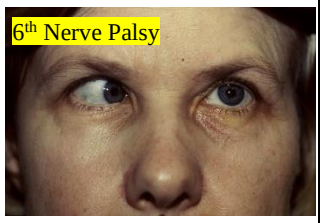
Idiopathic Intracranial Hypertension (IIH)

Secondary Headaches

AKA Pseudotumor Cerebri.
Disorder of increased intracranial pressure with unknown etiology. All brain imaging are normal and show no mass occupying lesions. Optic nerve is usually compressed so patients usually have headaches and visual problems such as papilledema and may lead to vision loss.
Epidemiology: Common in Young Obese Females.

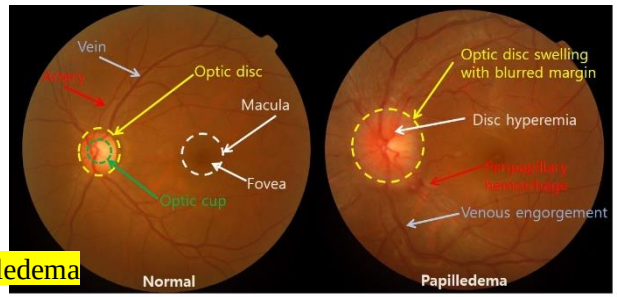


Increased ICP Clinical Features:
-Nausea, Vomiting (Compression of chemo triggers)
-Bilateral Papilledema (Compression of optic nerve)
-**Visual Obscurations** (Sudden transient bilateral visual loss with posture changes)
-Decreased Consciousness (Compression of reticular formation)
-Diplopia (Compression of Abducent nerve) → Eye rotated medially (Bi or Uni)
-Cough causes pain (ICP increases with it. And in IIH ICP is already too high)
-Tinnitus

Diagnosis: LP confirms high ICP (>40cm CSF) with normal CSF contents after excluding masses and hydrocephalus on brain imaging. Safe LP is done after excluding masses.

Treatment: Self limiting in some patients with weight loss or with one or more LPs. In other patients, it is chronic and threats vision. In such cases we use:
-Acetazolamide (Carbonic Anhydrase inhibitor, Decreases CSF formation)
-Chlortalidone (Diuretic)
-Corticosteroids (Not preferred due to SE, unwanted weight gain, withdrawal effects)
Surgery may be needed to protect optic disc or for CSF drainage techniques

DDx
Similar symptomatic syndromes:
-Cerebral Venous Sinus Thrombosis (CVST. Equivalent to a DVT)
-Excessive Vitamin A
-Calcium metabolism disturbances
-SLE
-Drugs: Tetracyclines and Corticosteroids (ironic)



Papilledema

Temporal Arteritis

Secondary Headaches

AKA Cranial Arteritis AKA Giant cell arteritis
Granulomatous inflammatory changes (with giant cells) in Carotid Artery branches, most commonly Superficial Temporal Artery but can occur elsewhere including ophthalmic A. Artery shows narrowing which may become superimposed with a thrombus
Important in 50yrs old and above. Onset is gradual and continuous.

Cause: Unknown etiology but viral infections and autoimmunity are involved. Commonly associated with Polymyalgia Rheumatica. (=girdle pains and morning stiffness. Dramatically responsive to steroids at lower doses, 7.5-15mg daily prednisolone)

Clinical Features:
•Headache localized to temples.
•Temple tenderness (Appears with hair combing)
•Pain chewing (Jaw claudication due to blood supply impairment)
•Diplopia (3rd or 6th nerve involvement due to ophthalmic artery involvement)
•Temporary unilateral vision loss (**Amaurosis Fugax**) High risk for blindness
•Optic disc pallor
•Swelling and **loss of pulsation** may occur
•Fever, night sweats, anorexia, weight loss
•Shoulder and/or Pelvic pain
•Rarely skin ulceration
More generalized arteritis shows liver function disturbance, intracranial vessels involvement (stroke) specially in vertebrobasilar area.
•Rarely causes peripheral neuropathy.

Diagnosis:
1. Increased inflammatory markers:
-ESR (erythrocytes sedimentation rate) = over 100mm/h *(sometimes can be normal)*
-CRP (c-reactive protein) = high *(Almost always high)*
2. Temporal artery biopsy
Negative finding does NOT exclude because of possibility of skip lesions)
3. Other tests:
-Liver function tests (increased alkaline phosphatase)
-Blood tests (normochromic normocytic anemia, glucose)

Treatment: If suspected, treat with urgent IV hydrocortisone after ESR is out and before biopsy is out. Corticosteroids are fortunately highly sensitive however initially high doses are required (40-60mg daily Prednisolone).
Rapid response to steroids = Dramatic relief within 1-2days.
Dose is tapered down according to symptoms and ESR. Treatment takes 1.5-2yrs.

Meningism

Secondary Headaches

Meningeal irritation caused by subarachnoidal hemorrhage or meningitis. Characteristically produces global or occipital headache with nuchal rigidity, photophobia and phonophobia.

-Subarachnoidal Hemorrhage: Very sudden onset and very severe, LOC may occur.
-Bacterial Meningitis: Acute onset but worsening over minutes or hours.

Nuchal rigidity is assessed by **K**ernig Sign (Pain and resistance to passive **K**nee extension with the hip flexed, any pain, resistance, inability to extend is a + sign)
Nuchal rigidity in children may be due to posterior fossa mass, however Kernig Sign will be not found (Negative)

Other Causes

Secondary Headaches

1) Headache can accompany Stroke especially when caused by:
-Hemorrhage
-Venous sinus thrombosis (CVST)
-Arterial dissection

2) Headache can be due to Metabolic Disturbances:
-Hypoxia
-Hypercapnia (Acidosis)
-Hypoglycemia

3) Products and drugs:
- Pheochromocytoma
-Vasoactive drugs
-Monosodium glutamate (MSG)
-Alcohol
-Nitrates and Nitrites

Cluster Headache

Primary Headaches

الصداع العنقودي
Unilateral usually around or behind the eye. Pain is always on the same side during a cluster but may switch side between clusters. character is excoriating pain (طحن).
Highest suicide rate in Primary Headaches.
Attacks last 20mins-3hrs and occur multiple times a day [1-8 times] (cluster).
They come as Clusters of attacks in one period followed by a period of no attacks hence the name. Clusters last weeks to months with remission of months to years.

Cause: Autonomic symptoms may be of Histaminergic and Humoral mechanisms
Epidemiology: Males (20-60yrs)

Clinical Features:
Unilateral pain with red, swollen watery eyes.
Parasympathetic symptoms UNILATERAL (tearing, stuffy nose, ptosis, miosis)
Agitated/restless during attacks
Unilateral facial sweating
Wakes patient up. More common at night.
Redness
Horner's syndrome unilaterally after attack
Horner's Syndrome:(Anhidrosis Miosis, Ptosis, Enophthalmos)

Horner's Syndrome

S	Sympathetic Nerve Fiber Injury
A	Anhidrosis
M	Miosis
P	Ptosis
L	Loss of ciliospinal reflex
E	Enophthalmos

Treatment:
For Acute attacks
Triptans (Sumatriptan subq)
Ergotamine (best as suppository at bedtime with caffeine)
60% high flow oxygen 6L (10-15mins) until patient feels well. Some patients have it at home

Prophylaxis

Verapamil, Methysergide, Pizotifen
Lithium (For chronic superrefractory cases but blood levels must be monitored) Dangerous
Steroids- Prednisolone (short reducing course of 2weeks to break the cycle of attacks)

DDx:
'Trigeminal-Autonomic' syndromes are rare but have unilateral headache and/or facial pain with autonomic features. These are highly responsive to Indomethacin (NSAID)

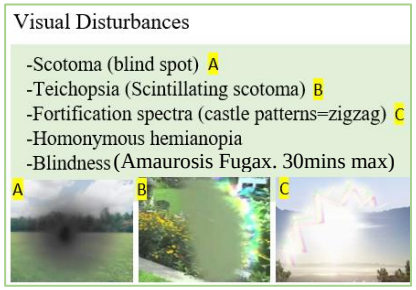
Migraine

Primary Headaches

Unilateral or bilateral periodic headache which may be associated with vomiting and visual disturbance. Pain is pulsating in character. Aura may precede.

Epidemiology: Common (>10% of general population experienced it at least once)
Any age, F>>, Youngs, Family history is common.
•Develops in people with travel sickness and cyclical vomiting in childhood.
•Relationship to HTN and head injury too.

