







Pharmacology Team 438

General Anesthetics

Important: The doctor said differences in males and females slides will not be in the exam

Objectives

By the end of the lecture , you should know:

- Define anesthesia, balanced anesthesia, and pre-anesthetic medication
- Be able to define MAC, potency, blood: gas partition coefficient and oil: gas partition coefficient.
- Distinguish between inhalation and intravenous anesthetics.
- Identify the pharmacokinetics, pharmacological actions, and side effects of inhalation anesthetics.
- Identify the pharmacokinetics, pharmacodynamics, and side effects of intravenous anesthetics.
- Know the difference between neuroleptanalgesia and neuroleptanesthesia.

Color index:

Black : Main content Red : Important Blue: Males' slides only Pink : Females' slides only Grey: Extra info or explanation Green : Dr. notes



Overview





Introduction:



Introduction:





Balanced Anesthesia:

Balanced anesthesia: is the use of more than one drug in combination to fulfil the patients needs, thus it will **increase** the **beneficial effects** & **decrease** the adverse effects

-Balanced anesthesia is achieved by a combination of:
1- I.V anesthesia
2-inhaled anesthesia
3- Pre-anaesthetic medications

But we don't have drug for the last two characteristics.
 smooth means its able to bypass the first two stages of anesthesia and reach stage 3.
 Loss of unwanted Autonomic reflexes

Pre-Anesthetic Medications

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

🔶 Drugs	Uses	Examples
opiates	Induce analgesia	Morphine
Anticholinergics	Prevent secretion of fluids into the respiratory tract ¹	Hyoscine
Sedatives & anxiolytics	Relieve anxiety	Diazepam
Antihistamines	Allergic reactions	Diphenhydramine
Antiemetics	Post surgical N&V	metoclopramide & prochlorperazine
H2-receptor blockers	Reduce gastric acidity	Ranitidine
Thiopental (Barbiturates) ²	Smooth induction	-
Adjunct to general anesthesia		
Neuromuscular blockers	 Facilitate intubation. suppress muscle tone. 	succinylcholine, vecuronium & atracurium

 so aspiration of fluids is avoided & decrease the vagomimetic action on the heart so bradycardia is avoided. parasympathetic antagonist= inhibit secretion.
 can be used alone I.V (discussed later on)

MOA of General Anaesthetics



Inhalation anesthetics

Induction: time elapsed between onset of administration of anesthetics 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.**

more related to IV drugs.
 more related to inhaled drugs.
 glutamate receptor.

Inhalation anesthetics

Rate of induction

P.K of Inhalation anesthetics

Depth of anesthesia and recovery

→ The an

Factors controlling induction & recovery:

- The anesthetic concentration in the inspired air \rightarrow Direct
- → Blood solubility= Blood : gas partition coefficient \rightarrow Inverse to induction rate¹
- → Rate and depth of ventilation \rightarrow Direct

Minimum alveolar concentration (MAC)

It is the concentration of **inhalation anesthetic** that produce immobility in **50%** patients in response to surgical incision.

- → Potency of anesthetic agents.
- → Oil: gas partition coefficient =lipid solubility (Direct with potency).
- → The lower the MAC value the more potent the drug (inverse)
- → MAC value increases with CNS stimulants & decreases with CNS depressants.²

Drugs	MAC value ⁴	Solubility	Induction & Recovery	Potency
methoxyflurane ³	Low MAC value 0.16	12	Slow	The Most potent
Halothane (Pleasant smell)	0.75	2.3	Slow	Potent
Isoflurane	1.4	1.4	Medium	Less potent
Enflurane (Pungent smell)	1.7	1.8	Medium	Less potent
Sevoflurane (Better smell)	2	0.69	Rapid	Less potent
Desflurane (Pungent smell)	6-7	0.42	Poor & Rapid	Less potent
Nitrious oxide ⁵	>100	0.47	Rapid	Least potent

1. How soluble is it within the blood? Does the drug have affinity to blood or not? The more soluble it is within the blood the longer time it'll take

- to saturate the blood before it reaches the site of action which is the CNS.
- 2. it lowers the concentration of anesthesia require, and elderly patients have hypersensitive neuronal receptors.
- 3. We don't use **methoxyflurane** anymore

4. Remember the concept not the value. But the value represents the concentration of the gas within the gas tank used for the patient. 5. Nitrous oxide has the lowest Solubility, the fastest induction and recovery, the highest MAC and least potent.

