جامعة الملك سعود
King Saud University

Pharmacology of Anesthesia

433
ANAESTHESIA

MED 433

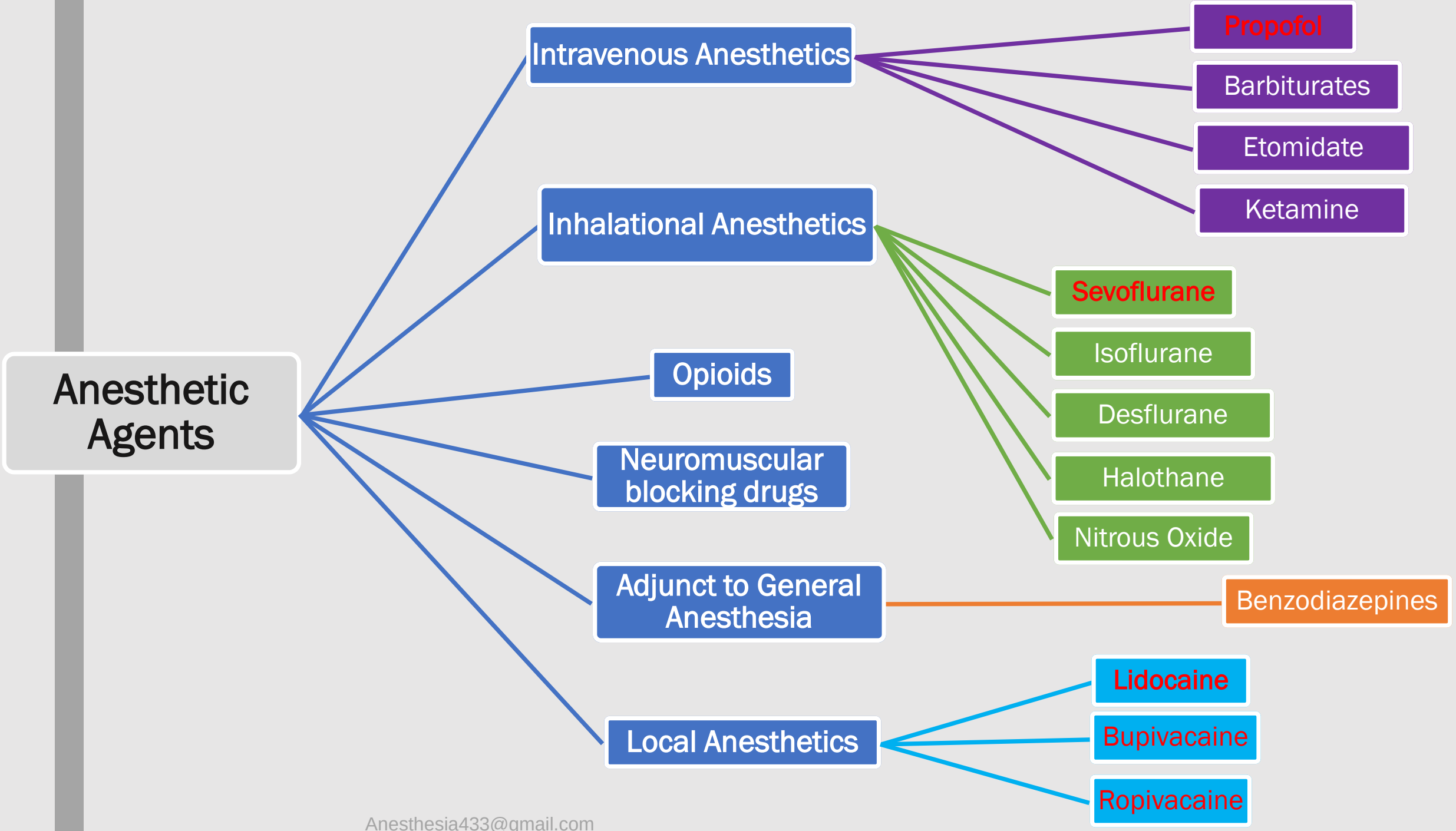
Objectives:

- IV anesthesia is mainly used in adults for anesthesia induction, while inhalation anesthesia is used to maintain it in adults.
- In pediatric the inhalation anesthesia is mainly used to induce the anesthesia.