Pathogenesis:
Triggered by stress (after stress is over, holidays & weekends), inadequate sleep, food, exercise, hormones (menstruation, menopause, menarche).
The following are solely theories and studies on the MOA:
1- Aura is thought to be caused by intracerebral vasoconstriction and a wave of depolarization across the cortex.
2- The headache is subsequently caused by vasodilation in the extracerebral vessels of the scalp and dura.
3- Serotoninergic pathways (5-HT) and vasoactive peptides are involved.
4- Calcium channels are involved.



Migraine Types:

A. Migraine with Aura (Classical Migraine)

Phase1: Prodromal symptoms:
Lasts for hours: Fatigue, mood changes, hunger, anorexia, yawning

Phase2: Aura:
The attack begins with aura: lasts 15-20mins or 1hr
There are visual symptoms (picture). Sensory symptoms are less common but unilateral numbness & paresthesia may occur in face/limbs. Dysphasia and limb weakness is rare. Aura can mimic a TIA or epilepsy. May overlap with headache.

Phase3: Headache:
Lasts for hours (4-72hrs). Typically, unilateral and periorbital with hemianopia on opposite side. Throbbing pain increased with cough, straining, bending (Jolt Phenomenon) Patients gain relief from sleeping and sitting in a dark room. Photophobia, phonophobia, N/V, pallor, diuresis are associated symptoms

Phase4: Postdrome:
Lasts 1-2days feels like a hangover

B. Migraine without Aura (Common Migraine) 90%

Aura is absent but vague prodromal symptoms may be present. Headache is similar to classical type but may occur upon waking up. Aggravated by simple physical activity.

C. Basilar Migraine (Bickerstaff variant)

Affects teenage females. During the aura, vertebrobasilar ischemic features occur such as vertigo, diplopia, dysarthria, ataxia and syncope

D. Hemiplegic and Ophthalmoplegic migraine

Rare syndromes. The migrainous headaches are accompanied by hemiplegia or ophthalmoplegia with focal neural deficits lasting days to weeks.
Diagnosed after structural causes have been excluded (ex: aneurysms)

Diagnosis: History dependent. Periodicity is important where the attacks last less than 3days with pain-free periods varying from days to months.
Weeks-long continuous headache can be **status migrainosus (rare)**
Neurological examination is normal unless hemiplegic or ophthalmoplegic migraine is present or if a migrainous cerebral infarction has occurred.
Cranial bruits may indicate a migraine associated with vascular malformation of the brain

Focal neurological features always recurring on the same side may prompt brain imaging to exclude an underlying lesion.

DDx (of transient focal neurologic symptoms):
Migraine
Transient cerebral ischemia
Epilepsy

Treatment:

For Acute attack

1- Analgesic (paracetamol) with antiemetic (for vomiting)
2- 5HT1 receptor agonists (sumatriptan, po, subq, nas)
Sumatriptan interacts with ergotamine, MAO inhibitors, selective serotonin reuptake inhibitors and lithium. Do not combine and don't use ergotamine or sumatriptan in IHD.

For Prophylaxis

1- Avoid dietary triggers
2- Caution with estrogen preparations (oral contraceptives, HRT)
For patients with frequent attacks (more than once a month):
3- Betablockers (Propranolol)
Betablockers are contraindicated in uncontrolled HF, obstructive airway disease, PAD, cardiac bradycardia
4- 5HT2 receptor antagonists (Pizotifen)
Pizotifen SE are weight gain, drowsiness, anticholinergic effects (cant use in glaucoma, urinary retention
5- Valproic acid, Verapamil, Topiramate
6- Methyl Sergide
Only for frequent severe unresponsive migraines. Under supervision for SE of retroperitoneal fibrosis
7- Tricyclic Antidepressants (Amitriptyline) and related drugs (Dosulepin)
Good for patients who have coexistent tension headache

Tension-Type Headache

Primary Headaches

Most common Primary Headache. Pain varies from dull at various sites to global pressure to feeling of tight band around the head. Gets worse at evening/night. Needs to stay >7days to diagnose.

Cause: Could be abnormal head and neck muscle contractions triggered by anxiety and depression or by local disease of head and neck such as cervical spondylosis or dental malocclusion

Clinical Features:
Normal physical examination
No associated symptoms (can have photophobia, phonophobia, N/V, blurred vision)
Coexists with Migraine

Treatment:
•Reassurance of no presence of sinister causes
•Physiotherapy (Muscle relaxation) and Psychotherapy (Stress management)
•Tricyclic Antidepressants: (in frequent or persistent cases. Used for 3-6mo)
-Amitriptyline
-Dosulepin

Chronic Daily Headache

Primary Headaches

Headache occurring minimum 15 days a month

Causes:
Medication overuse (patient will come complaining of drugs no longer effective)
Secondary Headaches
Chronic tension-type headache
Transformed migraine (migrainous features persist but normal periodicity is lost)

Treatment:
Withdrawal of overused medication and treatment with the remaining headache with NSAIDS, steroids, antiemetics, dihydroergotamines. Tell them to bare it for 1week without any drugs.

Prophylaxis:
Tricyclic antidepressants and related drugs are preventive measures and should be introduced at the earliest opportunity

Trigeminal Neuralgia

Facial Pain

Unilateral facial pain over one or more trigeminal sensory areas (Common at V2,V3).

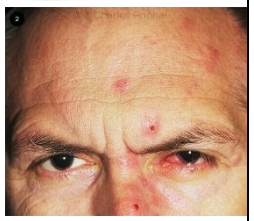
Clinical Features:
•Severe sharp, stabbing, electrical pain triggered even by a blow of air. Patients are reluctant to wash or shave their face. Even speaking can trigger. Chewing is more difficult and may cause weight loss
•Normal trigeminal function on physical exam
•Occurs multiple times a day 10-100times. High risk of suicide.
•Any abnormal neurological signs may indicate presence of a lesion (ex: cerebellopontine angle tumor)

Causes: Trigeminal sensory root compression by abnormal arterial loop (Superior Cerebral A) Or by cerebellopontine angle tumors
In younger patients, MS through trigeminal demylination
*Anxiety of the trigger areas causes **Tic Douloureux,** involuntary facial spasms
***Glossopharyngeal Neuralgia** is similar but rarer with pain in throat or deep inside ear
Diagnosis: Clinical + MRI shows trigeminal compression

Treatment:
1. Carbamazepine (Contraindicated in Myoclonic Jerks and absence seizures)
2. Baclofen, Phenytoin, Valproic acid, Gabapentin, Clonazepam, Tricyclics.
Simple analgesics do not relieve pain
3. Surgical treatment. May cause numbness + persistent pain: **Anesthesia Dolorosa**
4. Glycerol ganglion injection or radiofrequency thermocoagulation

Post-Herpetic Neuralgia

Facial Pain



Occurs unilaterally in patient who had shingles in the trigeminal nerve distributions
(Most commonly V1: Zoster Ophthalmicus) causing Persistent facial pain after the rash has healed. Pain can be extremely severe, lasting 2-3yrs after eruption.

Treatment: Sometimes responds to:
Tricyclic Antidepressants, Carbamazepine
Topical Capsaicin (Found in hot peppers, gives the burning sensation) – Qutenza®

Epilepsy

Epilepsy is the disorder of recurrent seizure attacks. A seizure is a sudden burst of uncontrolled electrical activity in the brain cortex (Grey matter) that results in transient Muscular/Behavioral/Emotional/Sensual/Awareness changes.
Epidemiology: Very common (1% of general population)

Some epilepsy attacks are triggered by flickering light (TV and computer screens)

Generalized seizure: Involves entire brain
Partial (focal) seizure: Involves one part of the brain

Simple seizure: Awareness is unaffected
Complex seizure: Awareness is affected

Diagnosis: Primarily clinical. EEG can confirm and classify especially in children. However, in adults, there are frequent false positives and false negatives.
Better EEG results are acquired by prolonged recordings especially with sleep deprivation. Ambulatory EEG or Telemetry with video recordings can diagnose.
Routine blood tests (Glucose and Calcium) can look for causes.
MRI and CT scan can be done.

Treatment: Prophylaxis is given after a second attack and not the first one.
Surgery may beconsidered for intractable refractory epilepsy.

Seizure Type	Drug of choice
Partial	Valproic acid Lamotrigine Phenytoin Carbamazepine
Absence	Valproic acid Lamotrigine Ethosuximide
Myoclonic	Valproic acid Lamotrigine Clonazepam
Generalized Tonic-Clonic	Valproic acid Lamotrigine Phenytoin Carbamazepine

•70% will be sufficiently treated with monotherapy. Others will need a second drug and others a third. The more drugs needed the lower the successfulness.

•Refractory epilepsy causes:
1. Non-concordance with medication
2. Pseudoseizures or non-epileptic attacks (with or without true seizures)
3. Structural brain diseases or anomalies
4. Alcohol and lifestyle.

