Lecture 7A
(Acute Brain Disorders)
Traumatic Brain Injury
Cerebrovascular Disease and Stroke
Cerebral Aneurysm and AVM
Central Nervous System Infections

Traumatic Brain Injury (TBI)

Etiology

- The majority are sustained in automobile accidents. Falls and sports injuries also contribute.
- In the US 15-24 year-olds are at highest risk.
- Early rescue from the trauma scene and emergency management are crucial.
- Half of TBI fatalities occur within 10 minutes of the traumatic event.
- The Glascow Coma Scale is used to assess the seriousness of TBI.
- The primary brain injury often leads to secondary brain injury (inflammation, cerebral edema, elevated ICP, reduced CCP, etc.)

Traumatic Brain Injury (TBI)

Types of TBI (based on the site of the primary injury)

- **Focal injury (coup)** is localized to the site of impact. The extent of damage is determined by depth and brain region.
  - Motor cortex injury is associated with contralateral muscle weakness.
  - Prefrontal cortex injury is associated with personality changes: poor judgment, impulsive behavior and apraxia (motor planning disorder)
- **Polar injury (aka coup contrecoup, aka closed head injury)** is a consequence of brain shift as occurs with acceleration-deceleration. The result is injury to opposite poles of brain tissue. Very common in automobile crashes.
- **Diffuse injury** occurs when movement within the cranium causes widespread neuronal damage.
  - Occurs in **Shaken Baby Syndrome**

Traumatic Brain Injury (TBI)

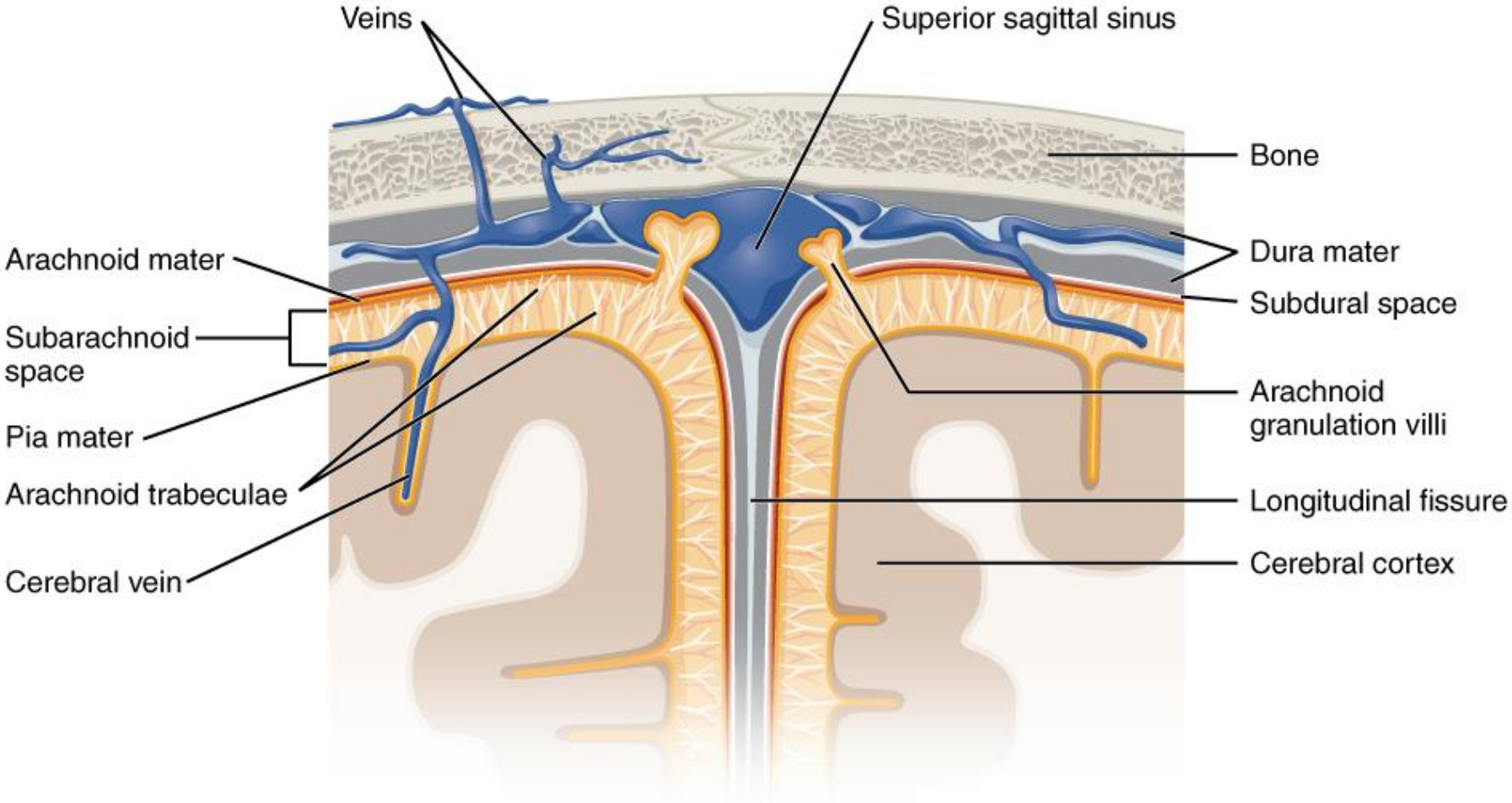
NOTE how the brain shifts forward when the head is thrown backward and visa versa. These injuries usually occur with some kind of rotation rather than exactly front to back.

Traumatic Brain Injury (TBI):

Types of TBI (based on mechanism of primary injury)

- **Concussion** occurs when brain injury causes neurological symptoms (blurred vision, memory loss, tinnitus) but no evidence of brain damage is found on physical or radiological exam. 90% of concussions involve no loss of consciousness. 10% cause brief loss of consciousness (a few minutes at most). Concussions are a hot topic lately especially as they affect military members in combat and athletes. The occurrence of multiple concussions in a single individual may have long-lasting effects.
- **Contusion** is present when CT or MRI reveals an area of brain tissue damage (necrosis, laceration, bruising). There is always loss of consciousness for at least 15 minutes.
- **Intracranial hematoma** is a localized collection of blood within the cranium resulting from vascular damage. There are three spaces into which bleeding most commonly occurs and thus three major types of intracranial hematoma. Hematomas are visible on brain scans.
- **NOTE: hematomas increase cerebral volume and thus ICP (intracranial pressure)!**

Meninges of the Brain



Meninges from superficial to deep: dura mater, arachnoid mater, pia mater. Note that the dura mater has two layers. The dural sinuses lie between those two layers.

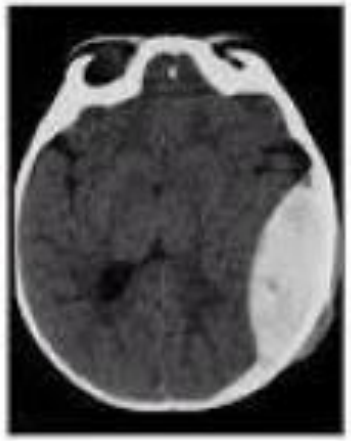
Traumatic Brain Injury (TBI)

Sites of Intracranial Hematoma Formation

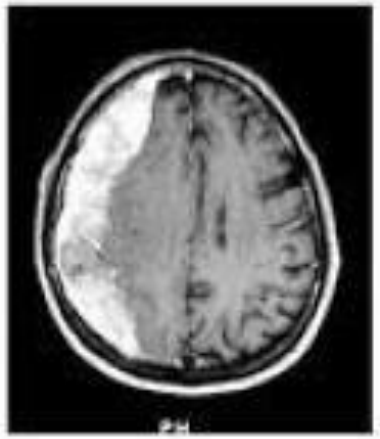
- **Epidural hematoma (EDH)**-between the skull and the dura mater.
  - The source of bleeding is usually an **artery**, so the hematoma expands rapidly causing rapid deterioration in consciousness. An EDH **doesn't cross the suture lines** of the skull (as seen on CT scan) because the dura is firmly attached to skull bone at suture lines. Fracture of the temporal bone is often associated with EDH.
- **Subdural hematoma (SDH)**-between the dura mater and the arachnoid mater
  - The source of bleeding is the **bridging veins (aka cerebral veins).** The blood is under low pressure, the rate of hematoma formation is slower than for an epidural bleed. An SDH **does cross suture lines.**
  - **Acute** SDHs produce delayed symptoms, up to 24 hours after injury. **Subacute** SDHs may not produce symptoms until 2-10 days post-injury. If SDH has been present for some time it enters a chronic stage in which granuloma formation occurs. **Chronic** SDHs are prone to rebleeding. They are a common autopsy finding in the elderly. SDH is also common in alcoholics and those taking anticoagulants.

Traumatic Brain Injury (TBI)

Epidural Hematoma



Subdural Hematoma



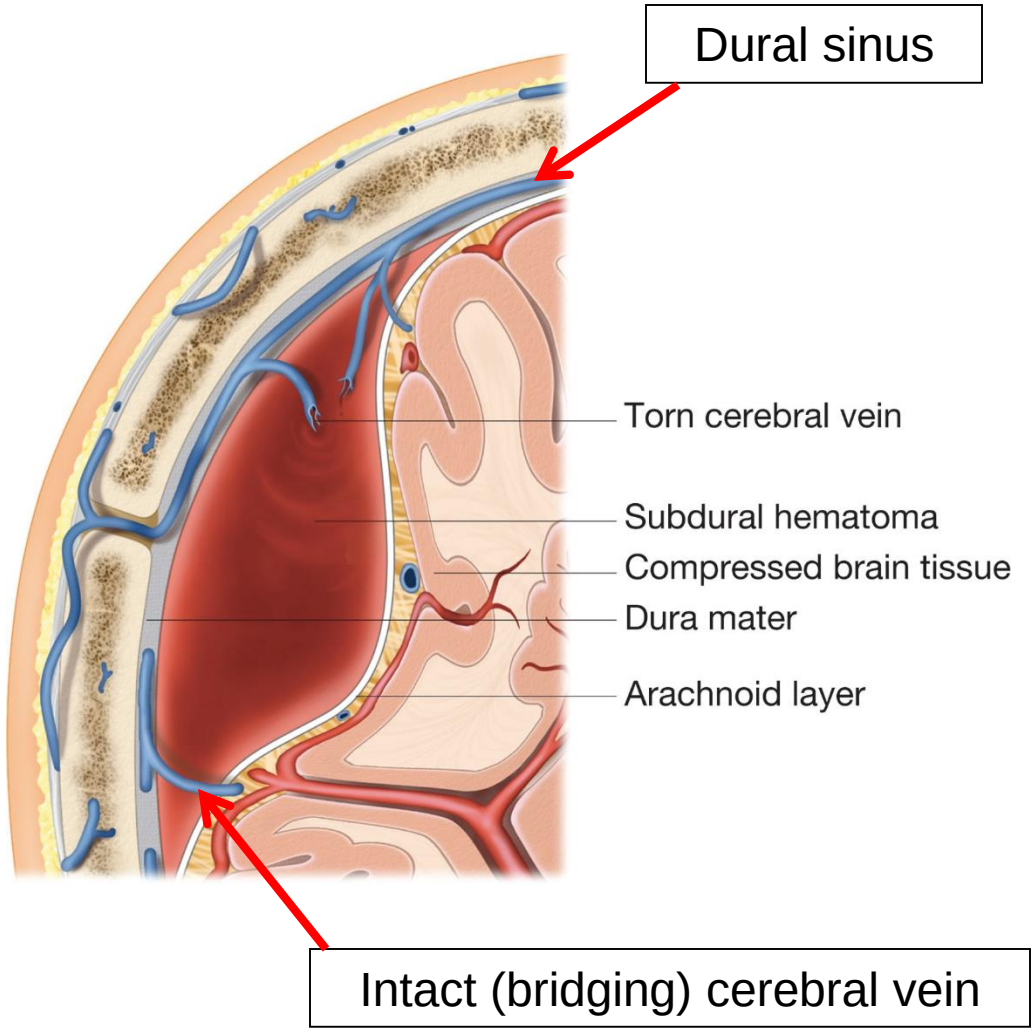
Traumatic Brain Injury (TBI)

Sites of Intracranial Hematoma Formation

- **Subarachnoid hematoma (SAH)/hemorrhage**-in the subarachnoid space, between the arachnoid mater and pia mater.
  - Subarachnoid hemorrhage may be due to trauma (bridging vein damage), but is most often associated with rupture of a **cerebral aneurysm or an arteriovenous malformation (AVM**).
  - Excruciating headache occurs immediately due to the presence of blood in the CSF. Spinal tap reveals the presence of blood in CSF.
  - Predisposes to secondary vasospasm and ischemia.
  - Predisposes to hydrocephalus because blood clots can obstruct CSF flow from the subarachnoid space through the arachnoid villi.

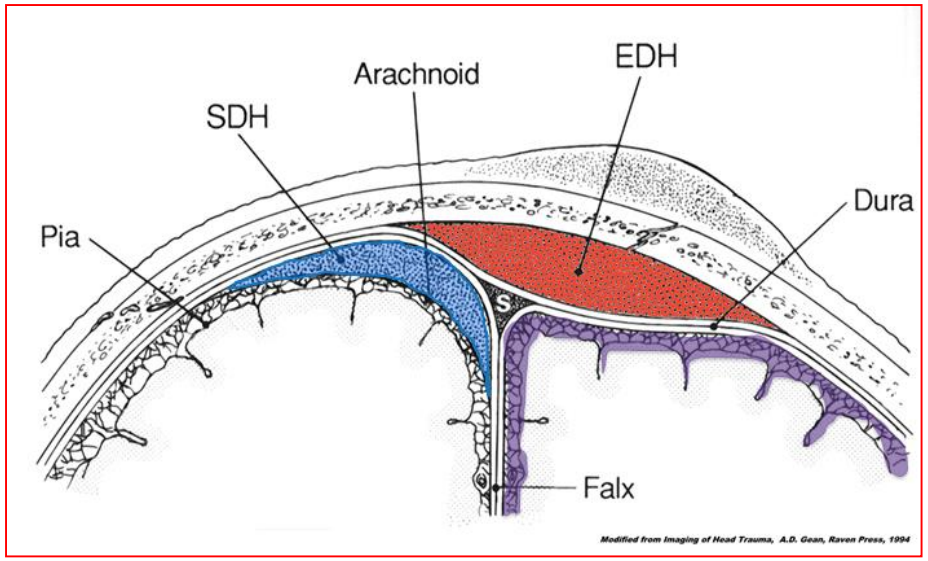
Traumatic Brain Injury (TBI)

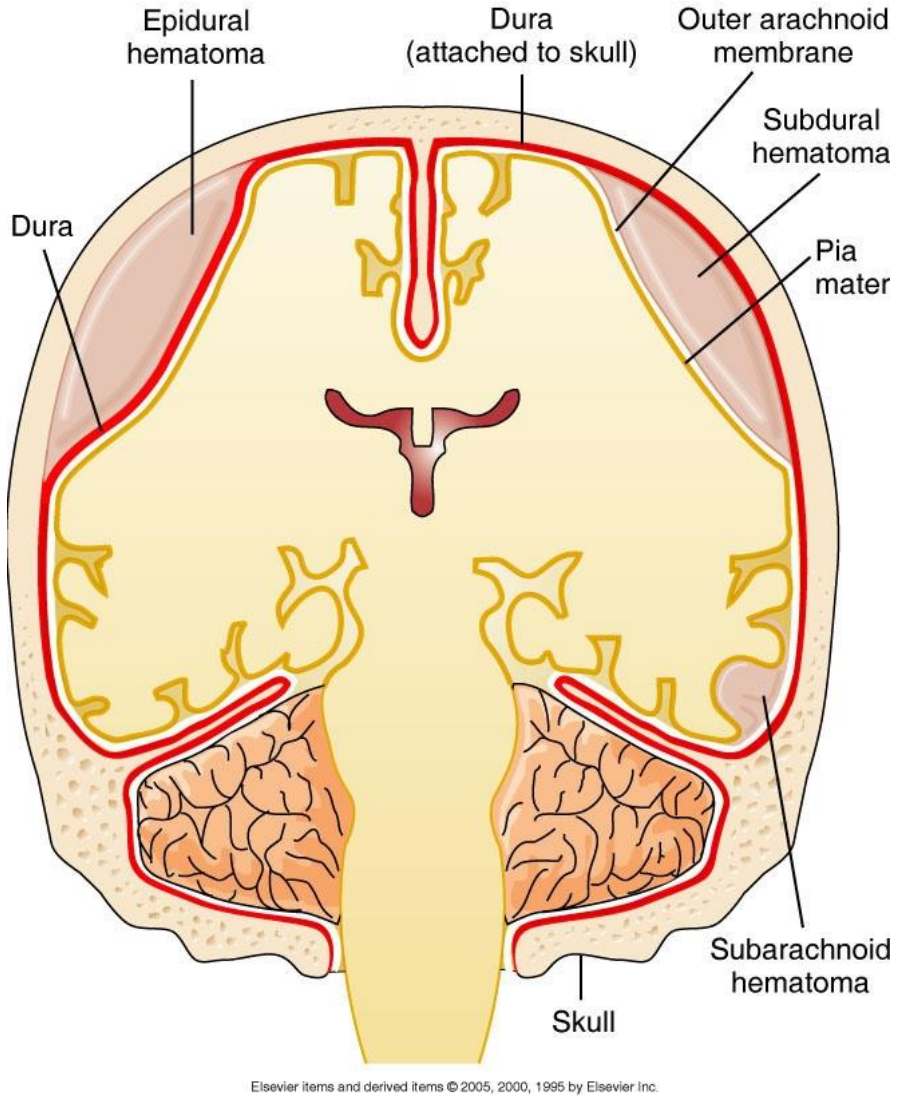
Bridging veins (cerebral veins) carry blood from the surface of the brain across the meninges and into the dural venous sinuses. In this diagram a torn bridging vein causes a subdural hematoma.



Traumatic Brain Injury (TBI)

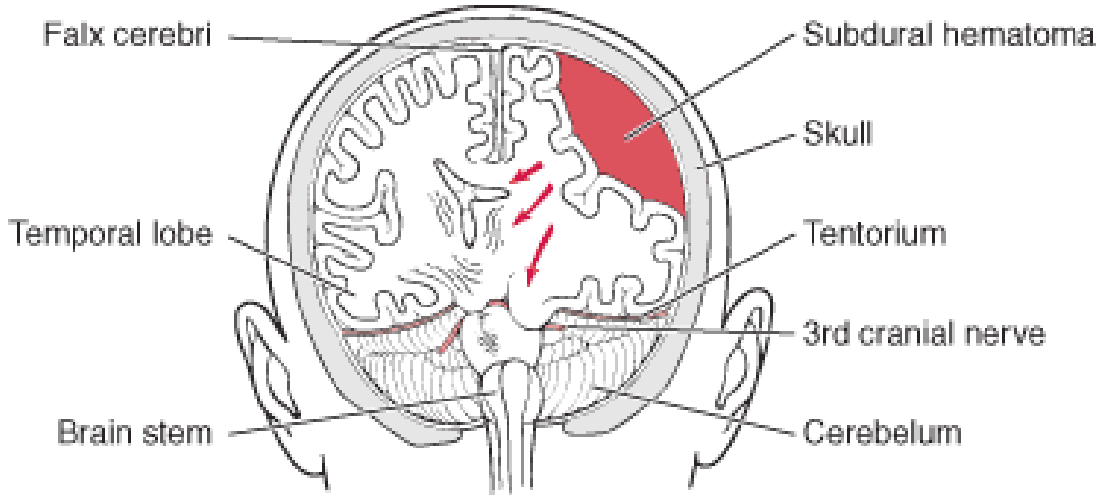
SDH=subdural hematoma.
EDH=Epidural hematoma.



