Chapter 7
Neurology

Clinical neurology is often treated with extreme trepidation by the MRCP(UK) candidates, for all three parts. This is in fact completely unfounded, because the subject matter of the neurology component is extremely predictable and logical. The questions tend to err on the easy side, because neurologists feel no need to over-complicate their specialty for the general physician (it is argued). For the purpose of the examination, clinical neurology is bundled together with clinical ophthalmology and psychiatry, which tends to reflect how these subjects actually go together in real life. As ophthalmology and psychiatry have their own Royal Colleges, the amount and depth of knowledge required to pass is modest.

A. NEUROLOGY

A7.1 Neurogenetics

You are expected to have knowledge of recent advances in the understanding of the genetic basis for various neurological disorders.

7.1.1 Myotonic dystrophy

Myotonic dystrophy (also called dystrophia myotonica) is an inherited myopathy with features developing at around 20-30 years old. It affects skeletal, cardiac and smooth muscle. These are trinucleotide repeats transcribed in RNA, but which are not translated into protein. There are two main types of myotonic dystrophy, DM1 and DM2.

Genetics

- autosomal dominant
- a trinucleotide repeat disorder
- DM1 is caused by a CTG repeat at the end of the DMPK (Dystrophia Myotonica-Protein Kinase) gene on chromosome 19
- DM2 is caused by a repeat expansion of the ZNF9 gene on chromosome 3

The key differences are listed in table below:

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<thead>
<tr>
<th></th>
<th>DM1</th>
<th>DM2</th>
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<tbody>
<tr>
<td>Genetics</td>
<td>- DMPK gene on chromosome 19q13.3</td>
<td>- ZNF9 gene on chromosome 3q21</td>
</tr>
<tr>
<td></td>
<td>- Distal weakness more prominent</td>
<td>- Proximal weakness more prominent</td>
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<tr>
<td></td>
<td></td>
<td>- Severe congenital form not seen</td>
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</tbody>
</table>

General features

- myotonic facies (long, 'haggard' appearance)
- frontal balding
- bilateral ptosis
- cataracts
- dysarthria
Other features

- myotonia (tonic spasm of muscle);
- weakness of arms and legs (distal initially);
- mild mental impairment;
- diabetes mellitus;
- testicular atrophy;
- cardiac involvement: heart block, cardiomyopathy;
- dysphagia.

7.1.2 Genetic aspects of Alzheimer's disease

Most cases are sporadic.

- 5% are inherited as an autosomal dominant trait
- mutations in the amyloid precursor protein (chromosome 21), presenilin 1 (chromosome 14) and presenilin 2 (chromosome 1) genes are thought to cause the inherited form

Apolipoprotein E allele E4 - encodes a cholesterol transport protein

An area of growing interest has been genetic testing for Alzheimer's disease. Until recently, clinical gene testing only included apolipoprotein E genotyping and testing for presenilin 1 mutations.

⚠️ In 2008, testing in the US expanded to include the presenilin 2 and amyloid precursor protein genes. Despite these advances, genetic testing is currently not appropriate for most individuals diagnosed with AD and has limited utility for predictive purposes.
7.2 Cell biology

Questions in this area will relate to advances in the cellular mechanisms of certain neurological disease processes which have provided better understanding of disease mechanisms and which might, in the future, lead to more rational therapy.

7.2.1 The genesis of tissue damage in stroke and the role of certain excitatory neurotransmitters

Knowledge of the molecular mechanisms that underlie neuron death following stroke is important to allow the development of effective neuroprotective strategies.

Neurological research focuses on information derived from animal models of ischemic injury. The two principal models for human stroke are induced in rodents either by global or focal ischaemia.

In both cases, blood flow disruptions limit the delivery of oxygen and glucose to neurons causing ATP reduction and energy depletion, initiating excitotoxic mechanisms that are deleterious for neurons. These include activation of glutamate receptors and release of excess glutamate in the extracellular space inducing neuron depolarisation and dramatic increase of intracellular calcium that in turn activates multiple intracellular death pathways.

The notion that excitotoxicity leads only to neuron necrosis has largely been abandoned now, as ultrastructural and biochemical analysis have shown signs of apoptotic and autophagic cell death in ischemic neurons and this has been further confirmed in neurons subjected to in vitro ischaemia models.
7.2.2 The role of the dopaminergic system in various extrapyramidal disorders

It is our understanding of the degeneration of the nigrostriatal dopaminergic system that is the rationale for using dopamine as an enhancer in Parkinson's disease. Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment.

Dopamine receptor agonists

• *e.g.* bromocriptine, ropinirole, cabergoline, apomorphine
• ergot-derived dopamine receptor agonists (*bromocriptine, cabergoline, pergolide*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advises that an ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored.

Levodopa

• usually combined with a decarboxylase inhibitor (*e.g.* carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
• reduced effectiveness with time (usually by 2 years)
• unwanted effects: dyskinesia, 'on-off' effect
• no use in neuroleptic induced parkinsonism

MAO-B (Monoamine Oxidase-B) inhibitors

• *e.g.* selegiline
• inhibits the breakdown of dopamine secreted by the dopaminergic neurons

Amantadine

• mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

COMT (Catechol-O-Methyl Transferase) inhibitors

• *e.g.* entacapone
• COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
• used in established PD

Antimuscarinics

• block cholinergic receptors
• now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
• help tremor and rigidity
• *e.g.* procyclidine, benztropine, trihexyphenidyl (benzhexol)
7.3 Neuropharmacology

You are expected to have some knowledge of new drug developments in neurology, as well as the established drug therapies.

7.3.1 Alzheimer’s disease

The pathogenesis of AD is complex and not yet fully understood. A number of factors, including amyloid plaques, NFTs, and inflammatory processes, are likely to contribute to development of the disease. Acetylcholine and glutamate are intimately involved in learning and memory.

Hypotheses implicating defects within both neurotransmitter systems in AD) are well recognized now in the literature, following the seminal paper by Bartus et al. (1979) implicating dysfunction of the cholinergic system.

This knowledge coupled with ongoing discoveries about the multiple pathophysiologic pathways involved in development and progression of AD has given rise to several plausible therapeutic targets. Therapies addressing some of these targets (i.e., acetylcholine, glutamate) have already shown clinical efficacy in treating AD while other targets continue to be investigated.

7.3.2 Atypical antipsychotics

Atypical antipsychotics should now be used first-line in patients with schizophrenia, according to 2005 NICE guidelines.

‘Schizophrenia – atypical antipsychotics’ NICE technology appraisal 43 (June 2002). NICE recommended the use of atypical (newer) oral antipsychotic drugs for a person who has been newly diagnosed with schizophrenia and for people who currently taking typical (older) antipsychotic drugs that are controlling their symptoms of schizophrenia but are causing side effects. The main advantage of the atypical agents is a significant reduction in extra-pyramidal side-effects.

Adverse effects of atypical antipsychotics

- weight gain
- olanzapine and risperidone are associated with an increased risk of stroke in elderly patients
- clozapine is associated with agranulocytosis (see below)

Examples of atypical antipsychotics

- clozapine
- olanzapine
- risperidone
- quetiapine
- amisulpride
Clozapine, one of the first atypical agents to be developed, carries a significant risk of agranulocytosis and full blood count monitoring is therefore essential during treatment. For this reason clozapine should only be used in patients resistant to other antipsychotic medication.

