ANESTHETICS

From Lippincott

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GENERAL ANESTHESIA

General anesthesia is a reversible state of central nervous system (CNS) depression, causing loss of response to and perception of stimuli. For patients undergoing surgical or medical procedures, anesthesia provides five important benefits:

- Sedation and reduced anxiety
- Lack of awareness and amnesia
- Skeletal muscle relaxation
- Suppression of undesirable reflexes
- Analgesia

Because no single agent provides all desirable properties, several categories of drugs are combined to produce optimal anesthesia

ANESTHETICS

PREOPERATIVE MEDICATIONS	Analgesics Antacids Anti emetics Benzodiazepines
ANALGESICS	Acetaminophen Celecoxib Gabapentin Ketamine Opioids
GERENERAL ANESTHETICS: INHALED	Halothane Desflurane Isoflurane Nitrous oxide Sevoflurane
GENERAL ANESTHETICS: INTRAVENOUS	Dexmedetomidine Etomidate Methohexital Propofol
NEUROMUSCULAR BLOCKERS	Cisatracurium Mivacurium

	Pancuronium Rocuronium Succinylcholine Vecuronium
LOCAL ANESTHETICS: AMIDES	Bupivacaine Lidocaine Mepivacaine Ropivacaine
LOCAL ANESTHETICS: ESTERS	Chloroprocaine Tetracaine

INHALATION ANESTHETICS

	THERAPUTIC USES	**ADVERSE EFFECTS**	
HALOTHANE	-Halothane is a potent anesthetic but a relatively weak analgesic. Thus, it is usually coadministered with nitrous oxide, opioids, or local anesthetics. -It is a potent bronchodilator. -Halothane relaxes both skeletal and uterine muscles and can be used in obstetrics when uterine relaxation is indicated. -Halothane is not hepatotoxic in children (unlike its potential effect on adults). -Combined with its pleasant odor, it is suitable in pediatrics for inhalation induction, although sevoflurane is now the agent of choice.	-Halothane is oxidatively metabolized in the body to tissue-toxic hydrocarbons (for example, trifluoroethanol) and bromide ion. These substances may be responsible for toxic reactions that some adults (especially females) develop after halothane anesthesia. This begins as a fever, followed by anorexia, nausea, and vomiting, and possibly signs of hepatitis. Although the incidence is low (approximately 1 in 10,000), half of affected patients may die of hepatic necrosis. To avoid this condition, halothane is not administered at intervals of less than 2 to 3 weeks. All halogenated inhalation anesthetics have been associated with hepatitis, but at a much lower incidence than with halothane. -Halogenated hydrocarbons are vagomimetic and may cause atropine-sensitive bradycardia. - cardiac arrhythmias (Halothane can sensitize the heart to effects of catecholamines such as norepinephrine) - Halogenated anesthetics produce concentration-dependent hypotension. -Malignant hyperthermia (MH causes a drastic and uncontrolled increase in	MANAGEMENT -Concentration dependent hypotension is best treated with a direct-acting vasoconstrictor, such as phenylephrine -For malignant hyperthermia, dantrolene is given as the anesthetic mixture is withdrawn, and measures are taken to rapidly cool the patient. Dantrolene blocks release of Ca2+ from the sarcoplasmic reticulum of muscle cells, reducing heat production and

		skeletal muscle oxidative metabolism, overwhelming the body's capacity to supply oxygen, remove carbon dioxide, and regulate temperature, eventually leading to circulatory collapse and death if not treated immediately.) -Burn victims and individuals with muscular dystrophy, myopathy, myotonia, and osteogenesis imperfecta are susceptible to MH.	relaxing muscle tone
ISOFLURANE		-produces dose-dependent hypotension. - It has a pungent odor and stimulates respiratory reflexes (for example, breath holding, salivation, coughing, laryngospasm) and is therefore not used for inhalation induction.	
DESFLURANE	-Desflurane provides very rapid onset and recovery due to low blood solubility. This makes it a popular anesthetic for outpatient procedures. - Its degradation is minimal and tissue toxicity is rare	- it has a low volatility, requiring administration via a special heated vaporizer. -Because it stimulates respiratory reflexes, desflurane is not used for inhalation induction. -It is relatively expensive and thus rarely used for maintenance during extended anesthesia.	
SEVOFLURANE	-has low pungency, allowing rapid induction without irritating the airways -suitable for inhalation induction in pediatric patients. - It has a rapid onset and recovery due to low blood solubility		
NITROUS OXIDE (Laughing gas)	-a nonirritating potent analgesic but a weak general anesthetic. -frequently used at concentrations of 30 to 50% in combination with oxygen for analgesia, particularly in dentistry. -it alone cannot produce surgical anesthesia, but it is commonly combined with other more potent agents. - least hepatotoxic of the inhalation agents	-Within closed body compartments, nitrous oxide can increase the volume (for example, causing a pneumothorax) or pressure (for example, in the sinuses), because it replaces nitrogen in various air spaces faster than the nitrogen leaves. - Its speed of movement allows nitrous oxide to retard oxygen uptake during recovery, thereby causing "diffusion hypoxia," which can be overcome by significant concentrations of inspired oxygen during recovery.	

