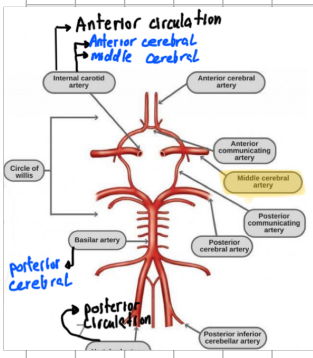
★Topic 1:- stroke & ↑intracranial pressure.

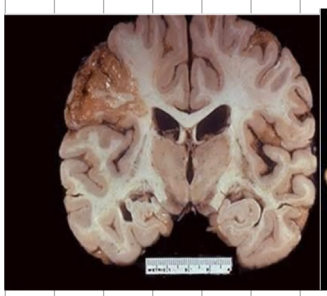
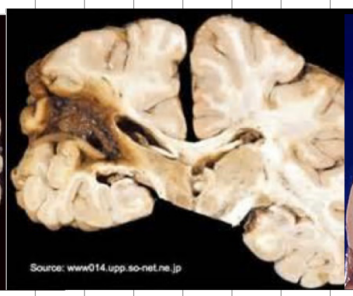
1) stroke or cerebrovascular accident:- Acute, Neurological
By a vascular cause, symptoms develops quickly → 24h

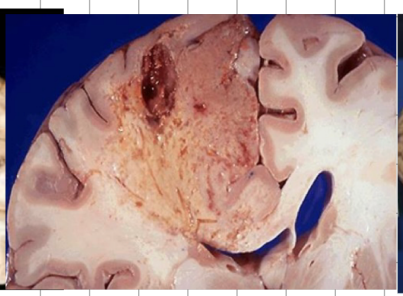
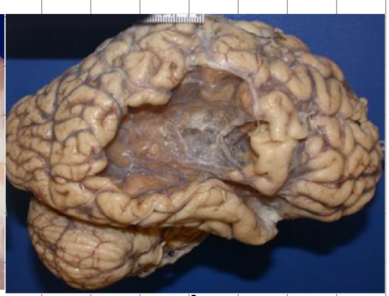
- <24 hours:- Transient ischemic attack (Risk of CVA)
- Types → Ischemic stroke:- (85%) occultion by thrombi or emboli
  - Thrombotic: comment sites → carotid bifurcation, origin of middle, Base of berilar
  - Embolic:- more common
    - source → cardiac mural thrombi:- valve, fib
      - arterial atheroma:- carotic & Aortic *
      - venous:- cardiac diffect (paradoxial) DVT (thigh), fat embolism.
    - comment site :★Middle cerebral artery★
      - vessels branch or stenotic (atherosclerosis)
  - Hemorrhagic :- 15%, vessel rupture (hypertension/vaculitis)



- Distinguish types:- Tx of anticoagulant.

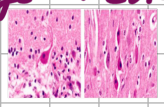
- Risk factors:- Same as atherosclerosis
  - Age, inactivity, HBP, Heart, DM, smoking, obesity.
- Clinical features:- (FAST)
  - F- Face:- dropped one side
  - A- Arms:- not able to Lift both arms (numbness in one arm).
  - S- speech:- slurred or garbled
  - T- Time:- Emersency.
- Macroscopic Apperance
  - early (<48h):- pale, soft swollen area (edema + Loss of neuron)
  - middle (2-10d):- gelatinous and friable.
  - Late (10d-3w):- Liquefaction necrosis (ischemic) → cavitation

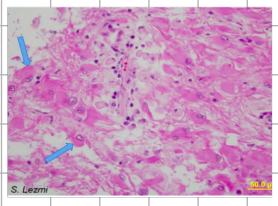
Infraction — Liquefaction → cavitation.

- Microscopic Apperence
  - Early (0-24h) :-
    - Red Neurons :- irrivisible damge → eosiophilia, pyknosis, karyorrhexis
    - neutrophilis infiltration
    - edema (soft



  - Subacute (24h - 2w)
    - Macrophages (Foamy)
    - gemistocytic astrocyte
    - Necrosis
    - vascular proliferation
    - Reactive gliosis (hard)
  - Repair (>2w)
    - Removal of necrotic tissue
    - Gliosis :- same as fibrosis, By Astrocytes.
    - Loss of CNS structures

- Gemistocytic astrocyte :-
  - Hyper (trophy & plasia)
  - enlarged nuclei
  - prominent nucleoli.
  - ↑pink cytoplasm
  - ↑, ramifying process.