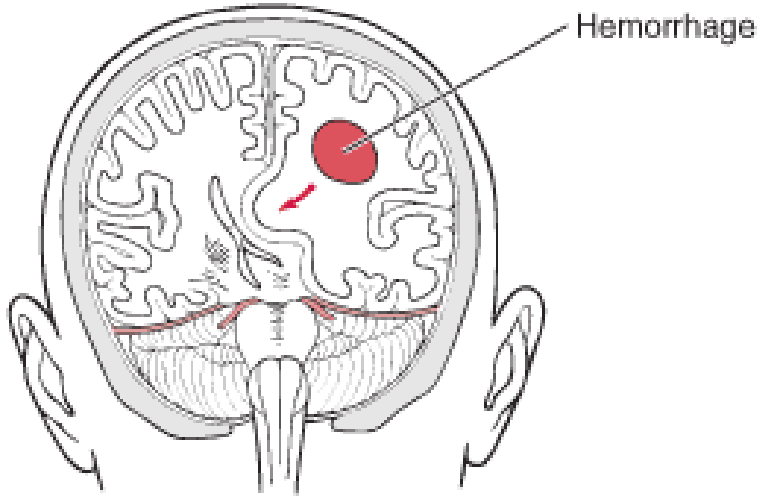


Traumatic Brain Injury (TBI)

Hematoma and Herniation



Tentorial Herniation



Subfalcine Herniation

Traumatic Brain Injury (TBI)

Treatment of TBI

•Cardiopulmonary stabilization first!

•Radiologic screening: CT scan to detect skull fracture, hematoma, hydrocephalus etc.

•Surgical decompression: craniotomy to relieve elevated ICP, insertion of ICP (intracranial pressure) monitors, CSF drainage devices

•Management of elevated ICP to maintain adequate CPP (central perfusion pressure)**. Remember, if ICP climbs too high, blood vessel compression occurs and brain capillary beds do not perfuse with blood properly because CPP is too low**. (MAP-ICP=CPP)

•The goal is to maintain normal blood pO2, pCO2 and glucose, and normal fluid volume with a CPP value no lower than 60 mm Hg.

•Repeated radiological examination is done to determine possible new lesions.

•Elevated ICP in the acute period is usually managed by administration of **mannitol**, an osmotic diuretic (Diuretics pull fluid into the urine.).

•Other treatments to **reduce intracranial pressure** include sedation, hypothermia (to reduce the rate of cellular respiration and pCO2) and mild hyperventilation (reduce pCO2), NMDA receptor blockers are used to reduce glutamate excitotoxicity. Drug-induced coma hypothermia (to reduce the rate of cellular respiration and pCO2) may be tried if ICP remains high.

•**Antibiotics** are used to prevent CNS infection in the case of open skull fracture

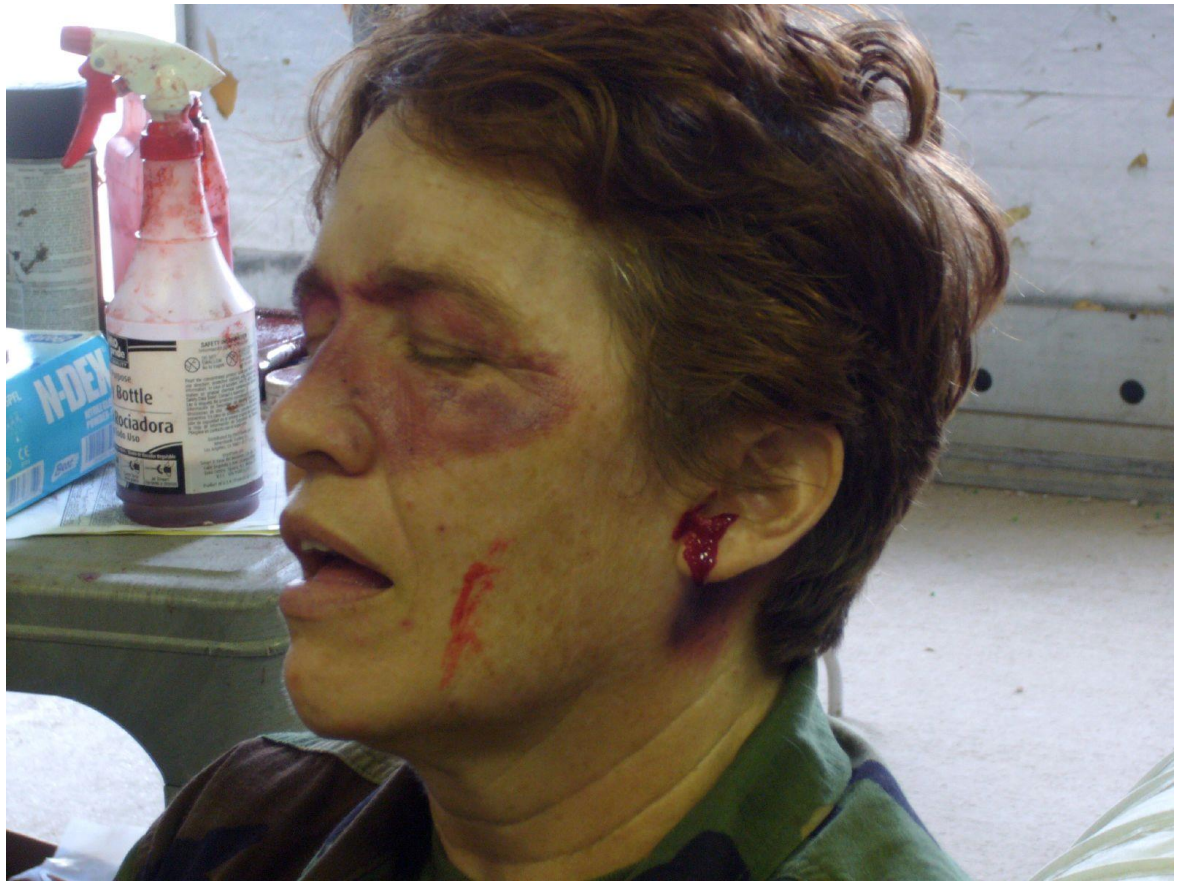
Traumatic Brain Injury (TBI)

Treatment of TBI

- Patients who have clear fluid (cerebral spinal fluid) draining from the nose or ears should be evaluated for **basilar skull fracture**. Such fractures are usually not visible by routine CT scan and increase the risk of cerebral infection.
- CSF on tissue paper creates a **"halo effect"** as it separates into layers due to its high glucose content. Ordinary nasal mucus does not separate in such a manner.
- Basilar skull fracture produces bilateral periorbital hematomas (black eyes aka **"raccoon sign"**) and bruising under the ears (**"battle sign"**).

Traumatic Brain Injury (TBI)

Basilar Skull Fracture
Raccoon Sign and Battle Sign



Cerebrovascular Disease and Stroke

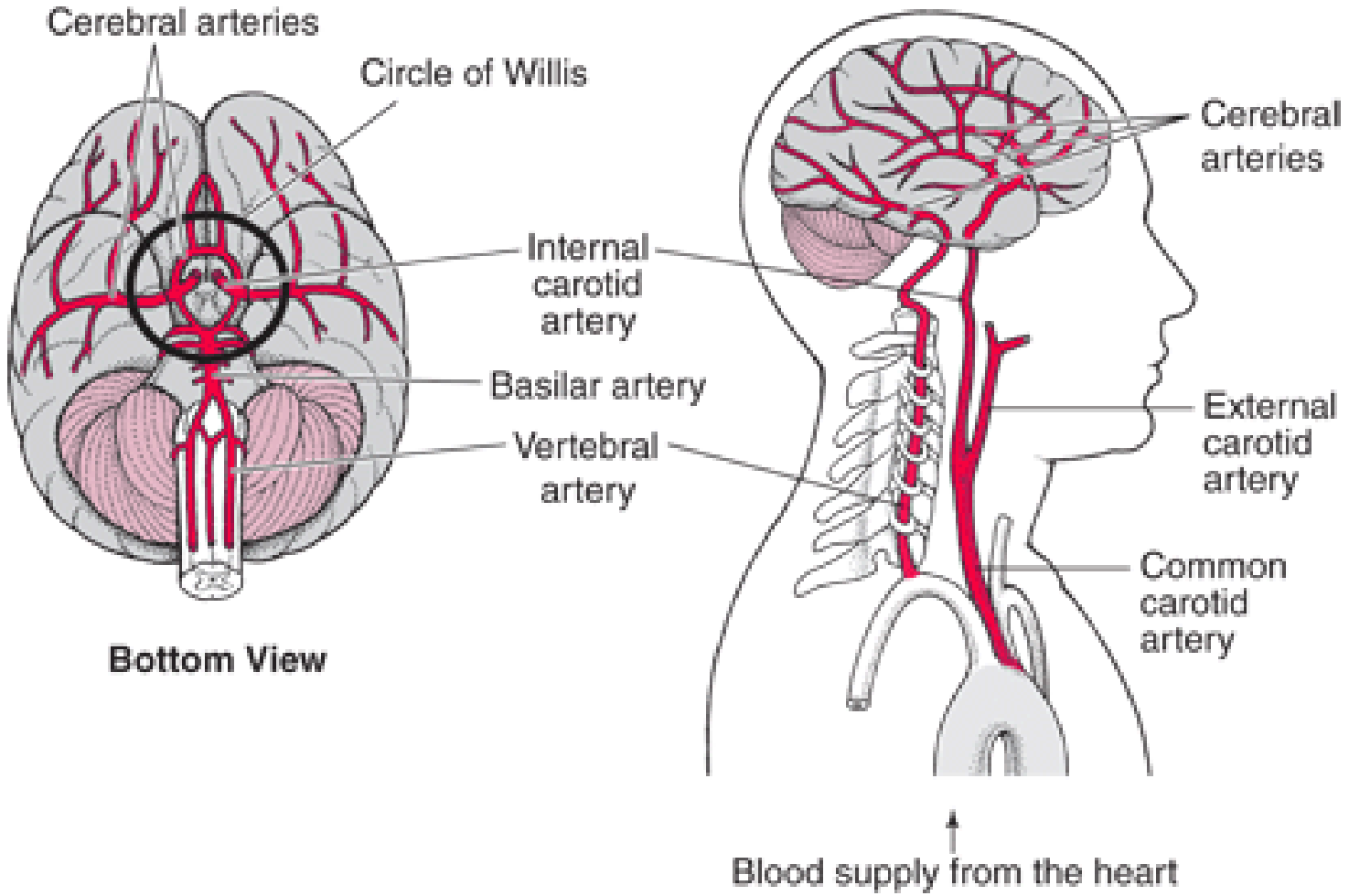
- Cerebrovascular diseases cause abnormalities of cerebral perfusion.
- A **stroke** is a cerebrovascular event that results in localized brain infarction (death of tissue).
- Stroke is the **third leading cause of death i**n the US and the leading cause of severe disability in the US.
- The majority of victims survive with most requiring long term care and rehab.
- Of those who survive longer than 6 months 50% have hemiparesis, 35% are clinically depressed, 30% cannot walk, 26% are institutionalized and 19% are aphasic (have language disorders).
- **Risk factors** for stroke: hypertension, diabetes, hyperlipidemia, smoking, advancing age, a previous stroke, and family history.

Cerebrovascular Disease and Stroke

Types of Stroke: Ischemic Stroke vs. Hemorrhagic

- Ischemic stroke is due to sudden occlusion of a **cerebral artery.**
- 88% of strokes are ischemic. There are two forms:
  - **Thrombotic strokes:** Ischemic strokes due to a thrombus in a cerebral artery, usually related to atherosclerosis.
  - **Embolic strokes:** Ischemic strokes due to an embolus (usually from a thrombus that formed on the heart wall or in a carotid artery) that travels from the site of its formation to the brain and occludes a cerebral artery. Atrial fibrillation increases the risk of embolic stroke by a **factor of 5**. Clots form in the left atrium if a leaky mitral valve is the cause of Afib.
- Neurologic deficits are evident within one minute.
- Ischemia for several minutes can cause irreversible cellular damage.
- **Middle cerebral artery** occlusion is the most common cause of ischemic stroke. That artery serves most of the cerebral cortex.

Cerebrovascular Disease and Stroke

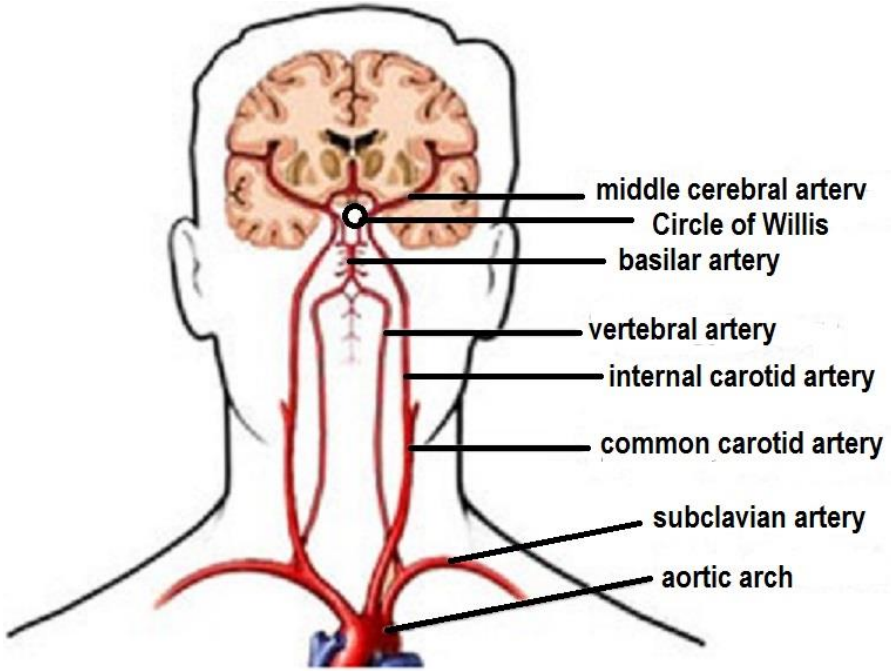


There are two major routes of blood flow from the heart to the **Circle of Willis.**

1. **Anterior Route**: via the internal carotid arteries
2. **Posterior Route:** via the vertebral arteries.

Cerebrovascular Disease and Stroke

Pathways of Blood Flow to the Brain

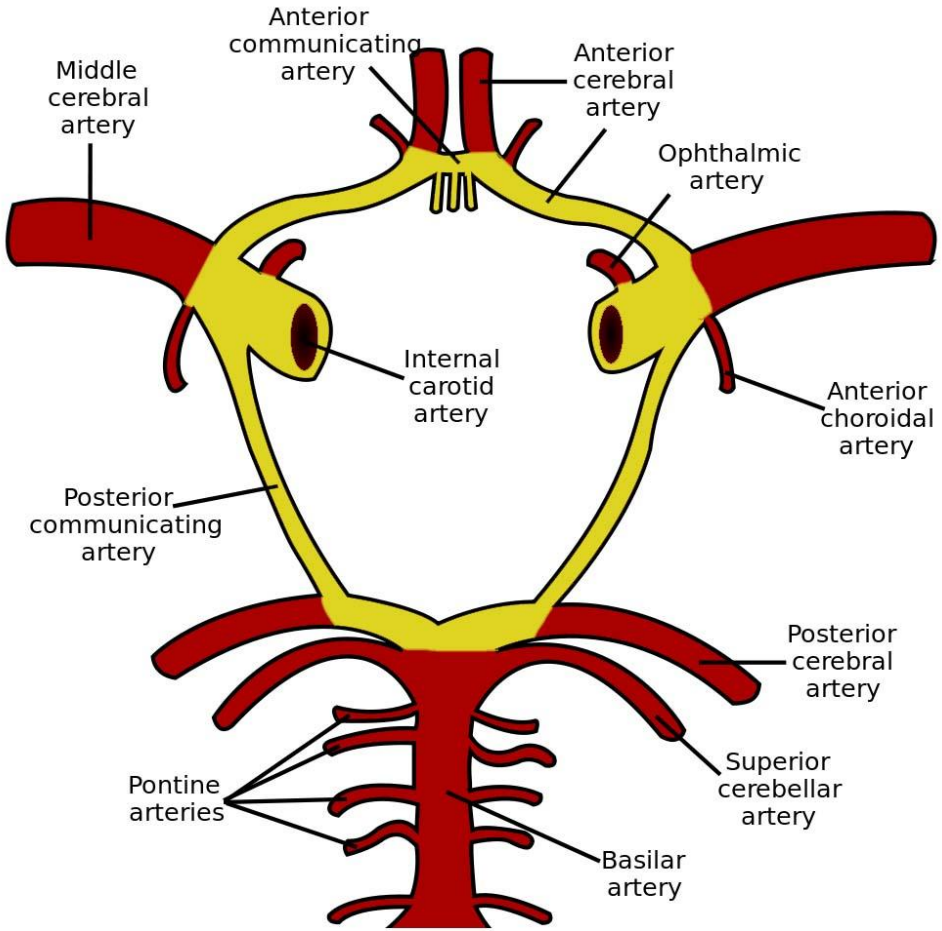


Anterior Route: aorta>L. common carotid artery>L. internal carotid artery>Circle of Willis **OR** aorta>brachiocephalic artery>R. common carotid artery> R. internal carotid artery>Circle of Willis

Posterior Route: aorta>L. subclavian artery>L. vertebral artery>basilar artery>Circle of Willis
OR
Aorta>brachiocephalic artery>R. subclavian artery>R. vertebral artery>basilar artery>Circle of Willis

Cerebrovascular Disease and Stroke

The Circle of Willis



The **Circle of Willis** is a roundabout for cerebral blood flow.

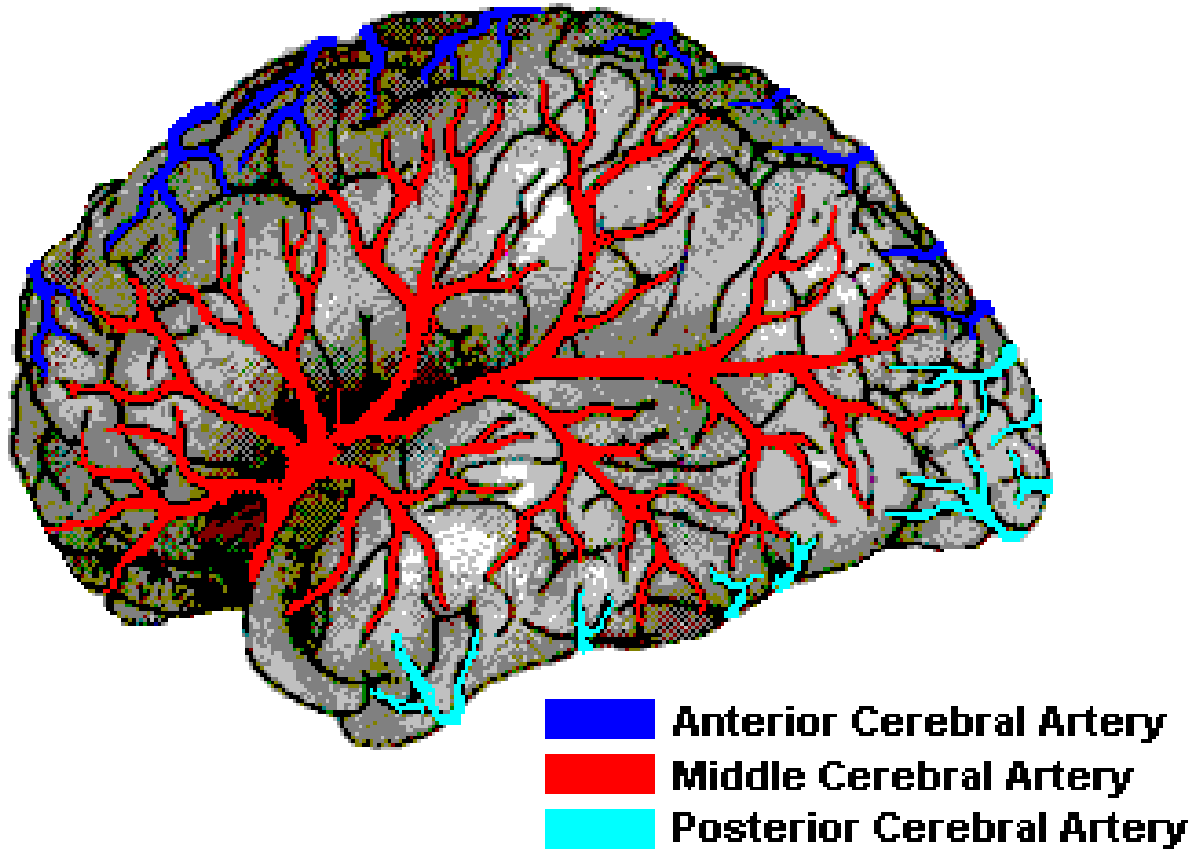
Note the relationship among the **internal carotid artery, the Circle of Willis (shown in yellow) and the middle cerebral artery (MCA).** The MCA is the artery that is most-often occluded in a stroke.

