stryker

SKILL™

Stroke **K**nowlege **I**nitiatives
for **L**earning and **L**eadership

BRAIN Training

Self-study Pre-Read

NP001825 v2.0

Background to stroke

NP001825 v2.0

Background to stroke

Stroke statistics

Stroke is the **number 5** cause of death in the United States.

Every **4 minutes** someone dies of a stroke.

60% of strokes are in women,
40% of strokes are in men.

Stroke kills nearly **130,000** people every year.

1 in every 20 deaths is a result of stroke.

Stroke is the **leading cause** of preventable disability.

http://www.strokeassociation.org/STROKEORG/AboutStroke/Impact-of-Stroke-Stroke-statistics_UCM_310728_Article.jsp#.Wodvba6nFhE

Background to stroke

Stroke

Stroke is the leading cause of serious, long-term disability in the United States and is the fifth leading cause of death (after cardiovascular disease and cancer). It accounts for the greatest expenditure of healthcare dollars and affects about 795,000 Americans per year. About 600,00 of these are first attacks, and 185,000 are recurrent attacks. Nearly three-quarters of all strokes occur in people over the age of 65.

The brain is composed of living cells that require blood supply for the oxygen and nutrients they need. It receives 15 percent of all blood pumped from the heart and consumes 20 percent of inspired oxygen.

Cerebral ischemia is a decrease in cerebral blood flow with resultant decrease in cerebral oxygenation. When blood flow is decreased, followed by subsequent reperfusion, one may see reversible or irreversible brain damage. The brain has no energy stores, therefore needs a constant supply of blood, oxygen, and glucose.

A stroke is an interruption in the blood supply that can lead to cell death and an interruption of function. This can be caused by an arterial blockage, leading to the more common ***ischemic stroke***, or by hemorrhage into the brain itself, leading to the more fatal ***hemorrhagic stroke,*** In either case, proper treatment must be under- taken as soon as possible. Having a stroke is an emergency!

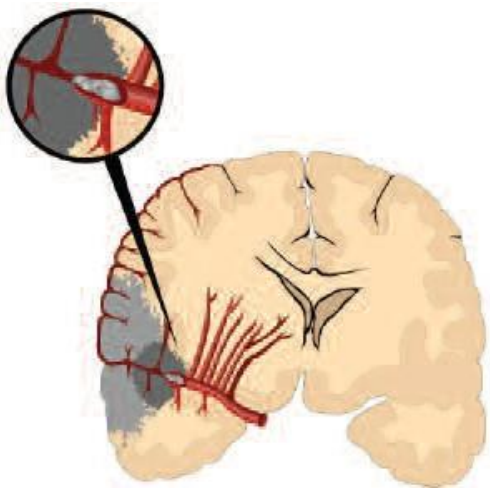


Figure 1.0. Ischemic

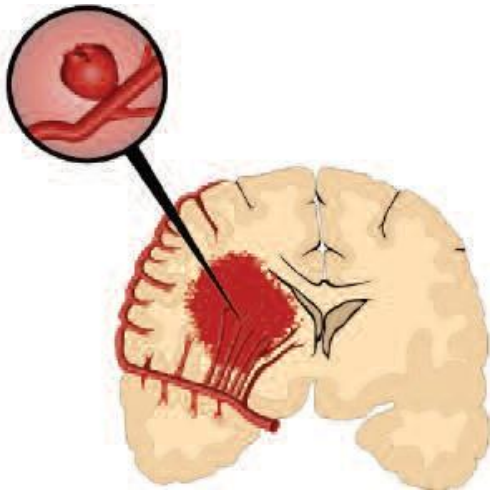


Figure 1.1. Hemorrhagic

Background to stroke

Ischemic stroke

Ischemic stroke comprises 87 percent of all strokes and may be caused by a blockage formed at a specific site, or it may be a piece of a clot that has dislodged from the heart or carotid artery and lodges in a cerebral vessel.

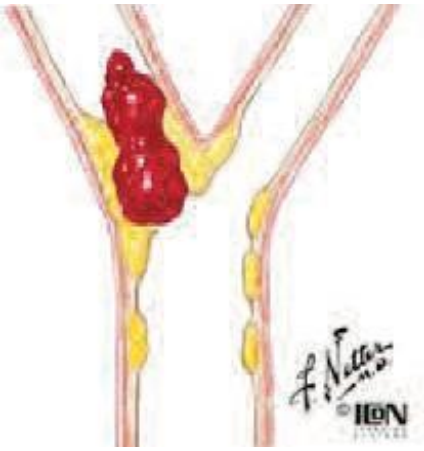


Figure 1.2. Thrombus.

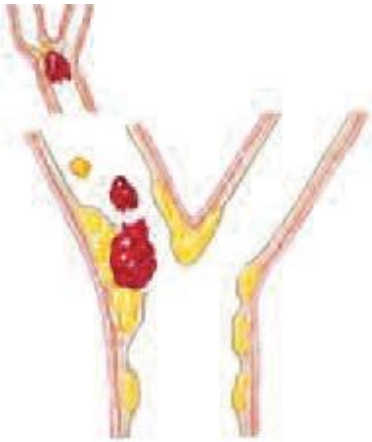


Figure 1.3. Embolus

Cerebral blood vessels may narrow as a result of plaque accumulation on arterial walls. Once plaque forms in the artery, platelets and fibrin can deposit on the plaque surface and form a ***thrombus*** (blood clot) that blocks blood flow. The blockage results in an insufficient amount of blood being delivered to that portion of the brain, which in turn stops functioning and may die if the blood vessel is not reopened within a certain amount of time. However, if the blockage is temporary, the blood supply may not be interrupted long enough to cause cell death. For ischemic stroke, restoration of blood flow and the nutrient supply is critical.

A ***transient ischemic attack*** (TIA) is a sudden neurological disturbance lasting minutes up to 24 hours without apparent, permanent neurological deficit. The most common cause of a TIA is a temporary interruption in the blood flow to the brain. Blood flow can drop to about one quarter of normal and cause symptoms, without resulting in permanent damage.

Determining the cause of the TIA is essential to preventing a stroke. About 30 percent of patients who suffer a major stroke previously experienced a TIA, with 20 percent of these occurring within the first month after the initial event.

A reversible ischemic neurologic deficit (RIND) is a deficit that persists for more than 24 hours, but with "complete" recovery within 3 weeks. A completed stroke has a duration greater than 3 weeks. Even a RIND with apparent complete recovery, however, may result in some area of true infarct.

Atherosclerosis of the carotid arteries often cause TIAs because pieces of the material that form the blockage (plaque) and blood clots that form on the plaque break off and are carried into the head where they can block vessels supplying the brain. Typical symptoms include weakness or numbness on one side of the body, inability to speak or understand speech, and changes in vision. If the blockage produced by this material is small and breaks up quickly, a TIA occurs. If there is blockage of a larger vessel or the blockage doesn't break up right away, a stroke results. Blockage of the vertebral arteries usually causes symptoms because of decreased blood flow to part of the brain, not because of plaque fragments and clot emboli. The symptoms of blockage of these vessels may get better or worse, or they may suddenly appear if a stroke occurs.

Unlike atherosclerosis of the carotid arteries, which often causes TIAs, intracranial atherosclerosis often is first found when a major stroke occurs. TIAs are a warning sign for stroke and should be viewed as an opportunity to prevent a major cerebrovascular event from occurring.

In most ischemic attacks, there is an area of irrecoverable tissue damage surrounded by a region that may be viable but close to cell death — the ***ischemic penumbra***. Even though saving all tissue in jeopardy would be ideal, it is this potentially salvageable ischemic penumbra that results in the clinical improvement in many cases and that is the true target of therapy. It is possible that there will be total cure in only a small number of patients; in most, however, the salvage of a portion of this viable ischemic penumbra is possible, resulting in a significant improvement in clinical condition.

The ischemic penumbra generally is thought to represent a geographic area of tissue surrounding a more profoundly ischemic central core. The amount of collateral supply to the affected territory determines the volume of recoverable tissue. The volume of tissue "teetering on the brink" can range from none to almost all of the affected territory.

So, even if some cells are permanently damaged in a stroke, other cells in the surrounding area sometimes take on the function of the dead cells. This is why some stroke patients eventually recover some or all of their abilities.

Background to stroke
Hemorrhagic stroke

Hemorrhagic stroke occurs less commonly and accounts for only 13 percent of all strokes. This type of stroke involves bleeding into the intra-parenchymal or subarachnoid space and can lead to immediate and delayed damage to the brain tissue.
There are two types of hemorrhagic stroke:

- Intracerebral hemorrhage.
- Subarachnoid hemorrhage.

An ***intracerebral hemorrhage*** (ICH), which is a hemorrhage into the brain parenchyma, can be caused by a number of problems including hypertension, vascular malformations, or as a complication of anticoagulation therapy.

Some brain tissue is destroyed by the initial bleed. Brain tissue and neurons surrounding the hemorrhage are at risk for secondary injury as the blood flow remains irregular, ischemia sets in, swelling exerts pressure, and toxic byproducts are released.

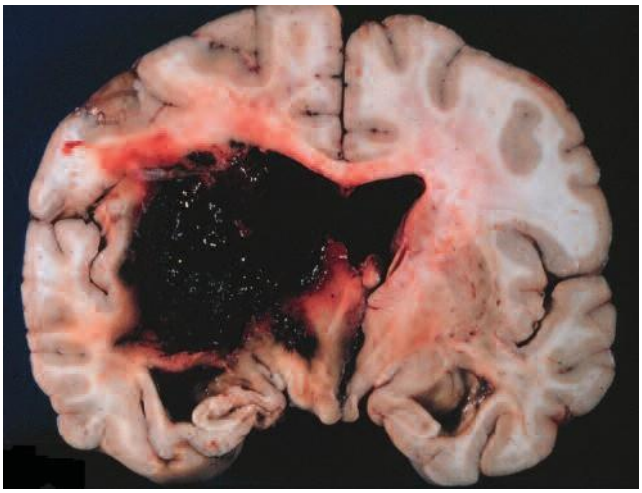


Photo of image taken by a BSC representative.

Figure 1.4. Intracerebral hemorrhagic can lead to hemorrhagic stroke.

A subarachnoid hemorrhage (SAH) occurs outside of the parenchyma and into the subarachnoid space and is most often caused by aneurysm rupture. Blood in the subarachnoid space is irritating to the meninges and blood vessels, potentially resulting in vasospasm and delayed ischemia.

Symptoms and risk factors

Some strokes are preventable. If the blockage can be prevented or if the hemorrhage can be prevented by controlling blood pressure or treating a vascular problem before rupture, a stroke can be prevented.

Some strokes are also treatable. If proper blood flow can be restored to the brain quickly, some of the damage done in the ischemic area can be reversed.

Recognizing and managing symptoms and risk factors play a vital role in preventing stroke. A stroke can cause different symptoms, depending upon which part of the brain is affected. Some regions of the brain can die and yet the patient will have no symptoms at all. Other areas of the brain are more important and even a tiny stroke in these locations can cause severe disabilities. Stroke symptoms include:

- Sudden numbness, weakness, or tingling on one or both sides of the body.
- Sudden blurred vision in one or both eyes.
- Slurred speech or difficulty understanding.
- Dizziness or stumbling.
- Severe headache with an abrupt onset.

Certain risk factors serve as warning signs to help identify patients who might be prone to a stroke. In addition, some patients will present with a warning sign, such as a headache, before they suffer a major intracerebral hemorrhage. Diagnostic and therapeutic interventions can be utilized.

Some risk factors can be modified to prevent a stroke. Modifications can include changing behavior or taking medications.

Following are the modifiable risk factors which are most concerning:
- Hypertension.
- Behavior, including smoking and obesity.
- Warning signs, including previous stroke(s) or TIAs.
- Headache.
- Cardiac disease.
- Carotid stenosis.

All of these risk factors are potentially recognizable and treatable. If managed properly, they can reduce the risk of stroke more than tenfold.

Some risk factors cannot be modified:

- Family medical history (relatives with a history of heart disease, diabetes, or cerebrovascular disease increase the risk of stroke).
- Gender (incidence of ischemic stroke is higher for women than men).
- Age (the chance of stroke more than doubles each decade after age 55).
- Race (African-Americans experience higher mortality from stroke).

Understanding unalterable risk factors is important in helping to identify patients who are at higher risk for stroke. These individuals need to be regularly screened for potential warning signs.

Hypertension (high blood pressure) is the leading risk factor for both ischemic and hemorrhagic stroke. Through direct effects on the arterial wall, hypertension can be involved in the etiology of both large and small vessel ischemia. Hypertension also can cause thickening and weakening of the smaller arteries within the brain. If these arteries burst or leak, intracerebral hemorrhage occurs. Increased blood pressure more than doubles a patient's chance of suffering an ICH.

Diagnosis

If stroke is suspected, a neurological examination will be conducted to assess the following:

- Level of consciousness
- Presence of seizure activity
- Glasgow Outcome Scale
- Pupils: size, equality, reactivity
- Limb movements

Depending on results of the physical examination, the patient may be taken for a CT scan (computed tomographic scan), which uses X-rays to produce a 3-D image of the brain. A CT scan is used to differentially diagnose hemorrhagic stroke, or ischemic stroke.

An MRI scan (magnetic resonance imaging) may be done to provide more detail of the brain and spinal cord. MR uses magnetic fields to produce a 3-D image of these structures.
One key factor that is critical to every type of stroke patient and to almost every treatment option available is time. With every minute that is wasted in starting treatment for a stroke, neurons are being permanently damaged and cannot be rescued.

To emphasize this point, many people refer to strokes as “brain attacks.” Because people clearly recognize the emergency nature of a heart attack, we hope to prompt patients to make the same association between stroke and “emergency.”

Following are common scales used by physicians to evaluate or classify stroke patients.

Hunt and Hess Neurological Scale
Classification of patients with intracranial aneurysms, according to surgical risk.

Category	Criteria
Grade 1	Asymptomatic, or minimal headache and slight nuchal rigidity.
Grade 2	Moderate to severe headaches, nuchal rigidity, no neurological deficit other than cranial nerve palsy.
Grade 3	Drowsiness, confusion, or mild focal deficit.
Grade 4	Stupor, moderate to severe hemiparesis, possibly early decerebrate rigidity and vegetative disturbances.
Grade 5	Deep coma, decerebrate rigidity, moribund appearance.

Glasgow Outcome Scale
An evaluation scale based on individual overall social capability (or dependence) of patients. It takes into account the combined effects of specific mental and neurological deficits.

Category	Description
Grade 1	Good recovery; full and independent life with a minimal neurologic deficit.
Grade 2	Moderately disabled; neurologic or intellectual impairment but is independent.
Grade 3	Severely disabled; conscious but totally dependent upon others.
Grade 4	Vegetative.
Grade 5	Death.

Modified Rankin Scale

Category	Description
Grade 1	No symptoms at all.
Grade 2	No significant disability, despite symptoms: able to carry out all usual duties and activities.
Grade 3	Slight disability: unable to carry out all previous activities, but able to look after own affairs without assistance.
Grade 4	Moderate disability: requiring some help, but able to walk without assistance.
Grade 5	Severe disability: bedridden, incontinent, and requiring constant nursing care and attention.
Grade 6	Death.

Ongoing research

Researchers understand more about the brain each day, and it is expected that ongoing research will help to minimize the effects of a stroke. Here are just a few examples of the types of work being done today:

- Research into how brain cells die is already helping physicians recognize which elements in the ischemic cascade are the most crucial for preventing permanent damage.
- Pharmacological agents are being developed that may extend the therapeutic window for treatment of stroke.
- Research on brain cell implants and transplants gives hope that destroyed tissues can be replaced or the function of surviving injured tissues can be augmented.

Background to stroke
Atherosclerosis

Atherosclerosis is a leading cause of ischemic stroke.

Extracranial atherosclerosis is "hardening" of the arteries that supply the head and neck (carotid and vertebral arteries), causing narrowing and blockage of these vessels.

Intracranial atherosclerosis is hardening of the arteries inside the head that supply the brain, causing narrowing and blockage of these vessels. They are both similar to atherosclerosis elsewhere in the body such as the heart or legs. If a vessel becomes completely blocked or even severely narrowed, blood flow to part of the brain can be blocked off and a stroke can occur. The same conditions that are associated with atherosclerosis elsewhere (such as in the vessels of the heart, causing heart attacks) are associated with intracranial atherosclerosis, such as diabetes, high blood pressure, high cholesterol, and smoking.

Atherosclerosis is a pathologic process mostly affecting large elastic arteries (e.g., the aorta and the iliac arteries) and medium-sized muscular arteries (e.g., the coronary and carotid arteries) of the extracranial circulation.

However, 8–10 percent of ischemic strokes result from intracranial atherosclerotic disease (ICAD). It is a degenerative process that is characterized by accumulation of plasma lipids, cholesterol, connective tissue fibers, and local and circulating cells in the tunica intima of these vessels.

Atherosclerosis often develops at branch points or curving portions along extracranial and intracranial large arteries where blood flow is slowed and more turbulent. Atherosclerosis has many manifestations, including plaque formation with stenosis, ulceration with thrombosis, distal emboli, and arterial dilatations and fusiform aneurysms.

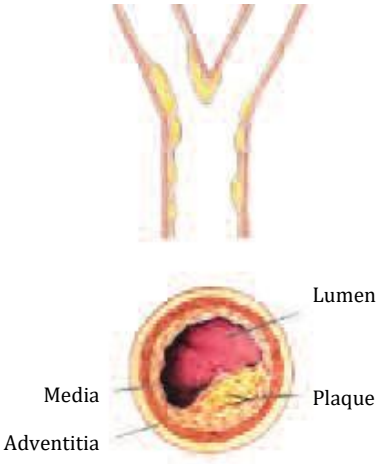


Figure 1.5. Atherosclerotic narrowing of vessel lumen.

The principal feature of atherosclerosis is the deposition of plasma lipids in arterial walls. Development of an ***atherosclerotic plaque*** occurs in several stages.

The intima may become injured through factors such as physical abrasion, hypertension, or abnormal blood substances. This injury causes disruption in the vessel lining, which allows lipid-rich cells to leak down inside the lining.

This initial intimal lesion, called a "fatty streak," creates a bump beneath the endothelial lining. In an attempt to promote healing, smooth muscle cells release a connective tissue matrix, which forms a fibrous plaque.

Plaque continues to harden as fibroblasts infiltrate the lesion.

In coronary vessels, plaque rupture occurs. This rupture activates platelets which leads to the formation of thrombus at the lesion site. Because ICAD has not been well studied, it is not known if intracranial plaque will rupture and lead to thrombus formation in a similar fashion.

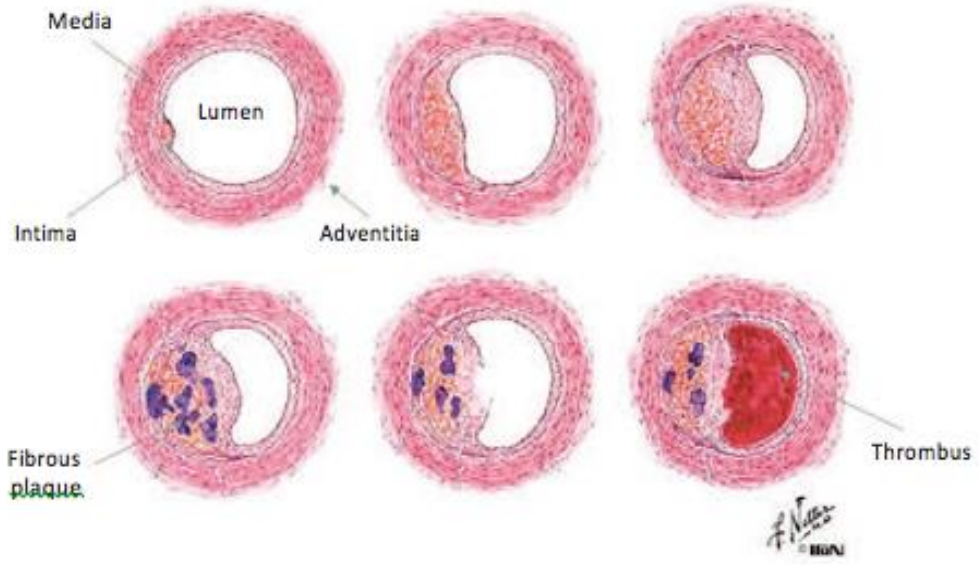
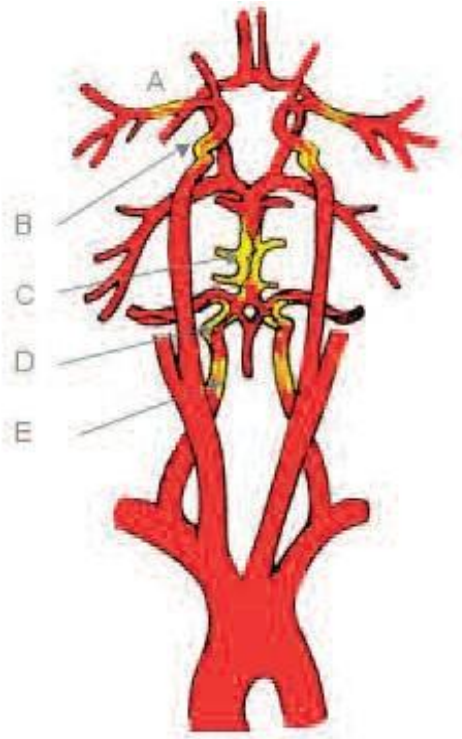


Figure 1.6. Atherosclerosis Fibrous Plaque Formation, shown in cross-sectional diagrams of a vessel.

Plaque is often eccentric and does not form evenly around the vessel wall. This cross-section of an atherosclerotic human vessel shows the plaque buildup primarily on one side of the vessel.

The pattern of plaque formation at sites where arteries bifurcate, in areas of geometric irregularity, and where blood undergoes sudden changes in velocity and direction of flow, suggests that local hemodynamic effects contribute to plaque formation. Stress generated by blood flow influences the endothelial cells. In the neck, plaques have a predilection for the great vessel origins, common carotid bifurcation, and proximal internal carotid artery (ICA).
The unique anatomy of the carotid bulb with its flow separation, flow stasis, and shear stress oscillations accounts at least in part for the high prevalence of atherosclerosis at this location.

Typical intracranial atherosclerotic lesions present primarily in five locations: main trunk of the MCA, carotid siphon, mid-portion of the basilar artery, vertebrobasilar junction, and distal vertebral artery. The distal vessels are less commonly affected.



A. Main trunk of the MCA
B. Carotid siphon
C. Mid-portion of the basilar artery
D. Vertebrobasilar junction
E. Distal vertebral artery

Figure 1.7. Typical intracranial atherosclerotic lesions primarily present in five locations.

Diagnosis

Clinical judgement in conjunction with conventional angiography remains the gold standard for diagnosing and determining treatment options for atherosclerosis. A vascular workup might also include TCD (transcranial doppler), CTA (computed tomographic angiography), or MRA (magnetic resonance angiography).

Treatment for carotid atherosclerosis

Medical treatment for atherosclerosis may be recommended if the narrowing is not very severe. If there is severe narrowing of a carotid artery, surgery (endarterectomy) to remove the plaque may be performed. If there are reasons surgery is not possible (such as poor health or previous radiation therapy to the neck), then opening of the carotid artery with a balloon catheter (angioplasty) may be performed under appropriate conditions.
Stents may also be used to keep the vessel open.

Medical Treatment

For patients with less than 50 percent stenosis, antiplatelet medications remain the cornerstone of treatment. These drugs decrease the adhesiveness of platelets and discourage thrombus buildup. Aspirin remains the therapy of choice, but there are several new medications available for patients who are not tolerant of aspirin; these include Clopidogrel (Plavix).

Surgical treatment

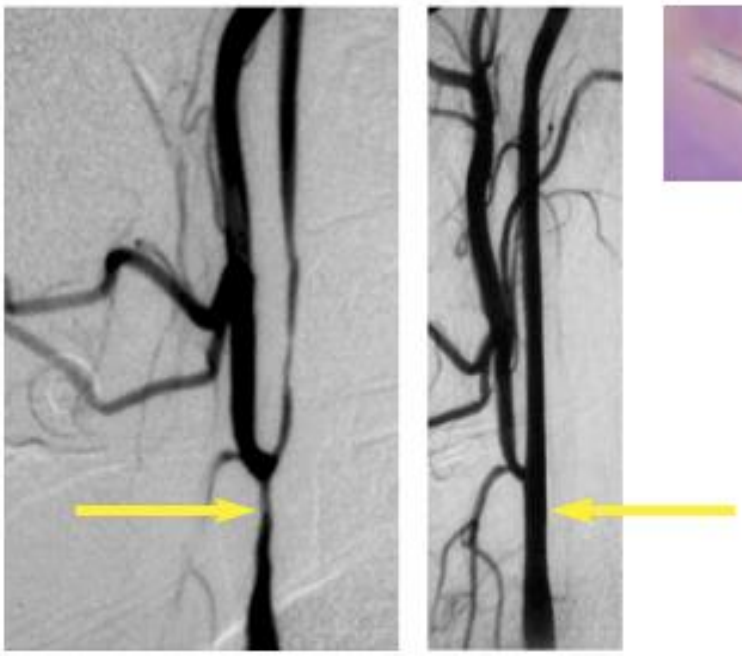
Carotid endarterectomy (CEA) is a surgical procedure that may reduce a patient's risk of stroke. During a carotid endarterectomy, the carotid artery is exposed and the plaque buildup is removed. This not only removes a stenosis and improves the blood flow through the artery, but it reduces the chance of thrombotic embolism from the ulcerated or irregular surface of the plaque.

Carotid endarterectomy is a relatively straight forward surgical procedure. The artery is generally easily accessible, the procedure can be performed under local anesthesia, and most patients go home within 48 hours of surgery.

Endovascular treatment

Neuroendovascular stenting is another treatment for carotid stenosis. Stenting might be considered as an alternative to carotid endarterectomy based on features of the stenosis, such as the size of the artery and location of the blockage, or certain risk factors for an open surgical procedure that are specific to the patient.

In this procedure, an angioplasty balloon catheter is placed across the region of stenosis and inflated to expand the plaque (predilation). Then the stent, a wire mesh tube, is placed over the balloon catheter (balloon-expandable stent) or mounted on a catheter tip (self-expandable stent) and moved into the area of the blockage. For the balloon-expandable stent, the system is designed so that when the balloon is inflated, the stent expands and locks in place. For the self-expandable stent, the stent mesh is "unsheathed" and the stent is delivered. In both cases, the stent forms a support (scaffold) to hold the artery open. The stent remains in the artery permanently. Carotid artery stenting is a less invasive alternative to CEA.



Pre-stenting **Post-stenting**

Figure 1.8. Carotid artery stenting. Results from Case Studies are not predictive of results in other cases. Results in other cases may vary.

Thrombolytic treatment
Intra-arterial thrombolysis is a method used to establish reperfusion that potentially has an extended therapeutic window. The goal of endovascular treatment is to use fibrinolytic agents locally infused into the clot intravascularly.

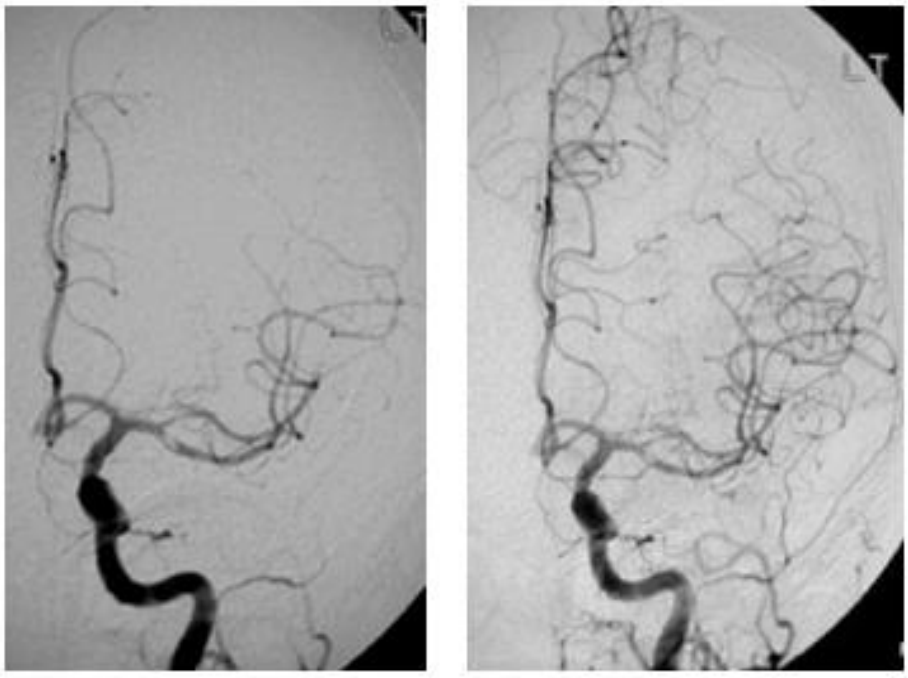


Figure 1.9. Endovascular intra-arterial therapy.

This type of therapy must be done within the indicated timeframe of the specific drug which is usually within several hours of the onset of symptoms. If too much time passes, the damage is permanent and reopening the vessel may make things worse by causing an intracerebral hemorrhage (ICH).

Intracerebral hemorrhage must also be recognized and treated quickly. Tissue plasminogen activator (tPA) and other thrombolytics cannot be given to patients with intracerebral hemorrhage.

In patients that present in the emergency room with ICH, the cause is usually hypertension. However, it can also be caused by anticoagulants, tPA, or can be the result of a ruptured vascular malformation in the brain, including an aneurysm.

Treatment for intracranial atherosclerosis
Intracranial atherosclerotic disease is currently treated primarily with medical management, both with antiplatelets such as aspirin and clopidrogrel (Plavix), and with the anticoagulant, warfarin (Coumadin). Bypass surgery may also be performed, but is far less common. Endovascular treatment is becoming more common as new devices are approved specifically for this use.

Medical treatment
The comparison of warfarin versus aspirin for symptomatic intracranial disease was studied in the WASID Trial. There was no statistically significant difference found in ischemic stroke rates for aspirin versus warfarin. The stroke rate in the territory of the symptomatic artery at one year was 12 percent for aspirin and 11 percent for warfarin. Warfarin was associated with a more statistically significant increase in incidence of hemorrhage and death.

Surgical treatment
Extracranial/Intracranial (EC/IC) Bypass, which requires a craniotomy, involves anastomosis of an arterial segment to bypass the narrowed atherosclerotic lesion.
The EC/IC Bypass Study, published in 1985, failed to confirm the hypothesis that extracranial-intracranial anastomosis is effective in preventing cerebral ischemia in patients with atherosclerotic arterial disease in the carotid and middle cerebral arteries.

Endovascular treatment
Until the early 2000s, there was no FDA-approved device in distribution for treating ICAD endovascularly in the U.S. However, some doctors determined it was in their patient's best interest to treat ICAD using angioplasty balloons and balloon-expandable stents "off-label."
The first self-expanding stent approved under a humanitarian device exemption (HDE) to treat ICAD was launched to the market in 2005 by Boston Scientific (now Stryker). The lesion is first pre-dilated with the Gateway® PTA Balloon Catheter, then the Wingspan® Stent System, mounted on a catheter tip, is unsheathed and the stent is deployed to form a scaffold to hold the artery open.*

* Humanitarian Device: The Wingspan Stent System with Gateway PTA Balloon Catheter is Authorized by Federal law for use in improving cerebral artery lumen diameter in patients 22 to 80 years old with recurrent (2 or more) strokes refractory to a comprehensive regimen of medical therapy and due to atherosclerotic disease of intracranial vessels with 70-99% stenosis that are accessible to the system. The most recent stroke must have occurred more than 7 days prior to treatment with the Wingspan Stent System. Patients are eligible for treatment with the Wingspan Stent System if their Modified Rankin Score (mRS) is 3 or less at the time of treatment.
The effectiveness of this device for this use has not been demonstrated.

Figure 2.0. Stenosed vessel.

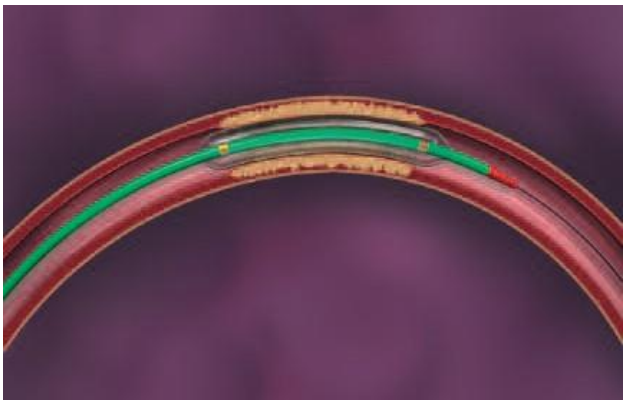


Figure 2.1. Balloon, pre dilation.

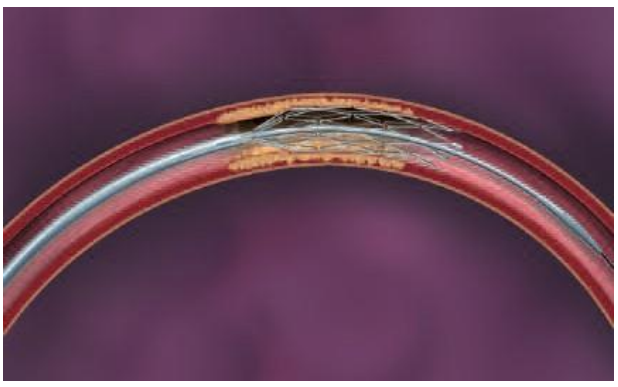


Figure 2.2. Stent deployment.

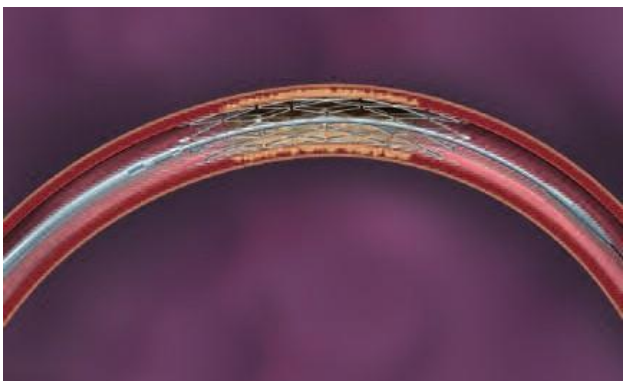


Figure 2.3. Stent deployed.

See package insert for complete indications, contraindications, warnings, precautions and instructions for use.

Humanitarian device. The Wingspan® Stent System with Gateway® PTA Balloon Catheter is Authorized by Federal law for use in improving cerebral artery lumen diameter in patients 22 to 80 years old with recurrent (2 or more) strokes refractory to a comprehensive regimen of medical therapy and due to atherosclerotic disease of intracranial vessels with 70-99% stenosis that are accessible to the system. The most recent stroke must have occurred more than 7 days prior to treatment with the Wingspan Stent System. Patients are eligible for treatment with the Wingspan Stent System if their Modified Rankin Score (mRS) is 3 or less at the time of treatment. The effectiveness of this device for this use has not been demonstrated.

Indications For Use

The Wingspan Stent System with Gateway PTA Balloon Catheter is Authorized by Federal law for use in improving cerebral artery lumen diameter in patients 22 to 80 years old with recurrent (2 or more) strokes refractory to a comprehensive regimen of medical therapy and due to atherosclerotic disease of intracranial vessels with 70-99% stenosis that are accessible to the system. The most recent stroke must have occurred more than 7 days prior to treatment with the Wingspan Stent System. Patients are eligible for treatment with the Wingspan Stent System if their Modified Rankin Score (mRS) is 3 or less at the time of treatment.

Contraindications

- Patients in whom antiplatelet and/or anticoagulation therapy is contraindicated.
- Lesions that are highly calcified or otherwise could prevent access or appropriate expansion of the Stent.
- For the treatment of stroke with an onset of symptoms within 7 days or less of treatment.
- For the treatment of transient ischemic attacks.

Adverse events

Observed adverse events:

Infection; TIA; stroke; hematoma; vasospasm; hemorrhagic event; hypertension; peripheral vascular diseases; neurological symptoms; pain; AMI; angina; arrhythmia; creatinine increase; hematuria; hypoglycemia/hyperglycemia; asymptomatic thromboembolic event; bradycardia (35 min); broken middle-foot left/V-fracture; chronical antrum gastritis; death; elevated bilirubin, GOT, GPT; fever; hiatus hernia; hypervolemia; new distal in stent stenosis; pulmonary edema; respiratory failure; seizure; syncope.

Potential adverse events:

Aneurysm, allergic reaction, cerebral ischemia, coagulopathy, drug reaction to contrast or antiplatelet medication, emboli (air, tissue, or thrombotic tissue), hypotension, intimal dissection, ischemia/infarct, restenosis, pseudoaneurysm, stent migration, stent misplacement, stent occlusion, stent embolization, stent thrombosis, thromboembolic event, vessel dissection, vessel occlusion, vessel perforation, vessel rupture, vessel spasm, vessel thrombosis, vessel trauma requiring surgical repair or intervention.

Please be aware that potential adverse effects may arise even with the proper use of medical devices. Accordingly, this device should only be used by persons qualified in the procedures for which it is indicated.

Warnings

- The Wingspan® Stent System is not designed or intended for contrast injections or injections other than heparinized saline.
- If excessive resistance is encountered during the use of the Wingspan Stent System or with the Gateway® PTA Balloon Catheter at any time during the procedure, discontinue use of the System. Movement of the System against resistance may result in damage to the vessel, or a System component.
- In animal evaluations, the severity of vessel stenosis/neointimal thickness appears to be correlated with the degree of trauma inflicted on the arterial walls by Stent placement or Stent radial expansion.
- Experience with stent implants indicates that there is a risk of restenosis. Subsequent restenosis may require repeat dilation of the vessel segment containing the stent. The risks and long-term outcome following repeat dilation of endothelialized stents is unknown at present.
- If the stent is implanted adjacent to or contacting other implanted metal, such as another stent or embolic coil, the metals should be of similar composition to avoid galvanic corrosion potential.
- The safety and probable benefit of the Wingspan System with Gateway PTA Balloon Catheter have not been established for treatment of patients with any of the following:
- New or unstable symptoms within 24 hours of treatment;
- Evidence on brain imaging study of subacute or acute ischemia in the vascular territory of the target lesion;
- A recent stroke of a size that would place the patient at risk for intracranial hemorrhage;
- Thrombolytic therapy within 24 hours prior to treatment with the device;
- The cause of the target stenosis is not atherosclerosis;
- The normal diameter of the target vessel that is not between 2.00 and 4.50 mm;
- A target lesion length greater than 14 mm;
- Severe calcification at the target lesion;
- A minimum lumen diameter of the target vessel of less than 2 mm after pre-dilation;
- Greater than 50% stenosis proximal or distal to the target intracranial lesion; OR
- A previous intracerebral or intracranial hemorrhage or a recent hemorrhagic infarction.
- Persons allergic to nickel titanium (Nitinol) may suffer an allergic response to this stent implant..

Warnings

- Since the use of this device carries the associated risk of subacute thrombosis, vascular complication and/or bleeding events, judicious selection of patients is necessary.
- Only physicians who have received training should perform intracranial angioplasty.
- Angioplasty and stenting procedures should only be performed at hospitals where emergency intracranial surgery can be readily performed in the event of a potentially injurious or life-threatening complicatio
- Contents supplied STERILE using an ethylene oxide (EO) process. Do not use if sterile barrier is damaged. If damage is found call your Boston Scientific Representative.
- For single patient use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure that, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness, or death of the patient.

Precautions/Cautions

- Federal Law (USA) restricts this device to sale by or on the order of a physician.
- After use, dispose of product and packaging in accordance with hospital, administrative and/or local government policy.
- Store in a dry, dark, cool place.
- Note product "Use By" date.
- Follow the Gateway® PTA Balloon Catheter preparation and use instructions carefully.
- **Do not prepare or pre-inflate the balloon** other than as directed. Use the balloon purging technique described in this Instructions for Use.
- Typical antiplatelet and anticoagulation regimen used for interventional intracranial procedure is an important adjunct to balloon angioplasty treatment. Do not use the Gateway PTA Balloon Catheter in patients in whom antiplatelet and/or anticoagulation therapy is contraindicated. Vessel thrombosis may occur during the procedure if proper antiplatelet and anticoagulation therapy is not administered.
- If difficulty is experienced during inflation, do not continue, remove the device and do not attempt to use it. Select another device.
- Angioplasty may lead to dissection of the vessel and may cause other complications (vasospasm/acute closure) of the vessel requiring additional intervention (i.e., further dilation, placement of stents).
- Use only the appropriate balloon inflation media. Do not use air or any gaseous medium to inflate the balloon because it may cause uneven inflation and complications.
- To reduce the potential for vessel damage, the inflated diameter of the balloon should approximate the lesser of the vessel diameters just proximal and distal to the stenosis.
- Do not use a guidewire having a diameter greater than 0.014 in/0.36 mm.
- When the delivery catheter is exposed to the vascular system, it should be manipulated while under high-quality fluoroscopic observation. If resistance is met during manipulation, determine the cause of the resistance before proceeding.
- Infusion of any medium other than a flush of heparinized normal saline through the guidewire lumen may compromise device performance.
- Do not attempt to reposition a partially deployed balloon. Attempted repositioning of a partially deployed balloon may result in severe vessel damage.

Precautions/Cautions

- Balloon pressures should be monitored during inflation. **Do not exceed rated burst pressure indicated on the product label**. Use of pressures higher than those specified on the product label may result in a ruptured balloon and potential intimal damage and dissection. The rated burst pressure is based on the results of in vitro testing. At least 99.9% of the balloons (with a 95% confidence interval) will not burst at or below their rated burst pressure. Use of a pressure monitoring device is recommended to prevent over pressurization.
- Before withdrawing the device, visually confirm complete balloon deflation by fluoroscopy. If the balloon has already been inflated and difficulty is experienced deflating (a non-deflate), connect a large-barrel syringe and manually attempt to deflate the device.
- **In order to achieve optimal performance of Gateway® Catheters and Boston Scientific steerable guidewires and to maintain the lubricity of the Bioslide surface, it is critical that a continuous flow of appropriate flush solution be maintained** between a) the Gateway Catheter and guide catheter, and b) the Gateway Catheter and any intra- luminal device. In addition, flushing aids in preventing contrast crystal formation and/or clotting on both the guidewire and inside the catheter lumen.
- The recommended continuous flush set up requires two stopcocks and two rotating hemostatic valves (RHV); the RHV's provide a fluid tight seal and are attached to the guide catheter and Gateway Catheter. The stopcocks attach to the RHV sidearms, which become infusion ports for appropriate flush or contrast medium injection.

Background to stroke
Aneurysms

An ***aneurysm*** is an abnormal, outward dilation of an artery resulting from a weakening in the arterial wall. Brain aneurysms, also called cerebral or intracranial aneurysms, are believed to be congenital in predisposition or may be associated with other medical conditions such as hypertension. It is estimated that up to one in fifteen people in the U.S. will develop a brain aneurysm during their lifetime.

Brain aneurysms affect more females (3:2) over males, and 20 percent of patients have multiple (two or more) aneurysms. The average age at presentation is usually 40–60 years old. Smoking predisposes to aneurysm formation.

Those aneurysms that involve the arteries in the brain are a serious medical condition that can rupture (bleed), causing a serious stroke or death, or compress surrounding brain tissue or cranial nerves causing neurological deficits.

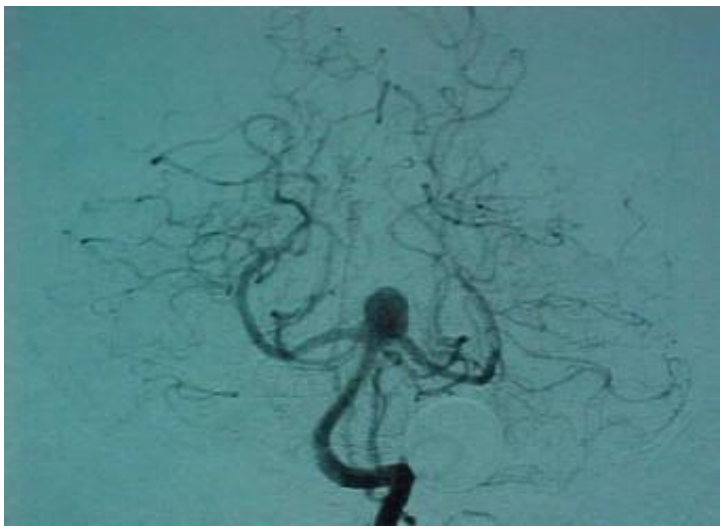


Photo of image taken by a BSC representative.

Figure 2.4.. Aneurysm on angiography.

Classifcations
Aneurysms are classified by their shape, size, and location.

Shape:

- A **saccular or berry aneurysm** is the most common type and typically forms due to hemodynamic stress. A small saccular-shaped aneurysm resembles a berry. These aneurysms appear more frequently in the anterior circulation.
- A **fusiform aneurysm** is an elongated, spindle-shaped dilation.
- A **dissecting aneurysm** is a splitting of an artery wall via a small tear.

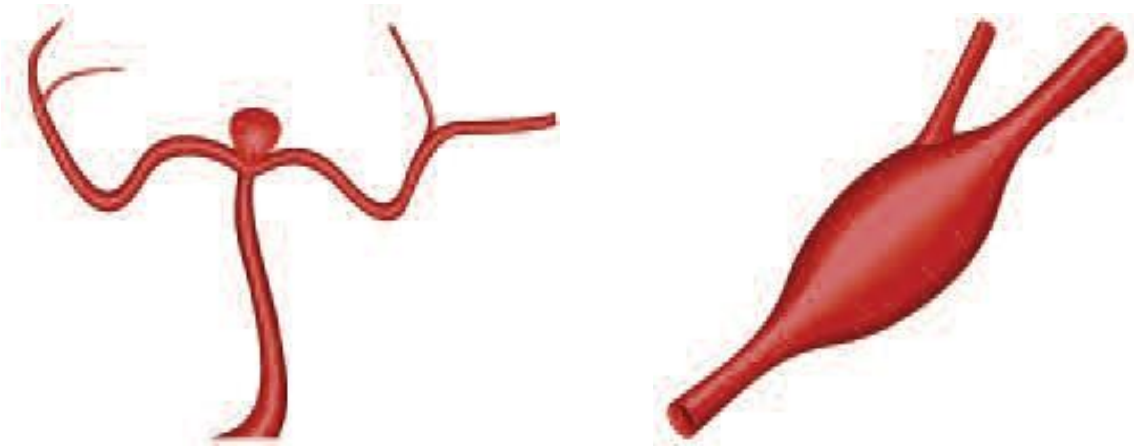


Figure 2.6. Saccular and fusiform aneurysms.

Size:
- A small aneurysm is smaller than 12 mm
- A large aneurysm is 12 - 25 mm (a U.S. dime is 18 mm)
- A giant aneurysm is larger than 25 mm

Aneurysm neck size refers to the width of the opening to the parent vessel.

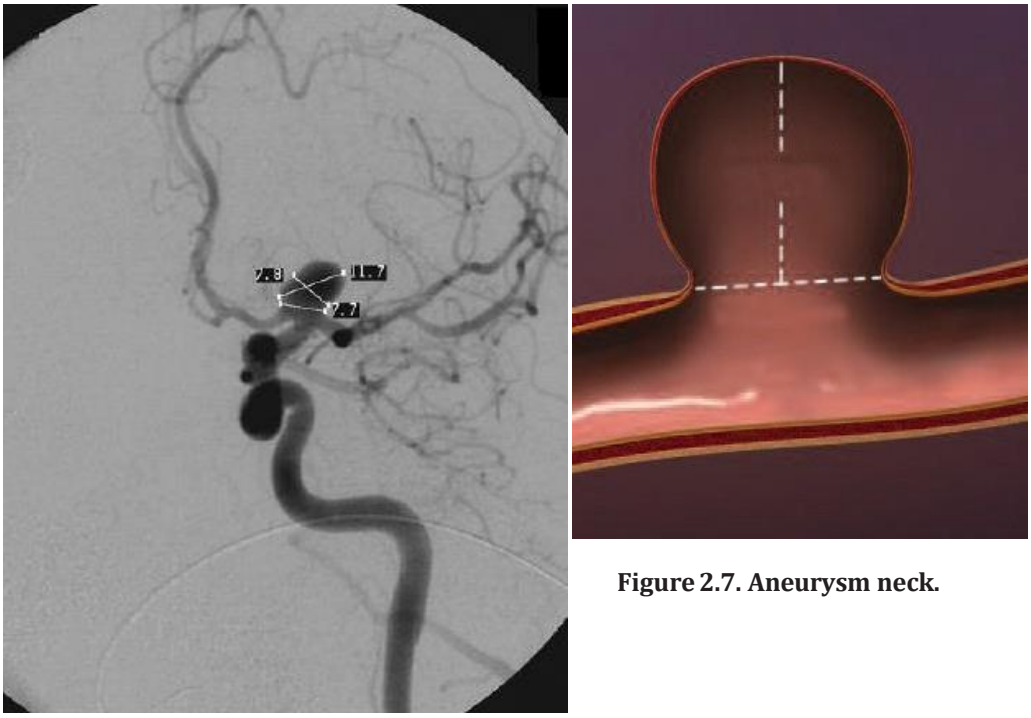


Figure 2.7. Aneurysm neck.

Location:
Aneurysms are named by the parent vessel from which they arise. For example, an aneurysm arising from the M1 segment of the MCA is referred to as an M1 aneurysm. Aneurysms are also characterized by the number of lobes they have.

Around eighty-five percent of brain aneurysms develop in the anterior circulation of the brain. Fifteen percent are found in the posterior circulation of the brain.

Aneurysm rupture

Patients often do not experience any symptoms of having a brain aneurysm before it ruptures. However, in many cases, people with unruptured aneurysms will experience some or all of the following aneurysm symptoms:

- Pain located above and behind the eye.
- Localized headache.
- Peripheral vision deficits.
- Thinking or processing problems.
- Speech complications.
- Perceptual problems.
- Sudden changes in behavior.
- Loss of balance and coordination.
- Decreased concentration.
- Short-term memory difficulty.
- Fatigue.

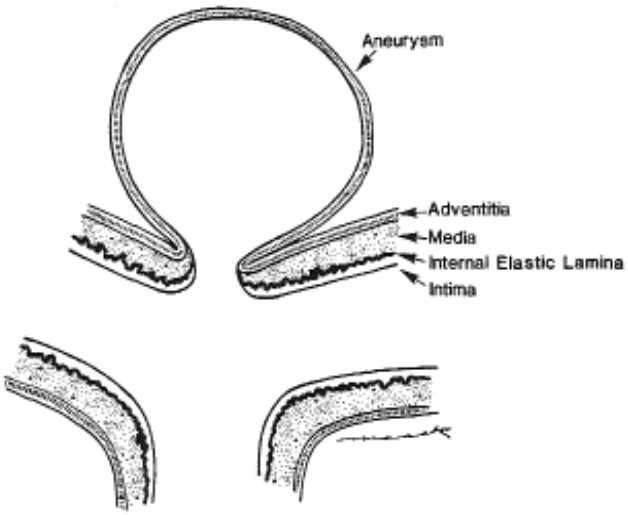


Figure 2.7. Aneurysmal sac.

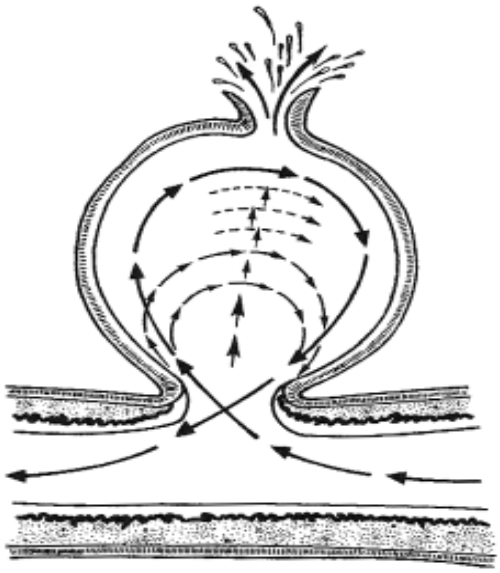


Figure 2.8. Rupture of an aneurysm.

The risk of an aneurysm rupture is estimated at 1–2 percent per year. The risk varies with aneurysm type, size, location, and history of previous aneurysm rupture. When a brain aneurysm does rupture, the blood usually goes into the subarachnoid space (a space that closely surrounds the brain), or less commonly, directly into the brain substance. These patients often complain of a severe headache and describe it as "the worst headache of my life." Unfortunately, aneurysms that have ruptured are at high risk for further bleeding.
A subarachnoid bleed is considered a medical emergency with potential major complications to the patient.

Each year, approximately 0.2–3 percent of Americans with undiagnosed brain aneurysms may suffer from bleeding. The annual incidence of aneurysmal subarachnoid hemorrhage in the U.S. exceeds 30,000 people. Between 10–15 percent of these patients will die before reaching the hospital, and over 50 percent will die within the first 30 days after rupture. Of those who survive, about half suffer some permanent neurological deficit. (*Statistic from 2012*)

Strokes caused by subarachnoid hemorrhage often occur one to two weeks after the hemorrhage itself. This happens because the blood from the hemorrhage irritates the blood vessels on the surface of the brain, causing them to close (vasospasm).

Less commonly, aneurysms can cause problems not related to bleeding. An aneurysm can form a blood clot within it that can break away and be carried downstream until it obstructs a small arterial branch, causing either a stroke or mini stroke. An aneurysm can also press against nerves (resulting in paralysis or abnormal sensation of one eye or the face) or the adjacent brain (resulting in seizures).

Vasospasm after aneurysm rupture

Vasospasm is the narrowing (spasm) of blood vessels. Vasospasm of the vessels that supply the brain can occur after a bleed from an aneurysm in the head and is the most significant complication of this kind of subarachnoid hemorrhage. The spasm can be severe enough to prevent enough blood from reaching the brain, causing a stroke. Of patients that survive the bleed from the aneurysm, 5–20 percent die from vasospasm. The use of drugs to help prevent vasospasm has decreased this number in recent years.

Vasospasm generally refers to either a mechanical stimulation of the vessel, a reactive protective mechanism for bleeding, or a response to local trauma. Intracranially, however, vasospasm can be a devastating complication related to subarachnoid blood arising from an aneurysmal or other rupture (e.g., arteriovenous malformation, cortical vein).

Vasospasm secondary to subarachnoid hemorrhage can be defined as either angiographic or clinical. After a subarachnoid bleed, up to 70 percent of individuals suffer some degree of intracranial vasospasm. This usually reaches maximum intensity from 4–12 days after the acute hemorrhage but still can be present as late as 3 weeks (or longer) after a bleed.

Angiographic vasospasm manifests more often than clinical vasospasm. True clinical vasospasm affects only 20–30 percent of patients with subarachnoid hemorrhage. It presents as a decrease in level of consciousness, confusion, delirium, or focal neurologic deficits. Clinical vasospasm can be reversible even when the symptoms are profound.

