INTRODUCTION AND OVERVIEW

Important clinical syndromes:

1. The Stroke Syndrome
   a. Rapid onset of localised damage to the CNS 2° to vascular haemorrhage/occlusion
   b. After a period of worsening there is a plateau and then gradual (slower) improvement
   c. Transient ischaemic attack – when complete recovery occurs in less than 24 hours

2. The Cerebral Tumour Syndrome
   a. Produced by an expanding intracerebral mass lesion → progressive effects
   b. Varying combination of progressive focal loss of function, signs and symptoms of raised intracranial pressure and epileptic seizures

3. The ‘System’ Degeneration Syndrome (e.g. motor neurone disease, Parkinson’s disease)
   a. Produced by degenerative disorders (cell death) of the CNS
   b. Characteristic clinical pictures attributable to progressive dying of cell groups with associated anatomical and physiological characteristics getting gradually worse

Important neurological symptoms (plus the others in the lectures, silly):

1. Sudden transient loss of consciousness leading to a fall:
   - Fit
     * Definition: Generalised seizure with paroxysmal electrical discharge
     * Loss of function due to abrupt reduction in cerebral perfusion
   - Faint
     * Definition: Loss of function due to abrupt reduction in cerebral perfusion
     * May have particular circumstances: Faintness, nausea, pallor, sweating, fading vision

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<tr>
<th>Fit</th>
<th>Faint</th>
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<tr>
<td>Definition</td>
<td>Generalised seizure with paroxysmal electrical discharge</td>
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<tr>
<td>Prodrome</td>
<td>Usually none</td>
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<tr>
<td>Attack</td>
<td>May have initial partial seizure</td>
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<td></td>
<td>Crashes stiffly</td>
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<td>Tonic spasm, clonic convulsions</td>
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<td>May have incontinence, cyanosis</td>
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<td>Injury common</td>
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<tr>
<td>Postictal</td>
<td>Confusion and drowsiness</td>
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<td>Headache</td>
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   a. Causes of syncope – vasovagal, 1° cardiac disorder, postural hypotension, peripheral neuropathy, hypovolaemia, acute increase in intrathoracic pressure (↓ venous return)

2. Weakness:
   - LMN
     * + Normal
     * Normal
   - UMN
     * + Normal
     * Normal
   - Extrapyramidal
     * Reduced
     * Normal
     * Up (abnormal)

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<thead>
<tr>
<th>Wasting</th>
<th>LMN</th>
<th>UMN</th>
<th>Extrapyramidal</th>
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<tr>
<td>Fasciculations</td>
<td>+</td>
<td>Normal</td>
<td>Normal</td>
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<tr>
<td>Tone</td>
<td>Normal</td>
<td>Increased (spastic)</td>
<td>Increased (rigid)</td>
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<tr>
<td>Power</td>
<td>Reduced</td>
<td>Reduced</td>
<td>Normal</td>
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<tr>
<td>Coordination</td>
<td>Normal</td>
<td>Reduced</td>
<td>Reduced</td>
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<tr>
<td>Tendon reflexes</td>
<td>Reduced</td>
<td>Increased</td>
<td>Normal</td>
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<tr>
<td>Babinski</td>
<td>Down</td>
<td>Up (abnormal)</td>
<td>Down</td>
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   a. Impaired function in a limb (described as weakness by the patient) may be due to non-paralytic disorder e.g. clumsiness, rigidity, bradykinesia, apraxia
   b. In ‘give-way’ weakness, it may be impossible to determine underlying weakness
   c. Not all the classical features may be present in an acutely developing lesion

3. Sensory symptoms other than pain – numbness (impaired sensation), paraesthesiae (tingling)
   - a. Common patterns:
     i. Generalised peripheral neuropathy – stocking/glove distribution
     ii. Isolated peripheral nerve – ulnar, median, lateral femoral cutaneous
     iii. Nerve root – dermatome
     iv. Spinal cord – sensory ‘level’
     v. Lateral medulla – pain/temperature on one side of face, other side of body
     vi. Upper brain stem and thalamus – hemianaesthesia of all modalities
     vii. Partial cerebral cortex – impaired joint position, touch, two-point discrimination and localisation, sensory inattention
   b. Aetiology of transient episodic symptoms – TIAs, focal sensory seizures, migraine, intermittent peripheral nerve compression (e.g. carpal tunnel syndrome)
   c. Note that in an alert and cooperative patient, important sensory abnormalities are uncommon where there is no complaint of sensory symptoms
Neurology

4. Disturbance of gait:
   a. Aetiology – leg/spine pain, neurological dysfunction, loss of confidence/psychogenic
   b. Neurological causes – UMN, LMN, extrapyramidal, cerebellar/sensory ataxia, vestibular dysfunction, apraxia of gait, involuntary movement disorder

