Introduction

Nutritionist → patients take different medicines

Objective: to know the drugs, to adjust the diet accordingly → object vs. non-object pathology

Getting sick is natural → natural, magical and religious remedies → healing: material, energetic or mixed

Therapeutic pharmacology

- Therapeutics: precepts and remedies
- Pharmacology: active substances (drugs)
  - Types
    - **Allopathic:** based on the opposite (counteract)
    - **Homeopathic:** based on a similar substance
    - **Substitutive:** based on correcting deficits

Drugs Vocabulary
Medication for human use: a substance which restores health by correcting physiological functions.
Active substance: substance with pharmacological, immunological or metabolic function.
Excipient: anything other than the active substance or the packaging material and is organoleptic.
Pharmaceutical form: method of administration of the drug. (solid, liquid, semi-liquid, semi-solid and gaseous

Drug types
Generic medication: a drug that has the same active substance and pharmaceutical form.
Compounding: specific medicinal product created on demand (medical prescription).
Officinal preparation: specific medicine created by a pharmacy (without prescription)
Investigational medicinal product: not marketed in the final stages or marketed with a known technical data sheet (cures something else new).

Drug sources
natural
semi-synthetics
synthetic
genetic engineering
cell procedure

Drugs Properties
Physicochemical properties: solubility and chemical structure (action)
Mechanism of action: how it acts in the body
Pharmacological effect: observable response to the medicine
Adverse effect: unexpected response
Therapeutic indication: conditions in which the drug is good
Contraindications: reasons why the medicine is not recommended to be taken
Interactions: changes in the therapeutic effect due to other substances.
Bioavailability: the amount of the active substance that reaches the blood intact.

Drug kind
those who need a prescription
advertising drugs
those for hospital use
those who need an inspection visa
foreigners (imported)

Therapeutic process
patient-treatment characteristics
therapeutic adherence
Medication error (avoidable)
Adverse reaction (not avoidable)

Way of transmission → affects efficacy of treatment

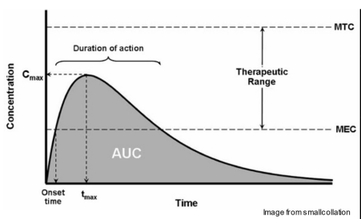
- Oral or enteral way
  - mouth, local or systemic effect, ≠ sublingual, absorption depends on pka and pH
    - Influence: pharmaceutical form, pH, peristalsis, drugs and food
- Parenteral way
  - sterile, apyrogenic and isotonic
    - **types**
      - **Intravenous: bolus** (max 20mL → minutes), **intermittent** (50-500mL → 30 minutes), **continuous** (500-1000mL → 24 hours)
      - **Intramuscular:** up to 5mL
      - **Subcutaneous:** up to 2mL
- Other ways
  - topical → "topos" = place
  - pericutaneous → systemic
  - inhalatory → inhalers
  - rectal → suppository
  - ocular → eye drops or ointments
  - nasal → drops or spray
  - otic → solutions

Nutritionist role: to know what drugs the patient takes and when:
fasted (1h before or 2h after)
with meal (during or right after)
separated (at least 2h)

Pharmacokinetics

studies the evolution of the drug in the body

LADME: liberation, absorption, distribution, metabolism and excretion



Plasma level curves
Cmax: Maximum concentration
Tmax: time to reach Cmax
MEC: Minimum effective concentration
LP: latent period
AUC: area under the curve (bioavailability)
Therapeutic range
MTC: Minimum toxic concentration
Duration of action
Intensity of action

Liberation: to disintegrate, dissolve and diffuse

Absorption. variability factors (physicochemical, drug formulation, physiological variables)

simple diffusion (liposolubility of the drug, pH, drug characteristics, ion trapping). **Filtration. Active transportation** (pinocytosis)

mouth→little absorption. **esophagus**→ no absorption. **stomach**→liberation and absorption. **intestine**→absorption of the rest

↑blood flow = ↑absorption
↑peristalsis = ↓absorption

Distribution. ↑speed of distribution = ↓drug effect

Distribution volume = administrated drug / plasma drug

fat-soluble drugs can get inside cells

forms of the drug:
free drug (1% active).
bond to proteins (albumin, b-globulin, a-glucoprotein) ***reversible*** (reservoir)

fat-soluble drugs can enter adipose tissue

Elimination. Metabolisation and/or Excretion

Metabolisation. chemical conversion into metabolites

Hydrosolubles easier to eliminate → liver, kidney, plasma, intestinal epithelium

inductor = ↑P-450 = ↓drug availability (ineffective)
inhibitor = ↓P-450 = ↑drug availability (toxicity)

Biotransformation reactions: **Phase I** (oxidation, reduction or hydrolysis) ↑polarity=↑elimination
Phase II (binding to endogenous polar substance) to ensure polarity ↑drug size

Factors: physiological, genetics (metabolisation speed), pathological and iatrogenic

Excretion. Renal or intestinal mainly...

3 phases

1. glomerular filtration → urine (filtration by size) free drug only

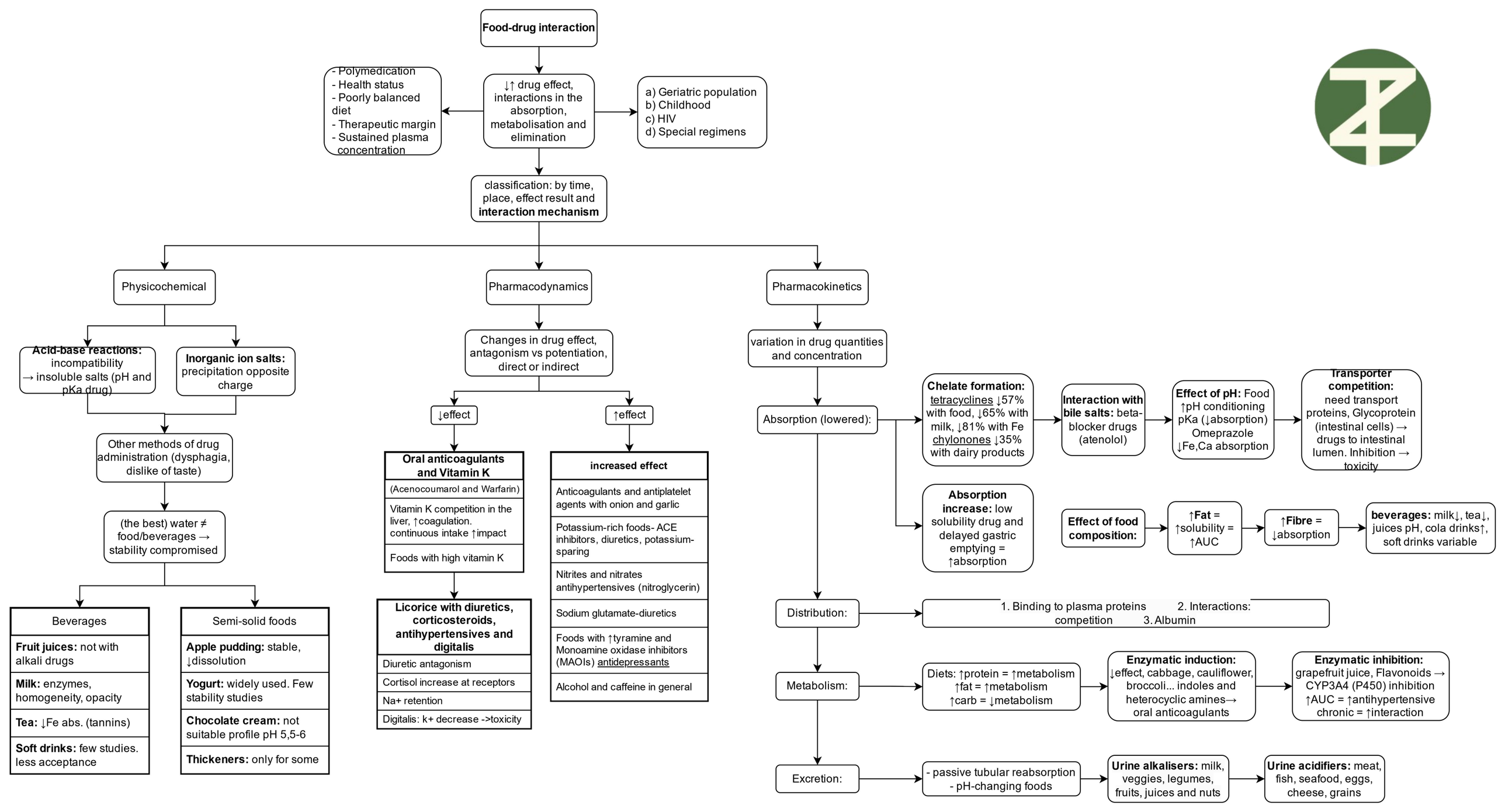
2. Active tubular secretion → proximal tubule (facilitated diffusion) ionised form