Pharmacological actions of inhalation anesthetics

System	Pharmacological action
CNS	 ↓ metabolic rate. ↑ ICP (due to cerebral vasodilatation) <u>thus contraindicated in head injuries.</u> Dose -dependent EEG changes (Enflurane) <u>Enflurane contraindicated in</u> <u>Epilepsy. Remember E with E</u>
Cardiovascular	 Hypotension Bradycardia Except (Isoflurane ,Desflurane). Myocardial depression (Halothane, Enflurane). Sensitize heart to catecholamines (Halothane)¹ Halothane contraindicated in pheochromocytoma
Respiratory	 All respiratory depressants Airway irritation (Desflurane-Enflurane due to pungent odor).
Liver	 Decrease hepatic flow Hepatotoxicity (Only halothane) only in adults. Remember (3 Hs). (:
Uterus & skeletal muscle	 Uterine relaxation BUT Nitrous oxide has minimal relaxant effect (labor) All are skeletal muscle relaxants. (of variable degrees)

	✤ Inhalation anest	hetics
Anesthetic drugs	Features	Side effects
Methoxyflurane (Not used anymore)	• For veterinary use only	Slow inductionnephrotoxicity
Halothane 3H	 Non irritant - Potent anesthetic, Weak analgesic. Can be used in children 	 Slow induction and recovery. Sensitization of <u>H</u>eart to catecholamines <u>H</u>epatotoxicity² Malignant <u>Hyperthermia</u>
Enflurane	 is metabolized to fluoride (8%) Contraindicated in patients with seizure disorders. Not for renal failures (release fluoride) 	 Pungent (less induction -Not for pediatrics). Airway irritation. CNS stimulation (Epilepsy-like seizure- abnormal EEG).
Isoflurane	 Stable compound (2%), Low biotransformation (Less fluoride). No nephrotoxicity - No hepatotoxicity. 	_
Sevoflurane	• Better smell, little effect on HR, No airway irritation (children)	_
Desflurane	 Less metabolized (0.05 %), low boiling point (special equipment) 	Pungent odorAirway irritation
Nitrous oxide	 Potent analgesics, Minimal CVS adverse effects, contraindicated in pregnancy (uterine relaxant). 	 Weak anesthetic (low potency, combined). Diffusion hypoxia³, Nausea and vomiting. Inactivation of B 12 megaloblastic anemia, congenital anomalies.
1: Halothane increases the sens	itivity of CVS to circulating catecholamines such as adrenaline a	and noradrenaline which are produced by the Adrenal

 Halothane increases the sensitivity of CVS to circulating catecholamines such as adrenaline and noradrenaline which are produced by the Adrenal medulla so if a patient has pheochromocytoma -tumor of adrenal gland that results in the excessive release of epinephrine and norepinephrine- the patient will suffer from severe tachycardia and severe elevation of BP. 2: in adults only.
 Nitrous Oxide is eliminated via respiration, and b/c it has low blood:gas solubility coefficient, rapid elimination of N2O will make it diffuse out of the blood in large volumes which will dilute the oxygen in lung alveoli reducing alveolar oxygen tension producing "Diffusion Hypoxia".

Inhalation anesthetics

Girls slides only

Drug	Desflurane
Potency	Less potent than Halothane
Induction & Recovery	• Rapid induction and fast recovery (Low solubility)
Smell	• Pungent (worst odor)
Metabolization	 Less metabolized (0.05%) Low boiling point (special equipment)
Disadvantages	• Pungent odor (irritation - cough)
Contraindication	• All of the inhalation anesthetic drugs are contraindicated in head injury.

Drug	Sevoflurane
Potency	Less potent than Halothane
Induction & Recovery	• Rapid onset and recovery (Low solubility)
Smell	Better smell
Metabolization	• Less metabolized (3-5% fluoride)
Uses	• No airway irritation (preferable for children)
Advantages	• Little effect on HR
Contraindication	• All of the inhalation anesthetic drugs are contraindicated in head injury.