**STUPOR AND COMA**
Normal consciousness has two components – alertness (reticular activating system) and content (cerebral hemispheres). Impairment may be judged by spontaneous activity and responsiveness:
1. Confusion/delirium
2. Stupor – temporary purposeful responses by vigorous stimulation, poor response to voice
3. Coma – no purposeful response to external stimuli

**Pathophysiology and Diagnosis**

**Pathophysiology of coma:**
1. Subtentorial mass/destructive lesions (15%) – compression/destruction, affects RAS directly
   a. Signs are usually asymmetric – impaired reflex eye movements and pupillary reflexes
   b. Destructive – brain stem haemorrhage/infarct, demyelination
   c. Compressive – cerebellar bleed/mass lesion, posterior fossa haematoma
2. Supratentorial mass lesions (20%) – transtentorial herniation, affects RAS indirectly
   a. Upper brain stem compressed/stretched caudally with interruption of basilar artery
   b. Uncus of medial temporal lobe may herniate through the tentorial notch compressing:
      i. Ipsilateral third cranial nerve (false localising sign)
      ii. Contralateral cerebral peduncle → ipsilateral hemiparesis
      iii. Posterior cerebral artery → causing homonymous hemianopia
   c. Focal signs – asymmetric reflexes, pupillary asymmetry, abnormal reflex eye movements. Early signs – reduced alertness, bilateral UMN signs (e.g. extensor plantar response) and frequent yawning. Late signs – papilloedema.
   d. Causes include intracerebral haemorrhage, ischaemic stroke with oedema, subdural or extradural haematoma, brain tumour, and brain abscess.
3. Metabolic encephalopathy (65%) – diffuse cerebral hemisphere and brain stem dysfunction
   a. Symmetric signs – asterixis, myoclonus, seizures (pupillary light reaction retained)
   b. Breathing often abnormal – hyperventilation (metabolic acidosis, respiratory alkalosis of hepatic failure, septic shock), hypoventilation (lung disease, CNS depression)
   c. Causes include:
      i. Deprivation of O₂, substrate (glucose) or co-factors (thiamine, niacin)
      ii. Organ failure – liver/kidney/lung/pancreatic, hypopituitarism, hypothyroidism
      iii. Poisons – sedatives, acids, psychotropics, anticholinergics, anticonvulsants
      iv. Electrolyte/acid-base abnormalities – ↑↓ Na⁺, ↑ Ca²⁺, ↑↓ Mg²⁺
      v. Disorders of temperature regulation
      vi. Infections/inflammation – encephalitis, meningitis
      vii. Others – post-epileptic seizure, head injury, subarachnoid haemorrhage

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<tr>
<th>Time course</th>
<th>Supratentorial</th>
<th>Subtentorial</th>
<th>Metabolic</th>
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<tr>
<td>Focal signs</td>
<td>Present</td>
<td>Present</td>
<td>Absent</td>
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**Differential diagnosis of coma:**
1. Locked-in syndrome – lesion in the basis pontis (ventral pons) interrupting the corticospinal and corticobulbar pathways, but spares the somatosensory pathways and RAS
   a. Paralysis of the arms and legs, facial and bulbar muscles
   b. Horizontal eye movements paralysed, but vertical eye movements intact
   c. Vision, hearing, somatosensory sensation intact
2. Psychogenic unresponsiveness
   a. Unresponsiveness to stimulation (including pain), often resist eye opening
   b. Pupils reactive (unless mydriatics used), ice cold calorics → nystagmus, EEG normal

**Assessment and Management**

**Assessment:**
1. History – onset, recent symptoms, trauma, previous medical/psychiatric illness
2. General examination – vital signs, signs of trauma, neck stiffness, others
Neurology

3. Neurological examination – respiratory pattern, tendon reflexes, muscle tone
   a. Glasgow coma scale – eye opening (4), speech (5), movement (6)
   b. Pupillary light reflexes:
      i. Normal – metabolic coma
      ii. Unilateral dilated pupil – transtentorial herniation
      iii. Mid-position, fixed pupils – midbrain lesion
      iv. Pinpoint pupils – pontine lesion, opiate overdose
   c. Reflex eye movements – Doll’s eye manoeuvre, cold caloric (normal → nystagmus)
      i. Conjugate deviation – metabolic encephalopathy (brainstem pathways intact)
      ii. Asymmetrical response – structural brain stem lesion
      iii. Bilateral absent response – structural (abnormal pupillary reflex) or metabolic

4. Investigations:
   a. Immediate – venous (glucose, electrolytes, creatinine, osmolality), ABG, CT, CSF
   b. Deferred – venous (drug screen, liver/thyroid/adrenal, coagulation, blood cultures, other electrolytes), arterial (ammonia), urine (drug screen, culture), EEG

Management:
1. Correct immediate threats to life (ABCs)
2. Glucose IV (50mL 50% dextrose), consider thiamine, consider naloxone (narcotic overdose)
3. Emergency treatment of impending herniation:
   a. Hyperventilation – lower pCO₂ to 25-30mmHg
   b. Osmotherapy – mannitol 0.5-2.0g/kg iv over 15 mins + 25g iv boosters
   c. Steroids – dexamethasone 100mg iv push, followed by 40-100mg/hour

