General Anesthesia

PHARMACOLOGY

COLLEGE OF DENTISTRY

DR. KHETAM ALHILALI

ANAESTHESIA

- **ANAESTHESIA** - is the reversible loss of response to noxious stimuli.

Definition of anesthesia It is a reversible blocking of pain feeling in whole body or in a part of it using pharmacology or other methods.

- **GENERAL ANAESTHESIA** - when anaesthesia is associated with loss of consciousness. loss of sensory perception of the entire body.

– Intravenous

– Inhalation (volatile)

– Combined, balanced

(TIVA -- Total Intra Venous Anaesthesia).

(VIMA-- Volatile Induction and Maintain Anaesthesia).

- **LOCAL ANAESTHESIA** - when consciousness is maintained during anaesthesia. loss of sensory perception over a small area of the body.
- **Regional Anesthesia:** loss of sensation over a specific region of the body (e. g. lower trunk)

Pharmacology

Anesthetic

Greek: an- “without” & aisthesis- “sensation”. Blocked or temporarily taken sensation (including the feeling of pain). Name is suggested by Oliver W. Holmes.

- Reversible, drug-induced loss of consciousness.
- Amnesia & unconsciousness
- Analgesia
- Muscle relaxation
- Attenuation of autonomic responses to noxious stimulation

- **An anesthetic** (American English) or **anaesthetic (British English)** is a drug used to induce anesthesia in other words, to result in a temporary loss of sensation or awareness. They may be divided into two broad classes: general anesthetics, which result in a reversible loss of consciousness, and local anesthetics, which cause a reversible loss of sensation for a limited region of the body without necessarily affecting consciousness.

Pharmacology

General Anesthesia

What Is General Anesthesia?

General anesthesia is medicine you get before some types of surgery to make you sleep and prevent you from feeling pain.

General Anesthesia Procedure

General anesthesia works by interrupting nerve signals in your brain and body. It prevents your brain from processing pain and from remembering what happened during your surgery.

Goal of anesthesia

- **Goal of anesthesia** : To create a reversible condition of comfort quiescence, and physiological stability in a patient before during and after performance of a procedure that would otherwise be painful frightening or hazardous.
- **Purpose**
  - **Analgesia-loss of response to pain**
  - **Amnesia-loss of memory,**
  - **Immobility- loss of motor reflexes**
  - **Hypnosis-loss of consciousness**
  - **Skeletal muscle relaxation**.

