

Central Nervous System

SHEET# 5 - PHARMACOLOGY

LEC. TITLE : GENERAL ANESTHETICS

WRITTEN BY : RAHMA MARIE

ABDALLAH ALKASHI

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kindly report it to
shaghafbatch@gmail.com



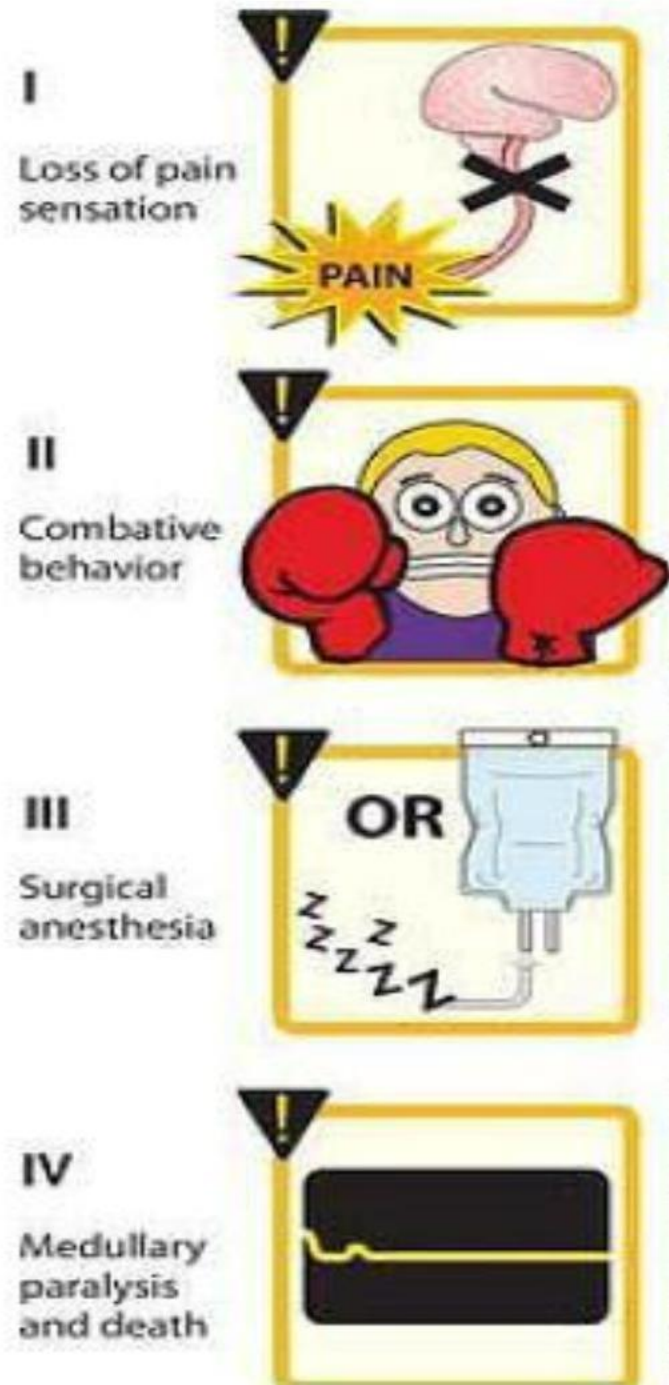


General Anesthetics

Dr. Romany H Thabet

Stage I Analgesia:

- ⌘ Loss of pain sensation results from interference with sensory transmission in the spinothalamic tract.
- ⌘ The patient is conscious and conversational.
- ⌘ Amnesia and a reduced awareness of pain occur as Stage II is approached.



Sheet #1

- "Ane" means sleep. "Sethia" means sensation. The goal of local anesthesia is to stop all feelings of pain, temperature, touch, pressure etc. in a localized area during operations. The goal of general anesthesia is similar + loss of consciousness while preserving the vital signs of the patient.

- Hernia removal surgeries require local anesthesia.