CONFUSIONAL STATE

Confusion refers to global impairment of higher mental function due to bilateral dysfunction of the cerebral hemispheres associated with drowsiness, inattentiveness, disorientation, illusions, reduced speed/clarity of thinking and impaired memory. It may be due to:

1. Primary diffuse brain disorders
   a. Meningitis or encephalitis, SAH, multifocal cerebral ischaemia (hyperviscosity, HT encephalopathy, DIC), head injury, post-epileptic seizure

2. Focal brain lesions – unilateral lesion → increased ICP, shift of intracranial contents
   a. Infarct, intracerebral haemorrhage, subdural haematoma, tumour, abscess

3. Systemic or metabolic disorders
   a. Drugs – sedatives, psychotropics, anticholinergics, amphetamine, digoxin, steroids, anticonvulsants, anti-Parkinsonian medications
   b. Acute systemic infections, organ failure – uraemia, liver/heart/lung failure
   c. Acid-base/electrolyte disturbances – ↑Na⁺, ↑Ca²⁺, ↓Mg²⁺, ↓BSL
   d. Co-factor deficiency – thiamine (Wernicke-Korsakoff syndrome), niacin (pellagra)

Delirium is a confusional state with agitation, tremulousness, visual hallucinations and autonomic overactivity. Causes include withdrawal states (alcohol, sedative drugs), intoxication (atropine, amphetamines, steroids), acute infections, encephalitis, head injury, and thyrotoxicosis (rare).

Differential diagnosis of acute confusional state:
1. Fluent (Wernicke’s) dysphasia – focal brain lesion in the superior temporal gyrus
2. Psychiatric disorder – e.g. psychosis
3. Dementia – acute metabolic/systemic illness may precipitate acute confusion

Management:
1. Investigations – looking for a systemic disturbance that can be treated
   a. FBC, U&Es (Na⁺, Ca²⁺, creatinine), LFTs, glucose, ABG (pH, pO₂, pCO₂), drug levels
   b. CXR, blood cultures, urine examination
   c. Others – CT or MRI (focal signs), CSF examination (fever)
2. Treatment:
   a. Treat the underlying cause – particularly stopping drugs that may cause confusion
   b. Environmental interventions – protect from injury, optimal stimulation
   c. Avoid sedatives if possible – Haloperidol 0.5-1mg bd or clonazepam 1-2mg
   d. Special situations – hypoglycaemia (50mL 50% dextrose), thiamine deficiency

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STROKE

Stroke is a syndrome caused by damage to the CNS by an abnormality of its blood supply, with sudden onset (abrupt, rapid progressive or stepwise), focal brain damage in the territory of a particular artery and symptoms and signs persisting >24 hours.

It is difficult to distinguish stroke subtypes clinically, and treatment differs by type (hence the utility of CT scans). Diagnosis of stroke should be made with caution if: poor history (unconscious, dysphasic, no eye witness), coma, gradual onset, no focal signs, associated with a blackout, unexplained fever.

- Ischaemic Stroke/Cerebral Infarction (80-85%)

Pathophysiology of ischaemic stroke:

1. Arterial disease – thrombosis at the site, or embolism of thrombus to distal arteries
   a. Atheroma – aortic arch, ends of internal carotids, proximal middle cerebral and basilar
      i. Thrombosis at site may be preceded by days to weeks of TIAs
      ii. Strong association with coronary artery disease, HT and diabetes mellitus
   b. Lipohyalinosis – penetrating branches of cerebral arteries → pons, deep white matter
      i. Blood vessels impregnated with a hyaline-lipid material, often chronic HT
   c. Other arterial diseases – dissection, vasculitis, fibromuscular dysplasia

2. Embolism – abrupt onset, multifocal TIAs or strokes
   a. Carotid artery (middle cerebral artery), vertebral artery (posterior cerebral or cerebellar artery). Anterior cerebral or small penetrating arteries not often occluded
   b. Cardiac causes – AF, valvular disease, bacterial endocarditis, mural thrombus, cardiac surgery/catheterisation, cardiomyopathy, paradoxical emboli, cardiac tumours
   c. Non-cardiac causes – thrombosed pulmonary veins (e.g. bronchiectasis)

3. Reduced cerebral perfusion pressure – global cerebral hypoxia/ischaemia
   a. Cardiac pump failure, hypovolaemic shock
   b. Usually borderzone (watershed) infarcts peripheral to major vascular supply areas

Clinical syndromes:

1. Total anterior circulation infarct (TACI) – internal carotid or middle cerebral artery
   a. Focal higher cerebral dysfunction (dysphasia, apraxia, agnosia)
   b. Homonymous visual field defect (optic radiation)
   c. Unilateral motor and/or sensory deficit involving at least 2 of face, arm, leg

