The illness and the sick

There is no clear definition for "Disease" (neither for "health")

Not diseases but sick people

Cannot use "normal" as a standard to define

the disease is defined in each case

Disease phases	Pathology areas
Causes (internal/external) (risk factor vs. risky practice)	Etiology
Mechanisms	Physiopathology
Injuries (structural & functional)	Pathological anatomy
Symptoms and signs (specific organic disorder → syndrome)	Semiology

Clinic: what the doctor does with the patient

Clinical history

Clinical Phases	
1. Diagnosis: anamnesis + examination (physical + complementary)	**Differential diagnosis:** know the actual disease
2. Prognosis: prediction of the course of the disease	
3. Treatment: etiologic, pathogenic or symptomatic	
4. Prevention: primary (no occurrence) secondary (no complications)	

The Infection

Aggression (incident) → Pro-inflammatory cytokines

Consequences
inflammation
febrile syndrome
acute phase response
systemic response
general adaptation syndrome
acute phase reactants
immune response

The body responds to Pathogen associated molecular patterns (**PAMPs**) and Damage associated molecular patterns (**DAMPs**) with the use of Pattern recognition receptors (**PRR**)

Infection (PAMPs) → TLR (PRR) → cytokines → inflammation

necrosis (DAMPs) → cytokines

Sepsis → necrosis (DAMPs)

Systemic inflammatory response syndrome (SIRS) → Sepsis

Inflammation → **local**; endothelium: **proadherent** (↑membrane receptors = ↑leukocytes and macrophages) and **procoagulant** (clotting) → **microthrombosis** → -itis

Systemic inflammatory response syndrome (SIRS) → SIRS (at least 2 of ↓)

SIRS (at least 2 of ↓)
Temperature >38ºC <36ºC
Leukocytes >12k/µL or <4k/µL
>10% immature neutrophils
Tachycardia >90bpm / Tachypnoea >20 rpm

Sepsis = SIRS + Infection + organ failure

↑cytokines = worse → Inflammatory Response

Inflammatory Response
- insufficient (malnutrition, immunosenescence, etc...)
- adequate
- excessive (sepsis, shock)

SOFA and Quick SOFA → Assessments → >22 respirations/min + mental disturbance + arterial pressure <100mmHg

Energetic Requirements

Harris-Benedict * PAL (1,2/1,3) * Sepsis (1,3-1,5)

Kwashiorkor like (mixed malnutrition)

Hospitals → serum (glucose) → insulin (no lipolysis) → muscle protein breakdown → gluconeogenesis

infection → inflammation → malnutrition → infection

The Inflammation

reaction of connective tissue in response to an aggression (etiological agents)

tumour, redness, heat, pain, functional impotence. local and/or systemic

it must be in irrigated tissues. Cartilage + infection → destruction (+neovascularisation)

Etiological agents
exogenous: physical, chemical and biological
endogenous: immunological, degenerative, atherosclerosis, neoplasm, foreign bodies, ↑CO2, ↓O2, bile

Detection of the inflammation: inflammasomes (receptors of PAMPs and DAMPs) → proteins that activate caspase and therefore, activation of pre-IL1 → IL-1

Inflammation phases	
phase 1: Vascular reaction (local). because of histamine, prostaglandin and NO	hyperaemia, protein exudation and altered spatial relation of blood cells
phase 2: Cellular reaction.	
2.1 early leukocyte phase: **recruitment** (adhesion to the membrane) + **diapedesis** (passage into the interior)	
2.2 late leukocyte phase: **chemotaxis** (chemokines bring them to the inflammatory focus) → **activation** (produces mediators) → **osponisation** (coating foreign particles) → **phagocytosis** (of marked particles)	

result: resolution, chronification or necrosis

Inflammation Mediators

Actions:
- vasodilation (histamine, prostaglandin and NO)
- ↑capillary permeability
- chemotaxis (recruitment)
- fever (IL-1, IL-6, prostaglandin)
- pain
- tissue damage (NO)

Chemical mediators characteristics: very short half-life, beneficial and harmful effects, stimulate other mediators, multiple mediators with complex interactions

Chemical → plasmatic → **systems: complement** (apoptosis), **coagulation** (to not spread infection), **fibrinolysis** (reactivates circulation → repair) and **kinins** (pain → immobilisation → repair)

Chemical → cellular → vasoactive **amines** (histamine, serotonin), **biolipids**, free **radicals**, **NO**, fat-soluble **enzymes**, pro-inflammatory **cytokines** (communication)

Cells → circulating → neutrophils, basophils, eosinophils, lymphocytes, platelets

Cells → tisular → mastocytes (histamine), fibroblasts (fibrosis → scar) macrophages lymphocytes

Pro-inflammatory cytokines:
- interleukins (IL-1 IL-6 pro-, IL-10 anti-)
- interferons IFN
- tumour necrosis factor TNF (pro- → cachexia)
- colony stimulating factors (leukocytes growth

IL-1, IL-6, TNF → endothelial activation, fever, ↓appetite, proteolysis (gluconeogenesis), ↓albumin, prealbumin and transferrin, ↑PCR, fibrinogen and ferritin → acute phase proteins → acute phase systemic reaction → systemic inflammatory response syndrome SIRS

The Fever

- General concepts
  - Hypothalamus controls body temperature
  - **Thermolysis**
    - Radiation 60%
    - Convection 12-15%
    - Evaporation 20-27%
    - Conduction (↓quantities)
  - Temperature Regulation
    - **Endocrine system**
      - thyroid → ↑TRH = ↑TSH → thermogenesis ↑metabolism
      - adrenal medullas → catecholamines
    - **Autonomic nervous system**
      - parasympathetic → rest
      - sympathetic → fight or flight
  - **Skin:** thermoregulation using anastomoses

Raynaud syndrome

- Definitions
  - ideal TºC measurement should be inside the body
  - rectal > buccal > axillary
    - **Fever:** ↑body TºC above diurnal elevation, caused by a new set point from the hypothalamus
    - **Hyperthermia:** ↑TºC of the body due to failure in heat elimination mechanisms (NO hypothalamus)
- Causes & Mechanisms
  - **Causes**
    - infection: viral and/or bacterial
    - tumours: lymphomas
    - connective tissue diseases
  - **Mechanisms**
    - exogenous pyrogen (inflammatory stimulus, necrosis, neoplasia, altered metabolism)
    - monocyte detects virus
    - IL-1 (endogenous pyrogen) has to reach the hypothalamus → cannot pass the blood-brain barrier
    - IL-1 goes to vascular organ of the lamina terminalis (VOLT)
    - Prostaglandin E2 is produced from arachidonic acid via cyclooxygenase→ passes blood-brain barrier
      - Fever = prostaglandin + thromboxane (thrombosis)
        - aspirin blocks cyclooxygenase → no prostaglandin = no fever = no thrombus
      - ↑TºC → fever

Hypersensitivity, autoimmunity and immune deficiency

- Hypersensitivity
  - tissue damage or functional alteration
  - type 1 anaphylactic: response to innocuous antigens
    - ↑1st contact awareness-raising 2nd contact allergic response → Cytokines involved
    - **Histamine, PAF and prostaglandin:** muscle contraction, vasodilator, ↑capillary permeability → hypotension = **edemas**
      - glottic edema = anaphylactic shock → treated with **Adrenaline** → ↑AMPc and phospholipase C inhibition → clinic → stop anaphylactic shock. angioedema most common

causes
aeroallergens (mites)
by sting (jellyfish)
intravenous (medication, radiology)
food (all 14 allergens)
heat or cold allergy
allergy to physical exercise, trauma
drugs (vancomycin → red man syndrome)

  - type 2 cytotoxic: IgM or IgG antibody (membrane antigen) → **inflammation**, frustrated **phagocytosis** (enzymes are released which then damage the membrane), **cellular dysfunction** (acetylcholine antibody → muscle paralysis)
    - aka it attacks the body's own structures → e.g. Goodpasteur syndrome → attacks kidneys and lungs (bloody sputum)
    - platelets, granulocytes. haemolytic anaemia
  - type 5 antibodies to receptors → variations of type 2
  - type 6 NK cells involved
  - type 3 circulating immunocomplexes → antigen (endogenous / exogenous) + antibody accumulate in natural filters
    - **local arthus-type:** precipitate where they enter
    - **systemic serum type:** infectious, complexes accumulate in filters → headache, muscle pain, urination
  - type 4 delayed or cellular → non-immunoglobulin cell-mediated contact dermatitis (sweat watches)
- Autoimmunity
  - loss of immunological tolerance (you no longer know what is yours).
  - it can be natural or acquired, specific or non-specific, central (thymus), peripheral (lymph nodes).
  - delection, allergy, clonal ignorance
- Immune deficiency
  - B-lymphocytes **humoral** ↓IgA → drugs, viruses, tumours, nephrotic syndrome
  - T-lymphocytes **combined** (live agents) → viruses (HIV) malnutrition diabetes, neoplasms, chronic renal failure

Etiology: the causes of disease

endogenous, exogenous; physical, chemical, biological agents

- Physical
- Chemical
- Biological

Mechanical
concussion (cerebral)
contusion (bruise)
wound (blood)
Motion sickness
body swaying (dizziness)
speed and acceleration (rollercoaster)
Gravity
orthostatism (getting up quickly from the couch)
sedentary lifestyle (↑CVDs)
prolonged stay in bed
Microgravity
cardiovascular, muscular atrophy, bone decalcification, urolithiasis, circadian rhythm alteration, cancer
Dysbarisms
absolute and relative hyperpressure (blast wave, diving)
absolute and relative hypopressure (altitude sickness, air cabin decompensation)
Vibrations
local or systemic (reynod, carpal tunnel)
Noise pollution
noise >55dB. damage= intensity/duration
Cold
hypothermia <35ºC. local or systemic. 1. fighting phase (maintain body heat) 2. claudification phase (body gives in to the cold)
erythema, immersion foot, frostbite (necrosis), cholestatoma
Heat
local or systemic. 1st degree burns (skin), 2nd degree burns (dermis), 3rd degree burns (all layers)
heat stroke >40ºC ambient
Radiation
ionising (cumulative) → cancer. natural, planned or emergency; external or internal
solar UV (in severe burns)
non-ionising: mobile phones, microwaves, electromagnetic waves
Electricity
low voltage → few problems (cut off current, do not touch electrocuted)
high voltage → many problems (cut substation and resuscitation)

