

Organic Psychiatry

Primary Dementia

- ‘A disorder characterized by both memory and thinking deterioration sufficient to impair personal activities of daily living. The memory impairment affects the registration, storage and retrieval of new information.’
- subcortical dementia (*Albert, 1974*) = slowing of cognition, difficulty with complex intellectual tasks, and affective disturbance without impairment of language, calculation, or learning. Causes include:
 - Huntington’s chorea
 - Parkinson’s disease
 - Progressive supranuclear palsy
 - Hydrocephalus
 - AIDS dementia
 - Steele-Richardson Syndrome (similar to Parkinson’s disease, but with abnormalities of conjugate gaze)

Clinical Features

- **Behaviour:** disorganized, inappropriate, distractible, restless. Few signs of interest or initiative. Disinhibition.
- **Speech:** syntactical errors and nominal dysphasia are common
- **Thought:** slow, impoverished. Concrete thinking, reduced flexibility, and perseveration. Judgement is impaired. False ideas, often persecutory.
- **Mood:** anxiety, irritability, and depression. As dementia progresses, emotions and responses become flattened, and sudden mood changes may occur without cause.
- **Cognition:** difficulty in new learning. Memory loss (especially for recent events). Patients often confabulate. Impaired attention and concentration. Disorientation for time, and later for person and place.
- **Insight:** lacking

Causes of dementia

1. Degenerative Alzheimer’s disease, Pick’s disease, FLD, Huntington’s chorea, Parkinson’s disease, normal pressure hydrocephalus, multiple sclerosis
2. SOL Tumour, subdural haematoma
3. Traumatic Severe single head injuries, repeated head injury (e.g. boxers)
4. Infections Encephalitis (any cause), neurosyphilis, cerebral sarcoidosis, HIV, prion diseases
5. Vascular Vascular dementia, carotid artery disease, cranial arteritis
6. Metabolic Sustained uraemia, liver failure, remote effects of carcinoma or lymphoma, renal dialysis
7. Toxic Alcohol, poisoning with heavy metal (lead, arsenic, thallium)

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|-----------------|---|
| 8. Anoxia | Anaemia, post-anaesthesia, carbon monoxide, cardiac arrest, chronic respiratory failure |
| 9. Vitamin lack | Sustained lack of Vit. B ₁₂ , folic acid, thiamine |
| 10. Endocrine | Hypothyroidism, Hypoparathyroidism |

Dementia in the Elderly

- Alzheimer's accounts for over 50 % of the dementias
- the most common other subgroup is caused by vascular disease
- prevalence of moderate and severe dementia is about 5 % of persons over 65 years, and 20 % of those over 80 years
- annual incidence for all forms is around 15 per 1000 persons over 65 years
- 80 % of demented people are in the community

Alzheimer's disease	> 50 % of total cases
Multi-infarct dementia	< 20 %
Alcohol-induced dementia	≈ 10 %
Reversible dementia	≈ 5 %
'Pseudodementia'	≈ 5 %

Neuropathology

Neurofibrillary tangles in:

- Alzheimer's disease
- 'Punch-drunk' syndrome
- Postencephalitic Parkinsonism
- Amyotrophic lateral sclerosis
- Progressive supranuclear palsy
- **Not in:**
 - Lewy body dementia
 - Pick's disease

Amyloid plaques in:

- Alzheimer's disease
- Lewy body dementia
- **Not in:**
 - Pick's disease
 - 'Punch-drunk' syndrome

Lewy bodies in:

- Alzheimer's disease
- Ataxia-telengectasia
- Progressive supranuclear palsy

Alzheimer's disease

Epidemiology

- F:M ratio is 2:1
- Prevalence of moderate/ severe Alzheimer's dementia is:
 - 5 % over the age of 65
 - approx. 30 % over the age of 85
- the condition generally lasts 7-15 years

Aetiology

1. *Trauma* :
 - a) is an independent risk factor but perhaps only in those with a genetic predisposition
2. *Genetic* :
 - a) a family history of Alzheimer's disease increases the risk of the disease four-fold
 - b) familial forms are inherited as an autosomal dominant trait
3. *Molecular genetics* :

Pattern of onset	Gene implicated	Chromosome	
<i>Early onset – autosomal dominant</i>	presenilin-1	14	causes 50 % of cases
	presenilin-2	1	2 mutations known
	Amyloid Precursor protein	21	rare cause
<i>Late onset – sporadic</i>	apolipoprotein ε4	19	affects age of onset
	α Macroglobulin		

- a) mutations in the **chromosome 14** locus are responsible for most early-onset, familial Alzheimer's disease
- b) the *apolipoprotein e* gene on **chromosome 19** has been implicated in late-onset Alzheimer's disease
 - i) the genotype ε4-ε4 confers a higher risk
- c) patients with trisomy of chromosome 21 (Down's syndrome) have a high risk of early-onset Alzheimer's disease - the gene for *b-amyloid precursor protein* is found on **chromosome 21**
- d) both the chromosome 14 genetic abnormality and chromosome 21 amyloid precursor protein mutations appear restricted to early-onset familial AD

Pathology

1. diminution of the cortex and subcortical white matter volume, with dilatation of the cortical spaces and enlargement of the lateral ventricles
2. *Loss of cortical neurones* :
 - a) particularly in outer 3 layers of cortex, but all layers affected

