

Anesthetics





Introduction

- General anesthesia: a reversible state of central nervous system depression resulting in loss of response to and perception of external stimuli
- For patients undergoing surgical and other medical procedures anesthesia provides these benefits:
 - Sedation and reduction of anxiety
 - Lack of awareness and amnesia
 - Skeletal muscle relaxation
 - Suppression of undesirable reflexes
 - Analgesia
- Because no single agent can provide all those benefits, several drugs are used in combination to produce optimal anesthesia

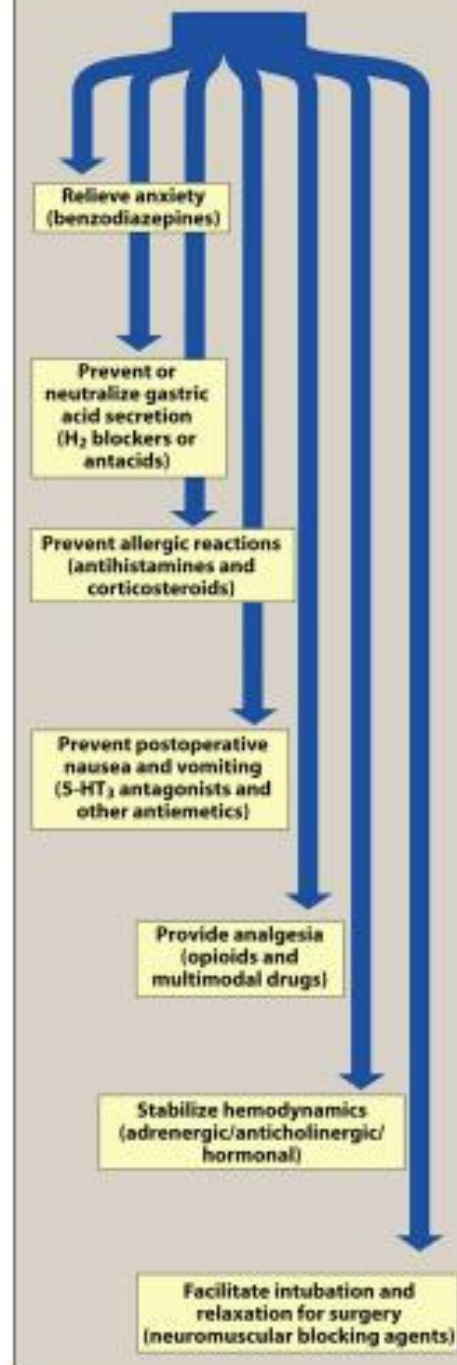


Preanesthetic medications

- Serve to calm the patient, relieve the pain and protect against undesirable effects of anesthetics or the surgical procedure
 - Antacids (neutralize stomach acidity)
 - H2 blockers like famotidine (Reduce gastric acidity)
 - Anticholinergics like glycopyrrolate (Prevent bradycardia and secretion of fluids)
 - Antiemetics like ondansetron (Prevent aspiration of stomach contents and postsurgical nausea and vomiting and)
 - Antihistamine like diphenhydramine (Prevent allergic reactions)
 - Benzodiazepines like diazepam (Relieve anxiety)
 - Opioids like fentanyl (Provide analgesia)
 - Neuromuscular blockers (Facilitate intubation and relaxation)



Some functions of adjuncts to anesthesia





Skeletal muscle relaxants

- Facilitate intubation of the trachea and suppress muscle tone to the degree required for surgery
- Used to stop reflexes to facilitate tracheal intubation, and to provide muscle relaxation as needed for certain types of surgery
- Mechanism of action is blockade of the nicotinic acetylcholine receptors in the neuromuscular junction
- Include pancuronium, rocuronium, succinylcholine, and vecuronium



Patient factors in selection of anesthesia

- Choice of anesthetic drugs are made to provide safe and efficient anesthesia based on the nature of the surgical or diagnostic procedures and patient's physiologic, pathologic and pharmacologic state