2) Intracranial pressure

- Cranium (عِظَام الرَّأْس) :- skull bone cannot exapnd
  - so ↑pressure = ↑intracranial pressure.
  - Inside cranium
    - 80% brain tissue :- 75% fluid (Intracellular & interstial)
    - 10% blood
    - 10% CSF

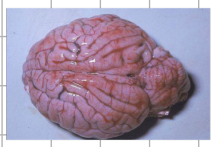
- Monro-Kellie hypotheris :-
  - Intracranial volume = V_{CNS} (Brain) + V_{CSF} + V_{Blood} + V_{Lesion}
    - any Lesion → ↑volume → ↑intracranial pressure.

- Intracranial pressure :- 7-15 mmHg

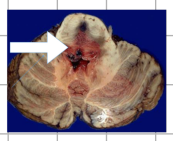
- Causes of Increase ICP
  - Mass :- tumor, hematoma, abcess
  - swelling :- ischemia, hypoxia, hypertension
  - ↑venous pressure :- HF.
  - Hydrocephalus :- ↑CSF (obstruction)
  - Idiopatic or unknown.

- **Clinical presentation**
  - Early → non-specific symptoms:- headache & vomiting.
    - Cushing reflex:- Hypertension (↑BP), bradycardia, Breathing.
  - more advanced:- neurological:- disturbed consciousness.
  - Later:- complications:- herniation & seizures

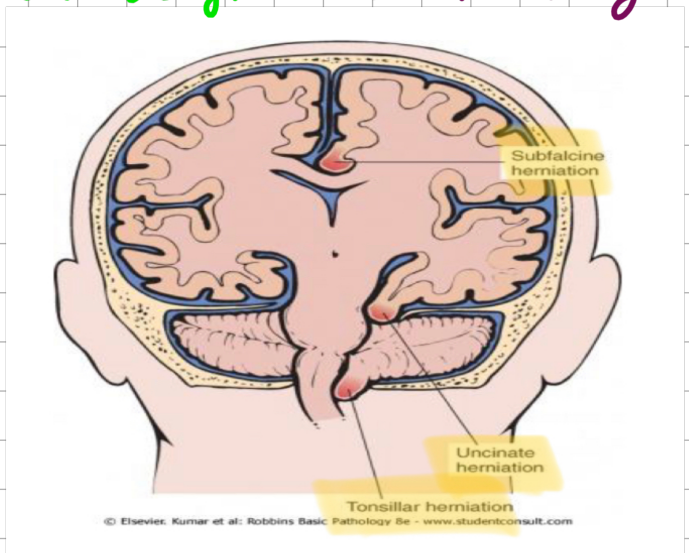
- **Brain edema / cerebral edema** :- fluid accumulation in brain parenchyma
  - vasogenic.
  - cytotoxic.
  - Distinction diminished
    - gyri :- widned by fluid
    - sulci :- filled with fluid → narrow



- **Hernation (complication)** :- ↑volume → ↑ICP → expansion of Brain
  - Subfalcine/cingulate
    - Location:- under edge of falx.
    - causes:- compress anterior cerebral artery → Ischemia.
  - Transtentorial / Uncinate
    - Location:- Medial temporal lobe / free margin of tentorium from supra → Infra-tentorial compartment.
    - causes
      1) III cranial nerve compress:- Dilated pupil, impaired ocular movement ipsilateral.
      2) posterior cerebral artery:- ischemia to visual cortex
         - Duret haemorrhage:- hemorrge in midbrain & pons → fatal



  - Tonsillar
    - Location:- Displaced tonsils through foramen magnum.
    - causes:- Brain stem compressing, (cardiac & Respiratory centers in medella).
    - Most dangrous:- Life threatning.



★ Topic 2:- Intracranial hemorrhage

- Non-Traumatic
  - hypertension
  - cerebral amyloid angiopathy. (الداء النشوائي)
  - Ruptured aneurysms (تمدد دموي).
  - vascular malformation.
  - Vasculitis
  - others:- Bleeding Disorders, Drug, cocaine, Tumors.
- Traumatic
  - Epidural
  - subdural
  - others:- subarachnoid, intraparenchymal.