Note also that the **basilar artery** is formed by the union of the two vertebral arteries (as seen on the previous slide).

Cerebrovascular Disease and Stroke

Blood Flow to the Cerebral Cortex

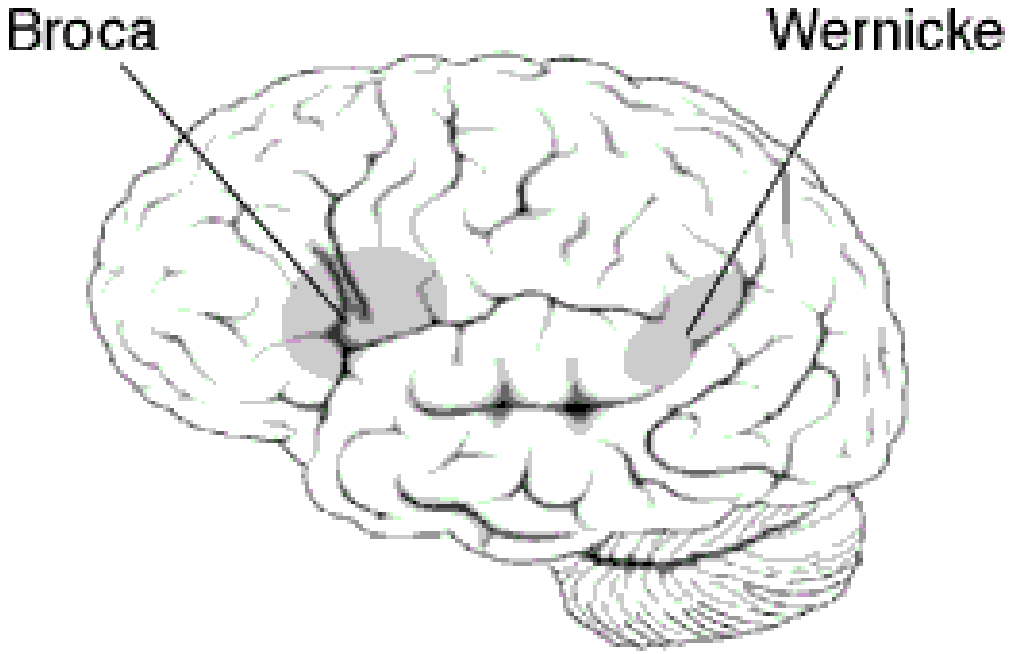
Note that the **middle cerebral artery** serves most of the cerebral cortex.



Cerebrovascular Disease and Stroke

Language Areas of the Cerebral Cortex

(Language Dominant Hemisphere is Usually Left.)



Front **Left Side View** Back

Cerebrovascular Disease and Stroke

Ischemic Events Other than Stroke:

- **Lacunar Infarcts**-occlusion of a small penetrating arteriole that serves a **subcortical** brain area.
  - Basal nuclei, pons, cerebellum, and internal capsule are common sites.
  - Prognosis for recovery is good.
  - Manifestations are often either purely motor or purely sensory.
- **Transient ischemic attack (TIA) aka "mini stroke"**
  - A brief occlusion of a cerebral artery; symptoms last less than 1 hour.
  - The clot is lysed by the fibrinolytic system before permanent damage occurs.
  - The occurrence of a TIA increases the risk of a true stroke about 10-fold.
  - TIA patients are started on daily aspirin therapy to prevent thrombus formation.
  - Carotid endarterectomy or carotid angioplasty is done if a carotid artery is occluded more than 70%.

Cerebrovascular Disease and Stroke

Manifestations of Middle Cerebral Artery Ischemic Stroke

- Areas served by the MCA: most of the lateral cerebral hemisphere, including its cortex, also the basal ganglia and the internal capsule.
- **Contralateral hemiplegia** (paralysis on side of the body opposite to the side of the brain damaged by the stroke)
- **Contralateral somatic sensory loss**
- **Aphasia**-speech problems (if stroke affects language areas of the cerebral cortex); the **LEFT** side of the cortex for most people.
- **Contralateral homonymous hemianopsia** (blindness in contralateral half of the visual field in both eyes). You will learn more about blindness later in the module.
- **Neglect syndrome**-For example, the patient doesn't realize that an affected (paralyzed) limb belongs to his or her body. Partial blindness contributes to neglect of body parts**.**

Cerebrovascular Disease and Stroke

Hemorrhagic Stroke

- Hemorrhagic stroke is due to bleeding from vessels into the brain tissue (intracerebral hemorrhage). The tissue normally served by those vessels is deprived of blood.
- This is usually due to capillary damage caused by high blood pressure.
- Hemorrhagic strokes are less common than ischemic strokes.
- They have a **higher rate of morbidity and mortality** than ischemic stroke.
- Most hemorrhagic strokes occur in the **basal nuclei or thalamus.**
- If the hemorrhage is large, it may significantly increase ICP leading to herniation and death.

Cerebrovascular Disease and Stroke

Treatment of Stroke

- **Respiratory and cardiovascular function** are assured first, then tests for neurological deficits, then CT scan to determine type.
- **In hemorrhagic stroke**
  - BP is often extremely high.
  - Bringing BP down into normal range could result in ischemia.
  - Best to keep the patient mildly hypertensive to keep CPP up.
- **In ischemic stroke**
  - 325 mg of aspirin is administered immediately to reduce platelet aggregation.
  - Patients who are candidates for thrombolytic (tPA-tissue plasminogen activator) therapy undergo CT scan first to rule out any hemorrhagic source.
  - Patients who have received thrombolytic therapy should NOT receive anticoagulant therapy (heparin-activates antithrombin III). The risk of bleeding is too high.
  - Clotting parameters must be monitored as a significant number of ischemic strokes convert to hemorrhagic lesions.

Cerebrovascular Disease and Stroke

Prevention of Stroke Recurrence

- For **hemorrhagic** stroke-careful monitoring of blood pressure and institution of life style changes
- For **embolic ischemic** strokes-control of dysrhythmias, anticoagulation therapy. Atrial fibrillation may be treated with medications, electrical cardioversion or radio ablation. If the source of the A-fib is a faulty mitral valve (mitral regurgitation), surgery to repair or replace the valve may be indicated.
- For **thrombotic ischemic** strokes-lifestyle modification including smoking cessation and lowering of serum lipids along with anticoagulation therapy. If carotid occlusion exists, carotid artery endarterectomy or angioplasty with stent insertion may be done. Thrombotic strokes and heart attacks have similar risk factors.

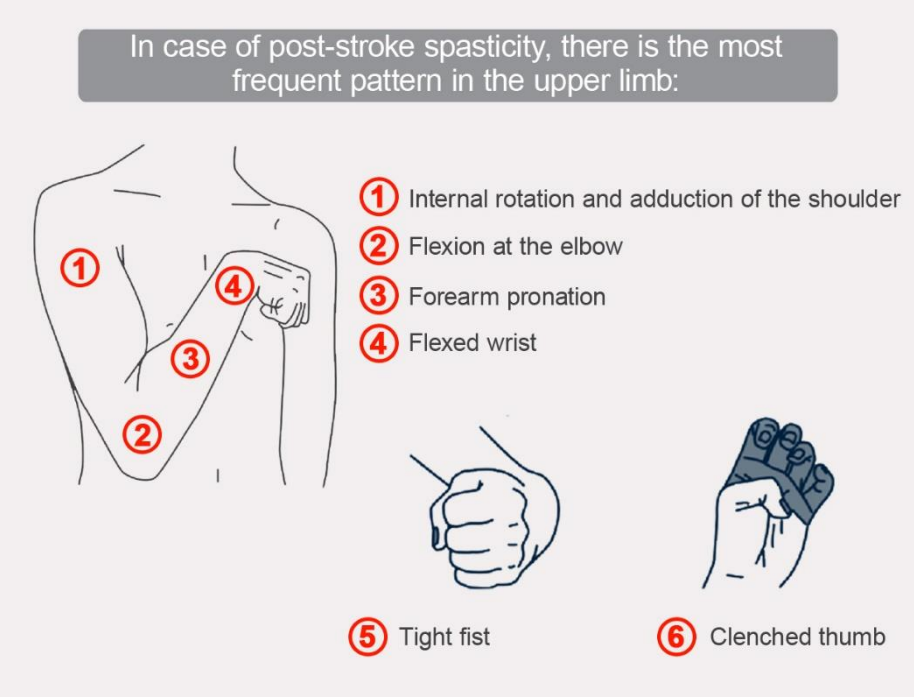
NOTE: It is extremely important to determine the TYPE of stroke before treatment. Using anticoagulants/antiplatelets/tPA for a hemorrhagic stroke would be a disaster!

Cerebrovascular Disease and Stroke

Stroke Sequelae Requiring Rehab

- **Motor paralysis** is commonly contralateral to the side of brain on which the stroke occurs due to decussation of motor fibers.
  - Initially paralysis is **flaccid** (Muscle tone is reduced or absent). Therapy is required to **prevent atrophy**: range of motion exercise (passive), elevation of edematous limbs, elastic stockings.
    - **Footdrop**, outward rotation with dependent edema, is common in lower extremity paralysis.
    - **Subluxation of the shoulder joint** may occur in upper extremity paralysis, if the arm is not supported.
  - After about six weeks motor function may begin to return in the form of **spasticity** (Muscle tone is increased and causes resistance to passive stretch.). Range of motion exercises (passive and active) are required to **prevent contractures.**
    - Increased **flexor** tone is common in the upper extremity (reduced extension ability). Contracture of the wrist is often seen.
    - Increased **extensor** tone (reduced flexion ability) is common in the lower extremity.
    - Subluxation of the shoulder joint becomes painful.

Cerebrovascular Disease and Stroke



Spastic Paralysis:

Upper Limb Flexion

Lower Limb Extension

Cerebrovascular Disease and Stroke

Stroke Sequelae Requiring Rehab

- **Sensory** (somatic) impairment occurs in the same locations as the motor paralysis.
- **Aphasia** requires speech therapy.
  - **Broca aphasia** causes poorly articulated speech with a sparse vocabulary. The speech of others is usually comprehended.
  - **Wernicke aphasia** speech that is fluent, but empty of content. The patient also has difficulty comprehending the speech of others. Word finding and naming difficulties are common features of this type of aphasia.
- **Cognitive deficits** may occur depending on stroke location.
  - Diffuse cortical or subcortical injuries affect the ability to be alert, to concentrate, to remember, and to reason.
  - Patients who do not retain the ability to learn are unlikely to benefit from rehabilitation.

Cerebral Aneurysm

Etiology

- An aneurysm is a congenital defect in the **tunica media** (smooth muscle layer) of an artery that results in dilation and ballooning of a segment of the vessel.
- Intracerebral aneurysms are the most common cause of **subarachnoid hemorrhage.**
- About 15% of patients with ruptured cerebral aneurysms die before they receive medical attention.
- About 60% of patients who suffered a ruptured cerebral aneurysm either die or are permanently disabled.
- High blood pressure, acute alcohol intoxication, and drug use (especially cocaine) are thought to precipitate aneurysm rupture.

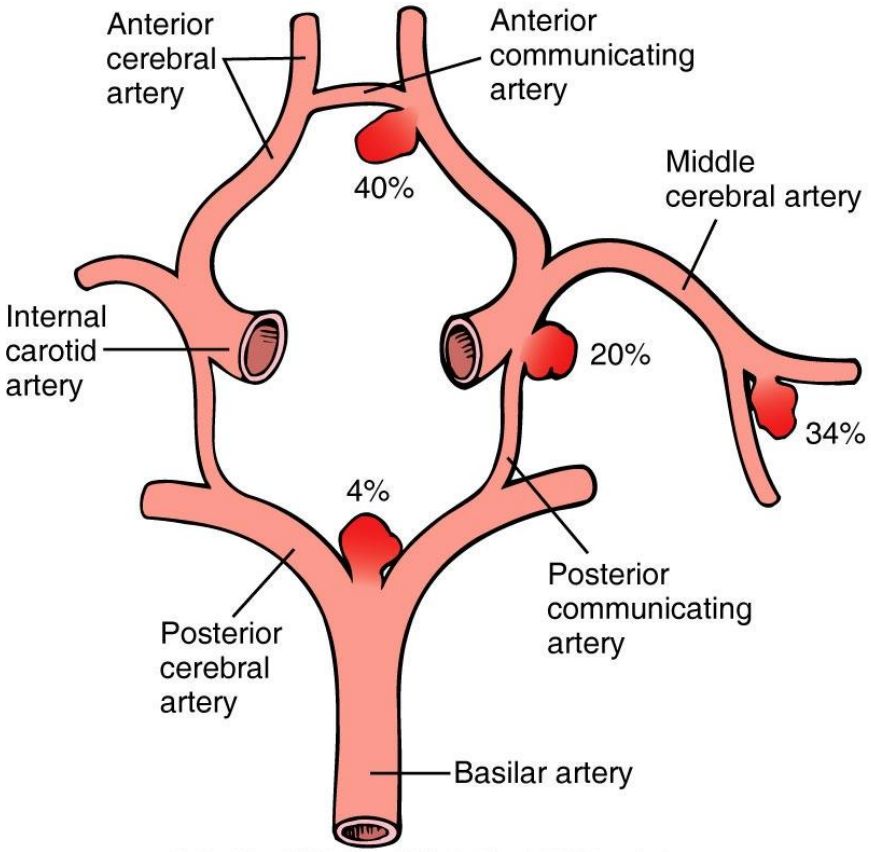
Cerebral Aneurysm

Pathogenesis

- Most (95%) of cerebral aneurysms are located in the **Circle of Willis.**
- **Warning leaks** may occur before rupture producing severe headache, photophobia, and stiff neck.
- **Pain** is due to the irritating effect of blood in the CSF.
- Rupture of an aneurysm causes a rush of blood into the **subarachnoid space**, raises ICP, and distorts brain structure.
- **Secondary cerebral vascular spasm** occurs from day 4 to day 14, reducing blood flow and causing ischemia and possibly infarction.
- The risk of **re-bleeding** is highest during the first 14 days after rupture.
- There is also a risk of **hydrocephalus** due to obstruction of flow of CSF by clotted blood in the subarachnoid space.

Cerebral Aneurysm

Most Common in the Circle of Willis



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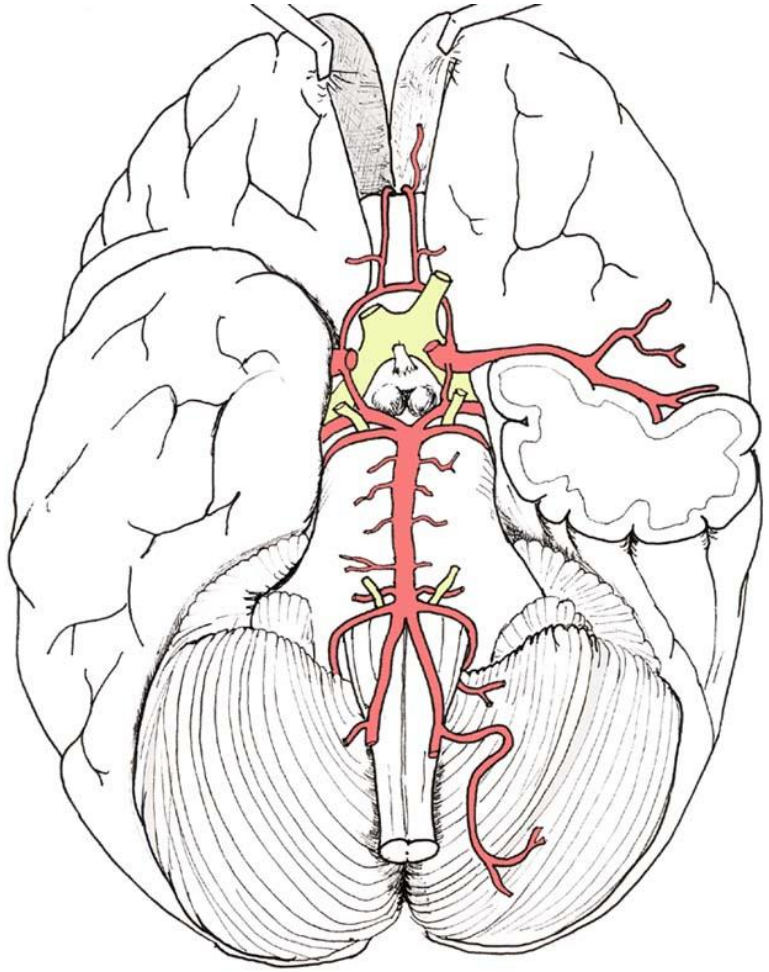


Cerebral Aneurysm

Diagnosis

- Unruptured aneurysms are often asymptomatic.
- Some patients experience:
  - Dilated pupils
  - Double vision
  - Pain above and behind the eye
  - Localized headache
- Ruptured aneurysms produce **excruciating** head pain due to blood in the CSF.
- Ruptured aneurysms are diagnosed by CT or MRI.
- If the scan is negative, but suspicion is high, a lumbar puncture is done to test for the presence of blood in the CSF.
- A **cerebral angiogram** is obtained to locate the site of the rupture in preparation for surgical intervention.

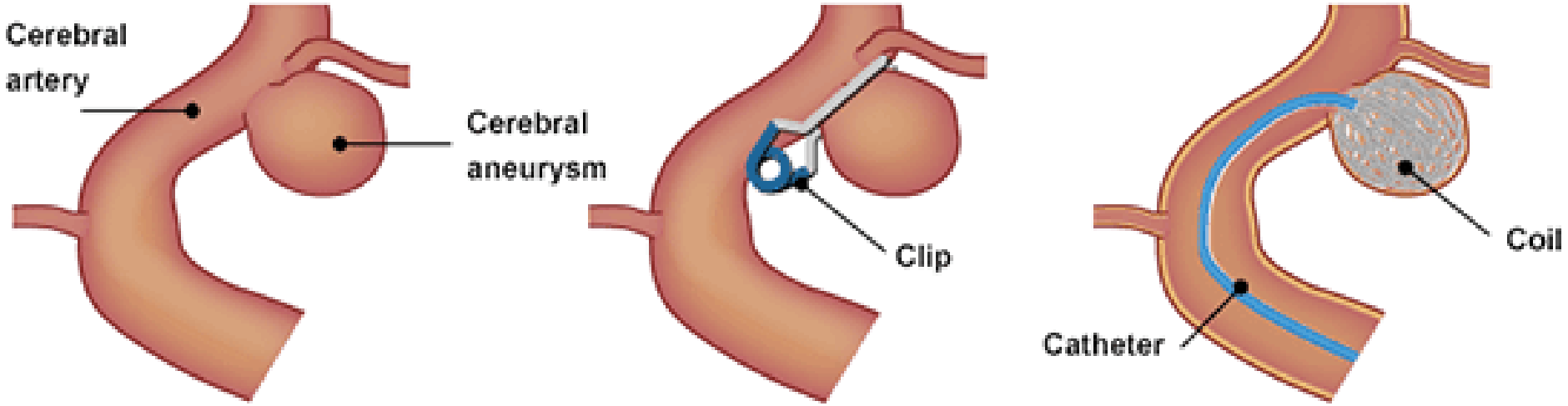
Cerebral Aneurysm

Treatment to Prevent Rupture or Stop Bleeding

- Medical Therapy
  - Smoking cessation and blood pressure management
- Surgical Therapy (Clipping)
  - The **skull is opened** to allow the surgeon to access the aneurysm.
  - A clip is inserted at the base of the aneurysm.
- Endovascular Therapy (Coiling)
  - A **catheter** may be placed inside the affected artery and used to place tiny coils of wire into the aneurysm. This promotes thrombus formation within the aneurysm.
- Frequent neurological monitoring is essential to detect the first signs of deterioration in clips or coils.

