

# General anesthetics (pharmacology)

General anesthetics are substances inducing *general anesthesia*, i.e. a **reversible** condition characterized by **unconsciousness, amnesia, analgesia, muscle relaxation**, maintenance of **physiological stability** and **reduced response to surgical stress**.

## Mechanism of action

General anesthetics represent such a heterogeneous group of drugs that the mechanism of their action is explained by two theories.

### Lipid theory

Lipid or biophysical theory considers a high lipophilicity to be the basic prerequisite for an overall anesthetic effect. This theory explains the effect mainly of inhalation anesthetics, the effect of which increases with increasing lipophilia.

Lipophilic substances tend to concentrate in the hydrophobic layer of cell membranes and thus affect their permeability. By this mechanism, they reduce excitability and conductivity and induce anesthesia.

### Protein-receptor theory

Another theory is protein, receptor, protein-receptor or biochemical. It is applicable mainly to intravenous anesthetics and according to it the basis of anesthesia is the interaction of the drug with receptors.

At the center of interest of this theory are the receptors associated with ion channels, mainly **GABA A'** (inhibitory), **NMDA** (receptor for glutamate, type N-methyl-D -aspartate – excitatory), **N-receptor** or receptor for **glycine** (inhibitory).

## Stages of general anesthesia

We can observe these stages when using inhalation anesthetics, although they were only really visible during anesthesia using ether, they are not very clear in today's anesthetic procedures - mainly stage II.

*AND. stage: period of analgesia* – The patient loses consciousness and the perception of pain is reduced.

*II. stage: period of excitation* – The patient is in unconsciousness, but many reflexes are strengthened, motor restlessness; at this stage the risk of death and cardiac arrest is greatest

*III. stage: the period of surgical anesthesia* – Begins with the reappearance of regular breathing and ends with the cessation of spontaneous breathing; muscle tone decreases, spontaneous movements disappear, all reflexes disappear with deepening anesthesia.

*IV. stage: period of spinal depression* – depression of the vasomotor respiratory center, death can occur within minutes.

## Inhalation anesthetics

They are gaseous substances or volatile liquids whose pharmacokinetics are very specific.

### Pharmacokinetics

The effect of general inhalation anesthetics practically affects **absorption**, **distribution** and elimination. The substances used today are practically not "metabolized" and are eliminated by the lungs in unchanged form. For most general anesthetics, this property, i.e. slight metabolism, is clearly desirable, as they tend to be biotransformed into toxic products (chloroform).

Factors affecting pharmacokinetics are determined by the "properties of the given substance" (primarily physico-chemical) and further by "physiological aspects":

*It is related to the properties of the substance:*

- **'blood/gas distribution coefficient** - in other words, solubility in blood; here it is true that the more soluble the substance is in the blood, the slower the distribution, thus the slower the onset and fading of the effect;
- **oil/gas partition coefficient** - i.e. solubility in lipids; here it can be said that the more liposoluble our anesthetic is, the more effective it will be, since it will like it in the CNS, but it will also readily distribute itself into adipose tissue.

The *physiological factors* affecting the effect of the anesthetic are then:

- **pulmonary ventilation;**
- **cardiac output** which affects blood flow through the lungs.

## Volatile organic liquids

The first general anesthetic was **ether** (more precisely, *diethyl ether*). Its significance today is rather historical. It induces anesthesia with strong analgesia and muscle relaxation. However, the side effects are significant: it often induces vomiting and stimulates bronchial secretion. The advantage is the low price, the disadvantage is the high explosiveness.

Today, mainly '*halogenated derivatives*' are used. Their advantage is that they are not flammable even when mixed with oxygen. They have a slower onset of action than intravenous anesthetics.

### Halothane

- Effective anesthetic, weak muscle relaxant and analgesic; suitable for maintaining anesthesia, has tocolytic properties.
  - "pharmacokinetics": slow onset of action, accumulation in adipose tissue, 20% "metabolized" to toxic "trifluoroacetic acid".
  - cardiovascular and respiratory effects*: **hypotension** due to vasodilation not followed by tachycardia, sensitizes the myocardium to catecholamines action .
  - Other adverse effects*: hepatotoxicity, malignant hyperthermia, **adverse effects are low in children**, so it is a suitable choice.

### Isoflurane

It is currently the **most used inhalation anesthetic**, depending on the dose hypotension occurs, heart rate is slightly increased.

- Unlike halothane*, it is 99% excreted by the lungs, so it is *not hepatotoxic*, and it does not sensitize the myocardium to catecholamines.

### Desflurane

Its properties are similar to isoflurane, only it is **transiently tachycardic**'.

Sevoflurane: It also has properties like isoflurane, it is not tachycardic, it is also used to induce anaesthesia.