- b) hippocampus, parietal regions, and nucleus basalis of Meynert usually affected first
 - c) visuosensory and sensorimotor areas relatively spared until later
 - d) loss of synapses correlates best with degree of cognitive impairment
3. *Amyloid plaques* :
- a) are the critical pathological feature of Alzheimer's disease - the plaques consist of amyloid peptide β -A4
 - b) seen in:
 - i) temporal cortex
 - ii) amygdala
 - iii) hippocampus
 - c) extent correlates with severity of clinical illness
4. *Neurofibrillary tangles* :
- a) abnormal phosphorylation of 'tau' proteins implicated in AD – e.g. A68 protein (Alzheimer disease associated protein – ADAP)
 - b) seen in hippocampus in normal ageing, but especially prevalent in the neocortex in Alzheimer's disease
 - c) the degree of cognitive impairment correlates with the number of neurofibrillary tangles
5. *Glial proliferation (gliosis)*
6. *Granulovacuolar degeneration* :
- a) especially in hippocampus
7. *Hirano bodies*
- a) in hippocampus, but not specific to AD
8. *Amyloid angiopathy*

Neurochemistry

1. *Cholinergic loss* :
 - a) substantial depletion of choline acetyltransferase (ChAT) and acetylcholine esterase is found, mainly in the temporal cortex
 - b) reduced cholinergic cells in nucleus basalis of Meynert, medial septum, diagonal band
 - c) cholinomimetics may improve cognitive deficits
2. *Noradrenergic loss* :
 - a) reduced noradrenaline concentrations in the cortex and hippocampus
 - b) cell loss in locus coeruleus, especially in early onset AD
 - c) correlates with depression in AD
3. *Serotonergic loss* :
 - a) loss of cortical 5-HT₂ receptors – especially in frontal and temporal lobes
 - b) cell loss and neurofibrillary tangles in nucleus raphe dorsalis
4. β -A4 amyloid may be neurotoxic, possibly altering calcium homeostasis and thereby altering neuronal susceptibility to the effects of excitotoxins such as glutamate
5. decreased somatostatin (especially in hypothalamus)
6. decreased GABA
7. decreased CK

8. decreased oestrogen-stimulated neurophysin (may reflect reduced cholinergic activity)
9. decreased CSF prolactin (correlates with cerebral atrophy)
10. deficiency of mitochondrial alpha ketoglutarate dehydrogenase complex or pyruvate dehydrogenase complex
11. raised prolactin (in senile form, but not the presenile form)
12. raised GH in the morning

Immunology

- localized inflammatory reaction
- complement found in senile plaques
- neuroglial reaction to amyloid
- increased acute phase reactants

Clinical features

- **Early** (until 2 years)
 - memory loss (STM > LTM)
 - personality changes
 - depression
 - fatigue and anxiety
 - inability to perform at normal level in everyday decision making
 - perceptible delay in word finding
 - speech can be hesitant
 - perseveration of words and phrases
 - early dementia is probable with a MMSE score of 24-27
- **Intermediate stages**
 - further deterioration in above
 - problems of language, praxis, and gnosis become increasingly apparent as the disease progresses
 - personal care deteriorates
 - neurological abnormalities start to appear:
 - extrapyramidal features
 - primitive reflexes
 - myoclonus
 - epileptic seizures in 5-10%
 - disorientation in time and space
 - misidentification (e.g. mirror sign)
 - emotional lability
 - catastrophic reaction
 - motor restlessness
- **Late stage**
 - all intellectual functions grossly impaired
 - neurological disability
 - increased muscle tone
 - wide-based unsteady gait
 - no communication

- no recognition
- speech replaced by jargon aphasia
- **Final stage**
 - no personality
 - no communication
 - emaciated
 - incontinent
 - limb contractures
 - death from pneumonia and inanition
- Early-onset AD is characterized by :
 - shorter survival
 - more rapid cognitive deterioration
 - greater frequency of language disturbance
 - more severe and widespread neurochemical abnormalities
 - greater density of neurohistologic lesions

Investigations

Psychometry:

- delayed recall is the best overall discriminator for early Alzheimer's disease

Electrophysiology:

- slowing of the dominant α rhythm
- appearance of θ and δ activity
- the P300 component of event-related potentials is either depressed or delayed
- slowing of peripheral motor nerve conduction, but normal sensory nerve conduction – the degree of slowing of peripheral nerve conduction correlates with the severity of dementia

SPECT:

- symmetrical reduction in grey matter perfusion, the degree of which correlates with the severity of dementia
- the earliest changes are seen in the temporoparietal cortex

PET:

- bilateral reduction of oxygen use and glucose uptake, initially in the temporal lobes but later involving the frontal lobes

CT:

- temporal lobe volume is reduced
- serial scanning can show progressive volume loss

Management

- cholinesterase drugs such as DONEPEZIL (ARICEPT[®]) have a role in delaying onset of the disease
 - DONEPEZIL has no effect on the disease process
 - there is evidence that DONEPEZIL produces improvement in a minority of patients with mild to moderate AD (MMSE between 10 and 26)
 - there is no evidence that DONEPEZIL has any effect on the non-cognitive manifestations of Alzheimer's disease

- depressive symptoms are best treated with SSRIs which are better tolerated
- low doses of neuroleptics are advised

Lewy body dementia

- average duration of survival of 6 years
- reported to be as much as 20 % of dementias over the age of 70 (Perry, 1990)

Pathology

- Lewy bodies are found in various parts of the cortex, accompanied by Lewy bodies in the substantia nigra
- there are morphological differences in the bodies found at these two sites
- senile plaques may be present but **neurofibrillary tangles are absent**

Pathophysiology

- widespread reductions in choline acetyltransferase in the neocortex
- loss of dopamine in the caudate nucleus

Clinical features

1. Fluctuating cognitive impairment with episodic confusion and lucid intervals
2. At least one of :
 - a) visual or auditory hallucinations with or without delusions
 - b) mild spontaneous extrapyramidal features or neuroleptic sensitivity
 - c) repeated unexplained falls or transient clouding or loss of consciousness
3. Clinical pattern persists over long periods
4. No underlying physical illness to account for the fluctuating mental state
5. Exclusion of CVA in history and by imaging

Treatment

- extrapyramidal features respond to L-Dopa

Vascular dementia

- includes multiple infarction, Binswanger's encephalopathy and the lacunar state

