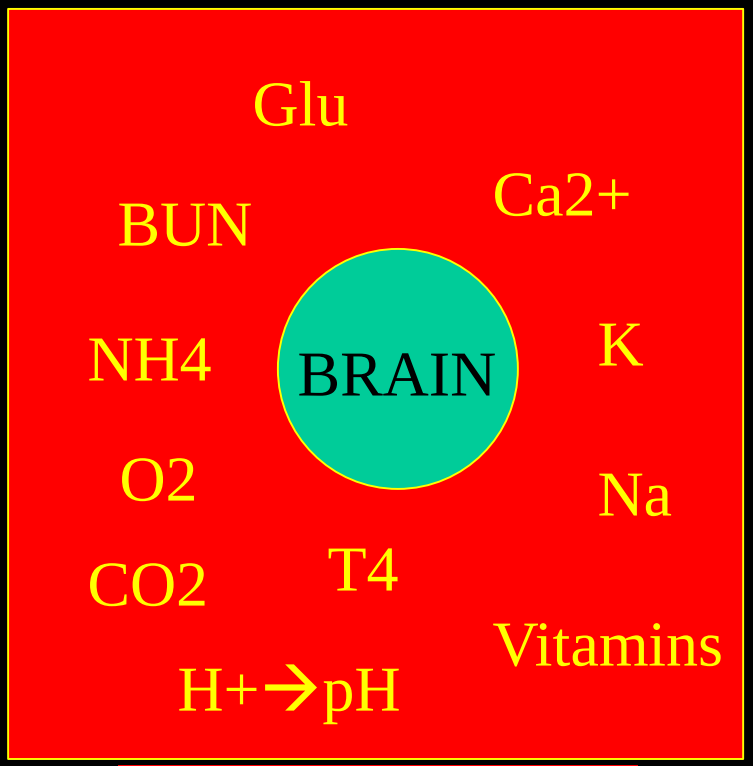
Neurological consequences of internal medicine diseases

Laszlo Olah

Neurological consequences of internal medicine diseases

- 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



Sepsis, endotoxins
Toxic agents

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  - failure of some other organ systems
    - metabolic abnormalities
    - blood gas alterations
    - hormonal changes
    - electrolyte disturbances
  - nutritional deficiencies
  - exogenous drugs and toxins

→

No structural abnormality in the CNS
CT, MR negative
No inflammation, CSF negative

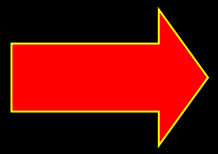
→ GLOBAL CEREBRAL DYSFUNCTION!!!
NO FOCAL NEUROLOGICAL SIGN

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

  → toxicologic examination!

Hypoxic-ischaemic encephalopathy

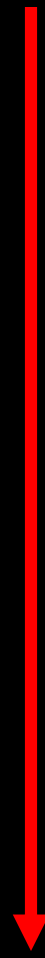
- There is not enough O2, no proper breathing, or no circulation
- Anaesthesia, mount climbers
- Suffocation/choking (blockage of the tracheal tube, aspiration, weakness of respiratory muscles, bilateral bronchopneumonia)
- Hgb cannot deliver O2 (severe anemia, CO)
- No circulation (MI, ventricular fibrillation, 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



Severity

Syncope

Epilepsy

Short lasting, transient
loss of consciousness

GLOBAL CEREBRAL ISCHAEMIA

SYNCHRON, ABNORMAL DISCHARGE OF NEURONS

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

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**

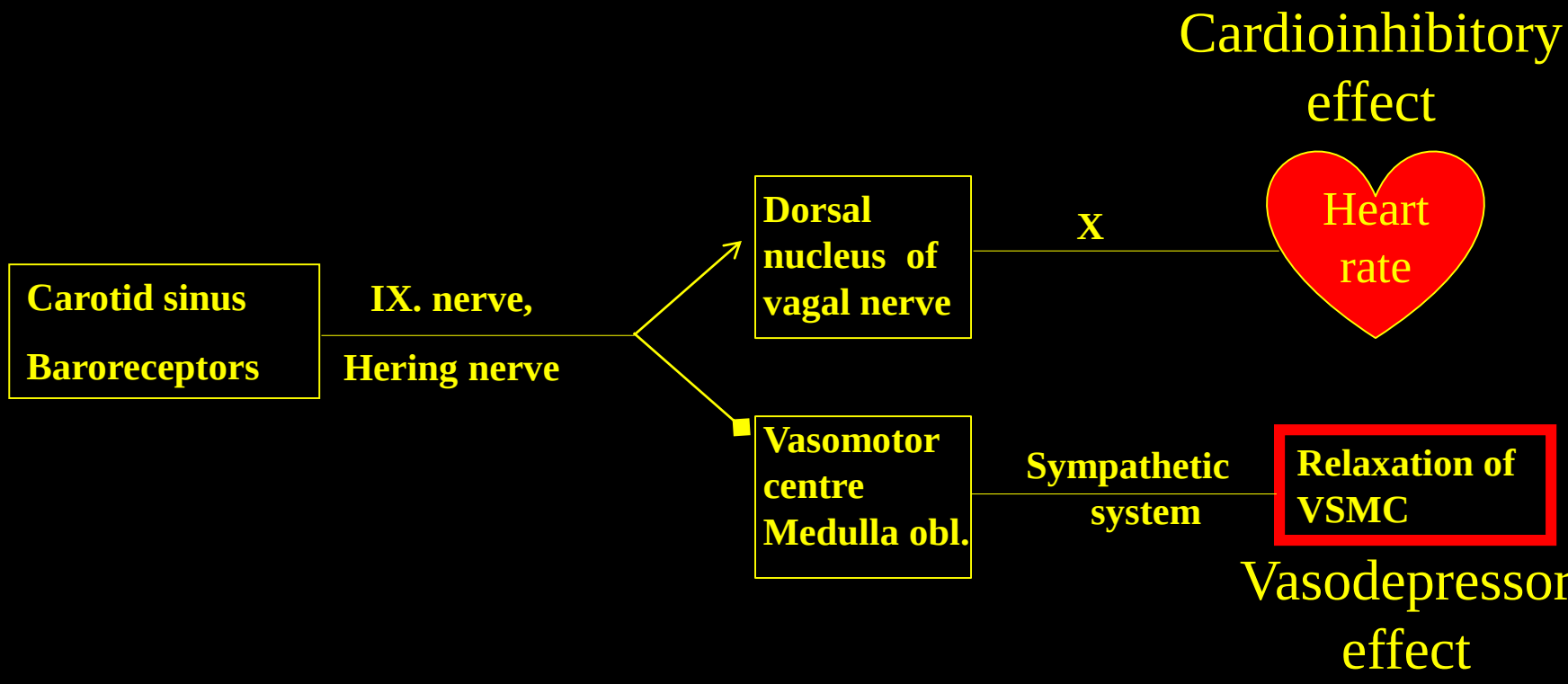
- Injection, blood drawing, pain may provoke
- Mostly in standing position
- Preceding signs: dizziness, blurred vision, nausea, perspiration
- Irregular twitches might be present
- Shorter disturbance of consciousness
- Pulse rate, BP↓
- Tongue biting is very rare
- Incontinence is rare
- Short, or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