Effects of general anesthesia

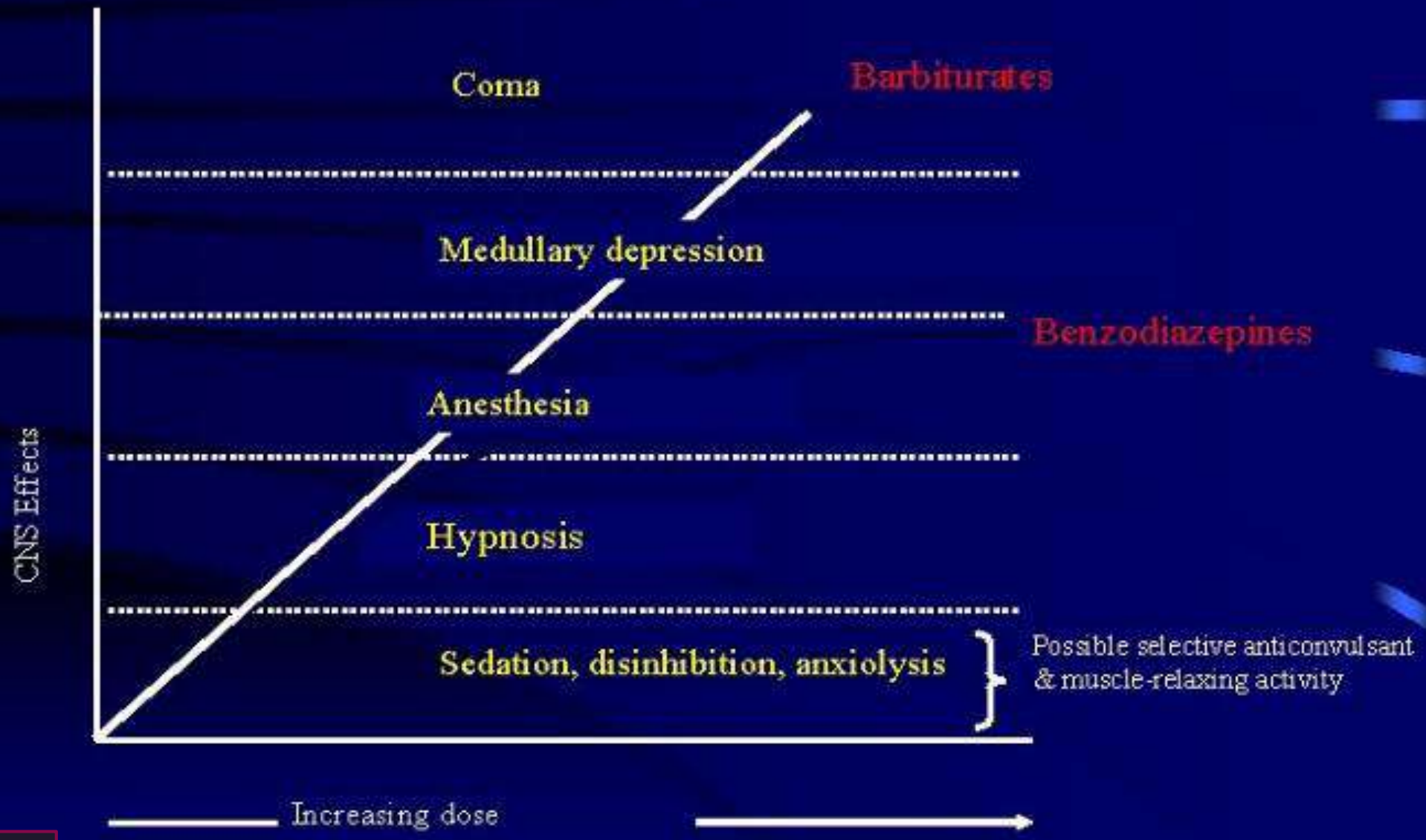
- **Low Dose Effects**

1. Amnesia
2. Euphoria
3. Analgesia
4. Hypnosis
5. Excitation
6. Hyperreflexia

- **• High Dose Effects**

1. Deep sedation
2. Muscle relaxation
3. Diminished motor responses
4. Diminished autonomic responses
5. Myocardial protection from ischemia
6. Cardiovascular/respiratory depression
7. Hypothermia
8. Nausea, vomiting
9. Death (1 per 250, 000)

Dose Response Relationships



A- General Anaesthesia

- General anaesthesia is a reversible state of central nervous system (CNS) depression,
- Causing loss of response to and perception of stimuli. For patients undergoing surgical or medical procedures, **anaesthesia provides five important benefits:**
- a. Sedation and reduced anxiety
- b. Lack of awareness and amnesia
- c. Skeletal muscle relaxation
- d. Suppression of undesirable reflexes
- e. Analgesia

Classification

There are two types of anaesthetics

- **A. INHALATIONAL**
- **Gases**

1. Nitrous oxide

- **Volatile Liquids**

1. Halothane
2. Enflurane
3. Isoflurane
4. Desflurane
5. Sevoflurane
6. Methoxyflurane
7. Trichloro-ethylene

- **B. Intravenous :**

❖ Ultra short Barbiturate

1. Thiopental

❖ Non Barbiturate:

1. Benzodiazepines
2. Propofol
3. Propanidid
4. Neurolept analgesia
5. Etomidate
6. Ketamine

Combination of drugs

- **Because no single agent provides all desirable properties,**
- **Several categories of drugs are combined to produce optimal anesthesia**
- Preanesthetics help calm patients, relieve pain, and prevent side effects of subsequently administered anesthetics or the procedure itself.
- In addition, the neuromuscular blockers facilitate tracheal intubation and surgery.
- Potent general anesthetics usually are delivered via inhalation and/or intravenous (IV) injection.

Minimal alveolar anesthetic concentration (MAC)

Minimal alveolar anesthetic concentration (MAC) :

Minimum alveolar concentration or **MAC** is the concentration of a vapour in the alveoli of the lungs that is needed to prevent movement (motor response) in 50% of patients in response to surgical (pain) stimulus. MAC is used to compare the strengths, or potency, of anaesthetic vapours.

MAC is small for potent anesthetics, as halothane & large for weak anesthetics as N2O

Anesthetic

- Anesthetic, also spelled anaesthetic, any agent that produces a local or general loss of sensation, including pain.
- Anesthetics achieve this effect by acting on the brain or peripheral nervous system to suppress responses to sensory stimulation. The unresponsive state thus induced is known as anesthesia.

The ideal anaesthetic agent

- **Ideal of anesthesia :**
- 1. Induce a smooth and rapid loss of consciousness
- 2. Allowing for a prompt recovery after administration is discontinued
- 3. The drug would also possess a wide margin of safety with less adverse effects
- 4. The modern practice of anesthesiology most commonly use of **combinations of intravenous and inhaled drugs . (so called balanced anesthesia technique)** which take advantage of the favorable properties of each agent while minimize their adverse reaction .

STAGES OF ANESTHESIA

- **Stage I : Analgesia Stage, or Disorientation (induction):** This phase occurs between the administration of the drug and the loss of consciousness. This stage is usually described as the "induction stage." Patients are sedated but conversational. Breathing is slow and regular. At this stage, the patient progresses from analgesia free of amnesia to analgesia with concurrent amnesia. This stage comes to an end with the loss of consciousness.

- **Stage II :Excitement, or Delirium (combative behavior)**

– dangerous state Stage The period following a loss of consciousness, characterized by excited and delirious activity. Breathing and heart rate becomes erratic, and nausea, pupil dilation, and breath-holding might occur. Airway manipulation during this stage of anesthesia should be avoided, including both the placement and removal of endotracheal tubes and deep suctioning maneuvers. There is a higher risk of laryngospasm (involuntary tonic closure of vocal cords) at this stage, which may be aggravated by any airway manipulation. Consequently, the combination of spastic movements, vomiting, and rapid, irregular respirations can compromise the patient's airway. Fast-acting agents help reduce the time spent in stage 2 as much as possible and facilitate entry to stage .

