

NEUROLOGY

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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?
 - vascular
 - infectious
 - neoplastic
 - degenerative
 - inflammatory-immunologic
 - congenital-developmental
 - traumatic
 - toxic
 - 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 vertigo nystagmus	clumsiness lack of coordination unsteadiness	tandem gait impairment dysdiadochokinesis abnormal heel-shin, finger-nose, nystagmus
brainstem	cranial nerve palsies vertigo nystagmus	diplopia, dizziness, deafness dysarthria, dysphagia decreased strength/sensation in face and body nystagmus	cranial nerve abnormalities UMN lesions (bilateral) sensory loss (crossed)
spinal cord	spinal cord syndromes ALS	sensory level distal weakness bowel and bladder changes	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 muscular dystrophies	proximal symmetric weakness no sensory loss	normal/decreased tone normal/decreased reflexes minimal atrophy
disorders not confined to one level	headache stroke multiple sclerosis CNS infections HIV/AIDS alcohol		

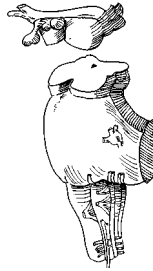
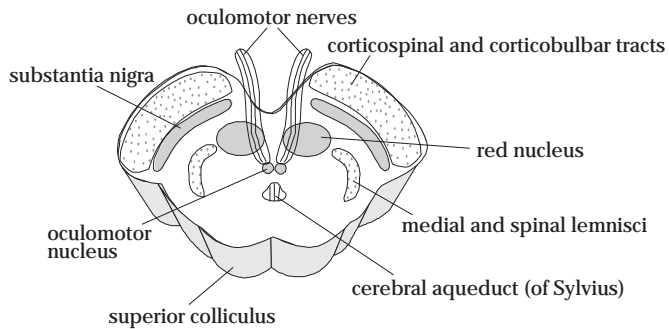


Figure 1. Section through the Midbrain at the Level of the Superior Colliculus

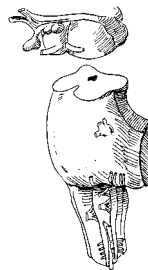
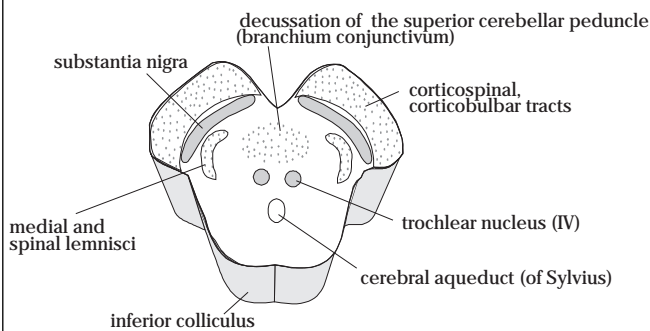


Figure 2. Section through the Midbrain at the Level of the Inferior Colliculus

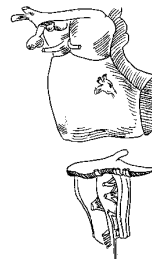
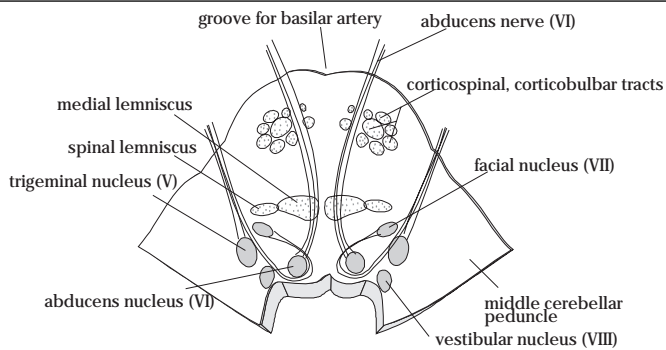


Figure 3. Section through the Pons

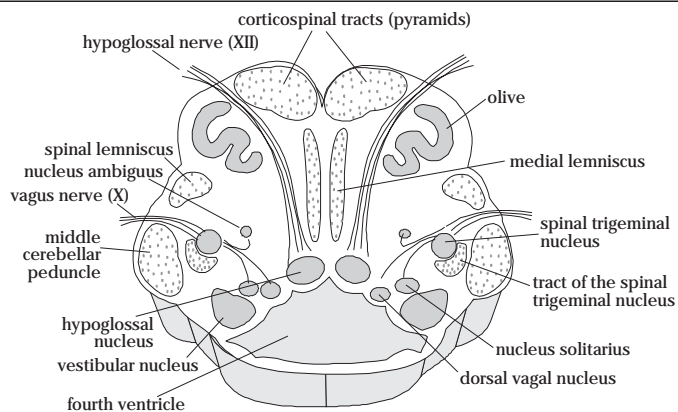


Figure 4. Section through the Open Medulla

Figures drawn by Dr. P. Stewart

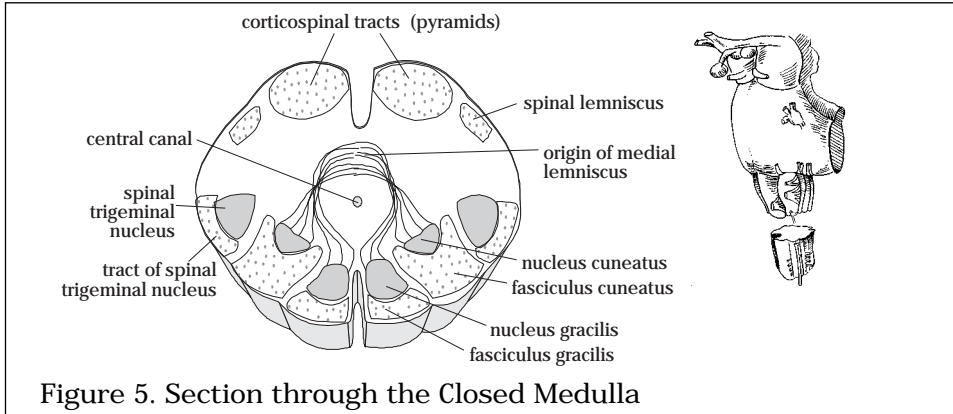


Figure 5. Section through the Closed Medulla

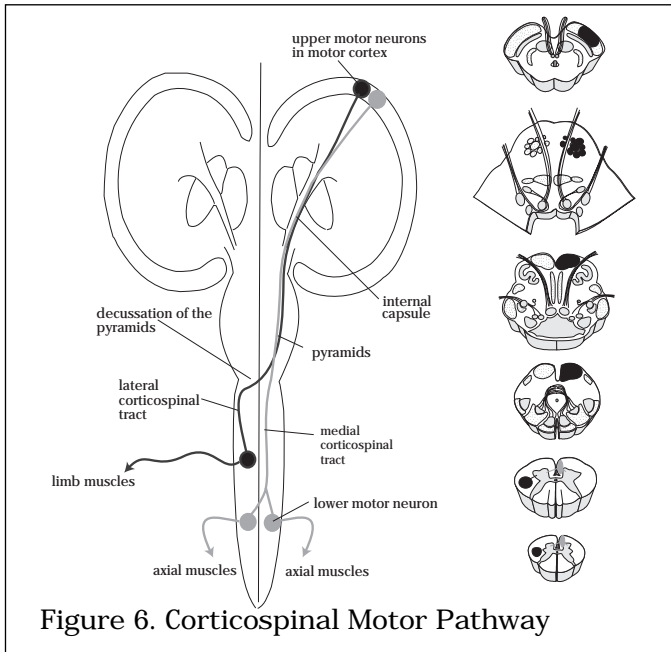


Figure 6. Corticospinal Motor Pathway

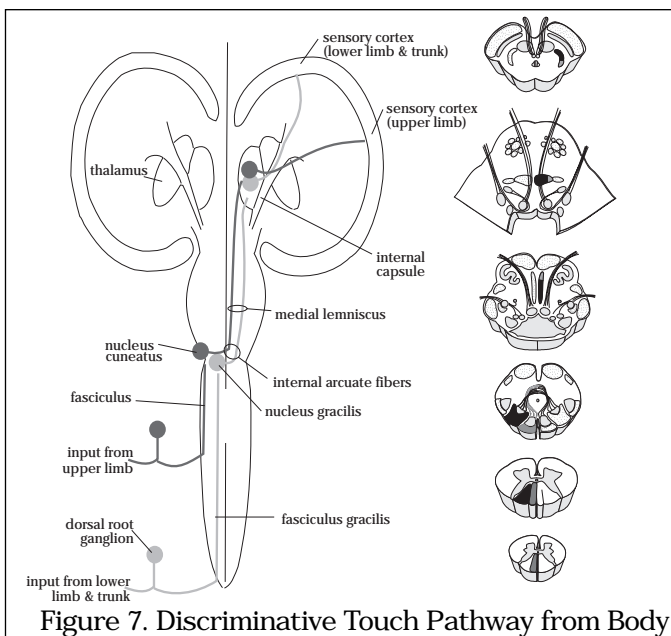
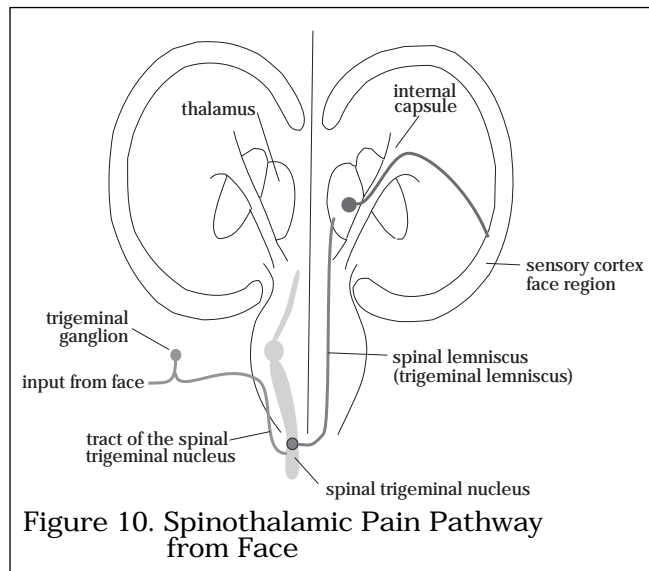
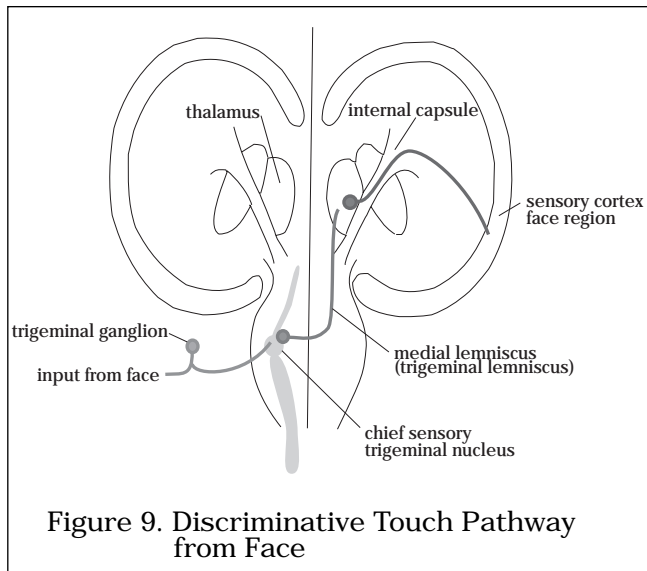
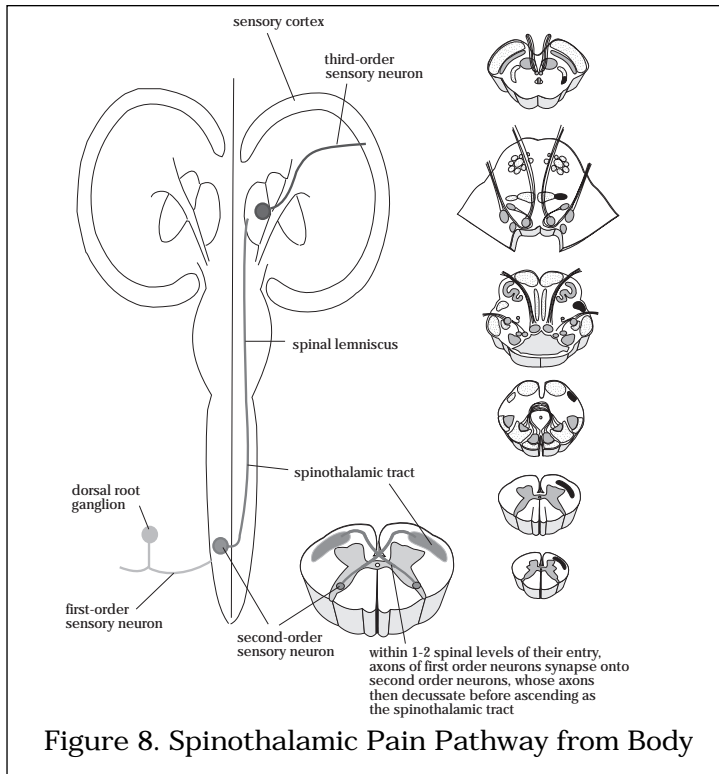