Once vasospasm does occur, there are several treatments that may be used to open the vessels back up and prevent damage to the brain. These may include:

- Medical therapy with pharmacological agents to increase the blood pressure and improve blood flow to the brain.
- Placement of a catheter in a cerebral artery to allow direct infusion of pharmacological agents to dilate the artery.
- Placing a balloon catheter into the vessel to dilate it (angioplasty).

Vasospasm occurs when the arterial wall becomes spastic, causing contraction in the vessel that can significantly constrict the lumen. Therefore, the procedure(s) that are used depend on how severe the spasm is and where in the blood vessels it occurs.

After a patient becomes symptomatic from vasospasm and has failed best available and possible medical treatment, the treating physician may initiate endovascular therapy.

The two techniques available for endovascular treatment of vasospasm are mechanical angioplasty and pharmacologic infusion (papaverine or another vasodilator).

Clinical response to therapy appears to be related more to the rate of increase in clinical symptoms than to the degree of radiographic vasospasm; some patients with incredible spasm may be essentially intact, whereas others with only moderate vasospasm may display profound symptoms. It is important to understand that the earlier therapy is performed, the better.

For focal stenoses in a proximal location along a primary intracranial vessel, direct angioplasty may yield excellent results and can be a straightforward solution.

Angioplasty is the treatment of choice for experienced interventional neuroradiologists. The angiographic results are more dramatic and immediate, and the clinical results appear to be more significant. The vasodilation is also permanent.

Angioplasty requires more technical skill than simple infusion. The possibility of vascular rupture or intimal tear makes this procedure more risky than papaverine infusion.

The indications for therapy are the same for papaverine as for angioplasty. It is important to treat vasospasm as soon as possible for two reasons: vascular response is better, and permanent ischemic damage is minimized. If there is true downstream parenchymal damage, even if there is good response to infusion, spasm recurs shortly after the infusion has ceased and can be even worse than before treatment, extending on occasion down to the extracranial (cervical) internal carotid artery and even down to the region of the carotid bifurcation. This appears to be a true protective mechanism, rather than a pathologic vascular behavior (i.e., the brain is trying to prevent normal pressure from reaching the damaged territories).

In angioplasty, the balloon occlusion catheter is delivered through a large-lumen guide catheter, and the use of a guidewire inside the balloon catheter facilitates the advancement of the system.

The balloon catheter system is then advanced to the area of spasm and slowly inflated. It is then deflated, advanced to the end of the dilated segment, and inflated again. This process is repeated. It is important that a low pressure balloon is selected for treatment of vasospasm.

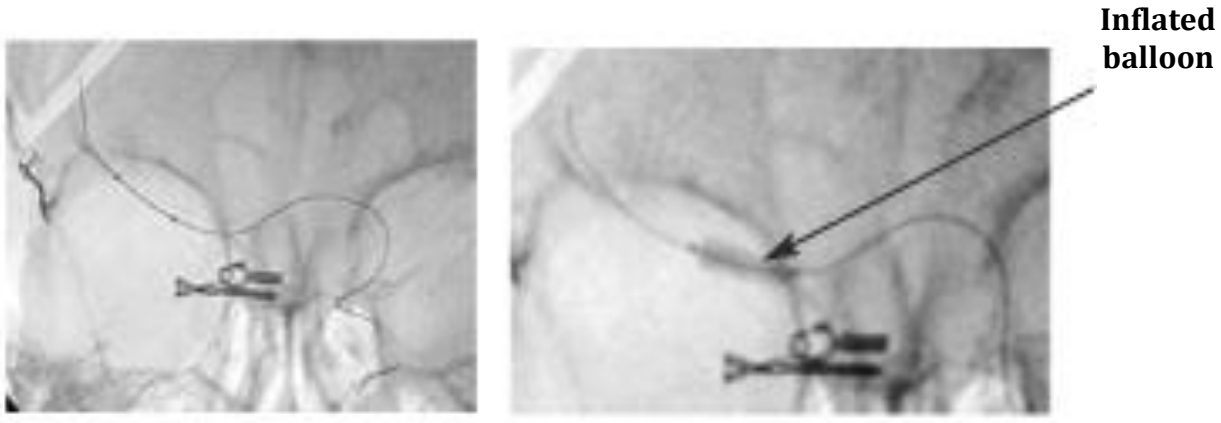


Figure 2.9. Angioplasty.

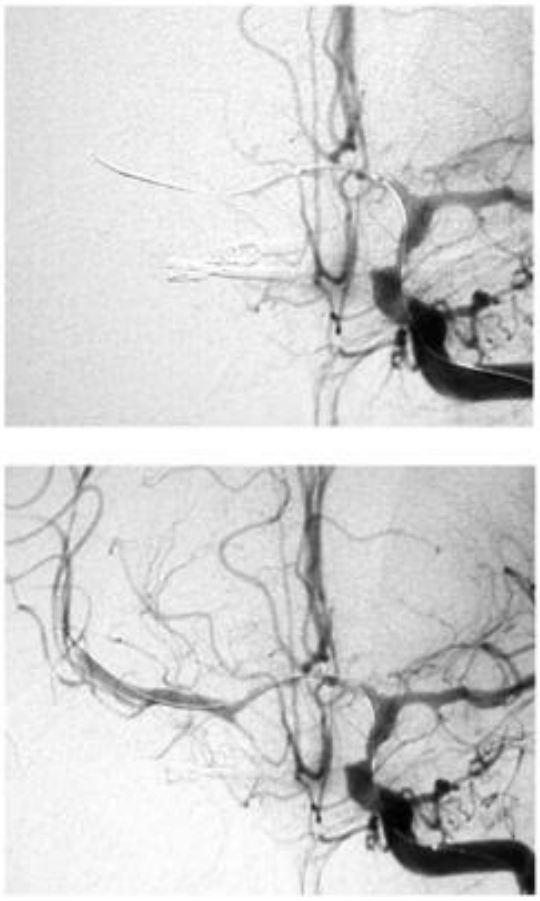


Figure 3.0. Angioplasty and paperverine infusion.

Diagnosis

Diagnosis of a ruptured cerebral aneurysm is commonly made by finding signs of subarachnoid hemorrhage on a CT scan. The CT scan is a computerized test that rapidly X-rays the body in cross sections, or slices, as the body is moved through a large, circular machine. If the CT scan is negative, but a ruptured aneurysm is still suspected, a lumbar puncture may be performed to detect blood in the cerebrospinal fluid (CSF) that surrounds the brain and spinal cord.

To determine the location, size, and shape of an aneurysm, ruptured or unruptured, neuroradiologists will use either cerebral angiography or computerized tomographic angiography.

Cerebral angiography, the traditional method, involves introducing a catheter into the artery (usually in the leg) and steering it through the blood vessels of the body to the artery involved in the aneurysm.

A special dye, called a contrast agent, is injected into the patient's artery, and its distribution is shown on X-ray projections. This method may not detect some aneurysms due to overlapping structures or spasm.

Treatment

Surgery or minimally invasive endovascular coiling techniques can be used in the treatment of brain aneurysms. It is important to note, however, that not all aneurysms are treated at the time of diagnosis or are amenable to both forms of treatment.

Surgical treatment

To get to the aneurysm, surgeons must first remove a section of the skull—a procedure called a *craniotomy*. The surgeon then spreads the brain tissue apart and places a tiny metal clip across the neck to stop blood flow into the aneurysm. After clipping the aneurysm, the bone is secured in its original place and the wound is closed.

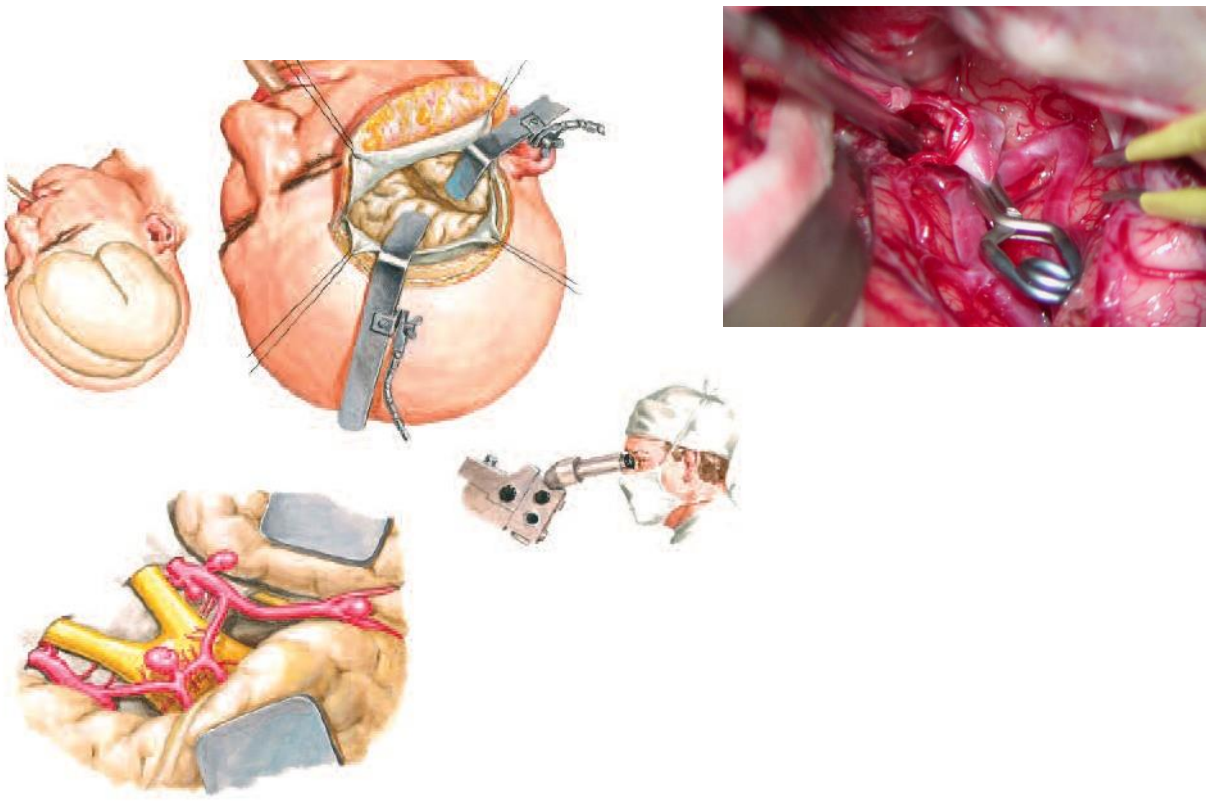


Figure 2.9. Craniotomy for aneurysm clipping.

Endovascular treatment

Endovascular treatment is a minimally invasive procedure that accesses the treatment area from within the blood vessel. In the case of aneurysms, this treatment is called coil ***embolization*** or coiling.

The goal of this aneurysm treatment is to cause considerable clot formation (thrombosis) inside the aneurysm to occlude the aneurysm completely, leaving the parent vessel patent. In patients for whom endovascular therapy is indicated, the rationale for treatment is to prevent bleeding in unruptured aneurysms or to prevent rebleeding in ruptured ones.

Endovascular coiling does not require open surgery. Instead, physicians use real-time X-ray technology, called fluoroscopic imaging, to visualize the patient's vascular system and treat the disease from inside the blood vessel.

Endovascular treatment of brain aneurysms involves insertion of a catheter into the femoral artery in the patient's leg and navigating it through the vascular system into the head and into the aneurysm. Tiny platinum coils are threaded through the catheter and deployed into the aneurysm, blocking blood flow into the aneurysm with the goal of preventing rupture. Each coil is attached to a delivery wire, allowing the physician to reposition or withdraw the coil to optimize ideal placement. Once properly positioned within the aneurysm, the coil is detached from the delivery wire using a variety of different detachment processes depending on the product.

The coils acutely occlude the neck of the aneurysm, and over time endothelial cells cover the neck of the aneurysm in some patients. In some patients, ***recanalization*** (regrowth of the aneurysm) occurs.

The coils are made of platinum designed to be flexible enough to conform to the aneurysm shape and visible via X-ray. Multiple coils must be packed into the aneurysm to create complete occlusion.

Sometimes the procedure is performed in stages where multiple coils are inserted during separate procedures (e.g., six months apart). It is very important to pack the coils into the aneurysm fully and thoroughly, otherwise there is a tendency for recanalization.

This endovascular coiling, or filling, of the aneurysm can be performed under general anesthesia or light sedation.

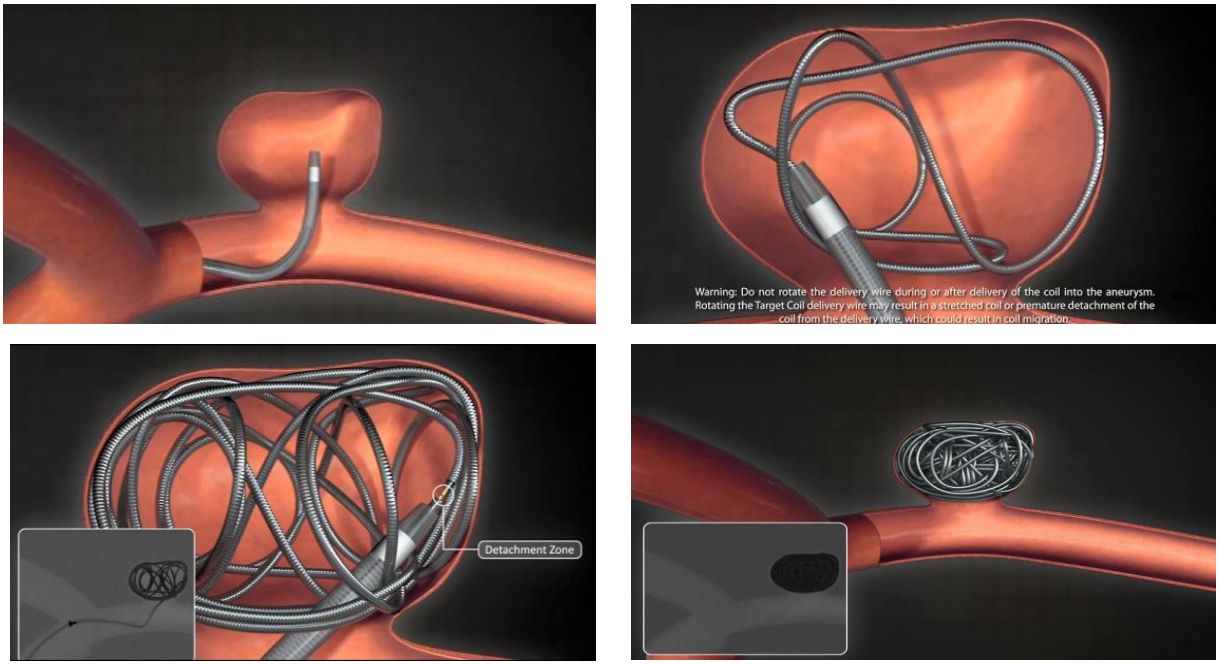


Figure 3.0. Treatment of a brain aneurysm with detachable coils.

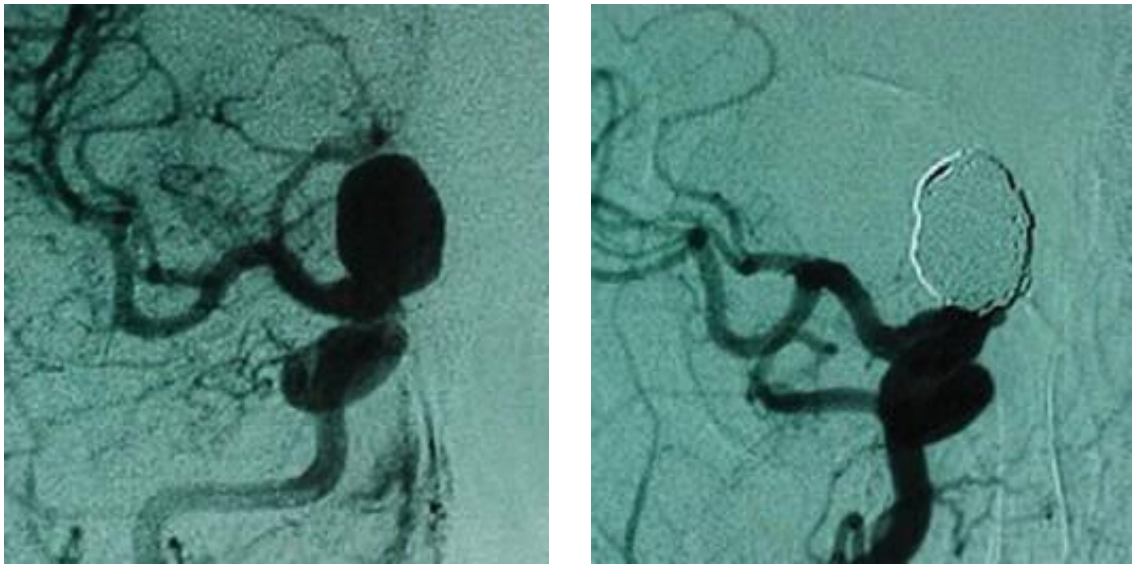


Figure 3.1 and Figure 3.2. Angiogram of an aneurysm before and after treatment.

Endovascular coiling vs. surgical clipping in treatment of ruptured aneurysms

Until the early 200s, most studies on surgical clipping and endovascular treatment of brain aneurysms were either small-scale studies or were retrospective studies that relied on analyzing historical case records. The only multicenter prospective randomized clinical trial (considered the "gold standard" in study design) comparing surgical clipping and endovascular coiling of ruptured aneurysms is the International Subarachnoid Aneurysm Trial (ISAT).

This study found that in patients equally suited for both treatment options, endovascular coiling treatment produced substantially better patient out- comes than surgery in terms of survival free of disability at one year. The relative risk of death or significant disability at one year for patients treated with coils was 23.9 percent lower than in surgically treated patients. This equates to an absolute risk reduction of 7.4 percent (3.6–11.2), which is equivalent to 74 patients avoiding death or dependency at 1 year for every 1,000 patients treated.

The study results were so compelling that the trial was halted early after enrolling 2,143 of the planned 2,500 patients, because the trial steering committee determined that it was no longer ethical to randomize patients to neurosurgical clipping.[9]

It is important to note that patients enrolled in the ISAT were evaluated by both a neurosurgeon and an endovascular coiling specialist, and both physicians had to agree that the aneurysm was treatable by either technique. Most patients were not deemed equally suitable for both treatment options and were therefore not randomized. Most of the 2,143 patients randomized into the trial had good-grade (88 percent in World Federation of Neurosurgical Societies (WFNS) grades I and II), small anterior circulation aneurysms (92 percent less than 11 mm in size). The ISAT findings are relevant to the types of patients randomized into the trial: good-grade patients with small anterior circulation aneurysms. The results suggest that these patients may be candidates for coiling and should receive an endovascular consultation as part of the treatment protocol. For patients that do not fit this profile, treatment decisions should be based on other research.

After publication of the preliminary results of ISAT, there was much controversy and discussion in the worldwide neurosurgical community. Several position statements were issued by groups in neurosurgery and related specialties, including the American Association of Neurological Surgeons, the American Society of Neuroradiology (ASNR), the American Society of Therapeutic and Interventional Neuroradiology (ASITN), and the respective German and Japanese societies. These statements drew attention to the many questions that the early results did not answer, in particular the durability and long-term efficacy of coil treatment at preventing re-rupture, applicability of the results, and possible challenges in the use of ISAT results to inform the treatment of all patients with subarachnoid hemorrhage. Criticisms mostly related to the proportion of eligible patients who were enrolled, which varied very widely between centers, and the expertise of the neurosurgeons who treated patients in ISAT, particularly those in the UK. These concerns have been noted in the final publication.

Long-term follow-up will be essential to assess the early advantage of endovascular coiling over conventional neurosurgical clipping for the treatment of brain aneurysms.

Molyneux A., Kerr R., Yu L., Clarke M., Sneade M., Yarnold J., Sandercock P., "International Subarachnoid Aneurysm Trial (ISAT) of Neurosurgical Clipping Versus Endovascular Coiling in 2,143 Patients With Ruptured Intracranial Aneurysms: a randomized comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion," *Lancet* 2005; 366: 809–817
Molyneux A., Kerr R., Stratton I., Sandercock P., Clarke M., Shrimpton J., Holman R., "International Subarachnoic Aneurysm Trial (ISAT) of Neurosurgical Clipping Versus Endovascular Coiling in 2,143 Patients With Ruptured Intracranial Aneurysms: a randomized trial," *Lancet* 2002; 360: 1267–74.
Harbaugh R.E., Heros R.C., Hadley M.N., "AANS Position Statement on the International Subarachnoid Aneurysm Trial (ISAT)," *Lancet* 2003; 361: 783–784.
Derdeyn C.P., Barr J.D., Berenstein A., et al., "The International Subarachnoid Aneurysm Trial (ISAT): a position statement from the executive committee of the American Society of Interventional and Therapeutic Neuroradiology," *Am J Neuroradiol* 2003; 24: 1404–08.
8 Raabe A., Schmiedek P., Seifert V., Stolke D., "German Society of Neurosurgery Section on Vascular Neurosurgery: position statement on the International Subarachnoid Aneurysm Trial (ISAT)," *Zentrabl Neurochir* 2003; 64: 99–

Treatment of unruptured aneurysms

Although no multicenter randomized clinical trial comparing endovascular coiling and surgical treatment of unruptured aneurysms has yet been conducted, retrospective analyses have been found that endovascular coiling is associated with less risk of bad outcomes, shorter hospital stays, and shorter recovery times compared with surgery. Studies have shown that:

- Average hospital stays are more than twice as long with surgery as compared to the endovascular coiling treatment.
- Four times as many surgical patients report new symptoms or disability after treatment as compared to coiled patients.
- There can be a dramatic difference in recovery times. One study showed that surgically treated patients had an average recovery time of one year compared to coiled patients who recovered in 27 days.

Balloon remodeling techniques

The ***balloon remodeling*** technique was developed to overcome the difficulties and limitations of the endovascular therapeutic approach in broad-based or wide-neck aneurysms. An occlusion balloon is inflated in the parent vessel, in front of the necks of the aneurysm, causing temporary occlusion of both neck and parent vessel as coils are advanced into the aneurysm.

Figure 3.3. Occlusion balloon catheter remodeling technique.

The theory behind the balloon remodeling concept was to stabilize coils during deployment. Some physicians may have believed that overcoming the inherent limitations of some coils would allow the treatment of a higher percentage of aneurysms and lower the failure rate.

Through the sheath, guide catheter(s) are inserted and positioned into the common carotid artery, internal carotid artery (ICA) or the vertebral artery (VA), depending upon the location of the aneurysm. The guide catheter with the two tip marker microcatheter has to be positioned more distally in the ICA or VA. The guide catheter with the balloon occlusion catheter is normally positioned more proximally.

Under ***biplane fluoroscopy***, the balloon catheter is placed first in the parent vessel in front of the neck of the aneurysm. The following images depict a balloon remodeling procedure.

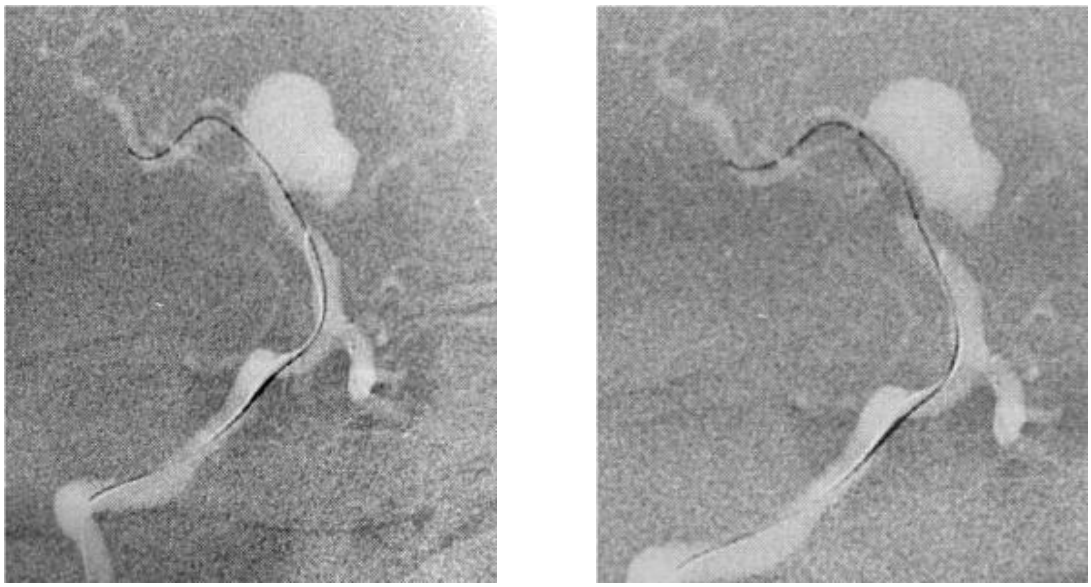
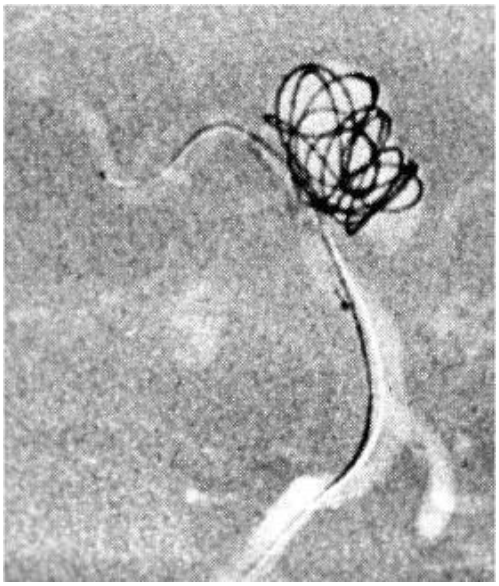


Figure 3.4. With the guidewire positioned past the distal tip of the microcatheter, the balloon has stability in front of the neck of the aneurysm during inflation and deflation.

Complications related to this technique include:

- Thromboembolic events.
- Rupture of the aneurysmal sac.
- Coil migration.
- Potential damage to the arterial wall.



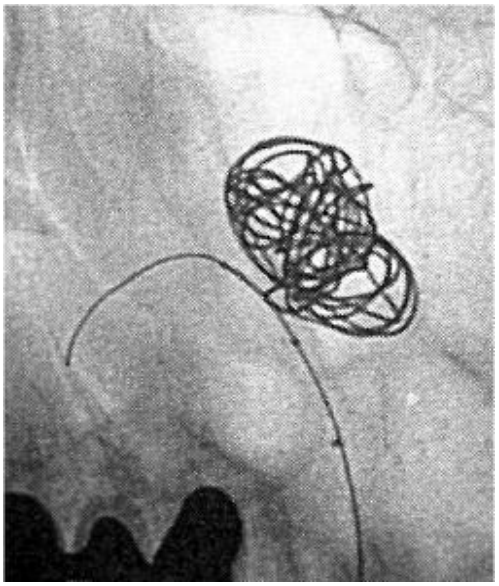


Figure 3.5. Under the protection of the balloon, the microcoils are then deposited into the aneurysm. Results from case studies are not predictive of results in other cases. Results in other cases may vary.

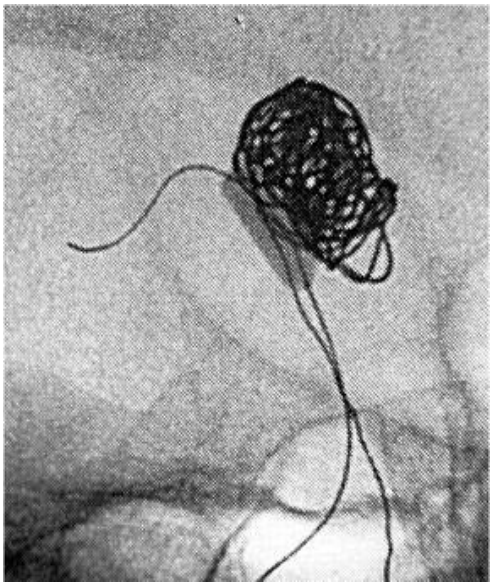


Figure 3.6. After each coil is positioned, but before detachment, the balloon is deflated in order to verify the stability of the coil. Results from case studies are not predictive of results in other cases. Results in other cases may vary.

Stenting

Since the introduction of intravascular stents to prevent occlusion and restenosis after transluminal angioplasty, improvements in endovascular techniques have allowed access for endovascular stent delivery to tortuous segments of the intracranial vasculature. These stents can be placed within the parent artery across the orifice of wide-necked intracranial aneurysms with the potential to isolate the lesion from the parent artery.

Two therapeutic strategies for stent deployment have emerged. The first involves simply placing a stent in the parent artery across the orifice of an intracranial aneurysm to alter intra-aneurysmal ***hemodynamics*** and reduce shear stress at the distal aneurysmal inflow zone by diversion of blood flow from the orifice of the aneurysm.

The second approach consists of stent placement across the interface between the aneurysm and parent artery combined with an endovascular packing technique. Following stent placement, the aneurysmal lumen can be obliterated with coils delivered via a microcatheter introduced into the aneurysm through the stent mesh. This technique may allow dense packing of wide-necked or fusiform intracranial aneurysms, because the stent acts as an endoluminal restraint, preventing herniation of the embolic agent into the parent artery.

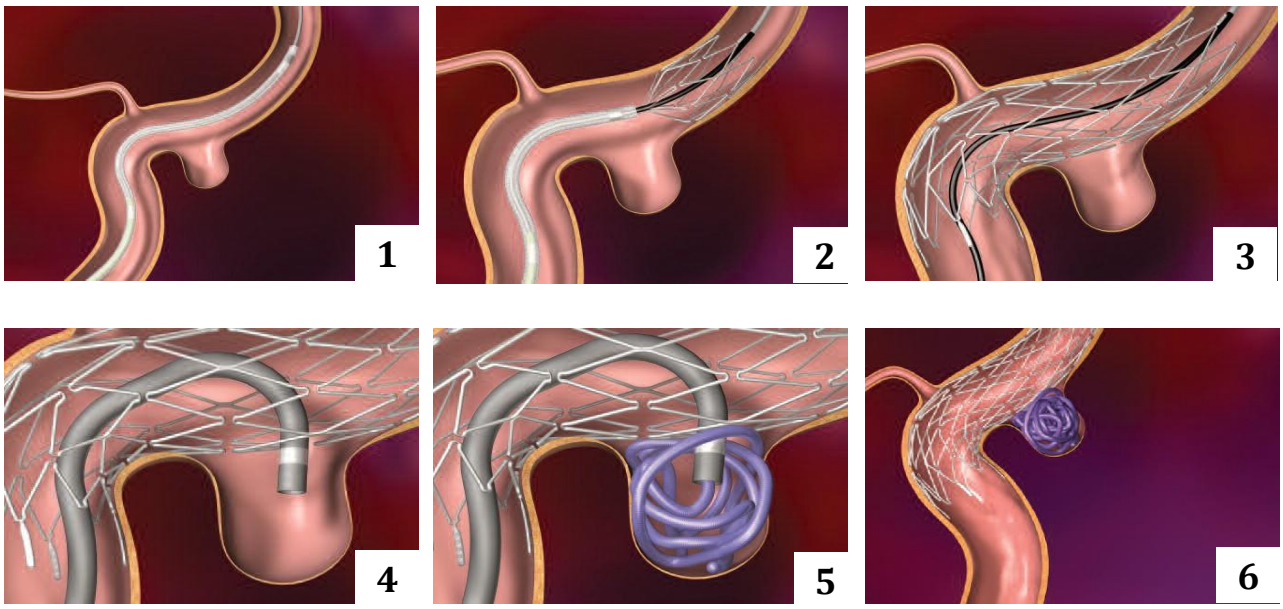


Figure 3.7. Stent deployment steps.

Background to stroke
Arteriovenous malformations

Arteriovenous Malformations (AVMs) are abnormal direct connections between arteries and veins that form a tangle of dilated blood vessels that bypass normal brain tissue and directly shunt blood from the arteries to the veins. AVMs can be located either within the brain or on the surface of the brain.

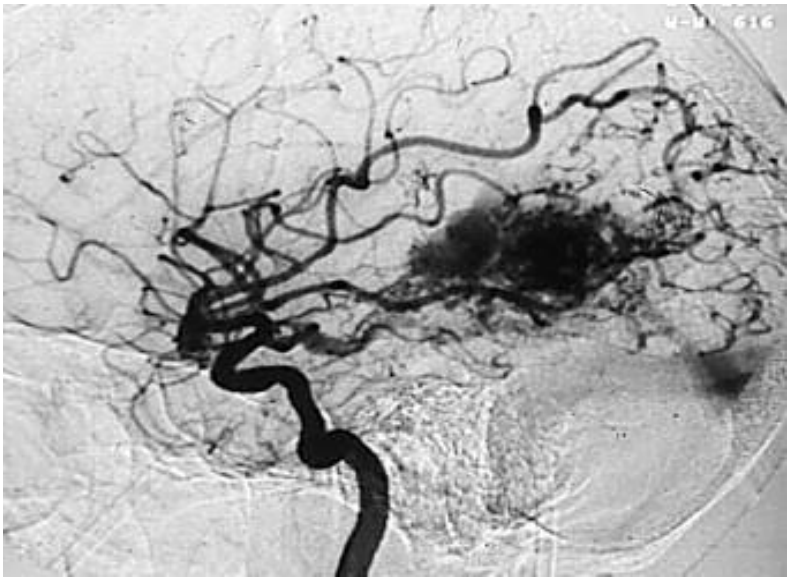


Figure 3.8. AVM on angiography.

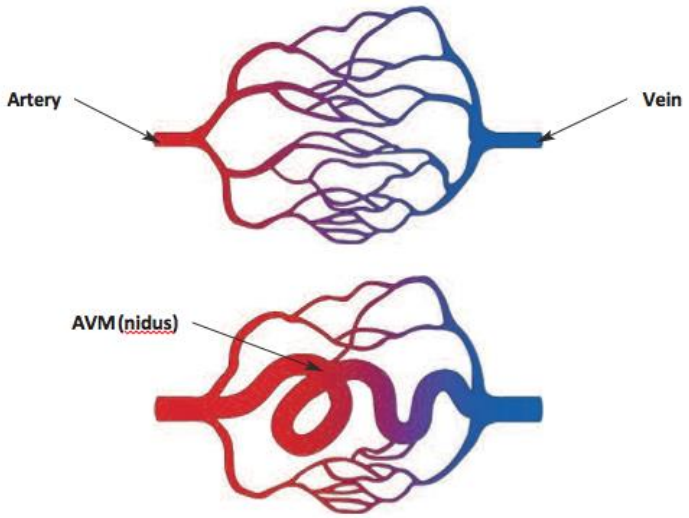


Figure 3.9. An arteriovenous malformation compared with normal anatomy.

Normally blood is pumped from the heart into the large arteries at a relatively high pressure and speed. The pressure and speed of blood flow decreases as it reaches smaller and smaller arteries.

Eventually the blood reaches the smallest vessels, called ***capillaries***. Capillaries are smaller than the diameter of a human hair, and as the blood flows slowly through these tiny vessels, it gives up oxygen and nutrients to the brain tissue and receives carbon dioxide and other waste products.

The pressure and speed of blood flow in the veins are normally very low compared with that of the arteries. The blood enters these tiny veins at a very low pressure, then these tiny veins join with larger veins to return the blood to the heart and lungs. The walls of the veins are, therefore, relatively thin and delicate compared to those of the arteries.

AVMs form early during embryonic life through the direct communication of an artery with a vein, without an intervening capillary bed. Because this is a low resistance shunt pathway, blood may selectively drain through this fistulous communication. There is, during embryonic as well as postnatal life, a progressive enlargement and dilatation of the feeding arteries and a concomitant dilatation of the draining veins. Very commonly the "***nidus***," which is the actual site of the abnormal communication, may be difficult to identify radiologically. Most of the lesion consists of the dilated feeding arteries and the dilated draining veins. The veins are usually of a much larger caliber than the arteries, because their walls are not supported by connective tissue and smooth muscle. Oftentimes the brain tissue in between the vascular channels becomes atrophic, gliotic, and even calcified. There may be associated ***atrophy*** in the brain tissue adjacent to the mass, because the mass represents a sump and low-resistance pathway that "steals" blood away from the normal tissue.

Brain AVMs can occur anywhere within the brain or on the covering of the brain. This includes:

- The four major lobes of the front part of the brain: frontal, parietal, temporal, or occipital.
- The back part of the brain (cerebellum).
- The brainstem.
- The ventricles—deep spaces within the brain that produce the cerebrospinal fluid (CSF).

Most AVMs do not grow or significantly change over time. However, there are some reported cases of AVMs shrinking or enlarging. This, how- ever, may be related to either clotting of parts of an AVM, causing it to shrink, or to recruiting adjacent blood vessels toward an AVM.

AVMs are most often congenital (present at birth) and usually have no specific identifiable cause. In the vast majority of cases, AVMs are not inherited, and other family members are not at an increased risk for having one.

Brain AVMs occur in 0.02–0.05 percent of the general population. About 64 percent of cases present by 40 years of age; 30–50 percent present secondary to hemorrhage.

Risks of AVMs

Because veins were never designed to handle the higher pressures and flows that arteries do, they expand and push against the neighboring areas of the normal brain when exposed to this abnormally high pressure and faster blood flow. This may damage the normal brain, causing weakness, numbness, loss of vision, or seizures. In addition, often the supplying arteries, the AVM itself, or the enlarged veins rupture, resulting in the most common presentation of an AVM—an intracranial hemorrhage, a type of stroke. There is a 2–4 percent chance per year of an existing brain AVM bleeding. If an AVM bleeds, it can affect one or more normal body functions. The functions affected by the brain AVM, and the extent of the damage, is dependent upon where the AVM is located. The risk of death from bleeding in a patient with an AVM is about 29 percent; an additional 20–30 percent of patients suffer neurological deficits.

Each time blood leaks into the brain, there is direct damage to the normal brain tissue. This results in permanent or temporary loss of normal function, such as arm or leg weakness or paralysis or difficulty with speech, vision, or memory.

Diagnosis

AVMs are usually diagnosed by medical imaging studies ordered after a patient develops symptoms. Symptoms of an AVM may include:

- Headache.
- Weakness.
- Numbness.
- Visual problems.
- Seizures.
- Abrupt onset of stroke.

The first imaging study in patients who are suspected to have an AVM is usually a CT scan or an MRI (magnetic resonance imaging). These studies are quite good at identifying an AVM and are relatively noninvasive, requiring only an injection of contrast material into a small vein during the study.

Further identification of the vessels involved in the AVM requires an angiogram. Angiography is the only test currently available that provides sufficiently detailed information to plan and carry out therapy on most AVMs.

Treatment
There are three major treatment methods that may be useful, either alone or in combination, in treating an AVM. The specific treatment chosen for an individual is a matter of medical judgment based on that patient's history, symptoms, and the anatomy of the AVM, including its size, feeding arteries, draining veins, and location within the brain. Treatments include:

- Endovascular embolization (closure of the AVM from within the blood vessels).
- Open surgical removal of the AVM.
- Radiosurgery.
- A combination of these techniques.

Treatment of an AVM is directed toward preventing brain injury, including that which might result from bleeding or rebleeding. No treatment currently exists that can repair damage already done to the brain by the AVM. This means, for example, that seizures might continue after embolization or even complete removal of the AVM. Patients with neurological deficits resulting from AVM hemorrhage would likely still have the deficits after treatment of the AVM, although improvement may occur.

Endovascular treatment

Embolization is an endovascular technique performed within the blood vessels to block vessels of the AVM. Embolization is performed using catheters and angiographic techniques. For the embolization procedure, a very tiny catheter is threaded from the groin directly into the AVM vessels within the brain. Under X-ray guidance, material is injected through the catheter to permanently block and close off the vessels of the AVM. Materials used might include particles of polyvinyl alcohol (PVA), small platinum coils, and/or liquid embolic agents.

Embolization of an AVM is usually performed before treatment by either surgery or radiosurgery. Embolization is often able to decrease the size of the AVM, making the surgery or radiosurgery much safer than would otherwise be the case. However, the blood flow of certain AVMs may be totally blocked by embolization techniques, and no further therapy may be required.

Surgical treatment

Open surgical treatment involves removing a portion of the skull so surgical instruments can be inserted to remove the AVM. Surgical treatment is often performed after embolization has closed portions of the AVM. The combination of embolization followed by surgical resection is frequently safer than surgical resection alone in treating an AVM.

Radiosurgery

Radiosurgery is a technique that uses focused beams of radiation to treat AVMs that are sufficiently small and located in appropriate areas of the brain. Despite the name, no opening of the skull is required. Instead, the radiation causes scarring in the blood vessels of the AVM, thereby eliminating it. After treating the AVM with radiosurgery, a period of two to three years is required for the full effect of the treatment to be determined. In the majority of cases where the AVM is sufficiently small, there is complete obliteration of the AVM.

Background to stroke
Arteriovenous fistulas

An ***Arteriovenous Fistula*** (AVF) is a congenital or acquired direct connection of variable length between an artery and a vein, with the absence of an intervening nidus. This connection results in high-volume arteriovenous shunting.

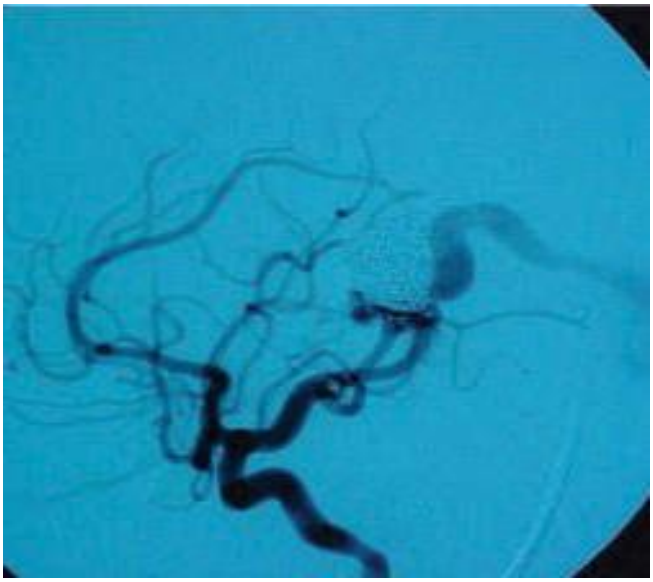


Figure 4.0. An arteriovenous fistula on angiography.

AVFs are most often acquired and usually result from penetrating trauma. They consist of a single communication between an artery and a vein and have low vascular resistance in the fistula, so blood preferentially flows through them.

Over time, the increased flow causes the more proximal supplying arteries and draining distal veins to enlarge. Chronic AVFs can be difficult to distinguish from AVMs, but differentiation between AVMs and AVFs is important for planning therapeutic treatment.

Treatment

The goal of treatment is complete occlusion of the fistula. Occlusion can be approached through an arterial or venous route. Coils or detachable balloons are used most commonly for vaso-occlusion. Usually an embolic device is placed in the segment of the vessel connecting the vein and artery, or it is placed immediately proximal and distal to the fistula. If feeders exist, occlusion of arterial-venous communication itself is necessary (or the venous outflow). If the supplying artery cannot be occluded safely, the device must be placed into the fistula.

Larger occlusive devices are used to occlude feeders. Small devices can go through the artery-to-vein (A-V) communication of the fistula and cause pulmonary embolization.

The vaso-occlusive device used for treatment must be carefully chosen for size so it will remain stable and not embolize due to high flow.

Amytal testing or temporary test occlusion is sometimes done with AVMs undergoing postprocedural surgery to determine proximity to the "eloquent" (functionally important) cerebral cortex.

Carotid-cavernous fistulas

Carotid-cavernous fistulas are abnormal connections between the carotid artery (or its branches) and a large vein (cavernous sinus) behind the eye that receives blood from the orbit, the pituitary gland, and the brain. These fistulas can form as a result of trauma, clotting of the sinus with subsequent reopening, or rupture of an aneurysm (weak spot) of the carotid artery where it passes through the sinus.

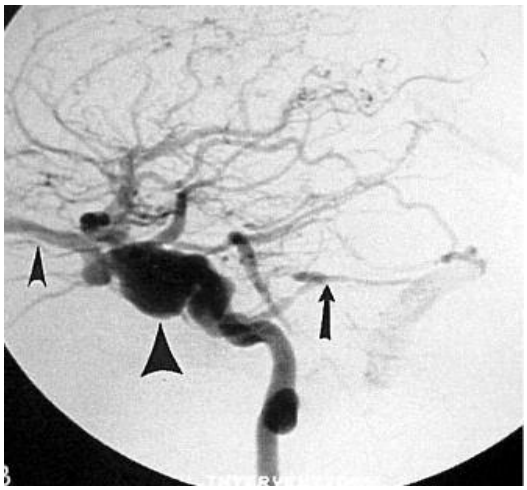


Figure 4.1. A carotid-cavernous fistula on angiography.

Symptoms include:

- Pulsating bulging of the eye (proptosis).
- Redness and swelling of the conjunctiva.
- Increased pressure in the eye (glaucoma).
- Loss of vision in the eye.
- Double vision.
- Pain.

Because of the location, these fistulas are difficult to treat surgically. Instead, they are often treated by placing a catheter into the blood vessels and injecting materials to block off the fistula and/or the vein. Sometimes, the carotid artery itself may be blocked off to close the fistula. If this is necessary, tests are done first to make sure there is enough flow from the other arteries to adequately supply the brain.

Dural arteriovenous fistulas

Dural arteriovenous fistulas are abnormal connections between arteries in the head and the large veins draining the brain that are found in the covering of the brain (dural sinuses). There is a direct connection between the arteries and the sinus without any vessels between.

These fistulas can result from:

- Trauma.
- Infections, such as sinus infections or mastoiditis.
- Clotting of the vein (the fistula forms as a result of the body trying to reopen the vein).

The symptoms of a fistula can vary. An unusual sound may be heard in one ear (e.g., pulsating or humming). If the fistula causes the pressure in the veins draining the brain to increase, there may be neurological symptoms and headaches.

The most dangerous complication of a fistula is rupture of the vein, resulting in hemorrhage in or around the brain.

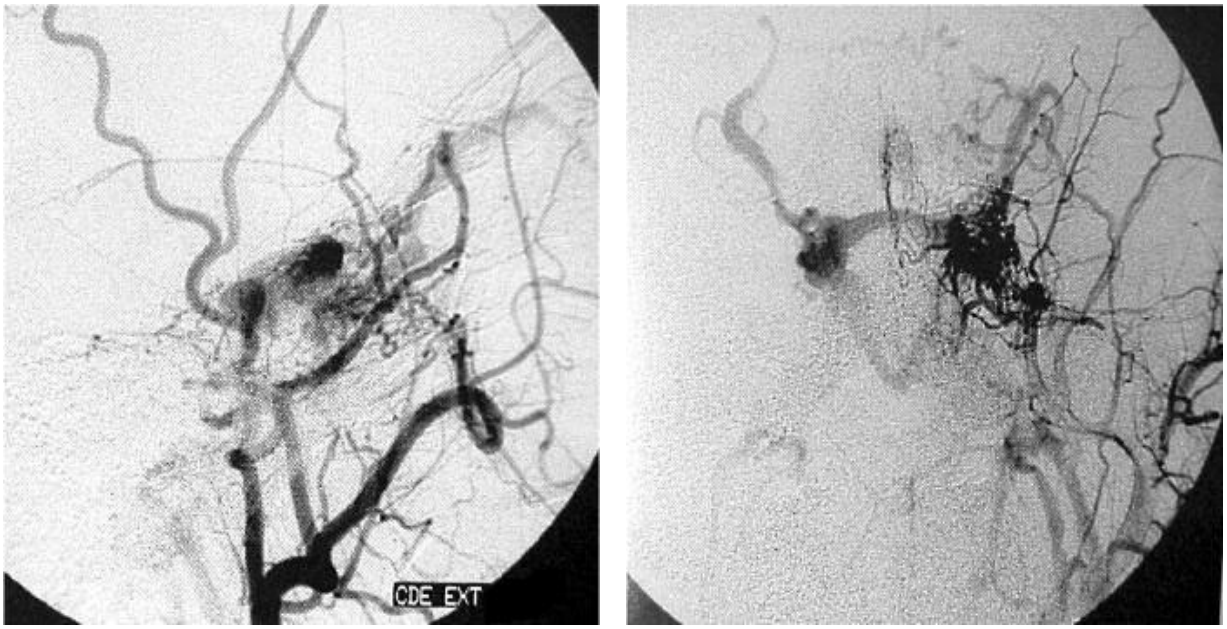


Figure 4.2. Dural arteriovenous fistulas on angiography.

The treatment for a dural fistula depends on the vessels involved. Surgery or radiation therapy may be recommended. Often, these fistulas are treated by the placement of a catheter into the blood vessels to inject materials to block off the vessels. Blockage of arteries, veins (sinus), or both may be needed. Multiple treatment may be needed to close the fistula.

Background to stroke
Tumors

The term ***tumor*** relates to abnormal tissue growth. A tumor involves abnormal cell proliferation due to lack of normal control on cell reproduction. Generally the terms ***neoplasm*** and tumor are synonymous.

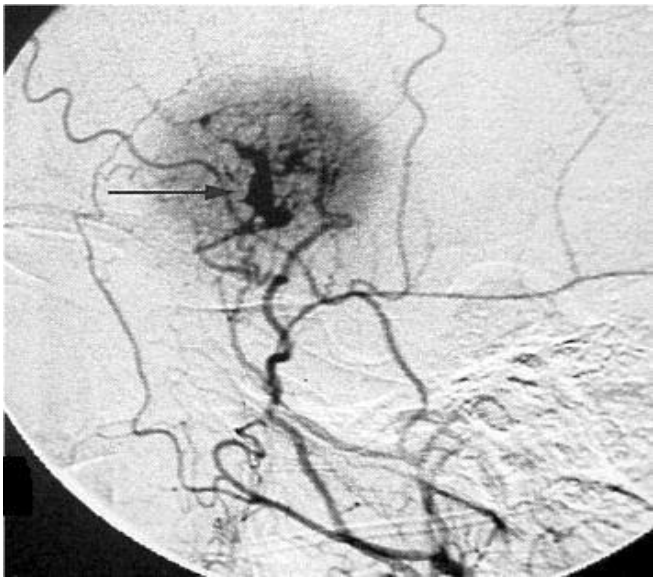


Figure 4.3. A brain tumor or angiography.

Classification of brain tumors

Tumors are generally classified by tissue of origin (histological classification), clinical behavior (***malignant*** or ***benign***), or location.

Primary Central Nervous System (CNS) tumors arise from the CNS and its linings (the meninges) and account for two-thirds of all brain tumors. This category includes tumors that arise from the brain tissue itself (neuronal-glial tumors and gliomas) and from various sources other than the brain tissue (meningiomas, hemangioblastoma, neuroblastoma, neuro- fibroma, schwannoma, hemopoetic tumors, and pituitary tumors).

Malignant tumors grow rapidly and aggressively, and most of them generate similar tumors within remote areas of the body (metastases) through either vascular or lymphatic channels. Metastatic brain tumors are remote metastases of tumors with various location and histological origin. They account for one-third of brain tumors.

Benign tumors grow slowly and may compress or destruct neighboring organs. They normally don't regrow if completely removed.

For both diagnostic and therapeutic purposes, CNS tumors are classified by location.

The CNS tumors can involve any part of the CNS, including the:
- Brain.
- Cranial nerves.
- Spine.
- Spinal nerves.
- Meninges.

In relation to the skull, intracranial tumors are located either in the posterior fossa, below the tentorium (infratentorial) or in the anterior and middle fossa above the tentorium (supratentorial).

Intracranial tumors are either located within the brain tissue (intra-axial tumors) or inside the skull but outside the brain (extra-axial tumors).

Craniofacial tumors (tumors of the head and neck) involve different tissues within the head and neck area other than the brain. They generally involve the base of the skull.

Tumor symptoms

A growing tumor mass will compress and displace the brain tissue, producing symptoms that are characteristic for the brain territory around the tumor site. This is known as ***mass effect***.

Tissue damage due to tumor growth destroys the blood-brain barrier (selective permeability of the capillary walls) within and around the tumor. As a result, water leaks from the capillary bed into the tissue (intercellular space). The increased water content of the tissue is called ***edema***.

The brain is held in a closed container (the skull). A growing tumor mass coupled with edema will increase the total volume of the skull's content. That results in elevated ***Intracranial Pressure*** (ICP). Elevated ICP generates symptoms like nausea, headaches, and vomiting. Seizures can result from mass effect and neuronal dysfunction from abnormal tissue and edema.

Diagnosis

CT and MRI demonstrate edema generated by tumor and displacement of normal brain structures by the tumor. Impairment of blood-brain barrier function within the tumor results in contrast leakage following contrast injection. This results in better visualization in most brain tumors by CT and MRI. Calcification is better seen by CT and, in general, MRI is superior in demonstrating brain tumor because of its better resolution and high sensitivity.

Angiography provides indirect signs of tumors by demonstrating characteristic displacement of cerebral vessels. In addition, angiography provides direct visualization of the angioarchitecture of hypervascularized tumors.

Treatment

The neurosurgical approach to treatment is removal of the tumor. It carries high morbidity due to bleeding from increased vascularity of the tumor and lack of knowledge about subsequent neurofunctional deficits.

There are two options for endovascular treatment:

- Chemotherapeutic agent infusion at the site of the tumor.
- Embolization of feeder vessels, presurgical assist.

Chemotherapy infusion is a less standardized procedure. Under general anesthesia, a microcatheter is advanced to the desired vessels. Bolus injections of chemotherapeutic agents are hand injected.

Preoperative embolization is the process of obstructing or diminishing blood flow within blood vessels, either permanently or transiently, by deposition of an occluding agent with a catheter into feeder vessels.

Embolic selection considerations include the type and location of the lesion to be treated, desire for permanent or temporary occlusion, and the goal of embolization. Occlusion can be accomplished with Polyvinyl Alcohol (PVA) particles, sclerosing agents like ethanol, or coils, which are permanent embolic agents.

Occlusion can occur at the arterial, capillary, or venous level, depending on the goal of embolization and the agent(s) used.

The goals of tumor embolization are to diminish tumor blood flow, intraoperative blood loss, and operative time.

Also, testing with Amytal to predetermine the extent of functional deficit to the patient by removing certain vessels or tissue is frequently done at the same time as embolization. Information is relayed to the neurosurgeon for use in tumor resection surgery.

Background to stroke
Diagnostic testing

Imaging techniques

A variety of imaging techniques used to diagnose neurovascular disease and abnormalities are available, including:

- Radiographic angiography.
- Computed Tomography (CT scan).
- Computed Tomographic angiography (CTA).
- Magnetic Resonance Imaging (MRI).
- Magnetic Resonance Angiography (MRA).
- Ultrasound (US).
- Transcranial Doppler (TCD).
- Intravascular Ultrasound (IVUS).

Conventional film-screen and high-resolution Digital Subtraction Angiography (DSA) remain the standards by which other diagnostic techniques are judged.

However, noninvasive modalities such as US, CT, and MRA have an increasingly important role in the evaluation of craniocerebral atherosclerosis and occlusive vascular disease.