- General anesthesia: step 1 involves (short acting) intravenous anesthetic while step 2 requires inhalation of anesthetic via the endotracheal tube. For this tube to enter smoothly, we need muscle relaxants to relax the muscles. So, first we give depolarizing succinylcholine (works for 5 minutes). Then, a second muscle relaxant is given during the operation: competitive NM blocker. After those are administered, the inhalation anesthesia is given. This anesthetic can also possess muscle relaxant properties. Why do we need to relax the muscles after the tube was already inserted? The muscles need to be relaxed for the sutures to be strong enough to close the incision.

- Ideal anesthetic:

No toxicity

Has muscle relaxant activity

Rapid recovery

Rapid induction

Stage II Excitement:

- ⌘ The patient experiences delirium and possibly violent, combative behavior.
- ⌘ There is a rise and irregularity in blood pressure.
- ⌘ The respiratory rate may increase.
- ⌘ To avoid this stage of anesthesia, a short-acting barbiturate, such as **thiopental**, is given intravenously before inhalation anesthesia is administered.

Reflexes start disappearing and the vital signs stabilize

Stage III Surgical anesthesia:

- ⌘ Regular respiration and relaxation of the skeletal muscles occur in this stage.
- ⌘ Eye reflexes decrease progressively, until the eye movements cease and the pupil is fixed.
- ⌘ Surgery may proceed during this stage.

Stage IV Medullary paralysis:

- ⌘ Severe depression of the respiratory and vasomotor centers occur during this stage.
- ⌘ Death can rapidly ensue unless measures are taken to maintain circulation and respiration.

This stage must be avoided. Depression of centers.

The therapeutic index of anesthetics: the toxic dose/therapeutic dose = dose produced in stage 4/dose produced in stage 3. The wider it is, the safer it is.


Inhalation Anesthetics



- ⌘ Inhaled gases are the mainstay of anesthesia and are used primarily for the maintenance of anesthesia after administration of an intravenous agent.
- ⌘ Inhalation anesthetics have a benefit as the depth of anesthesia can be rapidly altered by changing the concentration of the drug.
- ⌘ Inhalation anesthetics are also reversible, because most are rapidly eliminated from the body by exhalation.

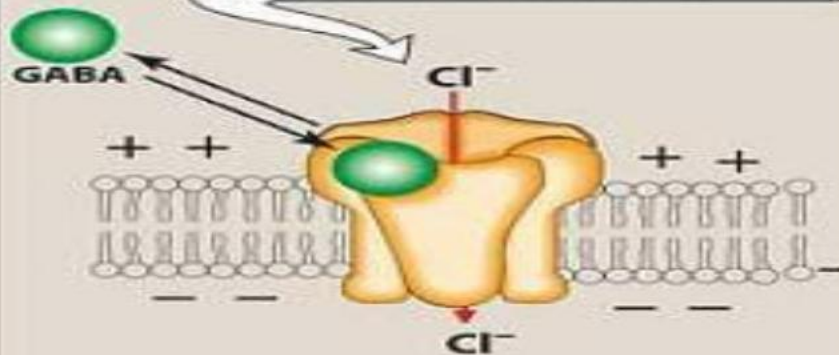
Sheet #2

- We need a lipophilic agent so it is properly absorbed. The inhalant anesthetic needs to be high lipid soluble and low blood soluble to not delay its action and not have a long recovery period.
- The higher the concentration of anesthesia, the more its depth.
- Minimal alveolar concentration of anesthetic: the least concentration in the alveoli that produces surgical anesthesia.
- Inhaled anesthetics leave the CNS through exhalation.

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- ⌘ The movement of these agents from the lungs to the different body compartments depends upon their solubility in blood and tissues as well as on blood flow.
 - ⌘ These factors play a role not only in induction but also in recovery.