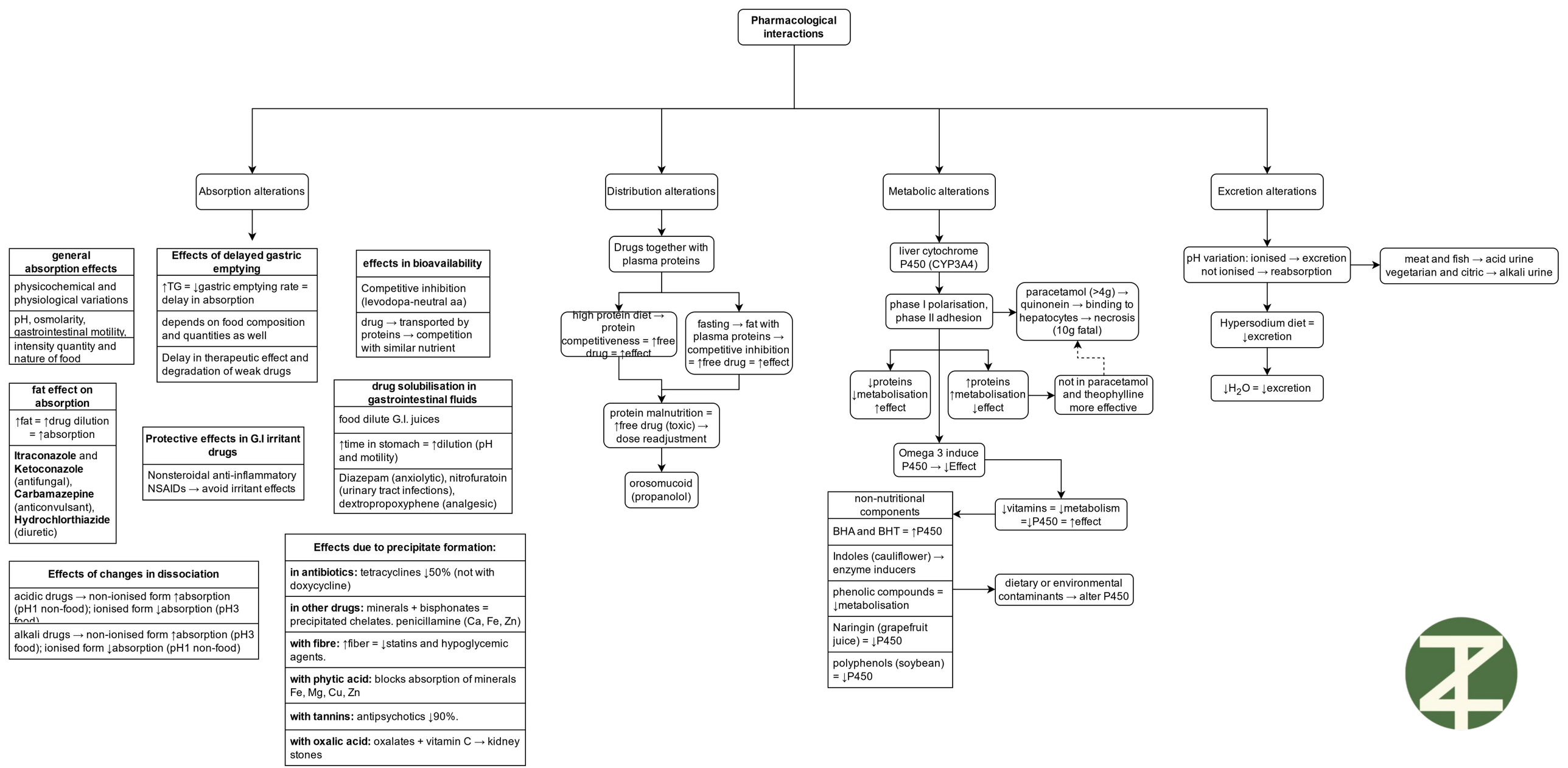
3. Passive tubular reabsorption → proximal and distal tubule, the non-ionised form

Excretion = filtration + active secretion - passive reabsorption

Nutrients

digestion and absorption mechanisms


Food-drug interaction
- Polymedication
- Health status
- Poorly balanced diet
- Therapeutic margin
- Sustained plasma concentration
↓↑ drug effect, interactions in the absorption, metabolisation and elimination
a) Geriatric population
b) Childhood
c) HIV
d) Special regimens
classification: by time, place, effect result and interaction mechanism
Physicochemical
Pharmacodynamics
Pharmacokinetics
Acid-base reactions: incompatibility → insoluble salts (pH and pKa drug)
Inorganic ion salts: precipitation opposite charge
Other methods of drug administration (dysphagia, dislike of taste)
(the best) water ≠ food/beverages → stability compromised
Beverages
Fruit juices: not with alkali drugs
Milk: enzymes, homogeneity, opacity
Tea: ↓Fe abs. (tannins)
Soft drinks: few studies. less acceptance
Semi-solid foods
Apple pudding: stable, ↓dissolution
Yogurt: widely used. Few stability studies
Chocolate cream: not suitable profile pH 5,5-6
Thickeners: only for some
Changes in drug effect, antagonism vs potentiation, direct or indirect
↓effect
↑effect
Oral anticoagulants and Vitamin K
(Acenocoumarol and Warfarin)
Vitamin K competition in the liver, ↑coagulation. continuous intake ↑impact
Foods with high vitamin K
Licorice with diuretics, corticosteroids, antihypertensives and digitalis
Diuretic antagonism
Cortisol increase at receptors
Na+ retention
Digitalis: k+ decrease ->toxicity
increased effect
Anticoagulants and antiplatelet agents with onion and garlic
Potassium-rich foods- ACE inhibitors, diuretics, potassium-sparing
Nitrites and nitrates antihypertensives (nitroglycerin)
Sodium glutamate-diuretics
Foods with ↑tyramine and Monoamine oxidase inhibitors (MAOIs) antidepressants
Alcohol and caffeine in general
variation in drug quantities and concentration
Absorption (lowered):
Chelate formation: tetracyclines ↓57% with food, ↓65% with milk, ↓81% with Fe chylonones ↓35% with dairy products
Interaction with bile salts: beta-blocker drugs (atenolol)
Effect of pH: Food ↑pH conditioning pKa (↓absorption) Omeprazole ↓Fe,Ca absorption
Transporter competition: need transport proteins, Glycoprotein (intestinal cells) → drugs to intestinal lumen. Inhibition → toxicity
Absorption increase: low solubility drug and delayed gastric emptying = ↑absorption
Effect of food composition:
↑Fat = ↑solubility = ↑AUC
↑Fibre = ↓absorption
beverages: milk↓, tea↓, juices pH, cola drinks↑, soft drinks variable
Distribution:
1. Binding to plasma proteins competition 2. Interactions: 3. Albumin
Metabolism:
Diets: ↑protein = ↑metabolism ↑fat = ↑metabolism ↑carb = ↓metabolism
Enzymatic induction: ↓effect, cabbage, cauliflower, broccoli... indoles and heterocyclic amines→ oral anticoagulants
Enzymatic inhibition: grapefruit juice, Flavonoids → CYP3A4 (P450) inhibition ↑AUC = ↑antihypertensive chronic = ↑interaction
Excretion:
- passive tubular reabsorption - pH-changing foods
Urine alkalisers: milk, veggies, legumes, fruits, juices and nuts
Urine acidifiers: meat, fish, seafood, eggs, cheese, grains


