

GENERAL ANESTHETICS

Prof. Hanan Hagar
Professor of Pharmacology
College of Medicine
King Saud University



Introduction

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

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Prof. Hanan Hagar



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.

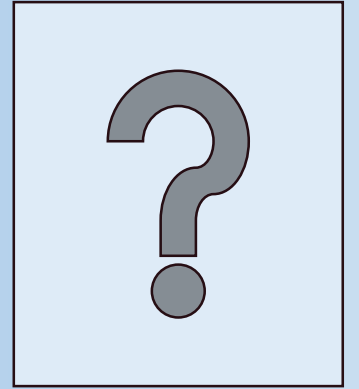


Beneficial effects



Adverse effects

HOW WE CAN OBTAIN BALANCED ANESTHESIA



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











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.

	RESPIRATION		OCULAR MOVE- MENT	PUPIL SIZE (no pre- medication)	EYE REFLEXES	MUSCLE TONE	RESPIRATORY RESPONSE TO SKIN INCISION
	inter- costal	diaphrag- matic					
STAGE I: ANALGESIA	Normal		Voluntary control	 Normal	Normal		
STAGE II: EXCITEMENT					Lid	Tense struggle	
STAGE III: SURGICAL ANESTHESIA	Plane 1				Corneal		
	Plane 2		No eye motion				
	Plane 3				Pupillary light	No response to skin incision	
	Plane 4				No light reflex		
STAGE IV: IMMINENT DEATH	Apnea					Flaccid	






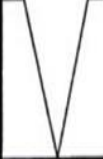





STAGES OF ANESTHESIA

- **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.

	RESPIRATION		OCULAR MOVE- MENT	PUPIL SIZE (no pre- medication)	EYE REFLEXES	MUSCLE TONE	RESPIRATORY RESPONSE TO SKIN INCISION
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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