Intoxications
toxic: harmful effects
toxicology: science that studies toxins.
toxin: natural substance
xenobiotic: foreign substance
drug: modifies body functions
WHO classification
recreational use: alcohol, tobacco, cocaine, heroin, cannabis
natural: caffeine
endogenous: most powerful ones
exogenous: factories
food: junk food, ultra-processed
cooking materials: aluminum, Teflon, heavy metals
plastic packaging: PVC (#3), polystyrene (#6), BPA (#7)
cosmetics and creams: asbestos, phthalates, lead, cadmium, additives
toxic additives in clothing: dark colors → heavy metals
pollution: air quality = quality of life
car air fresheners = chemicals
pesticides: DDT, organophosphates and carbamates

microorganisms: viruses, bacteria, parasites, prions

Objectives of the clinic

science of the sick

pathology ≠ disease
pathology is the way of falling ill

data collection: anamnesis (symptoms) and physical examination (signs) + medical history and anthropometric variation

semiology: study of symptoms and signs (sydromes)

diagnosis (differential)→ **prognosis** → **treatment** (cure, alleviate or comfort)

Immune system

- **natural immunity (not specific)**
  - no memory
  - physical, chemical, cellular and protein barriers
  - Levels of Barriers
    - **primary:** skin and mucosa; sweat, gastric acid and eye drops; microbiota
    - **secondary:** macrophages and neutrophils
      - **Inflammation**
        - macrophages, natural killer and neutrophils
- **adaptive immunity (specific)**
  - memory
  - antibodies and cellular lymphocytes immunity
    - humoral response
      - macrophages "teach" lymphocytes B about the pathogen
        - then antibodies production
    - cellular response
      - pathogen inside the cell → lymphocyte T (recognises the pathogen)
        - also use of the inoculated lymphocyte T (that already knows the pathogen)

Stable patient

Health (WHO): state of physical and social well-being

WHO levels of prevention:

- primary: prevents
- secondary: early stages
- tertiary: slow down aggravation

Prevention of cardiovascular disease

Risk factors:

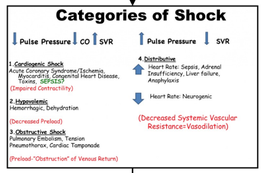
- High blood pressure: >140/90mmHg
- Diabetes mellitus: >126mg/dl >200mg/dl, HbA1C >6.5
- Obesity and Smoking
- Alcohol consumption: standard basic units (SBU)
- Hypercholesterolemia: >200mmHg
- **Low risk** <3♂ and <2♀ SBU, **moderate risk** >3♂ and >2♀ and **high risk** >6♂ (40w) and >5♀ (28w).
- Sedentary: 150 min of moderate aerobic activity per week
- together with strength and flexibility exercises. MET= metabolic equivalent of task

Management of the critically ill patient

extreme deterioration of vital functions with irreparable organic sequelae and even death

Complications of critical illness: sepsis, deep vein thrombosis, acute gastric ulcers, anaemia, malnutrition, acute renal failure.

Shock

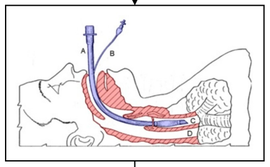


- **Decreased cardiac output** → assess extracellular volume (dehydration) and cardiac function
- **Increased cardiac output** → decrease in vascular resistance

Acute respiratory failure

arterial pO2 <60 mmHg.

- **Not severe** → resolution of predisposing disease
- **Severe** → orotracheal intubation and assisted ventilation



Partial pH= 7.47, pCO2 27, pO2 52, HCO3 24
Global pH= 7.26, pCO2 57, pO2 52, HCO3 24

Severe sepsis

lethal entity if not suspected and treated intensively and early

Acquired outside the ICU

Acquired in ICU: Leading cause of death (in non-coronary ICU) Frequent multi-resistant germs invasive interactions (intubations, probes, catheters...)

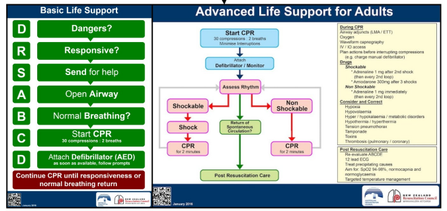
treatment: antibiotics, assisted respiration, nutrition, protection, water and electrolyte replenishment

Cardiovascular collapse, cardiac arrest and sudden death.

- **Cardiac arrest:** Sudden reversible interruption of pump function.
- **Sudden death:** Irreversible interruption of organ function.

Causes

- Ischaemic heart disease (AMI)
- Severe arrhythmias (ventricular fibrillation)



Acute confusional states and coma.

- Altered level of consciousness, fluctuating with acute onset and inattention.
- Pathological state of reactivity → the patient does not wake up.

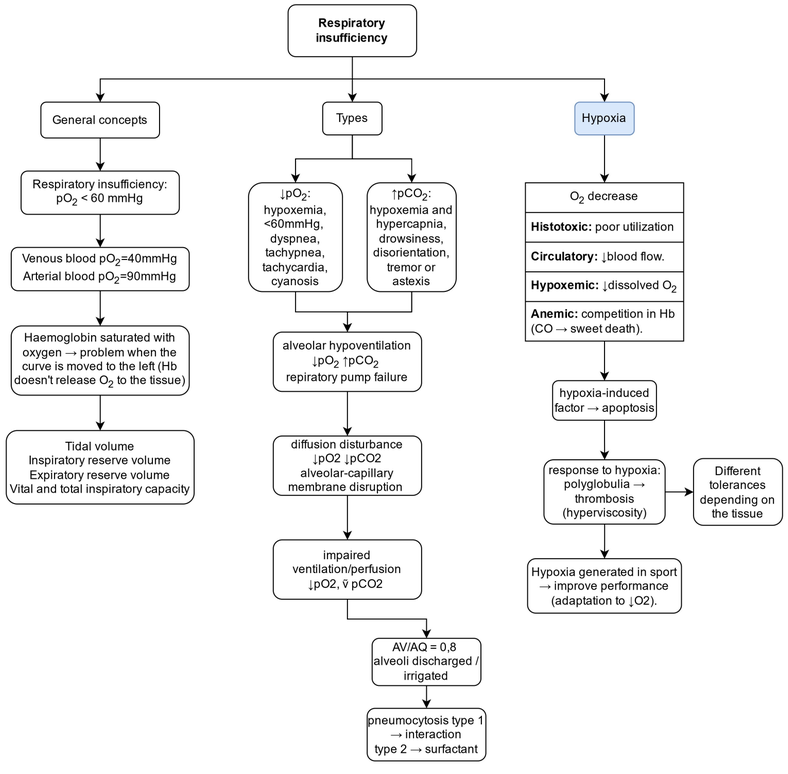
Causes: sepsis, intracranial pathologies, convulsions, hypoxia, hypertensive crises, shock, metabolic disorders, hypovitaminosis and electrolyte disorders, drugs: sedatives and analgesics and drug withdrawal.

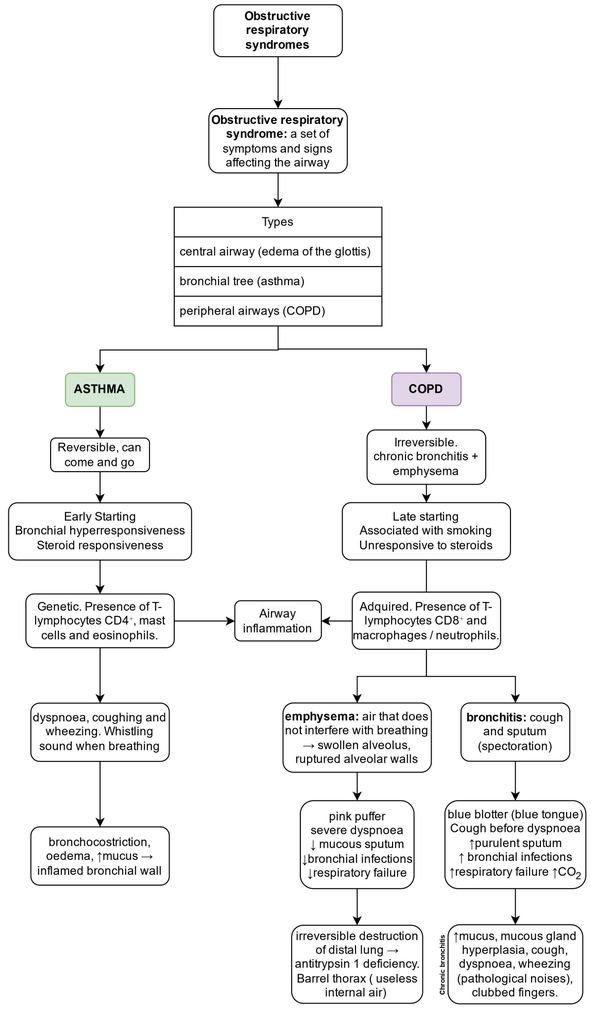
In relation to the central nervous system (CNS): Trauma, infections, epilepsy, haemorrhages, cerebral oedema

