Neuroscience Teaching

Cranial Nerves

I Test only if subjective change. Be aware of cold, old head injury – change sense

II VA, with correction of refractive error (pinhole if reduced)
Visual fields – screen four quadrants, including two stimuli together for neglect
If problem, map out extent
For central defect, use blind spots to find meridian plane, scan with pin
Colour vision – Ishihara plates
Pupil reflexes – Direct and consensual, accommodation, Relative Afferent Pupillary Defect (RAPD – swinging flashlight test)
Fundoscopy

III, IV, VI Eye movements ('H') – failure of movement, diplopia (false image is lateral), nystagmus
Saccadic movements
Internuclear Ophthalmoplegia – MLF lesion (VI rapid, nystagmus, III slower – input is to VI nucleus, then MLF to III nucleus)

V Sensation Va, Vb, Vc
Clench teeth – muscles of mastication
Corneal reflex

VII Facial expression (raise eyebrows, screw up eyes, smile, blow out cheeks)
Taste to anterior 2/3 tongue
Hyperacusis

VIII Hearing. If problem, Rinnes, Webers to localise

IX, X, XII Look at palate and uvula. Tongue wasting.
'Ah' – uvula rises symmetrically?
Protrude tongue, move left and right
Cough, swallow
Gag reflex

XI Test SCM – head movement, shrug

Other tests

Screening upper limbs

- Eyes closed, arms extended and supinated
- Look for wasting, tremor, weakness, pronator drift
- Tap hands, look for excess movement
- Touch nose with each finger

Screening lower limbs

- Walking normally
- Heel-toe, on toes, on heels (evidence of foot drop?)

Limbs

- Tone, clonus
- Power
- Co-ordination
- Reflexes
- Sensation (sharp/blunt, proprioception, vibration, temperature)

Dysarthria – ability to say "British Constitution" or "Yellow Lorry"
Frontal Release signs – Palmomental reflex, pout reflex, grasp reflex
Consider testing finger reflexes if others are brisk

Raised ICP

Symptoms:
- Headache (characteristic)
- Blurred vision
- Vomiting
- Lethargy

Signs
- Papilloedema
- Decreased LoC
- Herniation
- Late: hypertension/bradycardia

60% present with focal deficit, 50% with headache, 20% with seizures. <50% have papilloedema at presentation.

Causes – Mass lesion, oedema, obstructive hydrocephalus

Intracranial Tumours

Most commonly metastases (>50%) – common primaries are lung, breast, skin (melanoma). Primary tumours divide into benign/malignant, supratentorial/infratentorial, and intra-/extra-axial

Origins:
- Glial cells
  - Astrocytoma
    - 50% of SOL
    - Intra-axial
    - Grades I-II benign, III-IV malignant (cellular atypia, mitosis, necrosis, vascular proliferation). GBM most aggressive
  - Oligodendroglioma
  - Ependymoma
  - Choroid plexus papilloma/carcinoma
- Neuronal
  - All rare – neurones are normally mature, non-dividing cells
  - Medulloblastoma – posterior fossa/IV ventricle in children. Aggressive
    - Posterior fossa SOL presents with raised ICP, ataxia, diplopia
  - Ganglioneuroma/ganglioglioma
- Nerve sheath
  - Schwannoma (e.g. acoustic neuroma – actually a vestibular schwannoma)
  - Neurofibroma (rare)
- Meningioma
  - 15-20% of SOL
  - Extra-axial
  - Usually benign, some invasive. Rarely malignant. Rare in children
  - Arise from arachnoid cap cells/dural base, often parasagittal, convexity, sphenoid
- Lymphoma

    - Responds well to steroids for months, tends to recur and be less treatable
- Vascular
    - Haemangioma most common, but all very rare
- Pituitary
    - Adenoma
        - Benign
        - Functioning (GH/PRL/ACTH/TSH/FSH/LH) or non-functioning
        - Presentations:
            - Vision (bitemporal hemianopia, superior fields down, loss of colour vision in nasal field
            - Hypopituitarism
            - Hormonal hypersecretion
            - Cavernous sinus invasion – diplopia from III palsy
            - Pituitary apoplexy – ACTH suppression, shock – hydrocortisone, need urgent/emergency surgery
    - Craniopharyngioma

