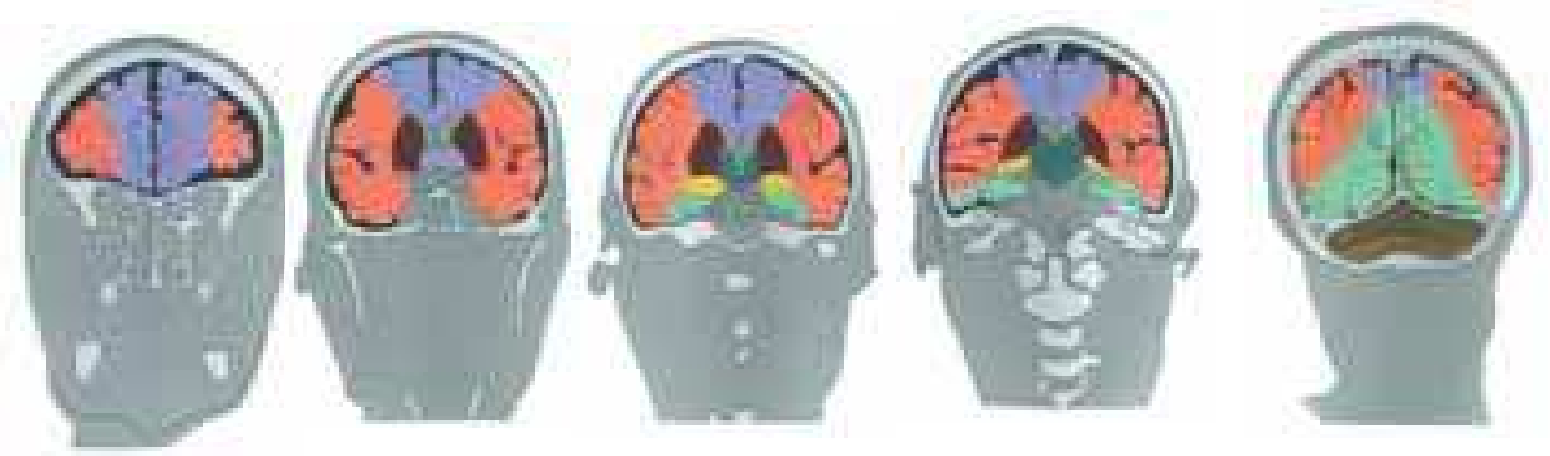
Intracerebral bleeds

- Mutations in the NOTCH3 gene lead to misfolding of the extracellular domain of the NOTCH3 receptor.
- NOTCH3 is preferentially expressed in vascular smooth muscle
- COL4A1 mutations also noted

MRI
Angiogram



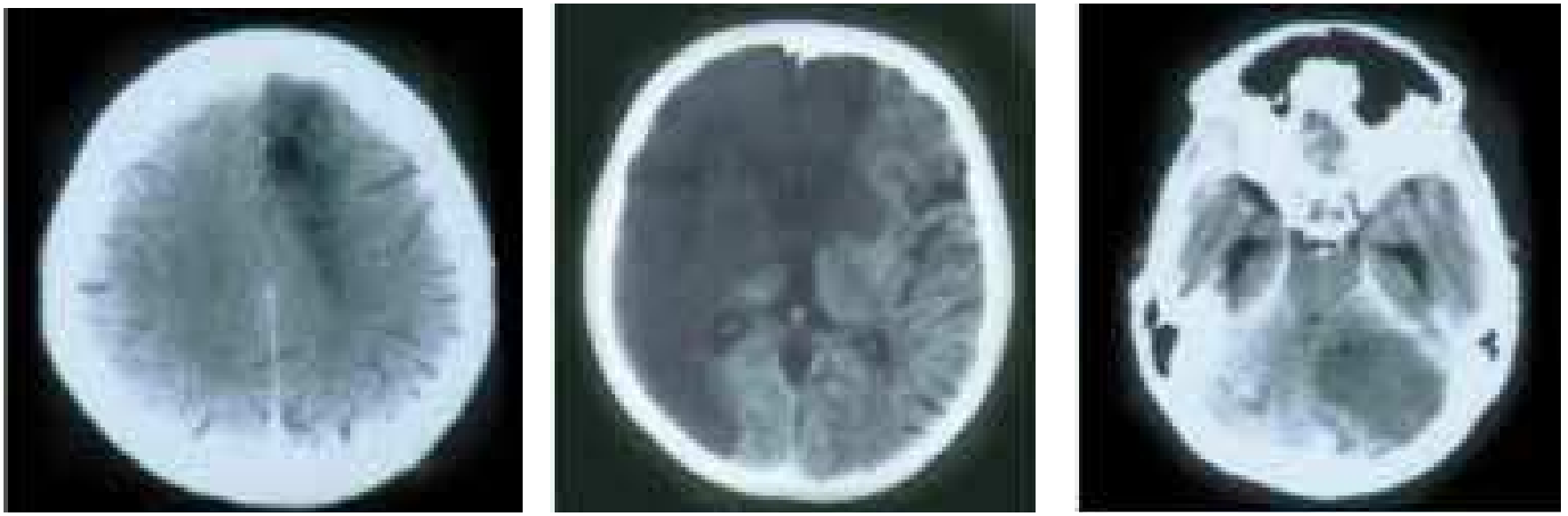
Regional arterial blood flow



Regional arterial blood flow as shown in frontal and coronal planes on CT.
Blue: anterior cerebral artery;
Red: middle cerebral artery;
Yellow: anterior choroidal artery;
Green: posterior cerebral artery;
Dark Brown: superior cerebellar and posterior inferior cerebellar artery

Rohkamm, R, Color Atlas of Neurology, Thieme. Stuttgart. 2004. p17 Accessed 11/08/2019

Causes of stroke infarction



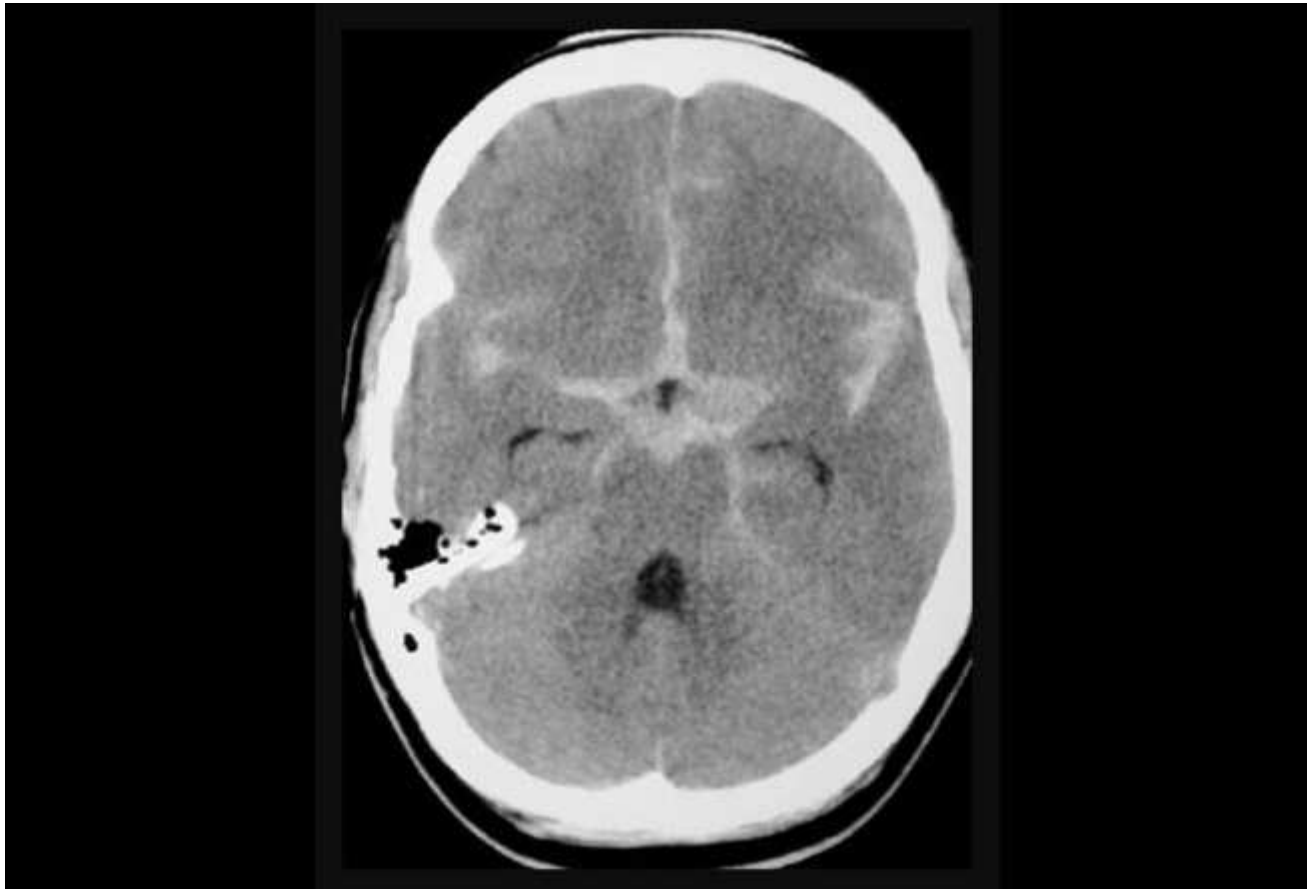
Dark areas are infarcted:
Left: Anterior cerebral artery, infarct;
Middle: anterior and middle cerebral arteries, infarct;
Right: posterior inferior cerebellar artery, infarct

Rohkamm, R, Color Atlas of Neurology, Thieme. Stuttgart. 2004. p167 Accessed 11/08/2019

