

Anesthesia



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History of Anesthesia



- Ether synthesized in 1540 by Cordus
- Ether used as anesthetic in 1842 by Dr. Crawford W. Long
- Ether publicized as anesthetic in 1846 by Dr. William Morton
- Chloroform used as anesthetic in 1853 by Dr. John Snow

History of Anesthesia



History of Anesthesia



- Endotracheal tube discovered in 1878
- Local anesthesia with cocaine in 1885
- Thiopental first used in 1934
- Curare first used in 1942 - opened the "Age of Anesthesia"

Basic Principles of Anesthesia



- Anesthesia defined as the abolition of sensation
- Analgesia defined as the abolition of pain
- “Triad of General Anesthesia”
 - need for unconsciousness
 - need for analgesia
 - need for muscle relaxation

Inhalational Anesthetic Agents



- Inhalational anesthesia refers to the delivery of gases or vapors from the respiratory system to produce anesthesia
- Pharmacokinetics--uptake, distribution, and elimination from the body
- Pharmacodynamics-- MAC value

Nitrous Oxide

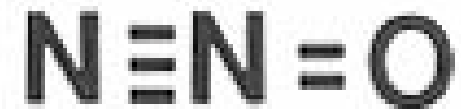


- Prepared by Priestly in 1776
- Anesthetic properties described by Davy in 1799
- Characterized by inert nature with minimal metabolism
- Colorless, odorless, tasteless, and does not burn

Nitrous Oxide



- Simple linear compound
- Not metabolized
- Only anesthetic agent that is inorganic



nitrous oxide

Nitrous Oxide



- Major difference is low potency
- MAC value is 105%
- Weak anesthetic, powerful analgesic
- Needs other agents for surgical anesthesia
- Low blood solubility (quick recovery)

Nitrous Oxide Systemic Effects



- Minimal effects on heart rate and blood pressure
- May cause myocardial depression in sick patients
- Little effect on respiration
- Safe, efficacious agent

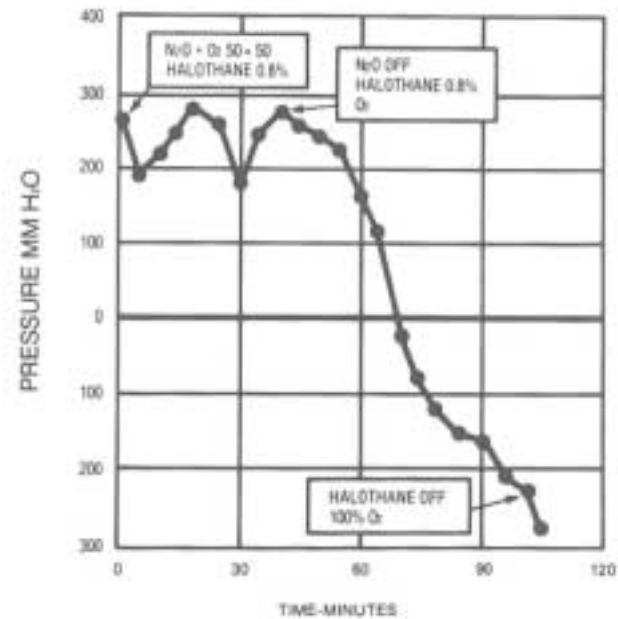
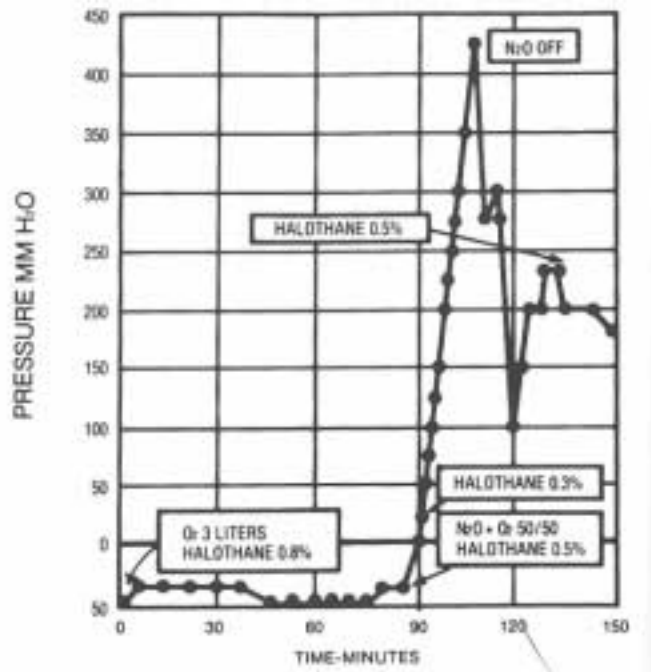
Nitrous Oxide Side Effects



