

Anesthetics

Anesthesia:

Anesthesia is a state characterized by unconsciousness, skeletal muscle relaxation, loss of reflexes and analgesia.

Remember, no single drug can produce all these characteristics. Because no single agent provides all desirable properties, several categories of drugs are combined to produce optimal anesthesia.

Pre-anesthetics:

Preanesthetics help calm patients, relieve pain, and prevent side effects of subsequently administered anesthetics or the procedure itself.

PREANESTHETIC MEDICATIONS

- Antacids
- Anticholinergics
- Antiemetics
- Antihistamines
- Benzodiazepines
- Barbiturates
- Opioids
- Muscle Relaxants

General Anesthetics

General anesthetics comprises of two types:

1. GENERAL ANESTHETICS: INHALED	2. GENERAL ANESTHETICS: INTRAVENOUS
<ul style="list-style-type: none">• Isoflurane• Desflurane• Enflurane• Sevoflurane (in children mostly)• Halothane• Nitrous oxide KEY: ID ESHN	<ul style="list-style-type: none">• Barbiturates• Benzodiazepines• Ketamine• Opioids• Propofol• Etomidate KEY: BB KO PE

Local Anesthetics

- Bupivacaine
- Lidocaine
- Tetracaine

Patient Factors in selection of Anesthesia

Drugs are chosen to provide safe and efficient anesthesia based on the type of procedure and patient characteristics such as organ function, medical conditions, and concurrent medications.

1. Cardiovascular system:

Anesthetic agents suppress cardiovascular function to varying degrees. This is an important consideration in patients with coronary artery disease, heart failure, dysrhythmias, valvular disease, and other cardiovascular disorders.

Hypotension may develop during anesthesia, resulting in reduced perfusion pressure and ischemic injury to tissues.

2. Respiratory system:

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

IV anesthetics and opioids suppress respiration. These effects may influence the ability to provide adequate ventilation and oxygenation during and after surgery.

3. Liver and kidney:

Liver is involved in distribution and kidney is involved in clearance of anesthetics. So these should be monitored before administering anesthesia.

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.
- 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 newborn.

Steps/Stages:

General anesthesia has three stages:

- 1) **Induction**
- 2) **Maintenance**
- 3) **Recovery**

1) Induction:

Induction is the time from administration of a potent anesthetic to development of effective anesthesia. It is very important to avoid the stage of depth of anesthesia. Induction of anesthesia depends on how fast effective concentrations of anesthetic reach the brain.

General anesthesia in adults is normally induced with an IV agent like propofol, producing unconsciousness in 30 to 40 seconds.

Combination of drugs may be used. Halothane and Sevaflurane(non-pungent) is used in children.

2) Maintenance:

After administering the anesthetic, vital signs and response to stimuli are monitored continuously to balance the amount of drug inhaled and/or infused with the depth of anesthesia. Maintenance is commonly provided with volatile anesthetics, which offer good control over the depth of anesthesia. Opioids such as fentanyl are used for analgesia along with inhalation agents.

3) Recovery:

For most anesthetic agents, recovery is the reverse of induction. The anesthetic admixture is withdrawn, and the patient is monitored for return of consciousness. The patient is monitored to assure full recovery, with normal physiologic functions (spontaneous respiration, acceptable blood pressure and heart rate, intact reflexes, and no delayed reactions such as respiratory depression).

Stages of Depth of Anesthesia

The depth of anesthesia has four sequential stages.

- 1- **Stage I—Analgesia**
- 2- **Stage II—Excitement**
- 3- **Stage III—Surgical anesthesia**
- 4- **Stage IV—Medullary depression/paralysis**

1) Stage I—Analgesia:

Loss of pain sensation result from interference with sensory transmission is spinothelmic tract. It begins with administration of anesthetics and lasts till consciousness is lost. Initially, analgesia without amnesia and later both analgesia and amnesia is there.

2) Stage II—Excitement:

It starts after loss of consciousness and proceed to beginning of anesthesia. Patient experiences delirium and can possibly be violent which is combat attitude and aggressive. Irregularity in blood pressure both volume and rate wise be there. Vomiting may occur and one may struggle.