Patient factors in selection of anesthesia

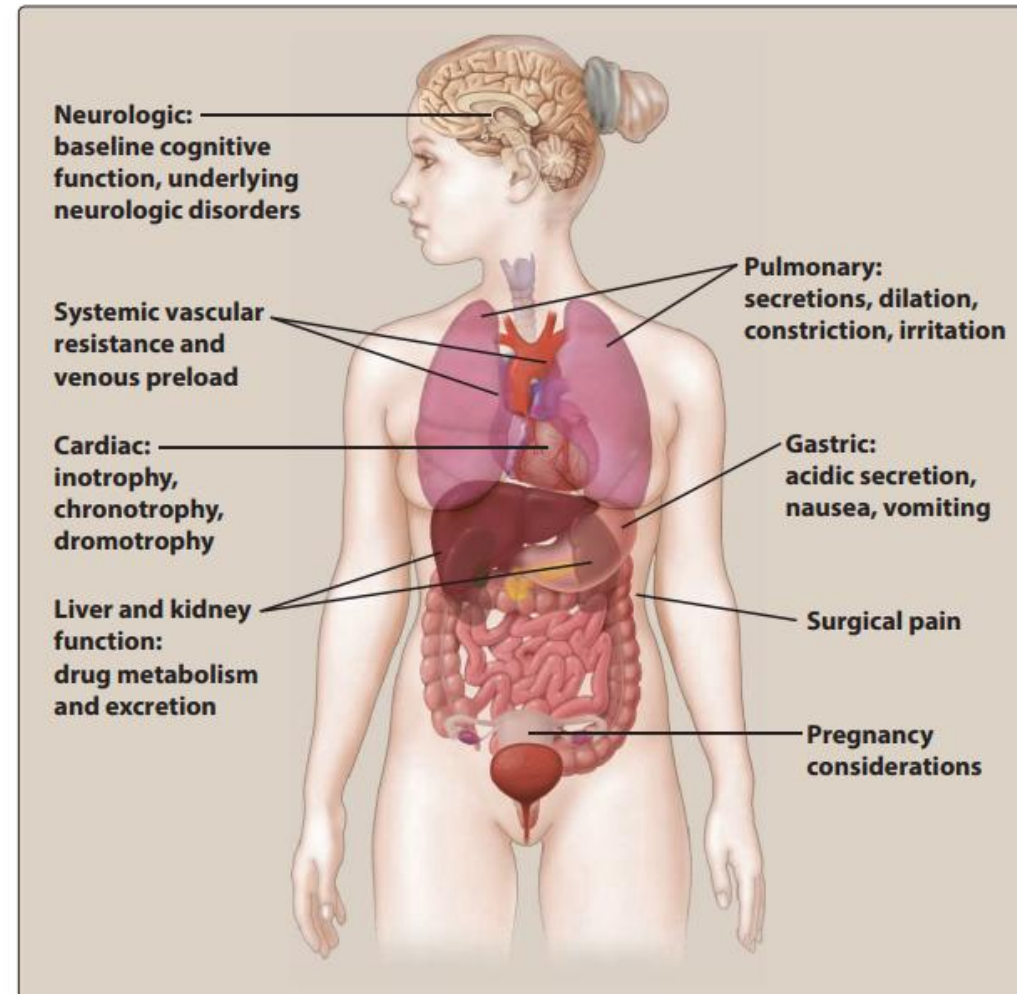


Figure 13.3

Overall considerations when delivering an anesthetic.



Patient factors in selection of anesthesia

- Two factors are important:
- **Status of organ system**
 - Cardiovascular system
 - Respiratory system
 - Liver and kidney
 - Nervous system
 - Pregnancy
- **Concomitant use of drugs**
 - Multiple adjunct agents
 - Nonanesthetic drugs



Status of organ systems

- **Cardiovascular system:**
 - Anesthetic agents suppress cardiovascular functions.
 - Ischemic injury to tissues may follow reduced perfusion pressure if a hypotensive episode occurs during anesthesia >> treatment with vasoactive substances may be necessary



Status of organ systems

- **Respiratory system**
 - Asthma may complicate control of inhalation anesthetic
 - Inhaled anesthetics depress the respiratory system
 - IV anesthetics and opioids suppress respiration
 - These effects may influence the ability to provide adequate ventilation and oxygenation



Status of organ systems

- **Liver and kidneys**
 - Affect distribution and clearance of anesthetics, and might be affected by anesthetic toxic effects
 - Their physiologic must be considered
- **Nervous system**
 - Presence of neurologic disorders like epilepsy, myasthenia gravis, problems in cerebral circulation
- **Pregnancy**
 - Effects of anesthetic agents on the fetus
 - Nitric oxide causes aplastic anemia in the unborn child
 - Benzodiazepines might cause oral clefts in the fetus



Concomitant use of drugs

- **Multiple adjunct agents**
- Multiple agents are administered preanesthesia, these agents facilitate induction of anesthesia and lower the needed dose of anesthetics
- They may enhance adverse effects of anesthesia like hypoventilation
- **Concomitant use of additional nonanesthetic drugs**
- Example: Opioid abusers may be intolerant to opioids



Stages of anesthesia

- **Induction:** the period of time from the onset of administration of the potent anesthetic to the development of effective surgical anesthesia in the patient.
 - Depends on how fast effective concentration of the drug reaches the brain
- **Maintenance of anesthesia:** providing a sustained surgical anesthesia
- **Recovery:** the time from discontinuation of administration of anesthesia until consciousness and protective physiologic reflexes are regained
 - Depends on how fast the drug leaves the brain



