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.

Types of Anesthesia

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

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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

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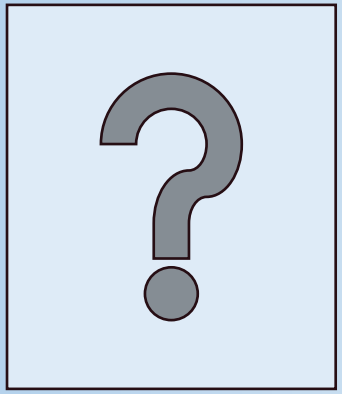
HOW WE CAN OBTAIN BALANCED ANESTHESIA



Balanced anesthesia is achieved by a combination of I.V and inhaled anesthesia and Pre-anaesthetic medications

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STAGES OF ANESTHESIA

- **Stage I (analgesia)**

-Loss of pain sensation.

-The patient is conscious and conversational.

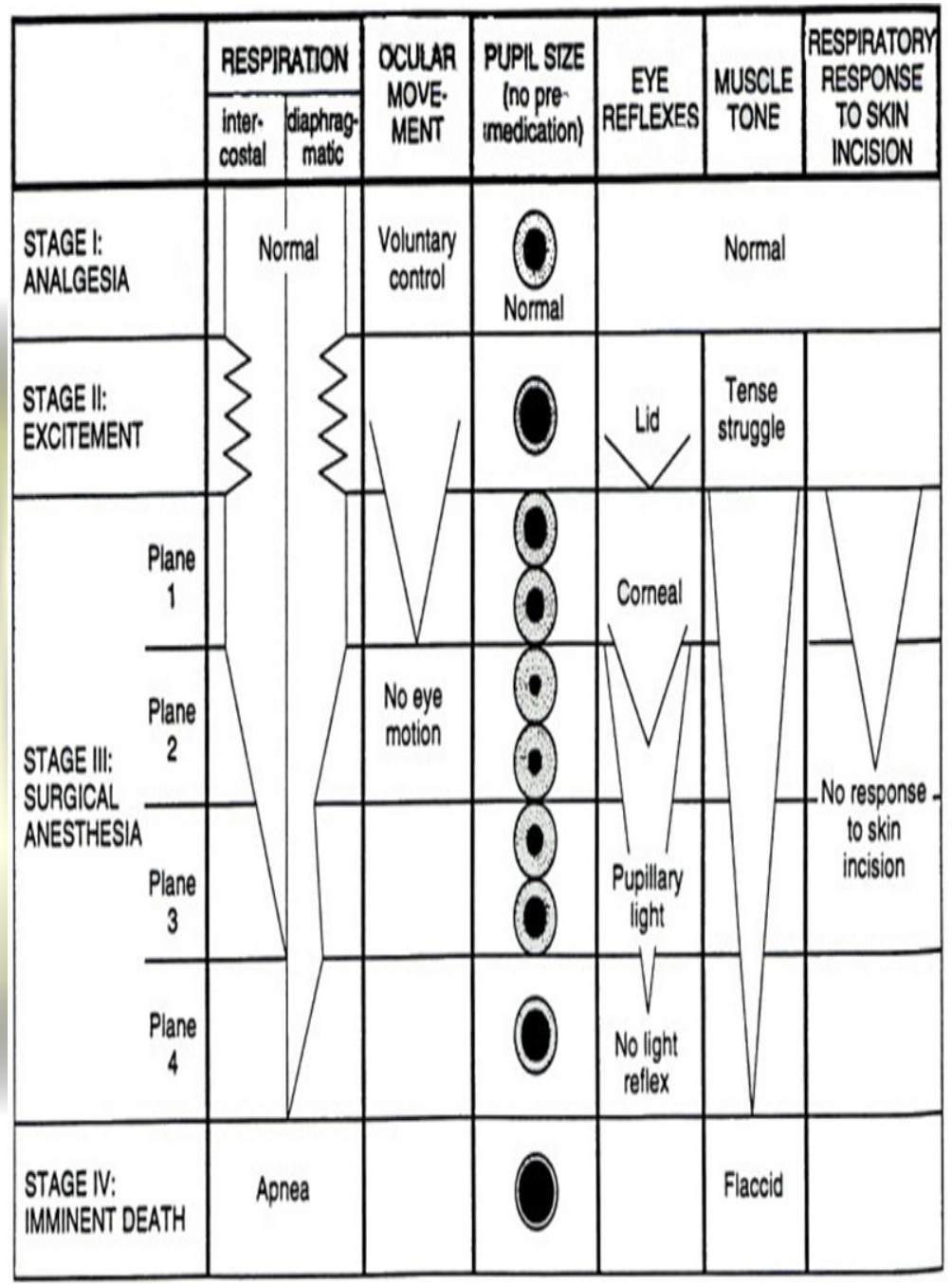
- **Stage II (Excitement)**

-Increased respiratory rate.

-Increased, irregular blood pressure.

-Patient may experience delirium & violent behavior.

-Eye dilated & reactive.