Presentation of SOL:
- Depressive
    - Generalised – raised ICP
    - Localised – focal deficit
- Irritative
    - Seizures – generalised or focal

Investigations:
- Imaging – CT/MRI
    - Location, number of lesions, surrounding oedema, hydrocephalus
    - Pituitary tumour and acoustic schwannoma are often clinical diagnoses
- Metastatic workup
    - CXR (lung primary?)
- Tumour markers
- Special – e.g. pituitary function tests

Treatment
- Steroids – reduce oedema, useful before surgery, or with lymphoma
- Anticonvulsants
- Surgery
    - Diagnostic (open or stereotactic)
    - Palliative – debulking (glioma, metastatic)
    - Curative – meningioma, acoustic, pituitary (transphenoidal approach)
    - Shunt for hydrocephalus
- Radiotherapy
    - Adjuvant or primary
    - Gliomas
    - Sometimes for benign SOL (meningioma, pituitary), but side effects especially in child <5
- Chemotherapy
    - Specific indications, rarely used

    - BBB limits effectiveness

Prognosis
- Depends on histology, treatment, neurological status, age
    - Very good for meningioma (but ~20% recurrence)
    - GBM median survival 12 weeks, 9/12 with debulking and radiotherapy

Head Injuries

Open
- Debridement required, plus antibiotic therapy (cef/met or similar).
- Primary closure within 12 hours (6 better), with repair of any defect
- Depressed #s are epileptogenic, so must be elevated and patient given phenytoin/carbamazepine for 6/12 minimum
- May or may not show neuro deficit – consciousness often preserved
- Any puncture wound to the scalp needs investigation

Closed
- Consciousness often impaired. May be associated scalp wound and/or skull fracture, both may be remote from site of injury
- Complications:
    - Haemorrhage from venous sinus/bridging veins/middle meningeal artery
    - Cranial nerve damage:
        - I most common in #, then VII/VIII (petrous bone), then III,IV,VI (Orbit), and II
    - CSF leakage – CSF ottorhoea or rhinorhoea
        - Will heal spontaneously in ~1/52 in undisplaced #
        - Dural repair required if displaced/comminuted # or if leak persists
        - No inoculation of brain so lower risk of infection – penicillin required against nose commensal (S. pneumoniae) only. Delayed meningitis/abscess is possible – radiological check
- Facial palsy – immediate suggests rip of VII, needs repair. Delayed suggests swelling after damage, and will resolve
- Deafness – sensorineural is permanent, conductive (ossicles displaced, ruptured tympanic membrane, blood in middle ear) may be treatable

Pathologies
- Contusion (coup/contra-coup)
- Laceration (edges of skulls or dura)
- Shearing (between grey and white matter – different coefficients of elasticity)
    - Diffuse Axonal Injury – often after rotational injury

Clinical Features
- Brainstem injury
    - Cord is relatively fixed, brain mobile – stress and distortion to brainstem
    - Especially reticular activating system (reduced consciousness) and respiratory centre (Cheyne-Stokes/hyperventilation/other pattern)

    - Also cardiovascular centres, temperature centres (pyrexia), vegative centres (vomiting, reduced GI absorption, hypersecretion)
- Neurogenic pulmonary oedema in extremis

- Motor disturbances
    - Eventual spastic quadraparesis from spinal level lesion
    - Extensor response ('decerebrate' posturing) from midbrain lesion – vestibular input to spinal cord preserved
- Swelling
    - Raised ICP causes drop in CPP (should be >40mmHg)
    - Limited compensation capacity:
        - CSF to spinal cord
        - Cerebral veins to general circulation
        - BP rises (Cushing's response)
    - Compensation fails – tentorial herniation with 2° brainstem compression
    - III compressed – pupil dilatation
- Focal signs