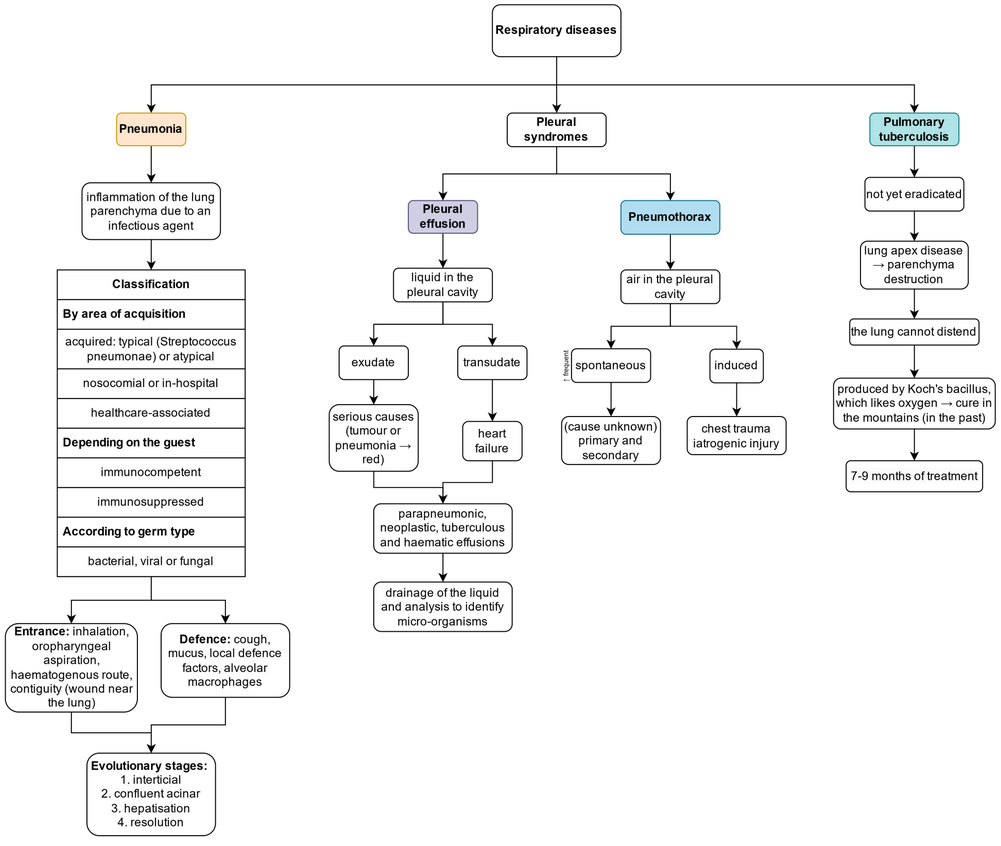
Not related to the CNS: drugs, hypoxia, hypercapnia, hepatic or renal insufficiency, electrolyte disturbances (Na, Ca, Mg)

Clinical: depends on the cause of the altered level of consciousness.

Treatment: that of the disease causing it.


Respiratory insufficiency
General concepts
Types
Hypoxia
Respiratory insufficiency: pO_2 < 60 mmHg
Venous blood pO_2=40mmHg
Arterial blood pO_2=90mmHg
Haemoglobin saturated with oxygen → problem when the curve is moved to the left (Hb doesn't release O_2 to the tissue)
Tidal volume
Inspiratory reserve volume
Expiratory reserve volume
Vital and total inspiratory capacity
↓pO_2: hypoxemia, <60mmHg, dyspnea, tachypnea, tachycardia, cyanosis
↑pCO_2: hypoxemia and hypercapnia, drowsiness, disorientation, tremor or astexis
alveolar hypoventilation ↓pO_2 ↑pCO_2 repiratory pump failure
diffusion disturbance ↓pO2 ↓pCO2 alveolar-capillary membrane disruption
impaired ventilation/perfusion ↓pO2, ↕ pCO2
AV/AQ = 0,8 alveoli discharged / irrigated
pneumocytosis type 1 → interaction type 2 → surfactant
O_2 decrease
Histotoxic: poor utilization
Circulatory: ↓blood flow.
Hypoxemic: ↓dissolved O_2
Anemic: competition in Hb (CO → sweet death).
hypoxia-induced factor → apoptosis
response to hypoxia: polyglobulia → thrombosis (hyperviscosity)
Different tolerances depending on the tissue
Hypoxia generated in sport → improve performance (adaptation to ↓O2).


Obstructive respiratory syndromes
Obstructive respiratory syndrome: a set of symptoms and signs affecting the airway
Types
central airway (edema of the glottis)
bronchial tree (asthma)
peripheral airways (COPD)
ASTHMA
COPD
Reversible, can come and go
Early Starting
Bronchial hyperresponsiveness
Steroid responsiveness
Genetic. Presence of T-lymphocytes CD4⁺, mast cells and eosinophils.
Airway inflammation
dyspnoea, coughing and wheezing. Whistling sound when breathing
bronchocostriction, oedema, ↑mucus → inflamed bronchial wall
Irreversible. chronic bronchitis + emphysema
Late starting
Associated with smoking
Unresponsive to steroids
Adquired. Presence of T-lymphocytes CD8⁺ and macrophages / neutrophils.
emphysema: air that does not interfere with breathing → swollen alveolus, ruptured alveolar walls
bronchitis: cough and sputum (spectoration)
pink puffer
severe dyspnoea
↓ mucous sputum
↓bronchial infections
↓respiratory failure
blue blotter (blue tongue)
Cough before dyspnoea
↑purulent sputum
↑ bronchial infections
↑respiratory failure ↑CO_2
irreversible destruction of distal lung → antitrypsin 1 deficiency. Barrel thorax (useless internal air)
Chronic bronchitis
↑mucus, mucous gland hyperplasia, cough, dyspnoea, wheezing (pathological noises), clubbed fingers.


Respiratory diseases
Pneumonia
Pleural syndromes
Pulmonary tuberculosis
inflammation of the lung parenchyma due to an infectious agent
Classification
By area of acquisition
acquired: typical (Streptococcus pneumonae) or atypical
nosocomial or in-hospital
healthcare-associated
Depending on the guest
immunocompetent
immunosuppressed
According to germ type
bacterial, viral or fungal
Entrance: inhalation, oropharyngeal aspiration, haematogenous route, contiguity (wound near the lung)
Defence: cough, mucus, local defence factors, alveolar macrophages
Evolutionary stages:
1. interticial
2. confluent acinar
3. hepatisation
4. resolution
Pleural effusion
Pneumothorax
liquid in the pleural cavity
exudate
transudate
serious causes (tumour or pneumonia → red)
heart failure
parapneumonic, neoplastic, tuberculous and haematic effusions
drainage of the liquid and analysis to identify micro-organisms
air in the pleural cavity
spontaneous
induced
↑ frequent
(cause unknown) primary and secondary
chest trauma
iatrogenic injury
not yet eradicated
lung apex disease → parenchyma destruction
the lung cannot distend
produced by Koch's bacillus, which likes oxygen → cure in the mountains (in the past)
7-9 months of treatment

Cardiac insufficiency

cardiac output: blood volume pumped per minute. ~70ml

cardiac output = (precharge*contractility*H.R.)/ (postcharge)

Cardiac insufficiency: when the cardiac output is lower than the blood supply needed by the tissues

Causes: ischemic cardiopathy and arterial hypertension

Symptoms: depending if before or after the congestion

Compensations mechanisms

Intrinsic: cardiac hypertrophy or dilatation

Extrinsic

Sympatic Nervous System (catecholamines → tachycardia)

Renin-Angiotensin-Aldosterone (↑Precharge ↑Cardiac output), ADH, Vasopressin

dyspnoea → nea = air

orthopnoea: dyspnoea when lying down

jugular hypertension → blood cannot enter the heart

Coronary heart disease

endo-, mio- and pericardium sinuses of valsalva → coronary artery origin.

coronary circulation → phasic flow of 80-100ml/100g myocardium/min.

Dominance →depends of posterior interventricular artery, if it's derived from left or right coronary artery

coronary insufficiency: flow unable to satisfy myocardial needs

↓coronary reserve ↑requirements ↓quantity.
↓O_2 ↓flow ↑O2 demand
↑ventricular strain ↑heart rate

Atheromatosis → atheroma plaque → changes pressure.

Causes: dyslipidemias, cholesterol, obesity, DM, smoking, arterial hypertension.

Consequences: myocardial necrosis → myocardial infarction.

Biochemicals: ↑ lactic acid, ↑protons (acidity) → pain. Clinical = ↑troponin. Electrolytes, arrythmias, stress (Sympathetic NS).

Mechanical: acute ischemia (partial necrosis), chronic ischemia (myocardial hibernation).

Coronary insufficiency syndromes
1. Silent ischemia (no symptoms)
2. Chronic coronary syndromes (stable angina → atheroma plaque pain on exercise).
3. Acute coronary syndromes (unstable angina → perpetual pain. transmural (Q) and non-Q acute myocardial infarction
4. sudden death (ventricular fibrillation → use of defibrillators)

High blood pressure

Chronic elevation of arterial blood pressure

affects the heart, the brain, the kidney and other disease

Main cause: atherosclerosis

Blood pressure is dynamic → changes a lot → differences between clinic and at home → masked hypertensives

Physiopathology

pressure exerted by the blood on the vessels

Regulation
1. rapid control system → baroreceptors, chemoreceptors, ischaemic response.
2. intermediate control system → Renin-Angiotensin-Aldosterone
3. Slow control system

Measures

avoid anxiety, constipation, pain, caffeine, smoking, urination.

comfortable and quiet environment.

comfortable posture, arm at heart level, feet touching the floor (without crossing).

Cuff according to arm circumference

Causes

epiphenomenon due to
1. aortosclerosis (hardening of the arteries).
2. coarctation of the aorta

↑ Systolic and diastolic pressures

Causes:
1. idiopathic or essential 90% → unknown causes.
2. Secondary (↑flow or ↑resistance) 10% → stress, alcohol, drugs, smoking

Consequences

1. Arterial thrombosis
2. Stroke
3. Angina pectoris
4. Myocardial infarction

Treatment

It depends on the age → lifestyle changes (balanced diet, lower sodium, physical exercise, healthy habits)

Shock → peripheral circulatory insufficiency

general hypoperfusion (acute severe decrease in blood flow) → medical emergency (life-threatening)

no feeding, neither by mouth, nor by nasogastric tube, nor parenterally → unstable individual (pressure rises and falls) low nutritional security

stop shock and then feed

Classification

Hypovolemic: ↓effective circulatory volume → ↓cardiac output → peripheral hypoperfusion

Acute haemorrhage, dehydration, third space

Distributive: dilatation of blood vessels → blood stagnation → hypoperfusion

Spesis, anaphylaxis, endocrinologic, toxic, neurogenic

Extracardiac obstructive: obstruction → retrograde accumulation → no blood outflow from the heart → hypoperfusion

obstruction: pulmonary thromboembolism or pneumothorax

Cardiogenic: drastic decrease in cardiac output → peripheral hypoperfusion.

cardiomyopathies, mechanical (valvular insufficiency) and arrhythmias

microcirculation consequences
1. Metabolic: ↓ATP, ↑lactate → acidosis
2. inflammation → ↑ capillary permeability
3. pre- and post-capillary sphincter disturbances
4. slow circulation
5. peripheral microthrombosis

Compensatory mechanisms
1. Hyperventilation
2. Mucosal necrosis gastrointestinal tract → bacterial translocation (inside of the organism)
3. Liver → centrolobular necrosis
4. ↓circulation kidney → urea ↑urea
5. Heart → tachycardia, dilatation, ↑contractility → depression

Metabolic disorders → hyperglycaemia, increased anaerobic metabolism → Renin-Angiotensin-Aldosterone system, ADH and Noradrenaline (catecholamines) all involved in shock.