1. Understand pharmacokinetics and pharmacodynamics of general anaesthetic agents: intravenous agents, inhalation agents, Opioids, neuromuscular blocking agents and reversal agents as well as local anaesthetic agents.

2. Learn about the main uses, advantages and disadvantages of these agents.

3. How to deal with adverse reactions diagnosis and management of Malignant hyperthermia and Succinylcholine apnea.



1- Intravenous Anesthetics

Even though we can give it to patient who has egg allergy

PROPOFOL

2, 6- diisopropylphenol

It is the most widely used induction agent. 1% isotonic oil-in-water emulsion, which contains egg lecithin, glycerol, and soybean oil.

Is the safest agent use nowadays

Mechanism of action	Facilitates inhibitory neurotransmission by enhancing the function (GABAA) receptors in CNS
Pharmacokinetics	Hepatic and extrahepatic metabolism leads to inactive metabolites which are excreted by renal route ,so you have to reduce the dose in hepatic or renal patient
Primary Uses	▪ A sedative/hypnotic in OR & ICU. ▪ Induction of anesthesia. ▪ Maintenance of anesthesia (TIVA).

Pharmacodynamics

CNS

- Induction : rapid onset of unconsciousness (30 to 45 seconds), followed by a rapid termination of effect by redistribution, so emergence is rapid .
- Weak analgesic effects .
- ↓ (ICP) and ↓ (CPP) due to markedly ↓ (MAP). Anticonvulsant .
- Less (PONV) occurs.

Cardiovascular System

- Dose-dependent ↓ in preload, afterload, and contractility lead to ↓ in (BP) and COP.
- **Hypotension** may be marked in hypovolemic, elderly, or hemodynamically compromised patients.
- Heart rate (HR) is minimally affected, and baroreceptor reflex is blunted.

Respiratory system

- Dose-dependent decrease in (RR) and (TV).
- ↓Ventilatory response to hypoxia and hypercarbia.

PROPOFOL

(2, 6- diisopropylphenol)

Dosage and administration	Induction: IV 1-2.5mg/kg Sedation : IV 25-100 µ/kg/min

Advantages

- Produces Laryngeal & pharyngeal muscle relaxation, **allowing LMA insertion**.
- **Safe in Malignant hyperthermia (MH) & Porphyria patients.**
- Antiemetic properties.
- **Suitable for day case surgery** to avoid prolong postoperative hangover (drowsiness, ataxia).
- **Situations where volatile anesthetics cannot be used (MH)**
- transfer of sedated patients, airway surgery).
  Adverse effects
- Total IV anesthesia (TIVA)

Adverse effects

- Venous irritation.
- Bacterial growth
- Lipid disorders. **used cautiously** in disorders of lipid metabolism (e.g., hyperlipidemia and pancreatitis).
- Myoclonus and hiccups
- Propofol infusion syndrome : a rare fatal disorder that occurs in critically ill patients (usually children) subjected to prolonged, high-dose propofol infusions. (Rhabdomyolysis, metabolic acidosis, cardiac failure, and renal failure).

- Titrate with incremental doses in hypovolemic, elderly, or hemodynamically compromised patients or if administered with other anesthetics

Barbiturates

Thiopental is a thiobarbiturate.

Mechanism of action	▪ Facilitate inhibitory neurotransmission by enhancing GABAA receptor function. ▪ Inhibit excitatory neurotransmission via glutamate and nicotinic acetylcholine receptors.
Pharmacokinetics	Metabolism and elimination is hepatic. Multiple doses or prolonged infusions may produce prolonged sedation or unconsciousness
Primary Uses	▪ Induction of anesthesia.

Pharmacodynamics

CNS

- Dose-dependent CNS depression. ↓ in (CMRO2) cause ↓ in ICP and (CBF).

Cardiovascular System

- Depress myocardial contractility, leading to dose-dependent ↓ in BP and cardiac output,
- Baroreceptor reflexes remain largely intact.