Adverse effects of clozapine

- agranulocytosis (1%), neutropaenia (3%)
- reduced seizure threshold - can induce seizures in up to 3% of patients
7.4 Localisation of function

7.4.1 Ulnar nerve

Overview

- arises from medial cord of brachial plexus (C8, T1)

Motor to

- medial two lumbricals;
- adductor pollicis;
- interossei;
- hypothenar muscles: abductor digiti minimi, flexor digiti minimi;
- flexor carpi ulnaris.

Sensory to medial 1½ fingers (palmar and dorsal aspects)

Patterns of damage

Damage at wrist

- 'claw hand'
- wasting and paralysis of intrinsic hand muscles (except lateral two lumbricals)
- wasting and paralysis of hypothenar muscles
- sensory loss to the medial 1½ fingers (palmar and dorsal aspects)

Damage at elbow

- as above
- radial deviation of wrist

7.4.2 Acoustic neuroma

Acoustic neuromas account for approximately five percent of intracranial tumours and 90 percent of cerebellopontine angle.

Features can be predicted by the affected cranial nerves

- cranial nerve VIII: hearing loss, vertigo, tinnitus
- cranial nerve V: absent corneal reflex
- cranial nerve VII: facial palsy

Bilateral acoustic neuromas are seen in neurofibromatosis type 2.

MRI of the cerebellopontine angle is the investigation of choice
7.4.3 Meralgia paraesthetica

Basics

- caused by compression of lateral cutaneous nerve of thigh
- typically burning sensation over antero-lateral aspect of thigh

7.4.4 Intracranial venous thrombosis

Overview

- can cause cerebral infarction, much less common than arterial causes
- 50% of patients have isolated sagittal sinus thromboses - the remainder have coexistent lateral sinus thromboses and cavernous sinus thromboses

Features

- headache (may be sudden onset)
- nausea and vomiting
- papilloedema

Sagittal sinus thrombosis

- may present with seizures and hemiplegia
- parasagittal biparietal or bifrontal haemorrhagic infarctions are sometimes seen

Cavernous sinus thrombosis

- other causes of cavernous sinus syndrome: local infection (e.g. sinusitis), neoplasia, trauma;
- ophthalmoplegia due to IIIrd, IVth and VIth cranial nerve damage;
- trigeminal nerve involvement may lead to hyperaesthesia of upper face and eye pain;
- central retinal vein thrombosis;
- swollen eyelids.

Lateral sinus thrombosis

- VIth and VIIth cranial nerve palsies
7.4.5 Pituitary apoplexy

Sudden enlargement of pituitary tumour secondary to haemorrhage or infarction.

Features

- sudden onset headache similar to that seen in subarachnoid haemorrhage;
- vomiting;
- neck stiffness;
- visual field defects: classically bitemporal superior quadrantic defect;
- extraocular nerve palsies;
- features of pituitary insufficiency e.g. Hypotension secondary to hypoadrenalism.

4.6 Nystagmus

Upbeat nystagmus

- cerebellar vermis lesions

Downbeat nystagmus - foramen magnum lesions

- Arnold-Chiari malformation
7.5 Clinical neurology – common conditions

7.5.1 Epilepsy

Generalised - no focal features, consciousness lost immediately

- grand mal (tonic-clonic)
- petit mal (absence seizures)
- partial seizures progressing to generalised seizures

Partial - focal features depending on location

- simple (no disturbance of consciousness or awareness)
- complex (consciousness is disturbed)
- temporal lobe ⇒ aura, déjà vu, jamais vu; motor ⇒ Jacksonian ‘march’

Myoclonus

- occur in a variety of conditions

Most neurologists now start antiepileptics following a second epileptic seizure. NICE guidelines suggest starting antiepileptics after the first seizure if any of the following are present:

- the patient has a neurological deficit
- brain imaging shows a structural abnormality
- the EEG shows unequivocal epileptic activity
- the patient or their family or carers consider the risk of having a further seizure unacceptable

Sodium valproate is considered the first line treatment for patients with generalised seizures with carbamazepine used for partial seizures.

Adverse effects
gastrointestinal: nausea and increased appetite and weight gain
alopecia: regrowth may be curly
ataxia
tremor
hepatitis
pancreatitis
teratogenic

Tonic-clonic seizures
sodium valproate
second line: lamotrigine, carbamazepine

Absence seizures (Petit mal)
sodium valproate or ethosuximide
sodium valproate particularly effective if co-existent tonic-clonic seizures in primary generalised epilepsy
Myoclonic seizures
sodium valproate
second line: clonazepam, lamotrigine

Partial seizures
carbamazepine
second line: lamotrigine, sodium valproate

7.5.2 Multiple sclerosis

Treatment in multiple sclerosis is focused at reducing the frequency and duration of relapses. There is no cure. High dose steroids (e.g. IV methylprednisolone) may be given for 3-5 days to shorten the length of an acute relapse. Baclofen is helpful in controlling spasticity. Hallucinations are occasionally seen on the withdrawal of baclofen.

Beta-interferon has been shown to reduce the relapse rate by up to 30%. Certain criteria have to be met before it is used:
relapsing-remitting disease + 2 relapses in past 2 years + able to walk 100m unaided
secondary progressive disease + 2 relapses in past 2 years + able to walk 10m (aided or unaided)
reduces number of relapses and MRI changes, however doesn’t reduce overall disability

Other drugs used in the management of multiple sclerosis include:
• glatiramer acetate: immunomodulating drug
• natalizumab: a recombinant monoclonal antibody that antagonises Alpha4Beta1-integrin found on the surface of leucocytes, thus inhibiting migration of leucocytes across the endothelium into parenchymal tissue
• symptom control
• spasticity: baclofen and gabapentin are first-line. Other options include diazepam, dantrolene and tizanidine

⚠️ For a review of the most up-to-date (at the time of publication) guidance on multiple sclerosis in the UK, please refer to the following link.

NICE CG8

http://guidance.nice.org.uk/CG8/NiceGuidance/pdf/English
7.5.3 Cluster headache

Cluster headaches are more common in men (5:1) and smokers.

Features

- constant, intense, and boring pain typical occurs once or twice a day, each episode lasting 15 mins - 2 hours;
- clusters typically last 4-12 weeks;
- intense unilateral pain around one eye (recurrent attacks 'always' affect same side);
- patient is restless during an attack;
- 80-90% have attacks at the same time each day;
- alcohol is often a trigger;
- accompanied by redness, lacrimation, lid swelling;
- nasal stuffiness;
- miosis and ptosis (in a minority).

Management

- acute: 100% oxygen, subcutaneous sumatriptan, nasal lidocaine
- prophylaxis: verapamil, lithium, sodium valproate, prednisolone
- consider specialist referral

7.5.4 Neurofibromatosis

There are two types of neurofibromatosis, NF1 and NF2. Both are inherited in an autosomal dominant fashion.

NF1 is also known as von Recklinghausen's syndrome. It is caused by a gene mutation on chromosome 17 which encodes neurofibromin and affects around 1 in 4,000.

NF2 is caused by gene mutation on chromosome 22 and affects around 1 in 100,000.

