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General anesthetics

Local anesthetics

Adsorbents

Mucilaginous

Astringents

Irritants

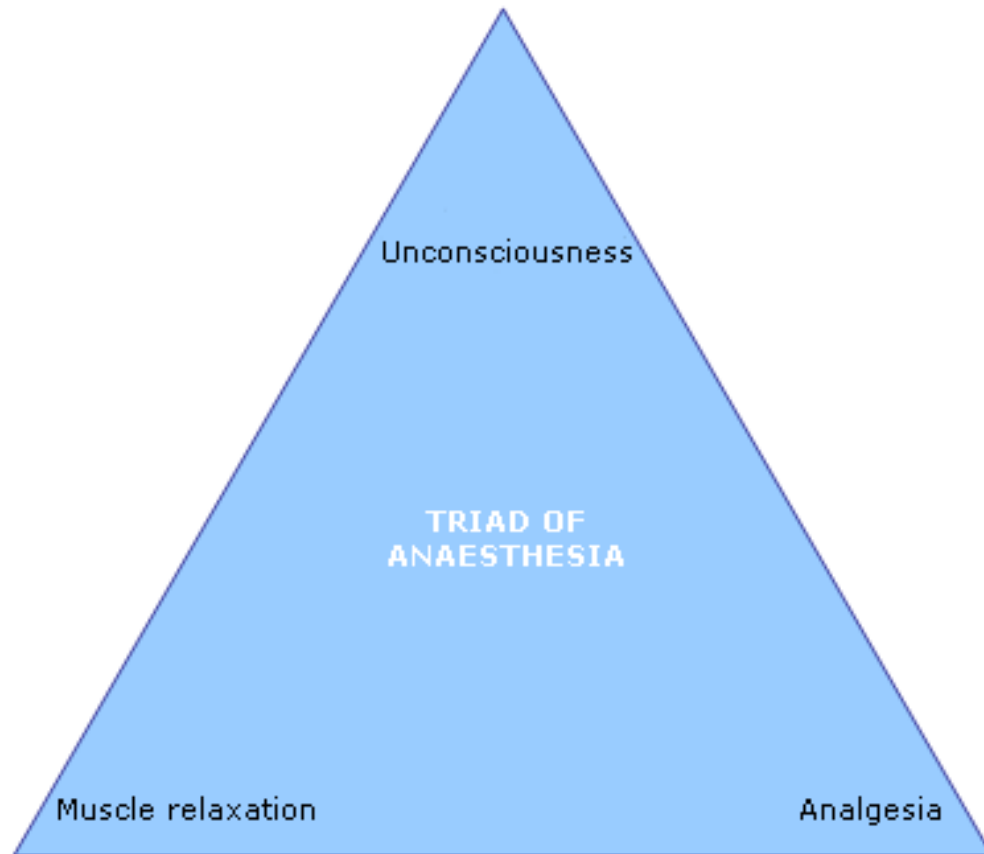
General anesthesia -

- **a state of unconsciousness, analgesia and amnesia, with skeletal muscle relaxation and loss of reflexes.**

General Anesthesia

- Alters responses of the Central Nervous system
- Causes one or more of the following
 - Pain relief
 - Muscle relaxation
 - Relaxation of reflexes
 - Deep sleep
- Commonly used during surgery

AIMS OF ANAESTHESIA



Triad of anaesthesia

- **Neuromuscular blocking agents** for muscle relaxation
- **Analgesics**/regional anaesthesia for analgesia
- **Anaesthetic agents** to produce unconsciousness



Why unconscious patient require analgesia ?

Anesthesiology

Preanesthetic medication:

It is the use of drugs prior to anesthesia to make it more safe and pleasant.

- To relieve anxiety – benzodiazepines.
- To prevent allergic reactions – antihistaminics.
- To prevent nausea and vomiting – antiemetics.
- To provide analgesia – opioids.
- To prevent bradycardia and secretion – atropine.

