MED437
KING SAUD UNIVERSITY

Pharmacology
Team 437

Revised By
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General Anesthetics

Objectives:

- Define anesthesia, balanced anesthesia, and pre-anesthetic medications.
- 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:

- Drugs names
- Doctors notes
- Important
- Extra

Editing File

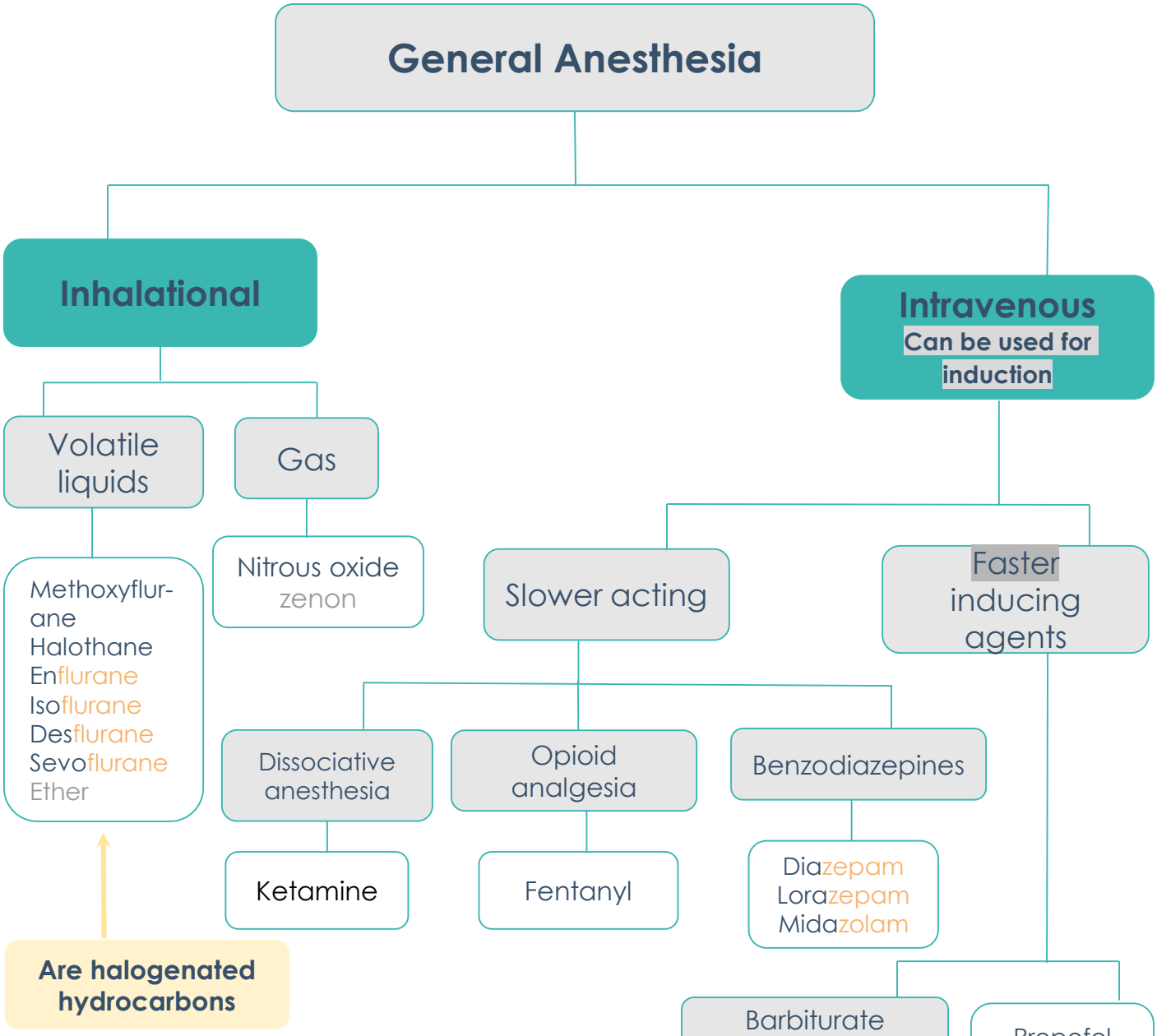
Important to know!!

