Drug		MOA	Primary uses + Pharmacokinetics	Pharmacodynamics	Advantages | Adverse effects
IV Anesthetics	Barbiturates	Enhance GABAA receptor & inhibit glutamate and nicotinic Ach receptors	- For Induction of anesthesia - Rapid onset (30-45s) - Short duration (5 – 8 min) initial dose; redistributed - Hepatic metabolism - Multiple doses or prolonged infusions → prolonged sedation or unconsciousness	**CNS:** ↓ CMRO2 → ↓ in ICP & CBF **Cardiovascular System:** -Depress myocardial contractility → ↓ in BP and COP - Intact Baroreceptor reflexes. **Respiratory system:** - ↓ RR & TV. - Apnea may last for 30 to 90s - Laryngeal reflexes remain more intact compared to propofol → cough & laryngospasm.	- Potent anticonvulsant properties. -Dose dependent histamine release (allergies). -Myoclonus and hiccups. - Absolutely contraindicated in Porphyria - 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
	propofol	- Enhance GABAA receptor - The safest & the most widely used	- Induction, sedative + hypnotic & Maintenance (TIVA) - Rapid onset (30 to 45 s) - Rapid termination of effect by redistribution, so emergence is rapid. - Weak analgesic effects. - Hepatic and extrahepatic metabolism - Inactive metabolites → excreted by renal route	**CNS:** - ↓ ICP & ↓ CPP due to markedly ↓ MAP. - Anticonvulsant. - Less PONV occurs. **Cardiovascular System:** - ↓ in preload, afterload, and contractility lead to ↓ in BP & COP. - HR is minimally affected, and baroreceptor reflex is blunted. **Respiratory system:** - ↓ RR and TV - ↓ Ventilatory response to hypoxia and hypercarbia.	- 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). - Total IV anesthesia (TIVA) - Venous irritation - Bacterial growth (b.c it contains soybeans) - Lipid disorders - Myoclonus and hiccups - Propofol infusion syndrome: Rhabdomyolysis, metabolic acidosis, cardiac failure, and renal failure - Titrate the dose in hypovolemic, elderly, or hemodynamically compromised patients, or if administered with other anesthetic → to prevent hypotension
	Etomidate	Enhance GABAA receptors	- Induction in CVD pts. - It has nothing to do with analgesia - Very high clearance in the liver and by circulating esterases to inactive metabolites - Redistribution	**CNS:** - No analgesic properties. - ↓ CBF, cerebral metabolic rate (CMR), and ICP **Cardiovascular System:** Minimal changes in HR, BP, and COP. **Respiratory system:** - ↓ RR & TV - Transient apnea may occur.	- 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. - N/V - 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 → increased mortality in ICU patients. - Respiratory depression even in small dose

	Ketamine	- non-competitive antagonism of NMDA receptors - Dissociative anesthesia	- For Induction, sedation & analgesia - (IV + IM) - Unconsciousness in 30 to 60 s after an IV. - Terminated by redistribution in 15 to 20 minutes. - Elimination half-life is 2 to 3h. - Metabolized by liver to multiple metabolites (norketamine).	**CNS:** ↑ (CBF), ↑ (CMR), and ↑ (ICP) - Amnesia & profound analgesia. **Cardiovascular System:** - ↑ HR, COP, and BP - Used in hemodynamically compromised pts. **Respiratory system:** - Mild ↓ in RR & TV - Potent bronchodilator. - Laryngeal reflexes are maintained.	- 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. - 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
Opioids		- Binding with opioid receptors (μ: mu, κ: kappa, δ: delta) - Morphine < 100x Fentanyl < 10x Sufentanil citrate < Remifentanil	- They mimic endogenous compounds: Endorphins, enkephalins & dynorphins. - Provides analgesia and some degree of sedation. - Large doses → GA. **Naloxone (antidote):** - A specific opiate receptor antagonist, duration of action: 30 to 45 min. Dose may need to be repeated or as an infusion. - Reversal of analgesia, N/V, Increased sympathetic nervous system activity.	**Fentanyl:** - Induction and maintenance of GA and to supplement regional and spinal anesthesia. - Maintain cardiac stability. **Sufentanil citrate:** Rapid elimination + Relatively more rapid recovery **Alfentanil:** Shorter duration of action **Remifentanil:** Ultra short acting + rapidly cleared + extrahepatic metabolism by blood and tissue nonspecific esterases **Morphine:** - Hypotension + bronchoconstriction → histamine-releasing action. - Poor choice for a pt with renal failure.	- Minimal cardiac effects - No myocardial depression. (Mnemonics: MORPHINES): - Miosis. - Orthostatic hypotension. - Respiratory depression & chest wall rigidity - Pain supression. - Histamine release: Some peripheral vasodilation and hypotension, itching - N/V, slow gastric emptying slow, constipation - Euphoria. - Sedation or drowsiness. - Bradycardia in large doses - Urinary retention & biliary colic
Benzodiazepines		Increasing the affinity of GABAA receptors for GABA.	- Used as premedication or as adjunct to general anesthesia. - Redistribution. - All are metabolized in the liver. - Hydroxymidazolam → sedation in Pt with renal failure. - Diazepam clearance → ↓ elderly. **Midazolam:** water soluble, so drug of choice for IV administration - More rapid onset and elimination - The most potent amnestic **Diazepam:** Water-insoluble, so IV use can cause local irritation/pain **Lorazepam:** Water-insoluble.	**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 ↓ in RR and TV. - Respiratory depression may be more if administered with an opioid (synergism)	- Drug interactions with anticonvulsant (valproate) - Pregnancy and labor: Risk of cleft lip and palate in the 1st trimester, CNS depression in the neonate. - Superficial thrombophlebitis + injection pain → diazepam + lorazepam. - Mild respiratory depression but can be marked in elderly leading to apnoea. **Flumazenil (antidote):** - 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 - Metabolized to inactive metabolites in the liver. - Contraindicated in patients receiving benzodiazepines for the control of seizures or elevated ICP.