Background to stroke
Diagnostic testing

Neuroangiography

Neuroangiography is a study of blood vessels in the brain. It is performed by a physician experienced and trained in performing and interpreting blood vessel examinations of the brain, using X-rays to map the specific blood vessels involved in the disease. A small tube or catheter is inserted into the femoral artery in the groin and maneuvered into the vessels in the neck that supply the brain. Material called contrast (or dye), which is visible on the X-ray, is injected into the vessel and images are taken as the liquid flows through the vessels. Vessels are rendered radiopaque by the injection of contrast medium. The angiogram gives a detailed picture of any disease in the cerebral vessels. Intra-arterial contrast angiography is still the most precise technique for evaluating intrinsic abnormalities of vessels in the head and neck. Before any consideration for treatment, a diagnostic cerebral angiogram is usually performed to fully map a plan for therapy.

Visualization of an artery during an angiogram requires that injected contrast be the equivalent of approximately 30 percent of the volume of flowing blood. Larger arteries and vessels with faster flow will require faster injections. Deciding on the rate of injection for a particular vessel depends on the caliber of the vessel, rate of flow, distal runoff, and catheter position.

Immediately after cessation of the injection, a process of dilution begins and opacification of the veins is less pronounced than that of the arteries. For this reason, in diseases where a foremost interest lies in the status of the venous system, consideration may be given to place emphasis on a longer injection rate with a higher total volume.

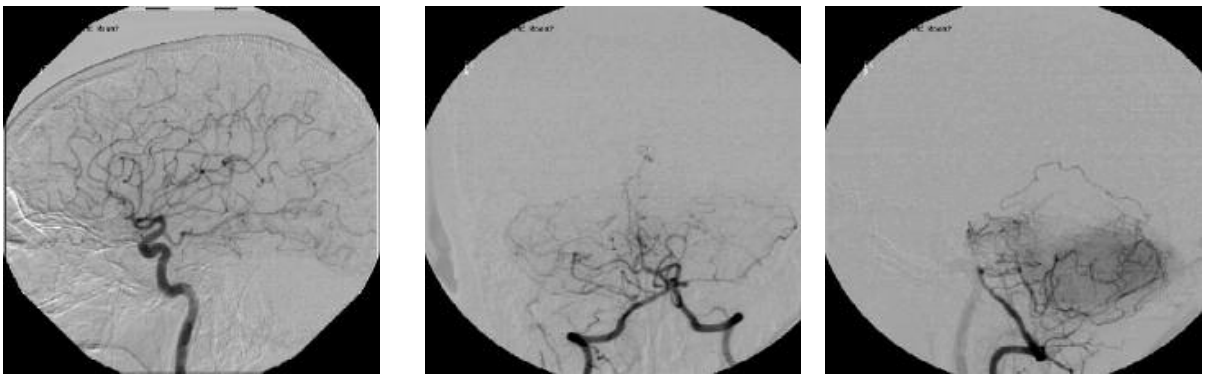


Figure 4.4. Examples of angiographic images.

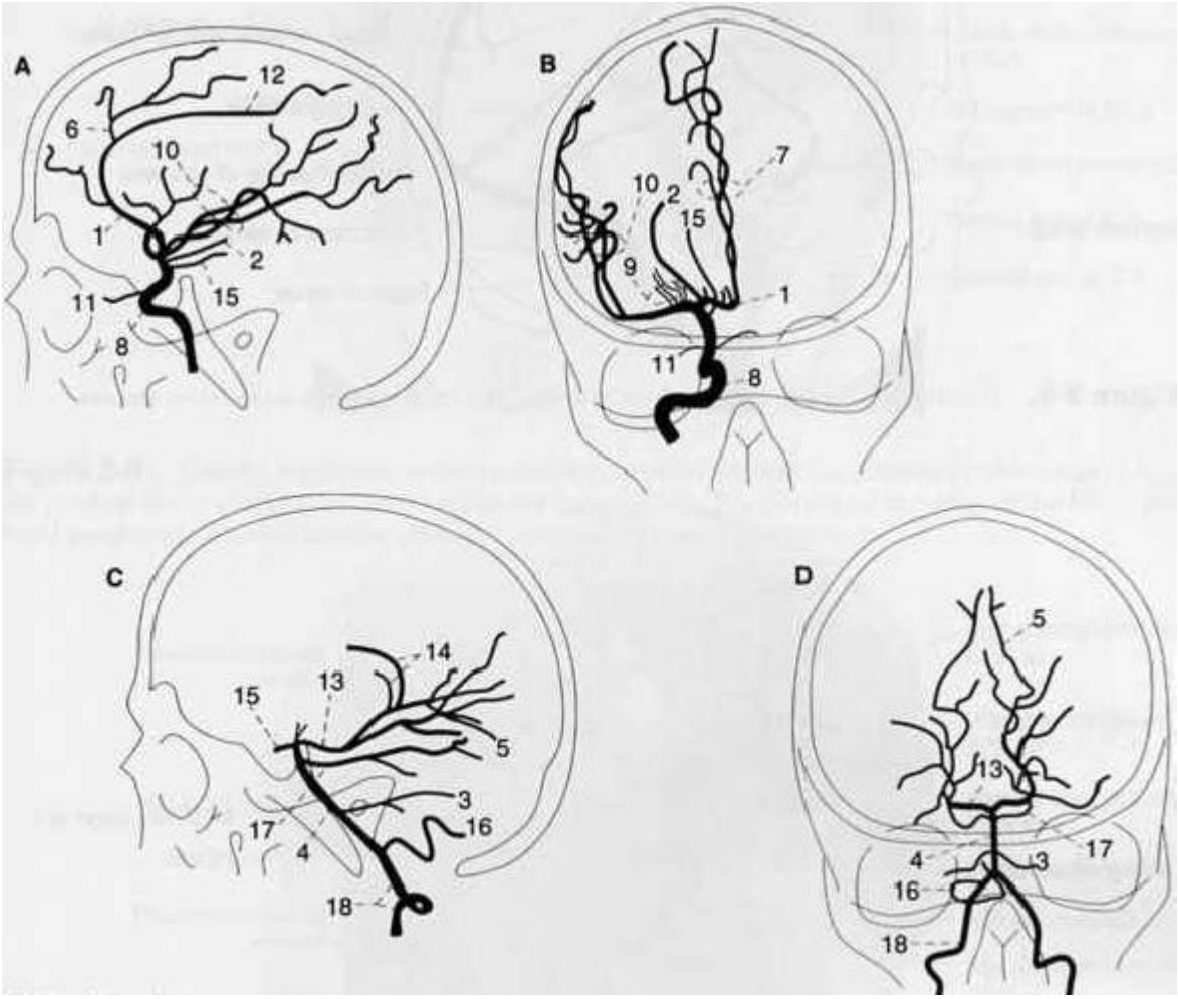


Figure 4.5. Neuroangiography views and circulations.

A. Lateral view, anterior circulation

B. A/P view, anterior circulation

C. Lateral view, posterior circulation

D. A/P view, posterior circulation

Test your knowledge

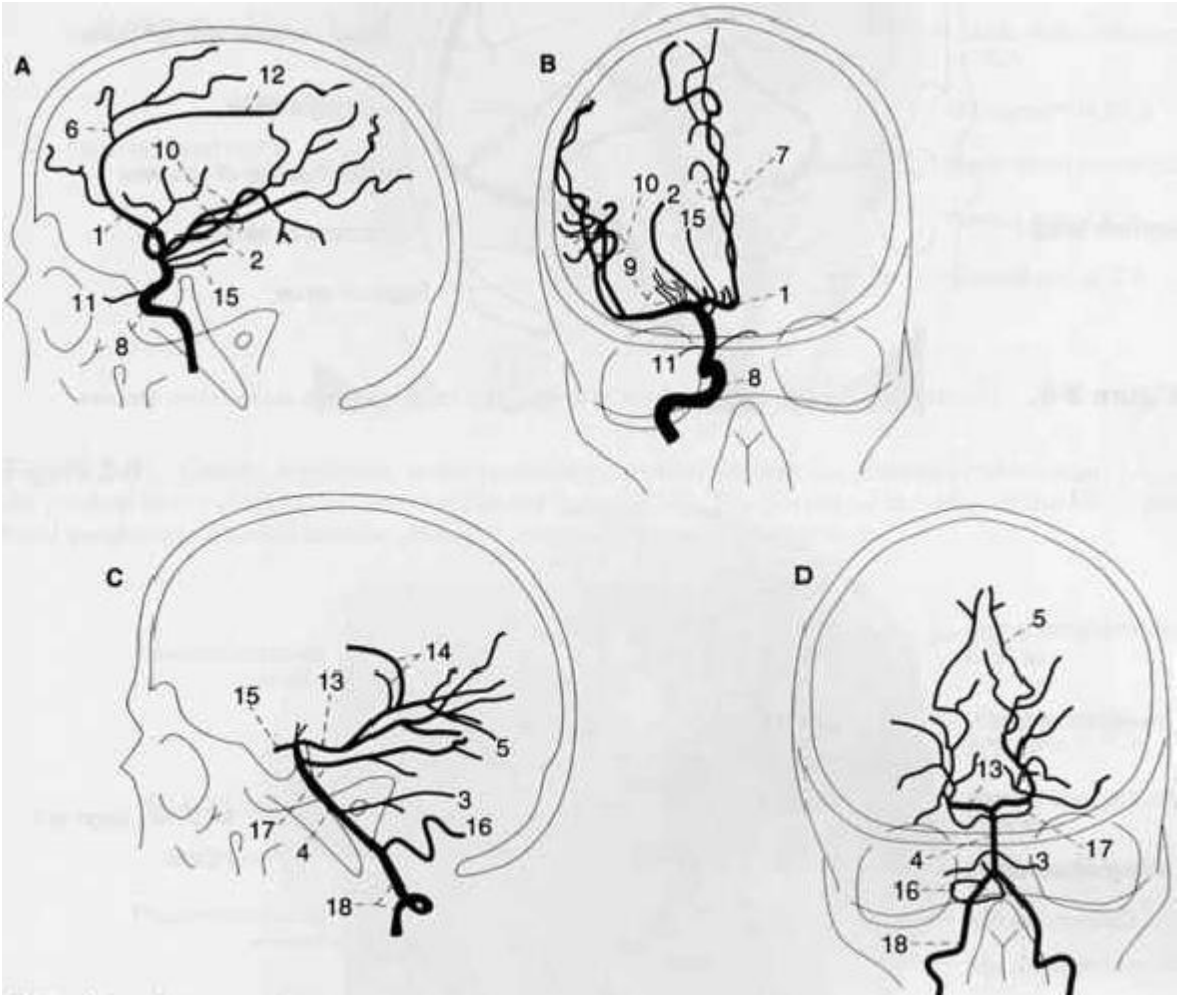


Figure 4.5. Neuroangiography views and circulations.

A. _____

B. _____

C. _____

D. _____

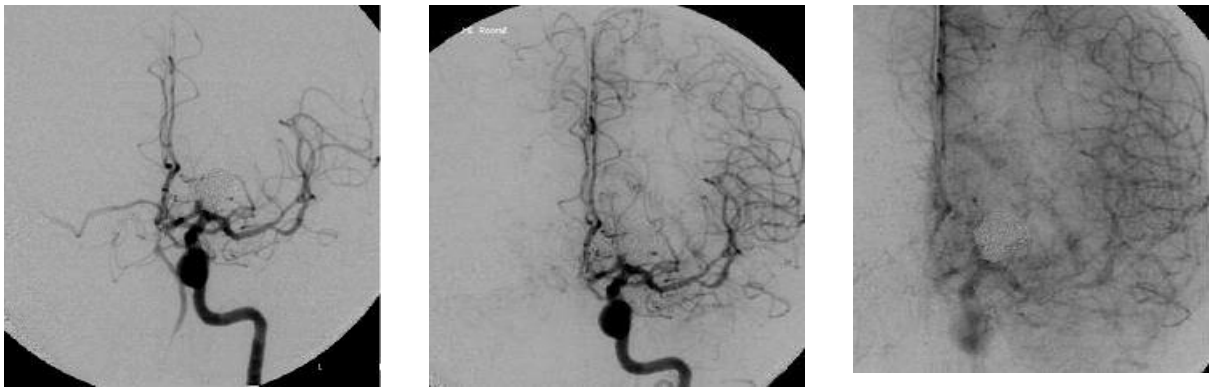


Figure 4.6. Examples of angiographic images.

Digital subtraction angiography stores images electronically and uses the computer to subtract images such as bone in real time, ideally showing nothing but those vessels filled with contrast media. This allows a clearer view of the vessels.

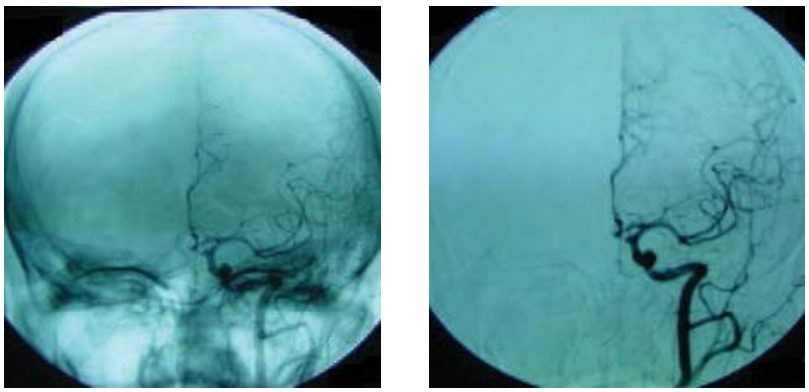


Figure 4.7. Native versus digital subtraction angiography.

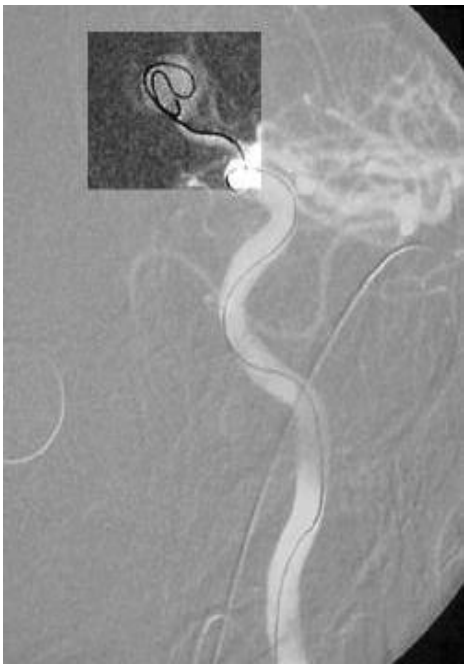
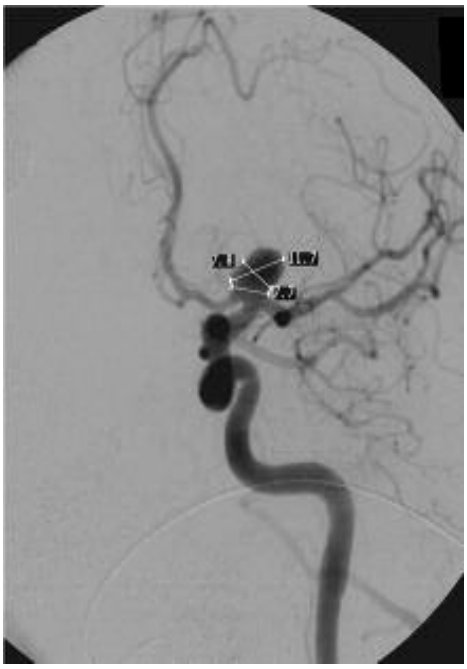


Figure 4.8. Creating a digital vascular roadmap of the lesion via angiography.

A digital vascular ***roadmap***, a feature available on many digital subtraction angiographic units, is obtained by contrast injection and storage of the resulting image for real-time subtraction during later fluoroscopy. When probing the lesion, this roadmap can be used to direct the manipulations.



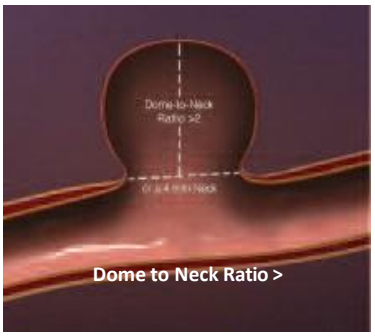


Figure 4.9. Determining the dimensions of an aneurysm via angiography.

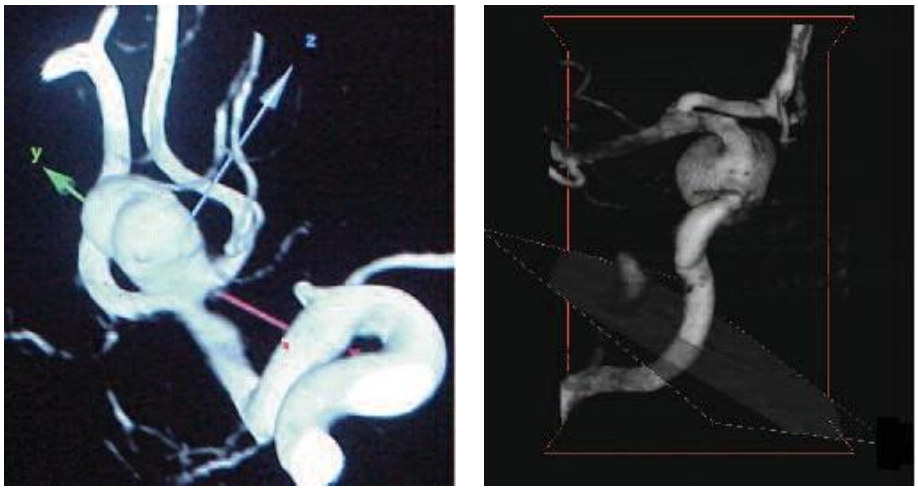


Figure 5.0. 3-D angiography of an aneurysm.

Rotational angiography in 2-D or 3-D mode is available in most neurointerventional rooms. The configuration of an aneurysm is more clearly demonstrated by 3-D angiography. Although requiring more contrast and radiation exposure, it provides a better understanding of extracranial and intracranial lesions. Rotational angiography increases the sensitivity of digital subtraction angiography to the severity of carotid stenosis present in patients with suspected atherosclerotic disease.

Computerized Tomography

Computerized Tomography (CT) is the imaging modality most often used in diagnosing and imaging stroke. CT scanning is a specialized X-ray examination in which a transaxial image is obtained from multiple angular projections. The X-ray tube within the scanning gantry is rotated 180° to 360° around the brain. The multiple angular projections thus obtained are detected by an array of either solid-state scintillation detectors or xenon gas ionization detectors, which are also located within the gantry. These detectors either rotate in conjunction with the X-ray tube or are stationary in a 360° circle around the patient. They are more sensitive than X-ray film and are able to detect variations of as little as 1 percent in the density of soft tissue (X-ray film detects differences of 10–15 percent).

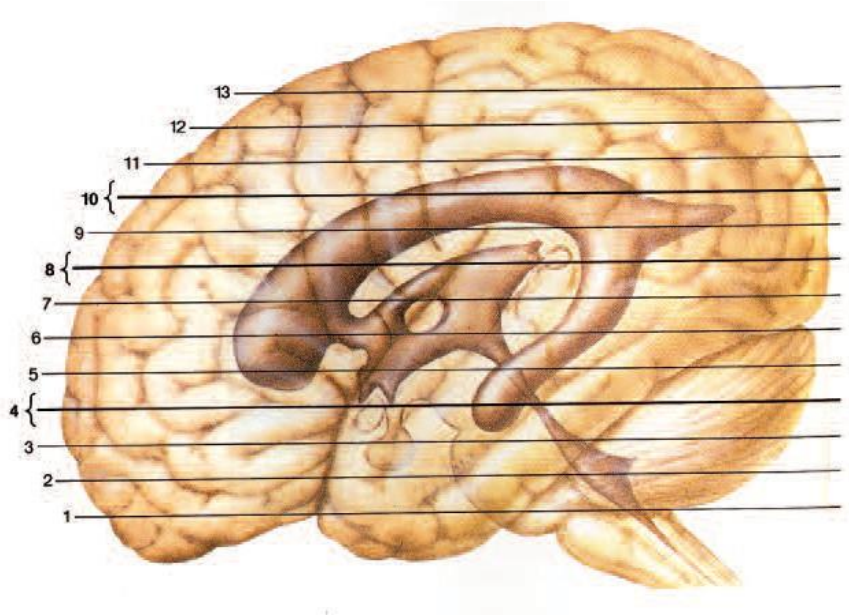


Figure 5.1. Planes of CT scan section.

The information obtained by these detectors is analyzed by a computer that constructs an image of the cross section of the region within the plane of the X-ray beam. The section may be 13mm, 10mm, 7mm, or 2mm thick (depending upon the type of CT scanner and the preselected image thickness), and it reveals the organs in an aspect that, until the development of the CT scanner, could be seen only in the cadaver lab

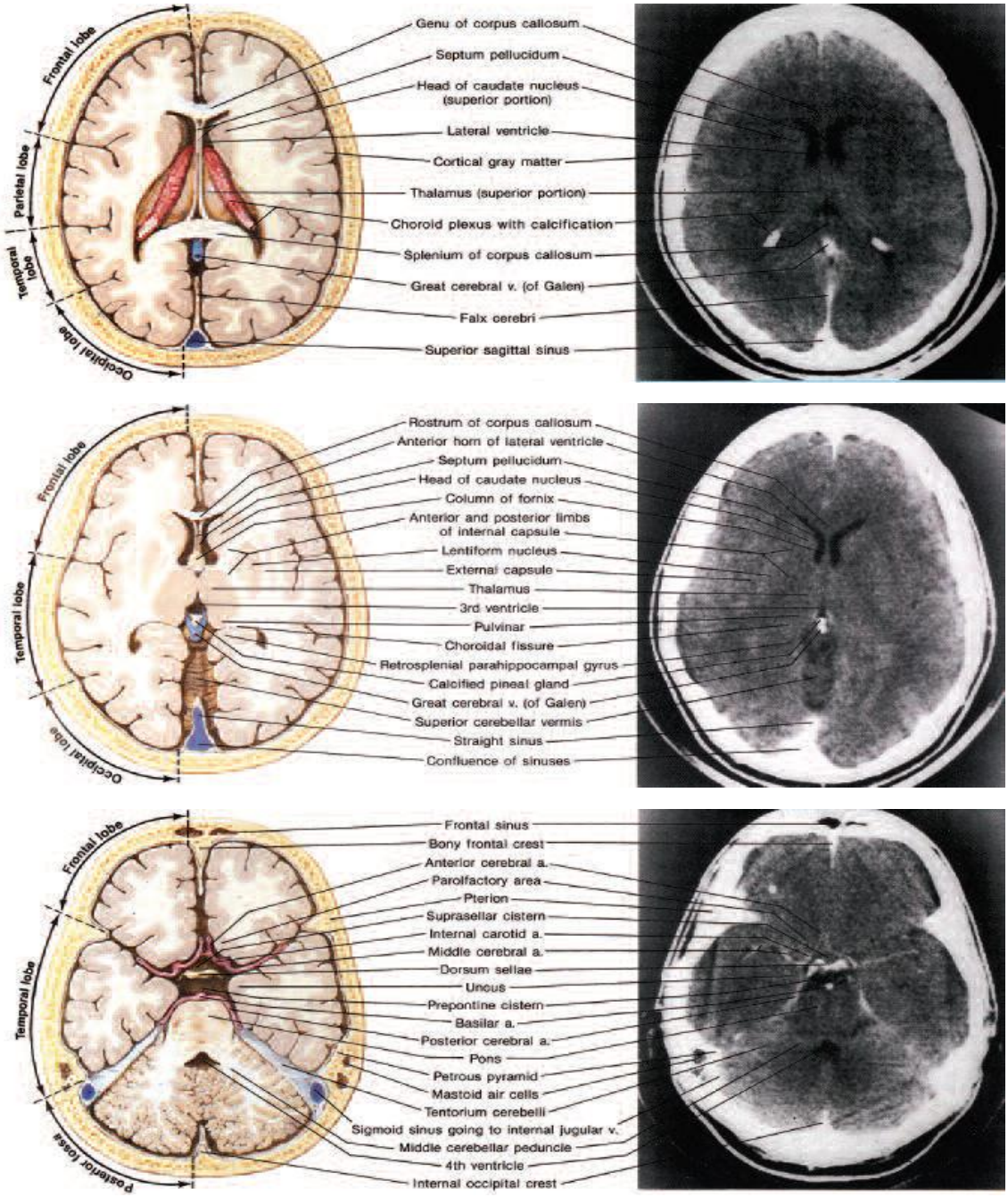
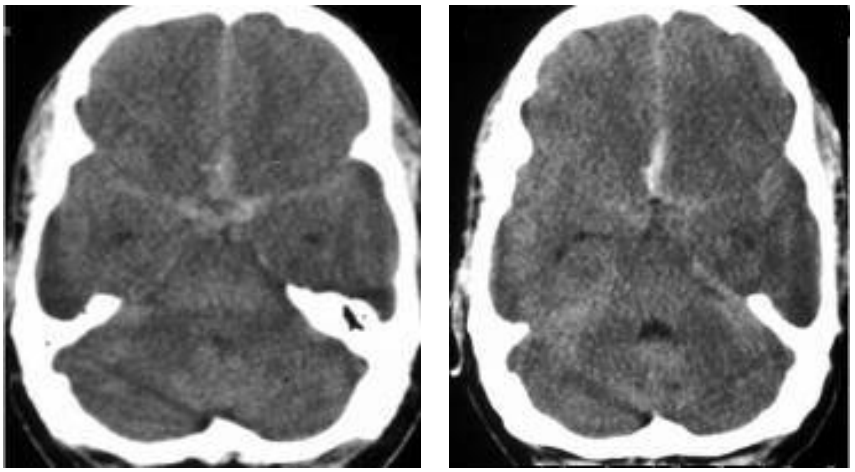
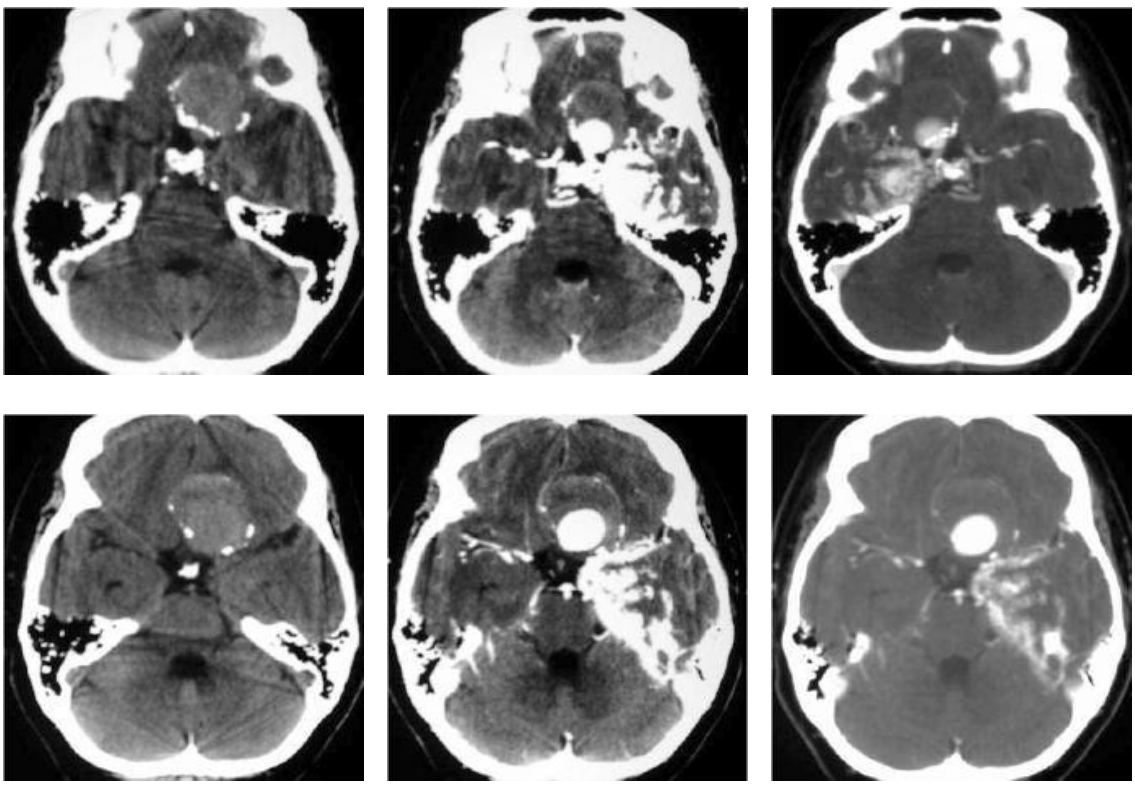


Figure 5.2. Normal brain anatomy, section 4.

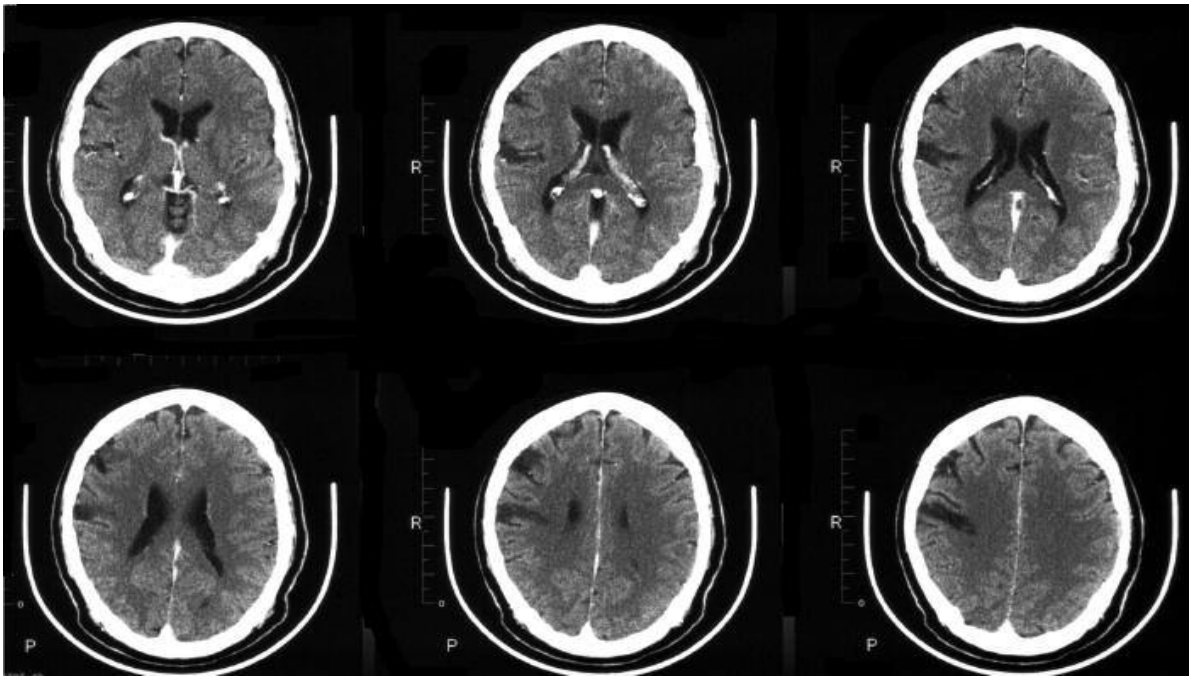
Hemorrhage (blood) can be easily seen on CT as an area of hyperdensity.



Photos of images taken by a BSC representative.
Figure 5.3. CT subarachnoid hemorrhage.



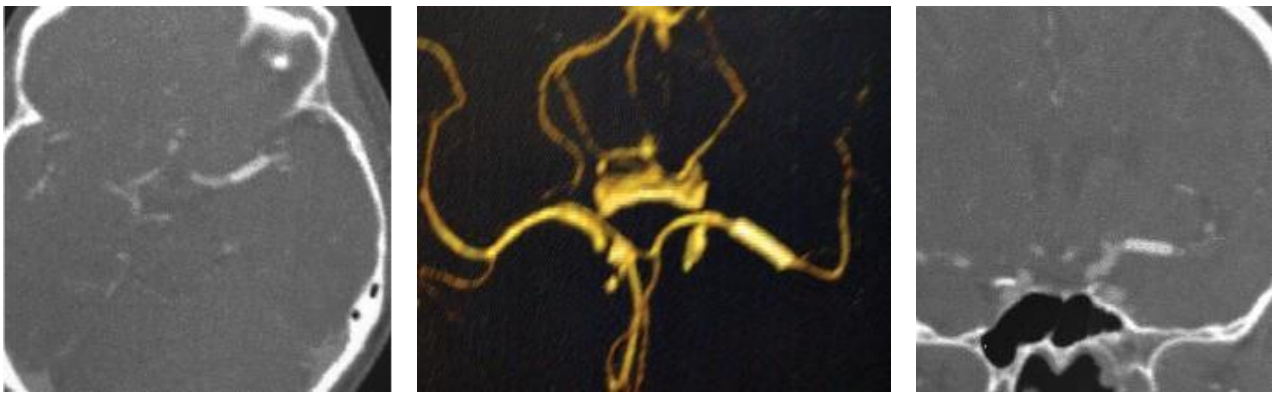
Photos of images taken by a BSC representative.
Figure 5.4. CT giant calcified ophthalmic aneurysm.



Photos of images taken by a BSC representative.
Figure 5.5. CT images of an aneurysm.

Computerized Tomographic Angiography

Computerized Tomographic Angiography (CTA) involves injecting a dye into a vein to provide contrast, which allows images to be taken of the blood vessels. The computer then generates 3-D reconstructions from the original cross-sectional images. The tentorium cerebelli, falx cerebri, choroid plexus of the lateral ventricles, dural venous sinuses, major deep veins, and major blood vessels at the base of the brain will be evident. Under normal circumstances, the contrast agent does not enter the brain, but if the blood-brain barrier is disrupted by a lesion, the contrast agent will leak into that area and produce better visualization (enhancement). Using CT scanning, the neuroradiologist can precisely locate an intracerebral lesion and assess its relationship to the intrinsic anatomy of the brain and the bony calvaria, without resorting to invasive techniques.



Photos of images taken by a BSC representative.
Figure 5.6. CT angiography.

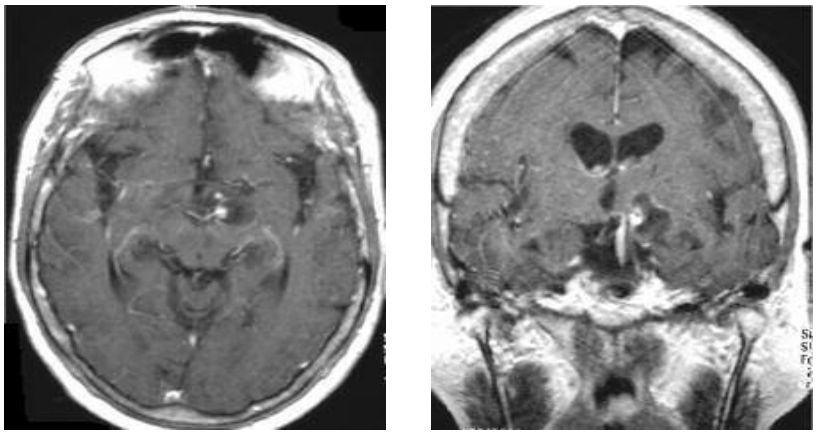
Magnetic Resonance Imaging

Magnetic Resonance Imaging (MRI) and ***Magnetic Resonance Angiography*** (MRA) are two noninvasive tests.

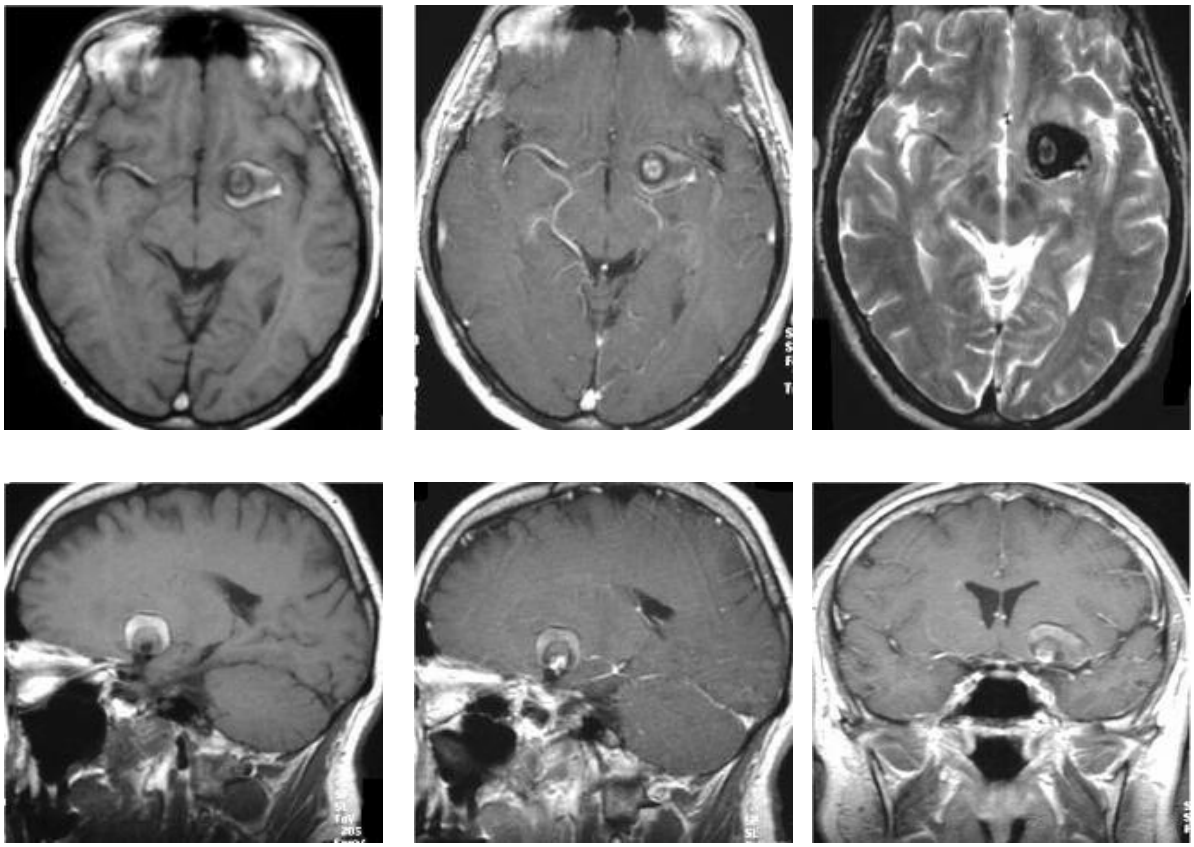
MRA uses blood flow as an intrinsic contrast agent and a magnetic field to produce detailed images of brain tissue and cerebral arteries.

The various MRA approaches depend on a recognition of moving signals from arteries coupled with a sufficiency of signal different from the back- ground to recognize the lumen of the vessel. It provides an accurate means to evaluate the patency and differentiation of cerebral arteries and veins. It provides information about flow direction, source of vascular supply, and identification of collateral flow patterns.

During an MRA, patients are placed on a table that slides into a magnetic resonance scanner, and the blood vessels are imaged to detect a cerebral malformation. Both of these screening tests are useful to detect most cerebral aneurysms larger than 3–5 mm (about 3/16 inch).



Photos of images taken by a BSC representative.
Figure 5.7. MRA images.



Photos of images taken by a BSC representative.
Figure 5.8. MRA images.

MRA is capable of imaging extracranial and intracranial arteries in a non- invasive fashion. In MRA, the vessel depiction is due to a more complex relationship than what we see on CTA or angiography. The goal of MRA is to differentiate vessel lumen from surrounding tissue, evaluate for the presence of stenosis, and evaluate characteristics of the vessel wall.

The following charts represent examples of normal and abnormal MR imaging interpretation. MR-T1 and MR-T2 represent sequences during imaging. For example, in normal tissue, dense bone will appear dark in both the first and second sequence. Water will appear dark in the first sequence and bright in the second sequence. These are compared to the appearance of the same tissue on X-Ray/CT.

Neuroimaging: normal tissue

Normal tissue	MR-T1	MR-T2	X-RAY/CT
Dense bone	Dark	Dark	Bright
Air	Dark	Dark	Dark
Fat	Bright	Bright	Dark
Water	Dark	Bright	Dark
Brain	Anatomic	Intermediate	Intermediate

Neuroimaging: abnormal tissue

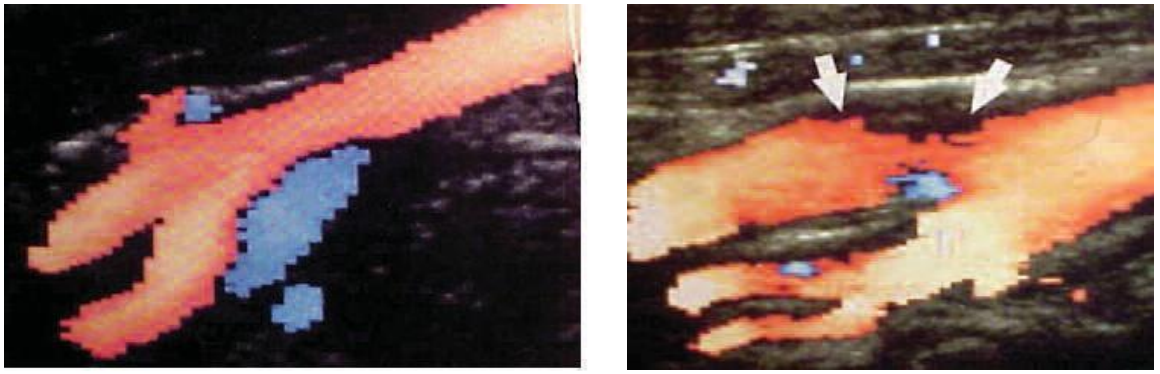
Abnormal tissue	MR-T1	MR-T2	X-RAY/CT	Enhancement
Infarct	Dark	Bright	Dark	Subacute
Bleed	Bright	Bright	Bright	No
Tumor	Dark	Bright	Dark	Yes
MS plaque	Dark	Bright	Dark	Acute

Carotid ultrasonography

Ultrasound (US) is a noninvasive screening modality. Color duplex US provides information on the flow conditions within a stenosed portion of the artery and also provides information on the morphology of plaque.

Intravascular Ultrasound (IVUS) may provide a more accurate measurement of the degree of arterial stenosis and plaque morphology.

Arterial stenosis is assessed by determining flow velocities in the narrowed vessel lumen.



Photos of images taken by a BSC representative.
Figure 5.9. Normal vessel vs. vessel with arterial stenosis.

Refinements in duplex sonography (color flow doppler sonography [CFDS]) now permit noninvasive detection of atherosclerosis plaque and vascular stenosis.

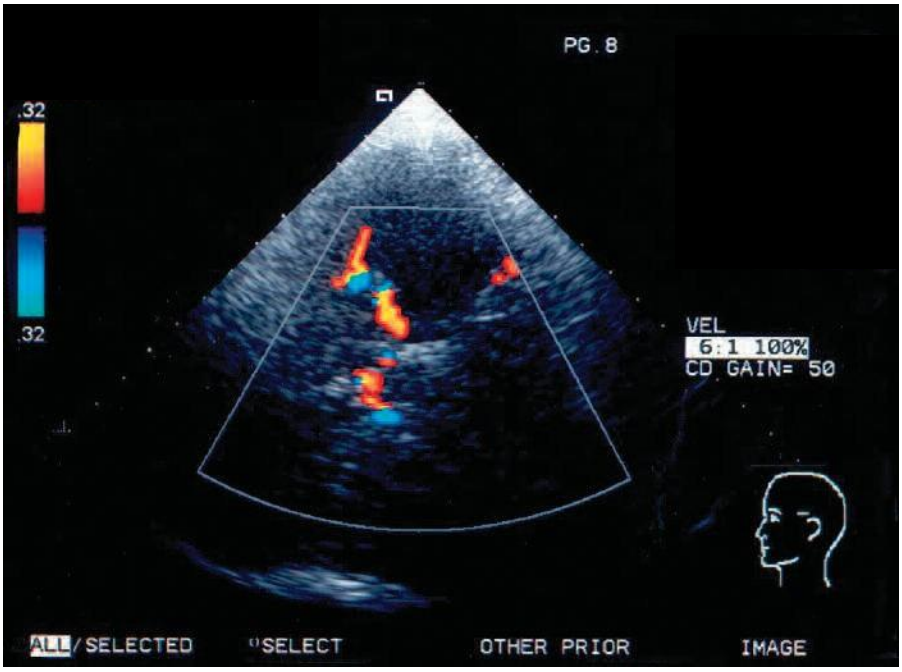
In CFDS, color saturation is directly related to flow velocity, and velocity is proportional to severity of obstruction. Elevated flow velocity is indicated by color shift areas (dark red to light pink) on CFDS. Spectral analysis measures flow velocity in cm/sec. Nonlaminar flow distal to a stenosis is indicated by a mixture of red and blue colors. Calcification within an atherosclerotic plaque appears as acoustic shadowing behind the plaque.

CFDS can also be used to detect surface irregularities in atherosclerotic plaques.

Clinical applications for neuroimaging

Cerebral infarction	CT, CTA, CT-perfusion, MR, MRA, angiogram, MR perfusion/diffusion
Aneurysm	CTA, MRA, MR, angiogram, 3-D
Dissection craniocervical arteries	CTA, MRA, MR, doppler sonography
Extracranial ICA stenosis	CTA, MRA
AVM	MR, MRA, CT, angiogram
Tumor	MR (contrast), angiogram

Transcranial Doppler



Photos of images taken by a BSC representative.

Figure 6.0. Transcranial Doppler (TCD)

Transcranial Doppler (TCD) is a noninvasive procedure in which a small probe is placed against the skull to measure blood flow velocity through the cerebral arteries with high frequency sound waves. TCD is more accurate in detecting intracranial artery stenosis than arterial occlusions.

Background to stroke
Pharmacology

Note: Please see the Pharmacologic Indications section at the end of this chapter for all of the drugs mentioned. Not all drugs are indicated and approved for use as discussed here. The following drug uses are taken from *Interventional Neuroradiology: Strategies and Practical Techniques* by J.J. Connors and Joan Wojack (W.B. Saunders Co.; 1999).

Many types of drugs are used surrounding interventional neuroradiological procedures. They may be drugs used during the procedure for functional testing, treating vasospasm, or sedating the patient so he/she doesn't move during the procedure. Other drugs include those that interfere with the normal blood coagulation process like ***antiplatelets***, ***anticoagulants***, or ***thrombolytic*** (clot-breaking) drugs. These drugs play a very important part in interventional neuroradiologic procedures, are used to treat strokes, or prevent complications of stenting or coiling. This chapter will focus first on a basic overview of blood coagulation and the drugs that impact this process. A brief description of several other drugs will follow.

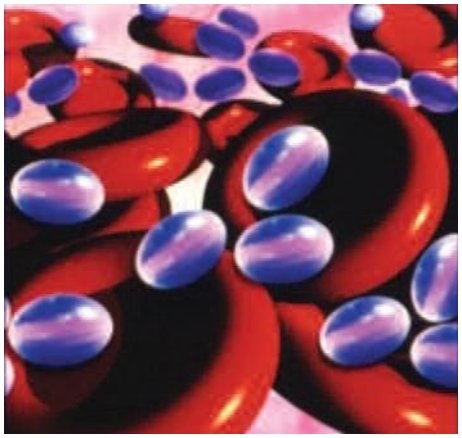


Figure 6.1. Platelets.

Blood coagulation

To understand how all the different drugs used in an interventional neurovascular procedure work, it is important to understand the coagulation process first. Everything starts with a platelet.

Platelets are small, enucleate, disc-shaped blood cells whose primary function is to maintain normal ***hemostasis*** by direct effects at the site of vascular injury and by indirect effects through interaction with the hemostatic cascades of circulating blood. There are 1.5 trillion platelets circulating throughout the body, each of which has a lifespan of approximately 10 days.

Platelets adhere to breaches in vessel ***endothelium***, and their cell membrane and shape are altered upon contact with activating substances. Upon activation, they secrete clotting factors, ***vasoconstrictors***, and growth factors.

Platelets play an important role in the body's response to injury. Injury may occur during any interventional procedure, such as when guidewires are used during coiling. Platelets may also be activated by the presence of a foreign body in the vessel such as a stent. In the presence of vessel injury, platelets release powerful substances that trigger a cascade of events, eventually leading to the cessation of bleeding and the formation of a blood clot.

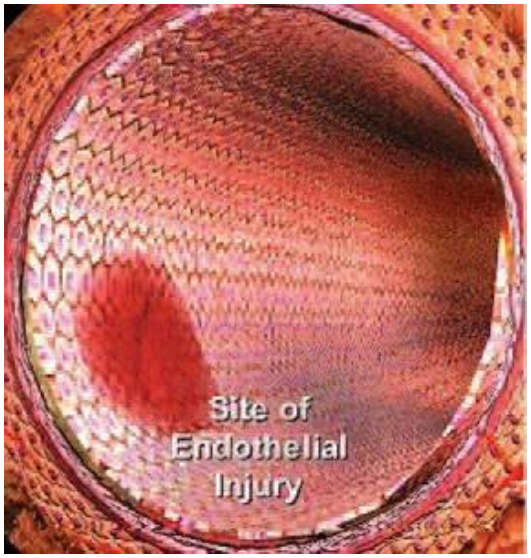


Figure 6.2. Endothelial injury.

In order for a clot to form, platelets must adhere to the site of injury. They then begin recruiting and activating other clotting factors, which leads to aggregation of the platelets to form a clot.

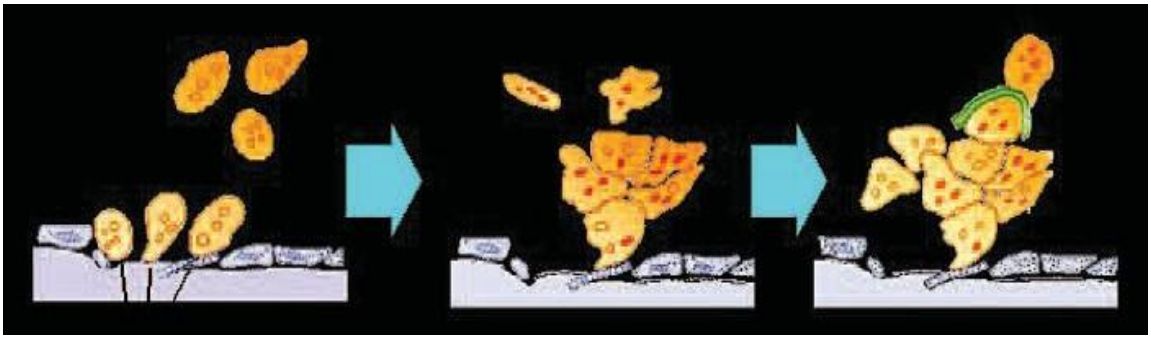


Figure 6.3. Platelet adhesion, activation, and aggregation.

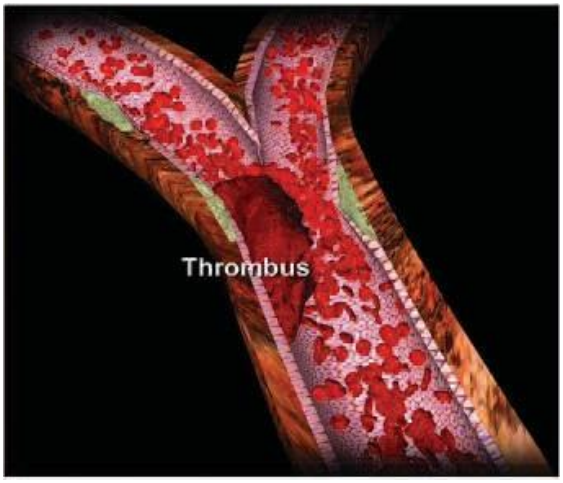


Figure 6.4. Platelets stick to each other to form a plug.

When an injury occurs to the vascular endothelium, platelets adhere to exposed collagen as well as other exposed sub endothelial tissues. Following platelet adhesion, release of adenosine phosphate (ADP) and other factors by the injured platelets leads to platelet aggregation. Hence the platelets will stick to each other to form a plug. The initiating event in blood coagulation is injury to the vessel wall or disturbance of blood flow.

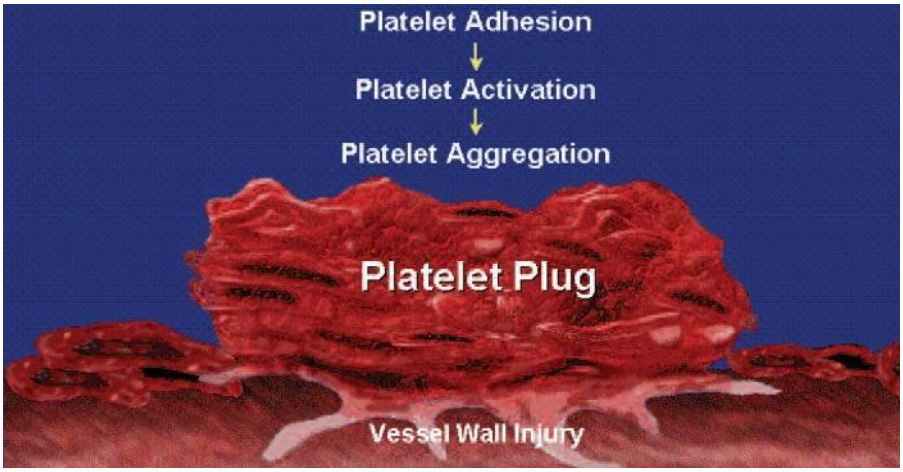


Figure 6.5. Platelet plug formation.

Platelet aggregates facilitate thrombin generation. Thrombin further activates platelets, initiates platelet contraction (clot consolidation), and activates coagulation—leading to fibrin deposition.

Fibrin strands reinforce the platelet plug and serve as sites for clotting factor deposition.
The site of the formation determines the proportion of red blood cells (RBCs), platelets, and fibrin within a ***thrombus***. In arteries, where the blood flow is fast, thrombi are mainly composed of platelet aggregates held together by strands of fibrin. These are platelet thrombi.

In the venous system, or where the blood flow is slower, these thrombi are RBCs interspersed with fibrin. These are coagulation thrombi.

Thrombogenic is a term used for "producing or tendency to produce a clot."

