CNS and Musculoskeletal Pathology

OPTH 727

Dave Chandra, DMD, PhD

Who treats these diseases?

Not on exam

- Neurologists
  - Pediatric Neurologists
- Neurosurgeons
- Interventional Radiologists
- Neuroradiologists
- Neurointensivists
- Therapists
  - Occupational
  - Physical
  - Speech
- Psychiatry

Diagnostic Tools

Not on exam

- Detailed clinical exam and patient interview
  - Symptoms (patient), also perspective from patient's family
- Functional testing
  - Mental: Cognition, memory, ability to concentrate,
  - Neuromuscular: Balance, strength, coordination
  - Senses: sight, hearing, touch
  - Speech
- Imaging ****
- Lumbar Puncture (spinal tap)
- EEG, EMG
- Blood, urine testing??
- Histopathology?

Facial pain, TMJ and other neuromuscular diseases that primarily affect the head and neck region will be covered in oral pathology courses

- **Bell Palsy**
- **Frey Syndrome**
- **Trigeminal Neuralgia**
- **Glossopharyngeal Neuralgia**
- **Giant cell arteritis**
- **Burning mouth disorder**
- **Dysgeusia and Hypoguesia**
- **Temporomandibular disorders**

- **Infectious**
  - **Meningitis, bacterial**
  - **Meningitis, viral**
  - **Encephalitis**
  - **Creutzefeldt-Jacob Disease**
    - Spongiform encephalopathy
- **Neurodegenerative Diseases**
  - **Alzheimer Disease**
  - **Parkinsons Disease**
  - **Huntington Disease**
  - **Multiple Sclerosis**
  - **Amyotropic Lateral Sclerosis (ALS)**
  - **Muscular Dystrophy**
  - **Myasthenia Gravis**
- **Cerebral Palsy**
- **Epilepsy**
- **(Errors in development)**
  - **Neural tube defects**
    - **Spina bifida**
- **Brain tumors (neoplasia)**
- **Vascular diseases of the brain**
  - **Stroke**

- Infectious
  - **Meningitis, bacterial**
  - **Meningitis, viral**
  - **Encephalitis**
  - **Creutzefeldt-Jacob Disease**
    - Spongiform encephalopathy

Infections

- Meningitis
  - Meningitis is an infection of the meninges
  - Meninges are three membranes (dura, arachnoid, and pia mater) that line the skull and enclose the brain and spinal cord.

- **Meningitis, bacterial**
- **Meningitis, viral**
- **Encephalitis**
  - Encephalitis is an infection of the brain parenchyma.
- **Creutzefeldt-Jacob Disease**
  - Bovine spongiform encephalopathy is a brain disorder in cattle that can be spread to humans through diseased meat. When spread to humans, it causes C-J Disease.
    - Most cases of Creutzefeldt-Jacob Disease are not caused by diseased meat
  - Caused by prion (an infectious agent comprised of protein)
  - Rapidly progressive neurodegenerative disease

Meningitis, bacterial vs. viral

- Bacterial
  - Less common than viral
  - Far more dangerous than viral
    - Death or permanent morbidity in ~40% of cases
    - Possible amputation of limbs (due to severe septicemia)
    - Must be treated with antibiotics immediately
  - Diagnosed via spinal tap
    - Turbidity (cloudiness) of cerebrospinal fluid,
  - Numerous bacteria may be involved
    - N. meningococci is most common
    - Vaccines available

- Viral
  - More common than bacterial
  - Usually self-limiting; resolves after 7-10 days
  - Often affects elderly, babies
  - Also diagnosed on spinal tap
  - Numerous types of viruses can cause