STAGES OF ANESTHESIA . Cont.

- **Stage III : Surgical anesthesia** / Extends from onset of regular respiration to cessation of spontaneous breathing. Muscles relax, vomiting stops and breathing is depressed. Eye movements slow and then cease. **Ceased eye movements and respiratory depression are the hallmarks of this stage. Airway manipulation is safe at this level.**
- The patient is ready to be operated on , This has been divided into 4 planes which may be distinguished as:

  -Plane 1 - roving movements of eyeballs.

  -Plane 2 - loss of corneal reflex (surgery).

  -Plane 3 - pupil starts dilating, muscle relaxation.

  -Plane 4 - only abdo respi, fully dilated pupils.

During plane 1, there is still regular spontaneous breathing, constricted pupils, and central gaze. However, eyelid, conjunctival, and swallow reflexes usually disappear in this plane. **During plane 2**, there are intermittent cessations of respiration along with the loss of corneal and laryngeal reflexes. Halted ocular movements and increased lacrimation may also occur. **Plane 3** is marked by complete relaxation of the intercostal and abdominal muscles and loss of the pupillary light reflex. This plane is referred to as **"true surgical anesthesia"** because it is ideal for most surgeries. Finally, **Plane 4** is marked by irregular respiration, paradoxical rib cage movement, and full diaphragm paralysis resulting in apnea.

STAGES OF ANESTHESIA . Cont.

- **Stage IV : Medullary paralysis (Overdose)** –Too much medication has been administered, leading to brain stem or medullary suppression. This results in respiratory and cardiovascular collapse.
- The anesthetist’s priority is to take the patient to stage 3 of anesthesia as quickly as possible and keep them there for the duration of the surgery.
- Not all stages are observed with modern GAs. all stages are Seen mainly with Ether
- This stage begins with respiratory cessation and ends with potential death.
- Skeletal muscles are flaccid, and pupils are fixed and dilated at this stage.
- Blood pressure is typically significantly lower than normal, with weak and thready pulses due to the suppression of the cardiac pump and vasodilation in the peripheral bloodstream. Without cardiovascular and respiratory support, this stage is lethal. Hence, the anesthetist's goal is to transition the patient as soon as possible to stage 3 of anesthesia and keep them there for the duration of the operation.

STAGES OF ANESTHESIA

I

Loss of pain sensation

II

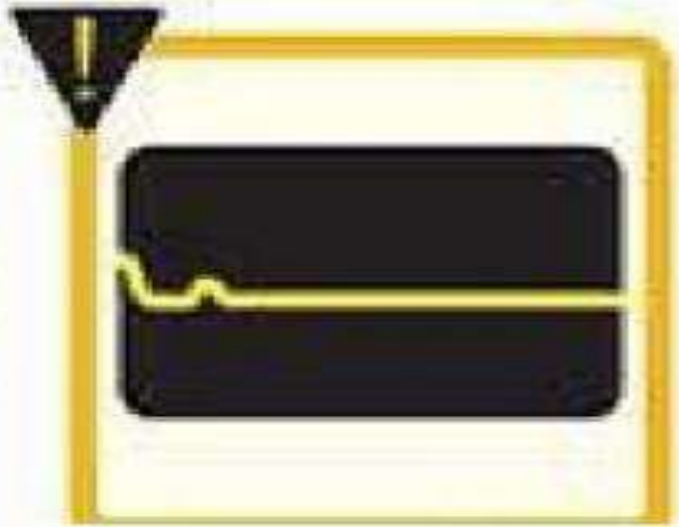
Combative behavior

III

Surgical anesthesia

IV

Medullary paralysis and death



Types of Mechanisms of Action Enhanced

- **Enhanced GABA effect on GABAA Receptors /** γ-Aminobutyric acid type A (GABAA) receptors, the major inhibitory neurotransmitter receptors responsible for fast inhibition in the basal ganglia

1. Inhaled anesthetics
2. Barbiturates
3. Benzodiazepines
4. Etomidate
5. Propofol

- **Block nicotinic receptor subtypes (analgesia) /** The nicotinic receptor is a channel protein that, upon binding by acetylcholine, opens to allow diffusion of cations. Moderate to high conc's of inhaled anesthetics
- **Activate K channels (hyperpolarize**) Hyperpolarization is a change in a cell's membrane potential that makes it more negative. It is the opposite of a depolarization. It inhibits action potentials by increasing the stimulus required to move the membrane potential to the action potential threshold.

Nitrous oxide, ketamine, xenon

- **Inhibit NMDA (glutamate) receptors**

NMDA receptor antagonists are a class of drugs that work to antagonize, or inhibit the action of, the N-Methyl-D-aspartate receptor (NMDAR). They are commonly used as anesthetics for animals and humans

Nitrous oxide, ketamine, xenon , high dose barbeturates.