Management
- History of time, trends, rate
- AcBCDE
- NG tube, dress/splint injuries, catheter, IV access
- Radiography – plain films, CT
- Neuro obs q 15mins
- Monitor CO_2 levels (CO2 vasodilator – ↑ICP/↓MAP)
- Evidence of ↑ICP – CT (Burr holes if CT unavailable)
    - Blood
        - Craniectomy/craniotomy to remove clot
    - Swelling
        - Mannitol bolus acutely (1g/kg IV over 20 mins)
        - Half life 4-6 hours
        - Single dose – leakage into injured area, so repeated doses exacerbate problem
        - Dangerous if bleed is present – remove tamponade. Commits to CT within 4 hours if given without definitive diagnosis made first
    - Fluid restriction
    - Ventilation (low normal pCO_2)
    - ICP monitoring

Long term sequelae
- Neurological – hemiplegia/dementia/focal defects/chronic vegetative state
- Epilepsy
- Psychological – memory/mood/behaviour/post concussion syndrome

Lumbar Puncture

Particularly indicated for:
- Guillan-Barre
- Meningitis
- Sub-Arachnoid Haemorrhage

C/I:

- Obstructive raised ICP
  - CT/MRI – axial section with lateral and III ventricles, basal cisterns
  - Basal cistern should be concave towards other structures
- Clotting disorders, inc. DIC
- Sepsis

	Glucose	Protein	Lymphocyte	Neutrophil	Abnormal Cells	RBC
Viral meningitis	-	↑	+	(+)	-	-
Bacterial meningitis	↓↓	↑↑	(+)	+	-	-
TB meningitis	↓↓	↑↑(↑)	++	-	-	-
SAH	-	↑	-	-	-	+
Malignant melanoma	↓	↑(↑↑)	+	-	+	-
Autoimmune	(↓)	↑	+	-	-	-

Cell type and glucose are most useful diagnostically.

Pressure will be elevated in all cases, but most notably in bacterial and TB meningitis, and in malignant melanoma.

SAH – will get equal blood staining in all samples (cf. trauma from LP, first sample most blood stained), plus Xanthachromia.

Hydrocephalus

Pathological excess of CSF (>140ml in cranial compartment). Normally produce 400-500ml/day – no useful drugs exist to reduce this production.

Classed as communicating (ventricles to subarachnoid space) or non-communicating

Never sedate a patient with ?elevated ICP – decreased respiratory rate leads to CO_2 retention and cerebral vasodilatation. GA is safer.

Congenital

- Aqueductal stenosis (NC)
- Spina bifida causing chiari malformation (cerebellar tonsils in foramen magnum, adhesions block CSF) (NC)
- Dandy-Walker – 4th ventricle outlet obstructed (NC)
- Maternal infection (toxoplasma, CMV) (C)

Trauma

- Mass lesion causing ventricular obstruction (NC)
- Blood in CSF
  - Prevent CSF reabsorption (C)
  - Inflammatory response in pia or arachnoid (C)
- Sagittal sinus thrombosis (C)

Infection

- Meningitis – inflammatory exudates reduces reabsorption (C)
- TB meningitis (C)

- Encephalitis – swelling of hemisphere causing obstruction (NC)
- Subdural empyema – veins thrombose – sagittal sinus thromboses (C)

Metabolic

- Hypercoaguable states lead to sagittal sinus thrombosis

Vascular

- Blood/clot
    - Ventricles (NC)
    - Subarachnoid space (C)

Neoplastic

- Mass effect
- Choroid plexus tumour – increased CSF production (rare)

Presentation – infants

- Skull not fused, so increased skull diameter
- Poor feeding, vomiting, irritable, sleepy
- Bulging fontanelle, palpable suture diastasis, scalp venous engorgement, 'sunsetting' eyes (conjugate downward deviation). Rarely papilloedema.
- US via fontanelles, ±CT, ±MRI