Stages of anesthesia:

- Stage I : Induction
- Stage II : Excitement, combative behavior – dangerous state

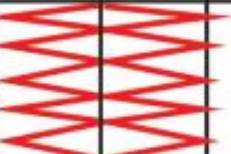













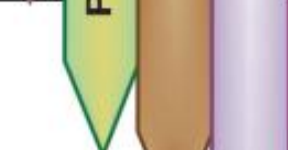











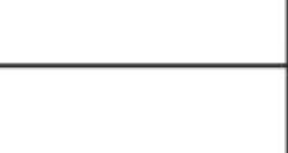






- Stage III : Surgical anesthesia

- *eyes initially rolling, then becoming fixed*
- *loss of corneal and laryngeal reflexes*
- *pupils dilate and loss of light reflex*
- *intercostal paralysis, shallow abdominal respiration, dilated pupil*

Stage IV : Medullary paralysis –

respiratory and vasomotor
control ceases.

Stages of anesthesia:

STAGE		Respiration		Ocular movem.	Pupil size	Reflexes	SK.mus. tone	B. P.	H. R.	USES									
		Thor.	Abd.																
I ANALGESIA				NORMAL						Labour, Incisions and Minor ops.									
II DELIRIUM				ROVING EYE BALLS						NIL									
SURGICAL ANAESTHESIA	1			FIXED EYES						Most of the surgical operations									
	2																		
	3																		
	4																		
IV MEDULLARY PARALYSIS													Never attempted						

Anesthetics Classification

1. Inhaled

- a. **Volatile liquids**
 - halothan
 - ether
 - enflurane
 - sevoflurane
 - isofluran
- b. **Gasses**
 - cyclopropan
 - nitrous oxide
 - xenon

Non-inhaled (intravenous) (1)

1. Barbiturates

- sodium thiopental**
- hexobarbital**
- thiobutabarbital**
- methohexital (used as sodium salts)**

2. Benzodiazepines

midazolam

diazepam

lorazepam

Non-inhaled (intravenous) (2)

3. Different structures

- Phencyclidine derivatives: ketamine
- Engenol derivatives: propanidide
- Diizopropylphenyl derivatives : propofol
- Imidazole derivatives: etomidate
- Opioid analgesics: fentanyl, alfentanyl, trimeperidine, morphine
- With steroid structure: hydroxidione
- GABA derivative: sodium oxybutirate
- Central alpha2-AM: dexmedetomidine

Hypotheses of General Anesthesia

1. Lipid Theory: based on the fact that anesthetic action is correlated with the oil/gas coefficients.
 - The higher the solubility of anesthetics is in oil, the greater is the anesthetic potency.

2. Protein (Receptor) Theory: based on the fact that anesthetic potency is correlated with the ability of anesthetics to inhibit enzymes activity of a pure, soluble protein. Also, attempts to explain the GABA_A receptor is a potential target of anesthetics action.

Other Theories included

- Binding theory:
 - Anesthetics bind to hydrophobic portion of the ion channel



Mechanism of Action

UNKNOWN!!

- **Most Recent Studies:**
 - General Anesthetics **acts on the CNS** by modifying the electrical activity of neurons at a molecular level by modifying functions of ION CHANNELS.
 - This may occur by anesthetic molecules binding directly to ion channels or by their disrupting the functions of molecules that maintain ion channels.