Cerebral Aneurysm

Management of Brain Aneurysm



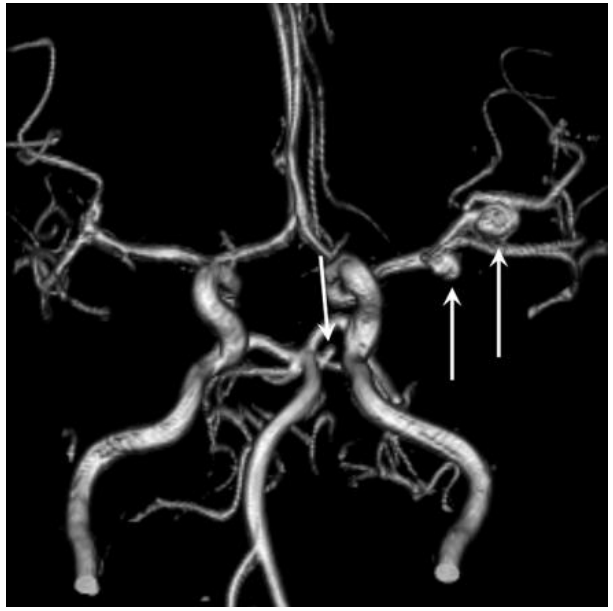
Pre-treatment

Brain surgery: Clipping of the cerebral aneurysm

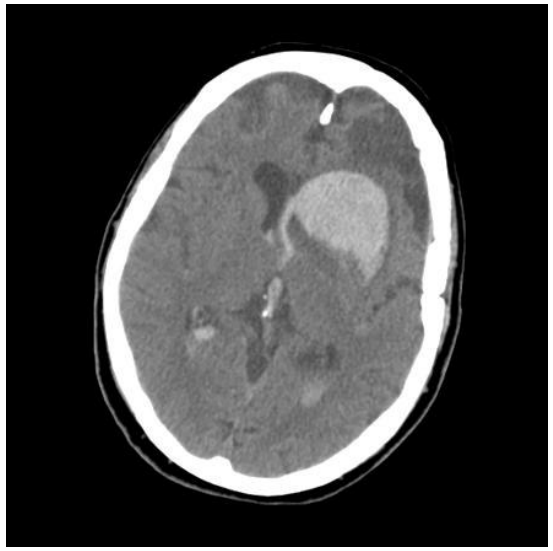
Catheter intervention: Coil embolization of the cerebral aneurysm

Cerebral Aneurysm

Cerebral Angiogram:
Multiple Aneurysms in and near the Circle of Willis



CT Scan:
Ruptured Cerebral Aneurysm



Arteriovenous Malformation (AVM)

Etiology and Pathogenesis

- Capillaries fail to develop between an arteriole and a venule so that the arterial blood is shunted directly into the venous system.
  - Exposure of the high-capacitance venous system to the high pressure of the arterial system causes the venous vessels to enlarge.
  - The arteries and veins that feed and drain the lesion also enlarge.
  - Eventually the AVM becomes a congested mass of enlarged vessels.
- AVMs are second most-common cause of subarachnoid hemorrhage.
- Most (90%) are found in the cerebral hemispheres.
- Mortality is much lower than that from ruptured aneurysms.

Arteriovenous Malformation (AVM)

Clinical Manifestations

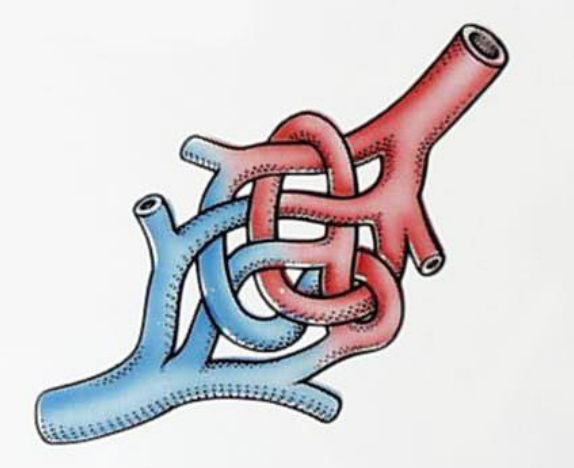
- Hemorrhage in 50% of cases
- Seizure in 25% of cases
- “Vascular steal syndrome” in 25% of cases; the AVM "steals" blood from surrounding tissue causing ischemia.

Treatment

- If possible the AVM is surgically removed.
- For deep or very large AVMs irradiation (gamma knife, for example) and catheterization and coiling or glue embolization may be used.
- Ruptured AVMs are treated in much the same way as ruptured cerebral aneurysms.

Arteriovenous Malformation (AVM)

Large Cerebral AVM



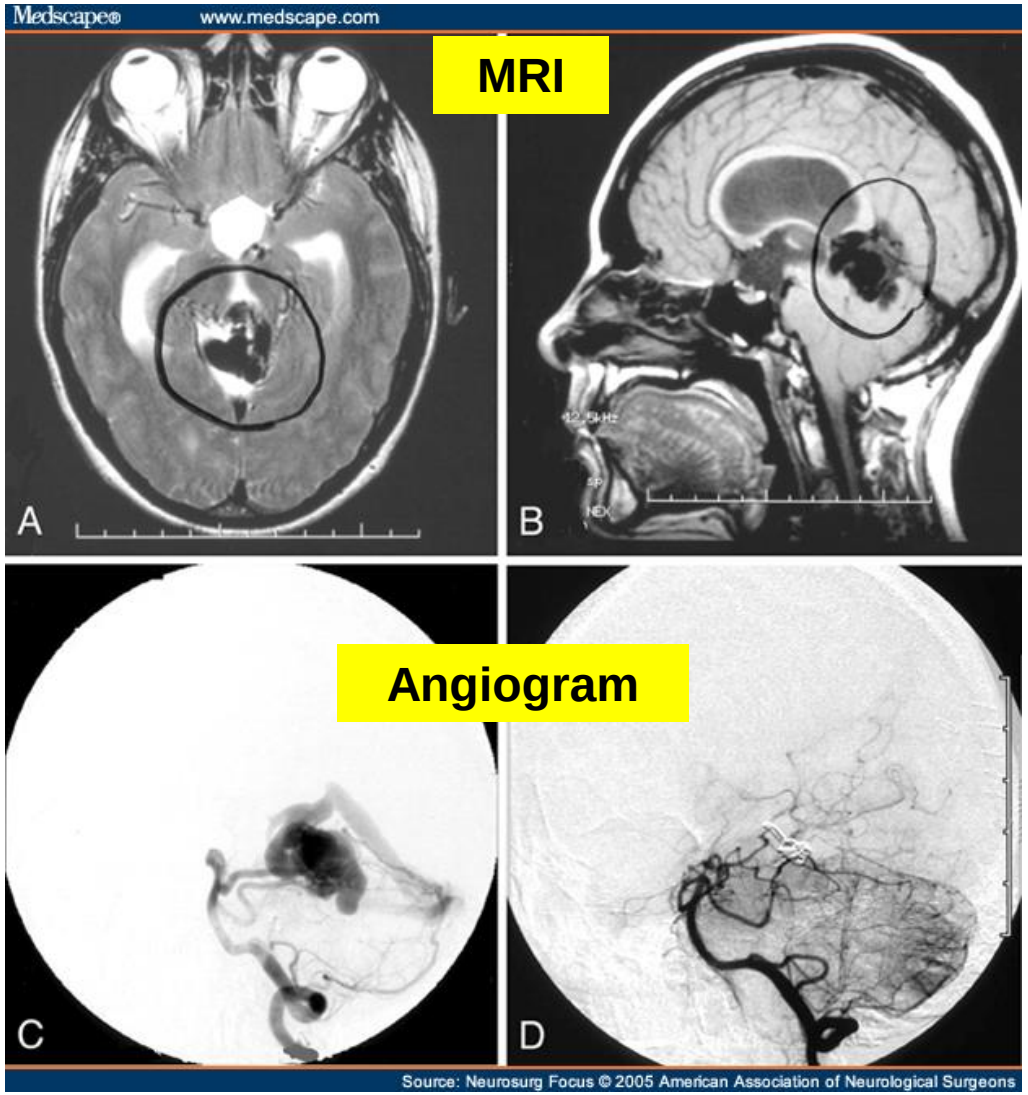


Image D is post-surgery. Rupture occurred during surgery. The patient did not survive.

Central Nervous System Infections: Meningitis

Etiology

- Meningitis is inflammation of the meninges, usually due to infection.
- **Usually bacterial** infection, but may be viral, fungal or parasitic infection (especially in immunocompromised individuals).
- In adults *Streptococcus pneumoniae* is most often causative. *Neiserria meningitidis,* if causative, has a poorer outcome.
- *Haemophilus influenza B* was formerly the most common cause of meningitis in children, but the **HIB vaccine** has changed that.
- Portals of entry: via the bloodstream or by extension from the paranasal sinuses, ears, skull fracture sites or neurosurgery sites.
- Mortality is highest in elderly patients.
- Survivors have 11%-19% chance of ongoing neurological deficits.

Central Nervous System Infections: Meningitis

Pathogenesis

- Bacterial meningitis is a pyogenic (pus making) infection that invades the pia mater, arachnoid mater and subarachnoid space.
- The infection travels readily around the brain and the spinal cord in CSF. Communicating hydrocephalus may result.
- Exudate may extend to blood vessel and cranial nerve sheaths.
- May cause brain abscess formation.

Clinical Manifestations

- Meningimus (headache, fever, stiff neck)
- Confusion and delerium; about one third of patients have seizures.
- Cranial nerve involvement is common and manifests as photophobia, ocular palsy, facial weakness, deafness, and/or vertigo.

Central Nervous System Infections: Meningitis

Diagnosis

- Diagnosis is made by lumbar puncture.
- Bacteria will likely be present.
- Gram stain will reveal the causative organism.
- CSF contains 1,000-10,000 WBCs/mm^3; mostly neutrophils. Normal is <10 WBCs/mm^3
- CSF contains **decreased glucose and greatly increased protein.**
  - Bacteria deplete CSF glucose.
  - Damage to BBB (blood brain barrier) and antibody production increases protein content.

Central Nervous System Infections: Meningitis

Treatment

- Supportive care and IV antibiotics

Complications

Visual impairment, optic neuritis, deafness, headache, seizure, personality changes, motor weakness, hydrocephalus, endocarditis, and pneumonia. CNS injury is largely due to inflammatory responses.

Prevention

- Prompt management of sinusitis, mastoiditis, ear infections, and pneumonia
- Vaccination against *N. meningitidis*
- Vaccination against HIB in children provides long-term protection.

Central Nervous System Infections: Encephalitis

Etiology

- Encephalitis is inflammation of brain tissue due to infection.
- **Usually viral,** may be bacterial or fungal
- **Herpes simplex type-1 (cold sore virus)** is the most common viral cause. It typically affects adults. 50% of patients die or are left impaired.
  - **West Nile virus and Western/Eastern Equine virus** are also causative, usually in the summer months, most often in children and elderly adults. Consequences are less serious than with HSV-1 encephalitis.
  - West Nile and Western Equine viruses are transmitted chiefly by **infected mosquitoes**. Birds are the preferred host. Infections occur in both horses and humans.

Central Nervous System Infections: Encephalitis

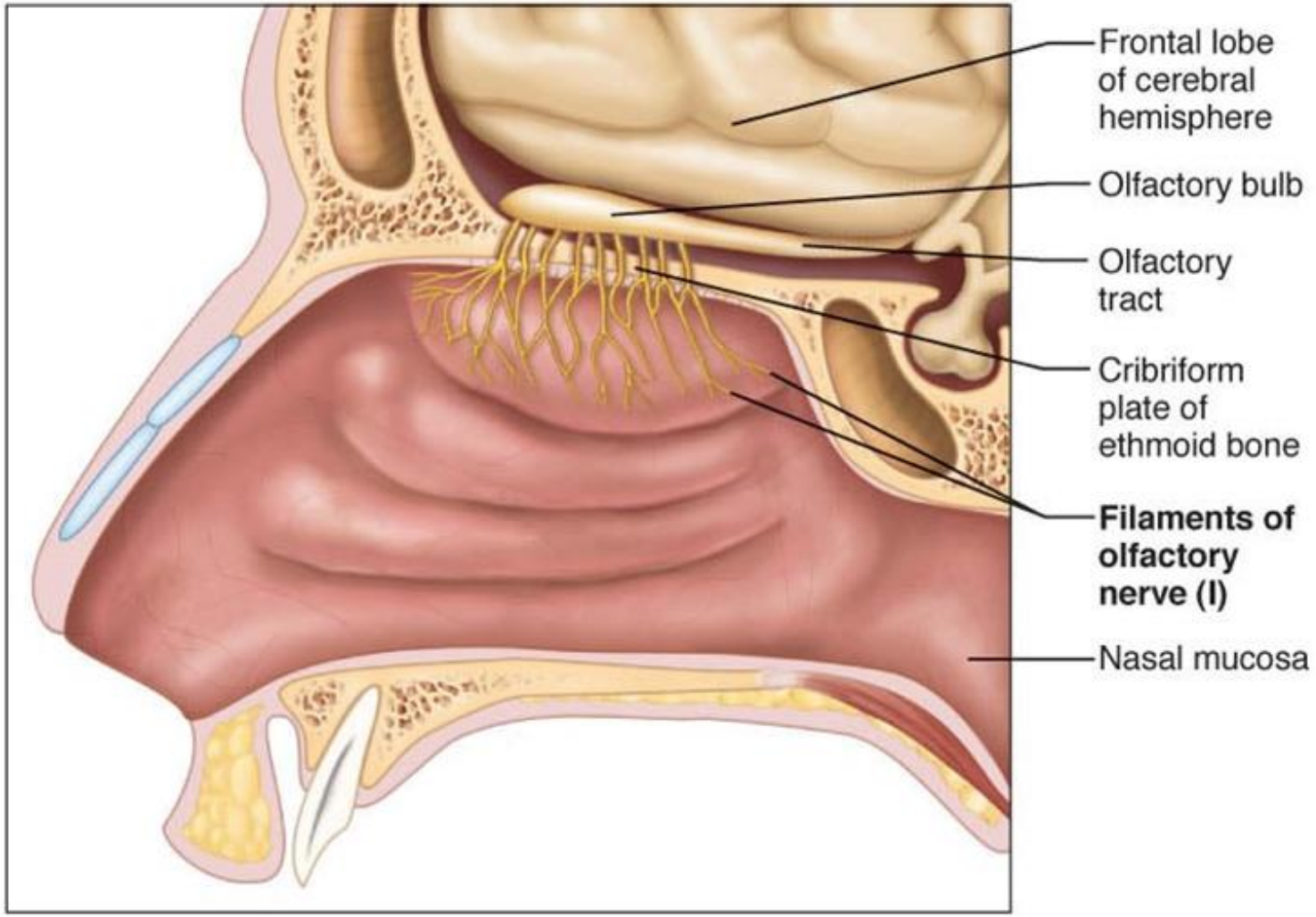
Pathogenesis

- **HSV-1** usually infects the nose/nasal cavity and travels into the fibers of **cranial nerve I (olfactory),** along the olfactory tracts, across the BBB and into brain tissue. (The virus may lie dormant in the ganglia of **cranial nerve V (trigeminal)** and then be reactivated.)
- The virus infects and kills neurons leading to inflammation. HSV-1 causes hemorrhagic necrosis of medial areas of the temporal and frontal lobes.
- The mechanism used by West Nile and Equine viruses to cross the BBB is unclear.

Clinical Manifestations

- Malaise, headache, stiff neck, photosensitivity, vomiting, confusion, delirium, weak muscles, and unsteady gait. A moderate fever develops and headache becomes more severe.

Central Nervous System Infections: Encephalitis Portal of Entry



Central Nervous System Infections: Encephalitis

Diagnosis

- Diagnosis is made by lumbar puncture. (See table next slide.)
  - CSF shows normal or mildly elevated WBCs
  - CSF contains small increases in protein with normal glucose level.
  - Some infections allow detection of antiviral antibodies in serum or CSF.

Treatment

- Supportive care and monitoring in accordance with symptoms.
- Corticosteroids, anticonvulsants, analgesics, and antipyretics may be given. HSV-1 encephalitis is treated with acyclovir.

Diagnostic Lumbar Puncture:

Bacterial Meningitis vs Viral Encephalitis

STUDENTS: Know these differences!

CSF	WBCs	Glucose	Protein
Bacterial Meningitis	**Greatly increased due mostly to elevated neutrophils**	**Decreased**	**Increased**
Viral Encephalitis	**Normal to slightly increased due to elevated lymphocytes**	**Normal**	**Slightly increased**

Brain Abscess

Etiology

- A collection of pus with a fibrous capsule embedded in brain tissue.
- Most are due to bacterial infections: streptococci, staphlococci and anaerobes.
- Portals of entry: penetrating wounds, extension from a neighboring structure (sinus), blood

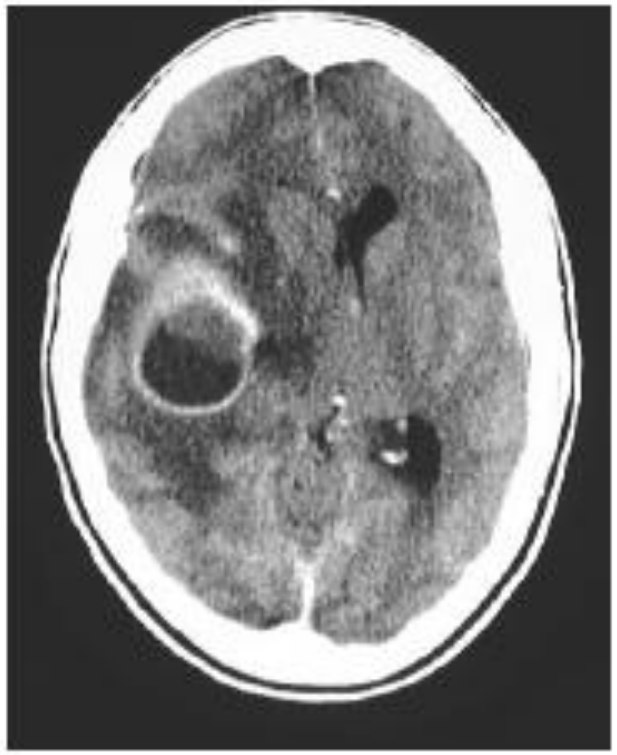
Pathogenesis/Diagnosis

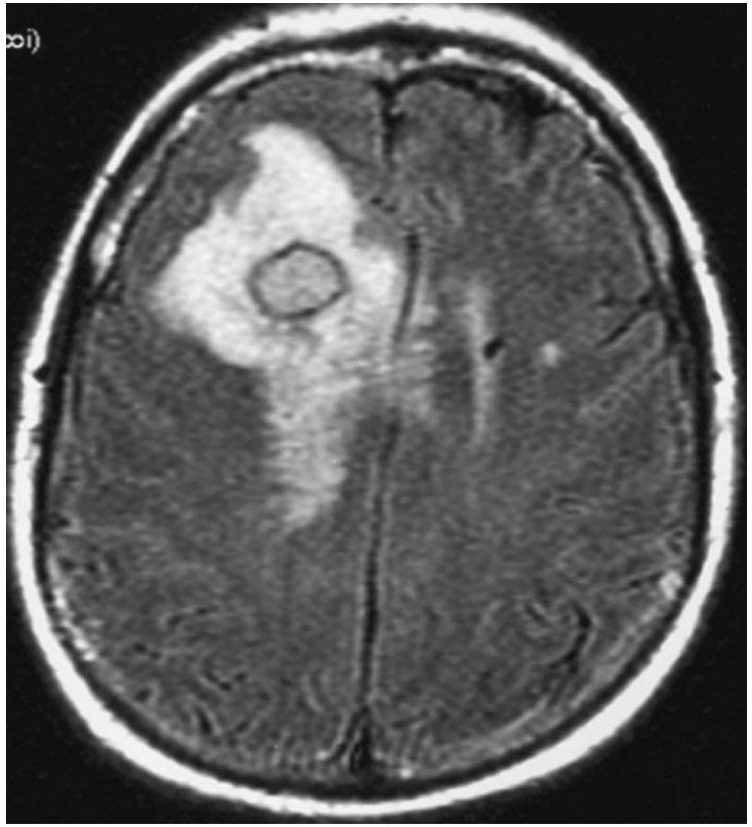
- Symptoms arise **1-4 weeks after** initial infection.
- Visible on CT scan as a round structure with a core (neutrophils at center, granulation tissue peripherally) and an outer ring (fibrous capsule). There is considerable edematous tissue surrounding the abscess.