Epidemiology

- slightly more common in men
- the prevalence increases with age, approximately doubling every 5 years
- incidence does not increase with age
- high rates in China, Japan, and the Russian Federation

Multi-Infarct dementia

Epidemiology

- less common than Alzheimer's type

Aetiology

- probably multiple emboli from extracranial arteries
- a genetic (**autosomal dominant**) predisposition has been suggested

Pathology

- localized or generalized atrophy and ventricular dilatation
- areas of cerebral infarction and evidence of arteriosclerosis in major vessels

Clinical features

- stepwise progression
- emotional and personality changes may appear first, followed by impairments of memory and intellect
- depression is frequent
- emotional lability and confusion are common, especially at night
- fits or minor episodes of cerebral ischaemia are usual
- focal neurological deficits are common
- the *Hatchinski index* may give a diagnostically indicative score:
 - <4 is non-vascular
 - >7 is likely to be vascular
 - includes items such as abrupt onset, step-wise progression, signs of cerebellar disease, emotional incontinence, hypertension

Investigations

- CT and MRI show areas of multiple infarction
- CT shows **leukoaraiosis** (term coined by Hatchinski)
 - describes appearance of reduced density of white matter
 - only affects white matter
 - patchy and diffuse
 - not associated with enlargement of cerebral sulci or ventricles
 - also found in non-demented subjects
- SPECT shows patchy blood flow reduction throughout the hemispheres
- PET reveals asymmetric cortical and subcortical changes

Management

- reduction of risk factors
- aspirin

Prognosis

- about 50 % of patients die from IHD
- life-span averages 5 years

Binswanger's encephalopathy (subcortical arteriosclerotic encephalopathy)

- slowly progressive disorder, with variations

Clinical features

- abnormalities of gait
- loss of sphincter control
- abnormal pyramidal function similar to that seen in normal pressure hydrocephalus

Investigations

- MRI shows striking periventricular signal change ('HIS' lesions – high intensity signal) on T2-weighted images

Frontotemporal Dementia (Pick's disease)

Epidemiology

- makes up 5 % of dementias and 20% of presenile dementias
- onset commonly between the ages of 45 and 60, but can present before 30 years as well as in the elderly
- F:M = 1:1

Aetiology

- possibly a single **autosomal dominant** gene, with variable penetrance

Pathological features

- pathology is circumscribed asymmetrical atrophy of the frontal and/ or temporal lobes accompanied by a lesser degree of general atrophy
- histological findings are of three types:
 - 1) Microvacuolar (60% of cases)
 - 2) Pick type (25% of cases)
 - severe neuronal loss in the outer layers of the atrophic cortex with argentophilic inclusions (Pick bodies) and swollen ('ballooned') chromatophilic neurones (Pick cells)
 - 'knife blade' atrophy is seen due to neuronal loss
 - 3) In 15% of cases, clinical features of both frontotemporal dementia and motor neurone disease are present during life and microvacuolar histological features are combined with those of motor neurone disease
- increased concentrations of zinc in the brain and red blood cells, with increased excretion of zinc in the urine
- senile plaques or neurofibrillary tangles are absent

Clinical features and diagnostic criteria

1) **Core features:**

- a) Insidious onset and gradual progression
- b) Early decline in social interpersonal conduct
- c) Early impairment in regulation of personal conduct
- d) Early emotional blunting
- e) Early loss of insight

2) **Supportive features:**

- a) *Behavioural disorder*
 - i) Decline in personal hygiene and grooming
 - ii) Mental rigidity
 - iii) Hyperorality and dietary changes
 - iv) Perseverative and stereotyped behaviour
 - v) Utilisation behaviour
- b) *Speech and language*
 - i) Altered speech:
 - (1) Aspontaneity and economy of speech
 - (2) Press of speech
 - ii) Echolalia

- iii) Perseveration
- iv) Mutism

Physical signs

- Incontinence
- Primitive reflexes
- Akinesia, rigidity, and tremor
- Low and labile blood pressure

Investigations

- EEG shows a lower incidence of abnormalities than Alzheimer's (50 % are normal)
- CT shows:
 - marked atrophy affecting the anterior portions of the frontal and temporal lobes
 - enlargement of the frontal horns
- neuropsychology shows impairment on frontal lobe tests in the absence of severe amnesia, aphasia, or perceptuospatial disorder

Treatment

- unlikely to respond to Cholinesterase inhibitors
- behavioural symptoms such as disinhibition, overeating, and compulsions may respond to SSRIs

Outcome

- mean duration of illness is 8 years (ranging from 2 to 20 years)

Dementia of frontal lobe type (FLD)

- 2nd most common form of dementia in the pre-senium
- cortical degeneration occurs mainly in the frontal lobes and is non-specific, with neural loss, slight gliosis, and spongiosis
- more common in men
- 50 % of patients have a family history
- onset usually in the mid-fifties
- normal duration is 7-10 years
- EEG is normal

Clinical features

- personality change
- social disinhibition
- progressive dementia
- relative sparing of memory loss and spatial impairment

Huntington's chorea (Hepatolenticular degeneration)

- described in 1872 by George Huntington

Epidemiology

- estimated prevalence = 4-7 per 100000
- equal sex ratio
- age at onset is usually 25-50

Aetiology

- autosomal dominant gene with 100 % penetrance
- due to a trinucleide repeat mutation - proximal arm of chromosome 4; all cases can be accounted for by this mutation
- from a genetic point of view, demonstrates:
 - *Imprinting* – different phenotype depending on whether it is inherited from the mother or father
 - due to methylation of expression genes
 - *Anticipation* – increase in severity and earlier onset with each successive generations
 - due to unstable trinucleide repeats
- decreased levels of GABA in the caudate nucleus
- decreased GABA biosynthesis and increased dopamine concentrations in parts of the basal ganglia