يوجد اختلاف كبير بين سلايدات البنات والعيال!!

- دكتور اشفاق حذف سلايدات كثيرة من عند العيال وقال اللي بيجي بالاختبار المشترك فقط.
- اللون الوردي موجود بسلايدات البنات فقط.
- جدول السميري مهم ، يحتوي على المعلومات المشتركة اللي ركزوا عليها الدكاترة من كلا الطرفين.
- الهايلايت الرمادي :هو اللي اضافته او عدلت عليه بروف حنان بعد ما ارسلنا لها شغل التيم.

- All inhalation anesthetics increase ICP contraidicated in head injuries.
- All intravenous anesthetics decrease ICP except ketamine & opioids.

overview:



Mnemonic:
The benzodiazepines family is small, happy, and hyperactive. They have 3 kids: Clara, Lora, and Dia.
Used as antidepressant bc they're happy. But also bc they're hyperactive they may fall, forget things, and run out of breath ~~(respiratory effect)~~

Mnemonic:
مها اندس في سنها سوس
م= Methoxyflurane
ها= Halothane
ان=Enflurane
دس:Desflurane
س= Sevoflurane
ن=Nitrous oxide

Introduction:

General Anesthetics: Drugs used to induce **loss of pain sensation, loss of consciousness**, skeletal muscle relaxation, analgesia, amnesia(فقد الذاكرة) and inhibitions of **undesirable autonomic reflexes.**

types of anesthesia

- General anesthesia
- Local anesthesia

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.
-Hyperactivity + irregularity of most the autonomic N.S

Stage III (Surgical anesthesia)

- **Regular** respiration & relaxation of Sk. muscles.
- Eye reflexes decrease until the pupil is fixed.
-the most desire stage.

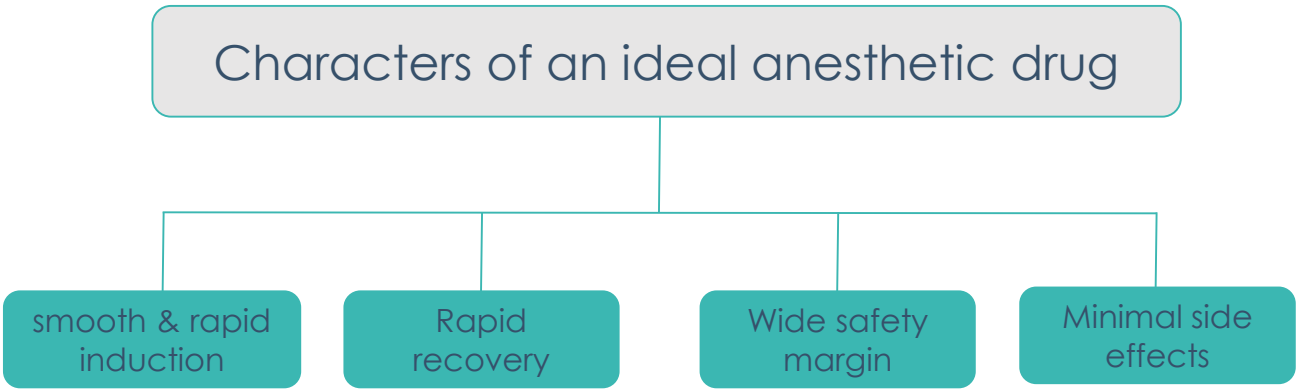
divided into 4 planes:
1. Cortical centers
2. Basal ganglia
3. Spinal cord
4. Medulla