Subarachnoid hemorrhage

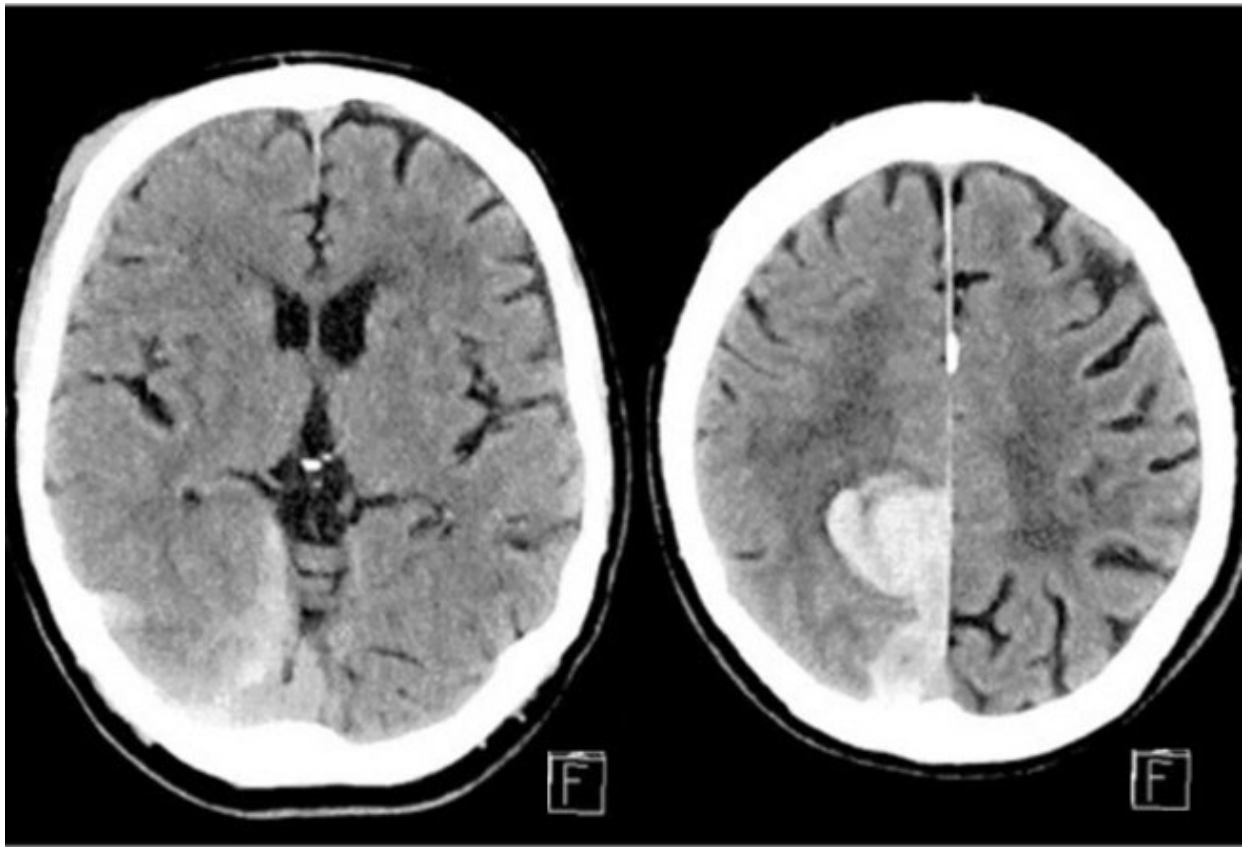
- Trauma is the most common cause
- 39% diagnosed with CT
- Arterial spasm may double mortality risk

Subarachnoid hemorrhage



https://reference.medscape.com/slideshow/traumatic-brain-injuries-6009819#13 Accessed 03/20/2020

Subarachnoid hemorrhage with subdural extension

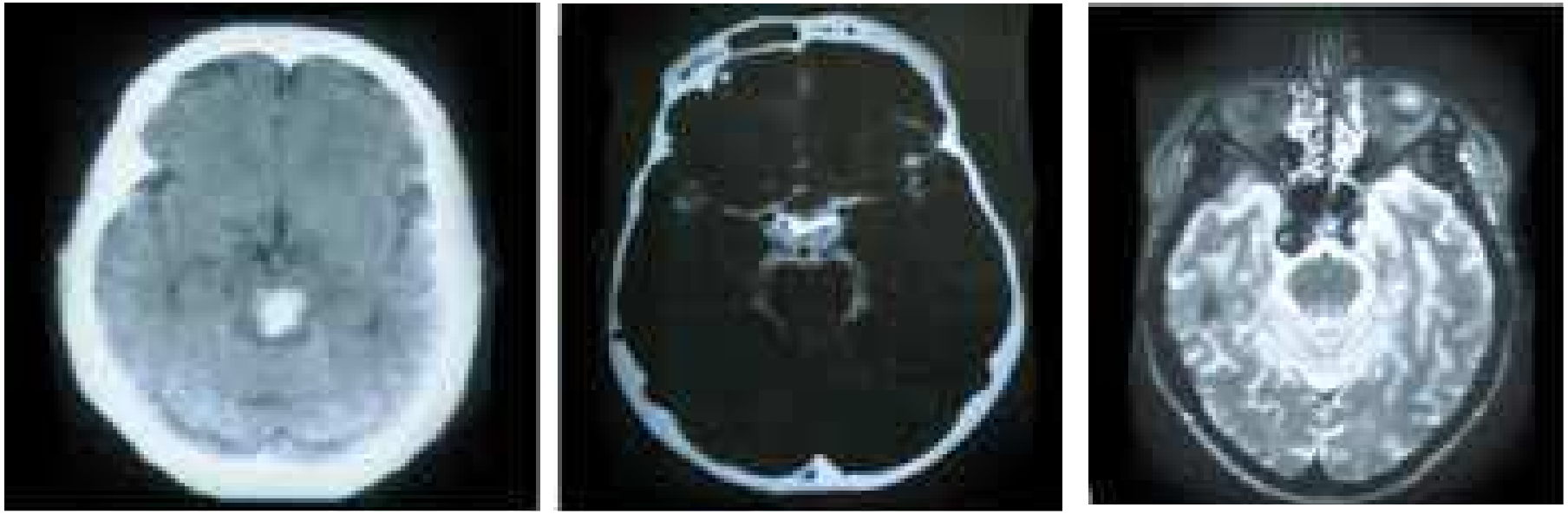


https://reference.medscape.com/slideshow/traumatic-brain-injuries-6009819#9 Accessed 03/20/2020

Major vascular lesions

Site	Vessels	Symptoms
Subarachnoid Hemorrhage	1. Junction of an Anterior Communicating Artery with an Anterior Cerebral Artery 40% 2. First bifurcation of a Middle Cerebral Artery in the Sylvian fissure 34% 3. Junction of a Posterior Communicating Artery with an Internal Carotid Artery 20%	Severe headache. 1. May only see decreased alertness or behavioral change 2. May see contralateral weakness and sensory loss, visual defects, language disturbance, or impaired spatial perception 3. Ipsilateral pupillary dilatation with loss of light reactivity

Intracerebral bleeds



Bright areas are fresh blood
Left: intracerebral hemorrhage;
Middle: subarachnoid hemorrhage;
Right: left internal carotid artery aneurysm

Rohkamm, R, Color Atlas of Neurology, Thieme. Stuttgart. 2004. p167 Accessed 11/08/2019

Subarachnoid hemorrhage

- Prevalence of aneurysms in general population is 4%
- Aneurysms < 1cm diameter rarely cause symptoms and rarely rupture.
- Aneurysms >1 cm diameter rupture at a rate of 0.5% per year.

Subarachnoid hemorrhage

- Saccular aneurysm is the most common type of intracranial aneurysm.
- The structural abnormality of the involved vessel (absence of smooth muscle and intimal elastic lamina) suggests that it represents a developmental disorder.
- Fusiform aneurysm is atherosclerotic
- Principally of the basilar artery

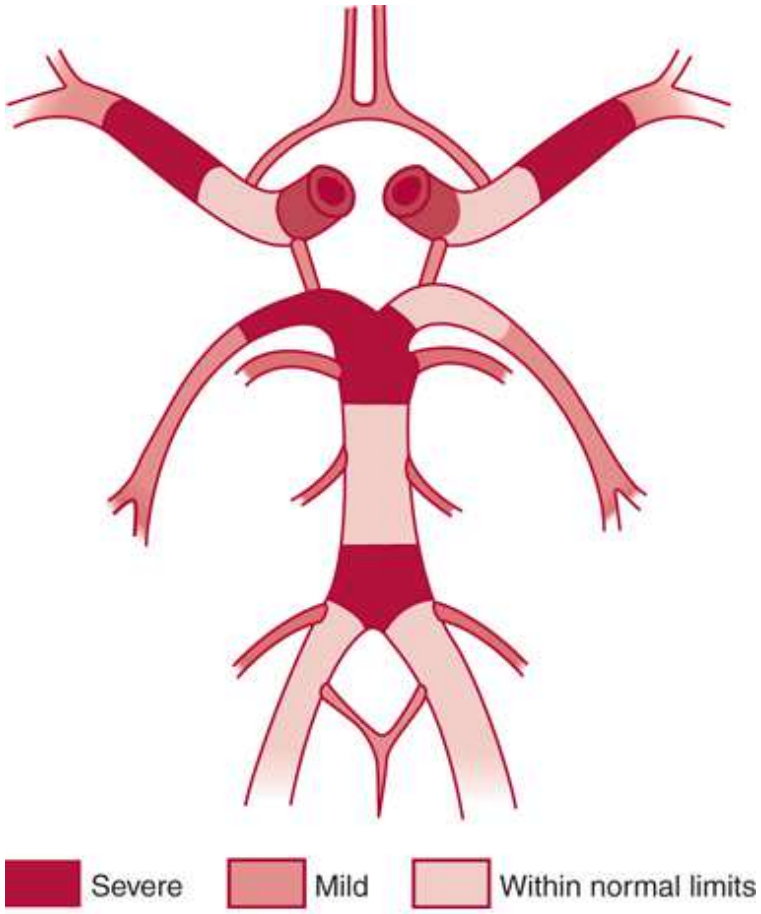
Subarachnoid hemorrhage

- 85% of subarachnoid hemorrhages are due to a rupture of a saccular aneurysm (“Berry”) in circle of Willis.
- Berry aneurysms in 2% of population.
- Increased risk in first degree relatives.
- Common sites:
- Junction of anterior communicating artery with anterior cerebral artery
- Junction of posterior communicating artery with the internal carotid artery
- Bifurcation of the middle cerebral artery.

Subarachnoid hemorrhage

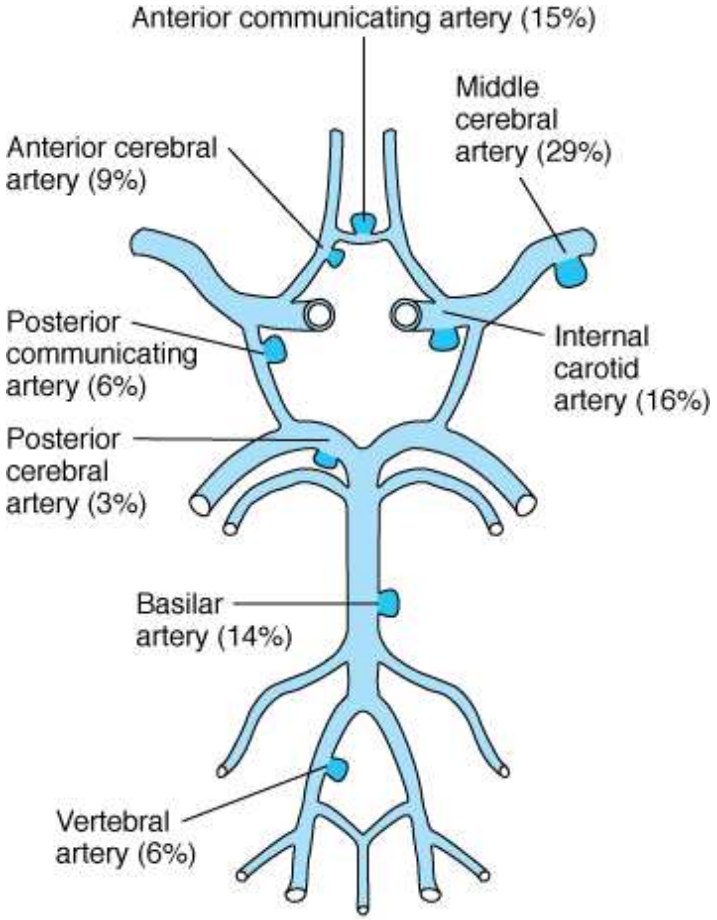
- Present with headache
- May be the worst headache one has ever experienced
- Stiff neck
- Change in mental status
- Fusiform aneurysm is found in the basilar artery.