Pathology

- pathological changes occur mostly in the frontal lobes and caudate nucleus; the basal ganglia are atrophied

Clinical features

- usually begins in the 3rd or 4th decade (mean age is in the forties)
 - 10 % present before the age of 20 – the juvenile form (*Westphal variant*) is characterised by rigidity rather than chorea
 - 10 % occur after 60
- onset of neurological and psychiatric symptoms may be many years apart
- **neurological signs:**
 - choreiform movements of the face, hands, and shoulders which are sudden, unexpected, aimless, and forceful
 - associated with changes in gait and dysarthria
 - eventually results in gross writhing contortions and ataxia
 - extrapyramidal rigidity and epilepsy also occur
- **psychiatric symptoms:**
 - dementia occurs in the later stages, after the development of chorea
 - cortical destruction is more extensive than in Alzheimer's and vascular dementias
 - memory is less affected
 - insight is often retained at a late stage

- distractibility is characteristic, with reduced ability to regulate attention and psychomotor speed
- depressive symptoms are frequent
- higher risk of suicide, including those in the family not affected
- paranoid symptoms are common, and schizophrenia may occur more frequently than in the general population

Investigations

- CT shows atrophy of the caudate and frontal lobes
- PET scanning shows a reduced striatal metabolism
- SPECT shows altered caudate and putaminal blood flow
- EEG is 'flat'

Management

- phenothiazines and butyrophenones for choreiform movements
- pallidectomy and thalamotomy have been used but there is a risk of worsening the dementia or causing neurological side effects
- antidepressants are used for major depressive symptoms

Prognosis

- adults : 13-16 years to death
- children : 8 years to death

Prion diseases (Creutzfeldt-Jacob Disease)

- transmitted by blood or tissues between human beings
- rapidly progressive degenerative disease of the nervous system

Epidemiology

- 50-100 cases occur each year in the UK
- equal sex ratio
- onset is 40-60

Aetiology

- due to accumulation of an abnormal prion protein in the brain (prions are small proteinaceous particles that resist inactivation by procedures that modify nucleic acid)
 - encoded on **chromosome 20**
- individuals with the E4 allele of apolipoprotein ε are at a higher risk of developing the disease
- the familial form (*Gerstmann-Straussler-Scheinker*) accounts for 10 % of patients and principally affects the cerebellum
 - autosomal dominant

Clinical features

- personality change
- seizures
- intellectual deterioration
- neurological deficits including:
 - cerebellar ataxia
 - spasticity
 - extrapyramidal signs
 - myoclonus sensitivity to noise or touch
- in new-variant CJD (nvCJD), initial psychiatric symptoms are followed by a cerebellar syndrome leading to memory failure and akinetic mutism
- 4 forms :
 - subacute spongiform encephalopathy (SSE 1), rapidly fatal
 - SSE 2 (*Heidenhaim's* – blindness and dementia)
 - thalamic form
 - ataxic form

Investigations

- **EEG:**
 - abnormal in 90 %
 - low voltage with bi/ triphasic discharges
 - repetitive complexes that coincide with the myoclonus
- atrophy may be apparent in the later stages with CT or MRI
- the CSF protein is sometimes moderately elevated

Prognosis

- rapidly progressive over 1-2 years

Normal pressure hydrocephalus

- not due to a block within the ventricular system but there is an obstruction in the subarachnoid space so that CSF can escape from the ventricles but is prevented from flowing over the ventricles
- more common in the elderly

Aetiology

- may be a history of SAH, head injury or meningitis

Clinical features

- progressive memory impairment and *dementia*
- slowness
- marked unsteadiness of *gait*
- urinary *incontinence*

Investigations

- removal of 50 ml of CSF can lead to a temporary improvement in cognition
- CT or MRI shows dilatation of the ventricular system and relatively normal sulci; periventricular lucencies are found on MRI

Management

- shunt to improve the circulation of CSF
- often the dementia may not improve

Organic disorders presenting with stupor

1. Raised intracranial pressure - medullary or midbrain pressure cone
2. Focal pathology in posterior diencephalon or upper midbrain
 - a) space occupying lesions (esp. craniopharyngiomas)
 - b) infarction
 - c) meningitis (esp. TB)
 - d) neurosyphilis
 - e) encephalitis lethargica
 - f) senile or presenile dementia
 - g) epileptic equivalents or postictal phenomena
3. Focal pathology in brainstem or anteromedial frontal lobes
4. Metabolic disorders
 - a) uraemia
 - b) hypoglycaemia
 - c) hepatic encephalopathy
 - d) electrolyte disturbance or water intoxication
5. Endocrine disorders
 - a) hypothyroidism
 - b) Cushing's disease
 - c) Addison's disease
 - d) hypopituitarism
 - e) hyperparathyroidism
6. Nicotinic acid deficiency encephalopathy
7. Substance abuse
 - a) alcohol intoxication
 - b) barbiturate intoxication
8. Adverse reaction to psychotropic medication
9. Terminal stages of infection

Organic disorders presenting with depression

1. Haematological
 - a) iron deficiency
 - b) pernicious anaemia
 - c) polycythaemia rubra vera (PRV)
2. Neoplastic
 - a) pancreatic Ca (often preceded by depression)
 - b) disseminated carcinomatosis
 - c) carcinoid syndrome
 - d) oat cell carcinoma
3. Metabolic
 - a) hepatic failure
 - b) uraemia
 - c) renal failure
 - d) electrolyte disturbance
 - e) acute intermittent porphyria
4. Endocrine
 - a) Cushing's syndrome
 - b) Hyperthyroidism
 - c) Hypothyroidism
 - d) Addison's disease
 - e) hypopituitarism
 - f) hyperparathyroidism
 - g) hypoparathyroidism
5. Neurological
 - a) systemic lupus erythematosus
 - b) intracranial tumours
 - c) disseminated sclerosis
 - d) epilepsy
 - e) subcortical dementia (e.g. Parkinson's disease)
6. Infective
 - a) AIDS
 - b) neurosyphilis
 - c) infectious mononucleiosis
 - d) post viral (e.g. influenza)
 - e) brucellosis
7. Drugs
 - a) alcohol
 - b) RESERPINE
 - c) L-DOPA
 - d) METHYLDOPA
 - e) CIMETIDINE
 - f) sympathetic blockers (e.g. PROPANOLOL)
 - g) DIGOXIN
 - h) diuretics
 - i) steroids
 - j) barbiturates
 - k) ACE-inhibitors (e.g. CAPTOPRIL)