Symptoms of meningitis

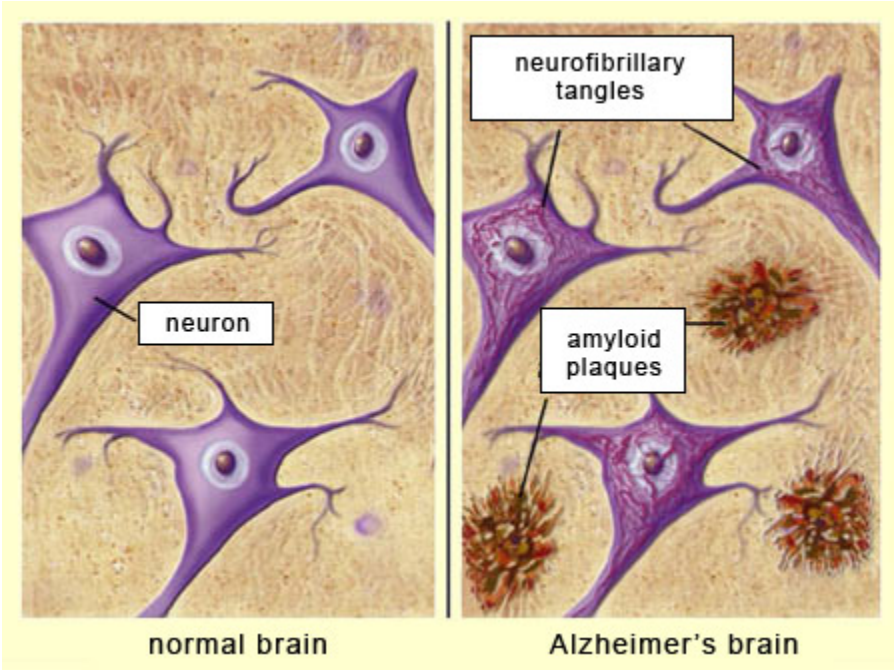
- Symptoms may be similar for bacterial and viral meningitis
- Severe headache
- Stiff neck
- High fever
  - Delirium
- Vomiting
  - Caused by increased intracranial pressure. Other disease processes that cause increased intracranial pressure (head trauma, stroke, tumors) produce vomiting

- **Infectious**
  - **Meningitis, bacterial**
  - **Meningitis, viral**
  - **Encephalitis**
  - **Creutzefeldt-Jacob Disease**
    - Spongiform encephalopathy
- **Neurodegenerative Diseases**
  - **Alzheimer Disease**
  - **Parkinsons Disease**
  - **Huntington Disease**
  - **Multiple Sclerosis**
  - **Amyotropic Lateral Sclerosis (ALS)**
  - **Muscular Dystrophy**
  - **Myasthenia Gravis**
- **Cerebral Palsy**
- **Epilepsy**
- **(Errors in development)**
  - **Neural tube defects**
    - **Spina bifida**
- **Brain tumors (neoplasia)**
- **Vascular diseases of the brain**
  - **Stroke**

Alzheimer's Disease

- #1 cause of dementia in elderly
- Slow onset, irreversible, progressive
  - Wide spectrum of disease
- Alzheimer's Disease only <u>definitively</u> diagnosed after death.
** - Based on brain histology…Amyloid plaques and tangles of tau protein found between neurons
- In real life, Alzheimer's diagnosis is based on ruling out other pathology
- No cure
- Very "hot" topic of research
  - Understanding genetic predisposition and other causes
  - Development of non-histology based diagnostics
  - Treatment- medications, etc.

- <u>Dementia</u> – an overall group of symptoms related to memory or other thinking skills that reduce a person's daily functioning, e.g.
  - Getting lost
  - Extreme forgetfulness
  - Trouble handling money and paying bills



Parkinson's Disease

- Adult onset movement disorder
  - Wide spectrum of disease
  - Symptoms: tremors, slowness of movement, difficulty walking
    - Advanced cases may present with cognitive, memory defects
- Definitive diagnosis – histopathology. Brain imaging rules out other diseases.
  - Loss of dopaminergic neurons in substantia nigra (in the basal ganglia)
  - Dopamine agonists relieve symptoms
- Cause is unknown, no cure, disease is progressive

Tremor - involuntary shaking (hands, legs, head)

- A symptom of Parkinson's and many other neurological disorders

Huntington's disease

- Genetic disease
  - Autosomal dominant
  - Caused by mutations in *Huntingtin* gene
    - CAG repeats within the gene
  - Symptoms typically have an adult onset
    - Age of onset related to number of CAG repeats within the gene

- Patients develop motor impairments (jerky involuntary movements) and dementia

Multiple Sclerosis

- Autoimmune destruction of myelin sheath
  - Leads to demyelinization – reduced nerve function (decreased conductance)
    - Affects CNS and PNS
- Very wide spectrum of disease
  - Weakness, fatigue, tingling/numbness, loss of vision, autonomic disturbances (bowel/bladder)
- Adult onset
  - Young adults may be affected. 20-60 yrs
- Disease may go into remission (disease not necessarily progressive)
  - True for many autoimmune diseases
- No cure
  - Corticosteroids often used (these are powerful anti-inflammatory agents)