Pharmacological interactions
Absorption alterations
Distribution alterations
Metabolic alterations
Excretion alterations
general absorption effects
physicochemical and physiological variations
pH, osmolarity, gastrointestinal motility,
intensity quantity and nature of food
Effects of delayed gastric emptying
↑TG = ↓gastric emptying rate = delay in absorption
depends on food composition and quantities as well
Delay in therapeutic effect and degradation of weak drugs
effects in bioavailability
Competitive inhibition (levodopa-neutral aa)
drug → transported by proteins → competition with similar nutrient
fat effect on absorption
↑fat = ↑drug dilution = ↑absorption
Itraconazole and Ketoconazole (antifungal), Carbamazepine (anticonvulsant), Hydrochlorthiazide (diuretic)
Protective effects in G.I irritant drugs
Nonsteroidal anti-inflammatory NSAIDs → avoid irritant effects
drug solubilisation in gastrointestinal fluids
food dilute G.I. juices
↑time in stomach = ↑dilution (pH and motility)
Diazepam (anxiolytic), nitrofuratoin (urinary tract infections), dextropropoxyphene (analgesic)
Effects of changes in dissociation
acidic drugs → non-ionised form ↑absorption (pH1 non-food); ionised form ↓absorption (pH3 food)
alkali drugs → non-ionised form ↑absorption (pH3 food); ionised form ↓absorption (pH1 non-food)
Effects due to precipitate formation:
in antibiotics: tetracyclines ↓50% (not with doxycycline)
in other drugs: minerals + bisphonates = precipitated chelates. penicillamine (Ca, Fe, Zn)
with fibre: ↑fiber = ↓statins and hypoglycemic agents.
with phytic acid: blocks absorption of minerals Fe, Mg, Cu, Zn
with tannins: antipsychotics ↓90%.
with oxalic acid: oxalates + vitamin C → kidney stones
Drugs together with plasma proteins
high protein diet → protein competitiveness = ↑free drug = ↑effect
fasting → fat with plasma proteins → competitive inhibition = ↑free drug = ↑effect
protein malnutrition = ↑free drug (toxic) → dose readjustment
orosomucoid (propanolol)
liver cytochrome P450 (CYP3A4)
phase I polarisation, phase II adhesion
paracetamol (>4g) → quinonein → binding to hepatocytes → necrosis (10g fatal)
↓proteins ↓metabolisation ↑effect
↑proteins ↑metabolisation ↓effect
not in paracetamol and theophylline more effective
Omega 3 induce P450 → ↓Effect
↓vitamins = ↓metabolism =↓P450 = ↑effect
non-nutritional components
BHA and BHT = ↑P450
Indoles (cauliflower) → enzyme inducers
phenolic compounds = ↓metabolisation
Naringin (grapefruit juice) = ↓P450
polyphenols (soybean) = ↓P450
dietary or environmental contaminants → alter P450
pH variation: ionised → excretion not ionised → reabsorption
meat and fish → acid urine vegetarian and citric → alkali urine
Hypersodium diet = ↓excretion
↓H_2O = ↓excretion

Influence of drugs on food

- Drug induces loss of appetite
  - primary
    - central
      - decrease appetite
        - catecholaminergic (dextroamphetamine), dopaminergic (levodopa), serotoninergic (fenfluramine), endorphins (naloxone)
    - peripheral
      - feeling of satiety
        - delayed gastric emptying, effect of TG
  - secondary
    - cause nausea and vomiting, hypogeusia, stomatitis, hepatotoxics
- Poor digestion and malabsorption
  - primary
    - at intestinal mucosa level → chelates with fibre or destruction of microvilli
  - secondary
    - at the level of absorption, distribution and metabolisation
      - diphenylmethane derivatives=statorrhoea, colchinine=microvilli damage, laxative abuse=malabsorption
- Alteration in the utilisation of substrates
- Increased elimination
- **most frequent interactions in clinical practice**

Thiazides and loop diuretics:
↑ K-elimination → hypokalaemia
magnesium depletion → asthenia, cramps, ↓concentration
↑ Ca elimination
thiamine deficiency

Spironolactone:
Increases K+ levels

Phenytoin and phenobarbital:
↓ Vit. D: Hypokalaemia, rickets, ostomalacia
no synthesis of plasma calcium-binding protein
phosphate incorporation into red blood cells

Carbamazepine and primidone:
biotin deficiency - inhibit intestinal transport (anaemia,

Antacids:
Malabsorption of vit A, carotenoids, Fe, P, thiamine
H_2 receptor inhibitors = ↓gastric acid = ↓vitamin B12

Biguanides:
10-20% decrease in vitamin B12
↑homocysteine → high gastrointestinal motility

Nutrients Pharmacological doses:
Vitamin A and E → Vitamin K
Fe → Zn
Vitamin C → Vitamin B12
Fibre → Ca, Mg, Fe, Zn

types

- Macronutrients
  - with carbs
    - alter absorption and digestion (intraluminal and brush border)
    - diarrhoea or intestinal damage
    - lactose intolerance
    - hyperglycemic or hypoglycemic
  - with fats
    - impede lipid digestion
    - 1. Lipase inhibition or mucosal damage
    - 2. Binding to bile salts
  - with proteins
    - Digest peptidase action
    - drug → intestinal mucosal damage
    - Inhibition of protein synthesis
    - protein catabolism (gluconeogenesis)
- Micronutrients
  - Generalities
    - **Marginal micronutrient intake:** age, pathologies, pharmaceuticals
    - **Decreased intake:** anorexia, dysgeusia, dysphagia
    - **maldigestion and malabsorption:** altered homeostasis
    - **Increased catabolism:** glucocorticoids (vit.D) and contraceptives (vit.B6)
    - **Increased elimination:** drugs (renal), antibiotics and diuretics (↓Vit.K), NSAIDs (↓Fe)
    - **Antinutrients:** converting enzyme inhibition, ↑ inactive form, complex active form
  - Vitamins
    - fat-soluble vitamins
      - laxatives, antibiotics, antigout, anticholesteromics, hypocholesteromics
        - vitamin K: drug → intestinal mucosal damage, steatorrhoea, inactive form of the vitamin. (lowered by A&E)
          - vitamin D: drug → ↑catabolism vitamin. isionazid → increases its inactive form. possible bone diseases
    - water-soluble vitamins
      - vitamin C: NSAIDs → alters concentration. ↑Excretion of basic drugs, destroy vit.B12, ↑absorption of Fe, anticoagulants.

B group vitamins
thiamine: diuretics ↑elimination
riboflavin: drugs inhibit active coenzyme conversion
niacin: form inactive complexes as for vit.B6
pyridoxine: isoniazid, hydrazine, penicillamine, l-dopa, cycloserine
biotin: antibiotics ↓ vitamin synthesis
folic acid: interacts with Zn absorption
cyanocobalamin: Neomycin, colchicine, antihistamines, oral contraceptives

  - Minerals

Minerals
sodium: mineralocortidoids → renal Na retention; diuretics→ hyponatraemia; SSRIs → hyponatraemia elderly
potassium: hypokalaemia → diuretics, mineralocorticoids; hyperkalaemia → potassium-containing drugs, b-blockers, diuretic-sparing drugs
phosphorus: disturbance in absorption and/or elimination
calcium: laxatives → absorption; furosemide → elimination; vit.D → calcium homeostasis
magnesium: hypomagnesia → alcohol, DM, malabsorption; tetracyclines → absorption; aminoglycosides → ↑elimination
iron: impaired absorption → antacids, antihistamines; secondary elimination → gastro-aggressive drugs
zinc: deficit = asthenia, delayed healing/growth; ↓absorption → other micronutrients (Fe, Cu, B9) and diarrhoeal drugs
copper: biliary elimination; ↓absorption → Fe, Zn, vit.C

Interactions in pathologies of the digestive system

peptide ulcer and gastro-oesophageal reflux

acid secretion controlled by 3 main receptors:
- gastrin (gastrin)
- histamine h2 (histamine)
- muscarinic receptors M1 and M3 (acetylcholine).

targets:
- treat H.pylori infection (if present)
- treat heartburn

reduction of acid secretion:

proton pump inhibitors

Omeprazole

prolonged use → hip fractures: ↓acid = ↓calcium ↓ B12

Lansoprazole and pantoprazole not P450 → good in polymedicates

food → ↓absorption iansoprazole and esomeprazole (best 30 min before meals)

digestive discomfort, nausea, diarrhoea, abdominal pain

H2-receptor agonists (h2-antihistamines)

cimetidine, ranitidine and famotidine

may mask gastric cancer symptoms

Less effective than proton pump inhibitors

to take in the evening, cimetidine on an empty stomach (not marketed)

dizziness, tiredness, skin rash

gastric mucosal enhancers:

misoprostol

synthetic prostaglandin E analogue

promotes healing of the mucosal barrier

not for hypotensive, nor for pregnant or lactating women (abortion)

diarrhoea and abdominal pain (spontaneous abortion)

chelates

Bismuth, subcitrate

inhibit pepsin action, ↑protective prostaglandins and ↑$HCO3^-$ secretion

not in renal failure and interacts with calcium (insoluble precipitates)

digestive discomfort, nausea, diarrhoea, abdominal pain

antacids:

Aluminium hydroxide, magnesium carbonate

alkaline salts → ↑pH stomach → bind to pepsin and inactivate it

not in hypophosphatemia. cause constipation and diarrhoea

together with citric acid → aluminium toxicity → space at least 3h apart

constipation (aluminium salts), diarrhoea (magnesium salts)

nausea and vomiting

vomiting is a natural reflex to ingestion of toxic substances, medicines and illnesses

can cause metabolic alkalosis

neural control by:

vomiting centre

in the medulla oblongata, stimulated by vestibular, visceral and CTZ stimuli

Chemoreceptor trigger zone (CTZ)

cluster of neurons near the emetic centre, with dopamine and serotonin receptors.