Sites of plaque and aneurysm in the Circle of Willis



Source: Waxman SG: *Clinical Neuroanatomy, 26th Edition*: http://www.accessmedicine.com

Fig. 12-16 Accessed 07/01/2010



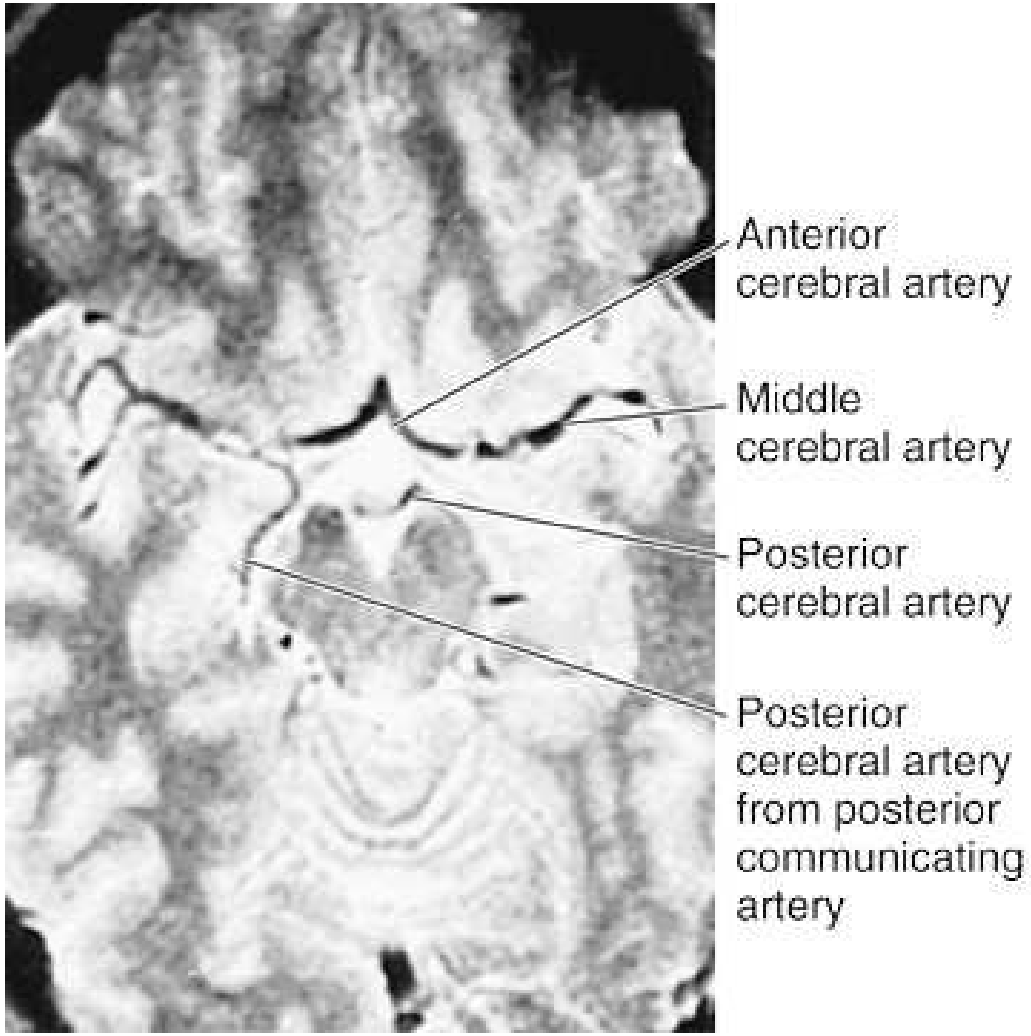
Source: Simon RP, Greenberg DA, Aminoff MJ: *Clinical Neurology, 7th Edition*: http://www.accessmedicine.com

Fig. 2-5 Accessed 07/01/2010

Atherosclerotic plaque

Lesion	Left (%)	Right (%)
Stenosis		
Brachiocephalic	—	4
Internal carotid (near bifurcation)	34	34
Anterior cerebral	3	3
Proximal vertebral	22	18
Distal vertebral	4	5
Occlusion		
Brachiocephalic	—	1
Internal carotid (near bifurcation)	8	8
Anterior cerebral	2	1
Posterior vertebral	5	4
Distal vertebral	3	3

Data from Hass WK, Fields WS, North RR, Kiercheff II, Chase NE: Joint study of extracranial arterial occlusion. JAMA *1968;203:961.*



Source: Waxman SG: *Clinical Neuroanatomy, 26th Edition*: http://www.accessmedicine.com

Figure 12-5 Accessed 07/01/2010

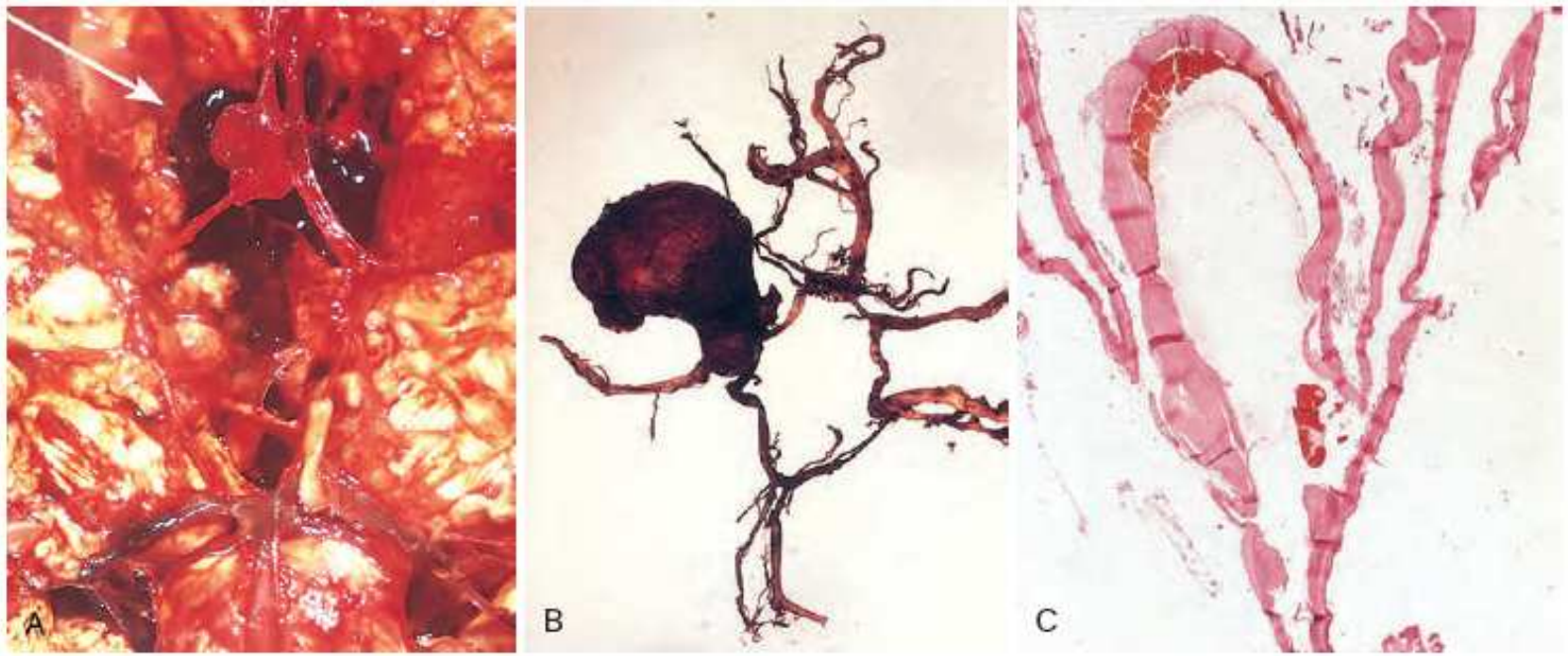


Figure 28-20 **A,** View of the base of the brain, dissected to show the circle of Willis with an aneurysm of the anterior cerebral artery *(arrow)*. **B,** Dissected circle of Willis to show large aneurysm. **C,** Section through a saccular aneurysm showing the hyalinized fibrous vessel wall (hematoxylin and eosin).

Arteriovenous malformation

- May involve vessels in the subarachnoid space, in the brain or both.
- A tangled network of wormlike vascular channels with prominent, pulsatile arteriovenous shunting with high blood flow.
- If involving vein of Galen, may lead to heart failure in newborn
- Composed of greatly enlarged blood vessels separated by gliotic tissue, often showing evidence of prior hemorrhage.

Arteriovenous malformation

- Some vessels can be recognized as arteries with duplication and fragmentation of the internal elastic lamina, while others show marked thickening or partial replacement of the media by hyalinized connective tissue
- Present usually between 10-30 years of age
- Seizure, subarachnoid or intracerebral hemorrhage

Cavernous malformation

- Distended, loosely organized vascular channels arranged back to back with collagenized walls of variable thickness.
- There is usually no brain parenchyma between vessels in this type of malformation.
- Low-flow channels
- May show calcifications
- Cerebellum, pons, subcortical regions
- Familial forms are autosomal dominant

Other vascular malformations

- Capillary telangiectasias are microscopic foci of dilated, thin-walled vascular channels separated by relatively normal brain parenchyma that occur most frequently in the pons.
- Venous angiomas (varices) consist of aggregates of ectatic venous channels
- Foix-Alajouanine disease (angiodysgenetic necrotizing myelopathy) is a venous angiomatous malformation of the spinal cord and overlying meninges, most often in the lumbosacral region, associated with ischemic injury to the spinal cord

Subarachnoid hemorrhage

- Non-contrast CT highly sensitive within first 12 hours
- Angiography is performed to assist in surgical plan
- Lumbar puncture deferred for 6-12 hours after the onset of a headache in a patient with a suspicious headache and a negative CT scan; then, xanthochromia in the cerebrospinal fluid is diagnostic

Subarachnoid hemorrhage

- Endovascular coiling preferred over surgical clipping for aneurysm repair in those >70 years of age
- OR Aneurysms of basilar apex
- Microclipping preferred for unruptured saccular aneurysms or ruptured middle cerebral artery aneurysms
- Or if large parenchymal hematoma
- Stenting of ruptured aneurysm is higher risk
- Consider urgent evacuation of hematoma if decreased consciousness and large intraparenchymal extension at time aneurysm is secured

Subarachnoid hemorrhage

- If aneurysm repair is delayed and there is increased risk of re-bleeding, consider short-term (< 72 hours) therapy with tranexamic acid or aminocaproic acid if not contraindicated
- After aneurysm repair, perform immediate cerebrovascular imaging to identify remnant or recurrence that may require treatment
- Begin oral nimodipine and continue 14-21 days if patient presents ≤ 96 hours after onset of hemorrhage and has adequate blood pressure
- Maintain circulating volume
- Elevate head 30º

Subarachnoid hemorrhage

- Complications following therapy include
- Cerebral vasospasm and ischemia
- Seizure
- Hydrocephalus
- Hyponatremia
- Neurogenic pulmonary edema
- Neurocardiogenic injury

STROKE

Stroke

- Thrombotic stroke may originate in large vessels.
- Carotid stenosis is a significant factor for large artery thrombotic stroke.
- Atherothrombosis is the most common pathologic process.
- Mural thrombus, valvular vegetations as other causes.
- Defects may wax and wane over days.