Molecular theories

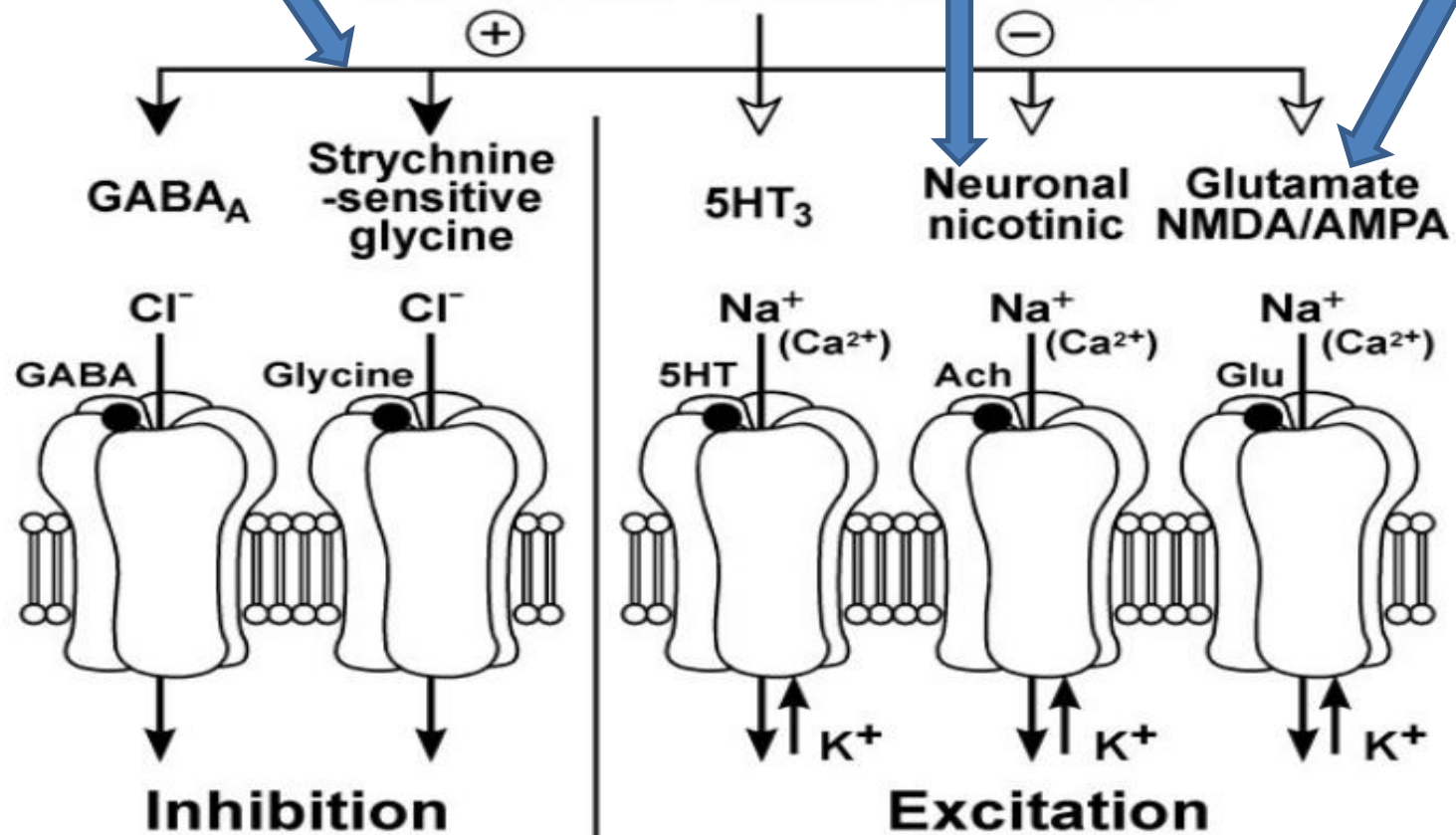
GABA – how do they work

- Critical volume hypothesis
 - Disruption of the function of ionic channels
- Perturbation theory
 - Disruption of annular lipids assoc. with ionic channels
- **Receptors**
 - **Inhibitory** – GABA_A, glycine  enhance
 - **Excitatory** - nACh, NMDA  inhibit