types of drugs

h1 antihistamines

Dimenhydrinate

blocks H1 and muscarinic receptors → sedation

caution in prostatic hypertrophy, urinary retention and glaucoma

sedation, somnolence.

dopamine agonists

Domperidone and metoclopramide

antagonise dopaminergic receptors in the CTZ

limit doses of metoclopramide

they cause drowsiness, sedation, hypotension and extrapyramidal symptoms

Domperidone only in adults and does not cross the blood-brain barrier.

slight delay in absorption of metoclopramide with food.

serotonin receptor agonists

Ondansetron

antagonise 5-HT3 receptors in the CTZ

causes constipation, diarrhoea, abdominal pain and dry mouth.

metabolised by CYP450 → caution with grapefruit juice

synthetic cannabinoid

Nabilone

antiemetic properties when it starts directly in the CTZ

intestinal motility

peristalsis with the aim of transporting, mixing and propelling the contents, in the caudal direction

neural control:

myenteric plexus and **submucosal** plexus (main target of drug treatment)

hormonal control:

endocrine (gastrin) as well as **paracrine** substances (histamine, secretin, CCK and VIP)

drugs:

motility stimulants

domperidone and metoclopramide

Antiemetics that may increase gastric and intestinal motility, without laxative effect.

they cause drowsiness, sedation, hypotension and extrapyramidal symptoms

antispasmodics

Muscarinic receptor antagonists

Atropine and dicycloverine

inhibit sympathetic activity → smooth muscle relaxation

not in gastro-oesophageal reflux, produces cholinergic adverse effects

dry mouth, blurred vision, dry skin, tachycardia and urinary retention

drugs acting directly on smooth muscle

mebeverine

reduces smooth muscle spasms

not in paralytic ileus. may produce nausea, headache and heartburn

constipation and diarrhoea

Constipation

laxatives

accelerate intestinal transit time and promote defecation.

relieve constipation and cleanse the bowel

types

dough formers:

methyl cellulose, ispaghula (plantago ovata)

↑volume of non-absorbable solid residue, distend colon and ↑peristalsis

not in dysphagia, intestinal obstruction, faecal impaction

may cause flatulence, abdominal distention and digestive obstruction

osmotic

Lactulose and macrogols

poorly absorbed, ↑osmotic load by trapping fluid in intestinal lumen (diarrhoea)

not in intestinal obstruction

cause flatulence, colic pain, abdominal discomfort, electrolyte disturbances

stimulants

senna, cascara sagrada, sodium picosulphate, bisacodyl

↑secretion of water and electrolytes from mucosa

not in intestinal obstruction

may give short-term: cramps → impaired bowel function and colon atony

emollients

liquid Paraffin

lubrication of the stool to promote intestinal transit

coats the stool with a hydrophobic layer, trapping the water inside, acts after 6-8h

not for children under 3 years of age

interaction with absorption of fat-soluble vitamins → space at least 2 hours.

Diarrhoea

Frequent, liquid stools. ↑motility ↑secretion ↓absorption of liquid

opiate-type antimotility

Loperamide

acts on opioid receptors in the myenteric plexus

↑ tonus and rhythmic contraction → ↓ propulsive activity

not in acute ulcerative colitis. not recommended in children.

causes nausea, vomiting, abdominal cramps, constipation, drowsiness.

other antidiarrhoeals

chalk and charcoal

act by adsorbing toxins

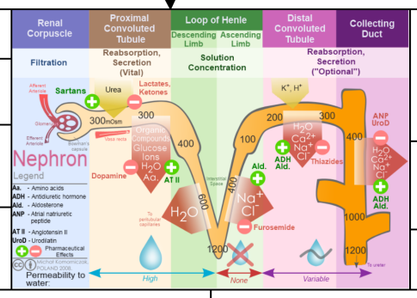
not in acute diarrhoea

may reduce the absorption of drugs

taken without food

Interactions in pathologies of the genitourinary system

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



Principal cells: reabsorb sodium and secrete potassium **Intercalary cells:** secrete hydrogen ions
presence of **aquaporins** for water reabsorption in the collecting duct
Renin-Angiotensin-Aldosterone system

Diuretics

↓Na^+ reabsorption and increase water excretion

prescribed for high blood pressure and oedemas

types

Loop diuretics

Furosemide, bumetanide, torasemide

sodium excretion: 15-25%

in the thick ascending portion → inhibit cotransporter $Na^+/K^+/2Cl^-$

↑Na in the collecting duct → ↑secretion of K^+ and H^+ (metabolic alkalosis)

inhibition of Ca and Mg reabsorption and vasodilatation

not prescribed in severe renal failure

food and gingseng may reduce the effect

liquorice antagonistic effect (Na and H2O retention, K excretion).

hypokalaemia, hyponatraemia, hypotension, hypovolaemia and metabolic alkalosis

Distal tube diuretics

thiazides: hydrochlorothiazide and **sulphonamides:** chlorthalidone and indapamide

sodium excretion: 5-10%.

inhibit Na+/Cl- cotransporter → increase secretion of K^+ and H^+ in the collecting duct

decrease Ca excretion

maximum effect 4-6h after taking them

not prescribed in ↓K^+ ↓Na^+ and ↑Ca (worsen)

caution in DM, thiazides cause hyperglycaemia

better tolerated than loop diuretics but still high frequency of urination

interaction with liquorice due to antagonistic effect

prolonged treatment → hypokalaemia
hypokalaemia → toxicity of other drugs

Potassium sparing diuretics

Sodium channel inhibitors: amiloride and triamterene. **Aldosterone antagonists:** spironolactone, eplerenone.

sodium excretion: 2-3%.

act in the end portion distal tubule and collecting duct

Sodium channel inhibitors

block reabsorption of Na^+ → lower secretion of K^+ and H^+

Aldosterone antagonists

no aldosterone = ↓Na^+ reabsorption and ↓K^+ and H^+ secretion

in heart failure and hyperaldosteronism.

not prescribed with ACE inhibitors (hyperkalaemia), not in renal failure.

cause digestive problems, hyperkalaemia and hyponatraemia.

aldosterone antagonists: gynaecomastia, menstrual disorders and male sexual dysfunction.

potassium-rich foods → risk of hyperkalaemia

urinary incontinence

Involuntary urine leakage

parasympathetic nervous system innervates the bladder (controls contractility)

Types of incontinence:
motor type. inability to inhibit contraction in filling phase.
overstimulation of sensory afferent pathways of the bladder
overactive musculature
due to prostate problems and neurological lesions

Muscarinic receptor antagonists

Oxybutynin, solifenacin, tolterodine, fesoterodine

relax detrusor muscle

not in bowel or bladder outlet obstruction, not in glaucoma.

Interaction with grapefruit juice may cause toxicity.

Urinary antispasmodic

Mirabegron

bladder smooth muscle antispasmodic (beta-3 adrenergic receptor agonist)

Not in severe and uncontrolled hypertension.

may cause tachycardia and urinary tract infections.

erectile dysfunction

repeated inability to achieve or maintain an erection.

may be due to adverse effects of other medications

Phosphodiesterase inhibitors → Sildenafil, tadalafil, vardenafil.

inhibit the degradation of cGMP (role of phosphodiesterase) → increasing the vasodilator effects of NO

not to use in recurrent nitrate treatment → may cause dyspepsia and visual disturbances.

vardenafil interacts slightly with food (delayed absorption).

Interactions in pathologies of the cardiovascular system.

blood: transport of nutrients and oxygen, as well as waste products → specific fluid to carry out these functions

cardiovascular risk

external: **lifestyle** internal; **RAA system**

disease vs **risk** (probability) vs **coronary risk** (development) vs **factor of CV risk** (idios)

non-modifiable: family history, age, gender (↑men)

arterial hypertension

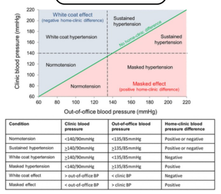
Introduction

force exerted by the blood in the blood vessels

RAA system increases osmolality and volemia

Healthy: 140/90
DM: 140/85
High CV risk: 135/80

Primary or secundary (comorbidities)



Condition	Clinic blood pressure	Out-of-office blood pressure	Home-clinic blood pressure difference
Normotension	<140/90mmHg	<135/85mmHg	Positive or negative
Sustained hypertension	≥140/90mmHg	≥135/85mmHg	Positive or negative
White coat hypertension	≥140/90mmHg	<135/85mmHg	Negative
Masked hypertension	<140/90mmHg	≥135/85mmHg	Positive
White coat effect	+ out-of-office BP	+ clinic BP	Negative
Masked effect	+ out-of-office BP	+ clinic BP	Positive

patient raiser (stays up at night)

HBP in pregnancy, pre-eclampia and refractory

lifestyle changes, diet, physical exercise

multi-drug approach with fewer doses of each drug → fewer adverse reactions

Drugs for hypertension

Diuretics: loop, thiazidics, K⁺-sparing drugs

Furosemide, Hydroclotiazide, Amiloride, Spirinolactone

β-adrenergic antagonists

block effect of adrenaline on cardiac contraction (β1) and vessels (β2).