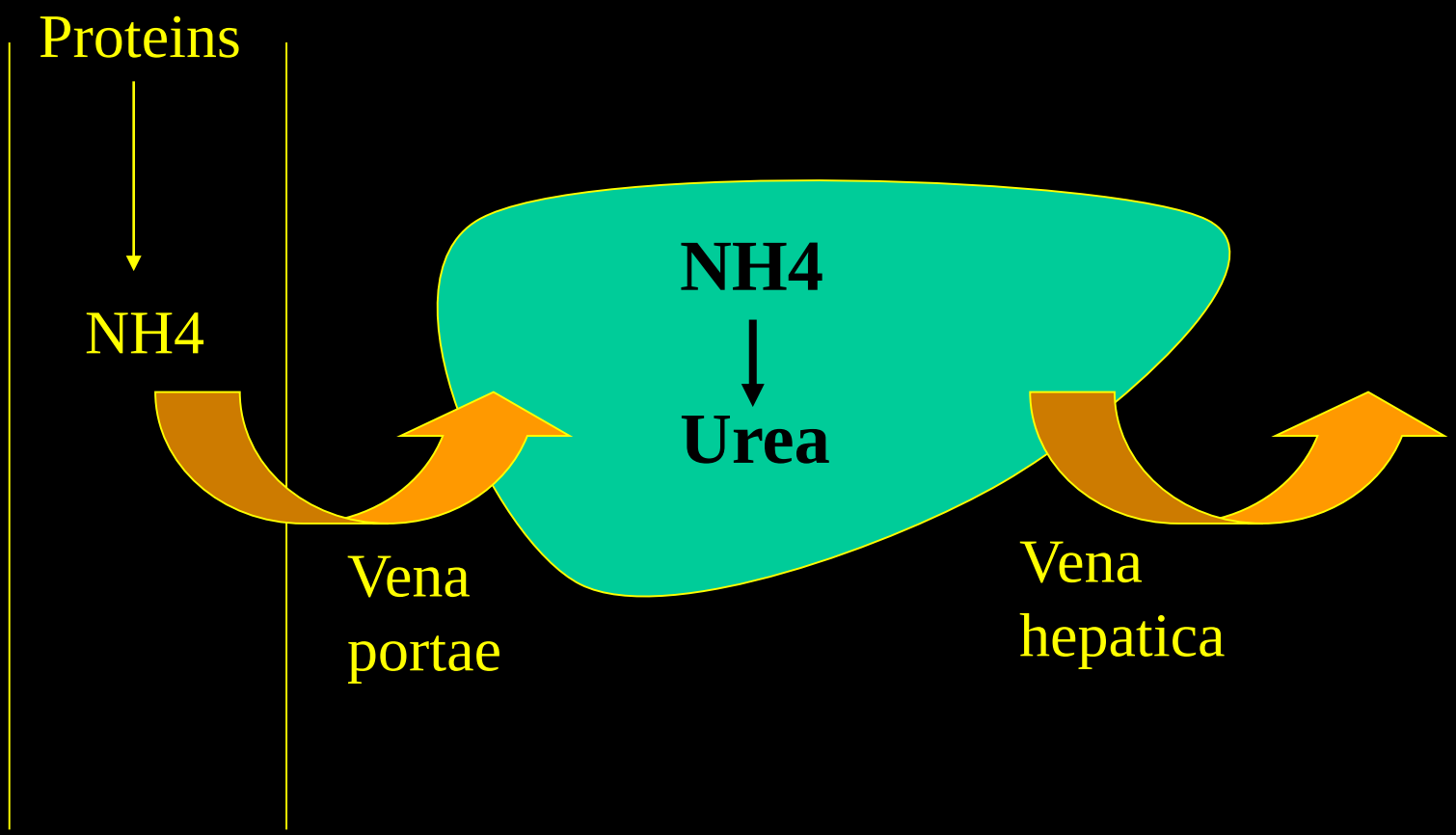
ECG, EEG, Holter ECG, EEG after sleep deprivation, carotis compressio n- ECG, HUTT
NO ABSOLUTE DIAGNOSTIC VALUE IN THE INTERICTAL PERIOD