2. Partial Anterior Circulation Infarct (PACI) – internal carotid, middle or anterior cerebral artery
   a. Two of the three TACI components, or
   b. Focal higher cerebral function alone, or
   c. Unilateral motor/sensory deficit more restricted than a lacunar infarct

3. Posterior Circulation Infarct (POCI) – vertebral, basilar or posterior cerebral artery
   a. Ipsilateral cranial nerve palsy, contralateral motor and/or sensory deficit
   b. Bilateral motor and/or sensory deficit
   c. Disorder of conjugate eye movements
   d. Cerebellar dysfunction without ipsilateral hemiparesis
   e. Isolated homonymous visual field defect
   f. Homer’s, nystagmus, vertigo/vomiting, coma, choreoathetosis, hemiballismus

4. Lacunar Infarct (LACI) – small penetrating arteries
   a. Pure motor – isolated hemiparesis affecting face, arm, leg
   b. Pure hemisensory – isolated hemisensory defect
   c. Dysarthria – e.g. clumsy hand
   d. Ataxic hemiparesis

Management:

1. Stroke units – NNT 18, no additional cost, variable availability
2. Aspirin (150-300mg) – 80% patients, NNT 83, inexpensive ($83 per patient saved)
3. IV tPA – beneficial if started within 3 hours of onset despite risk of early haemorrhage
4. Thrombolysis (3-6hrs) – few patients eligible (<5%), expensive, 10x haemorrhage rate
5. Heparin sc/iv, LMW heparin – uncertain long-term effects, may benefit some (dissection)
Intracerebral Haemorrhage (15%)

The clinical distinction between ischaemic stroke and intracerebral haemorrhage is difficult, and CT is required to distinguish the two. Clues include history of hypertension, no prodromal TIAs, severe headache, gradual onset (minutes to hours), reduced consciousness, and neck stiffness.

Pathophysiology of intracerebral haemorrhage:
1. **Systemic diseases**
   a. Hypertension – complex small vessel disease (lipohyalinosis) of basal ganglia, thalamus, cerebellum, pons → vessel tears, aneurysm dilation/rupture, lacunar infarct
   i. Chronic → degenerating penetrating arteries (Charcot-Bourchard aneurysms)
   b. Bleeding disorders – risk is 10x greater on anticoagulants, and risk increases with intensity (high INR), age, hypertension, past stroke and IDDM.
   c. Tumours – glioblastoma, metastases (melanoma, choriocarcinoma, RCC, Ca lung)
2. **Vascular abnormalities**
   a. Amyloid angiopathy – amyloid deposits in small and medium sized vessels → lobar haemorrhage in the elderly (grey-white matter junction), high rate of recurrence
   b. AV malformations, cavernous angiomas, saccular and mycotic aneurysms, vasculitis
3. **Exogenous factors** – sympathomimetic drugs (amphetamines, cocaine), trauma

Management:
1. Correct clotting abnormalities – vitamin K or FFP (warfarin), protamine sulphate (heparin), epsilon-aminocaproic acid and cryoprecipitate (thrombolytics), corticosteroids no benefit
2. Surgical evacuation:
   a. Large bleeds (e.g. supratentorial) have usually caused too much damage, while small bleeds respond well to medical treatment (surgery not required)
   b. Medium bleeds (2-4cm) may benefit, particularly if there are signs of ↑ ICP or ↓ LOC
   c. Cerebellar bleeds (>3-5cm) if reduced LOC, no loss of brainstem reflexes
3. TED stockings for DVT prophylaxis
4. Reduce intracranial pressure – hyperventilation, mannitol

Subarachnoid Haemorrhage (5%)

Despite diagnostic, medical and surgical advances, the incidence and fatality rate for subarachnoid haemorrhage has not changed in the last 30 years. Most subarachnoid bleeds are due to rupture of a berry aneurysm, occasionally an arteriovenous malformation or trauma and unknown in 10-20%.

1. Aneurysms occur at sites of weak arterial wall, affecting 5% of the population (10% rupture)
2. Terminal internal carotid artery, middle cerebral artery, anterior communicating arteries
3. Slowly increase in size, but generally asymptomatic until rupture
4. Thunderclap headache (abrupt onset, typically during exertion), vomiting ± loss of consciousness, focal signs not prominent, meningism (subacute with high fever, tachycardia)

Investigations:
1. Urgent non-contrast brain CT – positive in 95% within 24hrs, 50% at day 7, almost 0 at day 10
2. Lumbar puncture all CT negative patients 6-12hrs – RBCs, xanthochromia (12hrs to 4 weeks)
3. Cerebral angiography can be sued to localise the lesion, MRI not sensitive

Treatment – note that 15% of patients die before hospital. Of those who make it to hospital, 10% die on day one – of those that survive day one, 1/3 die within three months.
1. Surgical clipping of aneurysm (early <3 days, delayed >1 week)
2. Endovascular occlusion – can lead to rupture or embolisation, good for giant aneurysms
3. Risk of infarction after 1-2wks due to cerebral artery narrowing/spasm (Ca²⁺ blockers useful)
4. Blood pressure control debatable – rebled vs hypoperfusion infarct
5. Late complication is hydrocephalus – treated by ventriculo-peritoneal shunt