Drug	Halothane
Potency	Potent anesthetic
Induction & Recovery	Slow induction & recovery
Action	Weak analgesic, weak skeletal muscle relaxant
Metabolization	• Metabolized to toxic metabolites (trifluroethanol) hepatotoxic .
Disadvantages	 CVS depression Hypotension, bradycardia (vagomimetic action) ↓Myocardial contractility, ↓Cardiac output
Adverse effects	 Hepatotoxicity (repeated use). Malignant hyperthermia. Cardiac arrhythmias. Sensitizes heart to action of catecholamines → arrhythmias

Inhalation anesthetics

Girls slides only

Drug	Nitrous Oxide (N2O)
Potency	• the lowest potency
Induction & Recovery	• Rapid induction and recovery (the lowest solubility)
Uses	 Weak anesthetic (Low potency, combined) & potent analgesic Outpatient anesthesia (Dental procedures) & balanced anesthesia. Neuroleptanalgesia Delivery.
Advantages	 No muscle relaxation, no respiratory depression, not hepatotoxic, & minimal CVS adverse effects
Disadvantages	 Diffusion Hypoxia: (respiratory diseases). Nausea and vomiting. Inactivation of B12 → megaloblastic anemia. Bone marrow depression-Leukopenia (chronic use). Abortion - Congenital anomalies with repeated exposure eg. nurses
Contraindication	 Pregnancy(uterine relaxant), Pernicious anemia, & Immunosuppression.

Drug	Enflurane
Potency	Less potent than halothane
Induction & Recovery	• More rapid induction and recovery than halothane
Action	Better muscle relaxation, Better analgesic properties
Metabolization	• Metabolized to fluoride (8%), excreted in the kidney
Disadvantages	 Pungent (Less induction -Not for pediatrics). CNS stimulation (Epilepsy-like seizure- abnormal EEG)
Contraindication	 Patients with seizure disorders. Not for renal failures.

Drug	Isoflurane (Forane)
Potency	Potent anesthetic
Induction & Recovery	• More rapid induction & recovery than halothane
P.K	 Stable compound (2%) Low biotransformation (Less fluoride)
Advantages	 No nephrotoxicity - No hepatotoxicity. Good analgesic action. No sensitization of the heart. No cardiac arrythmias.
Disadvantages	 Pungent (Not for pediatrics).

Intravenous anesthetics



1: termination of action results from redistribution of the drug from the brain into adipose tissues (away from the site of action).

Intravenous Anesthetics

Ultrashort acting barbiturates		
Drug	Thiopental & Methohexital	
Onset	• Rapid (1 min) (high lipid solubility)	
Duration of Action	• Ultra short (15 - 20 min)	
Metabolization	 slowly by the liver Slow recovery Hangover. 	
Uses	 Potent anesthetic. ↓ICP (used in head injury) Induction in major surgery. Alone in minor surgery. 	
ADR	 CVS collapse, respiratory depression, precipitate porphyria attack,¹ & hypersensitivity reaction. 	
Contraindication	• COPD & severe hypotension (hypovolemic & shock patient)	
Propofol Hypnotic (Non Barbiturate)		
Onset	• Rapid	
Duration of Action	• Short	
Metabolization	 Rapidly in liver (10 times - Elimination ½ = 30 - 60 min). Faster recovery than thiopental 	
Uses	 ↓ICP Antiemetic action. 	
ADR	 Hypotension (↓PVR) Excitation (involuntary movements).² Pain at site of injection. Expensive. Clinical infections due to bacterial contamination. 	
	Benzodiazepines	
Drug	Midazolam, Diazepam, & Lorazepam	
Onset	Slower than other agent	
Induction & Recovery	Slow induction and recovery	
Uses	 No pain. Anxiolytic and amnesic action. Induction of general anesthesia. Alone in minor procedure (endoscopy). In balanced anesthesia (Midazolam). 	
ADR	Respiratory depression	

Barbiturates are liver microsomal enzymes inducers, they induce enzymes that are involved in the synthesis of porphyrins.
 EEG changes are seen.