Brain Abscess

Treatment

- Excision or drainage
- IV antibiotics for several weeks





From Grossman RI, Yousem DM: Neuroradiology, ed 2, St Louis, 2003, Mosby, p 285.

Lecture 7B
(Chronic Brain Disorders)
Seizure Disorders
Dementia
Parkinson Disease
Cerebral Palsy
Hydrocephalus
Cerebellar Disorders

Seizure Disorder

- **Seizure**-transient neurologic event of abnormal or excessive electrical discharge from neurons in the **cerebral cortex**; time between seizures is extremely variable; may be a single event; manifested by disturbances of skeletal motor function, sensation, autonomic visceral function, behavior or consciousness.
- **Epilepsy** refers to recurrent seizures. It affects 2 million Americans.

Seizure Disorder

Etiology

- Usually occur in conjunction with cerebral injury, a tumor, a blood clot, or an infection.
- Other causes: electrolyte/water imbalance, hypoxia, acidosis, alcohol withdrawal, drug overdose, or heavy metal toxicity.
- Seizures not associated with cerebral injury may be triggered by flashing lights, loud noises, rhythmic music, fever, exhaustion, emotional stress, menses, and inadequate nutrition.
- If no cause can be determined for a seizure it is called an idiopathic seizure.

Pathogenesis

- Alterations in membrane potential make certain neurons abnormally hypersensitive to changes in their environment.
- These abnormal neurons form an **epileptogenic focus** which functions autonomously, emitting large numbers of abnormal impulses. Neurons in the focus are able to **recruit** other local and distant (synaptically connected) neurons.

Seizure Disorder

Seizure Terminology

- **General Seizures:** The whole brain surface is involved at the outset. If the seizure spreads to the thalamus or RAS, it causes loss of consciousness.
- **Partial Seizures:** Only one hemisphere of the brain is involved. They may become general seizures.
- **Status Epilepticus**: series of seizures without a period of recovery in between. It can occur with any seizure type. Irreversible brain damage and death can occur if the seizure activity is not stopped.
- **Prodrome**: Some people have a sense of an impending seizure. This prodromal period may be characterized by myoclonic jerking, headache, lethargy, mood changes, palpitations, or epigastric sensations that precede the seizure by several hours.
- **Aura**: An odd movement or sensory experience occurs seconds before consciousness is lost, and it is remembered by the individual. The form of aura provides clues to the location of epileptogenic focus.

Seizure Disorder

7 Types of General Seizure

- **Absence or Petit Mal**: brief (2-10 sec), staring spell, occurs in children, may develop other seizure type later
- **Atypical Absence**: staring spell is accompanied by myoclonic jerks and automatisms (lip smacking)
- **Myoclonic**: extremely brief; single jerk or a few jerks of a one or more muscles
- **Atonic or Drop Attack**: sudden, complete loss of muscle tone
- **Clonic:** repeated jerking of a muscle or muscles; rare; more prolonged than myoclonic
- **Tonic:** sudden stiffening of a muscle or muscles
- **Tonic-Clonic or Grand Mal**: sudden loss of consciousness followed by three predictable phases.

Seizure Disorder

Grand Mal Seizure Phases

- **Tonic Phase (10-15 sec)**
  - The individual loses consciousness, usually falls, muscles become rigid, legs are extended, arms adducted (pulled close to the body).
  - Respiration is arrested and cyanosis may occur.
  - Bowel and bladder incontinence often occurs.
- **Clonic Phase (1 to 2 min)**
  - Individual is still unconscious. Violent, rhythmic muscle contractions occur, the eyes roll back, the face grimaces, and the pulse accelerates.
  - Salivation increases and patient may become diaphoretic.
  - The clonic phase ends with a deep inspiration.
- **Postictal Phase (may last several hours)**
  - Individual regains consciousness. There may be disorientation, confusion, headache, nausea.
  - The individual may sleep for several hours.
  - There is no memory of the event.

Seizure Disorder

Diagnosis

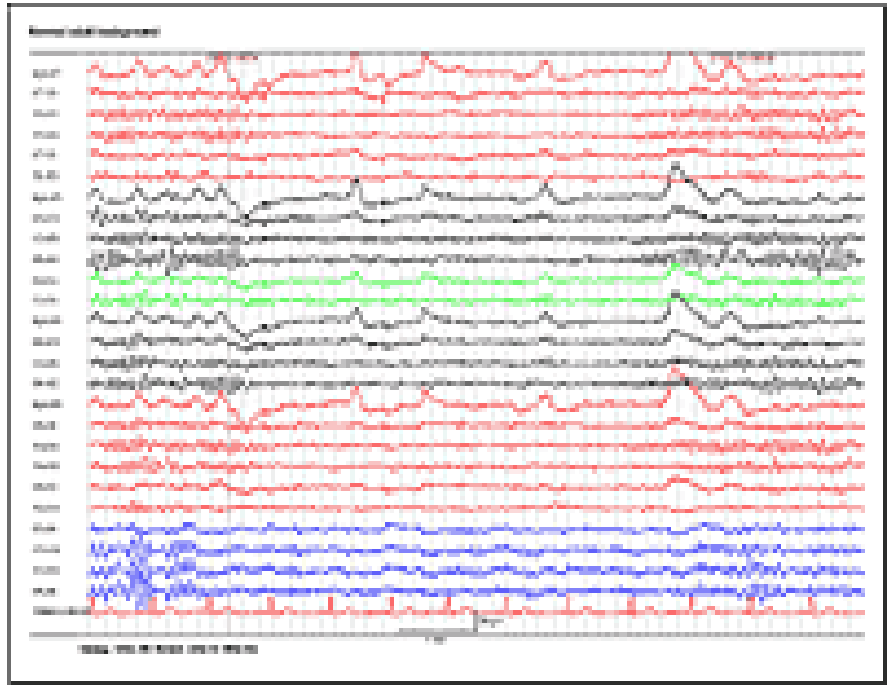
- Based on history, physical and neurological exam, EEG (electroencephalogram)
- Lab work may reveal metabolic causes
- CT or MRI may reveal structural causes.
- EEG is used to identify the type of seizure.

Treatment

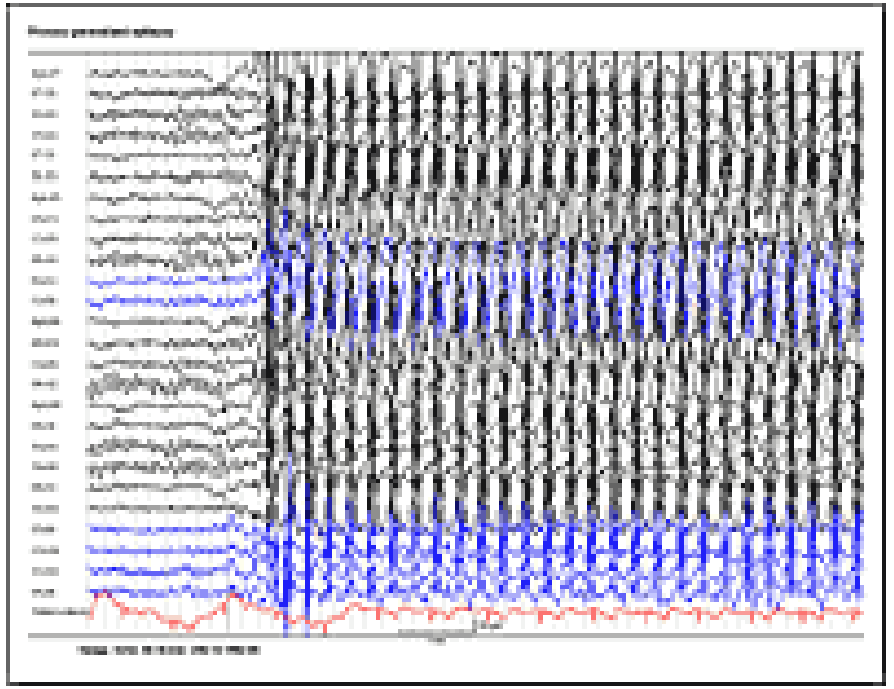
- Maintaining the airway; protecting the individual from injury
- Recording the course of the seizure is useful for treatment.
- Anticonvulsant medications specific to the seizure type are used until the patient is seizure free for two years.
- Surgical excision of the epileptogenic focus may be done if meds are not helpful.
- Patient education is important: avoid triggers and unsafe activity.

Seizure Disorder

NORMAL EEG



SEIZURE EEG



Dementia

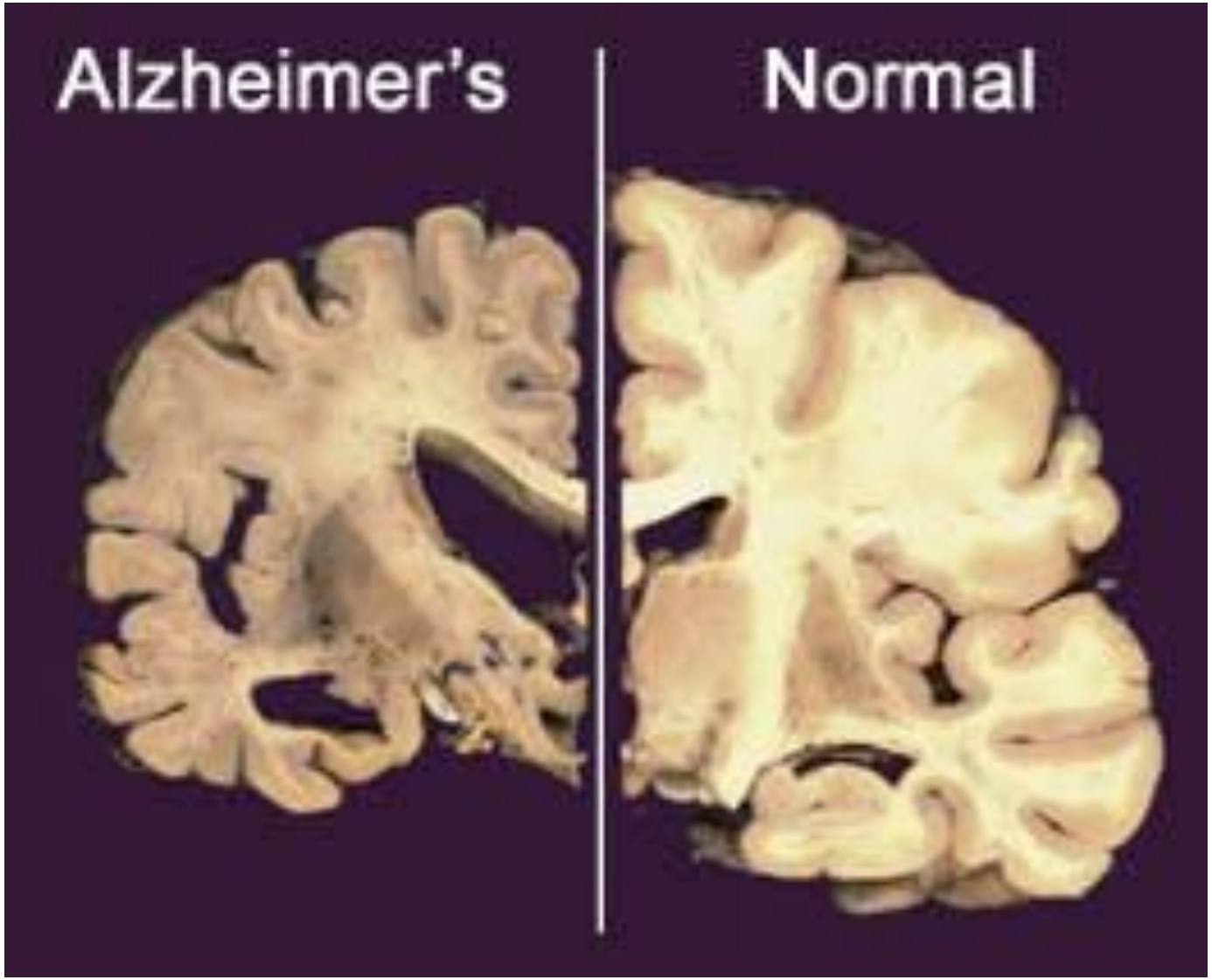
- **Dementia**-progressive deterioration of memory and other cognitive changes including changes in personality and behavior.
- **Alzheimer disease** underlies 60% to 80% of all cases of dementia.
  - 1 in 8 Americans over age 65 have AD. Women more than men.
  - Half of those over age 85 have AD.
- The second most-common cause of dementia is **vascular dementia**.
  - It results from single cerebrovascular events (such as infarctions), multiple lacunar infarcts or from microvascular pathology.
  - Studies suggest that vascular dementia predisposes one to developing late-onset Alzheimer disease.
- Alcoholism and many other brain disorders may lead to dementia.

Dementia: Alzheimer Disease

Pathogenesis

- Brain autopsy histology studies in Alzheimer disease shows two major types of lesions:
  - **Neurofibrillary tangles inside** neurons
  - **Amyloid plaques outside** neurons
- Tangles and plaques are accompanied by inflammation, complement activation, and activation of microglia and astrocytes.
- Autopsy shows **brain atrophy**. Brain weight decreases by up to 20% in advanced AD. Temporoparietal and anterior frontal lobe regions are most affected. Sulci and ventricles enlarge, and gyri atrophy.

Dementia: Alzheimer Disease



Dementia: Alzheimer Disease

Pathogenesis

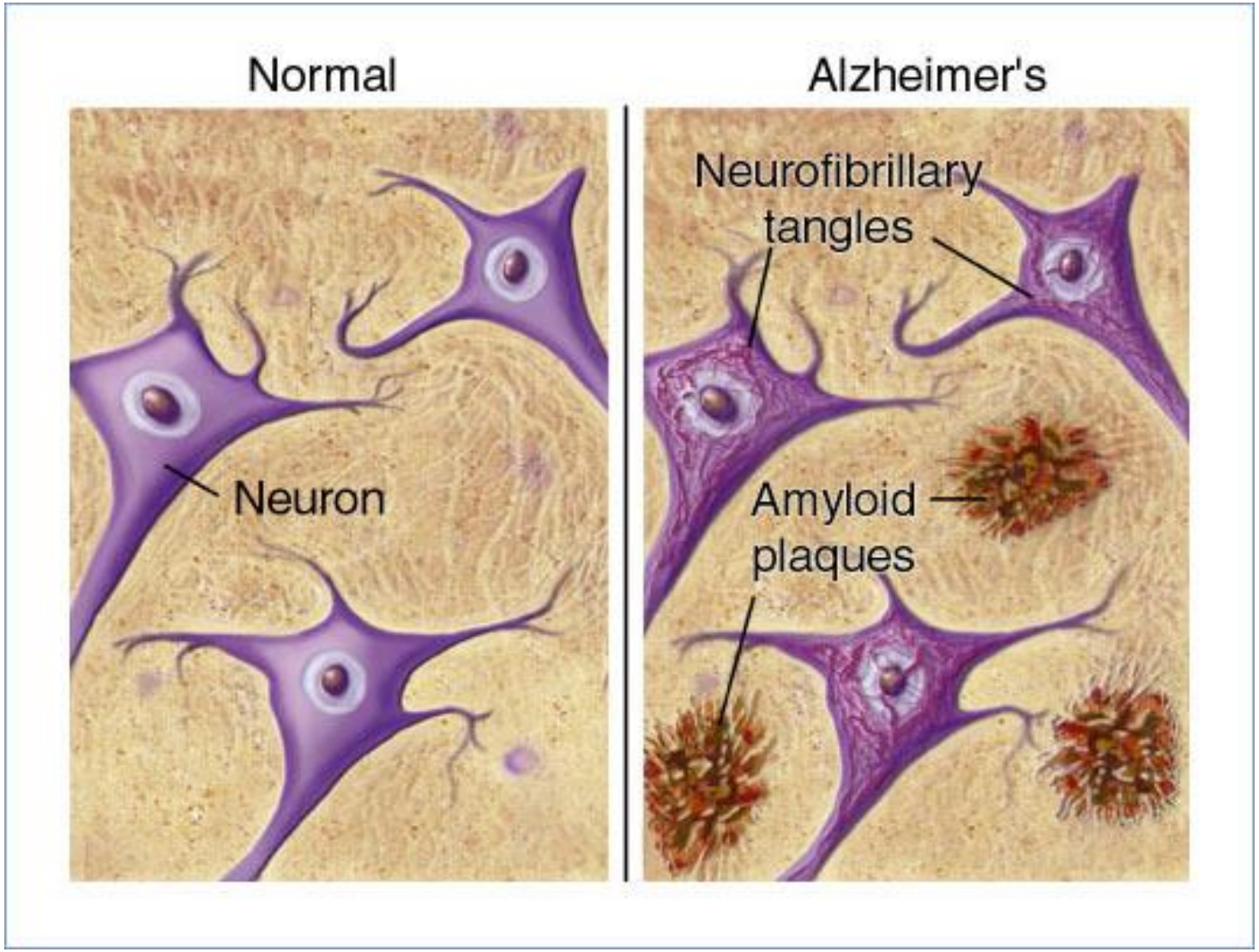
- **Hyperphosphorylated tau protein** is the main component of **neurofibrillary tangles**.
- Normal tau protein binds and stabilizes microtubules of the cytoskeleton of neurons. Hyperphosphorylation of tau reduces its ability to stabilize neuron structure and causes it to **self-assemble into a polymer** that accumulates in the cell.
- Enzymes that cause extra phosphate groups to be added to tau are activated by inflammation, lipid abnormalities and aging.
- Neurofibrillary tangles are also found in other neurodegenerative diseases.
- It is not known whether **amyloid plaques** are a cause or an effect of AD. The number of plaques is correlated with disease severity. Amyloid plaques consist of an abnormal protein, **β-amyloid**, in association with dead and dying neurons.