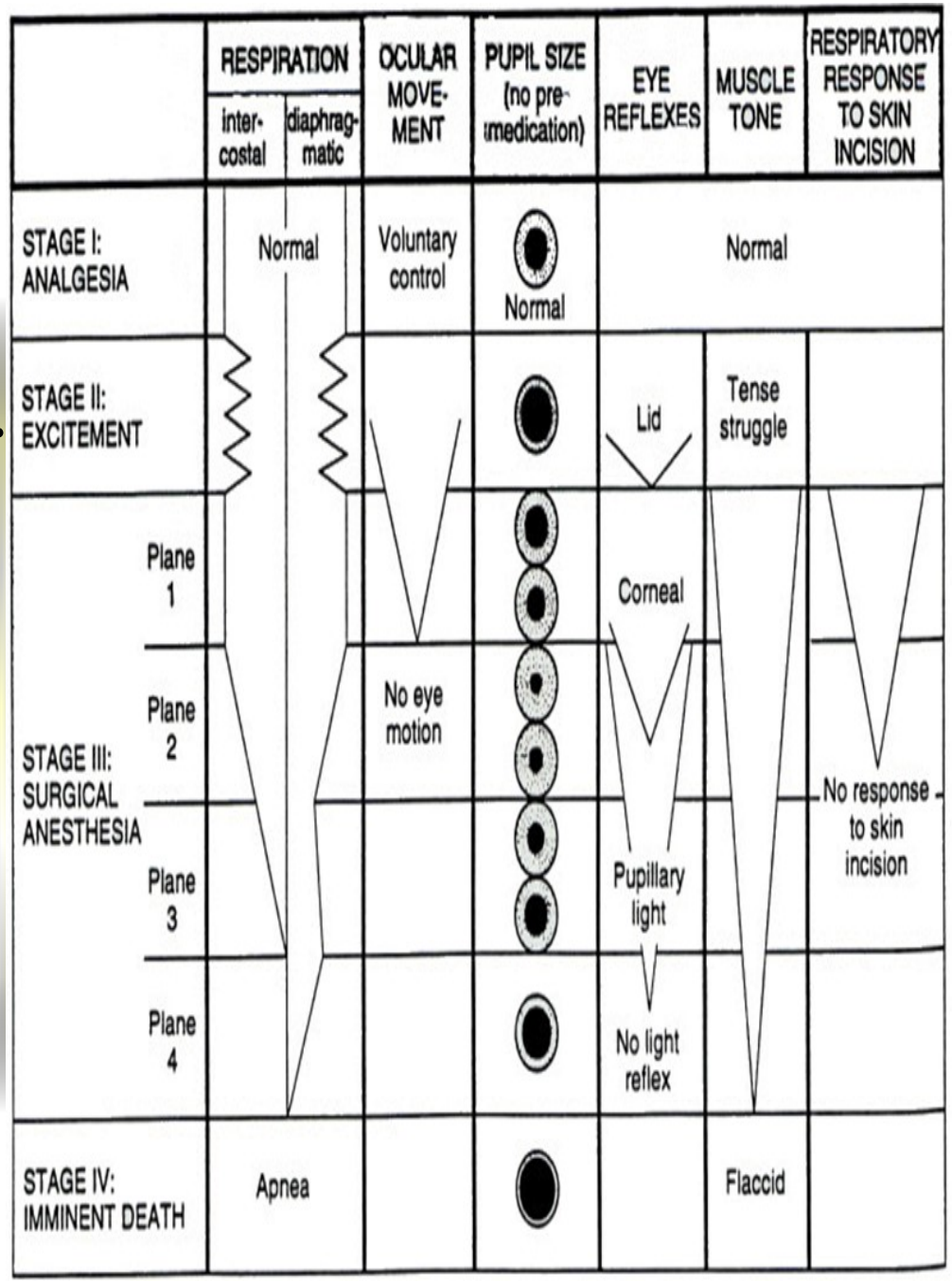


STAGES OF ANESTHESIA

- **Stage III (Surgical anesthesia)**
  - Regular respiration & relaxation of Sk. muscles.
  - Eye reflexes decrease until the pupil is fixed.
- **Stage IV (coma and death)**
  - Medullary paralysis.

  -Severe depression of vasomotor

  -Depression of respiratory centers.
  - Death may occur.



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

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PRE-ANESTHETIC MEDICATION

- **Calm the patient, relieve pain**
- **Protect against undesirable effects of the subsequently administered anesthetics or the surgical procedure.**
- **Facilitate smooth induction of anaesthesia**
- **Lowered the dose of anaesthetic required**

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ADJUNCTS TO GENERAL ANAESTHETICS

- **Pre-anesthetic medication.**

  Neuromuscular blocking agents

  - e.g. succinylcholine, vecuronium, atracurium
  - Facilitate intubation
  - Suppress muscle tone.