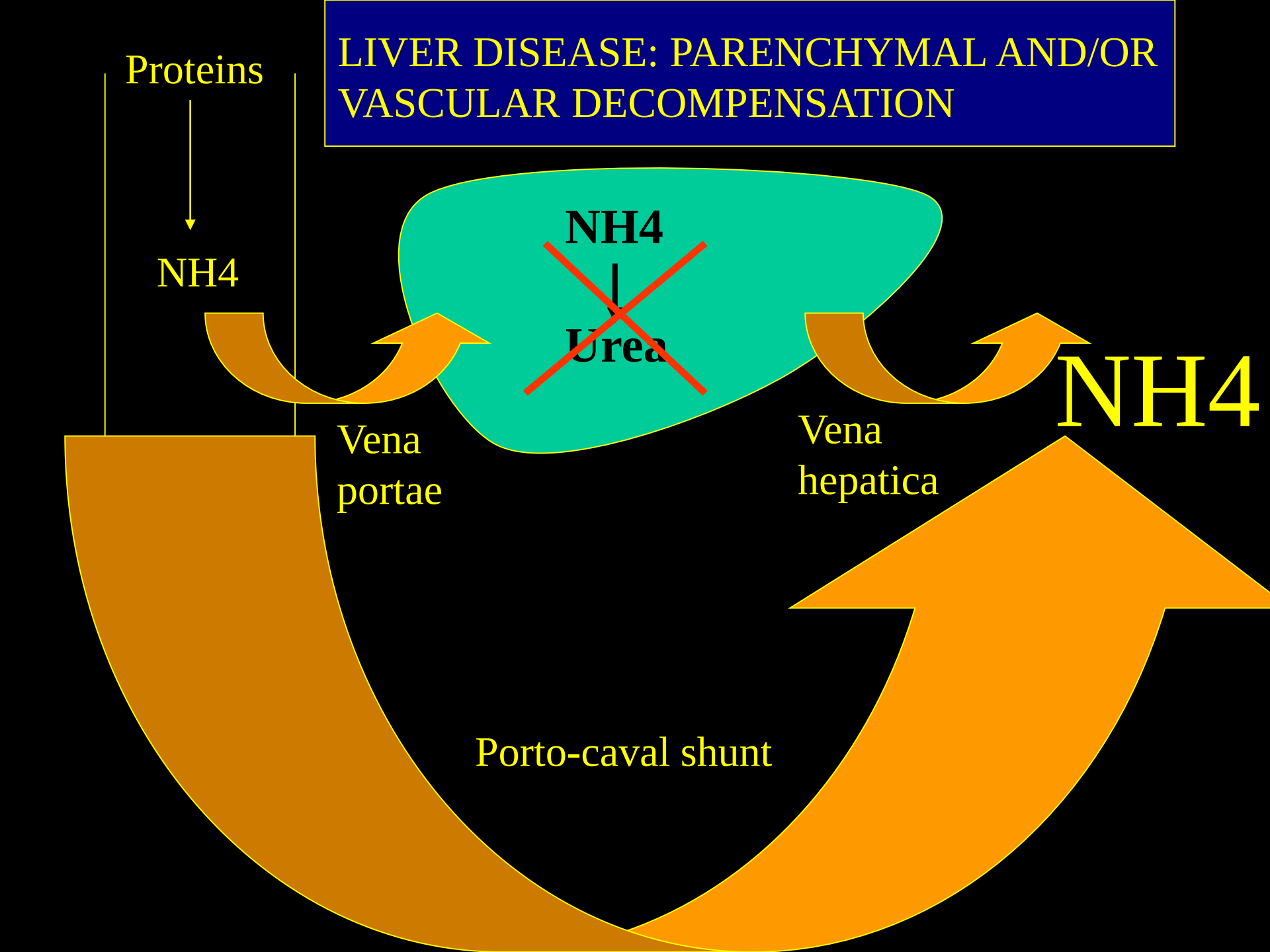
SYNCOPE

-CARDIOINHIBITORIC

-VASODEPRESSOR




Proteins
NH4
NH4
Urea
Vena
portae
Vena
hepatica


LIVER DISEASE: PARENCHYMAL AND/OR VASCULAR DECOMPENSATION
Proteins
NH4
NH4
Urea
NH4
Vena portae
Vena hepatica
Porto-caval shunt