1) Calcium antagonists (e.g. NIFEDIPINE)

Differentiation of pseudodementia from dementia

- rapid, acute onset
- no cognitive decline prior to depressive symptoms
- communication of a sense of distress
- patient complains of cognitive problems
- information in presenting complaint is well given, but direct testing of memory is poor
- “don’t know” responses are common
- inattention and poor concentration are main reasons for poor performance
- absence of higher cortical dysfunction, e.g. no dysphasias, dyspraxias, etc.
- presence of biological features of depression, esp. DVM

Head Injury and Focal Brain Damage

Epidemiology of head injuries

- 100,000 patients treated as inpatients in UK each year; 100,000 treated as out-patients
- 50 % are under 20 years
- 1000 people a year are severely disabled, 50 % never work again
- Apo E4 genotype is a predictor of poor outcome in head injury

Associated injuries

Cranial nerves

- I fracture of anterior cranial fossa
- II direct trauma
- III damage by herniated uncus of temporal bone impinging on the nerve or directly stretching the nerve
- VI torsion or herniation of the brain
- VII fracture of petrous temporal bone or direct effects of bleeding or swelling > facial palsy
- VIII fracture of petrous temporal bone > conductive deafness

Acute post-traumatic psychosis

- a.k.a. post-traumatic confusional state
- may result from anoxia, electrolyte disturbance, systemic infection, blood loss or brain injury
- results in residual impairment of consciousness and failure to retain new information, disorientation, paranoid ideation, misinterpretation

Amnesia in head injury

- duration of PTA in closed injury correlates with:
 - time taken to return to work
 - extent of brain injury
 - psychiatric disability
 - memory impairment

Post-traumatic amnesia (PTA) – a.k.a. anterograde amnesia

- *the time from the moment of injury to the time of resumption of normal continuous memory*
- may last several minutes or several weeks
- patient is insightless and may confabulate

Retrograde amnesia (RA)

- *time between the moment of injury and the last clear memory from before the injury that the patient can recall*
- RA is generally shorter than PTA
- may diminish in duration as time goes on - should not estimate until period of PTA of over

Psychiatric sequelae

- consequent on brain damage :
 - frontal lobe syndrome
 - reduced control over aggression
 - pathological intoxication (*mania a potu*)
- not consequent on brain damage :
 - fluctuating depression
 - morbid anxiety
 - obsessional traits
 - persistent irritability

Intelligence

- vocabulary-based intelligence is more resistant to head injury than non-verbal intelligence

Memory

- after head injury, there is impaired paired-associated learning
- memory impairment is proportional to the length of post-traumatic amnesia

Language

- non-fluent (expressive) dysphasia is the most common disorder of language

Psychoses after head injury

Schizophrenia:

- higher incidence than by chance
- paranoid forms especially common
- more common in milder injuries and those associated with temporal lobes

Paranoid psychoses:

- onset may be delayed by many years
- morbid jealousy is common feature

Affective psychoses

- may be associated with hypothalamic damage
- bipolar illness often of rapid cycling type
- depressive psychosis more common than hypomania
- hypomanic presentation is associated with frontal lobe damage

Suicide

- 14 % of all deaths in follow-up studies
- associated with frontal and temporal lobe injuries
- maximal risk 15-19 years post-injury
- 1/3 have reported personality change

Head injury associated with boxing ('Punch drunk' syndrome)

- neurological features :
 - dysarthria
 - facial immobility
 - poverty and slowness of movement
 - asymmetrical pyramidal signs
 - ataxia
 - rigidity and spasticity
- psychiatric features :
 - intellectual and personality change indicative of dementia
 - morbid jealousy
 - rage reactions
- CT Scan :
 - cerebral atrophy
 - ventricular dilatation
 - sulcal shrinkage
 - cerebellar atrophy
 - characteristic finding is perforation of septum pellucidum
- pathology :
 - similar to appearances in Alzheimer's disease
 - plaques are not seen

Occlusion of Specific arteries

Anterior cerebral

- contralateral lower limb paresis
- contralateral lower limb sensory deficits
- clouding of consciousness

Middle cerebral

- clouding of consciousness
- contralateral hemiplegia, hemianaesthesia and hemianopia
- motor and sensory aphasia if dominant

Posterior cerebral

- as for middle cerebral
- '*thalamic syndrome*'
 - contralateral hemianalgesia
 - spontaneous pain
- contralateral homonymous hemianopia
- amnesic syndrome

Posterior inferior cerebellar

- ipsilateral:
 - facial analgesia
 - Horner's syndrome
 - ataxia
 - weakness of vocal cords and tongue
- dissociated or contralateral analgesia
- alexia without agraphia (left occipital lobe and corpus callosum)
- visual agnosia

Basilar artery

- headache, vertigo, coma
- flaccid quadriplegia or monoplegia
- total anaesthesia
- hyperpyrexia
- ipsilateral cranial nerve palsies
- (ipsilateral) cerebellar signs

The Amnesic syndrome

- an organic mental disorder in which recent memory impairment is the single or predominant cognitive defect; other psychological functions remain relatively intact, in contrast with dementia