Multiple Sclerosis - Diagnosis

- Clinical evaluation and exclusion of other diseases
- Electrophysiology (EMG)
  - Shows increased conductance times (slower)
- MRI
  - May show small areas of demyelination
  - “White” matter looks “gray”
- CSF examination
  - Increase in lymphoid cells

Amyotropic Lateral Sclerosis (ALS)

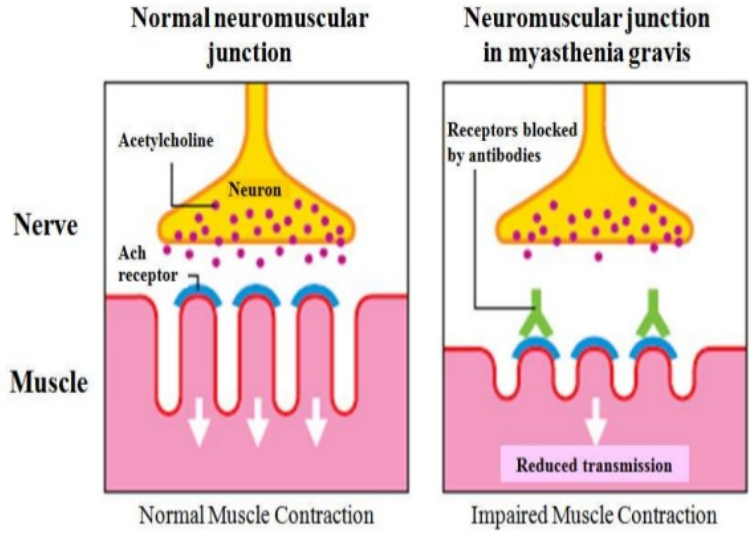
- ALS is a type of motor neuron disease
  - Destruction/deterioration of motor neurons
  - Motor neurons located in brain, spinal cord, brainstem
- Cause unknown, adult onset, progressive, irreversible
- Any process involving skeletal muscle may be affected
  - Movement
  - Speech
  - Eating/swallowing
  - Breathing
- Mental capabilities not affected

Muscular Dystrophy

- A group of genetic diseases that cause progressive weakness and loss of muscle mass.
  - A disease of muscle – not nerves.
  - Death of muscle cells and fibrotic replacement
- Many different diseases have been identified:
  - Age of onset – wide range (usually childhood). Symptoms – wide range.
  - Duchenne muscular dystrophy is most common. 1:5000 males affected.
    - What would you expect the inheritance pattern to be?
    - Progressive worsening of muscle function, may also affect cardiac muscle (a type of cardiomyopathy)
      - Lifespan ~30 yrs

Myasthenia Gravis

- An autoimmune disease caused by antibodies binding to nicotinic acetylcholine receptors at the neuromuscular junction.
- Symptoms: Generalized weakness and muscle fatigue, ptosis (droopy eyelid), dysphagia
- Diagnosis
  - Administer anti-cholinesterase drugs to see if function improves
  - Autoantibodies in blood
  - Muscle biopsy is non-diagnostic
- Treatment:
  - Corticosteroids
  - Anticholinesterase drugs
- Prognosis is good in most cases



Epilepsy

What is a seizure? A short period of symptoms – due to abnormally excessive neuronal activity in the brain.

Seizures may be "provoked" or "unprovoked". A provoked seizure is when a known event brings on the symptoms: i.e. low blood sugar, hyponatremia, brain infection, concussion. Unprovoked seizures are those that have no readily identifiable cause.

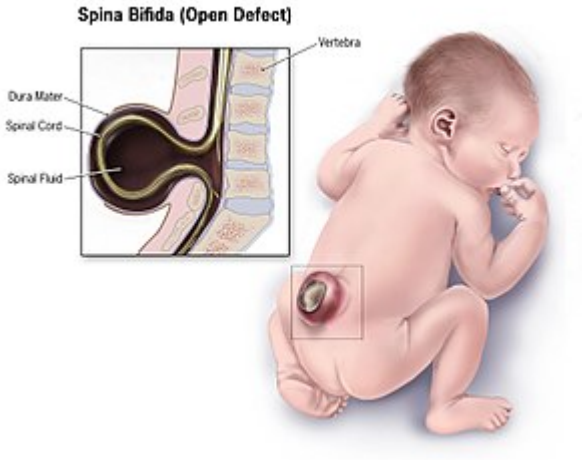
- A chronic disorder characterized by recurrent, unprovoked seizures.
- Numerous types of seizures
  - Tonic-clonic (grand mal) – uncontrolled shaking movements throughout body (often with loss of consciousness)
  - Absence seizures (petit mal) – subtle, momentary loss of awareness
- Wide range of symptoms
  - based on type of seizure (grand mal, petite mal, etc), frequency, duration, severity, etc.
- Epilepsy is common: 1% of population. Often manifests in childhood.
- Treatment: medications

