NEUROLOGY

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NEUROLOGY ... CONT.

INTRODUCTION

When approaching a patient with a neurologic disorder always ask yourself:

❑ where is the lesion?
- cerebrum
- cerebellum
- brainstem
- spinal cord
- nerve root
- peripheral nerve
- neuromuscular junction
- muscle
- not confined to one level

❑ what is the cause of the lesion?
- **V**ascular
- **I**nfectious
- **N**eoplastic
- **D**egenerative
- **I**nflammatory-immunologic
- **C**ongenital-developmental
- **A**utoimmune
- **T**oxic/ traumatic
- **E**ndocrine/ metabolic

❑ is the lesion focal, multifocal or diffuse?

Table 1. Temporal and Spatial Features of the Major Disease Categories

	Acute	**Subacute**	**Chronic**
Focal	Vascular (e.g. infarct, intraparenchymal hemorrhage)	Inflammatory (e.g. abscess, myelitis)	Neoplasm
Diffuse	Toxic Metabolic (e.g. anoxia)	Inflammatory (e.g. meningitis, encephalitis)	Degenerative

Table 2. An Anatomic Approach to Neurologic Disorders, Symptoms and Signs

Location	**Disorders**	**Symptoms**	**Signs**
Cerebrum	Seizure disorders Coma Confusion Dementia Aphasia Movement disorders	Aphasia, seizures Involuntary movements Visual field defects Cognitive/personality changes	Gaze preference Cortical blindness and sensory loss Homonymous field defects Neglect, apraxia, Anosognosia
Cerebellum	Cerebellar degeneration	Clumsiness Lack of coordination Unsteadiness Vertigo	Tandem gait impairment Dysdiadochokinesis Abnormal heel-shin, finger-nose, nystagmus
Brainstem	Cranial nerve palsies	Diplopia, dizziness, deafness Dysarthria, dysphagia Decreased strength/sensation in face and body Vertigo	Cranial nerve abnormalities UMN lesions (bilateral) Sensory loss (crossed) Nystagmus
Spinal Cord	Spinal cord syndromes Amyotrophic lateral sclerosis (ALM)	Sensory level Distal weakness Bowel and bladder changes	Upper motor neuron (UMN) signs Loss of superficial reflexes
Nerve Root	Nerve root compression	Same as peripheral nerve + pain (sharp, electric, radiating)	Weakness in myotomal group Sensory loss in dermatome
Peripheral Nerve	Neuropathies	Distal weakness with sensory change, atrophy	Normal or decreased tone Decreased reflexes
Neuromuscular Junction	Myasthenia gravis Lambert-Eaton syndrome	Proximal symmetric weakness No sensory loss Fatigable weakness	Repeated strength testing to elicit fatigability
Muscle	Polymyositis (PMY) Muscular dystrophies Metabolic Structural myopathies	Proximal symmetric weakness No sensory loss	Normal/ decreased tone Normal/ decreased reflexes Minimal atrophy
Disorders not confined to one level	Headache Stroke Multiple sclerosis (MS) CNS infections HIV/AIDS Alcohol		

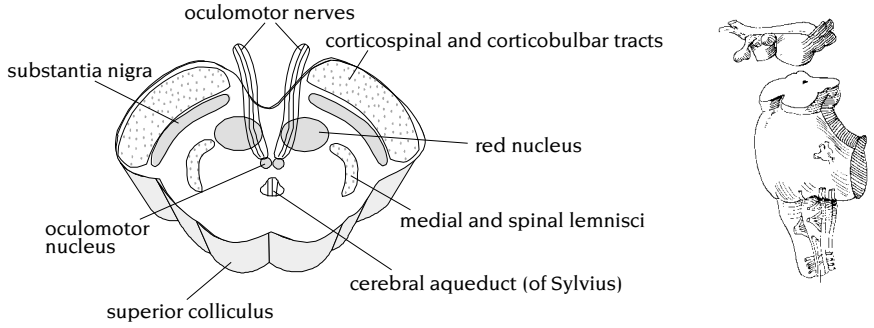

Figure 1. Section through the Midbrain at the Level of the Superior Colliculus

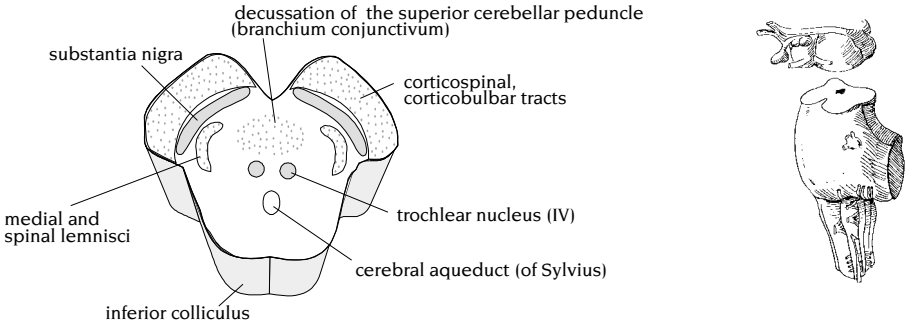

Figure 2. Section through the Midbrain at the Level of the Inferior Colliculus

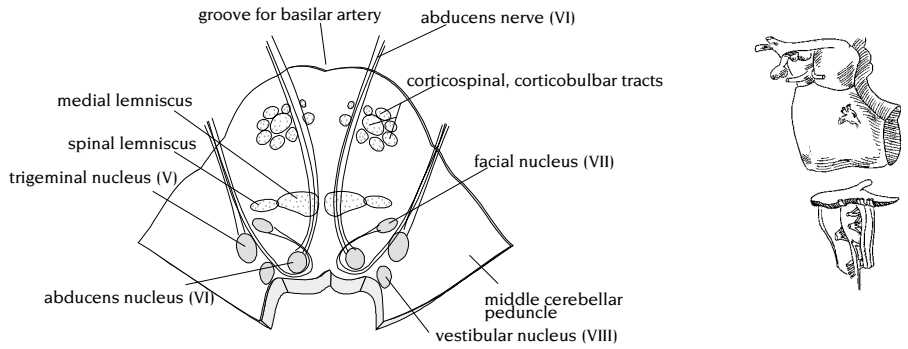

Figure 3. Section through the Pons

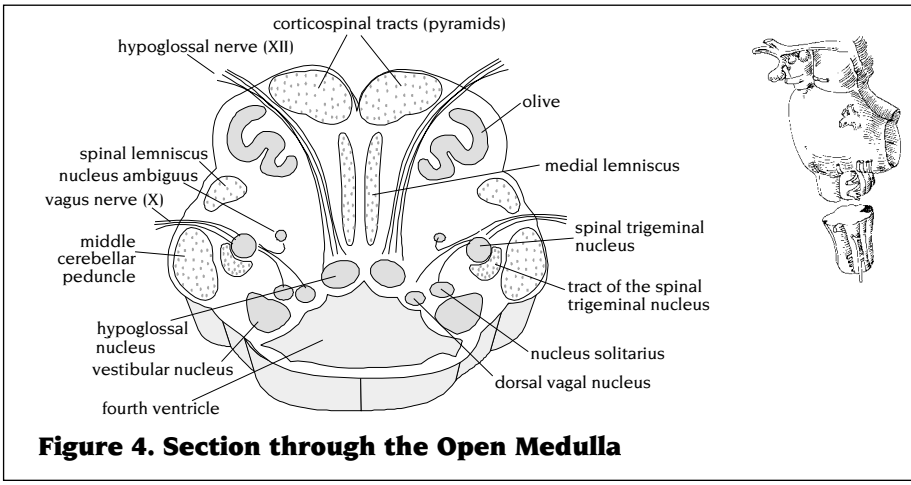

Figure 4. Section through the Open Medulla

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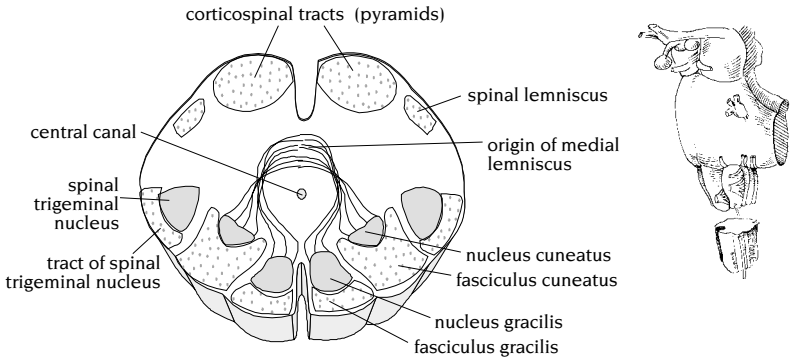


Figure 5. Section through the Closed Medulla

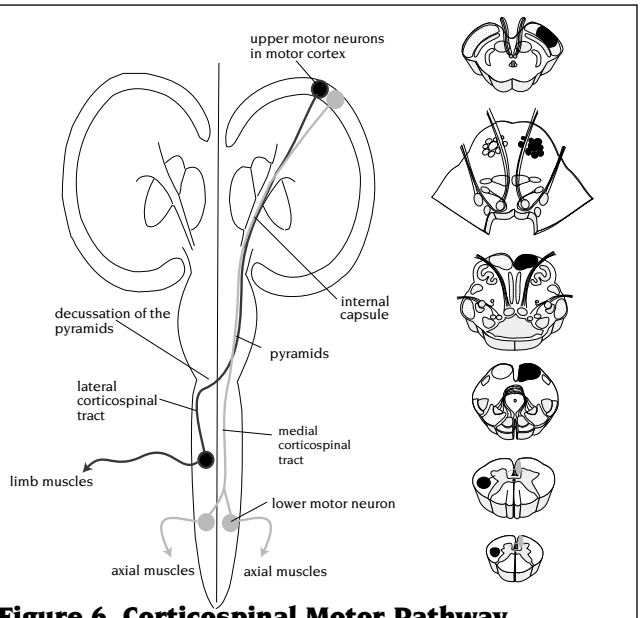


Figure 6. Corticospinal Motor Pathway

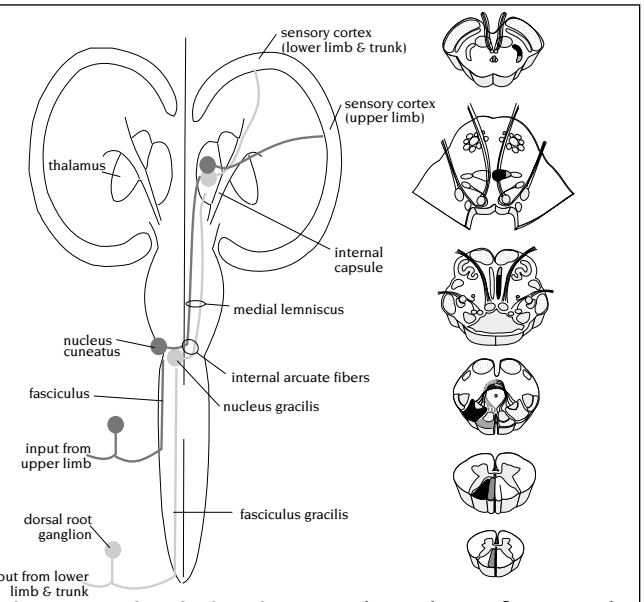


Figure 7. Discriminative Touch Pathway from Body

Illustrations by Dr. P. Stewart

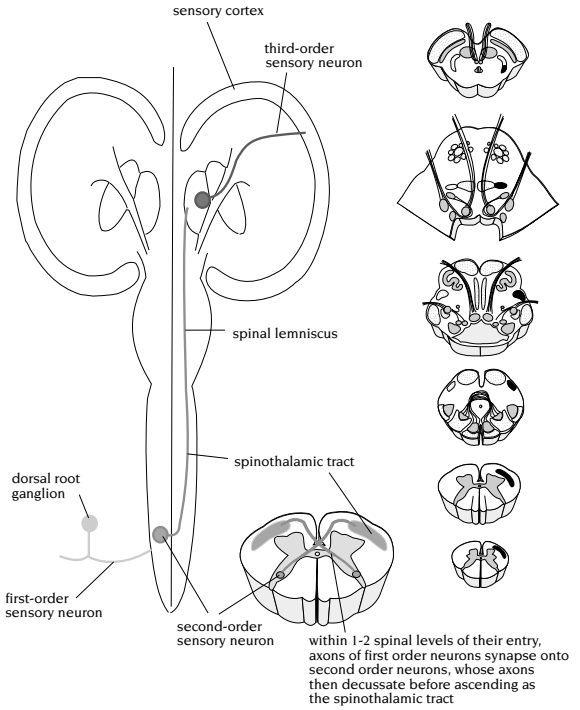


Figure 8. Spinothalamic Pain Pathway from Body

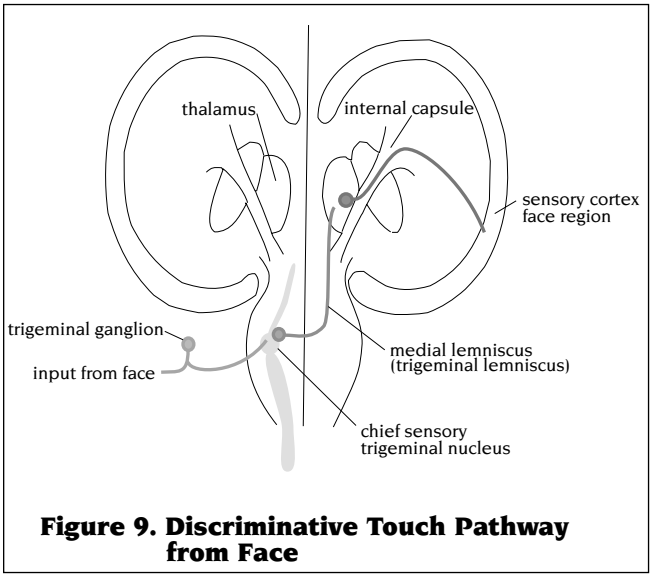


Figure 9. Discriminative Touch Pathway from Face

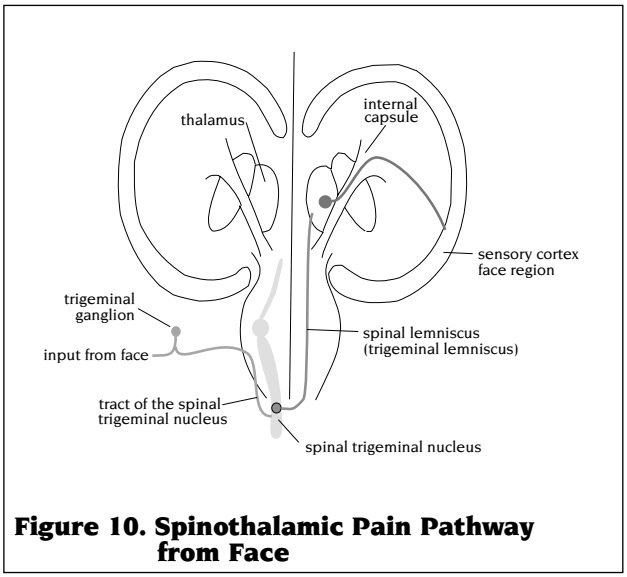


Figure 10. Spinothalamic Pain Pathway from Face

Illustrations by Dr. P. Stewart

DIAGNOSTIC INVESTIGATIONS

CT

X-Rays Attenuated in Proportion to the Density of Tissue
- ❑ black: air, fat, CSF, water
- ❑ gray: edematous or infarcted brain, normal brain, subacute hemorrhage (5-14 days)
- ❑ white: acute hemorrhage (hemoglobin), IV contrast, bone, metal
- ❑ CT with contrast is useful in detecting breakdown of Blood-Brain-Barrier, and in conditions such as neoplasm, abscess, vascular malformation

Clinical Pearl
- ❑ **CT with no contrast – bleeds, infarctions.**
- ❑ **CT with contrast – tumours, abscesses, vascular malformations.**

MRI

- ❑ better than CT in the evaluation of brainstem (posterior fossa), spinal cord lesions
- ❑ more sensitive for pathology

	Advantage	Black	Gray	White
T1-weighted	Anatomy	CSF, bone, often tumour/infarction	Normal brain	Fat, subacute hemorrhage
T2-weighted	Pathology	Bone	Normal brain	CSF, brain edema, infarction, tumour

- ❑ other MR images - proton density, diffusion, flair
- ❑ high velocity blood flow appears black on both T1 and T2, so intracranial blood vessels can be imaged
- ❑ good at differentiating periventricular pathology (e.g. white matter demyelination) from CSF
- ❑ MR angiography adequate for large-scale vascular lesions

OTHER INVESTIGATIONS

Table 3. Other Techniques of Neuroimaging

Imaging Technique	Basic Principle	Clinical Application
MRA (Magnetic resonance angiogram)	Special pulse sequences for blood	Visualization of blood vessels for lesions or abnormalities
fMRI (Functional MRI)	Ultrafast images of blood oxygenation	Changes in blood flow during functional activation
PET scan (Positron emission tomography)	Localization of positron-emitting radionuclides	Epilepsy surgery, dementia, degenerative diseases assess function
SPECT scan (Single photon-emission computed tomography)	Localization of gamma-emitting radionuclides	Localization of blood flow changes in dementia, epilepsy, degenerative diseases and cerebrovascular diseases

LUMBAR PUNCTURE (see Neurosurgery Chapter)

Indications
- ❑ infection (bacterial, tuberculous, fungal, viral meningitis) suspected
- ❑ subarachnoid hemorrhage (SAH) (since CT negative in 10% of SAH)
- ❑ non-infectious inflammation (SLE)
- ❑ CSF chemistry for diagnosis (gammaglobulin oligoclonal banding for MS)
- ❑ CSF dynamics (e.g. NPH or spinal block)
- ❑ cytology (e.g. carcinomatosis, meningeal cancer)
- ❑ therapeutic intrathecal drug administration
- ❑ therapeutic removal of CSF (e.g. pseudotumour cerebri)
- ❑ diagnostically for contrast injection during myelography
- ❑ inflammatory polyneuropathy (e.g. Guillain Barre syndrome)

DIAGNOSTIC INVESTIGATIONS . . . CONT.

Contraindications
- ❑ signs and symptoms of increased ICP (papilledema, decreased LOC, progressive deficit, headache) due to mass lesion
  - do CT first and then proceed to lumbar puncture (LP) if there is no shift
- ❑ neurologic findings suggestive of localized mass lesion
- ❑ obstructive hydrocephalus, or evidence of blood
- ❑ infection at LP site
- ❑ coagulopathy (e.g. anticoagulatn drugs) or thrombocytopenia
- ❑ developmental abnormality (i.e. tethered spinal cord)

Diagnostic Tests
- ❑ opening pressure, protein, glucose, cell counts, colour, VDRL, viral PCR, IgG levels, oligoclonal bands, fungal antigens, microbiological stains (Gram, ZN, fungal), bacterial culture and PCR

Typical
- ❑ see CSF Findings in CNS Infections section

Complications
- ❑ most common is bifrontal or generalized headache (10-40%)
- ❑ tonsillar herniation
- ❑ infection
- ❑ spinal epidural hematoma

SEIZURE DISORDERS AND EPILEPSY

Definitions
- ❑ a seizure is a paroxysmal alteration of behavior and/or EEG changes that results from abnormal and excessive activity of cerebral neurons
- ❑ epilepsy is a condition characterized by a tendency to have recurrent, unprovoked seizures

CLASSIFICATION OF SEIZURES

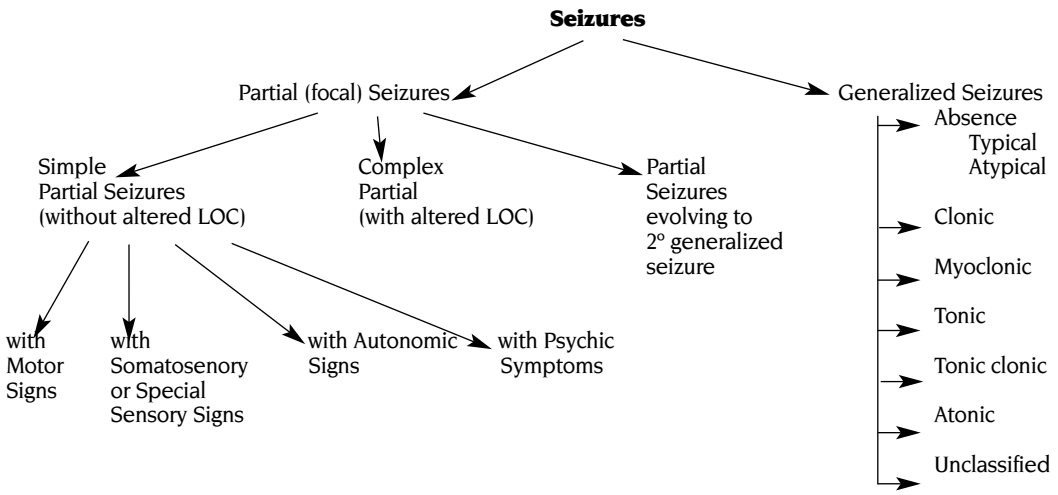


Figure 11. Classification of Seizures

CLINICAL APPROACH TO SEIZURES

History

- ❑ age of onset: primary generalized seizures rarely begin < 3 or > 20 years of age
- ❑ precipitants: sleep deprivation, drugs, EtOH, TV screen, strobe, emotional upset
- ❑ presence of aura: implies focal onset
- ❑ patient's responsiveness during attack
- ❑ nature of neurological features suggests location of focus
  - motor = frontal lobe
  - visual/olfactory/gustatory hallucinations = temporal lobe
- ❑ salivation, cyanosis, tongue biting, incontinence
- ❑ Jacksonian march: one body part is initially affected, followed by spread to other areas (e.g. fingers to hands to arm to face)
- ❑ adversive: head or eyes are turned forcibly to the contralateral frontal eye field
- ❑ automatisms: patterns of repetitive activities that look purposeful, (e.g. chewing, walking, lip-smacking)
- ❑ temporal lobe epilepsy: unilateral posturing, behavioral disturbances, automatisms, olfactory or gustatory hallucinatons
- ❑ post-ictal symptoms - limb pains, tongue soreness, headache, drowsiness, Todd's paralysis (hemiparesis)
- ❑ duration: ictus is short (seconds - minutes), post-ictus can be long (minutes - hours)
- ❑ family history of seizures
- ❑ past history of neurological insult: birth injury, head trauma, stroke, CNS infection, drug use/abuse
- ❑ fever: febrile seizures affect 4% of children between 3 months and 5 years of age, benign if brief solitary, generalized tonic clonic lasting less than 15 minutes and not more frequent than once/24 hours

Clinical Pearl

- ❑ **Stroke is the most common cause of late-onset (> 50 years of age) epilepsy, accounting for 50-80% of cases.**

Physical Examination

- ❑ pulse (especially rhythm), BP, heart auscultation
- ❑ complete neurological examination (CN, motor, reflexes, tone, sensory, coordination, mini mental exam)
- ❑ absence seizures can be precipitated by hyperventilation: have patient take up to 100 deep breaths and watch for a brief, transient cessation of activity and "glassy stare"
- ❑ asymmetry of fingernail, toe, and limb size (clue to early damage of contralateral hemisphere)
- ❑ arteriovenus malformations (AVM's) may present as focal seizures: auscultate for bruits (carotid, orbital, cranial, spinal), visual fields, optic fundi
- ❑ head exam for evidence of trauma (look, then feel)
- ❑ skin exam: look for characteristic lesions of neurocutaneous syndromes (neurofibromatosis (NF), tuberous sclerosis complex, Sturge-Weber syndrome)