Induction

- General anesthesia in adults is normally induced with an IV anesthetic like propofol
- At that time, additional inhalation and/or IV anesthetic drugs may be given to produce the desired depth of surgical anesthesia
- Often includes coadministration of an IV skeletal muscle relaxant such as rocuronium, vecuronium, or succinylcholine to facilitate intubation and muscle relaxation
- For children without IV access, inhalation induction is used such as sevoflurane, to induce general anesthesia



Maintenance

- Maintenance is the period during which the patient is surgically anesthetized
- Patient's vital signs and response to various stimuli are monitored continuously throughout the surgical procedure Opioids such as fentanyl are often used for pain relief
- IV infusions of various drugs may also be used



Recovery

- Postoperatively, the anesthetic admixture is withdrawn, and the patient is monitored for the return of consciousness
- If skeletal muscle relaxants have not been fully metabolized, reversal agents may be used
- The anesthesiologist continues to monitor the patient for full recovery, with normal physiologic functions



	MINIMAL (ANXIOLYSIS)	MODERATE	DEEP	GENERAL
Mentation	Responds normally to verbal stimuli	Responds purposefully to verbal or tactile stimuli	Responds purposefully to repeated verbal or painful stimuli	Unarousable to painful stimuli
Airway competency	Unaffected	Adequate	Intervention may be required	Intervention usually required
Respiratory system	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular system	Unaffected	Usually maintained	Usually maintained	May be impaired

Figure 20.3 Anesthetic levels of sedation.

Depth of anesthesia

- Depth of anesthesia is the degree to which the CNS is depressed
- Useful parameter for individualizing anesthesia
 - Stage I Analgesia
 - Stage II Excitement
 - Stage III Surgical anesthesia
 - Stage IV Medullary paralysis

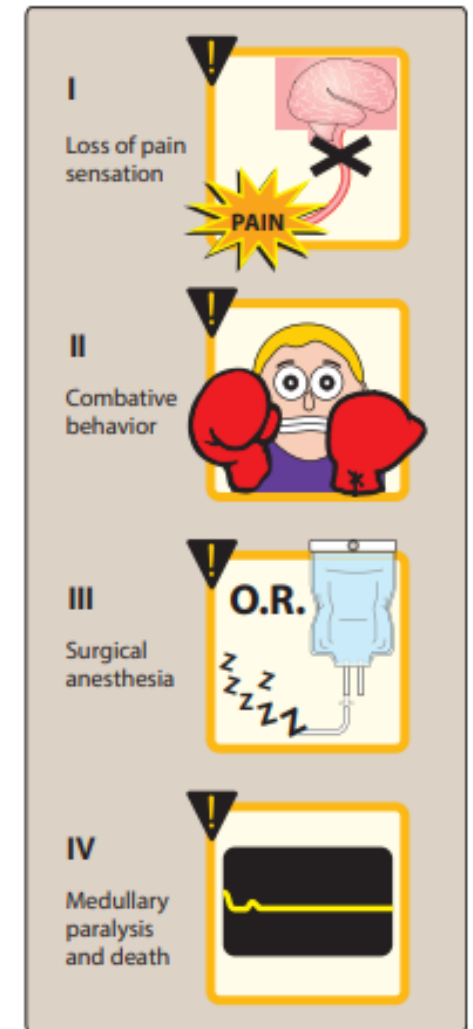


Figure 13.5
Stages of anesthesia.
O.R. = operating room.



Stages of anesthesia

- Stage I Analgesia
 - Loss of pain sensation
 - Drowsiness
 - Amnesia and reduced awareness of pain
- Stage II Excitement
 - Delirium
 - Rise and irregularity in blood pressure and respiration
 - Risk of laryngospasm
 - To shorten this period a rapid acting anesthetic like propofol is administered IV before inhaled anesthetic



Stages of anesthesia

- Stage III surgical anesthesia
 - Loss of muscle tone and reflexes
 - Ideal stage for surgery
 - Requires careful monitoring
- Stage IV Medullary paralysis
 - Severe depression of the respiratory and vasomotor centers
 - Death can occur unless respiration and circulation are maintained



Anesthetics

- Potent general anesthetics are delivered via inhalation or IV injection
 - Inhaled general anesthetics
 - Intravenous general anesthetics
- Local anesthetics