How a clot forms

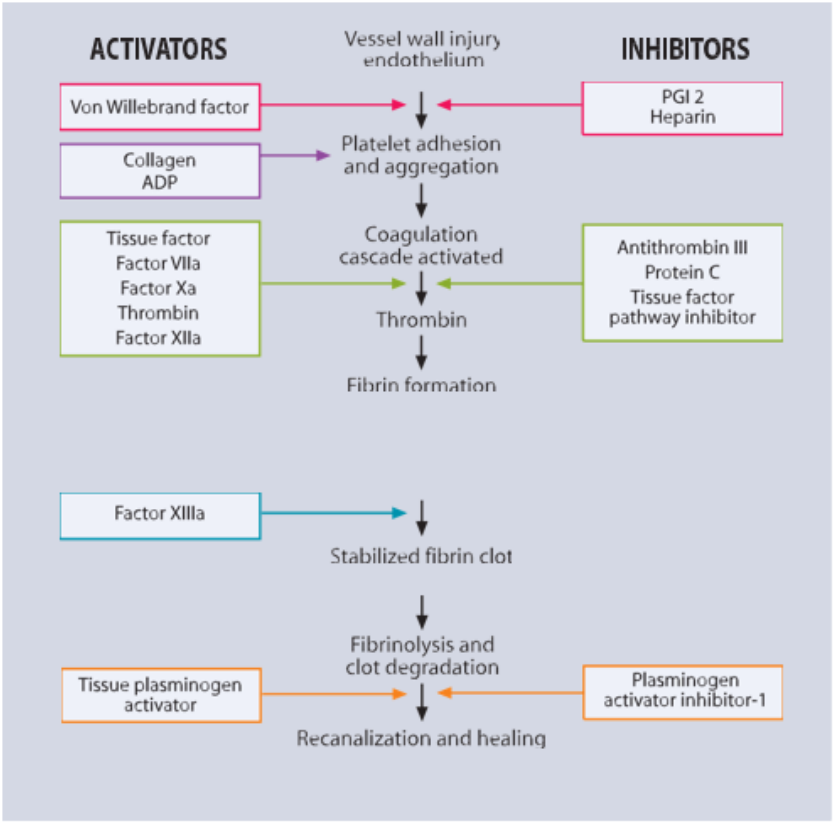


Figure 6.6. Coagulation cascade diagram.

Injury can be caused to the innermost lining of the arterial wall, called the intima, from a variety of factors including a plaque rupture or even guidewires and catheters. The intima is comprised of endothelial cells.

When the endothelial lining is disrupted, there is an exposure of collagen and other clotting factors. With this exposure of collagen, the platelets become activated and begin to expose their receptor sites. They adhere to each other with receptor sites. This is the beginning of a clot. This new clot starts to trap RBCs, a fibrin network begins, and a red clot is formed.
When the platelets adhere to the collagen and the formation of the unstable platelet plug, this requires the clotting factor called Von Willebrand's factor or factor VIII. This takes only minutes and is what binds the platelets to the collagen.

Fibrin consolidates the platelet plug and renders it stable in 24–48 hours.

Fibrinolysis (lysis is the dissolution by breaking down chemical bonds) is performed by fibrinolytic enzymes that dissolve the fibrin of the plug and render the plug unstable again. This enzyme is plasmin. Plasmin digests the fibrin threads and other substances in the clot and decreases the ability of the surrounding blood to clot.

Plasminogen is an inactive precursor of plasmin. Plasminogen is trapped inside the clot (also in the circulating blood). A tissue plasminogen activator is needed to activate the plasminogen into plasmin to start the dissolving process. The fibrin in the clot attracts the r-Tpa (recombinant tissue plasminogen activator) to start the fibrinolysis process.

Antiplatelet drugs

Antiplatelet agents directly inhibit platelet activation or aggregation and are therefore effective in preventing arterial thrombosis.

They are usually used in patients with atherosclerotic disease to prevent platelet plugs from forming and embolizing downstream. They may also be used to prevent thrombosis that could occur due to stent placement issues or a coil portion dangling into the parent vessel.

Treatment goals for acute antiplatelet therapy for stenting are:

- Limit downstream embolization of thrombus.
- Reduce risk of early adverse thromboembolic events.
- Improve safety and outcome of procedure.

Acetylsalicylic Acid (ASA) (Aspirin) produces inhibition of platelet aggregation by decreasing the synthesis of substances that mediate platelet aggregation. It keeps platelets slippery.

Clopidogrel (Plavix), in combination with aspirin, is the drug of choice to prevent stent thrombosis. It is an antiplatelet that helps keep blood platelets slippery, discourages formation of clots, and potentiates the effects of aspirin. This is called a synergistic effect.

Anticoagulant drugs

Anticoagulants inhibit thrombin generation and activity and fibrin formation.

Heparin is a rapid-acting anticoagulant that acts by keeping the RBCs from sticking together. It prevents the formation of new clot, but does not lyse existing clot.

Many interventional radiologists give heparin, which increases the Activated Clotting Time (ACT) in procedures involving temporary arrest of flow with balloons or other devices. Following an initial Intravenous Injection (IV) bolus dose, heparin is continued by IV infusion. The anticoagulant effect is noted immediately. In addition, significant ***systemic*** doses of heparin can be given in the flush system. Patients may also be maintained on a constant heparin infusion after a procedure.

Enoxaparin (low molecular weight heparin) preparations are smaller fractionated components produced by enzymes and are given to people who are allergic to heparin. It is administered subcutaneously (under the skin) or intravenously.

Protamine sulfate is a preparation of low-molecular-weight fish proteins, and it is a specific antidote of heparin. At the end of a case, the treating physician may confirm the reversal of the effect of heparin by protamine or by passage of time, which is important in avoiding arterial bleeding at the puncture site.

The protamine molecules bind to the heparin molecules to reverse the effects of the heparin. Some physicians will have protamine close at hand when coiling aneurysms in case of rupture while heparin is on board. One milligram of protamine neutralizes 100mg of heparin.

Warfarin sodium (Coumadin) is an anticoagulant that has similar effects as heparin. It is usually used as a long-term maintenance drug and is given orally as tablets. Frequent monitoring of Partial Thromboplastin Time (PPT) is important.

Glycoprotein IIb/IIIa inhibitors include:
- **Abciximab** (ReoPro).
- **Eptifibatide** (Integrilin).
- **Tirofiban** (Aggrastat).

Several powerful inhibitor agents that block the action of the GPIIb/IIIa receptors and thus prevent platelet aggregation are available.

The efficacy and safety of the GPIIb/IIIa inhibitors have been studied in a number of large studies of patients undergoing percutaneous procedures for atherosclerotic coronary disease. No study has been published yet regarding the use of these agents for cerebrovascular diseases.

Abciximab (ReoPro) immediately blocks platelet receptors and virtually completely blocks all platelet aggregation by preventing binding of fibri- nogen and other factors involved in aggregation. ReoPro is sometimes given as a clot-buster drug during interventional procedures. Because most clots that occur during a procedure are "platelet rich," ReoPro can attach itself to the platelet and disrupt the clot formation.

Eptifibatide (Integrilin), in contrast to ReoPro, binds to the GPIIb/IIIa receptor and is specific and reversible. After discontinuation of the drug, platelet function normalizes in about four hours.

Tirofiban (Aggrastat) is a reversible antagonist of fibrinogen binding with the GPIIb/IIIa receptor of platelets and provides a greater than 90 percent inhibition of platelet aggregation after a 30-minute loading dose.

Thombolytics (fibrinolytic agents)

All thrombolytic agents are intended to lyse thrombus, but also activate platelets directly and generate thrombin and plasmin that activate platelets. Thrombolytic agents are activators of plasminogen.

Streptokinase (Streptase) dissolves blood clots by activating the conversion of plasminogen to plasmin. This drug is derived from streptococci.

Urokinase (Abbokinase) is a substance produced by the kidneys that dissolves clots by activating the conversion of plasminogen to plasmin.

r-tPA (recombinant tissue plasminogen activator) (Activase) is a replicated substance that is similar to the tissue plasminogen activator that is produced in the body.

r-Pa (Retavase) is a recombinant derived from E. coli and is a smaller molecule than activase.

Regarding risks, all thrombolytic agents have been associated with bleeding complications, both intracranially and systemically. Thus doctors carefully screen patients (including history, PT/aPTT, fibrinogen level) and evaluate the computed tomographic scan before treatment (to exclude those patients with recent infarction or intracranial bleed) and to minimize the risks of subsequent catastrophic intracerebral hemorrhage or systemic hemorrhagic complication.

Drugs for functional neurologic testing

The most commonly utilized agent for functional neurological testing is amobarbital (Amytal). Methohexital (Brevital) is also used for this purpose.

For testing of a vessel before occlusion, the agent chosen depends on the location of the vessel. For evaluation of vessels supplying the brain, either amobarbital or methohexital may be used. When the vessel to be tested may supply cranial nerves, injectable lidocaine hydrochloride ("cardiac" lidocaine) is utilized.

Embolic agents

Ethyl alcohol and sodium tetradecyl sulfate (Sotradecol) are sclerosing agents used in the embolization of vascular malformations. Sotradecol can be used either transarterially or via direct puncture. Unlike alcohol, it is a painless agent and may cause less inflammatory reaction; therefore, less sedation is required for its use.

Local anesthetics

Local anesthetic agents are used to provide analgesia at the site of percutaneous needle or catheter entry during a procedure. They are also utilized in the performance of nerve blocks for diagnostic and therapeutic purposes. The most commonly used local anesthetic agents are lidocaine (Xylocaine) and bupivacaine (Marcaine, Sensorcaine). Lidocaine has a more rapid onset of action; bupivacaine has a longer duration of activity.

Vasodilators

Vasodilators are used by interventional neuroradiologists primarily for the prevention or treatment of catheter-induced vasospasm or for the treatment of vasospasm secondary to subarachnoid hemorrhage. They can also be used to lower systemic blood pressure in conjunction with temporary test occlusion of the internal carotid artery. Elective vasodilation can also be helpful during certain procedures. This might be used to allow more distal passage of a catheter for embolization, to allow particles to penetrate more distally, or to provoke hyperemia to aid in the identification of a bleeding source (e.g., when treating epistaxis).

Many interventional neuroradiologists apply nitroglycerin paste to the chest wall at the beginning of any procedure in which catheter-induced vasospasm might be anticipated. Some prefer to administer oral or sublingual nifedipine (Procardia), a calcium channel blocker, instead. Once vasospasm has occurred, nitroglycerin papaverine (an alkaloid with peripheral vasodilatory activity), or nimodipine (Nimotop) (another calcium channel blocker) can be administered through the catheter intra-arterially to relieve this spasm. Alternatively, inhaled amyl nitrite can be used for this purpose.

Vasospasm associated with subarachnoid hemorrhage continues to be a major source of morbidity and mortality. Currently, it is accepted practice in the neurosurgical community to place patients with aneurysmal sub- arachnoid hemorrhage on the calcium channel blocker nimodipine to help decrease the incidence and sequelae of vasospasm.

Sodium nitroprusside (Nipride) can be used to lower systemic blood pressure in conjunction with temporary test occlusion of the internal carotid artery. Alternatively, labetalol (Normodyne), a beta-blocker that also decreases blood pressure, can be administered.

Infusion of nitroglycerin directly into the pulmonary arteries has been used to treat acutely symptomatic pulmonary embolization associated with the use of particulate embolization agents, as well as in the treatment of cardiopulmonary collapse associated with alcohol embolization.

Neuroprotectants

Neuroprotectant agents are those drugs that help protect the brain from the effects of ischemia and reduce cerebral edema. At this time, only a limited number of these agents are available for use, other than as part of investigational protocols. Nimodipine is routinely administered to patients suffering from subarachnoid hemorrhage to help reduce vasospasm and help the brain withstand the ischemia associated with vasospasm.

The other widely available neuroprotectant agents are glucocorticoids. These act as free-radical scavengers, inhibiting lipid peroxidation and thereby stabilizing cell membranes to interrupt the ischemic cascade of injury. They are also effective in reducing cerebral edema. The gluco- corticoids most commonly used for these purposes include dexametha-sone sodium phosphate (Decadron Phosphate), and methylprednisolone sodium succinate (Solu-Medrol), which are administered intravenously. The major side effects associated with short-term use of glucocorticoids are hyperglycemia, peptic ulcers, and gastrointestinal perforation.

Pharmacologic indications, United States

The following indications are provided for your reference only and to show that not all drugs mentioned are indicated and approved for use as they are discussed in this chapter.

Abbokinase (urokinase) – is a protein (enzyme) which works to break up and dissolve blood clots which can block arteries. It is used in the treatment of very serious blood clots in lung blood vessels (pulmonary embolism).
http:/www.medicinenet.com/urokinase-injection/article.htm

Activase (alteplase) – is indicated for the management of acute ischemic stroke in adults for improving neurological recovery and reducing the incidence of disability. Activase is a Recombinant Tissue-Plasminogen Activator (rt-PA): a thrombolytic indicated for use in patients with Acute Myocardial Infarction (AMI), acute ischemic stroke, and acute, massive pulmonary embolism. Approved in 1996, Activase remains the only drug indicated for treatment of stroke.
http://www.lyticportfolio.com/activase/index.jsp

Aggrastat (tirofiban hydrochloride) – is indicated for the prevention of early myocardial infarction in patients presenting with unstable angina or non-Q-wave myocardial infarction with the last episode of chest pain occurring within 12 hours and with ECG changes and/or elevated cardiac enzymes. Patients most likely to benefit from Aggrastat treatment are those at high risk of developing myocardial infarction within the first 3-4 days after onset of acute angina symptoms including for instance those that are likely to undergo an early PTCA (see also "Posology and method of administration" and "Pharmacodynamic properties"). Aggrastat is intended for use with acetylsalicylic acid and unfractionated heparin.
http://emc.medicines.org.uk/emc/assets/c/html/displaydoc.asp?documentid=8398

Amytal (amobarbital) – some of the barbiturates may be used before surgery to relieve anxiety or tension. In addition, some of the barbiturates are used as anticonvulsants to help control seizures in certain disorders or diseases, such as epilepsy. Barbiturates may also be used for other conditions as determined by your doctor. The barbiturates have been used to treat insomnia (trouble in sleeping); but if they are used regularly (for example, every day) for insomnia they are usually not effective for longer than 2 weeks. The barbiturates have also been used to relieve nervousness or restlessness during the daytime. However, the barbiturates have generally been replaced by safer medicines for the treatment of insomnia and day- time nervousness or tension.
http://www.drugs.com/cons/amytal.html

Aspirin (acetylsalicylic acid) – is indicated for the treatment of light to moderately strong states of pain and fever, inflammation-related pain and fever.

Brevital (brevital sodium) – can be used in *adults* as follows:

For *intravenous* induction of anesthesia prior to the use of other general agents.

For *intravenous* induction of anesthesia and as an adjunct to subpotent inhalation anesthetic agents (such as nitrous oxide in oxygen) for short surgical procedures; Brevital Sodium may be given by infusion or intermittent injection.

For use along with other parenteral agents, usually narcotic analgesics, to supplement subpotent inhalational anesthetic agents (such as nitrous oxide in oxygen) for longer surgical procedures.

As *intravenous* anesthesia for short surgical, diagnostic, or therapeutic procedures associated with minimal painful stimuli.

As an agent for inducing a hypnotic state.

Brevital Sodium can be used in *pediatric patients older than 1 month* as follows:

For *rectal* or *intramuscular* induction of anesthesia prior to the use of other general anesthetic agents.

For *rectal* or *intramuscular* induction of anesthesia and as an adjunct to subpotent inhalational anesthetic agents for short surgical procedures.

As rectal or intramuscular anesthesia for short surgical, diagnostic, or therapeutic procedures associated with minimal painful stimuli.

http://www.drugs.com/pro/brevital-sodium.html

Coumadin (warfarin) – is an anticoagulant, which reduces the formation of blood clots and is used to prevent heart attacks, strokes, and blood clots in veins and arteries. It may also be used for purposes other than those listed here.
http://www.drugs.com/coumadin.html

Decadron Phosphate (dexamethasone phosphate) – is indicated:
By intravenous or intramuscular injection when oral therapy is not feasible for:
Endocrine disorders.

- Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the drug of choice; synthetic analogs may be used in conjunction with mineralocorticoids where applicable; in infancy, mineralocorticoids supplementation is of particular importance).
- Acute adrenocortical insufficiency (hydrocortisone or cortisone is the drug of choice; mineralocorticoid supplementation may be necessary, particularly when synthetic analogs are used).
- Preoperatively, and in the event of serious trauma or illness, in patients with known adrenal insufficiency or when adrenocortical reserve is doubtful.
- Shock unresponsive to conventional therapy if adrenocortical insufficiency exists or is suspected.
- Congenital adrenal hyperplasia.
- Nonsuppurative thyroiditis.
- Hypercalcemia associated with cancer.

Rheumatic disorders. As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in:

- Post-traumatic osteoarthritis.
- Synovitis of osteoarthritis.
- Rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy).
- Acute and subacute bursitis.
- Epicondylitis.
- Acute nonspecific tenosynovitis.
- Acute gouty arthritis.
- Psoriatic arthritis.
- Ankylosing spondylitis.

Collagen diseases. During an exacerbation or as maintenance therapy in selected cases of:

- Systemic lupus erythematosus.
- Acute rheumatic carditis.

Dermatologic diseases.
- Pemphigus.
- Severe erythema multiforme (Stevens-Johnson syndrome).
- Exfoliative dermatitis.
- Bullous dermatitis herpetiformis.
- Severe seborrheic dermatitis.
- Severe psoriasis.
- Mycosis fungoides.

Allergic states. Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment in:
- Bronchial asthma.
- Contact dermatitis.
- Atopic dermatitis.
- Serum sickness.
- Seasonal or perennial allergic rhinitis.
- Drug hypersensitivity reactions.
    - Uticarial transfusion reactions.
    - Acute noninfectious laryngeal edema (epinephringe is the drug of first choice).

Opthalmic diseases. Severe acute and chronic allergic and inflammatory processes involving the eye, such as:
- Herpes zoster ophthalmicus.
- Iritis, iridocyclitis.
- Chorioetinitis.
- Diffuse posterior uveitis and choroiditis.
- Optic neuritis.
- Sympathetic opthalmia.
- Anterior segment inflammation.
- Allergic conjuctivitis.
- Keratitis.
- Allergic corneal marginal ulcers.

Gastrointestinal diseases. To tide the patient over a critical period of the disease in:
- Ulcerative colitis (Systemic therapy).
- Regional enteritis (Systemic therapy).

Respiratory diseases.
- Symptomatic sarcoidosis.
- Berylliosis.
- Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy.
- Loeffler's syndrome not manageable by other means.
- Aspiration pneumonitis.

Hermatologic disorders.
- Acquired (autoimmune) hemolytic anemia.
- Idiopathic thrombocytopenic purpura in adults (I.V. only; I.M. administration in contraindicated).
- Secondary thrombocytopenia in adults.
- Erythroblastopenia (RBC anemia).
- Congenital (erythroid) hypoplastic anemia.

Neoplastic diseases. For palliative management of:
- Leukemias and lymphomas in adults.
- Acute leukemia of childhood.

Edematous states. To induce diuresis or remission of proteinuria in the nephrotic syndrome, without uremia, of the idopathic type, or that due to lupus erythematosus.

Miscellaneous.
- Tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate antituberculous chemotherapy.
- Trichinosis with neurologic or myocardial involvement.

Diagnostic testing of adrenocortical hyperfunction.

Cerebral edema associated with primary or metastatic brain tumor, craniotomy, or head injury. Use in cerebral edema is not a substitute for careful neurosurgical evaluation and definitive management such as neurosurgery or other specific therapy.

By intra-articular or soft tissue injection:
As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in:

- Synovitis of osteoarthritis.
- Rheumatoid arthritis.
- Acute and subacute bursitis.
- Acute gouty arthritis.
- Epicondylitis.
- Acute nonspecific tenosynovitis.
- Post-traumatic osteoarthritis.

By intralesional injection:

- Keloids.
- Localized hypertrophic, infiltrated, inflammatory lesions of: lichen planus, psoriatic plaques, granuloma annulare, and lichen simplex chronicus (neurodermatitis).
- Discoid lupus erythematosus.
- Necrobiosis lipoidica diabeticorum.
- Alopecia areata.
- May also be useful in cystic tumors of an aponeurosis or tendon (ganglia).

http://www.merck.com/product/usa/pi_circulars/d/decadron/decadron_phsinj_pi.pdf

Heparin – evidence is presented that heparin is useful for the prevention and/or treatment of venous thrombosis, pulmonary embolism, mural thrombus after myocardial infarction, post thrombolytic coronary rethrombosis, and unstable angina.
http://www2.kumc.edu/wichita/meded/cvresource/antithrombotic/heparin/

Integrilin (eptitibatide) – is indicated for the treatment of patients with acute coronary syndrome (UA/NSTEMI), including patients who are to be managed medically and those undergoing percutaneous coronary intervention (PCI), and for the treatment of patients undergoing percutaneous coronary intervention (PCI), including those undergoing intracoronary stenting.
http://www.integrilin.com/

Lovenox (enoxaparin; low molecular weight heparin) – is used to prevent blood clots in the leg in patients who are on bedrest or who are having hip replacement, knee replacement, or stomach surgery. It is used in combination with aspirin to prevent complications from angina (chest pain) and heart attacks. It is also used in combination with warfarin to treat blood clots in the leg. Enoxaparin is in a class of medications called low molecular weight heparins. It works by stopping the formation of substances that cause clots.
http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a601210.html
Integrilin is a trademark of Millenium Pharmaceuticals, Inc. Lovenox is a trademark of Aventis Pharmaceuticals S.A. Corporation.

Marcaine/Sensorcaine (bupivacaine HCL) – is an established long- acting local anaesthetic, used for surgical anaesthesia and acute pain management.
http://www.astrazeneca.com/productbrowse/4_74.aspx

Nimotop (nimodipine) – is indicated for the improvement of neurological outcome by reducing the incidence and severity of ischemic deficits in patients with subarachnoid hemorrhage from ruptured intracranial berry aneurysms regardless of their post-ictus neurological condition (ie, Hunt and Hess Grades I-V).
http://www.nimotopusa.com/

Nipride (nitroprusside) – is indicated for the treatment of acute hypertension refractory to standard therapeutic measures. Nitroprusside is also indicated for producing controlled hypotension during anesthesia in order to reduce bleeding in surgical procedures where surgeon and anesthesiologist deem it appropriate. In each case, the benefit-risk ratio should be carefully considered on an individual basis.
http://www.rxmed.com/b.main/b2.pharmaceutical/b2.prescribe.html/

Normodyne (labetalol) – is used alone or in combination with other drugs to reduce blood pressure.
http://www.medicinenet.com/labetalol/article.htm

Plavix (clopidogrel) – is an anti-thrombosis drug, more specifically known as an antiplatelet agent. It is indicated for the prevention of atherothrombotic complications in patients with a recent history of myocardial infarction, recent stroke, or established peripheral arterial disease.
http://en.sanofi-aventis.com/group/products/p_group_products_cardio_plavix.asp

Papaverine – is indicated for the relief of cerebral and peripheral ischemia associated with arterial spasm and myocardial ischemia complicated by arrhythmias.
http://www.rxlist.com/cgi/generic/papaverine_ids.htm

Procardia (nifedipine) – is indicated for the management of vasospastic angina confirmed by any of the following criteria: 1) classical pattern of angina at rest accompanied by ST segment elevation, 2) angina or coronary artery spasm provoked by ergonovine, or 3) angiographically demonstrated coronary artery spasm. In those patients who have had angiography, the presence of significant fixed obstructive disease is not compatible with the diagnosis of vasospastic angina, provided that the above criteria are satisfied. Procardia may also be used where the clinical presentation suggests a possible vasospastic component but where vasospasm has not been confirmed, e.g., where pain has a variable thresh- old on exertion or when angina is refractory to nitrates and/or adequate doses of beta blockers. Procardia is indicated for the management of chronic stable angina (effort-associated angina) without evidence of vasospasm in patients who remain symptomatic despite adequate doses of beta blockers and/or organic nitrates or who cannot tolerate those agents. In chronic stable angina (effort-associated angina) Procardia has been effective in controlled trials of up to eight weeks duration in reducing angina frequency and increasing exercise tolerance, but confirmation of sustained effectiveness and evaluation of long-term safety in these patients are incomplete. Controlled studies in small numbers of patients suggest concomitant use of Procardia and beta-blocking agents may be beneficial in patients with chronic stable angina, but available information is not sufficient to predict with confidence the effects of concurrent treatment, especially in patients with compromised left ventricular function or cardiac conduction abnormalities. When introducing such concomitant therapy, care must be taken to monitor blood pressure closely since severe hypotension can occur from the combined effects of the drugs.
http://www.rxlist.com/cgi/generic/nifedip_ids.htm

Protamine sulfate – is indicated in the treatment of severe heparin overdose resulting in hemorrhage. It is indicated to neutralize heparin that is administered during extracorporeal circulation in arterial and cardiac surgery or dialysis procedures; also, it may be used to neutralize the hemorrhagic effects following overdose of the low molecular weight heparin, enoxaparin. Transfusion of whole blood or fresh frozen plasma may also be required to replace lost volume if hemorrhaging has been severe; this may dilute, but will not neutralize, the effects of heparin.
http://www.drugs.com/mmx/protamine_sulfate.html

ReoPro (abciximab) – is indicated as an adjunct to PCI for the prevention of cardiac ischemic complications in patients undergoing PCI, and in patients with UA not responding to conventional medical therapy when PCI is planned within 24 hours. Safety and efficacy of ReoPro use in patients not undergoing PCI have not been established. ReoPro is intended for use with aspirin and heparin and has been studied only in that setting, as described in clinical studies.
http://www.reopro.com/index.jsp

Retavase (reteplase) – is indicated for use in the management of acute myocardial infarction (AMI) in adults for the improvement of ventricular function following AMI, the reduction of the incidence of congestive heart failure and the reduction of mortality associated with AMI.
http://www.retavase.com/RETLibrary/RETLib008/dld/Retavase_PI.pdf

Solu-Medrol (methylprednisolone) – is indicated for severe anaphylaxis, asthma/COPD, possibly effective as an adjunctive agent in the management of spinal cord injury.
http://www.dfdems.com/solumedrol.htm

Sotradecol (sodium tetradecyl sulfate injection) – is indicated in the treatment of small uncomplicated varicose veins of the lower extremities that show simple dilation with competent valves. The benefit-to-risk ratio should be considered in selected patients who are great surgical risks.
http://www.sotradecol.net/pdf/Sotradecol-PI.pdf

Streptase (streptokinase) – is an enzyme which works to break up and dissolve blood clots which can block arteries. It is used in the treatment of heart attack or lung clots (pulmonary embolism) as well as leg blood clots (deep venous thrombosis - DVT).
http://www.medicinenet.com/streptokinase-injection/article.htm

Tissue Plasminogen Activator - tPA – since 1996, tPA has been approved by the Food and Drug Administration (FDA) for the treatment of stroke and heart attack. According to the American Heart Association (AHA), if tPA is given within the first 3 hours of a stroke, it may reduce permanent disability. If given within 12 hours of the onset of a heart attack, the person has a better chance for survival and recovery.
http://health.allrefer.com/health/thrombolytic-therapy-tissue-plasminogen-activator-tpa-info.html

Verapamil HCl – Verapamil HCl immediate-release tablets are indicated for the treatment of the following:
Angina:

1. Angina at rest including vasospastic (Prinzmetal's variant) angina; Unstable (crescendo, pre-infarction) angina.
2. Chronic stable angina (classic effort-associated angina).

1. *Arrhythmias:*
2. In association with digitalis for the control of ventricular rate at rest and during stress in patients with chronic atrial flutter and/or atrial fibrillation (see WARNINGS, Accessory Bypass Tract).
3. Prophylaxis of repetitive paroxysmal supraventricular tachycardia. Verapamil HCl is indicated for the treatment of the following: essential hypertension.

http://www.rxlist.com/cgi/generic/verapsr_ids.htm

Xylocaine (lidocaine) – is a local anaesthetic, and is available in a wide range of presentations. Available presentations include:
Xylocaine injection is the most widely used local anaesthetic in dental procedures, and can be used for local infiltration, minor and major nerve blocks, epidural block, arthroscopy and intra- venous regional anaesthesia.
Several forms of Xylocaine for topical use are available including
Xylocaine jelly and *Xylocaine spray*.
http://www.astrazeneca.com/productbrowse/4_79.aspx

Neuroanatomy

NP001825 v2.0

Neuroanatomy

Neuroanatomy
The basics

Our brain is one of the most complex biological structures found in nature. It initiates and coordinates our bodily functions and movements. It processes all external sensory information we receive, creating our inner world of thoughts, feelings, and memories. And, it determines our personality. Damage to or disease of the brain profoundly influences our quality of life and ability to interact socially.

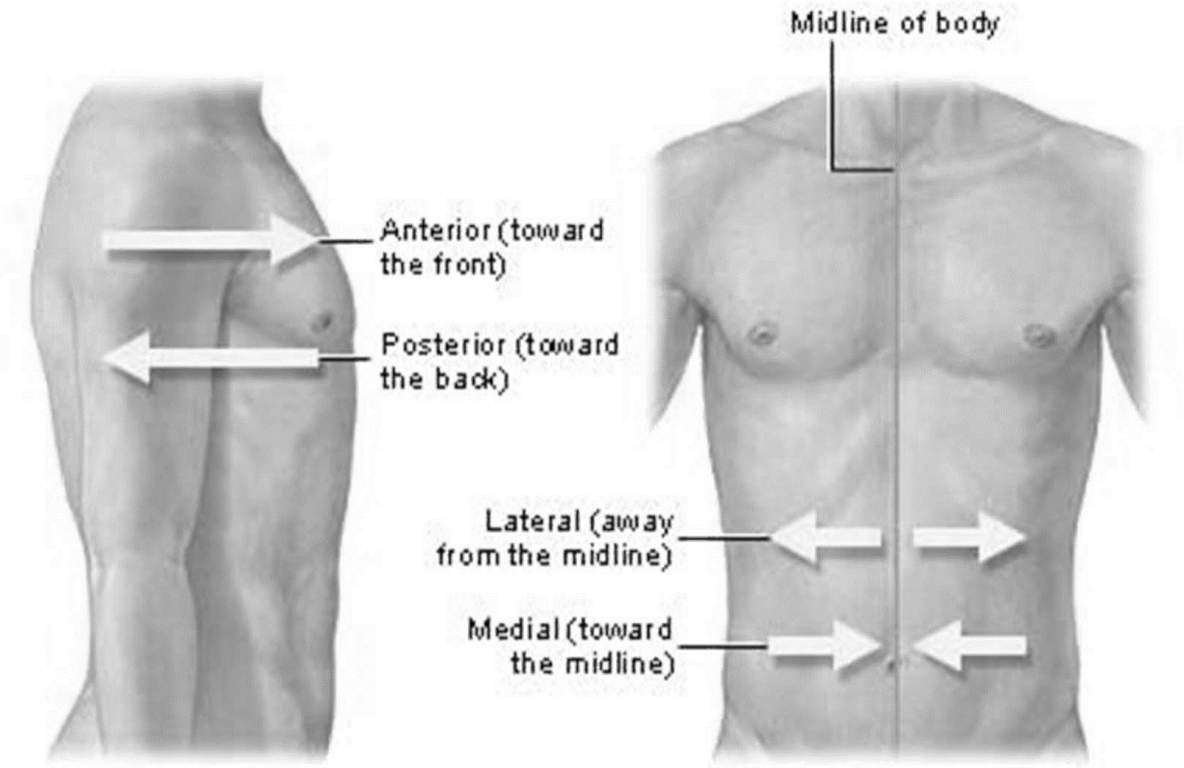


Figure 1.1. Body reference

Divisions of the brain

The central nervous system

Neurons are a class of brain cells that are very sensitive to lack of oxygen, known as ischemia. While other brain cells are less sensitive than neurons, continued ischemia also leads to death of these cells. In the end, death of neurons and other brain cells contributes to the final outcome of damage due to ischemia.

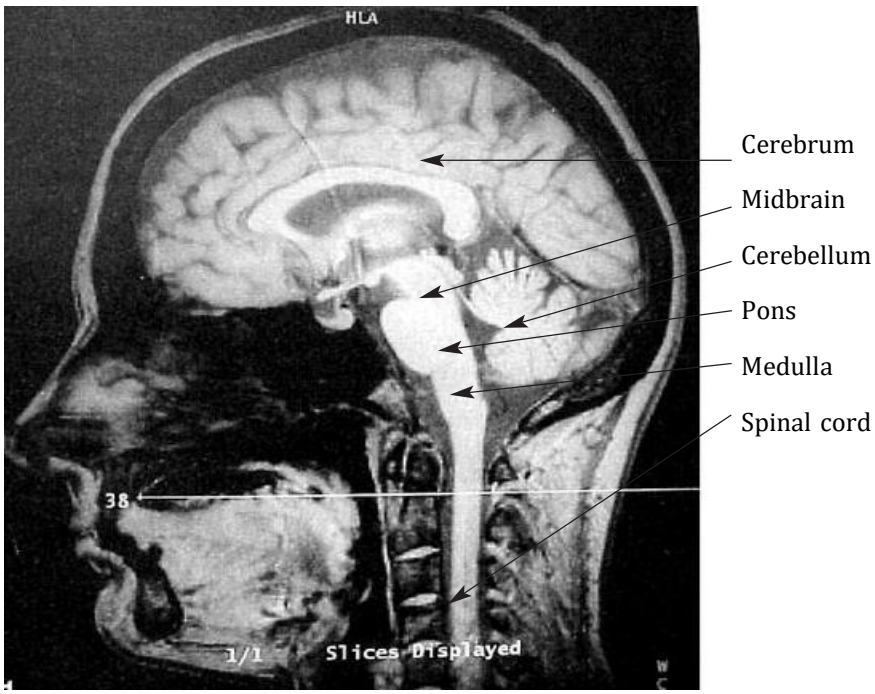


Figure 1.2. Central Nervous System

The Central Nervous System (CNS) *(see Figure 1.2)* includes:

- Cerebrum (right and left hemispheres
- Cerebellum.
- Midbrain.
- Pons.
- Medulla.
- Spinal cord.

Neuroanatomy
The basics

Forebrain (Prosencephalon)
- Telencephalon (Cerebrum)
- Diencephalon
    - Thalmus
    - Hypothalmus

Midbrain (Mesencephalon)
- Together with the hindbrain, makes up the brainstem

Hindbrain (Rhombencephalon)
- Cerebellum
- Medulla oblangata
- Metencephalon
- Myelencephalon
- Pons

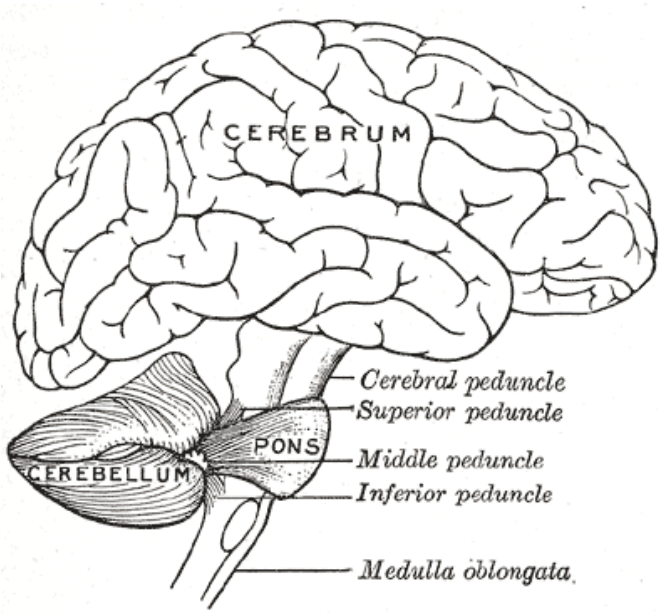


Figure 1.3. Divisions of the Brain

These regions assist in maintaining balance and equilibrium, movement coordination, and the conduction of sensory information.

The medulla oblongata is a relay station for information that is passed to the higher brain centers & cerebellum. It is responsible for controlling such autonomic functions as breathing, heart rate, blood pressure, swallowing, coughing and digestion.

The pons consists of the bulging brain stem region between the midbrain and the medulla oblongata. It includes a respiratory center that regulates the rate and depth of breathing

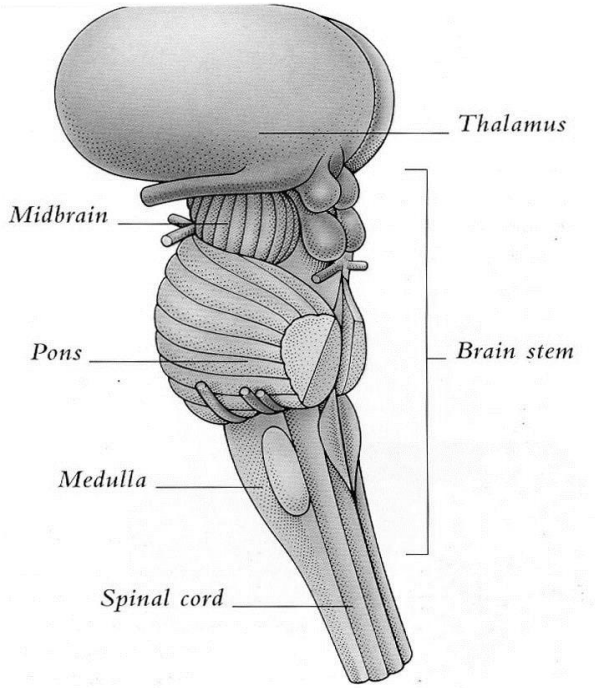


Figure 1.4. Diencephalon

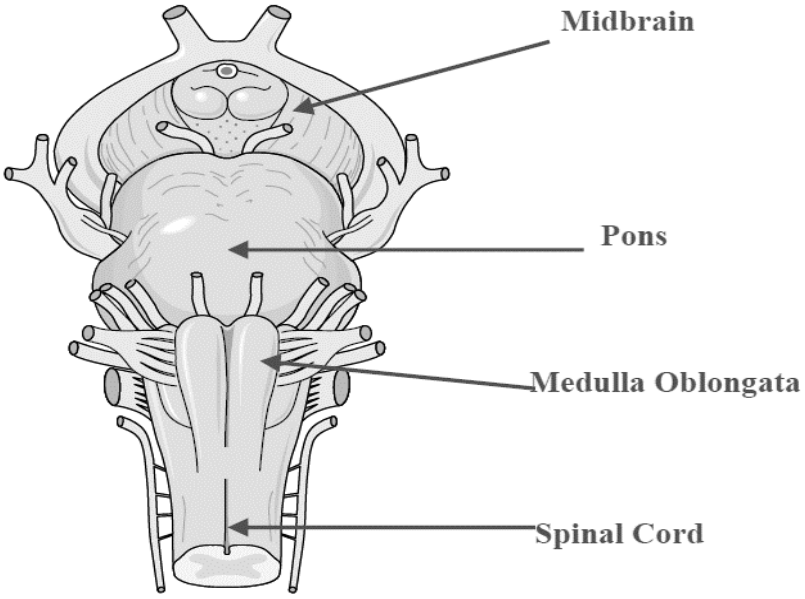


Figure 1.5. Mesencephalon

Divisions of the brain

Cerebrum

The ***cerebrum***, which forms the bulk of the brain, may be divided into two major parts: the right and left cerebral hemispheres. There is a fissure, or groove, that separates the two hemispheres called the great longitudinal fissure. The two sides of the brain are joined at the bottom by the corpus callosum. The corpus callosum connects the two halves of the brain and delivers messages from one half of the brain to the other. The surface of the cerebrum contains billions of neurons and glia that together form the cerebral cortex.

The cerebral cortex appears greyish brown in color and is called the "gray matter." The surface of the brain appears wrinkled. The cerebral cortex has small grooves (sulci), larger grooves (fissures), and bulges between the grooves (gyri). Beneath the cerebral cortex or surface of the brain, connecting fibers between neurons form the "white matter" (appear white in color). The cerebral hemispheres control the contralateral or opposite side of the body.

Each hemisphere has four lobes and a cerebellum that control daily functions.

The areas that produce movement of parts of the body are found in the primary motor cortex or precentral gyrus. These regions are found in the frontal lobe and also control memory, intelligence, concentration, temper, and personality. It helps us set goals, make plans, and judge our priorities.
The primary auditory cortex helps us hear sounds and gives sounds their meaning. The temporal lobes are the primary region responsible for memory.

The parietal lobes simultaneously interpret sensory signals received from other areas of the brain such as our vision, hearing, motor, sensory, and memory. It also coordinates right-left coordination.
The occipital lobe contains regions that contribute to our visual field or how our eyes see the world around us. They help us see light and objects and allow us to recognize and identify them. This region is called the visual cortex.

The ***cerebellum*** is located at the back of the brain beneath the occipital lobe. It is separated from the cerebrum by the tentorium (fold of dura). The cerebellum fine tunes our motor activity or movement (e.g., the fine movements of our fingers as they write a story or color a picture). It also helps us maintain our posture, our sense of balance or equilibrium by controlling the tone of our muscles, and senses the position of our limbs. In the cerebellum, right-sided abnormalities produce symptoms on the same side of the body, unlike the cerebral cortex that has ipsilateral control of the body. The cerebellum controls our balance and coordination. There are twelve pairs of nerves that come from the brain itself. These are called the cranial nerves.

The ***brain stem*** is located in front of the cerebellum and may be considered as a "stem" or structure holding up the cerebrum. It consists of three structures: the midbrain, pons, and medulla oblongata. It serves as a relay station, passing messages back and forth between various parts of the body and cerebral cortex. Many simple or primitive functions that are essential for survival are located here.
The majority of the cranial nerves arise from the brainstem to control many face and body functions. It is also the center for consciousness.

Each hemisphere has four lobes:

- Frontal.
- Temporal.
- Parietal.
- Occipital.

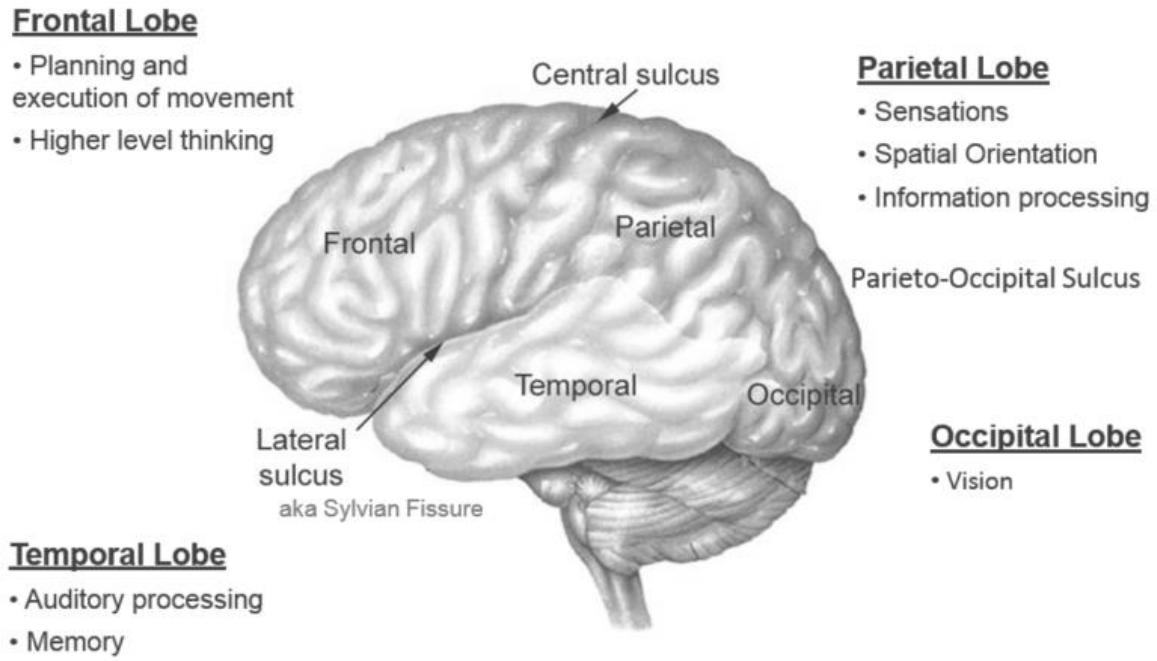


Figure 1.6. Hemispheres of the Brain

Divisions of the brain
Functionality

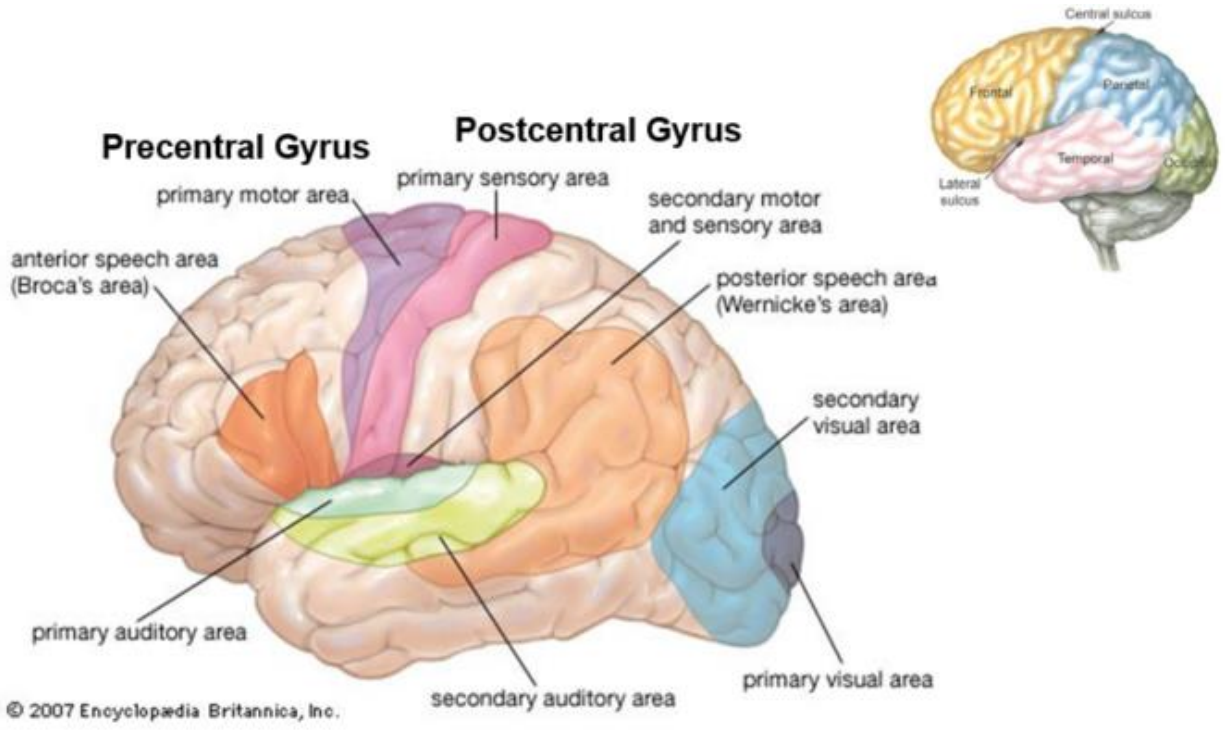
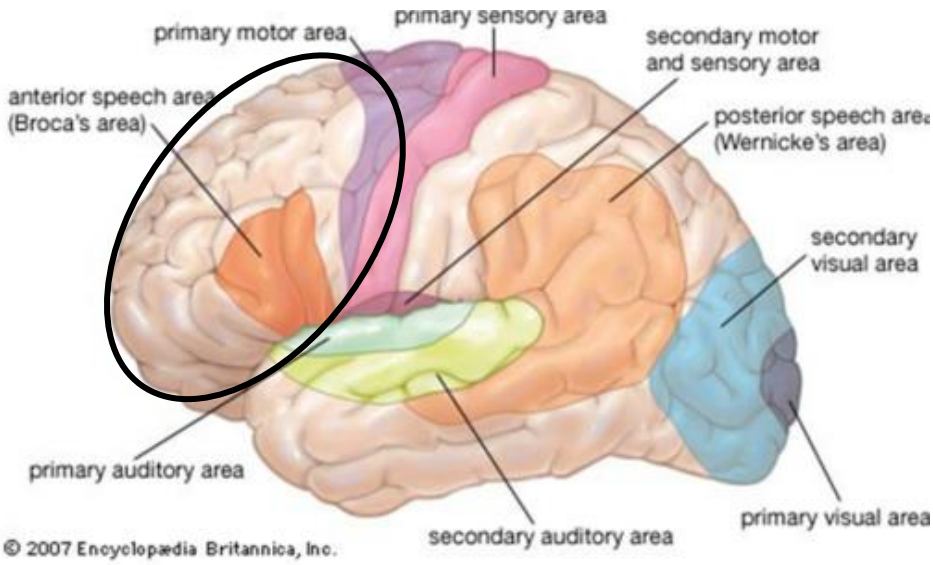


Figure 1.7. Brain Functionality

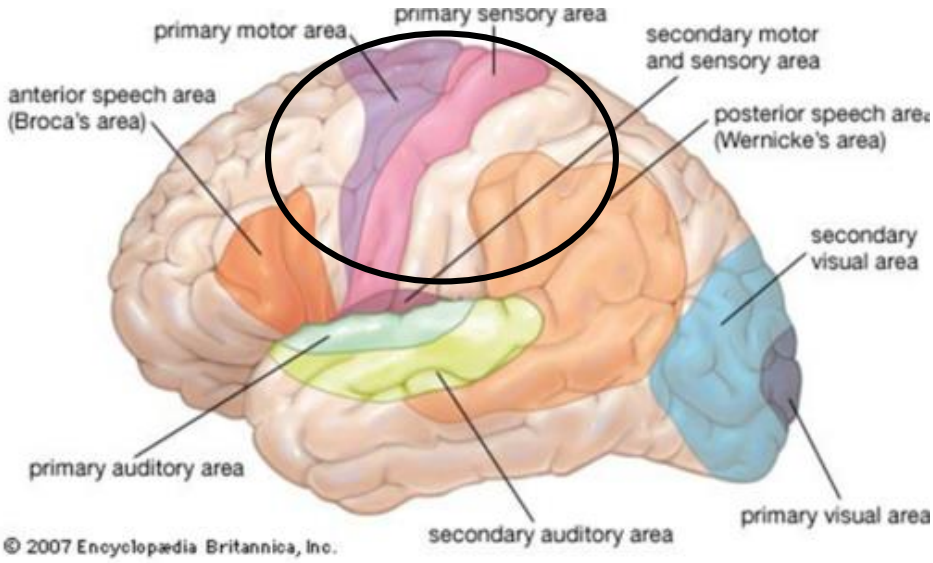
Divisions of the brain

The frontal lobe



Function	If injured
Intellect	Impairment of recent memory, inattentiveness, difficulty learning new information
Movement	Contains the precentral gyrus, which controls voluntary contraction of skeletal muscles, injury results in contralateral paralysis or paresis
Broca's area: language production	Difficulty producing sounds of speech, termed Broca's Aphasia
Personality psychological	Personality and behavior changes, flat moods, loss of inhibition/judgement

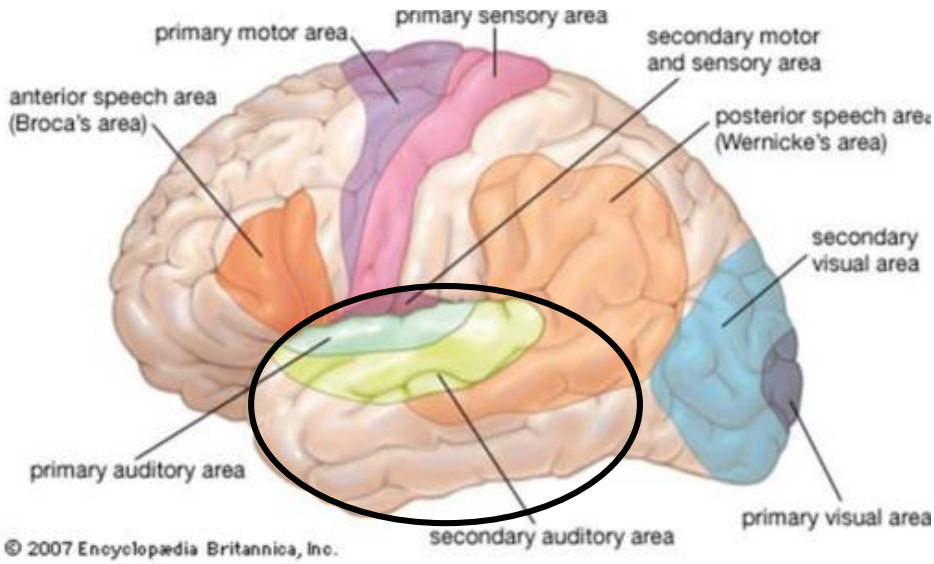
Divisions of the brain
Parietal lobes



Function	If injured
Sensation: post central gyrus is the primary sensory area	Inability to feel/localize touch, pressure, pain, temperature, prioprioception, locate/recognize parts of the body, and if severe, inability to recognize self

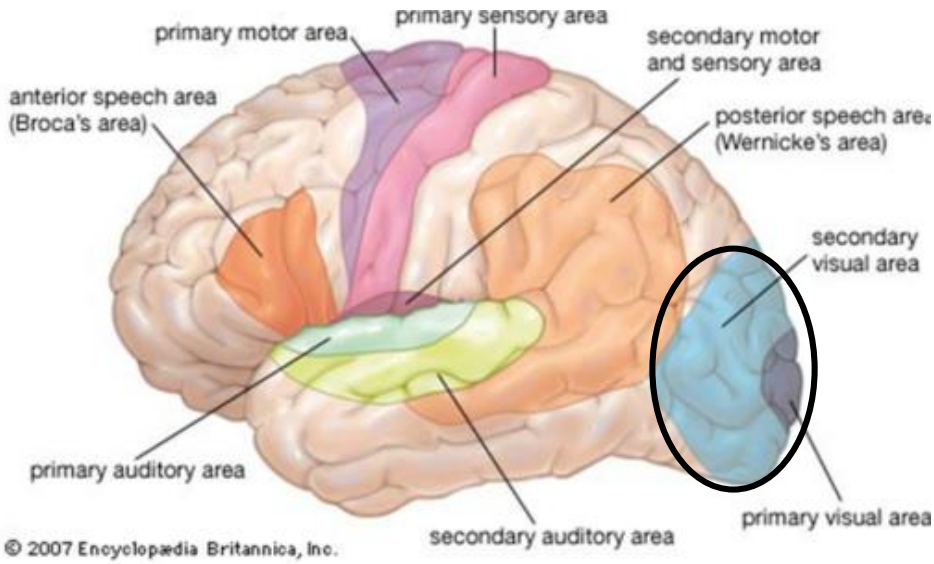
Divisions of the brain

Temporal lobes



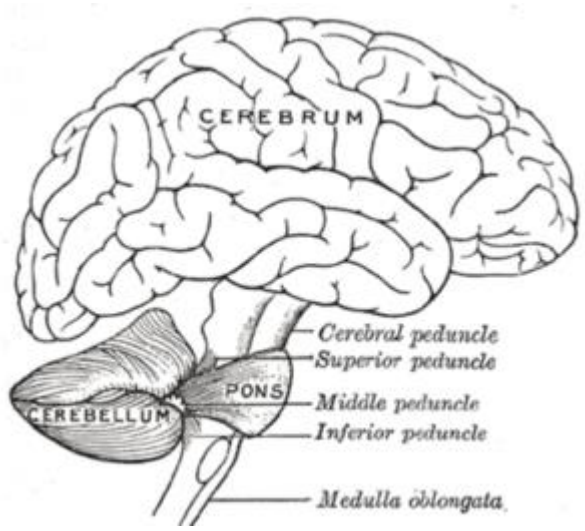
Function	If injured
Auditory	Difficulty evaluating, understanding, and/or remembering sounds, unable to give sounds meaning
Wernicke's area (left) language comprehension	Can cause devastating loss of ability to understand speech
Short term memory	Loss of short-term memory (visual, verbal)