Carotid artery disease

- The prevalence of carotid artery stenosis varies from 0.5% in those <50 years of age to 10% in those >90 years of age.
- Transient ischemic attack or embolic event.
- A bruit over the vessel has a positive likelihood ratio (LR+) of 4.0 for stenosis >70% in that vessel.
- The absence of a bruit does not exclude carotid artery stenosis.
- Carotid endarterectomy in asymptomatic patients with >70% occlusion or in patients with 50% occlusion and a history of TIA or embolic events.

Stroke

- Small vessel disease refers specifically to penetrating arteries.
- They may thrombose due to atheroma formation at their origin or in the parent larger artery, or
- Due to lipohyalinosis (hypertensive change).
- Can result in small deep (lacunar) infarcts.
- Evolve over hours.

Stroke

- Embolic fragments originate in the heart or aorta.
- Transthoracic echocardiography with “bubble test” unlikely to demonstrate patent foramen ovale in stroke patient (paradoxical embolism)
- Defects are of sudden onset, may resolve.
- Systemic hypoperfusion may lead to ischemia.
- Blacks, Asians, and women have a lower incidence of occlusive disease of the extracranial carotid and vertebral arteries than do men of European origin.
- Hypertensive intracerebral hemorrhage is more common among Blacks or Asians.

Chronic kidney disease

- **Laboratory diagnosis**
- GFR <60ml/min/1.73m^2 BSA
- albumin (mg)/creatinine (g) <30 (urine)
- eGFR groupings
- >90, 60-89, 45-59, 30-44,<30 ml/min
- eGFR based on cystatin -creatinine calculation corrected for sex, age, race, BMI most accurate
- BMI lower than 25 or higher than 31 also associated with diminished GFR

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Stroke

- Headache is typically a feature of hemorrhagic strokes.
- Reduced alertness favors hemorrhage.
- Accompanying neurologic signs favor intracerebral hemorrhage.
- Vomiting is common in patients with intracerebral hemorrhage, subarachnoid hemorrhage, and vertebrobasilar artery ischemia.
- Loss of consciousness favors vertebrobasilar artery ischemia.

Stroke criteria

- 10% of strokes occur in young patients.
- In patients >45 years old, with no history of seizures, who is not wheelchair bound or bedridden, (and whose blood glucose is between 60-400 mg/dl), the sudden (<24 hours) presence (and persistence for more than minutes) of any one of the following is diagnostic of an acute stroke:

  Facial asymmetry (show teeth or smile)

  Arm drift (patient closes eyes and extends both arms straight out for 10 seconds with the palms up; one arm drifts down)

  Weak grip (unilateral) or alteration in speech

Stroke criteria

- Any of the three symptoms, facial paresis, arm drift, or abnormal speech has an positive likelihood ratio (LR+) of 5.2 for stroke in emergency patients without trauma or not in coma. The probability of a stroke is >10%.
- If all three are present, the LR+ is 14. If the neurologic deficits persist, the LR+ is 40.
- If none are present though onset is acute, the LR+ is 0.14.

Stroke criteria

- Two additional screening criteria are:
- Balance problems
- Eye (vision) difficulties
- Deficits that last less than 4 hours are classified as a TIA. However, many are silent infarcts.
- The lower the NIHSS score, the greater the probability of excellent recovery.

Stroke

- Cortical watershed strokes are located between the cortical territories of the anterior cerebral, middle cerebral, and posterior cerebral arteries.
- Internal watershed strokes are subcortical infarcts located in the white matter along and slightly above the lateral ventricle
- Between the deep and superficial arterial systems of the middle cerebral artery
- Between the superficial systems of the middle cerebral and anterior cerebral arteries
- 10% of all ischemic strokes
- Hypoperfusion as cause

Oxford classification of subtypes of cerebral infarction

- Total anterior circulation infarction syndrome:
- Higher cerebral dysfunction such as dysphasia, dyscalculia, visuospatial disorder; with
- Homonymous visual field defect; and
- Ipsilateral motor or sensory deficit of at least two areas (face, arm, leg)
- Reflects proximal occlusion of the internal carotid or trunk of the middle cerebral artery

Oxford classification of subtypes of cerebral infarction

- Partial anterior circulation infarction syndrome:
- If face deficit with contralateral lower extremity involvement, anterior cerebral artery involved
- If aphasia with contralateral hemiparesis, middle cerebral artery involved
- Lacunar infarction syndrome:
- Pure motor stroke (internal capsule)
- Pure sensory stroke (thalamus)
- Sensorimotor stroke, or cerebellar dysfunction with ipsilateral long-tract deficit (ataxic hemiparesis) reflects infarct in pons

Oxford classification of subtypes of cerebral infarction

- Posterior circulation infarction syndrome:
- Any ipsilateral cranial nerve palsy with contralateral motor or sensory deficit, or
- Bilateral motor or sensory deficit, or
- Disorder of conjugate eye movement; or
- Cerebellar dysfunction without ipsilateral long-tract deficit; or
- Isolated homonymous visual field defect
- Reflects vertebrobasilar distribution stroke

Site involved

- Cerebrum: White matter

  “Long Tract” disorders of motor, sensory, visual, or cerebellar pathways
- Cerebellum:
- Ataxia, dysarthria, nystagmus, dysmetria, scanning speech, tremor

Site involved

- Brain stem:

  CN III-IV: midbrain

  CN V-VIII: pons

  CN IX-XII: medulla

  Crossed weakness if before decussation

- Spinal cord:

  Mixed upper and lower motor neuron changes; weakness sparing head

Pupil signs in stroke

- Pinpoint pupils (pons)
- Poorly reactive pupils (thalamus)
- Dilated pupils (putamen)

Speech

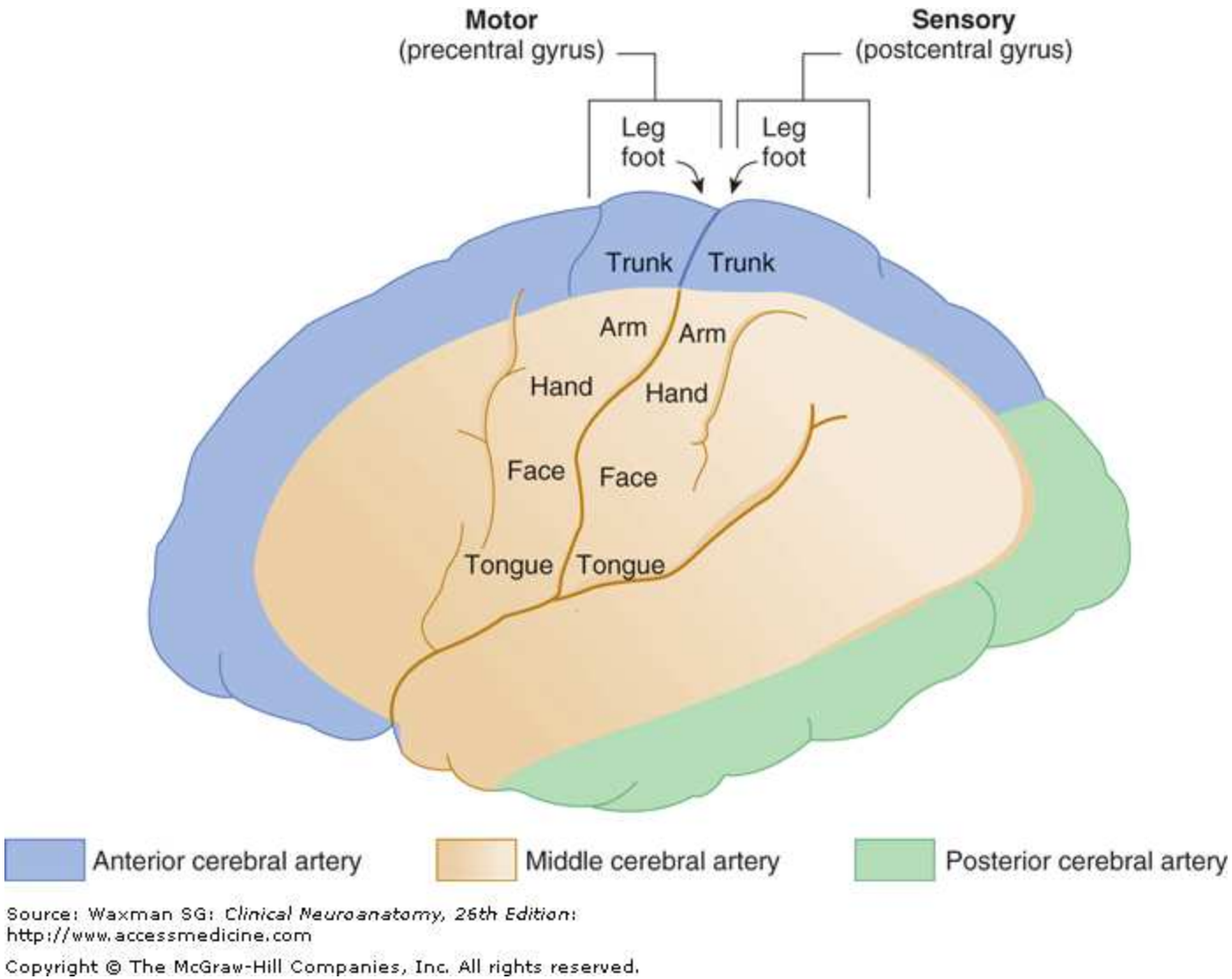
- Aphasia implies cortical dysfunction
- How did the problem begin?
- Global aphasia: “Uh..well..umm..like”
- Expressive aphasia: “1..2..days..bed”
- Receptive aphasia (phonemic paraphrasia): “When whence beside bespoke”
- Conductive aphasia: “Started..well..started”
- Broca aphasia results in deficits of speech and writing
- Dysarthria implies motor dysfunction

Speech

- Peripheral lesions are associated with slurred speech, dyspnea, hoarseness, or whispering. May "speak through nose".
- Cerebellar lesions associated with clipped, scanning speech.
- Basal ganglia lesions are associated with monotonous, soft, slurred speech. May see explosive, loud, uncoordinated, clipped speech, however.
- Slurred, effortful, slow speech is seen with metabolic disturbances.
- Monotonous, slow, hoarse, pressured speech is seen with white matter lesions. Deep, variable pitch.

Motor cortex lesions

- Irritative lesions
- May cause seizures that begin as focal twitching and spread (in a somatotopic manner, reflecting the organization of the homunculus) to involve large muscle groups (Jacksonian epilepsy).
- There may also be modification of consciousness and post-convulsive weakness or paralysis.
- Destructive lesions of the motor cortex (area 4)
- Produce contra-lateral flaccid paresis, or paralysis, of affected muscle groups.
- Spasticity is more apt to occur if area 6 is also ablated.