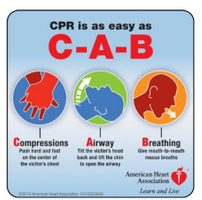
Per se has several phases and mechanisms → Treatment → restore peripheral perfusion

Cardiopathies

- 1. Cardiomyopathies
  - coronary heart disease
- 2. Valvulopathies
  - congenital, degenerative or inflammatory cause
    - **stenosis:** the valve does not open.
      - ↑ pressure before the valve → hypertrophy
        - ↑contractility but ↓preload
    - **insufficiency:** the valve does not close.
      - ↑volume in auricle and ventricle → dilatation
        - ↑preload but ↓contractility.
- 3. Pericardium
  - pericarditis, pericardial effusion or constrictive pericarditis.
- 4. Arrhythmias
  - heartbeat disturbances (formation or conduction of impulses)

management of ischemic heart disease

- stable angina
  - ↓symptoms ↓ischemia. Prevention of death and progression to other heart diseases
    - basic treatment
      - healthy lifestyle, ↓cardiovascular risk factors, identify and treat comorbidities
    - medical treatment
      - antiplatelet agents, antianginal drugs (nitrates, beta-blockers, Na channel blockers, Ranolazine), Statins
    - revascularisation
      - aortocoronary bypass or, less aggressive, angioplasty with stenting
- unstable angina
  - MONA treatment:
    Morphine
    Oxygenation
    Nitroglycerine
    Acetylsalicylic acid
- cardiac arrest or cardiorespiratory arrest
  - Basic vital support: Circulation, Airway, Breathing



  - Cardiopulmonary resuscitation

Pneumopathies

anatomy of the respiratory system:

3 right lobes, 2 left lobes.

thorax scavatum (sunken chest), keeled thorax (pigeon chest)

Breathing Phases
1. Ventilation (distensibility, flow, volume)
2. Diffusion (forced vital capacity, tiffenau index flow/volume, DLCO)
3. Perfusion

Pneumopathy

- obstructive ventilatory disorder (↓flow) ↓Tiffenau
  - in **upper** airways: **fixed** (felt at all times) or **variable** (extrathoracic inspiration, intrathoracic expiration)
  - in **lower** airways (bronchi and bronchioles): **asthma** or **COPD** (chronic bronchitis + emphysema).
- restrictive ventilatory disorder (↓volume) ↑Tiffenau
  - Limitation of lung **expansion** and/or decreased lung **compliance**

Main **cause** → tobacco and pollution
Sign → Drumstick fingers

diagnostic: bronchoscopy, spirometry, chest x-ray, pulse oximetry

Action in respiratory failure

Concepts

Dyspnoea is the sensation of breathing difficulty.

Cyanosis is the bluish discolouration of the skin and mucous membranes.

Diagnosis

history of respiratory problems

Features of semiological interest:

- respiratory pattern
- most affected breathing phase
- circumstances influencing the symptom
- presentation over time

Diag. based on arterial blood gas:
PaO2 = 85-100 mmHg → < 60 mmHg (RF)
PaCO2 = 35-45 mmHg → > 45 mmHg (RF)

Treatment

1.General measures: Airway ok?, O2, complete rest, ↓fever, NO sedation despite agitation, avoid aspiration of gastric contents → Diet, ↑pCO2? NO sleep!

2.Oxygen therapy: achieve an Hb saturation curve of 92%, LOW FLOW: nasal goggles, single mask, ventimax mask, HIGH FLOW: HF nasal cannula and reservoir mask

3.Aetiological treatment: specialised to the causing agent

remove foreign body if present, naloxone-flumacenil in poisoning, drainage of pleural effusion, drainage of pneumothorax (placement of pleural tube), analgesia and fixation of volet in rib fractures, treat PAD-ICC, promptly start antibiotics, bronchodilators, corticoids.

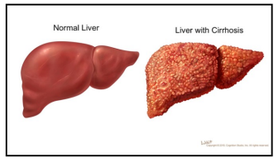
4.Non-invasive mechanical ventilation: Pressurised air ventilator with a determined amount of O2, it is not necessary to sleep or sedate the patient, it is a mask that is placed on the patient.

5. Intubation and mechanical ventilation: sedative or opioid (paralysis) → place endotracheal tube. Use of pleural tube with suctioning.

Hepatic insufficiency

functions of the liver:
detoxification and transformation of substances
synthesis of proteins, lipoproteins, coagulation factors
storage of glycogen, iron, vitamins
metabolism. glycogenolysis and gluconeogenesis

liver cirrhosis



hepatic, chronic, diffuse and irreversible

cirrhosis= fibrosis (strangulation)+ regeneration nodules

consequences:

hepatic insufficiency

acute due to intoxications (<1month), **chronic** due to liver cirrhosis (months-years)

Signs
↓**detoxification** → feminization
↓**albumin synthesis** → edemas
↓**synthesis of coagulation factors** → haemorrhages
↓**storage of glycogen** → hypoglycaemia
↓**bilirubin elimination** → jaundice
↓**ammonia elimination** → encephalopathy

All liver functions are affected causing: Hypoalbuminaemia, Hypogonadism, Coagulopathy, Jaundice and Hepatic encephalopathy.

portal hypertension

↑ hydrostatic pressure in the portal system. Normal porto-caval gradient of 2-5 mmHg.

Blood seeks to reach the heart:

blood through **oesophageal** ducts, through **foveal** vein of the liver → reaches the **umbilicus** and goes up to the heart through the skin. → goes also through the **rectum** without passing through the liver (**haemorrhoids**).

Consequences:
Hypersplenism
Ascites
Edemas
Collateral circulation: haemorrhoids and oesophageal varices
hepatic encephalopathy

Jaundice - Icterus

Excess of bilirubin → yellowing of skin and mucous membranes

Importance

often occurs in **neonates** → red blood cell change

from fetal haemoglobin to adult haemoglobin → **destruction of haemoglobin** = production of bilirubin

UV treatment to remove bilirubin when it is too high

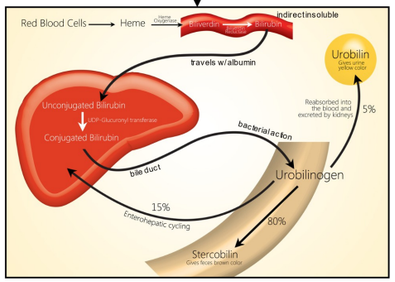
change **from indirect** bilirubin **to direct** bilirubin

Normal values of 1. **Indirect is toxic** and can damage neonatal brain.

Physiopathology

macrophages/monocytes trap and hydrolyse red blood cells when old

heme group cannot be recycled → modify within macrophage:



Classification

	prehepatic	hepatic	post-hepatic
cause	haemolysis, newborn	hepatitis	biliary calculus, pancreatic cancer
accumulates	Indirect bilirubin	both	Direct bilirubin
choluria	no	yes (variable)	yes (very much)
urine urobilinogen	high	variable	decreased

Pacreatitis

Inflammation of the pancreas. On the rise due to obesity and gallstones

Etiology

gallstones 70%: choledocho-pancreatic duct obstruction. more frequent in women.

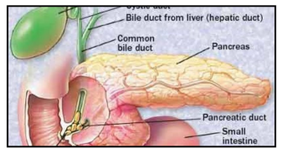
alcohol 30%: only 5% of alcoholics develop it. more frequent in men.

other: tobacco, ↑TG, radiography (radiation), drugs, idiopathic.

in the chronic: 50% due to alcohol

Classification

mild-acute: pain only
moderate acute: organ involvement
severe acute: 20% organ damage



Clinic

Persistent severe **abdominal pain** with **dyspnoea** due to pleural effusion or respiratory distress

↑amylase ↑lipase, ↑PCR ↑IL-6 ↑TNF, ↑immune system

Ultrasound, CT or MRI

in the chronic: chronic abdominal pain, steatorrhoea, pancreatic insufficiency and visible damage on imaging studies.

Complications

75% are **mild** with mortality <5%. 20% are **severe** with mortality <40%.

Treatment:

serotherapy + analgesia
absolute diet → Oral > Enteral > Parenteral
antibiotics if infection confirmed

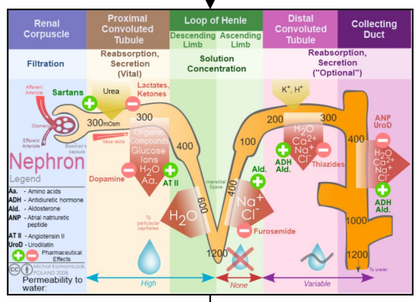
in chronic: smoking and alcohol cessation, pancreatic enzyme replacement therapy.

Acute renal failure

Kidney unable to perform its functions, for some hours or days:

Kidney functions

elimination of many of the body's waste products.
maintaining a constant and normal internal environment (heat, absorbs water; water excess elimination)
synthesis of various important substances (renin, erythropoietin and 1,25-dihydroxychalciferol aka



0.8g protein / kg / day → lower risk of developing renal insufficiency

Diagnosis

Blood: creatinine (assesses renal function) and urea (assesses dehydration).