Dementia: Alzheimer Disease

Pathogenesis

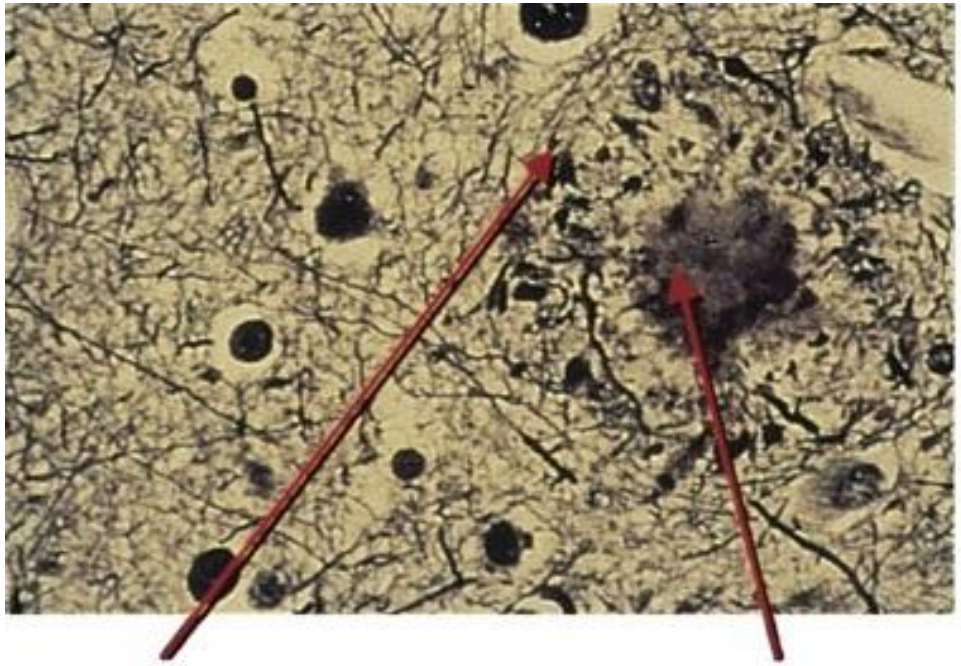
- **Amyloid precursor protein (APP)** is a normal transmembrane protein found in neurons.
- It is periodically recycled, a mechanism that includes cleavage of the portion of APP that lies in the cytoplasm by the protease, **alpha secretase**.
- Only if cleavage occurs at the wrong place, by other proteases, **β-amyloid protein** is produced and accumulates outside the cell.
- Accumulation of β-amyloid protein causes inflammation, lipid oxidation, activation of apoptotic genes, disruption of cell membranes and glutamate excitotoxicity.
- Damage in AD affects three mechanisms: neuron communication, neuron metabolism, and neuron repair.
- AD neurons have reduced levels of acetylcholine (ACH) neurotransmitter. They have reduced activity of the enzyme **choline acetyltransferase,** an enzyme required for the synthesis of **ACH**. In the brain ACH functions to increase attention, arousal and motivation. Imbalances in other neurotransmitters (glutamate, dopamine and serotonin) also occur.

Dementia: Alzheimer Disease

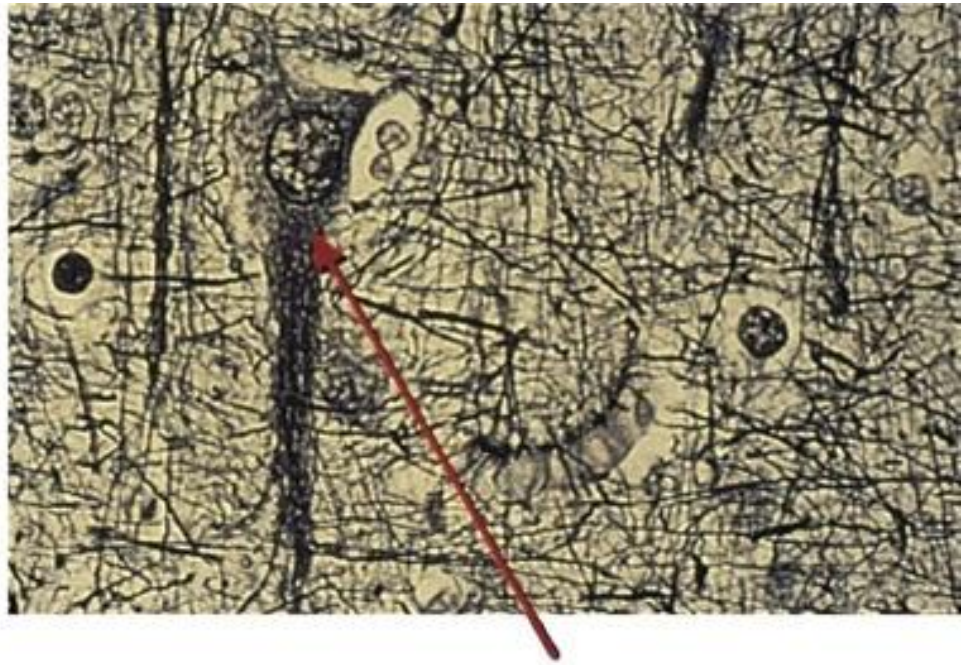


Dementia: Alzheimer Disease

Brain Tissue: Alzheimer's Disease



Plaque surrounding amyloid deposit



Neurons filled with neurofibrillary tangles

Dementia: Alzheimer Disease

Genetics and Alzheimer's Disease

- Risk factors for AD are age and family history. Having an affected first-degree relative increases the risk 4-fold.
- Four genes on four different chromosomes are tied to Alzheimer's Disease.
- Two forms of AD, late onset and early onset, have been identified. Late onset AD (disease develops after age 65) accounts for 90% of all cases.
- **AD1 (late onset AD)** is associated with the **E4** allele of the **apolipoprotein E gene** (chromosome 19).
  - The normal gene product, apolipoprotein E, is involved in carrying blood cholesterol. The APOE E4 allele produces a less active form of apolipoprotein E. Its role in Alzheimer's Disease is unclear.
  - Heterozygosity for the APOE E4 allele is associated with a 45% risk of developing AD by age 85. Homozygosity is associated with a 50-90% risk of developing AD by age 85.

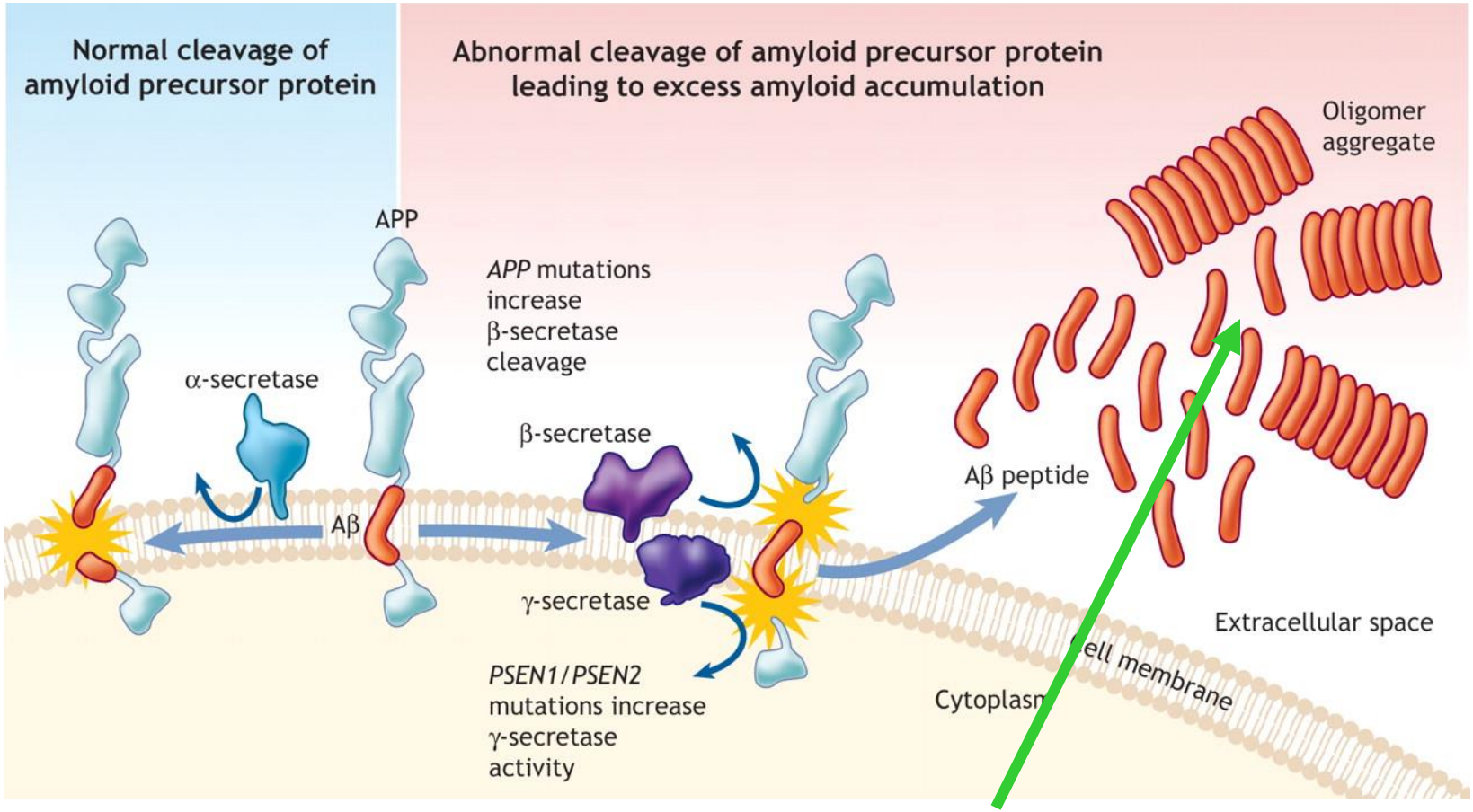
Dementia: Alzheimer Disease

Genetics and Alzheimer's Disease

- **AD2 (early onset AD)** is associated with the **presenilin-1 gene** (chromosome 14)
- **AD3 (early onset AD)** is associated with the **presenilin-2 gene** (chromosome 1).
  - Normal presenilin proteins function in the recycling of transmembrane proteins such as amyloid precursor protein (APP).
  - Abnormal presenilin allows "old" APP protein to accumulate.
- **AD4 (early onset AD)** is associated with an abnormal **APP gene** (amyloid precursor protein) (chromosome 21).
  - Abnormal or old amyloid precursor protein molecules are more likely to be abnormally cleaved by the wrong protease enzymes thus producing beta amyloid protein.

Dementia: Alzheimer Disease

Genetics and β-amyloid Protein Production in Alzheimer Disease



APO E4 allele decreases the ability to dispose of abnormal beta amyloid protein. Beta amyloid aggregates and accumulates extracellularly.

Dementia: Alzheimer Disease

Clinical Manifestations

- Gradual decline in cognitive function; memory loss (especially short-term) anxiety, agitation, depression, psychosis.
- With progression, difficulty with judgment, problem solving and communication
- Difficulty eating and swallowing; weight loss; loss of bowel and bladder control
- Inability to ambulate in later stages.
- Accidents and infections are common causes of death.

Diagnosis

Early diagnosis and intervention are key in management.

- Extensive blood testing and neuroimaging are done to rule out other disorders.
- Mental and functional status exams are recommended.
- Medications with anticholinergic effects mimic dementia in elderly and so may interfere with diagnosis.
- PET scans show promise as an early diagnostic tool. They measure glucose metabolism.

Dementia: Alzheimer Disease

Treatment

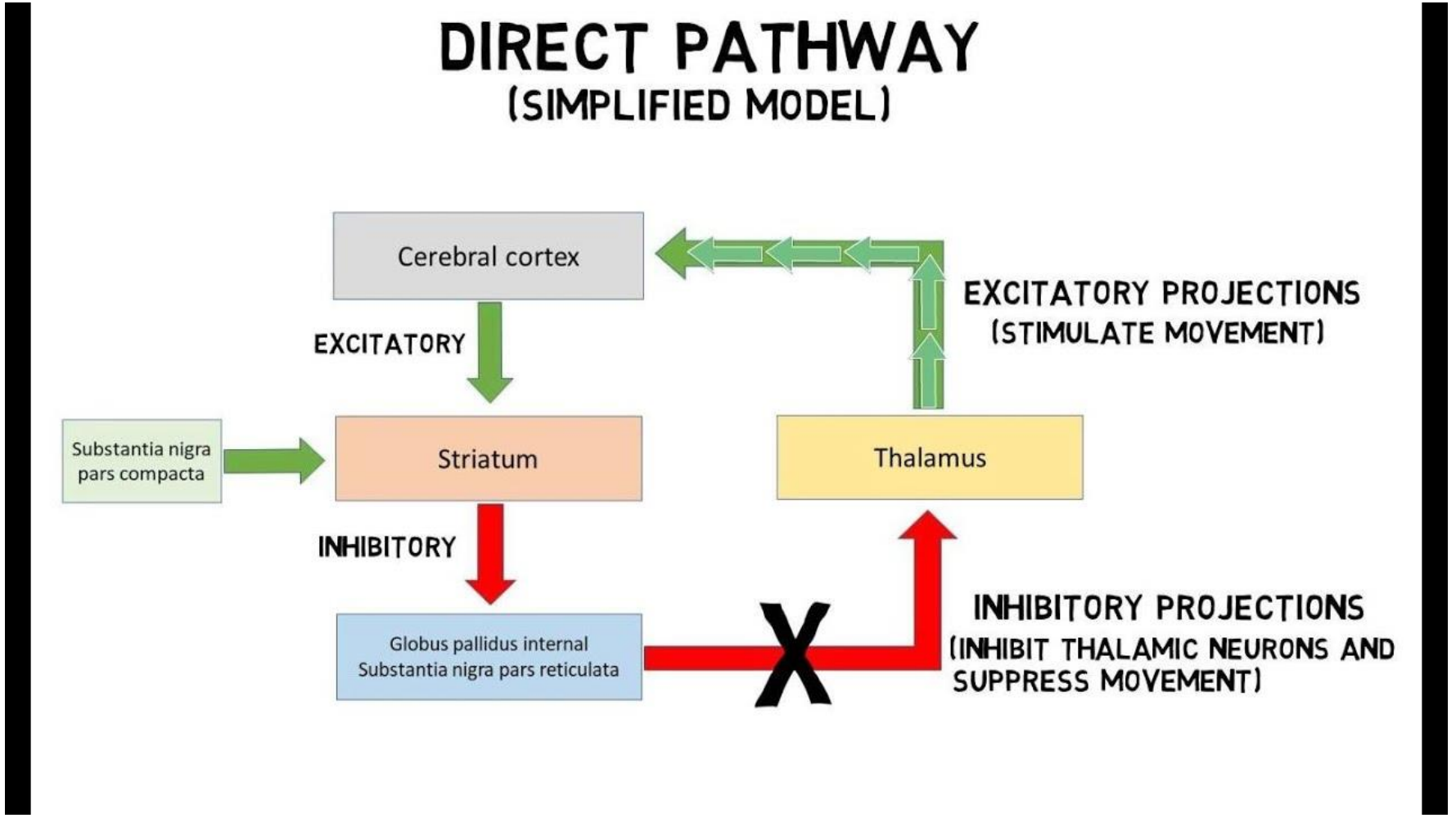
- Two classes of drugs are FDA-approved for the treatment of Alzheimer disease:
- **Acetylcholinesterase inhibitors** (Reminyl and Aricept) decrease synaptic destruction of ACH. They are indicated for mild to moderate AD. These drugs also benefit those who suffer from vascular dementia.
- **NDMA receptor antagonists** (Namenda) reduce glutamate excitoxicity by inhibiting the binding of glutamate to NMDA receptors. They are indicated for moderate and severe AD.
- Many other drugs are used to manage the symptoms.
- Early research--reduced occurrence of Alzheimer disease with NSAID, aspirin, antioxidant and statin use and a possible role for Herpes viruses in the etiology and pathogenesis of AD.
- Patients generally live at home in the early stages of dementia.
- Caring for the caregiver is important.

Control of Skeletal Muscle Movement

- **Initiation** of skeletal muscle movement requires stimulation of the cerebral cortex by glutamate-releasing neurons that have cell bodies in the thalamus.
- The thalamus to cerebral cortex pathway is regulated by the basal nuclei (aka basal ganglia) of the cerebrum and the substantia nigra of the midbrain by a mechanism called the Direct Pathway. Summary:
- Undesirable skeletal muscle movement is prevented by inhibition of that thalamus-to-cerebral cortex pathway. GABA is released to thalamic neurons by neurons with cell bodies in the **globus pallidus** (a basal nucleus) and neurons with cell bodies in the **substantia nigra pars reticulata.**
- When movement is desired, neurons from the cerebral cortex release glutamate to the **corpus striatum** (a set of basal nuclei), and the corpus striatum releases GABA to the globus pallidus and the **substantia nigra pars** reticulata (to remove the block on skeletal muscle movement).
- The neurons of the **substantia nigra pars compacta** release **dopamine** to the corpus striatum to facilitate the initiation of skeletal muscle movement.

By default skeletal muscle movement is inhibited by blocking a neural pathway from the thalamus to the cerebral cortex.
The block on that pathway is due to **GABA-releasing neurons with cell bodies in the globus pallidus and substantia nigra pars reticularis.**
Initiation of the skeletal muscle movement requires that the block on the thalamus-cortex pathway be removed. The **striatum is stimulated by the cerebral cortex and the substantia nigra pars compacta** to inhibit the blocking action.

