Neurological consequences of internal medicine diseases

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- At the interface of internal medicine and neurology
- Due to
  - failure of some other organ systems
    - metabolic abnormalities
    - blood gas alterations
    - hormonal changes
    - electrolyte disturbances
  - nutritional deficiencies
  - exogenous drugs and toxins

[Diagram showing various chemical elements and processes related to neurology and internal medicine, such as Glu, Ca2+, BUN, NH4, O2, CO2, T4, H+, pH, Brain, Vitamins, Sepsis, endotoxins, Toxic agents, etc.]
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⇒ GLOBAL CEREBRAL DYSFUNCTION!!!
⇒ NO FOCAL NEUROLOGICAL SIGN

No structural abnormality in the CNS
CT, MR negative
No inflammation, CSF negative
Neurological consequences of internal medicine diseases

- Frequent and important!
- Internal medicine disease → neurological symptoms
- The neurological symptoms are secondary, but may be more informative
- Clue to the diagnosis of the systemic disease
- Often reversible ..... but could be irreversible .....
Neurological consequences of internal medicine diseases

- Failure of other organs – Acquired metabolic disorders of the CNS
  - Lung and respiratory diseases
  - Heart disease, disturbance of circulation
  - Liver disease
  - Renal disease
  - Diabetes mellitus
  - Diseases of endocrine glands
  - Sepsis
  - Electrolyte disturbances

➢ Consequences
Secondary encephalopathies
- Hypoxic, ischemic
- Hepatic
- Uremic
- Hypo/hyper-glycemic
- Septic...
+others
- Polyneuropathy
- Macro- and microangiopathy
- Central pontine myelinolysis...
Secondary encephalopathies

- **Cause:** damage of other organ (than CNS)
- Global disturbance of cerebral functions - no focal signs
- Metabolic (hormonal, electrolyte, blood gas) alterations as well as exogenous drugs and toxins often lead to
  - difficulty of concentration, inattentiveness, headache, fatigue, irritability, confusion, later disturbance of consciousness – EEG
  - convulsions, myoclonus, action tremor, asterixis – flapping tremor
- Development of symptoms depends on
  - the severity of the alteration,
  - the dynamics of the development of abnormality (TIME)
Secondary encephalopathies

Obligatory laboratory examinations

- Blood count; ions, Glu, Urea (BUN), Creatinine, NH3, AST, ALT, CRP, blood gases, fT4, sTSH, osmolality
- In case of severe and long lasting metabolic encephalopathy, the symptoms may persist even after treatment of metabolic disturbances!!!
- Differential diagnosis: intoxication, poisoning
  \[\rightarrow\] toxicologic examination!
Hypoxic-ischaemic encephalopathy

- There is not enough O2, no proper breathing, or no circulation
- Anaesthesia, mount climbers
- Suffocation/choking (blockage of the tracheal tube, aspiration, weakness of respiratory muscles, bilateral bronchopneumonia)
- Hgb cannot deliver O2 (severe anemia, CO)
- No circulation (MI, ventricular fibrillation, cardiac arrest, shock, low blood pressure)
- Cortex ........................................brain stem
- Prognosis DURATION!!!
Global cerebral ischaemia

- Collapse, ....................................asystolia
- Duration of global ischaemia, temperature influence the consequences
- The gray matter is much more sensitive than the white matter, and the cortex is more vulnerable than the brain stem.
- Watershed areas are also sensitive to ischaemia
Global ischaemia - diffuse hypoxia

- Reversible damage
- Cognitive deficit, confusion, changing of personality, cortical blindness, myoclonus, epilepsy, extrapyramidal symptoms
- Cortical damage, but preserved brain stem functions
  - Hypnoid and not hypnoid disturbance of consciousness
- Cortical and brain stem damage
- Brain death
Syncope