Assessment and Management of Stroke

Assessment of stroke:
1. **Diagnosis:**
   a. Is it a stroke?
   b. Where is the lesion?
   c. Which type is it?
   d. What is the underlying cause?
Neurology

2. Clinical assessment:
   a. History – especially onset and progression of symptoms
   b. Neurological examination – where is the lesion?
   c. General examination – blood pressure both arms, heart, pulse, carotid bruits, fundi

3. Investigations:
   a. Basic – FBC, ESR, U+E, creatinine, glucose, ECG, CXR, CT head
   b. Ischaemic – coagulation, syphilis, echocardiography, USS, MRI, angiography
   c. Haemorrhagic – coagulation, blood cultures, angiography

Management:
1. Risk factors include age (75% are >66yrs), hypertension (reversible!), smoking (increases risk by 50%, cessation → normal risk by 2-5yrs), heart disease, hyperlipidaemia (unclear), DM and obesity, lack of physical inactivity
2. Primary prevention:
   a. Modify vascular risk factors – HT, smoking, diabetes, high cholesterol, low exercise
   b. Warfarin – prosthetic heart valves, AF, hypercoagulable states
   c. Surgery controversial (asymptomatic endarterectomy, aneurysms, AV malformations)
3. Secondary prevention:
   a. Antiplatelet therapy – aspirin, ticlopidine, aspirin + dipyridamole
   b. Anticoagulation (warfarin) – RR 12% to 4%/year, NNT 12
   c. Antihypertensives – NNT 46, cost varies
   d. No direct association, but statins reduce risk in patients with previous IHD (NNT 59)
   e. Carotid endarterectomy – symptomatic stenosis >70%

Complications:
1. Neurological:
   a. Progressing stroke – extension of the thrombus → enlargement of infarct, haemorrhage, oedema, seizures, metabolic abnormalities (fever, hypoxia)
   b. Cerebral oedema – 24-48hrs after large hemispheric ischaemic/haemorrhagic stroke
      i. Avoid hypooosmolar fluids, hypoxia, CO₂ retention, fever, ↑CVP, agitation
      ii. Osmotic diuretics (mannitol) may help temporarily, steroids not beneficial
   c. Hydrocephalus, brainstem compression – 1-4 days after cerebellar/post. fossa stroke
      i. Ventricular drainage and surgical decompression may be life-saving
   d. Seizures – prophylactic anticonvulsants not indicated until seizures occur, and even then early seizures may not progress to chronic epilepsy
2. Systemic:
   a. DVT, PE – 50% of patients with hemiplegia following stroke
      i. Heparin sc (haemorrhage/bleeding risk), DVT stockings, early mobilisation
      ii. Treat with full-dose heparin or LMW heparin
   b. Blood pressure:
      i. Hypertension – impairment of cerebral autoregulation in acute stroke
         1. Normalising blood pressure may → hypoperfusion, ischaemia
         2. Rest in quiet room, pain relief, urinary catheter, SLOWLY lower BP
      ii. Hypotension – commonly due to dehydration, anti-hypertensive medication
         1. Urgent correction – stop drugs, give fluids
         2. Monitor lying and standing BP as the patient mobilises
   c. Metabolic:
      i. Hypoxia – commonly due to aspiration pneumonitis, airway obstruction, hypoventilation. Give O₂ and protect airway with ET tube as indicated
      ii. Hyperglycaemia – associated with poor outcome, avoid glucose-containing IV fluids and administer insulin
      iii. Hyponatraemia – commonly due to SIADH causing acute confusional state, seizures. Treat with fluid restriction
   d. Fever and infection – common cause of mortality, diagnose and treat early

• Transient Ischaemic Attacks and Carotid Bruits

Transient ischaemic attacks are caused by a temporary cessation of blood flow to part of the brain or retina, often due to microembolisation, vasospasm or transient hypotension – symptoms resemble stroke but resolve within 24 hrs (usually within 15 min).
Neurology

1. **Aetiology** – large artery disease (atheroma – 50%), cardiac emboli (5-10%), miscellaneous causes (5-10%), idiopathic (25%)

2. **Clinical features:**
   a. Symptoms depend on site:
      i. Carotid artery (usually branches of MCA) → weakness, numbness, aphasia
      ii. Ophthalmic artery → transient monocular blindness (amaurosis fugax)
      iii. Vertebral/basilar artery → dizziness, diplopia, dysarthria, facial numbness or weakness, ataxia, blurred vision
   b. Note that isolated transient vertigo is rarely due to TIA – non-focal symptoms don’t suggest TIA unless focal symptoms are also present

3. **Prognosis:**
   a. TIs do not precede intracerebral haemorrhage
   b. Increased risk of stroke (5% per year, 3-5x risk) and mortality (5% per year, 2-3x risk)

**Carotid bruits:**
1. Often associated with stenosis at the origin of the ICA (bruit maximal at the angle of the jaw)
2. Note that they may also arise from ECA, and are not a specific or sensitive sign of stenosis
3. Risks include stroke (1-2% per year, 3-5% if >75% stenosis), mortality (3-5% per year)

**EPILEPSY**

Epilepsy is a symptom of disease, characterised by excessive neuronal activity commonly followed by reduced activity. Clinical manifestations depend on the spatial and temporal distribution of the excessive neuronal activity. Sub-clinical bursts of abnormal activity may also occur (epileptiform).