Many
inhalational
anaesthetics,
barbiturates,
benzodiazepines,
propofol

Fluorinated
anaesthetics
barbiturates

N₂O,
ketamine



Thiopentale

Intravenous anaesthetics

- **Problems with use**
 - Extremely painful and limb threatening when given intra-arterially
 - Hypersensitivity reactions 1: 15 000
- **Contraindications**
 - Porphyria

Propofol

- Phenolic derivative
- **Dose** 1- 2.5 mg/kg
- **Effects** : hypnosis
- **Side effects**
 - CVS: myocardiac depression, ↓SVR, ↓CO
 - Respiratory depression
 - Hypersensitivity 1 : 100 000



Propofol



- Other effects
 - Pain on induction
 - Nausea and vomiting less likely
 - Better for LMA placement than thiopentale
- Relative **contraindications**
 - Children under 3

Etomidate

- Ester
- **Dose** 0.3 mg/kg
- **Effects** : hypnosis
- **Side effects**
 - CVS: very little effect on HR, CO, SVR
 - Minimal respiratory depression



Etomidate

Intravenous anaesthetics

- **Problems with use**
 - Pain on injection
 - Nausea and vomiting
 - Adrenocortical suppression
 - Hypersensitivity reaction 1: 75 000
- **Relative Contraindications**
 - Porphyria

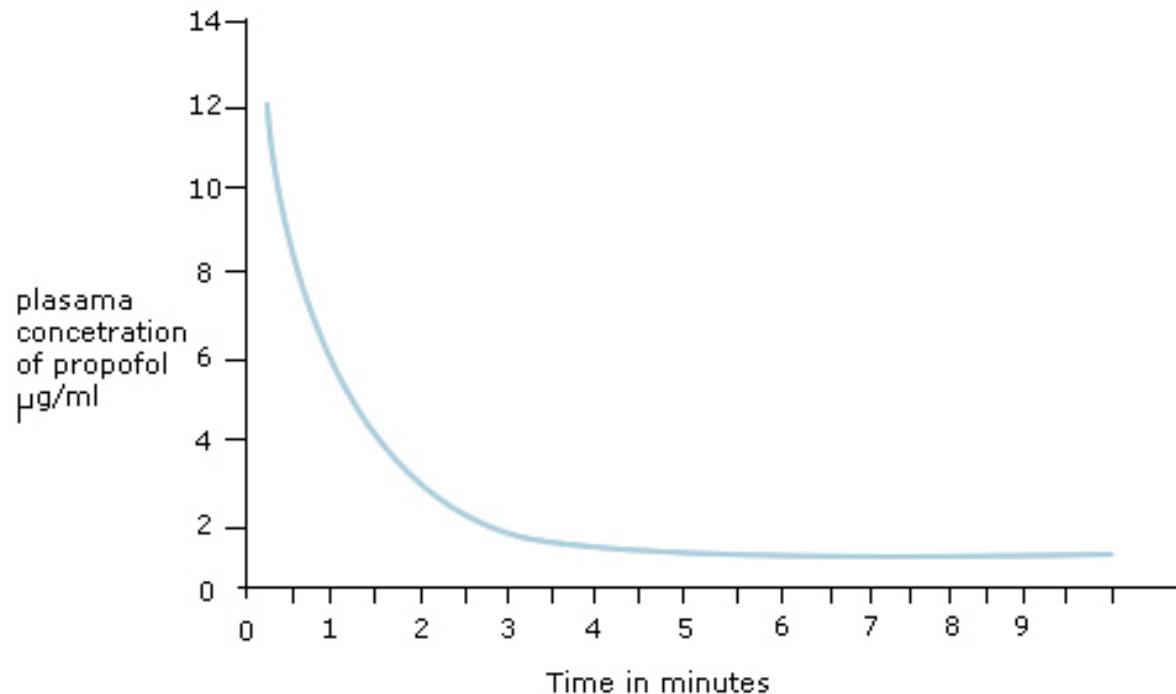
Ketamine

- Phencyclidine derivative
- CV effects - ↑ **HR, BP**, CO, O₂ consumption
- RS - ↑ RR, preserved laryngeal reflexes
- CNS – **dissociative anaesthesia, analgesia, amnesia**
- Use – analgesic in Emerg. Med