Figure 7. Discriminative Touch Pathway from Body

Figures drawn by Dr. P. Stewart



Figures drawn by Dr. P. Stewart

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, and new-onset seizures

MRI

- better than CT in the evaluation of brainstem, posterior fossa, intramedullary spinal cord lesions

	advantage	black	gray	white
T1-weighted	anatomy	CSF, bone, often tumour and infarction as well	normal brain	fat, subacute hemorrhage
T2-weighted	pathology	bone	normal brain	CSF, brain edema, infarction, tumour

- other MR images - proton density, diffusion, flare
- 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

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
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

Indications

- infection
- bleed (since CT is negative in 10% of SAH)
- non-infectious inflammation (GBS or SLE)
- CSF chemistry for diagnosis (gammaglobulin oligoclonal banding for MS)
- CSF dynamics (e.g. NPH or spinal block)
- cytology (e.g. carcinomatosis)
- therapeutic intrathecal drug administration
- therapeutic removal of CSF (e.g. benign increased ICP)
- diagnostically for contrast injection during myelography

Contraindications

- signs and symptoms of increased ICP (papilledema, decreased LOC, progressive deficit, headache)
- do CT first and then proceed to LP if there is no shift
- obstructive hydrocephalus, or evidence of blood
- infection at LP site
- coagulopathy or thrombocytopenia

Diagnostic Tests

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

Definitions

- a seizure is a paroxysmal alteration of behaviour that results from an abnormal and excessive activity of cerebral neurons
- epilepsy is a condition characterized by a tendency to have recurrent, unprovoked seizures

CLASSIFICATION OF SEIZURES

- partial (focal) seizures
 - simple partial seizures (without impairment of consciousness)
 - with motor signs
 - with somatosensory or special sensory symptoms
 - with autonomic symptoms or signs
 - with psychic symptoms
 - complex partial seizures (with impairment of consciousness)
 - partial seizures evolving to secondarily generalized seizures
- generalized seizures
 - absence seizures
 - typical absences
 - atypical absences
 - myoclonic seizures
 - clonic seizures
 - tonic seizures
 - tonic-clonic seizures
 - atonic seizures
 - unclassified seizures
 - West syndrome
 - Lennox-Gastaut syndrome

CLINICAL APPROACH TO SEIZURES

- is the episode in question indeed a seizure?
- what are the pattern and associated characteristics of the seizure?
- is there an underlying cause for the seizure?

History

- age of onset: primary generalized seizures rarely begin before 3 or after 20
- precipitants: sleep deprivation, drugs, EtOH, TV screen, strobe
- presence of aura: implies focal onset
- 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: anxiety, abdominal pains, nausea, dizziness, behavioural disturbances, or automatisms
- post-ictal symptoms - limb pains, tongue soreness, headache, drowsiness, Todd's paralysis (hemiplegia)
- duration: ictus is short (seconds - minutes)
post-ictus can be long (minutes - hours)
- family history of seizures
- past history of neurologic insult: birth injury, head trauma, stroke, CNS infection, drug use/abuse

Clinical Pearl

- Stroke is the most common cause of late-onset (after age 50) epilepsy, accounting for 50-80% of cases

Physical Examination

- pulse (especially rhythm), BP, heart auscultation
- look for focal neurological signs which point to location of focal lesion (asymmetry of reflexes, hemiparesis, upgoing toes, or hemiparetic posturing of a foot)
- 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)
- AVMs may present as focal seizures: auscultate for bruits (carotid, orbital, cranial), visual fields, optic fundi
- head exam for evidence of trauma (look, then feel)
- skin exam: look for characteristic lesions of neurocutaneous syndromes (neurofibromatosis, tuberous sclerosis complex, Sturge-Weber syndrome)

Investigations

- CBC, sodium, glucose, calcium, magnesium, creatinine, urea, LFTs
- CXR, ECG
- EEG (focal spikes/sharp waves, or generalized spike and wave complexes) - interictal EEG is normal in 60% of cases
- increased prolactin level with grand mal seizure
- 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 damage
 - vascular (cerebral hemorrhage, cortical infarcts, AVM, cavernoma)
 - cerebral tumours
 - infections (meningitis, encephalitis, cerebral abscess, subdural empyema, syphilis, TB, HIV)
 - inflammation (sarcoidosis, SLE)

DIFFERENTIAL DIAGNOSIS

Table 4. Seizures versus Syncope

characteristic	seizure	syncope
time of onset	daytime or night-time	daytime
position	any	upright (usually)
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

- syncope
 - causes
 - neurogenic vasodepressor and vasovagal reaction
 - sympathetic nervous system failure
 - reduced cardiac output or inadequate intravascular volume
 - others (e.g. hypoxia, anemia)

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

characteristic	pseudoseizure	epileptic seizure
age	any, less common in the elderly	any
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; other people usually present	day or night
physical injury	rare or non-serious	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

- pseudoseizures
 - can be impossible to differentiate without EEG
 - often occur in epileptics
 - history of sexual abuse
- narcolepsy (cataplexy)
 - migraine: associated with sensory or motor symptoms

CLINICAL FEATURES

Simple Motor

- arise in precentral gyrus (motor cortex), affecting contralateral face/trunk/limbs
- ictus
 - 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 humunculus)
 - 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: tonus 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 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: counselling and monitoring blood levels closely, teratogenicity of antiepileptic drugs, folate 4-6 mg/day for 3 months prior to conception
- 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 5 for indications and common side-effects of major anticonvulsants
- 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
- new anticonvulsants used as adjunctive therapy: clobazam (Frisium), gabapentin (Neurontin), vigabatrin (Sabril), lamotrigine (Lamictal)

Table 5. 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	morbilloform 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 increase 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

Surgical

- ❑ for selected cases of complex partial epilepsy with an identifiable focus

STATUS EPILEPTICUS

- ❑ a life-threatening state (5-10%) when a series of seizures occurs without the patient regaining full consciousness between attacks, lasting at least half an hour
- ❑ 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

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
- ❑ 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

Assess the Cause of the Status

- ❑ draw metabolic and drug screen (EtOH most commonly)
- ❑ measure anticonvulsant levels
- ❑ CXR, EEG and consider stat CT or MRI if first seizure or if focal neurologic deficits elicited

COMA

Definition

- ❑ a sleep-like state from which the patient cannot be aroused despite vigorous noxious stimuli

Pathophysiology

- ❑ consciousness consists of 2 components
 - arousal – alertness, sleep-wake cycle
 - content – responding to external stimuli
 - i.e. seeing, feeling, hearing, speaking
- ❑ consciousness requires
 - intact cerebral hemispheres
 - 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,
 - endogenous/exogenous toxins

INITIAL EVALUATION: GLASGOW COMA SCALE

Table 6. Glasgow Coma Scale

Eye Opening (E)	Verbal Response	(V)	Best Motor Response	(M)
spontaneous	oriented and converses	5	obeys commands	6
to speech	confused conversation	4	localizes pain	5
to pain	inappropriate words	3	withdrawal to pain	4
nil	incomprehensible sounds	2	abnormal flexion (decorticate)	3
	nil	1	abnormal extension (decerebrate)	2
			nil	1

GENERAL MANAGEMENT OF A COMATOSE PATIENT (ABCDE)

- Airway and C-spine control
- 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 (use unless stat glucometer says "no need")
- Evaluate patient

EVALUATING THE COMATOSE PATIENT

History

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

Physical Examination

- assess level of consciousness (drowsy, stuporous, comatose - GCS)
- eye findings
 - pupil size
 - large = atropinics/TCAs, brainstem lesion
 - small = opiates/parasympathomimetics, pontine lesion
 - pupil equality (inequality = structural lesion)
 - pupil reactivity (reactive = metabolic/drug, cortex)
 - movements (failing oculocephalic/vestibular = brainstem lesion)
 - papilledema (increased ICP)
- general (4 N's)
 - Noggin: head injury
 - eNt: otorrhea (head injury, abscess), rhinorrhea (head injury), tongue biting (ictal), breath (for acetone, alcohol, hepatic fetor, etc...)
 - Neck: nuchal rigidity (tonsillar herniation, meningitis, subarachnoid hemorrhage)
 - Needles: "tracks" of IV drug use
- neurological
 - decortication suggests cortical/upper brainstem lesion
 - decerebration suggests upper/lower brainstem lesion
 - absent motor response suggests lower brainstem lesion
 - look for tremor, myoclonus, asterixis, other "clues"
 - reflexes not too helpful usually (unless clear asymmetry)
 - respirations
 - if RR > 20, think acidosis, acute pulmonary edema, pneumonia, PE, adult respiratory distress syndrome, salicylates
 - if RR < 8, think opiates, ACh inhibitors

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 Differential Diagnosis

- orderly, progressive, loss of function - expanding supratentorial lesion is likely
 - hematoma, neoplasm, abscess, inflammation, hydrocephalus, etc...
 - massive infarction with edema (> 24 hours old)
- simultaneous onset of impaired consciousness, pinpoint (pons) pupils, 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
- scattered neurologic 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
- send for neurosurgeon and elevate head of bed to 30 degrees
- intubate and hyperventilate (pCO₂ to 20-25 mmHg to decrease ICP)
- mannitol IV 500 ml of 20% over 30 minutes (to decrease ICP)
- stat CT/MRI

Infratentorial Lesions

- ABCDE
- stat CT/MRI
- send for neurosurgeon if cerebellar hematoma demonstrated

Metabolic Coma

- ABCDE
- if meningitis or fever
 - CT (followed by LP if no mass lesion/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, look in A MUDPILE
 - ASA
 - Methanol
 - Urea (uremia)
 - Diabetic ketoacidosis
 - Phenformin/Paraldehyde
 - INH (isoniazid)
 - Lactate
 - Ethylene glycol
- calculate osmolality (for S.I. units): $2 \times \text{Na} + \text{BUN} + \text{glucose}$
- if osmol gap, think "ol"
 - ethanol
 - methanol
 - isopropanol
 - mannitol
 - ethylene glycol
 - glycerol

DEFINITION

- ❑ irreversible loss of brain function; vital structures of the brain necessary to maintain consciousness and independent vegetative survival are damaged beyond repair

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 to extent medically possible
- ❑ 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 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 O₂/minute to prevent anoxia (apnea test)

IN MOST 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
- ❑ brainstem auditory or short latency somatic evoked responses reflecting absence of function in vital brainstem structures
- ❑ angiographic examination shows no cerebral circulation

PERSISTENT VEGETATIVE STATE

- ❑ a state of permanent unresponsiveness due to irreversible loss of cerebral cortical function BUT with intact brainstem function
- ❑ patients have normal eye opening and sleep-wake cycles, and may survive for years in this state
- ❑ different from brain death

BEHAVIOURAL NEUROLOGY

ACUTE CONFUSIONAL STATES

Clinical Features of Delirium/Acute Confusional State

- ❑ impairment of consciousness
 - alertness, attention and concentration decreased
- ❑ 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 Notes)
- 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)
 - infection (encephalitis, cerebral abscess, meningitis, AIDS)
 - neoplasia
- extracranial (remember HIT ME)
 - Hypoxia (respiratory failure, cardiac failure, acute heart block, CO poisoning)
 - Infections (exanthemata, septicemia, pneumonia, UTI)
 - Toxins, especially withdrawal (EtOH, anticholinergics, beta-blockers, L-dopa, INH, etc...)
 - Metabolic (uremia, liver failure, carcinoma, electrolyte imbalance) and nutritional (thiamine, vitamin B₁₂, folate)
 - Endocrine (hyper/hypothyroidism, hypoglycemia, Addisonian crisis, etc...)