Inhaled Anesthetics

- Desflurane
- Isoflurane
- Sevoflurane
- Nitrous oxide



Inhaled Anesthetics

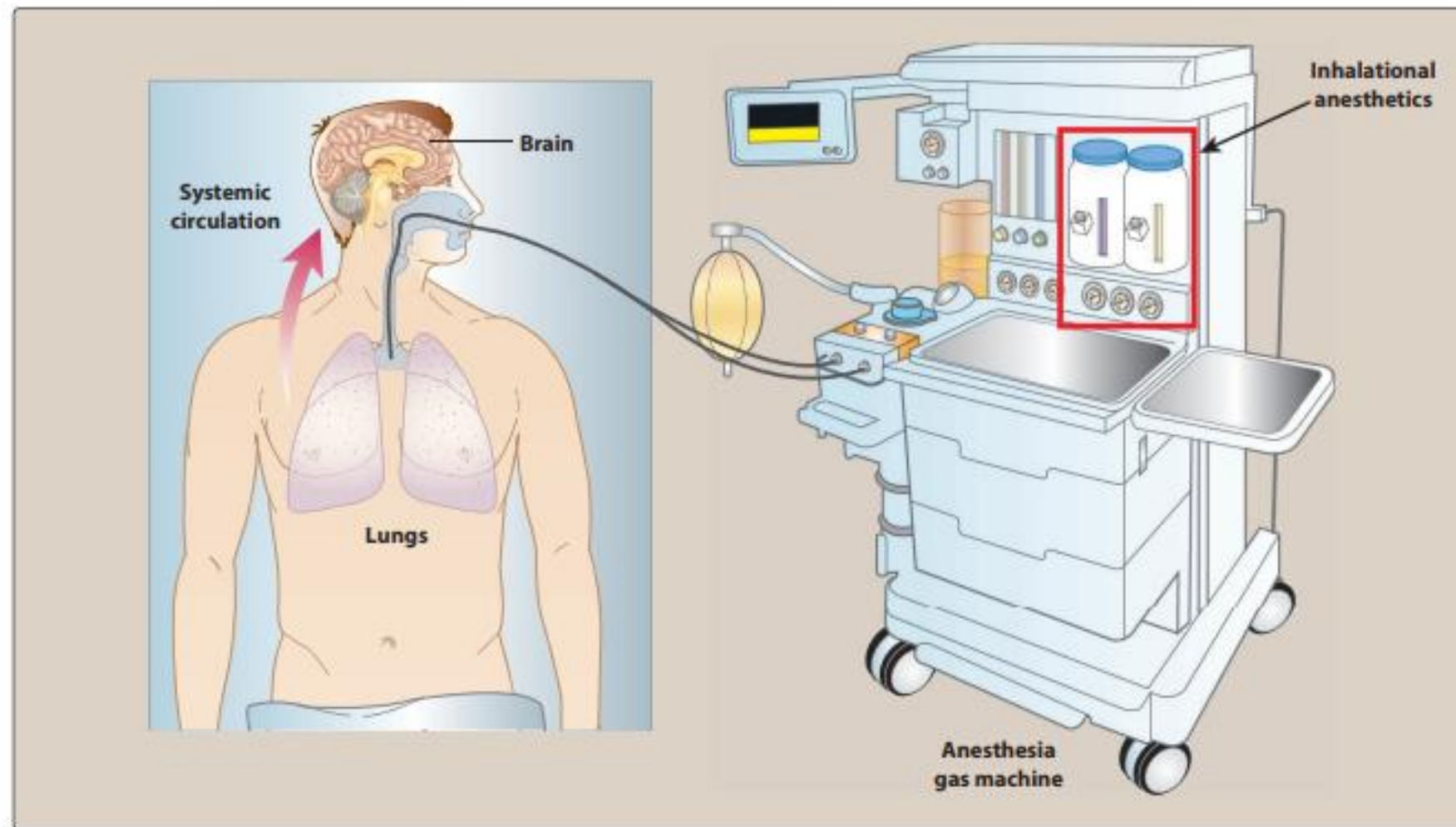


Figure 13.6

Volatile anesthetics delivered to the patient are absorbed via the lungs into the systemic circulation causing dose-dependent CNS depression.



Inhaled anesthesia

- Used for maintenance of anesthesia after administration of an IV agent
- The depth of anesthesia can be altered rapidly by changing inhaled concentration of the drug
- Narrow therapeutic index (from 2 - 4)
- The difference between the dose causing no effect, surgical anesthesia and severe cardiac and respiratory depression is **small**
- No antagonists exist



Inhaled anesthetics

- Potency of inhaled anesthetic is defined as the minimum alveolar concentration (MAC)
- MAC: the concentration of anesthetic gas needed to eliminate movement among 50% of patients
- Expressed as the percentage of gas in a mixture required to achieve the effect
- The smaller MAC is the more potent the drug
- Nitrous oxide alone cannot produce complete anesthesia