Urine: creatinine, urine volume, pH, ions, sediments (in case of ATN it is necrotic desquamated cells).

fractional excretion of sodium

urinary and plasma sodium divided by urinary and plasma creatinine per 100

Interpretation
<1 = Na^+ is being saved → pre-renal problem
>3 → renal or parenchymatous
1-3 → both occur

Types

Prerenal. Due to decreased renal perfusion

Intrarenal or parenchymal

- Vascular involvement → low flow
- Glomerular involvement → glomerulus is ruptured
- Interstitial involvement (very frequent 95%) → renal ischaemia or nephrotoxics → ATN

Acute tubular necrosis

Postrenal or obstructive. Obstruction to urine drainage

oligoanuric phase: ↓ urine

consequences
Na and H2O retention
↑K, P, uric, acidosis, plasma creatine
urine: dilute, ↓creatinine, ↓osmolarity

polyuric phase: ↑ urine

2-3 weeks

progressive **recovery of renal function**, possibility of dehydration and water-electrolyte disorders

	PRERENAL	ACUTE TUBULAR NECROSIS	POSTRENAL
[Na^+] urine	↓ it absorbs a lot	↑ the tubule does not work	↓ a lot of water is removed
[Creat] Blood (Always the same)	↑	↑	↑
[Creat] urine	↓ because it decreases the glomerular filtration rate	↓ because it decreases the glomerular filtration rate	↑ the kidney is able to excrete creatinine because it is healthy
urine osmolarity	↑ since the urine concentration is high	↓ since the tubule does not work	↓ since you need to remove water, sodium and solutes
sediment in urine	Normal	Pathological	Pathological

Consequences: oligoanuria, azotemia, sodium and water retention, hyperkalaemia, hyperphosphataemia, hypoerythaemia, acidosis

Toxic hepatitis

By paracetamol

N-acetylparabenzoquinoaimide (NAPQI) toxic

damages hepatocytes (10g hepatitis, 15g fatal)

Glutathione counteracts toxicity

Alcohol = ↓glutathione→ damage with 4-10g

N-acetyl cysteine = ↑Glutathione

By Alcohol

alcohol metabolism: ethanol → acetaldehyde → acetoacetic acid → acetyl-coa → (energy or fat)

NADH/NAD ratio imbalance: acetyl coa → fat → fatty liver. ↑ lactic acid → acidification

production of free radicals

acetaldehyde → damages intracellular proteins, ↑collagen synthesis, cancer

Phases of alcoholic liver disease:
steatosis → fat accumulation
inflammation (hepatitis)
fibrosis → destruction of structures
cirrhosis → fibres "choke" the hepatocytes
cancer

viral hepatitis

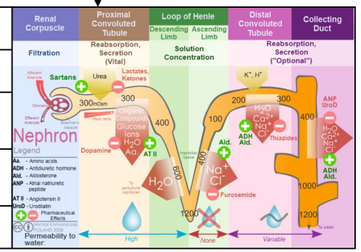
A: RNA, faecal-oral, benign ↓chronisation

B: DNA, sexual-parenteral, 5% chronification

C: RNA, parenteral, 80% chronification

Chronic Kidney Disease (CKD)

kidney functions:
1. eliminates toxins
2. hormonal function: erythropoietin and D3
3. water-electrolyte and pH balance
4. gluconeogenesis



pathology: when it is not capable of performing its functions

chronic: >3 months

detect kidney damage by direct (biopsy) or indirect (radiography) method

nephrons die, those that remain hypertrophy

filtration rate → uremia (↑creatinine ↑urea) where almost no nephrons remain.

Prognosis of CKD using albuminuria

CKD stage	GFR level (mL/min/1.73 m^2)	
Stage 1	≥ 90	normal function with
Stage 2	60–89	damage mild
Stage 3	30–59	moderate
Stage 4	15–29	severe
Stage 5	< 15	kidney failure → dialysis

100–130 average
125 mL/min/1.73m2

Causes
Local lesions
Diffuse lesions: direct or immunological aggression

Drugs: decrease the dose as CKD worsens and increase the interval between doses.

Beware of intoxications: antibiotics, anti-inflammatory drugs, analgesics.

Phases:

1. complete compensation

no symptoms

2. partial compensation

↑load filtered by each nephron or ↓absorption and ↑secretion

polyuria and nocturia, onset of arterial hypertension and anaemia.

Partial tubular compensation
P→secondary hyperparathyroidism → ↑PTH → hypercalcaemia
H^+ acidity ammoniogenesis bone.
uric acid ↓filtration, reabsorption of uric acid

total tubular compensation
Sodium
ADH
PTH

3. uremia period

No Vit.D3, no erythropoietin

oliguria <600ml, oedema, arterial hypertension, anaemia, pruritus, osteodystrophy

Diabetes mellitus

Islets of Langerhans:
α-cells: glucagon.
β cells: insulin.
δ-cells: somatostatin.

absolute or relative insulin deficiency

Types

Primary:

type1 destruction of β-cells → absolute deficiency. autoimmunity (genetic) or idiopathic.

↑Glucagon NO insulin → Risk of ketoacidosis

type 2 insulin resistance. genetic, obesity, sedentary lifestyle.

Fatty acids inhibit GLUT4 translocation → from hyperinsulinemia to hypoinsulinemia

Causes
sedentary lifestyle
excessive carbohydrate intake
glucotoxicity
islet hyperactivity and subsequent exhaustion
activation of the RAAS axis (angiotensin)

Secondary

↑counterinsulin hormones e.g. corticosteroid use.

↑pancreatic insufficiency, e.g. alcoholic pancreatitis.

Diagnosis

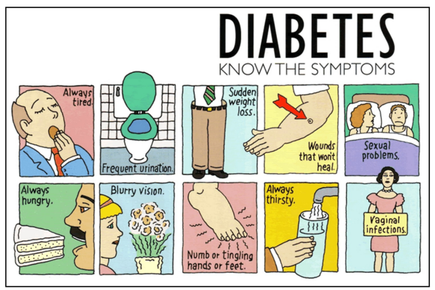
Fasting blood glucose **>126**mg/dL.
2h after any meal glucose **>200**mg/dl

glucose overload test when uncertain. 75g after 2h >180

In the clinic:

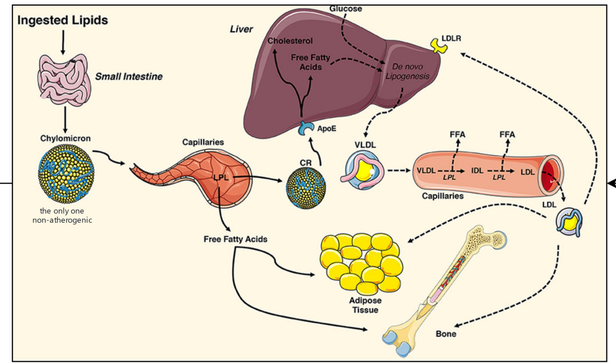
- hyperglycaemia
- weight loss → no nutrient utilisation
- **classic triad**: Polyphagia, Polyuria, Polydipsia
- ↑HbA1C → DM control marker
- diabetic microangiopathy → diabetic retinopathy, heart attacks, strokes, polyneuropathy.

Treatment:
- non-pharmacological: lifestyle changes
- pharmacological: insulin and incretins → GLP-1 agonists



Dyslipidemia

alteration of blood lipids, atherosclerotic plaque related → Cholesterol: essential TG: fasting energy source → They are transported by lipoproteins → Apoprotein: Maintaining structures so lipoproteins don't get screwed over

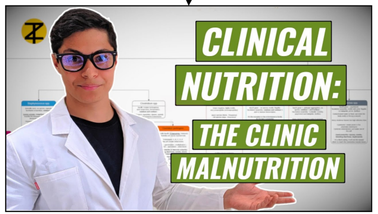


hypercholesterolemia, hypertriglyceridemia, or both → **Primary:** genetic (familial the most common) **Secondary:** diet, lifestyle or diseases
- **hormonal causes:** hypothyroidism, estrogens, anabolic steroids
- **metabolic causes:** diabetes, obesity, lipid dystrophy
- kidney diseases, liver diseases, lifestyle habits and medication

atherosclerotic cardiovascular disease

- how it is supposed to work: → ↑ nitric oxide → vasodilatation → inflammation (platelets) → foam cells (macrophages) eat the oxidised cholesterol → fatty streaks → microcalcifications + fibrin coating = atheromatous plaque
- diagnosis: → HDL <40mg/dl♂ <50mg/dl♀ Cholesterol >190mg/dl LDL cholesterol >115mg/dl Triglycerides >150mg/dl
- diet influence: → **saturated** ~↑risk, **monounsaturated** ↓risk, **polyunsaturated** ↓ risk, **trans** ↑↑ risk, **cholesterol** ~↑ risk → **protein** ↓ risk if vegetable, **carbohydrates** ↑ risk if sugars or ↑G.I. → **fibre** ↓risk ↑**calories** ↑risk, **alcohol** ↑ risk.
- lipid-lowering drugs: → **statins**, PCSK9 inhibitors, fibrates, cholesterol absorption inhibitors, nicotinic acid and its derivatives.

Malnutrition



- Marasm, Kwashiorkor, Caquexia → Marasm: Weight loss, normal albumin and preserved immunity. → Kwashiorkor: Low weight loss, low albumin and impaired immunity.
- Sarcopenia and vitamin deficiency → ↓hormones ↓proteins ↓exercise → pellagra and scurvy mainly
- Obesity → high blood pressure, increased cholesterol, diabetes

Inflammatory bowel disease

due to high processed food, modern countries

Causes
Genetic
Immunologic alterations of the intestinal mucosa
Environmental alterations: Microbiota alterations (*clostridium difficile*), diet alterations, vit.D, Tobacco protection, drugs NSAIDs

Crohn's

depends on what is affected:

↑inflammation, diarrhoea, mucus, blood, ↓weight, fever, anorexia, ↓eating, restriction → malnutrition

inflammatory diarrhoea, pain and general symptoms
stenotic (closing of the gastrointestinal tract) → bloating, colicky pain
fistulae: ileocecal > colonic > oesophageal and gastric (rare)

blind tract → abscess

ulcerative colitis

depending on extent and location

95% of the cases affect the rectum

blood and mucus in stool, fever, vomiting, urge to defecate all the time.

Diagnosis
Clinic
Laboratory
Radiology
Endoscopy
Biopsy

Diet: Healthy, with fibre and fruit could prevent...