Investigations

- ❑ CBC, sodium, glucose, calcium, magnesium, creatinine, urea, LFTs
- ❑ CXR, ECG
- ❑ EEG (symmetric bursts of sharp and slow, 4-7Hz in primarily generalized tonic clonic, focal epileptiform in secondarily generalized, spikes and slow waves at 3/second in absence) - interictal EEG is normal in 60% of cases
- ❑ increased prolactin level with generalized tonic-clonic seizures
- ❑ CT / MRI except for definite primary generalized epilepsy
- ❑ LP if signs of infection and no papilledema or midline shift of brain structures (generally done after CT or MRI, unless suspicious of meningitis)

Etiology

- ❑ generalized
  - idiopathic (family history in up to 40% of cases)
  - diffuse cerebral damage (encephalitis, anoxia, storage diseases)
  - metabolic (hypocalcemia, hypoglycemia, hyponatremia, porphyria, hypoxia, renal failure, hepatic failure)
  - drugs (EtOH withdrawal, TCAs, MAOIs, neuroleptics, cocaine, amphetamines)
- ❑ partial (focal)
  - cerebral trauma
  - birth injury
  - vascular (cerebral hemorrhage, cortical infarcts, AVM, cavernoma)
  - cerebral tumours
  - infections (meningitis, encephalitis, cerebral abscess, subdural empyema, syphilis, TB, HIV)
  - inflammation (sarcoidosis, SLE)

DDx

- ❑ syncope
  - causes
    - neurogenic vasodepressor and vasovagal reaction
    - sympathetic nervous system (SNS) failure
    - decreased cardiac output (CO) or inadequate intravascular volume
    - others (e.g. hypoxia, anemia)
  - NOTE: syncope may induce a seizure – this is not epilepsy
- ❑ pseudoseizure
  - can be impossible to differentiate without EEG
  - often occur in conjunction with epilepsy
  - history of sexual abuse
  - patterned after witnessed seizure (i.e. health care worker, sibling or friend with seizures)
  - see Table 5
- ❑ narcolepsy (cataplexy)
- ❑ migraine: associated with sensory or motor symptoms or vertebrobasilar migraine
- ❑ anxiety: hyperventilation, panic attacks
- ❑ transient ischemic attack
- ❑ hypoglycemia
- ❑ pheochromocytoma

Table 4. Seizures versus Syncope

Characteristic	Seizure	Syncope
Time of onset	Day or night	Day
Position	Any	Upright, not recumbent
Onset	Sudden or brief aura	Gradual (vasodepressor)
Aura	Possible specific aura	Dizziness, visual blurring, lightheadedness
Colour	Normal or cyanotic (tonic-clonic)	Pallor
Autonomic features	Uncommon outside of ictus	Common
Duration	Brief or prolonged	Brief
Urinary incontinence	Common	Rare
Disorientation, post-ictal	Can occur with tonic-clonic, complex partial	Rare
Motor activity	Can occur	Occasional brief tonic seizure or clonic jerks
Injury	Common	Rare
Automatisms	Can occur with absence or complex partial	None
EEG	Frequently abnormal, may be normal	Normal

Table 5. Seizures versus Pseudoseizures (non-epileptic "seizures")

Characteristic	Pseudoseizure	Epileptic Seizure
Age	Any, less common in the elderly F>>M	Any F=M
Triggers	Emotional disturbance	Uncommon
Duration	May be prolonged	Brief
Motor activity	Opisthotonus Rigidity Forced eye closure Irregular extremity movements Side-to-side head movements Pelvic thrusting Crying	Automatisms in complex Partial seizures Stereotypic Synchronous movements
Timing	Usually day; usually present other people	Day or night
Physical injury	Non-serious and only witnessed	May occur
Urinary incontinence	Rare	May occur
Reproduction of attack	Suggestion above or stimuli plus suggestion	Spontaneous
EEG	normal ictal and post-ictal patterns	Inter-ictal discharges frequent

TYPES OF SEIZURES

Simple Motor
- ❑ arise in precentral gyrus (motor cortex), affecting contralateral face/trunk/limbs
- ❑ ictus
  - no change in consciousness
  - rhythmical jerking or sustained spasm of affected parts (i.e. clonus)
  - characterized by forceful turning of eyes and head to side opposite the discharging focus (adversive seizures)
  - may start in one part and spread "up/down the cortex" (Jacksonian march - remember the homunculus)
  - duration from seconds to hours (which may result in Todd's paralysis for hours)

Simple Sensory
- ❑ somatosensory
  - arise in sensory cortex (postcentral gyrus), affecting contralateral face/trunk/limbs
  - numbness/tingling/"electric" sensation of affected parts
  - a "march" may occur
- ❑ other forms include: visual, auditory, olfactory, gustatory, vertiginous (may resemble schizophrenic hallucinations but patients recognize the unreality of phenomena)

Clinical Pearl
- ❑ **Motor and/or sensory partial seizures indicate structural disease until proven otherwise.**

Simple Autonomic
- ❑ symptoms/signs include: epigastric sensation, pallor, sweating, flushing, piloerection and pupillary dilatation

Simple Psychic
- ❑ disturbance of higher cerebral function
- ❑ symptoms rarely occur without impairment of consciousness and are much more commonly experienced as complex partial seizures

Complex Partial (Temporal Lobe Epilepsy, Psychomotor Epilepsy)
- ❑ often incorrectly called "petit mal" by patients
- ❑ seizures causing alterations of mood, memory, perception
- ❑ common form of epilepsy, with increased incidence in adolescents, young adults
- ❑ ictus
  - aura of seconds-minutes; forms include: dysphasic, dysmnesic (déjà vu, jamais vu), cognitive (dreamy states, distortions of time sense), affective (fear, anger), illusions (macropsia or micropsia), structured hallucinations (music, scenes, taste, smells), epigastric fullness
  - then patient appears distant, staring, unresponsive (can be brief and confused with absence seizures)
  - automatisms occur in 90% of patients (chewing, swallowing, lip-smacking, scratching, fumbling, running, disrobing, continuing any complex act initiated prior to loss of consciousness)
- ❑ recovery is characterized by confusion +/– headache
- ❑ can resemble schizophrenia, psychotic depression (if complex partial status)

Generalized Tonic-Clonic (Grand Mal)
- ❑ common
- ❑ all of the classic features do not necessarily occur every time
- ❑ prodrome of unease, irritability hours-days before attack
- ❑ ictus
  - aura (if secondary generalized from a partial onset) of olfactory hallucinations, epigastric discomfort, déjà vu, jerking of a limb, etc. seconds-minutes before attack
  - tonic phase: tonic contraction of muscles, with arms flexed and adducted, legs extended, respiratory muscles in spasm ("cry" as air expelled), cyanosis, pupillary dilatation, loss of consciousness, patient often "thrown" to the ground); lasting 10-30 seconds
  - clonic phase: clonus involving violent jerking of face and limbs, tongue biting, and incontinence; lasting 1-5 minutes
  - post-ictal phase of deep unconsciousness, with flaccid limbs and jaw, extensor plantar reflexes, loss of corneal reflexes; lasts a few minutes to several hours; headache, confusion, aching muscles, sore tongue, amnesia; serum CK elevated for hours

Absence (Petit Mal)
- ❑ relatively uncommon; onset in childhood
- ❑ hereditary
  - autosomal dominant
  - incomplete penetrance (~1/4 will get seizures, ~1/3 will have characteristic EEG findings)
  - 3 Hz generalized spike and slow-wave activity on EEG
- ❑ ictus
  - child will stop activity, stare, blink/roll eyes, be unresponsive; lasting approximately 5-10 seconds or so, but may occur hundreds of times/day
  - may be accompanied by myoclonus or akinetic/drop attacks
  - may be induced by hyperventilation
- ❑ often associated with decreasing scholastic performance
- ❑ 1/3 "convert" to tonic-clonic in adolescence

Myoclonic
- ❑ sudden, brief, generalized muscle contractions
- ❑ may be seen in association with absence and clonic-tonic-clonic seizures
- ❑ most common disorder is juvenile myoclonic epilepsy (benign, onset after puberty)
- ❑ also occurs in degenerative and metabolic disease (e.g. hypoxic encephalopathy)

Management
- ❑ psychosocial
  - educate patients and family
  - advise about swimming, boating, locked bathrooms, operating dangerous machinery, climbing heights, chewing gum
  - pregnancy issues: counseling and monitoring blood levels closely, teratogenicity of antiepileptic drugs, folate 4-6 mg/day for 3 months prior to conception (throughout child-bearing years)
  - inform of prohibition to drive and requirements to notify government
  - support groups, Epilepsy Association
  - follow-up visits to ensure compliance, evaluate changes in symptoms/seizure type (re-investigate)
- ❑ pharmacological
  - begin with one major anticonvulsant with a simple dosage schedule (see Table 6)
  - adjust dose to achieve plasma level in low therapeutic range
  - if no seizure control, increase dose until maximum safe dose or side-effects become intolerable
  - if no seizure control, change to or add second drug
  - clonazepam: mostly used for refractory myoclonic seizures
  - adjunctive therapy: clobazam (Frisium), gabapentin (Neurontin), vigabatrin (Sabril), lamotrigine (Lamictal)
- ❑ surgical
  - for selected cases of complex partial epilepsy with an identifiable focus

Table 6. Indications and Important Side-Effects of Major Antiepileptic Drugs

Drug	Indication	Major Side-Effects	
		Dose-Related	Idiosyncratic
Carbamazepine (Tegretol)	Partial or generalized tonic-clonic seizures	Diplopia Dizziness Headache Nausea Drowsiness Neutropenia Hyponatremia	Morbilliform rash Agranulocytosis Aplastic anemia Hepatotoxic effects Stevens-Johnson syndrome Teratogenicity
Phenytoin (Dilantin)	Partial or generalized tonic-clonic seizures status epilepticus	Nystagmus Ataxia Nausea Vomiting Gingival hyperplasia Depression Drowsiness Paradoxical ↑ in seizures Megaloblastic anemia	Acne Coarse facies Hirsutism Blood dyscrasias Lupus-like syndrome Rash Stevens-Johnson syndrome Dupuytren's contracture Hepatotoxic effects Teratogenicity
Valproate (Epival, Depakene)	All generalized seizures or partial seizures	Tremor Weight gain Dyspepsia Nausea Vomiting Alopecia Peripheral edema	Acute pancreatitis Hepatotoxic effects Thrombocytopenia Encephalopathy Teratogenicity
Ethosuximide (Zarontin)	Absence seizures	Nausea Anorexia Vomiting Agitation Drowsiness Headache Lethargy	Rash Erythema multiforme Stevens-Johnson syndrome Lupus-like syndrome Agranulocytosis Aplastic anemia

STATUS EPILEPTICUS
- ❑ a life-threatening state (5-10%) with either a continuous seizures lasting at least 30 minutes or a series of seizures occurring without the patient regaining full consciousness between attacks
- ❑ risks: repetitive grand mal seizures impair ventilation, resulting in anoxia, cerebral ischemia and cerebral edema; sustained muscle contraction can lead to rhabdomyolysis and renal failure
- ❑ may result in excitotoxic damage

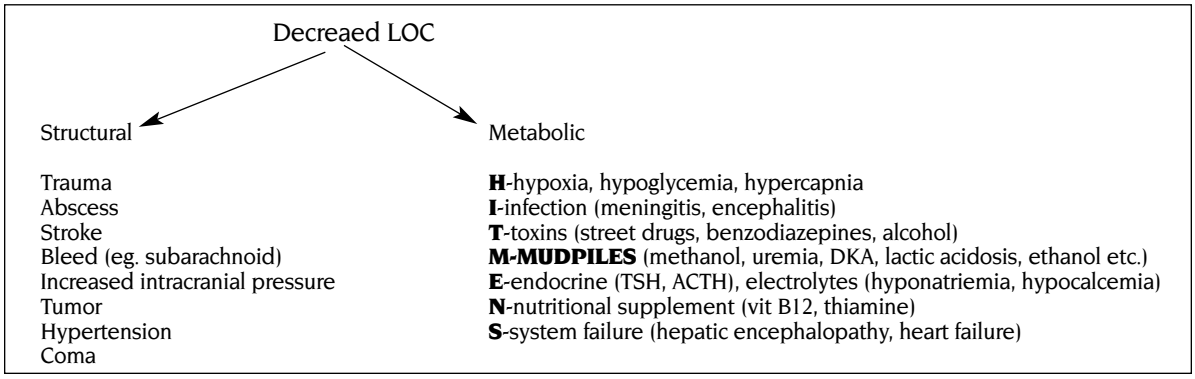
ABCs
- ❑ lateral semi-prone position, mandible pushed forward; use oropharyngeal/endotracheal tube with high-flow oxygen
- ❑ monitor RR, HR, BP and temperature

Interrupt Status
- ❑ give 50 ml 50% glucose IV and thiamine 100 mg IM
- ❑ lorazepam IV 2-4 mg (0.05 mg/kg)
- ❑ set up IV infusion of phenytoin (15-18 mg/kg loading dose with maintenance started 12 hours later); monitor BP and ECG during infusion
  - phenobarbital if no response (watch for hypotension and respiratory depression)
  - general anesthesia in ICU (e.g. pentothal) if no response to phenobarbital
- ❑ monitor lytes, glucose, urea, creatinine, lactate, myoglobin, blood gases, ECG
- ❑ midazolam drip (in ICU) or pentobarbital "coma"

Assess the Cause of the Status
- ❑ accucheck (rule out hypogycemia)
- ❑ draw metabolic and drug screen (most common is EtOH)
- ❑ measure anticonvulsant levels
- ❑ CXR, EEG and consider stat CT or MRI if first seizure or if focal neurological deficits elicited

ALTERED LEVEL OF CONSCIOUSNESS

APPROACH TO ALTERED LEVEL OF CONSCIOUSNESS (LOC)



COMA

Definition
- ❑ a state in which patients show no meaningful response to environmental stimuli from which they cannot be aroused

Pathophysiology
- ❑ consciousness consists of 2 components
  - arousal - alertness, sleep-wake cycle
  - content - responding to external stimuli
    - i.e. seeing, feeling, hearing, speaking
- ❑ consciousness requires
  1. intact cerebral hemispheres
  2. intact reticular activating system (RAS) in brainstem
- ❑ lesions diffusely affecting hemispheres or directly affecting the RAS cause impairment of consciousness and potentially coma
- ❑ focal hemispheric damage does not alter consciousness except by mass effect or by precipitating seizures

Classification
- ❑ structural lesions (tumour, pus, blood, CSF); (1/3 of all cases of coma)
  - expanding supratentorial mass: causes transtentorial herniation, leading to brainstem compression (and thus RAS dysfunction) or major shift (horizontal) with bilateral hemispheric dysfunction
  - posterior fossa lesion: may directly destroy the neurons of the brainstem RAS
- ❑ metabolic disorders/diffuse hemispheric damage (2/3 of comas)
  - deficiency of essential substrates, i.e. oxygen, glucose, vitamin B_{12}
  - endogenous/exogenous toxins, i.e. drugs, heavy metals, solvents
  - systemic metabolic diseases, i.e. uremia, hepatic encephalopathy, electrolyte imbalances

INITIAL EVALUATION: GLASGOW COMA SCALE (see Emergency Medicine Chapter)

Table 7. Glasgow Coma Scale

Eyes Open		Best Verbal Response		Best Motor Response	
spontaneously	4	answers questions appropriately	5	obeys commands	6
to voice	3	confused, disoriented	4	localizes pain	5
to pain	2	inapproriate words	3	withdraws to pain	4
no response	1	incomprehensible sounds	2	decorticate (abnormal flexion)	3
		no verbal response	1	decerebrate (abnormal extension)	2
				no response	1

GENERAL MANAGEMENT OF A COMATOSE PATIENT (ABCDE)

❑ Airway and C-spine stabilization
❑ Breathing
❑ Circulation
❑ Drugs
- thiamine 50 mg IM (think about alcoholism/nutritional causes)
- naloxone (Narcan) 0.4 mg/ml 2 ml IV (think about opiates)
- 50 ml 50% glucose IV

❑ Evaluate patient

EVALUATING THE COMATOSE PATIENT

History

❑ previous/recent head injury (hematomas)
❑ sudden collapse (intracerebral hemorrhage (ICH, SAH)
❑ limb twitching/incontinence (post-ictal state)
❑ slow onset of symptoms (mass or metabolic, bugs or drugs)
❑ diabetes mellitus (DM) (hypoglycemia or hyperglycemia)
❑ depression (drug overdose)
❑ telephone witnesses, read ambulance report, check for medic-alert bracelet

Physical Examination

❑ neurological – full examination essential but concentrate on
- GCS - follow over time
- respirations (rate and pattern)
  - apneustic or ataxic (brainstem)
  - Cheyne-Stokes (cortical, brainstem or toxic/metabolic)
- posture
  - decorticate: severe bilateral damage above midbrain
  - decerebrate: damage in midbrain, diencephalon
- movement
  - spontaneity, symmetry and seizure activity
- pupils - reactivity and symmetry (CN II, III), papilledema (increased ICP)
- reflexes
  - corneal reflex (CN V, VII)
  - gag reflex (CN IX, X)
  - oculocephalic reflex/doll's eye reflex (after C-spine clearance): test for brainstem integrity
  - oculovestibular reflex (rule out tympanic perforation and cerumen impaction first)
  - deep tendon reflexes and tone
  - plantar reflex
- caloric stimulation: normal response consists of ipsilateral slow gaze (brainstem mediated) and contralateral saccadic correction (cortically mediated); cannot be voluntarily resisted
- LP after normal CT to rule out meningitis, subarachnoid hemorrhage (SAH) (increasing evidence that lumbar puncture (LP) can be done as primary investigation if no evidence of increased ICP)

Clinical Pearl

❑ **Decorticate posturing i.e. arms flexed at elbow and wrist, and legs extended at knee and ankle in response to a noxious stimulus, points to a lesion below the thalamus but above the red nucleus.**
❑ **Decerebrate posturing i.e. arms extended at elbow, pronated and flexed at wrist, and legs extended at knee and ankle, suggests a lesion below red nucleus but above vestibular nucleus.**

Assessment and DDx
- ❑ orderly, progressive, loss of function - expanding supratentorial lesion is likely
  - hematoma, neoplasm, abscess, inflammation, hydrocephalus, etc.
  - massive infarction with edema
- ❑ simultaneous onset of impaired consciousness, pinpoint pupils (pons), and brainstem signs (i.e. skew deviation of eyes) suggests posterior fossa lesion
  - brainstem infarct or hemorrhage
  - cerebellar infarct or hemorrhage
- ❑ Note: abrupt onset of vertigo, nystagmus, vomiting, inability to stand/walk (with normal lower limb strength) with occipital headache, coma, miosis, and contralateral ocular deviation suggests cerebellar hemorrhage - call Neurosurgery for surgical compression
- ❑ scattered neurological dysfunction (i.e. intact brainstem with no focal signs) suggests metabolic coma
  - hypoxia, hypoglycemia, toxins, major organ failure
  - major endocrine disturbance (i.e. myxedema), major acid-base/electrolyte disturbance
  - Beware meningitis and SAH - can mimic metabolic coma!

MANAGEMENT OF SPECIFIC CAUSES

Expanding Supratentorial Lesion
- ❑ ABCDE
- ❑ elevate head of bed to 30 degrees
- ❑ intubate and hyperventilate (pCO_2 to 20-25 mmHg to decrease ICP)
- ❑ mannitol IV 500 ml of 20% over 30 minutes (to decrease ICP)
- ❑ stat CT/MRI
- ❑ call Neurosurgery

Infratentorial Lesions
- ❑ ABCDE
- ❑ stat CT/MRI
- ❑ send for neurosurgeon if cerebellar hematoma demonstrated
- ❑ Note: cerebellar infarction can cause hydrocephalus and decreased LOC - requires Neurosurgery

Metabolic Coma
- ❑ ABCDE
- ❑ if meningitis or fever
  - CT (followed by LP if no mass papilledema, lesion or hydrocephalus found)
  - if CT not available, start antibiotics for meningitis and transfer patient to neurological center
- ❑ ECG (continuous if TCA overdose a consideration)
- ❑ lytes, calcium, glucose, urea/creatinine, ABGs, osmolality, LFTs, hematology, drug levels/screen
- ❑ if increased anion gap, think 'MUDPILES', (see Nephrology Chapter)
- ❑ calculate osmolality (for S.I. units): 2 x Na + BUN + glucose
- ❑ if osmol gap, think "**ol**": ethanol, methan**ol**, isopropan**ol**, mannit**ol**, ethylene glyc**ol**, glycer**ol**

BRAIN DEATH

Definition
- ❑ irreversible loss of brain function; vital structures of the brain necessary to maintain consciousness and independent vegetative survival are damaged beyond repair
- ❑ cardiovascular activity may persist for as long as two weeks but usually CV collapse occurs within several days

MANDATORY CRITERIA FOR DIAGNOSIS
- ❑ no potentially anesthetizing amounts of either toxins or drugs present (e.g. barbiturates)
- ❑ hypothermia below 32°C or other physiologic (metabolic, endocrine) abnormalities must be corrected
- ❑ irreversible structural disease or a known and irreversible endogenous metabolic cause due to organ failure must be present
- ❑ 12 hour period of no cortical or brainstem functioning must have elapsed
  - no cerebral function
  - no brainstem reflexes
  - circulation may be intact, purely spinal cord reflexes may be retained
- ❑ no seizures
- ❑ no pupil reaction to bright light in both eyes
- ❑ absent corneal reflexes, no vestibulo-ocular reflex (VOR)
- ❑ no eye movements when ice water slowly injected into unoccluded external auditory meatus with head raised at 30°
- ❑ no gag reflex to bronchial stimulation with suction tube
- ❑ no motor response in the face or muscles supplied by cranial nerves to a painful stimulus (supraorbital pain, intranasal pain)
- ❑ no respiratory effort when disconnected from ventilator for 10 minutes after being hyperventilated with 6 L O_2/minute to prevent anoxia (apnea test)

Most Medical Centres
- ❑ evaluation has to be performed by two specialists (e.g. neurologist, anesthetist, neurosurgeon), patient has to be evaluated on two separate occasions

Supplemental Criteria
- ❑ isoelectric EEG for 30 minutes at maximum gain reflecting absence of electrical activity – may be normal in brain death
- ❑ brainstem auditory or short latency somatic evoked responses reflecting absence of function in vital brainstem structures
- ❑ angiographic examination shows no cerebral circulation

Clinical Pearl
- ❑ **If patient remains comatose, usual outcome is recovery, persistent vegetative state, or death within 2 weeks.**

PERSISTENT VEGETATIVE STATE
- ❑ no evidence of behavioural response to visual, auditory, tactile, or noxious stimuli
- ❑ no awareness of self or environment
- ❑ no language comprehension or expression
- ❑ due to irreversible loss of cerebral cortical function BUT with intact brainstem function and rudimentary movement
- ❑ patients have normal eye opening and sleep-wake cycles, and may survive for years in this state (average life expectancy = 2-5 years)
- ❑ EEG may be flat or nearly so

BEHAVIOURAL NEUROLOGY

ACUTE CONFUSIONAL STATES

Clinical Features of Delirium/Acute Confusional State
- ❑ impairment of consciousness
  - decreased alertness, attention and concentration
- ❑ memory disturbance
  - registration, retention and recall all affected
  - disorientation in time and place occur early, especially if in new environment
  - learning is impaired and recall of recent events is poor
- ❑ perceptual disturbance
  - illusions, hallucinations (usually visual and tactile; gustatory and olfactory suggest focal temporal lobe lesions)
- ❑ cognition
  - thought slowing, confusion
  - difficulty grasping essential features of the environment (events often misinterpreted, leading to persecutory delusions)
- ❑ psychomotor changes
  - retarded mental/motor activity
  - little spontaneity, with sparse speech and slow responsiveness
  - delirium: special subtype of acute confusion characterized by agitation, restlessness, hyperactivity along with illusions and hallucinations (see Psychiatry Chapter)
- ❑ emotional changes
  - anxiety, irritability and depression
  - in severe cases, apathy is present

Etiology
- ❑ usually "metabolic/toxic" or "beclouded dementia" (impaired cognition with precipitating event, e.g. sepsis)
- ❑ intracranial
  - trauma
  - vascular (TIA, cerebral hemorrhage/thrombosis, SAH, subdural hematoma)
  - epilepsy (post-ictal, non-convulsive status)
  - infection (encephalitis, cerebral abscess, meningitis, AIDS)
  - neoplasia
- ❑ extracranial (remember "**HIT ME**")
  - **H**ypoxia (respiratory failure, cardiac failure, acute heart block, CO poisoning)
  - **I**nfections (exanthemata, septicemia, pneumonia, UTI)
  - **T**oxins, especially withdrawal (EtOH, anticholinergics, β-blockers, L-dopa, INH, etc.)
  - **M**etabolic (uremia, liver failure, carcinoma, electrolyte imbalance) and nutritional (thiamine, vitamin B_{12}, folate)
  - **E**ndocrine (hyper/hypothyroidism, hypoglycemia, Addisonian crisis, hypopititarism etc.)