3) Stage III—Surgical anesthesia:

There is gradual loss of muscle tone and reflexes as the CNS is further depressed. Regular respiration and relaxation of skeletal muscles occurs.

It begins with reoccurrence of regular respiration and normal B.P and extends to complete cessation of spontaneous respiration. This is the ideal stage for surgery. Further four plans:

PLAN-1: (this plan should be maintained)

- Moving eye ball
- Pupil size normal
- Conjunctival reflexes normal
- Regular respiration
- Most of the surgeries are done in this stage

PLAN-2: (patient reach this plan occasionally)

- Fixed eye ball
- Pupil constricted at first
- Later on, pupil dilated
- Corneal reflex is abolished
- Respiration regular but shallower than Plan-1

Plan-3:

- Pupil dilated (completely)
- Light reflexed abolished
- Lagging of thoracic respiration behind abdominal respiration

PLAN-4:

- Pupil dilated (completely)
- Light reflex lost
- Lagging of thoracic respiration behind abdominal respiration but later cessation of respiration ensured.

4) Stage IV—Medullary depression/paralysis:

It starts by cessation of respiration and ends with the failure of circulation.

Properties of Ideal Anesthetics:

Divided into:

- 1- For Patient**
- 2- For surgeon**
- 3- For Anesthetist**

1- For Patient:

- It should be pleasant, non-irritant
- Should not cause nausea and vomiting
- Induction and recovery should be smooth with no after effects

2- For Surgeon:

- Should provide adequate analgesia
- Should be non-inflammable and non-explosive
- Should be good muscle relaxant

3- For Anesthetist:

- Administration should be easy, controllable and versatile.
- Margin of safety should be wide (no remarkable fall in b.p).
- Heart, liver and other organs should not be affected
- Should be potent at low concentration
- Rapid adjustment in depth of anesthesia should be possible.
- Should be cheap, stable and easily stored
- Should not react with rubber tubing
- Should not react with soda lime

Aims of Pre-anesthetics:

Pre-anesthetic medication refers to use of drugs before anesthesia to make it more pleasant and safe.

The aims are:

- 1) Relief of anxiety and apprehension
- 2) Pre-operatively to facilitate smooth induction
- 3) Amnesia for the pre and post-operative events
- 4) Supplements analgesic action of anesthetics and potentiate them so that less anesthetic is needed.
- 5) Decrease secretions and vagal stimulation caused by anesthetics.
- 6) Anti-emetic effect extending to the post-operative period
- 7) Decrease acidity and volume of gastric juices.

Inhalation Anesthetics

Inhaled gases are used primarily for maintenance of anesthesia after administration of an IV agent.

A. Common features of inhalation anesthetics:

- Modern inhalation anesthetics are nonflammable, non-explosive agents, including nitrous oxide and volatile, halogenated hydrocarbons.
- These agents decrease cerebrovascular resistance, resulting in increased brain perfusion.
- Cause Bronchodilation
- Also decrease both spontaneous ventilation and hypoxic pulmonary vasoconstriction (increased pulmonary vascular resistance in poorly aerated regions of the lungs, redirecting blood flow to more oxygenated regions).
- Movement of these agents from the lungs to various body compartments depends upon their solubility in blood and tissues, as well as on blood flow.
- These factors play a role in induction and recovery.

B. Potency:

- Potency is defined quantitatively as the minimum alveolar concentration (MAC). MAC is the median effective dose (ED₅₀) of the anesthetic, expressed as the percentage of gas in a mixture required to achieve that effect. Numerically, MAC is small for potent anesthetics such as sevoflurane and large for less potent agents such as nitrous oxide.
- The more lipid soluble an anesthetic, the lower the concentration needed to produce anesthesia and, thus, the higher the potency.