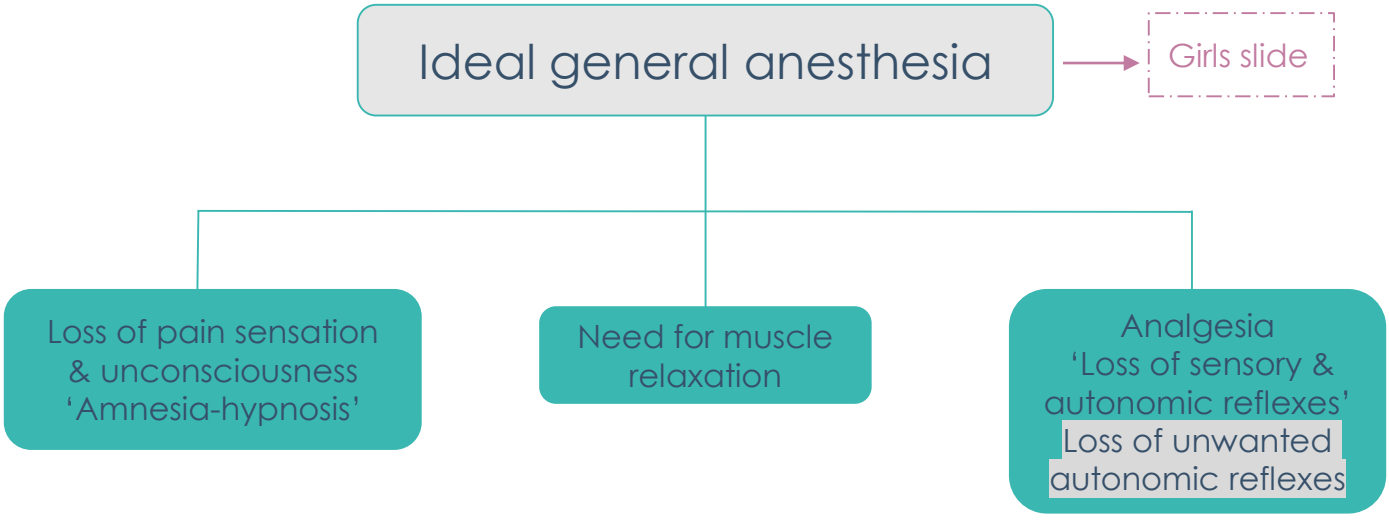
→ Girls slide

Stage IV (coma and death)

- Medullary paralysis.
-Severe **depression of vasomotor**
-Depression of respiratory centers.
- Death may occur.

Introduction:





Balanced Anesthesia

- Balanced anesthesia is achieved by a **combination of I.V and inhaled anesthesia , Pre-anaesthetic medications and also sk. muscle relaxants .**

- Thus it will increase the beneficial effects & decrease the adverse effects **of general anesthetics** which will fulfill the patient needs.

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.
- ★ Lowered the dose of anaesthetic required.

	Used to	Example
Opiates	Induce analgesia	**morphine**
Anticholinergics	Prevent secretion of fluids into the respiratory tract Protect the heart against vagal stimulation (bradycardia)	**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	Smooth induction	
Neuromuscular blockers	Facilitate intubation & suppress skeletal muscle tone.	**succinylcholine, vecuronium & atracurium**

MOA of General Anaesthetics

MOA:

-Disruption of the function of ionic channels

-Disruption of lipids associated with ionic channels

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Girls slide

Receptors

Enhanced

Inhibitory

- GABA A
- glycine

Excitatory

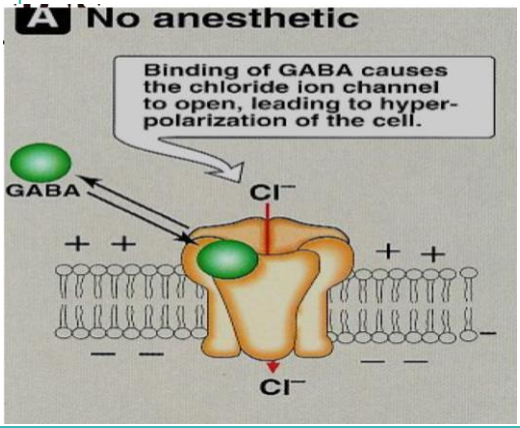
Inhibited

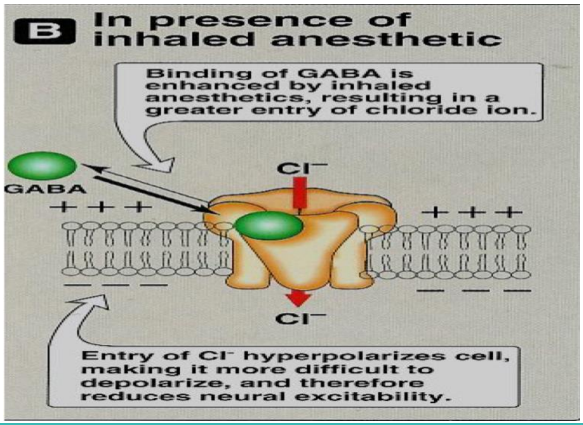
- nAch
  n= Nicotinic
- NMDA
  N-methyl-D-aspartate