Diagnosis

- history and physical
- urinalysis, blood cultures, and CXR
- electrolytes, urea, creatinine, glucose, ABGs, LFTs, calcium, phosphate, TSH, vitamin B₁₂, folate, CBC
- 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 if patient's behaviour disruptive
 - diazepam if DTs

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 – Intelligence, Memory, Personality

Operating Criteria for Dementia

- memory impairment plus at least two other criteria are needed for diagnosis
- memory impairment: recent before remote memory impairment
- impairment of judgement: due to inflexible thinking, and poor logic
- language impairment
- other cognitive signs
 - progressive word finding difficulty, hesitancy and inability to comprehend and communicate
 - aphasia, apraxia, agnosia, acalculia in varying degrees
- personality change
 - decline in personal manners/social awareness
 - disinhibited behaviour (sexually aggressive/criminal) occurs
 - 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
- 50-75% of dementia due to Alzheimer's disease; 10-25% due to vascular disease; 10-15% due to a mixed picture
 - ~ 75 other causes
 - medications and depression are important mimics

Approach to Dementia

- want to elicit treatable causes
- history
 - rate of cognitive decline: weeks, months/years, stepwise
 - degree of impairment of social function
 - general health
 - nutritional status
 - drug history
 - family history of dementia
- physical exam
 - mental status exam (Folstein a minimum)
 - focal neurological signs
 - involuntary movements
 - pseudobulbar signs
 - primitive reflexes (e.g. glabellar, pout, snout, palmomenta, grasp)
- investigations
 - labs: CBC, lytes, BUN, creatinine, glucose, AST, ALT, ALP, PT/PTT, albumin, Ca²⁺, phosphorus, ESR, TSH, vitamin B₁₂, folate, VDRL and FTA, urinalysis
 - CXR, ECG, EEG
 - CT or MRI
 - LP and neuropsychological testing may help

CAUSES OF DEMENTIA

D-Degenerative

Alzheimer's Disease

- most common dementia; females > males; ~ 15% of cases familial
- progression is slow over years
- memory problems, visual agnosia (ability to see but not recognize objects), apraxia (inability to perform certain motor tasks in absence of paralysis), language dysfunction
- diagnosis
 - exclusion of all other causes of dementia by history, physical and labs
 - physical exam: primitive reflexes; increased motor tone with motor dyspraxias; myoclonus/seizures may follow
- pathology: cortical atrophy, ventricular dilatation, neuritic plaques, neurofibrillary tangles, decrease in cholinergic neurons
- investigations: to find a treatable cause if present
- treatment
 - symptom relief and support (family/caregiver relief)
 - mild sedation (Trazadone) if aggressive behaviour
 - support groups
 - new acetylcholinesterase inhibitors (donepezil) may improve functional status and delay progression in mild to moderate 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: reduced 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

Other Degenerative Causes of Dementia Include

- Parkinson's disease, Huntington's disease (see Movement Disorders Section)
- progressive supranuclear palsy

E-Emotional

- depression, schizophrenia (see Psychiatry Notes)

M-Metabolic

- hypothyroidism/hyperthyroidism, hypocalcemia/hypercalcemia
- hypoglycemia/hyperglycemia
- hyperaldrenocorticism (Cushing syndrome)
- electrolyte abnormalities
- renal failure (uremia), hepatic encephalopathy
- Wilson's disease

E-Eyes and Ears

- severe hearing and visual impairment

N-Nutritional and Normal Pressure Hydrocephalus

- vitamin B₁₂ 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
 - 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
 - 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)
- alcohol - Wernicke-Korsakoff syndrome (thiamine deficiency)
- heavy metals

I-Infection

- tertiary syphilis
- AIDS
- chronic meningitis (e.g. TB)
- encephalitis
- Creutzfeldt-Jacob Disease
 - rapidly progressive, inevitably fatal prion disease of CNS characterized by progressive dementia and myoclonic seizures and affecting adults in midlife

- spread of disease: iatrogenic: corneal transplantation, injection of human growth hormone (prepared from pooled cadaveric pituitary glands)
- new variant CID - "mad cow disease" by oral ingestion
- prodromal symptoms: fatigue, depression, weight loss, insomnia, anorexia
- delirium; changes in behaviour, 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: changing over course of disease from one of diffuse nonspecific slowing to one of 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-Arteriosclerotic and Vascular

- multi-infarct dementia
 - most common vascular dementia, but often overdiagnosed
 - 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

APHASIA (Dysphasia)

- aphasia is a disorder of language produced by brain damage characterized by errors in speech production, impaired comprehension, 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

- 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)

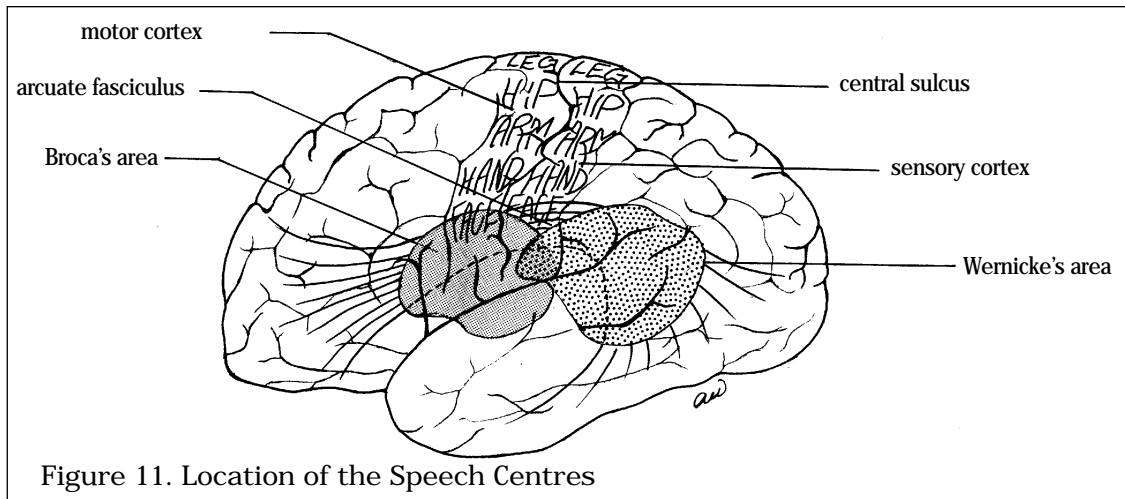


Figure 11. Location of the Speech Centres

Figure drawn 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
 - characteristics of aphasia (vs. dysarthria)
 - e.g. "sook" instead of "book", "table" instead of "chair"
- comprehension - verbal and written
- naming
- writing

Table 7. 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 - worse than spontaneous speech
naming	poor	poor	poor	poor
comprehension (verbal + written)	preserved	poor	poor	preserved
writing	poor	content abnormal good penmanship	poor	penmanship preserved
associated features	hemiparesis	none	hemiplegia hemianesthesia visual field defect	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

- 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, post-cardiac surgery, CO poisoning)
- 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

- lesion in parietal and/or premotor cortex
- disorder of skilled movement that cannot be accounted for either by weakness, ataxia or sensory loss
- 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

- lesion in parietal/occipital lobe
- examine sensory pathways: must be normal
- disorder in the recognition of the significance of sensory stimuli
- 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 paralysis (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**CLASSIFICATION**

- akinetic-rigid syndromes: characterized by a lack of movement (akinesia) or slowness of movement (bradykinesia), and increased muscle tone (rigidity), e.g. Parkinson's disease
- dyskinesias: characterized by abnormal involuntary movements, e.g. tremor, chorea, athetosis, ballism, myoclonus, dystonia, tics

NEURONAL CONNECTIONS OF THE BASAL GANGLIA

(see Figure 12)

- involved in regulating intended/programmed movement
- important in controlling the direction, speed, amplitude of movement
- two pathways link the putamen and globus pallidus pars interna (GPi)
 - the "indirect" pathway: from the putamen to globus pallidus pars externa (GPe) via the subthalamic nucleus (STN) to the GPi
 - the "direct" pathway: from the putamen to the GPi
- the output neurons in the indirect pathway utilize GABA and enkephalin, while the output neurons in the direct pathway utilize GABA and substance P

- ❑ the substantia nigra pars compacta (SNpc) is inhibitory to the neurons of the indirect pathway, but excitatory to the neurons of the direct pathway
- ❑ background activity in the putamen is low-frequency firing, whereas background activity in the GPi is high-frequency firing
- ❑ a burst of activity in the putamen (e.g. produced by a burst of activity from the cortex), facilitated by the SNpc, would produce a pause in the GPi via the direct pathway
- ❑ this burst would release the thalamus from tonic inhibition and excite the cortex, thus the direct pathway is a positive feedback circuit
- ❑ the same burst of putamenal neurons of the indirect pathway, dampened by the SNpc, would increase inhibition to GPe, thus decrease inhibition to the STN, and result in an excitation of the neurons of the GPi to even higher levels of activity, depressing the thalamus; thus the indirect pathway is a negative feedback circuit