Non-selective

Propanolol, oxprenolol, nadolol and carteolol

Oral and intravenous. with liquid, with or without food.

Not in patients with asthma

Hyperprotein diet increases 53% effect of propranolol and ↓glucose tolerance.

Selective, mainly on cardiac contraction (β1)

Atenolol, Bisoprolol, and nebivolol

Oral and intravenous. with or without food.

High doses give Bradycardia and hypotension

can give tiredness, insomnia, cold extremities and ↓glucose tolerance.

α-adrenergic antagonists

Doxazosin and terazosin

inhibit α1 receptor-mediated vasoconstriction → ↓peripheral resistance (↓LDL, VLDL, TG and ↑HDL).

Oral, with water, with or without food.

Not in chronic heart failure

may cause postural hypotension, dizziness, nausea and fatigue.

Calcium antagonists

Amlodipine, nicardipine, nimodipine

↓Ca entry into vascular cells→ vasodilatation and ↓arterial pressure.

Oral. with liquid, with or without food, best without grapefruit.

Not in aortic stenosis, give hypotension and bradycardia.

With grapefruit juice there is toxicity.

↓ nimodipine bioavailability with food ↑ bioavailability with lipids

Verapamil and diltiazem

↓Ca entry into cardiac cells → ↓contractility and ↓heart rate

Oral. take whole with liquid

Not in aortic stenosis, cause severe heart failure, do not combine with β-blockers.

With grapefruit juice there is toxicity.

tobacco/ethanol ↑metab. of verapamil. may cause heart block and constipation.

ACEIs Agiotensin Converting enzyme Inhibitors

first choice: **enalapril** (**captopril** in chronic)

inhibit the conversion of Angiotensin I to II → no hypertensive action with aldosterone.

Oral, with a glass of water

Not in pregnancy or aortic stenosis

Give cough, hypotension and dizziness.

↓absorption with food, liquorice mineralocorticoid effect, grapefruit juice inhibits, food ↑K⁺ (hyperkalemia).

ARA 2 angiotensin receptor antagonists

Valsartan, ibersartan, eprosartan, candesartan

angiotensin II receptor antagonists, cause vasodilatation

similar to the ACEIs

better absorption and fewer adverse effects (less coughing)

create vasodilatation, only for high blood pressure.

oral. Can cause cough and hypotension. Not for pregnant women

Aliskiren (new drug 2020)

renin inhibitor, similar to ACE inhibitor

Oral, with or without food, better without fruit juices

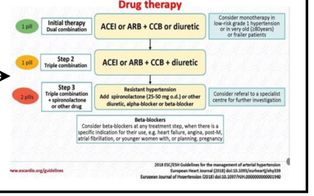
No cough as AR, interacts with grapefruit juice

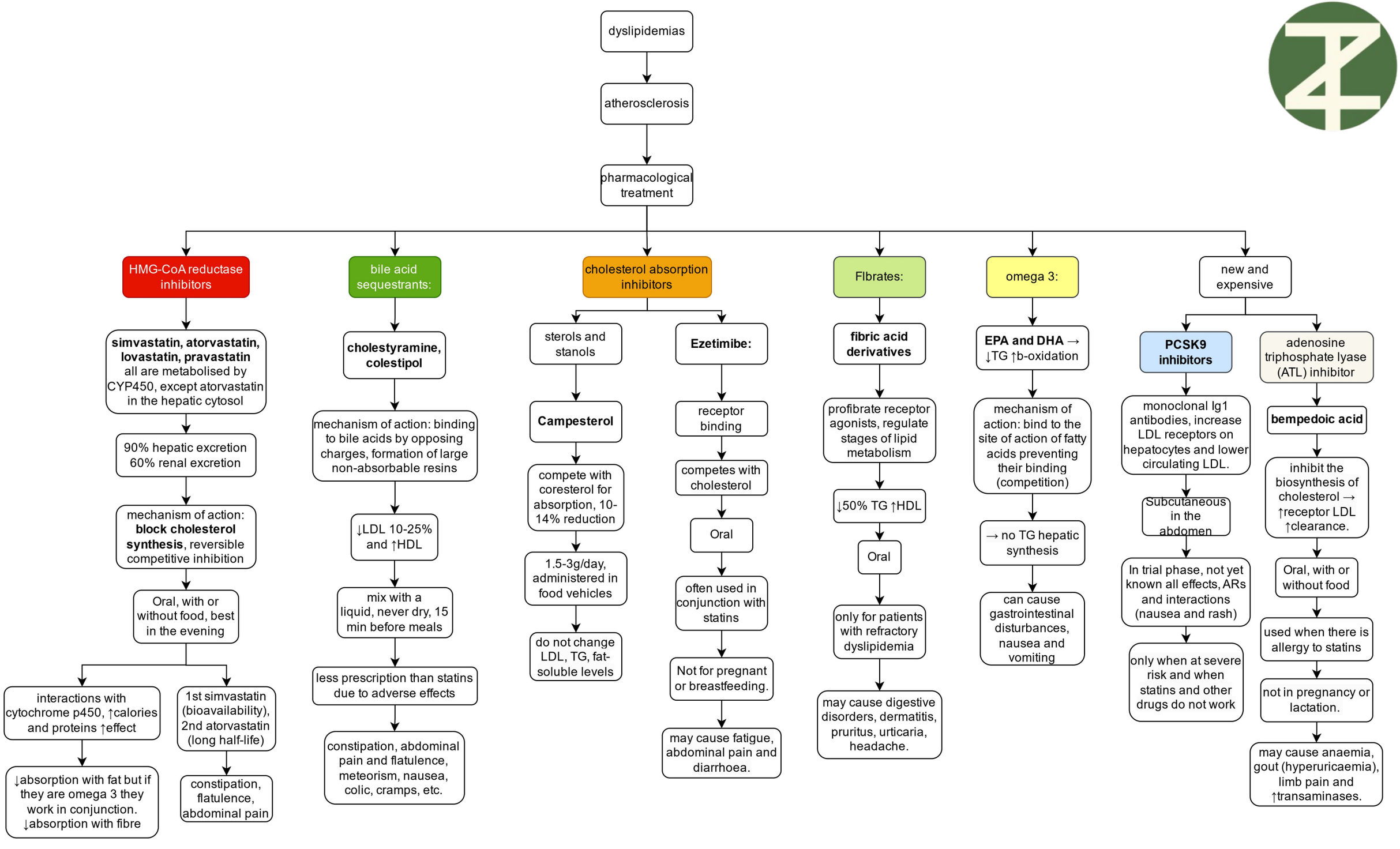
How prescription works:

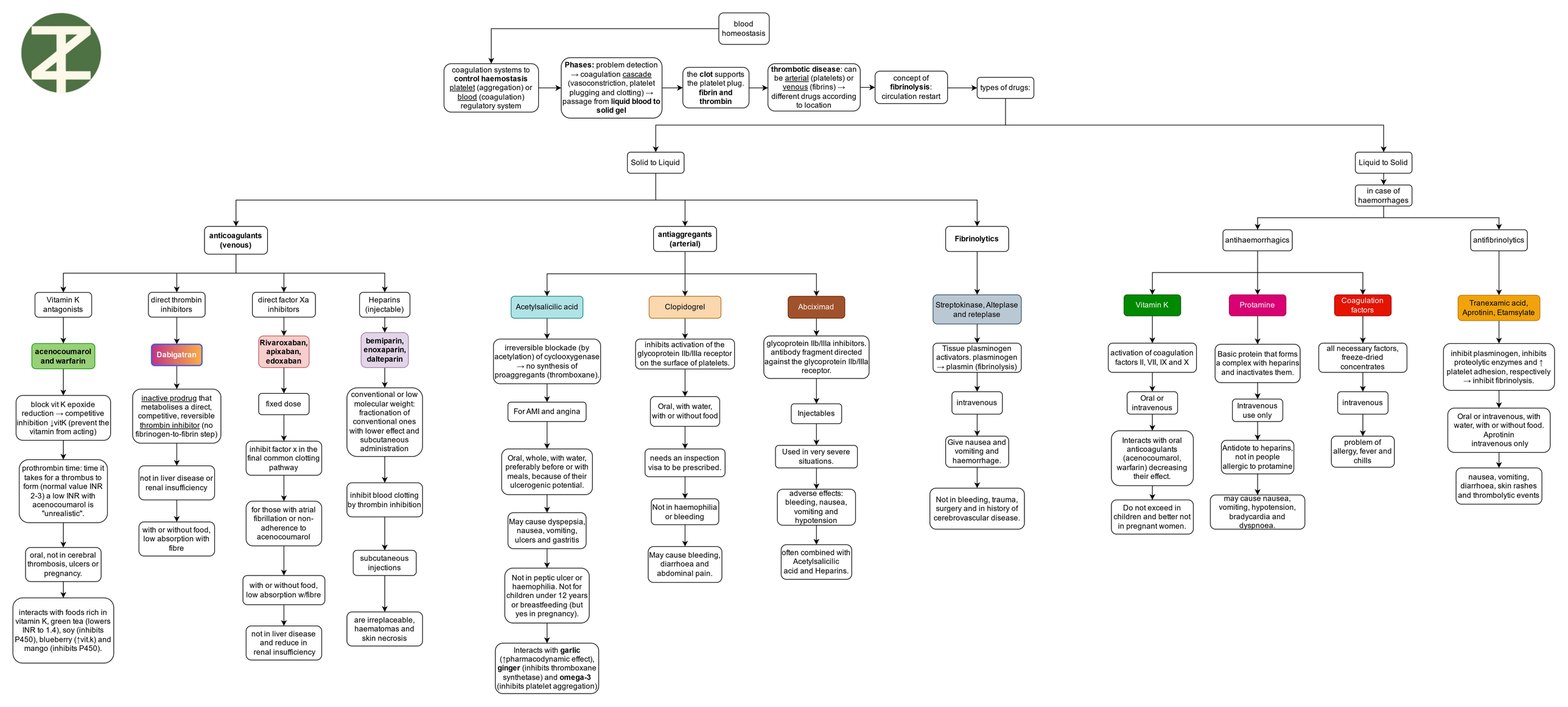
do not directly give full doses of input drugs

better to give less dose but in conjunction with other drugs

first line: ACEIs or ARA 2




dyslipidemias
atherosclerosis
pharmacological treatment
HMG-CoA reductase inhibitors
simvastatin, atorvastatin, lovastatin, pravastatin all are metabolised by CYP450, except atorvastatin in the hepatic cytosol
90% hepatic excretion 60% renal excretion
mechanism of action: block cholesterol synthesis, reversible competitive inhibition
Oral, with or without food, best in the evening
interactions with cytochrome p450, ↑calories and proteins ↑effect
↓absorption with fat but if they are omega 3 they work in conjunction. ↓absorption with fibre
1st simvastatin (bioavailability), 2nd atorvastatin (long half-life)
constipation, flatulence, abdominal pain
bile acid sequestrants:
cholestyramine, colestipol
mechanism of action: binding to bile acids by opposing charges, formation of large non-absorbable resins
↓LDL 10-25% and ↑HDL
mix with a liquid, never dry, 15 min before meals
less prescription than statins due to adverse effects
constipation, abdominal pain and flatulence, meteorism, nausea, colic, cramps, etc.
cholesterol absorption inhibitors
sterols and stanols
Campesterol
compete with coresterol for absorption, 10-14% reduction
1.5-3g/day, administered in food vehicles
do not change LDL, TG, fat-soluble levels
Ezetimibe:
receptor binding
competes with cholesterol
Oral
often used in conjunction with statins
Not for pregnant or breastfeeding.
may cause fatigue, abdominal pain and diarrhoea.
FIbrates:
fibric acid derivatives
profibrate receptor agonists, regulate stages of lipid metabolism
↓50% TG ↑HDL
Oral
only for patients with refractory dyslipidemia
may cause digestive disorders, dermatitis, pruritus, urticaria, headache.
omega 3:
EPA and DHA → ↓TG ↑b-oxidation
mechanism of action: bind to the site of action of fatty acids preventing their binding (competition)
→ no TG hepatic synthesis
can cause gastrointestinal disturbances, nausea and vomiting
new and expensive
PCSK9 inhibitors
monoclonal Ig1 antibodies, increase LDL receptors on hepatocytes and lower circulating LDL.
Subcutaneous in the abdomen
In trial phase, not yet known all effects, ARs and interactions (nausea and rash)
only when at severe risk and when statins and other drugs do not work
adenosine triphosphate lyase (ATL) inhibitor
bempedoic acid
inhibit the biosynthesis of cholesterol → ↑receptor LDL ↑clearance.
Oral, with or without food
used when there is allergy to statins
not in pregnancy or lactation.
may cause anaemia, gout (hyperuricaemia), limb pain and ↑transaminases.


blood homeostasis
coagulation systems to **control haemostasis** platelet (aggregation) or blood (coagulation) regulatory system
Phases: problem detection → coagulation cascade (vasoconstriction, platelet plugging and clotting) → passage from **liquid blood to solid gel**
the **clot** supports the platelet plug. **fibrin and thrombin**
thrombotic disease: can be arterial (platelets) or venous (fibrins) → different drugs according to location
concept of **fibrinolysis**: circulation restart
types of drugs:
Solid to Liquid
Liquid to Solid
in case of haemorrhages
anticoagulants (venous)
antiaggregants (arterial)
Fibrinolytics
antihaemorrhagics
antifibrinolytics
Vitamin K antagonists
direct thrombin inhibitors
direct factor Xa inhibitors
Heparins (injectable)
acenocoumarol and warfarin
Dabigatran
Rivaroxaban, apixaban, edoxaban
bemiparin, enoxaparin, dalteparin
block vit K epoxide reduction → competitive inhibition ↓vitK (prevent the vitamin from acting)
prothrombin time: time it takes for a thrombus to form (normal value INR 2-3) a low INR with acenocoumarol is "unrealistic".
oral, not in cerebral thrombosis, ulcers or pregnancy.
interacts with foods rich in vitamin K, green tea (lowers INR to 1.4), soy (inhibits P450), blueberry (↑vit.k) and mango (inhibits P450).
inactive prodrug that metabolises a direct, competitive, reversible thrombin inhibitor (no fibrinogen-to-fibrin step)
not in liver disease or renal insufficiency
with or without food, low absorption with fibre
fixed dose
inhibit factor x in the final common clotting pathway
for those with atrial fibrillation or non-adherence to acenocoumarol
with or without food, low absorption w/fibre
not in liver disease and reduce in renal insufficiency
conventional or low molecular weight: fractionation of conventional ones with lower effect and subcutaneous administration
inhibit blood clotting by thrombin inhibition
subcutaneous injections
are irreplaceable, haematomas and skin necrosis
Acetylsalicilic acid
Clopidogrel
Abciximad
irreversible blockade (by acetylation) of cyclooxygenase → no synthesis of proaggregants (thromboxane).
For AMI and angina
Oral, whole, with water, preferably before or with meals, because of their ulcerogenic potential.
May cause dyspepsia, nausea, vomiting, ulcers and gastritis
Not in peptic ulcer or haemophilia. Not for children under 12 years or breastfeeding (but yes in pregnancy).
Interacts with **garlic** (↑pharmacodynamic effect), **ginger** (inhibits thromboxane synthetase) and **omega-3** (inhibits platelet aggregation)
inhibits activation of the glycoprotein IIb/IIIa receptor on the surface of platelets.
Oral, with water, with or without food
needs an inspection visa to be prescribed.
Not in haemophilia or bleeding
May cause bleeding, diarrhoea and abdominal pain.
glycoprotein IIb/IIIa inhibitors. antibody fragment directed against the glycoprotein IIb/IIIa receptor.
Injectables
Used in very severe situations.
adverse effects: bleeding, nausea, vomiting and hypotension
often combined with Acetylsalicilic acid and Heparins.
Streptokinase, Alteplase and reteplase
Tissue plasminogen activators. plasminogen → plasmin (fibrinolysis)
intravenous
Give nausea and vomiting and haemorrhage.
Not in bleeding, trauma, surgery and in history of cerebrovascular disease.
Vitamin K
Protamine
Coagulation factors
activation of coagulation factors II, VII, IX and X
Oral or intravenous
Interacts with oral anticoagulants (acenocoumarol, warfarin) decreasing their effect.
Do not exceed in children and better not in pregnant women.
Basic protein that forms a complex with heparins and inactivates them.
Intravenous use only
Antidote to heparins. not in people allergic to protamine
may cause nausea, vomiting, hypotension, bradycardia and dyspnoea.
all necessary factors, freeze-dried concentrates
intravenous
problem of allergy, fever and chills
Tranexamic acid, Aprotinin, Etamsylate
inhibit plasminogen, inhibits proteolytic enzymes and ↑ platelet adhesion, respectively → inhibit fibrinolysis.
Oral or intravenous, with water, with or without food. Aprotinin intravenous only
nausea, vomiting, diarrhoea, skin rashes and thrombolytic events

Interactions in respiratory system pathologies.