Pharmakokinetics

Intravenous anaesthetics

- Recovery from single bolus 5-10 min



Intravenous anesthetics

Neuroleptanalgesia :

- It is characterized by general quiescence, psychic indifference and intense analgesia without total loss of consciousness.
- Combination of Fentanyl and Droperidol as **Talamonal**
- Used for endoscopies, angiography and minor operations.

INHALATION ANESTHETICS

- Primarily used for maintenance of anesthesia after administration of an IV agent (induction of A)
- Very steep dose–response curves
- Very narrow therapeutic indices
- Have no specific antagonists

INHALATION ANESTHETICS

Common features

- decrease cerebrovascular resistance→increased brain perfusion
- cause bronchodilation
- decrease both spontaneous ventilation and hypoxic pulmonary vasoconstriction
- Factors affecting lungs - body compartments movement:
 - solubility in blood and tissues
 - blood flow.

INHALATION ANESTHETICS

Potency

- is defined quantitatively as the minimum alveolar concentration (MAC), the end-tidal concentration of inhaled anesthetic needed to eliminate movement in 50% of patients stimulated by a standardized incision.
- MAC is the median effective dose (ED50) of the anesthetic, expressed as the percentage of gas in a mixture required to achieve that effect.

INHALATION ANESTHETICS

Halothane

- the prototype to which newer inhalation anesthetics are compared (replaced in most countries).

Indications:

- Potent anesthetic but a relatively weak analgesic. => coadministered with *nitrous oxide*, opioids, or local anesthetics.
- Potent bronchodilator. (Desflurane – bronchospasm)
- Relaxes both skeletal and uterine muscles => used in obstetrics when uterine relaxation is indicated.
- Is not hepatotoxic in children (unlike in adults), has pleasant odor => suitable in pediatrics for inhalation induction, although **sevoflurane** is now the agent of choice.

INHALATION ANESTHETICS

Halothane

Pharmacokinetics:

- oxidatively metabolized in the body to tissue-toxic hydrocarbons (ex. trifluoroethanol) and bromide ion => responsible for toxic reactions (1 in 10,000) in some adults (mainly females)

This begins as a fever, followed by anorexia, nausea, and vomiting, and possibly signs of hepatitis. 50% of affected patients may die of hepatic necrosis.

To avoid this condition, *halothane* is not administered at intervals of less than 2 to 3 weeks.

- For other halogenated inhalation anesthetics hepatitis has a much lower incidence than with *halothane*.

INHALATION ANESTHETICS

Halothane

- **Side effects**
- **CV:**
 - *atropine*-sensitive bradycardia.
 - Cardiac arrhythmias - *Halothane* can sensitize the heart to effects of catecholamines such as norepinephrine.
 - concentration-dependent hypotension (treated with alpha-AM, ex. *Phenylephrine*).
- **Hepatitis => hepatic necosis**

INHALATION ANESTHETICS

Halothane

Side effects

- **Malignant hyperthermia :**
 - drastic and uncontrolled increase in skeletal muscle oxidative metabolism, **SkM hypertonus**, overwhelming the body's capacity to supply oxygen, remove carbon dioxide, and regulate temperature (**hyperthermia**), eventually leading to **acute renal failure, circulatory collapse** and **death** if not treated immediately.
 - Burn victims and individuals with muscular dystrophy, myopathy, myotonia, and osteogenesis imperfecta are susceptible.
 - *Treatment:*
 - Dantrolene
 - Monitoring and support for respiratory, circulatory, and renal problems.