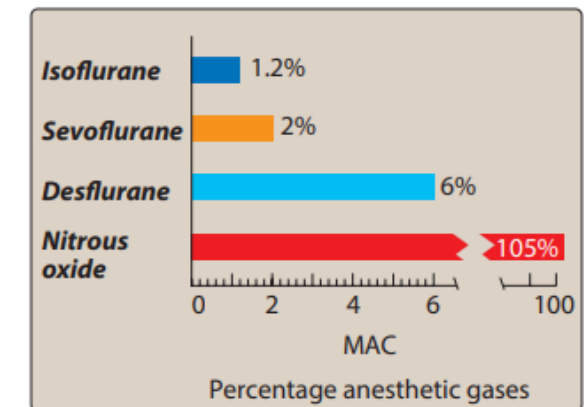


Figure 13.7

Minimal alveolar concentrations (MAC) for anesthetic gases are used to compare pharmacologic effects of different agents (high MAC = low potency).



Inhaled anesthetics

- The more the blood solubility, the more the anesthetic dissolves in the blood and the longer the induction
- and recovery time needed and slower changes in the depth of anesthesia occur as we change the concentration of inhaled drug
- isoflurane>sevoflurane>nitrous oxide >desflurane

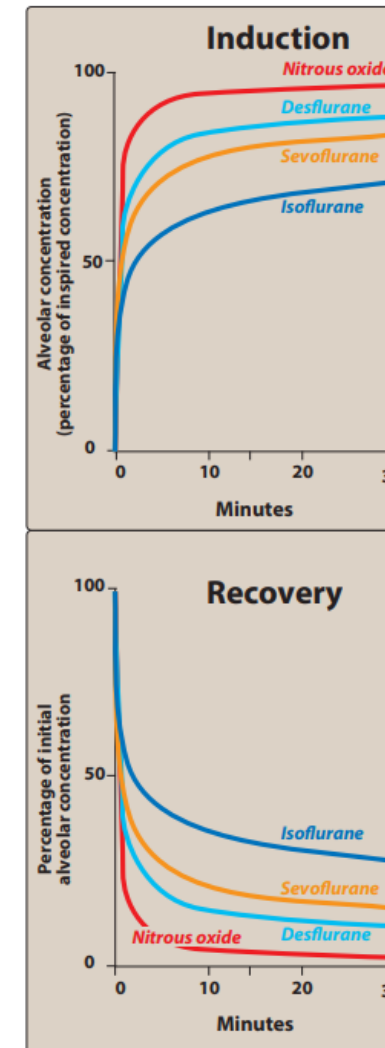


Figure 13.9
Changes in the alveolar blood concentrations of some inhalation anesthetics over time.

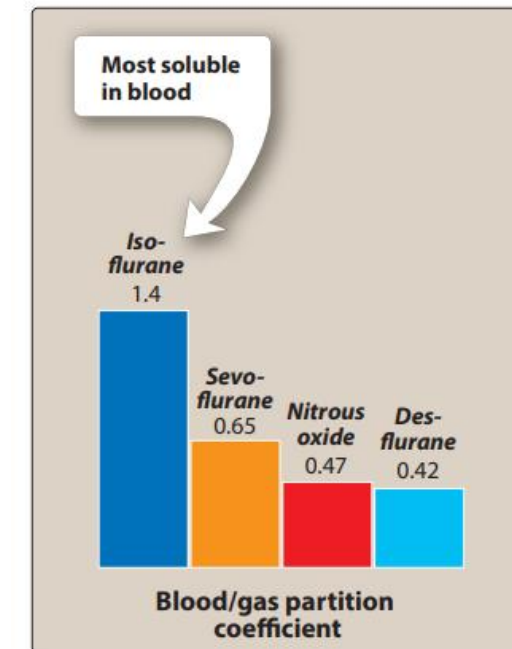


Figure 13.8
Blood/gas partition coefficients for some inhalation anesthetics.



Inhaled anesthetics

- Cardiac output affects the removal of anesthetic to peripheral tissues (not the site of action)
- The higher the cardiac output, the more the anesthetic is removed, the slower the induction time



Inhaled anesthetics

- Mechanism of action
 - No specific receptor has been identified as the locus of general anesthetic action
 - Anesthetics increase the sensitivity of GABA receptors to the neurotransmitter GABA prolonging the inhibitory chloride ion current after GABA release, reducing the postsynaptic neurons excitability
 - Anesthetics increase the activity of the inhibitory glycine receptors in the spinal motor neuron
 - Anesthetics block excitatory postsynaptic nicotinic currents
 - The mechanism by which the anesthetics perform these modulatory roles is not understood