☆Non-traumatic

1 Hypertension → primary/spontanous parenchymal heamorrage.

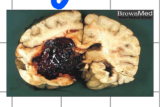
- 60y, due to rupture of small intra-parechymal vessels
- most common cause of non-traumatic hemorrahge.
- most effected site:- BG, thalamus, pon & cerebellum.

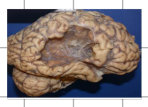
→ hylaine arteriosclerosis → weak → Rupture (↑BP)
- hylaine thiking (pink) + narrow lumen.

- can cause charcot-Bouchard micro aneurysms.

- symptoms
  - neurological symptoms related to area affected.
  - sympots of ↑intracranial pressure

- morphology:- Extravagated blood → cavitation





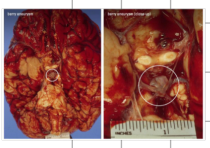
- hypertention effects
  - marrive intra-cranial pressure
  - Lacunar infracts:- small infracts in grey matter caused by narrowing of large cerebral artery.
  - vessel rupture:- small pentering vessels → slit hemorrhge
  - Acute hypertensive encephalopethy (edema)

2 Vasculitis:- Inflammation of vessels → weakens → rupture → hemorrghe.
- Infectious:- Syphilis, TB, cMV/herpes, aspergilliosis (↓immune)
- non-infectious
  - polyarthritis nodosa (localized middle cerebral
  - primary angitis → encephalopathy.

3 Cerebral amyloid angiopathy :- Amyloid deposition
- Usually Lobar hemorrhage , Long - standing.

- Amyloidosis:- Deposition of extracellular fibrillary proteins (misfolded) → chemically differs , same physically → Tissue damge
  - Microscope (Congo Red) :- continous, non - branching fibrils with a cross - β - pleated sheet.

4 Ruptured berry aneurysm:- most common non-Traumatic Subarchnoid hemorraghe , Due to ↑intracranial pressure
- other causes:- vascular malformation , trama, tumor, hemetological

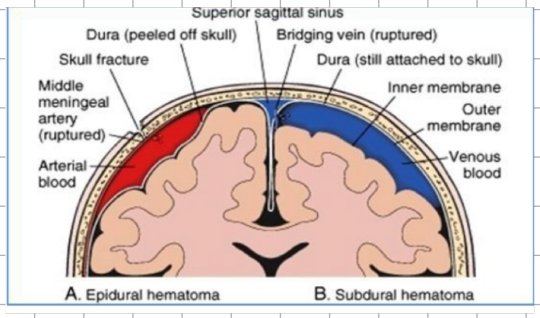


90% in the anterior circulation , near branching , 20-30% multiple

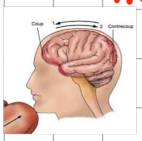
5 Vascular malformations
- cavernous malformation
- capillary telengectasia
- venous angioma
- Arteriovenous malformation:- Most common type , M>F, 10-30y
  - Symptoms:- seizures & hemorrage.

- Sites of hemorrage
  1) Intracranial :- non-traumatic
  2) subarcanoid :- Both (traumentic & non)
  3) subdural :- traumatic
  4) extra (epi) dural :- traumatic → Related to Dura

☆ Traumatic Lesion :- Mortality & disability , depends on extend & site
- Subdural:- Rapid movement during trauma , venous blood .
- Epidural:- fracture , Middle meningeal artery , Artirial blood.



- **Head injury :-** without / with external signs of injury, blunt / penetrating



- Coup :- injury in site of impact
- Counter coup :- injury opposite site of impact.

→ contusions

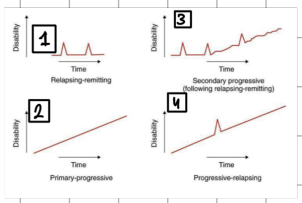
★ Topic 3 :- myleine diseases of CNS.

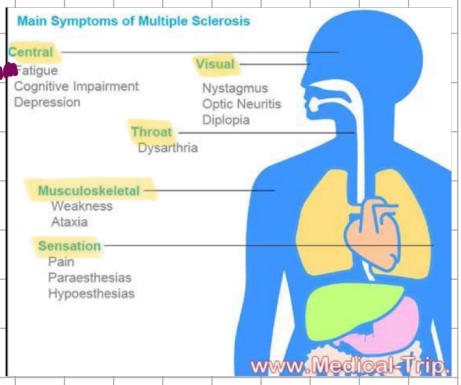
- Demyelinating :- acquired, damge to previosly myelinated axons due to enviromental cause → Autoimmune, viral, Drugs, toxins
- Dysmyelinating :- Leukodystrophy, inhirited mutations of proteins that form myelin.