Features

<table>
<thead>
<tr>
<th>NF1</th>
<th>NF2</th>
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<tbody>
<tr>
<td>Café-au-lait spots (= 6, 15 mm in diameter)</td>
<td>Bilateral acoustic neuromas</td>
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<tr>
<td>Axillary/groin freckles</td>
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<tr>
<td>Peripheral neurofibromas</td>
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<td>Iris: Lisch nodules in &gt; 90%</td>
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<td>Scoliosis</td>
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</table>
7.5.5 Paraneoplastic syndromes affecting nervous systems

Lambert-Eaton myasthenic syndrome

- associated with small cell lung cancer (also breast and ovarian)
- antibody directed against pre-synaptic voltage gated calcium channel in the peripheral nervous system
- can also occur independently as autoimmune disorder

Anti-Hu

- associated with small cell lung carcinoma and neuroblastomas
- sensory neuropathy - may be painful
- cerebellar syndrome
- encephalomyelitis

Anti-Yo

- associated with ovarian and breast cancer
- cerebellar syndrome

Anti-GAD antibody

- associated with breast, colorectal and small cell lung carcinoma
- stiff person syndrome

Anti-Ri

- associated with breast and small cell lung carcinoma
- ocular opsoclonus-myoclonus

7.5.6 Essential tremor

Essential tremor (previously called benign essential tremor) is an autosomal dominant condition which usually affects both upper limbs.

Features

- postural tremor: worse if arms outstretched
- improved by alcohol and rest
- most common cause of titubation (head tremor)

Management

- propranolol is first-line
- primidone is sometimes used
7.5.7 Multiple system atrophy

Shy-Drager syndrome is a type of multiple system atrophy.

Features

- Parkinsonism
- autonomic disturbance (atonic bladder, postural hypotension)
- cerebellar signs

7.5.8 Idiopathic intracranial hypertension

Idiopathic intracranial hypertension (also known as pseudotumour cerebri and formerly benign intracranial hypertension) is a condition classically seen in young, overweight females.

Features

- headache;
- blurred vision;
- papilloedema (usually present);
- enlarged blind spot;
- sixth nerve palsy may be present.

Risk factors

- obesity;
- female sex;
- pregnancy;
- drugs: OCP, steroids, tetracycline, vitamin A.

Management

- weight loss;
- diuretics e.g. acetazolamide;
- repeated lumbar puncture;
- surgery: optic nerve sheath decompression and fenestration may be needed to prevent damage to the optic nerve. [A lumbo-peritoneal or ventriculo-peritoneal shunt may also be performed to reduce intracranial pressure.]
7.5.9 Neuroleptic malignant syndrome

Neuroleptic malignant syndrome is a rare but dangerous condition seen in patients taking antipsychotic medication. It carries a mortality of up to 10% and can also occur with atypical antipsychotics.

Features

- more common in young male patients;
- onset usually in first 10 days of treatment or after increasing dose;
- pyrexia;
- rigidity;
- tachycardia;

A raised creatine kinase is present in most cases. A leukocytosis may also be seen.

Management

- stop antipsychotic;
- IV fluids to prevent renal failure;
- dantrolene may be useful in selected cases;
- bromocriptine, a dopamine agonist, may also be used.

7.5.10 Motor neuron disease: management

Motor neuron disease is a neurological condition of unknown cause which can present with both upper and lower motor neuron signs. It rarely presents before 40 years and various patterns of disease are recognized, including amyotrophic lateral sclerosis, progressive muscular atrophy and bulbar palsy.

Riluzole

- glutamate antagonist
- used mainly in amyotrophic lateral sclerosis
- prolongs life by about 3 months
- expensive

Respiratory care

- non-invasive ventilation (usually BIPAP) is used at night
- studies have shown a survival benefit of around 7 months

Prognosis

- poor: 50% of patients die within 3 years
7.5.11 Guillain-Barré syndrome

Guillain-Barré syndrome describes an immune mediated demyelination of the peripheral nervous system often triggered by an infection (classically *Campylobacter jejuni)*

Pathogenesis

- cross reaction of antibodies with gangliosides in the peripheral nervous system
- correlation between anti-ganglioside antibody (e.g. anti-GM1) and clinical features has been demonstrated
- anti-GM1 antibodies in 25% of patients

Miller-Fisher syndrome

- variant of Guillain-Barré syndrome
- associated with areflexia, ataxia, ophthalmoplegia
- usually presents as a descending paralysis rather than ascending as seen in other forms of Guillain-Barré syndrome
- anti-GQ1b antibodies are present in 90% of cases

Management

- plasma exchange
- IV immunoglobulins
- steroids and immunosuppressants have not been shown to be beneficial
- FVC regularly to monitor respiratory function

Prognosis

- 20% suffer permanent disability, 5% die

7.5.12 HIV: neurocomplications

Encephalitis

- may be due to CMV or HIV itself
- HSV encephalitis but is relatively rare in the context of HIV
- CT: oedematous brain
Cryptococcus

- most common fungal infection of CNS
- headache, fever, malaise, nausea/vomiting, seizures, focal neurological deficit
- CSF: high opening pressure, India ink test positive
- CT: meningeal enhancement, cerebral oedema
- meningitis is typical presentation but may occasionally cause a space occupying lesion

Progressive multifocal leukoencephalopathy (PML)

- widespread demyelination
- due to infection of oligodendrocytes by human papovirus (JC virus)
- symptoms, subacute onset: behavioural changes, speech, motor, visual impairment
- CT: single or multiple lesions, no mass effect, don’t usually enhance. MRI is better - high-signal demyelinating white matter lesions are seen

AIDS dementia complex

- caused by HIV virus itself
- symptoms: behavioural and cognitive changes predominantly, possible motor impairment
- CT: cortical and subcortical atrophy

Toxoplasmosis

- constitutional symptoms, headache, confusion, drowsiness
- CT: usually multiple ring enhancing lesions, mass effect may be seen
- management: sulfadiazine and pyrimethamine

Tuberculosis

- single enhancing lesion
7.5.13 Myasthenia gravis

Myasthenia gravis is an autoimmune disorder resulting in insufficient functioning acetylcholine receptors. Antibodies to acetylcholine receptors are seen in 90% of cases. Myasthenia is more common in women (2:1)

Features

- extraocular muscle weakness: diplopia
- proximal muscle weakness: face, neck, limb girdle
- ptosis
- dysphagia

Associations

- thymomas in 15%
- autoimmune disorders: pernicious anaemia, autoimmune thyroid disorders, rheumatoid, SLE
- thymic hyperplasia in 50-70%

Investigations

- Tensilon® test: IV edrophonium reduces muscle weakness temporarily
- CT thorax to exclude thymoma
- CK normal

Management

- long-acting anticholinesterase e.g. Pyridostigmine
- immunosuppression: prednisolone initially
- thymectomy

Management of myasthenic crisis

- plasmapheresis
- intravenous immunoglobulins
7.5.14 Tuberous sclerosis

Tuberous sclerosis (TS) is a genetic condition of autosomal dominant inheritance. Like neurofibromatosis, the majority of features seen in TS are neuro-cutaneous.

Cutaneous features

- depigmented 'ash-leaf' spots which fluoresce under UV light;
- roughened patches of skin over lumbar spine (Shagreen patches);
- adenoma sebaceum: butterfly distribution over nose;
- fibromata beneath nails (subungual fibromata);
- café-au-lait spots may be seen.