Aetiology

- thiamine deficiency (*Wernicke-Korsakoff's syndrome*)
- head trauma with damage to temporal region or diencephalon
- subarachnoid haemorrhage, especially involving the posterior cerebral artery which supplies the temporal region
- tumours involving the floor and walls of 3rd ventricle
- poisoning:
 - carbon monoxide
 - lead
 - arsenic
- intracranial infections:
 - herpes simplex
 - TB
- cerebral anoxia:
 - cardiac arrest
 - unsuccessful hanging attempts
- bilateral temporal lobectomy
- ECT
- epilepsy
- transient global amnesia

Korsakoff's syndrome

- normal digit span - able to pay attention and register information
- STM appears to be intact
- new learning and acquisition of memory is impaired at 'explicit' learning tests
- procedural memory, the response to priming, and well rehearsed aspects of semantic memory remain intact
- main defect may be in the retrieval of memory, or failure of consolidation/ transfer from STM to LTM
- diminished spontaneity and initiative
- reduced capacity to shift attention and thought - stereotyped thinking
- superficial jovial mood and euphoria
- lack of insight
- **disorientation** in time in both recent and remote memories, with jumbling of the sequential order of recalled events - *telescoping of information*
- **confabulation** :
 - falsification of memory in clear consciousness
 - due to hypothalamic-diencephalic lesions – **does not occur in bilateral hippocampal lesions** (insight also preserved)
 - two types:

1. *momentary* - brief in content and has to be provoked; can be traced to a time-dislocated true memory
2. *fantastic* - sustained; spontaneous and elaborate with grandiose, far-fetched content; ? due to frontal lobe involvement

Memory impairment with ECT

- verbal memory particularly affected
- worse affected if:
 - bilateral application
 - suprathreshold stimuli (dose not time relationship)
- Squire *et al* (1984) tested subjects following ECT:
 - retrograde amnesia from the preceding 1-3 years
 - anterograde deficit on recall and recognition tests
 - accelerated forgetting of newly learned information
 - some material acquired within a few hours of the convulsion may be permanently lost
 - performance of objective tests returned to normal after 6-9 months
 - complaints of poor memory persisted and were more obvious in those who recovered least from depression (? psychogenic)

Transient global amnesia

- occurs in middle or late life - usually men 50-70 years
- often episodes are isolated and do not recur

Clinical features

- characterized by abrupt episodes, lasting up to several hours, in which there is global loss of recent memory
- the patient remains alert and responsive, but is usually bewildered by his inability to understand his experience; motor skills are preserved
- personal identity is preserved
- recognition is intact
- there is impairment of new learning but not of other cognitive functions
- there is complete recovery, but with amnesia for the episode
- may be a link with migraine
- prognosis is good

Intracranial Infections

Neurosyphilis

- WR and VDRL are negative in 10 % of cases

Meningovascular

- usually 1-5 years after primary infection
- inflammation and exudate from leptomeninges
- headache, malaise
- lethargy, irritability
- delirium and/ or dementia
- cranial nerve disturbance – optic nerve, 8th nerve

Tabes dorsalis

- usually presents in middle age after an average of 10-15 years from infection
- atrophy of dorsal roots and posterior columns
- ataxia due to proprioceptive loss (Charcot joints)
- paraesthesias of limbs
- Argyll-Robertson pupils (in 2/3 of cases)

General Paralysis of the Insane (GPI)

- meningeal thickening
- cortical atrophy, mainly affecting the frontal and parietal lobes
- spirochaetes invade the brain, resulting in neuronal death, gliosis and patchy subcortical demyelination
- **Personality changes :**
 - irritable
 - emotional lability
 - impaired insight
- **Cognitive changes :**
 - poor concentration
 - dementia
- **Neurological changes :**
 - dysarthria
 - tremor (in 2/3 of cases)
 - seizures
 - Argyll-Robertson pupils
 - later, there is pyramidal deficit and incontinence
- Classic pictures :
 - simple dementing – 20-40 %
 - depressive – 25 %
 - grandiose – 10 %
- Wasserman reaction is always positive, with lymphocytosis, raised protein, and raised globulin

Encephalitis

- agents include *herpes simplex type 1* (most common in UK), *varicella zoster*, *cytomegalovirus*, *mumps*, *measles*, *EBV*, *polio*
- *rabies* presents in either an encephalitic or paralytic form

Pathology

- herpes affects mainly the basal frontal and temporal lobes – the lesions are often haemorrhagic
- polio causes perivascular inflammatory cell infiltration with petechial haemorrhages; the white matter is relatively spared

Clinical features

- prodromal illness
- fever
- headache
- depression of the conscious state
- focal or generalized seizures
- focal neurological signs
- 70 % fatal

Investigations

- EEG shows diffuse slow-wave activity; temporal localization of periodic epileptic discharges is suggestive of HSV infection
- CSF shows viral antigen

Psychiatric sequelae

- prolonged anxiety and depression
- dementia
- personality change
- epilepsy
- amnesic syndrome
- behavioural disorders in children

Subacute sclerosing panencephalitis

- follows measles infection after a mean period of 5 years
- does not occur after 25 years of age
- incidence = 1-3 per 1 000 000
- presents with a behavioural disturbance followed by dementia, myoclonus, and incoordination
- EEG shows repetitive slow-wave discharges alternating with periods of relative electrical silence
- CT or MRI identifies low-density lesions in the subcortex and periventricular areas
- the course is progressive and there is no specific treatment

AIDS dementia complex (ADC)

- high levels of unintegrated HIV-1 DNA are found in the brains of ADC patients
- neuropathological abnormalities are found in 75% of patients with AIDS
- 15 % of AIDS patients develop ADC

Pathology

- cerebral atrophy
- spongy white matter degeneration and focal demyelination
- perivascular and parenchymal infiltration by macrophages and lymphocytes
- characteristic multinucleated cells are found in the white matter and subcortical grey matter
- diffuse astrocytosis