Short lasting, transient loss of consciousness

Might be innocent, but may also indicate life-dangerous disease

Epilepsy

SYNCHRON, ABNORMAL DISCHARGE OF NEURONS

GLOBAL CEREBRAL ISCHAEMIA
Epilepsy – convulsive syncope

- Alcohol, sleep deprivation may provoke
- Posture is not typical
- Aura may precede
- **Tonic-clonic seizure**
- **Longer disturbance of consciousness**
- **Pulse rate, BP↑**
- **Tongue biting is frequent**
- **Incontinence is frequent**
- **Confusion after the event**

- Injection, blood drawing, pain may provoke
- Mostly in standing position
- Preceding signs: dizziness, blurred vision, nausea, perspiration
- Irregular twitches might be present
- Shorter disturbance of consciousness
- **Pulse rate, BP↓**
- Tongue biting is very rare
- Incontinence is rare
- Short, or missing confusion after the event
- Feeling of palpitation
- **In therapy-resistant epilepsy, think on this disease**

ECG, EEG, Holter ECG, EEG after sleep deprivation, carotis compression n- ECG, HUTT

**NO ABSOLUTE DIAGNOSTIC VALUE IN THE INTERICTAL PERIOD**
Carotid sinus
Baroreceptors

IX. nerve, Hering nerve

Dorsal nucleus of vagal nerve

Vasomotor centre Medulla obl.

Sympathetic system

Relaxation of VSMC

Vasodepressor effect

Cardioinhibitory effect

Heart rate

SYNCOPE
-CARDIOINHIBITORIC
-VASODEPRESSOR
Proteins

NH4

Vena portae

NH4

Urea

Vena hepatica
Proteins

NH4

Vena portae

Vena hepatica

NH4

Urea

Porto-caval shunt

LIVER DISEASE: PARENCHYMAL AND/OR VASCULAR DECOMPENSATION
Liver disease

- **Hepatic encephalopathy - hyperammonaemia**
  - proteins – microorganisms in bowels with urease enzyme – NH4
  - damage of the liver +/- porto-caval shunt – no utilisation of NH4 in the liver – hyperammonemia
  - inattentiveness, irritability, confusion, disturbance of consciousness
  - asterixis - **flapping tremor**, convulsion,
  - EEG: bilateral synchron slow waves, triphasic waves

- Coagulation disorders – bleeding
- Tendency for hypoglycaemia
Renal diseases

- **Uremic encephalopathy** - *uraemia*
  - Difficulty of concentration, fatigue, apathy, disturbance of consciousness
  - *myoclonus, action tremor, dysarthria, convulsion*

- **Uremic neuropathy**: *uraemia* + thiamin deficiency due to dialysis – burning feet, restless legs

- **Dysequilibrium syndrome** – osmotic gradient after rapid dialysis (EC → IC)
  - headache, nausea, muscle cramps, convulsions, delirium
IC

Blood

Urea...

Urea...

A F T E R D I A L Y S I S

Urea...

Urea...

OSMOTIC GRADIENT

IC EDEMA
Renal diseases

• Uremic encephalopathy - uraemia
  – Difficulty of concentration, fatigue, apathy, disturbance of consciousness
  – myoclonus, action tremor, dysarthria, convulsion

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Diabetes mellitus - 1

- Hypoglycaemia – disturbance of consciousness, convulsions, variable neurological signs
- Hyperglycaemia (with or without ketoacidosis)
  - confusion, disturbance of consciousness, convulsions
  - hyperosmolar coma
  - with ketoacidosis: + Kussmaul breathing!
Diabetes mellitus - 2

- Macro- and microangiopathies - stroke
- Diabetic neuropathies
  - Symmetric, sensory polyneuropathy
  - Diabetic amyotrophy (motor fibres are affected, leading to proxymal weakness, atrophy and pain in the lower extremity)
  - Autonomic neuropathy (orthostatic hypotension, impotence)
  - Ischemic neuropathy (oculomotor nerve)
Hypertension

- Hypertensive encephalopathy
  - headache, irritability, nausea, vomiting
  - later disturbance of consciousness, papilla-edema
  - treatment: decrease of blood pressure, but avoid sudden and pronounced decrease

- Headache (in the morning, occipital region)

- Macroangiopathy
  - Carotid stenosis, coronary disease, peripheral artery disease

- Microangiopathy
  - Lacunar cerebral infarctions, retinopathy...