Ultra-processed foods have a lot to do with the appearance

↑variable calorie and protein requirements

no specific diet, no restrictive if not necessary

↑risk of lactose intolerance, no insoluble fibres, intolerances reversible over time

Whenever possible: Oral > nutritional supplements > EN > NP

Diabetes management

Diagnosis
126mg/dl fasting plasma glucose
2h plasma glucose >200mg/dl
HbA1C >6,5
diabetes symptoms + random plasma glucose

all parameters are equally important

also control other parameters: fat, weight, blood pressure, lifestyle (tobacco, alcohol...)

lifestyle changes: correct diet & nutrition, aerobic exercise, no tobacco

control metabolic factors and **comorbidities**

nutrition, exercise, tobacco, self-control, psychological sphere and also social-economic factors

primary prevention: ↓weight ↑exercise ↑fibre

EVERY MOVE COUNTS!

fight sedentary lifestyle that's progressing nowadays

it lowers medication doses

type 2 more frequent than type 1

insulin deficiency

Treatment:

difference in control between 2008 and 2015: **individualisation**

Lifestyle changes:

Mediterranean diet → helpful for diabetes

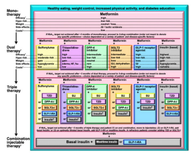
fruit & veggies, olive oil, grains, legumes, fish and nuts

40-55% Carbs
10-20% Proteins
30% Fats

prioritise ↓glycemic index foods

but the GI alone is not enough (mixing with other foods)

alcohol and sodium same as normal, then **individualise**



pharmaceutical changes:

2023 treatment: medication with cardiovascular and renal benefit

Metformin (side effect: lactic acidosis)

basal bolus therapy

2015 guidelines: mono, dual, triple and injectable therapy

2019 guidelines: importance to morbidity of comorbidities

2022 guidelines: importance to effectiveness and price

2023 guidelines: importance to great diagnosis, lifestyle and drugs

Conclusions: INTEGRATED AND INDIVIDUALISED TREATMENT

Metabolopathies

Primary alterations of metabolism leading to disease

dietary and nutritional treatment is possible

Inborn errors of metabolism

Accumulation of toxic substances

Accumulation of non-toxic substances

accumulation puts pressure on other anatomical structures

Energy deficit due to primary blockage of some pathway related to ATP synthesis

glycogenosis types 1,2 and 5 (Mackardel's syndrome), defects of fatty acid oxidation

End product deficit

primary blockage of an anabolic pathway e.g. albinism

Absence of detoxification

primary blockage of a catabolic pathway e.g. urea cycle defects

hemochromatosis (iron accumulation)

Impaired iron metabolism

hyperabsorption at intestinal level

Iron accumulates in the liver → liver cirrhosis

Diagnosis: ↑Fe, ↑transaminases

Treatment: frequent blood donation.

Hyperuricaemia → gout: due to increased uric acid or decreased excretion.

In cancer patients, due to cell death

should be excreted in the urine but may form stones.

Treatment:
anti-inflammatory drugs
Allopurinol (tricks xanthine oxidase → prevents uric acid production)
diet low in purines and pyrimidines (vegetarian)

Lysosomal diseases: inherited lysosomal storage diseases.

types
Gaucher → recessive
Fabry → female to male by gender
Hurler → variable penetrance (fast or slow progression)

There is no dietary change that can help

administration of enzymes from a bioreactor (e.g. lactase)

Porphyrins: alteration of heme metabolism. Dracula was porphyric (sunburn).

Wilson's disease disturbance of Cu metabolism, accumulation

Connective: Ehlers-Danlos → hyperelasticity
Osteogenesis imperfecta: children with glass bones
Dwarfism

Amino acids: Phenylketonuria, Albinism, Hyperoxaluria, Homocystinuria, Cystinosis

Membrane transport: Fanconi Syndrome

Glycogen: Pompe disease

Disorders of water and electrolyte metabolism

Volemia: It is the amount of volume in the blood.

Osmolality: It is the concentration of the blood

Body compartments:

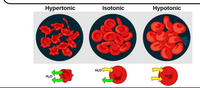
extracellular fluid (1/3): interstitial ⅔, plasmatic ⅓, transcellular

intracellular fluid (2/3): space inside the cells

water, sodium, chloride and bicarbonate

potassium and magnesium

normal osmolality pressure: 280 and 295 mOsmol/kg. **Goal:** to maintain those levels using water osmotic properties



starling's law → law of equilibrium of pressures ↓ oncotic pressure and ↑ hydrostatic pressure will give oedemas.

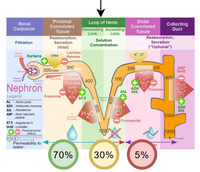
Water balance:
inputs: drink, food, endogenous.
losses: urine, faeces and insensible losses

Thirst: desire to drink when reaching ↑osmolality or hypovolaemia.

Renal regulation: ADH acts as a compensatory mechanism on ↑osmolality

↑Na ingested = ↑Na excreted ↑water reabsorbed

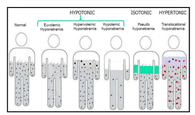
↑Na → Hypervolemia
↓Na → Hypovolemia
water follows Na



Physiopathology

Hyponatremia: plasma sodium concentration <135 mEq/L

types **hypotonic** (euvolemic, hypovolemic or hypervolemic), **isotonic** (pseudo- with glucose) and **hypertonic**.



Steps to follow
1. Na+ below 135 mEq/L
2. Measure osmolality (isotonic, hypotonic, hypertonic).
3. Observe plasma volume (hypovolaemic, euvolemic, hypervolaemic)
4. Measure urine sodium.

Hyponatremia
Serum sodium <135

Con 280295
Isotonic Hyponatremia
Pseudohyponatremia

Con <280
Hypotonic Hyponatremia

Con >295
Hypertonic Hyponatremia
Hyperglycemia
Hypertonic fluid administration

Hypovolemia
UNa >20: Renal failure
UNa <20: Heart failure, cirrhosis, nephrotic syndrome

Euvolemia
SIADH
Endocrinopathies
Diuretic Use

Hypervolemia
UNa >20: Renal solute loss
UNa<20: Extrarenal solute loss

main cause: SIADH

treatment: administration of hypertonic saline solution.

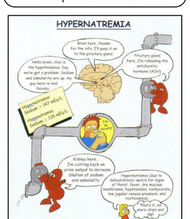
Hypernatremia: plasma sodium concentration >145 mEq/L.

~~**H2O and electrolyte deficits**~~, always with much higher water losses than sodium losses.

can appear as a consequence of **hyponatremia treatment** with hypertonic saline solutions

dehydrated: renal and extrarenal losses
normohydrated: diabetes insipidus
edematodes: iatrogenesis or ingestion of too much sea water when swimming

urine osmolality is **less than 300 mOsm/kg** = diabetes insipidus. Urine osmolality is **greater than 600 mOsm/kg** → adequate response with ADH



treatment: replenish the water deficit

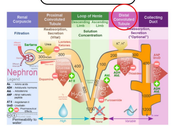
Disorders of K, Ca and P metabolism

Potassium K

4000mEq
98%intracellular
2%extracellular

Intake: diet, mineralocoricoids, acid-base balance

Excretion: renal 90% or intestinal 10%



↑excretion: diuretics, osmotic diuresis, mineralocorticoids and alkalosis

Na^+/K^- pump (KK in /NaNaNa out)

clinical factors: affected by catecholamines, insulin and alkalosis → ↑K intra

Hypokalaemia <3,5mEq/L

causes: catecholamines, insulin and metabolic alkalosis | ↓intake, ↑losses (diuretics) and RAA system

consequences: muscular (weakness, paralytic ileus and arrhythmias), renal (metabolic alkalosis and diabetes insipidus due to insensitivity to ADH)

Hyperkalaemia >5mEq/L

causes: no catecholamines, no insulin and metabolic acidosis | ↑intake, ↓losses (drugs) and tissue destruction

consequences: muscular (weakness, paralytic ileus and arrhythmias), renal (metabolic acidosis ↑HCO3- elmination)

Calcium Ca

99% in bone (support), **1% circulating** (coagulation, nerve conduction, muscle contraction)

PTH: hypercalcaemic ↑Ca ↓P (in urine ↓Ca ↑P)
Calcitonin: hypocalcaemic ↓Ca ↓P
Vit.D: hypercalemic and hyperphosphoremic ↑Ca ↑P

Hypoparathyroidism

Absence of the parathyroid glands or physical and autoimmune glandular damage

hypocalcaemia and hypocaliuria with hyperphosphatemia

Hypocalcaemia: calcium <8.5mg/dl

decreased blood calcium (hungry bones, tumours, pancreatitis) or **increased calcium to the tissues** (↓VitD)

paraesthesia, tetany, convulsions and arrhythmias

Hyperparathyroidism

primary: parathyroid adenoma
secondary: due to hypocalcaemia
tertiary: renal transplantation
ectopic: extraparathyroid tumours

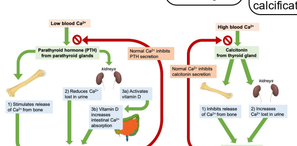
hypercalcaemia, osteoporosis, myopathies and anaemias

Hypercalcaemia: calcium >10.5mg/dl

increased blood calcium (PTH, vitD, tumours) or **decreased calcium to the tissues** (Paget)

acute: arrhythmias, acute renal insufficiency, neurological

chronic: digestive and renal disturbances and calcifications



Phosphorus P

↑intracellular.
↓extracellular (bone).
Always opposite to calcium.

Hypophosphataemia: P <2.5mg/dl.

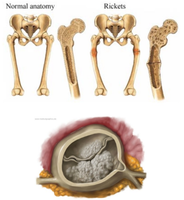
↓inputs (↓Vit.D) ↑losses (PTH)

Rickets, osteomalacia and muscle weakness.

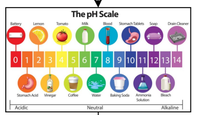
Hyperphosphataemia: P >4.5mg/dl.

↑inputs (tissue destruction, PN) ↓elimination (CKD, ↓PTH)

Hypocalcaemia, calcifications



Acid-base balance



Acids

Volatile Acids

CO2. Accounts for 98% of the total acid load

Lung elimination

↑ventilation ↓CO2 → **respiratory alkalosis**
↓ventilation ↑CO2 → **respiratory acidosis**

Fixed Acids

Represent 1-2% of the acid load. Oxidative catabolism of macros.

Renal elimination

Acidosis → [H+] (excreted), HCO_3^- (reabsorbed)
Alkalosis → [H+] (reabsorbed), HCO_3^- (excreted)

physiological buffers

regeneration needed, limited and short-lived action

Intracellular: proteins, inorganic phosphate and calcium carbonate from bone.

Extracellular: carbonic acid/bicarbonate

reference values

pH: 7.35 - 7.45.
pCO_2: 35-45 mmHg.
HCO_3^-: 24-28 mmol/L.