Neurological features

- developmental delay
- epilepsy (infantile spasms or partial)
- intellectual impairment
- (advers effects of medications)

Also

- retinal hamartomas: dense white areas on retina (phakomata)
- rhabdomyomas of the heart
- glomatous changes can occur in the brain lesions
- polycystic kidneys, renal angiomyolipomata

7.5.15 Subdural haemorrhage

- most commonly secondary to trauma e.g. old person/alcohol falling over
- initial injury may be minor and is often forgotten
- caused by bleeding from damaged bridging veins between cortex and venous sinuses

Features

- headache
- classically fluctuating conscious level
- raised ICP

Treatment

- needs neurosurgical review ? burr hole
7.5.16 Visual field defects

Some main points for the exam are:

- left homonymous hemianopia means visual field defect to the left, i.e. Lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

Homonymous hemianopia

- incongruous defects: lesion of optic tract
- congruous defects: lesion of optic radiation or occipital cortex
- macula sparing: lesion of occipital cortex

Homonymous quadrantanopia

- superior: lesion of temporal lobe
- inferior: lesion of parietal lobe
- mnemonic = PITS (Parietal-Inferior, Temporal-Superior)

Bitemporal hemianopia

- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma
7.5.14 Third nerve palsy

Features

- eye is deviated 'down and out'
- ptosis
- pupil may be dilated (sometimes called a 'surgical' third nerve palsy)

Causes

- diabetes mellitus;
- vasculitis e.g. temporal arteritis, SLE;
- false localizing sign due to uncal herniation through tentorium if raised ICP;
- posterior communicating artery aneurysm (pupil dilated);
- cavernous sinus thrombosis;
- Weber's syndrome: ipsilateral third nerve palsy with contralateral hemiplegia - caused by midbrain strokes;
- other possible causes: amyloid, multiple sclerosis.
7.5.14 Horner's syndrome

Features

- miosis (small pupil)
- ptosis
- enophthalmos (sunken eye)
- anhydrosis (loss of sweating one side)

Distinguishing between causes

- heterochromia (difference in iris colour) is seen in congenital Horner's
- anhydrosis: see below

<table>
<thead>
<tr>
<th>Central lesions</th>
<th>Pre-ganglionic lesions</th>
<th>Post-ganglionic lesions</th>
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<tbody>
<tr>
<td>Anhydrosis of the face, arm and trunk</td>
<td>Anhydrosis of the face</td>
<td>No anhydrosis</td>
</tr>
<tr>
<td>Stroke</td>
<td>Pancoast’s tumour</td>
<td>Carotid artery dissection</td>
</tr>
<tr>
<td>Syringomyelia</td>
<td>Thyroidectomy</td>
<td>Carotid aneurysm</td>
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<tr>
<td>Multiple sclerosis</td>
<td>Trauma</td>
<td>Cavernous sinus thrombosis</td>
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<tr>
<td>Tumour</td>
<td>Cervical rib</td>
<td>Cluster headache</td>
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<td>Encephalitis</td>
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7.5.15 Herpes simplex encephalitis

Herpes simplex (HSV) encephalitis is a common topic in the MRCP. The virus characteristically affects the temporal lobes - questions may give the result of imaging or describe temporal lobe signs e.g. aphasia.

Features

- fever, headache, psychiatric symptoms, seizures, vomiting
- focal features e.g. aphasia
- peripheral lesions (e.g. cold sores) have no relation to presence of HSV encephalitis

Pathophysiology

- HSV-1 responsible for 95% of cases in adults
- typically affects temporal and inferior frontal lobes

Investigation

- CSF: lymphocytosis, elevated protein
- PCR for HSV
- CT: medial temporal and inferior frontal changes (e.g. petechial haemorrhages) - normal in one-third of patients
- MRI is better (and often brings up the characteristic “cortical ribboning effect”)
- EEG pattern: lateralised periodic discharges at 2 Hz

Treatment

- intravenous aciclovir

The prognosis is dependent on whether aciclovir is commenced early. If treatment is started promptly the mortality is 10-20%. Left untreated the mortality approaches 80%
7.5.16 Normal pressure hydrocephalus

Normal pressure hydrocephalus is a reversible cause of dementia seen in elderly patients. It is thought to be secondary to reduced CSF absorption at the arachnoid villi. These changes may be secondary to head injury, subarachnoid haemorrhage or meningitis.

A classical *triad* of features is seen

- urinary incontinence
- dementia and bradyphrenia
- gait abnormality (may be similar to Parkinson’s disease)

**Imaging**

- hydrocephalus with an enlarged fourth ventricle

**Management**

- ventriculoperitoneal shunting
7.5.17 Restless legs syndrome

Restless legs syndrome (RLS) is a syndrome of spontaneous, continuous lower limb movements that may be associated with paraesthesia. It is extremely common, affecting between 2-10% of the general population. Males and females are equally affected and a family history may be present.

Clinical features

- uncontrollable urge to move legs (akathisia). Symptoms initially occur at night but as condition progresses may occur during the day. Symptoms are worse at rest
- paraesthesias e.g. ‘crawling’ or ‘throbbing’ sensations
- movements during sleep may be noted by the partner - periodic limb movements of sleeps (PLMS)

Causes and associations

- there is a positive family history in 50% of patients with idiopathic RLS;
- iron-deficiency anaemia;
- uraemia;
- diabetes mellitus;
- pregnancy.

The diagnosis is clinical although bloods to exclude iron deficiency anaemia may be appropriate.

Management

- simple measures: walking, stretching, massaging affected limbs;
- treat any iron deficiency;
- dopamine agonists are first-line treatment (e.g. pramipexole, ropinirole);
- benzodiazepines;
- gabapentin
7.6 Cerebrovascular medicine

7.6.1 Epidemiological aspects, in particular the risk factors for stroke

A stroke happens when the blood supply to your brain is disrupted. This can be by a blood clot blocking an artery in your brain (ischaemic stroke) or a blood vessel bursting in your brain (haemorrhagic stroke).

Risk factors for stroke include:

- smoking;
- high blood pressure;
- high cholesterol;
- being overweight or obese;
- diabetes;
- a family history of stroke/heart disease;
- abnormal heart beat (arrhythmia);
- conditions that increase your bleeding tendency (e.g. haemophilia);
- regular, heavy drinking;
- using illegal drugs, such as cocaine.

A stroke can also happen after an injury to an artery in your neck. This is called cervical artery dissection.

7.6.2 Management of stroke

Some very useful links on the management (at the time of writing) are:

www.rcplondon.ac.uk/pubs/brochure.aspx?e=250

http://www.nice.org.uk/guidance/index.jsp?action=download&co=38877

Antiplatelet therapy plays a major role in the secondary prevention of ischaemic stroke. The antiplatelet agents that are most used in the clinic include aspirin, dipyridamole and clopidogrel. These agents inhibit platelet activation through different mechanisms of action. A

Aspirin is the first-line drug in the secondary prevention of stroke; a combination of aspirin with dipyridamole produces a synergistic antithrombotic effect. Clopidogrel is slightly more effective than aspirin at reducing the risk of ischaemic events. Trials comparing the combination of aspirin and clopidogrel versus aspirin are underway. Intravenous antiplatelet therapy with glycoprotein IIb/IIIa receptor inhibitors for acute stroke and as an adjunct to carotid artery stenting appears promising. However, oral GPIIb/IIIa receptor inhibitors appear hazardous.