Cerebral Palsy

- A group of neurological disorders that appear in infancy or early childhood
  - Permanently affects body movement, muscle coordination, balance, gait
  - In serious cases, speech and bowel/bladder function may be affected

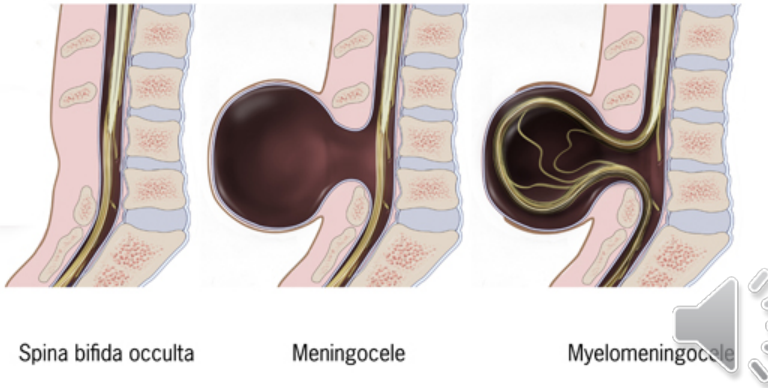
- Normal cognition
- Mostly due to insult/injury in utero or early infancy (e.g. hypoxia, infection)
- Wide range of severity
- NOT progressive – typically does not get worse over time
- NOT genetic

Neural tube defects



- A group of birth defects in which an opening in the spinal cord or brain remains past development.
  - Thusly, part of the brain/spinal cord may push out past the cranium or vertebral column
  - Vitamin deficiencies during gestation (particularly folate) are risk factors

- The most common neural tube defect is **spina bifida**
  - Incomplete closing of the spine and membranes around the spinal cord. Usually seen in lower back. 3 main types:
    - Spina bifida occulta
      - Malformation of vertebrae but no outpouching of spinal cord
        - Quite common – usually asymptomatic
    - Meningiocele
      - Outpouching of meninges only
    - Myelomeningiocele
      - Outpouching of meninges and neurons



Brain Tumors

- Primary brain tumors (benign or malignant)
  - Found in both children and adults
  - 2nd most common cause of childhood cancer (#1 is leukemia)
  - > 100 different types
- Metastatic disease
  - Most common cause of cancer affecting brain
    - Found mostly in adults (as you would expect… cancer typically is found in adults)
- Malignant tumors in brain (primary or metastatic) are very dangerous (as you would imagine)
  - Radiation, chemotherapy often first line of treatment
- Benign tumors of the brain are also potentially dangerous
  - Produce increased intracranial pressure (leading to symptoms- severe headache and others)
  - May damage adjacent brain parenchyma or blood vessels
- Rare for brain tumors to be of neuronal origin. Usually cell of origin are “support cells”. Glial cells or meninges.

Some brain tumors to know

- Malignant
  - **Medulloblastoma**- most common malignant pediatric brain tumor
  - **Glioblastoma**- most common malignant brain tumor seen in adults
    - Sometimes called glioblastoma multiforme
    - Glioblastoma is a type of astrocytoma. Astrocytomas are a spectrum of benign – malignant tumors. Glioblastomas always being malignant and often carrying a poor prognosis
- Benign
  - **Meningioma**
    - Common in adults
  - **Schwannoma**
  - **Neurofibroma**
  - **Ependymomas and Astrocytomas** may be benign or malignant.

Not on exam

- Malignant ependymomas are referred to as "**anaplastic ependymomas**".
- Malignant astrocytomas are "**anaplastic astrocytoma**" – which are malignant, but not as bad as glioblastoma.