Acidosis

Metabolic
↓HCO_3^-
pH < 7.35
< 24mEq/L
Respiratory compensation with ↑ventilation (↑**pCO_2**)

Respiratory
↑pCO_2
pH < 7.35
> 45mEq/L
Metabolic compensation with ↑**HCO_3^-**

Alkalosis

Metabolic
↑HCO_3^-
pH > 7.45
> 28mEq/L
Respiratory compensation with ↓ventilation (↓**pCO_2**)

Respiratory
↓pCO_2
pH > 7.45
< 35mEq/L
Metabolic compensation with ↓**HCO_3^-**

Osteopathies

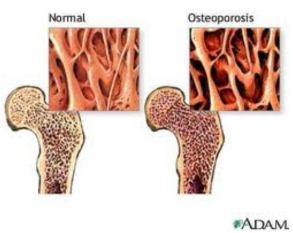
osteoporosis

systemic skeletal disorder characterised by **low bone mass**

Primary (senile or post-menopausal) or **secondary** (sporadic factors)

↓Ca, ↓Vit.D, alcohol, smoking, sedentary lifestyle, caffeine, ↓estrogens

vertebral fractures and deformities

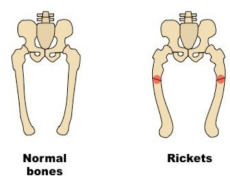


rickets and osteomalacia

softening of the bones caused by impaired bone metabolism ↓mass ↓**volume**

inadequate levels of available P, Ca, and Vit.D, or because of resorption of calcium

bone pain, muscle fatigue, crushing of the spine and bone fractures




Example of Rickets

Paget's disease

accelerated, but defective, **bone tissue turnover**

Phases
lytic: bone resorption ↑osteoclasts ↑vascularisation
mixed: bone remodelling ↑osteoclasts ↑osteoblasts
osteoclerotic: ↓replacement, ↓osteoclasts ↓osteoblasts ↓vascularisation

no symptoms, if any it is bone pain (specific or generalised)

rapid remodelling creates **new bones softer and weaker** than normal bones

Osteomyelitisis

infection that usually causes pain in the long bones in the legs

related with S.aureus in the majority of cases

pain and lump in the bone, redness of the area, fever, possible pus

Bone tumours

benign: osteochondroma, chondroma and osteoma.

cells from **normal** tissue, grow **slowly** and do **not invade** neighbouring structures

malignant: osteosarcoma, ewing's sarcoma, chondrosarcoma.

cells **different** from normal tissue, grow **rapidly**, **invade** structures and can **metastasise**.

Pathophysiology of the Hypothalamus and pituitary gland

nerve and hormonal communication signals

endocrine glands → secrete substances into the bloodstream

exocrine glands → secrete substances "out of the body"

Hypothalamus: source of several neurohormones that act on the pituitary gland.

Pituitary: small gland beneath the hypothalamus that divides into 2 parts:

Adenohypophysis (anterior): secretes various hormones when stimulated by releasing factors or RH from the hypothalamus.

Neurohypophysis (posterior): linked to the hypothalamus and releases hormones from the hypothalamus into the blood.

General Hormones	Gland Specific Hormones	General Hormones
Prolactin (PRL): milk production and mammary growth. has no RH, is stimulated by sucking at the breast and inhibited by dopamine.	**Thyrotrophin (TSH):** creation of thyroid hormones T3 and T4. Releasing factor: **TRH**	**Antidiuretic (ADH):** water reabsorption, stimulated by ↑**osmolarity**. vasoconstriction, stimulated by arterial **hypotension**
Growth hormone (GH): stimulates growth of all tissues and raises blood sugar. Releasing factor: **GHRH**	**Adrenocorticotropin (ACTH):** stimulates adrenal hormone production. Releasing factor: **CRH**	**Oxytocin:** contraction of the nipple to eject milk, stimulated by **sucking**. contraction of the uterus to facilitate **childbirth** by limiting postpartum hemorrhage.
	Follicle stimulating (FSH): ♂spermatozoa, ♀oocytes. Releasing factor: **GnRH**	
	Luteinising (LH): ♂testosterone, ♀ovulation and progesterone. Releasing factor: **GnRH**	

Negative feedback between the glands creates the **hypothalamic-pituitary axis** connected by the pituitary **portal** system.

Diseases of the hypothalamic-pituitary system

hypofunction or hyperfunction

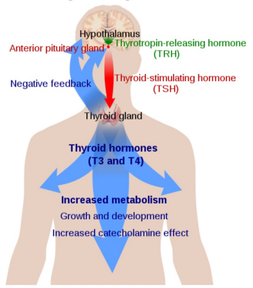
Most common
GH deficiency (pituitary dwarfism)
Global pituitary **insufficiency** (panhypopituitarism)
Prolactin-producing pituitary tumors: galactorrhea, menstrual disorders, low libido
GH-producing pituitary tumors: gigantism and acromegaly

Pathophysiology of the Thyroid

Hypothalamus-pituitary-thyroid axis

Hypothalamus: TRH
Adenohypophysis: TSH
Thyroid: T3 and T4 (using Iodine)

Thyroid system



thyroid hormones

90% of the hormone produced by the thyroid is T4.

Transform to T3: T3 is the active hormone.

Transform to reverse T3: Reverse T3 is an inactive T3 hormone to save energy.

Effects of thyroid hormones:
↑energy ↑oxygen consumption.
↑thermogenesis ↑metabolism ↑fat consumption
↑protein synthesis
↑cardiac output ↑pulmonary ventilation
↑cognitive capacity and speed of reflexes
↑sweating tremor
secretion of gastric juices and digestive enzymes

physiopathological manifestations

Goitre

enlargement of the thyroid due to:

Goitre Factors
Thyroiditis: inflammation. It is rare
Neoplasms: adenomas (benign) or carcinomas (malignant)
Response to hyperstimulation: TSH (↓iodine ↑TSH) or by thyroid-stimulating immunoglobulins (TSI antibodies) in Graves-Basedow disease

hyperthyroidism

thyroid overfunctioning

with symptoms it is called thyrotoxicosis

Causes
Graves-Basedow disease: TSI antibodies, diffuse stimulation, affecting the entire gland
Toxic thyroid adenoma: autonomous hormone production, ↓TSH → thyroid stops working (has been substituted).
Toxic multinodular goitre: thyroid with many adenomas

Diagnosis: blood tests, ultrasound and gamma scan.

Symptoms: palpitations, tachycardia, weight loss, mydriasis and exophthalmos (saucer eyes).

hypothyroidism

decreased thyroid hormone synthesis

Causes
Autoimmune such as Hashimoto's Thyroiditis, thyroid destroying antibodies
Removal of the thyroid

Symptoms:
Low concentration and tiredness
edema and thickened tongue (hoarseness)
weight gain
bradycardia

Adrenal glands physiopathology

CRH → ACTH → adrenal hormones

cortex → cortisol, aldosterone, androgen

medulla → catecholamines

Functions
protection against stressful situations
gluconeogenesis
↑Na^+ ↓K^+ ↑water retention
catecholamines: glucose and fat movilisation for energy

↑Na = ↓K
↑Na ↑water ↑hypertension
↑ACTH ↓cortisol → Addison
↑cortisol → cushing

Cortisol
Carbs: gluconeogenesis and insulin sensitivity. hiperglycemia
Proteins: protein catabolism
Lipids: lipolysis, ↓lypogenesis
circulation: hypertension
ions: Na retention, ↓K^+
CNS: euphoria
immunity: lowered (antiinflammatory drugs)

Aldosterone

Functions → ↑Na^+ reabsorption ↑water ↑volemia hypokalemia

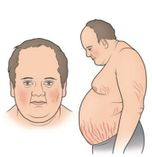
conn's syndrome (hyperaldosteronism) → 2% of hypertensives. young hypertensive? possible hyperaldosteronism

Pheochromocytoma → ↑catecholamines → hypertension and hyperactivity due to adrenal gland tumor.

Excess of Cortisol

↑corticoids → **cushing' syndrome** endogenous (ACTH dependent or independent) or exogenous (drugs)

Check ACTH levels... ↑levels: may be ectopic: not in place. ↓levels: adrenal problems (tumour)



measure cortisol in urine AM and PM, radiography, etc..
→ treat with drugs or surgery when there's a tumour

Deficit of Cortisol

Types
primary adrenal insufficiency Addison's (adrenal) ↑CRH ↑ACTH ↓cortisol
secondary pituitary ↓CRH ↓ACTH ↓cortisol
tertiary hypothalamic CRH

nausea, vomits, hypoglycemia, hypovolemic, hyponatremia, hyperkalemia, darkening of the skin, ↓energy, weight loss

Abrupt withdrawal of corticosteroids

do not stop taking them abruptly

the pituitary and ACTH are inhibited...

if so, the treatment is with a lot more corticosteroids

gradually decrease to let the pituitary adapt

Comas

Awareness: ability to know oneself and the environment.

content: perceptions-sensations, desires, memory, reasoning

state: waking-sleep

ascending activating reticular system RAAS → activates cerebral cortex via external impulses

activation of the a-motor neurons from the cortex to activate the muscles

Coma: unable to react to external stimuli, contrary to sleep

wakefulness → lethargy → obtundation → stupor → coma

numerical correspondence on the Glasgow scale

Glasgow parameters
eye opening
verbal response
motor response

from 15 to 3, lower = worse

dementia: difficulty to remember, learn, judge, think abstractively

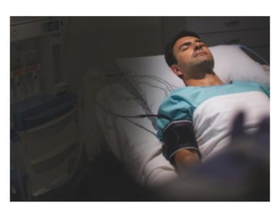
delirium: fluctuation, disorientation, not attention, agitation