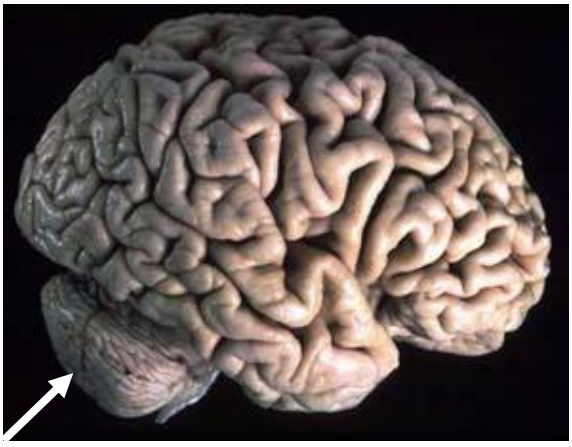
Divisions of the brain
Occipital lobes



Function	If injured
Contains visual cortex responsible for primary visual association Opposite lobe interprets visual signals from contralateral visual space	Visual defect in opposite field of vision, double-vision, functional blindness (no consciousness of what is being viewed)

Divisions of the brain
Cerebellum





Function	If injured
Contains visual cortex Responsible for primary visual association Opposite lobe interprets visual signals from contralateral visual space	Visual defect in opposite field of vision, double-vision, functional blindness (no consciousness of what is being viewed)

Neurovasculature

Neurovasculature

Territories of the brain

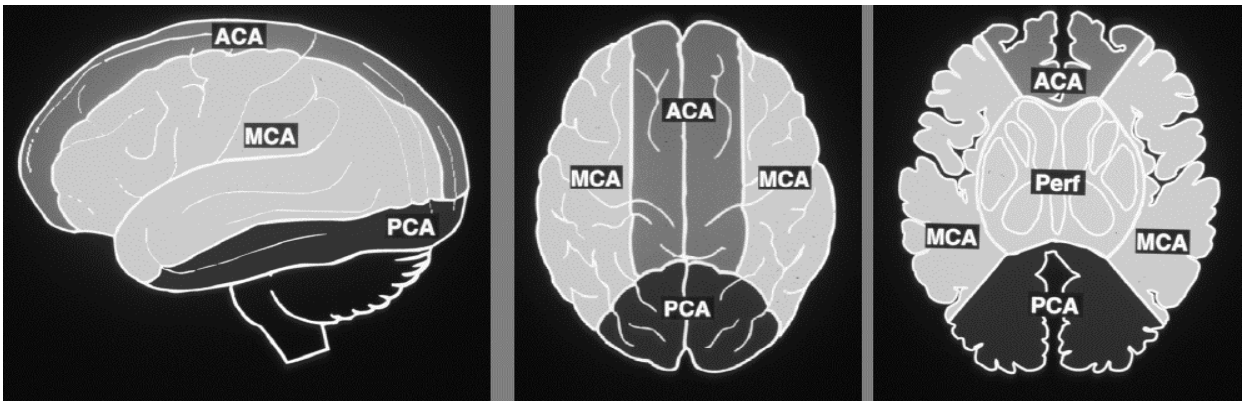


Figure 1.8. The territories of the brain

Neurovasculature

Arteries of the head and neck

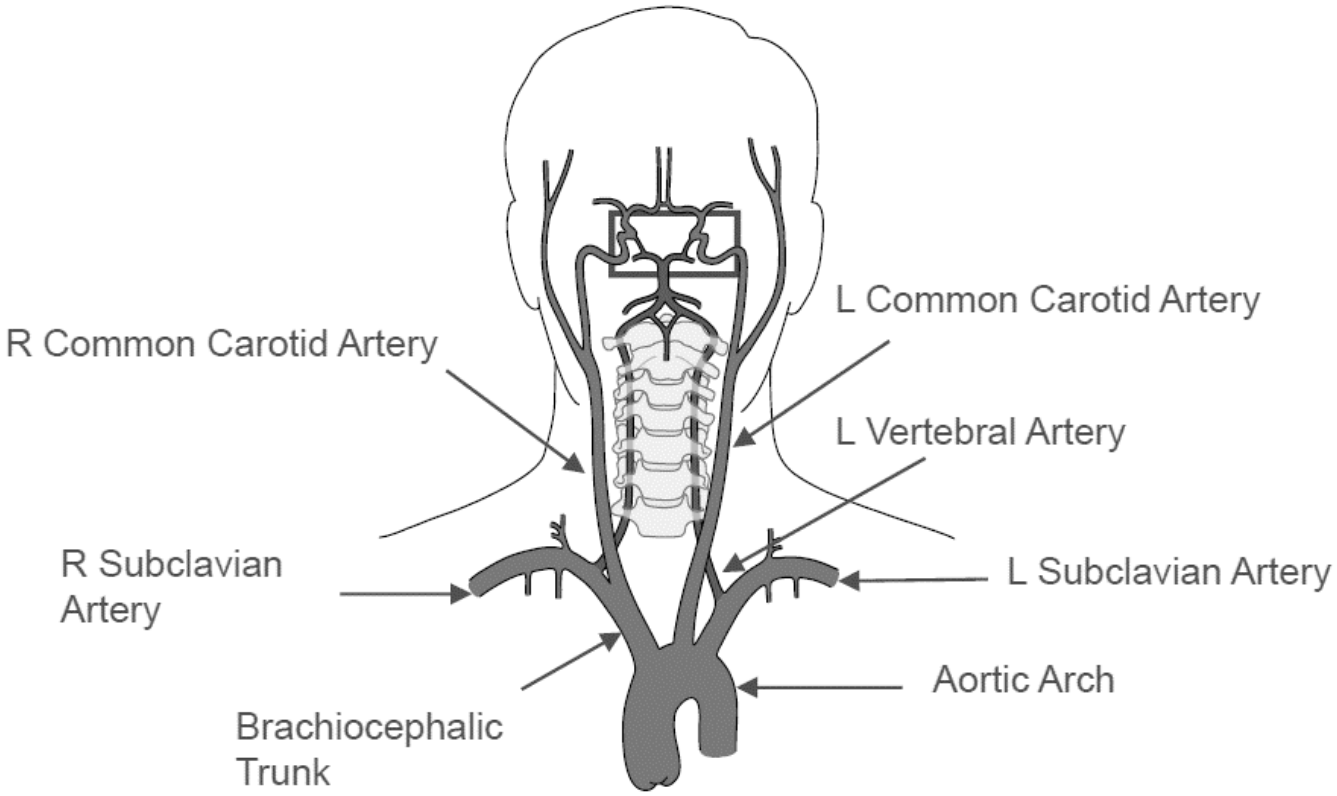


Figure 1.9. Arteries within the anatomy

Neurovasculature

Test your knowledge

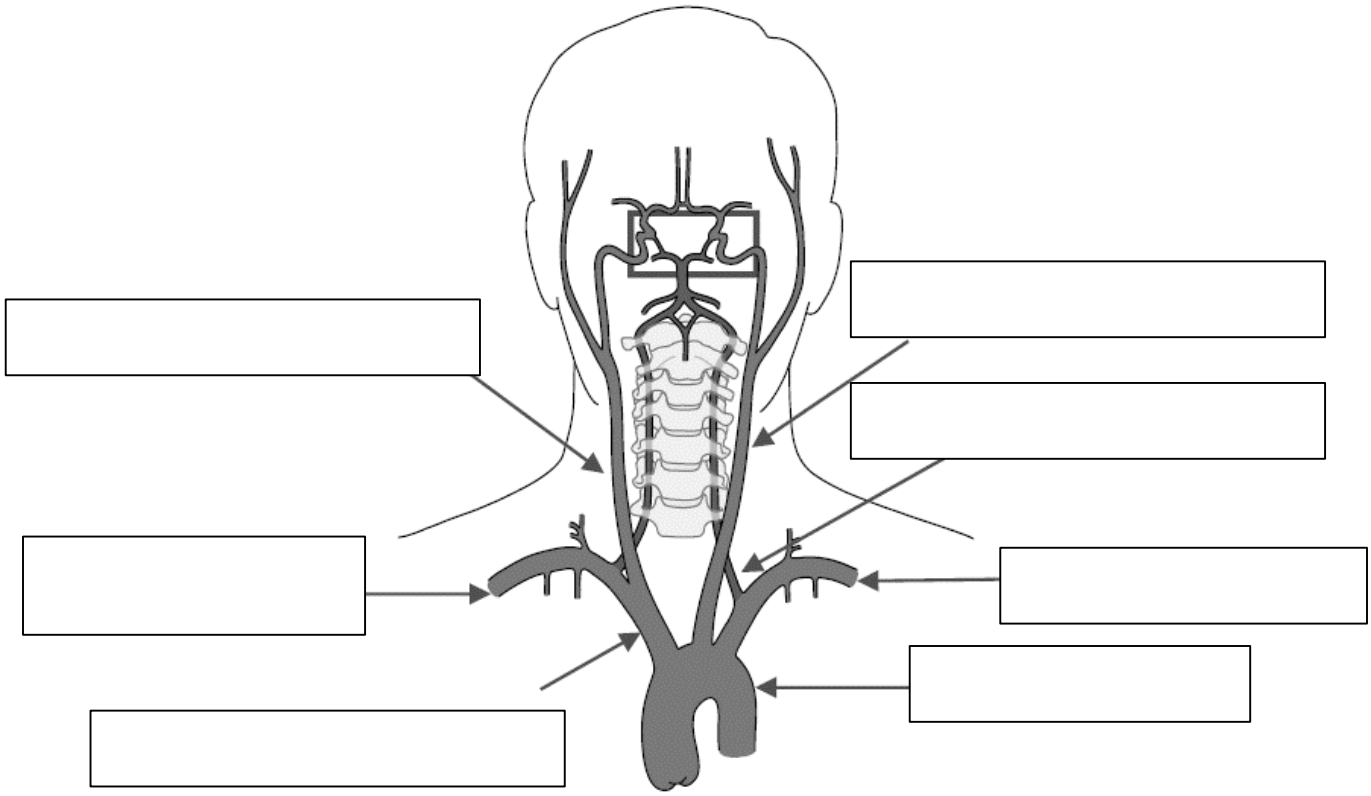


Figure 1.9. Arteries within the anatomy

1. Brachiocephalic artery
2. R Subclavian Artery
3. R Common Carotid
4. R Vertebral Artery
5. R Internal Carotid
6. R External Carotid
7. L Common Carotid
8. L Subclavian Artery
9. L Vertebral Artery
10. R Thyrocervical
11. L Thyrocervical

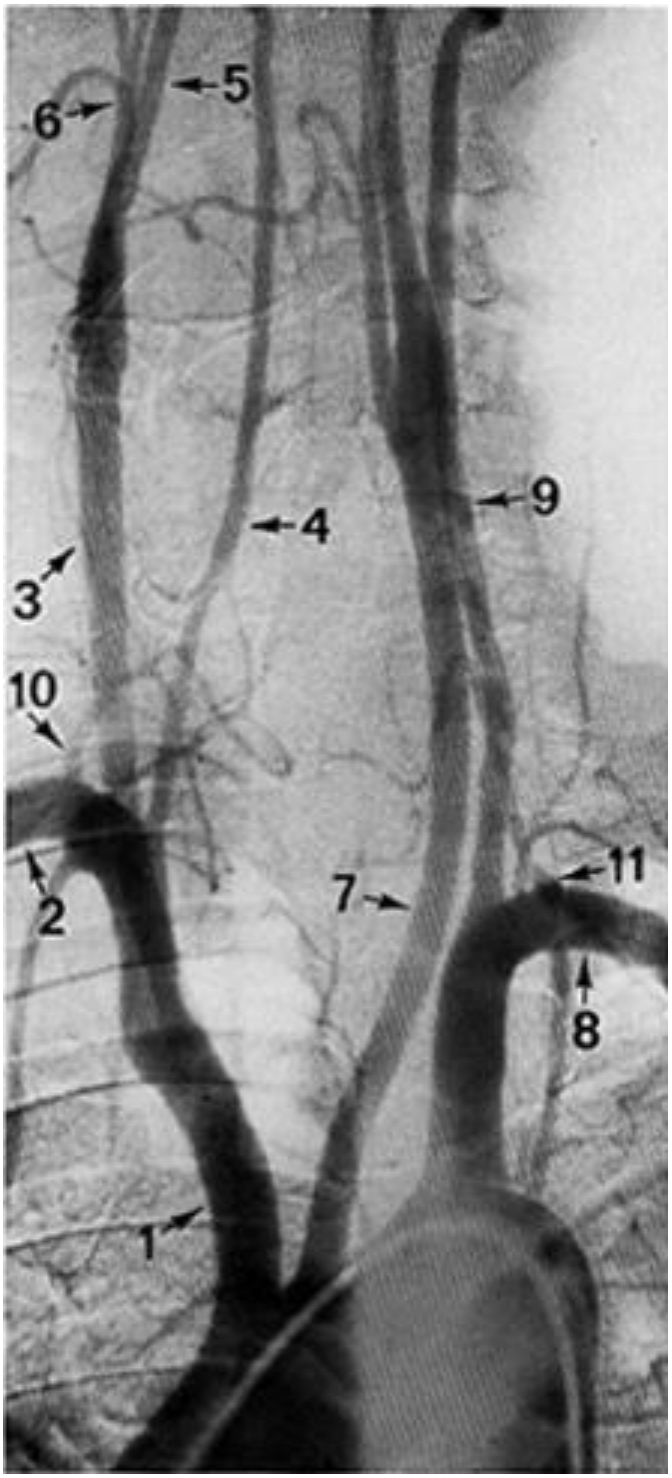


Figure 2.0. Imaging of the neuroanatomy

Neurovasculature

Test your knowledge

1. _____
2. _____
3. _____
4. _____
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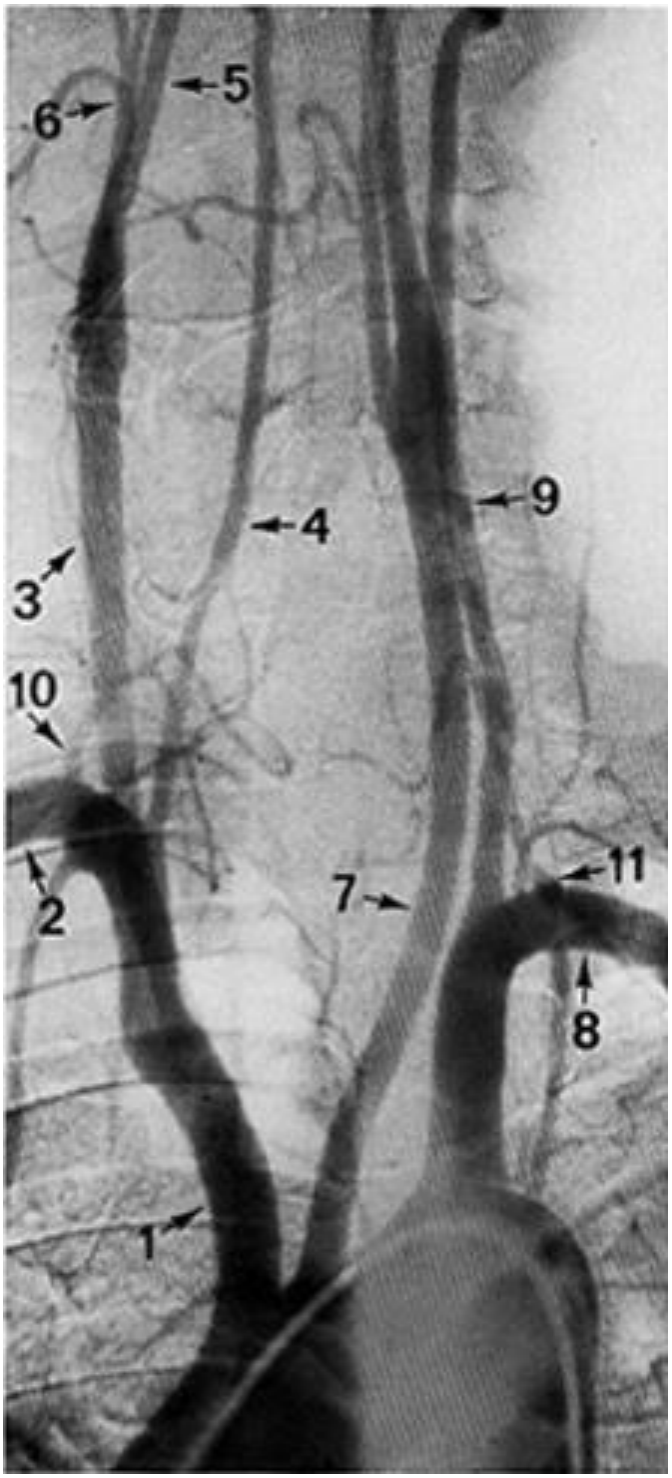

Figure 2.0. Imaging of the neuroanatomy

Neurovasculature
Aorta

The aorta is the largest artery in the body and carries oxygenated blood away from the heart.

It is comprised of 3 parts:

- Ascending aorta.
- Aortic arch.
- Descending aorta.

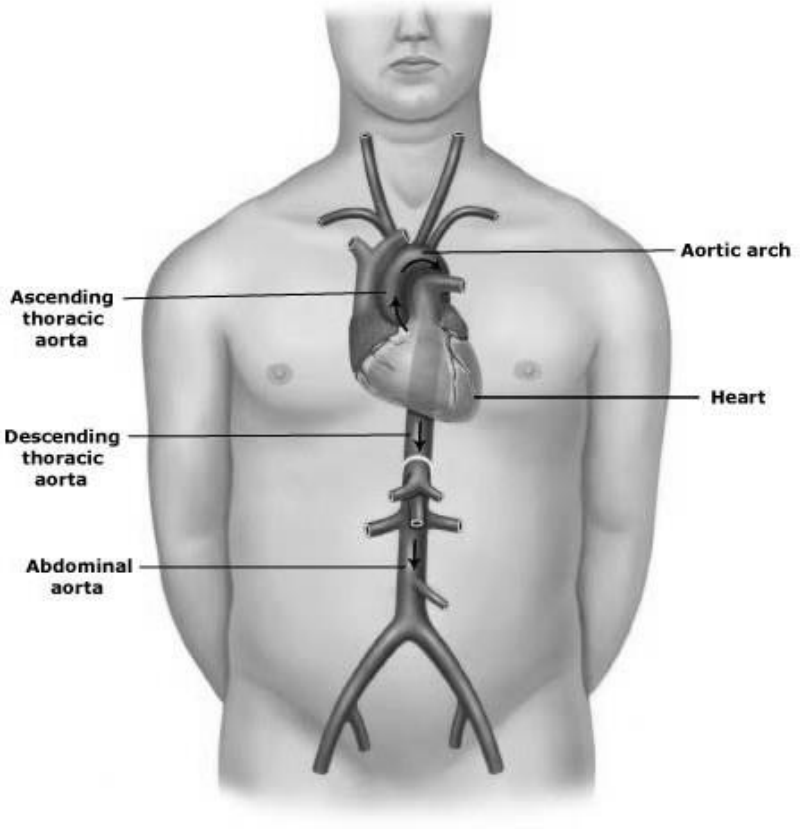

Figure 2.1. Segments of the aorta

Neurovasculature
Aortic arch

Gives rise to 3 Great Vessels:
- Brachiocephalic artery
- Left common carotid artery
- Left subclavian artery

These vessels supply:
- Upper extremities
- Neck
- Head

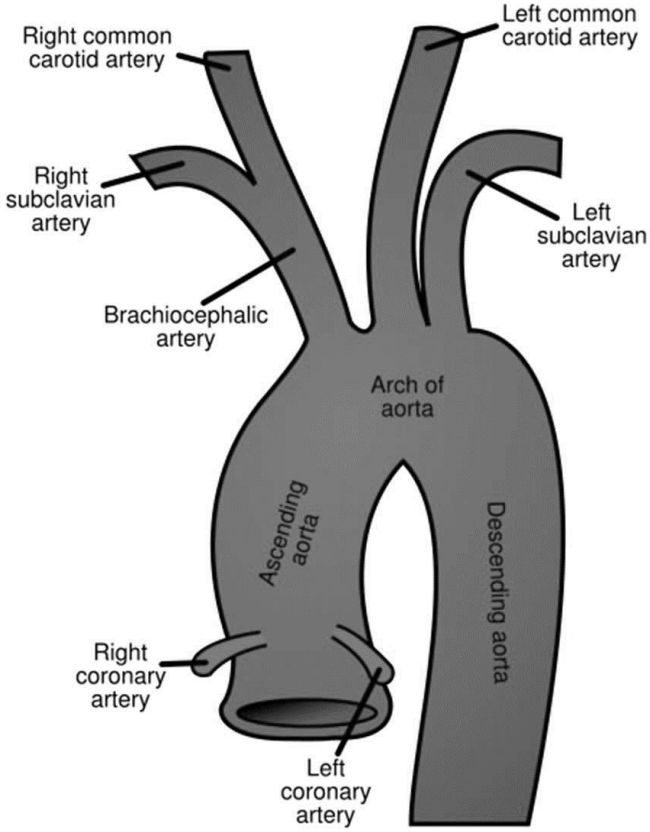

Figure 2.3. Segments of the aortic arch

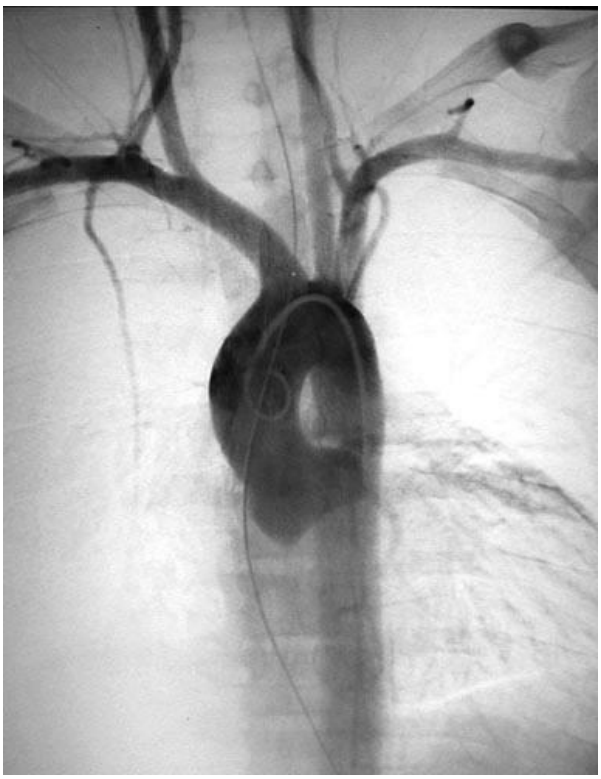

Figure 2.2. Imaging of the aortic arch

The innominate artery (brachiocephalic trunk) typically is the first large vessel arising from the ascending aortic arch. Two to three inches following its origin, it divides into the right subclavian and right common carotid arteries; the right and left common carotid arteries divide into internal and external carotid arteries

The right subclavian artery's primary function is to supply blood to the right arm. It additionally supplies the right chest wall and serves as the origin for the right vertebral artery. The vertebral arteries supply blood to the posterior portion of the brain.

The left subclavian artery ordinarily is the last major branch arising from the aortic arch in the chest. Its primary function is to supply blood to the left arm, but it also serves as the origin for the left chest wall vessels and the left vertebral artery.

Neurovasculature

Anterior and posterior circulation

Anterior circulation

Common carotid artery

- Supplies the majority of brain

Gives rise to:

- External carotid artery
- Internal carotid artery
- Anterior cerebral artery
- Middle cerebral artery
- Anterior communicating artery

Posterior circulation

Vertebrobasilar artery

- Vertebral a converge to form the basilar artery
- Supplies cerebellum and brainstem

Gives rise to:

- Posterior cerebral artery
- Posterior communicating artery

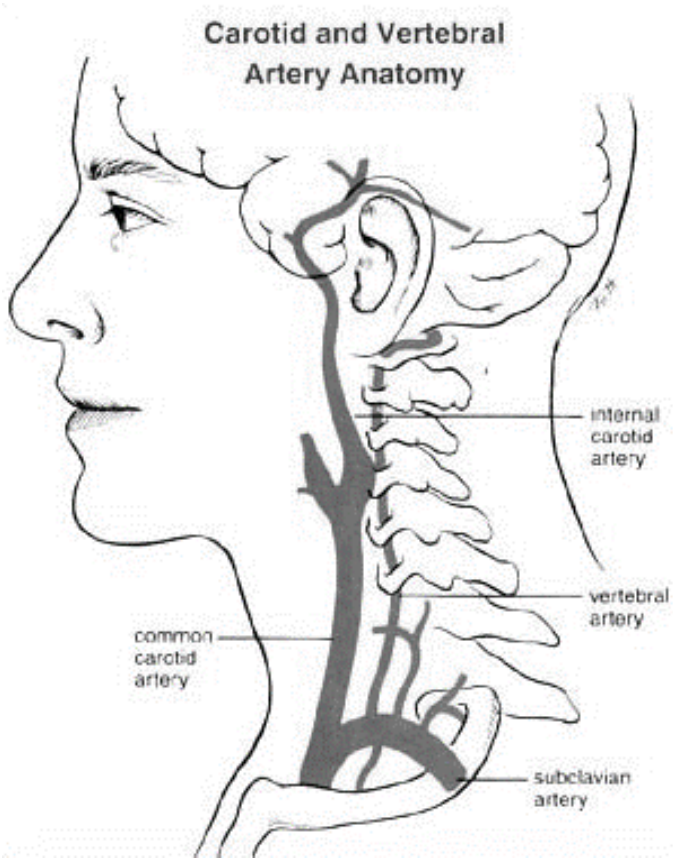

Figure 2.4. Anterior and posterior circulation

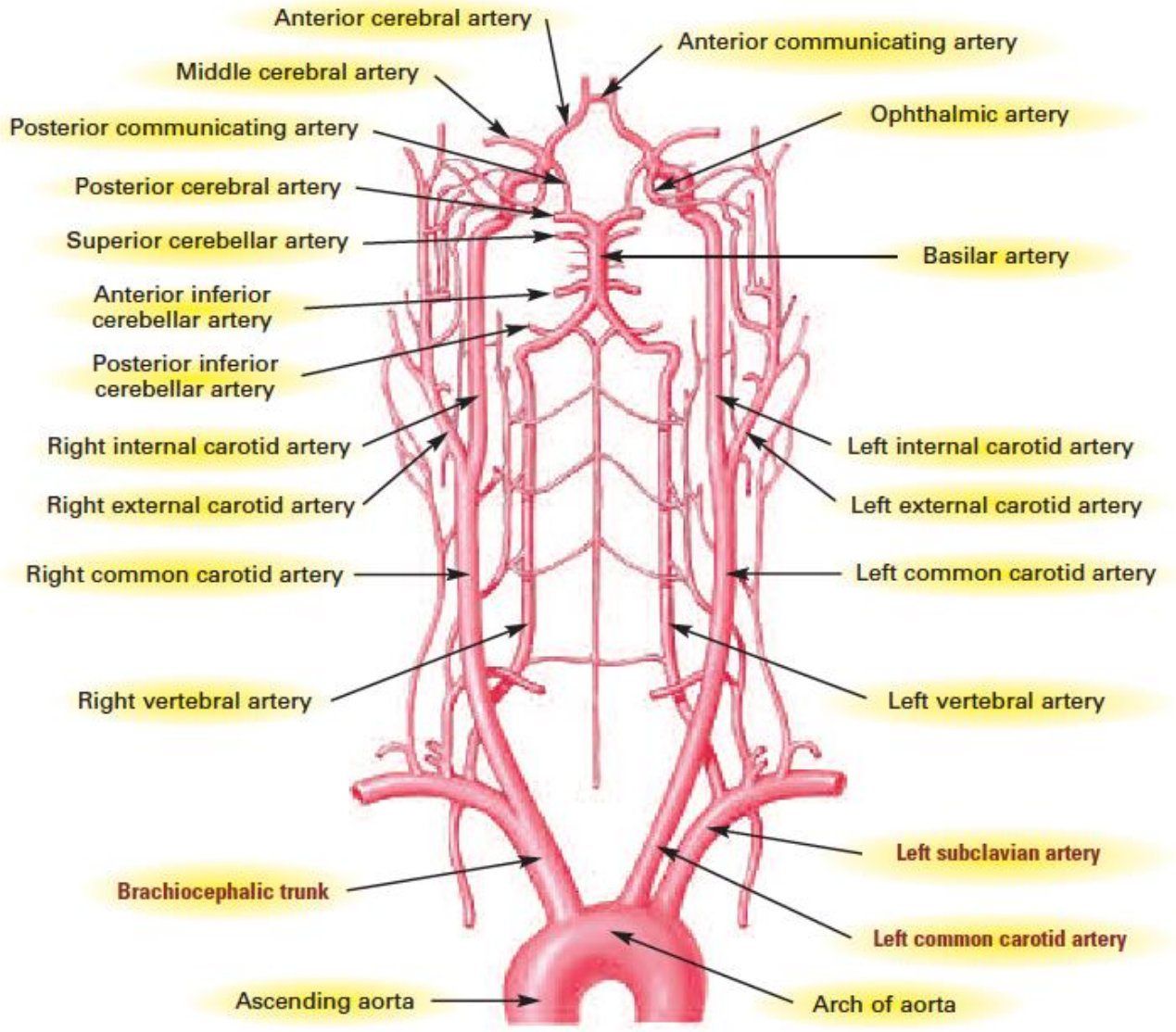

Figure 2.5. Arterial pathways from aortic arch

Neurovasculature

Test your knowledge

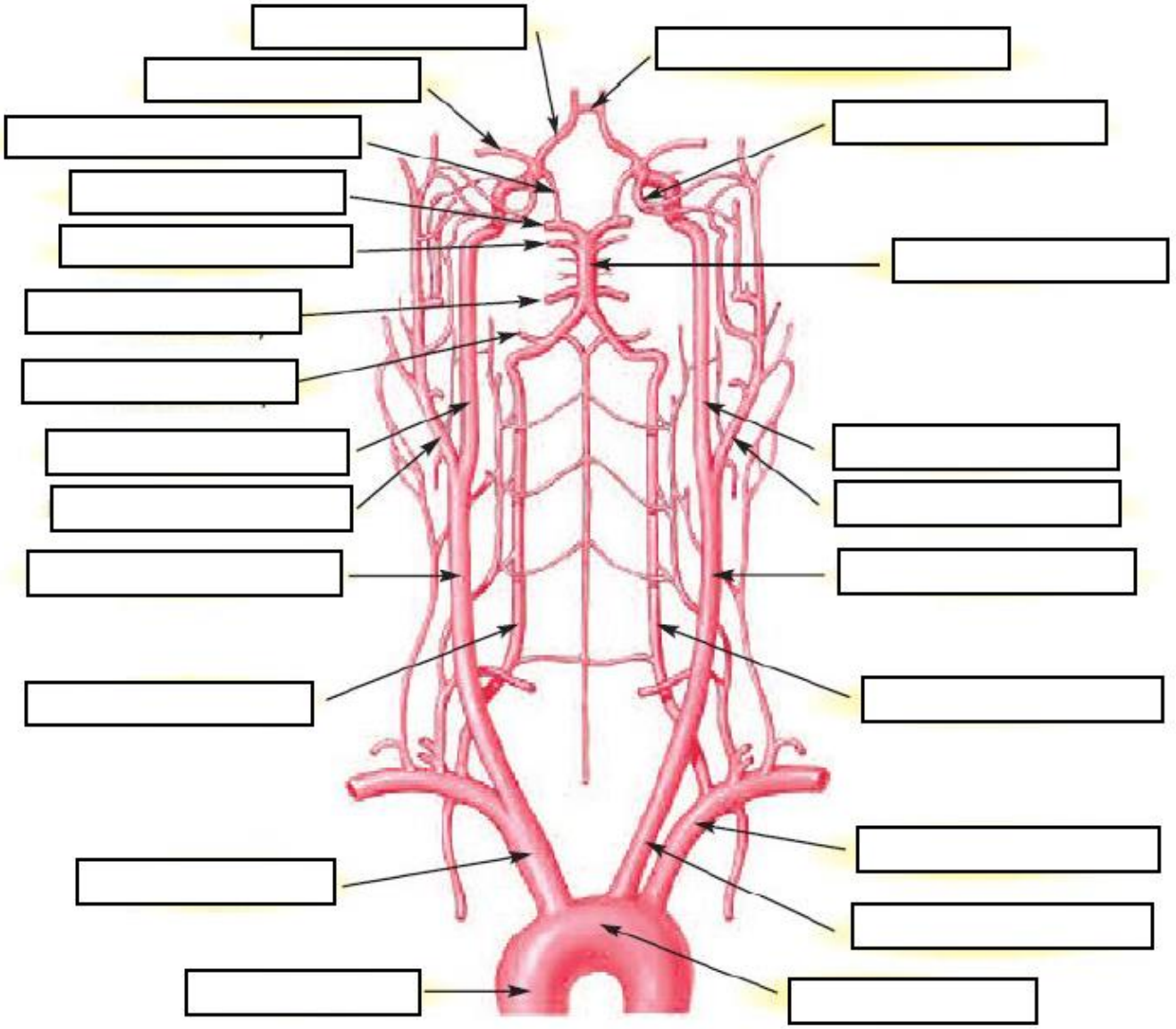

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Figure 2.5. Arterial pathways from aortic arch

Figure 2.6. Arterial pathways (frontal view)

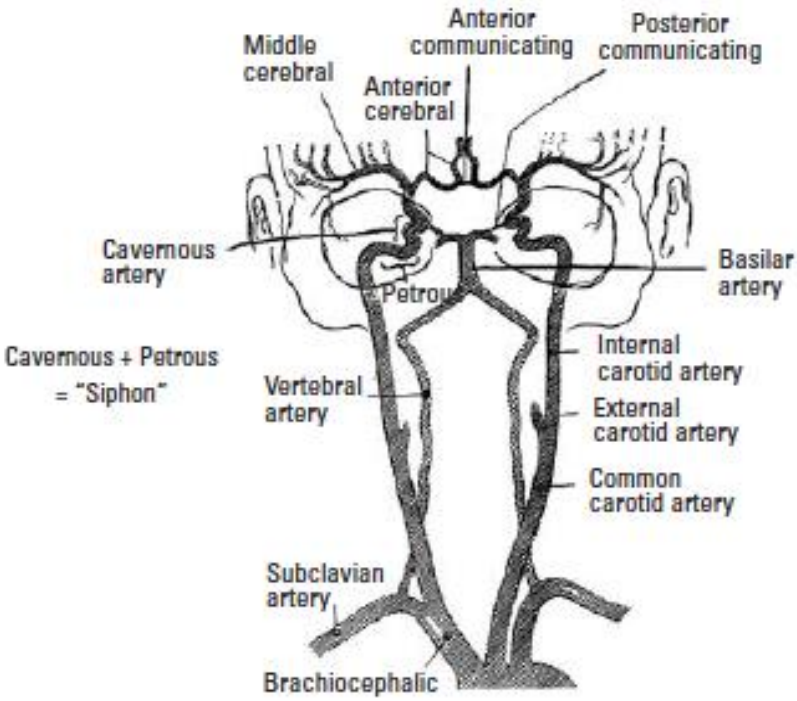
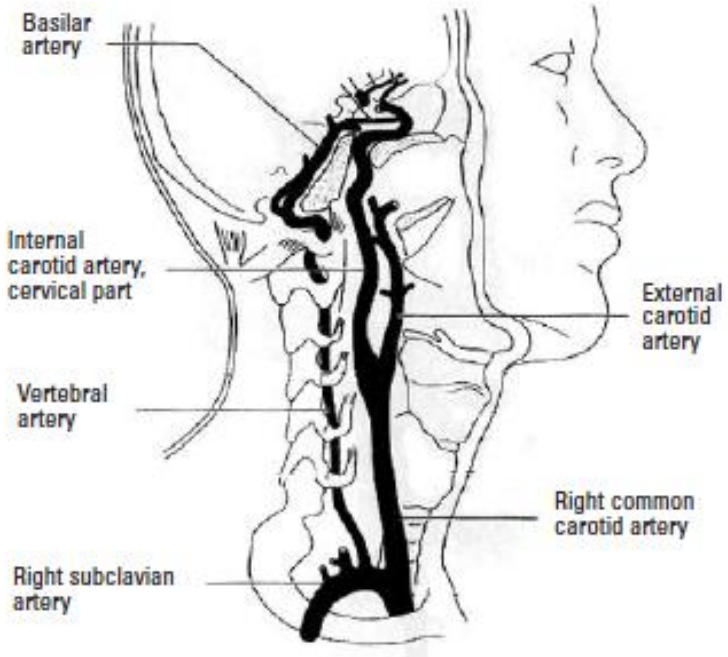
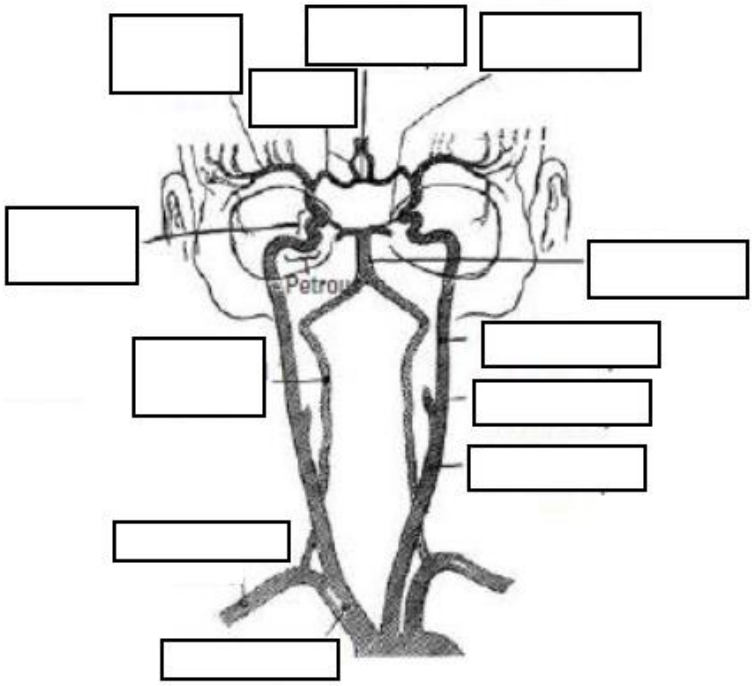


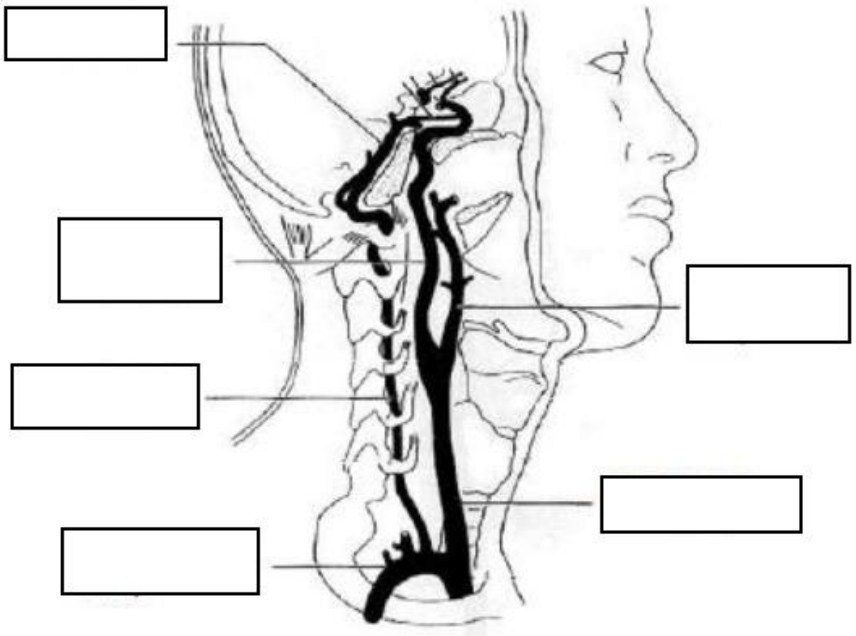
Figure 2.7. Arterial pathways (lateral view)



Neurovasculature

Test your knowledge





Blood supply to the brain, or cerebral circulation, is unique in that it derives from four major arteries that eventually coalesce to form the Circle of Willis. There are two paired sources: the vertebral arteries and the common carotid arteries. The vertebral arteries give rise to what we call the posterior circulation of the brain. They ascend the anterior surface of the upper spinal cord and the brainstem before fusing into the single basilar artery. The basilar artery divides into the two posterior cerebral arteries (PCA).

The common carotid arteries (CCAs) will eventually give rise to the anterior circulation of the brain. They supply the front of the brain, head, and neck, and divide into the internal carotid artery (ICA) and external carotid artery (ECA) between the C3 and C5 vertebrae. This is the carotid bifurcation.

The two internal carotid arteries (anterior circulation) run in the neck and then through the skull to meet the posterior circulation at the Circle of Willis. The Circle of Willis provides a connection between the anterior and posterior circulation.

The main arteries enter the subarachnoid space and divide many times before penetrating the substance of the brain to form smaller arterioles and capillaries. It is in the subarachnoid space where the branch points develop aneurysms and rupture to bleed into this space, giving rise to ***subarachnoid hemorrhage***. There is considerable individual variability in the exact pattern of the arterial blood supply to the brain. The capillaries form numerous anastomoses before coming back together into venules and veins. Venous blood is drained from the brain through a set of venous sinuses and then exits via the jugular veins.

The ***intracranial*** arteries are very complex. There are multiple vessels that feed the brain. All the vessels follow an extremely tortuous path, and there is tremendous variability from one person to another in the degree to which these connections allow flow. Several small branching arteries coming off the main trunk perfuse
critical, central structures of the brain.

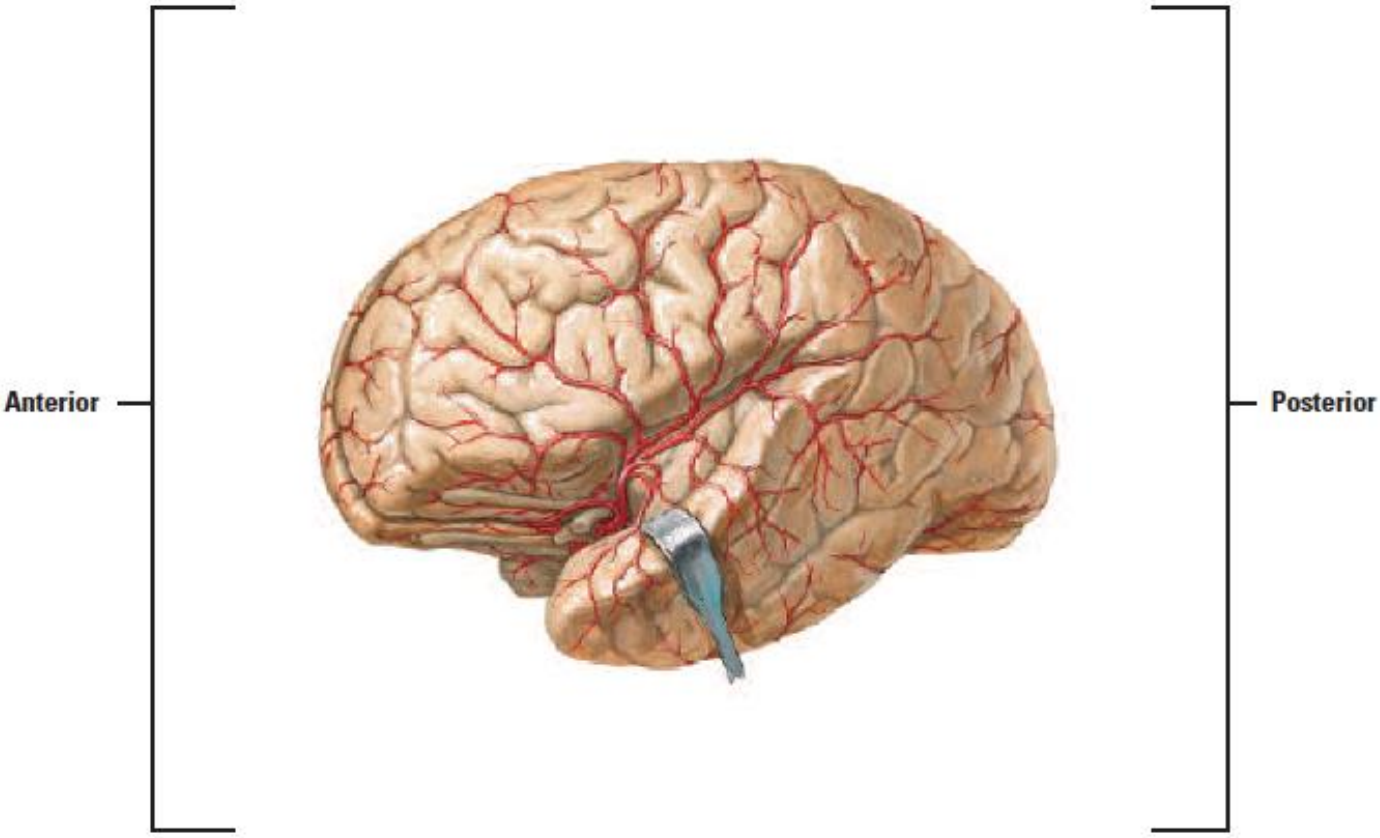


Figure 2.8. Anterior and posterior circulation

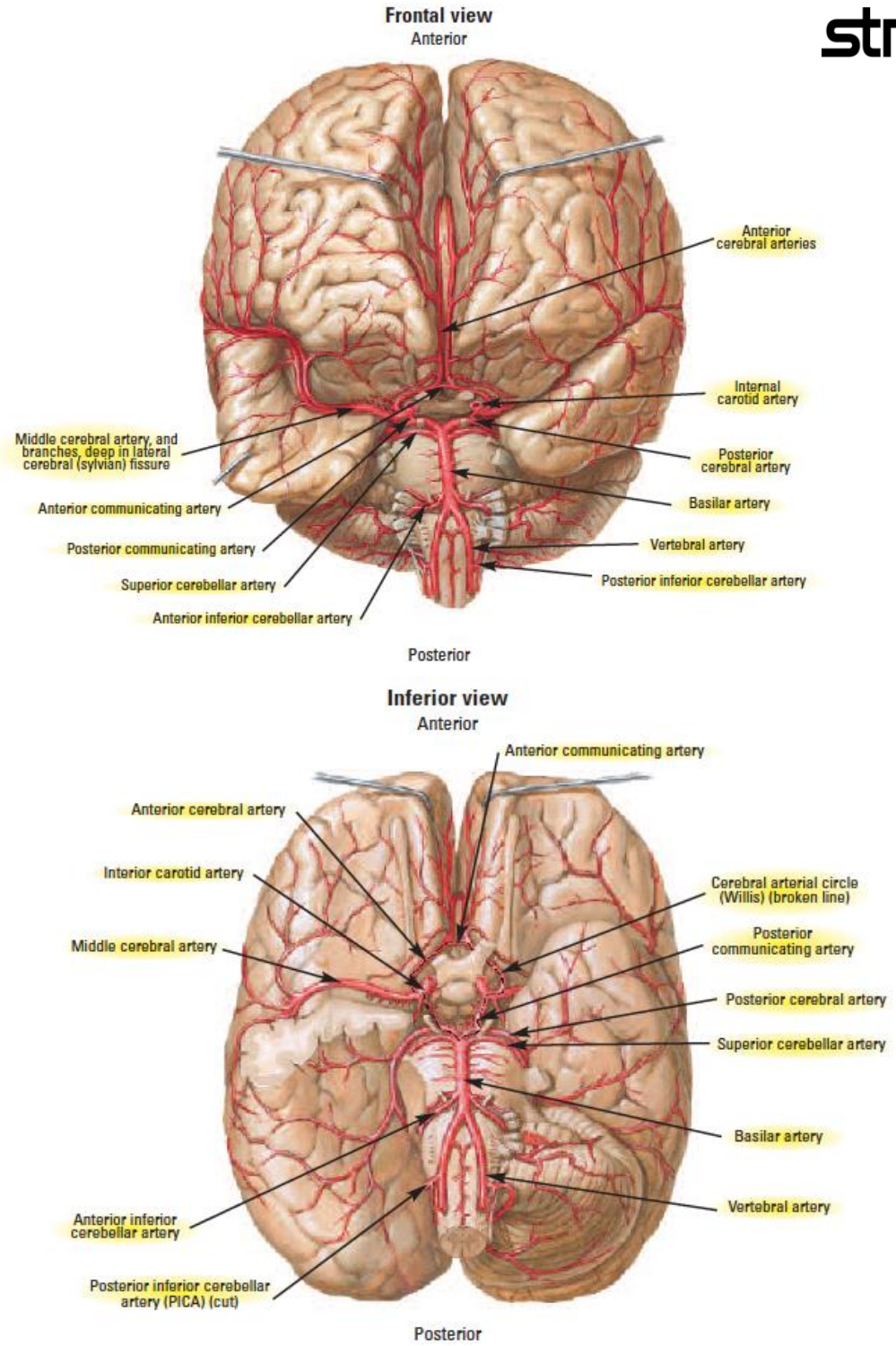


Figure 2.9. Anterior and posterior divisions

The external carotid artery (ECA) supplies the majority of the head and neck area outside the cranium: the scalp, the soft tissues of the deep face, the larynx, the pharynx, and the tongue.

Some branches of the external carotid artery enter the cranial cavity to supply the meninges and the cranial nerves.

Numerous connections (***anastomoses***) exist between branches of the external carotid artery and internal carotid artery.

The extracranial anastomoses include:

- The subclavian-vertebral, which connects branches between the ascending cervical (branch of the subclavian artery) and the vertebral artery.
- The subclavian-carotid, which is located between the deep cervical artery (branch of the subclavian artery) and the occipital artery.
- The carotid-vertebral, which is located between the occipital artery and the distal vertebral artery and between the ascending pharyngeal artery and the distal vertebral artery at the level of C1 and C2.

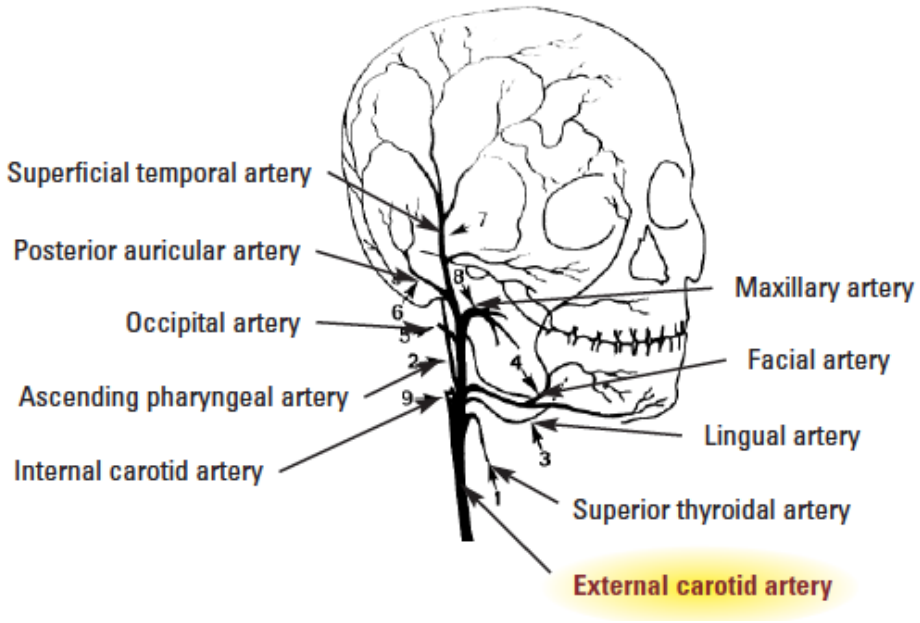


Figure 3.0. External carotid artery

Neurovasculature

Anterior circulation

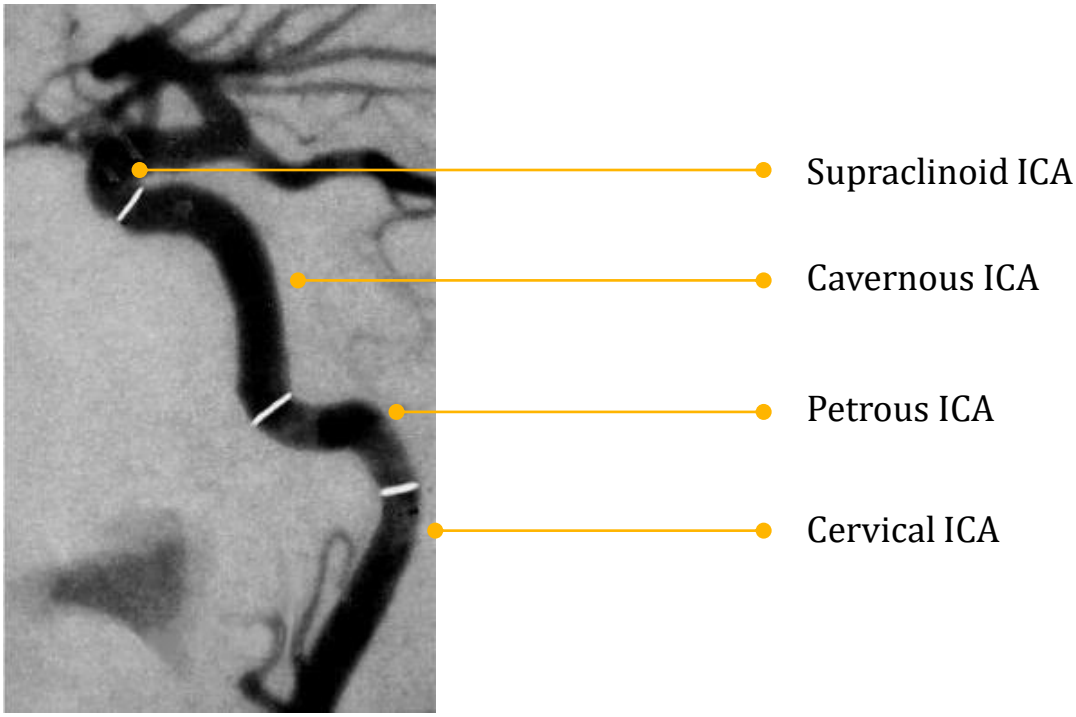


Figure 3.1. ICA segments

The internal carotid arteries (ICA) give rise to the anterior circulation of the brain. They are divided into four segments, which include: Cervical, Petrous, Cavernous, and Supraclinoid.

The ICA enters the cranial cavity at the apex of the petrous pyramid through the carotid canal and the cavernous sinus to supply the frontal (anterior) divisions of the brain.

The cervical ICA has no branching, ordinarily no narrowings, and extends from the common carotid bifurcation to the skull base.

The petrous ICA is surrounded by bone and is between the skull base and cavernous sinus.

The cavernous ICA, known as the carotid siphon, is an "S-shape" portion of the vessel that travels through the cavernous sinus (which is a venous room) and then exits the cavernous sinus as the supraclinoid portion of the ICA.

After passing anteriorly in the cavernous sinus, the ICA ascends to pierce the dura mater and becomes the supraclinoid segment. This is where it becomes intracranial. The supraclinoid carotid artery enters the subarachnoid space and divides into the anterior cerebral artery (ACA) and middle cerebral artery (MCA).