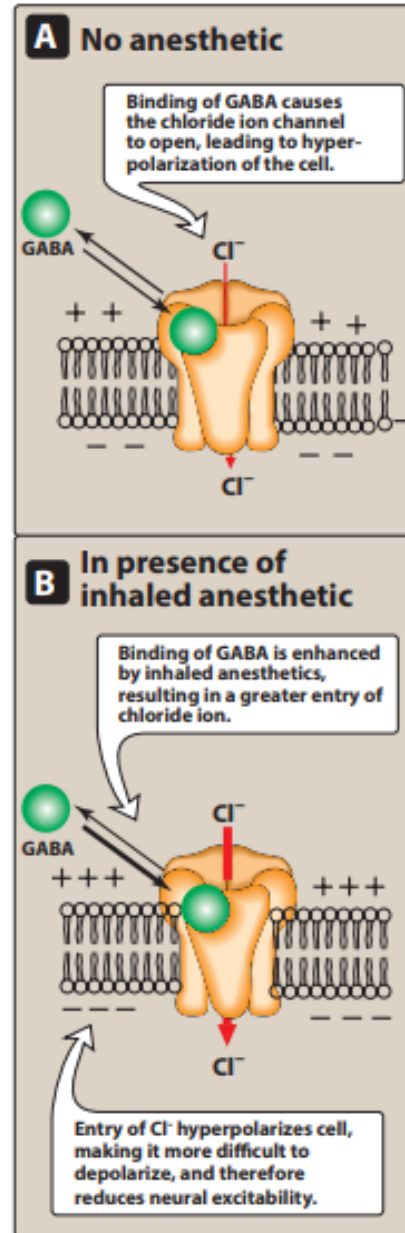


Figure 13.10

An example of modulation of a ligand-gated membrane channel modulated by inhaled anesthetics.
 Cl^- = chloride ion;
GABA = γ -aminobutyric acid.



Isoflurane

- Undergoes little metabolism, not toxic to the liver or kidney
- Does not induce cardiac arrhythmias
- Produces dose-dependent hypotension due to peripheral vasodilation



Desflurane

- Provides very rapid onset and recovery due to its low blood solubility, the lowest of all the volatile anesthetics
- Popular anesthetic for outpatient surgery
- Irritating to the airway and can cause laryngospasm, coughing, and excessive secretions
- Degradation is minimal, tissue toxicity is rare



Sevoflurane

- Low pungency, allowing rapid induction without irritating the airway, making it suitable for inhalation induction in pediatric patients
- Has replaced halothane for anesthesia
- Metabolized by the liver, and compounds formed in the anesthesia circuit may be nephrotoxic



Nitrous oxide

- Non-irritating and a potent analgesic but a weak general anesthetic
- Nitrous oxide is frequently employed at concentrations of 30–50% in combination with oxygen for analgesia, particularly in dental surgery.
- Nitrous oxide at 80 percent (without adjunct agents) cannot produce surgical anesthesia
- Combined with other, more potent agents to attain pain-free anesthesia
- Mechanism of action is unresolved, might involve activity on GABAA and NMDA receptors
- Least hepatotoxic of all inhaled anesthetics



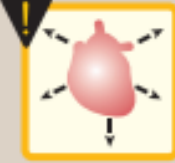
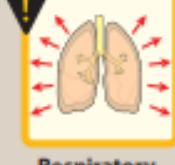
	Isoflurane	Desflurane	Sevoflurane
 Cardiac output	Decreased minimally	Decreased minimally	Decreased minimally
 Blood pressure	Dose dependent decreased	Dose dependent decreased	Dose dependent decreased
 Respiratory reflexes	Initial stimulation	Initial stimulation	Inhibited
 Hepatic toxicity	Low risk	Low risk	Low risk
 Renal toxicity	Low risk	Low risk	Some risk

Figure 13.11

Characteristics of some inhalation anesthetics.



Intravenous anesthetics

- Used in situations that require short duration anesthesia (outpatient surgery)
- Primarily used as adjuncts to inhalationals
- Administered first
- Rapidly induce unconsciousness
- In lower doses, they may be used to provide sedation



Intravenous anesthetics

- **Induction**
 - After entering the blood stream, a percentage of the drug binds to the plasma proteins, and the rest remains
 - unbound (free)
 - The drug is carried by venous blood to the heart
 - The majority of the CO (70%) flows to the brain, liver, and kidney
 - Once the drug has penetrated the CNS tissue, it exerts its effects
 - The exact mechanism of action of IV anesthetics is unknown
- **Recovery / Emergence**
 - Recovery from IV anesthetics is due to redistribution from sites in the CNS



Intravenous anesthetics

- Propofol
- Fospropofol
- Barbiturates
- Benzodiazepines
- Opioids
- Ketamine
- Etomidate