- Cerebral haemorrhage!!!
Blood pressure

Cerebral blood flow

HYPERTENSIVE ENCEPHALOPATHY
- ONE THEORY -

Higher BP → Higher CBF

Vasogenic edema

Extravasation

Higher BP → Constant CBF

Autoregulation

Higher BP → Higher CBF
Hypertension

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Cardiological diseases-stroke

• Source of cardiac embolisation - ischaemic stroke
  – Atrial fibrillation
  – Wall hypokinesis, or aneurysma after myocardial infarction
  – Dilatative cardiomyopathy
  – Arteficial heart valves
  – Infectious endocarditis

• Haemorrhagic transformation (reperfusion)
Cardiac diseases

Global cerebral ischaemia

• Decrease of cardiac output due to heart valve disease (e.g. aortic valve stenosis), or decreased pump function (e.g. AMI, dilatative cardiomyopathy)

• Decrease of cardiac output due to arrhythmia, or transient asystolia (SSS, AV-block, vasovagal syncope, carotis sinus hyperaesthesia)

• Differentiation of syncope and epilepsy
  • Holter ECG,
  • Blood Pressure Monitoring,
  • Echocardiography

DURATION!
Endocrine diseases

• ACTH, corticosteroids, Cushing’s syndrome
  – above dose of 100 mg prednisolone/day – 5%
  – hyperactivity, irritability, insomnia, euphoria, hypomania, confusion,

• Hyperthyroidism, thyreotoxicosis
  – tremor, irritability, confusion, convulsions

• Hypothyroidism
  – somnolence, slowness, neuropathy, periodic paralysis, weakness, dementia
Electrolyte disturbances - Na

- **Hypernatriaemia**
  - Head trauma, damage of hypophysis (ADH↓), no fluid intake
  - Myoclonus, convulsion, asterixis, somnolence
  - IC and brain volume ↓
  - Tearing of bridging veins, subdural haematoma

- **Hyponatraemia**
  - Head trauma (ADH↑), encephalitis, meningitis, SAH, „water poisoning”
  - Convulsion, confusion, disturbance of consciousness
  - After rapid correction
    - Central pontine myelinolysis
    - Extrapontine myelinolysis
Hypernatremia
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  - Extrapontine myelinalysis
Central pontine myelinolysis

- Not only in alcoholics
- Demyelinisation
- Most pronounced in the centre of the pons
- Cranial nuclei are preserved
- Tetraparesis, pseudobulbar lesion, but pupillary reaction and vertical eye movements are intact (locked-in syndroma)
- Rarely extrapontine localisation (thalamus, striatum, …)
Malignant diseases - metastases

- **Cerebral metastases**: lung, breast, melanoma, colon, rectum, kidney, testis
  - Focal and general signs

- **Meningeal metastases**: breast, lung, gastrointestinal tu., melanoma, leukaemia (lymphocytic, acute), lymphoma
  - Headache, back pain, polyradiculopathy, damage of cranial nerves, confusion, rarely hydrocephalus

- **Spine, skull (bone) metastases**: breast, prostate, myeloma
  - Usually there are no focal neurological signs, but painful!
  - Exception: cranial base – cranial nerve lesions.
  - Exception: fracture of vertebra – myelon compression.
Malignant diseases - paraneoplasia

- Due to indirect effect of systemic tumor on the CNS
- No compression, no direct involvement
- Ig against tumor antigens similar to proteins on the surface of neurons
  - Anti Hu, Anti Ri, Anti Yo, VGCC
- It may precede the signs and symptoms of the primary tu.!!!
- Treatment: removal of the primary tumor
- CSF, CT, MR usually negative, rarely T2 ↑
- Known form: Lambert-Eaton syndrome
Paraneoplastic syndromes