Prognosis: Good. Most patients have 5yr remission and many stopping treatment.
View pg88 table and other figures.

DDX: Pseudoseizures, syncope, cardiac dysrhythmia, hyperventilation/panic attacks, TIAs, Migraine, Narcolepsy, Hypoglycemia, Vestibular disorders

Partial Epilepsy

Epilepsy

Partial or focal seizure, can either be simple or complex. Symptoms vary a lot:
Sensory symptoms →Parietal lobe is affected
Visual hallucinations → Occipital lobe
Motor movements → Frontal lobe (Face & hands have the largest area = most affected)
Auditory hallucinations + mood changes + ANS → Temporal lobe

Temporal lobe seizures are the most common
Partial motor seizures can become generalized (2ndry generalized) and become tonic-clonic seizures

TEMPORAL LOBE SEIZURES (TLE)

In focal seizures, there is usually an aura or a warning of an upcoming attack. They are common in TLE but not everyone can remember them. Auras can be:
•Psychic symptoms
•Mood changes, Fear or Joy for no reason
•Olfactory/gustatory/visual hallucinations
•Déjà vu
•Rising sensation in the stomach (rollercoaster)

Symptoms of the attack include:
•Loss of consciousness
•Staring into space
•Anxiety/Confusion
•Stereotypical movements (automatism): chewing or lip smacking or rapid blinking.
•There might be more complex or violent movements sometimes.

After the seizure patients are confused, amnesic, fatigued.

Over time, repeated seizures in this part (epilepsy) can cause it to scar and atrophy, increasing the probability for Alzheimer's and memory problems (hippocampus).

JACKSONIAN EPILEPSY

Focal motor attacks beginning distally and spreads proximally.
Typically, from corner of the mouth, thumb, index finger or great toe.
Movements rapidly spread across face or ascend the limb (Jacksonian march)
Usually caused by an organic brain disease (ex. Tumor near the cortex).
After the attack, the affected limbs may become temporarily weak (Todd's Paralysis).

***Todd's Paralysis** Usually limited to one side of the body. Can last an average of 15hrs usually subsides on its own completely after about 2 days. Caused by severe and temporary suppression of the seizure affected area of the brain

***Epilepsia Partialis Continua** (EPC) is a rare form of Jacksonian epilepsy where the attack persists for days, weeks or even months. Attacks occur every few seconds or minutes, most commonly in the hands or face. Aka **Kojevnikov's epilepsia**

Primary Generalized Epilepsy

Epilepsy

Epilepsy occurring on its own. not secondary to a partial seizure.
All generalized seizures have some sort of awareness alteration (Complex).
Before an attack there might be vague symptoms such as dizziness or irritability.
An epileptic cry may precede the convulsions.

Subtypes (according to symptoms):

1. TONIC CLONIC (aka GRAND MAL)

The most common type. The one we see most.

1) Starts with the tonic phase where there is generalized muscle spasms (only few seconds) if the person is standing, it will cause them to fall. Support their head.
2) Followed by clonic phase where there are sharp repetitive muscle jerks (2-3mins). Remove any sharp objects so they don't hurt themselves.
3) As the seizure subsides, there may be associated tongue biting, Salivation and urine incontinence. Tongue biting may cause bleeding but its fine, do not put anything in their mouth. As seizure subsides, roll patient to one side so they breathe
4) After the jerk, patients remain unconscious for ~30mins and then wake up drowsy and confused for several hours (Post Ictal confusion)

Only call 911 if the seizure lasts longer than **5mins** (Status Epilepticus**)** or if a second seizure occurs before the patient is fully recovered or if the patient is pregnant.
It is normal to have irregular breathing during the seizure attack but if it doesn't get back to normal after the seizure, Call 911

Back pain is common. Muscular spasms of the back are strong enough to fracture the vertebra

2. MYOCLONIC

1) Starts with sudden very brief muscle jerk/s. Usually just one or both arms. But sometimes the person's head or whole body jerks. The jerks can be very mild like a twitch or very forceful. If it occurs in the leg, the patient may fall
2) After the seizure, recovering is immediate.

Although the seizure is brief, it can be very frustrating by causing spilt drinks or injuries.

3. CLONIC

Violent rhythmic contractions, more prolonged or violent than myoclonic. Very similar to the clonic phase of tonic-clonic seizures.

4. TONIC

More likely to happen during sleep.
Clusters may occur (multiple tonic seizures in short period of time)

1. Muscles stiffen either on one side or both sides of the body depending on the brain site. The neck extends, arms and leg contract. If patient is standing, they might fall down. Eyes open wide and roll up. Lips may turn blue and appear unbreathing due to stiffening of chest muscles. The seizure lasts no more than a minute.
2. Recovery is fast. Patient may be groggy for a few minutes if they had a cluster.

5. ATONIC (aka DROP ATTACKS)

1. All muscle tone is lost and patient drops heavily to the floor. Very brief and patient is usually able to get up straight away. Injuries can happen. Often to the nose, face or head (very short, lasts a few seconds)
2. Recovery is straight away.

6. ABSENCE (aka PETIT MAL)

Second most common

1. Unconscious for a few seconds. Patient stops what they are doing. But they don't fall. They might blink, have slight jerks or bite lips. Patients don't know what's happening and they can't be taken out of it.
2. Recovery is immediate

May occur multiple times a day even a 100. More common waking up or falling asleep.
If it occurs multiple times, avoid eating and stay away from sharp objects

Febrile Convulsions

Epileptic Syndromes with consequences in Adulthood

Seizures associated with fever. Occurs in children (3mo-5yrs) old. Takes place in 3% of otherwise normal children. Usually are brief seizures (less than 15mins). Uusally generalized but focal is possible, so are prolonged attacks with residual neurological signs

•70% occur as an isolated attack with NO recurrence.
•2-3% carry a risk of developing epilepsy

Does not usually require prophylaxis

Infantile Spasms (West's Syndrome)

Epileptic Syndromes with consequences in Adulthood

Consists of a Triad of:

1) Brief spasms within the first few months of life: Shock-like flexion of arms and neck with drawing up of knees (Salaam attack)
2) Progressive learning difficulties
3) Characteristic EEG (Hypsarrythmia= meaning chaotic, all over the place)

Causes:
Perinatal asphyxia
Encephalitis (TB)
Metabolic disorders
Cerebral malformations
Minority is idiopathic

Treatment: should be ASAP to stop seizures and avoid brain damage. Most anticonvulsants are ineffective. Treatment of choice is corticosteroids.

Absence Epilepsy

Epileptic Syndromes with consequences in Adulthood

Covered in (Primary Generalized Epilepsy)
Typically starts in childhood (Peak onset 4-8yrs) More common in girls

•10% risk of developing other seizure types as an adult.
•Characteristic EEG: 3Hz generalized, symmetrical spike-wave complexes.

Treatment: Valproic acid, Ethosuximide or both.

Juvenile Myoclonic Epilepsy (Janz Syndrome)

Epileptic Syndromes with consequences in Adulthood

Benign common form of primary generalized epilepsy. Typically starts in teenage years.
Consists of clinical triad of:

1) Infrequent generalized seizures often on waking
2) Daytime Absences
3) Sudden shock-like involuntary jerks (Myoclonus) usually in the morning. Consequently, patients spill or throw their breakfast (Kellogg's Epilepsy)

•EEG shows polyspike-wave discharges and photosensitivity
•must be distinguished from myoclonus and epilepsies that are associated with childhood underlying degenerative disease of the brain (**Progressive Myoclonic Epilepsies)**

Treatment: Valproic acid. Recurrence is likely if medication is stopped.
Valproic acid is not preferred for females in childbearing age as it is teratogenic.
Carbamazepine may be given.
Alternatives: Clonazepam, Levetiracetam and Lamotrigine.

Treatment of **Progressive Myoclonic Epilepsies** with carbamazepine instead of valproic acid worsens. Thus, the increasing importance to distinguish.

Stroke

Ischemic Stroke

Sudden focal neurological deficit attributed to vascular cause with evidence of infarction (cell death) with rapidly developing symptoms (within seconds or minutes). The symptoms last more than 24hrs or lead to death. Strokes are two types:

- Ischemic (Thrombotic, Embolic) → much more common
- Hemorrhagic (ICH, SAH)

TIA: Rapid loss of focal CNS function lasting less than 24hrs.

