Anesthesia

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

Pre-anesthetic 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)

Skeletal muscle relaxants

- Facilitate intubation of the trachea and suppress muscle tone to the degree required for surgery
  - Neuromuscular blockers
    - Pancuronium
    - Succinylcholine

- D Potent general anesthetics are delivered via inhalation or IV injection

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
- 2 factors are important

1. Status of organ system
   - Cardiovascular system
   - Respiratory system
   - Liver and kidney
   - Nervous system
   - Pregnancy
2. Concomitant use of drugs
   - Multiple adjunct agents
   - Non-anesthetic 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
  - Some anesthetics like halothane sensitize the heart to arrhythmogenic effects of sympathomimetics
- 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, which produces unconsciousness within 30–40 seconds after injection
- 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 halothane or sevoflurane, to induce general anesthesia

Maintenance of anesthesia

- 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 to carefully balance the amount of drug inhaled and/or infused with the depth of anesthesia
- Opioids such as fentanyl are often used for pain relief
- IV infusions of various drugs may also be used

Recovery

- Postoperatively, the anesthetic 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 (for example, spontaneous respiration, acceptable blood pressure and heart rate, etc.)

Depth of anesthesia

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

Stages and anesthesia

- Stage I Analgesia
  - Loss of pain sensation
  - Drowsiness

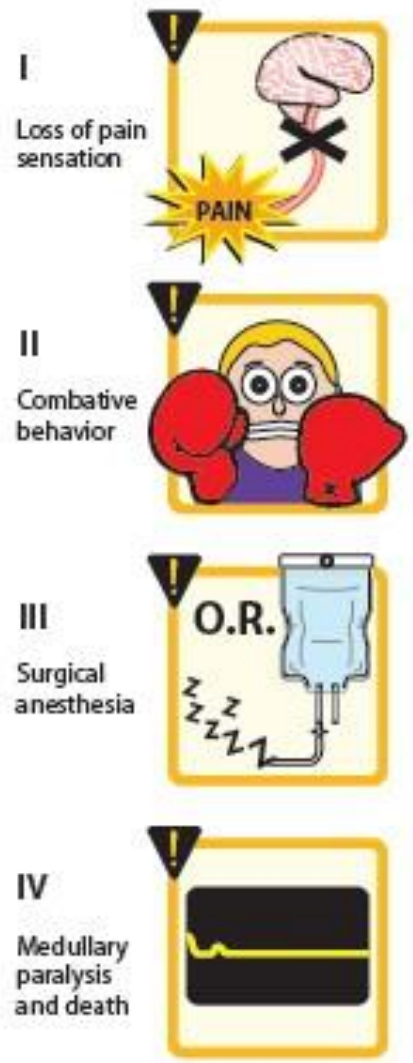
- Stage II Excitement
  - Delirium
  - Rise and irregularity in blood pressure and respiration
  - Risk of laryngospasm
  - To shorten this period a rapid acting anesthetic like propofol is administered IV before inhaled anesthetic

Stages and anesthesia

- Stage III Surgical anesthesia
  - Gradual loss of muscle tone and reflexes as CNS is further depressed
  - Ideal stage of anesthesia for surgery
  - Require careful monitoring

- Stage IV Medullary paralysis
  - Severe depression of respiratory and vasomotor centers
  - Death can occur unless measures are taken to maintain circulation and respiration

Stages of anesthesia



Anesthetics

- Inhaled general anesthetics
- Intravenous general anesthetics
- Local anesthetics

Inhaled anesthetics

- Desflurane
- Halothane
- Isoflurane
- Nitrous oxide
- Sevoflurane

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

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
- The smaller MAC is the more potent the drug

Inhaled anesthetics

- The more the blood solubility is 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
- Halothane> isoflurane> sevoflurane>nitrous oxide >desflurane

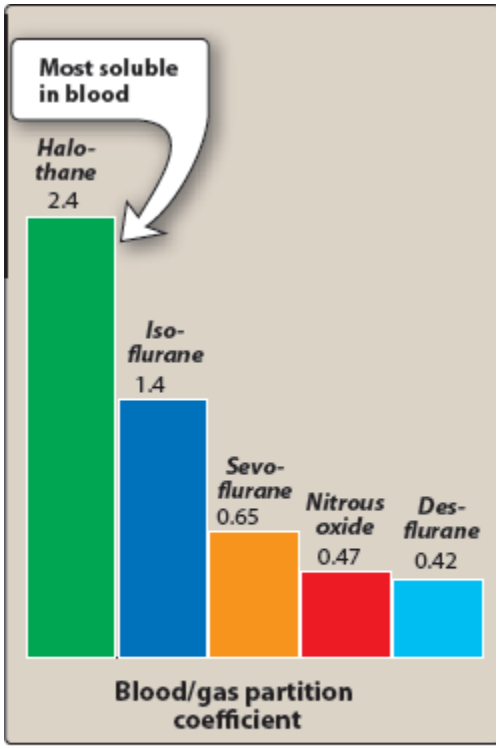


Figure 11.5
Blood/gas partition coefficients for some inhalation anesthetics.