Diagnosis
- ❑ history and physical
- ❑ urinalysis, blood cultures, and CXR
- ❑ electrolytes, urea, creatinine, glucose, ABGs, LFTs, calcium, phosphate, TSH, vitamin B_{12}, folate, CBC
- ❑ ECG, CXR, toxicological screen
- ❑ CT, LP (if CT negative, and no focal signs/papilledema), EEG

Management
- ❑ treat underlying cause
- ❑ supportive measures
  - nurse in a well-lit room
  - IV therapy (for fluid/lyte disturbance)
  - chlorpromazine or haloperidol (5-10 mg IM) if patient's behaviour disruptive
  - respiridone can be used for agitation
  - diazepam if DTs (delerium tremens)

DEMENTIA
- ❑ a clinical syndrome of acquired and progressive decline in higher cortical functioning in comparison with previous level of functioning, occurring in an alert patient
- ❑ remember:" **IMP**" - **I**ntelligence, **M**emory, **P**ersonality

Operating Criteria for Dementia
- ❑ memory impairment plus at least one of the following: aphasia, apraxia, agnosia, disturbance in executive functioning
- ❑ disturbance significantly interferes with work, social activities, or relationships
- ❑ disturbance does not occur exclusively during delerium
- ❑ memory impairment: recent before remote memory impairment
- ❑ other cognitive signs
  - learning and retaining new information
  - handling complex tasks
  - reasoning/ impaired judgment
  - spatial abilities and orientation
  - language (word finding)
- ❑ personality change
  - decline in personal manners/social awareness
  - disinhibited behaviour (sexually aggressive/criminal)
  - coarsening: an exaggeration of premorbid character traits
  - delusions may develop
  - deterioration in grooming/hygiene; urinary/fecal incontinence

Epidemiology
- ❑ incidence increases with age
- ❑ 4% population > 65 years severely demented
- ❑ 11% population > 65 years mild-moderate dementia
- ❑ 60-80% of dementia due to Alzheimer's disease; 10-20% due to vascular disease; 10-15% due to a mixed picture
  - ~ 75 other causes
  - medications and depression are important mimics
- ❑ risk factors: age, family history, diabetes

Approach to Dementia
- ❑ want to elicit treatable causes
- ❑ history
  - rate of cognitive decline: weeks, months/years, stepwise (strokes)
  - degree of impairment of social function
  - general health
  - nutritional status
  - drug history
  - family history of dementia
  - important to obtain collateral information
- ❑ physical exam
  - mental status exam (Folstein with a cutoff of 24/30 - sensitivity 87%, specificity 82%)
  - visual spatial testing, frontal lobe testing, supplementary memory tests
  - focal neurological signs
  - involuntary movements
  - pseudobulbar signs
  - primitive reflexes (e.g. glabellar, pout, snout, palmomental, grasp)
- ❑ investigations
  - all patients: CBC, lytes, BUN, creatinine, glucose, AST, ALT, ALP, PT/PTT, albumin, Ca^{2+}, TSH, vitamin B_{12}, folate, and VDRL
  - as clinically indicated: phosphorus, ESR, FTA, urinalysis
  - CXR, ECG, EEG, LP
  - CT or MRI
  - neuropsychological testing may help

CAUSES OF DEMENTIA (D-E-M-E-N-T-I-A)

D-Degenerative

Alzheimer's Disease
- ❑ most common dementia; females > males; ~ 15% of cases familial
- ❑ progression is slow over years
- ❑ triad of memory loss, language impairment and visual spatial dysfunction
- ❑ also visual agnosia (ability to see but not recognize objects), apraxia (inability to perform certain motor tasks in absence of paralysis)

- ❑ diagnosis
  - exclusion of all other causes of dementia by history, physical and labs
  - physical exam: primitive reflexes; ↑ motor tone with motor dyspraxias; myoclonus/seizures may follow
- ❑ pathology: cortical atrophy, ventricular dilatation, neuritic plaques, neurofibrillary tangles, decreases in cholinergic neurons
- ❑ investigations: to find a treatable cause if present
- ❑ treatment
  - symptom relief and support (family/caregiver relief)
  - mild sedation (Trazadone) if aggressive behavior
  - support groups
  - new acetylcholinesterase inhibitors (donepezil, tacrine, rivastagmine, galactamine) may be used for symptom relief but does not modify progression of disease

Lewy Body Disease
- ❑ extrapyramidal motor signs, progressive dementia
  - prominent fluctuations in mental status
  - visual hallucinations common
- ❑ management: DO NOT USE Haldol (phenothiazines) risk of severe extrapyramidal toxicity
- ❑ pathology: Lewy bodies throughout cortex and brainstem nuclei

Pick's Disease
- ❑ degenerative dementia affecting frontal and temporal lobes
- ❑ clinically similar to Alzheimer's
- ❑ personality changes of frontal lobe syndrome: disinhibition, loss of social graces, jocularity and apathy punctuated by irritability
- ❑ difficulty concentrating
- ❑ language dysfunction: decreased verbal output, word-finding difficulty (anomic aphasia)
- ❑ temporal lobe involvement: transcortical or fluent aphasias and memory loss
- ❑ peak onset 55-65 years, slightly greater female predominance
- ❑ thought to be autosomal dominant although cause unknown
- ❑ pathology: pick bodies in the neocortex and hippocampus

Other Degenerative Causes of Dementia Include
- ❑ Parkinson's disease, Huntington's disease (see Movement Disorders section)
- ❑ progressive supranuclear palsy, olivopontocerebellar degeneration

E-Emotional
- ❑ depression, schizophrenia (see Psychiatry Chapter)

M-Metabolic
- ❑ hypothyroidism/hyperthyroidism, hypocalcemia/hypercalcemia
- ❑ hypoglycemia/hyperglycemia
- ❑ hyperaldrenocorticism (Cushing syndrome)
- ❑ electrolyte abnormalities
- ❑ systemic organ failure - renal failure (uremia), hepatic encephalopathy
- ❑ Wilson's disease
- ❑ metachromatic leukodystrophy

E-Eyes and Ears
- ❑ severe hearing and visual impairment

N-Nutritional and Normal Pressure Hydrocephalus (NPH)
- ❑ vitamin B_{12} deficiency
  - subacute combined degeneration of spinal cord and brain
- ❑ folate deficiency
- ❑ other water soluble vitamin deficiency
- ❑ niacin deficiency
  - pellagra (diarrhea, dermatitis, dementia, death)
- ❑ normal pressure hydrocephalus (NPH)
  - history
    - temporal sequence of gait apraxia, incontinence, dementia
    - if sequence not followed, NPH unlikely
    - history of SAH, meningitis, trauma may be important and related to etiology
  - diagnosis: history, physical (frontal gait pattern), CT scan (markedly dilated ventricles without cortical atrophy), RISA scan, diagnostic CSF tap (Miller Fisher test – objective assessment of gait before and after removal of 30cc CSF)
  - treatment: CSF shunting may lead to improved clinical state
  - positive response to CSF tap is a good prognostic indicator
  - unlikely to benefit if demented

T-Trauma, Tumours, Toxins
- ❑ subdural hematoma
  - headache usually present
  - no history of trauma in 1/3 cases
  - suspect if drowsiness in elderly with recent personality change
- ❑ head injury
- ❑ primary or metastatic brain tumours
- ❑ drugs (e.g. barbiturates, anticholinergics, anticonvulsants, methyldopa)
- ❑ alcohol - Wernicke-Korsakoff syndrome (thiamine deficiency)
- ❑ heavy metals - lead, mercury, arsenic, thallium

I-Infection
- ❑ tertiary syphilis
- ❑ AIDS - HIV encephalopathy
- ❑ chronic meningitis (e.g. TB)
- ❑ encephalitis
- ❑ Creutzfeldt-Jacob Disease (CJD)
  - rapidly progressive, inevitably fatal prion disease of CNS characterized by progressive dementia, myoclonus and affecting adults in midlife
  - spread of disease: iatrogenic: corneal transplantation, injection of human growth hormone (prepared from pooled cadaveric pituitary glands)
  - new variant CJD - "mad cow disease" by oral ingestion
  - prodromal symptoms: fatigue, depression, weight loss, insomnia, anorexia
  - delirium, changes in behavior, emotional response, and intellectual function
  - cerebellar ataxia, visual disturbances, myoclonic contractions, dysarthria
  - startle myoclonus evocable by sensory stimuli of all sorts or may be spontaneous
  - stupor, coma
  - EEG pattern distinctive: triphasic waves changing over course of disease from diffuse nonspecific slowing to stereotyped periodic high voltage slow and sharp wave complexes on an increasingly flat background (burst suppression)
  - pathology: widespread neuronal loss and gliosis accompanied by a striking vacuolation of cerebral and cerebellar cortices

A-Atherosclerotic and Vascular
- ❑ multi-infarct dementia
  - most common vascular dementia, but often over diagnosed
  - history
    - abrupt onset
    - stepwise deterioration
    - history of strokes
    - focal motor/sensory/cognitive symptoms and signs
  - diagnosis: history; Hachinski Ischemic Score; confirmed by CT, MRI, SPECT
  - treatment (see Stroke Section)
- ❑ cerebral hemorrhage
- ❑ post-anoxic
- ❑ vasculitis
- ❑ severe stenosis of large neck vessels

APHASIA (Dysphasia)
- ❑ a disorder of language produced by a cerebral lesion characterized by errors in speech production, impaired comprehension, reading, writing and word-finding difficulty
- ❑ aphasia is an important localizing symptom usually indicative of dominant hemispheric dysfunction (usually the left hemisphere)

Preassessment Information Needed
- ❑ handedness (writing, drawing, using toothbrush, scissors)
- ❑ educational level
- ❑ native language
- ❑ preexisting learning difficulties

Language Representation
- ❑ in left hemisphere for almost all right-handed people and most left-handed people (75%)

Neuroanatomy of Aphasia (see Figure 12)
- ❑ posterior inferior frontal lobe (Broca's area) used for motor speech production
- ❑ Wernicke's area (posterior superior temporal and inferior parietal) used for comprehension of spoken language and for initiation of reply or action
- ❑ visual stimuli reach Wernicke's area through angular gyrus which is thought to be important for comprehension of written language
- ❑ these two areas connected through association bundle (arcuate fasciculus) and altogether comprise the perisylvian language zone
- ❑ aphasias may also result from damage to areas of the brain outside the perisylvian language zone (transcortical aphasias)

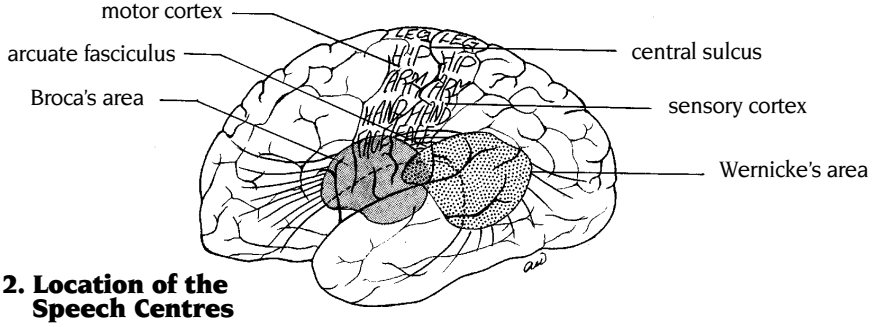


Figure 12. Location of the Speech Centres

Illustration by Aimee Warrell

Assessment of Aphasia

- ❑ fluency
  - nonfluent patients usually have damage in Broca's area
  - fluent patients have damage in Wernicke's area
- ❑ repetition
  - used to distinguish classical aphasias (arising from lesions in the perisylvian language zone) from the transcortical aphasias
  - repetition disturbance - classical aphasias: Broca's, Wernicke's, conduction aphasias, global
  - repetition intact - transcortical aphasias, anomic aphasias
- ❑ paraphasic errors
  - incorrect substitution of words or parts of words
  - characteristics of aphasia (vs. dysarthria)
  - e.g. "sook" instead of "book", "table" instead of "chair"
- ❑ comprehension - verbal and written
- ❑ naming
- ❑ writing

Table 8. Comparison of Classic Aphasias

Feature	Broca's	Wernicke's	Global	Conduction
Lesion Location	Broca's area	Wernicke's area	Both areas	Arcuate fasciculus
Fluency	Nonfluent Effortful "Telegraphic speech" Agrammatical	Fluent Paraphasic errors Circumlocutions Neologisms Pressure of speech	Nonfluent Agrammatic Neologisms Minimal volume	Fluent Paraphasic errors
Repetition	Effortful, poor	Poor	Poor	Poor to worse vs. spontaneous speech
Naming	Poor	Relative sparing	Poor	Poor
Comprehension (verbal + written)	Preserved	Poor	Poor	Preserved
Writing	Poor	Content abnormal	Poor	Penmanship preserved
Associated Features			Hemiplegia (right) Hemianesthesia Visual field defect (right hormonymous hemianopic)	Mild hemiplegia
Insight	Aware of deficit	Unaware of deficit	Aware	Aware

Transcortical Aphasias (Sensory, Motor, Mixed)

- ❑ lesions outside perisylvian language zone
- ❑ repetition relatively preserved

Anomic Aphasia

- ❑ inability to generate word names in confrontational tasks and in spontaneous speech
- ❑ if word-finding difficulty occurs in relative isolation, lesion can often be localized to posterior middle temporal/inferior parietal region or subcortical white matter
- ❑ may occur with metabolic disorders or space-occupying lesions

Important Aphasia Points

- ❑ clinical profile reflects cerebrovascular rather than functional anatomy
  - classical aphasias
    - typically produced by lesions in the MCA territory
  - transcortical aphasias
    - result from lesions in the border zone between ACA, MCA, and PCA territories (watershed areas)
    - are often associated with cerebral anoxia (i.e. post-MI, postcardiac surgery, carbon monoxide poisoning, hypotension)
- ❑ language deficit following acute stroke can change rapidly, especially if the initial impairment is mild
- ❑ with recovery, patient may evolve from one type of aphasia to another type
- ❑ most recovery occurs in first three months after onset but continues for more than one year
- ❑ conduction, transcortical, and anomic aphasias often recover completely; global aphasias have a poor prognosis

APRAXIA

- ❑ inability to perform voluntary motor sequences
- ❑ disorder of skilled movement that cannot be accounted for either by weakness, ataxia or sensory loss, comprehension, attention
- ❑ lesion in parietal and/or premotor cortex
- ❑ constructional - inability to draw or construct (R or L)
- ❑ dressing - inability to dress (R)
- ❑ ideomotor - inability to carry out skilled movements (L)
- ❑ ideational - inability to sequence actions (bilateral)

AGNOSIA

- ❑ disorder in the recognition of the significance of sensory stimuli although primary sensation and naming ability are intact
- ❑ lesion in parietal/occipital lobe
- ❑ important to examine sensory pathways: must be normal
- ❑ tactile, auditory, visual agnosia - inability to identify objects through a specific sensory modality (bilateral)
- ❑ prosopagnosia - loss of face recognition (bilateral)
- ❑ anosognosia - denial of illness, specifically hemiparesis (R)
- ❑ autotopagnosia - inability to identify body part
- ❑ finger agnosia - loss of finger recognition (L)
- ❑ spatial agnosia - inability to recognize places (R)
- ❑ Gerstmann's syndrome: acalculia, agraphia, finger agnosia, confusion of right and left (dominant parietal lobe lesion)

MOVEMENT DISORDERS

CLINICAL FEATURES

- ❑ negative features (primary functional deficit)
  - bradykinesia - loss or slowness of voluntary movement
  - postural disturbance - commonly seen in Parkinson's Disease (PD)
- ❑ positive features (secondary to disinhibition of normal brain regions)
  - involuntary movements - tremor, chorea, dystonia, ballismus
  - rigidity - affects extensors and flexors equally, not velocity dependent; when superimposed on tremor produces cogwheeling
- ❑ in akinetic rigid syndromes negative symptoms predominate (e.g. PD) whereas in dyskinesias positive symptoms predominate (e.g. Huntington's)

NEURONAL CONNECTIONS OF THE BASAL GANGLIA (see Figure 13)

- ❑ activity within the globus pallidus pars interna (GPi) prevents movement by tonic inhibition of cortical motor areas via the thalamus
- ❑ activity within the putamen acts to disinhibit cortical motor areas by directly inhibiting the GPi (direct pathway) and by inhibiting excitatory input into the GPi via the subthalamic nucleus (indirect pathway)
- ❑ activity within the substantia nigra pars compacta (SNpc) biases towards disinhibition of movement via excitation of the direct pathway and inhibition of the indirect pathway

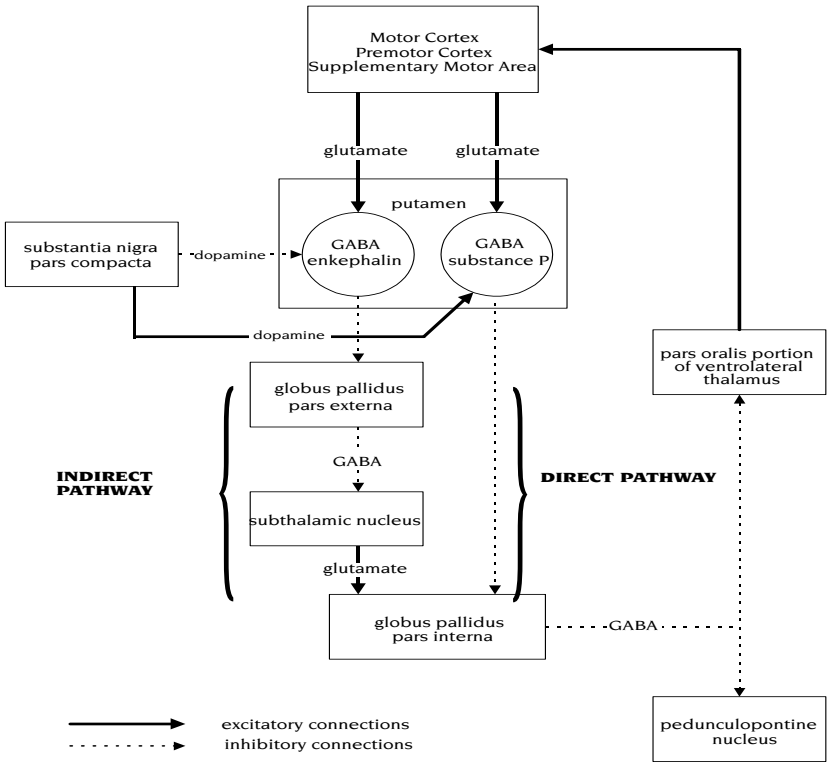


Figure 13. Neuronal Connections and Neurotransmitters of the Basal Ganglia

Illustration by David Chan

Table 9. Comparison of Corticospinal vs. Extrapyramidal Lesions

	Corticospinal	Extrapyramidal
Muscle Tone	Clasp-knife spasticity	Rigidity (lead-pipe or cogwheel) Hypotonia (cerebellar)
Distribution of Increased Tone	Arm flexors and leg extensors	Flexors and extensors of all limbs
Involuntary Movements	Absent	Tremor, chorea, athetosis, dystonia
Tendon Reflexes	Increased	Normal
Plantar Reflex	Extensor	Flexor
Paralysis or Weakness	Present	Absent

PARKINSON'S DISEASE (PD)

❑ an idiopathic, slowly progressive, degenerative CNS disorder
❑ insidious onset between 40-70 years

Clinical Features

❑ characteristic symptoms and signs (usually asymmetric onset)
- **T**remor (rest, pill-rolling, 4-7 Hz, can be suppressed by voluntary movement)
- **R**igidity (lead pipe and cogwheeling)
- **A**kinesia/Bradykinesia
- **P**ostural instability (festinating gait, retropulsion, falls)

❑ other features
- **D** - dysphagia, drooling, decreased voice
- **G** - gait: start hesitation, small shuffling steps, loss of arm swing
- **E** - eye: blepharoclonus (fluttering of closed eyelids), lack of blinking
- **M** - micrographia
- **M** - mask like face (hypomimia)
- **S** - subcortical dementia (apathy, forgetful, poor ability to use knowledge)

DDx

❑ therapeutic drugs: neuroleptics, metoclopramide
❑ toxins: MPTP (drug abusers), manganese, carbon disulfide, CO
❑ "Parkinson Plus" disorders
❑ Vascular Parkinson's
❑ post-infectious: 1914 flu epidemic (encephalitis lethargica "Awakenings")
❑ metabolic: Wilson's

Pathology

❑ loss of dopaminergic nigrostriatal neurons in substantia nigra's zona compacta
❑ dopamine neurons degenerate, upsetting normal balance between dopaminergic inhibition and cholinergic excitation of striatal output (GABA) neurons, results in relative acetylcholine (ACh) excess
❑ loss of neurons in multiple other selected areas
❑ result is relative increase in GABAergic output from striatum
❑ Lewy bodies (eosinophilic intraneural inclusion granules)
- not specific to PD