## Inorganic gases

Nitrous oxide (N<sub>2</sub>O, paradise gas):

- Colorless and odorless gas, non-flammable, must be mixed with oxygen.
- Effects*: **quick induction and awakening from anesthesia, however, it is weak** and therefore must be used **in combinations**; it is strongly analgesic and mildly euphoric.
- Effect on the cardiovascular system and breathing*: does not reduce heart function and has little effect on breathing, but reduces the body's response to hypoxia.

### Xenon

Xenon is free of adverse effects on the cardiovascular system, but its anesthetic effectiveness is not great and, above all, it is very expensive.

## Intravenous anesthetics

Intravenous anesthetics are mainly used for **short procedures** requiring anesthesia, they are used for **introduction to** inhalation anesthesia or when inhalation anesthetics are contraindicated in the so-called 'TIVA - **total intravenous anesthesia**.

They reach the brain quickly, anesthesia occurs *within tens of seconds* and its termination is caused by redistribution from the CNS, not metabolism.

Thiopental

- Cheap anesthetic *with rapid onset of effect*, lacks analgesic and myorelaxant effect.
- Pharmacokinetics*: the effect starts within 30 seconds and lasts for 5-10 minutes, after the effect wears off, the state of delirium persists (post-barbiturate hangover).
- Effect on cardiovascular system and respiration*: lowers blood pressure but increases heart rate, leads to bradypnea due to '*respiratory center depression*' .
- adverse effects* - **nausea, vomiting**, accumulation occurs upon repeated administration.

### Propofol

- An anesthetic similar to thiopental, but has a number of advantages compared to it; has antiemetic properties.
- Pharmacokinetics*: rapid onset of action, lasting 4-8 minutes, but unlike thiopental, there is no delirium after awakening.
- Effect on the cardiovascular system and breathing*: causes a drop in blood pressure, increases heart rate less than thiopental.

Etomidate

- It is an intravenous anesthetic with a profile similar to thiopental, but it is suitable *in patients with diseases of*

*the cardiovascular system.*

- *Pharmacokinetics*: effect lasts 4-8 minutes.
- *Effect on the cardiovascular system and respiration*: the effect on the cardiovascular system is **minimal** and the effect on respiration is also less than that of thiopental.
- *Adverse effects*: **myoclonic jerks**, suppression of corticosteroid synthesis, nausea, vomiting.

## Midazolam

- It is a benzodiazepine with **myorelaxant, anxiolytic, anticonvulsant and amnestic effects, but lacks analgesic effects; can be used to introduce and maintain anesthesia**; the advantage is the possibility of using "flumazenil" (a specific benzodiazepine antagonist).
- *Pharmacokinetics*: the effect begins more slowly than with thiopental.
- *Effect on the cardiovascular system and breathing*: the risk of cardiovascular and respiratory depression is 'very low'.

## Ketamine

- It is a **NMDA-receptor inhibitor and induces dissociative anesthesia** = a condition where the thalamocortical system is inhibited but limbic system stimulated; this has the effect of **inducing a hypnotic state but not unconsciousness**; characteristic is amnesia and analgesia, but spontaneous breathing and higher muscle tone.
- *Pharmacokinetics*: onset of effect takes about 2 minutes, effect lasts 10-15 minutes; administration does not have to be only i.v., but we can also use exotic routes of administration for general anesthetics, such as p.o., rectal or intranasal administration.
- *Effect on the cardiovascular system and respiration*: is the only general anesthetic that **increases heart rate and blood pressure** and does not depress respiration, which can be used in shock and hypovolemic states.
- *Side effects*: unpleasant vivid dreams to hallucinations – are reduced by simultaneous administration of benzodiazepines.

## Premedication and other drugs

The aim of today's premedication is primarily **anxiolysis**, not the suppression of adverse effects of anesthetics.

- **benzodiazepines** as an anxiolytic,
- **antihistamines** to prevent anaphylactic reactions,
- **anticholinergic** substances prevent reflex bradycardia,
- **H<sub>2</sub>-antagonists, antacids, prokinetics**, which prevent reflux and subsequent aspiration,
- **α<sub>2</sub>-mimetics** improve the stability of the cardiovascular system and contribute to sedation and anxiolysis,
- **neuroleptics** together with opioids serve to induce *neuroleptanalgesia*, a state of sedation, analgesia and amnesia, but not unconsciousness - the patient is able to cooperate,
- **opioids** then we use them for painful injuries.

## Links

### External links

- Template:Acute

### Related Articles

- Psychopharmaceuticals
- General anesthesia
- Anesthesia (pediatrics)
- Inhalation Anesthesia (Paediatrics)
- Anesthetics (Dentistry)
- Local anesthetics (pharmacology)

### References

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