Presentation – children/adults

- Raised ICP
- Visual disturbance (blurred/diplopia), neck stiffness (late)
- Ataxia, reduced papillary reactions, papilloedema, IV/VI palsy, nystagmus, conjugate downward deviation of eyes, reduced balance
- CT ± MRI

Presentation – elderly

- Raised ICP, OR:
- Normal pressure hydrocephalus (low grade, chronically raised ICP) – resistance to reabsorption.
    - Ataxia, dementia, incontinence

CT

- All ventricles uniformly enlarged?
- Sulci enlarged (evidence of atrophy) or effaced (raised ICP)?
- Peri-ventricular lucency (PVL)
    - In the young, CSF extravasation around ventricles
    - In elderly, sign of ischaemia (not indication of hydrocephalus)
- Third ventricular rounded? (Sign of hydrocephalus)
- Enlarged temporal horns?

Treatment

- Shunt has problems
    - Failure (especially if blood in ventricles)
    - Infection (~1:20 cases)
    - Excess CSF drainage
    - Pai/arachnoid adhesion
- Use only if no other options
- Communicating – repeat LP (acute) or lumbar drain (chronic)
- Non-communicating

    - Treat cause if possible
    - Consider external ventricular drain if acute, shunt if permanent
    - Alternative – Endoscopic Third Ventriculostomy (ETV) to open channel in floor of third ventricle, bypassing aqueduct/fourth ventricle

Shunt usually drains to peritoneum, occasionally to atrium. Normal CT does not exclude shunt malfunction.

Cognitive Impairment

Dementia – gradual deterioration (e.g. Alzheimers)
Acute confusional state – rapid onset (e.g. systemic infection, meningitis/encephalitis, drugs, organ failure)

Cognitive domains:

- Motor
    - Dyspraxia (follow command, copy action, copy with object, not at all)
    - Ataxia
- Sensory
    - Agnosia
    - Inattention
- Memory
    - Short/long term
        - Long term – episodic/semantic
    - Anterograde/retrograde
    - Explicit/implicit
- Language
- Attention
    - Impaired in acute confusional state, may not be in dementia
    - Tests:
        - GCS (esp. verbal component)
        - Mini Mental Score (esp. orientation, serial subtractions)
        - Digit span (5-7 normal), reverse digit span (3-5 normal)

Abscess

- Low density, ring enhancing lesion. Shows mass effect. Pus-filled – pressure makes lesion spherical
- Needs urgent treatment
- High index of suspicion
- Differential
    - Cystic tumour – less regular
    - Metastatic tumour with cystic component or nodules – less regular

Spinal Disease

Symptoms – usually a constellation of pain (muscular/radiculopathy), neurology, and deformity.

Sources:

- Bone (Degenerative, congenital, neoplastic, traumatic, infectious)
- Ligaments
- Discs
- Meninges
- Neural tissue

- Disc prolapse – pain from nerve root compression
  - Disc usually moves back and left or right – ligament prevents midline movement
  - 30-35% of asymptomatic people have CT/MRI evidence of disc abnormality – 50%+ of the over 60s
  - Schmalls node – end plate defect, disc fills – incidental finding of no clinical significance
- Discitis
  - Inflammation of discs
  - May be associated with osteomyelitis of vertebrae
- Spinal claudication
  - Reduced space in spinal canal
    - Degenerative disease of spine (most common)
    - Trauma
    - Achondroplasia, Paget's disease – rare
  - When increased blood supply is required, not enough space – pain
- Dysraphism
  - Abnormal formation of the spine
    - Spina bifida aperta (occulta)
    - Occult spinal dysraphism
  - Clinical features
    - Back mass
    - Cutaneous stigmata
    - Gait disturbance
    - Club foot
    - Back/extremity pain
    - Weakness
    - Bladder/bowel dysfunction
- 'Mechanical' (wear and tear type)
  - Most common cause of back pain
  - Acute – muscle spasm major component
    - Analgesia (NSAID) and muscle relaxant (benzo)
  - Chronic
    - Anti-inflammatory, physiotherapy
    - Most important – lifestyle change
      - Avoid contact sport, weight lifting, rowing machines (usually bad technique)
      - Exercise – 5x40min each week
      - Lose weight, improve posture
  - Surgical
    - Fuse vertebrae or replace disc (in trials)
    - Occasionally indicated
    - Benefits 30-40% of properly selected patients

