

GENERAL ANESTHETICS

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Introduction

Drugs used to induce loss of pain sensation, consciousness, skeletal muscle relaxation, analgesia, amnesia and inhibitions of undesirable reflexes.



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Types of Anesthesia

- **General anesthesia**
- **Local and regional anesthesia**



CHARACTER S OF AN IDEAL ANESTHETIC DRUG

- 1. Smooth and rapid induction.**
- 2. Rapid recovery.**
- 3. Wide safety margin.**
- 4. Minimal side effects.**

BALANCED ANAESTHESIA

Is the use of more than one drug in combination to fulfil the patient needs.



Beneficial effects



Adverse effects

PRE - ANAESTHETIC MEDICATION

- **Opiates:** induce analgesia.
- **Anticholinergics:** prevent secretion of fluids into the respiratory tract.
- **Sedatives & anxiolytics:** relieve anxiety. E.g. diazepam
- **Antihistaminics:** allergic reactions. e.g. diphenhydramine
- **Antiemetics :** post surgical N&V. e.g. metoclopramide, prochlorperazine
- **H2-receptor blockers:** reduce gastric acidity e.g. ranitidine
- **Thiopental:** smooth induction

ADJUNCTS TO GENERAL ANAESTHETICS

- **Pre-anesthetic medication.**
- **Neuromuscular blocking agents**
 - e.g. succinylcholine, vecuronium, atracurium
 - Facilitate intubation
 - Suppress muscle tone.