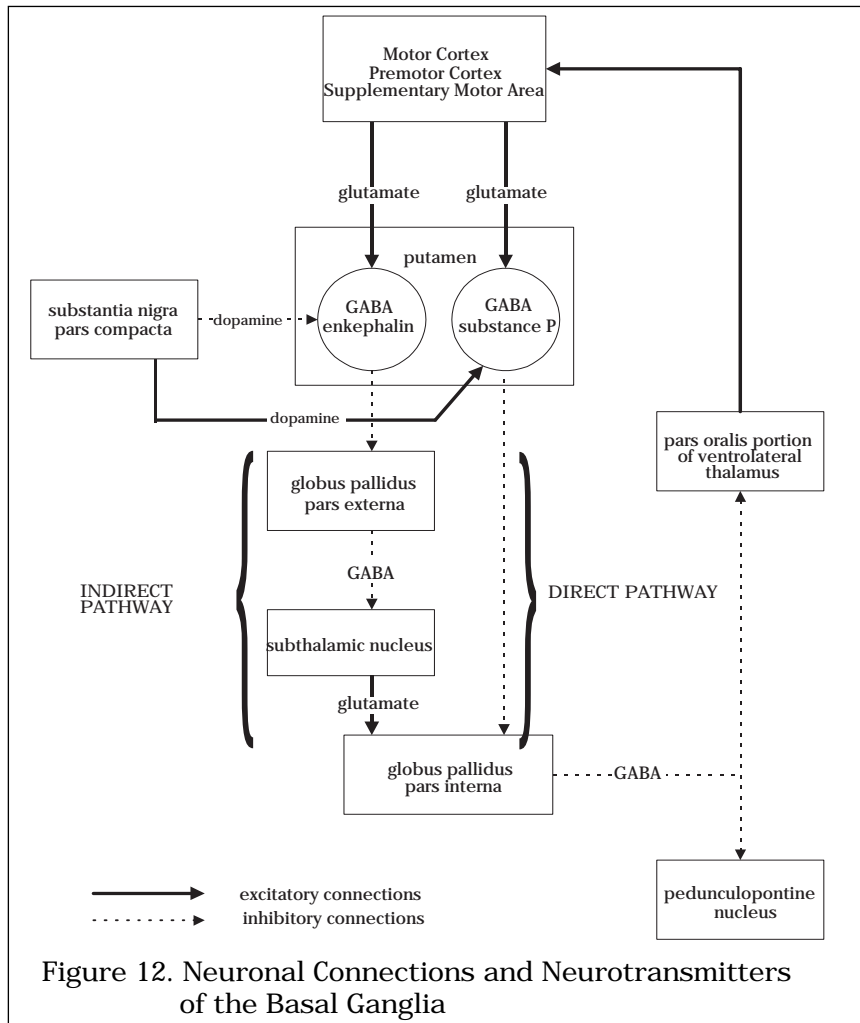


Figure drawn by David Chan

PARKINSON'S DISEASE

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

Clinical Features

- ❑ characteristic symptoms and signs ("TRAP")
 - Tremor (rest, pill-rolling, 4-7 Hz, can be suppressed by voluntary movement)
 - Rigidity (lead pipe and cogwheeling)
 - Akinesia/Bradykinesia
 - Postural instability (festinating gait, retropulsion, falls)

- other features
 - mask-like face (hypomimia), lack of blinking
 - blepharoclonus (fluttering of closed eyelids)
 - dysphagia, drooling, hypophonia
 - micrographia
 - gait: start hesitation, small shuffling steps, loss of arm swing
 - subcortical dementia

Differential Diagnosis

- therapeutic drugs: neuroleptics, metoclopramide
- toxins: MPTP (drug abusers), manganese, carbon disulfide, CO
 - “Parkinson Plus” disorders
 - 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
- result is relative increase in GABAergic output from striatum
 - Lewy bodies (eosinophilic intraneural inclusion granules)
 - not specific to PD

Treatment

- deprenyl (MAO-B inhibitor) may slow progressive course
- levodopa + peripheral decarboxylase inhibitor (i.e. Sinemet) for akinesia and rigidity
- dopamine agonists (bromocriptine, pergolide, ropinirole, pramipexole)
- anticholinergics (benztropine, trihexyphenidyl) for tremor
- NMDA antagonists (amantadone)
- neurosurgical options
- therapeutic problems: orthostatic hypotension, sudden loss of therapeutic effect, wearing off, dyskinesia, freezing

“PARKINSON PLUS” DISORDERS

Progressive Supranuclear Palsy (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, “anguished” facial expression
- may take years for characteristic syndrome to develop fully
 - supranuclear ophthalmoplegia - abnormality of vertical gaze (if eyes are fixated on a target and neck is flexed and extended, full or increased 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

Shy-Drager Syndrome

- Parkinsonian features
- autonomic insufficiency (orthostatic hypotension, impotence, incontinence, constipation, dysphagia)
- orthostatic hypotension associated with loss of intermediolateral horn cells and pigmented nuclei of the brainstem

TREMOR

Definition

- rhythmic oscillatory involuntary movement

Rest Tremor

- slow
- the characteristic tremor of Parkinsonism
- hands - pill rolling, alternating flexion/extension of fingers or hands, alternating pronation/supination of forearms
- best examined for with hands resting in lap, can be brought out by tasks of concentration

Postural and Action (Kinetic) Tremor

- fast
- seen best with arms and hands outstretched
- physiological
 - always present, imperceptible to the eye
- exaggerated physiological
 - anxiety, sleep deprivation
- drugs
 - theophylline, lithium, caffeine
- drug withdrawal
 - 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 beta-blocker contraindicated (diabetes, asthma)

Intention Tremor

- seen in diseases of cerebellar outflow (worsens with alcohol)
 - tremor of limbs or head
 - intention tremor worse at end point of movement; contra-axial tremor
 - may be associated with dysarthria, nystagmus and ataxia
- best examined for with finger to nose testing, heel to shin testing

Investigation of Tremor

- all patients under 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. anticipation)
- 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
- slight alterations in character are often the first signs: irritable, impulsive, eccentric
- emotional disturbances: depression, less communicative, more socially withdrawn
- gradual onset with subsequent progression of chorea and 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 counselling extremely important
- distinguish from benign hereditary chorea and exclude senile chorea
- treatment: haloperidol most effective for suppressing movement disorder, but increases postural instability

Other Types of Chorea

- Wilson's disease: autosomal recessive disorder of copper metabolism that produces neurologic and hepatic dysfunction (corneal Kayser-Fleischer rings and copper deposition in liver)
- Sydenham's chorea: primarily complication of previous GABHS 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
- senile chorea: no dementia, older age of onset
- benign hereditary: AD with incomplete penetrance, childhood onset, intellect preserved, mild

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
- neuroleptics are often effective for symptomatic treatment

DYSTONIA

- sustained torsion spasms of muscle contraction which distort the limbs, trunk or face into characteristic postures
- focal dystonia - disturbance restricted to localized muscle groups, e.g. writer's cramp
- segmental dystonia
- generalized dystonia e.g. idiopathic torsion 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

MYOCLONUS

- rapid, shock-like muscle jerks which are 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 neurologic symptoms
 - epileptic: seizure disorder predominates
 - symptomatic: part of another disorder - degenerative (Wilson's, Huntington's, Alzheimer's); infectious (Creutzfeldt-Jakob 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
 - also result from similar causes as generalized symptomatic
- treatment
 - treat underlying cause; valproate, clonazepam

TICS

- brief, rapid, involuntary movements, 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, and attention deficit hyperactivity disorder, or a mood disorder
 - often familial clustering, M > F
- treatment
 - simple tics may respond to benzodiazepines
 - haloperidol and pimozide are the most effective therapy for Tourette Syndrome
 - usually do not treat unless marked tic or disabling

Table 8. 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

CRANIAL NERVES

CRANIAL NERVE I (OLFACTORY)

Function

- special sensory – smell

Clinical Assessment

- must test both nostrils separately with non-irritating stimuli (e.g. coffee)
- irritating stimuli (e.g. ammonia) irritate free nerve endings

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: odours 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, subarachnoid hemorrhage, chronic meningeal inflammation
 - meningioma, aneurysm

CRANIAL NERVE II (OPTIC)

Function

- special sensory – vision

Clinical Assessment

- test each eye individually for:
 - visual acuity
 - visual fields
 - 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

- branchial 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
- 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 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
 - posterior communicating artery aneurysm: pupil involved early, headache over affected eye
 - cavernous sinus (internal carotid aneurysm, meningioma, sinus thrombosis): CN IV and VI also often involved, pain and proptosis may occur
 - ischemic (diabetes, temporal arteritis, hypertension)
 - pupil often spared

Clinical Pearl

- A pupil-sparing third nerve palsy usually has a medical etiology e.g. vasculitis, ischemia etc...
- Pupillary involvement usually indicates nerve compression e.g. tumour, aneurysm etc...

CRANIAL NERVE IV (TROCHLEAR)

Function

- branchial 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 (diabetic, hypertensive): most common
 - cavernous sinus (carotid aneurysm, thrombosis)
 - CN III and VI usually involved as well
 - orbital fissure (tumour, granuloma)
 - retroorbital pain; CN III and VI, CN IV may also be involved
 - at risk during neurosurgical procedures in the midbrain because of long intracranial course

CRANIAL NERVE V (TRIGEMINAL)

Function

- general sensory (V₁ - ophthalmic, V₂ - maxillary, V₃ - mandibular)
 - face, scalp to top of head, conjunctiva
 - mucous membranes of nasal and oral cavities
 - anterior 2/3 of tongue
 - part of tympanic membrane
 - meninges of anterior and middle cranial fossae
- branchial motor (V₃ - mandibular)
 - muscles of mastication
 - masseter, temporalis, pterygoids
 - tensor tympani, tensor veli palatini, mylohyoid, anterior belly of digastric

Clinical Assessment

- corneal reflex (V₁ sensory and VII motor)
- jaw jerk (V₃ sensory and motor)
- sensation on face, forehead
 - sensory loss in V₁, V₂ or V₃ distribution
 - root or peripheral nerve lesion
 - sensory loss in "onion skin" distribution
 - brainstem lesion

Trigeminal Nerve Lesions

- common lesions
 - pons (vascular, neoplastic, demyelinating, syringobulbia)
 - petrous apex (petrositis)
 - orbital fissure, orbit, cavernous sinus
 - skull base (nasopharyngeal or metastatic carcinoma, trauma)
 - cerebellopontine angle
 - acoustic neuroma, trigeminal neurilemmoma, subacute or chronic meningitis
 - other causes (diabetes, 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 V₃ distribution +/- V₂, V₁
 - 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
 - tumours of cerebellopontine angle (rare)
 - demyelination at root entry zone of trigeminal nerve
- 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

- branchial 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 raised ICP
 - cavernous sinus (carotid aneurysm, thrombosis)
 - vascular - may be secondary to DM, hypertension, or temporal arteritis

Clinical Pearl

- CN VI has the longest intracranial course and is thus vulnerable to raised intracranial pressures, 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

- lower motor neuron lesion
 - the entire face on ipsilateral side is weak
 - both voluntary and involuntary movements are affected
- upper motor neuron 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, GBS, diabetic mononeuropathy, parotid gland pathology

Bell's Palsy

- an idiopathic benign lower motor neuron 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
 - 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 hypertensive
 - if symptoms of hyperacusis, abnormal tearing

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)

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)
 - if heard better in 'deaf' ear = conductive loss
 - if heard better in 'good' ear = sensorineural loss in the 'deaf' ear
 - compare air and bone conduction (Rinné test)
 - air > bone conduction = sensorineural loss or normal
 - bone > air conduction = conductive loss
- more sophisticated tests (audiometry) usually required for formal assessment
- vestibular dysfunction is often manifested by nystagmus (see Vertigo Section, ENT Notes)

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)

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
 - to striated muscles of the pharynx, tongue and larynx
- visceral motor
 - to 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, affecting swallowing
 - pharyngeal weakness, affecting swallowing
 - laryngeal weakness, affecting 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
 - supplies 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
 - 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
 - as patient protrudes tongue, look for deviation to the 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 13)

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

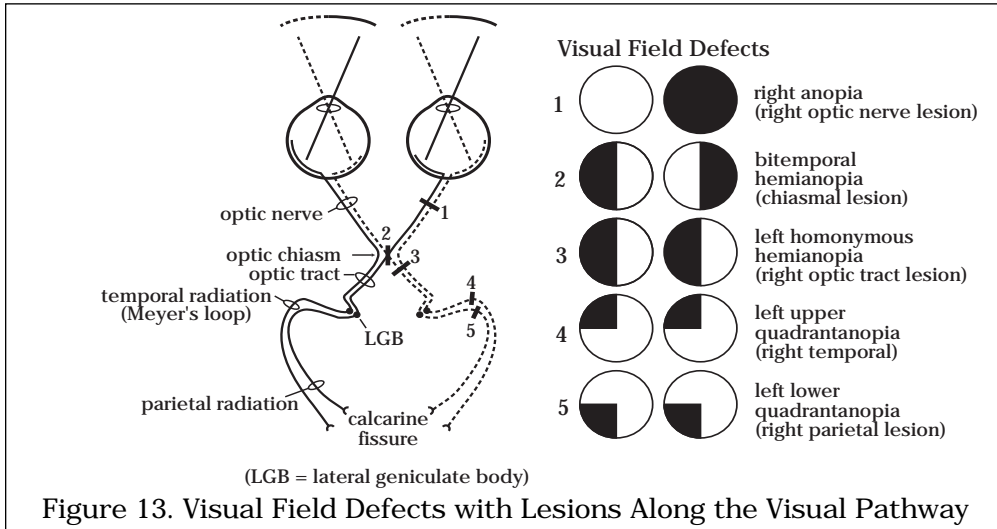


Figure drawn by Cecil Hahn

DISORDERS OF LATERAL GAZE

- ❑ voluntary eye movements are triggered in the frontal eye fields, located anterior to the precentral gyrus, bilaterally
- ❑ each frontal eye field controls voluntary saccades to the contralateral side
- ❑ 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, so the eyes deviate towards the side of the lesion
- ❑ in contrast, a unilateral lesion in the pons prevents voluntary saccades to the ipsilateral side, so the eyes deviate away from the lesion (this is because the corticopontine pathways cross)