- **Enhance glycine effect on glycine R's (immobility)** The glycine receptor (abbreviated as GlyR or GLR) is the receptor of the amino acid neurotransmitter glycine. GlyR is an ionotropic receptor that produces its effects through chloride current. It is one of the most widely distributed inhibitory receptors in the central nervous system and has important roles in a variety of physiological processes, especially in mediating inhibitory neurotransmission in the spinal cord and brainstem

Mechanism of general anesthetics action on synapse.

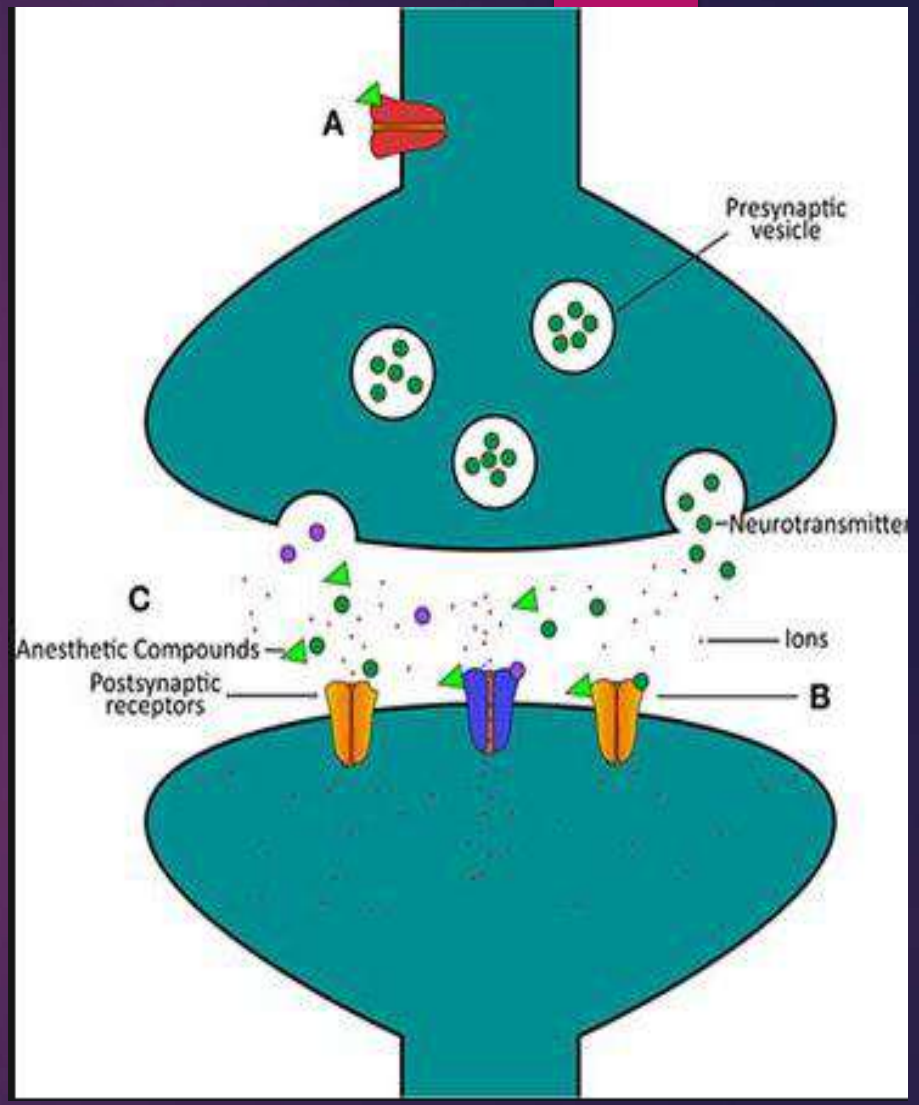
This figure simplified schematic highlighting certain actions of general anesthetics on the Lymnaea synapse.

(A) The anesthetic (green triangle)-activated potassium channel [red channel,] hyperpolarizes neurons, and thus will cause a reduction in presynaptic neurotransmitter release.

(B) A wide range of general anesthetics have been found to inhibit the response of the acetylcholine receptor to neurotransmitter, thus inhibiting synaptic communication.

(C) Represents various potential target sites of anesthetic actions on neurons and their synaptic communication, from presynaptic release of neurotransmitter to postsynaptic response.

Excitatory postsynaptic receptors for acetylcholine (yellow, excitatory, closed channels) are closed by anesthetic (green triangle) exposure, but at similar concentrations inhibitory postsynaptic channels (blue, inhibitory, open channels) remain open. As such, synaptic communication is preferentially suppressed in excitatory synapses as compared to inhibitory synapses at similar anesthetic concentrations .



The effect of Patient factors in selection of anaesthesia

- Drugs are chosen to provide safe and efficient anaesthesia based on the type of procedure and patient characteristics such as organ function, medical conditions and concurrent medications
- **A. Status of organ systems**
- **1. Cardiovascular system**: Anaesthetic agents suppress cardiovascular function to varying degrees. So, they should be used with caution in patients with coronary artery disease, heart failure, dysrhythmias, and other cardiovascular disorders
- **2. Respiratory system**: Respiratory function must be considered for all anesthetics.