Clinical features

- occurs late in the illness
- insidious onset of altered concentration and memory
- altered personality
- difficulty in walking and incoordination
- verbal and motor responses are slow and eye movement disorders appear, of the type seen in Parkinson's disease

Investigations

- CT shows cortical and deep atrophy
- MRI identifies the white matter changes

Parasitic infections in AIDS patients

- 33 % of patients are serum-positive for *Toxoplasma gondii*
- toxoplasmosis is the likeliest cause of a focal neurological deficit developing in an AIDS patient
- Cryptococcal meningitis is one of the most common CNS infections in AIDS patients

Cerebral abscess

- incidence of 1 per 10 000 general hospital admissions
- risk factors include congenital cyanotic heart disease, pulmonary AV malformations, and IV drug users

Pathology

- organisms are usually mixed and frequently include anaerobes
- most abscesses are secondary to infection in the paranasal sinuses or middle ear
- local spread from the ears or sinuses affects primarily the temporal lobes, frontal lobes, or cerebellum
- blood born infection localizes to the grey-white matter junction and is often multifocal

Clinical features

- fever, drowsiness, and seizures with no focal neurological deficit
- evidence of an expanding mass lesion without indications of its infective basis

Investigation

- EEG shows a focal slow wave disturbance
- Lumbar puncture is dangerous
- CT or MRI detects all symptomatic intracerebral abscesses

Cerebrovascular disease

Cerebrovascular accident

Epidemiology

- 3rd most common form of death in the industrialized world
- 4.5 million each year, worldwide
- 20 % of patients die within 30 days
- subsequent mortality approximately 16-18 % per year
- 90 % of survivors have residual deficit and 30 % are incapacitated

Pathology

- outcome depends on whether the cerebral ischaemia is global (e.g. cardiac arrest) or focal (single vessel occlusion)

Psychiatric sequelae

- personality change, irritability, apathy, lability of mood and aggressiveness
- 'catastrophic reactions' may occur
- depression:
 - may be associated with the size of the brain lesion
 - more common with left frontal lesions
 - is more severe the nearer the lesion to the frontal lobe
 - correlates with the degree of intellectual impairment
- anxiety is common after a stroke
- abnormal emotionalism (emotional lability) is frequent, and may be more common in patients with left frontal temporal lesions

Subarachnoid haemorrhage

- high incidence of mental disorder has been reported after SAH
- patients with neurological deficits are likely to suffer persistent cognitive impairment and social disability

Subdural haematoma

- occurs sometimes after falls associated with alcoholism

Clinical features

1. Acute:
 - a) coma
 - b) fluctuating level of consciousness
 - c) hemiparesis/ oculomotor signs
2. Chronic:
 - a) headache

- b) poor concentration
- c) vague physical symptoms
- d) fluctuating consciousness

Cerebral tumours

- 1 in 200 psychiatric inpatients (Parry 1968)
- almost any psychiatric symptomatology may be seen
- commonly:
 - impairment of conscious level
 - cognitive change
 - affective disturbance
 - hallucinations in any modality depending on site of lesion

Clinical features

- early mental symptoms are seen in 15 % of cases
- symptoms more common with meningiomas (30 %)
- symptoms more common when ant. or post. corpus callosum is affected (90 %)
- tumours in the cerebellopontine angle typically cause paranoid symptoms

Other Neurological Conditions

Brown-Sequard syndrome

- due to complete hemisection of the spinal cord
- causes ipsilateral dorsal column function loss and contralateral spinothalamic tract deficits

Benign Intracranial hypertension

- a.k.a. *pseudo-tumour cerebri*

Epidemiology

- predominates in obese women of child-bearing age
- annual incidence of 1 per 100,000

Aetiology

- usually idiopathic
- can occur with certain drugs, e.g., NALIDIXIC ACID, tetracyclines, or withdrawal of corticosteroid treatment
- manifestation of venous sinus thrombosis and its causes (e.g. polycythaemia)
- association with hypoparathyroidism

Clinical features

- headache:
 - typically of recent onset
 - generalized
 - often severe and exacerbated by straining
- nausea is common, vomiting less so
- visual symptoms:
 - blurred vision
 - diplopia (secondary to VI nerve palsy)
 - transient obscurations (typically triggered by posture change)

Signs

- papilloedema
- visual field defects - enlarged blind spots, inferonasal defects, peripheral constriction, central scotoma
- unilateral or bilateral VI nerve palsy

Investigations

- CT or MRI shows no lesion, but ventricles may be slightly narrowed or slightly dilated
- CSF pressure is elevated, but CSF is normal

Management

- ACETAZOLAMIDE is used
- lumboperitoneal shunting can be used for intractable cases (most remit within a few weeks)

Multiple sclerosis

- characterized by remissions and relapses and produces scattered areas of demyelination in the brain and spinal cord

Epidemiology

- prevalence is 1 per 1000
- condition is more common in women (2:1)
- peak incidence is about 30 years and is rare in children and in adults over 60
- North-South frequency gradient in the Northern Hemisphere (higher in the north)

Natural history

- 75 % have a relapsing-remitting illness
- 25 % have a progressive course from the onset
- median survival time is over 30 years
- shorter survival if:
 - older age at onset
 - male
 - cerebellar symptoms at onset
 - progressive course at onset

Pathology

- CNS demyelination with relative axonal preservation
- characteristic lesion consists of a demarcated periventricular plaque of demyelination
- predominantly in the white matter, but cortical lesions can occur

Pathophysiology

- partial demyelination permits saltatory conduction to occur but at a reduced velocity
- at a critical level of myelin loss, conduction fails and does so more rapidly if the environmental temperature is raised (i.e. symptoms worse after a hot bath = *Uhthoff's syndrome*)

Clinical features

- Motor symptoms
 - weakness
- Sensory symptoms
 - short-lived episodes of paraesthesiae
 - *Lhermitte phenomenon* is almost pathognomonic of MS in a young individual
- Cerebellar symptoms