- Spinal trauma
    - Ligaments are important in stability
    - Mechanisms
        - Hyperflexion (wedging of anterior body)
        - Hyperextension (avulsion of anterior body)
        - Compression (burst)
        - Shear (subluxation/dislocation)
        - Distraction
        - Rotation

    - Three columns. Disruption to middle column (acts as fulcrum) causes instability
        - Stable – pure flexion or extension
        - Unstable – burst/distraction/shear
- Syringomyelia
    - Syringomyelia/syrinx – CSF-filled cavity in cord
    - Hydromyelia – dilation of central canal
        - Differentiation only on post-mortem, and no clinical difference in management
    - Causes
        - Chiari malformation (cerebellar tonsil in foramen magnum)
        - Tumour causing obstruction
        - Trauma (adhesions/stenosis/haematoma) – can be years for syrinx to develop
        - Transverse myelitis
- Spinal tumours
    - Medullary – usually benign
        - Astrocytoma/haemangioblastoma
        - Ependymoma (low grade malignant)
    - Intradural extramedullary – usually benign
        - Meningioma/neuroma
        - Ependymoma (low grade malignant)
    - Extradural – usually malignant
        - From bone – usually mets
            - Prostate/breast/lung primary
        - Haematological
            - Lymphoma/myeloma

Surgery in Movement Disorders

Stereotactic surgery, utilising a Cartesian co-ordinate system referred to anatomical landmarks or relative to the anterior commissure-posterior commissure line. Detailed pre-operative neurological and radiological assessment is required.

Indications:
- Increasing resistance to pharmacotherapy
- Tremor predominant Parkinson's Disease
- Drug induced dyskinesias

Contraindications:

- Cognitive impairment

A frame is bolted to the outer table of the skull under local anaesthesia to give a firm and stable platform. The frame is attached to the operating table. A standard neural atlas is mapped to the patient imaging, and this then mapped onto the patient by computer.

Burr holes are drilled in the skull, and a microdrive is used to insert electrodes. Recordings are made from these as they progress to confirm the trajectory. Electrodes are usually multiple, each contact ~1.5mm long.

Each electrode is connected to an extension, and these are tunnelled under the scalp to a generator placed in a pouch below the clavicle.

Stimulation at ~110Hz is effective at reducing sub-thalamic nuclei activity. Mortality and morbidity are low (slightly higher in lesioning, low in deep brain stimulation).

Technique is widely used in Parkinson's disease and essential tremor (disabling, medication resistant), with other uses being researched.

Pathology – Cerebrovascular

Stroke

- 85% ischaemic, 15% haemorrhage (intracerebral, subarachnoid, subdural)
- 1hr – microvacuoles in neurons, swollen astrocyte processes
- 4-12hr – neurons hypereosinophilic, loss of Nissl, nuclear pyknosis. Leaky BBB
- 15h-1d – neutrophil migration
- 2d – macrophage migration
- 5d – end of neutrophils migration
- 7d+ –astrocytosis begins, leads to gliosis

Aneurysm

- Saccular
    - Elastica often reduced in thickness
    - Anterior/carotid – 85-95% of cases
        - Anterior cerebral 30%
        - Posterior communicating 25%
        - Middle cerebral 20%
    - Posterior/vertebral 5-15%
    - Multiple 20-30%
- Mycotic – 5-6% of all aneurysms
- Intracerebral aneurysm usually fusiform

Arteriovenous Malformation (AVM) Presentations:

- Haemorrhage 50%
- Seizures
- Mass effect
- Vascular steal leading to ischaemia
- Headache