Cerebrovascular disease

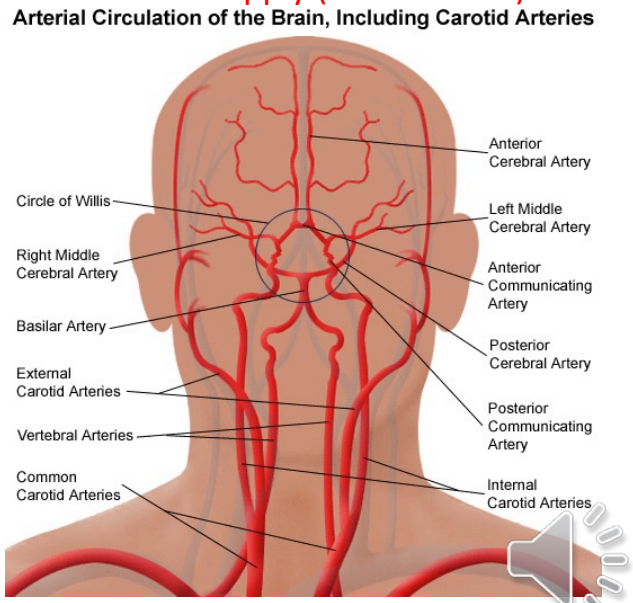
Cerebrovascular accident aka **Stroke**

- What is a **stroke**? – damage to the brain due to non-traumatic, interruption of blood supply (ischemia)
  - Due to diseased vessels that supply the brain
    - Atherosclerosis, arteriolosclerosis, aneurysm, thromboembolus

- 3rd leading cause of death in USA
  - #1 heart disease, #2 cancer

- What are the symptoms of a stroke?
  - Symptoms depend on which vessel(s) affected
  - Typical symptoms:
    - Numbness or weakness, particularly on one side
      - Face, arm, leg
    - Confusion/dizziness/severe headache/lack of coordination
    - Impaired vision or speech

Do not need to know the blood supply (for this class)



Transient ischemic attack (TIA) and silent stroke

- TIA (aka mini-stroke) is due to a temporary interruption of blood flow to the brain.
- Symptoms of TIA are similar to stroke
- What is the difference between stroke and TIA?
  - **TIA** -
    - Symptoms resolve quickly. Usually within minutes to one hour- (could be up to 24 hours)
    - TIA produces NO evidence of infarction on brain imaging (CT or MRI)
  - **Stroke**-
    - Symptoms last more than 24 hours (and often result in SOME permanent symptoms)
    - Stroke MAY or MAY NOT produce evidence of infarction (as seen on CT or MRI)
  - **Silent stroke**
    - Do not produce stroke symptoms.
    - Silent stroke produces evidence of infarction (as seen on CT or MRI)
- Why is a TIA worrisome?
  - 1 in 3 patients who have suffered a TIA, eventually suffer a stroke
  - High susceptibility of developing a stroke within 48 hours after a TIA

Questions about MI

Review of MI is not on exam

Respond at **PollEv.com/davechandra251**

1. What test is done to distinguish MI from unstable angina?

Work-up/diagnosis of stroke patient

- Symptomology
- Imaging of vessels- angiogram/ultrasound
  - Is there pathology in a vessel?
- Imaging of brain parenchyma (CT/MRI)
  - Brain infarcts (not always present with stroke patient)
- Rule out other causes of symptoms.
- Assess risk factors for cardiovascular disease
  - Hypertension, diabetes, heart disease, atherosclerosis of coronary vessels