  Asthma and ventilation or perfusion abnormalities complicate control of inhalation anesthetics.

The effect of Patient factors in selection of anaesthesia

A. Status of organ systems

- **3. Liver and kidney:** The liver and kidneys influence long-term distribution and clearance of drugs and are also target organs for toxic effects.
- **4. Nervous system:** The presence of neurologic disorders (for example, epilepsy, myasthenia gravis, neuromuscular disease, compromised cerebral circulation) influences the selection of anesthetic.
- **5. Pregnancy**: Special precautions should be observed when anesthetics and adjunctive agents are administered during pregnancy. Effects on fetal organogenesis are a major concern in early pregnancy. Transient use of nitrous oxide may cause aplastic anemia in the fetus. Oral clefts have occurred in fetuses when mothers received benzodiazepines in early pregnancy. Benzodiazepines should not be used during labor because of resultant temporary hypotonia and altered thermoregulation in the new born.

The effect of Patient factors in selection of anaesthesia

B- Concomitant use of drugs

- **B- Concomitant use of drugs**
- **1. Multiple adjunct agents:** Premedications play an important role in anesthesia as they can facilitate the smooth induction of anesthesia and lower required anesthetic doses. However, they can also enhance undesirable anesthetic effects (hypoventilation) and, when coadministered, may produce negative effects not observed when given individually.
- **2. Concomitant use of other drugs**: Patients may take medications for underlying diseases or abuse drugs that alter response to anesthetics. For example, alcoholics have elevated levels of liver enzymes that metabolize anesthetics, and drug abusers may be tolerant to opioids.

Pre-surgical evaluation

- Before general anesthesia is administered, patients will have a pre-surgery assessment to determine the most appropriate drugs to use, the quantities of those drugs and in which combination.

Some of the factors to be explored in a pre-surgical evaluation include:

1. body mass index (BMI)
2. medical history
3. age
4. current medications
5. fasting time
6. alcohol or drug intake
7. pharmaceutical drug use
8. mouth, dental and airway inspection
9. observation of neck flexibility and head extension

It is essential that these questions are answered accurately. For instance, if a history of alcohol or drug use is not mentioned, an inadequate amount of anesthesia might be given which could lead to dangerously high blood pressure or unintended intraoperative awareness.

PREANESTHETIC MEDICATION

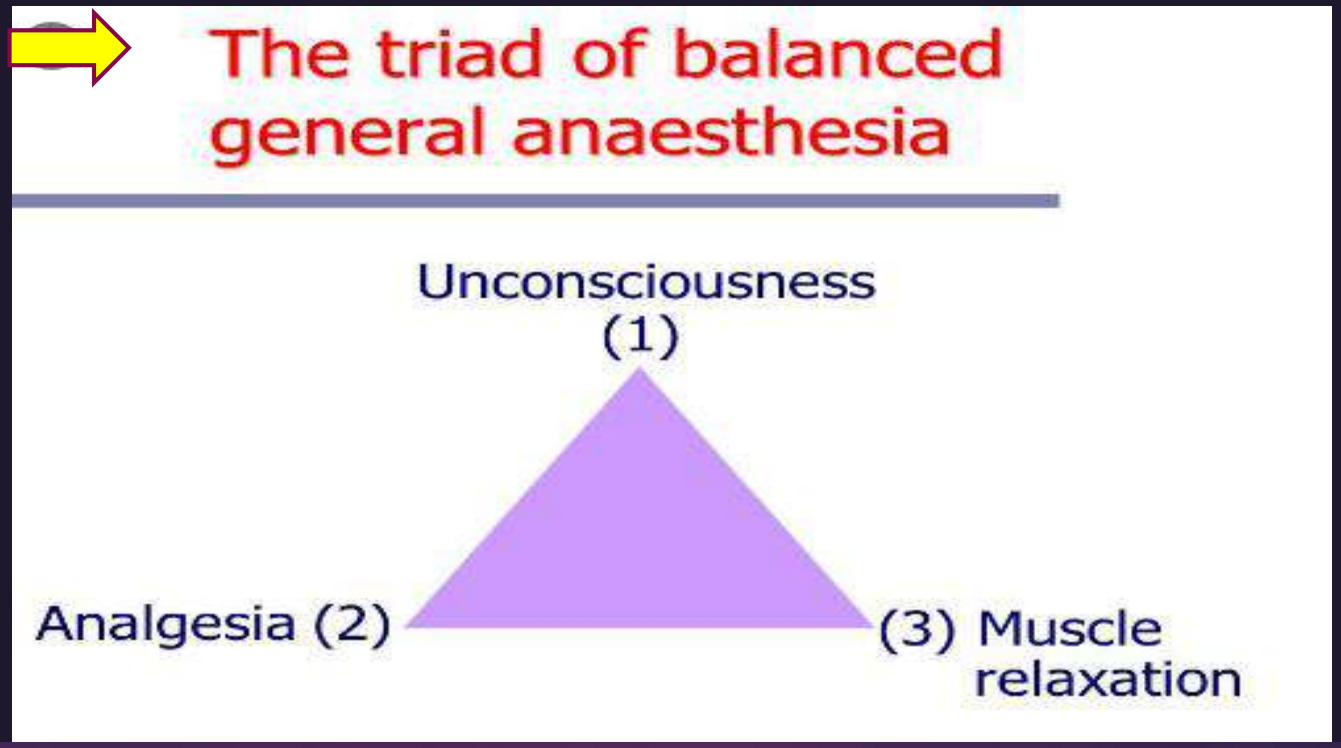
- It is the use of drugs prior to anesthesia to make it more safe and pleasant.
  - To relieve anxiety – Benzodiazepines.
  - To prevent allergic reactions – Antihistaminics.
  - To prevent nausea and vomiting – Antiemetics.
  - To provide analgesia – Opioids.
  - To prevent acidity – Proton Pump Inhibitor.
  - To prevent bradycardia and secretion – Atropine.