C. Uptake and distribution of inhalation anesthetics

- The principal objective of inhalation anesthesia is a constant and optimal brain partial pressure (P_{br}) of inhaled anesthetic (partial pressure equilibrium between alveoli [P_{alv}] and brain [P_{br}]).
- Alveoli are the “windows to the brain” for inhaled anesthetics.
- The partial pressure of an anesthetic gas at the origin of the respiratory pathway is the driving force moving the anesthetic into the **alveolar space** and, thence, into the **blood** (Pa), which delivers the drug to the **brain** and other **body compartments**.
- Because gases move from one body compartment to another according to partial pressure gradients, steady state is achieved when the partial pressure in each of these compartments is equivalent to that in the inspired mixture.

The time course for attaining this steady state (Equilibrium State) is determined by the following factors:

1. Alveolar wash-in:

This refers to replacement of normal lung gases with the inspired anesthetic mixture. The time required for this process is directly proportional to the functional residual capacity of the lung (volume of gas remaining in the lungs at the end of a normal expiration) and inversely proportional to ventilatory rate.

2. Anesthetic uptake:

It depends upon:

- gas solubility in the blood,
- cardiac output (CO),
- the gradient between alveolar and blood anesthetic partial pressures.

2a) Solubility in blood:

This is determined by a physical property of the anesthetic called the blood/gas partition coefficient and equilibrium.

Drugs with low versus high solubility in blood differ in their speed of induction of anesthesia.

When an anesthetic gas with low blood solubility such as nitrous oxide diffuses from the alveoli into the circulation, little anesthetic dissolves in the blood. Therefore, equilibrium between inhaled anesthetic and arterial blood occurs rapidly, and relatively few additional molecules of anesthetic are required to raise arterial anesthetic partial pressure i.e. the steady state is achieved.

In contrast, anesthetic gases with high blood solubility, such as halothane, dissolve more completely in the blood, and greater amounts of anesthetic and longer periods of time are required to raise blood partial pressure. This results in increased times of induction and recovery and slower changes in depth of anesthesia in response to changes in the concentration.

The solubility in blood is ranked as follows:

halothane > isoflurane > sevoflurane > nitrous oxide > desflurane.

2b) Cardiac output:

Cardiac output affects the delivery of anesthetics. CO affects removal of anesthetic to peripheral tissues, which are not the site of action. For inhaled anesthetics, higher CO removes anesthetic from the alveoli faster (due to increased blood flow through the lungs) and thus slows the rate of rise in alveolar concentration of gas.

- For inhaled anesthetics, higher CO equals slower induction.
- Low CO (shock) speeds the rate of rise of the alveolar concentration of gas, since there is less removal to peripheral tissues.

2c) Alveolar-to-venous partial pressure gradient of anesthetic:

This is the driving force of anesthetic delivery. For all practical purposes, pulmonary end-capillary anesthetic partial pressure may be considered equal to alveolar anesthetic partial pressure if the patient does not have severe lung diffusion disease.

The arterial circulation distributes the anesthetic to various tissues, and the pressure gradient drives free anesthetic gas into tissues. As venous circulation returns blood depleted of anesthetic to the lung, more gas moves into the blood from the lung according to the partial pressure difference.

The greater the difference in anesthetic concentration between alveolar (arterial) and venous blood, the higher the uptake and the slower the induction. Over time, the partial pressure in venous blood closely approximates that in the inspired mixture and no further net anesthetic uptake from the lung occurs.

3. Effect of different tissue types on anesthetic uptake:

The time required for a particular tissue to achieve steady state with the partial pressure of an anesthetic gas in the inspired mixture is **inversely proportional** to the blood flow to that tissue (greater flow results in a more rapidly achieved steady state).

It is also **directly proportional** to the capacity of that tissue to store anesthetic (a larger capacity results in a longer time required to achieve steady state).

Capacity, in turn, is **directly proportional** to the tissue's volume and the tissue/ blood solubility coefficient of the anesthetic.

Four major tissue compartments determine the time course of anesthetic uptake:

- a. **Brain, heart, liver, kidney, and endocrine glands:** These highly perfused tissues rapidly attain steady state with the partial pressure of anesthetic in the blood.
- b. **Skeletal muscles:** These are poorly perfused during anesthesia and have a large volume, which prolongs the time required to achieve steady state.
- c. **Fat:** Fat is also poorly perfused. However, potent volatile anesthetics are very lipid soluble, so fat has a large capacity to store them. Slow delivery to a high-capacity compartment prolongs the time required to achieve steady state in fat tissue.
- d. **Bone, ligaments, and cartilage:** These are poorly perfused and have a relatively low capacity to store anesthetic. Therefore, these tissues have minimal impact on the time course of anesthetic distribution in the body.