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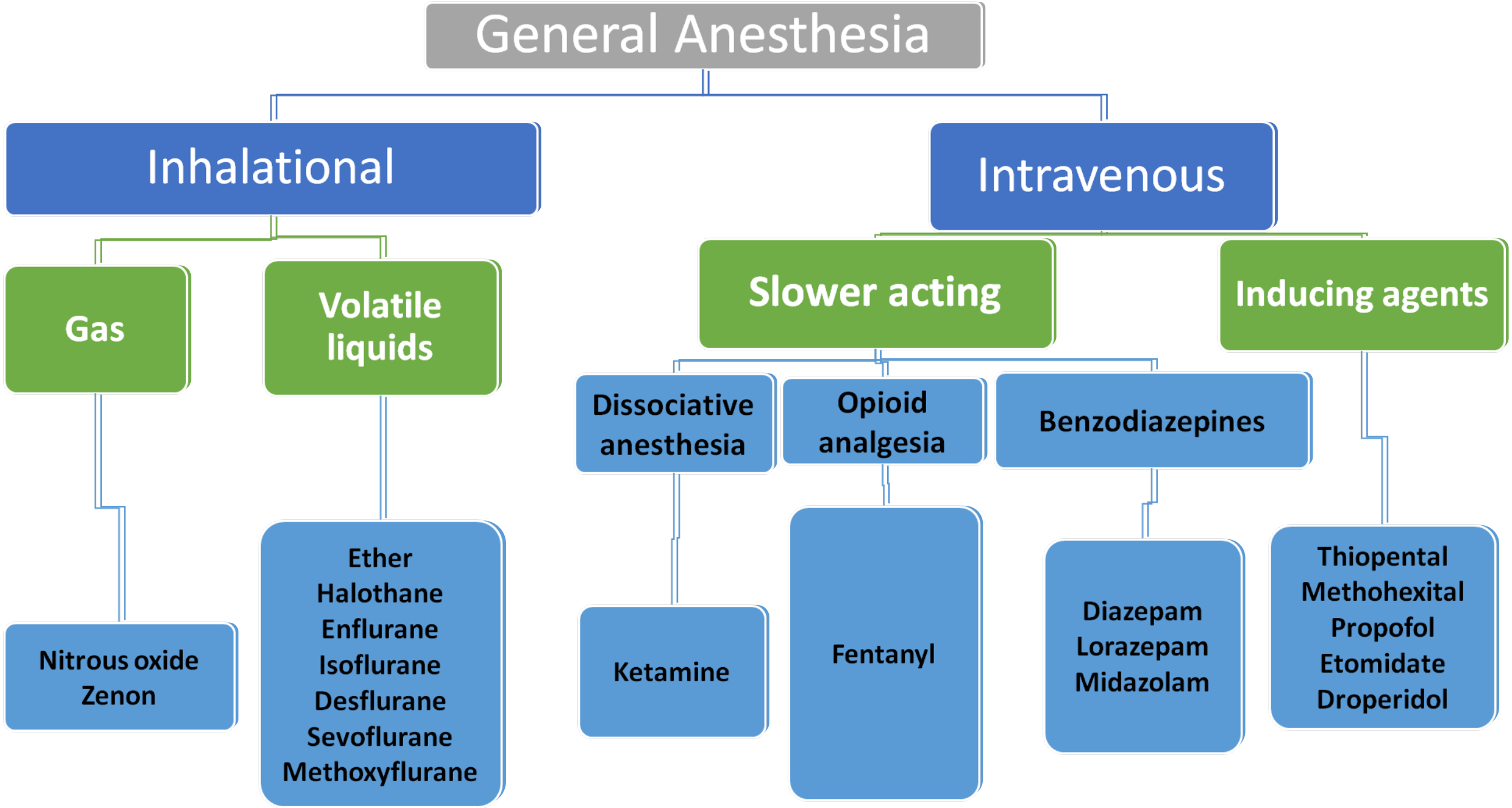
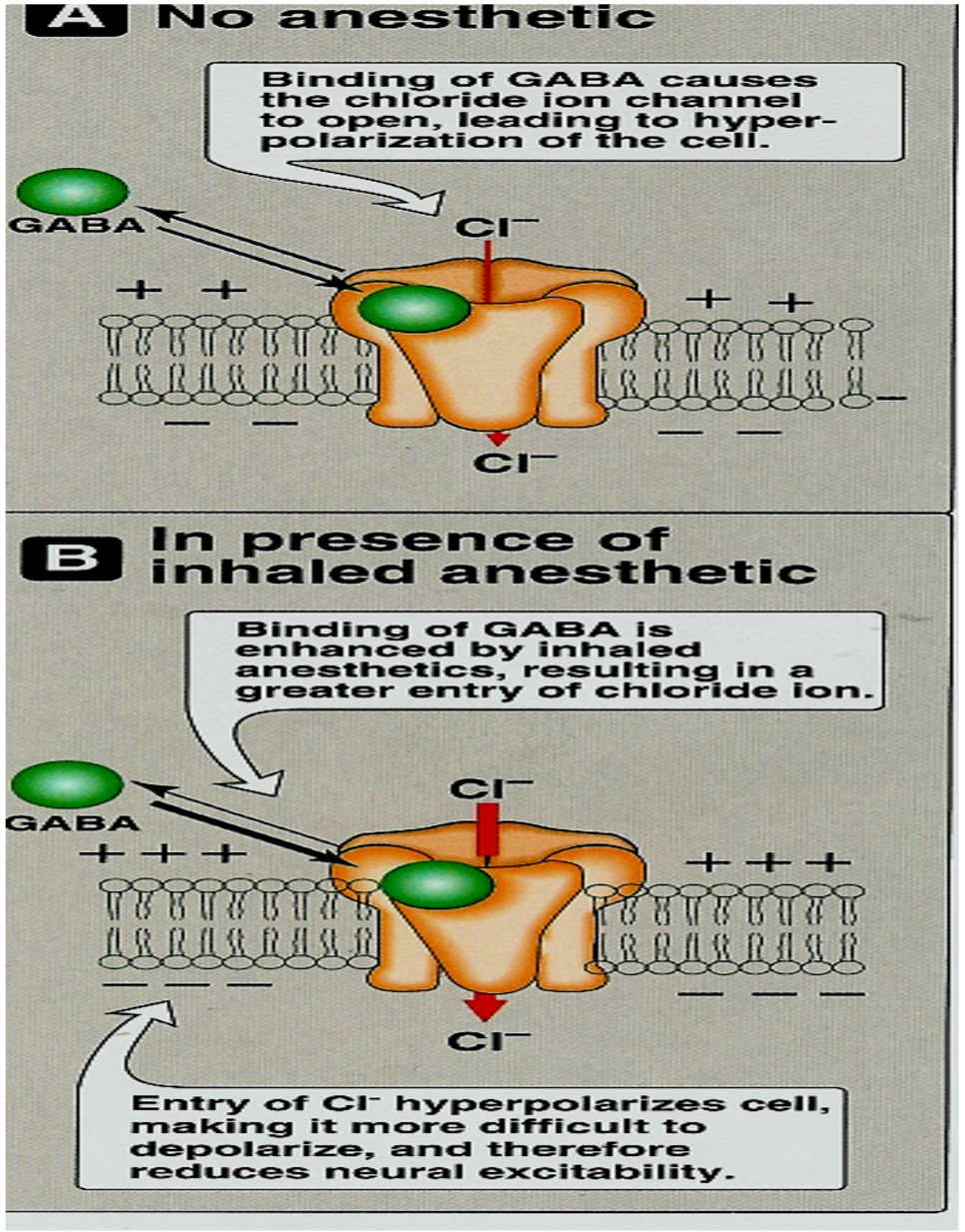