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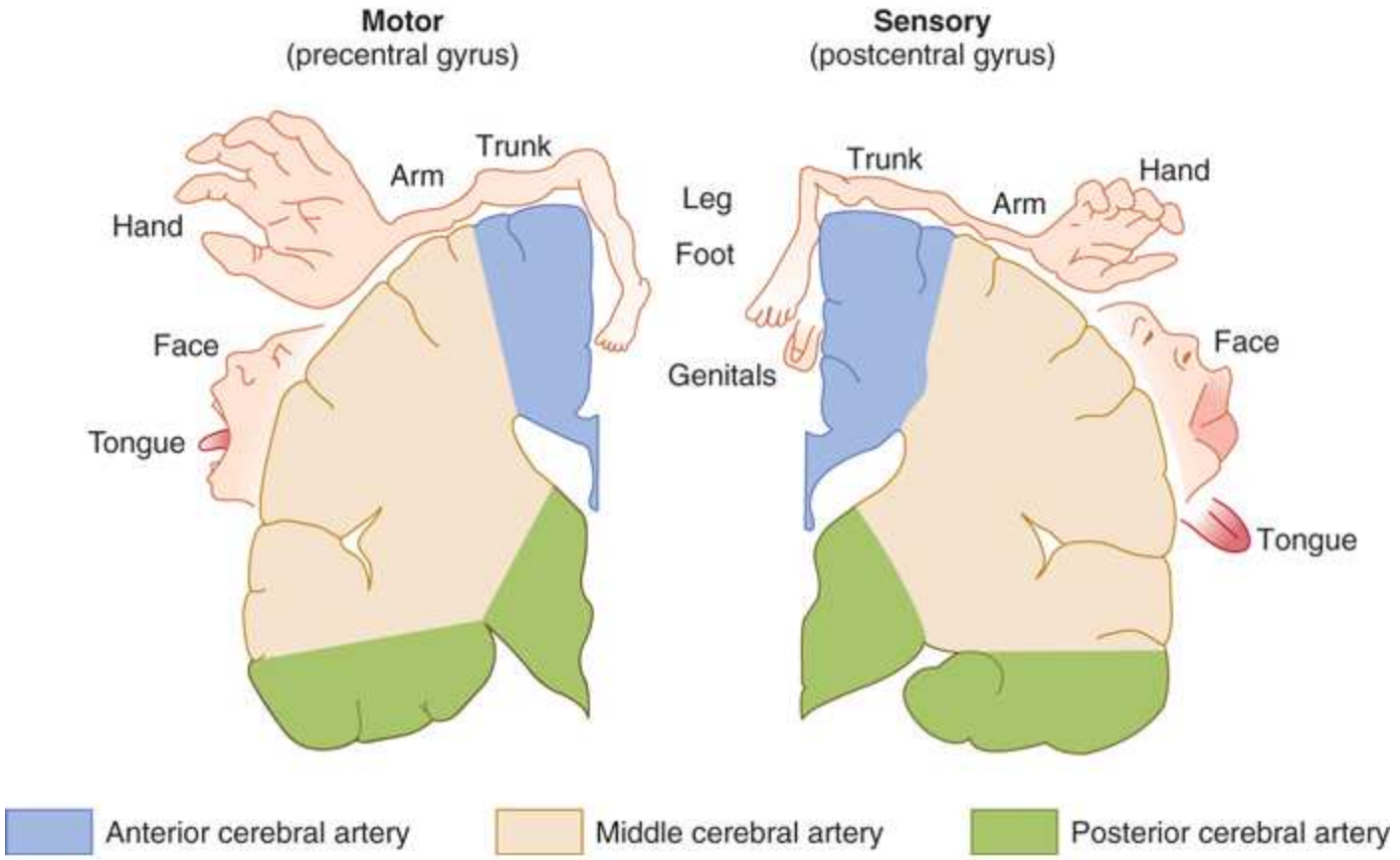

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Sensory cortex lesions

- Irritative lesions
- Paresthesias on the opposite side of the body.
- Destructive lesions
- Produce subjective and objective impairments in sensibility:
- Impaired ability to localize or measure the intensity of painful stimuli
- Impaired perception of various forms of cutaneous sensation.
- Complete anesthesia on a cortical basis is rare.

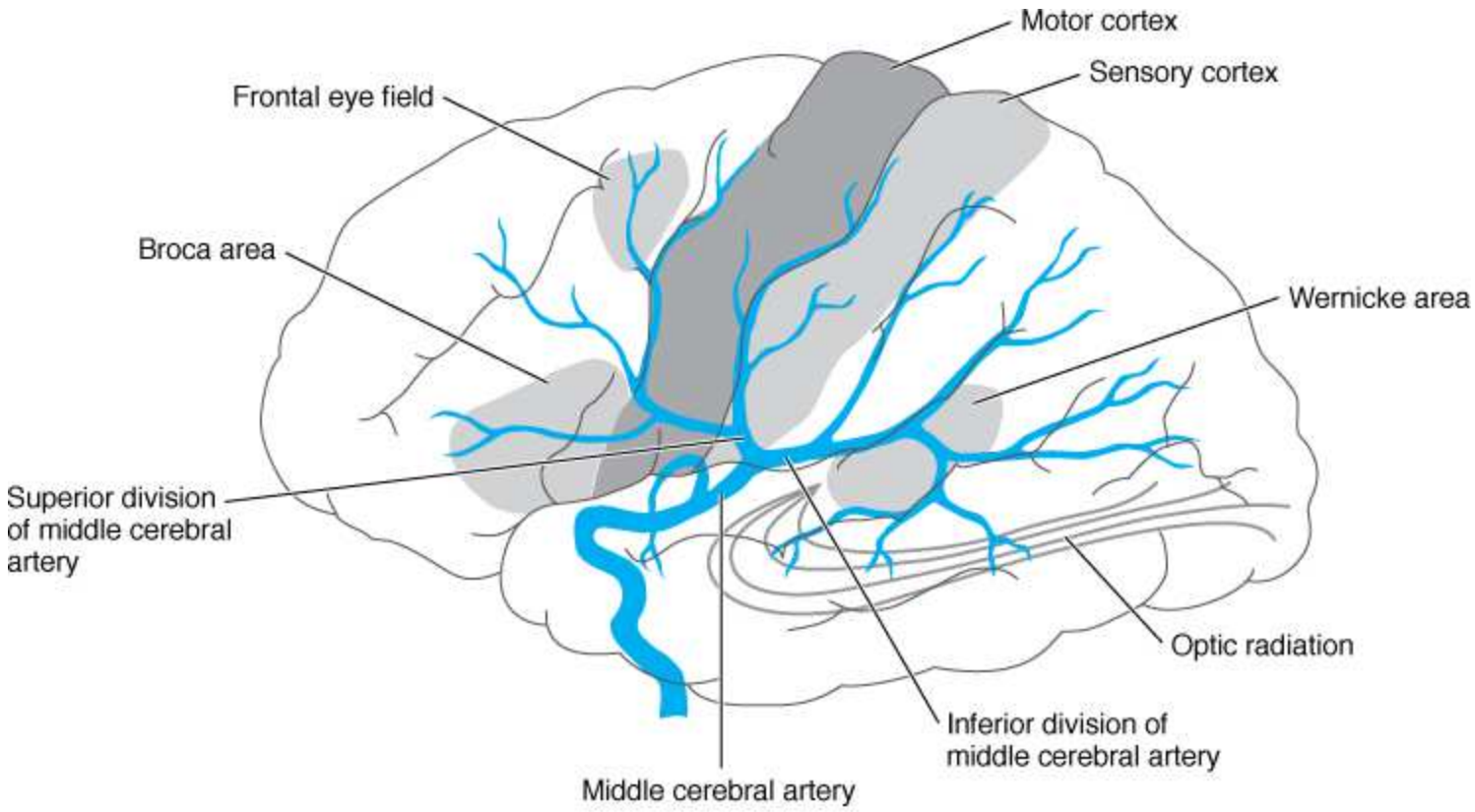


Figure 9-10 Accessed 07/01/2010

Visual cortex lesions

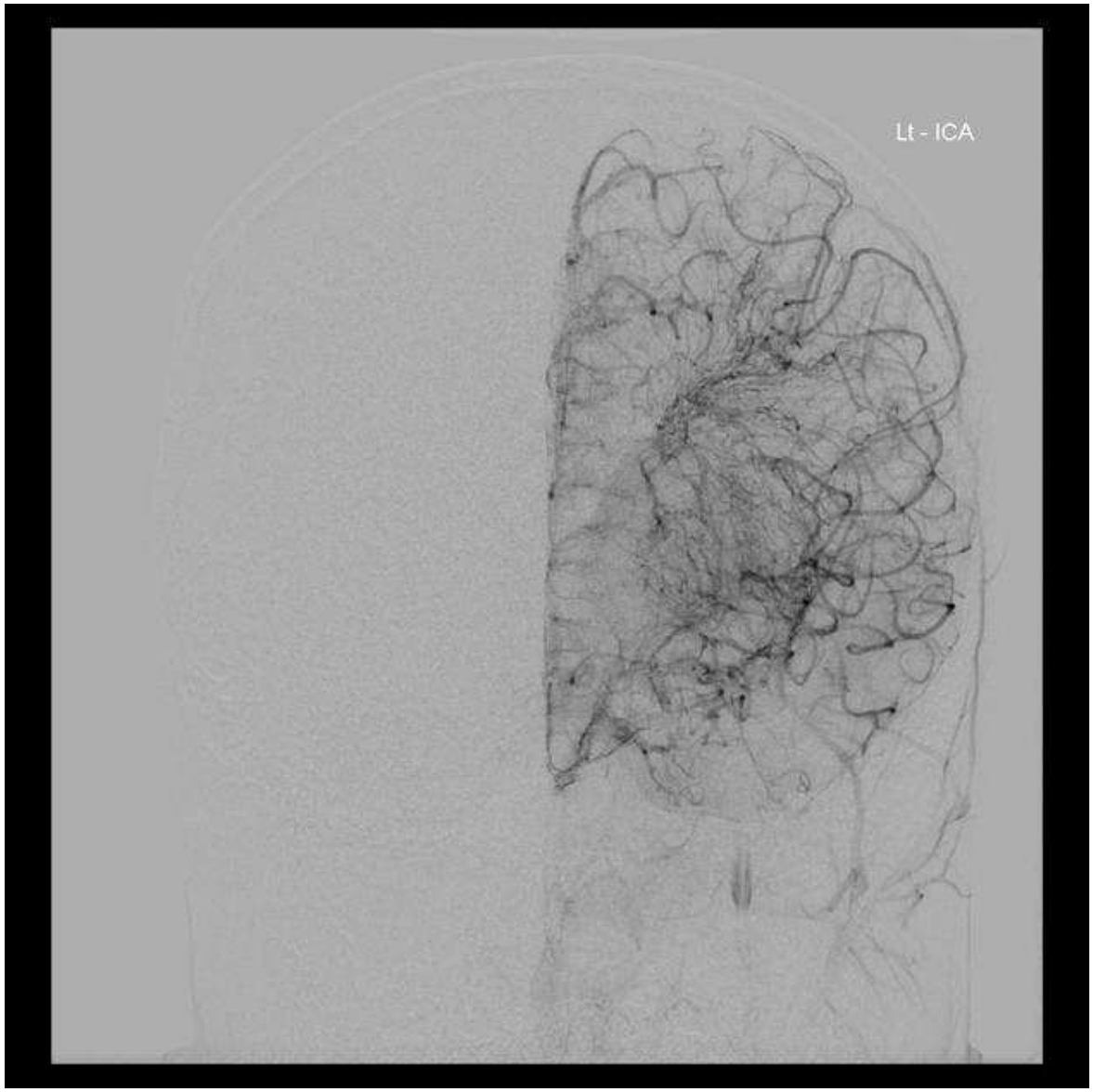
- Irritative lesions of area 17
- Produce such visual hallucinations as flashes of light, rainbows, brilliant stars, or bright lines.
- Destructive lesions
- Cause contralateral homonymous defects of the visual fields.
- This can occur without destruction of macular vision, a phenomenon called "macular sparing."
- Injury to areas 18 and 19 can produce visual disorganization with defective spatial orientation in the homonymous halves of the visual field.