A recent meta-analysis of 21 trials that enrolled 18,270 patients with prior ischaemic stroke and transient ischaemic attack (TIA) demonstrated that antiplatelet agents reduced the relative risk of vascular events by 17% as compared with controls (Antithrombotic Trialists. Collaborative meta-analysis of randomised trials of antiplatelet therapy for

7.6.3 Transient ischaemic attack

NICE issued updated guidelines relating to stroke and transient ischaemic attack (TIA) in 2008. They advocated the use of the ABCD2 prognostic score for risk stratifying patients who have had a suspected TIA:

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Age = 60 years</td>
<td>1</td>
</tr>
<tr>
<td>B Blood pressure = 140/90 mmHg</td>
<td>1</td>
</tr>
<tr>
<td>C Clinical features</td>
<td></td>
</tr>
<tr>
<td>- Unilateral weakness</td>
<td>2</td>
</tr>
<tr>
<td>- Speech disturbance, no weakness</td>
<td>1</td>
</tr>
<tr>
<td>D Duration of symptoms</td>
<td></td>
</tr>
<tr>
<td>- &gt; 60 minutes</td>
<td>2</td>
</tr>
<tr>
<td>- 10-59 minutes</td>
<td>1</td>
</tr>
<tr>
<td>Patient has diabetes</td>
<td>1</td>
</tr>
</tbody>
</table>

This gives a total score ranging from 0 to 7. People who have had a suspected TIA who are at a higher risk of stroke (that is, with an ABCD2 score of 4 or above) should have:

- aspirin (300 mg daily) started immediately
- specialist assessment and investigation within 24 hours of onset of symptoms
- measures for secondary prevention introduced as soon as the diagnosis is confirmed, including discussion of individual risk factors

If the ABCD2 risk score is 3 or below:

- specialist assessment within 1 week of symptom onset, including decision on brain imaging
  - if vascular territory or pathology is uncertain, refer for brain imaging

People with crescendo TIAs (two or more episodes in a week) should be treated as being at high risk of stroke, even though they may have an ABCD2 score of 3 or below.

NICE also published a technology appraisal in 2005 on the use of clopidogrel and dipyridamole.

Recommendations from NICE include:

- low-dose aspirin combined with modified-release dipyridamole is recommended as first-line treatment. After 2 years treatment should revert to low-dose aspirin alone
• if aspirin cannot be taken, clopidogrel alone

With regards to carotid artery endarterectomy:

• recommend if patient has suffered stroke or TIA in the carotid territory and are not severely disabled

Endarterectomy should only be considered if carotid stenosis > 70% according ECST [European Carotid Surgery Trialists’ Collaborative Group] criteria or > 50% according to NASCET [North American Symptomatic Carotid Endarterectomy Trial] criteria.
7.6.4 Stroke: highlighted points from the guidelines on management

Selected points relating to the management of acute stroke include:

- blood glucose, hydration, oxygen saturation and temperature should be maintained within normal limits
- blood pressure should not be lowered in the acute phase unless there are complications e.g. Hypertensive encephalopathy
- aspirin 300mg orally or rectally should be given as soon as possible if a haemorrhagic stroke has been excluded
- with regards to atrial fibrillation, the RCP state: 'anticoagulants should not be started until brain imaging has excluded haemorrhage, and usually not until 14 days have passed from the onset of an ischaemic stroke'
- if the cholesterol is > 3.5 mmol/l patients should be commence on a statin

7.6.5 Thrombolysis

Thrombolysis should only be given if:

- it is administered within 3 – 4½ hours (alteplase is currently recommended by NICE) of onset of stroke symptoms (unless as part of a clinical trial)
- haemorrhage has been definitively excluded (i.e. Imaging has been performed)
7.6 Dementia

The key points, relevant to medical care, are as follows (from CG42 NICE guidelines on dementia.)

- **Memory assessment services** (which may be provided by a memory assessment clinic or by community mental health teams) should be the single point of referral for all people with a possible diagnosis of dementia.

- **Structural imaging** should be used in the assessment of people with suspected dementia to exclude other cerebral pathologies and to help establish the subtype diagnosis. Magnetic resonance imaging (MRI) is the preferred modality to assist with early diagnosis and detect subcortical vascular changes, although computed tomography (CT) scanning could be used. Specialist advice should be taken when interpreting scans in people with learning disabilities.

- People with dementia who develop non-cognitive symptoms that cause them significant distress or who develop behaviour that challenges should be offered an assessment at an early opportunity to establish the likely factors that may generate, aggravate or improve such behaviour.

7.7 Nerve conduction studies

Nerve conduction studies (NCS) are useful in determining between axonal and demyelinating pathology.

**Axonal**

- normal conduction velocity
- reduced amplitude

**Demyelinating**

- reduced conduction velocity
- normal amplitude
B. OPHTHALMOLOGY

7.8 Macular degeneration

Macular degeneration is the most common cause of blindness in the UK. Degeneration of the central retina (macula) is the key feature with changes usually bilateral. Two forms of macular degeneration are seen:

- dry macular degeneration: characterised by drusen - yellow round spots in Bruch's membrane
- wet (exudative, neovascular) macular degeneration: characterised by choroidal neovascularisation. Leakage of serous fluid and blood can subsequently result in a rapid loss of vision. Carries worst prognosis.

Risk factors

- age: most patients are over 60 years of age
- family history
- smoking
- more common in Caucasians
- female sex

Features

- reduced visual acuity: 'blurred', 'distorted' vision, central vision is affected first
- central scotomas
- fundoscopy: drusen, pigmentary changes

General management

- stopping smoking
- high does of beta-carotene, vitamins C and E, and zinc may help to slow down visual loss for patients with established macular degeneration. Should be avoided in smokers due to an increased risk of lung cancer.

Dry macular degeneration - no medical treatments currently

Wet macular degeneration

- photocoagulation
- photodynamic therapy
- anti-vascular endothelial growth factor (anti-VEGF) treatments: intravitreal ranibizumab

7.9 Homocystinuria
Homocystinuria is a rare autosomal recessive disease caused by deficiency of cystathione beta-synthetase. This results in an accumulation of homocysteine which is then oxidized to homocystine.

Features

- often patients have fine, fair hair
- musculoskeletal: may be similar to Marfan's - arachnodactyly etc
- neurological patients may have learning difficulties, seizures
- ocular: downwards dislocation of lens
- increased risk of arterial and venous thromboembolism
- also malar flush, livedo reticularis

Diagnosis is made by the cyanide-nitroprusside test, which is also positive in cystinuria.

Treatment is vitamin B6 supplements.

### 7.10 Marfan's syndrome

Marfan's syndrome is an autosomal dominant connective tissue disorder. It is caused by a defect in the fibrillin-1 gene on chromosome 15.

Features

- tall stature with arm span > height ratio > 1.05;
- high-arched palate;
- arachnodactyly;
- *pectus excavatum*;
- *pes planus*;
- scoliosis of > 20 degrees;
- heart: dilation of the aortic sinuses (seen in 90%) which may lead to aortic regurgitation, mitral valve prolapse (75%), aortic dissection;
- lungs: repeated pneumothoraces;
- eyes: upwards lens dislocation (*superotemporal ectopia lentis*), blue sclera [the upward dislocation is in contrast to the downward dislocation in homocystinuria.]

### 7.11 Rheumatoid arthritis: ocular manifestations
Ocular manifestations of rheumatoid arthritis are common, with 25% of patients having eye problems

Ocular manifestations

- keratoconjunctivitis sicca (most common);
- episcleritis (erythema);
- scleritis (erythema and pain);
- corneal ulceration;
- keratitis.