	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 Temporal Arteritis bilateral rarely in adults may alternate in MS frequent in children	headache, nausea, vomiting, focal neurological deficits always	nonarteritic usually no other symptoms typically unilateral
Pupil	no anisocoria RAPD present	no anisocoria, no RAPD	no anisocoria RAPD present
Fundus	Retrobulbar - normal (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 increase relapse rate section for treatment if arteritic	treat specific cause of increased ICP	consider ASA for non-arteritic ischemic neuropathy see Temporal Arteritis section

Other Causes of Disc Edema

- central retinal vein occlusion
- systemic illness
- hypertension, vasculitis, hypercapnia
- toxic/metabolic/nutritional deficiency
- infiltration
 - neoplastic: leukemia, lymphoma, glioma
 - non-neoplastic: sarcoidosis
- pseudotumour cerebri
 - idiopathic signs and symptoms of high 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), and blood (CBC, PT, PTT, ANA)
- treatment: see Stroke Section

PUPILLARY SIGNS (see Table 10)

Relative Afferent Pupillary Defect (RAPD, Marcus Gunn Pupil)

- a failure of direct pupillary responses to light
- a sign of damage to the afferent portion of the pupillary reflex arc - (CNI)
 - 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 ptosis, miosis, and anhidrosis
- ❑ may occur anywhere along the sympathetic pathway on the affected side
 - 1st order neuron (preganglionic): hypothalamus brainstem stroke, spinal tumour
 - 2nd order neuron (preganglionic): apical lung cancer (Pancoast's tumour), paravertebral mass
 - 3rd order neuron (postganglionic): cluster headache, migraine, cavernous sinus mass
- ❑ 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 10. Summary of Pupillary Signs

	Site of Lesion	Features	Light and Near	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		not present	dilates/constricts	
light-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

Classification

- pendular
 - movements of equal velocity in two directions
- jerk
 - two components: a fast phase and a slow phase
 - nystagmus is named according to direction of the fast phase

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 H₂O instilled into ear decreases/increases relative stimulus from CN VIII, resulting in nystagmus to the opposite/same side
 - for caloric testing, remember COWS
 - Cold water results in nystagmus to Opposite side
 - Warm water results in nystagmus to Same side
- pathological
 - nystagmus towards normal side; may have torsional component
 - vertigo present; tinnitus and sensorineural deafness common in Ménière's, vestibular neuronitis, vascular disease
 - in benign positional vertigo, elicit by Hallpike's maneuver which fatigues with repetition

Cerebellar Disease

- horizontal jerk nystagmus towards the side of the cerebellar lesion (opposite to labyrinthine nystagmus)
- gaze-evoked nystagmus in all directions suggests drug (diltiazem, sedatives, EtOH) or diffuse cerebellar etiology

Brainstem Disease

- vertical nystagmus, jerk nystagmus with fast phase in direction of gaze; vertigo uncommon
- other signs of brainstem involvement present
- pons-midbrain, medial longitudinal fasciculus
 - "ataxic nystagmus"/ "internuclear ophthalmoplegia"
 - MLF links CN VI in pons with CN III in midbrain
 - a lesion causes disconjugation of lateral eye movements, especially during rapid changes of gaze, so that one eye is slow to adduct while the abducting eye shows coarse horizontal nystagmus
 - frequently bilateral
 - upbeating nystagmus on upgaze often present
 - usually indicates MS; but vascular disease, neoplasia, or Wernicke's encephalopathy may be etiological factor
- note: acquired pendular nystagmus signifies MS
- lower medulla
 - downbeating nystagmus on forward or lateral gaze can be seen in lesions around the cervicomedullary junction (e.g. Chiari malformation, cerebellar degeneration)
 - upbeating nystagmus in primary gaze can be seen in lesions in the medulla (e.g. MS, tumour, Wernicke's)

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

- ❑ vertigo is defined as an illusion of movement of self or surroundings (usually rotatory/spinning); vertigo must be distinguished from other causes of dizziness, such as presyncope, gait abnormalities and psychogenic phenomena

Causes related to anatomical structures

End organ --> CN VIII --> C.P.A. --> Brain Stem --> Cerebellum

<----- peripheral -----> <----- central ----->
(common) (uncommon)

Feature	Peripheral	Central
nystagmus	horizontal, sometimes torsional, increases when looking away from lesion	vertical or rotatory, increases when looking toward side of lesion, persistent
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	often falls toward the side of lesion
visual fixation	inhibits nystagmus	no change in nystagmus

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	

Assessment of Vertigo

- ❑ history
 - nature of vertigo: duration? positional? recurrent?
 - auditory symptoms?
 - neurological symptoms?
 - ototoxic drugs? (e.g. aminoglycosides)
- ❑ clinical examination
 - otoscopy, tuning fork tests
 - 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

- ❑ 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: 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, worse when watched, often confused with chorea

- ❑ 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

- ❑ vermis (midline)
 - coordinates trunk and leg movement
- ❑ lateral hemispheres
 - control ballistic and finely coordinated limb movements, mostly upper limb

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, staccato speech)
- ❑ 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

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
- ❑ with or without previous Wernicke's encephalopathy:
 - Wernicke's encephalopathy: confusion, ataxia, ophthalmoplegia (CN VI nerve)

Paraneoplastic Cerebellar Degeneration

- ❑ diffuse cerebellar atrophy
- ❑ 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

Spinocerebellar Degeneration

- ❑ Friedrich's ataxia
 - autosomal recessive (chromosome 9)
 - onset in childhood
 - progressive gait ataxia, followed by limb ataxia within 2 years
 - leg weakness, knee and ankle areflexia, positive Babinski
 - kyphoscoliosis, pes cavus
 - impaired joint position sense and vibration sense in legs
 - cerebellar dysarthria
 - degeneration of spinocerebellar, pyramidal and large sensory fibers

- ❑ cortical cerebellar atrophy
 - predominantly cerebellar (vermis)
 - late onset (30-50 years), sporadic and familial (AD)
 - slow progressive ataxia with gradual onset
- ❑ olivopontocerebellar atrophy
 - symptoms similar to cortical cerebellar atrophy
 - plus extrapyramidal and pyramidal dysfunction; and occasional dementia, autonomic insufficiency, and sensory impairment

DIFFERENTIAL DIAGNOSIS 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

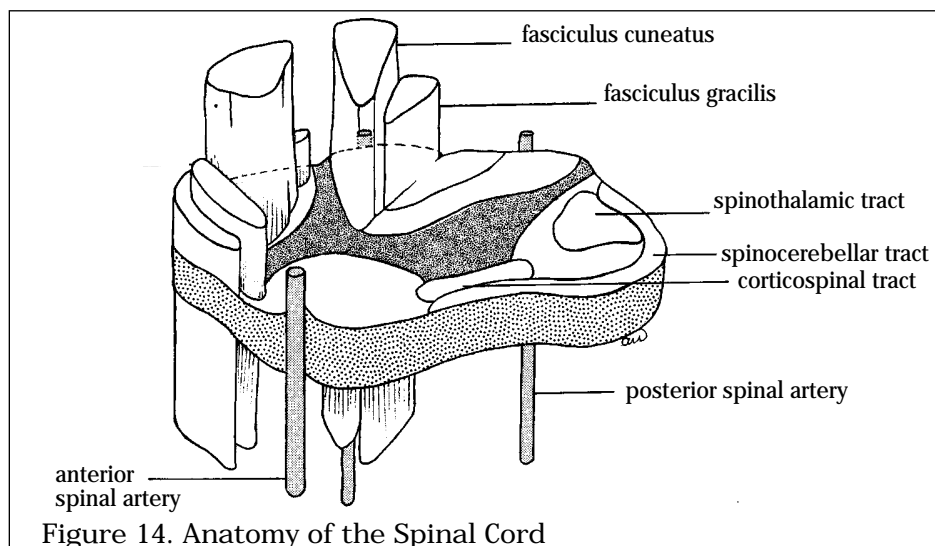


Figure 14. Anatomy of the Spinal Cord

Figure drawn 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
- radicular symptoms (pain, dermatomal sensory loss)
 - extradural: disc, trauma (cervical spondylosis), bone, tumour (metastases), abscess
 - intradural, extramedullary: meningioma, neurofibroma, arachnoid cyst
 - intradural, intramedullary: demyelination, tumour, infarct, hemorrhage (AVM), degeneration (ALS, SACS), syrinx

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**Brown-Sequard Syndrome**

- ipsilateral hemiplegia or monoplegia below lesion
- ipsilateral loss of vibration and proprioception below lesion
- contralateral loss of pain and temperature below lesion

Central Cord Syndrome

- 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), e.g. syringomyelia and intrinsic tumours

Anterior Spinal Artery Syndrome

- sparing of posterior columns

Subacute Combined Degeneration of the Spinal Cord

- corticospinal and posterior columns are affected e.g. vitamin B₁₂ deficiency

Conus Medullaris

- hypotonic bladder and rectal sphincters
- pain and loss of sensation in saddle distribution in perineum

MOTOR NEURON DISEASES**Spinal Muscular Atrophy**

- disorders beginning in infancy or childhood characterized by skeletal muscle wasting due to progressive degeneration of cells in the anterior horn and medulla
- infantile form
- floppy baby, survival < 1 year
 - Werdnig-Hoffmann disease
- 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
 - sparing of bowel and bladder function
- investigations
 - EMG: fibrillation, chronic neurogenic lesion
- treatment
 - supportive only

Table 13. Comparison of UMN and LMN Lesions

	Upper Motor Neuron	Lower Motor Neuron
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

SPINAL ROOT

- compression
 - by disc (C5-7, L4-S1)
 - by bone: trauma, osteophytes
 - by tumour: neurofibroma, schwannoma, meningioma, metastatic
- symptoms of radicular pain, dermatomal sensory and motor loss, muscle atrophy
- multiple spinal roots: think of carcinomatous meningitis