4. Washout:

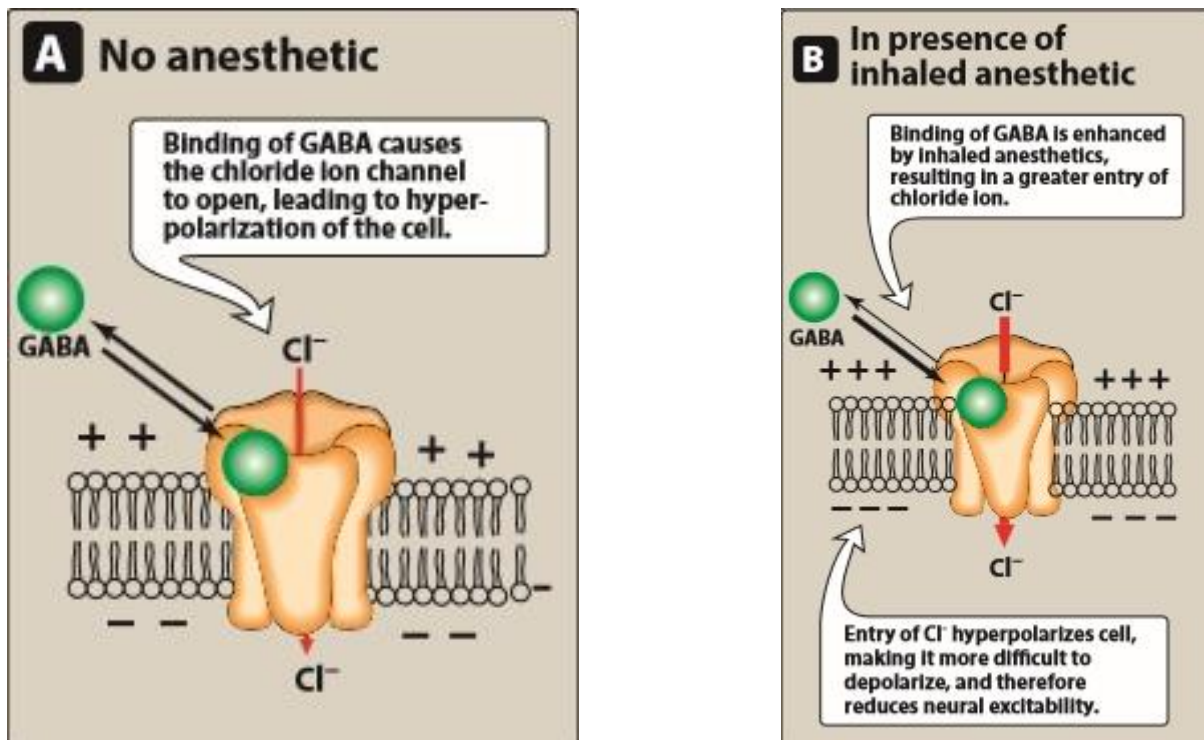
When an inhalation anesthetic is discontinued, the body becomes the "source" that drives the anesthetic back into the alveolar space. The same factors that influence attainment of steady state with an inspired anesthetic determine the time course of its clearance from the body.

Thus, nitrous oxide exits the body faster than halothane.

D. Mechanism of action:

It appears that a variety of molecular mechanisms may contribute to the activity of general anesthetics.

- At clinically effective concentrations, general anesthetics increase the sensitivity of the γ -aminobutyric acid (GABA) receptors to the inhibitory neurotransmitter GABA. This increases chloride ion influx and hyperpolarization of neurons.
- Postsynaptic neuronal excitability and, thus, CNS activity are diminished
- After hyperpolarization, it becomes difficult to depolarize and therefore reduces neuronal excitability.



Halothane:

Halothane is the prototype to which newer inhalation anesthetics are compared. Due to adverse effects and the availability of other anesthetics with fewer complications, halothane has been replaced in most countries.