Liver disease

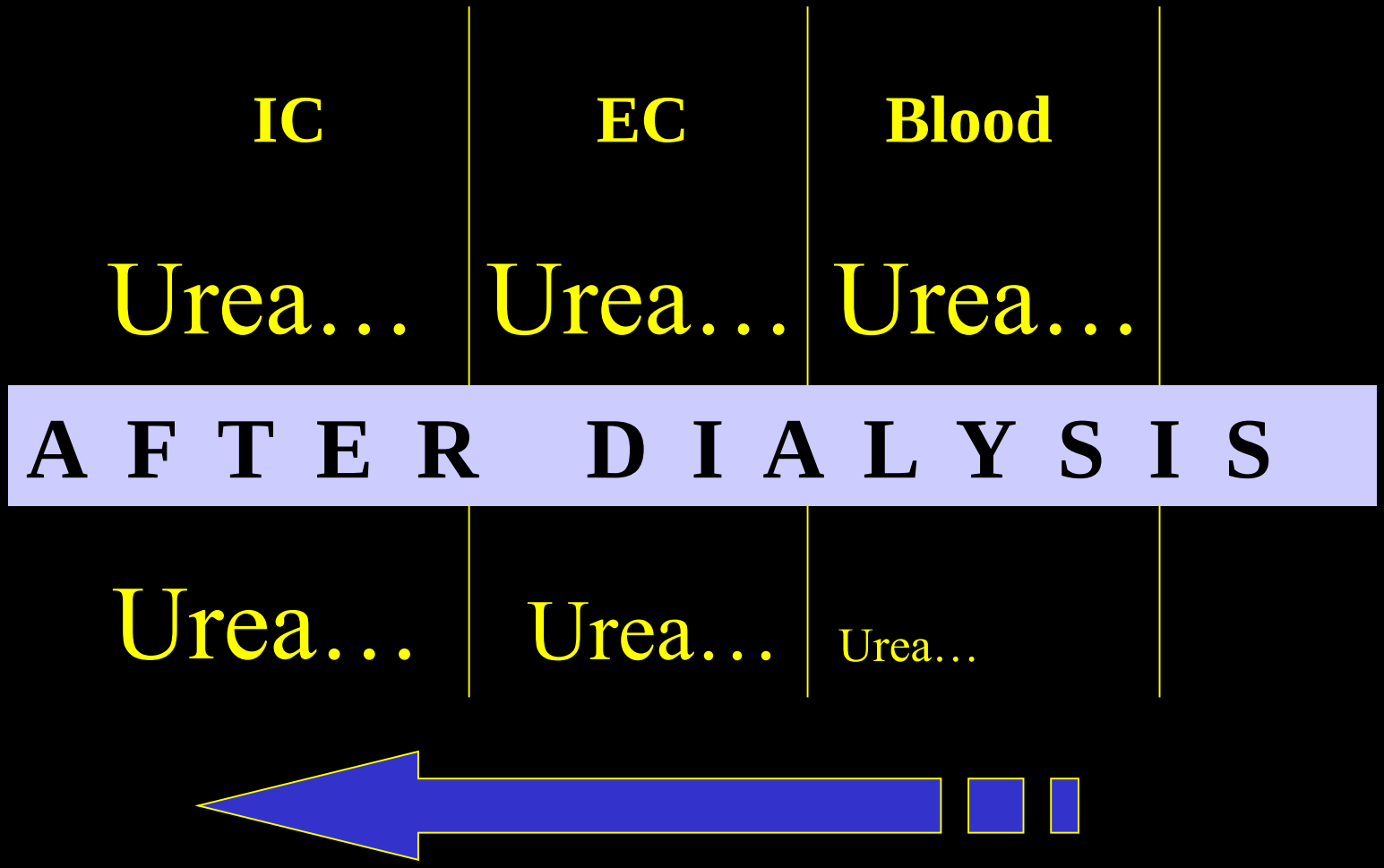
- Hepatic encephalopathy - **hyperammonaemia**
  - proteins – microorganisms in bowels with urease enzyme – NH4 – damage of the liver +/- porto-caval shunt – no utilisation of NH4 in the liver – hyperammonemia
  - inattentiveness, irritability, confusion, disturbance of consciousness
  - asterixis - 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
EC
Blood
Urea…
Urea…
Urea…
AFTER DIALYSIS
Urea…
Urea…
Urea…
OSMOTIC GRADIENT
IC EDEMA

Renal diseases

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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)