* 1	Intravenous Anesthetics	
	Etomidate Ultrashort acting hypnotic (Non Barbiturates)	
Onset & D.O.A	• Rapid onset & short D.O.A	
Metabolization	 Rapidly in liver. Fairly fast recovery Less hangover 	
ADR	 Minimal CVS and respiratory depressant effects. Involuntary movements during induction (diazepam)¹ Postoperative nausea & vomiting. Pain: at the site of injection. Adrenal suppression 	
Ketamine given IV, IM (can be used in Children)		
Onset & D.O.A	• Rapid onset but in comparison to other I.V or I.M. Short D.O.A	
Uses	 Dissociative anesthesia (Analgesic activity, Amnesic action immobility, complete separation from the surrounding environment). Used in (hypovolemic, shock & elderly) patients. Potent bronchodilator (asthmatics). 	
ADR	 Risk of hypertension and cerebral hemorrhage ↑ICP Postoperative: hallucination vivid dreams & disorientation & illusions ↑ BP & cardiac output → (↑ central sympathetic activity). Increases plasma catecholamine levels→↑ ICP 	
Contraindication	Head injuries & CV diseases (hypertension-stroke).	
Opiate drugs		
Drug	Fentanyl, Alfentanil, Sufentanil, Remifentanil	
Onset & D.O.A	• Rapid onset & short D.O.A	
Uses	 Potent analgesia. (NOT anesthetic) Cardiac surgery (morphine + nitrous oxide) Neuroleptanalgesia (Fentanyl+Droperidol). Neuroleptanesthesia (Fentanyl+Droperidol + nitrous oxide). 	
	 Respiratory depression, bronchospasm (wooden rigidity) 	

Hypotension

ADR

- nausea & vomiting
- Increase in ICP -Urinary retention.
 - Prolongation of labor & fetal distress.
- Head injuries.
 - Pregnancy.
- **Contraindication** Bronchial asthma.
 - Chronic obstructive lung diseases.
 - Hypovolemic shock (Large dose only)

Opiate drugs





Neuroleptanesthesia

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

Z

MCQ

- 1- Which of the following is an inhalation anesthetic?
 - A) Etomidate
 - B) Nitrous Oxide
 - C) Prochlorperazine
 - D) Diazepam
- 2- Which of the following can be used as an adjunct to general anesthetics?
 - A) Succinylcholine
 - B) Ranitidine
 - C) Prochlorperazine
 - D) Diphenhydramine

the MAC, the 3- The the Drug:

- higher, more potent A)
- B) higher, less potent
- C) lower, more potent
- D) lower, less potent
- 4- Which of the following is more potent?
 - Nitrous Oxide A)
 - Sevoflurane B)
 - C) Enflurane
 - D) Halothane

5- A patient with liver failure is undergoing surgery. Which of the following should not be used?

- A) Nitrous Oxide
- B) Sevoflurane
- C) Enflurane
- D) Halothane
- 6- Which of the following has analgesic and amnesic actions:
 - Thiopental A) B) Etomidate
 - C) Midazolam
 - D) Ketamine

7- A patient undergoing major surgery has a head injury. Which of the following is indicated?

- Ultrashort acting barbiturates A)
- B) Opioids
- C) Benzodiazepines
- D) Ultrashort acting hypnotics
- 8- Which of the following is indicated in asthmatics?
 - A) Ketamine
 - B) Diazepam
 - C) Fentanyl D)
 - Lorazepam

1- Name the adjuncts to general anesthetics with two examples:

2- Describe the mechanism of action of general anesthetics:

Extra Qs written by Abdulrahman M. Bedaiwi (Click Here)

SAQ

	N	ICQ		SAQ	
	Q1		Q1	1- Preanesthetics: Opiates (Morphine), Anticholinergics (hyoscine) 2- Neuromuscular blocking agents (Succinylcholine, vecuronium)	
	Q2	A	02	Info in the lecture	
	Q3				
	Q4	D			
	Q5	D			
Answers:	Q6	D			
	Q7	A			
	Q8	A			



Good Luck , Future Doctors!

Team Leaders:

May Babaeer Zyad Aldosari

This Stunning Work Was Done By:

Khalid Aldossari Naif Aldossari

Edited by: Salman Alagla