Epidemiology: 3rd cause of death after heart disease and cancer. Most strokes are cerebral infarcts

Causes:

a. **Thrombosis** (Risks: HTN, DM, HL, smoking, obesity, age)

Virchow's triad (3 factors to create a thrombus):

1. Vessel wall abnormalities:
   - inflammation (vasculitis),
   - trauma (dissection),
   - Degenerative diseases (atherosclerosis in large vessels/lipohyalinosis in small vessels).
2. Blood abnormalities: Polycythemia
3. Blood flow disturbances

b. **Embolism** may complicate degenerative arterial diseases or arise from the heart: (Valvular disease, Atrial fibrillation, Recent MI)

*Degenerative arterial disease is the most common cause of stroke.

*Smaller atherosclerotic plaques are more dangerous as their fibrous caps are softer and more prone to tear off

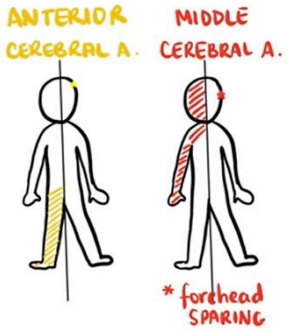
CNS ischemia causes edema:

Cytotoxic edema: When glial cells and neurons don't receive enough blood flow, they accumulate:

• Na^{+} which draws in water thus cells swell.

• Ca^{+2} which causes cells to rupture

Vasogenic edema: Inflammatory cells come in to remove damaged cells, resulting in BBB damage, allowing fluids/proteins to enter the BBB.



This edema/swelling causes deterioration within days after the stroke by increasing ICP and pushing adjacent structures

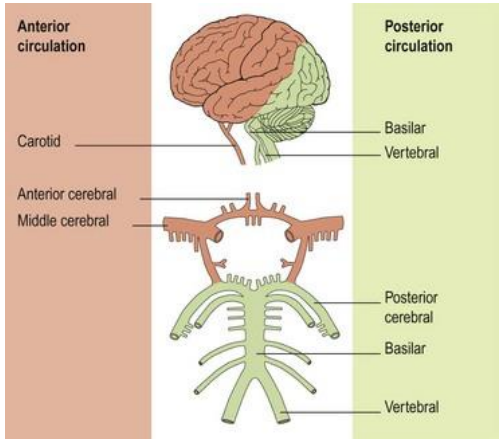
Smaller atherosclerotic plaques are more dangerous as their fibrous caps are softer and more prone to tear off

Clinical Features: (Depend on infarcted area)

ACA: feet + leg + hips + genitals
MCA: hands, arm, face, speech
PCA: visual + brainstem
Basilar: Locked in syndrome
Vertebrobasilar: Syncope
Carotid: visual

Anterior Circulation: ACA + MCA + **carotid**

Posterior Circulation: PCA + **basilar + vertebral**



• Total anterior circulation TACS:
Hemiplegia (upper corticospinal)
Hemianopia (optic radiation)
Cortical deficits (Dominant- Dysphasia, Non-Dominant- Visuo-spatial loss)

• Partial anterior circulation PACS:
Two of the above or cortical deficit alone

• Lacunar LACS:
Due to lipohyalinosis in small arteries causing a characteristic syndrome:
Pure motor OR pure sensory OR sensorimotor OR ataxic hemiparesis

• Multiple lacunar infarcts may produce:
Multi-infarct dementia (cognitive impairment)
Marche a petits pas (small steps gait)
Gait apraxia (difficulty starting walking: ignition failure)

• Posterior circulation (vertebrobasilar) POCS:
Homonymous Hemianopia
Brainstem deficit (vertigo, diplopia, altered consciousness)

Complications: (severely affected patients)
-Pneumonia
-Fluid imbalance
-DVT and PE
-MI, Arrythmias, HF

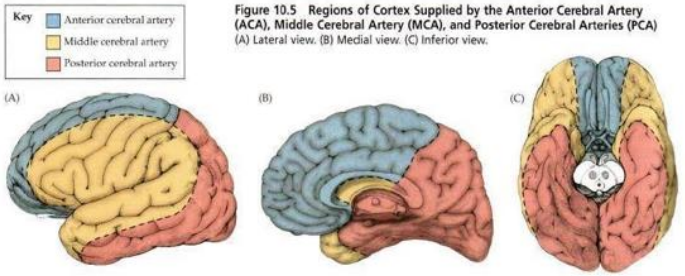


Figure 10.5 Regions of Cortex Supplied by the Anterior Cerebral Artery (ACA), Middle Cerebral Artery (MCA), and Posterior Cerebral Arteries (PCA) (A) Lateral view. (B) Medial view. (C) Inferior view.

10% of cerebral infarction patients die within a month
50% of survivors have longtime disability. Factors:
-Pressure sores
-Epilepsy -Spasticity
-Recurrent falls and fractures -Depression

Diagnosis:
Diagnosis is clinical. We do investigations to find the cause, prevent recurrences.
Common stroke investigations:
-Blood count and ESR
-Urea, electrolytes, glucose and lipids
-Chest radiograph and ECG
-CT cranial scan (hemorrhagic vs ischemic. Also eliminates tumors)

Treatment:
-**Aspirin** 300mg daily. Good if given 48hrs of onset.

-**Thrombolysis**: (15% of patients are eligible) Thrombolysis is done with intravenous tissue plasminogen activator (**alteplase**). Must be started within 3hrs of onset but we can extend to 4.5hrs or more. The faster, the less risk to permanent brain damage.
If uncertain about onset time = ineligible

-**Surgery** (rare) in cases where infarction swelling is compressing brainstem or obstructing CSF flow, we drain ventricles and decompress post. Fossa (brainstem)
-Young patients with total MCA infarction develop massive edema with high risk of increased ICP, compressed brainstem, death → (**Malignant MCA occlusion syndrome**)
We can save their lives by temporary removal of skull vault over infarcted area (**hemicraniectomy**)

Prevention:
-Smoke cessation, low fat/salt diet, no alcohol
-Use cholesterol lowering agents (statins)
-Control of blood pressure (no additional hypertensive drugs beyond pre-existing treatment should be given for the first 2weeks after an ischemic stroke unless there is malignant HTN)
-Lifelong antiplatelets starting directly after attack. 300mg Aspirin can be reduced to 75mg after a month. Aspirin is a daily medication
-Anticoagulation (warfarin) is beneficial in presence of A.fib and other cardiac emboli sources.

Both prevent formation and growth of blood clots but with different mechanisms and uses:
Antiplatelet: Prevents platelets from clumping (Aspirin) → Endothelial damage where platelets stick
Anticoagulation: Reduces fibrin formation (Warfarin, Heparin) → stasis and clots formation

Rehabilitation in stroke unit is life-saving.

Transient Ischemic Attacks (TIAs)

Ischemic Stroke

Focal neurological deficit attributed to a temporary vascular cause but with no infarction (cell death) of brain tissue. Resolves within 1hr and without evidence of acute infarction

Causes:
1- Thromboembolism from atherosclerotic neck vessels (most common)
2- Lipohyalinosis of small intracranial vessels
3- Cardiogenic embolism
4- Vasculitis or hematological disease (rare)

Clinical features: (Depend on Artery affected)
Carotid (Most common)
-Hemiparesis
-Hemisensory loss
-Dysphasia
-Temporary monocular visual loss (Amaurosis Fugax)

Vertebrobasilar
-Bilateral or alternating Paresis or Sensory loss
-Bilateral sudden visual loss (in older patients)
-Diplopia, ataxia, vertigo, dysphagia (at least two simultaneously)

Neurological signs are usually absent by the time the patient presents, but cholestrol emboli can be seen on ophthalmoscope in patients with Amaurosis fugax.

Diagnosis:
Carotid bruit – Most likely Carotid TIA
Cardiac arrythmias and murmurs – Cardiac source embolism
Subclavian steal syndrome – Proximal subclavian artery stenosis, may lead to retrograde blood flow to vertebral artery when arm is exercised. Stenosis can cause a bruit low in the neck and BP + pulse reduction in ipsilateral arm.
Investigations are made to identify cause and to prevent strokes:
- Full blood count, ESR
- Blood glucose and cholesterol
- Syphilis serology
- ECG
- Chest radiograph, echocardiogram, 24hr ECG if cardiogenic embolism is suspected
- CT cranial scan – to detect previous cerebrovascular disease and exclude structural lesions (tumor)
- Carotid ultrasound or angiography for carotid stenosis for patients with carotid TIA
- Blood cultures when infective endocarditis is suspected

Treatment:
Highest risk of getting a stoke is within the first hours, days, weeks and year after a TIA.
Also, there's an increased risk of a myocardial infarction after a TIA.
Stroke preventive measures:
• Treating hypertension
• Stopping smoking
• Reducing serum cholesterol by diet and drugs
• Anticoagulants (Warfarin)
• Antiplatelet drugs (low-dose Aspirin)
• Surgical endarterectomy

^ Aspirin is contraindicated in active peptic ulcer disease
^ Evidence suggests a synergistic effect of Aspirin + Dipyridamole
^ Clopidogrel is an alternative for patients who can't tolerate Aspirin.
^ Warfarin is used when cardiogenic embolism is identified and in non-rheumatic Afib
^ Endarterectomy: surgery to clear Internal Carotid Artery atheroma. Done in patients with severe carotid stenosis (>70%) after a TIA.
^ Carotid stenting and angioplasty are alternatives to surgery.
^ Surgery in less severe or asymptomatic carotid stenosis is not well established
^ No surgical option for most vertebrobasilar TIAs (except subclavian steal syndrome)

ABCD^2 for risk of upcoming stroke: Risk of 4 and above needs intervention.