Seizures usually occur for no apparent reason, but may be induced by a number of factors and stimuli. They tend to be abrupt in onset and self-limiting, lasting less than a minute or two. Prolonged or recurrent seizures without full recovery between attacks are called status epilepticus – prolonged partial or general seizures may produce permanent cerebral damage.

### Pathophysiology of Epilepsy

**Causes of epilepsy:**
1. **Intrinsic cerebral disturbance**
   a. Basic predisposition to seizures, often inherited and not associated with demonstrable disease of the brain → idiopathic epilepsy (generalised seizures)
   b. Structural lesion (particularly cortex) – trauma, tumours (gliomas, benign tumours), infarct, infection, cortical dysgenesis, AV malformation, scar, hippocampal sclerosis

2. **Systemic metabolic disturbance** – hypoxia, hypocalcaemia, hypoglycaemia, hyponatraemia, uraemia (renal failure), fever (in children), drug use (phenothiazines, antidepressants) or withdrawal (EtOH, benzodiazepines, barbiturates)

Idiopathic epilepsy – no underlying brain disease
Symptomatic epilepsy – underlying brain disease present
Cryptogenic epilepsy – presumed underlying brain disease present

**Differential diagnosis** includes syncope, pseudoseizures (psychogenic), TIs in vertebrobasilar circulation (impaired consciousness) or ICA (sensory)

### Clinical Features of Epilepsy

**Classification of seizures:**
1. **Generalised seizures**
   a. Generalised convulsion (tonic/clonic, grand mal) - may need eyewitness account
      i. Initial stiffening (tonic phase) lasting up to 30s associated with cyanosis
      ii. Limb jerking (clonic phase) and brief coma → confusion, headache
      iii. May be followed by sleep, may have tongue biting, urinary incontinence
   b. Absence seizure (petit mal) – onset in childhood
      i. Brief lapses of awareness, associated with myoclonus (eyelid flickering)
      ii. No aura or post-ictal drowsiness, may be precipitated by hyperventilation
      iii. Typical EEG abnormality – generalised 3-4Hz spike and wave
   c. Atonic seizures (epileptic drop attacks), tonic seizures (without clonic jerks, bilateral myoclonic jerks (not always epileptic, not always benign)
Neurology

2. **Partial (focal seizures)** – in simple partial seizures consciousness is retained; in complex partial seizures the patient loses awareness of their surroundings
   a. Focal motor – localised (foot, head, mouth), Jacksonian march, versive (head turning), epilepsia partialis continue (focal motor status epilepticus)
      i. May be followed by Todd’s paresis (temporary hemiparesis)
   b. Focal sensory – somatosensory (localised or Jacksonian march), visual (unformed spots or lights), auditory (unformed sounds)
   c. Temporal lobe seizures – psychosensory/cognitive, illusions/hallucinations, altered perception of time, déjà vu, jamais vu, visceral/affective symptoms, impaired LOC

**Epileptic syndromes:**

1. **Characterised by partial seizures**
   a. Temporal lobe epilepsy – simple partial and complex partial seizures characterised by
      i. Aura – visceral, hallucinations, psychosensory
      ii. Begin with motionless stare → oro-alimentary (lip smacking, chewing) and motor (fumbling, picking at clothes, walking, undressing) automatisms
      iii. Dystonic posturing – if unilateral, seizure usually in contralateral hemisphere
      iv. Usually marked post-ictal confusion, may progress to generalised seizure
   b. Frontal lobe epilepsy – 20-30% of partial seizures
      i. Often very short, frequently at night, often occurring in clusters
      ii. Usually no aura, consciousness preserved, no post-ictal confusion
      iii. Often bizarre – prominent vocalisation, violent dramatic movements
      iv. Discharge spreads rapidly, often generalise, status epilepticus common
   c. Benign Rolandic epilepsy (benign childhood epilepsy with centrotemporal spikes)
      i. Primary partial epilepsy (not associated with underlying structural disorder)
      ii. Features include unilateral paraesthesia and clonus of tongue and face, speech arrest, preservation of consciousness, nocturnal, 2° generalisation
      iii. Children otherwise normal, seizures stop at puberty