Respiratory system

- Dose dependent decrease in RR and TV. Apnea may last for 30 to 90 seconds after induction dose.
- **Laryngeal reflexes remain more intact** compared to propofol so higher incidence of cough and laryngospasm.

Barbiturates
Thiopental is a thiobarbiturate.

Dosage and administration	▪ Induction: IV 3-6 mg/kg ▪ Sedation IV 0.5-1.5 mg/kg N.B. Reduce doses in hypovolemic, elderly, or hemodynamically compromised patients..**because it cause hypotension**

Advantages	Adverse effects
▪ Rapid onset (30 - 45 sec), ▪ short duration (5 – 8 min) initial dose; redistributed from brain to muscle resulting in return of consciousness. ▪ It has potent anticonvulsant properties.	▪ Dose dependent histamine release. ▪ Myoclonus and hiccups . ▪ **Absolutely contraindicated in Porphyria, it cause spasm** ▪ Venous irritation and tissue damage ▪ Thiopental can cause **severe pain and tissue necrosis** if injected subcutaneously or intra-arterially. ▪ **If** intra-arterial administration occurs, heparin, vasodilators, and regional sympathetic blockade may be helpful in treatment. ▪ Hangover effect ▪ Not for one day surgery

Etomidate

It is a carboxylated imidazole.

Mechanism of action	Facilitates inhibitory neurotransmission by enhancing the function (GABAA) receptors.
Pharmacokinetics	▪ Effects of a single bolus dose are terminated by redistribution. ▪ Very high clearance in the liver and by circulating esterases to inactive metabolites
Primary Uses	▪ Induction of anesthesia in patients with cardiovascular problems. (hypertension , ischemic heart disease , shock , trauma , bleeding) ▪ It has nothing to do with analgesia

Pharmacodynamics

CNS	Cardiovascular System	Respiratory system
▪ **No analgesic properties.** ▪ ↓ (CBF), cerebral metabolic rate, (CMR), and (ICP).	▪ Minimal changes in HR, BP, and COP.	• Dose-dependent ↓ in (RR) & (TV). Transient apnea may occur.

Dosage and administration	▪ Induction: IV 0.2-0.5mg/kg

Etomidate

It is a carboxylated imidazole.

Advantages	Adverse effects
▪ **Short acting and potent, with CVS and RS stability, suitable for elderly and shocked patients.**	▪ Excitatory phenomena (Involuntary limb twitches), myoclonus, so you have to give it with propofol or fentynel in small dose to reduce twitches. ▪ Nausea and vomiting . ▪ Venous irritation and superficial thrombophlebitis ▪ Adrenal suppression, (Inhibits 11β & 17 α hydroxylase). ▪ A single dose suppresses adrenal steroid synthesis for up to 24 hours. ▪ Repeated doses /infusion is associated with increased mortality in ICU patients. ▪ Respiratory depression even in small dose

Ketamine

It is phencyclidine derivative causing ‘dissociative anesthesia’

Mechanism of action	Mainly attributed to noncompetitive antagonism of NMDA receptors in the CNS
Pharmacokinetics	▪ Unconsciousness in 30 to 60 s after an IV. ▪ Terminated by redistribution in 15 to 20 minutes. ▪ Metabolized rapidly in the liver to multiple metabolites, some of which have modest activity (e.g.,norketamine). , have long duration of action. ▪ Elimination half-life is 2 to 3 hours.
Primary Uses	▪ Induction of general anesthesia. ▪ Sedation and analgesia.

Pharmacodynamics

CNS

- Amnesia and profound analgesia.
- ↑ (CBF), ↑ (CMR), and ↑(ICP) pressure.

Cardiovascular System

- ↑ HR, COP, and BP .
- Used in hemodynamically compromised patients.