- Bruit
- Raised ICP

Vasculopathy
- CADASIL
- Amyloid angiopathy
- Arteriosclerosis

Brain Purpura
- Fat embolism
- Malaria
- Poisons
- Acute Haemorrhagic Leukoencephalopathy

Vasculitis
- Virus
    - HIV arteritis, VZV, CMV
- Virus-like
    - Ricketsia
- Bacteria
    - Meningitis leading to secondary vasculitis
- Fungi
    - Aspergillus
- Idiopathic
    - Takayau's, polyarteritis nodosa, temporal arteritis, Wegener's granulomatosis, Churg-Strauss, primary angiitis of CNS, lymphatoid granulomatosis

Neuroradiology – Stroke

Sub-insular cortex region – typical site for lacunar infarct. Seen as low density, surrounded by normal tissue.

Ischaemic/infarcted region is hypodense on CT. Can be haemorrhagic however, with hyperdense blood seen.

For a region to enhance with contrast, need vascularity (usually 3-5 days post-infarct to allow for capillary formation), and damage to BBB. Usually gyral pattern.

Watershed/junctional infarcts are a consequence of an acute drop in blood supply against a background of underlying atherosclerosis. Causes include trauma, cardiac surgery, septic shock, heart failure, etc.

Stroke investigation:
- CT head
- Carotid Doppler US/MR angiography to screen

    - Angiogram to confirm
        - Carotid endarterectomy is 70%+ stenosis. Medical treatment better for <30-40%, equal risk for 40-70%
- BP/diabetes/cholesterol/smoking
    - Investigate and control

Stroke care:

- Patient should be treated in MDT stroke unit
- If appropriate, thrombolyse early – ↓ risk of haemorrhage if done <3 hours
- May be a role for neuroprotective drugs (unproven in humans) – block neurochemical cascade

	Lacunar	Partial anterior circulation	Total anterior circulation	Posterior circulation
Signs	Motor OR Sensory	2 of: • Motor/sensory • Hemiplegia • Cortical symptoms	All of:	• Hemianopia • Brain stem • Cerebellar
Dead at 1 year	10	20	60	20
Dependant at 1 year	25	30	35	20

Neuroradiology – Tumours

Mass lesion may be intra- or extra-axial. Usually need contrast enhancement to determine clearly.

Features:
Enhancement indicates either a vascular tumour (e.g. meningioma) or BBB breakdown (e.g. glioma)
Glial tumours will often calcify
Multiple tumours are suggestive of metastases (often vary in size, shape, etc)
Meningioma has dural base, oedema, and enhances
Rapidly resolving – 'vanishing' or 'ghost' tumour (especially after steroid)
Lymphoma
Primary – brain only (often adjacent to ventricles)
Secondary – spread from elsewhere (often to skull base, meninges and often affects cranial nerves)

Neuroradiology – Spinal Disease

Non-invasive

- Plain films*
- Tomography
- Isotope bone scan*
- US
- CT*
- MRI*

* - more useful techniques

Invasive

- Myelography*
- Epidurography
- CT myelography*
- Vascular studies (spinal angiography, epidural venography)
- Discography
- Facet joint arthroscopy
- Needle biopsy*

Principles:

- Safest method better (often no radiation method – especially if young/pregnant)
- Non-invasive better than invasive
- Cheapest suitable method better

Plain films are generally useless in back pain +/- sciatica

Useful Tips

Abscess in the brain tends to cause fibrosis. Most other pathology causes gliosis

Motor structures tend to be anterior, sensory structures posterior

Partial volume effect – artefact seen on scans where subject is tilted. Part of a structure is rotated into a different slice to the rest of the structure, giving an apparent asymmetry in the slice

Poor resolution in a CT image is often due to patient movement

Haematoma – subdural cresentic, extradural bi-convex

Typical IV contrasts for CT are iodine based, for MRI are gadolinium based

Rapid growth of SOL tends to give more marked symptoms and more rapid ↑ in ICP