*NB: General anesthetics do **NOT** combine with GABA receptors (they just enhance their action)

Enhance the action of GABA A and glycine receptors leading to **greater entrance of chloride ion** → hyperpolarization → thus **decrease neuronal excitability.**

-CNS depressant most of them act to stimulate or inhibit of exist neurotransmitter .





Inhalation anesthetics

induction : time elapsed between **onset** of administration of anesthetics(drug) and development of effective **surgical anesthesia** (stage no.3)**.**

The faster the better

Maintenance : Time during which the patient is surgically anesthetized(keeping the patient stage 3).

Recovery: The time from discontinuation(stopping)of anesthetic drug until **consciousness is regained**

The faster the better

Inhalation anesthetics

Pharmacokinetics of Inhalation anesthetics:

- Rate of induction
- Depth of anesthesia and Recovery

Factors controlling induction & recovery :

1- The anesthetic concentration in the inspired air → **Direct**

2- Blood solubility : Blood gas partition coefficient → **Inverse relation** (means it need more time to reach CNS to produce an effect.)

3- Rate and depth of ventilation → **Direct**

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	0.42	Poor & Rapid
Nitrious oxide	0.47	Rapid

Nitrous oxide has the lowest solubility,the fastest induction and recovery, the highest MAC and least potent

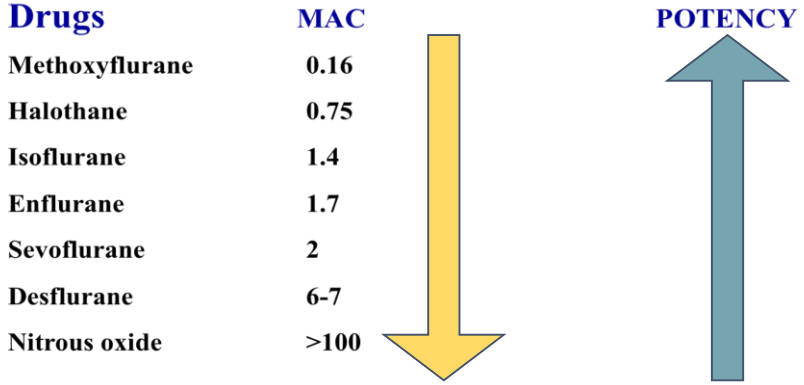
Minimum alveolar concentration (MAC)

It is the concentration of **inhalation anesthetic** that produce immobility (affect) 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.
- Decreased by CNS depressants, old people.
- Increased by CNS stimulants.
- Potency is inversely proportional to MAC value of anesthetic agents.

Girls slide

Drug	MAC value	Induction & recovery	Potency
Methoxyflurane	**low** MAC value 0.16	**slow** induction & recovery	The **most** potent
Halothane (Pleasant odor)	0.75	Slow	Potent
Enflurane (Pungent odor)	1.4	Medium	Less potent
Isoflurane	1.7	Medium	Less potent
Sevoflurane (Better smell)	2	Rapid	Less potent
Desflurane (Pungent odor)	6-7	Rapid	Less potent
Nitrous oxide	>100	Rapid	**Least** potent



Pharmacological actions of inhalation anesthetics

System	Pharmacological action
Central nervous	- ↓ metabolic rate. - ↑ ICP (due to cerebral vasodilatation) # in head injuries. - Dose -dependent EEG changes (**Enflurane**). - - **Enflurane** contraindicated in epilepsy
Cardiovascular	- Hypotension - Bradycardia **Except** (**Isoflurane** ,**Desflurane** & Sevoflurane). - Myocardial depression (**Halothane – Enflurane**). -Sensitize heart to catecholamines (**Halothane**) **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
Uterus & skeletal muscle	-Uterine relaxation **BUT** Nitrous oxide has minimal relaxant effect (labor) - All are skeletal muscle relaxants. (of variable degrees)