Preanesthetic Medications

- Benzodiazepines
  - Reduce anxiety
  - Midazolam, diazepam
- Barbiturates
  - Sedation
  - Pentobarbital
- Antihistamines
  - Prevention of allergic reactions
  - Diphenhydramine
- Antiemetics
  - Prevent aspiration of stomach contents
  - Reduce postsurgical nausea and vomiting
  - Ondansetrone **Brand name: Zofran**
- Opioids
  - Provide analgesia
  - Fentanyl
- Anticholinergics
  - Amnesia, prevent bradycardia, and fluid secretion
  - Scopolamine
- Muscle relaxants
  - Facilitation of intubation

Balanced Anaesthesia

- **Balanced anaesthesia uses selective drugs**
  1. Unconsciousness Intravenous and inhalational ➡ anaesthetics
  2. Analgesia ➡ Opioids
  3. Muscle Relaxation ➡ Neuromuscular blockers



The Process of General Anaesthesia

- 1.Preparation
  - Monitoring
  - IV access
  - IV infusion
  - other “lines”Preoxygenation
- 2.Induction
  - IV Muscle relaxant
  - Manual ventilation
  - Tracheal intubation
  - Maintenance
- 3. Maintenance
  - Ventilation

Oxygen 30% . Nitrous oxide 70%. Isoflurane 0.5 - 1 %

- plus as required: Muscle relaxant, Opioid

± Regional block

- 3.Emergence
  - Cessation of inhaled agents
  - Reversal of muscle relaxants
  - Extubation
- 4. Recovery
  - Return of consciousness
  - Analgesia
  - Management of complications
    - Nausea and vomiting
    - Cardiorespiratory
    - Hypothermia

Physical Property

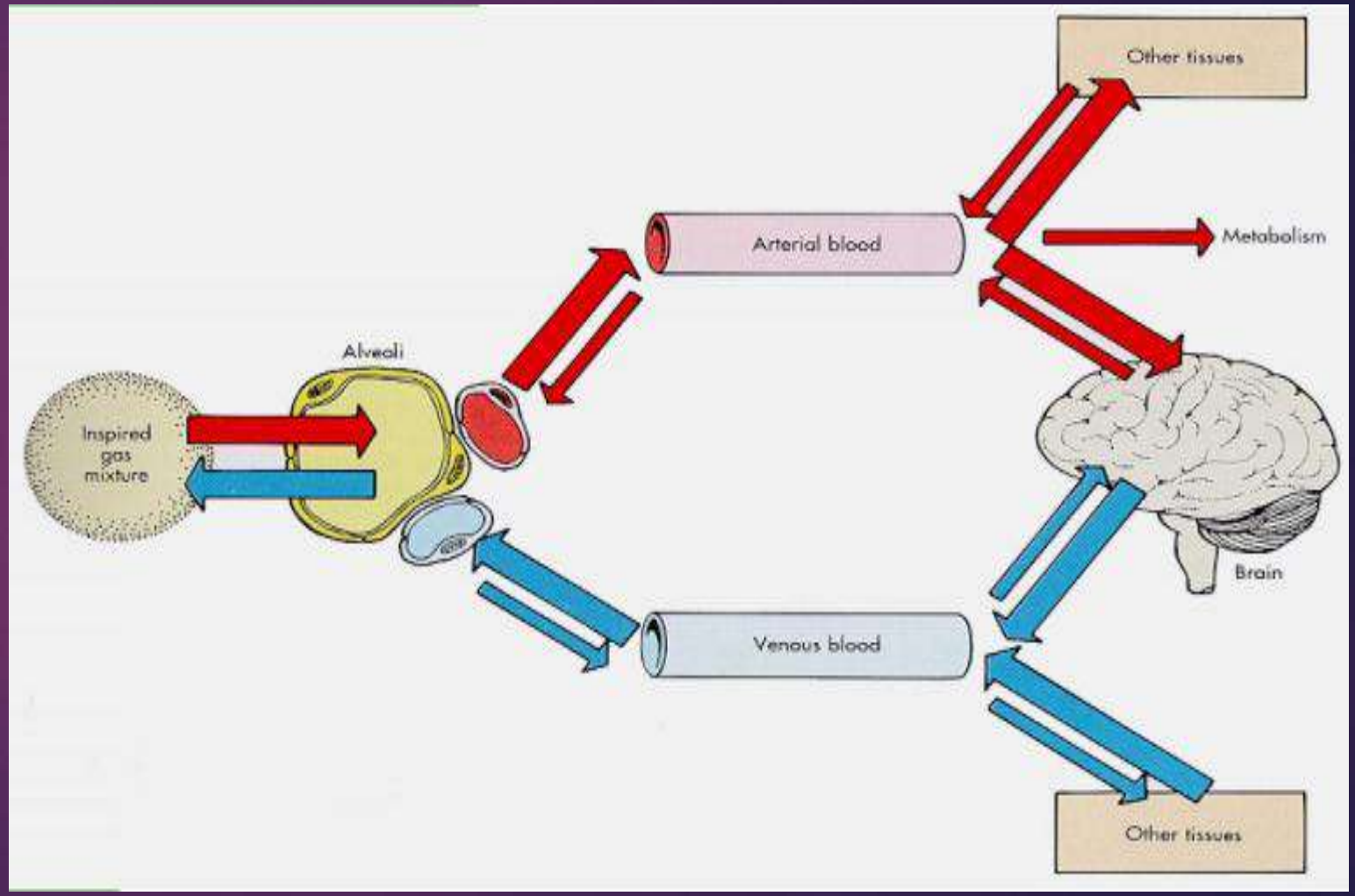
1. Non-flammable, non-explosive at room temperature
2. Stable in light
3. Liquid and vaporizable at room temperature i.e. low latent heat of vaporization
4. Stable at room temperature, with a long shelf life
5. Stable with soda lime, as well as plastics and metals