Symbol	Parameter	Score
A: Age	< 60 ≥ 60	0 1
B: BP	< 140/90 > 140/90	0 1
C: Clinical	Motor Speech Others	2 1 0
D: Duration	≥ 60mins 10-59mins < 10mins	2 1 0
D: Diabetes	Present Not Present	1 0

Cerebral Venous Sinus Thrombosis (CVST)

Ischemic Stroke

Venous infarction caused by formation of a clot (thrombosis) within intracranial dural venous sinuses. It is a rare type of stroke. This produces syndromes different than arterial infarction. Produces thunderclap headache

Clinical features:

Superior sagittal sinus thrombosis
- Acute headache (worsen over days)
May present as different headache types and locations
40% of cases, headache is the only symptom
- Early Seizures
- Bilateral focal neurological deficits (most commonly motor), often progressive & with impairment of consciousness. It has many causes:
• Coagulopathies
• Dehydration
• Cachexia
• Oral contraceptives
• Puerperium (6 weeks of childbirth where reproductive organs return to their baseline)

Cavernous sinus thrombosis
- Red swollen eyelid and conjunctiva
- Third, Fourth, V1 V2, Sixth cranial nerve palsies
- Papilledema

Transverse/Lateral sinus thrombosis
- Increased ICP symptoms
- Seizures
- Drowsiness

Cavernous and Transverse sinus may undergo thrombosis due to an infection spread
- From face to orbit to cavernous sinus
- From ear to transverse sinus (lateral sinus)

Treatment: (according to cause mainly)
- Antibiotics if underlying cause is infection
- Intravenous Heparinization if non-infective. Anticoagulants is a concern in presence of hemorrhagic venous infarction

Hypotension

Ischemic Stroke

Effect of hypotension on the brain and ischemic stroke formation
If blood flow falls below the autoregulatory range (normal range) ex: Hypovolemic shock
Cerebral infarction may result as blood vessels cannot dilate further thus blood flow falls.
The most affected areas are the **Watersheds** (border zones between vascular territories) as perfusion pressure is usually lowest at these areas.
Example: Infarction at the border zone between PCA and MCA causes visual field defects or more complex visual disturbances (visual agnosia)

Hypertension

Ischemic Stroke

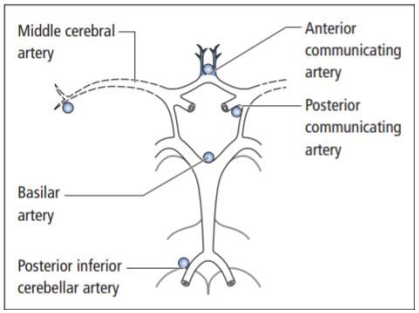
Effect of hypertension on the brain and ischemic stroke formation
Autoregulatory range may be exceeded in severe hypertension (Malignant hypertension MHT) causing increased blood flow and vessel walls damage (Fibrinoid Necrosis) causing cerebral edema. Patients develop ↑ ICP symptoms

Clinical features: (of ↑ ICP)
Headache
Vomiting
Drowsiness
Papilledema
Seizures and focal neurological signs

Treatment: (of hypertensive encephalopathy)
Prompt lowering of blood pressure, aiming at 100-110 diastolic.
More drastic lowering my cause cerebral infarction if long-standing hypertension has shifted the autoregulatory shift to the right)

Subarachnoid Hemorrhage (SAH)

Hemorrhagic Stroke



Bleeding into the subarachnoid space.

Causes:
● Aneurysm rupture (congenital weakness occurring typically at circle of Willis' junctions. See photo)
● Arteriovenous malformations (Angiomas)
● Trauma -rare-
● Coagulopathies -rare-
● Vessels weakened by infarctions (ex septic emboli from infective endocarditis → Mycotic aneurysms) -rare-

Clinical features:
Because blood irritates the meninges, we will have meningeal signs:
• Sudden (within seconds) very severe headache
• Photophobia, phonophobia, N/V
• Neck stiffness and Kernig's sign

With more severe hemorrhages, intracranial pressure may rise:
• Altered consciousness
• Papilledema and retinal hemorrhage

Focal neurological signs develop due to:
• False localizing sign of increased ICP
• Coexistent intracerebral hemorrhage
• Vessel spasm due to irritation of blood and consequent ischemia

Systemic features:
• Bradycardia and hypertension (hypothalamic damage caused by increasing ICP + fever)
• Pulmonary edema and cardiac arrythmias (sometimes)

Diagnosis and Investigation:
•CT cranial scan (non-contrast) reveals subarachnoid blood in most but not all cases
•Small bleeds are not detectable on CT. LP may be needed to diagnose.
•No contraindication to LPs once masses are excluded
•LPs can be made as long as there is no bleeding diathesis (easy bleeding and bruising)
•For an LP to diagnose SAH, there must be frank blood that fails to clear in different taps
•After 3hrs, hemoglobin breaks down forming yellow CSF (Xanthochromia)
•Chest cardiograph and ECG can be made to investigate pulmonary edema and cardiac arrythmias
•Bleeding disorders must be excluded
•Glycosuria is sometimes present

•If patient is alert/mildly drowsy, do cerebral angiography ASAP to look for aneurysms

Prognosis:
•30-40% of people die in the first few days of aneurysmal SAH (High mortality)
•Bleeding arteriovenous malformations have lower mortality than aneurysmal bleeding.
•There is a high risk for a 2nd rebleed especially in the first 6weeks. The 2nd bleed may be worse. Thus, prevention is very important.

Treatment:
● Bed rest and analgesia are initially instituted
● Nimodipine (Calcium antagonist) reduces ischemic morbidity
● Aneurysmal neck clipping or wrapping are substituted by endovascular interventional neuroradiological approaches: aneurysm occlusion by detachable coils
● Arteriovenous malformations with no bleeding (discovered with epilepsy) should usually not be treated surgically

Complications:
Hydrocephalus (CSF obstructed by blood) → Early
Communicating hydrocephalus → Later

Spontaneous Intracerebral Hemorrhage (sICH)

Hemorrhagic Stroke

Spontaneous bleeding inside the substance of the brain. HTN is the most common risk. 10% of all strokes

Causes:
- Hypertension with microaneurysms (Charcot-Bouchard Aneurysms)
- Bleeding tumors
- Trauma
- Blood disorders
- Blood vessels disorders (arteriovenous malformations, vasculitis, amyloidosis)

Clinical Features: (depending on site of bleed)
- Focal neurological signs
- Seizures
- Increased ICP signs

Complications: Hydrocephalus and coning
Diagnosis: can't differentiate ischemic from hemorrhagic stroke. Need non-contrast CT

Treatment:
Initially – Antihypertensives
For seizures – Antiepileptics
Increased ICP – Mannitol
Correction of coagulopathies

Surgical interventions:
- Hematoma evacuation – For cerebellar or cerebral lobar hemorrhages with progressive deterioration
- Ventricular drainage: For acute hydrocephalus

Parkinson's Disease (PD)

Movement Disorders

Degeneration of Dopaminergic neurons (Extrapyramidal pathways). It is progressive, adult onset. Characterized by a triad of:
1— Bradykinesia
2— Rigidity
3— Tremor

Epidemiology: 2nd most common degenerative neurological disease after Alzheimer's 1-2% of the 60+ aged population. No gender bias. Worldwide distribution but more commonly the US and Europe

Environmental relation:
MPTP, a synthetic heroin by-product produces acute parkinsonism by selective CNS damage, has led to the theory of the presence of widely present environmental factor that acts the same way. Further support to the environmental relation:
* Predominance increases with age (mean onset is 60)
* Genetic factors are present but usually not in idiopathic cases
* Weak association between the disease and different objects (wood pulp and pesticides)

Pathology:
The dopaminergic neurons affected in the disease are those projecting from Substantia Nigra (Midbrain) to striatum of basal ganglia (Caudate and Putamen). Those neurons are degenerated due to alpha synuclein protein aggregation (**Lewy Bodies**). Dopaminergic damage causes an imbalance in the extrapyramidal system in favour of Ach and other neurotransmitters. Dopamine is Inhibitory while Acetylcholine is Excitatory
Symptoms appear when 60-80% of dopaminergic neurons are lost.