Clinical Pearl

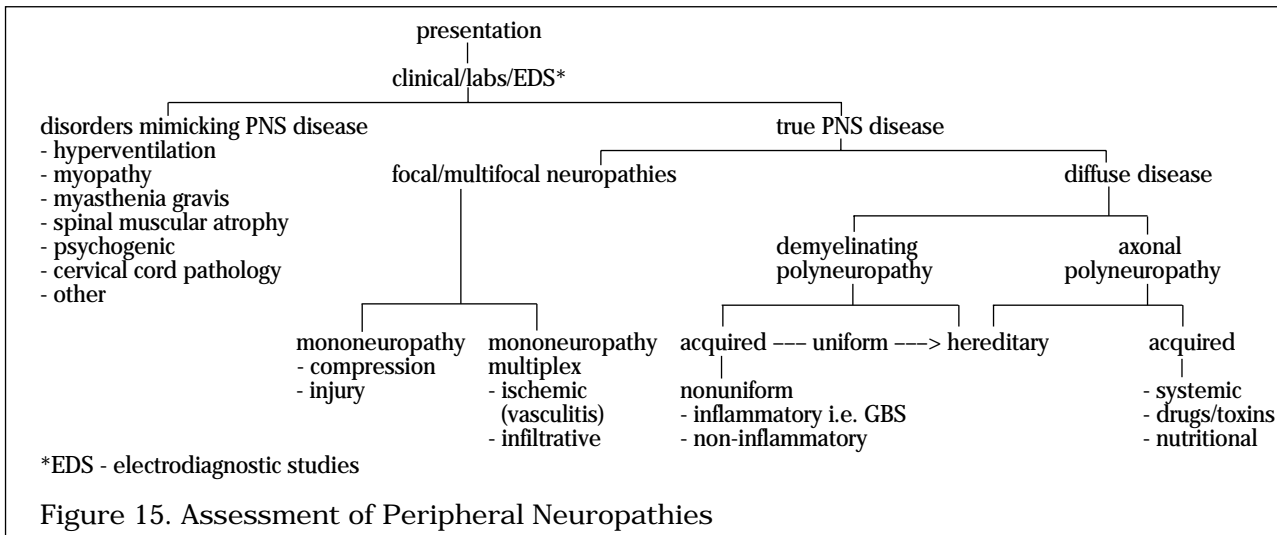
- Diseases of the spinal roots often resemble peripheral neuropathies, and are associated with pain radiating down the limb (the hallmark of root disease)

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
 - if sensory, may have paresthesias in addition to sensory loss
 - autonomic dysfunction includes anhidrosis, orthostatic hypotension, impotence, bladder/bowel dysfunction, impairment of pupillary responses
 - focal vs. diffuse disease
 - proximal vs. distal
 - upper vs. lower extremities
 - fibre size selectivity
 - large: weakness, loss of joint position, vibration, and touch/pressure
 - small: pain and temperature loss, autonomic dysfunction
 - relationships to systemic illness (DM, RA)
 - drugs, EtOH, environmental factors

- family history, especially with unexplained polyneuropathy from childhood (hereditary) whereas in 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, QST)
 - 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



Clinical Pearl

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

FOCAL AND MULTIFOCAL NEUROPATHY

Etiology

- ❑ most common for focal involvement: injury/entrapment
- ❑ ischemic: diabetes, 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

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 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, diabetic, inflammatory, vascular)
- ❑ pathology: axonopathy vs. myelinopathy vs. neuronopathy
- ❑ fibre 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

MYELINOPATHIES

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

Hereditary Motor Sensory Neuropathy (HMSN)

- ❑ HMSN Type I (Charcot-Marie-Tooth)
 - etiology: AD, occasionally AR
 - epidemiology: late childhood/adolescence
 - 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
 - main disability is difficulty walking
 - pathology: segmental demyelination and onion bulb

Acquired Myelinopathies

Guillain-Barré Syndrome (GBS) / Acute Inflammatory

Demyelinating Polyneuropathy (AIDP)

- ❑ acute, usually rapidly progressive form of polyneuropathy characterized by proximal muscle weakness 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
 - 60% preceded by mild respiratory or GI infection, particularly *Campylobacter jejuni*, CMV, EBV, *Mycoplasma pneumoniae*
- ❑ etiology
 - unknown, may be autoimmune
 - inflammation of nerve roots and peripheral nerves
- ❑ diagnosis
 - 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 Guillain-Barré syndrome
 - > 50% have pain and aching in muscles of hips, thighs, back
 - paresthesias early on
 - can progress to total muscle paralysis and death from respiratory failure
 - occasionally autonomic disturbances
 - cellular rise in total protein in CSF by end of first week of symptoms
 - Miller-Fisher variant 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
 - 10% have a relapsing or fluctuating course
- ❑ treatment
 - IV gamma globulin and plasmapheresis
 - shorten 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, with maximal severity after weeks or months
- ❑ more likely to have relapsing or fluctuating course

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
 - diabetes, hypothyroid
 - 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 fibre (i.e. pain/temperature, absent ankle jerk)
- ❑ malignancy
 - subacute motor neuropathy in lymphoma
 - sensorimotor neuropathy in lung carcinoma
 - sensory in paraneoplastic small cell lung or breast carcinoma
- ❑ drugs
 - usually dose-related: cisplatin, vincristine, disulfiram, dapsone, antiretrovirals, nitrofurantoin, isoniazid, 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 neuronitis, carcinomatous sensory neuronopathy

DIABETIC POLYNEUROPATHIES

- ❑ 15% of diabetics have symptoms of mixed, focal, multifocal, or polyneuropathies
 - ~ 50% will have abnormal NCS

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
- 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
- acute painful neuropathy: weight loss, intense foot pain, good response to glucose control

NEUROMUSCULAR JUNCTION DISORDERS

MYASTHENIA GRAVIS

Epidemiology

- bimodal age of onset: 20's female/60's male
- < 60 years associated with thymic hyperplasia
- > 60 years associated with thymomas
- associated with other autoimmune diseases: IDDM, thyroid disease, vitiligo

Pathophysiology

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

Signs and Symptoms

- episodic muscle weakness, chiefly in muscles innervated by cranial nerves, and characteristically improved by cholinesterase-inhibiting drugs
- fatigability with use, relief with rest
- remitting and exacerbating course

Clinical Pearl

- Fatigability is the hallmark of diseases affecting the neuromuscular junction, with 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 CXR, CT, or MRI

Treatment

- anti-ACh inhibitors (increased ACh at receptor site)
- immunosuppressive drugs to attack underlying process:
 - steroids, azathioprine
- IVIG (intravenous gamma globulin)
- plasmapheresis
- thymectomy if indicated

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

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 lower motor neuron lesion
- myopathies cause diffuse weakness, usually worse in axial and proximal limb girdle muscles
- muscle disuse causes type II fibre atrophy

Table 14. Comparison of Muscle and Nerve Disorders

	Myopathy	Neuropathy
weakness	proximal (except myotonia)	distal (except Guillain-Barré)
bulk	decreased late	decreased
reflexes	normal, decreased late	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

Clinical Pearl

- Proximal and symmetric limb weakness with normal sensation are hallmark symptoms and signs of muscle diseases

POLYMYOSITIS/DERMATOMYOSITIS

- 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)
- 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
- diagnosis
 - increased CPK
 - circulating antibodies - RF, ANA
 - EMG myopathic (myopathic motor units on EMG and spontaneous activity - fibrillation potentials, increased insertional activity)
 - muscle biopsy showing destruction of muscle fibres with inflammatory cells
- treatment
 - steroids or immunosuppressives (prednisone 60-80 mg/day, Imuran)
- see Rheumatology Notes for additional information

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
 - 1/4000 live male births
 - X-linked recessive, onset 3-6 years, 40% sporadic
- signs and symptoms
 - hip girdle weakness (waddling gait), 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 elevated
 - 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 11 years

- ❑ signs and symptoms
 - less severe than Duchénne
 - cardiac muscles spared
 - mental retardation rare
 - same gene, different mutation

Myotonic Dystrophy

- ❑ epidemiology
 - autosomal dominant (19q), 5/100 000, age of onset of 20-30 years
- ❑ signs and symptoms
 - distal weakness, myopathic facies (thin, narrow face, ptosis, temporal 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
 - autosomal dominant (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

HEADACHE

- ❑ arises when pain-sensitive structures of head and neck are stimulated; the brain itself is insensitive to pain

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, raised ICP, tumour, abscess
- ❑ when to be concerned? (see Table 15)

Table 15. Warning signs of serious headache

- new-onset headache
- different or more severe than any previous headache; the worst headache ever
- sudden onset
- headache associated with
 - fever
 - meningeal irritation
 - projectile vomiting
 - altered level of consciousness
 - focal neurological symptoms or signs
 - recent head injury
 - optic disc edema

Differential Diagnosis

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

MIGRAINE

- ❑ recurrent attacks of headache, often severe and throbbing, usually accompanied by nausea, vomiting, photophobia or phonophobia
- ❑ 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
- familial 60%

Signs and Symptoms

- pulsating or throbbing
- typically unilateral, can be bilateral
- gradual onset, lasts hours to days
- worse with movement, straining, coughing, bending over, noise, light, odours
- 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

- the headache is preceded or accompanied by aura lasting 10-30 minutes, characterized by
 - transient focal neurologic 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
- bright light
- hormonal factors (menstruation, ovulation, exogenous estrogen, pregnancy, menopause)
- dietary factors (fasting, caffeine withdrawal, tyramine (cheeses), nitrites (bacon, salami), MSG, chocolate, alcohol (red wine))

Management Strategies

- general: identify and avoid trigger factors, get enough sleep, eat regularly, stress management
- symptomatic treatment: (acetaminophen, NSAIDs), antiemetics, ergotamine derivatives (avoid consecutive days, wait 24 hours after ergotamine), newer nasal tryptans or dihydroergotamine, IV metoclopramide, IV chlorpromazine, IV DHE (dihydroergotamine), IV prednisone if severe and prolonged
- prophylactic treatments if frequent and severe headaches, in order of increasing efficacy and rate of serious side-effects: pizotyline, TCAs, propranolol, methysergide
- other: relaxation training, biofeedback, hypnosis, acupuncture
- admit if severe headache persists for longer than two days

TENSION-TYPE HEADACHE

- very common
- F > M; onset before 40's
- signs and symptoms
 - can occur daily
 - psychological factors are present, especially anxiety, depression

- multiple episodes lasting 1/2 hour to 1 week
- pressing or tight pain, not severe, felt bilaterally or front-to-back, not aggravated by routine activity
- no aura, nausea/vomiting, phonophobia nor photophobia
- ❑ treatment
 - counselling with reassurance and education
 - removal of precipitants
 - physical methods (massage, heat, biofeedback, relaxation)
 - non-narcotic analgesics (NSAIDs probably more effective than acetaminophen)
 - prophylaxis - TCAs (e.g. amitriptyline) +/- psychotherapy

CLUSTER HEADACHE

- ❑ uncommon
- ❑ M > F; middle-age
- ❑ signs and symptoms
 - abrupt onset, often in early a.m. (waking patient up from sleep)
 - alcohol may precipitate
 - excruciating, unilateral pain surrounding a red, watery Horner's eye with a dripping, stuffy nose
 - no nausea/vomiting
 - last an hour or so, at least 1/day, everyday, for weeks to months; reappears months later
- ❑ treatment
 - prophylaxis with verapamil, methysergide (young patient), lithium, prednisone
 - acute treatment with ergotamine tryptans and/or O₂ inhalation

MEDICATION-INDUCED HEADACHE

- ❑ signs and symptoms
 - chronic daily/near daily headache
 - refractory to standard medications
 - 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
 - usually neurosurgical (see Neurosurgery Notes)

MENINGEAL IRRITATION

(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 a 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
 - see Neurosurgery Notes
 - non-contrast CT
 - lumbar puncture with CSF studies if CT negative (CT alone does not rule out SAH) or CT unavailable
 - LP contraindicated if depressed LOC, papilledema, or focal neurological signs (see LP section below)

TEMPORAL ARTERITIS

(Giant Cell Arteritis/Cranial Arteritis)

- "a local symptom for a systemic disease!"
- M = F; older age groups (> 60 years)
- signs and symptoms
 - headache is slight, transient -> severe, constant, throbbing, temporal
 - +/- visual symptoms (transient or permanent blindness)
 - +/- jaw and/or tongue claudication
 - polymyalgia rheumatica common
 - constitutional features are almost always present
 - examination reveals a firm, nodular, incompressible, tender temporal artery with little/no pulsatility
- diagnosis
 - elevated ESR +/- leukocytosis/anemia/altered serum proteins
 - temporal artery biopsy is confirmatory if positive; does not rule out if negative (because of 'skip lesions')
- treatment
 - high-dose prednisone until asymptomatic and normal ESR --> low-dose; treat if suspicious (don't wait for biopsy result)
- prognosis
 - 50% go blind or have other vascular catastrophes (i.e. MI, mesenteric infarction, stroke) if untreated