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**

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

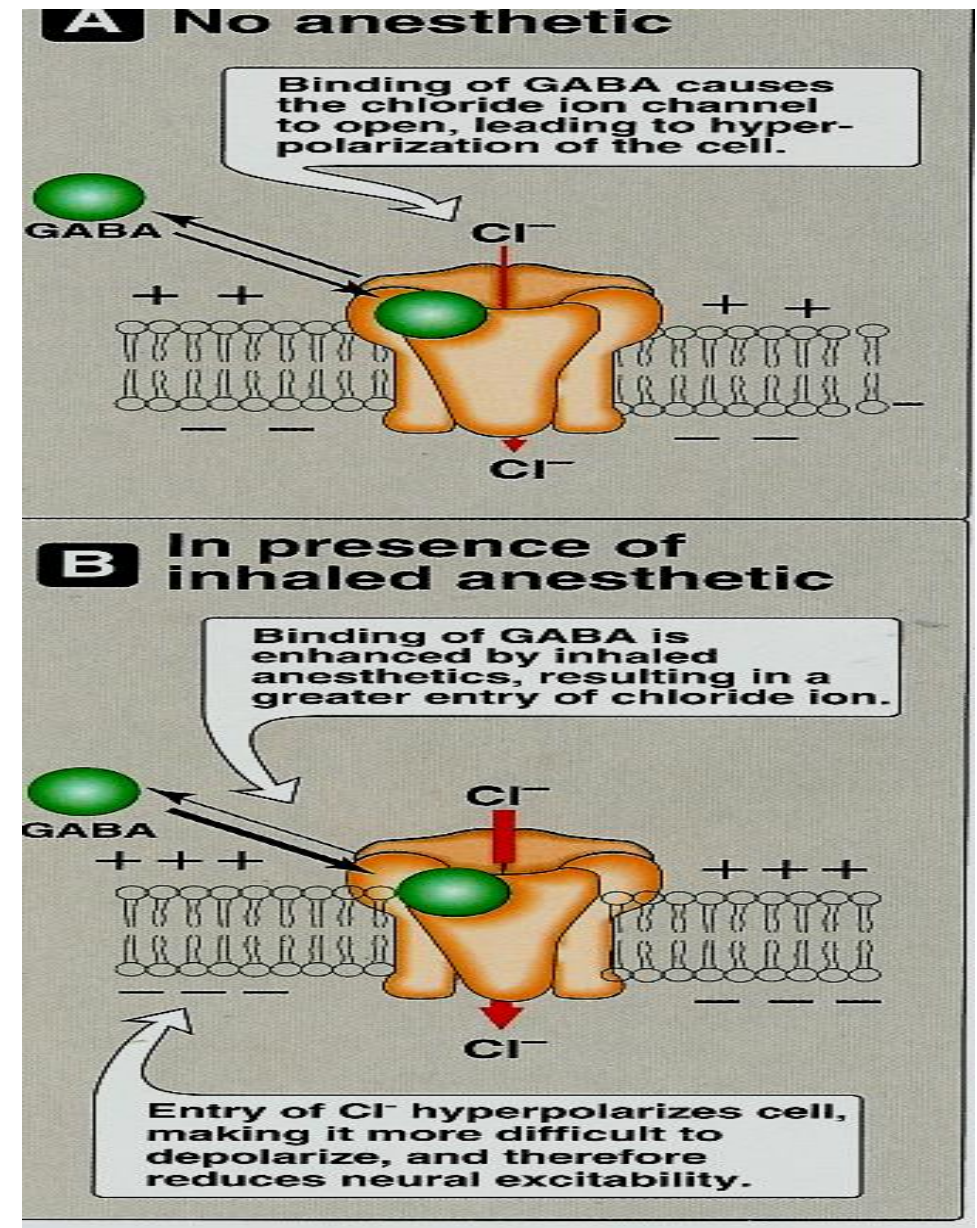
Diazepam
Lorazepam
Midazolam

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

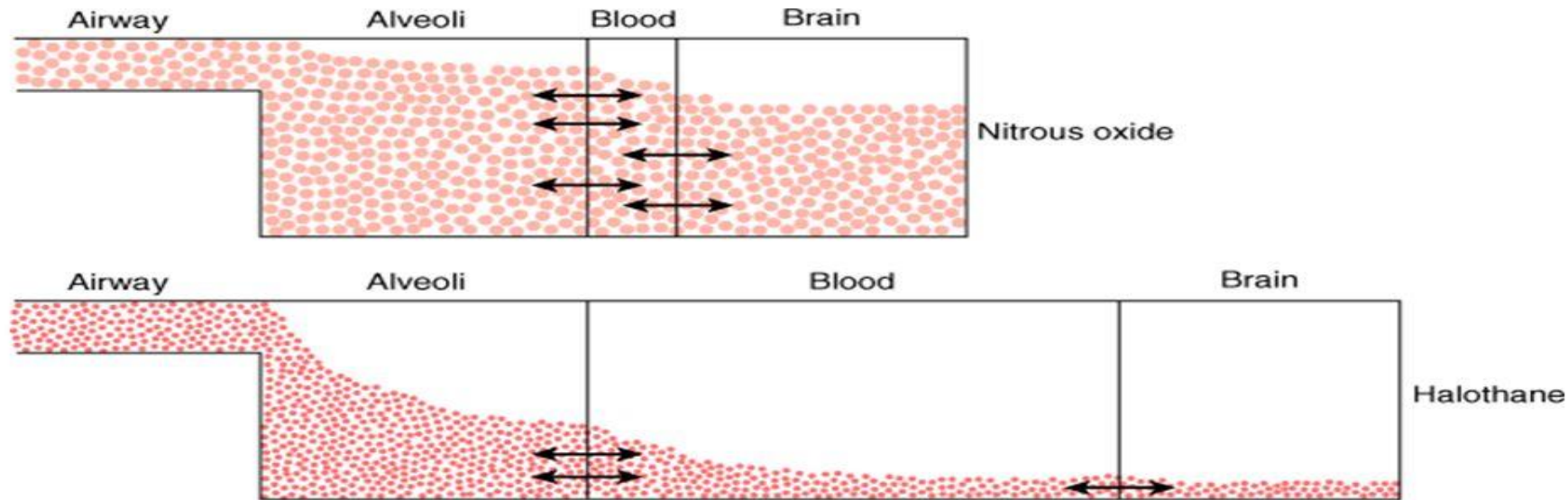
Nitrous Oxide

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

Drugs

MAC (%)

POTENCY

Methoxyflurane

0.16

Halothane

0.75

Isoflurane

1.4

Enflurane

1.7

Sevoflurane

2

Desflurane

6-7

Nitrous oxide

>100



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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

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)

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.

Side effects of inhalation anesthetics

Anesthetic drugs	Side effects
Methoxyflurane	Slow induction, nephrotoxicity
Halothane	Slow induction and recovery (?????). 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

Inhalation anesthetics

Anesthetic drugs	
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).

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.**

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 (GABA 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.**

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**
- **Postoperative nausea & vomiting.**
- **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, Faster recovery than thiopental**
- **Rapidly metabolized in liver (10 times - Elimination $t_{1/2} = 30 - 60$ min).**
- **Decreases \downarrow ICP, Antiemetic action.**

Side Effects

- **Hypotension (\downarrow 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	↑	↑


Summary of the side effects

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 Minimal CVS and respiratory depression
Opioids	Respiratory depression, Bronchospasm (wooden rigidity). Hypotension, Nausea & vomiting, Increase in ICP, 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