Questions about MI

Review of MI is not on exam

Respond at **PollEv.com/davechandra251**

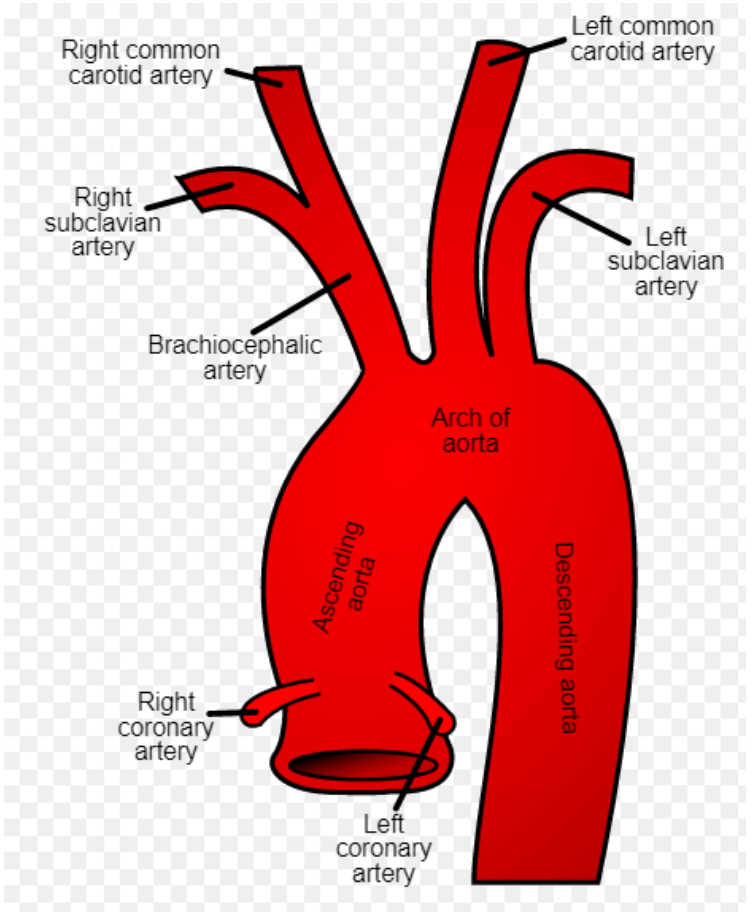
1. What test is done to distinguish MI from unstable angina?
2. What is the most common cause of a heart attack (or unstable angina)? More specifically, what type of insult/injury/pathology to the coronary vessel takes place?

Questions about MI

Review of MI is not on exam

Respond at **PollEv.com/davechandra251**

1. What test is done to distinguish MI from unstable angina?
2. What is the most common cause of a heart attack (or unstable angina)? More specifically, what type of insult/injury/pathology to the coronary vessel takes place?
3. What is a treatment that can be used in a patient that is suffering from an MI?
4. Thrombus around atheroma is the most common cause of a MI. Thromboembolus is rare. However for stroke, both are likely. Why?


Right common carotid artery
Left common carotid artery
Right subclavian artery
Left subclavian artery
Brachiocephalic artery
Arch of aorta
Ascending aorta
Descending aorta
Right coronary artery
Left coronary artery

Questions about MI

Review of MI is not on exam

Respond at **PollEv.com/davechandra251**

1. What test is done to distinguish MI from unstable angina?
2. What is the most common cause of a heart attack (or unstable angina)? More specifically, what type of insult/injury/pathology to the coronary vessel takes place?
3. What is a treatment that can be used in a patient that is suffering from an MI?
4. Thrombus around atheroma is the most common cause of a MI. Thromboembolus is rare. However for stroke, both are likely. Why?
5. What may be other mechanisms of coronary artery disease that may lead to an MI? Think back to other complications of an atheroma.

Strokes: Two main types: “ischemic” and “hemorrhagic”. But don’t be confused. Both produce ischemia and infarction of brain tissue.

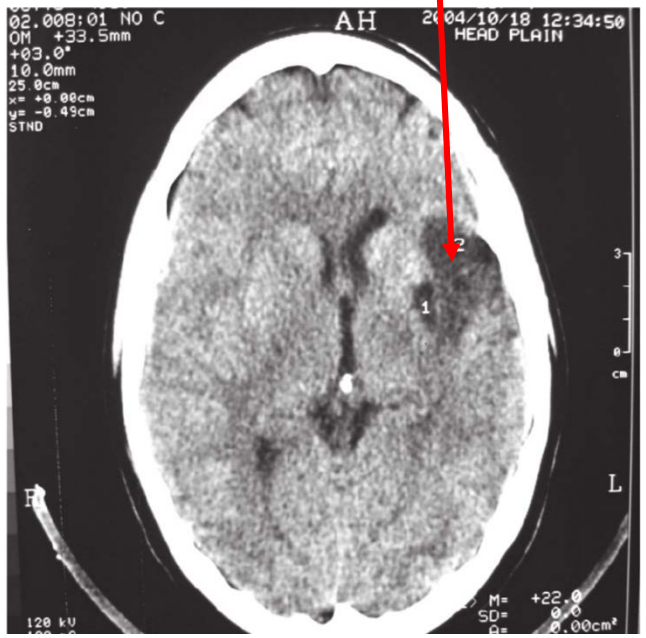
- Ischemic stroke
  - 85% of strokes
  - Caused by occlusion of vessels
    - Usually due to occlusion of large/medium vessels (thrombus/thromboembolus)
  - Treated with thrombolytic therapy
  - Better prognosis
- Hemorrhagic stroke
  - 15% of strokes
  - Caused by rupture of vessels
  - More common in younger persons
  - Cannot be treated with thrombolytic therapy
  - Worse prognosis