General Anesthesia

Inhalational

Gas

Nitrous oxide
Zenon

Volatile liquids

Ether
Halothane
Enflurane
Isoflurane
Desflurane
Sevoflurane
Methoxyflurane

Intravenous

Slower acting

Dissociative anesthesia

Ketamine

Opioid analgesia

Fentanyl

Benzodiazepines

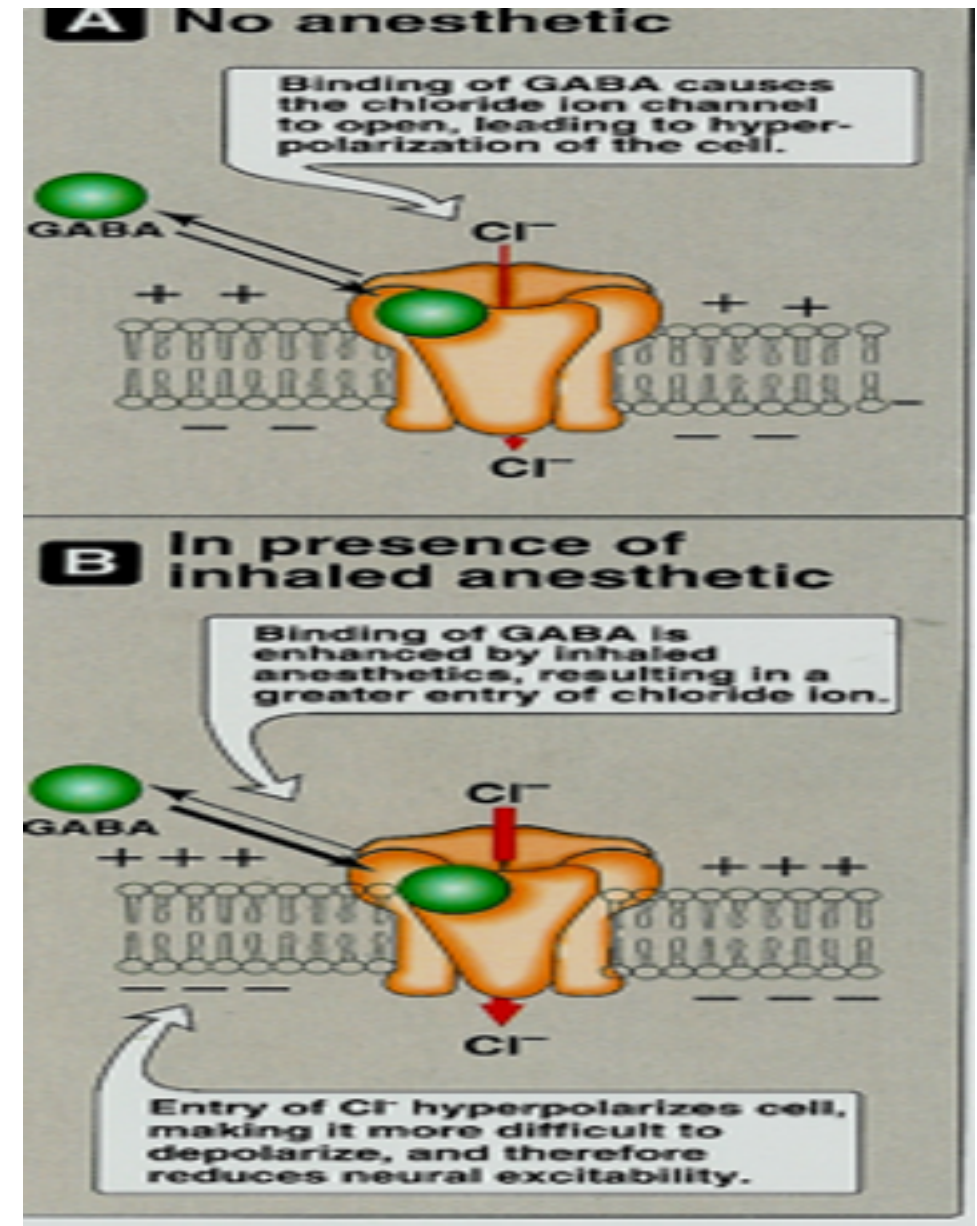
Diazepam
Lorazepam
Midazolam

Inducing agents

Thiopental
Methohexital
Propofol
Etomidate
Droperidol

MECHANISM OF ACTION OF GENERAL ANAESTHETICS

- Enhance the action of GABA and glycine on receptors thus decrease neuronal excitability.



Inhalation anesthetics

Volatile liquids

- **Methoxyflurane**
- **Halothane**
- **Enflurane**
- **Isoflurane**
- **Desflurane**
- **Sevoflurane**
- **Nitrous oxide (Gas)**

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Pharmacokinetics of Inhalation anesthetics

- **Rate of induction**
- **Depth of anesthesia and recovery.**

Inhalation anesthetics

Induction

Time elapsed between onset of administration of anesthetic and development of effective surgical anesthesia.

Maintenance

Time during which the patient is surgically anesthetized.

Recovery

The time from discontinuation of anesthetic drug until consciousness is regained.

Pharmacokinetics of Inhalation anesthetics

Factors controlling induction & recovery

- **The anesthetic concentration: (Direct).**
- **Blood solubility: Blood: gas partition coefficient (Inverse relation).**
- **Rate and depth of ventilation (Direct).**

Drugs

Solubility

Induction & Recovery

(Blood : gas partition coefficient)

Methoxyflurane

12

Slow

Halothane

2.3

Slow

Enflurane

1.8

Medium

Isoflurane

1.4

Medium

Sevoflurane

0.69

Rapid

Desflurane (low volatility)

0.42

poor & Rapid

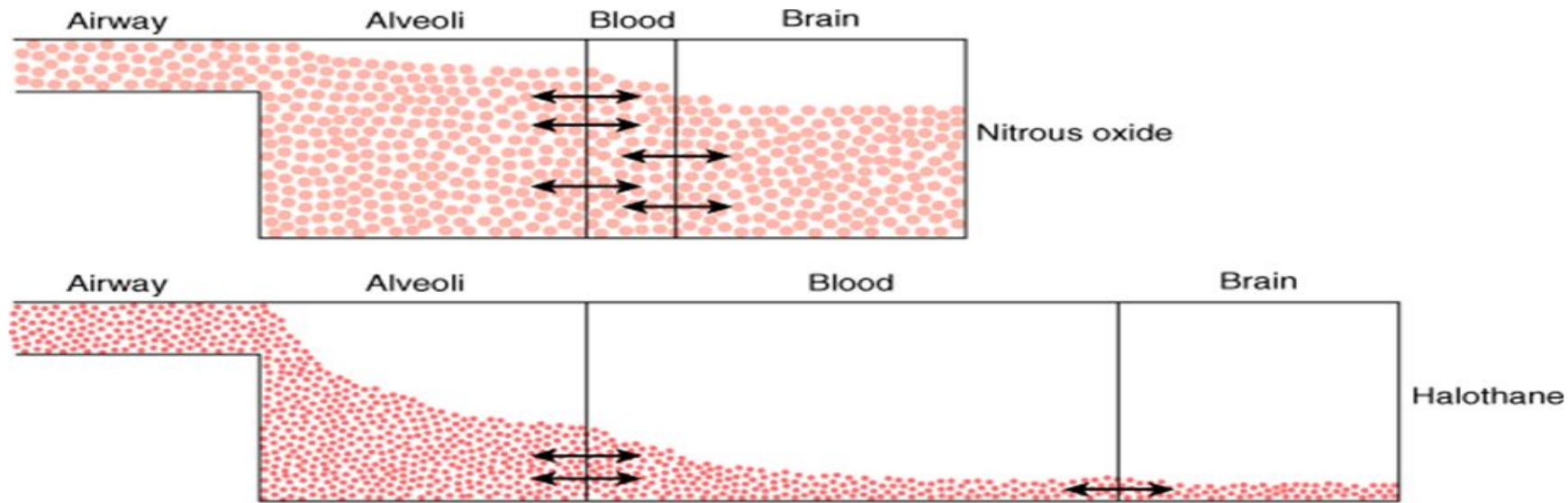
Nitrous Oxide

0.47

Rapid



Solubility and induction of anesthesia



Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology*, 11th Edition: <http://www.accessmedicine.com>