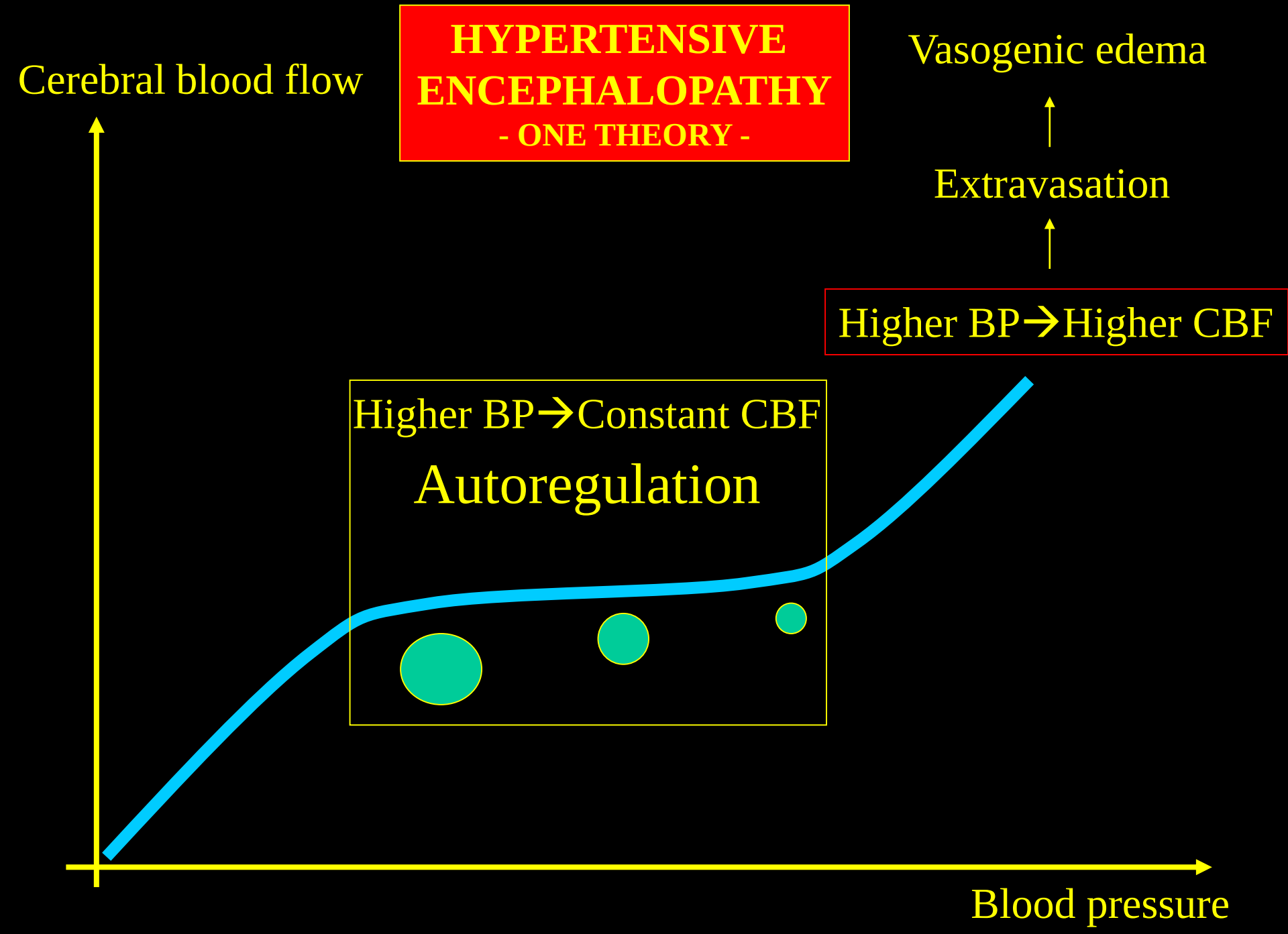
Hypertension

- 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!!!

HYPERTENSIVE ENCEPHALOPATHY
- ONE THEORY -



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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)

DURATION!

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

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

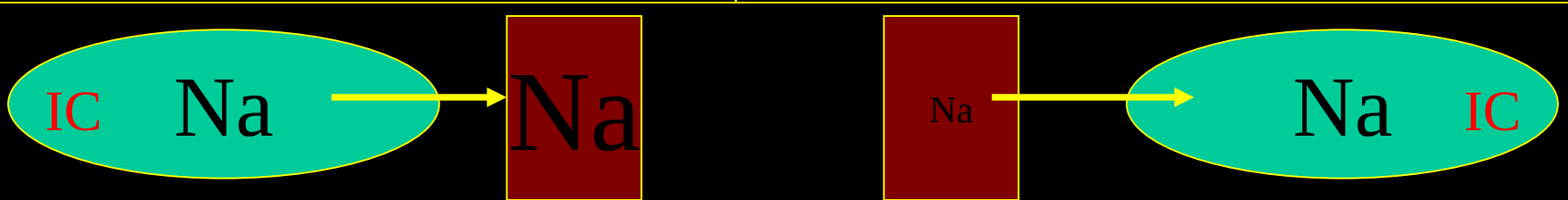
Electrolyte disturbances - Na

- **Hypernatriaemia**
  - Head trauma, damage of hypophysis (ADH↓), no fluid intake
  - Myoclonus, convulsion, asterixis, somnolence

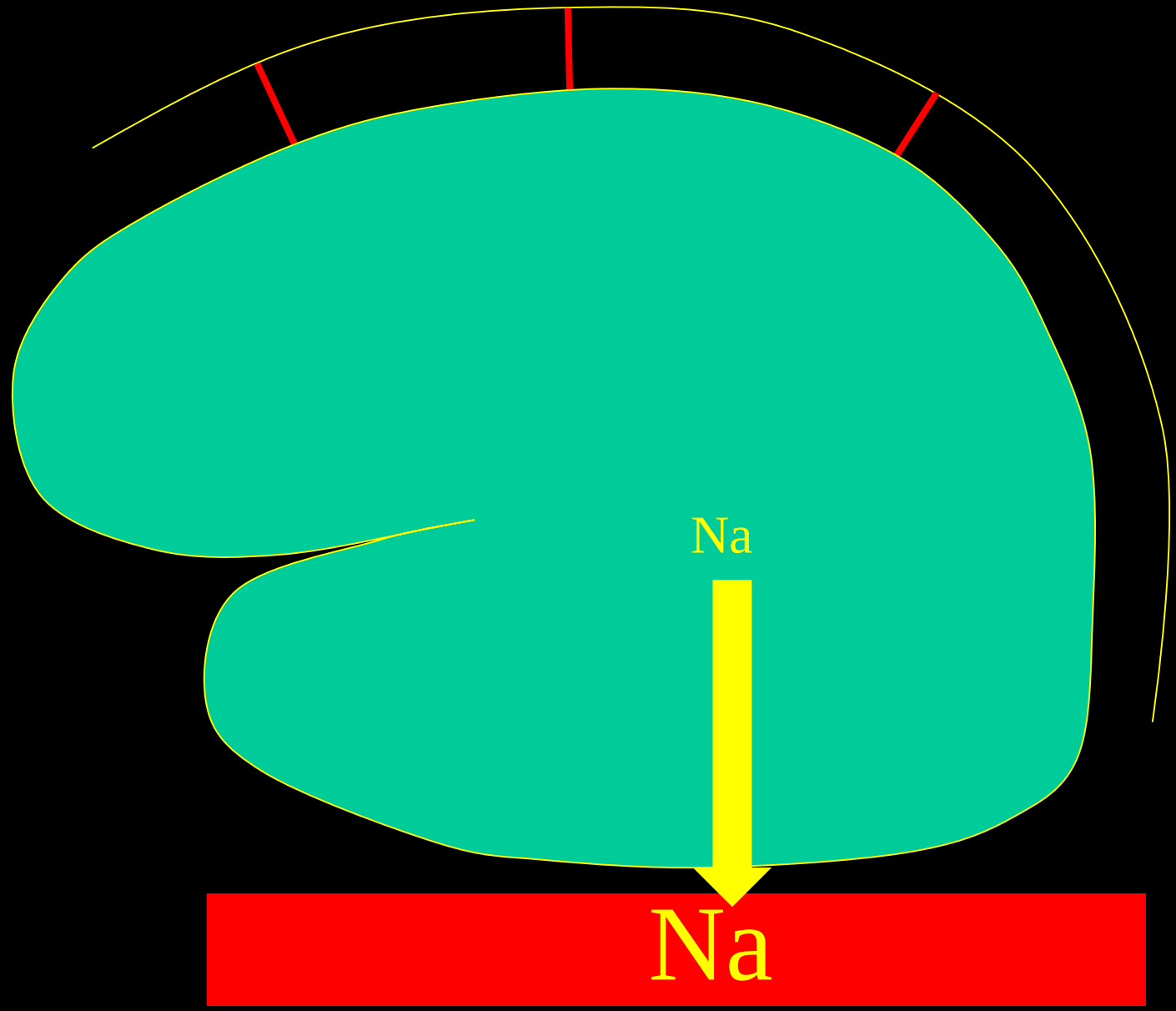
  - IC and brain volume ↓
  - ⬇
  - Tearing of bridging veins, subdural haematoma