Iatrogenic

- steroid-induced cataracts
- chloroquine retinopathy

7.12 Angioid retinal streaks

Angioid retinal streaks are seen on fundoscopy as irregular dark red streaks radiating from the optic nerve head. The elastic layer of Bruch's membrane is characteristically thickened and calcified

Causes

- pseudoxanthoma elasticum (this makes a nice PACES case!)
- Ehler-Danlos syndrome
- Paget's disease
- sickle-cell anaemia
- acromegaly

7.13 Optic atrophy
Optic atrophy is seen as pale, well demarcated disc on fundoscopy. It is usually bilateral and causes a gradual loss of vision. Causes may be acquired or congenital.

**Acquired causes**

- multiple sclerosis;
- papilloedema (longstanding)
- raised intraocular pressure (e.g. glaucoma, tumour);
- retinal damage (e.g. choroiditis, retinitis pigmentosa);
- ischaemia;
- toxins: tobacco amblyopia, quinine, methanol, arsenic, lead;
- nutritional: vitamin B<sub>1</sub>, B<sub>2</sub>, B<sub>6</sub> and B<sub>12</sub> deficiency

**Congenital causes**

- Friedreich's ataxia
- mitochondrial disorders e.g. Leber's optic atrophy
- DIDMOAD - the association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also known as Wolfram's syndrome)

### 7.14 Relative afferent pupillary defect
Also known as the Marcus-Gunn pupil, a relative afferent pupillary defect is found by the 'swinging light test'. It is caused by a lesion anterior to the optic chiasm i.e. optic nerve or retina.

Causes

- retina: detachment
- optic nerve: optic neuritis e.g. multiple sclerosis

Pathway of pupillary light reflex

- afferent: retina ➔ optic nerve ➔ lateral geniculate body ➔ midbrain
- efferent: Edinger-Westphal nucleus (midbrain) ➔ oculomotor nerve

7.15  Mydriasis

Causes of mydriasis (large pupil)

- third nerve palsy;
- Holmes-Adie pupil;
- traumatic iridoplegia;
- phaeochromocytoma;
- congenital.

Drug causes of mydriasis

- topical mydriatics: tropicamide, atropine
- sympathomimetic drugs: amphetamines
- anticholinergic drugs: tricyclic antidepressants
C. PSYCHIATRY

7.16 Schizophrenia and related syndromes

Schneider's first rank symptoms may be divided into auditory hallucinations, thought disorders, passivity phenomena and delusional perceptions:

Auditory hallucinations of a specific type

- two or more voices discussing the patient in the third person
- thought echo
- voices commenting on the patient's behaviour

Thought disorder/thought alienation

- thought insertion
- thought withdrawal
- thought broadcasting

Passivity phenomena

- bodily sensations being controlled by external influence
- actions/impulses/feelings - experiences which are imposed on the individual or influenced by others

Delusional perceptions

- a two stage process) where first a normal object is perceived then secondly there is a sudden intense delusional insight into the objects meaning for the patient

Other features of schizophrenia

- impaired insight;
- incongruity/blunting of affect (inappropriate emotion for circumstances);
- decreased speech;
- neologisms (made-up words);
- catatonia;
- negative symptoms: incongruity/blunting of affect, anhedonia (inability to derive pleasure), alogia (poverty of speech), avolition (poor motivation)

Epidemiology
Risk of developing schizophrenia

- monozygotic twin has schizophrenia = 50%
- parent has schizophrenia = 10-15%
- sibling has schizophrenia = 10%
- no relatives with schizophrenia = 1%
Prognostic factors

Factors associated with poor prognosis

• strong family history;
• gradual onset;
• low IQ;
• premorbid history of social withdrawal;
• lack of obvious precipitant

Treatment

See section on neuropharmacology above. The pharmacological management has been heavily influenced by the dopamine hypothesis of schizophrenia, and *vice versa*. 
7.17 Affective disorders

Characteristics of anxiety (after Lewis)
1. An emotional state with the subjectively experienced quality of fear
2. An unpleasant emotion which may be accompanied by a feeling of impending death
3. A feeling directed towards the future, perceiving a threat of some kind
4. There may be no recognizable threat or one which, by reasonable standards, is out of proportion to the emotion it seemingly provokes
5. There may be subjective bodily discomfort and manifest bodily disturbance

Biological markers of anxiety

Cardiac function

Electrodermal response

Peripheral blood flow
• more vasodilatation
• decreased renal and splanchnic flow

Neurotransmitter abnormalities
• increased circulating adrenaline
• increased circulating noradrenaline
• increased platelet MAO
• increased central NA and 5-HT activity

Behaviour therapies

Systematic desensitization
• gradual exposure to phobic stimulus along hierarchy of increasing intensity until patient habituates and avoidance response is extinguished gain
• severe obsessions

Flooding (implosion)
• supervised maximum exposure to feared stimulus until anxiety reduction, or exhaustion
• effective for phobias where free-floating anxiety is prominent

Modelling
• observation of therapist engaging in non-avoidance behaviour with the feared stimulus
• a combination of flooding, associated modelling, and moderate doses of diazepam given four hours before sessions may be particularly effective in agoraphobia
Phobic anxiety disorders

Mowrer’s two-step conditioning [1971] aims to explain fear, and phobias:
1. pairing of stimulus with fear (classical conditioning)
2. reinforcing avoidance by anxiety reduction (operant conditioning)

Bipolar Illness (mania)

- depression tends to present first, with onset of mania after the age of 30
- manic episodes usually begin abruptly and last from 2 weeks to 5 months (median = 3-4 months)
- more than 50% of episodes last less than one month with treatment
- depressive episodes tend to last longer (median = 6 months)

Mood disorders and suicide

- risk of suicide in those with depressive disorder is 30 times the normal population
- 11-17% of patients who have had a severe depressive illness will eventually commit suicide
- highest risk period is 1-2 years after hospitalization
- 90% of completed suicides suffer with depression at some time
- it is estimated that 25-50% of those with bipolar disorder will make a suicide attempt at some time (Goodwin and Jamison, 1990)

Depression: selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are consider first line for the majority of patients with depression. Citalopram and fluoxetine are currently the preferred SSRIs. Citalopram is useful for elderly patients as it is associated with lower risks of drug interactions. Sertraline is useful post myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants.

Adverse effects
- gastrointestinal symptoms are the most common side-effects
- patients should be counselled to be vigilant for increased anxiety and agitation

Following the initiation of antidepressant therapy patients should normally be reviewed by a doctor after 2 weeks.

If patients make a good response to antidepressant therapy they should continue on treatment for at least 6 months after remission as this reduces the risk of relapse.

When stopping a SSRI the dose should be gradually reduced over a 4 week period to avoid the well-known “serotonin discontinuation syndrome”.

Hypomania vs. mania
The presence of psychotic symptoms differentiates mania from hypomania,
Psychotic symptoms

- delusions of grandeur
- auditory hallucinations

The following symptoms are common to both hypomania and mania.

Mood

- predominately elevated
- irritable

Speech and thought

- pressured
- flight of ideas
- poor attention

Behaviour

- insomnia
- loss of inhibitions: sexual promiscuity, overspending, risk-taking
- increased appetite

Seasonal affective disorder

Seasonal affective disorder (SAD) describes depression which occurs predominately around the winter months. Bright light therapy has been shown to be more effective than placebo for patients with SAD.
**Grief and bereavement**

- normal grief has 3 phases:
  1. stunned (shock) phase (few hours to 2 weeks)
  2. mourning (pinning) phase (lasts for several weeks)
  3. acceptance and adjustment
- initial shock and disbelief – ‘a feeling of numbness’;
- increasing awareness of the loss is associated with painful emotions of sadness and anger;
- anger may be denied;
- irritability;
- somatic distress:
  - sleep disturbance
  - tearfulness
  - loss of appetite
  - weight loss
  - loss of libido
  - anhedonia
  - early morning wakening
- identification phenomena – in which the mannerisms and characteristics of the deceased person may be taken on;
- preoccupation with deceased;
- transient hallucinatory phenomena.