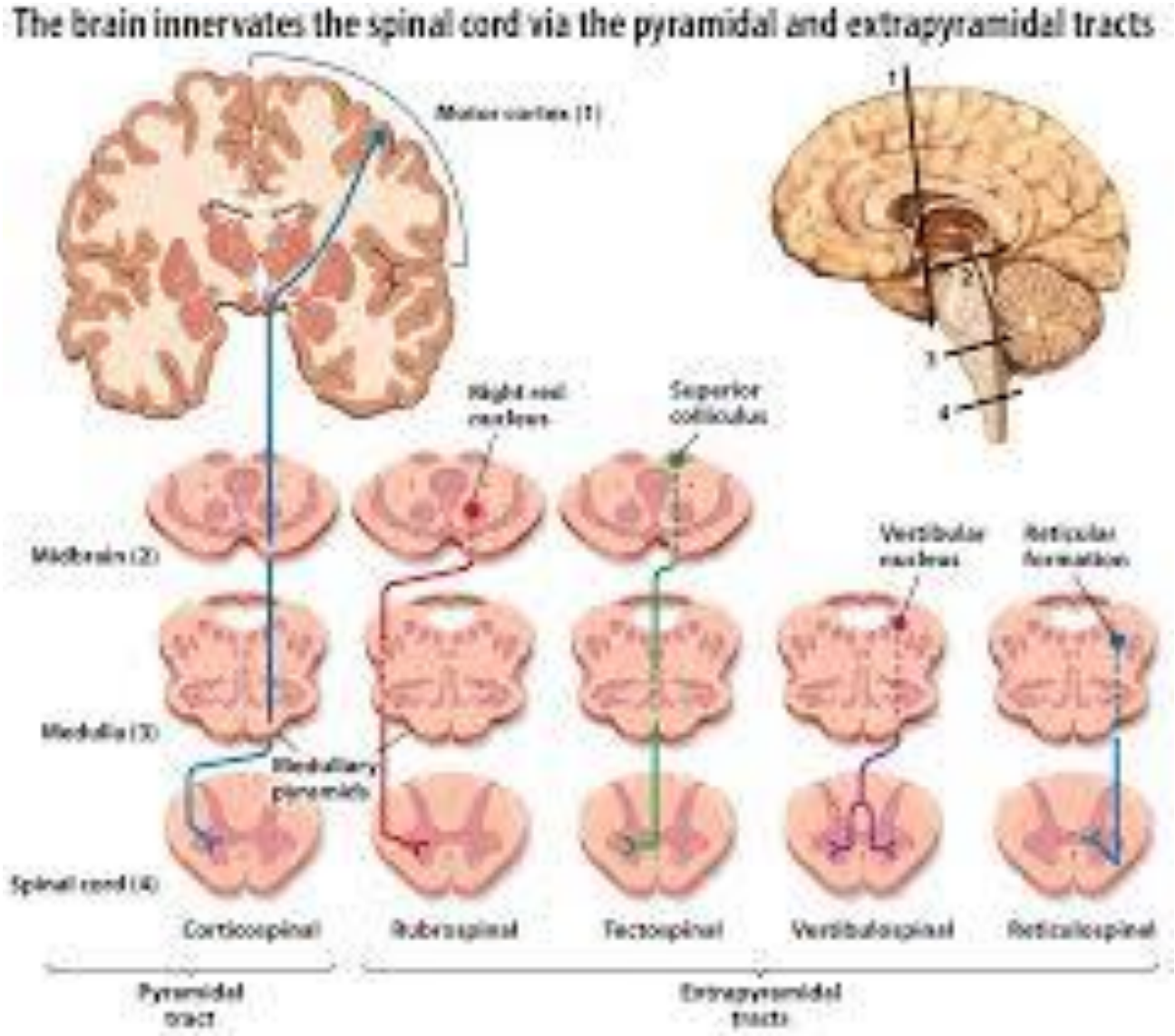
The Direct Pathway



Control of Skeletal Muscle Movement

- Once initiated, skeletal muscle movement is controlled by the upper motor neurons and the lower motor neurons.
- **The axons of upper motor neurons** are located in the pyramidal motor tracts and the extrapyramdal motor tracts.
  - The **pyramidal motor tracts control** have their cell bodies in the cerebral cortex (primary motor cortex). They form ridges known as **pyramids** on the anterior surface of the brain stem. Their axons synapse with the lower motor neurons.
  - The **extrapyramidal motor tracts** have their cell bodies in brainstem nuclei. They synapse with lower motor neurons.
- There are tons of motor impulses that descend from the brain toward the lower motor neurons. Skeletal muscle movements are “refined” by **inhibiting inappropriate motor outputs from upper motor neurons before they are passed along to the lower motor neurons** and by **synchronizing** the motor output of the cerebral cortex.

Pyramidal and Extrapyramidal Tracts



Parkinson Disease

Etiology

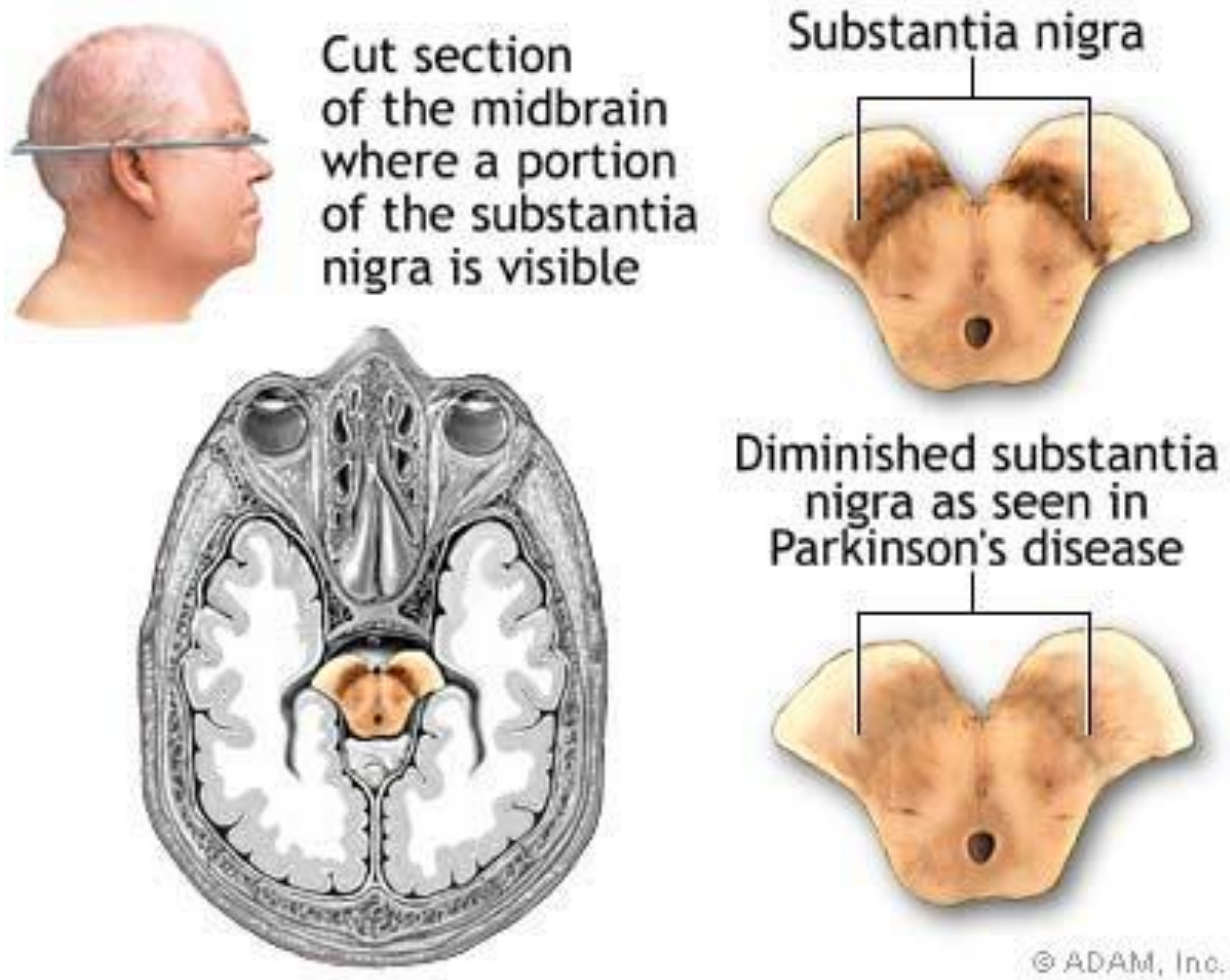
- Disorder that affects 1 million Americans, usually age 65 or older, but about 4% are diagnosed before age 40.
- May be acquired through genetics, infection, intoxication or trauma, but is most often idiopathic. Side effects of certain drugs mimic PD symptoms at toxic levels.

Pathogenesis

- Degeneration of the dopamine-producing neurons in the **substantia nigra** ("black substance") of the midbrain and, to some extent, elsewhere in the brain.
- As described above, degeneration of the dopamine-producing neurons of the substantia nigra pars compacta **interferes with the initiation of skeletal muscle movements by the Direct Pathway.**
- Eosinophilic (stain with the red dye, eosin) cytoplasmic inclusions called **Lewy bodies** are found in surviving neurons. Lewy bodies are also associated with a severe form of dementia (Lewy dementia). Lewy bodies contain an abnormal version of the protein, **alpha-synuclein**. The normal protein plays a role in mitochondrial function and maintenance.
- Another protein called **parkin**, is involved in disposal of old, misfolded proteins, particularly proteins located in mitochondrial membranes. Mutations in in the **PRKN gene** are tied to familial (early onset) forms of Parkinson disease.

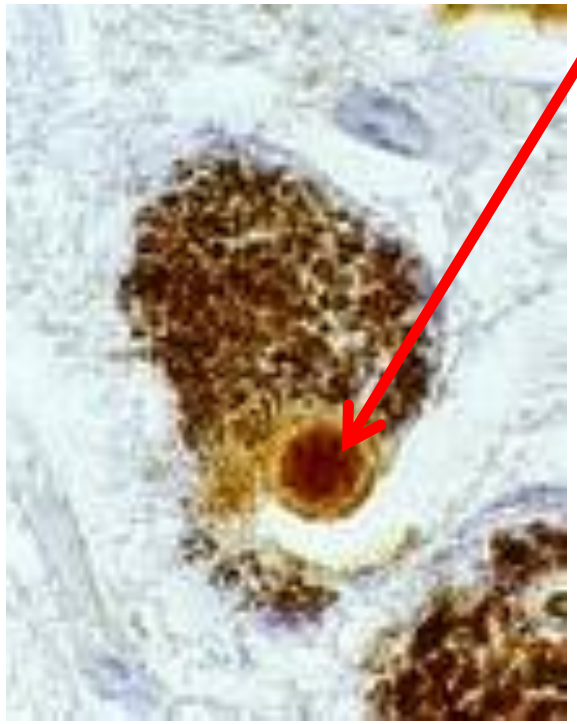
Parkinson Disease

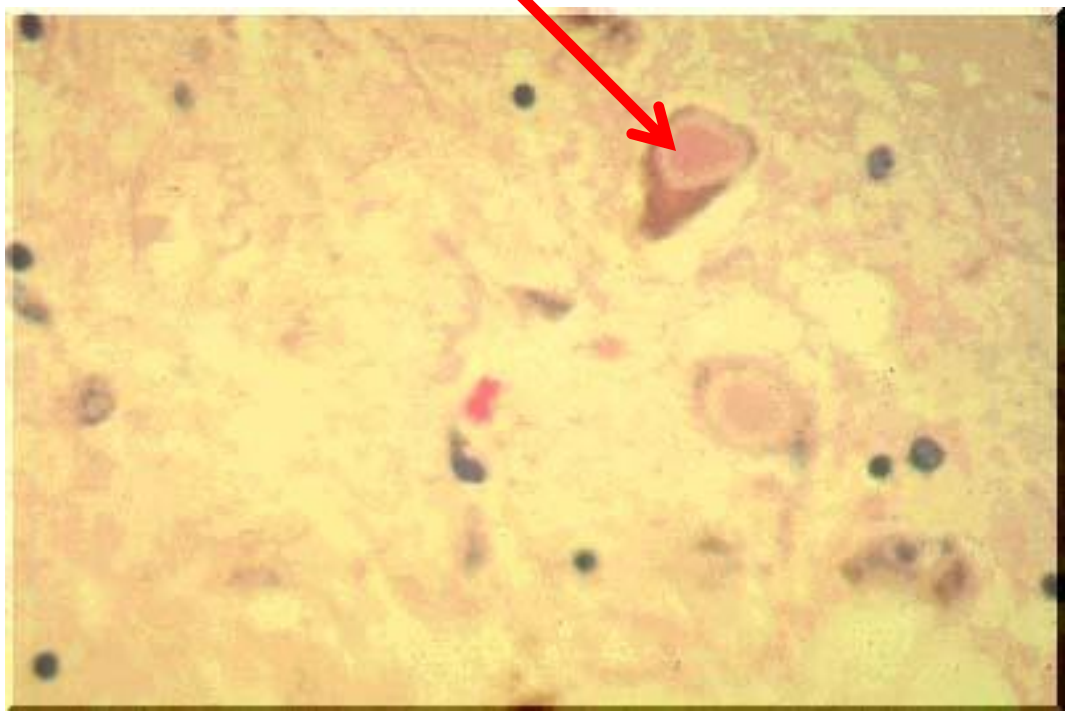
Substantia Nigra in Parkinson Disease



Parkinson Disease

Lewy bodies in the cytoplasm of neurons in Parkinson disease





Parkinson Disease

Clinical Manifestations

- **Early signs**
  - Loss of flexibility, fatigue, bradykinesia (slow movement)
  - Loss of facial expression, infrequent eye blinking
  - Tremor occurs in 70% of cases; prompts patient to seek medical attention; unilateral “pill-rolling” hand tremor is common early on.
- **Later signs**
  - Tremor becomes bilateral and more generalized.
  - Handwriting becomes small and cramped.
  - Speech is low in volume, monotonous and dysarthric.
  - Delayed swallowing (drooling, danger of aspiration)

Parkinson Disease

Clinical Manifestations

- Later Signs, cont.
  - Lack of arm swinging while walking, shuffling gait; stooped posture
  - Inability to initiate movement
  - Difficulty maintaining balance; risk of falling.
- Sleep disturbances and restless leg syndrome
- Depression and dementia are prevalent.

Treatment

- Medications
  - **Levadopa**, a dopamine precursor that can cross the BBB, is administered. Dopamine, itself, cannot cross the BBB, so levadopa is administered along with carbidopa, a drug that prevents levadopa from being converted to dopamine before it crosses the BBB.

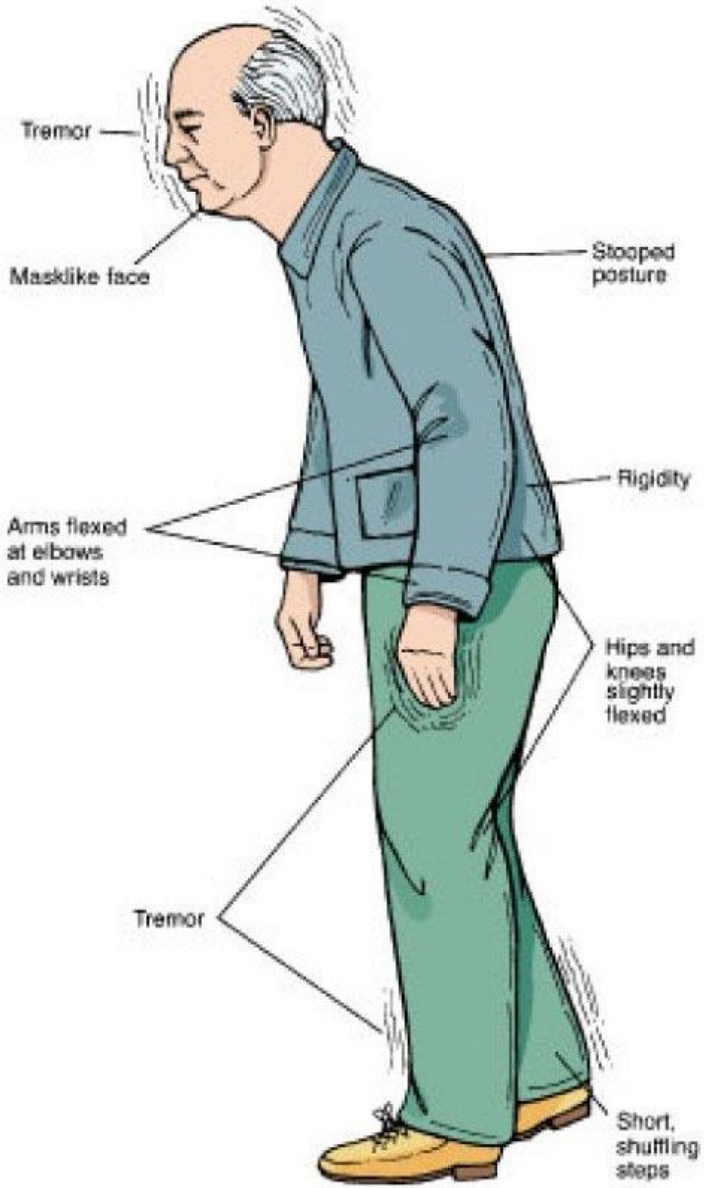
Parkinson Disease

Treatment

- Other medications stimulate the activity, slow the catabolism, or enhance the release of dopamine.
- Anticholinergic medications help with tremor, rigidity, or drooling. An AD med is used to slow dementia development.

- Deep brain stimulation
  - Surgical implant of electrodes into the thalamus to interrupt the tremor-causing nerve impulses and decrease the need for meds.
- Surgical interventions
  - Lesions in the globus pallidus or the thalamus improve rigidity, tremor, and bradykinesis, and also makes the patient more responsive to meds. Rarely used due to high morbidity
- Future treatments may include transplantation of dopamine-producing neurons from animals; antioxidant treatments; gene therapy.

Clinical Manifestations of Parkinson's Disease



From Monahan FD, Neighbors M: Medical-surgical nursing: foundations for clinical practice, Philadelphia, 1998, Saunders, p 787.

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Cerebral Palsy

Etiology and Pathogenesis

- Cerebral palsy is a group of crippling syndromes involving permanent, non-progressive **brain damage incurred before, during or shortly after birth.**
- Affects 2 to 2.5 per 1000 live births=very common.
- Damage to the **upper motor neurons (or brain areas that control them)** produces a wide-range of problems including, but not limited to chronic pain, scoliosis and respiratory problems.
- Seizures may occur.
- Major types involve spasticity, ataxia, dyskinesia or any combination thereof.
- Etiologic factors: prenatal infections, disease of the mother, head trauma, exposure to neurotoxins, hypoxia of brain tissue
- Risk factors: prematurity, neonatal hypoglycemia or kernicterus.

Cerebral Palsy

Clinical Manifestations

- **Spastic CP: Muscles are stiff--**hypertonia, abnormal reflexes, clonus, rigidity of extremities, scoliosis, contractures, due to damage in the motor area of the **cerebral cortex.** Spastic paralysis may affect one entire side, both legs, both legs and one arm or all four extremities. A "scissor" gait and toe walking are common.
- **Dyskinetic CP: Muscle movements are difficult to control--** extreme difficulty in purposeful movement and fine motor coordination, movements are slow, jerky and poorly controlled due to damage to the **basal nuclei or extrapyramidal tracts.** Symptoms may increase during stress and decrease during sleep.
- **Ataxic CP: Problems with balance and coordination--** due damage to the **cerebellum.**
- NOTE: Most CP cases are a combination of the above types.

Cerebral Palsy

Treatment

- Depends on the nature and extent of the disorder.
- Muscle spasticity and contractures are treated with muscle relaxants and Botox injections.
- Anticonvulsant drugs for seizures.
- Orthopedic surgery, casts, braces and traction are used to correct some forms of disability.

Hydrocephalus

Etiology

- Abnormal accumulation of CSF
  - Usually congenital and associated with a neural tube defect.
  - Occasionally it occurs in adults due to brain injury.
- Three types

1. Normal Pressure Hydrocephalus

- CSF volume increases, but there is no increase in CSF pressure
- Occurs if brain tissue has been lost as in Alzheimer disease.
- Congenital forms are linked to neurotoxins or viral infections during pregnancy.

2. Noncommunicating or Obstructive Hydrocephalus

- Due to an abnormality that obstructs interventricular CSF flow. Obstruction of the **cerebral aqueduct** is the most common cause. (lateral and third enlarge)
- CSF volume and pressure increase behind the blockage.