Respiratory system

- Mild depression of (RR) and (TV).
- **Potent bronchodilator** .
- Laryngeal protective reflexes **are maintained.**

Dosage and administration	▪ Induction: IV 1-2mg/kg , IM 3-5mg/kg **N.B. Useful for IM induction in patients with no IV access (e.g., children).**

Ketamine

It is phencyclidine derivative causing ‘dissociative anesthesia’

Advantages	Adverse effects
▪ **CVS stability makes it suitable for shocked patients.** ▪ **Preservation of airway reflexes & less respiratory depression** makes it suitable for procedures – radiological interventions, radiotherapy, burns & dressing changes.	▪ ↑ salivation, PONV. (post-op nausea & vomiting) ▪ Emotional disturbance, agitation & **hallicunations**.so we give it with propofol to decrease the chances of getting hallicunations ▪ Contraindicated in patients with **head trauma.** ▪ **Not in LMA insertion , cause the laryngeal reflexes are intact**

2- Opioids

Opioids produce moderate sedation and profound analgesia. Fentanyl, Sufentanil, Alfentanil, Remifentanil, Meperidine, Morphine.

Mechanism of action	They exert their effects by binding with opioid receptors in CNS 3 major opioid receptors μ (mu), κ (kappa), and δ (delta).
Primary Uses	▪ They mimic endogenous compounds: Endorphins, enkephalins & dynorphins. ▪ Principally provides **analgesia and some degree of sedation.** ▪ Large doses can produce general anesthesia.

Advantages	Adverse effects
▪ Minimal cardiac effects ▪ No myocardial depression.	▪ Miosis ▪ Nausea & vomiting, slow gastric emptying, constipation does not occur from single dose. ▪ Drowsiness or sedation ▪ Chest wall rigidity & respiratory depression ▪ Bradycardia in large doses ▪ Some peripheral vasodilation and histamine release – hypotension ▪ Itching ▪ Urinary retention & biliary colic,

Fentanyl Best used for induction	▪ A potent synthetic opioid agonist with100 times, the analgesic potency of morphine. ▪ Used for **induction** and maintenance of G.A and to supplement regional and spinal anesthesia. ▪ Ability to **maintain cardiac stability**.
Sufentanil citrate (Sufenta)	▪ 10 times as potent as fentanyl ▪ Rapid elimination ▪ Relatively more **rapid recovery** as compared with fentanyl.
Alfentanil	▪ **Shorter duration** of action compared to fentanyl and sufentanil,
Remifentanil (Ultiva) best used intraoprative.	▪ **Ultra short acting and rapidly cleared** ▪ widespread extrahepatic metabolism by blood and tissue nonspecific esterases
Morphine Best used post-op	▪ May produce hypotension and bronchoconstriction as a consequence of its histamine-releasing action., itching ▪ Morphine may be a poor choice for a patient with renal failure, reduce the dose in elderly
Naloxone (antidot) A specific opiate receptor antagonist, binding the receptor. The effective dose is 1 to 4 µg/kg IV, and the duration of action is 30 to 45 min. Dose may need to be repeated or as an infusion	
Adverse effects	▪ Reversal of analgesia, nausea, vomiting, Increased sympathetic nervous system activity, (tachycardia, hypertension, pulmonary edema, and cardiac dysrhythmias). Need monitoring

3- Adjunct to General Anesthesia

Benzodiazepines

Midazolam, lorazepam, and diazepam.

Mechanism of action	Enhance inhibitory neurotransmission by increasing the affinity of GABAA receptors for GABA.
Pharmacokinetics	▪ Effects are terminated by redistribution. ▪ All are metabolized in the liver. ▪ Hydroxymidazolam cause sedation in Pt with renal failure. ▪ **Diazepam clearance is reduced in the elderly.**
Primary Uses	▪ **Sedation, amnesia, anxiolytic use as premedication** or as adjunct to general anesthesia. Have anticonvulsant and hypnotic effect also

Pharmacodynamics

CNS

- Amnestic, anticonvulsant, anxiolytic, and sedative-hypnotic (dose-dependent manner).
- **No analgesia.**

Cardiovascular System

- Mild systemic vasodilation and ↓ in cardiac output.
- HR is usually unchanged.