- Paraneoplastic cerebellar degeneration
  - Lung (small cell cc), breast, ovarium, Hodgkin’s disease, …

- Paraneoplastic sensory neuropathy
  - Lung – distal onset → proximal signs, cranial nerves, vegetative signs

- Paraneoplastic opsoclonus-myoclonus-ataxia
  - Neuroblastoma (children) + breast, lung

- Paraneoplastic encephalomyelitis
  - Bronchus, lung – confusion, hallucination, agitation, dementia

- Necrotizing myelopathy + motor neuropathy
  - Bronchus, lymphoma (Hodgkin) – mainly motoros symptoms, ~ALS
Malignant diseases – complications of treatment

Treatment: cytostatic drugs, immunosuppression

– polyneuropathy
– anaemia - dizziness
– infections – brain abscess, herpes zoster, meningitis
Diseases of the nervous system caused by nutritional deficiency

- Starvation
- Dietary causes
- Malabsorption
- Alcoholism
  - Acute effect of alcohol (intoxication)
  - Chronic alcoholism
    - Nutritional deficiency
    - Chronic toxicity
    - Withdrawal syndromes
Vitamin B12 deficiency

- Stomach surgery, no intake of B12 vitamin (vegetarians), no absorption of B12 vitamin
- Combined degenerative disorder of spinal cord
  - Dementia
  - Polyneuropathy
  - Pernicious anaemia

OTHERS

- Vitamin E deficiency: spinocerebellar degeneration
- Vitamin A: impairment of vision
- EXCESS of Vitamin A: pseudotumor cerebri
Vitamin B1 deficiency

- Polyneuropathy
- Wernicke disease and Korsakoff psychosis
Wernicke disease
(Polioencephalitis haemorrhagica superior)
Carl Wernicke, 1881

- **Deficiency of thiamine** (alcoholism, hyperemesis, gastric cancer)
- Acute or subacute onsets
- *Ocular signs* (nystagmus \(\leftrightarrow^{\uparrow\downarrow}\), weakness of external eye muscles, diplopia, weakness of conjugate gaze)
- *Ataxia* (severe trunk and gait ataxia)
- *Disturbance of consciousness and mentation* (apathetic, inattentive, hallucinations, agitation, drowsiness, amnesia)
Korsakoff psychosis

- Amnestic confabulatory state
- Usually associated with Wernicke disease
  - pathology is the same (mamillary body)
- *Retrograde amnesia* for memories of the recent past but not of the remote past
- *Lack of short memory*
- *Confabulation* - fills the gaps in his memory with confabulation
Treatment of Wernicke - Korsakoff Syndrome

• Immediate administration of *thiamine* (100-300 mg /day parenterally)
• Administration of all the B vitamins
• Recovery of ocular signs > ataxia > memory disturbance
# Neurological complications of chronic alcoholism

**Site of damage**

- Muscles
- Peripheral nerve
- Optic nerve
- Myelon
- Diencephalon
- Brainstem
- Cerebellum
- Cortex
- Corpus callosum

**Disease**

- Myopathy
- Polyneuropathy-N
- Alcoholic amblyopia-N
- Myelopathy-N
- Wernicke disease-N
- Korsakoff disease-N
- Central pontine myelinolysis
- Vermis atrophy-N
- Cerebral atrophy-?
- Marchiafava-Bignami disease-?
Intoxication, poisoning

- Benzodiazepines
  - (flumazenil-Anexate)
- Alcohol, metanol, ethylene-glycol
  - Acidosis!!
- Carbamazepine (iatrogenic)
  - Ataxia, double vision, nystagmus, somnolence
- Warfarin, acenocumarol (iatrogenic)
  - Increased bleeding risk! Appropriate INR control!!!