Neurovasculature
Anterior circulation

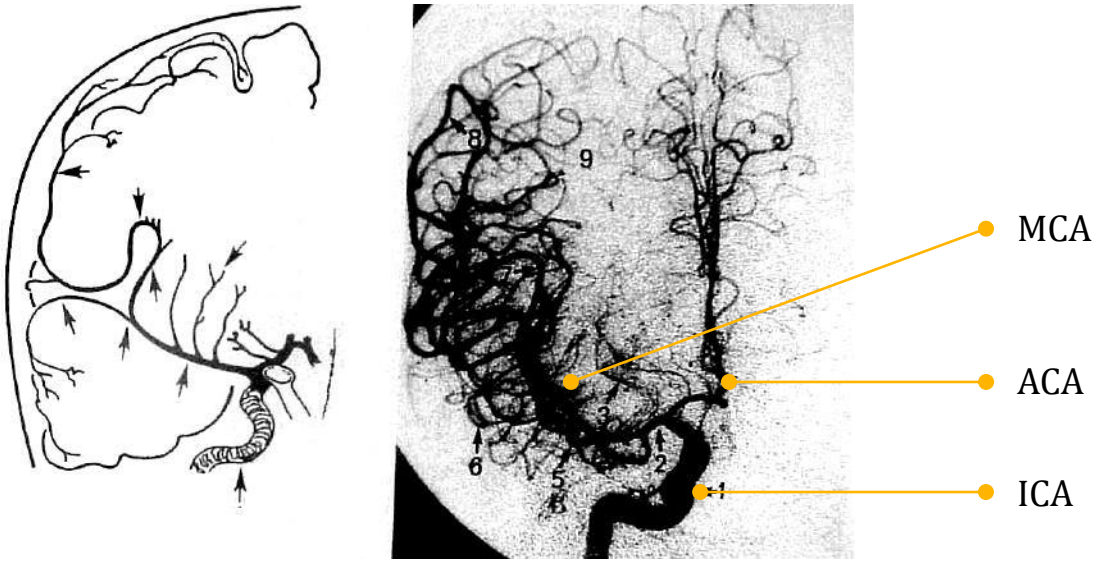


Figure 3.2. Anterior circulation (anterior-posterior view)

The ACA supplies the medial portions of the frontal and parietal lobes. The opposite side of the ACA is joined by the anterior communicating artery (AComA). The ACom artery connects bilateral anterior circulations.

- A1. This segment refers to the section from the carotid bifurcation to the ACom artery.
- A2. The segment distal to the ACom artery.

The MCA branches supply the posterior part of the frontal lobe, and the anterior, mid, and posterior parietal lobes. The MCA is the largest of the two terminal branches of the ICA. The exact course of the proximal MCA segment varies with different factors (e.g., age).

- M1. The segment approximately 1.5cm from the MCA origin.
- M2. This segment divides into two or three branches.

The anterior circulation includes:

- Internal carotid artery (ICA).
- Middle cerebral artery (MCA).
- Anterior cerebral artery (ACA).
- Anterior communicating artery (ACom artery).

Neurovasculature

Test your knowledge

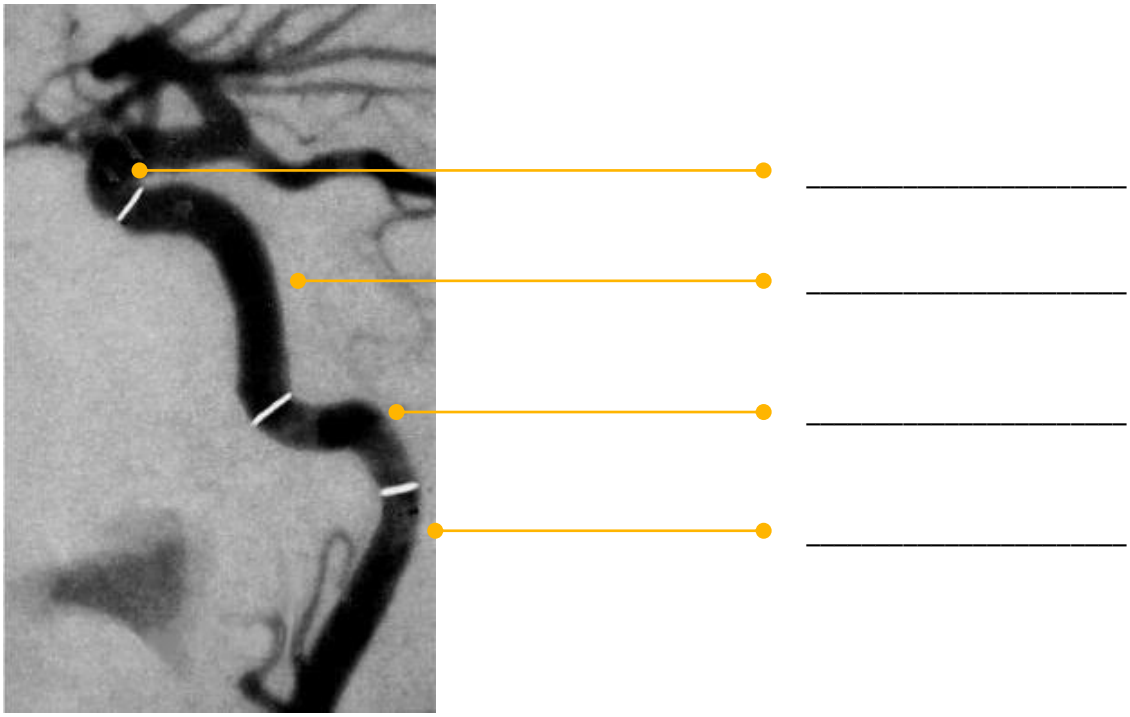


Figure 3.1. ICA segments

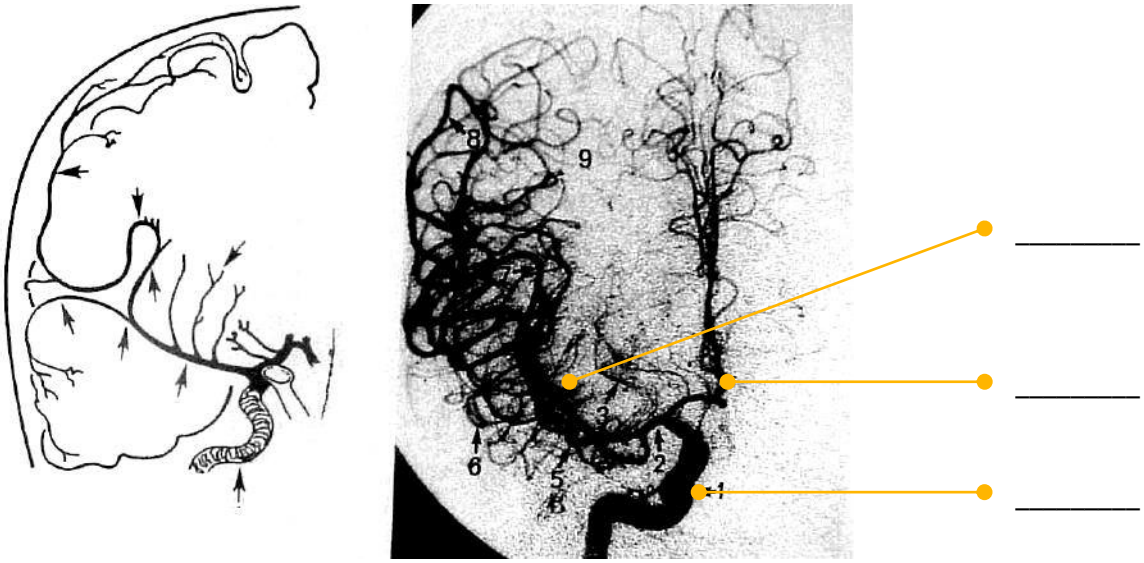


Figure 3.2. Anterior circulation (anterior-posterior view)

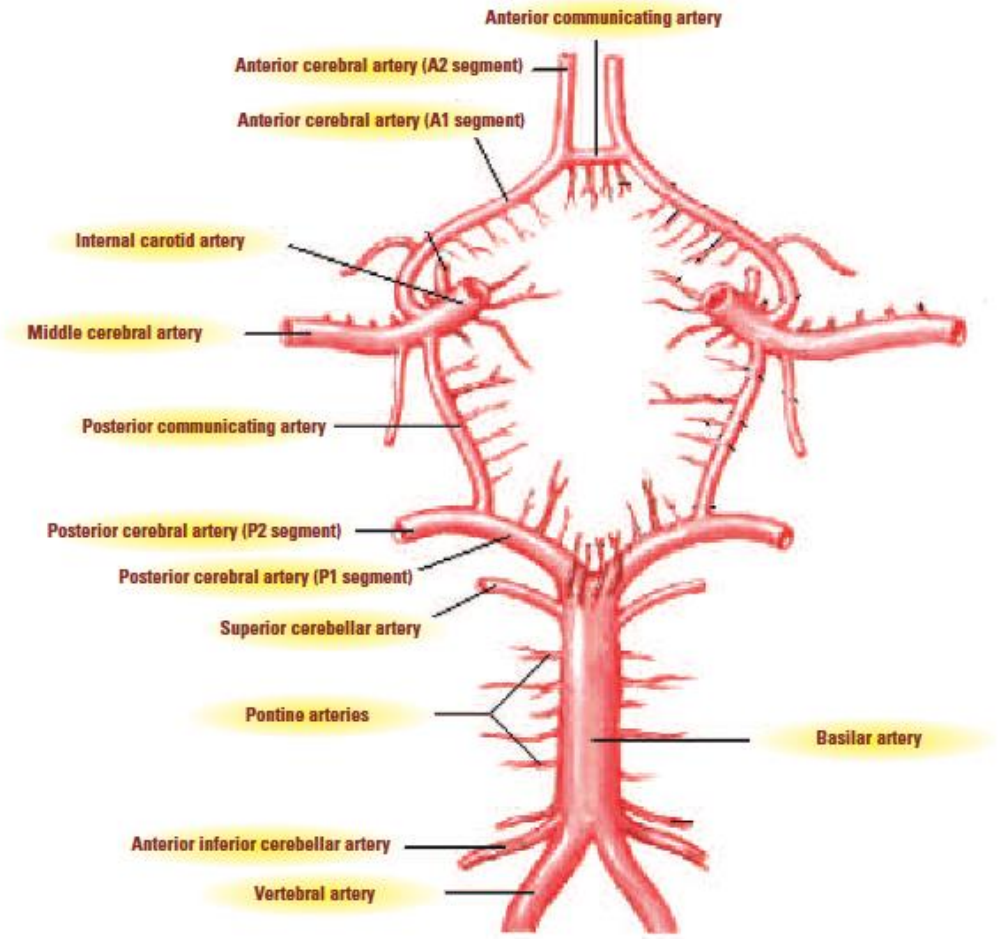


Figure 3.3. Circle of Willis

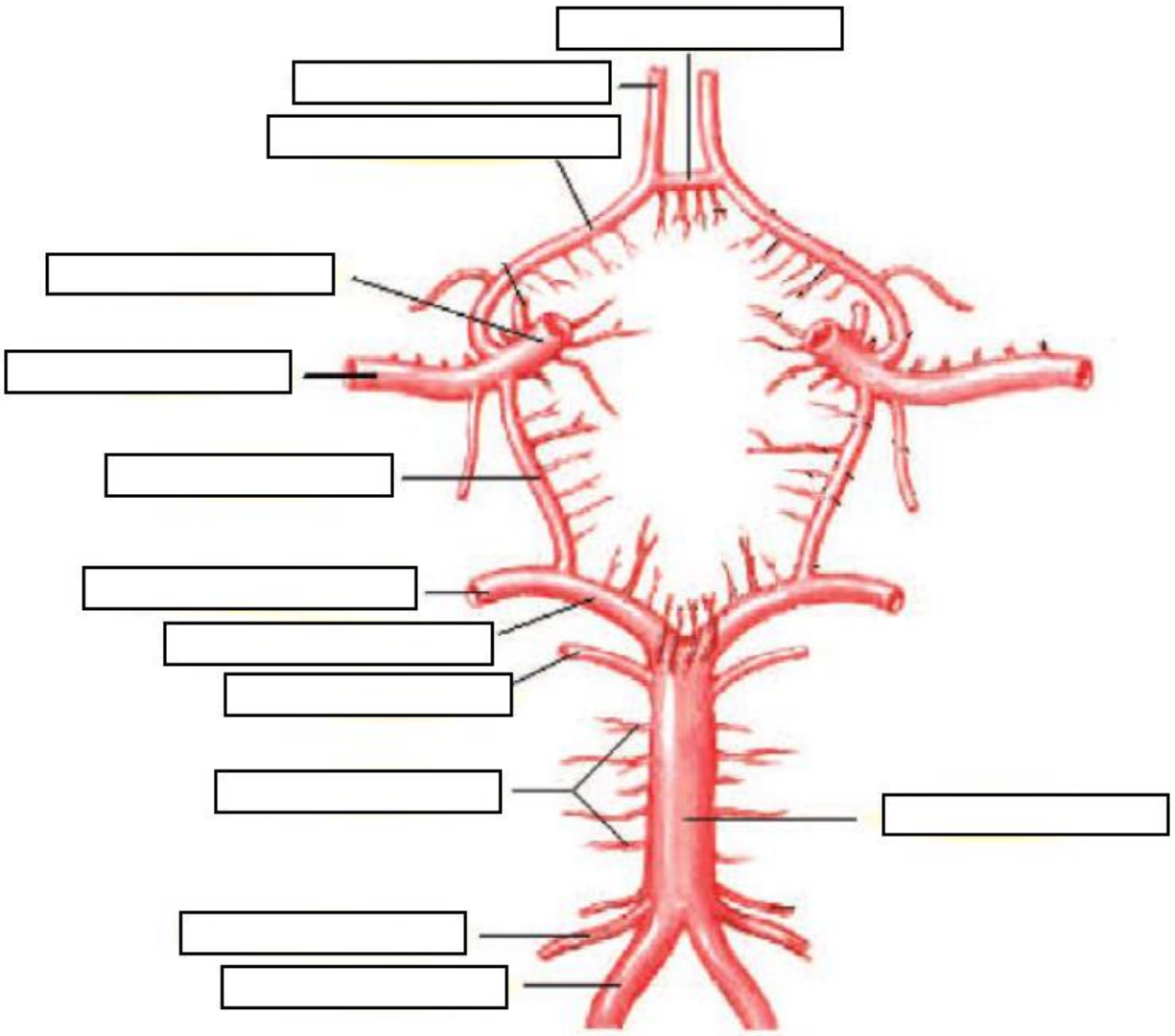
The three major arteries at the base of the skull—the two internal carotid arteries (ICAs) and the Basilar Artery (BA)—are connected to each other through an arterial network called the ***Circle of Willis.***

The Circle of Willis consists of the:

- Anterior communicating artery (ACom artery).
- Anterior cerebral artery (ACA).
- Internal carotid artery (ICA).
- Posterior communicating artery (PCom artery).
- Posterior cerebral artery (PCA).
- Basilar artery (BA).

Neurovasculature

Test your knowledge



The Circle of Willis allows blood that enters by either internal carotid (anterior circulation) or vertebral arteries (posterior circulation) to be distributed to any part of both cerebral hemispheres. It allows communication between anterior and posterior circulation.

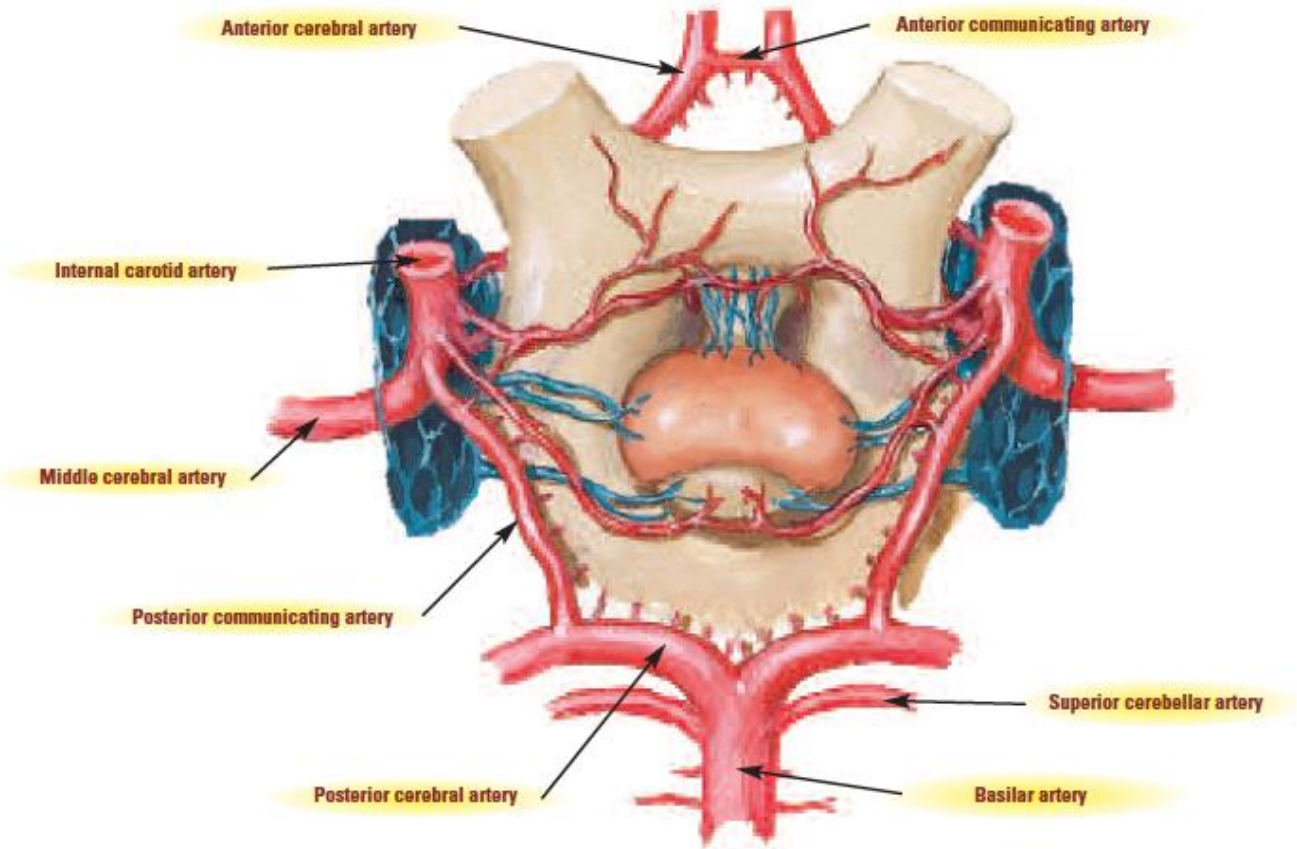
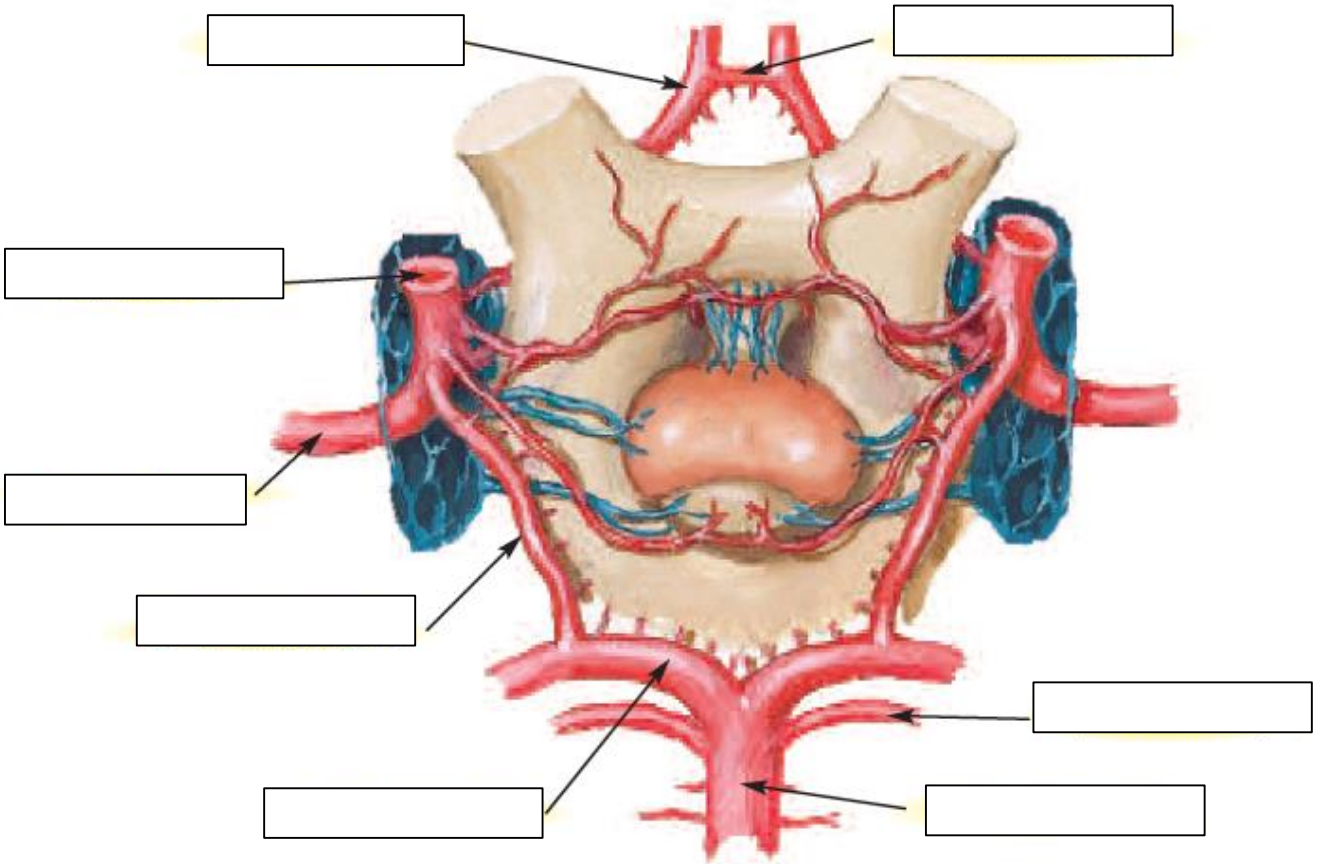


Figure 3.4. Circle of Willis

Neurovasculature

Test your knowledge



Neurovasculature
Posterior circulation

The right vertebral artery is the most proximal major branch of the right subclavian artery. Dominant or larger than the left vertebral artery in 25 percent of individuals, it supplies posterior portions of the brain and joins with the left vertebral artery to form the basilar artery.

The basilar artery, named because of its position at the base of the skull, is a single trunk formed by the junction of the two vertebral arteries. It extends from the lower to the upper border of the pons, lying in its median groove, under cover of the arachnoid. It ends by dividing into the two posterior cerebral arteries.

The pontine branches are a number of small vessels that branch off at right angles from either side of the basilar artery and supply the pons and adjacent parts of the brain.

The posterior cerebral arteries (PCAs) originate from the basilar bifurcation, just above the superior cerebellar artery origin and supply the occipital lobe, cerebellum, and posterior temporal lobes.

The three segments are:
- P1. The short segment extending laterally from the basilar bifurcation to the PCA junction with the PComA.
- P2. Courses from the PCA-PComA junction posteriorly around the midbrain.
- P3. The quadrigeminal segment courses behind the midbrain.

Superior cerebellar arteries (SCA) take off at the top of the cerebellum near the termination of the basilar and form a loop above and then behind the cerebellum to join with the PICAs.

Anterior inferior cerebellar arteries (AICAs) arise from the basilar artery just above the convergence of the vertebral arteries into the basilar artery.

Posterior inferior cerebellar arteries (PICAs) are important branches arising from the vertebral arteries before the vertebral arteries join together to form the basilar artery.

The posterior circulation includes:

- Vertebral arteries (VA).
- Basilar artery (BA).
- Posterior cerebral arteries (PCA).
- Superior cerebellar arteries (SCA).
- Anterior inferior cerebellar arteries (AICA).
- Posterior inferior cerebellar arteries (PICA).

As noted, common abbreviations for the arteries discussed are:

- Anterior cerebral artery (ACA).
- Anterior communicating artery (AComA).
- Anterior inferior cerebellar artery (AICA).
- Basilar artery (BA).
- Common carotid artery (CCA).
- External carotid artery (ECA).
- Internal carotid artery (ICA).
- Middle cerebral artery (MCA).
- Posterior cerebral artery (PCA).
- Posterior communicating artery (PComA).
- Posterior inferior cerebellar artery (PICA).
- Superior cerebellar artery (SCA).
- Vertebral artery (VA).

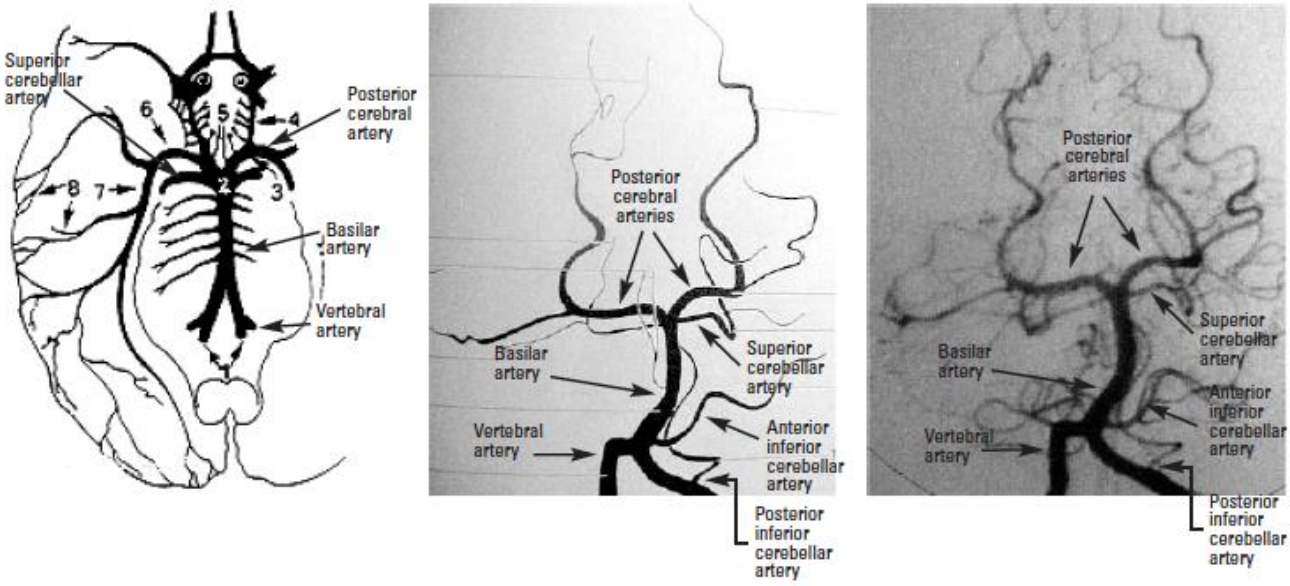


Figure 3.5. Posterior circulation (anterior-posterior view)

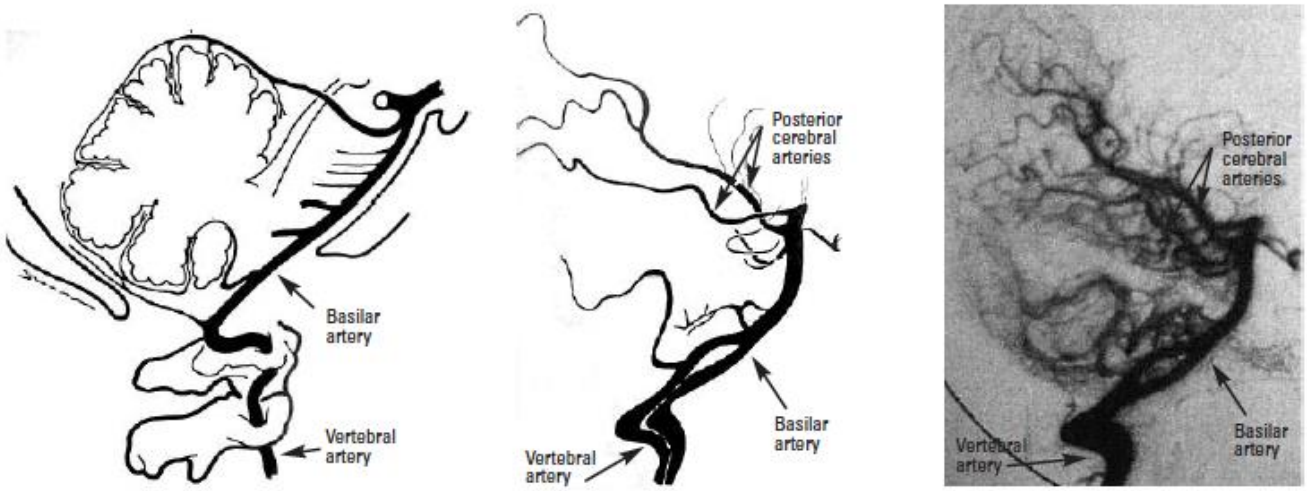


Figure 3.6. Posterior circulation (lateral view)

Neurovasculature
Meninges

Meninges cover and protect the CNS, enclose venous sinuses, control cerebrospinal fluid, and form partitions within the skull and the connective tissues. There are three layers of meninges. From the outermost layer inward, they are:

- Dura mater.
- Arachnoid mater.
- Pia mater.

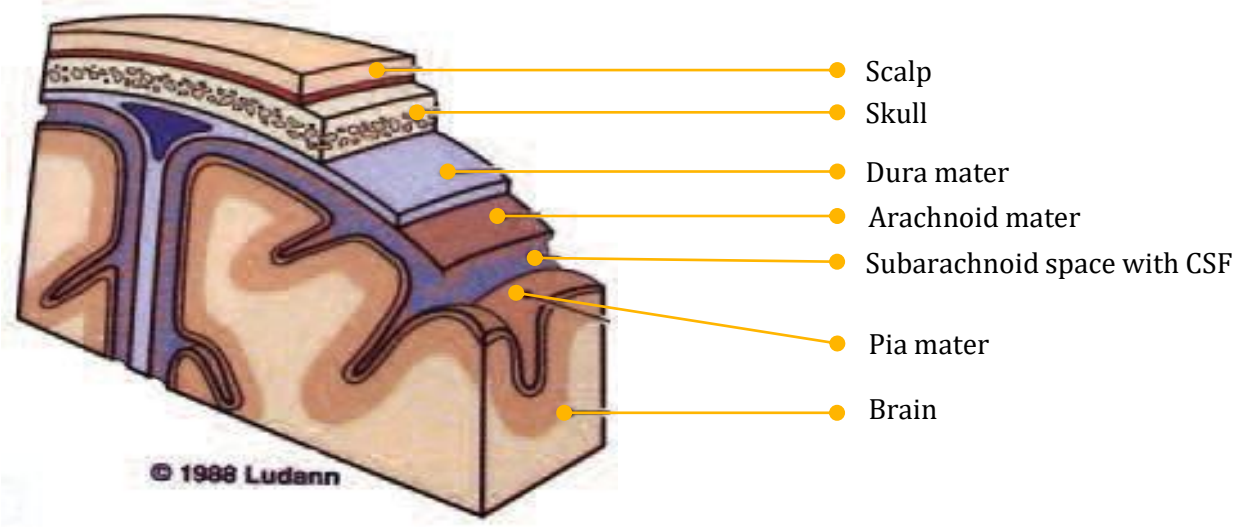


Figure 3.7. The meninges.

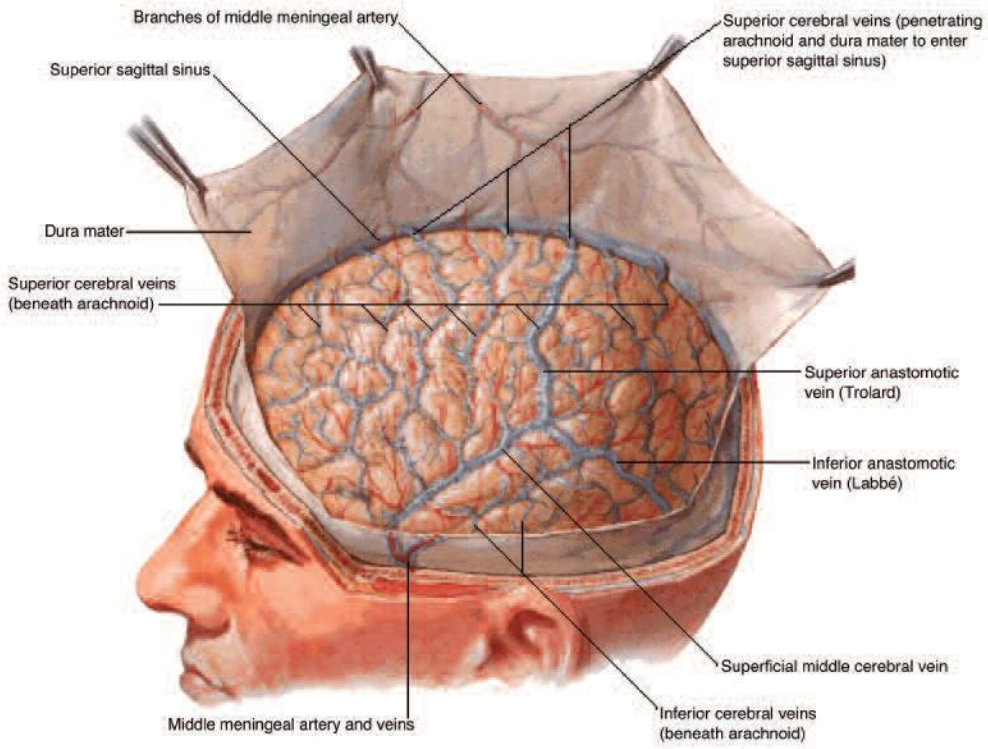


Figure 3.8. Dura mater

There are two special folds of the dura in the brain: the falx and the tentorium. The falx separates the right and left half of the brain and the tentorium separates the cerebrum (higher functioning cortex) and the cerebellum (balance center, located below the cerebrum). The ***dura mater*** itself has two layers that when split give rise to the above folds and enclose the dural venous sinuses.

The second layer of the meninges is the ***arachnoid mater***. This membrane is thin and delicate and covers the entire brain. There is a space between the dura and the arachnoid membranes that is called the ***subdural*** space. The arachnoid is made up of delicate, elastic tissue and blood vessels of different sizes.

The layer of meninges closest to the surface of the brain is called the ***pia mater***. The pia mater has many blood vessels that reach deep into the surface of the brain. The pia, which covers the entire surface of the brain, follows the folds of the brain. The major arteries supplying the brain provide the pia with its blood vessels. The space that separates the arachnoid and the pia is called the ***subarachnoid*** space. It is here where the cerebrospinal fluid flows.

Neurovasculature

Arterial layers

Arteries carry oxygenated blood from the heart to all organs and tissues of the body. Veins carry deoxygenated (or used) blood back to the lungs to be reoxygenated. The arterial system is a much higher pressure system than the venous system. To better understand disease processes of the neurovasculature, it is helpful to discuss the different layers of arteries at this point. Arteries are comprised of the following layers:

- ***Intima***. The innermost arterial layer is paper-thin and composed primarily of endothelial cells. It provides a smooth, thrombi- resistant surface and is nourished by the blood flowing through the artery. It is easily damaged by guidewires, catheters, or plaque. Atherosclerosis is a disease caused by thickening of the intima.
- ***Internal elastic lamina (IEL)***. Located between the intima and media.
- ***Media***. The middle layer of the artery, composed of smooth muscle tissue, provides strength to the artery by allowing constriction and/or dilation. Weakening of this layer usually results in an aneurysm. This layer receives blood supply by diffusion and is innervated by the sympathetic nervous system. Intracranial arteries, when compared with extracranial arteries of similar size, have a thinner media.
- ***External elastic lamina (EEL)***. Located between the media and adventitia in most arteries. The EEL is not present in intracranial arteries.
- ***Adventitia***. The outer layer of the artery, composed primarily of connective tissue and elastic fibers, provides elastic and structural strength to the artery.

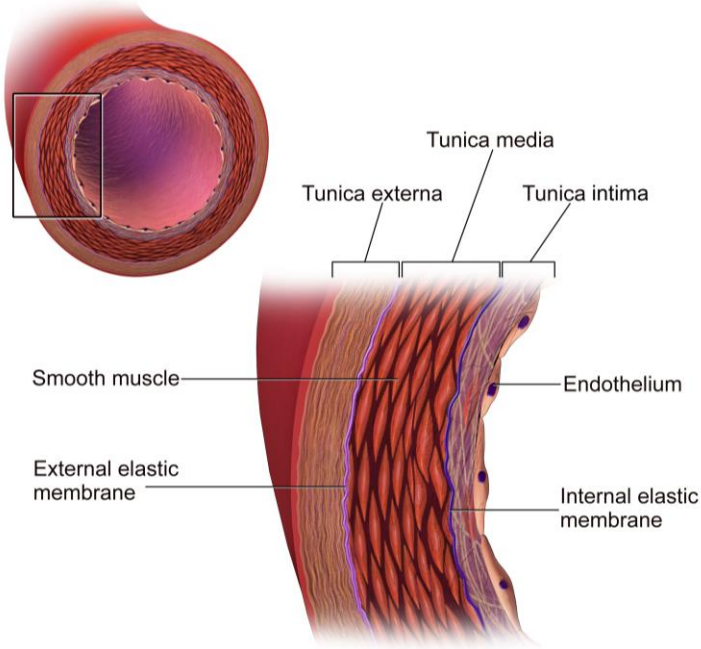


Figure 3.9. Arterial Layers

Neurovasculature

Venous drainage

There are three dural sinuses in the brain that function as a venous return route or collection space for blood to ultimately return from the arterial system to the heart.

They are:

- Sagittal sinus (superior and inferior).
- Transverse sinus.
- Sigmoid sinus.

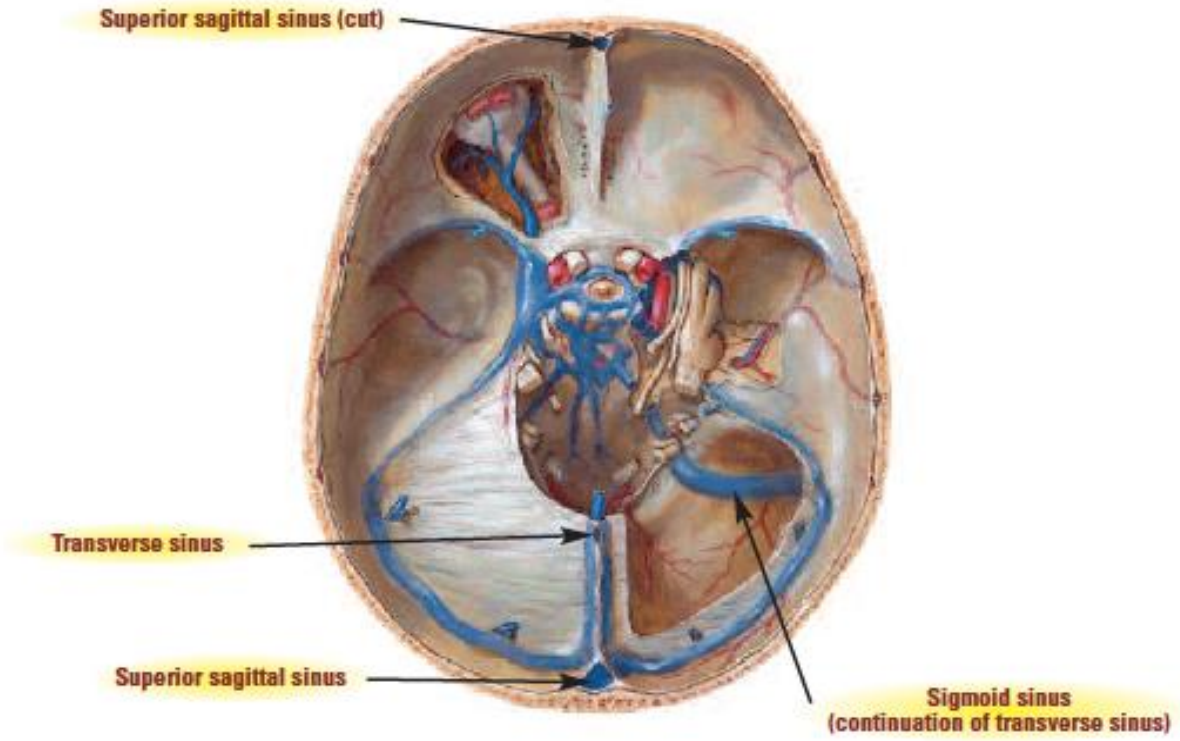


Figure 4.0. Dural sinuses

Neurovasculature

This table shows the abbreviation, full name, and average diameter of the basic neurovascular arteries.

ABBR	Artery name	Mean diameter
Anterior Circulation		
ICA	Internal Carotid Artery	5.0mm
MCA	Middle Cerebral Artery	2.5mm
ACA	Anterior Cerebral Artery	2.0mm
ACom	Anterior Communicating Artery	1.5mm
PComA	Posterior Communicating Artery	1.0mm
Posterior Circulation		
VA	Vertebral Artery	2.5mm
BA	Basilar Artery	3.5mm
PCA	Posterior Cerebral Artery	2.0mm
SCA	Superior Cerebellar Artery	1.0mm
AICA	Anterior Inferior Cerebellar Artery	1.0mm
PICA	Posterior Inferior Cerebellar Artery	1.5mm
PComA	Posterior Communicating Artery	1.0mm

The table is divided into anterior and posterior circulation with the posterior communicating artery standing out as it arises from both circulations. Artery diameters are approximate values rounded to the nearest .5 mm for ease of memorization.

Wollschlaeger, P.B., et al., "The Arteries of the Basal Ganglia, The Sustaining Diagnostic Pattern of the Perforant Arteries (A Comparative Study of Pre- and Post-Mortem Cerebral Angiography)," VIII Symposium Neuroradiologicum, Paris, 1967.

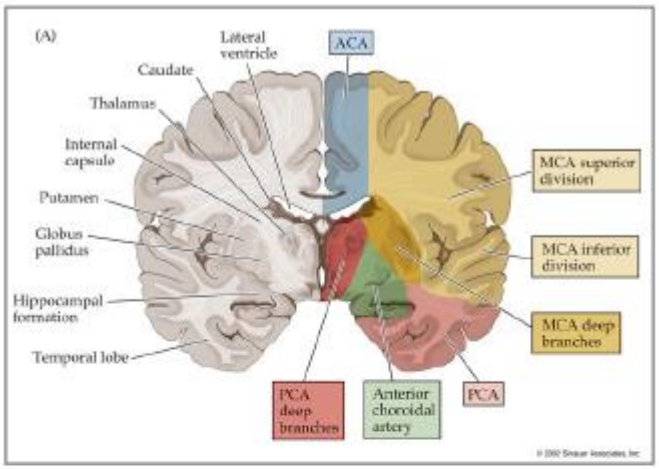
Diamond, M.C., Scheibel, A.B., Elson, L.M., *The Human Brain Coloring Book* (New York: Harper Collins, 1986) 1.1–1.6; 9.1–9.12.

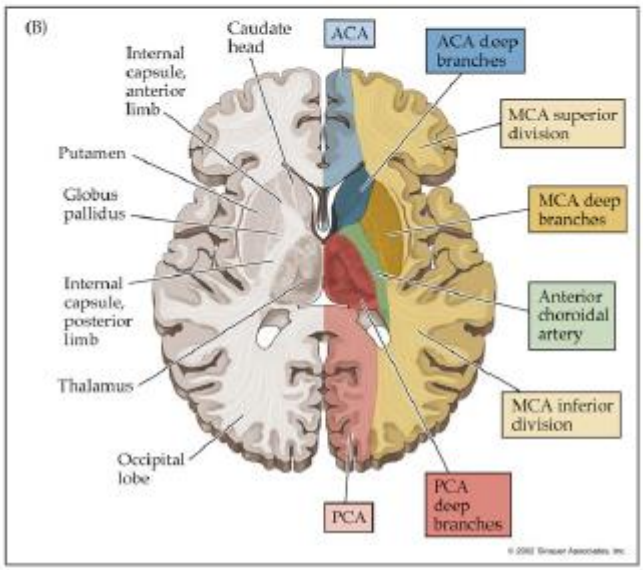
Cerebrovascular territories & ischemic stroke symptoms

Clinical signs and symptoms
MCA occlusion

Left MCA - typically dominant hemisphere (~90%)
- Difficulty with language expression and reception (aphasia)
- Right body (face/arm) motor and sensation
- Right-sided neglect and vision loss (homonymous hemianopia)
- Eyes deviate to left – driven by right frontal eye fields

Right MCA
- Constructional tasks – ie getting dressed (apraxia)
- Left body (Face/arm) motor and sensation
- Left-sided neglect and vision loss (homonymous hemianopia)
- Eyes deviate to right – driven by left frontal eye fields





~60% of ischemic strokes occur in the MCA

50% (of all strokes) in M1

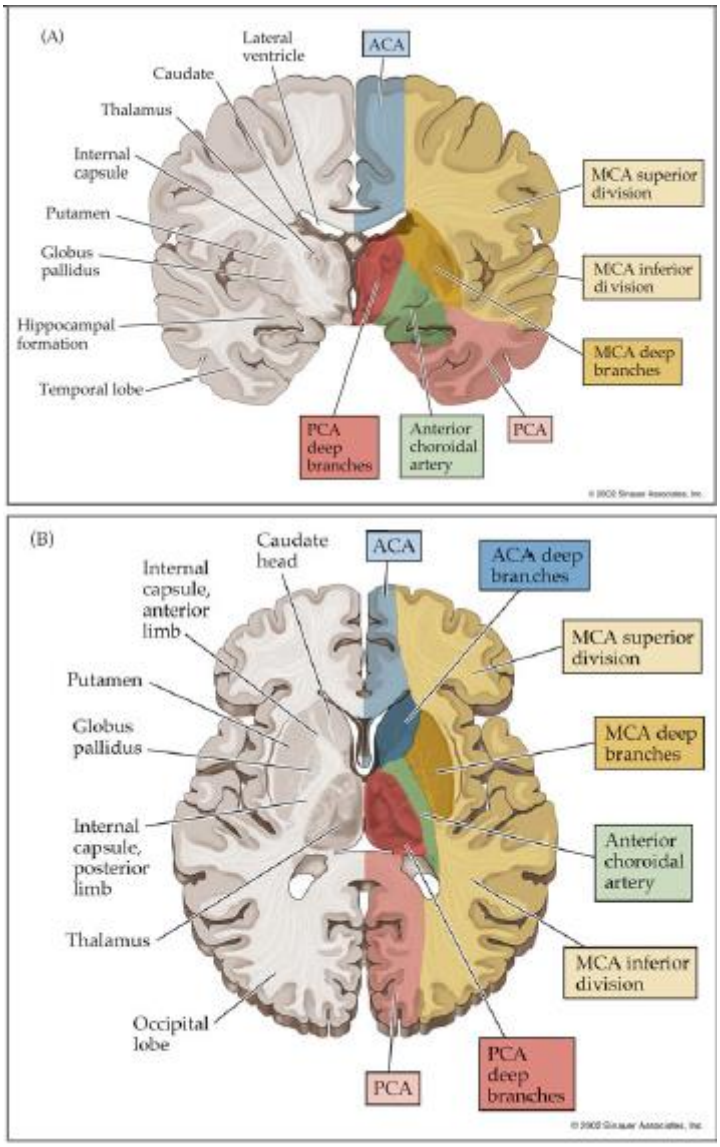
10% (of all strokes) in M2

Clinical signs and symptoms

ACA occlusion

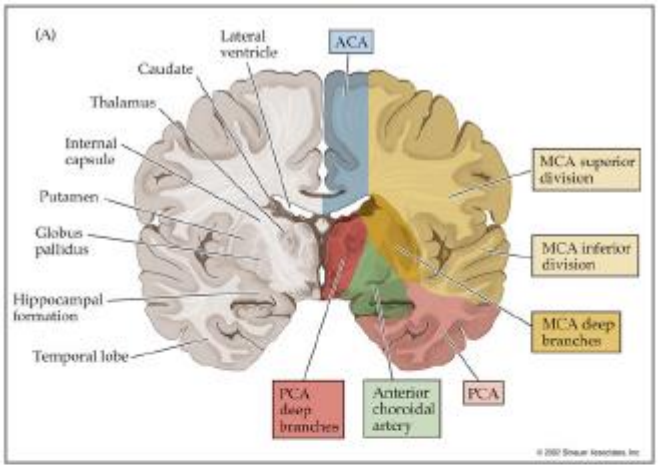
Left ACA
- Loss of motor & sensation in right leg
- Behavior disturbances: anger, hostility

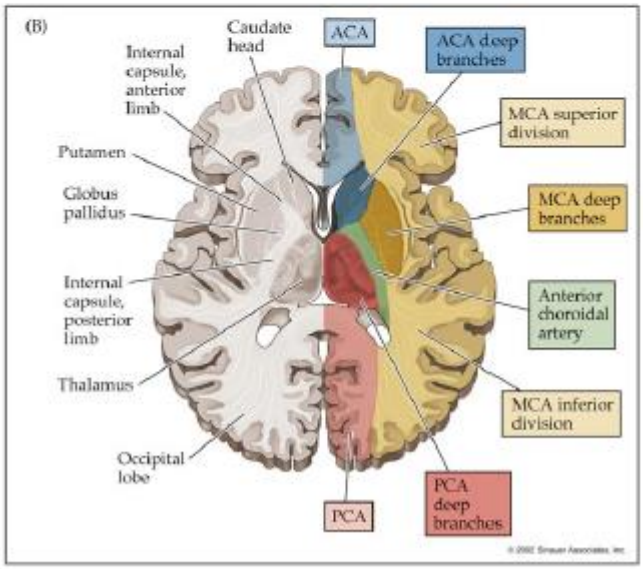
Right ACA
- Loss of motor & sensation in left leg
- Behavior disturbances: anxiety, depression



Clinical signs and symptoms
ICA occlusion

- Combined MCA and ACA presentations
- Occluded ophthalmic artery causing monocular blindness
- Dissection a common etiology – neck pain





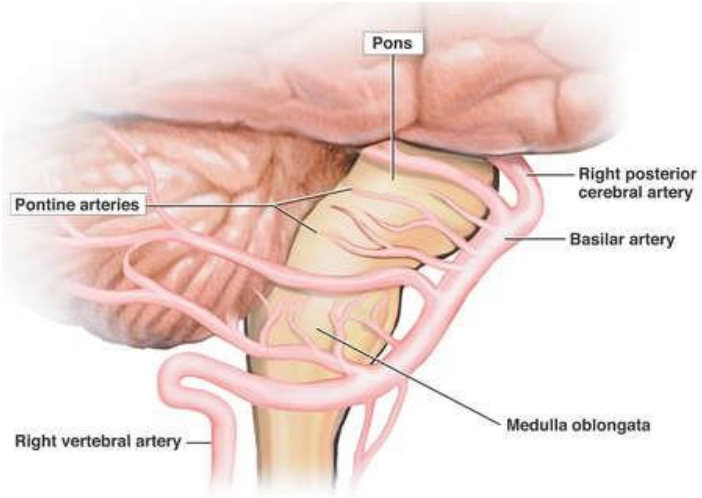
30-35% of ischemic strokes occur in the ICA

Clinical signs and symptoms
Posterior circulation

Asymptomatic to comatose presentation
- Based on artery involved

The 5 Ds:
- Dizziness
- Diplopia
- Dysarthria
- Dysphagia
- Dystaxia

Clinical hallmark: crossed findings
- Cranial nerve deficits – Ipsilateral
- Motor/sensory deficits – Contralateral



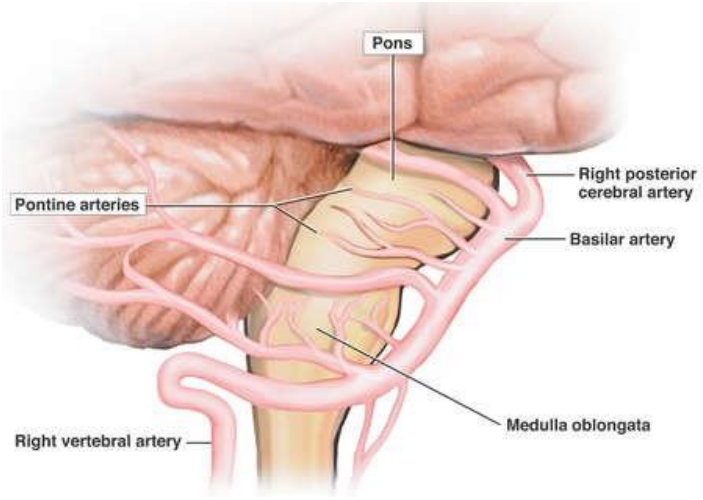
Clinical signs and symptoms
Vertebral occlusion

Often caused by trauma – leading to dissection

Produces PICA occlusion

Occlusion by vertebral artery or PICA can lead to lateral medullary syndrome

- Patients present with crossed findings

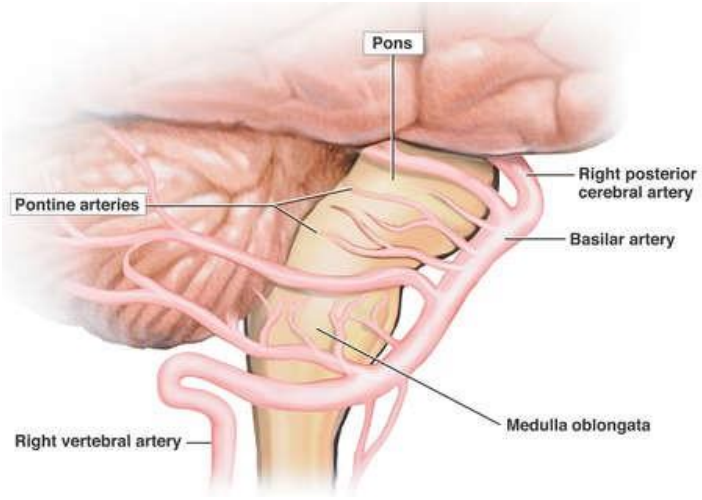


8-10% of ischemic strokes occur in the vertebrobasilar vessels

Clinical signs and symptoms
Basilar occlusion

Affects brainstem (vital organs/systems)

- Brainstem tolerates an ischemic condition better, slower to infarct
- Very high mortality rate, usually due to respiratory failure
- Can result in "locked-in" syndrome, patient can think and see, but cannot respond
- **Routinely treated much later (up to 12 hours with tPA)**



Lesions to one side of the brainstem will cause crossed body findings:

- Ipsilateral cranial nerve symptoms
- Contralateral sensory / motor of body via ascending and descending nerve tracts