Treatment

❑ deprenyl (MAO-B inhibitor) acts by blocking dopamine breakdown and may slow progressive course
❑ levodopa + peripheral decarboxylase inhibitor (i.e. Sinemet)
❑ dopamine agonists (bromocriptine, pergolide, ropinirole, promipexole) can be used as 1st line or as add on therapy when levodopa responsiveness diminishes
❑ anticholinergics (benztropine, trihexyphenidyl) for tremor
❑ NMDA antagonists (amantadine)
❑ neurosurgical options (lesions or stimulators)
❑ therapeutic problems: orthostatic hypotension, sudden loss of therapeutic effect, wearing off, dyskinesia, freezing, psychiatric (psychosis, paranoia)

Clinical Pearl
❑ **In Parkinson's disease, postural instability generally appears later in the course of the disease. If postural instability occurs earlier consider alternative diagnosis e.g. Parkinson's plus, Vascular Parkinson's.**

Vascular (pseudo) Parkinsonism
- ❑ parkinson's-like state due to multiple strokes
- ❑ imaging usually shows basal ganglia lacunae or white matter change
- ❑ generally occurs in elderly; associated with hypertension
- ❑ often have signs and symptoms of Parkinson's below the waist (short stepped gait, start hesitation, freezing, postural instability) but relative sparing above the waist (normal voice and facial expression, absence of rest tremor and bradykinesia)
- ❑ poor response to L-dopa
- ❑ patients with true PD may also have cerebrovascular disease in addition their PD
- ❑ CT/MRI helpful in distinguishing vascular parkinsonsim from true PD

"PARKINSON PLUS" DISORDERS

Progressive Supranuclear Palsy (PSP)
(Steele, Richardson, Olszewski Syndrome)
- ❑ age of onset 50 to 70 years
- ❑ onset characterized by difficulty in balance, abrupt falls, ocular disturbances, slurred speech, dysphagia, vague personality changes, depression, abnormal facial expression
- ❑ may take years for characteristic syndrome to fully develop
    - supranuclear ophthalmoplegia - abnormality of vertical gaze (if eyes are fixated on a target and neck is flexed and extended, full or ↑ movements can be obtained)
    - pseudobulbar palsy - UMN spastic weakness of pharyngeal musculature, slurred speech, mouth held open, swallowing difficulties, exaggerated jaw jerk
    - axial dystonia - gradual stiffening and extension of the neck (contrast to Parkinson's where neck is flexed)
    - affected neurons in subthalamus, thalamus, basal ganglia, and peri-aqueductal grey
    - pathology: neurofibrillary tangles (like in Alzheimer's)
    - L-dopa not very effective in PSP
    - fatal within 2-5 years
    - may have prominent dementia or normal cognition

Multiple System Atrophy
- ❑ includes striatonigral degeneration, sporadic olivopontocerebellar atrophy, Shy-Drager Syndrome
- ❑ Parkinsonian features
- ❑ early dysautonomia (orthostatic hypotension, impotence, bladder dysfunction, mottled cold hands)
- ❑ other features are cerebellar dyfunction, pyramidal tract signs, stimulus sensitive myoclonus of hands and feet, extreme forward neck flexion, inspiratory stridor, dysarthria
- ❑ 20% respond to L-dopa initially, 13% sustained response

TREMOR

Definition
- ❑ rhythmic oscillatory involuntary movement about an axis

Rest Tremor
- ❑ slow (3-7 Hz), coarse, distal
- ❑ the characteristic tremor of Parkinsonism
- ❑ hands - pill rolling, alternating flexion/extension of fingers or hands, alternating pronation/supination of forearms
- ❑ best examined with hands resting in lap, can be brought out by tasks of concentration

Postural and Action (Kinetic) Tremor
- ❑ fast (6-12 Hz), fine, usually upper limbs, head (titubation)
- ❑ seen best with arms and hands outstretched
- ❑ physiological
    - always present, imperceptible to the eye
- ❑ exaggerated physiological
    - anxiety, sleep deprivation
- ❑ drugs (e.g. theophylline, lithium, caffeine, amphetamines, decongestants)
- ❑ drug withdrawal (e.g. EtOH)
- ❑ hyperthyroidism, hypoglycemia
- ❑ essential tremor
    - AD inheritance
    - patient complains of shaking when carrying teacup, putting a glass to the mouth, or trying to drink soup
    - affects handwriting, and voice
    - head titubation is seen
    - tremor diminishes with alcohol
- ❑ treatment: propranolol, nadolol; primidone if β-blocker contraindicated (diabetes, asthma), surgery

Intention Tremor (Cerebellar Tremor)
- ❑ seen in diseases of cerebellar outflow (worsens with alcohol)
    - coarse tremor of limbs or head; absent at rest
    - intention tremor worse at end point of movement
    - may be associated with dysarthria, nystagmus and ataxia
- ❑ examination maneuvers: finger to nose testing, heel to shin testing

Investigation of Tremor
- ❑ all patients < age of 45 exhibiting tremor should be screened for Wilson's disease (serum and urine copper high, ceruloplasmin low); and have TSH (postural tremor) and CT/MRI (if cerebellar disease suspected) performed

CHOREA

Definition
- ❑ involuntary, irregular, jerky movements; affect head and neck, face, shoulders commonly
    - other manifestations include grimacing and respiratory sounds

Huntington's Disease
- ❑ AD transmission (single gene defect on chromosome 4p), usual onset 40-60 years, age of onset inversely correlated with number of CAG trinucleotide repeats present in gene on chromosome 4p (i.e. paternal inheritance associated with expansion —> earlier and more severe presentation)
- ❑ no cure; fatal 10-20 years after clinical onset
- ❑ pathology: atrophy of head of caudate nucleus and putamen bilaterally, moderate gyral atrophy in frontal and temporal regions
- ❑ associated with decreased levels of GABA and ACh and decreased activity of glutamic acid decarboxylase and choline acetyltransferase
- ❑ chorea: initially hands and face involved, seem fidgety, restless
- ❑ chorea eventually progresses to gross involuntary movement that interrupts voluntary movements
- ❑ slight alterations in character are often the first signs: irritable, impulsive, eccentric
- ❑ emotional disturbances: depression, less communicative, more socially withdrawn
- ❑ subcortical dementia
- ❑ diminished work performance, inability to manage responsibilities, sleep disturbances
- ❑ reduced memory and attentiveness, loss of fine manual skills, tongue cannot be held protruded, increased frequency of blinking
- ❑ dysarthric and explosive speech
- ❑ later appearance of akinetic-rigid states
- ❑ diagnosis: clinical plus family history, DNA testing available, CT (atrophy of caudate), MRI (increased signal of caudate in T2)
- ❑ genetic counseling extremely important
- ❑ distinguish from benign hereditary chorea and senile chorea, which is a diagnosis of exclusion
- ❑ treatment: haloperidol most effective for suppressing movement disorder, but increased postural instability

Other Types of Chorea
- ❑ Wilson's disease: AR disorder of copper metabolism that produces neurological and hepatic dysfunction (corneal Kayser-Fleischer rings and copper deposition in liver)
- ❑ Sydenham's chorea: primarily a complication of previous Group A β-hemolytic *Streptococcus* infection, acute onset and remits in weeks
- ❑ chorea gravidarum: acute onset during pregnancy (many related to SLE and/or antiphospholipid antibody syndrome)
- ❑ SLE
- ❑ drugs (tardive chorea): L-dopa, amphetamine, oral contraceptives
- ❑ senile chorea: no dementia, older age of onset
- ❑ benign hereditary: AD with incomplete penetrance, childhood onset, intellect preserved, mild, rarely progressive

Hemiballismus
- ❑ unilateral, large amplitude flinging of the limbs, especially in proximal limb muscles
- ❑ lesion in contralateral subthalamic nucleus or its neuronal projections
- ❑ usually self-limited, resolving in 6-8 weeks
- ❑ most common cause is stroke (PCA territory)
- ❑ neuroleptics are often effective for symptomatic treatment

DYSTONIA
- ❑ sustained co-contraction of agonist and antagonist muscles which distort the limbs, trunk or face into characteristic postures
- ❑ focal dystonia - disturbance restricted to localized muscle groups, e.g. writer's cramp
- ❑ spasmodic torticollis – unilateral deviation of the head
    - geste antagoniste – patient uses finger pressure to turn head to neutral position
- ❑ idiopathic torsion dystonia
    - childhood onset, sporadic or dominant inheritance
    - initially intermittent progressing to constant disabling generalized dystonia
- ❑ abnormal movements are not present during sleep, and are enhanced by emotional stress and voluntary activity
- ❑ perinatal anoxia, birth trauma and kernicterus are common causes
- ❑ treatment
    - often unsatisfactory
    - anticholinergics and botulinum toxin injection, surgery

MYOCLONUS

❑ rapid, shock-like muscle jerks, sufficient to move a joint; often repetitive and sometimes rhythmic
❑ generalized myoclonus
- widespread distribution
- physiologic: occurring during falling asleep or awakening (nocturnal myoclonus); and hiccups
- essential: benign condition, sometimes inherited, occurring in absence of other neurological symptoms
- epileptic: seizure disorder predominates
- symptomatic: part of another disorder - degenerative (Wilson's, Huntington's, Alzheimer's); infectious (CJD disease, AIDS dementia complex, SSPE); metabolic (hepatic and renal failure)

❑ segmental myoclonus
- restricted to particular part of body
- arise from lesions affecting cerebral cortex, brainstem or spinal cord

❑ treatment
- clonazepam may suppress myoclonic movements
- treat underlying condition (e.g. valproate)

TICS

❑ brief, rapid, stereotyped and irresistable actions, often resembling fragments of normal behaviour
❑ worsen with stress, diminish during voluntary activity or mental concentration, and disappear during sleep
❑ most frequent forms: blinking, sniffing, throat clearing, hitching the shoulder, or throwing the head to the side or backwards
❑ simple tics (e.g. eye blinking)
- begin in childhood as nervous mannerisms and disappear spontaneously

❑ Gilles de la Tourette Syndrome
- multiple motor tics
- vocal tics: sniffing, snorting, involuntary vocalizations and the compulsive utterance of obscenities (coprolalia - very rare)
- may be associated with obsessive compulsive disorder, attention deficit hyperactivity disorder, or a mood disorder
- often familial clustering, M > F

❑ treatment
- simple tics may respond to benzodiazepines
- haloperidol and pimozide are traditional treatments
- usually do not treat unless marked tic or disabling

CRANIAL NERVES

CRANIAL NERVE I (OLFACTORY)

Function

❑ special sensory - smell

Clinical Assessment

❑ must test both nostrils separately with non-irritating stimuli (e.g. coffee, vanilla, peppermint)
❑ irritating stimuli (e.g. ammonia) irritate free nerve endings (therefore if person does not recognize it than consider deficit may not be organic)

Anosmia

❑ absence of the sense of smell
❑ characteristics
- usually associated with a loss of taste sense (ageusia); if taste is intact, consider malingering
- usually not recognized by patient if it is unilateral

❑ classification
- nasal: odors do not reach olfactory receptors because of physical obstruction
  - heavy smoking, chronic rhinitis, sinusitis
- olfactory neuroepithelial: destruction of receptors or their axon filaments
  - influenza, herpes simplex, hepatitis virus, atrophic rhinitis (leprosy), esthesioneuroepithelioma (rare)
- central: olfactory pathway lesions
  - congenital: Kallman syndrome (anosmia and hypogonadotropic hypogonadism), albinism
  - head injury, cranial surgery, SAH, chronic meningeal inflammation
  - meningioma, aneurysm
  - Parkinson's disease

CRANIAL NERVE II (OPTIC)

Function
❑ special sensory - vision

Clinical Assessment
❑ test each eye individually for:
- visual acuity i.e. Snellen chart, count fingers, detect hand movements or changes from light to dark
- visual fields by confrontation (finger counting) or red test object because may identify subtle defects

❑ inspect for symmetry, contour
❑ test pupillary responses to light and accommodation
❑ perform fundoscopy, noting disc margins, cup to disc ratio, disc pallor (see Neuro-Ophthalmology section)

CRANIAL NERVE III (OCULOMOTOR)

Function
❑ somatic motor
- control of eye movement via extraocular muscles
  - superior, inferior and medial rectus muscles
  - inferior oblique muscle
- control of elevation of upper eyelid
  - levator palpebrae superioris muscle

❑ visceral motor
- control of pupillary constriction
  - sphincter pupillae muscle
- control of lens accommodation
  - ciliary muscle

Clinical Assessment
❑ test extraocular movements in the six cardinal directions of gaze and convergence
❑ test pupillary responses to light and accommodation

Oculomotor (III) Nerve Palsy
❑ clinical features
- ptosis, eye is "down and out" (depressed and abducted), divergent squint, pupil dilated
- pupillary constrictor fibers are on periphery of nerve
  - external compression of the oculomotor nerve results in pupil dilation with subsequent progression to extraocular muscle paresis
  - vascular infarction results in extraocular muscle paresis with sparing of the pupil

❑ common lesions
- midbrain (infarction, hemorrhage): may/may not affect pupil, may be bilateral with pyramidal signs contralaterally
- PCA aneurysm: pupil involved early, headache over affected eye
- cavernous sinus (internal carotid aneurysm, meningioma, sinus thrombosis): CN IV, V, and V, also travel in the cavernous sinus, pain and proptosis may occur
- ischemic (DM, temporal arteritis, HTN, atherosclerosis)
  - pupil often spared

Clinical Pearl
❑ **Medical Pupil: A pupil-sparing CN III palsy usually has a medical etiology e.g. vasculitis, ischemia etc.**
❑ **Surgical Pupil: Pupillary involvement usually indicates nerve compression e.g. tumour, aneurysm etc.**

CRANIAL NERVE IV (TROCHLEAR)

Function
❑ somatic motor
- control of superior oblique muscle which mainly intorts and also depresses and adducts the eye

Clinical Assessment
❑ test extraocular movements in the six cardinal directions of gaze

Trochlear (IV) Nerve Palsy
❑ clinical features
- diplopia, especially on downward and inward gaze
- patient may complain of difficulty going down stairs or reading
- patient may hold head tilted to side opposite of palsy to minimize diplopia (Bielschowski head tilt test)

❑ common lesions
- trauma
- ischemic (DM, HTN): most common
- cavernous sinus (carotid aneurysm, thrombosis)
  - CN III and VI usually involved as well
- orbital fissure (tumour, granuloma)
  - retro-orbital pain; CN III, IV and VI may also be involved
- at risk during neurosurgical procedures in the midbrain because of long intracranial course
- only CN that exits posteriorly – it is completely crossed

CRANIAL NERVE V (TRIGEMINAL)

Function

❑ general sensory (V_1 - ophthalmic, V_2 - maxillary, V_3 - mandibular)
- face, scalp to top of head, conjunctiva
- mucous membranes of nasal and oral cavities
- anterior 2/3 of tongue (not taste)
- jaw proprioception
- part of tympanic membrane
- meninges of anterior and middle cranial fossae

❑ somatic motor (V_3 - mandibular)
- muscles of mastication
  - masseter, temporalis, pterygoids
- tensor tympani, tensor veli palatini, mylohyoid, anterior belly of digastric

Clinical Assessment

❑ corneal reflex (V_1 sensory and VII motor)
❑ jaw jerk (V_3 sensory and motor)
❑ sensation on face, forehead
- sensory loss in V_1, V_2 or V_3 distribution
  - root or peripheral nerve lesion
- sensory loss in "onion skin" distribution
  - brainstem lesion

❑ motor – inspect and palpate temporal and masseter muscles while patient clenches teeth

Trigeminal Nerve Lesions

❑ common lesions
- pons (vascular, neoplastic, demyelinating, syringobulbia)
- petrous apex (petrositis)
- orbital fissure, orbit, cavernous sinus (II, III, IV, VI also affected)
- skull base (nasopharyngeal or metastatic carcinoma, trauma)
- cerebellopontine angle
  - +/– VII, VIII
  - acoustic neurilemmoma, trigeminal neurilemmoma, subacute or chronic meningitis
- other causes (DM, SLE)
- herpes zoster
  - usually affects ophthalmic division (V1)
  - tip of nose involvement —> watch out for eye involvement

Trigeminal Neuralgia (Tic Douloureux)

❑ excruciating paroxysmal shooting pains in cheeks, lips, gums
❑ history
- characterized by: severe, sharp, short, stabbing, unilateral shocks in a series - usually in V_3 distribution +/– V_2, V_1
- pain typically lasts only a few seconds to minutes, and may be so intense that the patient winces (hence the term tic)
- may be brought on by triggers: touching face, eating, talking, cold winds
- lasts for days/weeks followed by remission of weeks/months
- F > M; usually middle-aged and elderly

❑ physical examination is normal
❑ diagnosis
- clinical diagnosis (make sure no sensory loss over CN V)
- sensory loss in trigeminal distribution suggests mass lesion
  - must do MRI to rule out mass lesion
- beware the young patient with tic Douloureux (demyelination, tumour)

❑ etiology
- redundant or tortuous blood vessel in the posterior fossa, irritating the origin of the trigeminal nerve
- demyelination at root entry zone of trigeminal nerve
- tumours of cerebellopontine angle (rare)

❑ treatment
- medical
  - carbamazepine (which helps confirm diagnosis)
  - clonazepam, phenytoin, gabapentin and baclofen may also be beneficial
- surgical (all methods are 80% effective, for ~ 5 years)
  - microvascular decompression of redundant blood vessel at origin of trigeminal nerve
  - percutaneous thermocoagulation
  - injection of glycerol/phenol into trigeminal ganglion

CRANIAL NERVE VI (ABDUCENS)

Function
- ❑ somatic motor
  - control of lateral rectus muscle which abducts the eye

Clinical Assessment
- ❑ test extraocular movements in the six cardinal directions of gaze

Abducens Nerve Palsy
- ❑ clinical features
  - inability to abduct the eye on the affected side
  - patient complains of horizontal diplopia, which is worse on lateral gaze to the affected side
- ❑ common lesions
  - pons (infarction, hemorrhage, demyelination)
    - may be associated with facial weakness and contralateral pyramidal signs
  - tentorial orifice (compression, meningioma)
    - may be a false localizing sign in increased ICP
  - cavernous sinus (carotid aneurysm, thrombosis)
  - vascular - may be secondary to DM, HTN, or temporal arteritis

Clinical Pearl
- ❑ **CN VI has the longest intracranial course and is thus vulnerable to increased ICP, creating a false localizing sign.**

CRANIAL NERVE VII (FACIAL)

Function
- ❑ branchial motor
  - muscles of facial expression
    - buccinator, platysma, orbicularis oculi and oris, frontalis, occipitalis
  - stapedius muscle, stylohyoid, posterior belly of digastric
- ❑ visceral motor
  - control of the lacrimal, submandibular, sublingual glands
- ❑ general sensory
  - small supply to ear, tympanic membrane
- ❑ special sensory
  - taste from anterior 2/3 of the tongue

Clinical Assessment
- ❑ inspect the face for asymmetry in the muscles of facial expression
- ❑ look at nasolabial folds
- ❑ test power of muscles of facial expression
- ❑ ask patient to raise eyebrows, frown, close eyes tightly, show teeth, smile, puff out cheeks

Facial Palsy
- ❑ LMN lesion
  - the entire face on ipsilateral side is weak
  - both voluntary and involuntary movements are affected
- ❑ UMN lesion
  - weakness of contralateral lower face; forehead is spared
  - voluntary control of facial expression is lost but involuntary emotional movements are spared
- ❑ look for associated brainstem or cortical symptoms and signs to help localize lesion
- ❑ pathologic differential diagnosis
  - idiopathic = Bell's palsy (see below)
  - trauma
  - infection (otitis media, mastoiditis, EBV, HZV, Lyme disease, HIV)
  - other
    - sarcoidosis, Group B *Streptococcus*, DM mononeuropathy, parotid gland pathology

Bell's Palsy (see Otolaryngology Chapter) **(see Colour Atlas OT9)**
- ❑ an idiopathic benign LMN facial nerve palsy
- ❑ acute onset of unilateral (rarely bilateral) LMN facial weakness
- ❑ diagnosis of exclusion
  - must rule out symptoms and signs of brainstem and hemispheric dysfunction and systemic disease
- ❑ etiology
  - unknown; thought to be due to swelling and inflammation of facial nerve in its canal within the temporal bone

- ❑ associated features which may be present
  - pain behind ipsilateral ear (often precedes weakness)
  - prodromal viral URTI
  - hyperacusis
  - decreased taste sensation
  - abnormal tearing (decreased lacrimation)
  - facial numbness/altered sensation
- ❑ treatment
  - patient education and reassurance
  - eye protection (because of inability to close eye)
    - artificial tears, lubricating ointment
    - patch eye closed at night
  - steroids: controversial (weigh risks and benefits)
    - typical regime is prednisone 40-60 mg tapered over 7-10 days
- ❑ prognosis
  - spontaneous recovery in 85% over weeks to months
  - poor outcome
    - if complete paralysis lasts 2-3 weeks
    - if elderly or HTN
    - if symptoms of hyperacusis, abnormal tearing
  - synkinesis – due to aberrant regeneration; fibers cross – get tearing while eating, etc.