Choice of induction agent

Intravenous anaesthetics

- 1. Are any agents absolutely contraindicated ?
 - Hypersensitivity, porphyria
- 2. Are there any patient related factors ?
 - CVS status
 - Epilepsy
- 3. Are there any drug related factors ?
 - Egg allergy

DRUGS ACTING ON AFFERENT NS

(Diminish the sensitivity
of nerve endings)

LOCAL ANESTHETICS

- Local anesthetics are drugs used to prevent or relieve pain in specific regions of the body without loss of consciousness
- Local anesthetics block pain sensation by blocking nerve conduction
- **Mechanism of action**
- Local anesthetics reversibly bind to the voltage-gated Na⁺ channel, block Na⁺ influx, and thus block action potential and nerve conduction.

Classification

A. According to the origin

- ***Natural***
 - Cocaine
- ***Synthetic***
 - Tetracaine, procaine, chloroprocaine, lidocaine,
 - cynocaine, prilocaine, mepivacaine, bupivacaine,
 - ethidocaine, benzocaine, articaine;
- ***From different groups***
 - phenol,
 - diphenhydramine,
 - chlorpromazine

Classification

B. According to the chemical structure

- ***Amide-linked local anesthetics (acetalinidine derivatives)***

- | | | |
|---------------|-----------------|-------------|
| – Articaine | Lidocaine | Mepivicaïne |
| – Prilocaine | Etidocaine | Bupivicaïne |
| – Ropivicaïne | Levobupivicaïne | |

- ***Ester linked local anesthetics (paraaminobenzoic acid derivatives)***

- | | | |
|--------------|----------------|----------|
| – Benzocaine | Chloroprocaine | Procaine |
| – Tetracaine | Cocaine | |

Classification

C. According to the potency

- ***Very potent***
 - tetracaine, bupivacaine, etidocaine, cinchocaine,
 - articaine;
- ***Of medium potency***
 - Lidocaine, trimecaine, mepivacaine,
 - benzocaine, cocaine, prilocaine;
- ***Of low potency***
 - Procaine Chlorprocaine

Classification

D. According to the duration of action

- ***Short acting (20-60 min.)***
 - Procaine Chloroprocaine
 - Cocaine Tetracaine
- ***Of medium duration: (1-2 h.)***
 - Lidocaine Trimecaine Prilocaine
 - Mepivacaine Articaine
- ***Long acting (>3 h.)***
 - Bupivacaine Etidocaine Cincocaine
 - Benzocaine

Classification

E. According to the type of anesthesia (1)

- ***Superficial (terminal, contact) anesthesia***
 - Tetracaine Benzocaine Trimecaine
 - Lidocaine Articaine
- ***Infiltrative anesthesia***
 - Procaine Chloroprocaine Trimecaine
 - Lidocaine Mepivacaine Articaine
 - Prilocaine Bupivacaine Etidocaine

Classification

E. According to the type of anesthesia (2)

- ***Conduction anesthesia***

- Procaine Chloroprocaine Trimecaine Lidocaine
- Mepivacaine Articaine Prilocaine
- Mepivacaine Bupivacaine Etidocaine

- ***Spinal anesthesia***

- Lidocaine Mepivacaine Bupivacaine
- Cincocaine Articaine

- ***All types of the anesthesia***

- Lidocaine

Indications

- Infiltration anesthesia
- Field block
- Nerve block
- Intravenous regional block
- Spinal nerve block
- Epidural nerve block
- Topical anesthesia
- Ventricular tachyarrhythmias (lidocaine)

Metabolism of local anesthetics

- Most ester-linked local anesthetics are quickly hydrolyzed by enzymes (pseudocholinesterase) in blood.
- Amide-linked local anesthetics can be widely distributed via the circulation and are hydrolyzed in the liver.
- Water-soluble metabolites are excreted in the urine.

Toxicity and side effects

A. Central nervous system

- Stimulatory effects: restlessness, tremor, convulsion.
- Suppression at high dosage may lead to respiratory failure.