8-10% of ischemic strokes occur in the vertebrobasilar vessels

Clinical signs and symptoms

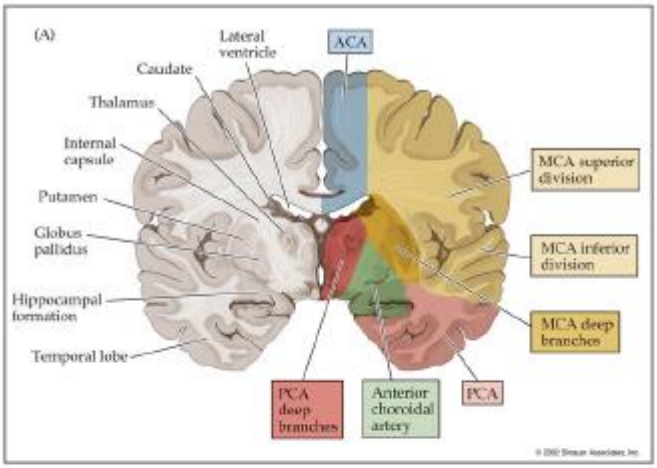
PCA occlusion

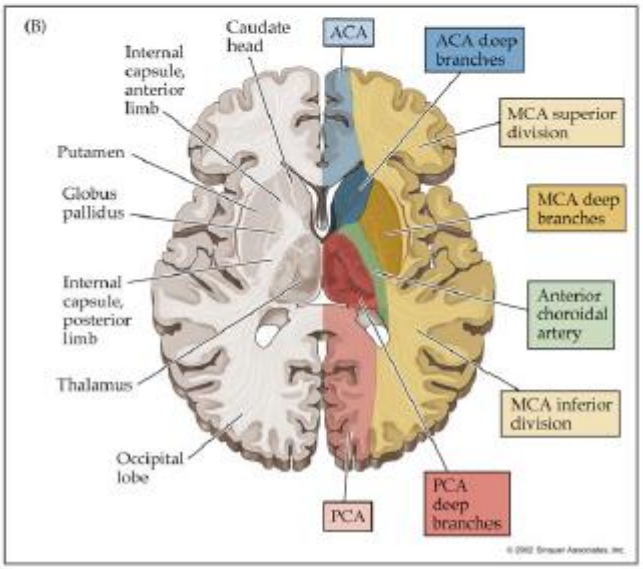
Contralateral homonymous hemianopsia

Thalamic lesions result in contralateral face and limb sensory loss

Temporal and/or parietal-occipital lobes

- Neuropsychologic deterioration of memory, language, or visual-cognitive dysfunction
- Cortical blindness – denial of blindness (Anton"s Syndrome) – bilateral medial occipital
- Alexia without agraphia – lateral occipital – dominant hemisphere

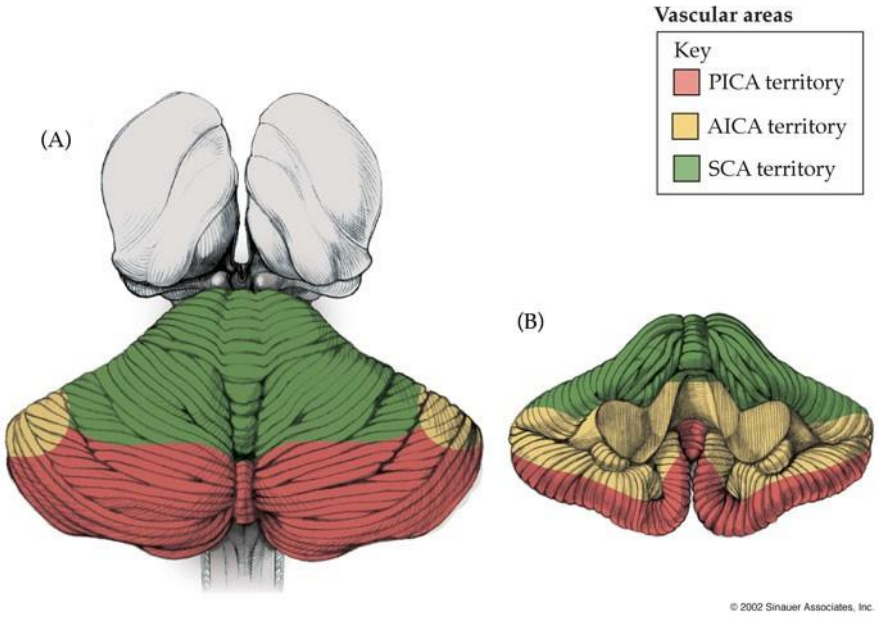




Clinical signs and symptoms

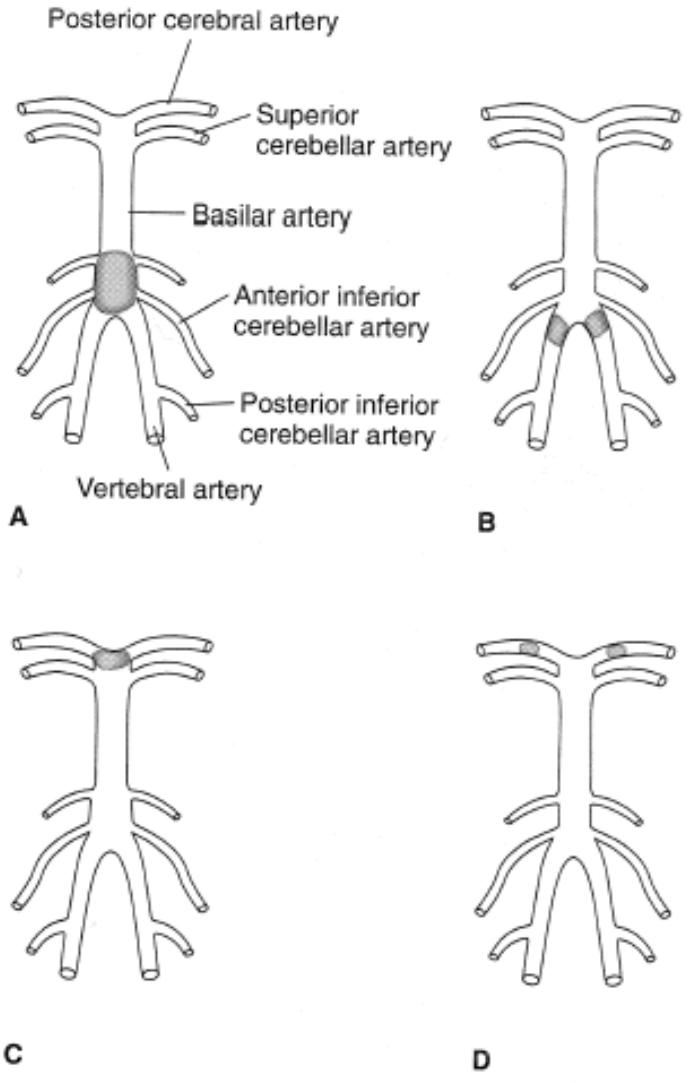
Cerebellar stroke

- Occlusions of SCA, AICA, and/or PICA
- Cause ipsilateral ataxia, trouble with balance
- May cause compression – an emergent situation



Sites of thrombotic and embolic
Vertebrobasilar occlusions

Top of basilar vs. mid-basilar
- ~50/50 split
- Top of basilar is usually embolic
- Mid-basilar is usually caused by atherothrombosis



A. Thrombotic occlusion of basilar artery
B. Thrombotic occlusion of both vertebral arteries
C. Embolic occlusion at the apex of the basilar artery
D. Embolic occlusion of both posterior cerebral arteries

Clinical signs and symptoms

Ischemic stroke symptoms summary

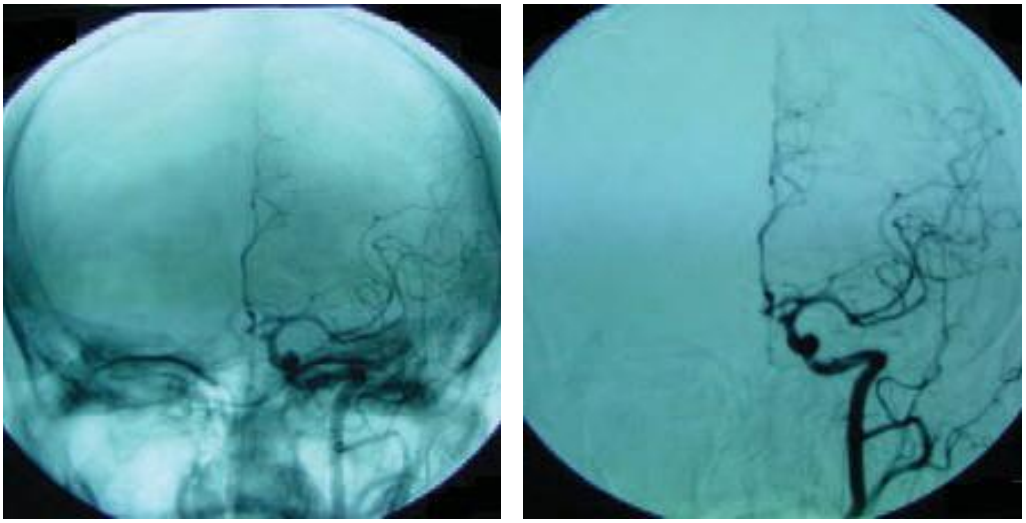
Artery	AIS Symptoms
Left Middle Cerebral Artery	Difficulty with **language expression and reception** (aphasia) Right body (face/arm) motor and sensation Right-sided neglect and vision loss (homonymous hemianopia) Eyes deviate to left – driven by right frontal eye fields
Right Middle Cerebral Artery	Constructional tasks – ie getting dressed (apraxia) Left body (face/arm) motor and sensation Left-sided neglect and vision loss (homonymous hemianopia) Eyes deviate to right – driven by left frontal eye fields
Anterior Cerebral Artery	Contralateral motor, sensory (leg), behavior disturbances (left: anger; right: depression)
Internal Carotid Artery	Combined MCA/ACA symptoms; possible monocular blindness
Posterior Cerebral Artery	Contralateral neglect and vision loss, face and limb sensory loss, memory (dominant side only), reading
Basilar Artery	Nausea, vomiting, headache, vision, motor, sensory loss, difficulty swallowing, consciousness
Vertebral Artery	Dizziness, vertigo, vision, difficulty swallowing, balance, lateral medullary syndrome

Image interpretation

NP001825 v2.0

Angiographic interpretation
Imaging

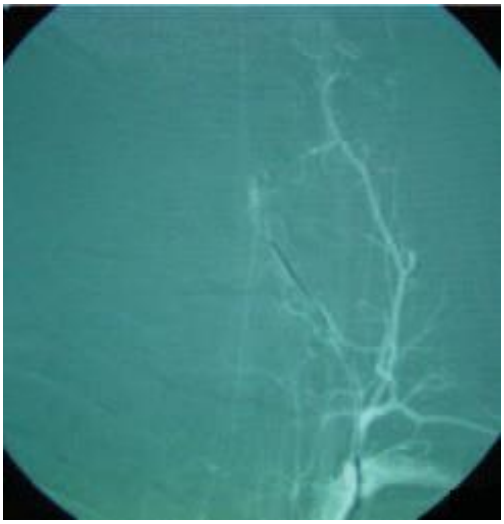
Angiography in general is the study of blood vessels. ***Fluoroscopy*** is the visual observation of the forms and motion of blood vessels using X-ray shadows projected on a fluorescent screen. This is the method of diagnostic imaging that you will see most commonly when working with physicians in the angiography suite. It involves injection of contrast into the blood vessels of the brain. The contrast renders the blood vessels radiopaque and allows them to be visible on X-ray. Information gained from these pictures assists the physician in diagnosing the disease and determining appropriate treatment options. In this section, we will discuss how these films are interpreted at a very basic level.



Photos of images taken by a BSC representative.

Figure 1.0. Native vs. digital subtraction angiography.

Digitally subtracted angiography stores images electronically and uses the computer to subtract images such as bone in real time, revealing only the vessels filled with contrast media. This enables the physician to obtain a clearer view of the vessels.



Photos of image taken by a BSC representative.

Figure 1.1. A “roadmap” image.

A ***roadmap*** is obtained by contrast injection and storage of the resulting images. A live fluoroscopic image will be superimposed on this stored film later to provide a path or “roadmap” for navigating the vasculature.

There are three projections, or angles, used in viewing fluoroscopic images. The three most common are:

- Anterior-posterior (AP or PA).
- Lateral (LAT).
- Oblique.

Figure 1.2. Anatomy planes: anterior-posterior and lateral.

AP is taken from front to back or back to front. Lateral is taken from the side. Oblique is taken in between AP and lateral.

All of these projections may be taken from the right or left side of the patient and will be indicated “R” or “L.”

If the left carotid artery is injected, the vessels in the left hemisphere of the anterior circulation will fill and be visible, and vice versa.

Regardless of which vertebral artery (R or L) is injected, the contrast will flow into the basilar artery, which will fill the entire posterior circulation.

The anterior and posterior circulations of the brain are very distinguishable on fluoroscopy.

The following pages, taken from the *Atlas of Radiologic Anatomy* (Lothar Wicke, Third Edition, Urban & Schwarzenberg, Baltimore, MD, 1982), superbly illustrate AP and lateral projections of both the anterior and posterior circulations. Please focus only on the highlighted vessels.

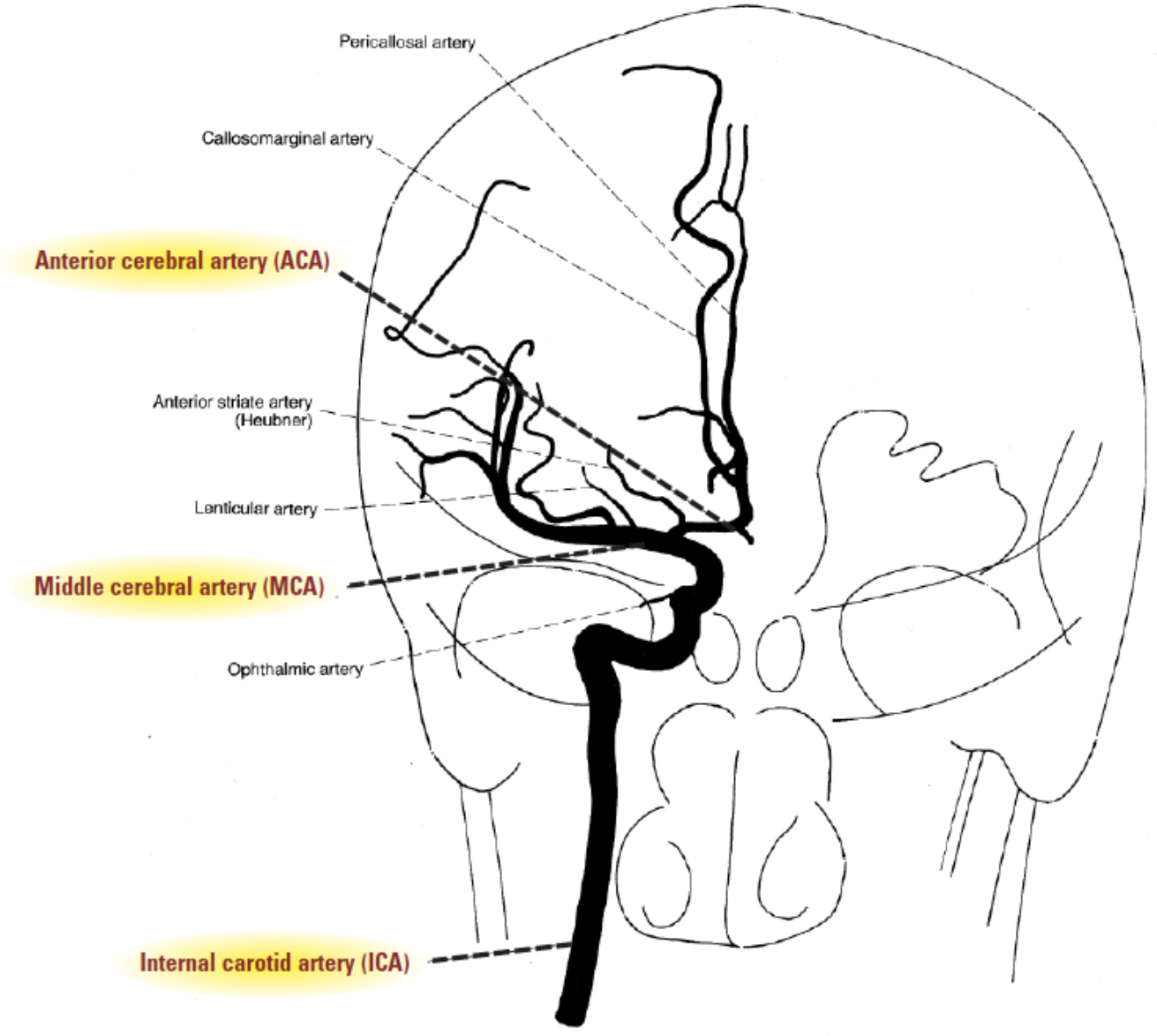


Figure 1.3. Anterior circulation, anterior/posterior (AP) projection.

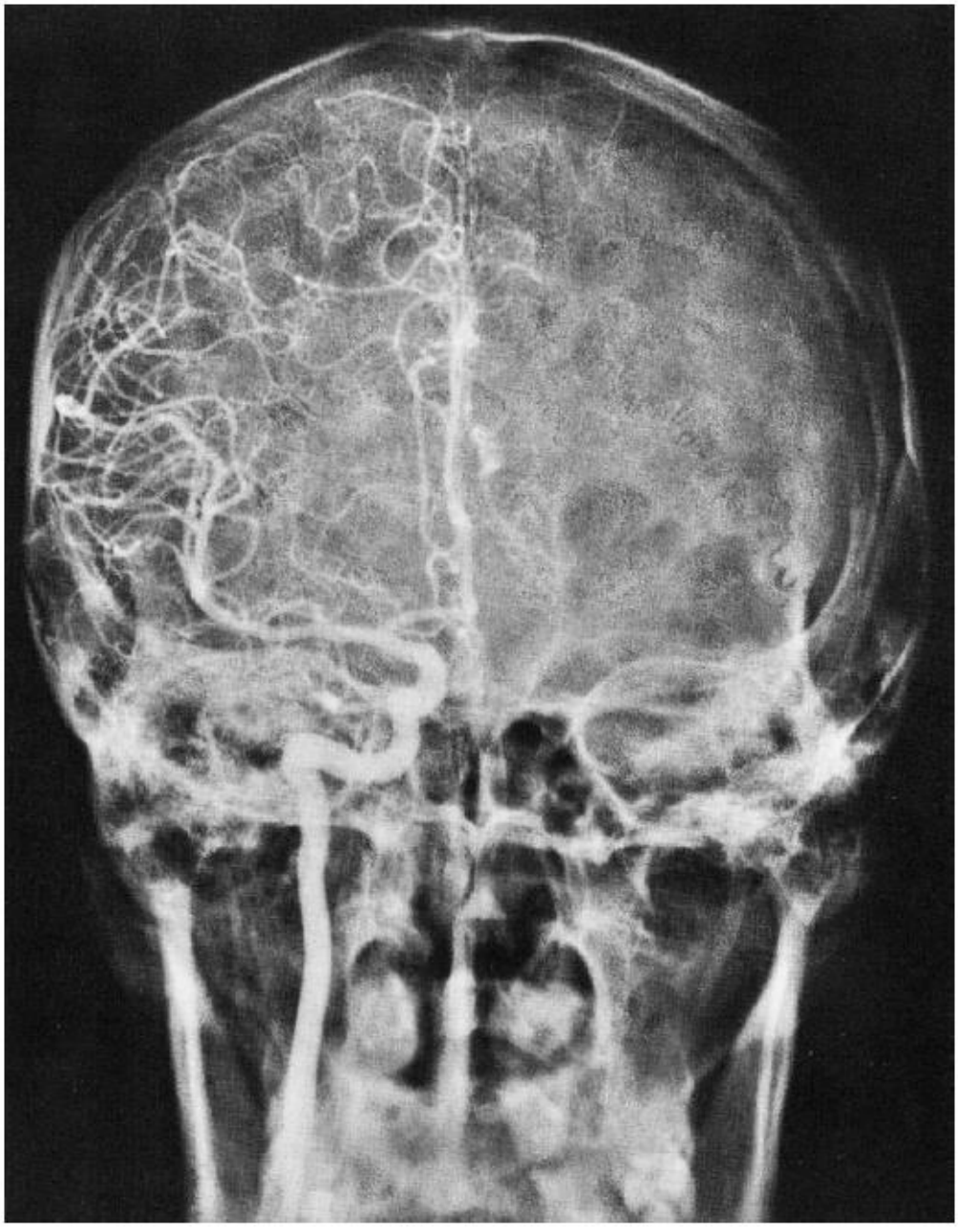


Figure 1.4. Anterior circulation, anterior/posterior (AP) projection.

Identify the ACA, MCA, and ICA on this angiographic image.

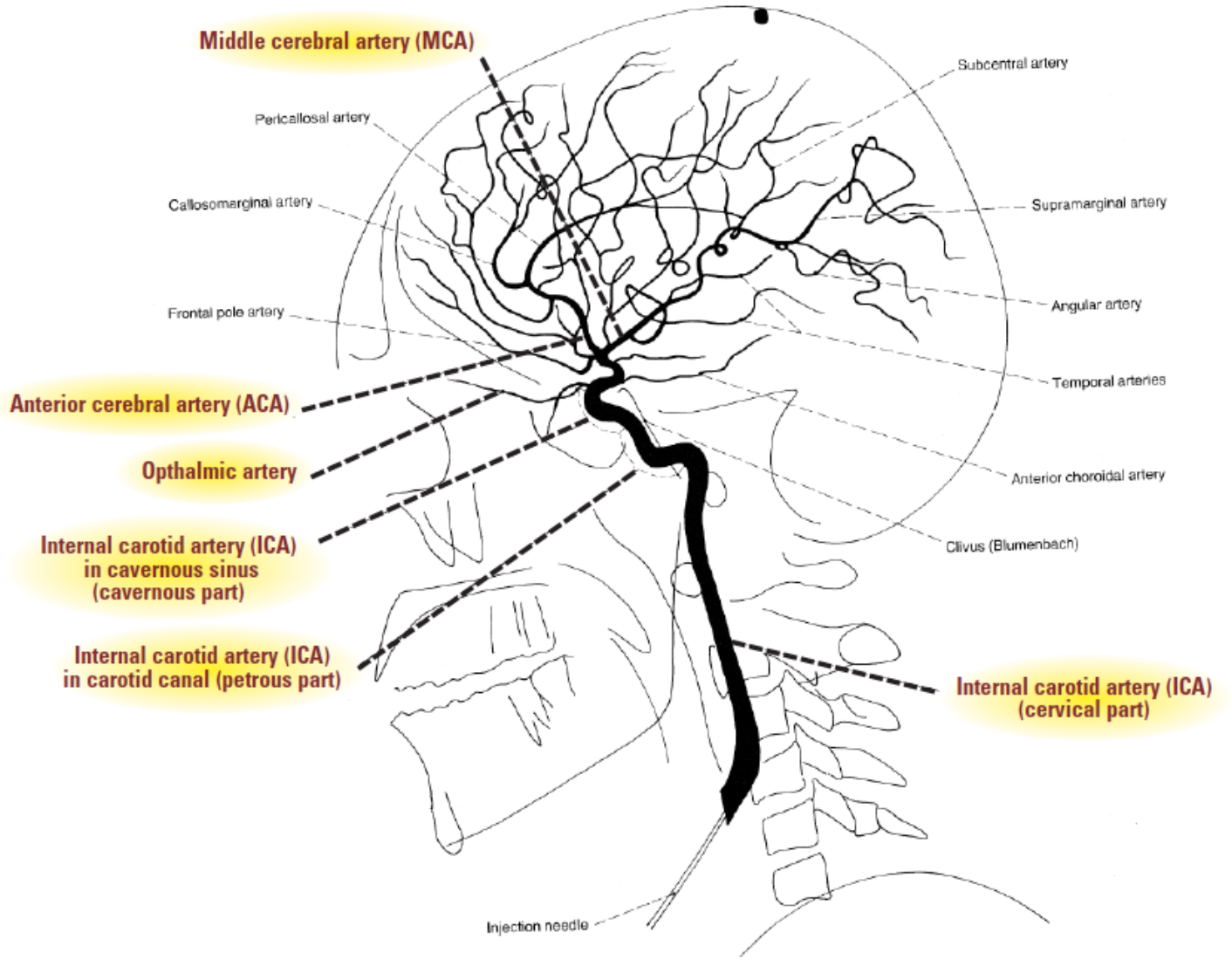


Figure 1.4. Anterior circulation, lateral projection.

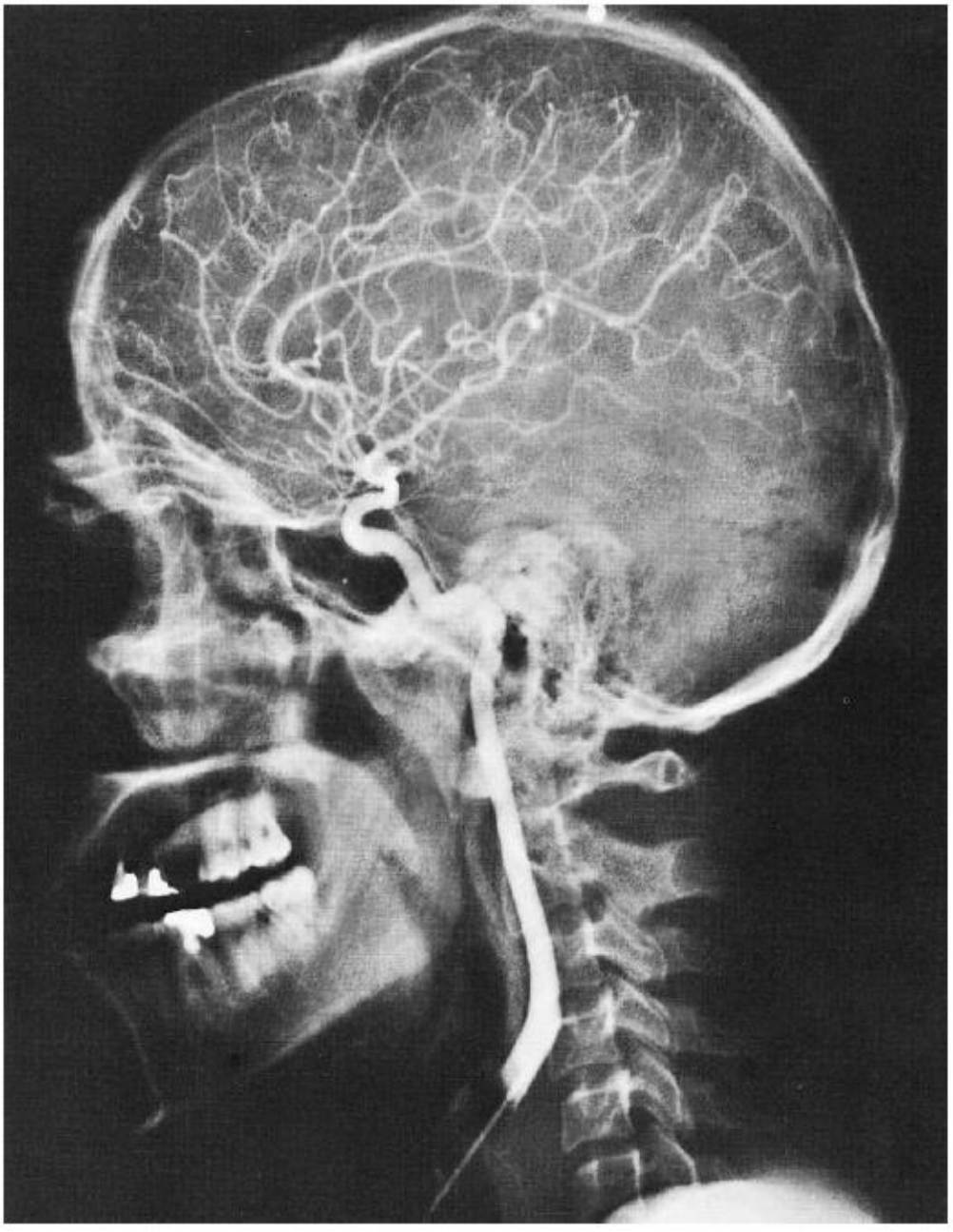


Figure 1.5. Anterior circulation, lateral projection.

Identify the ACA, MCA, ICA (cavernous, petrous, and cervical) on this angiographic image.

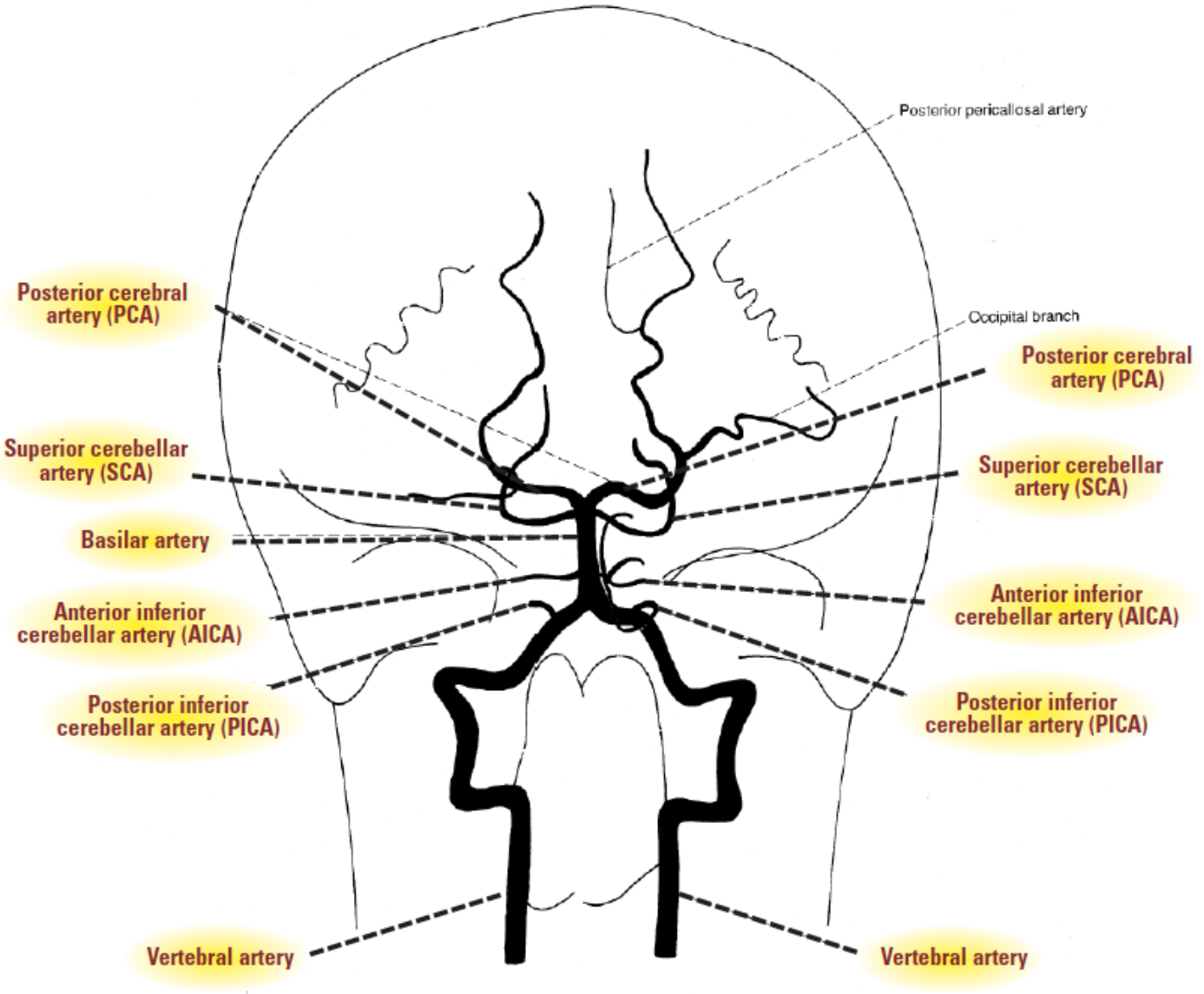


Figure 1.6. Posterior circulation, anterior/posterior (AP) projection.

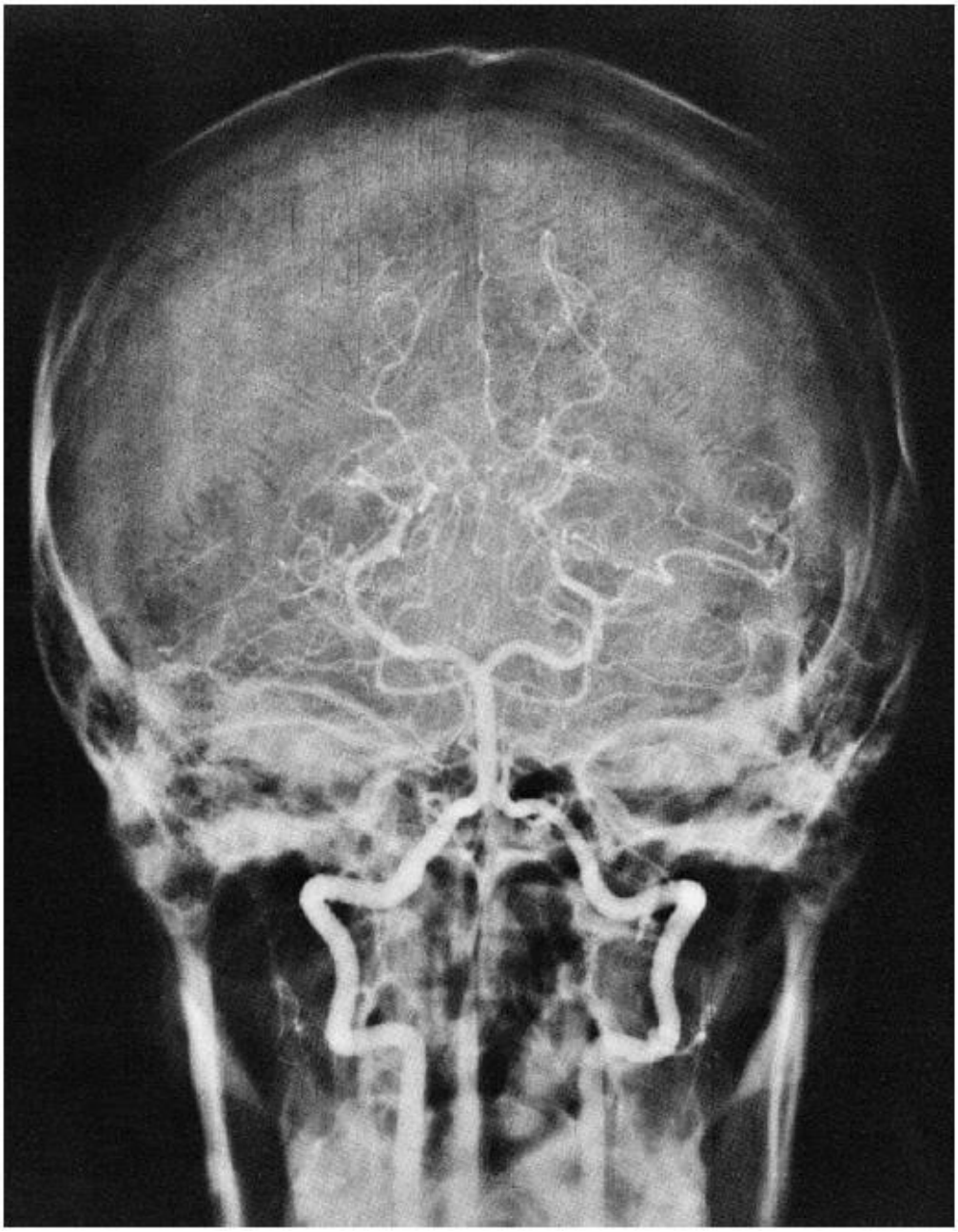


Figure 1.7. Posterior circulation, anterior/posterior (AP) projection.

Identify the vertebral arteries, basilar artery, PCAs, SCAs, AICAs, and PICAs on this angiographic image.

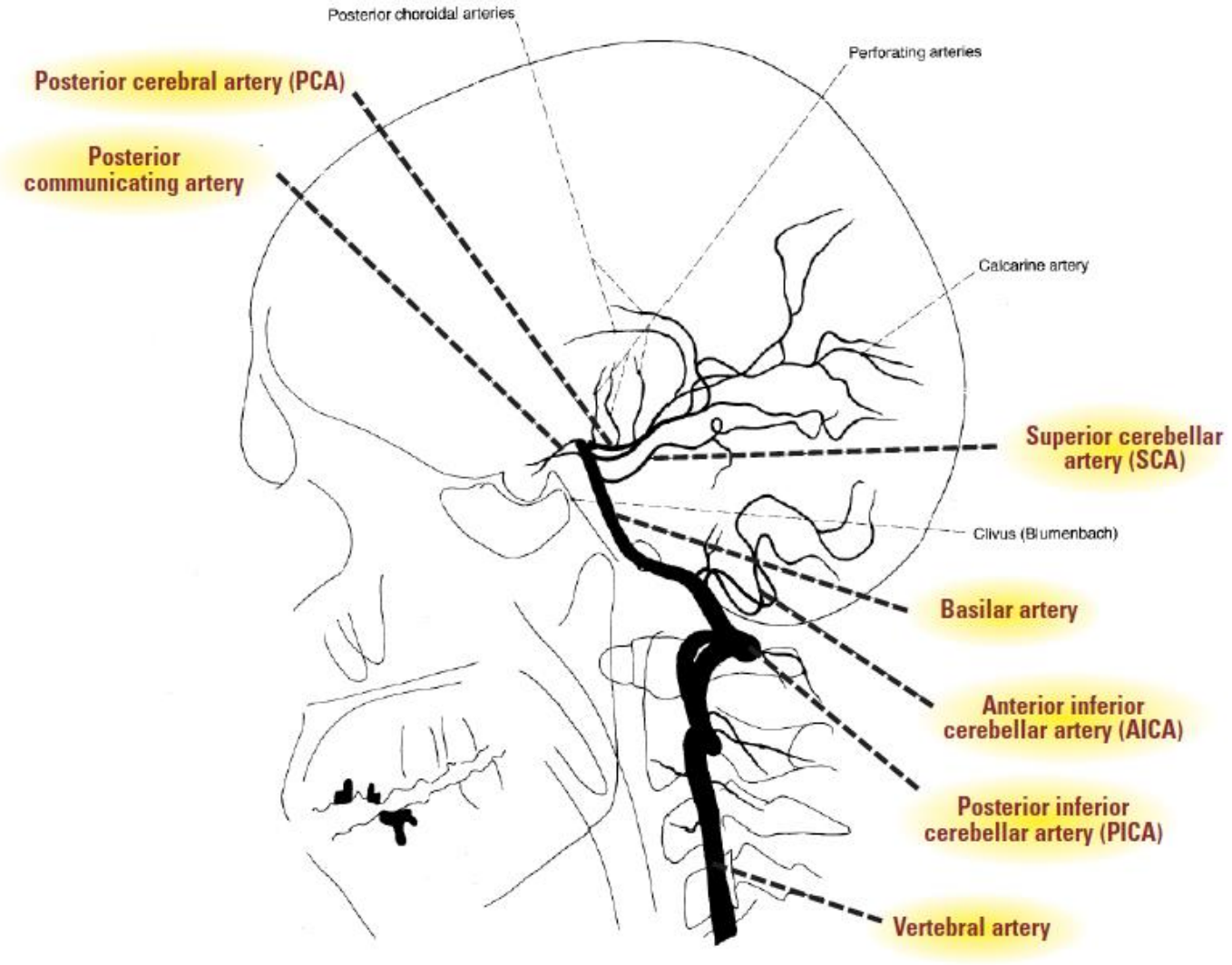


Figure 1.8. Posterior circulation, lateral projection.

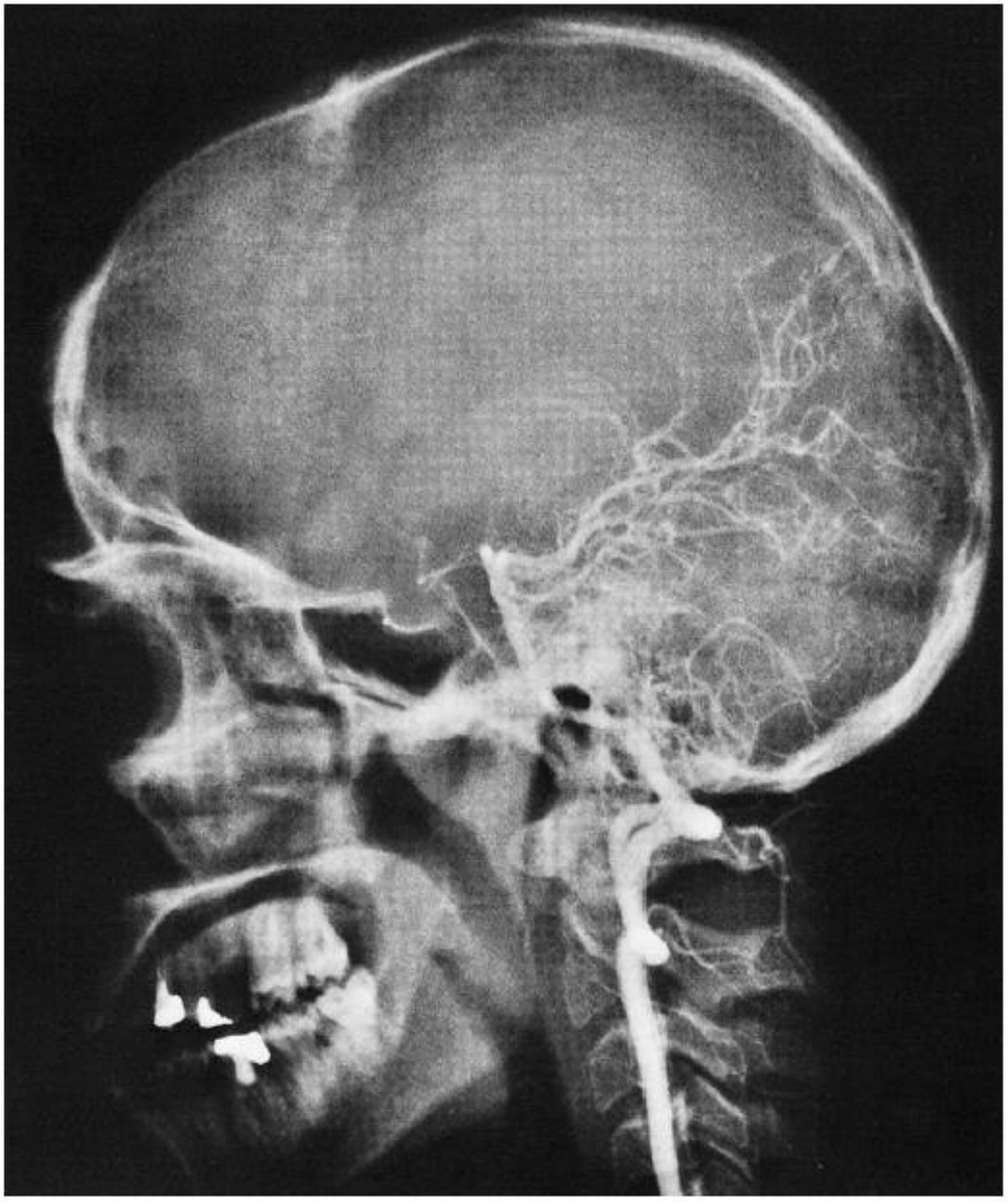


Figure 1.9. Posterior circulation, lateral projection.

Identify the vertebral artery, basilar artery, PCA, and SCA on this angiographic image.

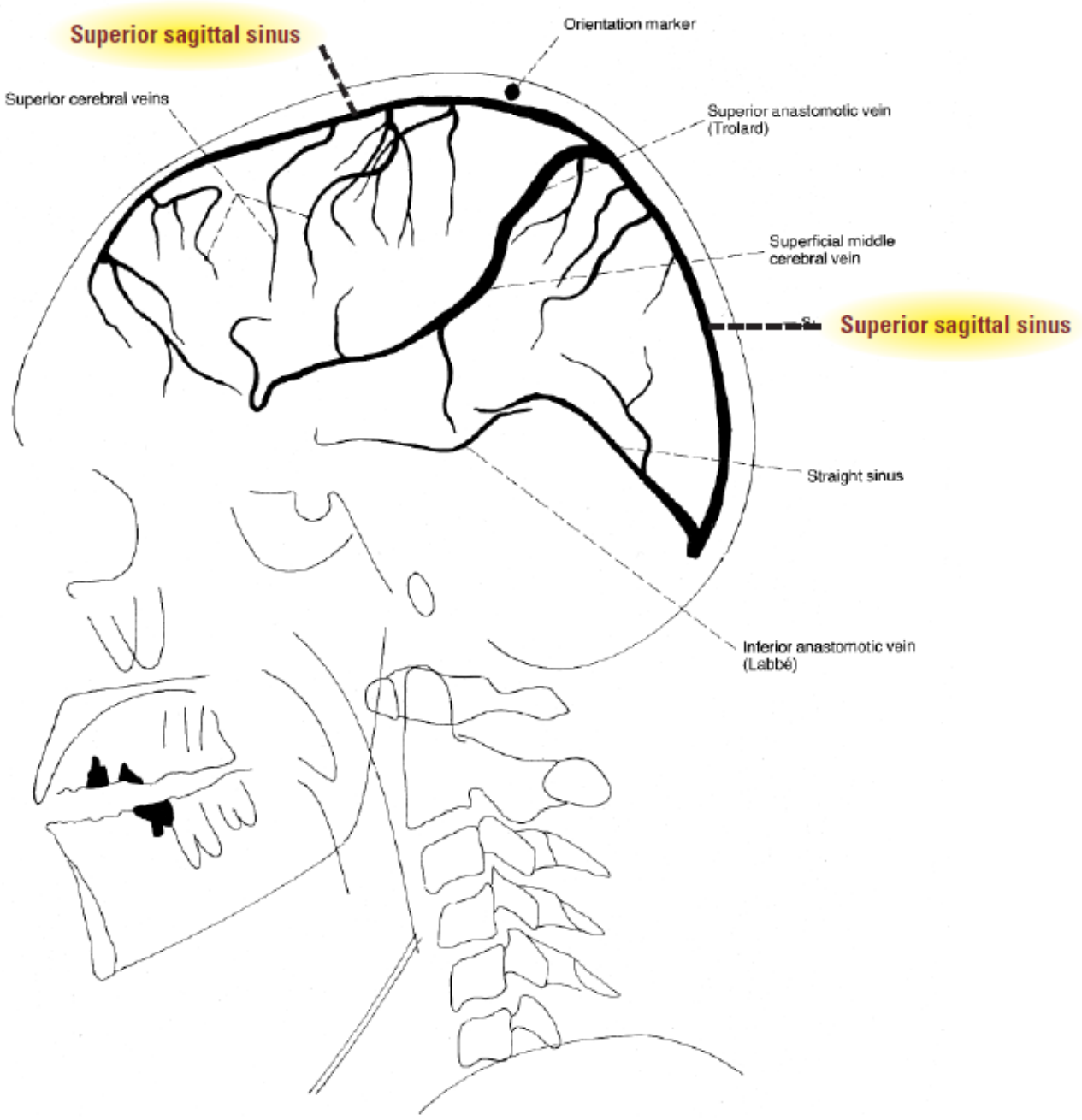


Figure 2.0. Anterior venous circulation, lateral projection.

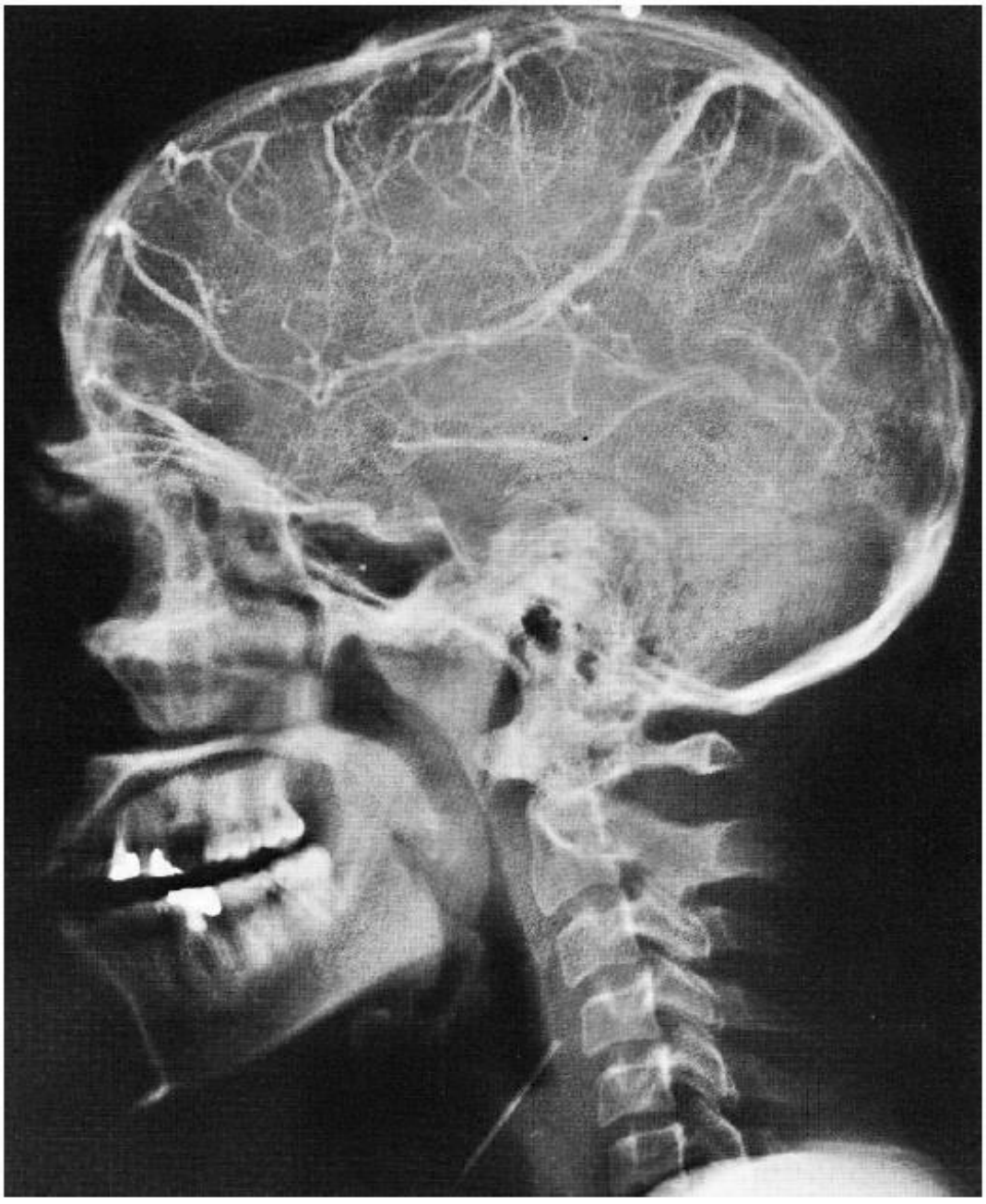


Figure 2.1. Anterior venous circulation, lateral projection.

Identify the superior sagittal sinus on this angiographic image.

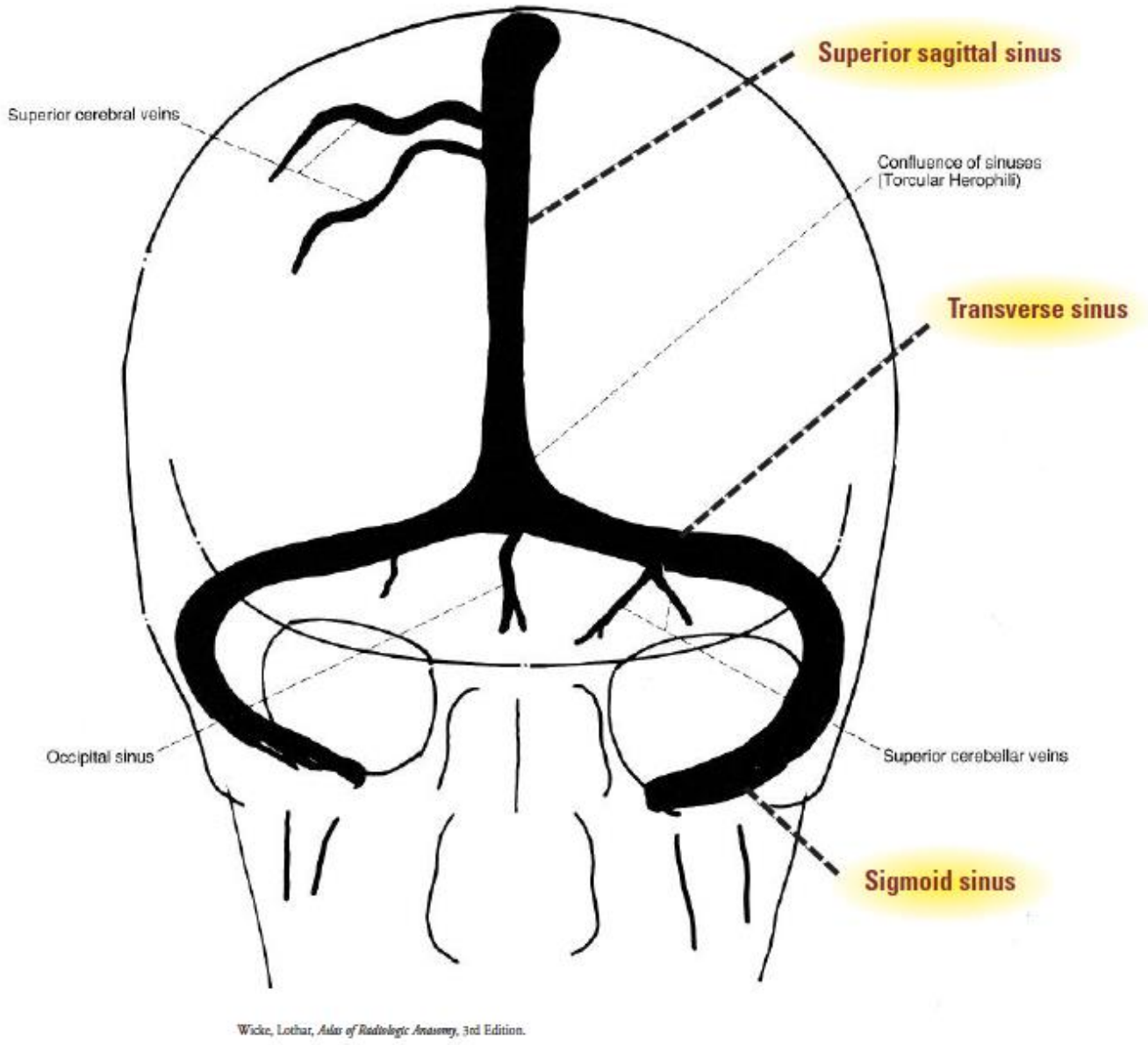


Figure 2.2. Venous sinuses, AP projection.