Therapeutic uses:

- ✓ Halothane is a potent anesthetic but a relatively weak analgesic. Thus, it is usually co-administered with nitrous oxide, opioids, or local anesthetics.
- ✓ It is a potent bronchodilator.

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- ✓ Halothane relaxes both skeletal and uterine muscles and can be used in obstetrics when uterine relaxation is indicated.
- ✓ Halothane is not hepatotoxic in children (unlike its potential effect on adults).
- ✓ Combined with its pleasant odor, it is suitable in pediatrics for inhalation induction, although sevoflurane is now the agent of choice.

Pharmacokinetics:

Halothane is oxidatively metabolized in the body to tissue-toxic hydrocarbons and bromide ion.

Halothane is not administered at intervals of less than 2 to 3 weeks.

Adverse effects:

- **Cardiac effects** (bradycardia, cardiac arrhythmias, concentration-dependent hypotension)
- **Malignant hyperthermia** (a rare life-threatening condition. MH causes a drastic and uncontrolled increase in skeletal muscle oxidative metabolism, overwhelming the body's capacity to supply oxygen, remove carbon dioxide, and regulate temperature, eventually leading to circulatory collapse and death if not treated immediately)

Isoflurane:

- Undergoes little metabolism and is, therefore, not toxic to the liver or kidney.
- Does not induce cardiac arrhythmias or sensitize the heart to catecholamines.
- Produces dose-dependent hypotension.
- It has a pungent odor and stimulates respiratory reflexes (for example, breath holding, salivation, coughing, laryngospasm) and is therefore not used for inhalation induction.

Desflurane:

- Very rapid onset and recovery due to low blood solubility.
- Low volatility, requiring administration via a special heated vaporizer.
- Like isoflurane, it decreases vascular resistance and perfuses all major tissues very well.
- Because it stimulates respiratory reflexes, desflurane is not used for inhalation induction.
- Its degradation is minimal and tissue toxicity is rare.

Sevoflurane:

- Has low pungency, allowing rapid induction without irritating the airways. This makes it suitable for inhalation induction in pediatric patients.
- Rapid onset and recovery due to low blood solubility.
- Metabolized by the liver.

Nitrous oxide:






























- Nitrous oxide ("laughing gas") is a nonirritating potent analgesic but a weak general anesthetic.

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- Used at concentrations of 30 to 50% in combination with oxygen for analgesia, particularly in dentistry.
- Nitrous oxide alone cannot produce surgical anesthesia, but it is commonly combined with other more potent agents.
- Nitrous oxide is poorly soluble in blood and other tissues, allowing it to move very rapidly in and out of the body.
- Nitrous oxide does not depress respiration and does not produce muscle relaxation.
- Within closed body compartments, nitrous oxide can increase the volume or pressure because it replaces nitrogen in various air spaces faster than the nitrogen leaves and causing “diffusion hypoxia,”
- When co-administered with other anesthetics, it has moderate to no effect on the cardiovascular system or on increasing cerebral blood flow, and it is the least hepatotoxic of the inhalation agents. Therefore, it is probably the safest of these anesthetics, provided that sufficient oxygen is administered simultaneously.

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Additional Information (Mainly for Objective)

	<i>Halothane</i>	<i>Isoflurane</i>	<i>Desflurane</i>	<i>Sevoflurane</i>
 Arrhythmias	 Increased	—	—	—
 Sensitivity to catecholamines	 Increased	—	—	—
 Cardiac output	 Decreased	 Decreased to a lesser extent than <i>halothane</i>	 Decreased to a lesser extent than <i>halothane</i>	 Decreased to a lesser extent than <i>halothane</i>
 Blood pressure	 Dose dependent decreased	 Dose dependent decreased	 Dose dependent decreased	 Dose dependent decreased
 Respiratory reflexes	 Inhibited	 Initial stimulation	 Initial stimulation	 Inhibited
 Hepatic toxicity	 Some risk	 Low risk	 Low risk	 Low risk
 Renal toxicity	 Low risk	 Low risk	 Low risk	 Some risk

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