Respiratory system

- Mild dose-dependent ↓ in RR and TV.
- Respiratory depression may be more if administered with an opioid
- Respiratory depression can be marked and lead to apnea in elderly

Adverse effects	▪ Drug **interactions with anticonvulsant (valproate)** ▪ Pregnancy and labor : Risk of cleft lip and palate in the first trimester. CNS depression in the neonate. ▪ Superficial thrombophlebitis and injection pain by diazepam and lorazepam. ▪ They cause mild respiratory depression **but can be marked in elderly leading to apnoea**.
Midazolam (Dormicum)	▪ Water soluble, so drug of choice **for IV administration** ▪ More rapid onset and more rapid elimination ▪ The most potent amnestic
Diazepam (Valium)	▪ Water-insoluble, so IV use can cause local irritation/pain
Lorazepam (Ativan)	▪ Water-insoluble. **Premed**

Midazolam can be given in receiving area pre-op to deferentiated from real HTN and anxiety >> B.P goes to normal if it was due to anxiety

Flumazenil (antidot)

- **A competitive antagonist** at the benzodiazepine binding site of GABAA receptors in the CNS.
- Reversal of sedative effects occurs within 2 min; peak effects at 10 min.
- Half-life is shorter than the benzodiazepine 1 hour
- Metabolized to inactive metabolites in the liver.
- Dose. 0.3 mg IV every 30 to 60 seconds (to a maximum dose of 5 mg).
- **Contraindicated in patients receiving benzodiazepines for the control of seizures or elevated ICP.**

4- Inhalational Anesthetics

Characteristics of the ideal inhaled anesthetic agent	Volatile anesthetics	The minimum alveolar concentration (MAC)
▪ Non - toxic, non-.allergenic, non - irritant. ▪ Stable in storage, non – flammable & no extra specialist equipment required. ▪ Low solubility in blood and tissues. ▪ Resistance to physical and metabolic degradation. ▪ Analgesic. ▪ CVS stable. ▪ No respiratory depression. ▪ Environmentally inert. ▪ No reaction to soda lime/ breathing circuit. ▪ Not a malignant hyperthermia (MH) trigger.	▪ Present as liquids at room temperature and pressure. ▪ Vaporized into gases for administration	▪ The amount of vapour (%) needed to render 50% of spontaneously breathing patients unresponsive to a standard painful surgical stimulus.' ▪ Halothane, isoflurane, sevoflurane, and desflurane are 0.75%, 1.15%, 1.85%, and 6.0% at one atmosphere. ▪ **First sign for low MAC is tachcardia**

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Sevoflurane , Desflurane , Isoflurane , Halothane

Mechanism of action	Various ion channels in the CNS involved in synaptic transmission (including GABAA, glycine, and glutamate receptors) may play a role.
Pharmacokinetics	**The higher the vapor pressure, the more volatile the anesthetic.** Blood solubility determines the speed of build-up / elimination from blood / brain Lower blood solubility means (faster induction/recovery) **Inspired air → Alveolar air → Blood → Brain** Metabolism: hepatic . Exhalation:This is the predominant route of elimination

Pharmacodynamics

CNS

- Unconsciousness and amnesia . ↑ cerebral blood flow (CBF).

Cardiovascular System

- Myocardial depression & systemic vasodilation.
- HR tends to be unchanged, except desflurane
- Sensitize the myocardium to the arrhythmogenic effects of catecholamines.

Respiratory system

- Dose-dependent respiratory depression
- Airway irritation and, during light levels of anesthesia, may precipitate coughing, laryngospasm, or bronchospasm (sevoflurane makes it more suitable)
- **Bronchodilator (with the exception of desflurane).**
- Inhibit hypoxic pulmonary vasoconstriction.

All volatile agents can trigger MH. if so stop the inhalation agent and shift to TIVA (total IV analgesia)

Pharmacodynamics

Neuromuscular system

- Dose-dependent ↓ in skeletal muscle tone.
- May precipitate malignant hyperthermia **… A dramatic increase in body temperature**, acidosis, electrolyte imbalance and shock.
- Management is removal of triggering agent, 100% Oxygen,
- active cooling measures & Dantrolene (1 to 10 mg/kg)

Renal system.