INHALATIONAL ANESTHETICS

DRUG	THERAPEUTIC USES	ADVERSE EFFECTS	OTHER POINTS
PROPOFOL	-an IV sedative/hypnotic used for induction and maintenance of anesthesia -is widely used and has replaced thiopental as the first choice for induction of general anesthesia and sedation -It has less of a depressant effect than volatile anesthetics on CNSevoked potentials, making it useful for surgeries in which spinal cord function is monitored. - incidence of postoperative nausea and vomiting is very low, as this agent has some antiemetic effects.	-Although propofol depresses the CNS, it is occasionally accompanied by excitatory phenomena, such as muscle twitching, spontaneous movement, yawning, and hiccups. - Transient pain at the injection site is common. -reduces intracranial pressure, mainly due to systemic vasodilation. -It does not provide analgesia, so supplementation with narcotics is required.	-Induction is smooth and occurs 30 to 40 seconds after administration. -initial redistribution half-life is 2 to 4 minutes
BARBITURATES	-quickly enter the CNS and depress function, often in less than 1 minute.	-diffusion out of the brain can also occur very rapidly because of redistribution to other tissues -Thiopental may contribute to severe hypotension in patients with hypovolemia or shock -All barbiturates can cause apnea, coughing, chest wall spasm, laryngospasm, and bronchospasm (of particular concern for asthmatics).	-Barbiturates require supplementary analgesic administration during anesthesia
BENZODIAZEPINES	-The benzodiazepines are used in conjunction with anesthetics for sedation.	-Minimal cardiovascular depressant effects are seen, but all are potential respiratory depressants (especially when administered IV). -can induce a temporary form of anterograde amnesia in which the patient retains memory of past events, but new information is not transferred into long-term memory	-The most commonly used is midazolam. Diazepam and lorazepam are alternatives. -They are metabolized by the liver with variable elimination half-lives, and erythromycin

			may prolong their effects.
OPIOIDS	-Because of their analgesic property, opioids are commonly combined with other anesthetics -hey may be administered intravenously, epidurally, or intrathecally (into the cerebrospinal fluid).	-pioids are not good amnesics, and they can all cause hypotension, respiratory depression, and muscle rigidity, as well as postanesthetic nausea and vomiting. Opioid effects can be antagonized by naloxone	-The most commonly used opioids are fentanyl, sufentanil and remifentanil, because they induce analgesia more rapidly than morphine
ETOMIDATE	-Etomidate is a hypnotic agent used to induce anesthesia, but it lacks analgesic activity. -little to no effect on the heart and circulation. -usually only used for patients with coronary artery disease or cardiovascular dysfunction.	-decreased plasma cortisol and aldosterone levels, which can persist up to 8 hours. -Injection site reaction and involuntary skeletal muscle movements are not uncommon, which can be managed by administration of benzodiazepines and opioids.	- Induction is rapid, and the drug is short-acting.
KETAMINE	-Ketamine, a short-acting, nonbarbiturate anesthetic, induces a dissociated state in which the patient is unconscious (but may appear to be awake) and does not feel pain. This dissociative anesthesia provides sedation, amnesia, and immobility -Ketamine stimulates central sympathetic outflow, causing stimulation of the heart with increased blood pressure and CO. It is also a potent bronchodilator. Therefore, it is beneficial in patients with hypovolemic or cardiogenic shock and in asthmatics - is lipophilic and enters the brain very quickly -used mainly in children and elderly adults for short procedures.	-contraindicated in hypertensive or stroke patients. -It is not widely used, because it increases cerebral blood flow and may induce hallucinations, particularly in young adults.	
DEXMEDETOMIDINE	-is a sedative used in intensive care settings and surgery. -It is relatively unique in its ability to provide sedation without respiratory depression.		

	-Dexmedetomidine has sedative, analgesic, sympatholytic, and anxiolytic effects that blunt many cardiovascular responses. -It reduces volatile anesthetic, sedative, and analgesic requirements without causing significant respiratory depression.		