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Why induction of anesthesia is slower with more soluble anesthetic gases. In this schematic diagram, solubility in blood is represented by the relative size of the blood compartment (the more soluble, the larger the compartment). Relative partial pressures of the agents in the compartments are indicated by the degree of filling of each compartment. For a given concentration or partial pressure of the two anesthetic gases in the inspired air, it will take much longer for the blood partial pressure of the more soluble gas (halothane) to rise to the same partial pressure as in the alveoli. Since the concentration of the anesthetic agent in the brain can rise no faster than the concentration in the blood, the onset of anesthesia will be slower with halothane than with nitrous oxide.

Minimum alveolar concentration (MAC)

- **It is the concentration of inhalation anesthetic that produce immobility in 50 % patients in response to surgical operation.**
- **The lower the MAC value the more potent the drug.**

Drugs

MAC (%)

POTENCY

Methoxyflurane

0.16

Halothane

0.75

Isoflurane

1.4

Enflurane

1.7

Sevoflurane

2

Desflurane

6-7

Nitrous oxide

>100



POTENCY & INDUCTION AND VELOCITY

Drugs

Methoxyflurane: The most potent, low MAC value, slow induction & recovery

Halothane: Potent, slow induction & recovery (pleasant odor)

Enflurane: less potent, medium induction & recovery (pungent odor)

Isoflurane: less potent, rapid induction & recovery

Sevoflurane : less potent, rapid induction & recovery (better smell)

Desflurane: Rapid induction & rapid recovery (pungent odor)

Nitrous oxide: The least potent, high MAC value, rapid induction & recovery

Pharmacological actions of inhalation anesthetics

CNS

- ↓ metabolic rate.
- ↑ ICP (due to cerebral vasodilatation) # in head injuries.
- Dose dependent EEG changes (Enflurane).

CNS

- Hypotension
- Bradycardia Except (**Isoflurane & Desflurane**).
- Myocardial depression (**Halothane – Enflurane**).
- Sensitize heart to catecholamines (**Halothane**)

Pharmacological actions of inhalation anesthetics

Respiratory

- All respiratory depressants.
- Airway irritation (Desflurane-Enflurane).

Uterus & Skeletal Muscles

- Uterine relaxation [nitrous oxide has minimal relaxant effect (labor)].
- skeletal muscle relaxants.

Inhalation anesthetics

Anesthetic drugs	Properties and Side effects
Methoxyflurane	For veterinary use only Slow induction, nephrotoxicity
Halothane	Non irritant - Potent anesthetic, Weak analgesic. Can be used in children, Sensitization of heart to catecholamines Hepatotoxicity, Slow induction and recovery (?????). Malignant hyperthermia
Isoflurane	Stable compound (2%), Low biotransformation (Less fluoride). No nephrotoxicity - No hepatotoxicity. Less myocardial depression
Enflurane	is metabolized to fluoride (8%) Contraindicated in patients with seizure disorders. renal failures (release fluoride) . Pungent (less induction -Not for pediatrics). Airway irritation, CNS stimulation (Epilepsy-like seizure- abnormal EEG).
Desflurane	Less metabolized (0.05 %), low boiling point (special equipment) Pungent odor, Airway irritation
Sevoflurane	Better smell, little effect on HR , No airway irritation (good for children)
Nitrous oxide	Potent analgesics, Minimal CVS adverse effects, contraindicated in pregnancy (uterine relaxant). Weak anesthetic (low potency, combined). Diffusion hypoxia, Nausea and vomiting. Inactivation of B 12 → megaloblastic anemia, congenital anomalies

Intravenous anesthetics

- **Ultra short acting barbiturates e.g. thiopental**
- **Benzodiazepines (diazepam, lorazepam, midazolam)**
- **Opioids (fentanyl)**
- **Ketamine**
- **Propofol**
- **Etomidate**

Intravenous anesthetics

- **NO need for special equipments.**
- **Rapid induction & recovery EXCEPT BZs**
- **Injected slowly (rapid induction).**
- **Recovery is due to redistribution from CNS.**
- **Analgesic activity: Opioids & ketamine**
- **Amnesic action: BZs & ketamine.**
- **Can be used alone in short operation & Outpatients anesthesia.**