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 anesthetic

- Mechanism of 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

Halothane

- Potent anesthetic, weak analgesic.
- Administered with nitrous oxide, opioids or local anesthetics
- Adverse effects

  Cardiac effects: Bradycardia

  Malignant hyperthermia: rare and life threatening condition if untreated would cause circulatory collapse and death

Inhaled anesthetics

- Desflurane
- Halothane
- Isoflurane
- Nitrous oxide
- Sevoflurane

Intravenous Anesthetics

- Used in situations that require short duration anesthesia (outpatient surgery)
- To supplement inhalation anesthetics
- Primarily used as adjuncts to inhalationals
- Administered first
- Rapidly induce unconsciousness

IV Anesthetics

- Barbiturate

  -Thiopental- rapid onset and potent, but no analgesia

- Benzodiazepines

  -Diazepam, Lorazepam, Midazolam- produce sedation but not analgesia; produce amnesia

- Opioids-Fentanyl-good analgesia; for intra-operative pain
- Propofol -Commonly used for sedation during procedures or in the ICU

- Etomidate

  -a potent hypnotic agent used for induction of surgical anesthesia. Unconsciousness develops rapidly and lasts about 5 minutes. no analgesic action

- Ketamine -Good analgesia, produces delusions

Local Anesthetics

- Amides (lidocaine) and esters (procaine)
- Stop axonal conduction
- Block sodium channels
- Causes rapid loss of sensation in limited part of body

Local Anesthetics

- They reversibly block impulse conduction along nerve axons that utilize sodium channels to generate an action potential.
- Cocaine was the first such agent used but then abandoned due to its addictive properties

Short-acting-procaine (1 hour)

Intermediate-acting- lidocaine (1-2.5 hours)

Long-acting- tetracaine (3-9 hours)

- Vasoconstrictor substances such as norepinephrine are co-administered so as to limit absorption and concentrate them at the site of injection

Adverse Effects

CNS- anxiety, restlessness, blurred vision, seizures. CNS depression with unconsciousness followed by respiratory arrest.

CV- Occurs under high doses- myocardial depression, bradycardia, arrhythmias, hypotension, and cardiac arrest.

Dermal- burning sensation at site of injection, hypersensitivity reactions.

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.

Muscle Relaxants

Muscle Relaxants

Drugs that affect skeletal muscle function fall into two groups:

- Neuromuscular (NMJ) blockers- used in intensive care units to cause paralysis and as a preanesthetic medication

- Spasmolytics - used to reduce spasticity in a variety of neurologic disorders

NMJ Blockers

- Relax skeletal muscles during surgery, to reduce the intensity of muscle spasms in electrically-induced convulsions, help manage patients who are fighting mechanical ventilation.

Nondepolarizing agents- curare alkaloids such as **tubocurarine**, **pancuronium**, and **vecuronium**. Block neurotransmitter action of acetylcholine. NMJ agents do not cross the blood–brain barrier and have no action on the CNS. For this reason, anesthesia is induced before neuromuscular blockade is started.

- The neuromuscular blocking actions of tubocurarine may be reversed with anticholinesterases such as neostigmine, pyridostigmine, and edrophonium.

Depolarizing agents (succinylcholine) cause excessive depolarization which desensitizes muscles and renders them unresponsive.

Spasticity

- **Clinical conditions associated with (Cerebral palsy, Multiple sclerosis, Stroke)**

- **Spasmolytics**- these are skeletal muscle relaxing agents that relieve acute musculoskeletal pain, spasm or spasticity.

Spasmolytics (Central)

- **Baclofen**

  GABA analog acting at $GABA_B$ receptors which depresses neuronal activity, decreasing the frequency and degree of muscle spasms and reduces muscle tone

  Drug of choice because it produces less sedation than diazepam and less peripheral muscle weakness than dantrolene.

  Used for paraplegic or quadraplegic patients with spinal cord lesions caused by either multiple sclerosis or trauma.

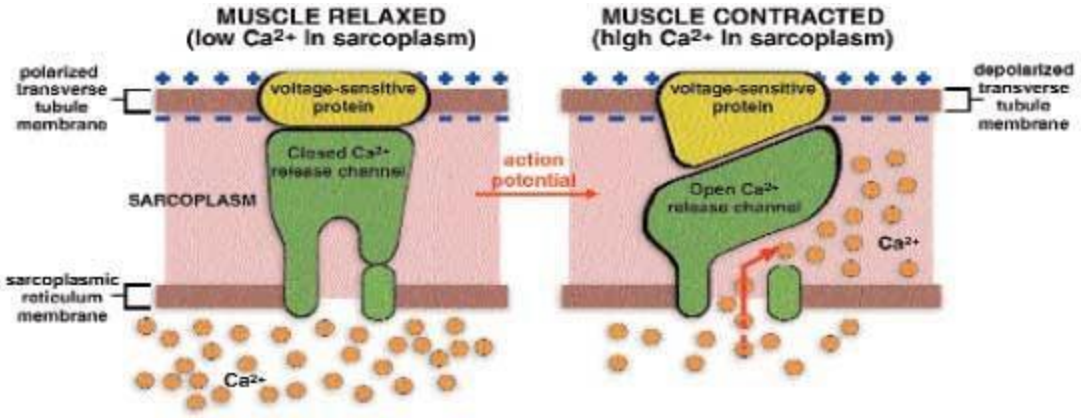
  Intrathecal Baclofen use for management of severe spasticity/pain when nonresponsive to medication by other routes of administration.

- **Diazepam**

  Effective for both acute spasms and chronic spasticity. Indicated for patients with spinal cord lesions or those with cerebral palsy.

  Anti-spasmolytic effect in part due to action in the spinal cord

Spasmolytics (Peripheral)



Dantrolene has similar effects to other central drugs but it works directly on the muscle by inhibiting calcium release necessary for muscle relaxation. It is most effective for spasticity with cerebral origin (multiple sclerosis, cerebral palsy)