Auditory cortex lesions

- Irritation of the region in or near the primary auditory receptive area
- Causes buzzing and roaring sensations.
- A unilateral lesion in this area may cause only mild hearing loss, but bilateral lesions can result in deafness.
- Destruction of area 22 in the dominant hemisphere
- Produces a syndrome of pure word deafness (in which words cannot be understood although hearing is not impaired), also called Wernicke's aphasia.

Moyamoya syndrome

- Stenosis or thrombotic obstruction of cerebral arteries
- Not atherosclerosis
- Proliferation of inner layers of vessels
- Collateral circulation around obstruction leaks blood due to increased pressure
- Puff of smoke appearance on angiography
- Increased risk in Down's syndrome, neurofibromatosis 1, and head trauma
- Associated with chromosome 17 abnormality
- TIA in children; hemorrhagic stroke in adults



https://radiopaedia.org/articles/moyamoya-syndrome-1?lang=us
Accessed 03/10/2020

CT imaging

- When a patient presents with stroke or TIA or neurological signs indicating a possible vascular ischemic etiology, a CT scan must be performed first.
- The CT scan is used to diagnose or exclude any other cause that may have mimicked a stroke;
- and to recognize the extent of ischemia and the significance of mass effect on adjacent structures.
-

CT imaging

- If there is a discrepancy between the clinical status and the CT finding, or
- if the patient is a candidate for aggressive thrombolytic therapy,
- it will be necessary to obtain an MRI, including diffusion and perfusion studies, eventually followed by angiography
- TTE (trans esophageal echocardiogram) with bubble test rarely detects a PFO (patent foramen ovale) as stroke origin

CT imaging

- In the acute phase about 60% of CT scans may be considered normal within the first few hours
- However, some subtle early signs may be detected depending upon the area of insult:
- Loss of grey/white matter interface,
- Obscuring of the lentiform nucleus,
- Hyperdensity of the horizontal portion of the middle cerebral artery within the Sylvian fissure.

CT imaging

- A rapid development of the picture may be seen after 6-8 hours with the development of cytotoxic edema.
- The infarcted area becomes markedly hypodense with involvement of both grey and white matter, usually in a wedge-shaped area corresponding to the region of distribution of the occluded vessel.

CT imaging

- In about 15-20% of cases hemorrhagic foci may be detected after 24-48 hours, particularly in the basal ganglia in cases of occlusion of the middle cerebral artery.
- Enhancement following contrast injection may be observed as early as 3–4 days and may persist for as much as 2 months.
- The infarcted area goes through a short phase of isodensity around the second and third week. The edema and mass effect disappear.
- In the chronic phase a porencephalic cavity with the tissue density of cerebrospinal fluid may be noted.

MRI imaging

- With MRI, diffusion-weighted images show hyperintense areas in the infarcted area as early as the first 2 hours following the insult.
- Cytotoxic edema is present.
- MRI perfusion sequences show absence of flow in the vessels leading to the infarcted area and early gyral edema,
- While spin echo sequences show T2 hyperintensity subsequently involving also the white matter.
- These changes are detected earlier than with CT.

Imaging of the basal ganglia

- The CT picture is that of hypodensity involving the head of caudate, putamen and globus pallidus.
- MRI shows marked T2 hyperintensity in the same area.
- Marked homogeneous enhancement following contrast injection can be observed.

Therapeutic strategy

- Early treatment with t-PA (within 3 hours of onset of symptoms) is associated with better outcomes.
- Tenecteplase is drug of choice to promote clot lysis in both acute myocardial infarction and acute stroke.
- Protects ischemic tissue
- IV bolus (ateplase is given by infusion)
- Increased hemorrhagic risk compared to ateplase
- Patients with symptoms that mimic stroke show little adverse effect if administered t-PA
- Contraindicated if recent surgery or active bleeding

Therapeutic strategy

- In patients with moderate to severe symptoms or without pre-stroke severe disability,
- AND confirmed occlusion of proximal anterior circulation (including terminal internal carotid artery as well as proximal middle cerebral artery)
- OR basilar artery or posterior cerebral artery occlusion,
- Thrombolytic therapy followed by endovascular thrombectomy or if stroke onset <6 hours
- If onset 6-24 hours, thrombectomy ONLY if limited infarct core volume noted on CT perfusion or MRI weighted imaging studies

Therapeutic strategy

- If the patient does not have disabling symptoms (a decision by the patient), then aspirin or clopidogrel for 30-90 days followed by 81mg aspirin daily is appropriate therapy for a TIA.
- No impact on stroke prevention
- Medical management of carotid stenosis has better outcome than does stent placement
- If high-grade stenosis, intervene within 2 weeks of stroke
- Angiography is the best method for evaluating stenosis

Summary

- Anterior cerebral artery
- Affects lower limbs
- Contralateral paralysis
- Urinary incontinence
- Personality changes
- Middle cerebral artery
- Contralateral paralysis of upper limbs and face
- Aphasia if dominant side affected
- Neglect syndrome if non-dominant side affected
- Eyes deviate to the side of the lesion

Summary

- Lacunar infarcts
- Middle cerebral artery origin
- Pure motor stroke
- Contralateral hemiparesis
- Ataxia
- Parkinsonian signs
- Thalamus stroke is purely sensory

Summary

- Anterior spinal artery
- Medial medullary syndrome
- Contralateral hemiparesis of and lower limbs
- Diminished proprioception
- Tongue deviates to side of lesion

Summary

- Posterior inferior cerebellar artery
- Lateral Medullary Syndrome (Wallenberg)
- Horner's syndrome on the side of the lesion
- Contralateral changes manifest as dysphagia, hoarseness, loss of gag reflex
- Ataxia and vertigo
- Dysmetria (lack of coordination of movement)
- Nystagmus

Summary

- Anterior inferior cerebellar artery
- Lateral pontine syndrome
- Horner's syndrome to the side of the lesion
- Paralysis of face
- Loss of taste on the tongue
- Diminished tearing and salivation
- Ataxia and vertigo
- Dysmetria (lack of coordination of movement)
- Nystagmus

Summary

- Posterior cerebral artery
- Contralateral hemianopia with macular sparing
- Inability to recognize faces
- Basilar artery
- Locked in syndrome
- Preserved consciousness
- Quadriplegia
- Loss of facial and mouth movements
- Able to blink

CLINICAL NEUROANATOMY REVIEW

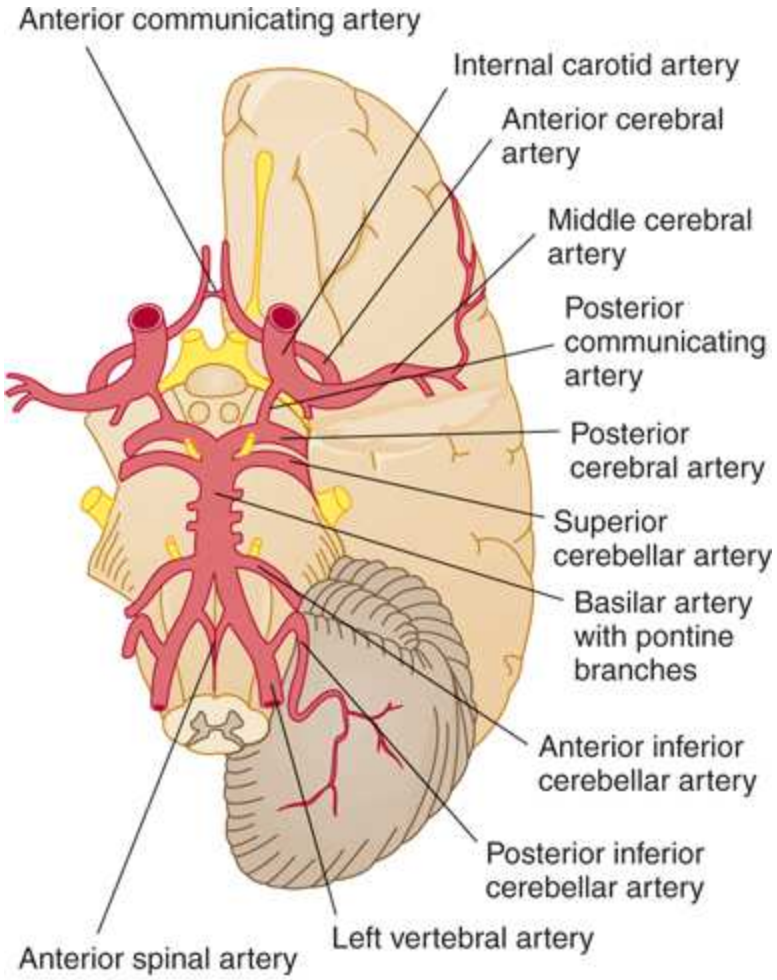


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Figure 12-1 Accessed 07/01/2010

Anterior cerebral artery

Branch	Effects of occlusion
Orbital/frontopolar	Apathy with some memory loss
Medial striate	Paresis of face and arm
Callosomarginal	Paresis and hypesthesia of face and arm; may see abulia, mutism, or inability to reach across field
Pericallosal	Ideomotor alexia (anterior lesion) Tactile anomia (posterior lesion)

Middle cerebral artery

Branch	Effects of occlusion
Orbitofrontal	Prefrontal syndrome
Left precentral	Broca's aphasia
Right precentral	Motor aprosodia
Central	Loss of motor function (possibly sensory as well) in face and arm
Inferior parietal	Hemineglect
Either angular branch Left angular Right angular	Hemianopsia alexia Wernicke's aphasia
Right Temporal	Receptive aprosodia

Major vascular lesions middle cerebral artery

SEGMENT	CLINICAL EFFECTS OF OCCLUSION
Either Stem Left Stem Right Stem	Hemiplegia, hemihypesthesia, hemianopsia global aphasia sensory neglect
Either Upper Division Left Upper Division Right Upper Division	Paresis and hypesthesia of face and arm, dysarthria Broca's aphasia hemineglect or expressive aprosodia
Either Lower Division Left Lower Division	Hemianopsia; possibly agitated state Wernicke's aphasia, alexia, ideomotor apraxia

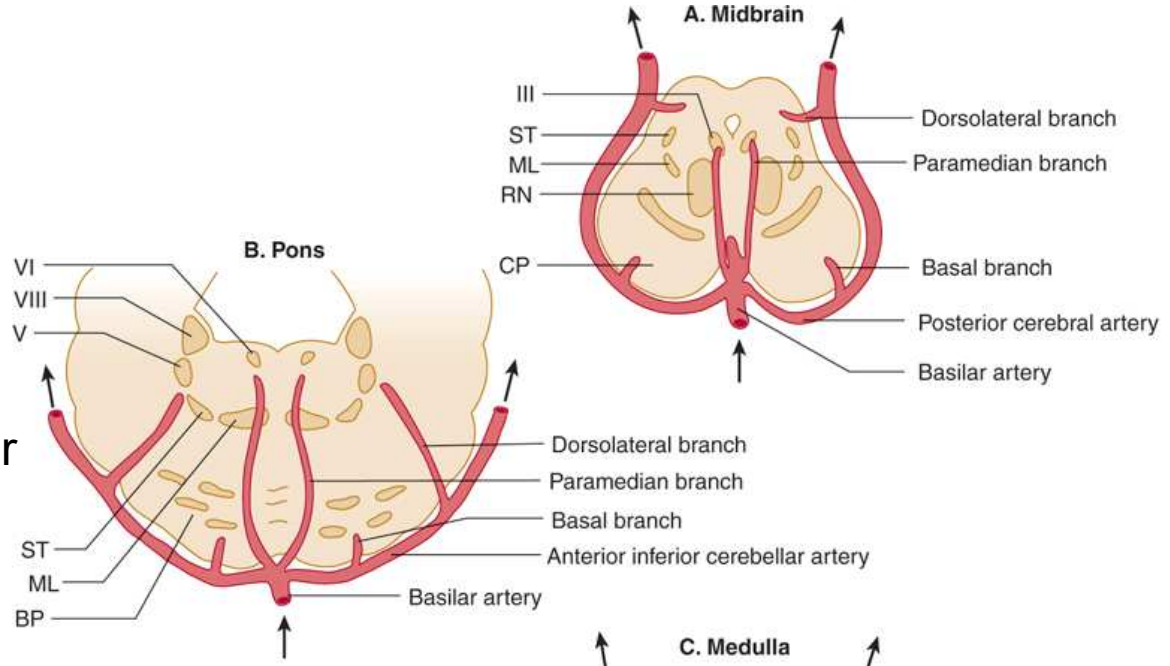
Lateral striate arteries most often affected in stroke and in Charcot-Bouchard microaneurysms (result from chronic hypertension).