- ↓ renal blood flow
.

Hepatic System

- ↓ hepatic perfusion.

Sevoflurane , more potent

Advantages

- Low solubility in blood-- produces rapid induction and emergence
- **Pleasant smelling** (suitable for children)
- Has good **bronchodilating** properties
- **Agent of choice in asthma, bronchitis, and COPD.**
- It has little effect on the heart rate., good for CVS problems
- Mild respiratory and cardiac suppression

Disadvantages

- Carbon dioxide absorbents in anesthesia machines degrade sevoflurane to Compound A

Desflurane

Advantages

- Rapid onset and recovery of anesthesia (outpatient procedures)
- One of least metabolized to toxic byproducts
- Irritant not for induction

Disadvantages

- Requires a **special vaporizer**
- Pungent and irritating to the airway (leading to more coughing, laryngospasm)
- High inspired gas concentrations lead to **a significant ↑ in the patient's BP & HR.**

Isoflurane

Advantages

- It causes peripheral **vasodilation** drop BP and increased coronary blood flow .

Disadvantages

- Moderate solubility, so recovery from anesthesia may be delayed
- Isoflurane can make the heart "more sensitive" to circulating catecholamines (like epinephrine).

Halothane not used anymore

Used for induction in children (sweet pleasant odor);
Sensitize the myocardium to the arrhythmogenic effects of catecholamines.
Blood pressure usually falls.
Very soluble in blood and adipose tissue
Prolonged emergence
"Halothane hepatitis" (rare).

Nitrous Oxide

MAC is 104% at one atmosphere

Pharmacodynamics

CNS

- Antagonism of NMDA receptors in CNS.
  Weak anesthetic, produce analgesia.
- Usually combined with other anesthetics.
- Used alone e.g. dental procedures.

Cardiovascular System

- Mild myocardial depressant
- mild sympathetic stimulant.HR and BP are usually unchanged.
- ↑ pulmonary vascular resistance.

Respiratory system

- Little effect on respiration

Adverse effects

- Nausea/vomiting.
- Risk of bone marrow depression
- Inhibits vitamin B-12 metabolism
- Expansion of closed gas spaces. Nitrous oxide is 35 times more soluble in blood than nitrogen.
  Contraindicated in (e.g. air embolus, pneumothorax, Middle Ear Surgery etc)
- Diffuse into the cuff of ETT.
- Diffusion hypoxia. After discontinuation, its rapid elimination from the blood into the lung may lead to a low partial pressure of oxygen in the alveoli.

5- Neuromuscular blocking drugs (NMBD)

Primary Uses

- Perform tracheal intubation.
- Facilitate ventilation.
- Provides optimal surgical operating conditions.

A/ Depolarizing (Succinycholine)

Structurally similar to acetylcholine .activate the acetylcholine receptors (Ach) .depolarization of post junctional membrane.

Advantages

- **Very short duration of action** (onset 60 seconds/ duration 10 minutes)
- For short time intubation **(Rapid sequence induction)**
- Metabolized very quickly by plasma cholinesterase.
- Characterized by transient muscle fasciculations followed by relaxation.
- **Acetylcholine esterase (AChE) inhibitors potentiate rather than reverse the block.**

Disadvantages

- **Cardiac dysrhythmias**: sinus bradycardia, junctional rhythm, and even asystole after the first dose in children and following repeated dose within a short time interval in adults.
- **Hyperkalemia**.(burns, RF, muscular dystrophies & paraplegia)
- A transient increase in intraocular pressure
- Increase in intracranial & intragastic pressure.
- Myalgia : abdomen, back, and neck.
- Histamine release.
- Dual block.

Succinylcholine apnea (side effect)

- Low levels of plasma cholinesterase (severe liver or kidney disease, starvation, malignancy or cardiac failure) result in prolongation of the effect
- A drug-induced inhibition of its activity, a genetically atypical enzyme.
- Management is **supportive**, especially to avoid awareness.
- Anaphylaxis. over 50% of anaphylactic reactions to NMBDs.
- Malignant hyperthermia (MH).