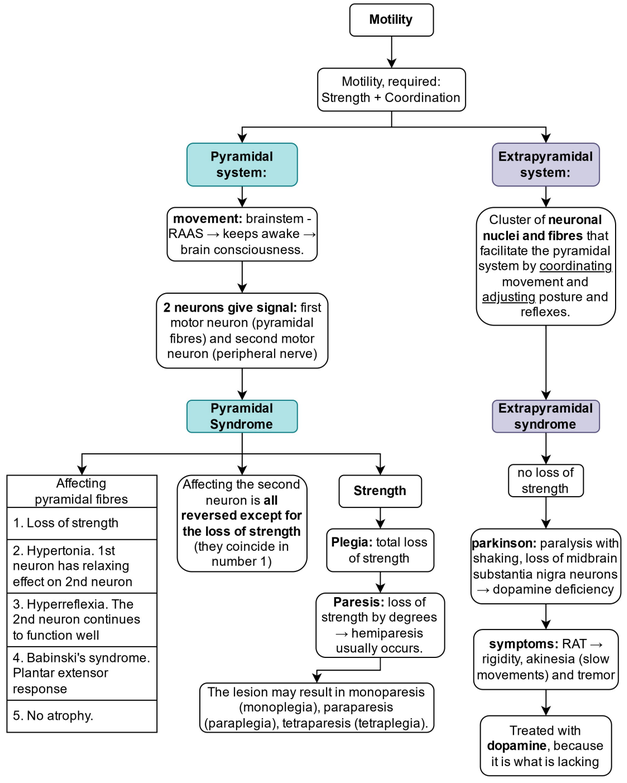
neurological coma: structural lesions

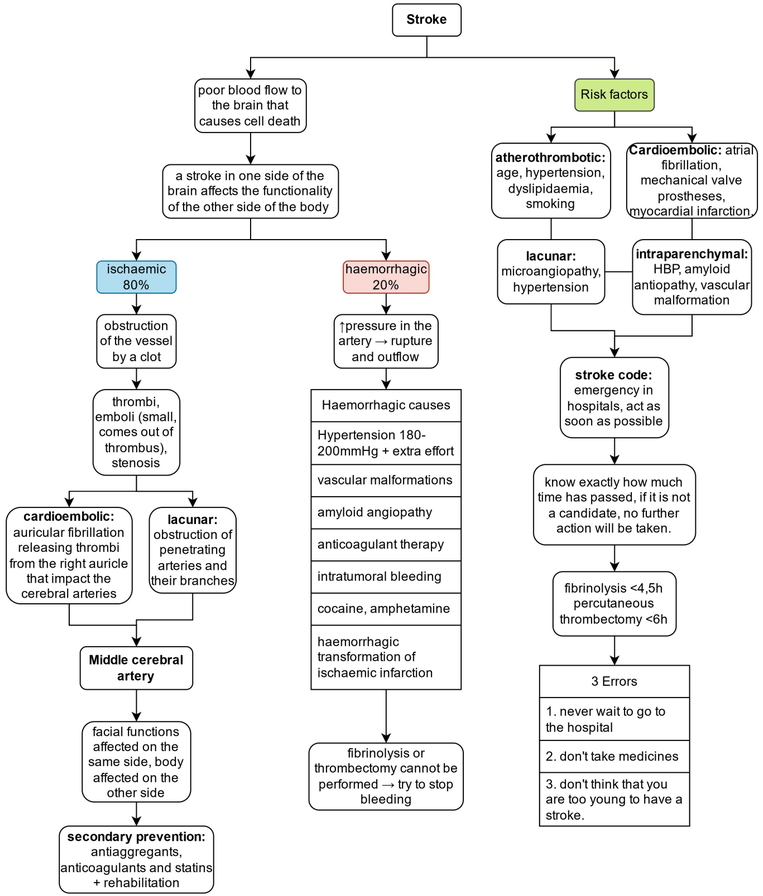
Causes
extensive cortical lesions: repeated heart attacks, meningo-encephalopathy, leukoencephalopathy
supratentorial expansive processes: haemorrhages, abscesses, cysts, tumors, toxoplasmosis, encephalitis, cerebral edema and hypertension
infratentorial injuries: brain herniation and various strokes

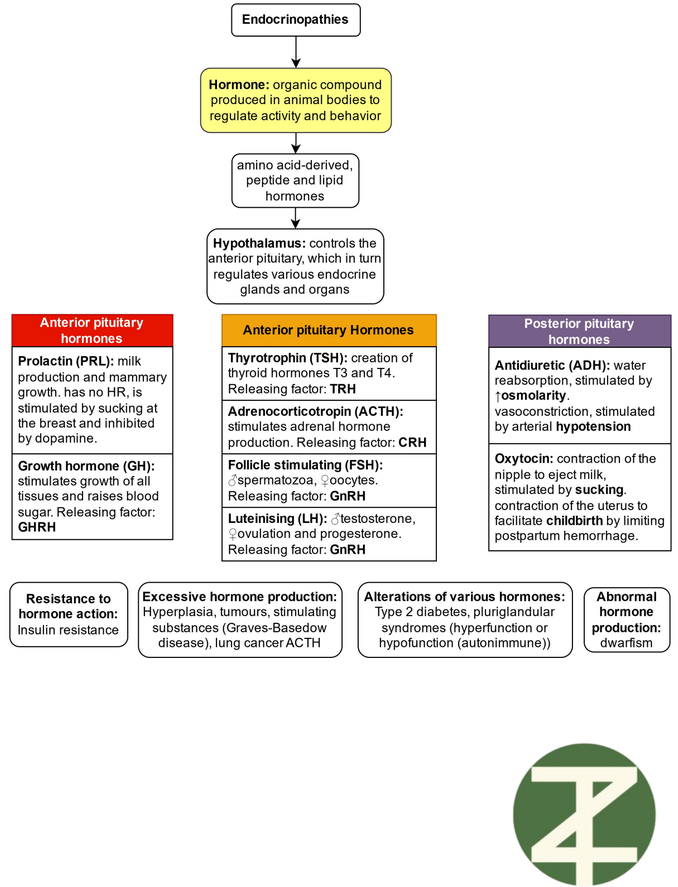
metabolic coma: functional alteration

Causes
energy production alterations: hypoxia, hypoglycemia, ↓B1 (Wernicke), hypothermia-hypothyroidism
hydroelectrolitic alterations: hypo or hypernatremia, hypercalcemia, hypophosphatemia, metabolic acidosis
depressant substances: alcohol, opiates, neuroleptics, benzodiazepines, barbiturates, salicylates, anticholinergics
endogenous intoxications: uremic, hypercapnic, hepatic, septic encephalopathy




Motility
Motility, required: Strength + Coordination
Pyramidal system:
movement: brainstem - RAAS → keeps awake → brain consciousness.
2 neurons give signal: first motor neuron (pyramidal fibres) and second motor neuron (peripheral nerve)
Pyramidal Syndrome
Affecting pyramidal fibres
1. Loss of strength
2. Hypertonia. 1st neuron has relaxing effect on 2nd neuron
3. Hyperreflexia. The 2nd neuron continues to function well
4. Babinski's syndrome. Plantar extensor response
5. No atrophy.
Affecting the second neuron is all reversed except for the loss of strength (they coincide in number 1)
Strength
Plegia: total loss of strength
Paresis: loss of strength by degrees → hemiparesis usually occurs.
The lesion may result in monoparesis (monoplegia), paraparesis (paraplegia), tetraparesis (tetraplegia).
Extrapyramidal system:
Cluster of neuronal nuclei and fibres that facilitate the pyramidal system by coordinating movement and adjusting posture and reflexes.
Extrapyramidal syndrome
no loss of strength
parkinson: paralysis with shaking, loss of midbrain substantia nigra neurons → dopamine deficiency
symptoms: RAT → rigidity, akinesia (slow movements) and tremor
Treated with dopamine, because it is what is lacking


Stroke
poor blood flow to the brain that causes cell death
a stroke in one side of the brain affects the functionality of the other side of the body
ischaemic 80%
obstruction of the vessel by a clot
thrombi, emboli (small, comes out of thrombus), stenosis
cardioembolic: auricular fibrillation releasing thrombi from the right auricle that impact the cerebral arteries
lacunar: obstruction of penetrating arteries and their branches
Middle cerebral artery
facial functions affected on the same side, body affected on the other side
secondary prevention: antiaggregants, anticoagulants and statins + rehabilitation
haemorrhagic 20%
↑pressure in the artery → rupture and outflow
Haemorrhagic causes
Hypertension 180-200mmHg + extra effort
vascular malformations
amyloid angiopathy
anticoagulant therapy
intratumoral bleeding
cocaine, amphetamine
haemorrhagic transformation of ischaemic infarction
fibrinolysis or thrombectomy cannot be performed → try to stop bleeding
Risk factors
atherothrombotic: age, hypertension, dyslipidaemia, smoking
Cardioembolic: atrial fibrillation, mechanical valve prostheses, myocardial infarction
lacunar: microangiopathy, hypertension
intraparenchymal: HBP, amyloid antiopathy, vascular malformation
stroke code: emergency in hospitals, act as soon as possible
know exactly how much time has passed, if it is not a candidate, no further action will be taken.
fibrinolysis <4,5h percutaneous thrombectomy <6h
3 Errors
1. never wait to go to the hospital
2. don't take medicines
3. don't think that you are too young to have a stroke.


Endocrinopathies
Hormone: organic compound produced in animal bodies to regulate activity and behavior
amino acid-derived, peptide and lipid hormones
Hypothalamus: controls the anterior pituitary, which in turn regulates various endocrine glands and organs
Anterior pituitary hormones
Prolactin (PRL): milk production and mammary growth. has no HR, is stimulated by sucking at the breast and inhibited by dopamine.
Growth hormone (GH): stimulates growth of all tissues and raises blood sugar. Releasing factor: GHRH
Anterior pituitary Hormones
Thyrotrophin (TSH): creation of thyroid hormones T3 and T4. Releasing factor: TRH
Adrenocorticotropin (ACTH): stimulates adrenal hormone production. Releasing factor: CRH
Follicle stimulating (FSH): ♂spermatozoa, ♀oocytes. Releasing factor: GnRH
Luteinising (LH): ♂testosterone, ♀ovulation and progesterone. Releasing factor: GnRH
Posterior pituitary hormones
Antidiuretic (ADH): water reabsorption, stimulated by ↑osmolarity. vasoconstriction, stimulated by arterial hypotension
Oxytocin: contraction of the nipple to eject milk, stimulated by sucking. contraction of the uterus to facilitate childbirth by limiting postpartum hemorrhage.
Resistance to hormone action: Insulin resistance
Excessive hormone production: Hyperplasia, tumours, stimulating substances (Graves-Basedow disease), lung cancer ACTH
Alterations of various hormones: Type 2 diabetes, pluriglandular syndromes (hyperfunction or hypofunction (autonimmune))
Abnormal hormone production: dwarfism