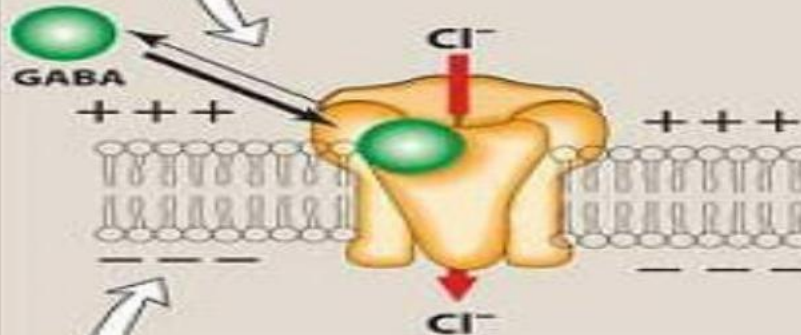
A No anesthetic

Binding of GABA causes the chloride ion channel to open, leading to hyperpolarization of the cell.



B In presence of inhaled anesthetic

Binding of GABA is enhanced by inhaled anesthetics, resulting in a greater entry of chloride ion.



Entry of Cl^- hyperpolarizes cell, making it more difficult to depolarize, and therefore reduces neural excitability.

Halothane



⌘ Therapeutic uses:

1. coadministered with nitrous oxide, opioids, or local anesthetics.
2. Relaxes both skeletal and uterine muscle, and it can be used in obstetrics when uterine relaxation is indicated.
3. Is not hepatotoxic in pediatric patients (unlike its potential effect on adults), and combined with its pleasant odor, this makes it suitable in children for inhalation induction

Adverse effects:



Cardiac effects: vagomimetic and causes atropine sensitive bradycardia. cardiac arrhythmias, concentration-dependent hypotension.

Malignant hyperthermia: idiosyncratic reaction due to abnormal release of calcium from sarcoplasmic reticulum

⌘ **Dantrolene** is lifesaving given as the anesthetic mixture is withdrawn.

⌘ The patient must be carefully monitored and supported for respiratory, circulatory, and renal problems.

Sheet #3

- Halothane has a sweet scent. It is used with other anesthetics. Has a rapid induction and causes muscle relaxation. No need for external muscle relaxants when Halothane is used. Succinylcholine followed by Halothane are enough. Competitive NM blocker is not allowed. Hepatotoxic for adult patients and causes liver cirrhosis even years after the surgery. Also hypotensive which is very expected of Inhaled anesthetics.
- In some patients, the muscles' sarcoplasmic reticulum expels the calcium at a very high rate when Halothane is given. This is called Malignant hyperthermia. It is genetic and can occur as a response to succinylcholine as well.
- Extra info: you do not hook up a patient to a mechanical ventilator unless there is respiratory depression.

Enflurane



- ⌘ Less potent than halothane,
- ⌘ But it produces rapid induction and recovery.
- ⌘ **contraindicated in patients with kidney failure.**

Enflurane anesthesia exhibits the following differences from halothane anesthesia: fewer arrhythmias, less sensitization of the heart to catecholamines, and greater potentiation of muscle relaxants due to a more potent curare-like effect.

A disadvantage of enflurane is that it causes CNS excitation (**not used in patients with seizure disorders**).

Isoflurane



- ⌘ Does not induce cardiac arrhythmias and does not sensitize the heart to the action of catecholamines.
- ⌘ However, it produces concentration-dependent hypotension due to peripheral vasodilation.
- ⌘ It also dilates the coronary vasculature, increasing coronary blood flow and oxygen consumption by the myocardium. This property may make it beneficial in patients with ischemic heart disease.

Sevoflurane



- ⌘ Suitable for **induction in children** (replacing halothane for this purpose).
- ⌘ Recovery is faster than with other anesthetics.
- ⌘ It is metabolized by the liver, releasing fluoride ions; thus, like enflurane, it may prove to be nephrotoxic.