Clinical Pearl
- ❑ **An isolated cranial nerve defect, especially of CN VI and VII, is most likely the result of a peripheral, and not brainstem, lesion.**

CRANIAL NERVE VIII (VESTIBULOCOCHLEAR) (see Otolaryngology Chapter)

Function
- ❑ special sensory
  - auditory information from cochlea
  - balance information from semicircular canals

Clinical Assessment
- ❑ test hearing
- ❑ if hearing loss is present, one must distinguish
  - conductive causes (external/middle ear disease) from sensorineural causes (damage to cochlea/VIII nerve)
  - test for lateralization (Weber test with 512 Hz tuning fork)
  - compare air and bone conduction (Rinné test), should conduct better in air than bone unless obstructed for air conduction
- ❑ more sophisticated tests (audiometry) usually required for formal assessment
- ❑ vestibular dysfunction is often manifested by nystagmus

CRANIAL NERVE IX (GLOSSOPHARYNGEAL)

Function
- ❑ branchial motor
  - stylopharyngeus muscle, which elevates soft palate
- ❑ visceral motor
  - stimulates secretion by parotid gland
- ❑ visceral sensory
  - input from carotid body and carotid sinus
- ❑ general sensory
  - posterior 1/3 of tongue, external ear, tympanic membrane
- ❑ special sensory
  - taste from posterior 1/3 of tongue

Clinical Assessment
- ❑ gag reflex (afferent on CN IX and X, efferent on CN X)
- ❑ open mouth widely and say "ah…ah…": symmetric elevation of soft palate demonstrates normal function of CN IX, X, uvula should remain midline

Glossopharyngeal Neuralgia
- ❑ brief, sharp, attacks of pain affecting posterior pharynx
- ❑ pain radiates toward ear and triggered by swallowing
- ❑ treatment
  - carbamazepine (Tegretol)
  - surgical lesion of CN IX

CRANIAL NERVE X (VAGUS)

Function
- ❑ branchial motor
  - striated muscles of the pharynx, tongue and larynx
- ❑ visceral motor
  - smooth muscle and glands of the pharynx, larynx and thoracic and abdominal viscera
- ❑ visceral sensory
  - input from larynx, trachea, esophagus, thoracic and abdominal viscera, stretch receptors in aortic arch, chemoreceptors in aortic bodies
- ❑ general sensory
  - pharynx, skin at back of ear, external acoustic meatus, part of tympanic membrane

Clinical Assessment
- ❑ listen to voice
  - hoarseness suggests vocal cord paresis
  - nasal quality suggests paralysis of the palate
- ❑ ask patient to say "ah" and note symmetry of palatal movement
  - watch for deviation of uvula as it is pulled away from the side of the lesion by the intact muscles of the opposite side
- ❑ test gag reflex (afferent CN IX and X, efferent CN X)
- ❑ disorders of the Vagus result in
  - palatal weakness: affects swallowing
  - pharyngeal weakness: affects swallowing
  - laryngeal weakness: affects speech

Clinical Pearl
- ❑ **Testing for the presence of a gag reflex is not sufficient for screening for the presence of dysphagia and assessing the patient's risk for aspiration. The correct screening test is to observe the patient drinking water from a cup. Any coughing, choking, or "wetness" of the voice implies that it is not safe for the patient to eat or drink.**

CRANIAL NERVE XI (ACCESSORY)

Function
- ❑ branchial motor
  - sternomastoid and trapezius muscles

Clinical Assessment
- ❑ test strength of trapezii as patient shrugs shoulders
- ❑ ask patient to turn head to each side against your hand, and observe strength of contraction of the opposite sternomastoid

Accessory Nerve Lesions
- ❑ this nerve is vulnerable to damage during neck surgery, which results in shoulder drop on the affected side, and weakness when turning the head to the opposite side

CRANIAL NERVE XII (HYPOGLOSSAL)

Function
- ❑ somatic motor
  - supplies intrinsic and extrinsic muscles of tongue, except palatoglossus (CN X)

Clinical Assessment
- ❑ listen to patient's speech/articulation
  - dysarthria may be caused by lesions of CN V, VII, X or XII
- ❑ inspect the tongue
  - look for atrophy or fasciculations, indicating an ipsilateral LMN lesion non-functioning side
    - caused by an ipsilateral LMN lesion or a contralateral UMN lesion

Location of Lower (CN IX, X, XI and XII) Cranial Nerve Lesions
- ❑ intracranial/skull base
  - meningiomas, neurofibromas, metastases, osteomyelitis, meningitis
- ❑ brain stem
  - infarction, demyelination, syringobulbia, poliomyelitis, tumours (astrocytoma)
- ❑ neck
  - trauma, surgery, tumours

Clinical Pearl
- ❑ **Clinical symptoms or signs suggesting lesions of both cranial nerve lesions and long tract signs imply a brainstem localization disease.**

VISUAL FIELD DEFECTS

❑ lesions anywhere in the visual system, from the optic nerve to the occipital cortex will produce characteristic visual field defects (see Figure 14)

Definitions

❑ scotoma = an area of absent or diminished vision within an otherwise intact visual field
❑ hemianopia = loss of half of the visual field
❑ homonymous = loss of either the right or left half of the visual field in both eyes
❑ bitemporal = loss of both temporal visual fields
❑ quadrantanopia = loss of one quarter of the visual field

Table 10. Definition of Different of Eye Movement

Eye Movement	Definition	Site of Control
1. Saccadic	Rapid movement from one point of fixation to another	Frontal lobe
2. Pursuit	Slow eye movement to maintain fixation on a moving object	Occipital lobe
3. Vestibular-positional	Eye movements which compensate for head movement in order to maintain fixation	Cerebellar vestibular nuclei
4. Convergence	Maintenance of fixation as object is brought closer to face	Midbrain

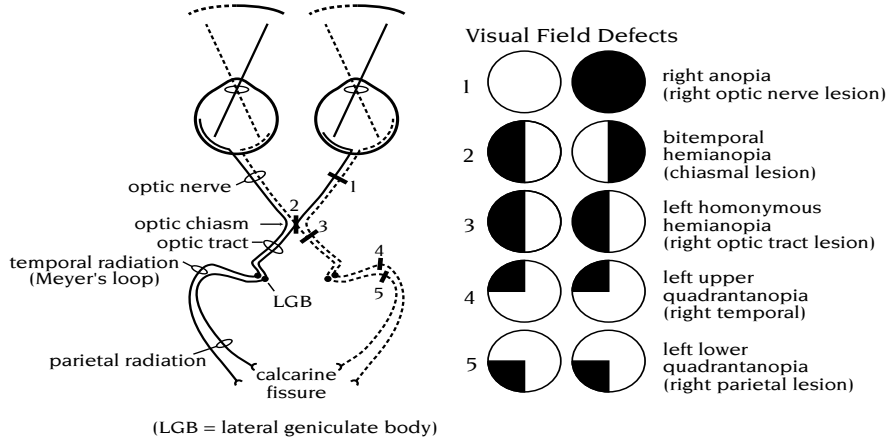


Figure 14. Visual Field Defects with Lesions Along the Visual Pathway

Illustration by Cecil Hahn

DISORDERS OF LATERAL GAZE

❑ voluntary eye movements are triggered in the frontal eye fields, located anterior to the precentral gyrus, bilaterally in frontal lobe
❑ each frontal eye field controls voluntary saccades to the contralateral side via connections to the contralateral paramedian pontine reticular formation (PPRF)
❑ a seizure involving a frontal eye field will cause eye deviation towards the opposite side
❑ a unilateral lesion in one frontal eye field prevents voluntary saccades to the opposite side, eyes deviate toward the side of the lesion (may also occur with large parietal lobe lesion)
  • can be overcome with doll's eye maneuver
❑ in contrast, a unilateral lesion in the pons prevents voluntary saccades to the ipsilateral side, eyes deviate away from the lesion (because the corticopontine pathways cross)
  • cannot be overcome with doll's eye maneuver

❑ Vertical gaze palsy = lesions in upper brainstem
❑ common causes of lateral and vertical gaze palsies are brainstem infracts, MS, tumours

Internuclear Opthalmoplegia (INO)
- ❑ results from a lesion in medial longitudinal fasciculus (MLF) which causes a disconjugate gaze
  - MLF links CN VI in pons with CN III in midbrain
- ❑ adduction of contralateral eye is impaired but there is full excursion of abducting eye + nystagmus
  - cannot be overcome by caloric testing
  - adducts normally with convergence
- ❑ frequently bilateral
- ❑ up beating nystagmus on up gaze often present
- ❑ usually indicates MS; but vascular disease, neoplasia, or Wernicke's encephalopathy may be etiological factor

One and a Half Syndrome
- ❑ lesion in MLF and PPRF
- ❑ have an INO with inability to gaze toward side of lesion
- ❑ ipsilateral eye immobile in horizontal plane and movement of contralateral eye restricted to abduction

OPTIC DISC EDEMA

Table 11. Causes of Optic Disc Edema

	Optic Neuritis	Papilledema	Ischemic Neuropathy
Vision	• Rapidly progressive loss • Central vision loss • Acuity affected • Decreased colour vision	• Usually no loss of vision • Possible transient obscuration • Variable acuity • Normal colour vision	• Acute field defects (commonly altitudinal) • Decreased colour vision
Other Symptoms	• Tender globe, painful on motion • Arteritic (see Rheumatology Chapter) • Bilateral rarely in adults • May alternate in MS • Frequent in children	• Headache, nausea, vomiting • Focal neurological deficits	• Monarteritic usually no other symptoms • Typically unilateral
Pupil	• No anisocoria • RAPD present	• No anisocoria • No RAPD	• No anisocoria • RAPD present
Fundus	• Retrobulbar - normal in 2/3, 1/3 have unilateral disk swelling (physician & patient see nothing) • Papillitis - variable • Disc swelling, few flame hemorrhages	• Variable disc swelling and hemorrhages • Absent venous pulsations	• Pale segmental disc edema with flame hemorrhages
Treatment	• IV methylprednisolone (shortens attacks) • Oral prednisone may • Increaed relapse rate • Section for treatment if arteritic • Associated with MS in 74% of • females and 34% of males	• Treat specific cause of increased ICP	• Consider ASA for non-arteritic ischemic neuropathy

Other Causes of Disc Edema
- ❑ central retinal vein occlusion
- ❑ systemic illness
- ❑ HTN, vasculitis, hypercapnia
- ❑ toxic/metabolic/nutritional deficiency
- ❑ infiltration
  - neoplastic: leukemia, lymphoma, glioma
  - non-neoplastic: sarcoidosis
- ❑ pseudotumour cerebri
  - idiopathic signs and symptoms of increased ICP, with a normal CT
  - usually in obese young women
- ❑ compressive
  - meningioma, hemangioma, thyroid ophthalmopathy

TRANSIENT MONOCULAR BLINDNESS

(Amaurosis Fugax/Retinal TIA)
- ❑ history: sudden, transient, painless loss of vision in one eye
- ❑ central retinal artery occlusion: complete loss of vision
- ❑ branch retinal artery occlusion: altitudinal loss of vision

- ❑ patients with TIAs are at increased risk for stroke, CAD, permanent retinal infarction
- ❑ diagnosis: investigations look at heart (ECG, holter monitor), carotid arteries (doppler, angiography), blood (CBC, PT, PTT, ANA) and hypercoagulability work up
- ❑ treatment: see Stroke section

PUPILLARY SIGNS (see Table 12)

Relative Afferent Pupillary Defect (RAPD, Marcus Gunn Pupil) (see Ophthalmology Chapter)
- ❑ a failure of direct pupillary responses to light
- ❑ a sign of damage to the afferent portion of the pupillary reflex arc - (CNII)
  - optic nerve (optic neuritis, ischemia, compression)
  - optic chiasm (severe compression, e.g. pituitary tumour)
  - optic tract to pretectal nucleus
- ❑ clinical assessment: swinging light test
  - swing light from one eye to the other
  - when normal side is illuminated, both pupils constrict
  - when damaged side is illuminated, both pupils paradoxically dilate

Clinical Pearl
- ❑ **Lesions which result in a RAPD must be prechiasmal, and almost always involve the optic nerve.**

Horner's Syndrome
- ❑ a sympathetic defect causing partial ptosis, miosis, and anhydrosis and apparent enopthalmos
- ❑ may occur anywhere along the sympathetic pathway on the affected side
  - 1st order neuron (preganglionic): hypothalamus, medulla (brainstem stroke), spinal tumour, MS, intracranial tumours, syringomyelia
  - 2nd order neuron (preganglionic): apical lung cancer (Pancoast's tumour), paravertebral mass, carotid artery dissection
  - 3rd order neuron (postganglionic): cluster headache, migraine, cavernous sinus mass, trauma (including surgical)
- ❑ clinical confirmation with cocaine test: cocaine does not dilate a miotic Horner's pupil
- ❑ no test to differentiate central from preganglionic lesion
- ❑ paredrine (hydroxyamphetamine) will not dilate a post-ganglionic Horner's pupil
- ❑ most preganglionic Horner's are serious, whereas most post-ganglionic Horner's are benign

Table 12. Summary of Pupillary Signs

	Site of Lesion	Features	Light and Accomodation	Anisocoria	Mydriatics/ Miotics	Special Tests
Simple Anisocoria	No associated disease	Round, regular; 1 mm difference	Both brisk		Dilates/constricts	
RAPD (Marcus Gunn)	Unilateral optic nerve or retina	Round, regular, "swinging light test" positive	Poor to light Better to near	Not present	Dilates/constricts	
Fight-near Dissociation	Midbrain/ciliary ganglion	Mid-dilated; may be oval; bilateral if midbrain	Poor to light; better to near		Dilates/constricts	
Argyll-Robertson (syphilis)	Midbrain	Miotic, irregular; usually bilateral	Poor to light; better to near		Dilates/constricts	
Atropinized	Iris sphincter	Very dilated, round; uni- or bilateral	Fixed at 7-8 mm	Greater in light	Does not constrict (one side only)	Pilocarpine will not constrict
oculomotor palsy	CN III	Dilated, round acutely	+/– fixed (acutely) at 7-9 mm	Greater in light	Dilates/ constricts	Pilocarpine will constrict
Adie's tonic	Ciliary ganglion, globe	Vermiform motion; usually larger in bright light	Poor to light; tonic to near; tonic redilation	Greater in light	Dilates/ constricts	Dilute (0.1%) pilocarpine constricts
Horner's syndrome	Sympathetic system	Small, round; unilateral	Both brisk	Greater in dark	Dilates (see special tests)/ constricts	Cocaine: poor dilation; paredrine: no dilation if postganglionic, dilation if central or preganglionic

NYSTAGMUS (see Otolaryngology Chapter)

Definition
- ❑ a rhythmic movement of eyes composed of a quick and a slow component and may be rotatory, vertical or horizontal
- ❑ direction of nystagmus defined by direction of quick component

Classification
- ❑ pendular
  - movements of equal velocity in two directions
  - onset usually in infancy (congenital and acquired) as a result of some visual impairment but can occasionally be a symptom of cerebellar or brainstem disease
- ❑ congenital nystagmus
  - poor fixation
  - rapid, pendular, jerk on lateral gaze
  - often with head tremor
  - may be associated with congenital cataract, congenital macular defect, albinism
  - persistent throughout life
- ❑ jerk
  - two components: a fast phase and a slow phase
  - nystagmus is named according to direction of the fast phase
  - benign jerk nystagmus, at extremes of lateral gaze is a common finding without pathological significance
- ❑ two nystagmus syndromes are most common
  - gaze evoked
    - occurs with gaze toward a direction
    - often adverse effect of sedative or anti-convulsant
    - can also result from cerebellar or central vestibular dysfunction
  - vestibular
    - increases with gaze toward the fast phase
    - usually associated with vertigo when lesion is in peripheral vestibular apparatus

Labyrinthine Disease
- ❑ due to a left-right imbalance of stimulation from vestibular system
- ❑ causes a slow drift of eyes towards side with damage/decreased stimulus (thus nystagmus, i.e. fast phase is away from lesion)
- ❑ physiological
  - rotational acceleration with nystagmus pointing to direction of turning, i.e. slow phase points to visual image
  - cold/hot H_2O instilled into ear decreased/increased relative stimulus from CN VIII, resulting in nystagmus to the opposite/same side
  - for caloric testing, remember "**COWS**"
  - **C**old water results in nystagmus to **O**pposite side
  - **W**arm water results in nystagmus to **S**ame side
- ❑ pathological
  - characteristically unidirectional horizontal (toward normal side) or horizontal rotary
  - nystagmus towards normal side; may have torsional component
  - vertigo present; tinnitus and sensorineural deafness common in Meniere's, vestibular neuritis, vascular disease
  - in benign positional vertigo, elicit by Dix-Hallpike maneuver (see OT7) which fatigues with repetition

Cerebellar Disease
- ❑ horizontal jerk nystagmus towards the side of the cerebellar lesion (opposite to labyrinthine nystagmus)

Brainstem Disease
- ❑ vertical nystagmus, jerk nystagmus with fast phase in direction of gaze; vertigo uncommon
- ❑ other signs of brainstem involvement present (cranial nerve abnormalities)
- ❑ pons-midbrain, medial longitudinal fasiculus (MLF)
  - "ataxic nystagmus"/"internuclear ophthalmoplegia"
- ❑ note: acquired pendular nystagmus signifies MS
- ❑ lower medulla
  - down beating nystagmus on forward or lateral gaze can be seen in lesions around the cervicomedullary junction (e.g. Chiari malformation, cerebellar degeneration)
  - up beating nystagmus in primary gaze can be seen in lesions in the medulla (e.g. MS, tumour, Wernicke's)

VERTIGO

❑ defined as an illusion of movement of self or surroundings (usually rotatory/spinning) often associated with impulsion (sensation of body pulled in space) or oscillopsia (visual illusion of moving back and forth) as well as nausea and vomiting and gait ataxia ; vertigo must be distinguished from other causes of dizziness, such as presyncope, gait abnormalities and psychogenic phenomena

Causes related to anatomical structures
Cerebellum —> Brain Stem —> Central Pontine Angle—> CN VIII —> Vestibular labyrinth
<—— central ——————————————————> <—— peripheral————————>
(common) (common)

Assessment of Vertigo (see Cardiology and Otolaryngology Chapter)

❑ history
- distinguish from presyncope (feeling lightheaded and faint) (see Cardiology Chapter)
- nature of vertigo: duration? positional? recurrent?
- auditory symptoms (hearing loss and tinnitus)?
- neurological symptoms?
- ototoxic drugs? (e.g. aminoglycosides)

❑ clinical examination
- otoscopy, tuning fork tests for hearing
- nystagmus, cranial nerves - especially CN V (including corneal reflex)
- long tract signs: cerebellar, pyramidal, sensory
- fundoscopy

❑ investigations
- audiometry, caloric testing
- evoked potentials, ENG, CT/MRI
- VDRL

Table 13. Peripheral vs. Central Vertigo

Feature	Peripheral	Central
Nystagmus	Horizontal, sometimes torsional, ↑ when looking away from lesion Direction does not change when direction of gaze changes	Vertical or rotatory, ↑ when looking toward side of lesion, persistent May change when direction of gaze changes
Caloric Test	Abnormal on side of lesion	May be normal
Brainstem or Cranial nerve signs	Absent	Often present
Hearing loss, Tinnitus	Often present	Absent
Nausea and Vomiting	Usually present	Usually absent
Vertigo	Severe, often rotational, always present	Usually mild, often absent
Falling	Often falls to the side opposite nystagmus (fast phase) i.e. toward lesion	Often falls toward the side of lesion but may be variable direction
Visual fixation	Inhibits nystagmus	No change in nystagmus

Table 14. Major Causes of Vertigo

Peripheral	Central
*Benign positional vertigo Trauma Ménière's disease Vestibular neuronitis Ear infections Fistulae Drug toxicity Acoustic neuroma Vascular loop	Brainstem or cerebellar Vascular disease: vertebrobasilar system ischemia and infarction: Tumour TIA MS Migraine

* BPV is the most common cause of vertigo in office practice

❑ **Purely vertical or purely torsional nystagmus are almost always due to a central cause.**

GAIT DISTURBANCES

❑ observe for posture, arm swing, length of stride, width of stance, symmetry and balance

Clinical Approach
❑ length of stride short
- Parkinson's (posture is stooped with no arm swing)
- Marche à petit pas (Parkinson's/"Parkinson's plus" multi-infarct state)

❑ width of stance (length of stride normal)
- crossing over, think spastic paresis
- wide based: cerebellar ataxia,
- wide with high stepping, slapping feet: sensory ataxia

❑ look at knees (stride and width normal)
- high knees: foot drop/ LMN

❑ look at pelvis and shoulders (stride, width, and knees normal)
- waddling gait (i.e. proximal muscle myopathy)

❑ look at whole movements
- disjointed movements: apraxic gait (cortical lesion from NPH, CVD)
- bizarre, elaborate and inconsistent: functional gait

❑ look for asymmetry
- think of pain, bony deformity, or weakness

Category of Disorders	Clinical Features of Gait
Hemiparesis/focal brain injury	Spastic extended leg and flexed arm, circumduction of affected foot
Paraparesis/spinal cord injury	Toe-walking or scissoring gait, bilateral circumduction
Sensory ataxia/peripheral or central deafferentation	Wide-based stance and gait, high steppage, positive Romberg's sign
Cerebellar disease	Wide-based gait, ataxia, titubating posture
Parkinsonism	Stooped posture, festination/shuffling gait, difficulty initiating and terminating steps, turns "en bloc", many stepped turn
Movement disorders (chorea, athetosis, dystonia)	Lurching gait, may have adventitial movements
LMN disease	High steppage, distal weakness
Myopathy	Proximal weakness with difficulty arising from chair or climbing stairs
Apraxia/hydrocephalus or frontal lobe injury	Magnetic gait (feet barely off the ground) and shuffling, difficulty initiating steps
Cerebral palsy/congenital or perinatal brain injury	Scissoring gait, spastic extended legs and flexed arms, adventitial movements
Functional gait	Bizarre, elaborate, inconsistent with rest of exam

CEREBELLAR DISORDERS

❑ disorders of the cerebellum, or its inflow or outflow tracts, produce deficits in the rate, range, and force of movement
❑ signs are present ipsilateral to the side of the cerebellar lesion
❑ cerebellar lesions do not produce motor weakness or sensory loss

FUNCTIONAL ANATOMY OF THE CEREBELLUM
❑ paleocerebellum (superior and inferior vermis)
- coordinates trunk and leg movement

❑ neocerebellum (anterior and posterior lobes)
- coordinates planning of ballistic and finely coordinated limb movements, mostly upper limb

❑ archicerebellum (flocculonodular lobe)
- maintenance of balance and eye movements during stance and gait

SYMPTOMS AND SIGNS OF CEREBELLAR DISEASE
❑ ataxia
- a disturbance in the smooth performance of voluntary motor acts
- can affect gait, trunk, limbs, speech, eye movements
- examples
  - dysmetria (inability to control range of movement)
  - dysdiadochokinesia (inability to perform rapid alternating movements)

❑ intention tremor
❑ muscle hypotonia
- impaired check/rebound and pendular reflexes

❑ dysarthria (e.g. scanning speech, telegraphic)
❑ nystagmus
- fast component of beat is toward side of lesion

- ❑ consider other disorders
  - sensory ataxia (loss of joint position sense)
  - pyramidal and extrapyramidal disorders which interfere with controlled movement
- ❑ symptoms improve gradually with time if underlying disease does not progress

Clinical Pearl
❑ **Clumsiness, incoordination, and tremor of the limbs, associated with brainstem symptoms are typical of cerebellar disorders.**

ACQUIRED CEREBELLAR DISEASES

Alcoholic Cerebellar Degeneration
- ❑ midline (superior vermis) atrophy
  - truncal and gait ataxia, broad-based stance
  - less frequent are arm ataxia, nystagmus, dysarthria, hypotonic and truncal instability
- ❑ progressive, but partly reversible with abstinence
- ❑ presentation may be acute, subacute or chronic
- ❑ with or without previous Wernicke's encephalopathy
  - confusion, ataxia, opthalmoplegia (CN VI nerve)

Paraneoplastic Cerebellar Degeneration
- ❑ diffuse cerebellar atrophy
- ❑ rapidly progressive
- ❑ gait and limb ataxia are prominent, often with dysarthria and myoclonus
- ❑ associated with particular neoplasms
  - small cell carcinoma of lung, breast, ovary, and lymphoma

HEREDITARY ATAXIAS

Friedrich's Ataxia
- ❑ AR (chromosome 9)
- ❑ age of onset between 5 and 20 years
- ❑ progressive gait ataxia, followed by limb ataxia within 2 years
- ❑ leg weakness, knee and ankle areflexia, positive Babinski
- ❑ musculoskeletal abnormalities (kyphoscoliosis, pes cavus)
- ❑ impaired joint position sense and vibration sense in legs
- ❑ cerebellar dysarthria
- ❑ degeneration of spinocerebellar, pyramidal and large sensory fibers
- ❑ death from cardiac (cardiomyopathy) or pulmonary (kyphoscoliosis) causes within 10-20 years of onset

Ataxia Telangiectasia
- ❑ AR (chromosome 11)
- ❑ multisystem disorder characterized by progressive cerebellar ataxia, ocular and cutaneous telangiectasia and immunodeficiency
- ❑ progressive ataxia develops in infancy; telangiectasia develops later

Autosomal Dominant Cerebellar Ataxia (adult onset)
- ❑ type 1 – ataxia, ophthalmoplegia, dementia, spasticity
- ❑ type 2 – ataxia, retinopathy with progressive visual loss
- ❑ type 3 – ataxia alone, age of onset >50 years