- may involve:
  - projection;
  - wish fulfillment;
  - denial;
  - introjection;
  - identity diffusion.
7.18 Suicide, attempted suicide and deliberate self-harm

Factors associated with risk of suicide following an episode of deliberate self harm:

- efforts to avoid discovery
- planning
- leaving a written note
- final acts such as sorting out finances
- violent method

These are in addition to standard risk factors for suicide

- male sex;
- increased age;
- unemployment or social isolation;
- divorced or widowed;
- history of mental illness (depression, schizophrenia);
- history of deliberate self harm;
- alcohol or drug misuse.
7.19 Alcohol dependence

DCR-10

at least three of the following:
A. A strong desire or sense of compulsion to drink
B. Difficulty in controlling the amount drunk
C. Physiological withdrawal state after drinking stops, with the possible use of alcohol to relieve this
D. Evidence of tolerance may appear
E. Progressive neglect of alternative pleasures and interests
F. Persistence of drinking in spite of evidence of harmful effects

Aetiology

Genetic
1. Family Studies:
   7-fold increase in risk of alcoholism among 1st degree relatives of alcoholics.
2. Twin Studies:
   a) MZ: DZ = 70 %: 43 % for males
   47 %: 32 % for females
3. Adoption Studies:
   a) sons of alcoholics are 4 x more likely to be alcoholic than sons of non-alcoholic, regardless of the drinking patterns of adoptive parents
   b) sons of alcoholics raised by non-alcoholic adoptive parents are no more susceptible to other non-alcoholic adult psychiatric disorder
4. Chromosomal abnormalities
5. Vulnerability markers
6. Risk factors

Complications of alcohol abuse

Hepatic:
1. may be due to toxic effects of acetaldehyde / damage to immune system by alcohol
2. women are more susceptible than men
3. Fatty liver:
   a) may be present in 90 % of drinkers
   b) reversible with abstinence
4. Alcoholic hepatitis:
   a) abstinence aids resolution, but cirrhosis may follow
5. Cirrhosis:
   a) 10 % of chronic alcoholics
   b) more common in women
   c) vulnerability may be due to HLA-B8 antigen, found in 25 % of population
   d) HLA-A28 may have a protective effect
   e) fibrosis of the liver and decompensation of liver function
   f) stigmata of liver disease may be present
6. Carcinoma:
   a) 15 % of patients with cirrhosis go on to develop hepato-cellular carcinoma
7. Portal hypertension
**Gastrointestinal:**
1. Barrett’s oesophagitis
2. Oesophageal varices
3. Mallory-Weiss tears
4. Gastritis and gastric erosions
5. Peptic ulceration – 20% of alcoholics; bleeding may be exacerbated by Vitamin K deficiency secondary to cirrhosis
6. Pancreatitis – both acute and chronic
7. Gastric carcinoma
8. Possible association with colorectal carcinoma
9. Diabetes mellitus

**Haematological:**
1. Alcoholism is the commonest cause of macrocytosis
2. Thrombocytopenia and anaemia may also occur
3. Zieve’s syndrome is a rare form of alcoholic haemolysis

**Neurological:**
1. Delirium Tremens
2. Alcoholic Hallucinosis:
   a) rare conditions in which auditory hallucinations occur alone in clear consciousness
   b) usually clears in a few days, but may be followed by secondary delusional misinterpretation
   c) up to 50% go on to develop symptoms of schizophrenia (Benedetti, 1952)
3. Epilepsy of late onset (> 25 yrs) is the most common neurological complication
   a) trauma
   b) alcohol withdrawal
   c) brain damage
4. Peripheral neuropathy is probably due to thiamine deficiency (Dry Beriberi)
5. Optic atrophy:
   a) loss of visual acuity
   b) blindness associated with methanol poisoning, thiamine and B12 deficiency, and heavy tobacco smoking
6. Korsakoff’s syndrome is caused by global cortical brain impairment
7. Wernicke’s encephalopathy
8. Central pontine myelinolysis
9. Cerebellar atrophy/ degeneration
10. Widening of sulci on CT scan
11. EEG abnormalities – P300 is decreased, and other wave abnormalities have been reported in detoxified alcoholics

**Cardiovascular:**
1. moderate drinking is considered beneficial, due to changes in the lipoprotein profile
2. heavy drinking has the following effects:
   a) increase in blood pressure
   b) weakened contraction of myocardium, leading to heart failure
   c) cardiac arrhythmia
   d) cardiomyopathy
Laboratory tests

- MCV may be raised
- GGT may be raised after a single heavy drinking bout
- CDT (carbohydrate deficient transferrin) can detect if someone has been drinking more than 7 units a day for a week
- AST > ALT in alcoholism

Psychiatric disorders associated with alcoholism

- Affective disorders
- Anxiety
- Schizophrenia
- Personality disorder
- Morbid jealousy
- Delirium tremens

Treatment

1. Antabuse *
2. Group therapy
3. Individual counselling
4. In-patient detoxification
5. Alcoholics anonymous

Pharmacotherapy

1. naltrexone
2. acamprosate
7.20 Eating disorders

Anorexia nervosa

Anorexia nervosa is associated with a number of characteristic clinical signs and physiological abnormalities which are summarised below.

Features

- loss of axillary and pubic hair
- bradycardia
- hypotension
- enlarged salivary glands

Physiological abnormalities

- hypokalaemia;
- low FSH, LH, oestrogens and testosterone;
- raised cortisol and growth hormone;
- impaired glucose tolerance;
- hypercholesterolaemia;
- hypercarotinaemia;
- low T₃.

Bulimia nervosa

Bulimia nervosa is a type of eating disorder characterised by episodes of binge eating followed by intentional vomiting.

Management

- referral for specialist care is appropriate in all cases
- cognitive behaviour therapy (CBT) is currently consider first-line treatment
- interpersonal psychotherapy is also used but takes much longer than CBT
- pharmacological treatments have a limited role - a trial of high-dose fluoxetine is currently licensed for bulimia but long-term data is lacking
7.21 Obsessive Compulsive Disorder

Characteristics of compulsive acts (DSM III-R)
1. the act has to be a purposeful one
2. it has to be performed in accordance with a certain set of rules
3. the act is not an end in itself, but is designed to bring about another state of affairs (e.g. averting disaster)
4. there has to be a disconnection between the act itself and the state of affairs it is likely to engender - a magical quality between what the patient is doing and what he is trying to achieve or prevent must be present

Clinical features
Obsessions tend to increase anxiety in a sufferer of OCD, whilst carrying out a compulsive ritual tends to decrease anxiety

Types of obsessions
1. obsessional thoughts / ideas
2. obsessional images
3. obsessional ruminations
4. obsessional doubts
5. obsessional convictions
6. compulsive rituals
7. obsessional slowness

Phenomenology
- obsessive doubts 42 %
- fears of contamination 45 %
- bodily fears 36 %
- insistence on symmetry 31 %
- aggressive thoughts 28 %
- checking compulsions 63 %
- washing 50 %
- counting 36 %