NEUROMUSCULAR BLOCKERS

DRUG NAMES	Cisatracurium Mivacurium Pancuronium Rocuronium Succinylcholine Vecuronium
MOA	blockade of nicotinic acetylcholine receptors in the neuromuscular junction.
MANAGEMENT	Sugammadex is a selective relaxant-binding agent that terminates the action of both rocuronium and vecuronium.
THERAPEUTIC USES	- Neuromuscular blockers are clinically useful during surgery to facilitate tracheal intubation and provide complete muscle relaxation at lower anesthetic doses, allowing for more rapid recovery from anesthesia and reducing postoperative respiratory depression - During surgery, they are used to facilitate endotracheal intubation and provide complete muscle relaxation at lower anesthetic doses. This increase the safety of anesthesia by allowing patients to recover quickly and completely - NMBs are also used in ICU as adjuvant therapy to facilitate intubation and mechanical ventilation in critically ill patients

	NON DEPOLARIZING (COMPETITIVE) BLOCKERS	**DEPOLARIZING AGENTS**
DRUG NAMES	Curare Tubocurarine Cisatracurium Mivacurium Pancuronium Rucuronium	Succinylcholine is the only depolarizing muscle relaxant in use today

	Vecuronium	
MOA	AT LOW DOSES: competitively block ACh at the nicotinic receptors i.e. they compete with ACh at the receptor without stimulating it. Thus, these drugs prevent depolarization of the muscle cell membrane and inhibit muscular contraction. Their competitive action can be overcome by administration of cholinesterase inhibitors, such as neostigmine and edrophonium, which increase the concentration of ACh in the neuromuscular junction. Anesthesiologists employ this strategy to shorten the duration of the neuromuscular blockade. At low doses the muscle will respond to direct electrical stimulation from a peripheral nerve stimulator to varying degrees, allowing for monitoring of the extent of neuromuscular blockade. AT HIGH DOSES: Nondepolarizing agents can block the ion channels of the motor endplate. This leads to further weakening of neuromuscular transmission, thereby reducing the ability of cholinesterase inhibitors to reverse the actions of the nondepolarizing blockers. With complete blockade, the muscle does not respond to direct electrical stimulation.	Succinylcholine attaches to the nicotinic receptor and acts like ACh to depolarize the junction. Unlike ACh, which is instantly destroyed by AChE, the depolarizing agent persists at high concentrations in the synaptic cleft, remaining attached to the receptor for a relatively longer time and providing constant stimulation of the receptor. The depolarizing agent first causes the opening of the sodium channel associated with the nicotinic receptors, which results in depolarization of the receptor (Phase I). This leads to a transient twitching of the muscle (fasciculations). Continued binding of the depolarizing agent renders the receptor incapable of transmitting further impulses. With time, continuous depolarization gives way to gradual repolarization as the sodium channel closes or is blocked. This causes a resistance to depolarization (Phase II) and flaccid paralysis
ACTION	Not all muscles are equally sensitive to blockade by competitive agents. Small, rapidly contracting muscles of the face and eye are most susceptible and are paralyzed first, followed by the fingers, limbs, neck, and trunk muscles. Next, the intercostal muscles are affected and, lastly, the diaphragm. The muscles recover in the reverse manner.	-The duration of action of succinylcholine is dependent on diffusion from the motor endplate and hydrolysis by plasma pseudocholinesterase. Genetic variants in which plasma pseudocholinesterase levels are low or absent lead to prolonged neuromuscular paralysis. -As with the competitive blockers, the respiratory muscles are paralyzed last. Succinylcholine initially produces brief muscle fasciculations that cause muscle soreness. This may be prevented by administering a small dose of nondepolarizing neuromuscular blocker prior to succinylcholine. Normally, the duration of action of succinylcholine is extremely short, due to rapid hydrolysis by plasma pseudocholinesterase. However, succinylcholine that gets to the NMJ is not

		metabolized by AChE, allowing the agent to bind to nicotinic receptors, and redistribution to plasma is necessary for metabolism (therapeutic benefits last only for a few minutes)
THERAPEUTIC USES	-used to facilitate endotracheal intubation	-Because of its rapid onset of action, succinylcholine is useful when rapid endotracheal intubation is required during the induction of anesthesia (a rapid action is essential if aspiration of gastric contents is to be avoided during intubation). -It is also used during electroconvulsive shock treatment
ADVERSE EFFECTS	In general, these agents are safe with minimal side effects.	-can potentially induce **malignant hyperthermia** in susceptible patients -Administration of succinylcholine to a patient who is deficient in plasma cholinesterase or who has an atypical form of the enzyme can lead to **prolonged apnea** due to paralysis of the diaphragm. -The rapid release of potassium may also contribute to prolonged apnea in patients with electrolyte imbalances who receive this drug. In patients with electrolyte imbalances who are also receiving digoxin or diuretics (such as heart failure patients) succinylcholine should be used cautiously or not at all - Hyperkalemia
MANAGEMENT	-Drugs such as neostigmine, physostigmine, pyridostigmine, and edrophonium can overcome the action of nondepolarizing neuromuscular blockers. However, with increased dosage, cholinesterase inhibitors can cause a depolarizing block as a result of elevated ACh concentrations at the endplate membrane. If the neuromuscular blocker has entered the ion channel, cholinesterase inhibitors are not as effective in overcoming blockade	
DRUG INTERACTIONS	-desflurane act to enhance neuromuscular blockade by exerting a stabilizing action at the NMJ. These agents sensitize the NMJ to the effects of neuromuscular blockers -gentamicin and tobramycin inhibit ACh release from cholinergic nerves by competing with calcium ions. They synergize with pancuronium and other competitive blockers, enhancing the blockade.	