SIDE EFFECTS OF INTRAVENOUS ANAESTHETIC DRUG

Drug	Main side effects
Thiopental	<p>CVS collapse and respiratory depression (Laryngospasm, bronchospasm), porphyria (Porphyria is a group of liver disorders in which substances called porphyrins build up in the body, negatively affecting the skin or nervous system).</p>
Etomidate	<p>Adrenocortical suppression, Excitatory effects during induction pain at site of injection, Post-operative NV</p>
Propofol	<p>CVS and respiratory depression, Excitation (involuntary movements) Pain at injection site, expensive.</p>
Ketamine	<p>Psychotomimetic effects following recovery (vivid dreams, hallucination) Postoperative nausea, vomiting, salivation Risk of hypertension and cerebral hemorrhage</p>
Midazolam	<p>Slow induction & recovery , Minimal CVS and respiratory depression</p>
Opioids	<p>Respiratory depression, Bronchospasm (wooden rigidity). Hypotension, Nausea & vomiting, Increase in ICP, Urinary retention.</p>

CONTRAINDICATION OF INTRAVENOUS ANAESTHETIC DRUGS

Drug	Contraindications
Thiopental	Porphyria (severe abdominal pain, numbness, anxiety and confusion) , severe hypotension (hypovolemic & shock patient) Chronic obstructive lung disease.
Propofol	CVS and respiratory depression
Fentanyl	Head injuries, Pregnancy, Bronchial asthma, Chronic obstructive lung diseases. Hypovolemic shock (Large dose only).
Ketamine	CV diseases (hypertension-stroke). Head injuries.
Midazolam	respiratory patients

Ultrashort acting barbiturates

e.g. Thiopental, Methohexital

- **Rapid onset of action 1 min (high lipid solubility).**
- **Ultra short duration of action 15 - 20 min**
- **Metabolized slowly by the liver (slow recovery)**
- **Potent anesthetic.**
- **CNS: ↓ ICP (Used in head injuries).**
- **CVS collapse & respiratory depression, precipitate porphyria attack, hypersensitivity reaction.**
- **Used for induction in major surgery and alone in minor surgery.**

Benzodiazepines

Midazolam, Diazepam , Lorazepam

- **No pain, have anxiolytic and amnesic action**
- **Slow induction & recovery.**
- **Cause respiratory depression.**
- **Used in induction of general anesthesia.**
- **Alone in minor procedure (endoscopy).**
- **In balanced anesthesia (Midazolam).**

Etomidate

- **Ultrashort acting hypnotic (Non Barbiturates).**
- **Rapid onset of action, short duration of action.**
- **Rapidly metabolized in liver (less hangover).**
- **Minimal CVS and respiratory depressant effects.**
- **Involuntary movements during induction**
- **Pain at sit of injection.**
- **Adrenal suppression**

ketamine

- **Dissociative anesthesia (Analgesic activity & Amnesic action. immobility, complete separation from the surrounding environment).**
- **Rapid onset of action, short duration, is given IV, IM (Children).**
- **↑ Potent bronchodilator (asthmatics **BP & cardiac output (↑central sympathetic activity).****
- **↑ Increases plasma catecholamine levels, ↑ ICP).**
- **Used in (hypovolemic, shock & elderly) patients.**
- **Post operative **hallucination vivid dreams & disorientation & illusions****
- **Risk of hypertension & cerebral hemorrhage, ↑ ICP**

Propofol

- Hypnotic (Non Barbiturate).
- Rapid onset, short duration of action
- Rapidly metabolized in liver (10 times - Elimination $\frac{1}{2}$ = 30 – 60 min).
- Decreases ↓ ICP, Antiemetic action.

Side Effects

- Hypotension (↓PVR)
- Excitation (involuntary movements), Pain at site of injection
- Expensive

Opiate drugs

Fentanyl, Alfentanil,

Rapid onset, Short duration of action, Potent analgesia.

Uses

Cardiac surgery (morphine + nitrous oxide).

Neuroleptanalgesia (Fentanyl + Droperidol).

Neuroleptanesthesia (Fentanyl+Droperidol+ nitrous oxide).

Side Effects

Respiratory depression, bronchospasm (wooden rigidity).

Hypotension, nausea & vomiting

Neuroleptanalgesia

- **A state of analgesia, sedation and muscle relaxation without loss of consciousness.**
- **used for diagnostic procedures that require cooperation of the patient.**
- **Innovar (Fentanyl + Droperidol).**
- **Contraindicated in parkinsonism.**

Neuroleptanesthesia

A combination of (Fentanyl + Droperidol + nitrous oxide).

Contraindication

- 1. Head injuries.**
- 2. Pregnancy.**
- 3. Bronchial asthma.**
- 4. Chronic obstructive lung diseases.**
- 5. Hypovolemic shock (Large dose only).**

Induction drugs effects on CVS system

Drug	Systemic BP	Heart rate
Propofol	↓	↓
Etomidate	No change or slight ↓	No change
Ketamine	↑	↑