B/ Nondepolarizing blockers have 2 types

Mechanism of action	They act by competitively blocking the binding of ACh to its receptors and inhibit muscular contraction. (Slower onset than suxamethonium)
characterized by	▪ Absence of fasciculations. ▪ Potentiation by other nondepolarizing NMBDs and volatile anesthetic agents. ▪ Reversal by AChE inhibitors.

1ST type : Benzylisoquinoliniums : A/ MIVACURIUM

- Short-acting, rapidly hydrolyzed/metabolized by plasma cholinesterase.
- Histamine release causing a transient **hypotension and tachycardia**.

B/ ATRACURIUM

Widely used and have an **intermediate onset** and duration of action.
No direct cardiovascular effects.
Metabolism is by Hofmann degradation and ester hydrolysis in the plasma > causing **Histamine release.**
Its duration of action is independent of renal and hepatic function.
A breakdown product of atracurium, (laudanosine) may accumulate and **cause seizures**

C/ CISATRACURIUM

Isomer of atracurium
Hofmann degradation and does not accumulate in renal failure.
Relatively **slow** onset of action.
Does not release histamine. Less laudanosine .

2ND Type is Aminosteroids : ROCURONIUM

The most rapid onset of the clinically available non-depolarizing NMBDs.
Intubating conditions can be achieved in 60-90 seconds after an induction dose of 0.6 mg/Kg. Increasing the dose to 1.2 mg/kg shortens the time can **be used for rapid sequence induction when Suxamethonium is contraindicated.**
An **intermediate** duration of action. **Histamine is not released Or minimal release. Cardiovascularly is stable**
Higher incidence of anaphylactic reaction.

Anticholinesterases (Neostigmine)

They inhibit the action of the acetylcholinesterase enzyme at the NMJ by increasing the concentration of Ach at NMJ.
Clinical tests of adequate resolution of neuromuscular block include the ability to lift the head from the bed for 5 seconds.
Intravenous injection at a dose of 0.05 mg/kg (maximum 5mg).
To minimize adverse effects such as bradycardia, miosis, GI upset, nausea, bronchospasm, increased sweating, salivation & bronchial secretions, an an antimuscarinic such as glycopyrronium 0.01 mg/kg or atropine 0.02 mg/kg **must be administered along with the anticholinesterase.**

Table 9–1. Depolarizing and nondepolarizing muscle relaxants.

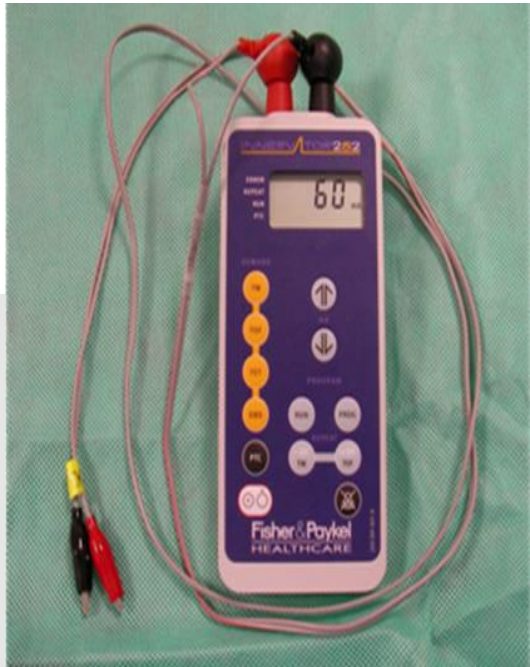
Depolarizing	Nondepolarizing
Short-acting	Short-acting
Succinylcholine	Mivacurium
	Intermediate-acting
	Atracurium
	Cisatracurium
	Vecuronium
	Rocuronium
	Long-acting
	Doxacurium
	Pancuronium
	Pipecuronium

CHOICE OF NMBD

- **Urgency for tracheal intubation.**
- Duration of the procedure,
- Coexisting medical conditions that may affect the NMJ.
- Side effects & metabolism
- Cost-effectiveness
- Suxamethonium makes it a good choice for rapid intubation .
- **Rocuronium will decrease the risk of hyperkalemia in patients with burns.**
- Pancuronium can produce a tachycardia that is undesirable in patients **with severe IHD**, **but its vagolytic effects may be appropriate in pediatrics..**

Peripheral nerve stimulator

- Check the depth of neuromuscular blockade
- Determine that neuromuscular blockade **is reversed**
- At least 3 twitches on a train of four should be detected before attempting reversal.