DDX OF ATAXIA

Onset	Disease Process
Acute (minutes to hours)	Cerebellar hemorrhage/infarction Trauma Intoxication Migraine
Subacute (hours to days)	Posterior fossa tumour/abscess MS Toxins Hydrocephalus Guillain-Barré syndrome Viral cerebellitis
Chronic (days to weeks)	Alcoholic cerebellar degeneration Paraneoplastic cerebellar syndrome Foramen magnum compression Chronic infection (CJD, rubella, panencephalitis) Hydrocephalus Vitamin E deficiency Hypothyroidism Hereditary ataxia Idiopathic degenerative ataxias
Episodic	Recurrent intoxications MS TIA (if accompanied by other symptoms) Dominant periodic ataxia (in children)

DISEASES OF THE SPINAL CORD

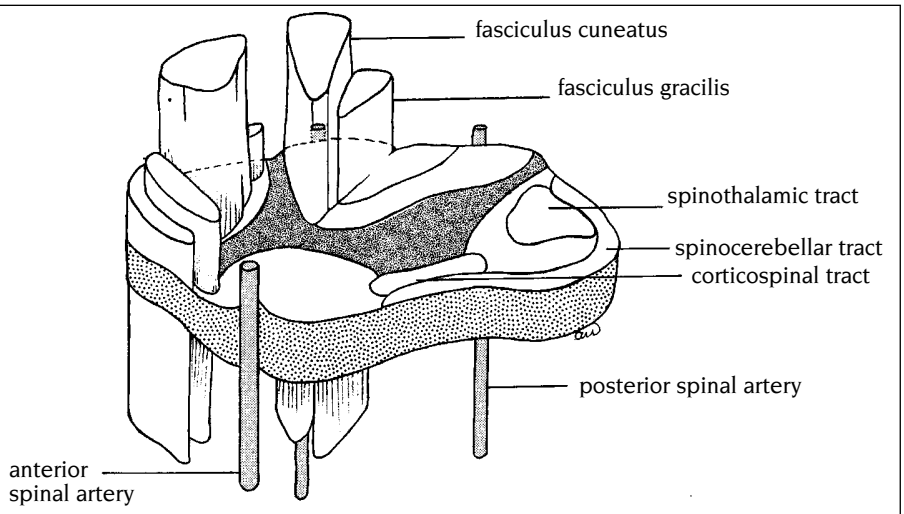


Figure 15. Anatomy of the Spinal Cord

Illustration by Aimée Warrell

CLINICAL FEATURES

- ❑ paraplegia or quadriplegia
- ❑ deficit corresponding to a sensory level
  - T4-nipple, T10-navel, L5-dorsum of foot, S1-lateral foot
- ❑ bladder and bowel incontinence
- ❑ LMN signs at the level of the lesion and UMN signs below the level of the lesion (see Table 15)
- ❑ radicular symptoms (sharp, shooting radicular pain, dermatomal sensory loss)
  - causes
    - extradural: disc, trauma, cervical spondylosis, bone, tumour (metastases), abscess
    - intradural, extramedullary: meningioma, neurofibroma, arachnoid cyst
    - intradural, intramedullary: demyelination, inflammatory (transverse myelitis) tumour, infarct, hemorrhage (AVM), or degeneration (subacute combined degeneration (SACD)), syrinx

Table 15. Comparison of UMN and LMN Lesions

	Upper Motor Neuron (UMN)	Lower Motor Neuron (LMN)
Bulk	Normal (unless disuse)	Muscle wasting
Tone	Increased (spastic)	Decreased
Fasciculations	Absent	Present
Weakness	Pyramidal pattern Upper extremity: extensors weakest Lower extremity: flexors weakest	Specific to lesion i.e. root, nerve
Reflexes	Increased	Decreased —> absent
Plantar Reflex	Extensor	Flexor

Clinical Pearl

❑ **Spinal cord diseases usually cause a triad of: parasthesia at a sensory level (hallmark symptom); bilateral corticospinal (spastic) weakness; bowel and bladder problems.**

SPINAL CORD SYNDROMES (see Neurosurgery Chapter)

Brown-Sequard Syndrome

- ❑ lateral compression of one half of spinal cord (hemisection)
- ❑ ipsilateral LMN signs at level of lesion
- ❑ ipsilateral hemiplegia or monoplegia below lesion & UMN signs
- ❑ ipsilateral loss of vibration and proprioception below lesion
- ❑ contralateral loss of pain and temperature below lesion
- ❑ common causes – tumour, radiation

Central Cord Syndrome
- ❑ common causes are syringomyelia and intrinsic tumours
- ❑ suspended or cape sensory loss over shoulders from cervical lesion most common
- ❑ dissociated sensory loss
  - loss of pain and temperature sensation with spared touch, joint position and vibration
- ❑ atrophy of intrinsic hand muscles (anterior horn cells),

Anterior Spinal Artery Syndrome
- ❑ sudden para/quadriplegia; initial flaccidity and areflexia ("spinal shock"); within days develop UMN signs below lesion
- ❑ preserved vibration and position sense (spared posterior columns)
- ❑ due to occluded anterior spinal artery, usually at thoracic level

Subacute Combined Degeneration of the Spinal Cord
- ❑ corticospinal and posterior columns are affected e.g. vitamin B_{12} deficiency, HIV
- ❑ system degeneration therefore no distinct motor or sensory level

Conus Medullaris (Cauda Equina Syndrome)
- ❑ hypotonic bladder and rectal sphincters
- ❑ pain and loss of sensation in saddle distribution in perineum
- ❑ foot drop, absent ankle jerks
- ❑ causes: cord disc herniation, tumour, inflammatory

Foramen Magnum Syndrome
- ❑ quadriparesis, neck/head pain, hand atrophy +/– cerebellar signs
- ❑ cause: tumours

Transverse Myelitis
- ❑ back pain, rapid onset cord syndrome
- ❑ cause: post-infections, inflammatory, demyelination

Epidural Abscess
- ❑ severe back pain and tenderness, rapidly progressive cord syndrome
- ❑ may not have systemic signs/symptoms of infection
- ❑ surgical emergency!!!

Complete Transection of Cord
- ❑ trauma, tumour
- ❑ loss of all sensation and voluntary motor function below level (UMN)

MOTOR NEURON DISEASES
- ❑ diseases of cortical —> anterior horn motor neurons

Spinal Muscular Atrophy (SMA)
- ❑ disorders beginning in infancy or childhood characterized by skeletal muscle wasting due to progressive degeneration of cells in the anterior horn and medulla
- ❑ acute infantile SMA (Werdnig-Hoffmann disease)
- ❑ floppy baby, survival < 1 year
  - childhood forms
  - Wohlfart-Kugelberg-Welander disease
- ❑ adult forms
  - proximal and distal muscles (may look like myopathy)
  - slowly progressive, good prognosis

Amyotrophic Lateral Sclerosis (ALS)
- ❑ motor neuron disease of unknown etiology characterized by progressive degeneration of corticospinal tracts and anterior horn cells or bulbar efferent neurons
- ❑ 10% familial
- ❑ onset age = 40-60 (very rare < 20)
- ❑ progressive, fatal 2-6 years (50% at 3 years)
- ❑ signs and symptoms
  - no sensory findings
  - fasciculations, muscle cramps
  - segmental, asymmetrical weakness and atrophy
  - upper and lower motor neuron signs (tonic atrophy)
  - bulbar palsy, atrophy and tongue fasciculations
  - dysarthria, dysphagia
  - sparing of bowel and bladder function, and ocular muscles
- ❑ investigations
  - EMG: diffuse denervation, fibrillation with normal nerve conduction
  - Don't miss high spinal cord lesion!
- ❑ treatment
  - Riluzole in bulbar causes prolongs survival
  - supportive treatment

SPINAL ROOT (see Neurosurgery Chapter)

PERIPHERAL NEUROPATHIES

APPROACH TO PERIPHERAL NEUROPATHIES

❑ signs and symptoms
- onset, progression (acute, subacute, chronic)
- determine if motor, sensory, autonomic dysfunction
  - if chronic motor, see muscle atrophy and absent reflexes
  - if sensory, may have paresthesias in addition to sensory loss
  - autonomic dysfunction includes anhydrosis, GI dysmotility, orthostatic hypotension, impotence, bladder/bowel dysfunction, impairment of pupillary responses
- mononeuropathy vs. polyneuropathy
- proximal vs. distal
- upper vs. lower extremities
- fiber size selectivity
  - large: motor weakness, loss of joint position, vibration, and touch/pressure
  - small: pain and temperature loss, autonomic dysfunction
- relationships to systemic illness (DM, RA, EtOH)
- family history, especially with unexplained polyneuropathy from childhood (hereditary); later life, paraneoplastic or paraproteinemic causation is more likely
- pes cavus, thickened nerves in hereditary causes

❑ lab investigations (based on clinical suspicion)

❑ electrodiagnostic studies (NCS, EMG, quantitative sensitivity testing)
- confirm neuropathy and elimination of non-neuropathic disorder
- localization of focal lesion, prediction of pathology

❑ nerve biopsy has limited use
- vasculitides, sarcoid, amyloid, inherited storage disorders

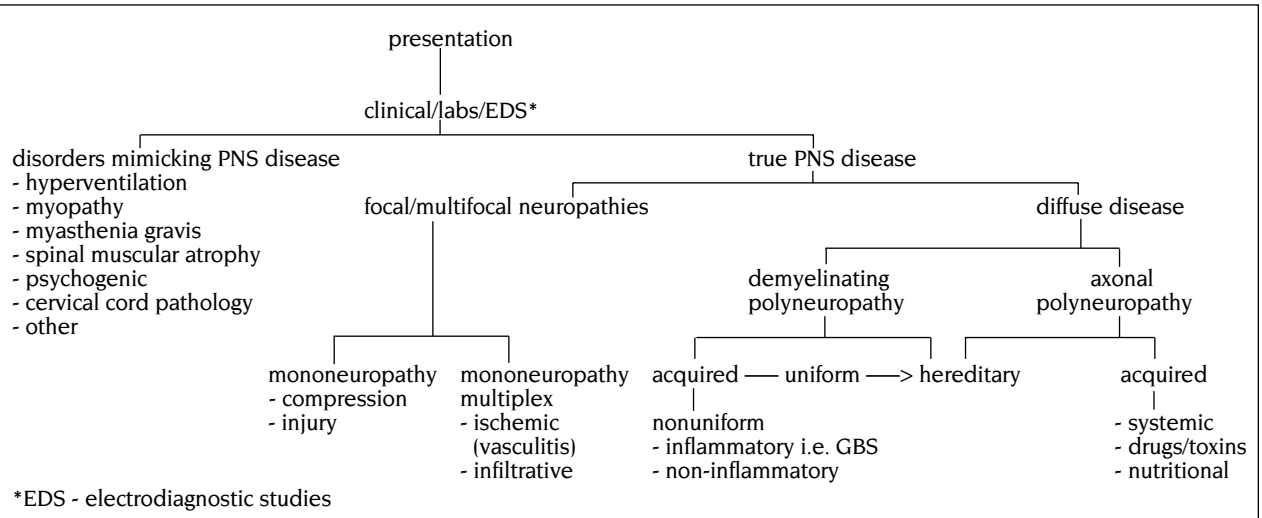


Figure 17. Assessment of Peripheral Neuropathies

Clinical Pearl

❑ **Distal and asymmetric weakness with denervation and sensory changes are characteristic of peripheral neuropathies.**

FOCAL AND MULTIFOCAL NEUROPATHY

Etiology
- ❑ mononeuropathy
  - single motor/sensory neuron
  - most common for focal involvement: injury/entrapment
  - ischemic: DM, vasculitides
  - infiltrative: sarcoid, amyloid, leukemia or lymphoma, leprosy

Nerve Plexopathies
- ❑ brachial (C5-T1)
  - trauma, compression, inflammation, post-radiation
  - Pancoast's tumour: lung cancer compressing T1
  - most common: deltoid, supraspinatus muscles affected
- ❑ lumbosacral (L2-S2)
  - retroperitoneal tumours, hemorrhage, surgical trauma, inflammation, DM

Mononeuropathy Multiplex
- ❑ simultaneous/sequential involvement of individual noncontiguous nerve trunks over days to years that seems random and multifocal
- ❑ may be "patchy" initially but progress to more symmetric picture (pattern of early symptoms important for diagnosis)
- ❑ 1/3 demyelinating disorder: multifocal conduction block variant of chronic inflammatory demyelinating polyneuropathy (CIDP)
- ❑ 1/3 axonal involvement caused by vasculitis (PAN, RA, SLE, MCTD)
- ❑ 1/3 axonal involvement but no diagnosis

Diffuse Polyneuropathies
- ❑ classification
  - onset: acute, subacute, chronic
  - etiology: hereditary vs. acquired (infectious, carcinomatous, DM, inflammatory, vascular)
  - pathology: axonopathies vs. myelinopathies vs. neuropathy
  - fiber type: large vs. small, motor vs. sensory vs. both
- ❑ signs and symptoms
  - classically, a bilaterally symmetric disturbance of function
  - distal LMN weakness
  - "stocking/glove" sensory loss
  - early reflex loss

MYELINOPATHIES
- ❑ functional failure of large myelinated fibers, leading to decreased light touch, position, vibration sensation; weakness, and decreased/absent deep tendon reflexes
- ❑ usually symmetrical, may affect both proximal and distal fibers equally
- ❑ can be associated with entities such as DM, hypothyroidism, malignancies, amiodarone, diphtheria toxin, dysproteinemias, CIDP, GBS

Hereditary Motor Sensory Neuropathy (HMSN)
- ❑ there are 7 distinct types
- ❑ HMSN Type I (Charcot-Marie-Tooth)
- ❑ 2 forms: I Hypertrophic, II Neuronal
  - etiology: AD, occasionally AR
  - epidemiology: late childhood/adolescence (40/100,000)
  - signs and symptoms: distal muscle atrophy beginning in feet and legs, later hands, due to very slowly progressive chronic degeneration of peripheral nerves and roots, slight degree of sensory impairment ('star legs' or 'upside down champagne bottle' legs)
  - main disability is difficulty walking
  - pathology: slowly progressive segmental demyelination and onion bulb formation
- ❑ treatment: supportive

Acquired Myelinopathies

Guillain-Barré Syndrome (GBS) / Acute Inflammatory Demyelinating Polyneuropathy (AIDP)
- ❑ acute, ascending, usually rapidly progressive neuropathy characterized by weakness, hyporeflexia and parasthesia involving proximal > distal muscle often beginning 1-3 weeks following viral infections, surgery, pregnancies, immunizations, or other immune altering events
- ❑ epidemiology
  - bimodal distribution affecting young adults and 50-74 years
  - slightly more common in males
  - incidence 1.7/100,000 per year < 40 and 8.6/100,000 > 70
  - 60% preceded by mild respiratory or GI infection 2-4 weeks earlier, particularly *Campylobacter jejuni*, CMV, EBV, HIV, *Mycoplasma pneumonia* as well as some medications (penicillamine, captopril, heroin, streptokinase, etc.)
- ❑ pathology
  - acute inflammatory demylinating polyradiculoneuropathy
  - may also have acute axonal degeneration
  - changes maybe caused by cross-reacting antibodies to GMI ganglioside (found in peripheral nerve myelin)

- ❑ diagnosis
  - The 4 P's of GBS
  - **P**ain (back, flanks, hips, thighs)
  - **P**arasthesia (toes and fingers)
  - **P**aralysis (ascending pattern involving proximal muscles more than distal muscles)
  - **P**alsies in 45-75% of cases (typically cranial nerves VII, IX-X)
  - roughly symmetric weakness, often but not always in ascending pattern (legs, up trunk to arms and face)
  - rapidly progressive weakness with absent reflexes and little/no sensory changes is almost always GBS
  - can progress to total muscle paralysis and death from respiratory failure
  - autonomic disturbances 50% (labile BP, cardiac dysrhythmia, paralytic ileus, bladder dysfunction, and abnormal sweating)
  - rise in total protein in CSF by end of first week of symptoms, normal glucose, opening pressure, and few or no cells (albumino-cytologic dissociation)
  - electrophysiological studies most specific and sensitive diagnostic tool
  - Miller-Fisher variant (5% of the GBS cases) characterized by areflexia, ataxia and ophthalmoplegia
- ❑ course
  - monophasic course, with weakness progressing for several days to weeks, reaching a plateau, and then recovering over a period of several weeks to months
  - 10% of patients have lasting disability
  - 3% of patients do not survive due to respiratory failure, a complication of immobility such as pulmonary embolism (PE)
  - 10% have a relapsing or fluctuating course
- ❑ treatment
  - IV gamma globulin or plasmapheresis
    - shortens disease course
  - supportive management focuses on day-to-day concerns of respirators, vital signs (autonomic function), nutrition, and other aspects of critical care

Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP)

- ❑ similar to GBS with following differences:
- ❑ uncommon to have preceding illness
- ❑ develops slowly, maximal severity after weeks or months
- ❑ more likely to have relapsing or fluctuating course
- ❑ motor weakness with areflexia
- ❑ increase in protein in CSF
- ❑ treatment: IVIG, steroids

AXONOPATHIES

- ❑ degeneration of the distal ends of long axons, usually causing an equal loss of all sensory modalities with motor involvement in “stocking/glove" distribution occurring as sensory loss spreads more proximally
- ❑ associated with systemic disease
  - DM, hypothyroidism
  - uremia: 60% patients in end-stage renal failure, usually painless mild symmetrical distal weakness
  - porphyria: may be proximal > distal and may have atypical proximal sensory deficits
  - SLE, RA, PAN, scleroderma, amyloidosis, sarcoidosis
- ❑ alcohol-nutritional
  - legs > arms
  - sensory usually occurs before distal motor weakness
  - “burning feet”
  - small fiber (i.e. pain/temperature, absent ankle jerk)
- ❑ malignancy
  - subacute motor neuropathy in lymphoma
  - sensory motor neuropathy in lung carcinoma
  - sensory in paraneoplastic small cell lung or breast carcinoma
- ❑ drugs
  - usually dose-related: cisplatin, disulfiram, dapsone, antiretroviral, nitrofurantoin, ISH, metronidazole, hydralazine
- ❑ toxins
  - heavy metals, lead (motor, wrist drop)
- ❑ infection
  - HIV, Lyme disease

NEURONOPATHIES

- ❑ affects cell body of sensory/motor nerves, causing acute/gradual onset of sensory and/or motor loss, often no recovery
- ❑ classified as motor, sensory, autonomic
- ❑ associated with motor neuron diseases, herpes zoster neuritis, paraneoplastic sensory neuronopathy

DIABETIC POLYNEUROPATHIES

❑ 15% of diabetics have symptoms of mixed, focal, multifocal, or polyneuropathies
- ~ 50% will have abnormal NCS with > 20 years DM
- decreased incidence with close glucose control

Symmetric Polyneuropathy Syndromes

❑ most common is distal symmetrical sensory polyneuropathy
- feet/legs > hands

❑ symmetrical proximal motor weakness (lower limbs > upper limbs) without pain

Focal or Multifocal Neuropathy Syndromes

❑ focal limb and truncal neuropathy: femoral or sciatic most common, good potential for recovery
❑ ophthalmoplegia: CN III (pupil sparing, severe eye pain), CN VI, CN IV
❑ multifocal neuropathy: pain in low back or hip spreading to thigh and knee (deep ache with superimposed lancinating jabs, worse at night, self-limited, recovery in months to years), pathology localized to lumbosacral plexus

Other

❑ autonomic neuropathy: orthostatic hypotension, gastroparesis, impotence, diarrhea, bladder dysfunction
❑ acute painful neuropathy: weight loss, intense foot pain, good response to glucose control

NEUROMUSCULAR JUNCTION (NMJ) DISORDERS

MYASTHENIA GRAVIS

Epidemiology

❑ bimodal age of onset: 20's female > males / 60's males > females
❑ thymoma in 10% of patients (more often in those aged 30-60)
❑ associated with other autoimmune diseases: IDDM, thyroid disease, vitiligo

Pathophysiology

❑ an autoimmune disease: production of antibodies to acetylcholine (ACh) receptors at nicotinic post-synaptic neuromuscular junction
❑ decreased number of ACh receptors

Signs and Symptoms

❑ fluctuating course of muscle weakness, chiefly in muscles innervated by cranial nerves, causing ptosis, diplopia, dysphagia and characteristically improved by cholinesterase-inhibiting drugs
❑ fatigability with use, relief with rest
❑ remitting and exacerbating course
❑ fatigability is the hallmark of diseases affecting the neuromuscular junction, weakness that worsens with activity and improves with rest

Classification

❑ based on distribution of weakness
- generalized: proximal weakness (neck flexors, deltoids, hip flexors)
- ocular: ptosis, ophthalmoplegia
- bulbar: dysphagia, dysarthria

Diagnosis

❑ EMG shows muscle fatigability with repetitive stimulation
❑ single fiber-EMG: increased jitter (variability in the firing of individual muscle fibers of a motor unit)
❑ Tensilon test (edrophonium) with transient reversal of weakness within 30-60 seconds
❑ anti-acetylcholine receptor (AChR) antibodies (90% of generalized myasthenia compared to 50% of pure ocular myasthenia have detectable serum antibodies)
❑ thymic hyperplasia/thymomas visualized by CT or MRI

Treatment

❑ anti-ACh inhibitors (increased ACh at receptor site) Mestinon, pyridostigmine
❑ immunosuppressive drugs to attack underlying process:
- steroids, azathioprine

❑ for acute crisis
- IVIG, plasmapheresis

❑ thymectomy if indicated (after CT of chest to assess for thymoma)

LAMBERT-EATON SYNDROME

- ❑ pathophysiology
  - a myasthenic syndrome due to autoimmune process which targets mechanism releasing ACh, resulting in inadequate release of ACh from nerve terminals
  - associated with small cell lung carcinoma and other malignancies
- ❑ signs and symptoms
  - progressive proximal muscle weakness and fatigue but, unlike myasthenia gravis, bulbar and eye symptoms are uncommon
  - may be a temporary increase in muscle power during first few contractions
  - may have autonomic symptoms: dry mouth, impotence, orthostatic hypotension, constipation, difficult micturition, paresthesias, hyporeflexia, aching pain
- ❑ diagnosis
  - EMG shows paradoxical increase in successive muscle contractions
  - poor response to edrophonium
- ❑ treatment
  - therapy of underlying neoplasm
  - plasmapheresis
  - immune suppression
  - 3,4 diaminopyridine (experimental)

Clinical Pearl

❑ **Approximately 50-60% of patients with Lambert-Eaton syndrome have small cell carcinoma of the lung at the time of presentation or will be diagnosed with it within 2 years.**

MUSCLE DISEASES

- ❑ muscle disorders have features of a LMN lesion
- ❑ myopathies cause diffuse weakness, usually worse in axial and proximal limb girdle muscles
- ❑ muscle disuse causes type II fiber atrophy

Table 16. Comparison of Muscle and Nerve Disorders

	Myopathy	Neuropathy
Weakness	Proximal (except myotonia)	Distal (except Guillain-Barré)
Bulk	Decreased (late finding)	Decreased
Reflexes	Normal, Decreased (late finding)	Decreased
Sensation	Normal	Decreased
EMG	Myopathic; NCS normal	Neuropathic; NCS may be slow
Muscle enzymes	Increased	Usually normal
Muscle biopsy	Diffuse loss	Group fibre loss