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

1. 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
2. HEMORRHAGIC STROKE (20%)
 - abrupt onset with focal neurological deficits, due to spontaneous (non-traumatic) bleeding into the brain
 - includes intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (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 loss of vision in one eye

Reversible Ischemic Neurological Deficit (RIND)

- neurological abnormalities similar to acute completed stroke, but the deficit disappears after 24 to 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)

- neurologic 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 2^o to stroke
 - temporal profile may differentiate between TIA's, 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 2^o hemorrhage)
 - hemorrhage
- 4. What is the pathogenesis? (i.e. mechanism of the stroke)
 - it will guide acute and chronic therapy

1. DIFFERENTIAL DIAGNOSIS: IS IT A STROKE?

- focal seizures
- other focal lesions: tumours, abscesses, subdural hematoma, demyelination, focal encephalitis (herpes simplex)
- lower motor neuron 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

2. WHERE IS THE LESION?

- see Figure 16 for vascular territories of major cerebral arteries

Hemispheric

- carotid territory (see Table 16)
- vertebrobasilar territory (posterior cerebral arteries)
 - homonymous hemianopia (without motor deficit)
 - cortical blindness

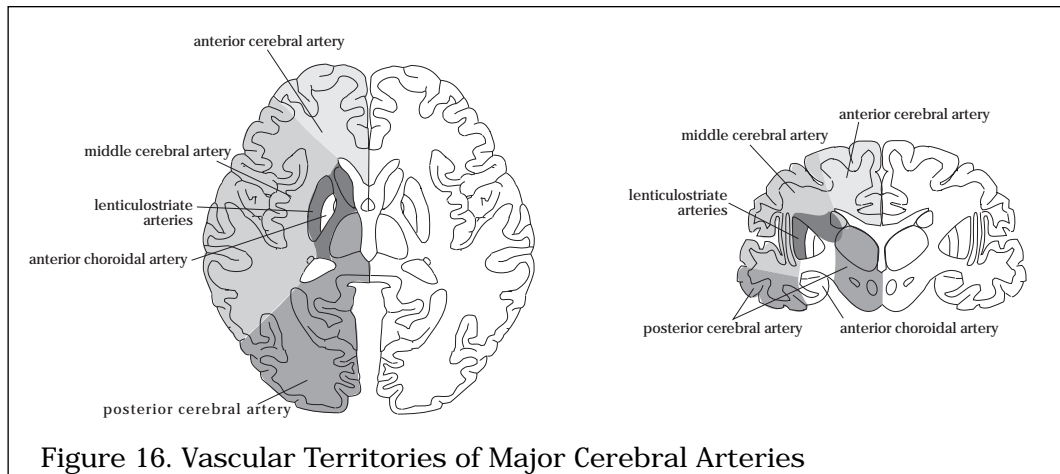


Figure 16. Vascular Territories of Major Cerebral Arteries

Figure drawn by Dr. P. Stewart

Anterior Cerebral Artery	Middle Cerebral Artery
Hemiplegia of LE	Hemiplegia of UE and face
Hemianesthesia of LE	Hemianesthesia of UE and face
Incontinence	Hemianopia
Grasp, snout, palmomental reflexes	Aphasia (if dominant hemisphere)
Behavioural and memory disturbances	Neglect of contralateral limbs
and constructional apraxia (if non-dominant hemisphere)	(if non-dominant hemisphere)
Gaze preference (away from hemiparesis)	

Brainstem

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

Indeterminate

- ☐ "hemisyndromes": hemiparesis, hemisensory loss, dysarthria

3. WHAT IS THE LESION?

	Hemorrhage	Infarct
hypertension	usually present	often present
preceding TIA	no	30% of cases
onset	often with activity	often at night or no activity
course	rapidly progressive	static (rarely stepwise)
increased ICP	yes	no
CT scan	shows blood	normal or changes of infarction
<ul style="list-style-type: none"> • CT (or MRI) is the only reliable way to rule out hemorrhage 		

4. 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
 - diabetes
 - cigarette smoking
 - high cholesterol
- treatment
 - control atherosclerotic risk factors
 - carotid endarterectomy in selected patients (see below)
 - antiplatelet agents: aspirin, ticlopidine

Cardiogenic Origin

- an embolus of clot
 - risk factors: atrial fibrillation (commonest cause), LV aneurysm, LV dysfunction, increased age, mitral annulus calcification
- air emboli - during surgery or diving
- valvular vegetations
- treatment
 - risk of embolization can be reduced with anticoagulation (heparin and warfarin)
 - higher risk of hemorrhagic infarction implying that it is imperative to exclude the presence of bleeding prior to starting anticoagulants (i.e. do 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
 - thalami
 - pons
- clinical syndromes
 - pure motor or pure sensory
 - clumsy hand dysarthria
 - ataxic hemiparesis
- risk factors
 - hypertension
 - diabetes
 - increasing age
- treatment
 - control hypertension
 - use antiplatelet drugs

Other Causes

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

INVESTIGATIONS

- laboratory
 - CBC, ESR, PT, PTT, VDRL, glucose, lipids
- 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, clopidogrel
- 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
 - limit or prevent neuronal death
 - avoid secondary complication of immobilization (e.g. pneumonia, pulmonary embolus)
 - prevent recurrent cerebral infarction
- practical steps
 - ensure the ABC's
 - DO NOT LOWER THE BP, avoid acute administration of anti-hypertensive agents, especially given parenterally or sublingually; most patients with an acute cerebral infarct are initially hypertensive and their BP will fall spontaneously within 1-2 days
 - avoid hyperglycemia which will increase the degree of lactic acidosis in ischemic tissue, increasing 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 to decrease the risk of aspiration
 - start ambulation early, and if not feasible, use subcutaneous heparin to avoid DVTs
 - make the correct etiological diagnosis so you have a rational approach to secondary prevention of stroke
 - remember that myocardial infarction is an important cause of morbidity and mortality in these patients; screen for and manage the patient's coronary artery disease
 - consider transfer to stroke centre 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

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 but rather one of the above secondary complications

- ❑ a relapsing or progressive disease of CNS myelin (oligodendrocytes) characterized by disseminated patches of demyelination in the brain and spinal cord, resulting in multiple and varied neurologic symptoms and signs usually with exacerbations and remissions

Epidemiology

- ❑ onset usually 20-40, but can be younger or older
- ❑ F:M = 3:2
- ❑ prevalence in North America 1/1000; 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

Signs and Symptoms

- ❑ weakness e.g. hemiparesis, paraparesis (myelopathy)
- ❑ numbness/paresthesias
- ❑ optic neuritis
- ❑ diplopia, nystagmus, dysarthria, vertigo, hearing loss
- ❑ incoordination, cerebellar ataxia
- ❑ bladder and bowel dysfunction
- ❑ fatigue
- ❑ cortical symptoms are less frequent (seizures, aphasia, memory and attention deficits, depression)
- ❑ important clues
- ❑ internuclear ophthalmoplegia (lesion in medial longitudinal fasciculus causing failure of adduction of the ipsilateral eye and nystagmus of the abducting eye on attempted lateral gaze)
- ❑ optic neuritis
- ❑ Lhermitte's symptom (forward flexion of the neck causes electric shock sensation down the back, 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

Course of Illness

- ❑ relapsing remitting
- ❑ chronic progressive
- ❑ clinically inactive disease
- ❑ mixed pattern

Diagnosis

- ❑ evidence from history and examination of lesions disseminated in both time and space
- ❑ slowing of evoked potentials (visual/auditory/somatosensory)
- ❑ CSF (oligoclonal Ig bands and increased IgG concentration)
- ❑ MRI (plaques show as hyperintense lesions on T2 MRI)

Management

- ❑ patient education and counselling (disclosure, prognosis, future expectations, support groups, psychosocial issues: divorce, depression, suicide not uncommon)
- ❑ corticosteroids are the most commonly used treatment for MS
- ❑ the Optic Neuritis Treatment Trial verified that methylprednisolone but not prednisone increased the recovery rate and increased the time to next relapse

- current recommendation is to treat disabling attacks with 500 to 1000 mg of IV methylprednisolone for 3-5 days with or without short tapering dose
- physiotherapy, speech therapy, occupational therapy, nutrition, social work
- symptomatic treatment for spasticity (baclofen), painful symptoms, bladder dysfunction (ditropan), fatigue (amantadine), depression
- monitor closely for infection especially UTI
- interferons are a class of drugs that have antiviral and immunoregulatory function
- β -interferon (beta 1b betaseron) shown to decrease relapse rate, decrease progression of disability in patients with relapsing/remitting and progressive disease
- β -interferon (beta 1a avonex) appears promising with similar effectivity to betaseron, with less common side-effects and less incidence of neutralizing antibodies than betaseron
- copolymer also decreases relapse rate in relapsing remitting disease

CNS INFECTIONS

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 *streptococcus*, *Listeria 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: *Listeria monocytogenes*
- viral ("aseptic")
 - enteroviruses, influenzae, HIV, HSV, adenovirus
- fungal
 - cryptococcus
- other
 - *Treponema pallidum* (meningeal neurosyphilis)
 - *Borrelia 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 neurologic signs (i.e. CN palsies)

Diagnosis

- CBC + differential
- electrolytes for SIADH
- X-rays may indicate primary infection site (CXR, sinuses, mastoid bone)
- CSF profile (see Table 17)
- Gram stain, culture
- PCR and/or 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, culture and sensitivity results become available
- neonates: ampicillin + cefotaxime (better CSF penetration than gentamycin)
- infants and children: ampicillin + ceftriaxone/cefotaxime
- adolescents and adults: penicillin
- elderly: penicillin + ampicillin
- CSF leak: cloxacillin + gentamycin
- reportable to Public Health

Complications

- headache, seizures, cerebral edema, hydrocephalus, SIADH, residual neurologic 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 neurologic signs

Prevention

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

Table 18. CSF Profile for CNS Infections

	Normal	Bacterial	Viral/Syphilis	TB/Fungal
appearance	clear	N/cloudy	N/cloudy	cloudy
glucose (mmol/L)	2.8-4.4	↓	N	↓
protein (g/L)	0.2-0.45	↑	↑	↑↑
cell count	< 6	↑	↑	↑
predominant cell	lymphocytes	PMNs	lymphocytes	lymphocytes
pressure (mmHg)	100-200 < 20 cm H ₂ O	maybe ↑	n/a	↑

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
- 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: Creutzfeldt-Jakob disease (prion)

Signs and Symptoms

- acute febrile illness, malaise, chills, nausea, vomiting
- meningeal involvement: headache, stiff neck
- parenchymal disease: seizures, mental status changes, focal neurologic signs
- increased 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
- 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

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
 - headache, stiff neck, vomiting, hemiparesis, and focal or generalized seizures
 - note signs of temporal lobe (HSV target) dysfunction
 - 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)
- 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 neurologic 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 Notes - intracranial mass (pus)
- etiology: focal infection leading to hematogenous, or local spread,
 - sometimes idiopathic
- extension from ear
 - Group A Strep, *S. pneumoniae*, *H. influenzae*, anaerobic Strep, *Bacteroides sp.*, *Enterobacteriaceae*
 - 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*, *Enterobacteriaceae*
 - 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*

HIV/AIDS AND THE NERVOUS SYSTEM

- HIV infection can present with abnormalities anywhere in the nervous system

Epidemiology

- brain involvement occurs in over 50% of HIV infected individuals
- 1/3 of people with AIDS have signs and/or symptoms of nervous system involvement
- nearly all people have CNS lesions on autopsy