Inhalation Anesthetics

Drug	Halothane	Enflurane	Isoflurane (Forane)
Potency	Potent	Less potent than **Halothane**	Potent, stable compound (2%)
Induction & Recovery	Slow induction and recovery	More rapid induction and recovery than halothane	Rapid induction and recovery
Smell	Pleasant odor used in children	Pungent	Pungent
Metabolization	Metabolized to toxic metabolites (trifluoroethanol) hepatotoxic	Metabolized to fluoride (8%), excreted in the kidney (lead to nephrotoxicity)	Low biotransformation (Less fluoride)
Uses	Potent anesthetic, Weak analgesic, Weak skeletal muscle relaxant	Better muscle relaxation, Better analgesic properties	Potent anesthetic, Good analgesic action
Advantages	Profs. Notes on Halothane: 1- Slow induction 2- Very potent 3- Hepatotoxicity in adults 4- Arrhythmias (sensitizes heart to catecholamines)	---	- No nephrotoxicity - No hepatotoxicity - No sensitization of the heart - No cardiac arrhythmias
ADRs / Disadvantages	- CVS depression: Hypotension, bradycardia (vagomimetic action) ↓Myocardial contractility, ↓Cardiac output - Hepatotoxicity (repeated use). (only in adults, not in children) - Malignant hyperthermia. (can't be predicted) - Cardiac arrhythmias. - Sensitizes heart to action of catecholamines →arrhythmias.	**Pungent** (Less induction in comparison to other inhalation it's slow Not for pediatrics) -CNS stimulation (Epilepsy-like seizure - abnormal EEG)	Pungent (Not for pediatrics)
CI.	- **Pheochromocytoma**	-Patients with seizure disorders (epilepsy) -Not for renal failures	---

Inhalation Anesthetics

Drug	Desflurane	Sevoflurane	Nitrous Oxide (N2O)
Potency	Less potent than **Halothane**	Less potent than **Halothane**	**the Lowest potency**
Induction & Recovery	Rapid induction and fast recovery (Low solubility)	Rapid onset and recovery (Low solubility)	Rapid induction and recovery (Low solubility)
Smell	Pungent (worst odor)	Better smell	---
Metabolization	Less metabolized (0.05%) Low boiling point (special equipment)	Less metabolized (3-5% fluoride)	---
Uses	---	No airway irritation (preferable for children)	Weak anesthetic (Low potency, combined) Potent analgesic - Outpatient anesthesia (Dental procedures). - Balanced anesthesia. - Neuroleptanalgesia - Delivery.
Advantages	---	Little effect on HR	No muscle relaxation, No respiratory depression Not hepatotoxic, minimal CVS adverse effects
ADRs / Disadvantages	Pungent odor (irritation - cough)	---	- 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
CI.	**All of the inhalation anesthetic drugs are contraindicated in head injury.**		- Pregnancy(uterine relaxant) - Pernicious anemia. - Immunosuppression.

Intravenous Anesthetics

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

Patient with hypovolemia or shock suffer from severe hypotension so I can't give them Barbiturates, Propofol, Etomidate and Benzodiazepines since they decrease BP. We can give them Katamine because it's the only one that increase sympathetic→↑BP.