Posterior cerebral artery

Stem or branch	Effects of occlusion
Either stem Left stem Both stems	Homonymous hemianopsia Alexian visual field Cortical blindness, possibly amnesia
Midbrain Branch	Ipsilateral CN3 palsy and contralateral hemiplegia
Thalamus Branch	Contralateral numbness, possibly hemianopsia, thalamic syndrome
Subthalamic Nucleus Branch	Contralateral ballism
Corpus Callosum Branch	Alexia in contralateral visual field

The posterior cerebral artery continues [arrows] to supply the thalamus, occipital lobe, and medial temporal lobe.

anterior inferior cerebellar artery [arrows]



posterior inferior cerebellar artery [arrows]

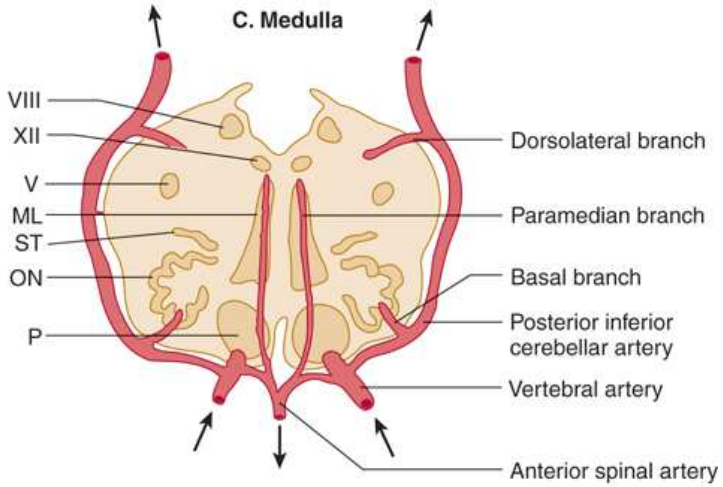


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Fig. 12-4 Accessed 07/01/2010

Lacunar lesions

Location	Effects
Genu of Internal Capsule	Dysarthria, clumsy hand; possibly dysphagia
Posterior limb of Internal Capsule	Pure motor hemiparesis
Ventral posterior nucleus of Thalamus	Pure sensory syndrome, possibly with sensory ataxia

Basal ganglia lesions

Site of Lesion	Effect
Globus Pallidus	Involuntary, continuous muscle contractions that lead to rotatory movements and abnormal postures of hand, an arm, neck , or face (Athetosis is a localized dystonic movement).
Subthalamic Nucleus	Hemiballismus (proximal flinging movement of limbs; violent)
Putamen	Chorea. Overshooting; spontaneous, abrupt, alternating irregular movements. Varies from restlessness with little gesticulation to hesitant dance-like gait impairment to violent hyperkinesia.
Caudate and Putamen	Huntington's Chorea
Substantia Nigra	Parkinson's Disease

Limbic syndromes

Syndrome	Presentation	Region lesioned
Delerium, acute confusional state	Disturbance of consciousness, attention, perception. Fluctuating. Visual hallucinations. Disturbance of affect.	Bilateral mediobasal temporal lobe (hippocampus, amygdala), hypothalamus
Pathologic laughing and crying	Uncontrollable.	Internal capsule, basal ganglia, thalamus, corticonuclear tract
Aggressive, violent behavior; fits of rage	Out of proportion.	Mediobasal temporal lobe (amygdala)
Apathy, indifference, akinetic mutism		Bilateral septal area, cingulate gyrus
Memory deficit, transient global amnesia	Only short-term memory and sense of time impaired	Mammillary bodies; mediobasal temporal lobe
Disturbed sexuality		Septal area; hypothalamus

Hypothalamic function

Region Stimulated	Physiological Effects
Anterior Hypothalamus (preoptic area)	Decreased blood pressure, heart rate; Increased GI motility and secretion; Bladder contraction; Pupillary constriction; Decreased body temperature
Posterior Hypothalamus (lateral nuclei)	Increased blood pressure, heart rate; Vasoconstriction of skin vessels; Decreased peristalsis; Pupillary dilation; Increased blood glucose; shivering; eccrine sweating
Lateral Hypothalamus (zona incerta)	Increased water intake
Medial Hypothalamus (ventromedial nucleus) Amygdala	Decreased food intake, docile Fear or rage

Basilar artery

Site of lesion	Presentation
Midbrain	Vertical gaze palsy; impaired convergence; retractional nystagmus. May see strabismus with diplopia. Sensation of movement of surroundings with walking or movement of head. No central paralysis. Pupils may be constricted but reactive or dilated and non-reactive to light.
Thalamus, part of temporal and occipital lobes	Visual field defects. May see somnolence, dream-like scenic hallucinations, memory impairment, disorientation, psychomotor hyperactivity.

Midbrain syndromes

Anterior midbrain (peduncle)	
Site of Lesion	**Presentation**
Intramesencephalic fibers of the oculomotor nerve	Ipsilateral oculomotor paralysis, dilated pupil unreactive to light
Pyramidal tract	Contralateral central paralysis and facial paralysis (supranuclear facial palsy); spasticity; may see dysarthria (supranuclear hypoglossal palsy)
Substantia nigra	Rigidity

Midbrain syndromes

Medial midbrain (tegmentum)	
Site of Lesion	**Presentation**
Intramesencephalic fibers of the oculomotor nerve	Ipsilateral oculomotor paralysis; dilated pupil unreactive to light
Medial lemniscus	Contralateral impairment of touch, position, vibration sense
Red nucleus	Contralateral tremor
Substantia nigra	Rigidity
Superior cerebellar peduncle	Contralateral ataxia

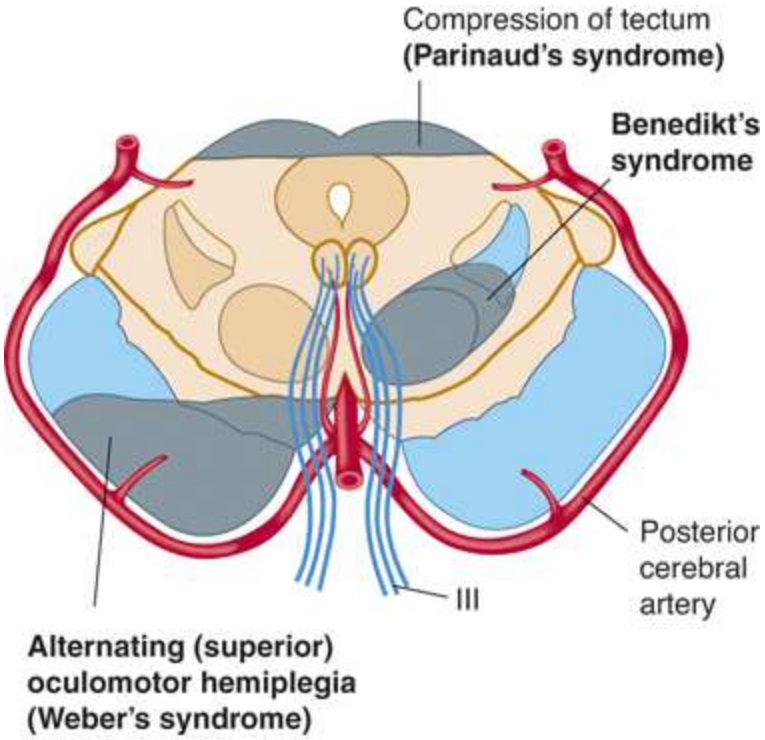

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Figure 7-13 Accessed 07/01/2010

Midbrain syndromes

Dorsal midbrain (tectum)	
Site of Lesion	**Presentation**
Oculomotor nuclei	Overactive levator palpebrae superioris muscle (retraction). Over time, pupils dilate and do not react to light but do constrict upon convergence.
Medial longitudinal fasciculus	Supranuclear palsy of upward conjugate gaze (eyes move upward passive deflection of the head but not voluntarily). Convergence nystagmus with lid retraction on upward gaze.
Trochlear nucleus	Trochlear nerve palsy.
Aqueduct	Hydrocephalus, papilledema

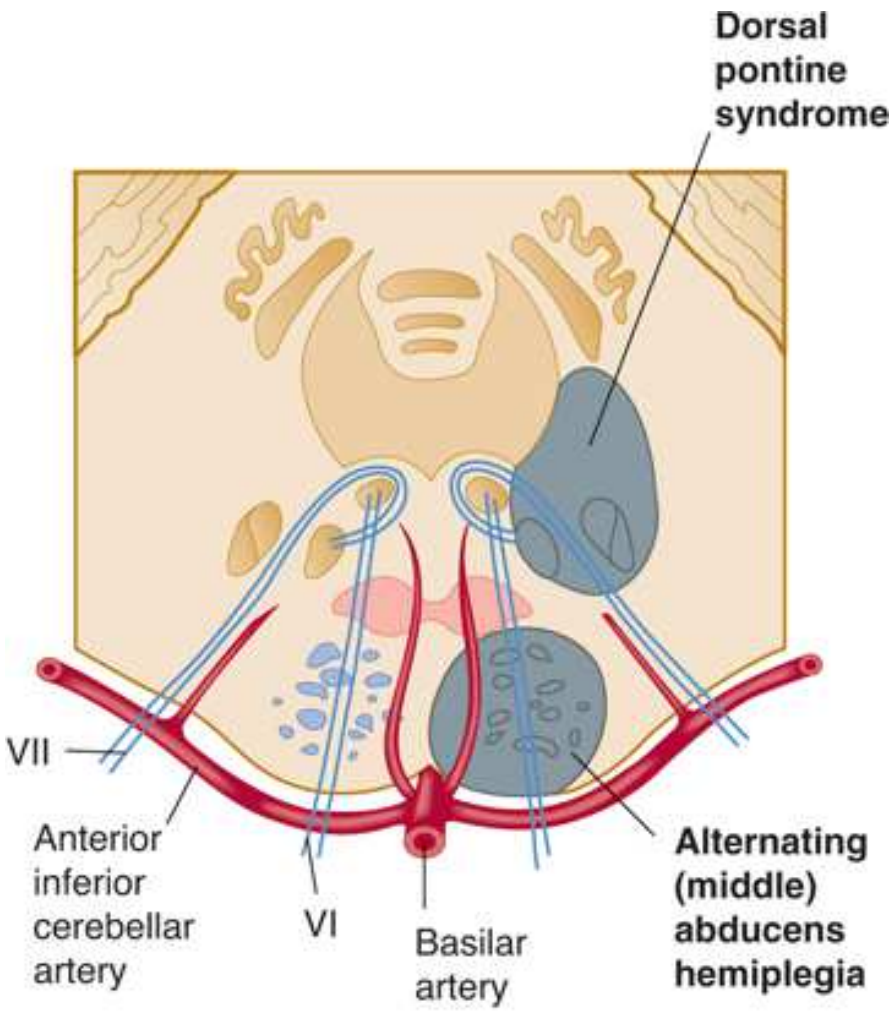

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Fig. 7-12 Accessed 07/01/2010