- clumsiness
- unsteady gait
- Visual symptoms
 - diplopia
 - optic neuritis > unilateral blurring or visual loss, with pain on movement
- brief impairment of balance with vertigo and dizziness
- epilepsy is more common than the general population
- erectile dysfunction has been reported in 40 % of males with MS

Investigation

- CSF :
 - elevated cell count
 - elevated IgG ratios
 - oligoclonal bands in the IgG region on electrophoresis
- Visual evoked potentials :
 - abnormal in 70 %
 - shows delay
- Imaging :
 - MRI criteria for MS (any two) :
 1. a lesion adjacent to the body of a lateral ventricle
 2. a lesion below the tentorium
 3. a lesion ≥ 6 mm in diameter

Psychiatric symptoms

- depression is more common than in other disabling illnesses (lifetime risk is 50 %)
- cognitive impairment
- dementia is common in the later stages

Parkinson's disease

- defined as the combination of bradykinesia, rest tremor, cogwheel rigidity, and the impairment of postural reflexes

Epidemiology

- around 30-300 per 100 000
- incidence increases with age
- more common in men
- higher risk in:
 - pesticide exposure
 - non-smokers
 - family history

Aetiology

- complex 1 of the mitochondrial respiratory chain is deficient in the substantia nigra

- decreased glutathione and glutathione peroxidase activity is found in the substantia nigra

Pathology

- substantia nigra shows a loss of at least 50 % of its melanin-containing cells
- Lewy bodies are also found

Pathophysiology

- rigidity is due to enhancement of long-latency stretch reflexes
- tremor is probably due to rhythmic neuronal discharges within the thalamus and is associated with alpha-gamma co-activation

Clinical features

1. Bradykinesia
 - a) asymmetrical at onset
 - b) results in difficulty dressing, *micrographia*, slower walking, reduced arm swing when walking, and quieter speech
 - c) reduced facial expression, with infrequent blinking
2. Tremor
 - a) present in 70 % of patients
 - b) asymmetrical
 - c) 3-4 Hz; 'pill-rolling'
 - d) inhibited briefly by purposeful movement
 - e) a postural tremor at a higher rate may be seen
3. Rigidity
 - a) increase in muscle tone throughout movement of a joint
 - b) cogwheeling is a fluctuant increase in tone, whose rate corresponds to the postural rather than the resting tremor frequency
4. Autonomic symptoms
 - a) urinary urgency
 - b) constipation
5. Postural reflexes
 - a) posture becomes stooped

Psychiatric features

- a true, cortical **dementia** is found in 15-20 %
- dementia is more common in:
 - older patients
 - those with a longer duration of illness
 - men
 - those with more parkinsonian disability
- disturbance of frontal lobe function, in the absence of dementia, results in thought slowing, apathy and inattention
- higher incidence of **depressive illness** (40 % of patients)

Wilson's disease

Aetiology

- autosomal recessive
- leads to copper deposition in various organs, especially the liver and the brain

Course

- onset usually in childhood, with liver disease, renal disease, or haemolytic anaemia
- individuals with adult-onset (rare beyond 40 yrs) present with neurological or psychiatric features

Clinical features

- movement disorders:
 - tremor
 - dystonia
 - choreo-athetoid movements
- dysphagia
- dysarthria
- Kayser-Fleischer ring usually visible in psychiatric patients due to copper deposition in Descemet's membrane of the cornea
- psychopathology in 51 % of cases
 - changes in personality and behaviour
 - depression
 - cognitive impairment
- psychiatric symptoms are related to the severity of the neurological rather than the hepatic symptoms

Pseudobulbar palsy

- more common than bulbar palsy
- UMN lesion
- due to a bilateral lesion above the midpons

Aetiology

- MS
- Motor Neurone Disease

Clinical features

- small, spastic tongue
- increased jaw jerk
- 'Donald Duck' speech
- emotional lability

Bulbar palsy

- LMN lesion of brainstem motor nuclei

Aetiology

- Motor neurone disease
- Guillain-Barre syndrome
- polio
- syringobulbia
- brainstem tumours
- central pontine myelinolysis

Clinical features

- flaccid tongue – shows fasciculation
- normal/ absent jaw jerk
- speech is quiet, hoarse, or nasal

Bell's Palsy

Clinical features

- sagging mouth
- dribbling
- impaired taste
- eye waters
- hyperacusis
- crocodile tears (salivation produces tears)

Gilles de la Tourette syndrome

- described first by Itard in 1825, and later by Gilles de la Tourette in 1885

Epidemiology

- prevalence = 0.5 per 1000
- M:F = 4:1
- 10 times more prevalent in children and adolescents than in adults

Aetiology

1. **Biochemical:**

- possibly related to Dopamine function
- Post Mortem studies:
 - decreased 5-HT and glutamate in several areas of the basal ganglia

2. **Genetic:**

- MZ:DZ = 53:8
- multiple tics without vocal tics are more common in the families of probands with Gilles de la Tourette syndrome than in the general population

Clinical features

- multiple tics beginning before the age of 16, together with vocal tics (grunting, snarling, spitting) – 1/3 present initially with vocal tics
- 1/3 of people show coprolalia
- 10-40 % show echolalia or echopraxia
- stereotyped movements such as jumping and dancing
- the tics usually precede other disorders, with the exception of abnormal sensations which may occur before the tics
- other features include:
 - over-activity
 - difficulties in learning
 - emotional disturbances
 - social problems
- obsessive-compulsive symptoms occur frequently, and are also more common in the families of these patients
- ADHD has also been reported to be more common

Treatment

- Haloperidol seems to be the most effective
- the obsessive-compulsive symptoms are said to respond to SSRIs

Prognosis

- little data, but generally poor
- coprolalia disappears in 1/3
- the tics and obsessive-compulsive symptoms are usually lifelong

References

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