Intravenous Anesthetics

Drugs	Ultrashort acting barbiturates -Thiopental -Methohexital Ends with al or one, Hypnotic	Propofol Hypnotic(Non Barbiturate) Hypnotic	Benzodiazepines -Midazolam -Diazepam -Lorazepam Hypnotic anxiolytics
Onset D.O.A *	Rapid (1 min) (high lipid solubility)	Rapid	slower than other agent
	Ultra short (15 - 20 min) they undergo **Redistribution**	short	---
Metabolization	slowly by the liver . • slow recovery. • hangover.	Rapidly in liver (10 times - Elimination ½ = 30 – 60 min). • Faster recovery than thiopental	**Slow induction and recovery** *reserved for preanesthetic
Uses	-Potent anesthetic. -Induction in major surgery. - Alone in minor surgery. -In head injuries : ↓ ICP.	-Antiemetic action. - ↓ICP.	-No pain. -anxiolytic and **amnesic action.** -Induction of general anesthesia. -Alone in minor procedure (endoscopy). -In balanced anesthesia (Midazolam).
ADR	-CVS collapse and respiratory depression **(laryngospasm,bronchospasm)**. -precipitate **porphyria** attack. (enzyme inducers) -hypersensitivity reaction.	-CVS collapse (Hypotension) -CVS and respiratory depression. **-Excitation (involuntary movements).** (like enflurane) **- Pain at site of injection.** **-Expensive.** -Clinical infections due to bacterial contamination.	- respiratory depression. -CVS collapse (Hypotension)
C.I	**-Respiratory patients** **-COPD** **-Porphyria** -severe hypotension **(hypovolemic & shock patient)**	---	---

*D.O.A =duration of action

Intravenous Anesthetics

Drugs	Etomidate Ultrashort acting hypnotic (Non Barbiturates)	Ketamine given IV, IM **(Children)**	Opiate drugs -Fentanyl -Alfentanil -Sufentanil - Remifentanil
onset	Rapid	rapid but in comparison to other I.V it's slow	Rapid
D.O.A	short	short	Short
Metaboli zation	Rapidly in liver. • fairly fast recovery • less hangover	---	---
Uses	----	**-Dissociative anesthesia** (**Analgesic activity, Amnesic action** ,immobility, complete separation from the surrounding environment). **-Used in (hypovolemic, shock & elderly) patients.** **-Potent bronchodilator (asthmatics).**	- Potent analgesia. NOT anesthetic **-Neuroleptanalgesia** (Fentanyl+Droperidol). **-Neuroleptanesthesia** (Fentanyl+Droperidol+ nitrous oxide).
ADR	-Minimal CVS and respiratory depressant effects. **-Involuntary movements during induction (diazepam).** -Postoperative nausea & vomiting. -Pain: at the site of injection. **-Adrenal suppression**	**-Risk of hypertension and cerebral hemorrhage ICP** -Postoperative: -**hallucination vivid dreams & disorientation & illusions**. - BP & cardiac output → (central sympathetic activity). Increases plasma catecholamine levels→ ICP ADRs: طبعاً على حسب استخدامنا لهم ممكن يكون ساید افیکت وممكن نستخدمه بطريقة تفيدنا	-Respiratory depression, bronchospasm . -(wooden rigidity). -Hypotension -nausea & vomiting -Increase in ICP -Urinary retention. -Prolongation of labor & fetal distress.
C.I	---	-Head injuries -CV diseases (hypertension-stroke). But is the drug of choice in **hypovolemic & shock patient**	-Head injuries. -Pregnancy. -Bronchial asthma. -Chronic obstructive lung diseases. -Hypovolemic shock (Large dose only)

Opiate drugs

Girls slide only

Neuroleptanalgesia :

(Opiate drugs)

- 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).** Blocks dopamine release
- Contraindicated in parkinsonism.

Neuroleptanesthesia :

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

*Prof. Hanan said it's important to know the characteristic of each drug that make it unique (summarized here)