Biological Properties

1. Pleasant to inhale, non-irritant, induces bronchodilatation
2. Low blood: gas solubility - i.e. fast onset
3. High oil: water solubility - i.e. high potency
4. Minimal effects on other systems - e.g. cardiovascular, respiratory, hepatic, renal or endocrine
5. No biotransformation - should be excreted ideally via the lungs, unchanged
6. Non-toxic to operating theatre personnel

Pathway for General Anesthetics

Inhalational anesthesia refers to the delivery of gases or vapors from the respiratory system to produce anesthesia.



Pharmacology

Methods of general anesthesia / CIRCUITS:

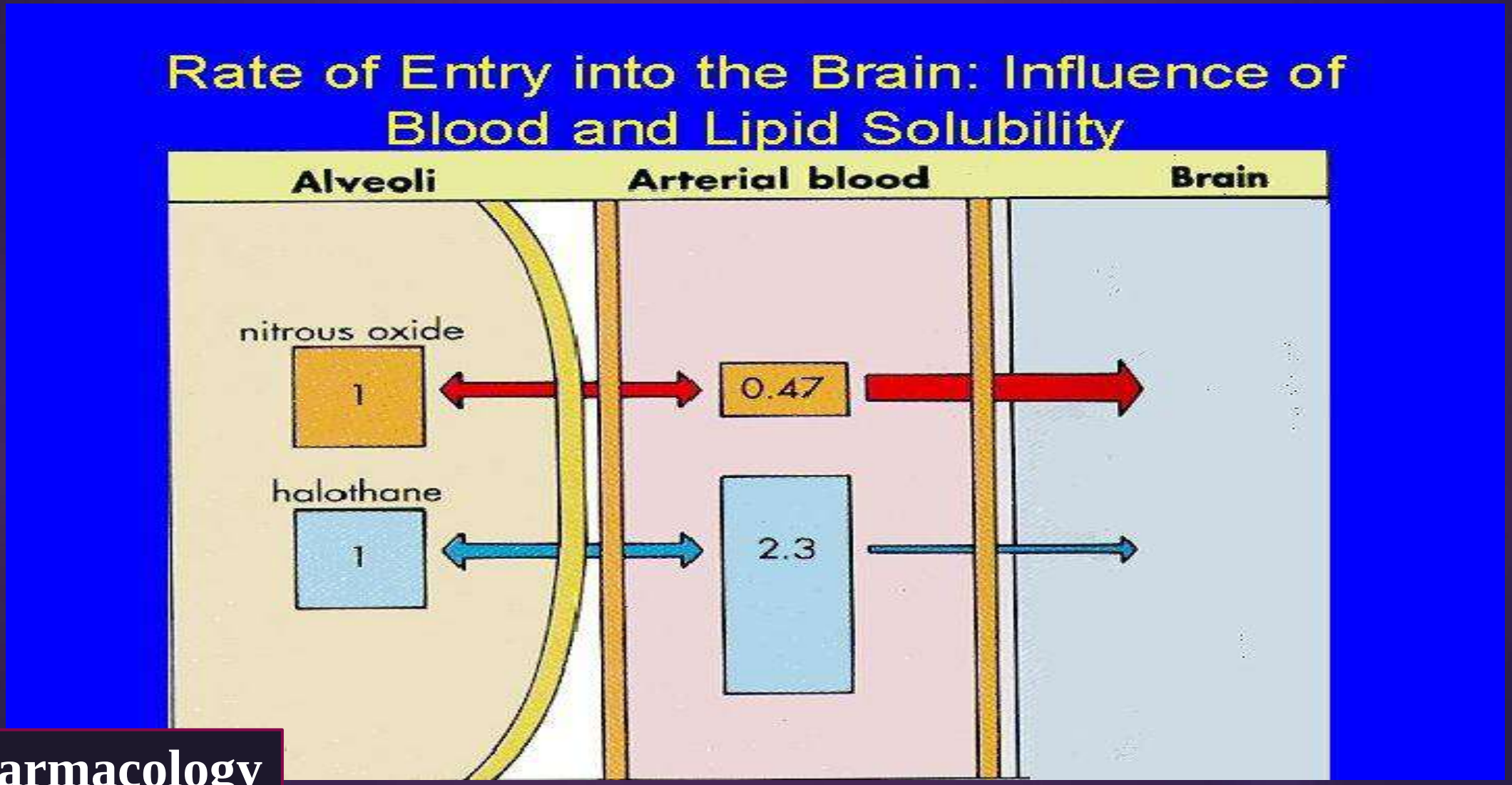
- **No rebreathing ---No reservoir → Open**
- **Reservoir --- No rebreathing → Semi-open**
- **Reservoir ---Partial rebreathing → Semi-closed**
- **Reservoir --- Complete rebreathing → Closed**