They are the main reason for first consultations in primary medicine.

Third leading cause of death in Europe.

Cough

reflex action with a protective function

Productive: there is expectoration (without treatment).
Non-productive or dry: there is no expectoration (requires treatment).

Can be acute or **chronic** (>10 days).

is initiated by **irritant** stimuli carried by the **vagus** nerve (neuomogastric)

vagal sensory fibers: **fast** adapting receptors, **capsaicin**-sensitive and bronchopulmonary afferent **C-fibers** (cough reflex)

integration in the **cough center** in the **medulla oblongata** (independent of the respiratory centre)

cough centre efferent pathways → muscle response → **act of coughing**: inhalation, ↑intrathoracic pressure and then expulsion.

Antitussive Drugs

opioid antitussives

Codeine

Depresses the medullary **cough centre**, inhibits the production of **tachykinins**, the main neurotransmitters of the **C-fibers** of this center.

Oral, with or without food, **syrups**? directly or **dissolved** in another liquid.

Not in COPD, severe asthma, Causes **respiratory depression**.

Not in pregnancy → neonatal astinence syndrome (**FDA category C**).

May give **nausea**, vomiting, constipation. Interacts with **alcohol** ↑effect.

Dextromethorphan

Codeine **analog**. Depresses the medullary **cough centre**, inhibits **tachykinins** (**C-fiber** neurotransmitters).

Rapidly absorbed **orally**, with or without food. **avoid grapefruit juice** or bitter oranges.

Not in asthma or COPD, children and lactation.

May give **dizziness**, drowsiness, **nausea**, vomiting, intestinal discomfort, fatigue.

Lacks narcotic effects. **Alcohol** and **grapefruit** juice ↑effect.

Noscapine

Depresses the medullary **cough centre**. inhibits **tachykinins** (**C-fiber** neurotransmitters).

Oral or suppositories, preferably after meals.

Not respiratory depressant, not ↓mucociliary clearance, not ↓bronchial secretions, **bronchodilator**

Yes in children from 2 years old, not in pregnancy/lactation

It causes **nausea**, headache and drowsiness. Interacts with **alcohol** ↑effect.

non-opioid antitussives

Cloperastine

possible depression of the **cough center** + **bronchodilation** and local **anesthesia** in the bronchi

syrup, oral suspension → shake before use, can be taken **with or without food**

Does **not** result in **dependence** or nervous depression like opioids

Yes in **children** from 2 years of age

They have **anticholinergic** effects (be careful in children as they are more sensitive).

Levodropropizine

Interference in the release of sensory neuropeptides in the respiratory tract (inhibits **capsaicin**-induced cough).

Oral, 3 **fasting** doses → at least 6 hours apart.

Greater effects than cloperastine if cough is induced by **peripheral** stimuli.

10x **less effective** than codeine in cough of **central** origin.

May cause **nausea**, **vomiting**, **diarrhea**, abdominal pain, gastric hyperacidity, dyspepsia, somnolence, headache, vertigo, palpitations.

other antitussives

Mepiromide

Xanthine. Nonspecific **H1 antihistamine**, produces slight bronchodilator effect.

Oral with food

Not in porphyria

May cause **nausea**, **vomiting**, constipation, diarrhea, epigastric pain, anorexia, dry mouth (symptoms **decrease** if taken **with food**).

With **alcohol** there is drowsiness

Ipratropium bromide

bronchodilator and antisecretory + cough reflex impulse blocker.

Inhaled

may cause **nausea**, dry mouth and dyspepsia.

Diphenhydromine

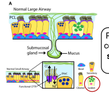
Central cough suppressant and H1 antihistamine.

with sufficient **liquid**, with or without **food**. before going to **bed**.

May cause **dry** mucous membranes and **thickening** of mucus.

With **alcohol** produces drowsiness

Mucus



Produced by **goblet** cells (MUC5AC) and **submucosal** gland cells (MUC5B)

purpose: to **protect** the tracheal mucosa

mature **glycoproteins** or mucins, high molecular weight: **gel-like mucus**.

increased mucus **viscosity** due to the presence of high amounts of **DNA**

Mucous **drainage**: ciliary activity and coughing

Drugs

Expectorants

eucalyptus and menthol

Essential oils of the terpenes group

Iodides (potassium iodide)

increase the **aqueous secretion** of the **submucosal glands** by direct action or by activation of the **gastropulmonary vagal reflex.**

potassium iodide: **gastrointestinal** discomfort, rhinorrhea, iodism and thyroid alterations.

Guaifenesin

guaiacol glyceryl ether. Stimulates the production of **bronchial** secretions by reflex mechanism of **irritation** of the gastric mucosa

Oral, syrup directly **and then a glass of water**, with or without food.

Not in **porphyria**, not in children <2 years.

Adverse effects: **nausea**, vomiting, diarrhea, drowsiness, dizziness, headache.

Mucolytics

Thiol derivatives

Acetylcysteine

They **break disulfide bridges**, reducing mucus viscosity. maximum effect at pH 7-9.

Oral, best with food, best in the **morning**.

Reduces mucus **hyperviscosity** in common **cold** and **flu**

Not in hypersensitivity, caution in children.

May cause **nausea**, vomiting, diarrhea and gastric hyperacidity

Carbocisteine

increases the **synthesis of sialomucins**, thus re-establishing the normal composition of mucus secretion, **normalizing mucus viscoelasticity**.

Oral, maximum dose 600mg once a day. **glass of water after each dose**, plenty of water during the day.

Not in **peptic ulcer** (aggravation), not in <2 years.

May give **nausea**, vomiting, dyspepsia and abdominal pain.

Vasicin derivatives

Bromhexidine

activation of **sialyl-transferase**, responsible for synthesizing **sialomucins**

normalization of mucus composition. Activation of **lysozyme** which induces the **breakdown of muco-polysaccharides**.

Oral, inhalation or injectable, **glass of water after each dose**, plenty of water during the day.

Reduces mucus **hypervicosity** in common cold and flu. Not in hypersensitivity, **caution** in children

May cause **nausea**, vomiting, diarrhea and abdominal pain.

Ambroxol

increased synthesis of **sialomucins** → **normalizes** mucus composition.

Mucous glands of the brochial epithelium increasing **lysozyme** → **breakdown** **mucopolysaccharides** and stimulation of mucociliary activity.

Oral

Reduces mucus hypervicosity in common **cold and flu**

Not in children <2 years. May cause **nausea**, dysgeusia and hypoesthesia.

Enzymes

Dornase Alpha

Degradation of **DNA** molecules from **neutrophil lysis** (the cause of mucus hypervicosity).

Inhalation

For **cystic fibrosis** (treatment >5 years). Not in hypersensitivity.

May cause **hoarseness and pharyngitis**, rash with urticaria and conjunctivitis, possible chest pain

Streptodornase

deoxyribonuclease that produces an **enzymatic degradation** of suppurative and viscous exudates.

Nebulisation

Indicated **in very specific cases** and only for a few days.

Can cause **bronchospasm** and **hypersensitivity** reactions of varying severity.

Highly **variable efficacy** and low yield.

Asthma

Chronic inflammatory disease with bronchial **hyperresponsiveness** and variable airflow **obstruction**.

Goal of approach:
- To achieve and maintain **control** of the pathology.
- **Prevention** of future risk (exacerbations)

Prevalence: increasing 112.6% from 1990 to 2015, more in **middle age** and **women**.

Many **risk factors**: host, perinatal, environmental, and medication.

Exaggerated contraction of bronchial smooth muscle (**hyperresponsiveness**) to allergens causing mast cell degranulation.

Inflammatory mediators → inflammatory reaction in bronchi (damage and further hyperresponsiveness).

everything is based on the **severity** of asthma

forced expiratory volume in the first second (**FEV1**) and forced vital capacity (**FVC**). FEV1/FVC <0,7

Drugs

Bronchodilators

for **immediate** phase response

B2-adrenergic agonists

Salbutamol (ventolin) and Terbulin → short action **Salmeterol**, Formoterol, vilanterol, indacaterol → long action

Taken by inhalation

short-acting, on demand, 3-5 hours of action. **Long-acting**, twice daily, 12 hours of action.

For asthma and COPD, give mild **tremor**, tachycardia or **hypokalaemia** after high doses.

Caution in hyperthyroidism, **cardiovascular disease** or arrhythmias.

Anticholinergics

Ipratropium bromide → short action **Tiotropium** → long action

They **block muscarinic receptors**, (M3), which respond to **parasympathetic** bronchoconstrictor tone

Inhaled

Not in glaucoma, prostatic hypertrophy and pregnancy.

may cause dry mouth. Systemic effects are rare.