Pontine syndromes

Mid-ventral pons	
Site of lesion	**Presentation**
Pyramidal tract	Contralateral central paralysis sparing the face
Intrapontine fibers of trigeminal nerve Middle cerebellar peduncle	Ipsilateral facial hyperesthesia, weakness of muscles of mastication Ipsilateral ataxia

Pontine syndromes

Lacunar lesion **Site of lesion**	**Presentation**
Pyramidal tract	Contralateral central paralysis more pronounced in the legs and possibly sparing the face
Middle cerebellar peduncle	Ipsilateral ataxia with dysarthria and dysphagia; may also see a “clumsy” hand

“Locked-in” syndrome Site of Lesion	Presentation
Ventral pons (corticobulbar and corticonuclear tracts) bilaterally; abducens nucleus, pontine paramedian reticular formation, fibers of trigeminal nerve	Quadriplegia, aphoria, inability to swallow, horizontal gaze palsy (including absence of caloric response), loss of corneal reflex Eyelid and vertical eye movements, sensation, wakefulness, and spontaneous breathing remain intact.

Pontine syndromes

Superior pontine tegmentum	
Site of Lesion	**Presentation**
Trigeminal nucleus and fibers	Ipsilateral facial hyperesthesia; paralysis of muscles of mastication
Superior cerebellar peduncle	Ipsilateral ataxia, intention tremor
Medial lemniscus	Contralateral impairment of touch, position, and vibration sense
Spinothalamic tract	Contralateral loss of pain and temperature sensation
Paramedian pontine recticular formation	Ipsilateral loss of conjugate movement (loss of optokinetic and vestibular nystagmus but vestibulo-ocular reflex intact)
Pyramidal tract	Contralateral paralysis sparing the face.

Pontine syndromes

Caudal pontine tegmentum	
Site of Lesion	**Presentation**
Pyramidal tract	Contralateral central paralysis sparing the face
Facial nerve nucleus and fibers	Ipsilateral facial palsy
Abducens nerve fibers	Ipsilateral abducens paralysis (eyes drift away from the lesion); loss of vestibulo-ocular reflex
Central sympathetic pathway	Ipsilateral Horner syndrome
Paramedian pontine reticular formation	Loss of ipsilateral conjugate movement
Medial and lateral lemniscus	Contralateral loss of touch, position, and vibration sense
Lateral spinothalamic tract	Contralateral loss of pain and temperature sensation

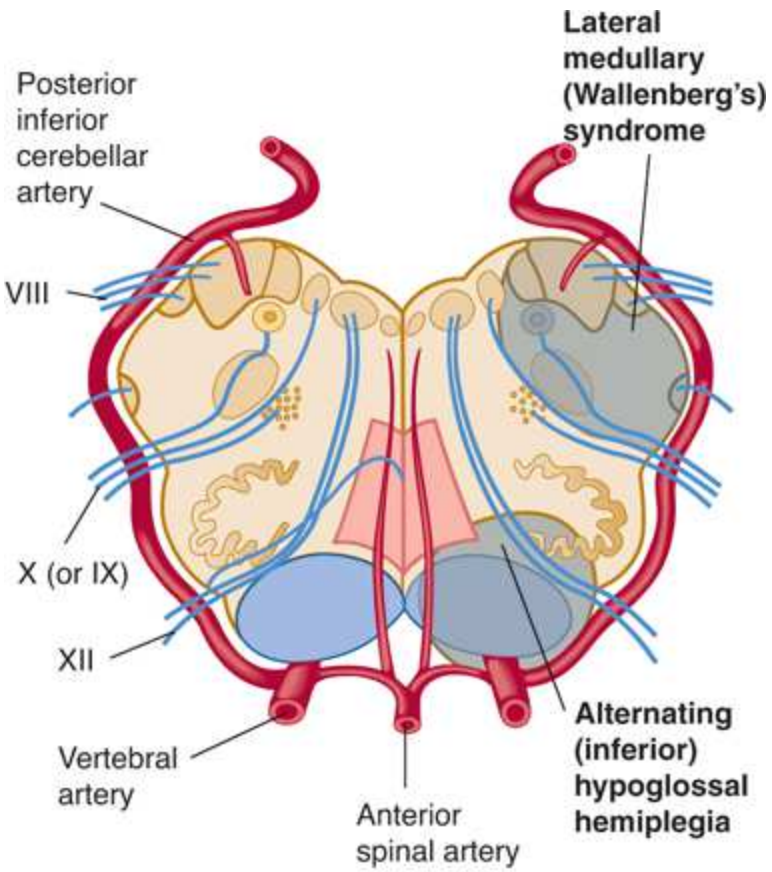


Figure 7-11 Accessed 07/01/2010

Medullary lesions

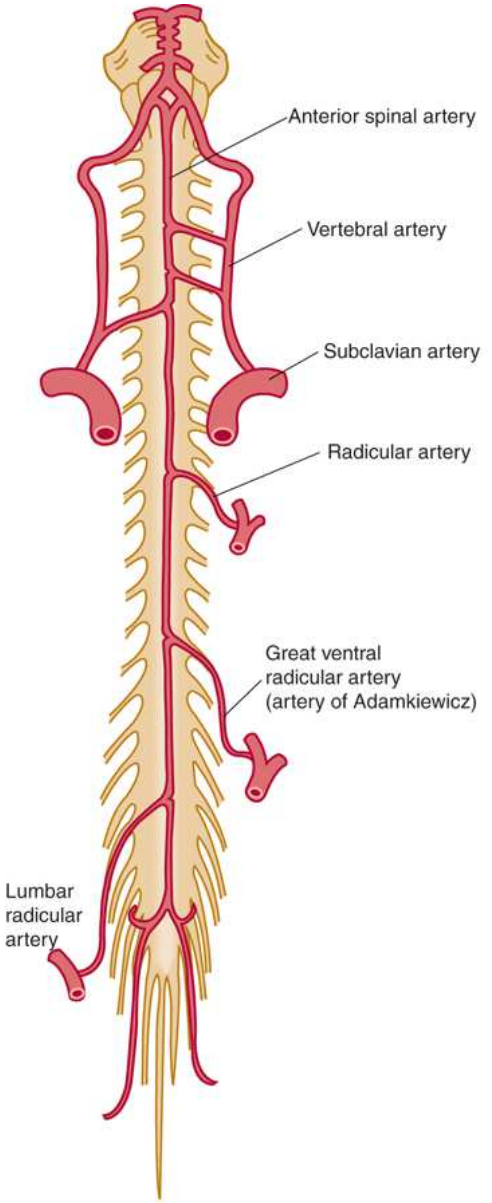
Medial medullary lesions	
Site of Lesion	**Presentation**
Hypoglossal nucleus and fibers	Ipsilateral hypoglossal paralysis
Pyramidal tract	Contralateral central paralysis (flaccid) sparing the face
Medial lemniscus	Contralateral loss of touch, position, vibration sense with intact pain and temperature sensation
Medial longitudinal fasciculus	Upbeat nystagmus

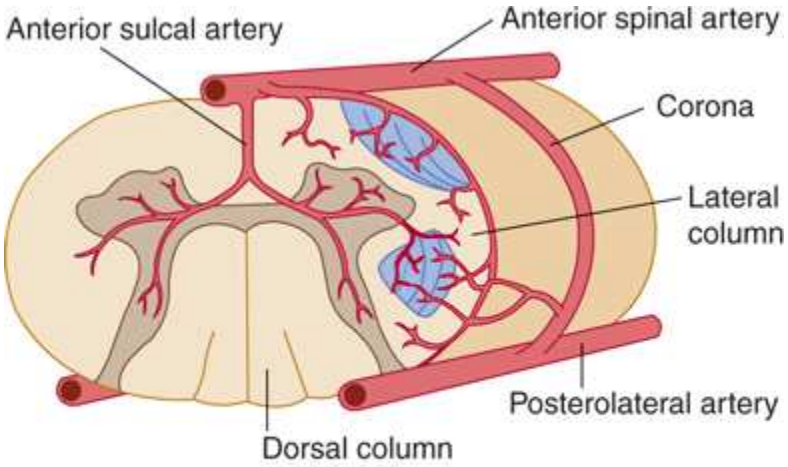
Medullary syndromes

Lateral medullary lesions	
Site of lesion	**Presentation**
Spinal nucleus of trigeminal nerve	Ipsilateral analgesia/thermanesthesia with sparing of the face and absence of corneal reflex
Cochlear nucleus	Ipsilateral hearing loss
Nucleus ambiguus	Ipsilateral paralysis of pharynx and larynx with tongue movement intact
Solitary nucleus	Impaired sense of taste
Dorsal nucleus of vagus nerve	Tachycardia and dyspnea
Inferior vestibular nucleus	Nystagmus away from the lesion while falling to the side of the lesion
Central tegmental tract	Ipsilateral tremor of the soft palate and pharynx
Central sympathetic pathway	Ipsilateral Horner’s syndrome

Medullary syndromes

Lateral medullary lesions	
Site of lesion	**Presentation**
Reticular formation	Singulitis (hiccups)
Inferior cerebellar peduncle	Ipsilateral ataxia and intention tremor
Anterior spinocerebellar tract	Ipsilateral hypotonia
Lateral spinothalamic tract	Contralateral loss or pain and temperature sensation while preserving touch, position, and vibration sense





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Figs. 6-4 and 6-5 Accessed 07/01/2010

Arterial supply to the spinal cord

- The anterior spinal artery arises within the cranium by union of branches from the vertebral arteries. Unpaired.
- The posterior spinal artery arises from the vertebral arteries. Paired. May arise from the posterior inferior cerebellar artery.
- Segmental medullary arteries supplement the anterior and posterior vertebral arteries.

Arterial supply to the spinal cord

- Watershed between T3 and T9 as segmental arteries are small, arise from spinal or posterior intercostal arteries, and supplement blood supply to the cord.
- The ventral great radicular artery of Adamkiewicz arises from a spinal segmental artery and joins the anterior spinal artery (generally on the left side) at T12 or L1. As with the larger lumbar radicular arteries, it also supplements the blood supply to the cord. May be compromised with aortic aneurysm or its repair.
- The dorsal horn and columns are supplied by the posterior spinal artery.