•NCS = nerve conduction studies

Clinical Pearl

❑ **Proximal and symmetric limb weakness with normal sensation are hallmark symptoms and signs of muscle diseases.**

POLYMYOSITIS (PMY)/DERMATOMYOSITIS (DMY) (see Rheumatology Chapter)

- ❑ an inflammatory and probably autoimmune muscle disease characterized by the subacute onset (weeks to months) of symmetrical, proximal muscle weakness of limbs and girdle
- ❑ 15% have accompanying skin rash (dermatomyositis)
- ❑ heliotrope rash, rash on extensor surfaces, "shawl" sign, ectopic calcifications in subcutaneous tissue
- ❑ muscles may be painful and tender
- ❑ pharyngeal and laryngeal muscle involvement leads to dysphagia and dysphonia
- ❑ accompanying features include Raynaud's phenomenon, arthralgia, malaise, weight loss and low-grade fever
- ❑ epidemiology
  - 8 per 100,000, age 30-60
  - 10% of adults with myopathy have neoplasia, usually carcinoma
  - 60% of adults > 40 years with dermatomyositis have neoplasia
  - 15% may have symptoms and signs of a collagen vascular disease (CVD)

- ❑ diagnosis
  - clinical signs/symptoms
  - increased CPK
  - may have circulating antibodies - RF, ANA
  - EMG myopathic (myopathic motor units on EMG and spontaneous activity - fibrillation potentials, insertional activity)
  - muscle biopsy showing destruction of muscle fibers with inflammatory cells
- ❑ treatment
  - steroids or immunosuppressives (prednisone 60-80 mg/day, Imuran)

Other Inflammatory Myopathies
- ❑ inclusion body myositis
- ❑ infectious
  - viral - Enteroviruses: Coxsackievirus, Echovirus
  - parasitic - toxoplasmosis, schistosomiasis
- ❑ drug-induced - penicillamine, clofibrate, bezafibrate

METABOLIC MYOPATHIES
- ❑ correction of the endocrine disturbance results in recovery
- ❑ acromegaly: with proximal weakness and fatigue
- ❑ thyrotoxicosis: weakness in 20%, shoulder girdle > pelvic
- ❑ hypothyroidism: proximal weakness, pelvic girdle > shoulder, associated with painful cramps and muscle stiffness
- ❑ hyper- or hypoadrenalism: proximal myopathy due to these conditions, also due to steroids used to treat hypoadrenalism

INHERITED MUSCLE DISEASES

Duchénne Muscular Dystrophy
- ❑ epidemiology
  - 1/4,000 live male births, prevalence 3/100,000
  - X-linked recessive (Xp21), dystrophin gene
  - onset 3-6 years, 40% sporadic
- ❑ signs and symptoms
  - progressive muscle weakness
  - hip girdle weakness (waddling gait, hard to climb stairs, Gowers sign)
  - pseudohypertrophy of calves
  - axial muscles involved, leads to kyphoscoliosis and respiratory distress
  - cardiac muscle involved late in course
  - mean IQ 15-20 points lower than normal
  - progressive, death during adolescence
- ❑ investigations
  - CK substantially increased - early sign
  - EMG
  - ECG - conduction abnormalities and rhythm disorders
  - muscle biopsy - no staining of dystrophin

Becker Muscular Dystrophy
- ❑ epidemiology
  - 1/20,000 live male births
  - mean age of onset 12 years, 90% by age 20
- ❑ signs and symptoms
  - less severe than Duchénne
  - cardiac muscles spared in 50% of patients
  - mental retardation rare
  - same gene, different mutation

Myotonic Dystrophy
- ❑ epidemiology
  - AD (19q), triplet repeat
  - 5/100,000, age of onset of 20-30 years
- ❑ signs and symptoms
  - distal weakness, myopathic facies (thin, tenting of upper lip, narrow face, ptosis, temporal, masseter and sternocleidomastoid atrophy)
  - myotonia = failure of muscle to relax immediately after voluntary contraction has stopped
  - males: frontal balding, testicular atrophy
  - multisystem features including ocular, cardiac, respiratory, skeletal and endocrine manifestations
  - slight mental retardation

Fascioscapulohumeral Dystrophy
- ❑ epidemiology
  - 1-2/100,000
  - AD (4q), onset 6-20 years
- ❑ signs and symptoms
  - weakness of shoulder girdle (spares deltoids) and proximal arm muscles
  - winged scapula an early sign
  - myopathic face
- ❑ arises when pain-sensitive structures of head and neck are stimulated; the brain itself is insensitive to pain

HEADACHE

Classification
- ❑ benign (primary) headaches - vast majority of headaches are of this type; migraine, tension-type headache, cluster headache
- ❑ serious (secondary) headaches - the headache is a symptom of underlying disease e.g. meningitis, SAH, temporal arteritis, increased ICP, tumour, abscess
- ❑ when to be concerned? (see Table 17)

Table 17. Warning signs of serious headache

- New-onset headache
- Different or more severe than any previous headache; the worst headache ever
- Sudden onset (maximal at onset - no increase over min.)
- Headache associated with
  - Fever
  - Meningeal irritation
  - Projectile vomiting
  - Altered level of consciousness
  - Focal neurological symptoms or signs
  - Recent head injury
  - Optic disc edema

DDx
- ❑ headache can arise from disease of ears, nose, sinuses, teeth, jaw, TMJ,eyes, C-spine, and systemic disease
- ❑ see Otolaryngology Chapter

MIGRAINE
- ❑ recurrent attacks of headache, often severe and throbbing, usually accompanied by nausea, vomiting, photophobia, phonophobia or osmophobia
- ❑ two main types
  - migraine without aura (common migraine) - 85%
  - migraine with aura (classical migraine) - 15%

Epidemiology
- ❑ common: 17% of adult Canadian population
- ❑ F:M = 3:1, young > old
- ❑ peak age 25-34 years
- ❑ familial 60%

Migraine without Aura
- ❑ pulsating or throbbing
- ❑ typically unilateral, can be bilateral
- ❑ gradual onset, lasts 2-72 hours (if untreated or unsuccessfully treated)
- ❑ interferes with activities of daily living and ability to work
- ❑ associated with nausea and vomiting
- ❑ may be associated with photo/phonophobia
- ❑ worse with movement, straining, coughing, bending over, odors
- ❑ better with rest, immobility, quiet, darkness, pressure on scalp, cold compress
- ❑ may have dilated, inflamed extracranial vessels
- ❑ prodrome and post-headache phases with changes in mood, activity, appetite, polyuria, autonomic symptoms

Migraine With Aura
- ❑ follows pattern of migraine without aura but is preceded or accompanied by aura lasting 10-30 minutes
- ❑ characterized by
  - transient focal neurological symptoms: visual (most common), sensory, motor, language, perception
  - visual symptoms: fortification spectra (zig zags), scintillating scotomata (spots), teichopsia (flashing lights)
  - correlates with vasoconstriction of intracranial vessels

Atypical Migraine
- ❑ migraine aura without headache
- ❑ basilar migraine (usually young women, occipital headache, mimics vertebrobasilar insufficiency i.e. visual field defects, diplopia, vertigo, ataxia, alterations in consciousness)
- ❑ hemiplegic/hemisensory migraine (deficit may persist for hours)
- ❑ ophthalmoplegic migraine (rare, e.g. CN III palsy; rule out aneurysm)
- ❑ retinal migraine (monocular scotoma or blindness)
- ❑ migraine in childhood: recurrent abdominal pains, vomiting and motion sickness; recurrent sleepwalking

Triggers
- ❑ stress and relaxation
- ❑ fatigue, sleep excess or deprivation
- ❑ weather
- ❑ medications: exogenous estrogen and nitroglycerin
- ❑ bright light
- ❑ hormonal factors (menstruation, ovulation, pregnancy, menopause)
- ❑ dietary factors (fasting, caffeine withdrawal, tyramine (cheeses), nitrites (bacon, salami), MSG, chocolate, alcohol (red wine)

Management Strategies
- ❑ non-pharmacologic: education (avoid triggers, stress management), relaxation training*, biofeedback*, cognitive behavioural therapy (CBT), hypnosis, accuputure
  *Grade A evidence
- ❑ pharmacologic (symptomatic treatment):
  - analgesia: NSAIDS, acetominophen, summatriptan (Immitrex), ergotamine derivatives (avoid consecutive days, wait 24 hours after ergotamine)
  - NSAIDS, acetominophen, ergotamine often combined with each other and/or caffeine
  - others (benzodiazepines, opioids, barbiturates)
  - antiemetics (eg. metaclopramide)
  - NB: Beware rebound H/A caused by long-term use of analgesics
- ❑ prophylactic treatments
  - consider in patients with frequent H/A lasting longer than 12 hours
  - beta blockers
  - calcium channel blockers
  - others (TCA, SSRI, cyproheptadine, methysurgide, phenelzine, valproate, NSAIDs, riboflavin lisinopril)
- ❑ homeopathic remedies: some evidence for feverfew
- ❑ admit if severe headache persists for longer than two days

TENSION-TYPE HEADACHE
- ❑ very common (30%)
- ❑ F > M; onset before 40's
- ❑ signs and symptoms
  - non-throbbing, pressing or tightening, bilateral occipital head pain, no nausea and vomiting, no phono/photophobia and no prodrome, can occur daily
  - psychological factors are present, especially anxiety, depression
  - multiple episodes lasting 1/2 hour to 1 week
- ❑ treatment
  - counseling with reassurance and education
  - removal of precipitants
  - physical methods (massage, heat, biofeedback, relaxation)
  - non-narcotic analgesics (NSAIDs probably more effective than acetaminophen)
  - prophylaxis - TCAs (imipramine, amitryptylline) +/– psychotherapy

CLUSTER HEADACHE
- ❑ uncommon
- ❑ M > F; middle-age, mean age of onset is 25 years of age, rarely family history
- ❑ signs and symptoms
  - clusters of brief (15 min - 3 hour) severe constant, non-throbbing pain
  - abrupt onset, often in early a.m. (waking patient up from sleep)
  - last an hour or so, at least 1/day, everyday, for cluster of weeks to months; reappears months later
  - unilateral, orbital, supraorbital, and/or temporal
  - alcohol may precipitate
  - associated with conjunctival ingection, lacrimation, nasal congestion, rhinorrhea, forehead and facial sweating, miosis, ptosis, eyelid edema
  - no nausea/vomiting
- ❑ treatment
  - prophylaxis with verapamil, methysergide (young patient), lithium, prednisone
  - acute treatment with ergotamine, tryptans +/– O_2 inhalation

MEDICATION-INDUCED HEADACHE
- ❑ signs and symptoms
  - chronic daily/near daily headache
  - having characteristics of both migraine and tension-type headaches
  - occurring in patients who are chronic (over) users of analgesic medication: (vicious cycle of headache —> analgesic use —> headache)

TRACTION HEADACHE

❑ pathophysiology
- caused by an intracranial mass lesion (e.g. tumour, blood, pus)

❑ signs and symptoms
- mild and intermittent —> more severe/persistent; unlike previous headaches
- precipitated by head-low, Valsalva, lying down, exertion
- worse in a.m.
- constant in location or diffuse
- accompanied by other neurological symptoms/signs
- +/– vomiting, papilledema

❑ diagnosis
- requires imaging
- contrast CT or MRI

❑ treatment (see Neurosurgery Chapter)

MENINGEAL IRRITATION (see Neurosurgery Chapter)

(Meningitis, Subarachnoid Hemorrhage)

❑ any sex, any age, any time

❑ signs and symptoms
- severe, generalized headache with nausea/vomiting and photophobia
- meningitis is maximal in hours to days, SAH is maximal in seconds to minutes
- SAH may have "sentinel bleed": severe headache may be preceded by warning headache

❑ physical exam
- positive Kernig's sign (knee extension with hip in flexion arrested due to pain)
- positive Brudzinski's sign (gentle, passive, forward neck flexion is arrested, while other head movements are normal)
- meningitis presents with symptoms/signs of infection, SAH may have a fever

❑ diagnosis
- non-contrast CT
- lumbar puncture with CSF studies if CT negative (CT alone does not rule out SAH) or CT unavailable
- LP contraindicated if decreased LOC, papilledema, or focal neurological signs (see LP section)

GIANT CELL ARTERIES (see Rheumatology Chapter)

STROKE

❑ a clinical syndrome characterized by sudden onset of a focal neurological deficit presumed to be on a vascular basis; avoid 'CVA' ('confused vascular assessment')

CLASSIFICATION

Ischemic Stroke (80%)
❑ ischemic stroke results from focal ischemia leading to cerebral infarction. Mechanisms include embolism from heart or proximal arteries, small vessel thrombosis, or hemodynamic from a drop in the local perfusion pressure. Global ischemia (e.g. from cardiac arrest or hypotension) causes a diffuse encephalopathy.
❑ ischemic strokes vary according to their size, anatomical location in the brain, and temporal pattern

Hemorrhagic Stroke (20%)
❑ abrupt onset with focal neurological deficits, due to spontaneous (non-traumatic) bleeding into the brain
❑ includes ICH and SAH
❑ subdural and extradural hemorrhages are not usually classified as strokes as they are associated with trauma
❑ hemorrhage into an area of cerebral infarction (commonly following cardiogenic embolism) is a hemorrhagic infarct which should be considered an ischemic stroke complicated by secondary hemorrhage; not a hemorrhagic stroke

STROKE TERMINOLOGY

Transient Ischemic Attack (TIA)
❑ stroke syndrome with neurological symptoms lasting from a few minutes to as much as 24 hours, followed by complete functional recovery

Amaurosis Fugax, Transient Monocular Blindness (TMB)
❑ due to episodic retinal ischemia, usually associated with ipsilateral carotid artery stenosis or embolism of the retinal arteries resulting in a sudden, and frequently complete, transient loss of vision in one eye

Reversible Ischemic Neurological Deficit (RIND)/Minor Stroke
❑ neurological abnormalities similar to acute completed stroke, but the deficit disappears after 24 - 36 hours, leaving few or no detectable neurological sequelae (a better term is minor stroke)

Completed Stroke (CS)
❑ stroke syndrome with a persisting neurological deficit suggesting cerebral infarction; the ensuing neurological defect can last days, weeks, or permanently; even after maximal recovery, at least minimal neurological difficulties often remain

Progressing Stroke (Stroke In Evolution)
❑ neurological deficits begin in a focal or restricted distribution but over the ensuing hours spread gradually in a pattern reflecting involvement of more and more of the particular vascular territory

MAKING THE COMPLETE DIAGNOSIS: "THE FOUR QUESTIONS"

❑ 1. Has the patient had a stroke?
- not all acute focal neurological deficits are 2º to stroke
- temporal profile may differentiate between TIAs, progressing stroke, and minor and severe completed stroke

❑ 2. Where is the lesion and what is the blood supply?
- vascular territory: carotid vs. vertebrobasilar

❑ 3. What is the lesion?
- ischemia/infarction (with or without 2º hemorrhage)
- hemorrhage

❑ 4. What is the pathogenesis? (i.e. mechanism of the stroke)
- it will guide acute and chronic therapy

DDx: IS IT A STROKE?

❑ focal seizures
❑ other focal lesions: tumours, abscesses, subdural hematoma, demyelination, focal encephalitis (herpes simplex)
❑ LMN lesions: Bell's Palsy, plexopathies, mononeuropathy
❑ previous cerebral infarction (i.e. focal signs are old)
❑ confusion, dementia and coma (without focal signs) are rarely modes of presentation for strokes and usually suggests diffuse disturbance of cerebral function

WHERE IS THE LESION?

❑ see Figure 17 for vascular territories of major cerebral arteries

Hemispheric (see Figure 17 and Table 18)
❑ carotid territory (ACA, MCA)
❑ posterior cerebral arteries (vertebrobasilar supplies)

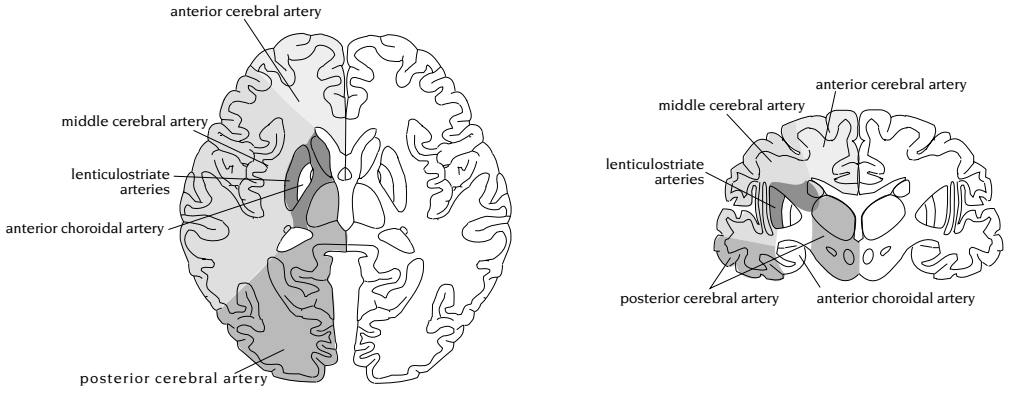


Figure 17. Vascular Territories of Major Cerebral Arteries

Illustration by Dr. P. Stewart

Table 18. Anterior vs. Middle Cerebral Arteries vs. Posterior Cerebral Arteries
* UE = upper extremities, LE = lower extremities

Anterior Cerebral Artery	Middle Cerebral Artery	Posterior Cerebral Artery
• Hemiplegia of LE • Hemianesthesia of LE • Incontinence • Grasp, snout, palmomental reflexes • Behavioural and memory disturbances and constructional apraxia (if non-dominant hemisphere) • Gaze preference (away from hemiparesis)	• Hemiplegia of UE and face • Hemianesthesia of UE and face • Hemianopia • Aphasia (if dominant hemisphere) • Neglect of contralateral limbs (if non-dominant hemisphere)	• Homonymous hemianopia or cortical blindness (if bilateral) • If dominant hemisphere - alexia without agraphia • If thalamus - contralateral hemisensory loss - spontaneous pain • If subthalamic - hemiballismus • If midbrain - ipsilateral CN III palsy - contralateral motor deficit

Brainstem
❑ vertebrobasilar territory
- cranial nerves
  - diplopia, gaze palsies, nystagmus
  - vertigo
  - dysarthria and dysphagia (sometimes hemispheric if patient hemiplegic)
  - other cranial nerve palsies (III-XII)
- cerebellum
  - ataxia
  - incoordination
  - crossed sensory loss (face and opposite side of body)
  - bilateral motor deficits

Indeterminate
❑ 'hemisyndromes': hemiparesis, hemisensory loss, dysarthria

WHAT IS THE LESION?

Table 19. Hemorrhagic vs. Ischemic Stroke

	Hemorrhage	Infarct
Hypertension	Usually present	Often present
Preceding TIA	No	30% of cases
Onset	Often with activity	Often at night or no activity, on waking
Course	Rapidly progressive	Static (rarely stepwise)
Increased ICP	Yes	No
CT scan	Shows blood	Normal or changes of infarction

- **CT (or MRI) is the only reliable way to rule out hemorrhage**

WHAT IS THE PATHOGENESIS?

Atherosclerotic Plaque
- ❑ inadequate perfusion of brain due to
  - an embolus from an atherosclerotic plaque in a large vessel (artery to artery embolus) (most common)
  - a large vessel thrombosis with low distal flow
- ❑ risk factors
  - hypertension (HTN)
  - diabetes mellitus (DM)
  - cigarette smoking
  - high cholesterol
- ❑ treatment
  - control atherosclerotic risk factors
  - carotid endarterectomy in selected patients (see below)
  - antiplatelet agents: aspirin, ticlopidine, clopidogrel, aggrenox (dipyridamole and ASA)

Cardiogenic Origin
- ❑ an embolus of clot
  - risk factors: A fib (commonest cause), LV aneurysm, LV dysfunction, increased age, mitral annulus calcification
- ❑ air emboli - during surgery or diving
- ❑ valvular vegetations (infection, tumour)
- ❑ treatment
  - risk of embolization can be decreased with anticoagulation (heparin and warfarin)
  - increase risk of hemorrhagic infarction implying that it is imperative to exclude the presence of bleeding prior to starting anticoagulants (i.e. do CT scan at 48 hours post-bleed)
  - if moderate sized infarct, delay anticoagulation 5-14 days

Lacunar Infarction
- ❑ small (< 2 cm) and deep infarcts (lacune means lake)
- ❑ most < 5 mm, only 1% > 10 mm = "giant lacunes"
- ❑ pathology
  - lipohyalinosis of small penetrating arteries of basal ganglia and brain stem; microatheroma; junctional plaques (atherosclerosis of parent vessel blocking orifices of penetrating vessels)
- ❑ sites
  - putamen
  - internal capsule - pure motor
  - thalamic - pure sensory
  - pons - brainstrm signs
- ❑ clinical syndromes
  - pure motor or pure sensory
  - clumsy hand dysarthria
  - ataxic hemiparesis
- ❑ risk factors
  - HTN
  - DM
  - increasing age
- ❑ treatment
  - control HTN
  - use antiplatelet drugs

Other Causes
- ❑ large artery diseases (Moya Moya, Takayasu's arteritis)
- ❑ dissection, trauma, vasculitis (PAN, meningovascular syphilis)
- ❑ coagulation/viscosity problems (especially in younger patients)
- ❑ venous infarction (cortical vein or sinus thrombosis)
  - seen in "hypercoagulable states" (e.g. pregnancy, dehydration) and results in cortical infarction, often complicated by 2° hemorrhage and seizures

Risk Factors for Stroke
- ❑ hypertension (HTN)
- ❑ smoking
- ❑ myocardial infarction (MI)
- ❑ atrial fibrillation (A fib)
- ❑ diabetes mellitus (DM)
- ❑ alcohol abuse
- ❑ homocysteinemia
- ❑ obesity
- ❑ severe carotid stenosis
- ❑ parental stroke (family history)

Investigations

❑ laboratory
- CBC, ESR, PT, PTT, VDRL, glucose, lipids and hypercoagulability work-up (Protein C, Protein S, Factor V Leiden, anti cardiolipin antibody, lupus anticoagulant, PT/INR, PTT, anti-phospholipid antibody and heparin cofactor II)

❑ neuroimaging
- CT, MRI, functional imaging (SPECT, PET)
- for acute stroke, unenhanced CT head is imaging method of choice

❑ cardiac
- ECG, echocardiogram (transesophageal), Holter monitor

❑ non-invasive studies
- duplex doppler of carotids, transcranial doppler to look at intracranial vessels, MR angiography

❑ angiography

Management

❑ Asymptomatic Carotid Bruit
- suggests the presence of atherosclerotic stenosis and signifies increased risk for both cerebral and myocardial infarction
- modify risk factors, +/– antiplatelet therapy
- if stenosis > 60%, risk of stroke is 2% per year

❑ TIA, Mild Stroke
- investigate to determine the vascular territory and etiology, then treat accordingly for atherosclerotic pathogenesis: manage risk factors and use antiplatelet agents - ASA, ticlopidine (Ticlid), clopidrogel (Plavix), Persantine with ASA (Aggrenox)
- for carotid territory event, consider carotid endarterectomy by a good experienced surgeon if there is severe ipsilateral, extracranial carotid stenosis (> 70% by angiography)
- if angiography shows 50-69% stenosis refer to stroke neurologist to assess indication for carotid endarterectomy