Hydrocephalus

Etiology

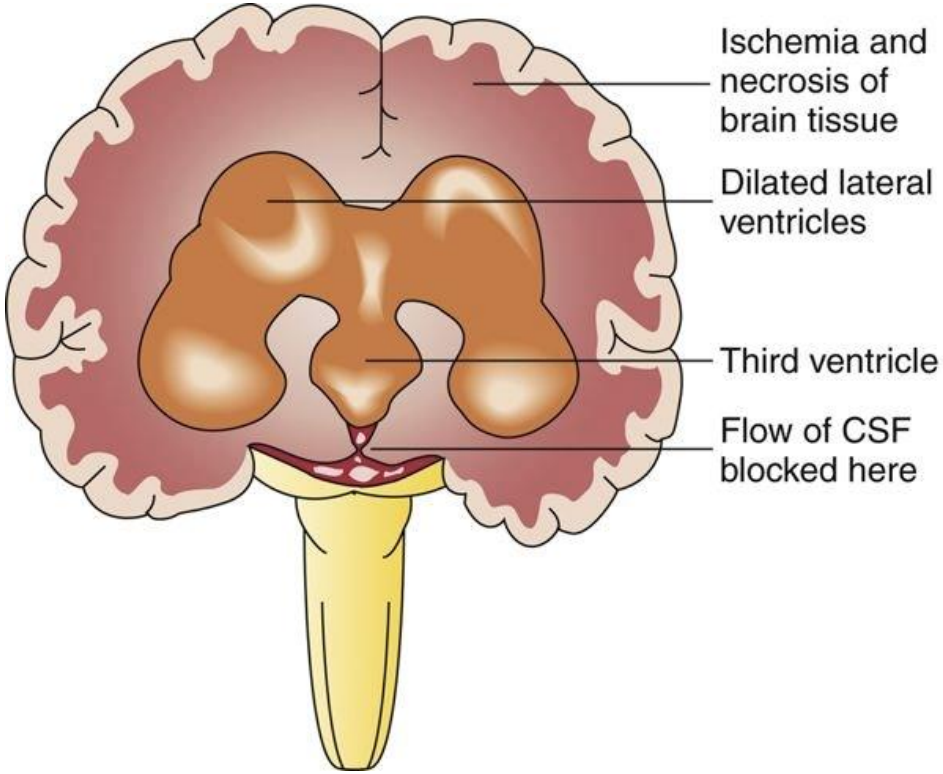
3. Communicating Hydrocephalus

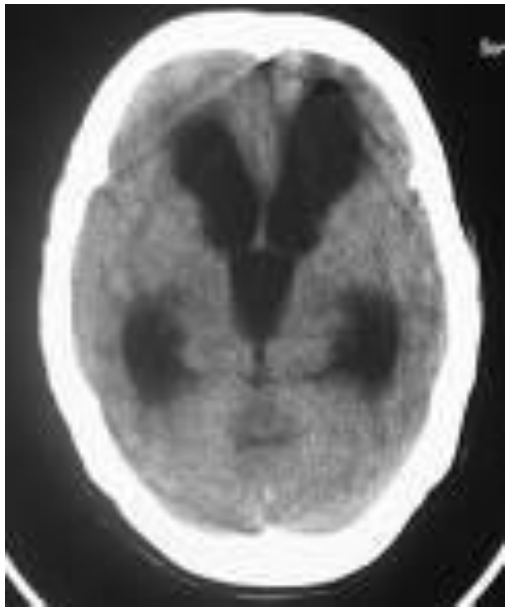
- Due to an abnormality in the capacity to absorb fluid from the subarachnoid space through the arachnoid villi and into the blood.
- Occurs in infection (meningitis) or trauma (subarachnoid hemorrhage)
- There is no obstruction of flow between the ventricles.
- Causes increased CSF volume and pressure in all ventricles and in the subarachnoid space.
- Brain tissue is compressed.
- The head may swell tremendously in infants before the fontanels have closed.

Hydrocephalus

Noncommunicating Hydrocephalus

CSF Accumulation in the Lateral and Third Ventricles

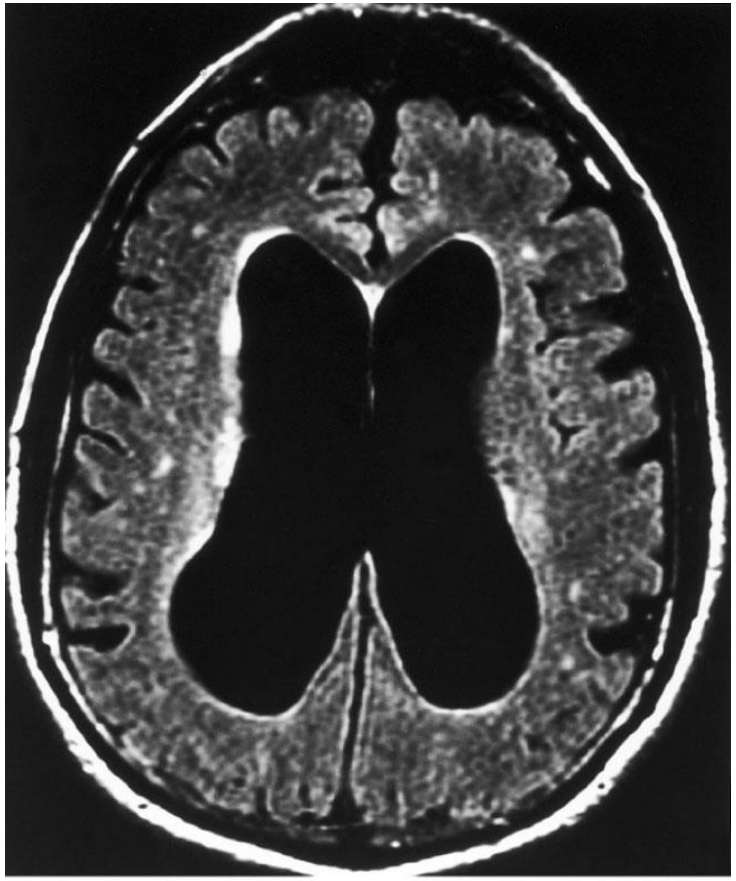




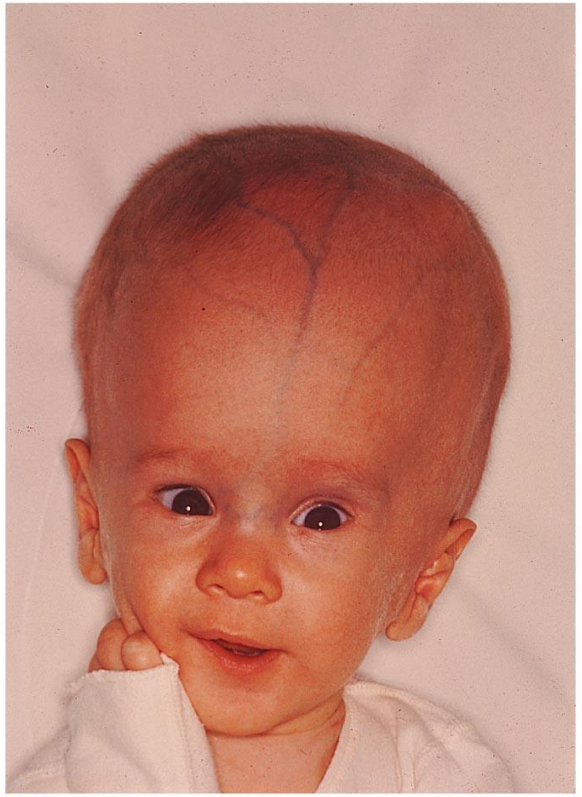
Hydrocephalus

Communicating Hydrocephalus

CSF Accumulation in All Ventricles and the Subarachnoid Space



From Grossman RI, Yousem DM: Neuroradiology, ed 2, St Louis, 2003, Mosby, p 377.



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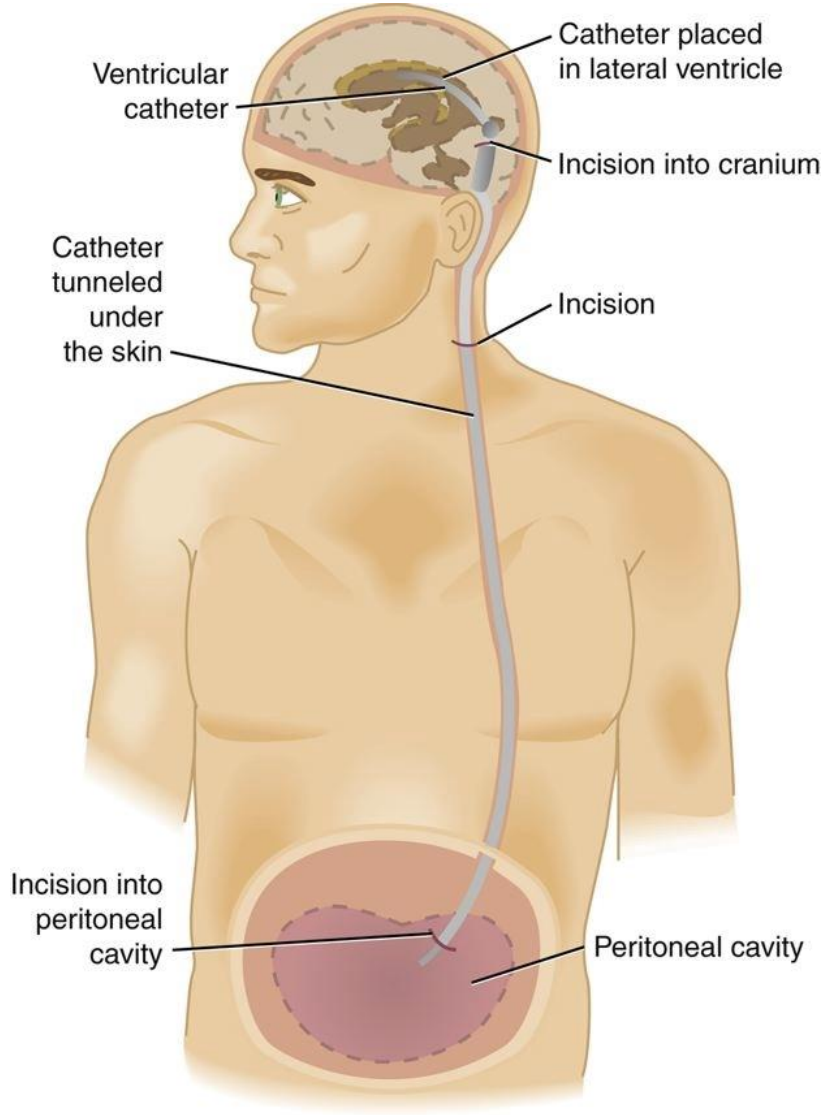
Hydrocephalus

Treatment

- **Ventriculoperitoneal shunting**
  - A catheter may be inserted into one of the ventricles. A one-way valve directs fluid away from the ventricle. The distal end of the catheter is most often positioned in the peritoneal cavity where the excess fluid may be absorbed and excreted.
  - With shunting, two thirds of children with uncomplicated hydrocephalus may have normal or nearly normal intellect.
- **Endoscopic third ventriculostomy (ETV)**
  - Guided by endoscopy a hole is made in the bottom of the third ventricle. This allows excess CSF to enter the subarachnoid space between the pituitary gland and the ventral surface of the midbrain. This procedure is most often used when the cerebral aqueduct is occluded.

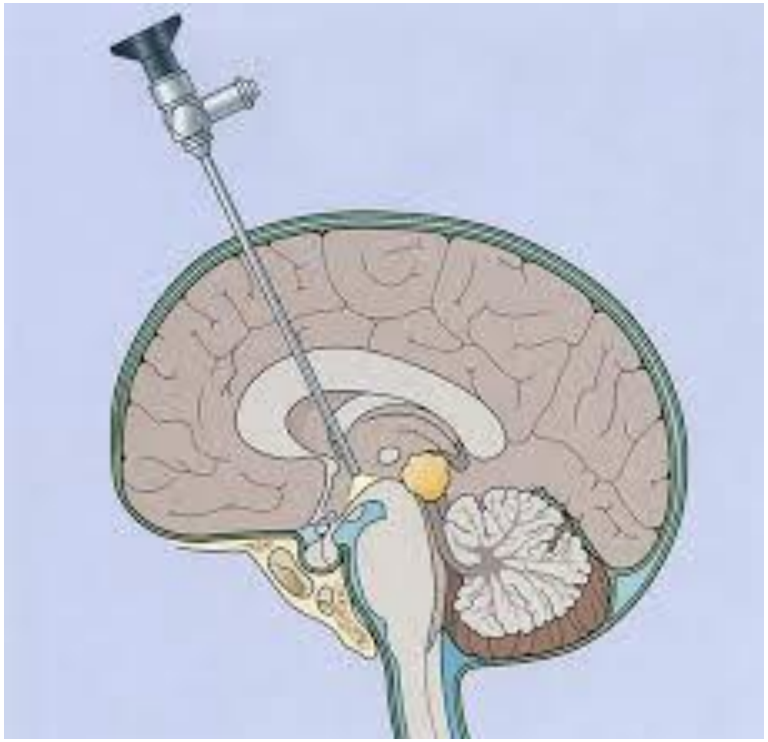
Hydrocephalus

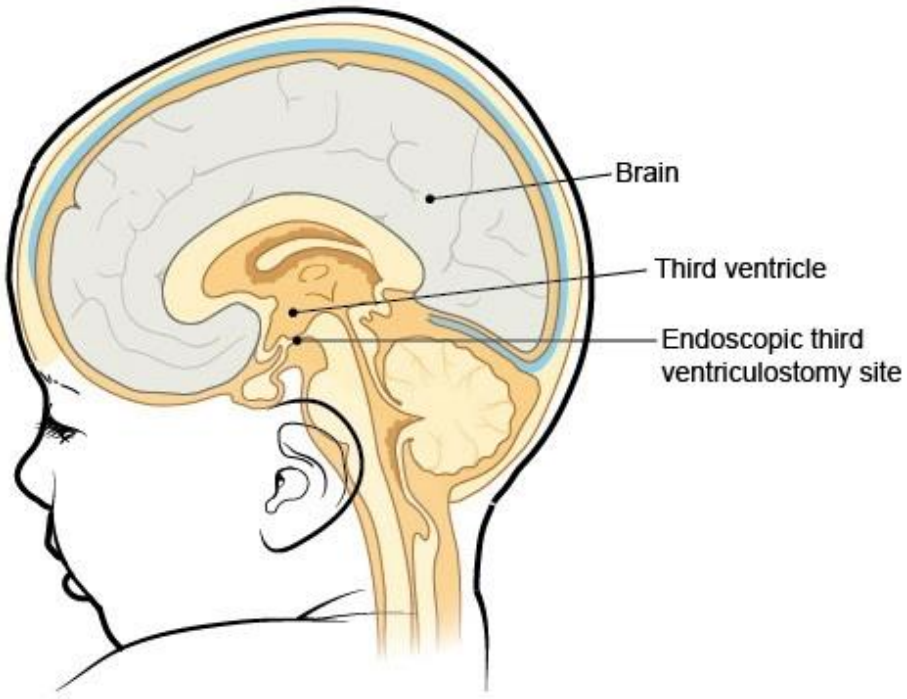
Ventriculoperitoneal Shunt



Hydrocephalus

Endoscopic Third Ventriculostomy (ETV)





Cerebellar Function

Cerebellar Function

- The cerebellum receives sensory information about the **current position of the body** from **proprioceptors** in the muscles and joints and from **equilibrium receptors** in the inner ear via the vestibular nucleus in the brainstem.
- It also receives information from the **primary somatic sensory cortex** and the **primary motor cortex** about the "next" **intended** skeletal muscle movements. The cerebellum has **two jobs**:

1. The cerebellum uses the information it receives to **make a plan for the "next" voluntary skeletal muscle movements**. It sends the plan up through the thalamus to the primary motor cortex. The primary motor cortex then puts the plan into action by sending impulses down to the spinal cord in the **upper motor neurons** via the **pyramidal motor tracts**.

Cerebellar Function

2. Information from the cerebellum also travels to **brainstem nuclei** that further control skeletal muscle movements by sending impulses via the **extrapyramidal motor tracts** down into the spinal cord to affect (mostly **INHIBIT**) **lower motor neurons**. Those tracts are:
   - **Rubrospinal tracts from the red nuclei**
   - **Reticulospinal tracts from the reticular nuclei**
   - **Vestibulospinal tracts form the vestibular nuclei**
   - These tracts don't originate in the cerebral cortex. That explains why we are NOT conscious of their operation.

- Cerebellar fine-tuning allows movements that produce the intended action while maintaining balance**. Inhibition of impulses in upper motor neurons is key to smooth skeletal muscle function!**

Cerebellar Disorders

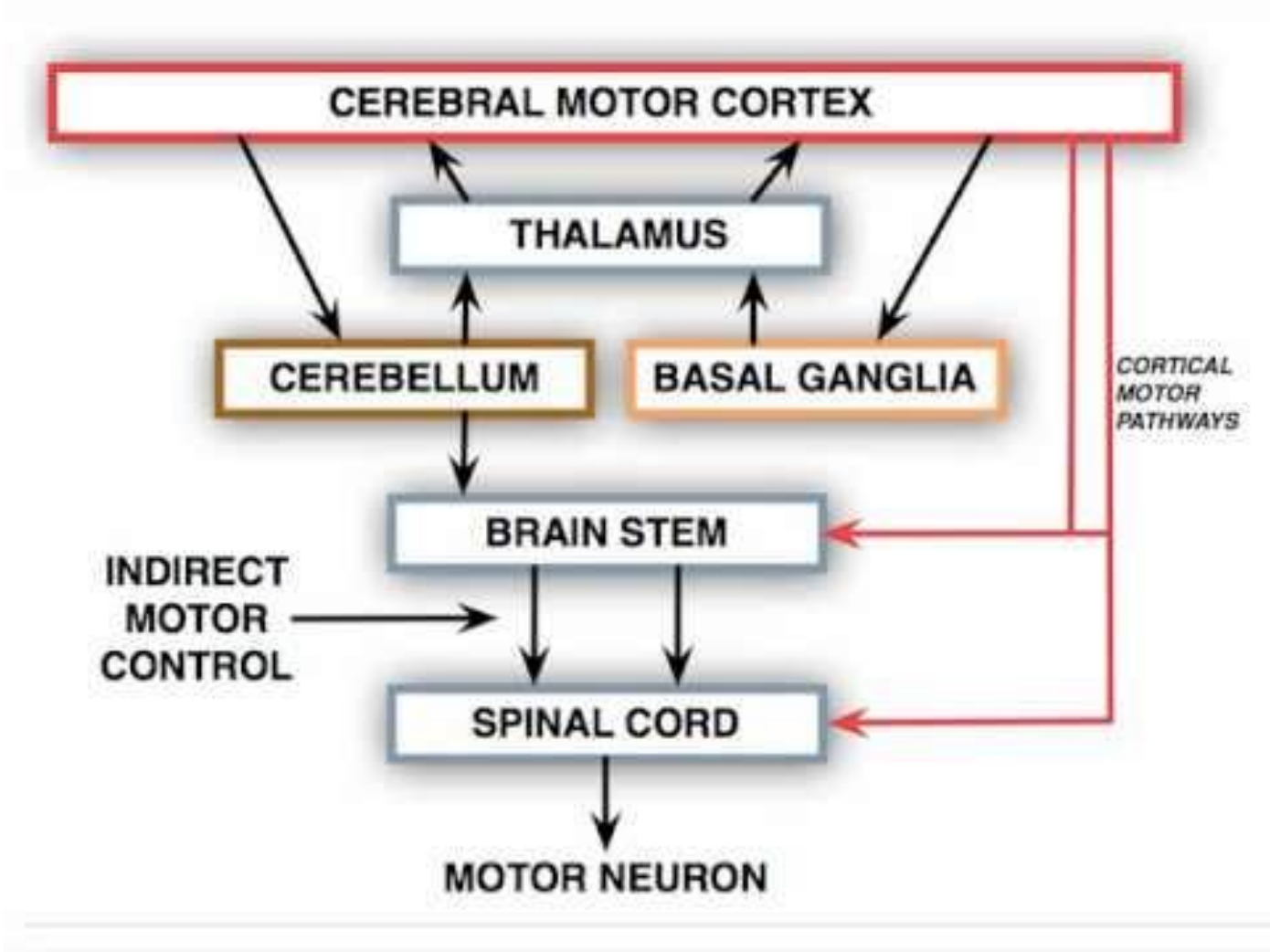
Etiology and Pathogenesis

- Cerebellar disorders may result from abscess, hemorrhage, tumor, trauma, viral infection, alcoholism, multiple sclerosis, NARP and other causes that damage cerebellar neurons.

Clinical Manifestations

- Cerebellar disorders cause uncoordinated skeletal muscle movement (ataxia). Gait disturbances and trouble maintaining balance and posture are common symptoms.
- Paralysis does not occur.

Simplified Diagram of Motor Controls



QUIZ 7AB

- COMPLETE QUIZ 7AB.
- THEN GO ON TO MODULE 7CD PPT.