Clinical Features:
1) **Akinesia (Bradykinesia)**
Slowed down movement
Difficulty with complex motor tasks – Dressing/Writing (often micrographia, small handwriting)
Lack of spontaneous movement:
- Facial expression (Mask-like face)
- Difficulty changing position (ex: turning in bed)
- Quiet and monotonous speech
- Abnormal gait and stance (due to akinesia and loss of normal postural control)

2) **Rigidity**
-Lead pipe rigidity, meaning constant rigidity
-Cogwheel rigidity may be found due to the tremor of Parkinson's (superimposed)
^ Tone is best tested on joints with smaller range of movement (wrist)

3) **Tremor**
-Hand tremor primarily in Parkinson's. Face, Jaw or Trunk may be involved
-Pill rolling look in the hands
-Present at rest, improves or disappears with movement. Exacerbated by stress
-Characterized by 3-6Hz frequency
-Early in the disease, tremor and other signs are usually unilateral

Other clinical features:
●Gait
-Stooped or flexed posture
-Patients may fall forward (propulsion) or backwards (retropulsion).
-Increased risk of falls with severe Parkinson but it comes later in the disease. If patient presents with frequent falls early on, we think of parkinsonism plus diseases.
-Initiation of walking or turning may be difficult (freezing)
-Shuffling gait with small steps, described as **festinant** as if patient hurries up back to balance with gravity.
-Arm swing is lost
●Cranial Nerves
-Eye movement test: Mild impairment of upgaze
-Tremor in eyelids (Blepharoclonus)
-Difficulty swallowing (even one's own saliva) which causes drooling (Sialorrhea)
-Glabellar tap is positive (Normally, eyes will blink for the first 3times but then get fatigued. However, here it will keep blinking)
●Limbs
-Power, Deep tenson reflexes, sensation and Babinski are normal.
-Pain in the muscles is common, many develop a frozen shoulder
●Autonomic symptoms
-Greasy seborrheic skin
-Constipation is common
-Bladder disturbances and erectile dysfunction is common
-Postural Hypotension is mild
●Depression is common and develops independently of degree of motor symptoms
●Dementia: Cognitive impairment is common in advanced Parkinson's
●Hallucinations: vivid and visual occurring especially at night. Not necessarily indicative of psychosis or cognitive impairment.
●Psychosis: worsening hallucinations may lead to psychosis, especially when there is cognitive impairment already
●Insomnia is common
●Anosmia may start before motor symptoms in years.

Diagnosis:
-Presence of at least 2 of the triad.
-Standard CT or MRI is useless
-If diagnosis is in doubt, the patient's response to drugs helps

Treatment:
-Symptomatic treatment.
-Treatment to restore neurochemical balance: Anticholinergic or dopamine enhancers:

1- L-DOPA
Crosses BBB unlike Dopamine. Usually given orally, but most of the dose is metabolized to Dopamine by peripheral DOPA decarboxylase. We stop this by combining L-DOPA with a DOPA decarboxylase inhibitor like
Benserazide or **Carbidopa**. This combination reduces peripheral side effects of N/V.
Co-careldopa (L-DOPA + Carbidopa)
Co-beneldopa (L-DOPA + Benserazide)
Both may have central side effects (Postural Hypotension, Confusion, Hallucinations, Delusions). But most patients with Idiopathic Parkinson's benefit from these at least early in the disease.

Side Effects: (of long-term L-DOPA):
* After 2-5yrs, it stops being effective in treating motor fluctuations and dyskinesias

Effect on motor fluctuations:
Wearing-off: Short lived effects are produced
On/off: patient switches from benefited state to akinetic-rigid state often unpredictable to timing of drug doses.

Effect on dyskinesia:
Peak-dose dyskinesia: Involuntary muscle movement (twisting, turning) occurring with high dopamine levels
Wearing-off dystonias: Painful sustained muscle contraction (feet usually) with low dopamine levels.

Dopamine dysregulation syndrome: A small proportion of patients crave additional levodopa at higher doses than what they take which results in bizarre, repetitive, compulsive behaviors

Motor fluctuations and dyskinesia can be alleviated in some patients by:
- Frequent small doses of drugs containing Levodopa
- Controlled release preparations
- L-DOPA combined with selegiline, entacapone or direct dopamine agonists
- Tolcapone is restricted because it can cause severe liver failure

Other routes of administration besides oral levodopa:
Rotigotine (dopamine agonist) given subdermally
Apomorphine (dopamine agonist) given by subcutaneous infusion
Duodenal infusion of levodopa

2- Selegiline
Many neurologists treat early Parkinson with selegiline alone.
L-DOPA's requirement may be delayed up to 12months.
Rasagiline is a newer MOA_B inhibitor

3- Dopamine agonists
Includes: **Bromocriptine, Cabergoline, Pergolide, Ropinirole, Pramipexole, Rotigotine** and **Apomorphine.**
Important in early Parkinson and delays L-DOPA too.
The first 3 drugs are associated with pulmonary and retroperitoneal fibrosis.
Up to 1/3 of Pergolide users develop fibrotic cardiac valvulopathy. Thus, non-ergoline dopamine agonists are preferred.
Ropinirole and Pramipexole cause excessive drowsiness, sudden sleeping, bizarre behaviors such as pathological gambling.

4- Amantadine
Mildly beneficial in early Parkinson.
Later, it reduces L-DOPA induced dyskinesia but only for 6-9mo.

5- Anticholinergics
Includes: Trihexyphenidyl, Orphenadrine and Benztropine.
Minor effects, helps with tremor which L-DOPA doesn't.
Side effects are serious: Urinary retention, dry mouth, blurred vision (glaucoma), Confusion and hallucinations particularly in elderly

Having a diary of periods can be helpful in manipulating the timing and dosage of drugs

Symptomatic treatment:
Nausea – Domperidone
Hallucinations in patients with cognitive impairment –
*Atypical neuroleptics (Risperidone, Olanzapine, Quetiapine, Clozapine)
*Cholinesterase inhibitors (Donepezil, Rivastigmine)

Surgery:
Stereotactic thalamotomy: used for severe tremor unresponsive to medications
Interruption of globus pallidus (pars interna/subthalamus) output: by a lesion or by implanted deep brain stimulation device. These nuclei are overactive due to the imbalance, so cutting off the output helps in dyskinesia and motor fluctuations.
Cell transplantation: using fetal substantia nigra, helps in MPTP-induced parkinsonism

Chorea

Movement Disorders

Irregular, random and variable movements that have a flowing or dancing quality.
Might appear semi purposeful and it affects any part of the body.

Causes:
Chronic L-DOPA therapy
Postinfectious especially after rheumatic fever (Sydenham's Chorea)
Polycythemia rubra vera
SLE
Thyrotoxicosis
Pregnancy and oral contraceptives
Phenytoin, alcohol, neuroleptics (antipsychotics)
Hereditary (Huntington's Disease)

Treatment:
Monoamine depleting drugs (Tetrabenazine) but may cause severe depression.
Neuroleptics (Sulpiride or Haloperidol).

Hemiballismus: Movements are more jerky and violent occurring unilaterally on the opposite side of the lesion (subthalamic nucleus damage)

Athetosis

Movement Disorders

Movements slower and more writhing than chorea.
Causes:
Typically associated with congenital brain damage (cerebral palsy), particularly the one that occurs with neonatal hyperbilirubinemia (Kernicterus)

Myoclonus

Movement Disorders

Rapid, abrupt, jerky, shock-like movements of full body or parts of it.
May occur due to abnormal electrical discharge of the cortex, hence in association with epilepsy. However, myoclonic jerks can arise elsewhere in the CNS including spinal cord thus can arise in degenerative and metabolic disorders.
Valproic acid and clonazepam are 1st line drugs for myoclonic epilepsies

Tremor

Movement Disorders

Causes:
Resting tremor:
Parkinson's
Other akinetic-rigid syndromes
Postural tremor (maximal with maintained posture):
Essential tremor
Physiologic tremor, exaggerated by:
Anxiety
Thyrotoxicosis
Alcohol
Drugs (Bronchodilators)
Intention tremor (cerebellar diseases):
Multiple sclerosis
Hereditary ataxias
Tumor, infarct or hemorrhage of cerebellum

Postural or intention (kinetic) tremors may be associated with dystonia and some peripheral neuropathies

Essential tremor is common and characterized by:
• Positive family history
• Postural tremor of BOTH hands (thus difficulty holding cups or writing)
• Other body parts can be affected too, including head (titubation)
• Tremor absent at rest
• No extrapyramidal or cerebellar features
• Tremor may be relieved by alcohol
• May respond to propranolol or primidone