Ischemic Stroke… caused by occlusion of vessels

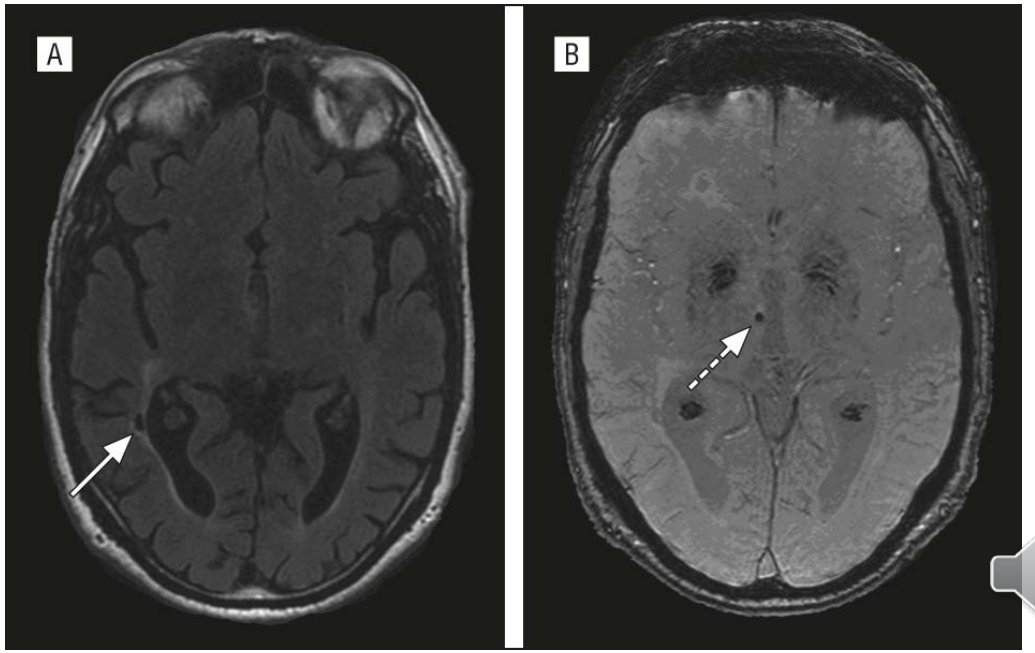
- Large vessel disease (large/medium size arteries)
  - Two main causes:
    - Thrombus forms around atheroma in carotid/cerebral vessels
    - Thrombus from heart, aorta, carotid embolizes and occludes smaller cerebral arteries
  - Produces large regional infarcts – infarction may be seen around affected vessel
    - Remember, infarcts may not always be seen in stroke patients on CT or MRI. Often seen only post-mortem.
  - Large vessel disease produces the symptoms seen in stroke
- Small vessel disease (arterioles)
  - Arteriolosclerosis caused by uncontrolled diabetes or hypertension
    - Produces hyalinization (thickening) leading to arteriolar stenosis which produces occlusion
    - Produces multiple infarcts throughout brain (lacunar infarcts)
      - Lacunar infarcts themselves usually do not produce stroke symptoms
        - Often a cause of "silent stroke"

Not on exam

Regional infarct



Lacunar infarcts



Hemorrhagic stroke… caused by rupture of vessels

- Rupture of vessel weakened by aneurysm
  - Aneurysm caused by atheroma
  - Congenital aneurysm (berry aneurysm)
    - Rupture of berry aneurysm is a common cause of stroke in young persons
- Rupture of vessels weakened by prolonged, uncontrolled hypertension
- Rupture of vessels due to malignant hypertension
  - Malignant hypertension – severe, sudden onset hypertension
    - Vessels do not have time to adapt and may easily rupture
    - Often a drug induced (e.g. cocaine) cause of stroke in young persons