Nitrous oxide



- ⌘ A potent analgesic but a weak general anesthetic.
- ⌘ It is therefore frequently combined with other, more potent agents to attain pain-free anesthesia.
- ⌘ Move very rapidly in and out of the body.
- ⌘ Does not depress respiration, nor does it produce muscle relaxation.
- ⌘ it is the **least hepatotoxic of the inhalation anesthetics.**
- ⌘ It is therefore probably the safest of these anesthetics, provided that at least 20 percent oxygen is always administered simultaneously.

**Causes muscle spasms (not a grimace) that looks like a laugh.
Causes diffusion hypoxia so 20% oxygen needs to be administered.**

Intravenous Anesthetics

- ⌘ Are often used for the rapid induction of anesthesia, which is then maintained with an appropriate inhalation agent.
- ⌘ They rapidly induce anesthesia and must therefore be injected slowly.
- ⌘ Recovery from intravenous anesthetics is due to redistribution from sites in the CNS.

All intravenous anesthetics (except for ketamine which is not used anymore and causes disassociated anesthesia) have redistribution.


Barbiturates (as Thiopental)

- ⌘ Thiopental is a potent anesthetic but a weak analgesic.
- ⌘ An ultrashort-acting barbiturate
- ⌘ Has a high lipid solubility
- ⌘ Quickly enter the CNS and depress function, often in less than 1 minute.
- ⌘ However, diffusion out of the brain can occur very rapidly as well because of redistribution of the drug to other body tissues, including skeletal muscle and, ultimately, adipose tissue.
- ⌘ [Note: This latter site serves as a reservoir of drugs from which the agent slowly leaks out and is metabolized and excreted.]

Thiopental: potent anesthetic, weak analgesic

Fentanyl : potent anesthetic, potent analgesic

Thiopental is an irritant and irritates the upper respiratory system. Not appropriate for asthmatics.

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- ⌘ May contribute to severe hypotension in patients with hypovolemia or shock. All barbiturates can cause apnea, coughing, chest wall spasm, laryngospasm, and bronchospasm. [Note: The latter is of particular concern for asthmatic patients.]
 - ⌘ Barbiturates are contraindicated in patients with acute intermittent or variegate porphyria.

B. Benzodiazepines



- ⌘ Are used in conjunction with anesthetics to sedate the patient.
- ⌘ The most commonly employed is midazolam.
- ⌘ Diazepam and lorazepam are alternatives.
- ⌘ All three facilitate amnesia while causing sedation.

C. Opioids



- ⌘ Because of their analgesic property, opioids are frequently used together with anesthetics;
- ⌘ For example, the combination of morphine and nitrous oxide provides good anesthesia for cardiac surgery.
- ⌘ The most frequently employed opioids are **fentanyl** and its congeners, sufentanil or remifentanil, because they induce analgesia more rapidly than morphine does.

Therapeutic Disadvantages

- Must be delivered using a special vaporizer

- Incomplete anesthesia
- No muscle relaxation
- Must be used with other anesthetics for surgical anesthesia

- Reduces hepatic and renal blood flow
- Lowers blood pressure
- Sensitizes myocardium to actions of catecholamines
- Hepatic toxicity
- Arrhythmias

- Poor analgesia
- Potent anesthesia
- Little muscle relaxation
- Laryngospasm

- Poor analgesia

Inhalation anesthetics

Desflurane

Nitrous oxide

Halothane

Enflurane

Isoflurane

Sevoflurane

Intravenous anesthetics

Thiopental

Ketamine

Fentanyl

Propofol

Therapeutic Advantages

- Good analgesia
- Rapid onset/recovery
- Safe, nonirritating

- Best agent in pediatric patients
- Bronchial smooth muscle relaxation good for patients with asthma

- Good muscle relaxation
- Rapid recovery
- Stability of cardiac output
- Does not raise intracranial pressure
- No sensitization of heart to epinephrine

- Rapid onset/recovery
- Not irritating; useful in children

- Rapid onset of action
- Potent anesthesia

- Good analgesia

- Rapid onset
- Lowers intracranial pressure