Sugammadex (a cyclodextrin) binds irreversibly to rocuronium and vecuronium, rendering them inactive. It has a role in failed intubation/ventilation scenarios by reversing muscle relaxation when rapid resumption of airway reflexes and respiratory function is required.

6- Local anesthetics (LAs)

LAs are drugs which reversibly prevent the transmission of pain stimuli locally at their site of administration.

Mechanism of action	Reversibly blocking sodium channels to prevent depolarization
Lipid solubility	▪ potency, plasma protein binding determines, duration of action of local anesthetics.
Addition of vasoconstrictor	▪ Prolongation of anesthetic action, decreased risk of toxicity and decrease in bleeding from surgical manipulation.

Esters (metabolized by plasma cholinesterase)	**Amides** (metabolized by cytochrome p-450)
▪ Cocaine (out of date) ▪ Benzocaine ▪ Procaine , Tertracaine	▪ Lidocaine ▪ Bupivacaine ▪ Mepivacaine , Prilocaine , Ropivacaine

Applications of local anesthesia

- Nerve block: (e.g., dental and other minor surgical procedures)
- Topical application: To skin for analgesia (e.g., benzocaine) or mucous membranes (for diagnostic procedures)
- Spinal & epidural anesthesia:
- Local infiltration: At end of surgery to produce long-lasting post-surgical analgesia (reduces need for narcotics)
- I/V infusion: For control of cardiac arrhythmias (e.g., lidocaine for ventricular arrhythmias)

LIDOCAINE

- The most commonly used amide type local anesthetic.
- Rapid onset and a duration of 60-75 minutes, extended with epinephrine for up to 2 hours.
- Metabolized in the liver and excreted by the kidneys.
- Contraindicated in patients with **a known sensitivity.**
- Has also **antiarrhythmic action.**

BUPIVACAINE

- Onset of action is **slower** than lidocaine and anesthesia is long acting - 2-4 hours, extended with epinephrine for up to 7 hours.
- **More cardio-toxic than lidocaine**, difficult to treat.
- Metabolized in the liver and excreted by the kidneys
- Contraindication: known **hypersensitivity**

ROPIVACAINE

Less toxic, long-lasting LA.
Undergoes extensive hepatic metabolism, with only 1% of the drug eliminated unchanged in the urine.
Ropivacaine is slightly less potent than bupivacaine.

Choice of local anesthetics

- Onset & Duration
- Sensory vs. motor block
- Potential for toxicity

Local Anesthetic Toxicity

- **CNS**: Initially circumoral numbness, dizziness, tinnitus, visual change. Later drowsiness, disorientation, slurred speech, loss of consciousness, convulsions & finally respiratory depression
- **Cardiovascular System**: Myocardial depression and vasodilation-- hypotension and circulatory collapse
- **Allergic reactions**: rare (less than 1%) rash, bronchospasm

Prevention and Treatment of Toxicity

- All Cases: **Assure adequate ventilation & administer supplemental Oxygen.**
- Seizures: Midazolam
- Hypotension: Trendelenburg position (head down , legs up),
- IV fluid bolus (Isotonic Saline or LR),
- Vasopressor (Dopamine if refractory to above).
- Dysrhythmias: As per ACLS protocol (but do not administer further Lidocaine)

Other side effects:
Allergy is common with the esters, especially with procaine but very rare with amides. It is more likely to be related to additives such as vasoconstrictors or preservatives.
Prilocaine metabolism produces toludine, which reduces Hb to metHb. Excess prilocine can therefore cause methaemoglobinaemia. It is treated with methylene blue.

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Color reference:
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Red-important

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