Epidemiology

Lifetime prevalence (ECA study) = 1.9 - 3.1 %
1. Biological
   a) dysregulation of serotonin function
   b) genetic:
      i) MZ: DZ = 50-80 %: 25 %
      ii) 35 % of 1st degree relatives also have OCD

2. Psychosocial
e.g. personality:
   i) 15 - 35 % of OCD patients have been noted to have previous
      anankastic personality traits
   ii) some personality traits which are said to characterize OCD
      sufferers are:
         a) abnormally high expectations of unpleasant outcomes
         b) failure to live up to perfectionist ideals should be punished
         c) magical rituals can prevent catastrophes
         d) erroneous perception of threat
         e) deficiency in ability to link concepts and integrate them
         f) give single events undue credence
         g) “islands of certainty amid confusion”

Treatment
1. Psychological
   Cognitive behavioural therapy and supportive therapy may be useful
2. Pharmacotherapy e.g. clomipramine and SSRIs
3. Psychosurgery

Prognosis
  • better with:
    • mild symptoms
    • predominance of phobic ruminative ideas, absence of compulsions
    • short duration of symptoms
    • no childhood symptoms or abnormal personality traits
  • worse if:
    • symptoms involving the need for symmetry and exactness
    • male sex
    • early onset
    • family history of OCD
    • presence of hopelessness, hallucinations, or delusions

Associations
  • depression (30%)
  • schizophrenia (3%)
  • Sydenham's chorea
  • Tourette's syndrome
  • anorexia nervosa
7.22 Abnormal illness behaviour

Post-concussion syndrome
Post-concussion syndrome is seen after even minor head trauma.

Typical features include

- headache
- fatigue
- anxiety/depression
- dizziness

Post-partum mental health problems
Post-partum mental health problems range from the 'baby-blues' to puerperal psychosis.

<table>
<thead>
<tr>
<th>'Baby-blues'</th>
<th>Postnatal depression</th>
<th>Puerperal psychosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seen in around 60-70% of women</td>
<td>Affects around 10% of women</td>
<td>Affects approximately 0.2% of women</td>
</tr>
<tr>
<td>Typically seen 3-7 days following birth and is more common in primips</td>
<td>Most cases start within a month and typically peaks at 3 months</td>
<td>Onset usually within the first 2-3 weeks following birth</td>
</tr>
<tr>
<td>Mothers are characteristically anxious, tearful and irritable</td>
<td>Features are similar to depression seen in other circumstances</td>
<td>Features include severe swings in mood (similar to bipolar disorder) and disordered perception (e.g. auditory hallucinations)</td>
</tr>
<tr>
<td>Reassurance and support, the health visitor has a key role</td>
<td>As with the baby blues reassurance and support are important</td>
<td>Admission to hospital is usually required</td>
</tr>
<tr>
<td></td>
<td>Cognitive behavioural therapy may be beneficial.</td>
<td>There is around a 20% risk of recurrence following future pregnancies</td>
</tr>
</tbody>
</table>
7.23 Unexplained symptoms

There are a wide variety of psychiatric terms for patients who have symptoms for which no organic cause can be found:

**Somatisation disorder**

- multiple physical symptoms present for at least 2 years
- patient refuses to accept reassurance or negative test results

**Hypochondrial disorder**

- persistent belief in the presence of an underlying serious DISEASE, e.g. cancer
- patient again refuses to accept reassurance or negative test results

**Conversion disorder**

- typically involve loss of motor or sensory function
- some patients may experience secondary gain from loss of function
- patients may be indifferent to their apparent disorder

**Dissociative disorder**

- dissociation is a process of 'separating off' certain memories from normal consciousness
- in contrast to conversion disorder involves psychiatric symptoms e.g. amnesia, fugue, stupor
- dissociative identity disorder (DID) is the new term for multiple personality disorder as is the most severe form of dissociative disorder

**Munchausen's syndrome**

- also known as factitious disorder
- the intentional production of physical or psychological symptoms

**Malingering**

- fraudulent simulation or exaggeration of symptoms with the intention of financial or other gain
7.24 Post-traumatic stress disorder

It is worth looking at the 2005 NICE PTSD guidelines (CG26). These guidelines are subject to regular review and revision.

Current link:

http://guidance.nice.org.uk/CG26/NiceGuidance/pdf/English

Post-traumatic stress disorder (PTSD) can develop in people of any age following a traumatic event, for example a major disaster or childhood sexual abuse. It encompasses what became known as 'shell shock' following the first world war. One of the DSM-IV diagnostic criteria is that symptoms have been present for more than one month.

Features

- re-experiencing: flashbacks, nightmares, repetitive and distressing intrusive images
- avoidance: avoiding people, situations or circumstances resembling or associated with the event
- hyperarousal: hypervigilance for threat, exaggerated startle response, sleep problems, irritability and difficulty concentrating
- emotional numbing - lack of ability to experience feelings, feeling detached from other people
- depression
- memory loss – due to the excitotoxic effect of the stress hormone cortisol on the hippocampus
- drug or alcohol misuse
- anger
- unexplained physical symptoms

Management

- following a traumatic event single-session interventions (often referred to as debriefing) are not recommended
- watchful waiting may be used for mild symptoms lasting less than 4 weeks
- trauma-focused cognitive behavioural therapy (CBT) or eye movement desensitisation and reprocessing (EMDR) therapy may be used in more severe cases
- drug treatments for PTSD should not be used as a routine first-line treatment for adults. If drug treatment is used then paroxetine or mirtazapine are recommended.
26 Psychiatric features of medical disease

You should be aware of the psychiatric presentations of physical disease including:

Metabolic, Biochemical, and Endocrine disorders

1. Endocrinopathies

- hyperthyroidism
- hypothyroidism
- Cushing's syndrome
- adrenocortical deficiency
- hyperparathyroidism
- hypoparathyroidism
- acromegaly
- hypopituitarism
- diabetes mellitus
- diabetes insipidus
- insulinoma
- phaeochromocytoma
- hepatic dysfunction
- deficiency of substrates of cerebral metabolism
- cerebral anoxia
- carbon monoxide poisoning
- hypoglycaemia

2. Disorders of electrolyte, acid-base, and fluid balance

- uraemia
- hypernatraemia
- hyponatraemia
- hyperkalaemia
- hypokalaemia
- hypercalcaemia
- hypocalcaemia
- hypomagnesaemia
- hypocalcaemia
- zinc deficiency
- alkalosis
- water intoxication
- water depletion
- disorders of vitamins
- vitamin B deficiency
- pellagra (nicotinic acid deficiency)
- alcoholic pellagra encephalopathy
- Wernicke's encephalopathy
- Korsakoff's psychosis
- folic acid deficiency
- vitamin excess
3. Miscellaneous disorders (very rare)

Wilson’s disease
porphyria
Hallervorden-Spatz disease
neuroacanthocytosis
Niemann-Pick disease
Tay Sachs disease (GM2 gangliosidosis)
the Leucodystrophies

4. Epilepsy

- increasing tension, irritability, and depression are sometimes apparent as prodromata for several days before a seizure
- transient confusional states and automatisms may occur during seizures (especially complex partial) and after seizures (usually those involving generalized convulsions, and complex partial seizures)
- occasionally, non-convulsive seizures may continue for days or even weeks (absence status and complex partial status)
- automatic behaviour is most commonly due to abnormal electrical discharge originating in the periamygdaloid region
- pain