- **Hyponatriaemia**
  - 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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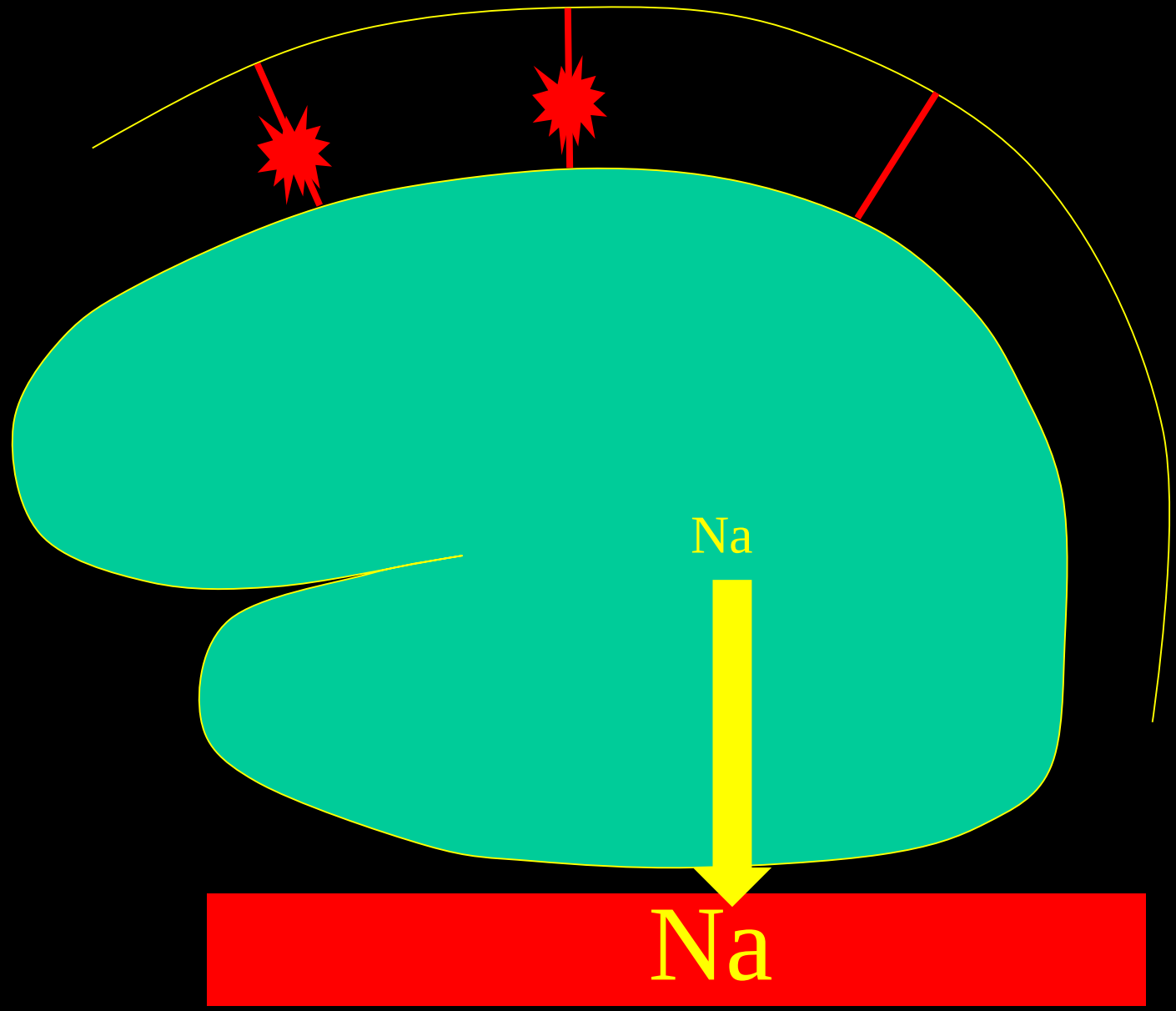