	-Calcium channel blockers may increase the neuromuscular blockade of competitive blockers.	

LOCAL ANESTHETICS

MOA	Local anesthetics block nerve conduction of sensory impulses and, in higher concentrations, motor impulses from the periphery to the CNS. Na+ ion channels are blocked to prevent the transient increase in permeability of the nerve membrane to Na+ that is required for an action potential
DELIVERY TECHNIQUES	topical administration, infiltration, peripheral nerve blocks, and neuraxial (spinal, epidural, or caudal) blocks
DRUG NAMES	Bupivacaine Lidocaine Mepivacaine Ropivacaine Tetracaine Prilocaine
THERAPEUTIC USES	-Prilocaine is a dental anesthetic -lidocaine is an IV antiarrhythmic
ACTIONS	-Local anesthetics cause vasodilation, leading to rapid diffusion away from the site of action and shorter duration when these drugs are administered alone.
DRUG INTERACTIONS	By adding the vasoconstrictor epinephrine, the rate of local anesthetic absorption and diffusion is decreased. This minimizes systemic toxicity and increases the duration of action.
ADVERSE EFFECTS	-Allergies -. Psychogenic reactions to injections may be misdiagnosed as allergic reactions and may also mimic them with signs such as urticaria, edema, and bronchospasm.
OTHER POINTS	-Before administering local anesthetic to a child, the maximum dose based on weight should be calculated to prevent accidental overdose. -Because some degree of cardiovascular compromise may be expected in elderly patients, reducing the dose of epinephrine may be prudent. - Local anesthetics are safe for patients who are susceptible to MH
MANAGEMENT	-Treatment for systemic local anesthetic toxicity includes airway management, support of breathing and circulation, seizure suppression and, if needed, cardiopulmonary resuscitation. -Administering a 20% lipid emulsion infusion (lipid rescue therapy) is a valuable asset.

ANESTHETIC ADJUVANTS

GIT MEDICATIONS	H2 receptor antagonist (Ranitidine)	Help reduce gastric acidity in event of aspiration
	Proton pump inhibitors (Omeprazole)	Help reduce gastric acidity in event of aspiration
	Nonparticulate antacids (Sodium citrate/ citric acid)	Quickly increase pH of stomach contents (used in obstetric population going to surgery, along with other patients with reflux
	Dopamine receptor antagonist (Metoclopramide)	Used as a prokinetic to speed gastric emptying and increase lower esophageal sphincter tone
MEDICATIONS OF PONV **(Post operative nausea and vomiting)**	5-HT3 receptor antagonist (Ondansetron)	Usually administered towards the end of surgery to prevent PONV (caution is advised in patients with long QT intervals on ECG)
	Anticholinergic and antihistamine (Promethazine)	It can be used, however, sedation, delirium, and confusion can complicate the postoperative period, esp in the elderly
	Glucocorticoids (dexamethasone)	Usually given at start of surgery
	Neurokinin-1-antagonist (Aprepitant)	Has been shown to reduce PONV
	Transdermal scopolamine	-given post operatively to patients with multiple risk factors or a history of PONV -Caution is advised bcz it can produce central anticholinergic effects
ANXIETY MEDICATIONS	Benzodiazepenes (Midazolam, Diazepam)	They can also elicit anterograde amnesia, which can help promote a more pleasant surgical experience
	Alpha 2 agonists (Clonidine, Dexmedetomidine)	Alleviate anxiety
	H1 receptor antagonist (Diphenhydramine)	Alleviate anxiety

ANALGESIA	Opioids	-mainstay in anesthesia for pain control -However, multiple analgesia is becoming more common due to long term risks of opioid consumption in surgical patients
	NSAIDs (Ketorolac, Celecoxib)	-common adjuncts to opioids -caution should be used in patients with coagulopathies, and in those with a history of peptic ulcer or platelet aggregation abnormalities
	Acetaminophen	-can be used PO and IV -caution is advised in impaired hepatic function
	Analogs of GABA (Gabapentin, Pregablin)	-are becoming more common as pretreatment to reduce opioid consumption both during and after surgery -also have multiple uses in neuropathic pain and addiction medicine
	NMDA Antagonist (Ketamine)	Used to reduce overall consumption both intra and post operatively