Propofol

- IV sedative/hypnotic used in the induction or maintenance of anesthesia
- Widely used and has replaced thiopental as first choice for anesthesia induction and sedation, because it does not cause postanesthetic nausea and vomiting
- The induction of anesthesia occurs within 30–40 seconds of administration
- Supplementation with narcotics for analgesia is required
- Propofol decreases blood pressure without depressing the myocardium
- It also reduces intracranial pressure due to systemic vasodilation



Fospropofol

- Approved only for sedation
- Prodrug of propofol



Barbiturates

- The barbiturates are not significantly analgesic, require some type of supplementary analgesic administration during anesthesia to avoid objectionable changes in blood pressure and autonomic function
- Can cause apnea, coughing, chest wall spasm, laryngospasm, and bronchospasm
- Barbiturates tend to decrease blood pressure, which may cause a reflex tachycardia.
- **Methohexital**
- **Thiopental**
 - Potent anesthetic but a weak analgesic
 - Ultrashort-acting barbiturate



Benzodiazepines

- Used in conjunction with anesthetics to sedate the patient
- Midazolam
- Diazepam
- Lorazepam
- Facilitate amnesia while causing sedation
- Enhance the inhibitory effects of various neurotransmitters, particularly GABA
- Minimal cardiovascular depressant effect
- Potential respiratory depressants
- 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
 - Important treatment information should be repeated to the patient after the effects of the drug have worn off



Opioids

- Commonly used with anesthetics due to their analgesic property
- The choice of opioid used perioperatively is based primarily on the duration of action needed
- **Fentanyl, remifentanyl**
 - Induce analgesia more rapidly than morphine
 - Administered intravenously, epidurally, intrathecally
- Not good amnesics
- Can cause hypotension, respiratory depression, muscle rigidity and postanesthetic nausea and vomiting
- Opioid effects can be antagonized by naloxone



Ketamine

- A short-acting nonbarbiturate anesthetic
- Used for short procedures
- 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
- Interacts with the N-methyl-D-aspartate receptor
- Stimulates the central sympathetic outflow, which, in turn, causes stimulation of the heart with increased blood pressure and CO
- Beneficial in patients with hypovolemic or cardiogenic shock and in patients with asthma)
- Not used in hypertensive or stroke patients
- Causes post-operative hallucinations



Etomidate

- A hypnotic agent used to induce anesthesia, but it lacks analgesic activity.
- Induction is rapid, and the drug is short acting.
- Has minimal impact on cardiac output and systemic vascular resistance.
- Used for patients with cardiovascular dysfunction or patients who are acutely critically ill.
- Decreases plasma cortisol and aldosterone levels.
 - Etomidate should not be infused for an extended time, because prolonged suppression of these hormones is dangerous.
- Adverse effects: Injection site pain, involuntary skeletal muscle movements, and nausea and vomiting.