- **Demylinating diseases :- Acurid destruction.**
  - multiple sclerosis (MS) :- most common, autoimmune
  - Neuromeylities optica :- Autoimmune → optic Nerve & spinal cord
  - post infectious demyelination
  - central pontine myelinotysis

1 Multiple sclerosis :- Episodes of neurologic deficits separated in time (symptom → another symptom) & separated in space (diffirent in the site) which attributed to white matter (axon).

- epidemiology :- F > M, young female (20-40), rare in old & young.
- clinicaly :- variable (site), revesible but the disease can recur
  - course
    - relapsing-Remitting :- Normal - symptom
    - primary progressive :- No remission & get worse by time.
    - secondary progressive :- 1 then 2
    - progressive relapsing :- 2 + periods
  - cannot be predict, time will tell



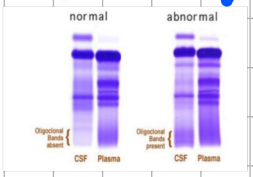


- outcomes
  - capcity to regenerate myline
  - secondary damge of axons :- after repeated relapses (usually don't effect axon but with repeated attacks autoimmune response → secondary axial damge (late))

- pathogenesis :- Autommune disease, onset of symptoms by enviromental Trigger (viral) & Gentic
  - Loss of Tolerance of self-protein in myleine sheath.
  - Genitcs :- x15 1st dgree relaves, 25% twins, HLA DR2 & gene for encoding cytokines receptors (IL2 & 7).
  - CD4 (T-helper) → TH1 :- secrete Interferon gamma → Mecrophge
    - TH 17 :- recruits WBC → cytokines

(Cellular immunity)

- CD8 & B Lymphocyte play a role
- oligoclonal bands :- IgG (IgM) in CSF by elecrophoresis (seperate protein accourding to size & charge.
  - Normally CSF proteins ≤ plasma proteins.
  - extra bands = intrathecally (in CSF)



- Morphology :- white matter (axons), multiple plagues (sclerotic)
  - 2 Types of plagues
    - Active plagues :- ongoing myleine brakedown (inflammation)
    - Quiescent (inactive) plagues :- No Inflammation
      - Astrocytic proliferation.
      - prominent gliosis.

2 Neuromyelitis optica :- inflammatory demylinating disease affecting mainly optic Nerve & spinal Cord.
- pathogenisis :- Antibodies against aquaporin-4 (Diagnostic), humoral

3 post infectious demyelination :- After viral (not direct, autoimmune)
- Acute dissminating encephalitis :- 1-2 w, non-Localized symptoms.
- Acute necrotizing heamorrgic encephalomyelitis :- more danger

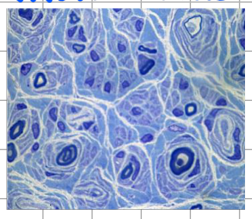
4 central pontine myelinolysis :- not immune, edema of oligodendrogyte → seperting myleine from axons (pons)
- occurs after rapid correction of hyponatremia (change in osmolarity).
- Pons :- motor relay center → quadriplegia (Lock in syndrome)

- Locked in syndrome :- aware but cannot move due to comple paralysis of all voluntary muscles in the body execept vertical eye movement & blinking (runs dorsally) (damge of ventral pons)

- Dysmylinating diseases :- Leukodystrophies, Inhirted disease
  - mostly autosomal recesive, sometimes X-linked (mutation)
  - Normal in children → Losing developmental milestones in infancy.
  - prosressivly & fatal.

★ Topic 4:- myelin disease of the PNS.

- **myelin:-** protein - Lipid complex wrapped around the axons
  - by → CNS:- oligodendrocyte.
  - by → PNS:- schwann cells.
  - predominant component of white matter.
- **Diseases of myelin in PNS.**
  - Main pattern:- segmental demyelination
    - primary:- injury to schwann or myline → Hereditary. / Autoimmune.
    - secondary:- demyelination due to underlying axonal abnormalities.
      - Toxins, alchol, Drugs, ischemia, ↓ vitamins.
  - re-myelination occurs by schwann cells porliferation → function restored
  - hypertropic neuropathy (onion bulb):-
    repeated demelination-re-myelination cycles
    → ↑number of schwann cells → enlarged nerve.