Classification

- HIV with neurological disease means "AIDS-Related Complex"
- secondary malignancy/infection is needed for "AIDS" designation

Pathophysiology

- HIV infects
 - macrophages, which travel to brain, releasing cytokines (toxic to myelin/neurons)
 - astrocytes/oligodendrocytes
 - T4 cells, which results in inhibited cell-mediated immunity (thus mycobacteria, herpes viruses, and fungi will be predominant infectious organisms)
 - human DNA (thus is oncogenic)
- see Infectious Diseases Notes for more detailed information

CLINICAL PRESENTATIONS**OPPORTUNISTIC INFECTIONS****Cerebral Toxoplasmosis**

- most common cause of intracerebral mass lesion
- signs and symptoms
 - headache, fever, confusion, lethargy, seizures
 - dementia, ataxia, hemiparesis
- diagnosis
 - CT with contrast: multiple ring-enhancing lesions
- treatment: sulfadiazine + pyrimethamine + folate (replace sulfadiazine with clindamycin if allergic)

Progressive Multifocal Leukoencephalopathy

- ❑ pathophysiology
 - human papillomavirus causing widespread hemispherical demyelination
- ❑ signs and symptoms
 - often clinically normal (i.e. with normal mental status functioning)
 - presents with dementia, lethargy, hemiparesis, ataxia, dysphasia, visual disturbance --> death in weeks/months
- ❑ diagnosis
 - CT shows multiple, nonenhancing, white matter lesions
- ❑ treatment
 - high dose zidovudine (no proven effective treatment)

CMV Encephalitis

- ❑ signs and symptoms
 - presents with acute onset of headache (+/- fever), progressing to alterations in cognitive function; may also cause acute myelopathy and cranial neuropathies
- ❑ diagnosis
 - tissue culture or serology (must be done with CBC and differential, metabolic screen, CT, EEG)
- ❑ treatment
 - gancyclovir to help limit extent of disease

Herpes Encephalitis

- ❑ see Herpes Simplex Encephalitis in CNS Infections section above

Fungal Encephalitis

- ❑ caused by *Candida*, *Aspergillus*, *Cryptococcus*, *Coccidiomycosis*, *Histoplasmosis*

Cryptococcal Meningitis

- ❑ commonest CNS fungal infection
- ❑ diagnosis
 - CSF - India ink stain (see halos), culture; serum cryptococcus antigen
 - radiology often normal
- ❑ treatment
 - 5-flucytosine and Amphotericin B

Tuberculous Meningitis

- ❑ signs and symptoms
 - meningeal involvement is most marked at base of brain (i.e. CN V-XII)
 - may also produce spinal abscess (causing an acute myelopathy)
- ❑ diagnosis
 - CSF - serology, Ziehl-Neelsen stain (acid fast bacilli), culture (takes ~ 2 months)
 - high mortality rate due to delayed diagnosis
- ❑ treatment
 - INH, rifampin, pyrazinamide (give pyridoxine supplement), streptomycin

Neurosyphilis

- ❑ signs and symptoms
 - atypical presentations (usually is asymptomatic / meningovascular/ general paresis of the insane or tabes dorsalis)
- ❑ treatment
 - benzathine penicillin is inadequate in HIV with neurosyphilis

DIRECT HIV EFFECTS

Dementia-Encephalopathy

- signs and symptoms
 - cognitive, behavioural, and motor involvement (especially mental slowing, apathy, and social withdrawal)
 - often hyperreflexic, with upgoing toes and primitive reflexes (e.g. glabellar tap)
 - depression is a common presentation
- diagnosis
 - clinical : rule out infections/malignancies
 - CT/MRI: atrophy, white matter abnormalities
- treatment
 - supportive

Myelopathy

- signs and symptoms
 - presents in a fashion similar to subacute combined degeneration of the cord
 - muscle weakness, myalgia, weight loss
- diagnosis
 - increased CK, EMG, muscle biopsy
- treatment
 - zidovudine reduction or withdrawal

Neuropathy

- acute inflammatory demyelinating neuropathy
- chronic inflammatory demyelinating neuropathy
- distal symmetric neuropathy
- shingles (herpes zoster)
 - multiple and/or frequent lesions means AIDS
 - treatment: analgesics

NEOPLASIA

Cerebral Lymphoma

- most common CNS neoplasm in AIDS
- may occur in other locations (i.e. spinal cord)
- signs and symptoms: headache, lethargy, cognitive changes, hemiparesis, aphasia
- diagnosis: CT/MRI shows enhancing lesions
- treatment: radiation

Kaposi's Sarcoma

- epidemiology
 - believed to be related to sexual transmission
 - most commonly present in homosexual males in US
 - uncommon among other risk groups
- signs and symptoms
 - predilection for oral cavity and skin, also commonly occurs in GI tract, lungs, lymph nodes, but can occur in any organ, including the brain
- treatment
 - chemotherapy for systemic/disseminated disease
 - radiation or interferon-alpha for cutaneous/mucosal lesions

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

- can be fatal
- occurs within 1 week after reduction/cessation of drinking, lasts 3-5 days
- signs and symptoms
 - tremulousness
 - starts 8 hours after patient stops drinking, peaks at 24 hours
 - normalizes after 7-10 days
 - visual hallucinations
 - autonomic hyperactivity - tachycardia, fever, sweating
- treatment
 - high dose chlordiazepoxide, lorazepam or diazepam
 - clonidine, atenolol for autonomic hyperactivity
 - maintain fluid and electrolyte balance

Wernicke Encephalopathy (Thiamine Deficiency)

- signs and symptoms
 - nystagmus on horizontal/vertical gaze; bilateral CN VI or gaze palsy
 - ataxia
 - recent memory loss and confabulation
- treatment
 - thiamine

Polyneuropathy

- due to deficiency of vitamin B complex (thiamine B₁, riboflavin B₂, nicotinic acid B₃, pantothenic acid B₅ or pyridoxine B₆)
- loss of ankle jerks and sometimes knee jerks
- mild distal weakness, lower limbs initially
- pain, burning feet, paresthesias
- sensory loss in "stocking/glove" distribution

Cerebellar Degeneration

- M > F
- midline structures (vermis) especially affected, i.e. trunk and leg movement coordination problems
- wide-based gait and truncal instability

Myopathy

- proximal muscle weakness
- may get rise 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 neurologic 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 decline in serum Na⁺
- rapid correction causes central pontine myelinolysis

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

Thyrotoxicosis

- exophthalmos
 - diplopia due to inflammation of extraocular muscles
- myopathy
 - M > F
 - upper extremity weakness and wasting, with brisk reflexes, periodic paralysis and occasionally myasthenia gravis
- movement
 - tremor
 - may have choreiform movements
- sensorium
 - delirium, seizure or even coma in acute thyroid storm
- risk of stroke due to atrial fibrillation

Hypothyroidism

- myopathy: proximal weakness, delayed relaxation of ankle jerks
- carpal tunnel syndrome
- mental apathy and physical inertia, a cause of dementia

Hyperparathyroidism

- hypercalcemia
- myopathy: proximal weakness
- personality changes and increased risk of psychosis
- choreiform movements, parkinsonism

Hypoparathyroidism

- hypocalcemia
- risk of convulsions and papilledema in children
- extrapyramidal movements (e.g. chorea)
- myopathy: proximal weakness
- personality changes

Diabetes Mellitus

- 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 nerve (painful, pupil sparing), CN IV nerve
 - autonomic neuropathy
 - postural hypotension, impotency, 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 behaviour, focal signs mimicking strokes, seizure, coma
 - chronic: progressive dementia, spasticity, dysarthria, extrapyramidal signs, ataxia

COLLAGEN VASCULAR DISEASES

Systemic Lupus Erythematosus

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

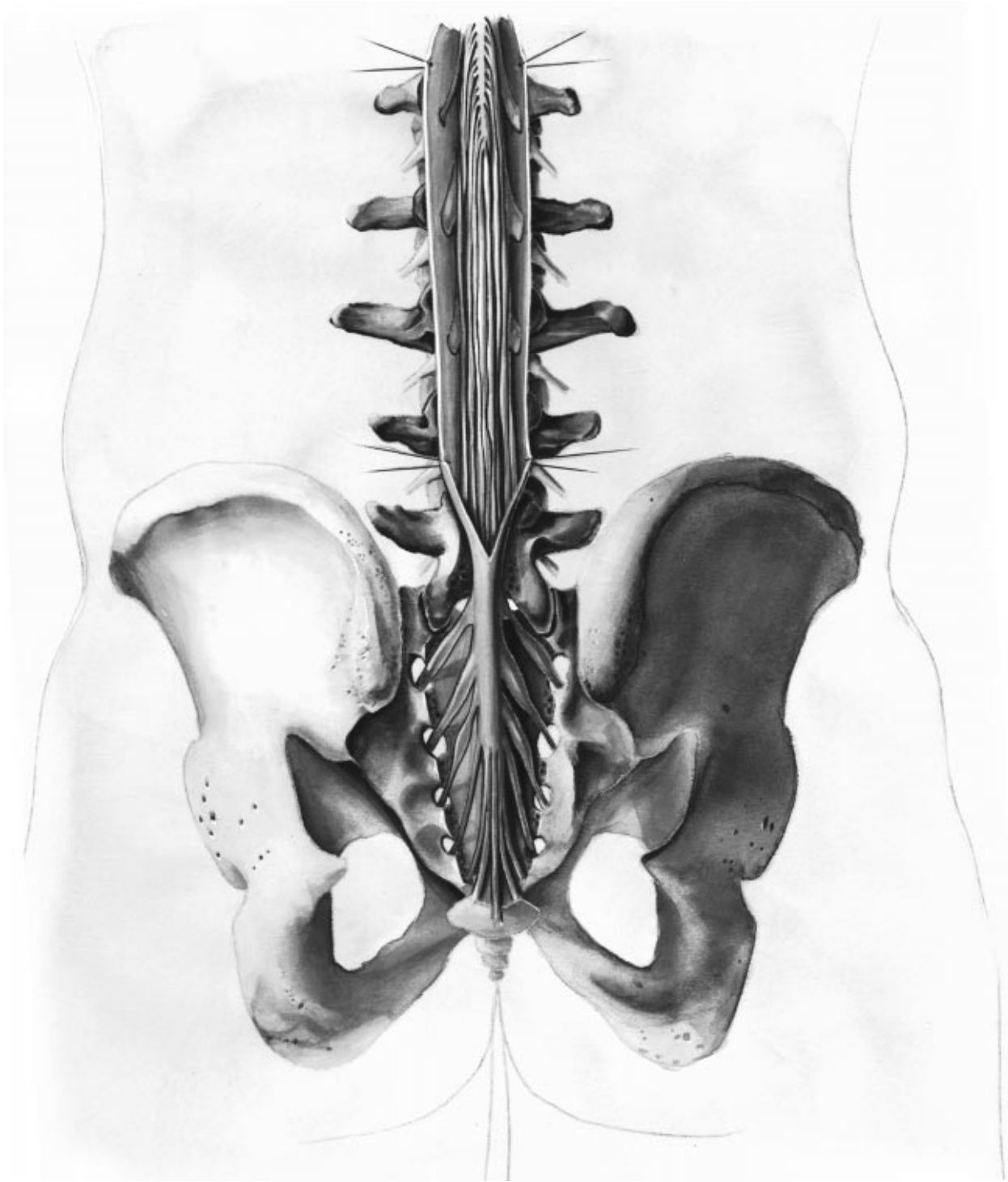
Rheumatoid Arthritis

- commonly due to periarticular tissue damage
- 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

Temporal Arteritis (see Headache Section)



Drawing by M. Brierley