2. **Characterised by generalised seizures**
   a. Idiopathic (primary) generalised epilepsy (centrencephalic epilepsy)
      i. Combinations of absence, tonic/clonic and myoclonic seizures
      ii. Onset in childhood/early adult life – major genetic component
      iii. Patient otherwise normal, normal development, normal neuroimaging
      iv. Tonic-clonic seizures also occur as 2° generalised seizures in symptomatic epilepsies – do not make diagnosis without convincing history of myoclonic jerks or absences or characteristic 3-4Hz spike and wave on EEG
   b. Absence epilepsy:
      i. Onset usually 3-10yrs, characterised by recurrent absence seizures where the patient stares and is momentarily unresponsive. No aura or confusion.
      ii. 30-50% also have tonic-clonic seizures, 80% remit before the age of 30
      iii. Atypical absences – clinically similar but slower onset, slower recovery
         1. Seen with underlying brain disease (e.g. Lennox Gastaut syndrome)
         2. 1-2Hz spike and wave on EEG
   c. Juvenile myoclonic epilepsy
      i. Common (5% of epileptics), onset during teens, lifelong tendency to seizures
      ii. Frequent myoclonic jerks followed by infrequent tonic-clonic seizures
      iii. 30-40% have absence seizures as well (but not usually clinically apparent)

3. **Others**
   a. Symptomatic and cryptogenic epilepsy – in diffuse/multifocal brain disease, often many seizure types (tonic-clonic, atonic-tonic, myoclonic jerks, atypical absences)
   b. Febrile seizures – 3% of children 6mo-5yrs, increased incidence if family history
      i. Most are simple (brief, symmetrical tonic-clonic); complex if duration >15min, recurrent during single febrile episode, focal or lateralizing features
      ii. ~5% develop epilepsy, increased risk if complex seizures

The most important localising feature of an epileptic attack is the very first symptom, often called the **aura** – note that it is misleading to give this a special name as it is actually part of the seizure process.

**Diagnosis and Management of Epilepsy**

The EEG (spontaneous and evoked brain activity recorded from the scalp) is one of the key tools:
Neurology

1. **Diagnosis** – only interictal sign, sensitivity ~50% (higher with multiple tests), specificity 98%
   a. Limited role for detection of structural brain disease, CT/MRI are better
2. **Classification** – particularly valuable in distinguishing absence from complex partial seizures
3. **Aetiology** – detection of associated EEG disorders may suggest cause

Management of epilepsy – see therapeutics tutorial, it’s a good one

1. **General principles**
   a. Safety – during seizures, interictally (risk of sudden unexpected death of epilepsy)
   b. Avoidance of precipitating factors helps, but drugs are often necessary
   c. Importance of education and support (e.g. support groups), taking responsibility
2. **Principles of drug therapy** (see below)
   a. Use the correct drug for the correct type of epilepsy
   b. Start with one drug, increasing until patient is seizure free or side-effects intolerable
      i. If this is unsuccessful, change to another drug (overlap for 6 weeks)
   c. If two individual drugs fail, consider a combination – choose one for baseline and try various second drugs (do not continue if no obvious benefit)
      i. If this fails, be prepared to reconsider the diagnosis (e.g. pseudoseizures)
   d. Serum levels are useful for checking compliance, unusual metabolism and suspected toxicity, but therapeutic range should only be used as a guide (don’t get obsessed)
3. **Pregnancy:**
   a. Risks of uncontrolled tonic-clonic seizures is greater than the risk of adverse effects
   b. Teratogenicity – 2-6x risk, may be >10% on polytherapy
   c. Folic acid before conception may reduce valproate-induced neural tube defects
   d. Note that enzyme-inducing anti-epileptic drugs reduce efficacy of the OCP
4. **Driving:**
   a. Must stop for 1 year unless the seizure was due to unusual provocative factors unlikely to recur – may be reduced to 6 months on neurologist recommendation
   b. Must stop for 6 months when drugs therapy is changed or reduced – if a seizure occurs, the patient may drive 6 months after resuming prior therapy that worked
   c. Any history of epilepsy results in a permanent ban from passenger service vehicles, ambulances, vehicle recovery and heavy vehicles (only 1 year if clearly provoked)
   d. Sleep epilepsy – may drive if seizure-free for >1 y or only nocturnal seizures >3 yrs
5. **Prognosis:**
   a. 40% of those seen in hospital with their first seizure have recurrence in 2 years (most within 6 months), and 70% of those who have 2 seizures have a third within 2 years
   b. Increased risk with structural lesions or if there are epileptiform discharges on EEG

**Status epilepticus** – prolonged or frequent seizures without consciousness between attacks

1. Medical emergency – risk to life and of developing permanent cerebral damage
2. General – search for causes early on, carefully maintaining ABCs
3. IV anticonvulsants necessary, but only if the patient is in true status (not recovered)
4. Use only one drug at a time, carefully recording dosage and rate of administration