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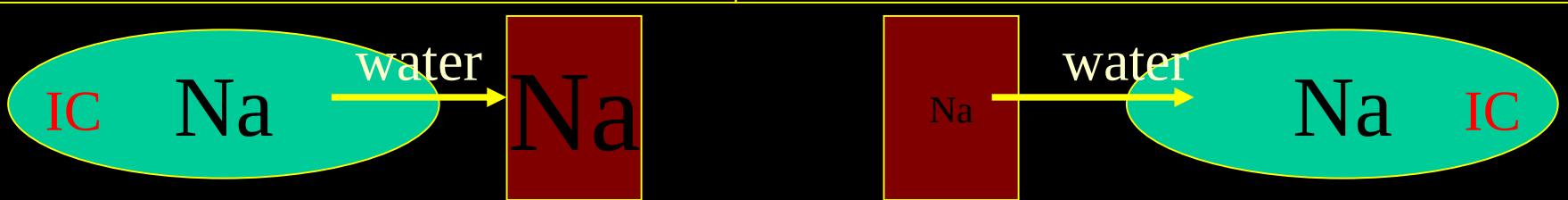

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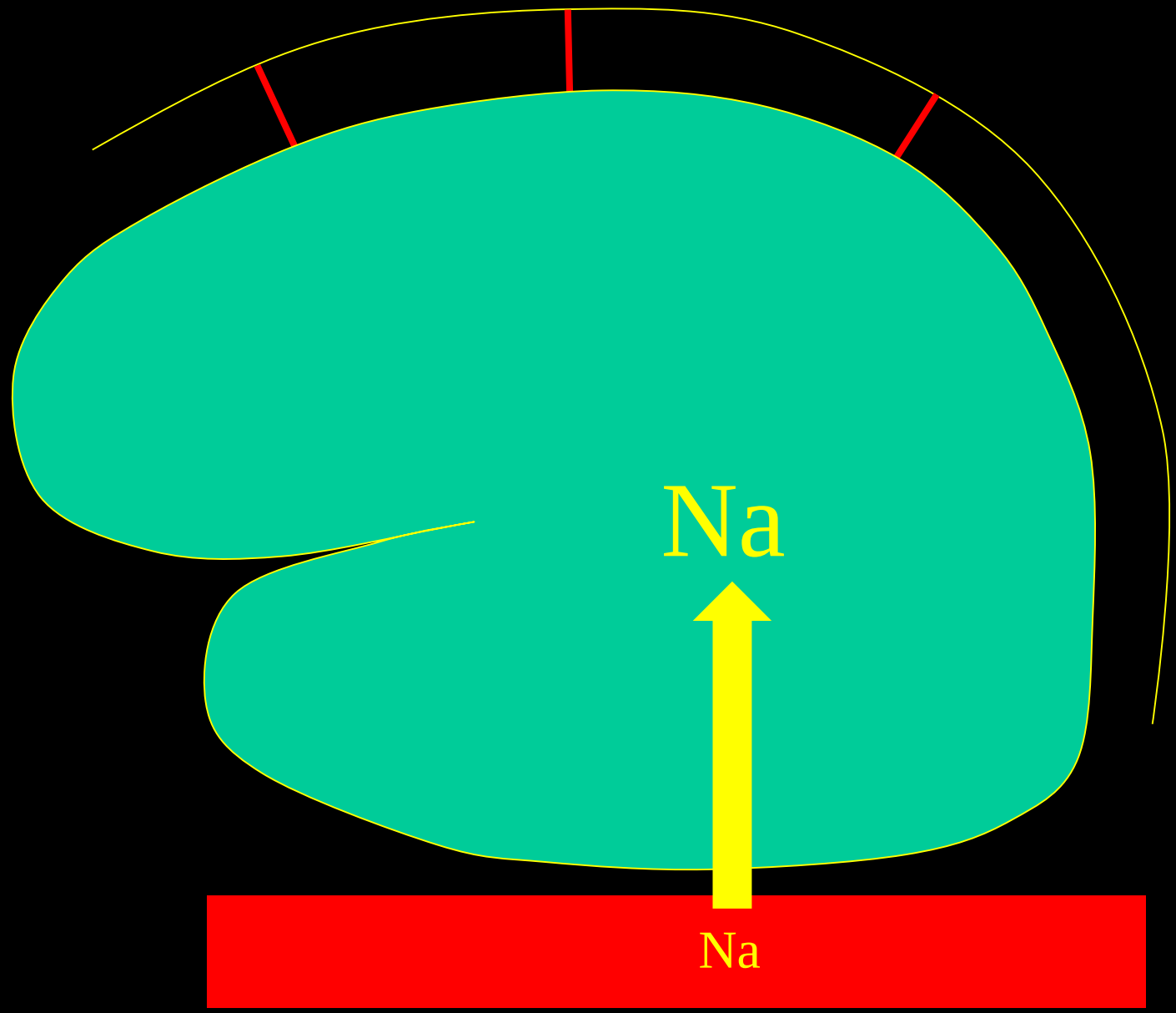