❑ Acute Cerebral Infarction
- management goals
  - ensure medical stability
  - limit or prevent neuronal death
  - avoid secondary complication of immobilization (e.g. pneumonia, pulmonary embolus)
  - prevent recurrent cerebral infarction
- practical guidelines
  - ensure the ABC's
  - patient with vertebrobasilar ischemia or bihemispheric ischemia can have decreased respiratory drive or muscular airway obstruction
  - consider heparin in patients who are not eligible for tPA who have a larger artery atherosclerotic stroke, progressing thromboembolic stroke, or cardioembolic stroke and who do not have a large infarct, uncontrolled hypertension or bleeding condtions
  - make the correct etiological diagnosis so you have a rational approach for secondary prevention of stroke
  - remember that MI is an important cause of morbidity and mortality in these patients; screen for and manage the patient's CAD
  - consider transfer to stroke center if patient seen in first few hours for neuroprotective or thrombolytic therapy (both under evaluation by clinical trials)
  - consider thrombolysis if early in course (< 3 hours from onset)
  - IV tPA if severe deficit, < 3 hours from onset and no evidence of hemorrhage on CT
  - ineligible for tPA if
    - history of intracranial hemorrhage
    - major surgery within 14 days
    - GI bleed within 21 days, head trauma or stroke within 3 months
    - LP within 7days, rapidly improving
    - BP greater than 185/110, seizures at onset
    - symptoms suggest SAH, post MI pericarditis, pregnant, evidence of hemorrhage on CT
    - PTT greater than 15s on warfarin, increased INR on heparin,
    - platelets less than 100,000/mm^3
    - glucose less than 50 or greater than 400mg/dl
    - severe anemia
  - BP: DO NOT LOWER THE BP, avoid acute administration of anti-hypertensive agents; unless hypertension is extreme
  - most patients with an acute cerebral infarct are initially hypertensive and their BP will fall spontaneously within 1-2 days
  - acutely elevated BP is necessary to maintain brain perfusion
  - anytihypertensive therapy is withheld for at least 10days after thromboembolic stroke unless there is cardiac failure, aortic dissection, or a systolic above 220mmHg or a diastolic BP above 120mmHg
  - IV labetalol is usually first line

- avoid hyperglycemia which will increase the degree of lactic acidosisin ischemic tissue, increase the infarct size
- keep patient well hydrated, this will keep blood viscosity low and maintain perfusion of ischemic tissue
- keep patient NPO if there is any hint of abnormal swallowing due to the risk of aspiration

- aspirin 325mg should be started within 48 hours of stroke onset, optimal dose uncertain, no compelling evidence that any specific dose more effective
- give antiplatelets clopidogrel if ASA not suitable (e.g. Anaphylaxis, ulcers)
- clopidogrel (75mg/d) preferred over ticlopidine because of risk of neutropenia with ticlopidine
- start ambulation early, and if not feasible, use subcutaneous heparin to avoid DVTs

- glycoprotein IIB/IIIA platelet receptor antagonists, most powerful antiplatelet agents, have been used in cardiac revascularization and are currently being evaluated in ischemic stroke patients

Clinical Pearl
- ❑ **The leading causes of death during the first month following a stroke are pneumonia, pulmonary embolus, cardiac disease and the stroke itself.**
- ❑ **If a patient survives beyond the first week following a stroke, the cause of death is not directly related to the stroke.**

MULTIPLE SCLEROSIS

- ❑ a relapsing or progressive disease of CNS myelin characterized by disseminated patches of demyelination in the brain and spinal cord, resulting in multiple and varied neurological symptoms and signs usually with exacerbations and remissions
- ❑ lesions separated in time and space

Epidemiology
- ❑ onset usually 20-40, but can be younger or older
- ❑ F:M = 3:2
- ❑ prevalence in North America 1/1,000; most common in European races and in countries farther from the equator
- ❑ genetic predisposition: 3% risk for first degree relatives, 30% concordance for identical twins, HLA DR2 and Dw2 association

Etiology
- ❑ unknown but immunological and viral theories

Pathology
- ❑ multiple discrete lesions of myelin destruction (plaques)
- ❑ common plaque sites include optic nerve, periventricular areas, corpus callosum, brainstem, spinal cord

Course of Illness
- ❑ 5 Types
  1. relapsing remitting (80% present this way initially, F>M)
  2. primary progressive (gradually progressive clinical course from presentation, F=M)
  3. secondary progressive (starts with relapsing remitting becomes progressive)
  4. clinically inactive disease
  5. mixed pattern

Signs and Symptoms
- ❑ signs: hyperreflexia, ataxia, nystagmus, spasticity and limb weakness
- ❑ symptoms: parasthesia, gait disorder, weakness (e.g. hemiparesis, paraparesis (myelopathy)) and incoordination, visual loss (optic neuritis) and diplopia, incontinence, fatigue

Common Features
- ❑ internuclear ophthalmoplegia (lesion in MLF causing failure of adduction of the ipsilateral eye and nystagmus of the abducting eye on attempted lateral gaze)
- ❑ optic neuritis
- ❑ Lhermitte's sign (forward flexion of the neck causes electric shock sensation down the back to limbs, indicative of cervical cord lesion)
- ❑ Uhthoff's phenomenon (worsening of symptoms with heat e.g. hot bath, exercise)
- ❑ trigeminal neuralgia in young patient

Clinical Pearl
❑ **MS is a common cause of internuclear ophthalmoplegia.**

Diagnosis
❑ evidence from history and examination of multiple lesions disseminated in both time and space
❑ slowing of evoked potentials (visual/auditory/somatosensory)
❑ CSF (oligoclonal Ig bands in 90%, increased IgG concentration, mild lymphocytosis and increased protein)
❑ MRI (plaques show as hyperintense lesions on T2 MRI in periventricular distribution)

Management
❑ patient education and counseling (disclosure, prognosis, future expectations, support groups, psychosocial issues: divorce, depression, suicide not uncommon)
❑ acute treatment
- corticosteroids are the most commonly used treatment for acute attacks
- current recommendation is to treat disabling attacks with 500 to 1,000 mg of IV methylprednisolone for 3-5 days with or without short oral tapering dose of prednisone

❑ symptomatic treatment
- symptomatic treatment for spasticity (baclofen), painful symptoms, bladder dysfunction (ditropan), fatigue (amantadine), depression
- monitor closely for infection especially UTI
- physiotherapy, speech therapy, occupational therapy, nutrition, social work

❑ disease suppressing agents
- interferons, copolymers are being used to suppress disease activity
- mechanism uncertain
- disease suppressing medications are indicated for ambulating patients with frequent relapses
- β-interferon (beta 1b, Betaseron) shown to decrease relapse rate, decreased rogression of disability in patients with relapsing/remitting and progressive disease
- β-interferon (beta 1a, Avonex) appears promising with similar efficacy to betaseron
- Copolymer also decreases relapse rate in relapsing remitting disease and is currently under investigation for use in secondary progressive
- trials under way for chronic and primarily progressive

CNS INFECTIONS

❑ see Infectious Diseases Chapter

MENINGITIS
❑ inflammation of the meninges

Predisposing Factors
❑ systemic (especially respiratory) or parameningeal (otitis media, odontogenic, sinusitis) infections
❑ head trauma
❑ anatomical meningeal defects
❑ previous neurosurgical procedures
❑ cancer, alcoholism, and other immunodeficiency states

Etiology
❑ bacterial
- neonates: E. *coli*, Group B S*treptococcus*, L*isteria monocytogenes*
- infants and children: H. *influenzae*, S. *pneumoniae*, N. *meningitidis*
- adolescents and adults: S. *pneumoniae*, N. *meningitidis*
- elderly: S. *pneumoniae*, N. *meningitidis*, Gram negatives
- CSF leak: S. *aureus*, Gram negatives
- immunocompromised: L*isteria monocytogenes*

❑ viral ("aseptic")
- Enteroviruses, H. *influenzae*, HIV, HSV, Adenovirus

❑ fungal
- cryptococcus

❑ other
- T*reponema pallidum* (meningeal neurosyphillis)
- B*orrelia burgdorferi* (Lyme disease)
- TB

Signs and Symptoms
- ❑ neonates and children: fever, vomiting, lethargy, irritability, and poor feeding
- ❑ older children and adults: fever, headache, neck stiffness, confusion, nausea and vomiting, lethargy, meningeal signs (i.e. Kernig's, Brudzinski's)
- ❑ other signs include altered level of consciousness, petechial rash (septic microemboli), seizures, focal neurological signs (i.e. CN palsies)

Diagnosis
- ❑ CBC + differential
- ❑ lytes for SIADH
- ❑ X-rays may indicate primary infection site (CXR, sinuses, mastoid bone)
- ❑ CSF profile (see Table 20)
- ❑ Gram stain, culture
- ❑ PCR +/– serology (viral)
- ❑ do CT, EEG if focality

Treatment
- ❑ initial choice of antibiotics is empirical, based upon the patient's age and predisposing factors
- ❑ therapy is adjusted as indicated when Gram stain, C&S results become available
- ❑ neonates: ampicillin + cefotaxime (better CSF penetration than gentamicin)
- ❑ infants and children: ampicillin + ceftriaxone/cefotaxime
- ❑ adolescents and adults: penicillin
- ❑ elderly: penicillin + ampicillin
- ❑ CSF leak: cloxacillin + gentamicin
- ❑ reportable to Public Health

Complications
- ❑ headache, seizures, cerebral edema, hydrocephalus, SIADH, residual neurological deficit (especially CN VIII), death

Morbidity and Mortality
- ❑ S. *pneumoniae*: about 25%; N. *meningitidis*: 10%; H. *influenzae*: 5%
- ❑ worse prognosis with extremes of age; delays in diagnosis and treatment; complicating illness; stupor or coma; seizures; focal neurological signs

Prevention
- ❑ regular childhood immunization against H. *influenzae*
- ❑ vaccinate against N. *meningitidis* if traveling to endemic meningitic areas
- ❑ prophylactic Rifampin for household and close contacts of H. *influenzae* and N. *meningitidis* meningitis-affected patients

Table 20. CSF Profile for CNS Infections

	Normal	Bacterial	Viral/Syphilis	TB/Fungal	Aseptic Meningitis
Appearance	Clear	Normal/cloudy	Normal/cloudy	Cloudy	
Glucose (mmol/L)	2.8-4.4	Decreased	Normal	Decreased	Normal
Protein (g/L)	0.2-0.45	Increased	Increased	Increased	Increased
Cell Count (cell #/mm³)	< 6	Increased	Increased	Increased	Increased
Predominant Cell	Lymphocytes	PMNs	Lymphocytes	Lymphocytes	Lymphocytes
Pressure (mmHg)	100-200 < 20 cm H_2O	Maybe increased	N/A	Increased	N/A

Clinical Pearl
- ❑ **For suspected tuberculosis (TB) meningitis, confirm with PCR, AFB stain, TB culture.**

ENCEPHALITIS

Pathophysiology
- ❑ an acute inflammatory disease of the brain due to direct viral invasion or to hypersensitivity initiated by a virus / foreign protein
- ❑ common portals of viral entry into host include respiratory (mumps, measles, influenza), enteric (rabies, CMV, HIV), genitourinary tract (enteroviruses), and venereal spread (HSV, CMV, HIV)
- ❑ other viruses reach CNS via peripheral nerves (rabies, HSV)

Etiology
- ❑ viral (usual cause): HSV, mumps, measles, rabies, arbovirus, HIV, poliovirus, CMV, varicella zoster
- ❑ bacterial, mycobacterial and spirochetal: Mycoplasma pneumoniae, syphilis, Listeria, TB, typhoid fever
- ❑ fungal: cryptococcosis, histoplasmosis, candida, coccidiomycosis
- ❑ parasitic: toxoplasmosis, falciparum malaria, protozoal (cysticercosis)
- ❑ rickettsial: Rocky Mountain spotted fever
- ❑ unclassified: CJD (prion)

Signs and Symptoms
- ❑ acute febrile illness, malaise, chills, nausea, vomiting
- ❑ meningeal involvement: headache, stiff neck
- ❑ parenchymal disease: seizures, mental status changes, focal neurological signs
- ❑ increasing ICP if a significant brain volume is damaged by the infectious process

Diagnosis
- ❑ typically is based on clinical picture
- ❑ CSF can confirm inflammatory process
- ❑ CSF profile (cell count and differential, glucose, protein), cultures, stains may help provide specific diagnosis or limit possibilities
- ❑ serologic studies are valuable in diagnosing encephalitis
- ❑ CT/MRI/EEG to define anatomical substrata affected may show focus
- ❑ brain tissue biopsy for culture, histological examination, ultra structural study, and immunocytochemistry

Treatment
- ❑ general supportive care plus measures directed against specific infecting agent
- ❑ monitor vital functions carefully (BP, HR, respirations)
- ❑ maintain nutritional status (hyperalimentation/gastroscopy feeds)
- ❑ reportable to Public Health

Clinical Pearl
- ❑ **With meningitis, cerebral function remains normal.**
- ❑ **With encephalitis, patients often have altered mental status (speech, movement).**

Herpes Simplex Encephalitis
- ❑ pathophysiology
  - acute, necrotizing, asymmetrical hemorrhagic process with lymphocytic and plasma cell reaction, which usually involves the medial temporal and inferior frontal lobes
  - associated with HSV-1, but herpes encephalitis can also be caused by Varicella
- ❑ signs and symptoms
  - typically sudden onset
  - headache, stiff neck, vomiting, hemiparesis, and focal or generalized seizures
  - note signs of temporal lobe (HSV target) dysfunction (olfactory hallucinations, behavioral disturbance, complex partial seizures)
  - usually rapidly progressive over several days and may result in coma or death
  - common sequelae in surviving patients are memory and behaviour disturbances (reflecting limbic involvement)
  - can present as supratentorial mass lesion
  - may also cause acute myelopathy
- ❑ diagnosis
  - CT/MRI: medial temporal lobe necrosis
  - EEG: early focal slowing, periodic discharges
  - biopsy: when diagnosis uncertain
  - PCR of CSF for HSV DNA: for rapid diagnosis
- ❑ treatment
  - IV acyclovir if diagnosis is suspected

Arbovirus Encephalitis
- ❑ epidemic, sporadic, virus type by location (Eastern Equine is the worst, summer worst)
- ❑ newly recognized in North America - West Nile virus
- ❑ severe mortality/morbidity > 50%
- ❑ signs and symptoms
  - rapid onset drowsiness, stupor, or coma with convulsive seizure, headache, vomiting, neck stiffness, high fever
  - CN palsies, hemiplegia, and other focal neurological signs common
  - patients who recover often have sequelae: mental deficiency, cranial nerve palsies, hemiplegia, aphasia, and convulsions are common
- ❑ treatment
  - entirely supportive in acute stage

INTRACRANIAL ABSCESS (see Neurosurgery Chapter) **(see Colour Atlas NS8)**
- ❑ etiology: focal infection leading to hematogenous, or local spread,
  - sometimes idiopathic
- ❑ extension from ear
  - Group A *Streptococcus*, S. *pneumoniae*, H. *influenzae*, *anaerobic Streptococcus*, *Bacteroides sp.*, *Enterobacteriaciae*
  - treatment: penicillin G + metronidazole + ceftriaxone/cefotaxime
- ❑ extension from paranasal sinuses
  - anaerobes, Strep sp., S. *pneumoniae*, H. *influenzae*
  - treatment: penicillin G + metronidazole
- ❑ post-surgery or trauma
  - S. *aureus*, *Enterobacteraciae*
  - treatment: cloxacillin + ceftriaxone/cefotaxime + rifampin
- ❑ spread from extracranial site
  - site-specific organisms
- ❑ HIV-infected
  - Toxoplasma gondii
  - treatment: pyrimethamine + sulfadiazine or pyrimethamine + clindamycin
- ❑ chronic abscess
  - M. *tuberculosis*, C. *neoformans*

NEUROLOGIC COMPLICATIONS OF SYSTEMIC DISEASE

METABOLIC DISEASES

Alcohol Intoxication

Seizures
- ❑ alcohol withdrawal seizures
  - arise 12-48 hours after ingestion
  - patient is tremulous
  - cluster of 2-3 seizures
  - normal or slow interictal EEG
  - treatment: benzodiazepines
- ❑ seizure precipitated by alcohol
  - intrinsic CNS lesion (e.g. subdural hematoma, meningitis)
  - focal seizure, EEG has focal abnormality
  - occurs during the time of intoxication

Delirium Tremens
- ❑ mortality rate 20% if left untreated
- ❑ occurs from 24 h – 7 days after reduction/cessation of drinking, lasts 3-5 days
- ❑ signs and symptoms
  - tremulousness
  - symptoms of delirium
  - visual hallucinations
  - autonomic hyperactivity - tachycardia, fever, sweating
- ❑ treatment
  - high dose chlordiazepoxide, lorazepam or diazepam +/– haldol
  - clonidine, atenolol for autonomic hyperactivity
  - maintain fluid and electrolyte balance

Wernicke's Encephalopathy (Thiamine Deficiency)
- ❑ signs and symptoms
  - nystagmus on horizontal/vertical gaze; bilateral CN VI or gaze palsy
  - ataxia
  - recent memory loss and confabulation
- ❑ up to 80% develop Korsakoff's (short term memory loss, anterograde amnesia, confabulation)
- ❑ treatment
  - thiamine

Polyneuropathy
- ❑ due to deficiency of vitamin B complex (thiamine B_1, riboflavin B_2, nicotinic acid B_3, pantathenic acid B- or pyridoxine B_6)
- ❑ loss of ankle jerks and sometimes knee jerks
- ❑ progressive distal weakness, lower limbs initially
- ❑ pain, burning feet, paresthesias
- ❑ sensory loss in "stocking/glove" distribution
- ❑ autonomic dysfunction – impotence, orthostatic hypotension

Cerebellar Degeneration
- ❑ M > F; commonest cause of acquired ataxia
- ❑ midline structures (vermis) especially affected gait ataxia and lower limb inco-ordination; upper limbs spared; nystagmus rarely present

Myopathy
- ❑ proximal muscle weakness
- ❑ may get increase in myoglobin and creatinine kinase

Fetal Alcohol Syndrome / Fetal Alcohol Effects
- ❑ low birth weight and size, failure to catch up
- ❑ mental retardation
- ❑ birth defects (facial, cardiac)

Electrolyte Disturbances

Hyponatremia
- ❑ among the many causes of hyponatremia, SIADH is of special importance since it may complicate many neurological diseases (head trauma, bacterial meningitis and encephalitis, cerebral infarction, SAH, neoplasm, and GBS)
- ❑ may present with decreased level of alertness, confusion, seizure, coma
- ❑ severity of the clinical effects is related to the rapidity of decrease in serum Na^+ which leads to brain edema and increased ICP
- ❑ rapid correction causes central pontine myelinolysis (acute progression of bulbar weakness and tetraparesis, decrease in LOC, coma, death)

Hypernatremia
- ❑ major causes include diabetes insipidus, nonketotic diabetic coma, chronic hydrocephalus, and stuporous patients not receiving any fluids
- ❑ extreme high levels cause impairment of consciousness, asterixis, myoclonus, seizures, choreiform movements, muscular weakness and rhabdomyolysis
- ❑ degree of CNS disturbance is related to the rate of change in serum Na^+
- ❑ rapid rises shrink the brain and may cause subdural hematomas by rupturing a bridging vein

Hypokalemia
- ❑ presents as generalized neuromuscular weakness, mental confusion

Hyperkalemia
- ❑ presents as generalized muscular weakness in addition to the serious risk of cardiac arrest

ENDOCRINE DISEASES (see Endocrinology Chapter)

Hyperthroidism
- ❑ myopathy
  - M > F
  - upper extremity weakness and wasting, with brisk reflexes, periodic paralysis and occasionally myasthenia gravis
- ❑ movement
  - fine tremor
  - may have choreiform movements
- ❑ sensorium
  - delirium, seizure or even coma in acute thyroid storm
- ❑ risk of stroke due to A fib
- ❑ additionally in Grave's disease
  - exophthalmos and diplopia due to inflammation of extraocular muscles
  - optic neuropathy

Hypothyroidism
- ❑ myopathy: proximal weakness (may actually have enlarged muscles despite weakness), delayed relaxation of ankle jerks "hung reflexes"
- ❑ carpal tunnel syndrome
- ❑ mental apathy and physical inertia, a cause of dementia

Hyperparathyroidism
- ❑ hypercalcemia
- ❑ myopathy: proximal weakness, easy fatigability, wasting
- ❑ personality changes and increased risk of psychosis
- ❑ choreiform movements, Parkinsonism

Hypoparathyroidism
- ❑ hypocalcemia
- ❑ tetani & hyporeflexia
- ❑ risk of convulsions and papilledema in children
- ❑ extrapyramidal movements (e.g. chorea)
- ❑ myopathy: proximal weakness (rare)
- ❑ personality changes

Diabetes Mellitus (DM)
- ❑ peripheral neuropathy
  - Mononeuritis Multiplex
    - due to compression and impaired microcirculation of the nerves
    - e.g. femoral nerve, common peroneal nerve, upper lumbar roots
  - mononeuropathy
    - CN III (painful, pupil sparing),
    - CN IV, CN VI
    - wrist, foot drop
  - autonomic neuropathy
    - gastroparesis, bladder dysfunction postural hypotension, impotence, sweating
- ❑ visual defects
  - poor vision or blindness can result from retinal vasculopathy, cataracts, embolic events, progressive neuropathy, and ischemic optic neuropathy
- ❑ cerebrovascular and vascular lesions of the spinal cord
  - lacunar infarcts and large vessel infarcts (secondary to accelerated atherosclerosis)
- ❑ manifestations of metabolic syndromes in DM
  - DKA —> coma
  - hyperosmolar hyperglycemic nonketotic syndrome
    - seizures, pyramidal or extrapyramidal signs, coma
  - hypoglycemia
    - confusion, altered behavior, focal signs mimicking strokes, seizure, coma
    - chronic: progressive dementia, spasticity, dysarthria, extrapyramidal signs, ataxia

COLLAGEN VASCULAR DISEASES

Systemic Lupus Erythematosis
- ❑ microvascular pathology leads to neurological disease
- ❑ 50% have abnormal EEG, and 30% may develop seizures and psychosis
- ❑ may present with intractable H/A, cerebrovascular disease, chorea, extraocular neuropathy, peripheral neuropathy (mononeuritis multiplex, GBS), and polymyositis
- ❑ cerebral infarction related to an associated antiphospholipid antibody syndrome (hypercoagulable state)

Rheumatoid Arthritis
- ❑ neuro problems due to 1) peripheral nerve entrapment, 2) cervical spine instability, 3) vasculities
- ❑ may present with carpal tunnel syndrome, ulnar nerve palsy, mononeuritis multiplex, GBS, polymyositis, etc.
- ❑ may cause spastic tetraparesis due to avulsion/absorption of odontoid process, atlantoaxial subluxation, basilar invagination

Polyarteritis Nodosa
- ❑ results from peripheral nerve and nerve root infarction
- ❑ mononeuritis multiplex, GBS and roots at C5-7 and L2-4 may be involved
- ❑ multiple mononeuropathies occur in at least 50% of patients

Giant Cell Arteritis (see Rheumatology Chapter)

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