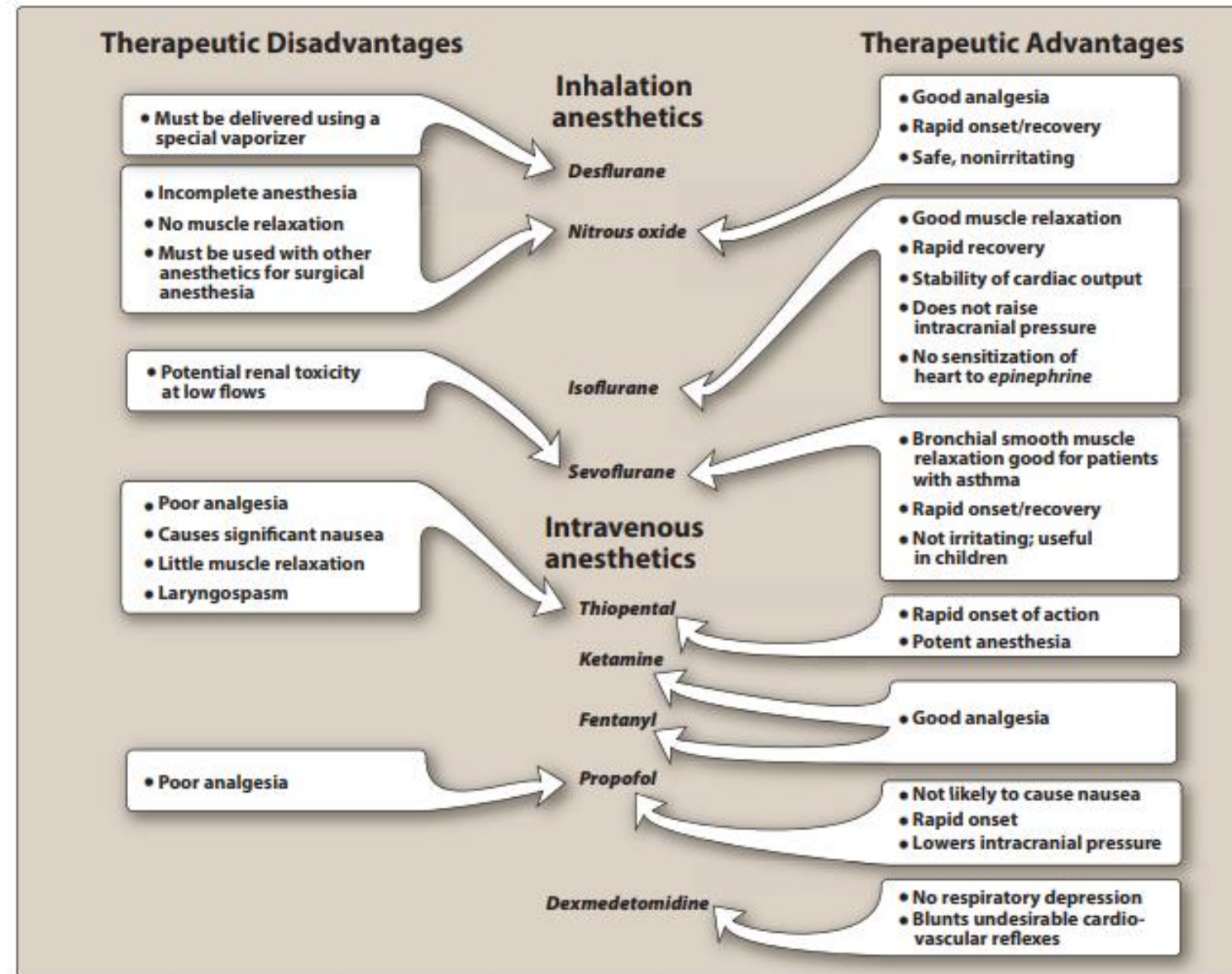


Figure 13.14
Therapeutic disadvantages and advantages of some anesthetic agents.



Local anesthetics

- Amides (lidocaine) and esters (procaine)
- Cause loss of sensation and, in higher concentrations, motor activity in a limited area of the body
- Applied or injected to block nerve conduction of sensory impulses from the periphery to the CNS



Local anesthetics

- **Mechanism:**
- Local anesthesia is induced when propagation of action potentials is prevented, so that sensation cannot be transmitted from the source of stimulation to the brain
- Work by blocking sodium ion channels to prevent the transient increase in permeability of the nerve membrane to sodium that is required for an action potential to occur

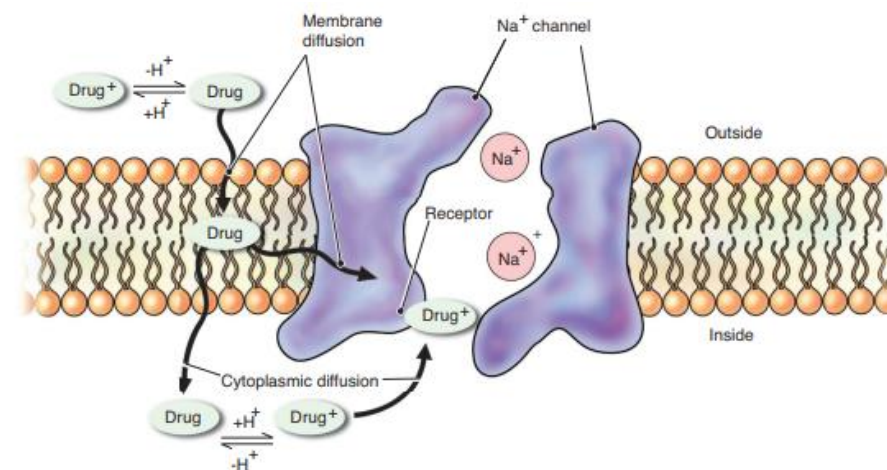


Figure 13.15
Mechanism of local anesthetic action.



Local anesthetics

- Lidocaine
- Bupivacaine
- Procaine
- Ropivacaine
- Tetracaine
- Mepivacaine
 - Not used in obstetric anesthesia due to its increased toxicity to the neonate



Local anesthetics

- Local anesthetics cause vasodilation, which leads to rapid diffusion away from the site of action and results in a short duration of action
- Adding the vasoconstrictor epinephrine to the local anesthetic, the rate of local anesthetic diffusion and absorption is decreased
- This both minimizes systemic toxicity and increases the duration of action



Topical anesthetics

- They are applied directly to the skin or mucous membranes
- Benzocaine is the major drug in this group
- Lidocaine and tetracaine can be used topically
- They are used to relieve or prevent pain from minor burns, irritation, itching
- They are also used to numb an area before an injection is given.
- Expected adverse effects involve skin irritation and hypersensitivity reactions