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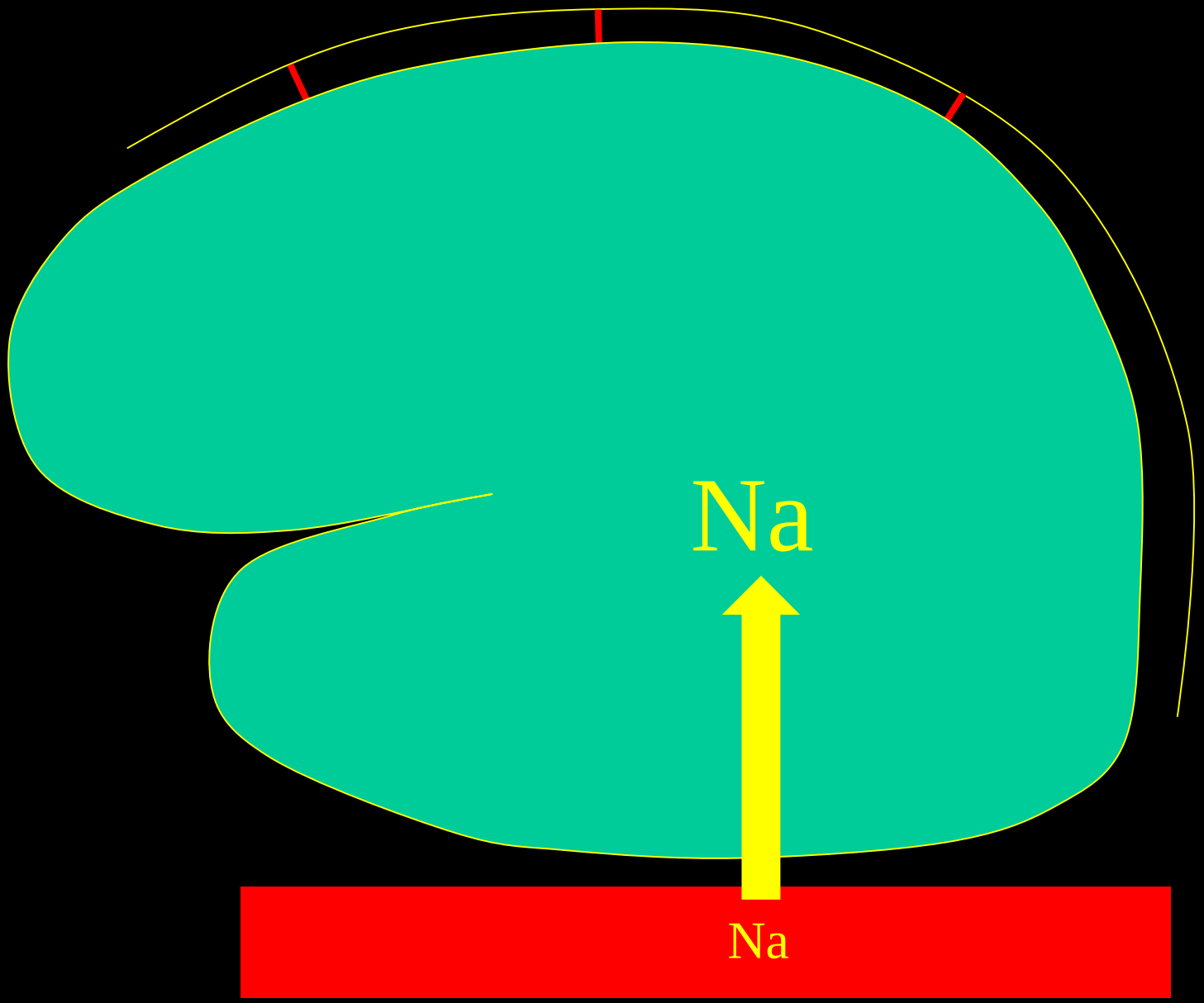

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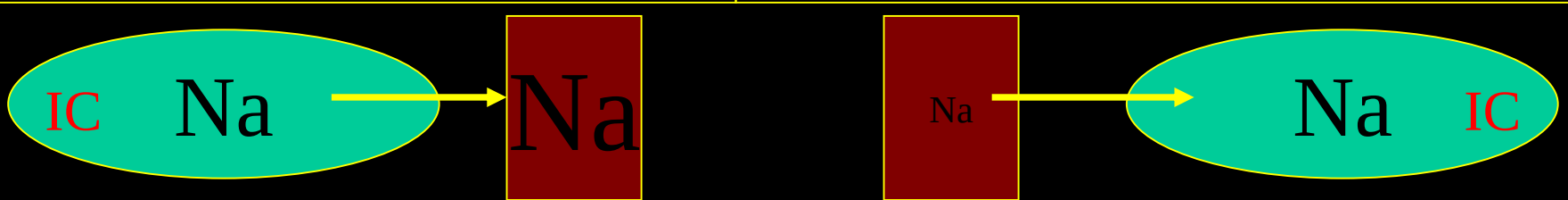


Central pontine myelinolysis

- Not only in alcoholics
- Demyelinisation
- Most pronounced in the centre of the pons
- Cranial nuclei are preserved
- Tetraparesis, pseudobulbar laesion, 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

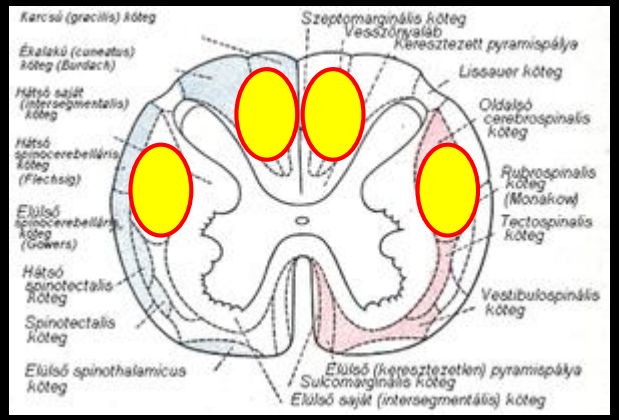
Diseases of the nervous system caused by nutritional deficiency

- 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 ↔↑↓, weakness of external eye muscles, diplopia, weakness of conjugate gaze)
- ***Ataxia*** (severe trunk and gait ataxia)
- ***Disturbance of consciousness and mentation*** (apathetic, inattentive, hallucionations, 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	Disease
Muscles	Myopathy
Peripheral nerve	Polyneuropathy-N
Optic nerve	Alcoholic amblyopia-N
Myelon	Myelopathy-N
Diencephalon	Wernicke disease-N
	Korsakoff disease-N
Brainstem	Central pontine myelinolysis
Cerebellum	Vermis atrophy-N
Cortex	Cerebral atrophy-?
Corpus callosum	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!!!