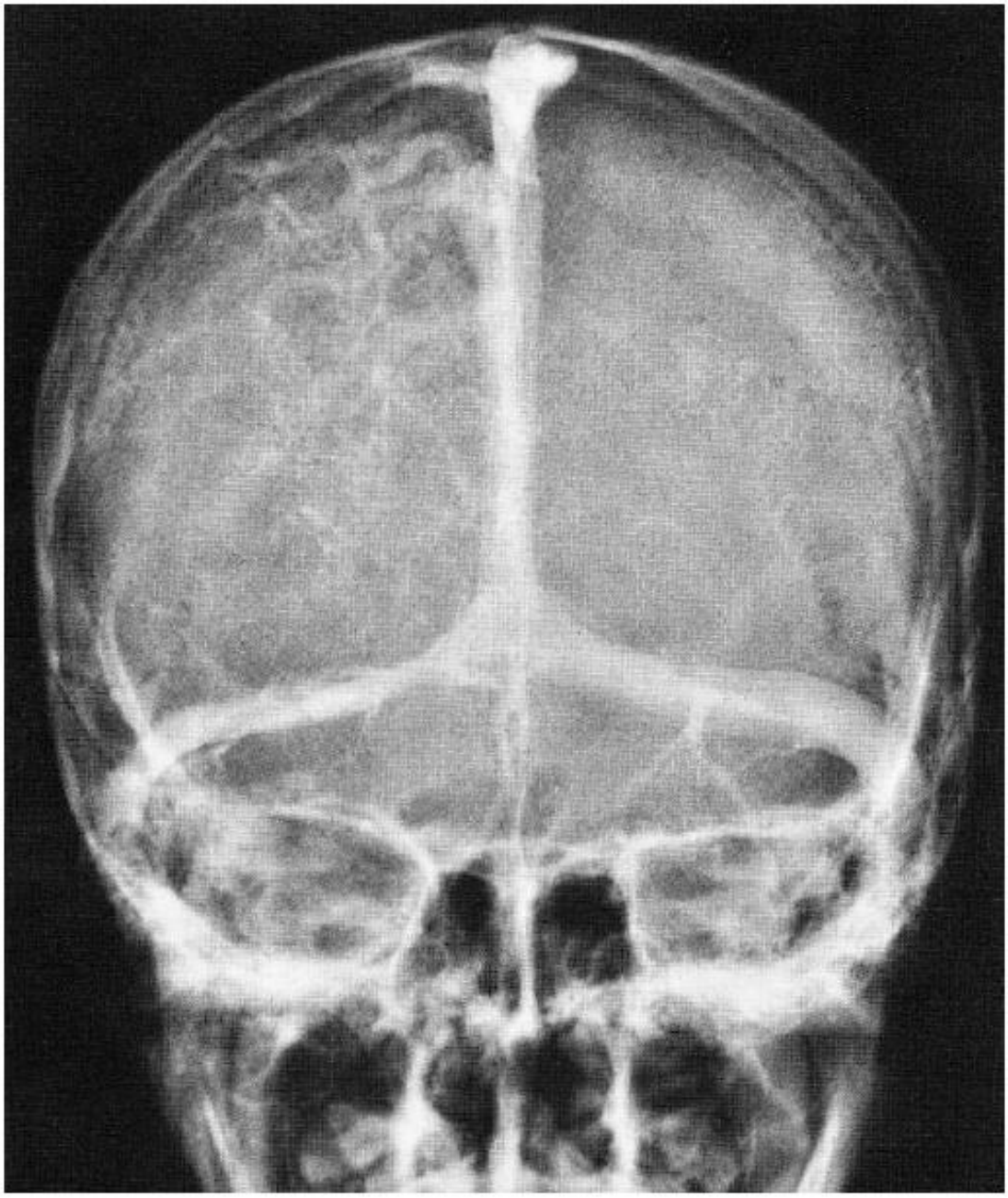


Figure 2.3. Venous sinuses, AP projection.

Identify the superior sagittal, transverse, and sigmoid sinuses on this angiographic image.

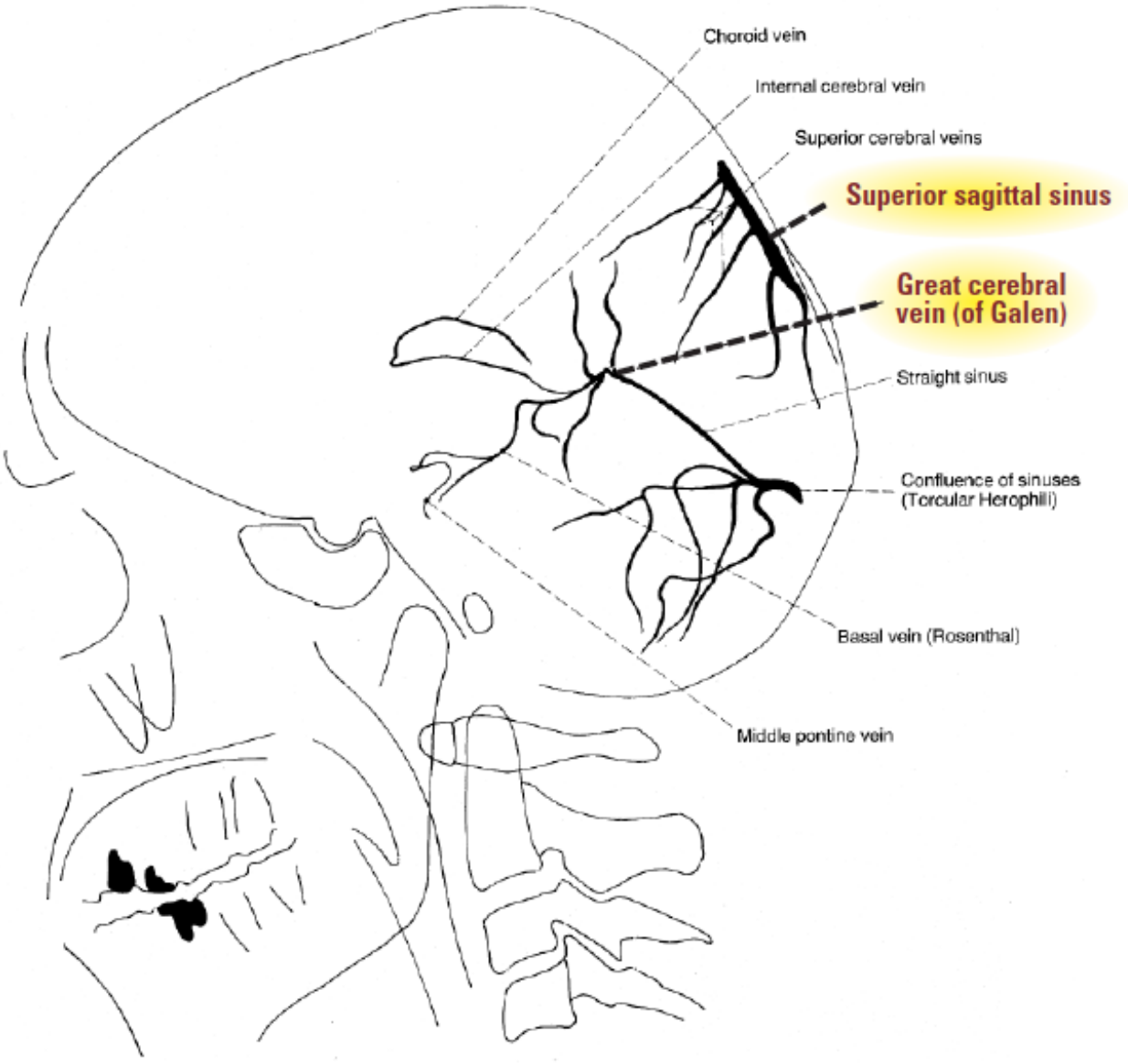


Figure 2.4. Posterior venous circulation, lateral projection.

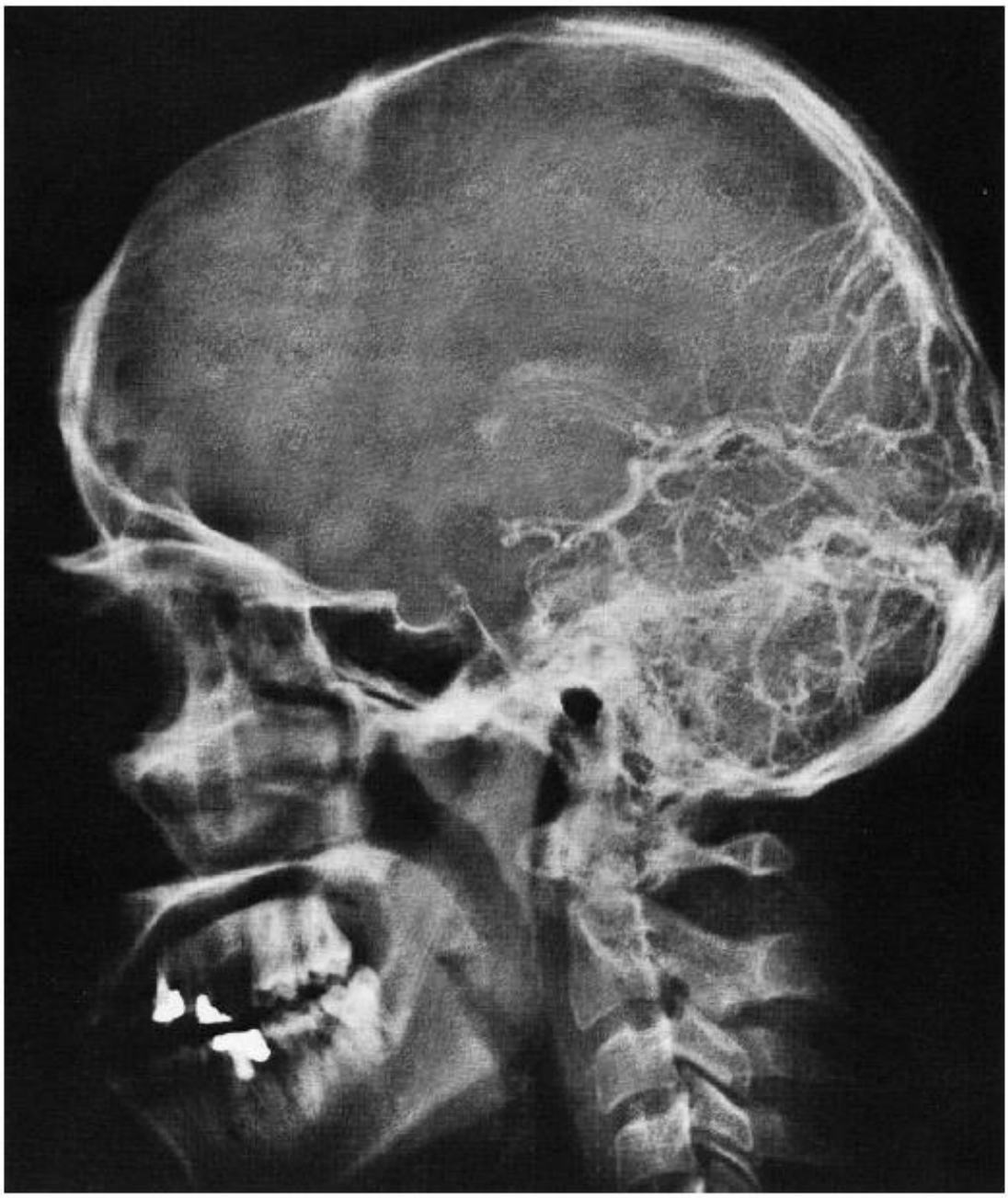


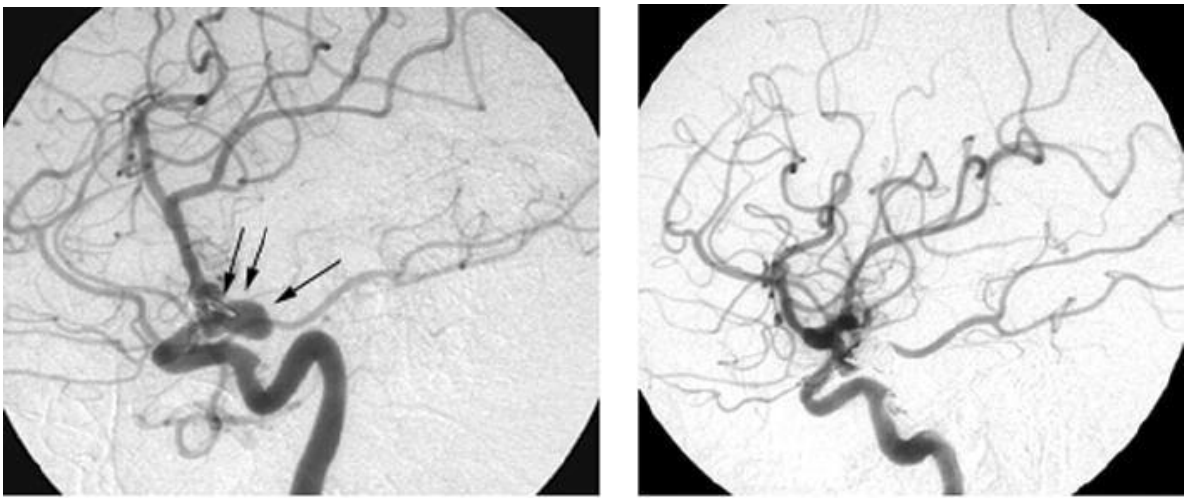
Figure 2.5. Posterior venous circulation, lateral projection.

Identify the superior sagittal sinus on this angiographic image.

Angiographic interpretation
Aneurysms

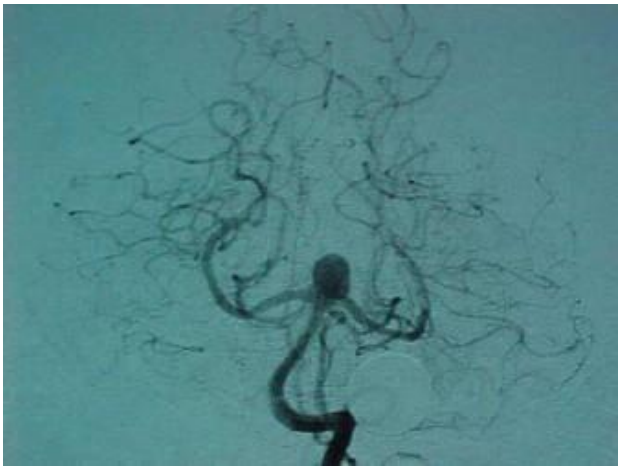
Aneurysms:

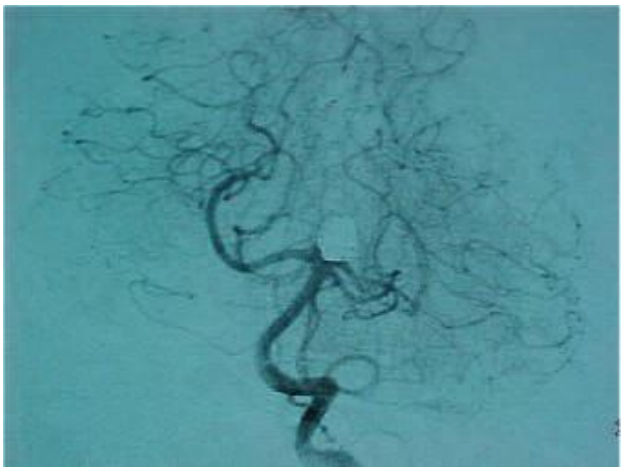
- Are an abnormal outward dilation of a weakened artery.
- Appear as a dense, dark, somewhat irregularly round mass on angiography.
- Are named for the vessel from which they arise (parent vessel).
- Can present a danger of rupture.
- Are treated to exclude flow into the aneurysm.



Photos of images taken by a BSC representative.
Figure 2.6.

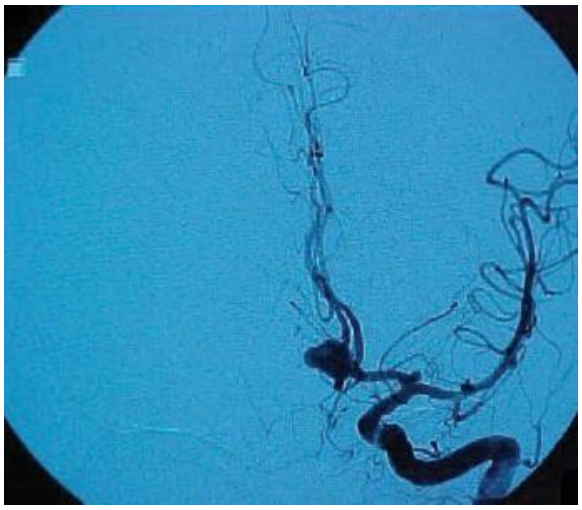
Identify the circulation, view, and aneurysm location on these angiographic images.

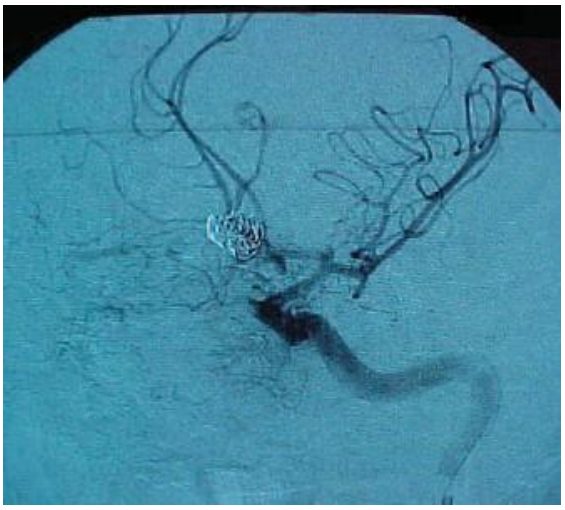




Photos of images taken by a BSC representative.
Figure 2.7.

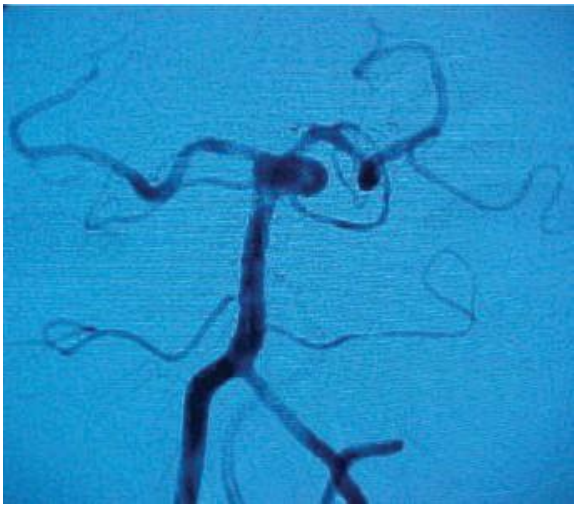
Identify the circulation, view, and aneurysm location on these angiographic images.

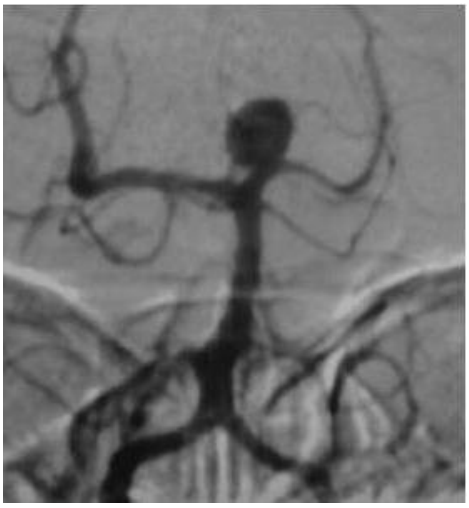




Photos of images taken by a BSC representative.
Figure 2.8.

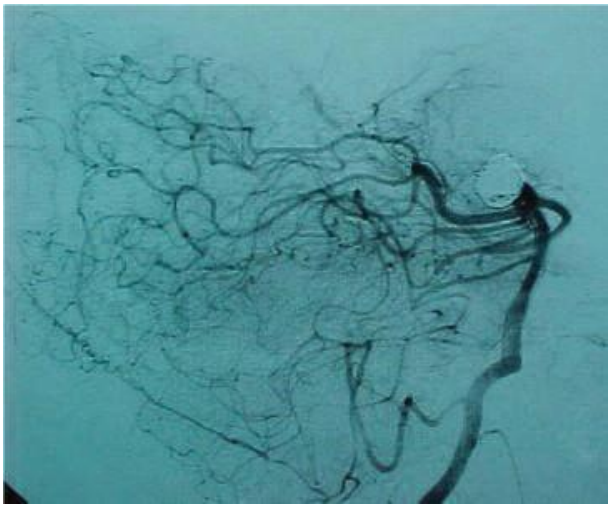
Identify the circulation, view, and aneurysm location on these angiographic images.





Photos of images taken by a BSC representative.
Figure 2.9.

Identify the circulation, view, and aneurysm location on these angiographic images.



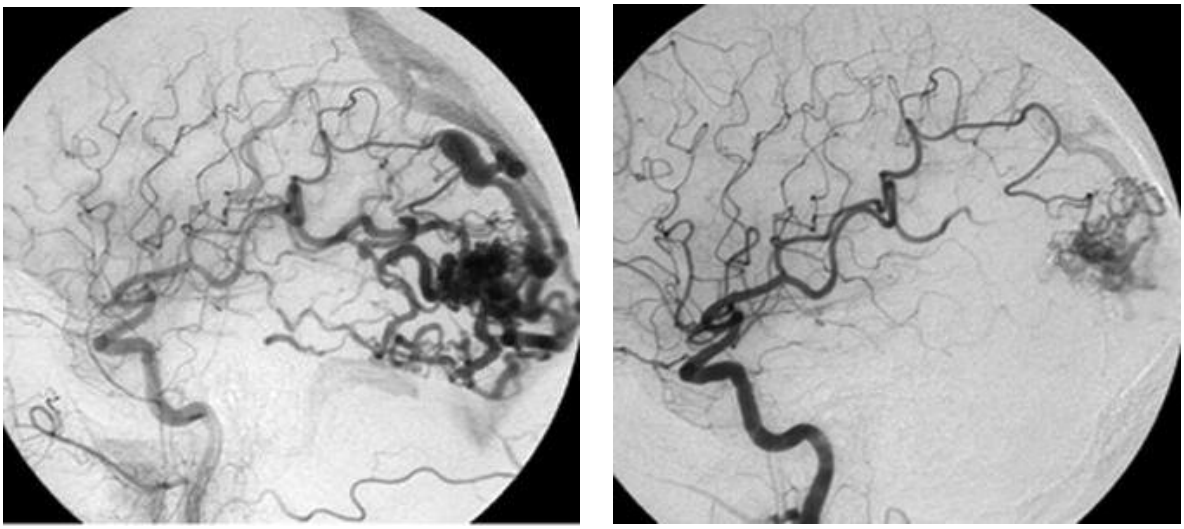
Photos of images taken by a BSC representative.
Figure 3.0.

Identify the circulation, view, and aneurysm location on these angiographic images.

Angiographic interpretation
Arteriovenous malformations (AVMs)

AVMs:

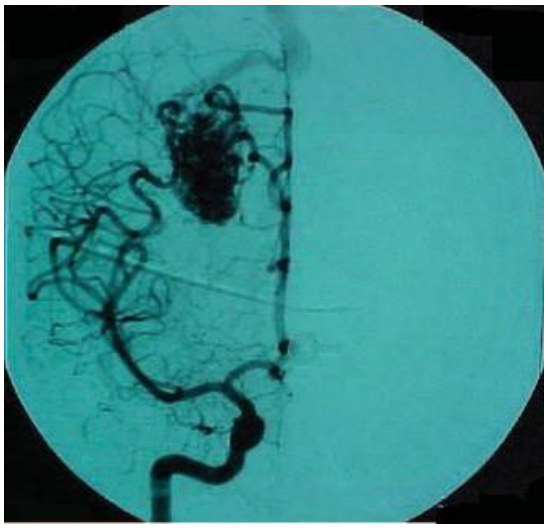
- Are abnormal, direct connections between arteries and veins that form a “tangle” of dilated blood vessels.
- Appear as an abnormal “tangle” or clump-like mass of blood vessels on angiography.
- Are named for the area of the brain they occupy.
- Can present a danger of bleeding.
- Are treated via removal or reduction of blood flow to the AVM (using liquid embolics,* PVA, ethanol, or coils).
- Can be treated via surgical excision or gamma knife radiation reduction.



Photos of images taken by a BSC representative.

Figure 3.1.

Identify the circulation, view, and feeder vessels on these angiographic images.



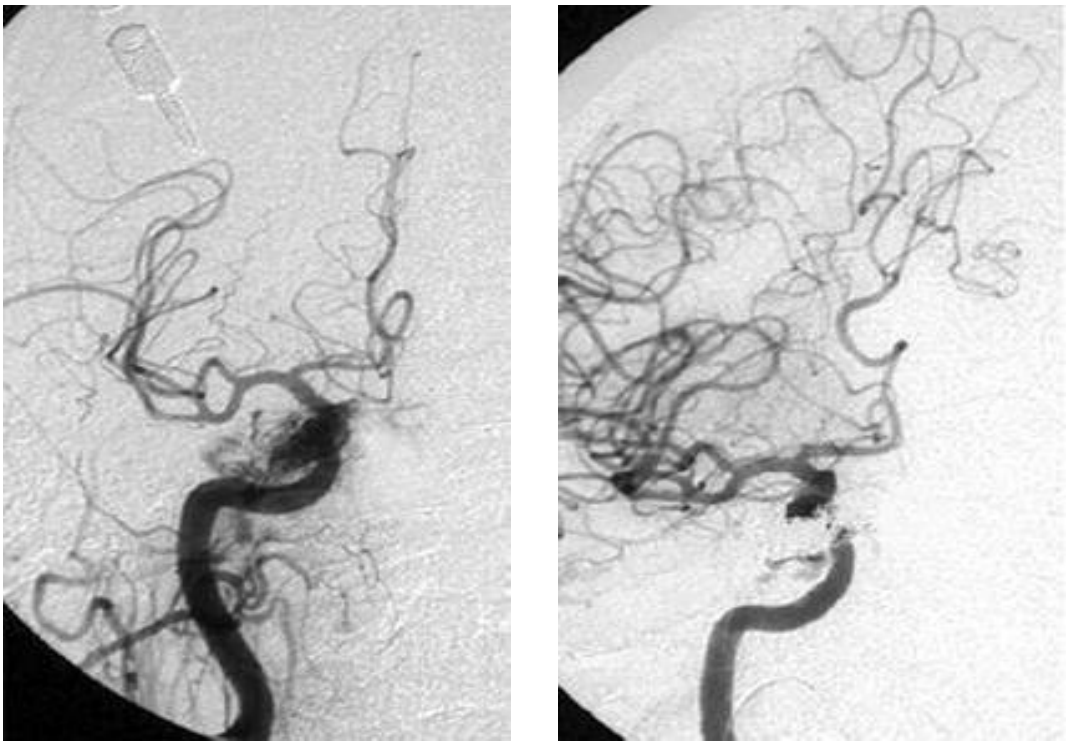
Photos of images taken by a BSC representative.
Figure 3.2.

Identify the circulation, view, and feeder vessels on this angiographic image.

Angiographic interpretation
Arteriovenous fistulas (AVFs)

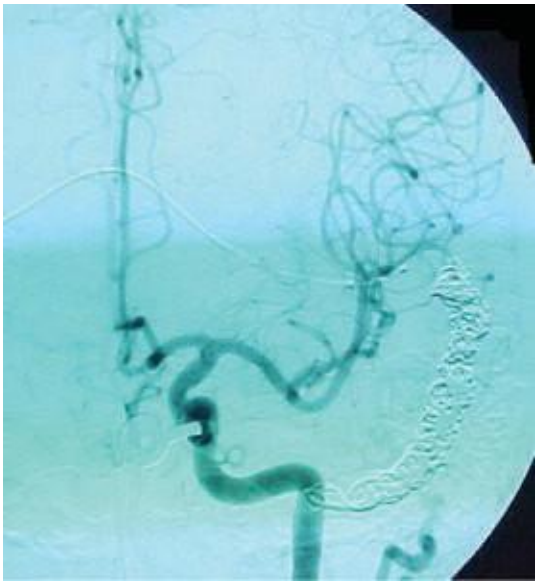
AVFs:

- Are a direct connection between an artery and a vein, shunting blood between the two, without the presence of a nidus.
- Appear as a shadowy venous structure in the same phase as arteries.
- Are named for the vessels that they connect.
- Are treated to stop the shunt (using coils, balloons, liquid embolics,* or a combination of these treatments).



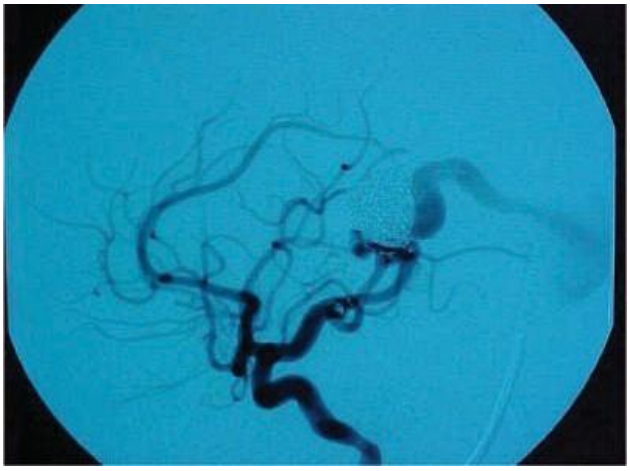
Photos of images taken by a BSC representative.
Figure 3.3.

Identify the circulation, view, area coiled, and fistula on these angiographic images.



Photos of images taken by a BSC representative.
Figure 3.4.

Identify the circulation, view, area coiled, and fistula on this angiographic image.



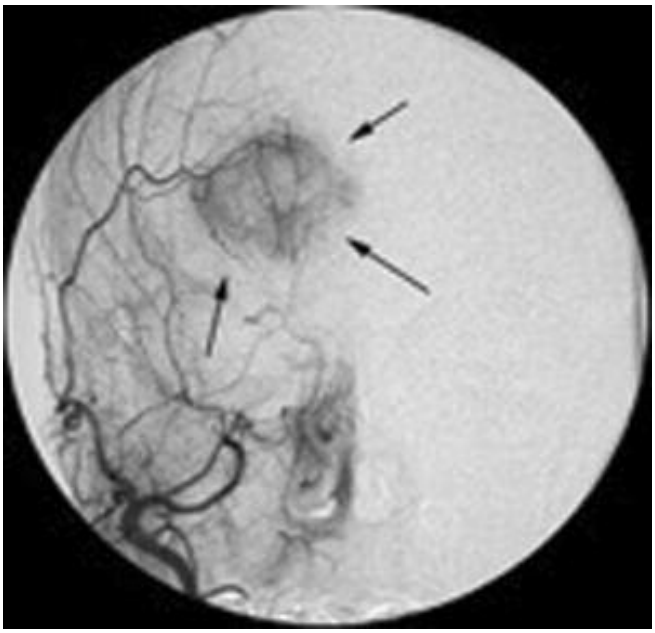
Photos of images taken by a BSC representative.
Figure 3.5.

Identify the circulation, view, area coiled, and fistula on this angiographic image.

Angiographic interpretation
Tumors

Vascular tumors:

- Are a mass of abnormal tissue growth.
- Appear as a concentrated “blushy” area with fuzzy border on angiography.
- Are treated by blocking blood flow (using PVA, liquid embolics,* coils, or surgery to excise) to them.

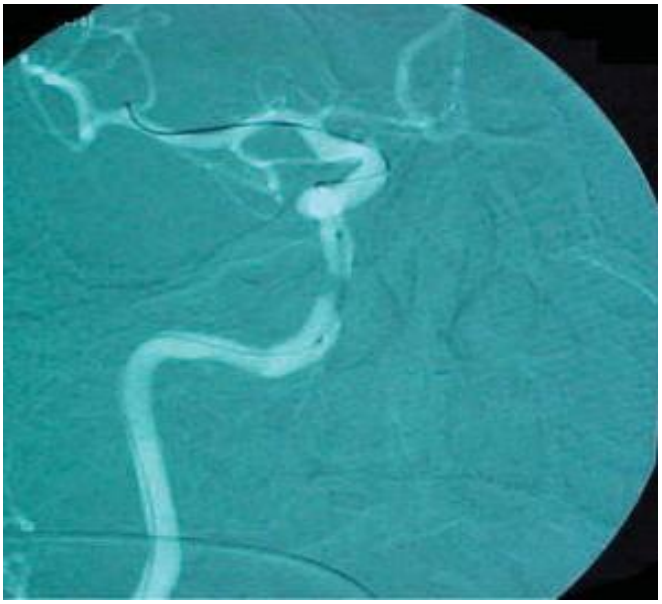


Photos of images taken by a BSC representative.
Figure 3.6.

Angiographic interpretation
Occlusive disease

Occlusive disease is the narrowing of an artery by atherosclerosis or vasospasm.

- ***Atherosclerosis*** is the buildup of plaque in the artery, which constricts the vessel lumen.
- ***Vasospasm*** is a spastic vessel wall due to trauma or hemorrhage.

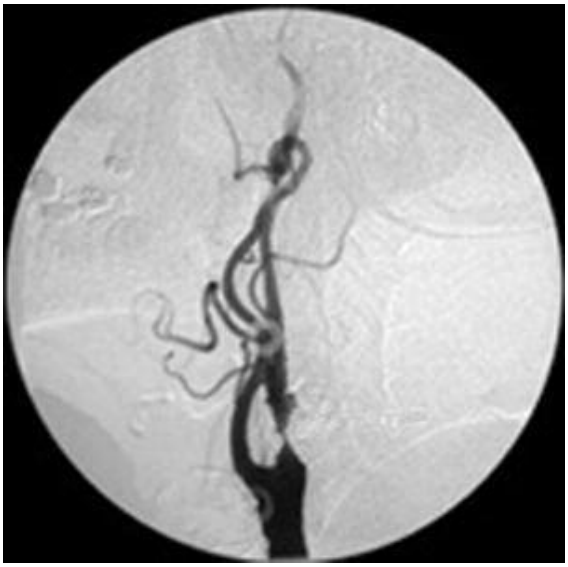


Angioplasty performed.

Stent deployed.

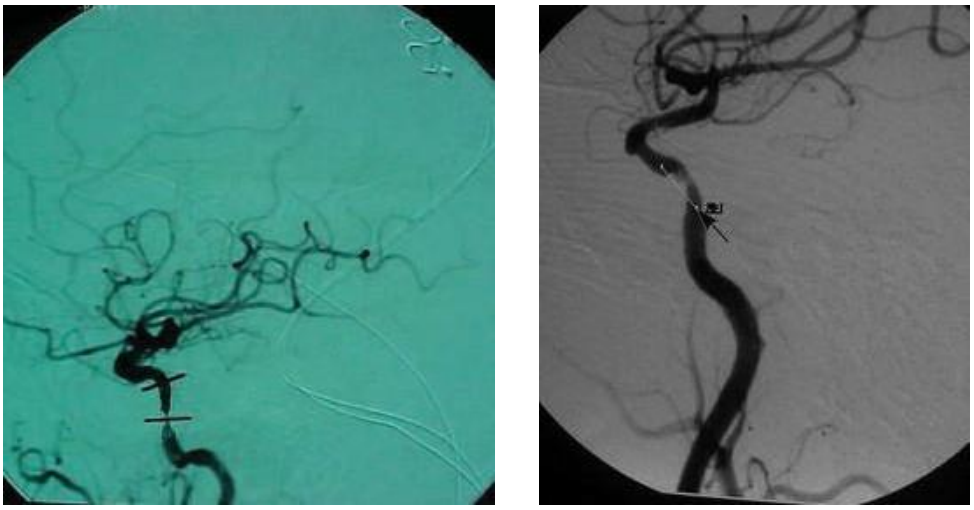
Photos of images taken by a BSC representative.
Figure 3.7.

Identify the atherosclerotic narrowing and its location on these angiographic images.



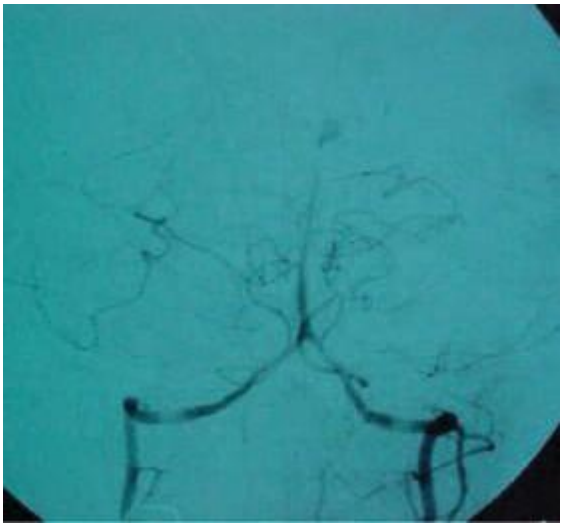
Photos of images taken by a BSC representative.
Figure 3.8.

Identify the atherosclerotic narrowing and its location on this angiographic image.

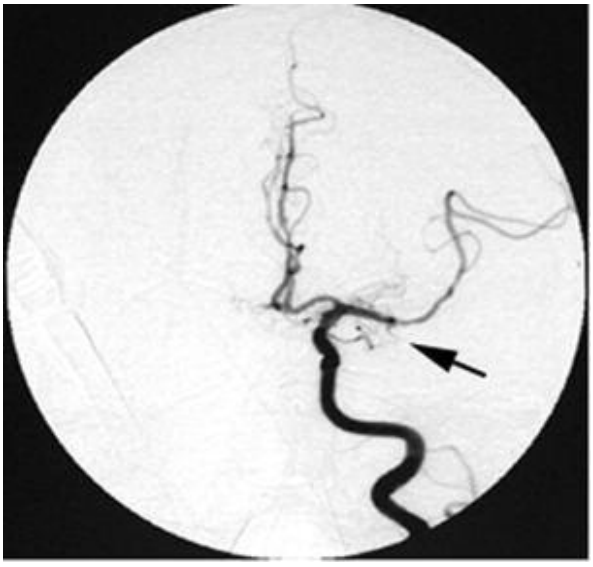


Photos of images taken by a BSC representative.
Figure 3.9.

Identify the circulation, view, and affected vessel on these angiographic images.

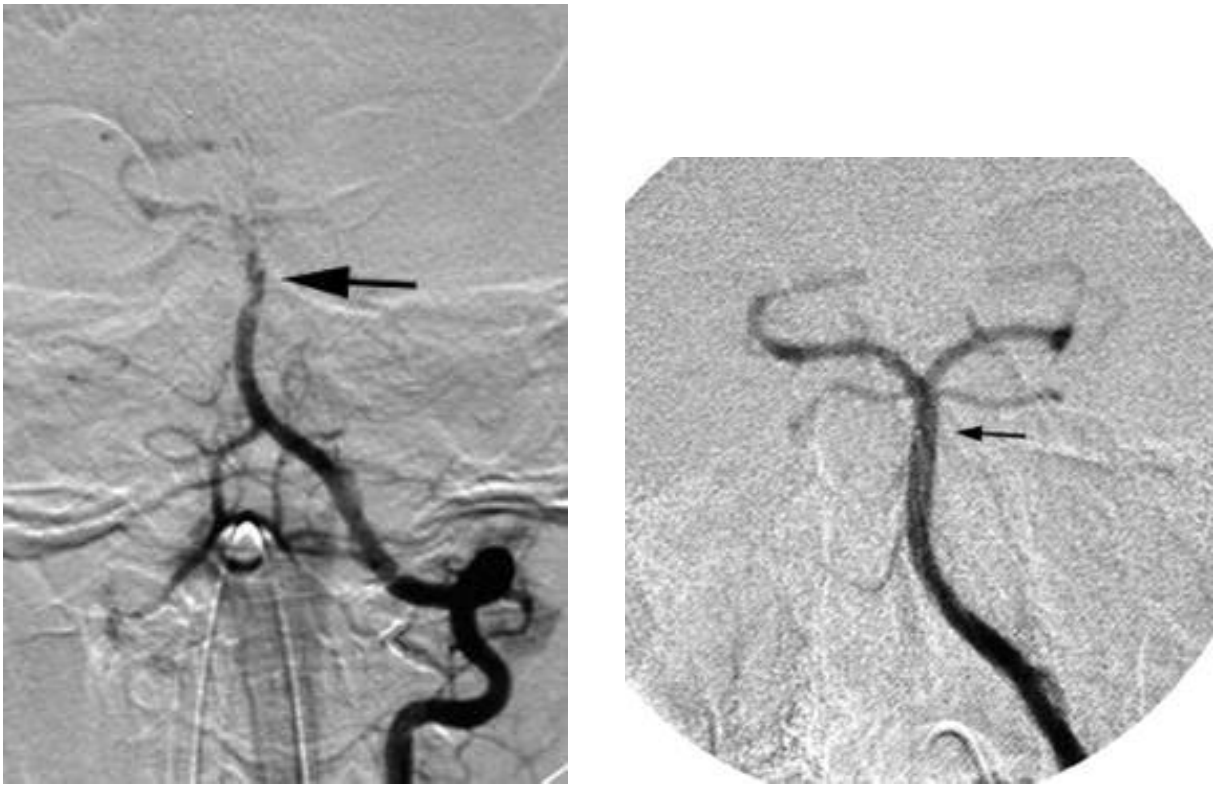


Photos of images taken by a BSC representative.
Figure 4.0. Vasospasm caused by SAH, which was caused by manipulation.



Photos of images taken by a BSC representative.
Figure 4.1.

Identify the circulation, view, and affected vessel on this angiographic image.



Photos of images taken by a BSC representative.
Figure 4.2.

Identify the circulation, view, and missing vessel on these angiographic images.

Glossary

NP001825 v2.0

Glossary
Terminology

Definitions of words and terms

AVF (arteriovenous fistulae) – an abnormal, direct passageway between an artery and a vein.

AVM (arteriovenous malformation) – an abnormal collection of blood vessels in which blood flows directly from arteries to veins without an intervening capillary bed.

Adventitia – the outermost lining of a blood vessel, composed primarily of connective tissue and elastic fibers; provides elastic and structural strength to the artery.

Agnosia – loss of ability to recognize objects, people, sounds, shapes or smells. Usually classified according to the sense or senses affected.
Symptom common to damage to parietal lobes of cerebral hemispheres.

Anastomosis – a connection between two vessels or tubes such as arteries.

Aneurysm – a thin-walled outpouching or dilation of a blood vessel.

Angiogram – also referred to as arteriogram; a radiographic technique used for visualization of the blood vessels using standard radiographic methods in conjunction with the intra arterial injection of iodinated contrast medium.

Anticoagulants – medications that prevent or slow blood coagulation.

Antiplatelets – medications that prevent or slow aggregation of platelets, a critical step in the blood clotting process.

Aphasia – loss of ability to speak or write; loss of ability to understand speech or written words.

Apraxia – inability to perform purposeful movements.

Arachnoid mater – the thin, delicate membrane interposed between the dura mater and the pia mater of the entire brain and with them constituting the brain meninges — a protective covering of the brain made up of delicate, elastic tissues and blood vessels.

Arrhythmia – irregular heartbeat.

Atherosclerosis – arterial disorder characterized by thickening, loss of elasticity and calcification of arterial walls resulting in decreased blood supply.

Ataxia – lack of coordination in bodily movements.

Atrophy – a “wasting away”; a diminution in the size of a cell, tissue, organ or part.

Benign – not malignant, not recurrent, favorable for recovery.

Brain stem – the stemlike portion of the brain connecting the cerebral hemispheres with the spinal cord, and comprising the pons, medulla oblongata, and midbrain; considered by some to include the diencephalon.

Bruit – an abnormal sound or murmur heard while auscultating (listening to) an organ or body.

CSF (cerebral spinal fluid) – the fluid that flows through and protects the four ventricles of the brain, the subarachnoid space and the spinal canal.

CT (computed tomography) – a computerized x-ray device that produces images of cross section of the brain. A dye may be used to help visualize abnormal tissue.

Capillary – one of the minute vessels connecting the arterioles and venules, the walls of which act as a semipermeable membrane for inter- change of various substances between the blood and tissue fluid.

Carotid “siphon” – the cavernous portion of the internal carotid artery is an “S-shape” portion of the vessel that travels through the cavernous sinus (which is a venous room) and then exits the cavernous sinus as the supra- clinoid portion of the ICA.

Catheter – a hollow, flexible tube for insertion into a body cavity, duct, or vessel. Used in the endovascular treatment of cerebral aneurysms.

Caudal – toward the distal end of the spine.

Cerebellum – the part of the brain situated on the back of the brainstem, to which it is attached by three cerebellar peduncles on each side; it consists of a median lobe and two lateral lobes.

Cerebral aneurysm – a weak bulging spot on the wall of a brain artery; also called a brain or intracranial aneurysm.

Cerebrum – the main portion of the brain, occupying the upper part of the cranial cavity; its two hemispheres, united by the corpus callosum, form the largest part of the central nervous system in humans.

Circle of Willis – allows blood that enters by either internal carotid (anterior circulation) or vertebral arteries (posterior circulation) to be distributed to any part of both cerebral hemispheres. Allows communication between anterior and posterior circulation.

Congenital – present at and existing from the time of birth.

Contrast – a radiopaque material used to visualize arteries and veins in an angiogram.

Coumadin® – tradename for the anticoagulant Warfarin Sodium.

Craniotomy – surgical procedure where a section of the skull cap is temporarily removed.

Decerebrate posture – a position in which the arms are extended and internally rotated and the legs are extended with the feet in forced plantar flexion. This condition usually indicates compression of the brainstem.

Digital subtraction angiography – subtraction of bony images from an angiographic image to allow clearer visualization of opacified vessels.

Decorticate posture – a position in which the upper extremities are rigidly flexed at the elbows and wrists. This indicates a lesion in the mesencephalic region of the brain.

Dura mater – the outermost, toughest, of the three meninges (mem- branes) of the brain and spinal cord; a protective covering for the brain.

Dysarthria – impairment of speech caused by damage or impairment of the tongue or speech muscles. Symptom may indicate pressure on the brainstem or elsewhere in the posterior fossa.

Dysphagia – difficulty swallowing.

Dysphasia – language disorder. Inability to speak words which one has in mind or to think of correct words. Inability to understand spoken or written words.

Dysplasia – abnormality in development of a tissue or organ.

Dyspnea – difficulty breathing.

EEL (External elastic lamina) – thin, elastic layer between the media and adventitia of an artery. Not present in intracranial arteries.

Edema – swelling due to an excess of water.

Embolization – a technique, also referred to as coiling, that seals off the cerebral aneurysm and stops further blood from entering into the aneurysm. This treatment is done endovascularly.

Embolus – a foreign object, quantity of gas, a bit of tissue or thrombus that circulates in the bloodstream until lodging in a vessel.

Endothelium – the layer of epithelial cells that lines the cavities of the heart and of the blood and lymph vessels, and the serous cavities of the body.

Endovascular – within the vascular system.

Epidemiology – the study of the distribution of disease and its impact upon a population using measures such as incidence, prevalence and mortality.

Etiology – the study of cause of disease.

Extracranial – outside the cranial cavity.

Fibrinolysis – the dissolution of fibrin by enzymatic action.

Fluoroscopy – an examination by means of the fluoroscope to visually observe the form and motion of blood vessels by means of x-ray shadows projected on a fluorescent screen.

Glasgow outcome scale (GOSS) – an evaluation scale based on individual overall social capability (or dependence) of patients. It takes into account the combined effects of specific mental and neurological deficits.

Guide catheter – in the endovascular treatment of cerebral aneurysms, these flexible tubes are introduced into the patient's carotid artery in the neck to function as a working channel through which devices, like micro- catheters, may be introduced into the brain.

Guidewire – a thin, usually flexible wire that can be inserted into a con- fined or tortuous space to guide and facilitate passage of instrumentation, such as a catheter. Used in the endovascular treatment of cerebral aneurysms.

Hematoma – a collection of extravasated blood trapped in the tissues of the skin or in an organ.

Hemiparesis – muscle weakness on one side of the body.

Hemodilution – a reduction in the concentration of blood cells in a given volume of blood.

Hemodynamics – the study of the movements of the blood and of the forces concerned therein.

Hemorrhage – a loss of a large amount of blood in a short amount of time.

Hemorrhagic stroke – a stroke caused by a ruptured blood vessel and characterized by bleeding in or surrounding the brain. Subarachnoid hemorrhage from a ruptured cerebral aneurysm can lead to a hemorrhagic stroke.

Hemostasis – the arrest of bleeding, either by the physiological properties of vasoconstriction and coagulation or by surgical means. Interruption of blood flow through any vessel or to any anatomical area.

Heparin – an anionic mucopolysaccharide that acts as an anticoagulant and is used for prevention and treatment of venous and arterial thromboembolism.

Hydrocephalus – excess water in the brain due to blockage of CSF flow, increased production or reduced absorption.

Hyperplasia – an increase in the number of cells in a body part.

Hypertension – elevated blood pressure.

Hypervolemia – an increase in the amount of extracellular fluid.

Hunt & Hess grade – a neurological scale used to determine the patient's surgical risk following the hemorrhage of an aneurysm.

ICAD (intracranial atherosclerotic disease) – the buildup of plaque on the inside walls of arteries within the brain.

ICP (Intracranial pressure) – pressure within the cranium that can be caused by increased blood or fluid in a closed, non-expandable space.

IEL (Internal elastic lamina) – thin, elastic layer between the intimal and medial layers of an artery.

IVUS (intravascular ultrasound) – ultrasound within a vessel or vessels used for diagnostic purposes.

Infarct – a localized area of necrosis (death) in a tissue, vessel or organ resulting from tissue anoxia caused by the cessation of blood flow.

Intima – the innermost lining of an artery, composed of endothelial cells. Provides a smooth, thrombiresistant surface and is nourished by the blood flowing through the artery.

Intracerebral hemorrhage – bleeding within the cerebrum as a result of trauma or aneurysm rupture.

Intracranial – within the cranial cavity or skull.

Ischemia – lack of oxygen due to decreased blood supply to a body organ or part.

Ischemic penumbra – the region surrounding dead brain tissue that is close to cell death, but still potentially viable.

Ischemic stroke – stroke caused by a lack of blood supply and subsequent lack of oxygen to affected brain tissue.

MRA (magnetic resonance angiography) – uses blood flow as an intrinsic contrast agent and a magnetic field to produce detailed images of brain tissue and cerebral arteries.

MRI (magnetic resonance imaging) – a computerized scanning device utilizing a magnetic field and radio waves.

Malignant – tending to become progressively worse and possibly result in death.

Media – middle layer of an artery, composed of smooth muscle tissue, provides strength to the artery by allowing constriction and/or dilation.

Medical therapy – the use of pharmacological agents. Sometimes also referred to as medical management or medical treatment.

Meninges – the three membranes covering the brain and spinal cord for protection: dura mater, arachnoid, and pia mater.

Mass effect – symptoms produced by compression or displacement of brain tissue, specific to the brain territory around a physical mass.

Meningioma – a hard, usually vascular tumor, occurring mainly along the meningeal vessels and superior longitudinal sinus, invading the dura and skull and leading to erosion and thinning of the skull.

Microcatheter – a very small catheter used to deliver diagnostic and therapeutic agents such as devices used in the endovascular treatment of cerebral aneurysms. Over-the-wire microcatheters follow along a guidewire to the area of the body for treatment. Flow-directed microcatheters utilize the forward blood flow to reach their destination in the body.

Myelography – a radiographic process by which the spinal cord and spinal subarachnoid space are viewed and photographed after the introduction of contrast media.

Neoplasm – tumor: any new and abnormal growth, specifically one in which cell multiplication is uncontrolled and progressive.

Neuroangiography – the study of blood vessels in the brain.

Nidus – the point of origin or focus of a morbid process.

Non-ruptured aneurysm – an aneurysm that has not hemorrhaged.

PET (positive emission tomography) – a scanning technique using low-dose radioactive glucose to measure metabolic activity of an organ.

Pathogenesis – the source or cause of a disease.

Pia mater – the innermost and most delicate of the three meninges covering the entire brain and spinal cord. Contains many blood vessels that reach deep into the surface of the brain.

Plaque – a fatty deposit inside an arterial wall, made up of plasma lipids, cholesterol, connective tissue fibers and other cells in the intima of the vessel; an abnormal patch on or inside the body.

RIND (reversible ischemic neurologic deficit) – deficit that persists for more than 24 hours, but with complete recovery within 3 weeks.

Radiosurgery – a technique that uses focused beams of radiation to treat AVMs that are sufficiently small and located in accessible areas of the brain. It causes scarring in the blood vessels of the AVM, thereby eliminating it.

Rebleed – to bleed again after an initial bleed such as in an aneurysm rupture.

Recanalization – regrowth of an aneurysm.

Restenosis – occurs after a vessel has been treated with angioplasty or stenting. It is the repair process caused by mechanical injury induced by ballooning and stenting and is different than the original plaque or atherosclerotic lesion.

Roadmap – superimposing a "real time" image over a stored subtracted reversed image, to enable more effective navigation through the vasculature.

Ruptured aneurysm – an aneurysm that has hemorrhaged prior to coil treatment. Acute rupture has occurred within the last fifteen days and non-acute rupture has occurred over fifteen days ago.

SAH (subarachnoid hemorrhage) – an intracranial hemorrhage (bleed) into the CSF filled subarachnoid space. The pathologic hallmark of aneurysm rupture as cerebral arteries are within the subarachnoid space.

SPECT (single photon emission computed tomography) – a variation of CT imaging.
Shunt – a diversion or redirection of bodily fluid from one cavity or vessel to another.

Stenosis – a narrowing of the artery lumen generally due to thrombus, atherosclerotic plaque or vasospasm in the vessel.

Stent – a device used to support and maintain patency of a bodily cavity, channel, or vessel.

Stroke – any disease process which results in the death of cells in any region of the brain. Cerebral vascular accident.

Subarachnoid space – between the arachnoid mater and pia mater of the brain, in which flows cerebrospinal fluid.

Subdural space – between the dura mater and the arachnoid mater of the brain.

Systemic – pertaining to or affecting the entire body as a whole.

TIA (transient ischemic attack) – an episode of cerebrovascular insufficiency , usually associated with partial occlusion of an artery by atherosclerotic plaque or an embolism.

Thrombogenesis – clot formation.

Thrombogenic – producing or tendency to produce a clot.

Thrombolytics – agents that lead to dissolution of a thrombus.

Thromboembolism – obstruction of a blood vessel with thrombotic material carried by the blood from the site of origin to plug another vessel.

Thrombus – an aggregation of platelets, fibrin, clotting factors and cellular elements of blood that adheres to blood vessel walls.

Transcranial Doppler – noninvasive procedure in which a small probe is placed against the skull to measure blood flow velocity through the cerebral arteries with high frequency sound waves.

Tumor – neoplasm: a new growth of tissue in which cell multiplication is uncontrolled and progressive.

Ultrasonography – the imaging of deep structures of the body by recording the echoes of pulses of 1-10 megahertz ultrasound reflected by tissue planes where there is a change in density

Vasoconstriction – constriction or narrowing of blood vessels.

Vasospasm – acute, abnormal narrowing of arteries due to irritation by blood in the subarachnoid space; often develops several days after an aneurysm rupture.

Ventricles – a small cavity or chamber such as in the heart or brain. Brain ventricles manufacture and circulate cerebrospinal fluid.

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