General Anesthesia
Inhalational
Intravenous
Gas
Volatile liquids
Slower acting
Inducing agents
Dissociative anesthesia
Opioid analgesia
Benzodiazepines
Nitrous oxide
Zenon
Ether
Halothane
Enflurane
Isoflurane
Desflurane
Sevoflurane
Methoxyflurane
Ketamine
Fentanyl
Diazepam
Lorazepam
Midazolam
Thiopental
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.**

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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.

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Pharmacokinetics of Inhalation anesthetics

Factors controlling induction & recovery

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

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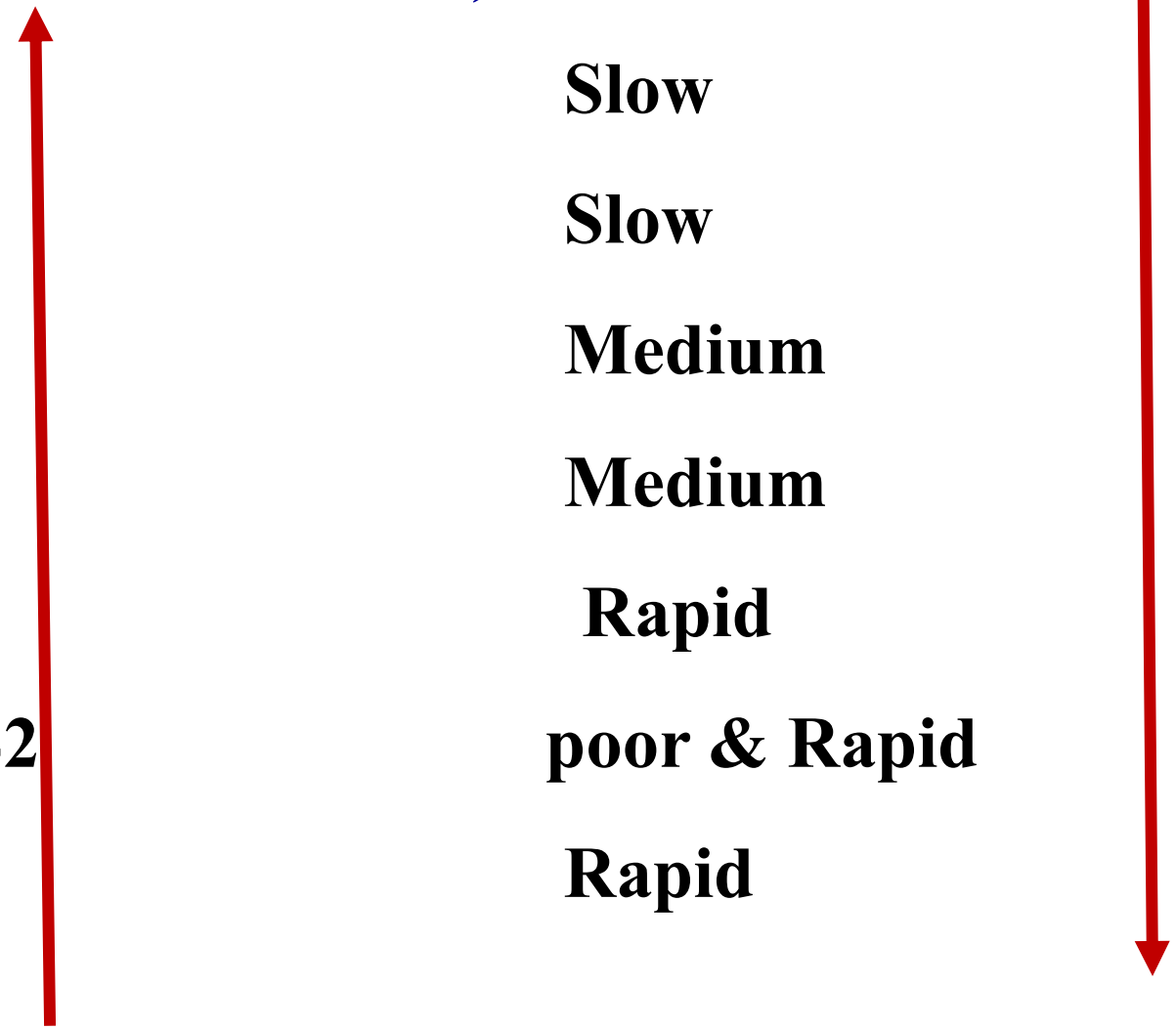
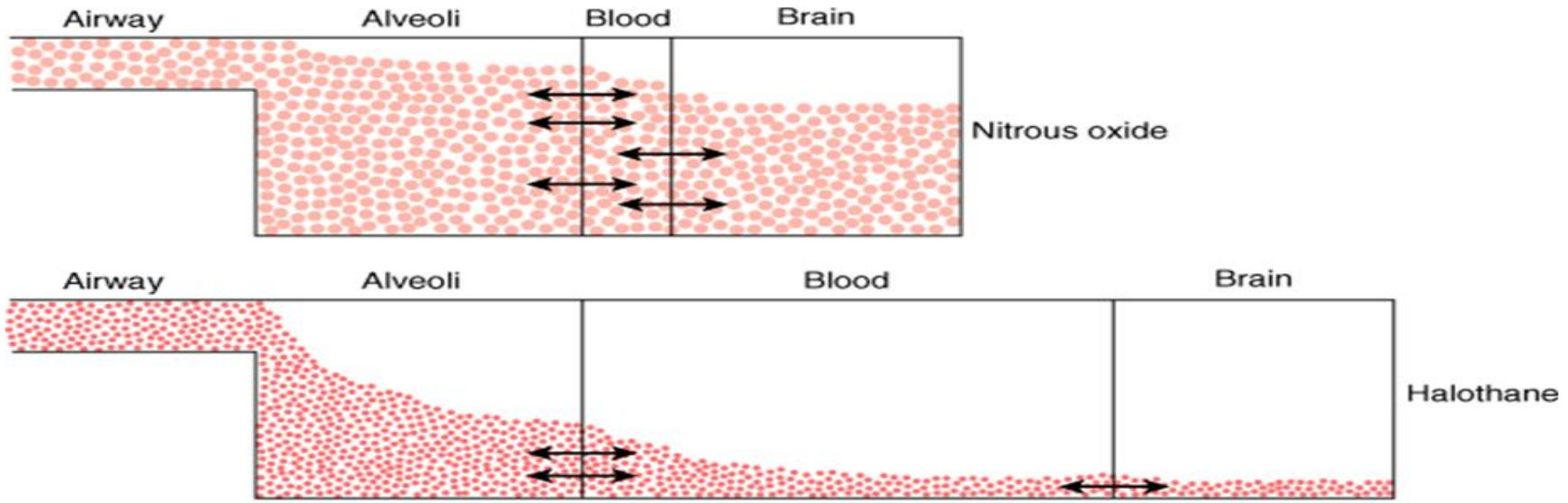
Drugs	Solubility (Blood : gas partition coefficient)	Induction & Recovery
Methoxyflurane	12	Slow
Halothane	2.3	Slow
Enflurane	1.8	Medium
Isoflurane	1.4	Medium
Sevoflurane	0.69	Rapid
Desflurane (low volatility)	0.42	poor & Rapid
Nitrous Oxide	0.47	Rapid



Solubility and induction of anesthesia



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

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.**
- **Mac value increases with CNS stimulants and decreases with CNS depressants.**

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Drugs	MAC (%)
Methoxyflurane	0.16
Halothane	0.75
Isoflurane	1.4
Enflurane	1.7
Sevoflurane	2
Desflurane	6-7
Nitrous oxide	>100

POTENCY

Pharmacological actions of inhalation anesthetics

CNS

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

CVS

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

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Pharmacological actions of inhalation anesthetics

Respiratory

- All respiratory depressants.