Pharmacokinetics of Inhaled Anesthetics

- 1. Amount that reaches the brain Indicated by oil: gas ratio (lipid solubility)
- 2. Solubility of gas into blood,

The lower the blood: gas ratio, the more anesthetics will arrive at the brain

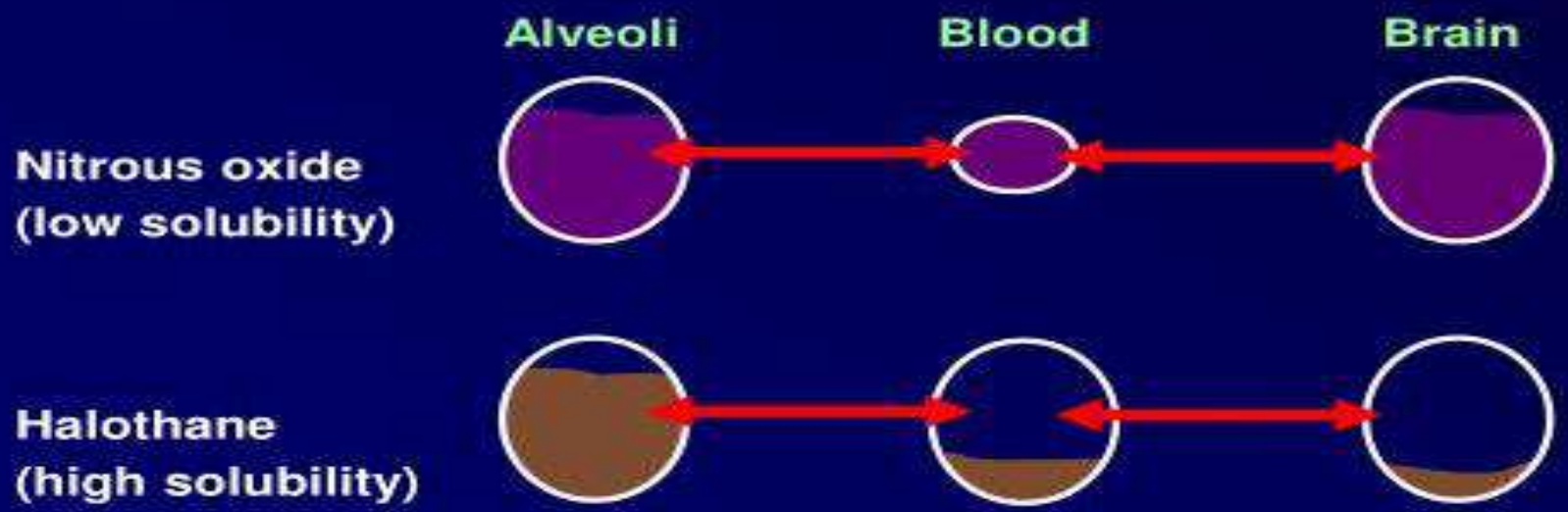
Rate of Entry into the Brain: Influence of Blood and Lipid Solubility



I. Inhalation anesthetics

Pharmacokinetics

- The concentration of a gas in a mixture of gases is proportional to the partial pressure
- Inverse relationship between blood:gas solubility and rate of induction



WHY INDUCTION OF ANESTHESIA IS SLOWER WITH MORE SOLUBLE ANESTHETIC GASES

SOME FEATURES OF INHALED ANESTHETICS

Drug	B/G *	MAC(%)	B(%)**	Onset	Recovery
Nitrous oxide	0.47	>100	none	rapid	rapid
Desflurane	0.42	6	0.02	rapid #	rapid
Sevoflurane	0.65	2	< 3	rapid	rapid
Isoflurane	1.40	1.2	< 1	medium	medium
Halotane	2.30	0.75	> 20	slow	slow

* Blood/gas partition coefficient
** biotransformation
# poor induction because of irritant properties