**Drugs for Epilepsy**

**Drug choice based on seizure type:**

1. **Generalised seizures (tonic-clinic)** – valproate, carbamazepine
   a. Second line – phenytoin, clobazam
   b. Third line – topiramate, lamotrigine
   c. Fourth line – phenobarbitone, primidone
2. **Generalised seizures (myoclonic or absence)**, sodium valproate, ethosuximide (kids only)
   a. Second line – clobazam, clonazepam
   b. Third line – lamotrigine, acetazolamide
   c. NOT carbamazepine, vigabatrin, gabapentin
3. **Partial seizures** – carbamazepine, sodium valproate
   a. Second line – phenytoin, clobazam
   b. Third line – topiramate, lamotrigine
   c. Fourth line – gabapentin, tiagabine, phenobarbitone, vigabatrin

**Summary of common drugs:**

1. **Carbamazepine** (Tegretol)
Neurology

1. Carbamazepine (Tegretol)
   a. Indications – tonic-clonic seizures an partial seizures (simple or complex), ineffective for absence seizures and juvenile myoclonic epilepsy
   b. Dosage – start slowly (100mg nocte) and increase the dose by 100mg every few days to twice-daily dosage, usually to 600-1600mg/day
   c. Adverse effects – rash, sedation and cognitive side effects, hyponatraemia, cardiac conduction defects, neutropenia, liver disease, toxic → ataxia, diplopia, nystagmus
   d. Interactions – induces metabolism of other drugs (contraceptive, warfarin)
2. Sodium valproate (Epilim)
   a. Indications – broad spectrum: tonic-clonic, absence, partial and myoclonic seizures
   b. Dosage – start at half dose (200-400mg bd), increase according to clinical response (can be done quicker than carbamazepine), usually to 800-3000mg over two doses
   c. Adverse effects – nausea, weight gain, hair loss, hand tremor, liver failure, thrombocytopenia, pancreatitis, teratogenic (neural tube defects)
   d. Interactions – inhibits metabolism of lamotrigine
3. Phenytoin (Dilantin)
   a. Indications – tonic-clonic (1° or 2°), partial seizures, ineffective for absence seizures
   b. Dosage – start as a loading dose (1000mg po or 18mg/kg iv at <50mg/min) or normal maintenance dose (300mg od – takes longer to reach therapeutic levels). Note that metabolism is saturable so small dose changes → marked effects on blood levels.
   c. Adverse effects – cosmetic (hirsutism, coarsening of facial features), sedation and other cognitive side effects, peripheral neuropathy or cerebellar ataxia (chronic use), osteomalacia, toxic → ataxia, nystagmus
4. Clobazam (Frisium)
   a. Indications – tonic-clonic (1° or 2°), partial and absence seizures. Seldom effective in monotherapy and usually used as additional therapy when a single agent fails
   b. Dosage – start with 10mg nocte, increasing to 10-60mg/day nocte
   c. Adverse effects – sedation, dizziness, honeymoon effect (loss of effect long-term)
5. Ethosuximide (Zarontin)
   a. Indication – only indicated for absence seizures
   b. Dose – 15-40mg/kg/day as a single daily dose
   c. Adverse effects – cognitive/behavioural changes, drowsiness, headache, GI symptoms, anorexia, rash. Rarely – SLE, agranulocytosis
6. Lamotrigine (Lamictal)
   a. Indications – broad spectrum: tonic-clonic (1° or 2°), absence and partial seizures (expensive, so restricted to patients unsuccessfully treated on older agents)
   b. Dose – start slowly (12.5mg/day), increase weekly to 100-400mg/day
   c. Adverse effects – skin rash early on, otherwise well tolerated
   d. Interactions – metabolism inhibited by valproate, carbamazepine
7. Other drugs:
   a. Phenobarbitone (60-200mg/day), primidone (750-1000mg/day) – effective for tonic-clonic and partial seizures, limited by adverse effects (sedation, cognitive impairment)
   b. Vigabatrin (2-4g/day) – effective for complex partial seizures and 2° generalised seizures, not for idiopathic generalised seizures (tonic-clonic and absence seizures). Side effects – irreversible retinal damage (40%), sedation, depression, psychoses
   c. Gabapentin – add-on treatment in refractory partial seizures, ineffective for idiopathic generalised seizures (tonic-clonic and absence seizures). Minimal interactions and side effects, but less effective than most other drugs
   d. Topiramate – add-on treatment for refractory partial seizures and 2° generalised tonic-clonic seizures. Induces metabolism for OCP, but otherwise minimal interactions and side effects. Use limited by high cost.

Drug-resistant epilepsy:

1. If a patient still has seizures after an adequate trial of an appropriate 1° line anti-epileptic, there is only a 10-20% chance that they will become seizure free with other drugs
2. Surgery is appropriate for some patients with drug resistant epilepsy – it should be considered early (2-5 yrs) after onset of symptoms:
   a. Seizures need to be refractory to medical treatment, significantly interfere with the patient’s life, unlikely to resolve spontaneously, and the patient is fit for surgery
   b. Only useful if the patient has partial seizures arising from a single site, that can be confidently identified and resected without producing a significant clinical deficit.