-Airway irritation (Desflurane-Enflurane).

Uterus & Skeletal Muscles

-Uterine relaxation [nitrous oxide has minimal relaxant effect].

- skeletal muscle relaxants.

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POTENCY & INDUCTION AND VELOCITY (Summary keep in mind solubility and MAC values)

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

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Inhalation anesthetics

Anesthetic drugs	Properties
Methoxyflurane	For veterinary use only
Halothane	Non irritant - Potent anesthetic, Weak analgesic. Can be used in children
Isoflurane	Stable compound (2%), Low biotransformation (Less fluoride). No nephrotoxicity - No hepatotoxicity.
Enflurane	is metabolized to fluoride (8%) Contraindicated in patients with seizure disorders. renal failures (release fluoride).
Desflurane	Less metabolized (0.05 %), low boiling point (special equipment)
Sevoflurane	Better smell, little effect on HR, No airway irritation (children)
Nitrous oxide	Potent analgesics, Minimal CVS adverse effects, contraindicated in pregnancy (uterine relaxant).

Side effects of inhalation anesthetics

Anesthetic drugs	Side effects
Methoxyflurane	Slow induction, nephrotoxicity
Halothane	Slow induction and recovery (why ??????). Sensitization of heart to catecholamines Hepatotoxicity Malignant hyperthermia
Desflurane	Pungent odor Airway irritation
Enflurane	Pungent (less induction -Not for pediatrics). Airway irritation CNS stimulation (Epilepsy-like seizure- abnormal EEG).
Nitrous oxide	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**

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Intravenous anesthetics

- **NO need for special equipments.**
- **Rapid induction & recovery EXCEPT benzodiazepines (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.**

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CHARACTER S OF INTRAVENOUS ANAESTHETIC DRUGS

Drug	Induction and recovery
Thiopental	Fast onset, slow recovery, hangover
Etomidate	Fast onset, fairly fast recovery, less hangover
Propofol	Fast onset, rapidly metabolized, very fast recovery
Ketamine	Slow onset, Produces **good analgesia and amnesia.**
Midazolam	Slower onset than other agents, **has amnesic effect.**

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.**

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.
- Postoperative nausea & vomiting.
- Pain at sit of injection.
- Involuntary movements during induction
- Adrenal suppression

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Propofol

- **Hypnotic (non barbiturates).**
- **Rapid onset, short duration of action, Faster recovery than thiopental**
- **Rapidly metabolized in liver (10 times - Elimination ½ = 30 – 60 min).**
- **Decreases ↓ ICP, Antiemetic action.**

Side Effects

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

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Benzodiazepines

Midazolam, Diazepam , Lorazepam

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

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ketamine

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

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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

Nausea & vomiting
Respiratory depression, bronchospasm (wooden rigidity).
Hypotension

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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).

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Contraindication of opiate drugs

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

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Induction drugs effects on CVS system

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

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SIDE EFFECTS OF INTRAVENOUS ANAESTHETIC DRUG

Drug	Main side effects
Thiopental	CVS collapse and respiratory depression (Laryngospasm, bronchospasm), porphyria
Etomidate	**Adrenocortical suppression, Excitatory effects during induction** pain at site of injection, Post-operative NV
Propofol	CVS and respiratory depression, Excitation (involuntary movements) Pain at injection site, expensive.
Ketamine	Psychotomimetic effects following recovery **(vivid dreams, hallucination**) Postoperative nausea, vomiting，salivation Risk of hypertension and cerebral hemorrhage
Midazolam	Slow induction & recovery
Opioids	Increase in ICP, Respiratory depression, Bronchospasm (wooden rigidity). Hypotension, Nausea & vomiting, Urinary retention. Prolongation of labor & fetal distress.

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

Thank you