Inhalational Anesthetics	Various ion channels in the CNS involved in synaptic transmission (including GABAA, glycine, and glutamate receptors)	- Present as liquids at room temperature and pressure. - Vaporized into gases for administration - Halothane, isoflurane, sevoflurane, and desflurane are 0.75%, 1.15%, 1.85%, and 6.0% at one atmosphere - The higher the vapor pressure, the more volatile the anesthetic. - Blood solubility determines the speed of build-up / elimination from blood / brain - Metabolism: hepatic - Exhalation → predominant route of elimination --- - **Nitrous Oxide**: MAC is 104% at one atmosphere	**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:** - Respiratory depression - Airway irritation and, during light levels of anesthesia, may precipitate coughing, laryngospasm, or bronchospasm (sevoflurane makes it more suitable) - Bronchodilator (except desflurane). - Inhibit hypoxic pulmonary vasoconstriction **Neuromuscular system:** - ↓ in skeletal muscle tone. - May precipitate malignant hyperthermia **Renal system:** ↓ renal blood flow. **Hepatic System:** ↓ hepatic perfusion. --- **Nitrous Oxide:** **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	**Sevoflurane (more potent):** - Low solubility in blood→ 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 - Carbon dioxide absorbents in anesthesia machines degrade sevoflurane to Compound A --- **Desflurane:** - Rapid onset and recovery of anesthesia (outpatient procedures) - One of least metabolized to toxic byproducts - Requires a special vaporizer - Pungent & irritating to the airway (leading to more coughing, laryngospasm) - High inspired gas concentrations lead to a significant ↑ in BP & HR --- **Isoflurane:** - It causes peripheral vasodilation (drop BP) and increased CBF. - 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); - Very soluble in blood and adipose tissue → Prolonged emergence - Blood pressure usually falls. - Sensitize the myocardium to the arrhythmogenic effects of catecholamines. - Halothane hepatitis (rare). --- **Nitrous Oxide:** - N/V - Risk of bone marrow depression - Inhibits vitamin B-12 metabolism - Expansion of closed gas spaces. N_2O is 35x more soluble in blood than N. - Contraindicated in (e.g. air embolus, pneumothorax, Middle Ear Surgery) - Diffuse into the cuff of ETT. - Diffusion hypoxia → low partial pressure of oxygen in the alveoli.

Neuromuscular blocking drugs (NMBD)	**Depolarizing (Succinycholine: Suxamethonium)**	Structurally similar to acetylcholine, activate the acetylcholine receptors (Ach), depolarization of post junctional membrane.	- Perform tracheal intubation. - Facilitate ventilation. - Provides optimal surgical operating conditions	- 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. --- - 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. **<u>Succinylcholine apnea (side effect):</u>** - Low levels of plasma cholinesterase (severe liver or kidney disease, starvation, malignancy or cardiac failure) result in prolongation of the effect - Drug-induced inhibition of its activity, a genetically atypical enzyme. - Management is supportive (avoid awareness). - Anaphylaxis. over 50% of anaphylactic reactions to NMBDs. - Malignant hyperthermia (MH).
	Nondepolarizing blockers (2 types)	They act by competitively blocking the binding of ACh to its receptors and inhibit muscular contraction. (Slower onset than suxamethonium)	- Absence of fasciculations. - Potentiation by other nondepolarizing NMBDs and volatile anesthetic agents. - Reversal by AChE inhibitors. **Neostigmine:** - They inhibit the action of the AChE 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. - To minimize adverse effects, an antimuscarinic such as glycopyrronium or atropine must be administered along with the anticholinesterase. **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	**<u>1ST type: Benzylisoquinoliniums:</u> 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. **<u>2ND Type is Aminosteroids:</u> 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, Increasing the dose 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. - Decrease the risk of hyperkalemia in patients with burns.

Local anesthetics		- LAs are drugs which reversibly prevent the transmission of pain stimuli locally at their site of administration. - Reversibly blocking sodium channels to prevent depolarizatio	**2 types:** - Esters. - Amides (2i): - Lidocaine - Bupivacaine - Mepivacaine , Prilocaine , Ropivacaine - Potency of local anesthetics is determined by lipid solubility - ↑ lipid solubility → ↑ potency - Increase plasma protein binding of a drug → prolong it action → ↑ potency **Addition of vasoconstrictor:** Prolongation of anesthetic action, decreased risk of toxicity and decrease in bleeding from surgical manipulation. **Choice of local anesthetics**: - Onset & Duration - Sensory vs. motor block - Potential for toxicity	**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. **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 O_2. - **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)

Good luck!
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