Primary orthostatic tremor: unsteadiness or tremor in the leg triggered by prolonged standing. Clonazepam may helpful

Dystonia

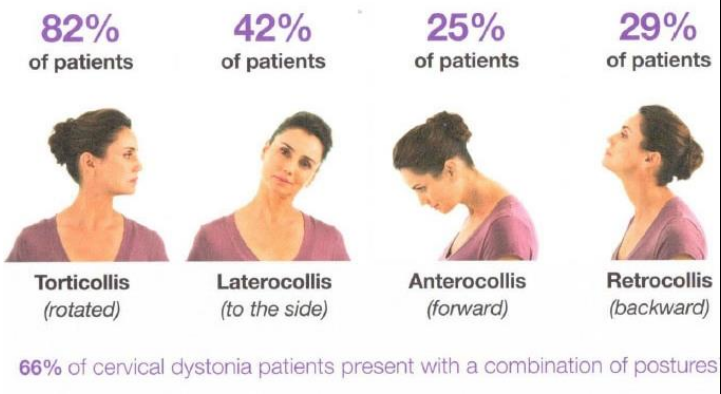
Movement Disorders

Involuntary sustained muscle contraction that results in abnormal posture or slow repetitive movements.
1 – Focal
2 – Generalized

1. Focal:
Blepharospasm: Involuntary eye closure
Oculogyric crisis: Eyes rolled upwards as seen in postencephalitic parkinsonism
Laryngospasm: With stridor
Trismus: Jaw spasm
Writer's Cramp: abnormal painful hand posture, task specific and stops patient writing.
Spasmodic torticollis: Wry neck, painful SCM contraction, neck muscles atrophy resulting in head turning to:
One side – Torticollis
Forward – Antecollis
Backward – Retrocollis

2. Generalized:
Primary torsion dystonia: (AKA dystonia musculorum deformans) it is inherited but also occurs with drug reactions or with cerebral damage

Treatment: Drugs are generally unsatisfactory
Generalized dystonias may respond to high doses of anticholinergics (Trihexyphenidyl)
L-DOPA is good for a rare type of inherited childhood dystonia occurring in lower limbs
Focal dystonias may be treated with botulinum toxin (botox) injection in affected muscle
Paroxysmal dystonias which are rare, may respond to antiepileptics



Tics

Movement Disorders

Rapid, compulsive (irresistible urge), stereotyped movements thus known as 'habit spasms'. The movement can be resisted voluntarily for a limited time but then hits more violently, immediately after resistance is stopped.

Gilles de la Tourette syndrome: complex tics associated with involuntary utterances (A spoken word, statement or vocal sound)
which are often repetitive (echolalia) and obscene/offensive (coprolalia).

Treatment: Drug treatment is difficult but neuroleptics may help.

Drug-Induced movement disorders

Movement Disorders

Neuroleptic drugs unsurprisingly through its dopamine inhibitory effect causes many motor side effects such as:
• Acute dystonic reactions
• Akathisia (restlessness, jittery, unable to sit down)
• Drug induced parkinsonism
• **Tardive dyskinesia (TD)** (involuntary repetitive movement of the face, neck, tongue, mouth which may persist after the neuroleptics (the causative drug) has been discontinued.

Neuroleptic malignant syndrome (NMS): most severe, life-threatening disorder seen with neuroleptics.

Clinical features: (neuroleptic malignant syndrome)
- Generalized muscular rigidity: which is sufficient enough to produce muscle damage and elevated serum creatinine kinase and sometimes myoglobinuria as patient keeps moving restlessly for days.
- Tremor
- Fever
- Incontinence
- Altered consciousness
- Autonomic dysfunction
- Cardiovascular changes

Treatment: Resuscitative measures and withdrawal of the offending drug, dopamine agonists to restore balance (Bromocriptine) and use of muscle relaxants (Dantrolene)

Miscellaneous Movement Disorders

Movement Disorders

Various types and forms of diseases grouped together; they include:

1. Restless Leg Syndrome (Ekbom's Syndrome)

Common. Patients have distressing irresistible desire to move the legs (akathisia), associated with uncomfortable deep-seated sensation in the legs, worse at night.
Symptoms are brought by rest and relieved by movement.
Early onset is usually familial.

Other associations:
Old female patient with no family history (common presentation)
Underlying peripheral neuropathy
Lumbar root disease
Iron deficiency
Renal failure

Treatment: If condition is severe enough to need drug therapy, we use first line dopaminergic agents, either dopamine agonists or L-DOPA.
Other drugs: Opiates, clonazepam, gabapentin and iron replacement therapy.

2. Painful legs and moving toes syndrome

Rarer condition and hard to treat. Patients have severe pain in their legs with involuntary continuous writhing movements of the toes.

Associated:
There may be underlying lumbar root disease or peripheral neuropathy

3. Stiff Person Syndrome

Very rare. Slowly progressive rigidity of the trunk and proximal limbs with superimposed painful muscle spasms

Cause: May be autoimmune
Associated: Diabetes and Epilepsy
Diagnosis: EMG, presence of autoantibodies in some cases, oligoclonal bands in CSF.
Treatment: Steroids, IV immunoglobulins, plasma exchange or symptomatic treatment with Benzodiazepines (calms and sedates patients)

There are other more progressive forms of spinal rigidity, some which may be paraneoplastic.

4. Psychogenic movement disorders

Must be diagnosed with caution. Suspected if movements are unusually variable, disappear with distraction and associated with other clinical features that suggests a non-organic cause.

Multiple Sclerosis (MS)

CNS Demyelinating Diseases

Most common chronic neurological condition of young people.

Epidemiology: More common in temperate weather than tropical. More common in females (3:1) but more severe in males. Can occur at any age but less common in children and elderly. It is the disease of the young (20-40).

Pathogenesis:
Genetic factor (MHC most likely) triggered by an environmental factor (virus, VitD def) Primarily affects white matter of the brain and spinal cord and the optic nerve. It can also affect the grey matter too especially in late stages. Caused by autoimmune self-destruction of the myelin in the CNS while relatively sparing the axons (at least initially). The damage is not uniform, rather it is interspersed in foci =Plaques. There are chronic inflammatory cells. Demyelination leads to reduction in speed of nerve conduction and eventually loss of information. Stages of MS:

1. Local breakdown of BBB
2. Evidence of inflammation and edema
3. Loss of myelin
4. Gliosis (scarring)

At the glial stage (4), the sclerotic area will be shrunken and improved clinically due to the relative remyelination. Symptoms are worse when the plaque is active. This remyelination gives the relapsing-remitting nature

Clinical Features:
Commonly presents with: 1) Visual Disturbance 2) Limb Weakness 3) Sensory Disturbance

1) Visual Disturbance:

Optic (retrobulbar) neuritis is very characteristic and may indicate the onset of MS caused by the inflammatory demyelination of one optic nerve or both (less common)
Unilateral optic neuritis comes as:
- Pain around one eye especially with movement
- Blurred vision which may become monocular blindness with days or weeks
- Impaired colour vision and visual acuity
- Pink swollen optic discs on fundoscopy (if affected area is immediately behind)
- Visual field defect, typically a central scotoma on affected eye
- Relative afferent pupillary defect

In the acute phase, if the optic disc swelling is bilateral, it should be differentiated from increased ICP where visual acuity would not be much affected. The only field defect in early papilledema is enlargement of the blind spot
Visual defects usually resolves over weeks or months but there will still be some visual impairment. Fundoscopy will show optic disc pallor caused by optic atrophy
Optic neuritis does not necessarily mean MS, it may be a monophasic illness especially if it was bilateral or occurred in children

2+3) Sensorimotor disturbances

Generally, implies a lesion in the spinal cord or cerebrum.
Lhermitte's Phenomenon: Neck flexion causes rapid tingling sensation shooting down the arms or legs. usually indicated dorsal column lesion.
Uhthoff Phenomenon: Visual, sensory or motor symptoms are temporarily much worse after a hot bath because conduction velocity decreases with heat, especially on already slowed down demyelinated nerves.