Summary

النقاط المهمة واللي ركزوا عليها بروف حنان ودكتور اشفاق موجودة بالجدولين

Inhalation Anesthetics

Drug	Characters	S/E	C/I	Uses	
Methoxy-flurane NOT USED	For veterinary use only	Slow induction, nephrotoxicity		No longer used	highest solubility , potency - slowest induction & recovery lowest MAC
Halothane (Pleasant odor)	●non-irritant. ●Slow induction ●Very potent ●Weak analgesic. ●Can be used in children.	●Hepatotoxicity (adult only) ●Malignant hyperthermia. ●Sensitization of heart to catecholamines → arrhythmias.	pheochromocytoma	since it does not cause hepatotoxicity in children and has pleasant smell, can be used with children	
Enflurane (pungent odor)	Metabolized to fluoride (8%), excreted by kidney	Airway irritation CNS stimulation (Epilepsy-like seizure- abnormal EEG).	●patients with seizure disorders. ● renal failures. ●Epilepsy patient		
Isoflurane (Forane) (Pungent odor)	●Stable compound. ●No nephrotoxicity. ● No hepatotoxicity.				
Sevoflurane (better smell)	●No airway irritation (preferable for children)			with children.	
Desflurane (Powerful pungent odor)	●Low boiling point (special equipment).	Its pungent odor lead to airway irritation and cough			
Nitrous oxide (Pungent odor)	●Potent analgesic. ●weak anesthetic.	●Diffusion Hypoxia. ●Inactivation of B12→ megaloblastic anemia. ●Abortion -	●Pregnancy. ●Pernicious anemia. ●Immunosuppression	●Dental procedures ●Balanced anesthesia.(not used alone) ●Neuroleptanalgesia	lowest solubility fastest induction & recovery highest MAC and

Summary

Intravenous Anesthetics

Drugs:		Characters	S/E	C/I	Uses:
Barbiturates (Ultrashort acting)	Thiopental	●Rapid onset of action ●Short duration (Redistribution) ●Potent anesthetic ●↓ ICP	●CVS & respiratory depression ●precipitate porphyria attack ●hypersensitivity reaction(sulfat)	●Hypotensive patient ●porphyria patients ●chronic obstructive lung disease	●induction in major surgery and alone in minor surgery. (dentistry) ●in head injuries
	Methohexital				
Hypnotic(NonBarbiturate)	Propofol	↓ICP Has Antiemetic action.	Excitation (involuntary movements)1	---	---
	Etomidate	●Rapidly metabolized in liver (less hangover). ●Minimal CVS and respiratory depressant effects.	●Involuntary movements during induction (like diazepam). ●Adrenal suppression	---	a safe Cardiovascular and respiratory risk profile
Ketamine		●Dissociative anesthesia (Analgesic activity Amnesic action) ●Can be given IV or IM (especially in children) ●↑central sympathetic activity2 ●Potent bronchodilator.	●Psychotomimetic effect after recovery (hallucination vivid dreams) ●↑ICP - salivation ●hypertension ●cerebral hemorrhage.	●Head injury ●Hypertensive patient ●Cardiovascular disorders	hypovolemic, shock & elderly patients
Opioids	fentanyl	Potent analgesia.	●bronchospasm (wooden rigidity). ●Hypotension ●↑ICP ●prolong labor and fetal distress ●Urinary retention.	●Head injury. ●Pregnancy. ●Bronchial asthma +COPD ●Hypovolemic shock	Neuroleptanalgesia Neuroleptanesthesia
	Alfentanil				
	Sufentanil				
	Remifentanil				
Benzodiazepines	diazepam	anxiolytic and amnesic action	---	Respiratory patients	●induction of general anesthesia. ●Alone in minor procedure (endoscopy). ●In balanced anesthesia (Midazolam)
	lorazepam				
	Midazolam (pre-anesthetic)				

Questions

MCQs

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

3- The ____ the MAC, the ____ the Drug:

A) higher, more potent
B) higher, less potent
C) lower, more potent
D) lower, less potent

4- Which of the following is more potent?

A) Nitrous Oxide
B) Sevoflurane
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

MCQs Answers:
1- B
2- A
3- C&B
4- D
5- D

Questions

MCQs

6- Which of the following has analgesic and amnesic actions:

A) Thiopental
B) Etomidate
C) Midazolam
D) Ketamine

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

A) Ultrashort acting barbiturates
B) Opioids
C) Benzodiazepines
D) Ultrashort acting hypnotics

8- Which of the following is contraindicated in asthmatics?

A) Ketamine
B) Diazepam
C) Fentanyl
D) Lorazepam

MCQs Answers:
6- D
7- A
8- C

Questions

SAQ

Name the adjuncts to general anesthetics with two examples:

1. Preanesthetics: Opiates (Morphine), Anticholinergics (Hyoscine)
2. Neuromuscular blocking agents (Succinylcholine, vecuronium)

Describe the mechanism of action of general anesthetics:

Info in the lecture

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References:

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