  - clinical features
    - Motor nerve:- muscle weakness & atrophy.
    - Sensory nerve → sensory loss.
      - pain
      - parasthesia:- → numbness & tingling & prickly
        - → burning sensation with no physical explanation (e.g. legs)
    - Autonomic → loss of bowel & bladder control.
      - cardiac abnormalities:- arrthmia, BP changes.
  - Types
    - axonal neuropathy (80-90%):- Any disease effect nerve or Blood supply.
    - demyelination neuropathy:- hereditary or Autoimmune

1 Diabetic neuropathy:- most common cause of generalized phephral neuropathy & most common complication of DM.

- Risk → Duration of DM.
  - Lvl control of blood sugar
- can manifest as polyneuropathy or mononeuropathy
- forms
  - 1 Distal symmetric sensomotor polyneuropathy:- most common, stocking-gloves
  - 2 autonomic:- Bowel, bladder, cardiac (dangerous).
  - 3 Lumbosacral:- pain/Loss of sensation in lower legs.
- Symptoms:- Numbness, ↓ability to feel pain, burning sensation sharp pain/cramps, ↑sensitivity to touch, muscle weekness Loss of reflexes, Loss of balance, foot problem (ulcer, infection).
- pathogenesis
  - 1 AGE:- damge vessels → ischemic damge to nerves
  - 2 polyol pathway:-
    - ↑sorbitol
    - ↓NADPH
    - ↓glutatione
    - → direct damge to nerves.

1 Advanced glycation end products (AGE)

- formed by nonenzymatic interaction between Glucose derived precursors & Amino acids (protein + Glucose). formes glycated proteins.

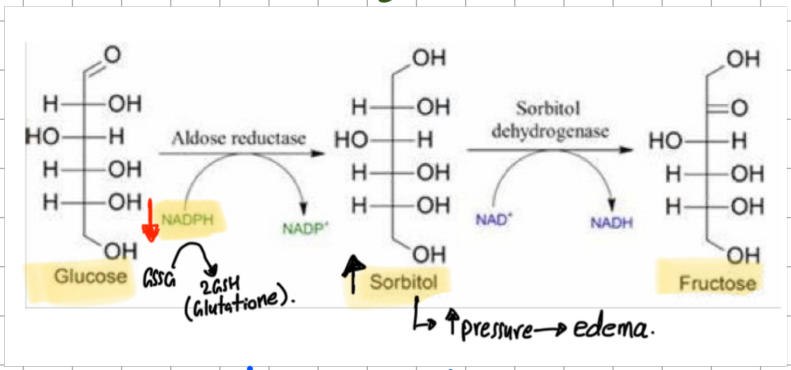
- glycated proteins + RAGE receptors

RAGE present in → inflammatory cells :- macrophages + T-Lymphocytes
RAGE present in → Blood vessels :- endothial & vascular smooth muscle cells

- effects of AGE + RAGE
  - Direct
    - formation of reactive oxygen species.
    - cytokines & growth factor formation.
  - Ischemic
    - procoagulant (↓Lumen)
    - proliferation of SM & ↑extracellular matrix
      - Microangiopathy :- Thickness of vessels

2 polyol pathway

- ↑sorbitol.
- ↓NADPH.
- ↓glutatione.



- sorbitol can't cross plasma membrane → ↑osmotic pressure → edema → damge.

- polyol pathway uses NAPH → ↓NAPH → ↓glutatione → ↑oxidative stress

2 Guillan Barre syndrome :- autoimmune neuropathy for myline or axon

- follows
  - Infections :- campylobacter Jejuni (most common), CMV, EBV
  - immunization or surgery.
- CSF :- ↑proteins, ↓WBC.

covid 19

- clinical feasures :- Acute, Symmetric, paralysis, begins distally → ascends proximally.
  - may cause respiratory difficulty if it reach diaphragm.
  - Autonomic involvment → cardiac arrhythmia (↑BP, ↓BP)
- outcome :- resolves 2-4 weeks after onset.

- Chronic inflammatory demyelinating polyneuropathy (CIDP)
  - similar to Guillian Barre syndrome. But chronic (2m or more).
  - immune mediated with no history of infection.
  - associated with Autoimmune diseases & AIDS.