Other presentations:

- Trigeminal neuralgia due to brainstem plaques. Or pain in limbs.
- Epilepsy is becoming commoner however it mostly presents in late stages (grey matter)
- Bladder disturbance (urgency or retention)
- Impotence (Erectile dysfunction)

Course:
Relapsing-Remitting (70-80%): Clinical features worsen over days or weeks, reaches a plateau then gradually resolve partially over weeks or months. Then there will be recurrent attacks with at least a 1mo window and hitting a different site. (Disseminated in time and space = DIT, DIS)

Secondary progressive: When there is no longer resolution of RRMS

Primary progressive (10-20%): No clear-cut relapses and remission. Straight line progression from the very beginning. Typically present with progressive spastic paraparesis

Diagnosis:
- Brain and Spinal cord MRI. It is possible to diagnose MS based on the first attack on basis of MRI (Clinically isolated syndrome)
- Visual evoked potentials, shows delayed conduction due to previous optic neuritis
- CSF: lymphocytosis and high protein (Abs) and oligoclonal bands indicates local immunoglobulin synthesis in the CNS

DDx:
MSRR → Sarcoidosis, SLE, TIA
Progressive → Motor neuron disease, Spinal and cerebellar degenerations

Treatment:

Acute relapse:

Severe attacks are treated with corticosteroids (high dose methylprednisolone IV or PO) 500mg to 1g daily for 3-5days. It helps with speed but not degree of recovery. Before using, exclude UTIs (corticosteroids are immunosuppressants).
Prolonged corticosteroids show no effect.

Course modification:

- Interferon Beta and Glatiramer acetate (protects against relapses 30%)
- Natalizumab (more effective, used in aggressive RRMS) however it has a low risk of progressive multifocal leukoencephaly.
- Mitoxantrone (chemotherapy, alternate to natalizumab) has cardiotoxicity side effect and 0.2% acute leukemia

Control of symptoms:

- Spasticity and flexor spasms: Baclofen, Dantrolene, Tizanidine, Diazepam (those can increase weakness and cause drowsiness) Botox muscle injections can be used.
- Cerebellar tremor: (mild tremor) Clonazepam, isoniazid, gabapentin
- Fatigue (common): Amantadine, selegiline, modafinil (anti-narcolepsy)
- Bladder disturbances: Anticholinergics (Oxybutynin, tolterodine).
- Depression: Tricyclic and family (Amitriptyline, dosulepin), selective serotonin reuptake inhibitors (Sertraline)
- Erectile impotence: Phosphodiesterase type 5 inhibitors (Sildenafil)
- Pain/Seizures: Carbamazepine, gabapentin

Surgical for extreme instances:

- Tenotomy for spasticity and flexor spasms
- Dorsal column stimulation for pain
- Stereotactic thalamotomy for severe cerebellar ataxia (destroying part of the thalamus which is responsible for tremor)

Inherited Disorders

Dysmyelination: abnormal myelin chemistry rather than demyelination. Aka Leucodystrophies. Usually present at infancy and childhood. They are rare, progressive and fatal. No specific treatments but enzyme replacement by bone marrow transplantation or gene therapy can be used.
In adults may present with dementia, ataxia, spasticity, optic atrophy or polyneuropathy

Acute Disseminated Encephalomyelitis (ADEM)

CNS Demyelinating Diseases

Rare, acquired disease. Acute multifocal inflammatory demyelination throughout CNS. May follow viral infection or post immunization thus AKA **Postinfectious Encephalomyelitis**

Clinical Features:

Fever, Headache, Meningism.
Possible impairment of consciousness
Focal neurological symptoms (cerebrum, cerebellum, brainstem, optic nerve)
Patients with postinfectious bilateral optic neuritis or transverse myelitis present with localized variants of ADEM.

Investigations:

CSF lymphocytosis (several hundreds) and raised protein
Nonspecific EEG changes
CT may be normal
MRI appears similar to MS

DDx:

Acute viral encephalitis (infectious not postinfectious)
Acute attack of MS

Treatment:

Corticosteroids (High dose IV methylprednisolone)

Prognosis:

Long term prognosis is good wit complete recovery and no relapse. However, a minority dies in the acute phase

Neuromyelitis Optica (NMO) (Devic's Disease)

CNS Demyelinating Diseases

Rare. Inflammatory demyelinating disease caused by the Immune system where it damages the optic nerves and the spinal cord. Thus, characterized by optic neuritis (unilateral or more commonly bilateral) and transverse myelitis.

Destruction is caused by antibodies secreted by B cells while in MS, destruction is cellular (T cells). The optic neuritis in MS is less severe and likely to get better.

Central Pontine Myelinolysis

CNS Demyelinating Diseases

Electrolyte imbalance causing edema of oligodendrocytes resulting in separation of myelin from the axons in the Pons mainly (non-immune).
The primary function of the pons is to act as a motor relay center, thus any problem there will give give motor sypmtoms

Cause: Iatrogenic due to rapid correction of hyponatremia or other ions.
Hyponatremia should be corrected at a rate no more than 8-12mmol/L of sodium per day

Clinical Features:
Rapid Quadriplegia. Can cause Locked in syndrome.

Locked In Syndrome (LIS)

CNS Demyelinating Diseases

Complete paralysis of nearly all voluntary muscles except for Vertical eye movement and blinking because the supranuclear ocular motor pathways run dorsally (not affected) while every other motor pathway passes and synapses in the ventral part of pons.

Cause: Any damage to pons ventrally, not necessarily central pontine myelinolysis (demyelinating) only. Could be, pontine infarction, pontine hemorrhage, trauma, tumor or encephalitis.

Clinical Features:
Consciousness and cognitive functions are intact
Vertical eye movement and blinking are intact
Every other voluntary muscle is paralyzed.

Alzheimer Disease (AD)

Dementia: Degenerative Diseases

Most common cause of dementia. Neurodegenerative disorder characterized by protein aggregations of AB amyloid initially (extracellular neuritic plaques) and later on Tau (intracellular neurofibrillary tangles). This aggregation occurs in the **cortex** and causes cell death and dysfunction. First symptom to occur is dementia, which is memory and cognitive impairments severe enough to affect patient's daily life.

Pathology:
Neuritic plaques consist of amyloid beta protein which is a fragment of a larger protein, Amyloid precursor protein (APP) encoded by a gene in chromosome 21. Patients with down syndrome have higher risk for AD and in earlier ages.
Apolipoprotein E has also been identified as a risk factor
Sites: Affected sites are hippocampus and adjacents, temporal neocortex, nucleus basalis of Meynert in the frontal lobe. Cholinergic neurons are affected (degenerated)

Clinical Features:

Early
~ Short-term memory loss
- difficulty learning or retaining new information
- patients might be unaware of these problems. History is taken by relative.

Later
~ Memory impairment and attention deficits leads to disorientation in time.
- Word finding difficulties
- Loss of general knowledge
- Hallucinations and delusions

Finally
~ Severe global cognitive impairment
- Amnesia, Dysphasia, Dyspraxia, Agnosia
- Disintegration of personality and behavioral disturbances
- Incontinence
- Increased dependency and death within 5-10yrs

Diagnosis:
by clinical diagnostic criteria. Important to exclude other causes of dementia

Management:
- Systemic illnesses like infections can exacerbate dementia. So, it's important to look after one's health and avoid alcohol, sedative drugs and fatigue
- Simple memory aids like labels and diaries are helpful early in the diseases
- Cholinergic drugs may enhance memory early in the disease only for a few months (Cholinesterase inhbitors: Donepezil, Rivastigmine, Galantamine) → also nicotinic agonist
- Memantine is used in moderate to severe disease (affects glutamate transmission)
-Non cognitive treatment: Antidepressants, neuroleptics, anxiolytics

Creutzfeldt-Jakob Disease (CJD)

Dementia: Degenerative Diseases

Prion disease. Both inherited and transmissible. Infectious prion proteins (PrP) with no evidence of nucleic acid. Highly resistant to heat and formaldehyde.
Epidemiology: Most cases are sporadic. Familial form is autosomal dominant.
Gene: PrP gene mutations

A lot of infectious transmission is iatrogenic and incubation time is several years.

Clinical Features:
- Rapidly progressive dementia
- Cortical visual problems
- Motor Features (Myoclonus, muscle wasting and fasciculation)
- Death within 1-2yrs or less

Children variant:
- Psychiatric features
- Sensory disturbance
- Ataxia
- THEN dementia

Investigations:
- EEG in classical CJD may show **'Periodic Complexes'**
- CSF shows neuronal proteins

Diagnosis: is only confirmed by brain or lymphoid tissue (tonsil) biopsy or at autopsy

Frontotemporal Lobar Degeneration (FTLD)

Dementia: Degenerative Diseases

Heterogenous group of diseases characterized by the degeneration of frontal and/or temporal lobes. Causes frontotemporal dementia where changes in personality and language precede memory loss
Epidemiology: More common in younger patients

Clinical Features:
Frontal Dementia: Personality and social behavior changes + Motor (non-fluent aphasia)
Semantic Dementia (temporal): Word finding difficulty and loss of general knowledge
The progressive dysphasia in semantic dementia remains fluent

موفقين جميعا

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