B. Peripheral nervous system

- Inhibition of transmission at neuromuscular junctions and ganglionic synapse.

C. Smooth muscles

- Depress contractions of intestinal, vascular and bronchial smooth muscles.

Toxicity and side effects

D. Cardiovascular system:

- Decreases the electrical excitability, conduction rate and force of contraction in myocardium.
- Causes dilation of blood vessels.
- Cocaine may cause vasoconstriction, hypertension and cardiac arrhythmias.
- Bupivacaine may cause cardiovascular collapse and ventricular tachycardia.

E. Allergic reactions

ASTRINGENTS

- Any of a group of medicines that shrink mucous membranes and stop or slow secretion of blood, mucous, or other fluids from human body;
- Astringents decrease fluids by:
 - narrowing small blood vessels,
 - drawing water away from organ,
 - coagulating the superficial layers of organ into a crust.

Classification

1. Organic drugs

- Tannin, tannalbin etc.;
- Infusions, decoctions, extracts and tinctures of: sage leaves, chamomile flowers, oak bark, etc.

2. Nonorganic drugs

- | | |
|--------------------------|------------------|
| – Lead acetate; | Silver nitrate; |
| – Basic bismuth nitrate; | Zinc oxide; |
| – Zinc sulphate; | Alum; |
| – Aluminum sulphate | Copper sulphate; |

ASTRINGENTS

- Used to reduce swollen mucous membranes that result from inflammations of the nasal, gastrointestinal, and urinary tracts
- Used to dry up excessive secretions and (in this connection they are often known as styptics) to stop bleeding.

ASTRINGENTS

- Astringent medicines cause shrinkage of mucous membranes or exposed tissues and are often used **internally** to manage discharge of blood serum or mucous secretions (**sore throat, hemorrhages, diarrhea, or with peptic ulcers**).
- **Externally** applied astringents, which cause mild coagulation of skin proteins, dry, harden, and protect the skin (**acne, skin irritations resulting from superficial cuts, allergies, insect bites, or fungal infections such as athlete's foot**).

IRRITANTS

- Mustard plaster
- Oil of turpentine
- Menthol
- Ammonia

EMMOLIENTS (moisturizers)

- Emollients are topical drugs, which reduce water loss from the outer layer of skin (epidermis) by covering it with a protective film.
- Emollients keep the water in the skin where it is needed and allow damaged skin cells on the skin's surface to repair themselves.
- As well as helping the skin to retain water, emollients:
 - moisturize dry skin
 - ease itching
 - reduce scaling
 - soften cracks
 - allow other topical treatments to enter the skin

EMMOLIENTS (moisturizers)

Classification

- Glycerin, vaseline, lanolin;
- Peach oil, olive oil, sunflower oil;
- Regesan (grape seed oil);
- Vinyl

Adverse reactions to emollients

- Irritant reactions
- Allergy
- Folliculitis
- Facial rashes

MUCILAGINOUS DRUGS

- Vegetable or animal substances, which form a colloidal film that protects sensitive endings against irritation thereby reducing harmful pathological reflexes.

Classification

1) Vegetable:

- Starch mucilage;
- Linseed mucilage;
- Infusion of marshmallow;

2) Of protein origin (animal):

- Lizozim

ADSORBENTS

Classification (1):

- ***Active charcoals:***
 - carbo medicinalis, carbosem, Medicas E,
 - carbolong, carbovit, antralen
- ***Anionic resin, synthetic polymers:***
 - cholestyramine, colestipol,
- ***Silicas***
 - silica gel, enterosgel, polysorbate, silard,
 - white clay, smecta

ADSORBENTS

Classification (2):

- ***Natural organic dietary fibers, pectins, alginates***
 - microcrystalline cellulose
 - polifepan,
 - multisorb,
 - algisorb,
 - micoton
- ***Combined drugs:***
 - sums,
 - ultrasorb