Xanthines

Theophylline

inhibits **phosphodiesterase** by increasing **cAMP** levels → smooth muscle relaxation and **bronchodilatation**

also anti-inflammatory

Oral

Not in heart disease, may cause **digestive problems**, nausea, vomiting, tremor, **insomnia** and tachycardia

interacts with **tobacco**, **lowering** the effect of thiophylline.

Anti-inflammatories

for **late** phase response

Leukotriene receptor antagonists

Montelukast

inhibit the effect of endogenous **leukotrienes** and produce **bronchodilation**.

Oral

may cause **inflammation** of blood vessels, **nausea**, vomiting, abdominal pain and **diarrhoea**.

interacts with **orange juice** lowering its **bioavailability** and **efficacy**.

Glucocorticoids

Budesonide, beclomethasone, dipropionate, fluticasone propionate

reduce mucosal **inflammatory** response → **reduce** bronchial **hyperresponsiveness**.

inhaler, oral or intravenous is reserved for severe chronic asthma

more potent and effective treatment, may give oral or pharyngeal candida, cough, pharyngitis

Interacts with **grapefruit juice** ↑effect, **alcohol** (ulcers), **Ca** (must be supplemented), **echinacea** (↓effect), **liquorice** (↑effect), **tobacco** (↓effect).

Interactions in nervous & hormonal system pathologies.

Thyroid

Primary hypothyroidism: thyroid gland abnormalities
Secondary hypothyroidism: reduced TSH secretion - Pituitary gland
Tertiary hypothyroidism: reduced TRH secretion - Hypothalamus

Autoimmune hypothyroidism vs. **triggering** factors.

5% population

Iodine deficient countries. Spain

TRH → TSH → iodination and tyrosine binding → T4 and T3 → **increased metabolism**

Hypothyroidism

Levothyroxine

Synthetic **analogue of T4**. normalises deficiency.

Oral or parenteral. take whole with little **water**, **in the morning** on an empty stomach **30 minutes before breakfast**.

Not in Addison's or AMI. may cause **symptoms of hyperthyroidism.**

Fibre, milk, coffee, juices, papaya, calcium, iron, chromium **lower T4**. Soy ↑**TSH**. Vitamin C ↓TSH ↑**T3 and T4.**

Hyperthyroidism

Carbimazole, Methimazole and Thiamizole

Antithyroid, **inhibits iodine oxidation** by inhibiting peroxidases.

Oral with liquid, with or without food. **Effective after 2 weeks** and can be stopped after 2 years (**may not be chronic**).

Causes **liver toxicity**, agranulocytosis, neutropenia and thrombocytopenia.

Iodine, radioactive iodine

Antithyroid, excess **inhibits iodine uptake** by the thyroid, if **radioactive** it **destroys** the thyroid.

Hyperthyroidism **returns** in a few weeks, limited utility.

may cause **hypersensitivity reactions**: angioedema, skin haemorrhages, serum sickness.

Mood disorder

Depression

depression: mood **without interest** or pleasure, ↓**energy**, lasts 2 weeks, present and **unrelated to previous events** maybe due thyroid disorders, medication, narcotic drugs

depressive disorders: sadness only
bipolar depressive disorders: sadness + mania

may be mild or severe → leading to **incapacitation of daily habits** (a lot of suicide in severe)

Non-pharmacological treatment:

Cognitive-behavioural psychotherapy treatment → this is what the psychologist/psychiatrist treats and is the most effective.

Electroconvulsive therapy → epileptic seizure with CNS stimulation

Drugs

Acute, continuation or maintenance treatment

Selective serotonin reuptake inhibitors

Escitalopram, Fluoxetine, Paroxetine

selectively **inhibits reuptake** of **serotonin** by neuronal presynaptic membrane → **increased serotonin** to the **CNS.**

Oral, with liquid, with or without food

May cause **nausea**, dry mouth, **sedation** and **constipation** (paroxetine), **weight loss** (fluoxetine) and **weight gain** (paroxetine).

grapefruit juice ↑toxicity, **tryptophan** → serotonergic syndrome, **hyperic** P450, **alcohol** CNS depression

Serotonergic agonist antidepressant

Vortioxetine

modulator of serotonergic **transmission** and **inhibitor** of serotonin **transporters**

Oral, with liquid, with or without food

Decreases the risk of **relapse**, may cause **nausea** and vomiting.

Serotonin and noradrenaline reuptake inhibitors

Duloxetine, venlafaxine and desvenlafaxine

Oral, with liquid, with or without food

↓absorption **duloxetine** with food, **venlafaxine** ↑Cmax with fat, **tryptophan** serotonergic syndrome, **alcohol** CNS depression

alprazolam-alcohol ↑**aggression**, diazepam-**alcohol** ↑effect, **caffeine** ↓effect, **grapefruit juice** ↑effect and toxicity

Tricyclic antidepressants

Amitriptyline

for **major** depressive episodes

Oral, with liquid, with or without food, **at night**.

non-specific, many AR. give **sedation** and drowsiness.

Fibre ↓absorption, **DAO enzyme** → histamine-rich foods, **hypericum** ↑effect and toxicity, **alcohol**: increases CNS depressant effect.

Serotonergic receptor antagonists and serotonin uptake inhibitors

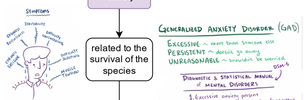
Mirtazapine, Trazodone

have an antiemetic effect for oncology patients.

Oral, with liquid, with or without food, **at night.**

Dry mouth, drowsiness, **sedation**

Anxiety



related to the survival of the species

anticipation of future harm or misfortune, fear of any situation - insecurity

Benzodiazepines

Diazepam (Valium), **alprazolam** (Xanax), clonazepam (Klonopin), Lorazepam (anxiolytic and hypnotic)

they **calm or sedate** by raising the level of the inhibitory neurotransmitter **GABA** in the brain.

Rectal or injectable solution (diazepam) and **oral**, with liquid, with or without food (alprazolam).

Give the lowest possible dose that is effective.

Treatments should not exceed 4-6 months.

Reduce the dose progressively.

Grapefruit juice ↑effect. **Caffeine** ↓effect. **Ethanol** ↑effect. Alprazolam-alcohol: increased **aggressiveness**.

Diabetes

Increased insulin sensitivity

Metformin

Biguanides. acts at **three levels** (liver, muscle and intestine), improves **lipid** profile and **weight reduction**.

Oral

HbA1c (1.5-2%)

Delayed absorption with food.

↑absorption of **vitD**, ↑**effect with** vit A,C,E, prebiotics, alcohol, fibre and spirulina. **plantago ovata** (improves glycaemia), and ↓**absorption of vitB12**.

Pioglitazone

Thiazolidinediones. may lead to **weight gain**. HbA1c (1-1.6%)

oral with or without food, **better** on an **empty stomach**

caution with bioflavonoids (**grapefruit**) **increases** hypoglycaemic **effect**.

Treatment lasts 6-8 weeks until improvement

Increased insulin secretion

Glibenclamide

HbA1c 1-1.8%.

Oral, with or without food (shortly before or during meal).

Risk of hypoglycaemia.

fibre decreases bioavailability, **Plantago ovata**: improves hypoglycaemic effect and metabolic control **(use together to improve glycaemia)**

Repaglinide

HbA1c 1.5-2%.

Oral, with or without food. Recommended **15-30 minutes before a meal.**

Can be administered **3 times a day** (effect of about 6 hours).

Risk of hypoglycaemia, forcing insulin secretion.

Sitagliptin

HbA1c 0.6-0.8%.

Oral, with or without food

No **hypoglycaemia** or pancreatic depletion.

Usually used **in combination with metformin** as a second step.

Flavonoids ↑effect

Reduced digestive absorption of glucose

Acarbose

Slight postprandial decrease and HbA1c less than 1%.

Oral, **always with food**

Do **not** produce **hypoglycaemia** as they do not affect insulin

Can cause **diarrhoea** (very frequent) and **low** vitamin **K** and/or **B12** absorption.

Flavonoids ↑effect.

Guar gum

Inhibits renal tissue reabsorption of glucose

Dapagliflozin, empagliflozin

hypoglycaemic effect depends on **renal status**.

Hb1Ac 0.7-1.1%.

Oral, with or without food

Not for **DM1**, monitor patient's **hydration**, increases **diuresis**, urinary glucose **excretion**.

(GLP-1)

Semaglutide

helps the pancreas to **secrete** the **correct dose** of **insulin** when there is hyperglycaemia.

Hb1Ac 1.5-2%.

Oral. **30 minutes before** ingesting food or drugs to **improve their bioavailability** given their poor absorption.

Not for **DM1**, monitor the patient's **hydration**, introduce gradually (avoid digestive discomfort).

In DM2 it goes **together** with another **hypoglycaemic agent** (Metformin)