- Manufacturing impurities toxic
- Hypoxic mixtures can be used
- Large volumes of gases can be used
- Beginning of case: second gas effect
- End of case: diffusion hypoxia

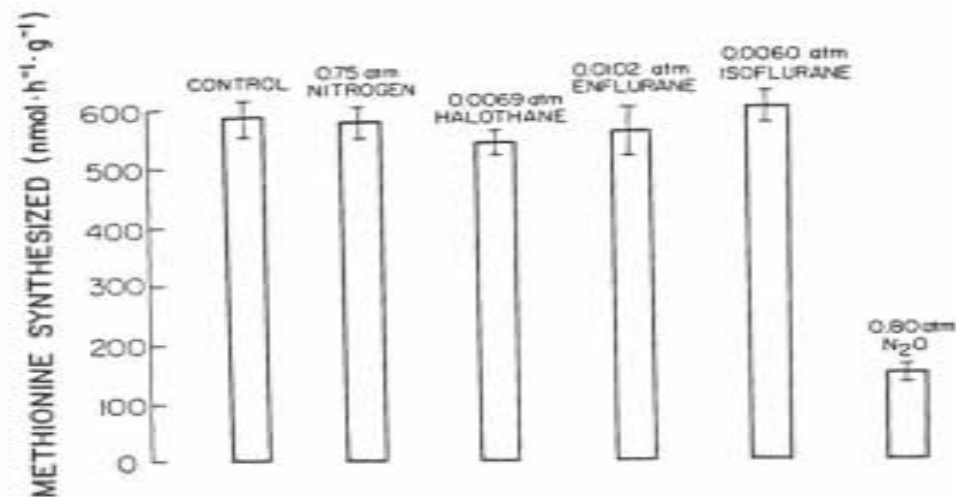
Nitrous Oxide Side Effects

- Diffusion into closed spaces



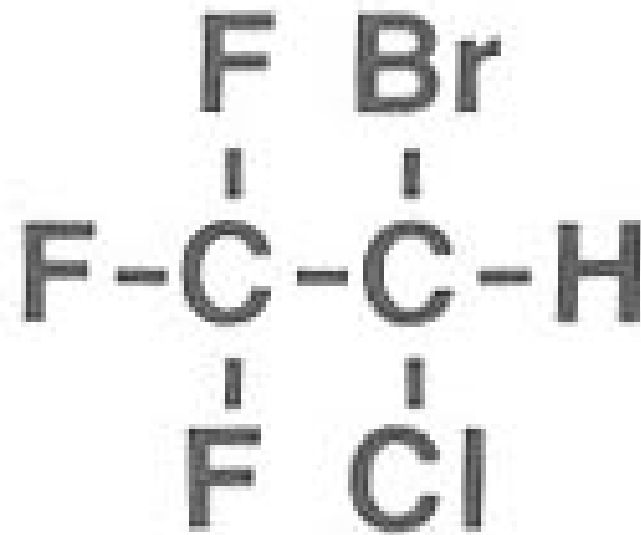
Nitrous Oxide Side Effects

- Inhibits methionine synthetase (precursor to DNA synthesis)
- Inhibits vitamin B-12 metabolism
- Dentists, OR personnel, abusers at risk



Halothane

- Synthesized in 1956 by Suckling
- Halogen substituted ethane
- Volatile liquid easily vaporized, stable, and nonflammable



halothane

Halothane



- Most potent inhalational anesthetic
- MAC of 0.75%
- Efficacious in depressing consciousness
- Very soluble in blood and adipose
- Prolonged emergence

Halothane Systemic Effects



- Inhibits sympathetic response to painful stimuli
- Inhibits sympathetic driven baroreflex response (hypovolemia)
- Sensitizes myocardium to effects of exogenous catecholamines-- ventricular arrhythmias
 - Johnson found median effective dose 2.1 ug/kg
 - Limit of 100 ug or 10 mL over 10 minutes
 - Limit dose to 300 ug over one hour
 - Other medications

Halothane Systemic Effects



- Decreases respiratory drive-- central response to CO_2 and peripheral to O_2
 - Respirations shallow-- atelectasis
 - Depresses protective airway reflexes
- Depresses myocardium-- lowers BP and slows conduction
- Mild peripheral vasodilation

Halothane Side Effects



- “Halothane Hepatitis” -- 1/10,000 cases
 - fever, jaundice, hepatic necrosis, death
 - metabolic breakdown products are hapten-protein conjugates
 - immunologically mediated assault
 - exposure dependent

Halothane Side Effects



- Malignant Hyperthermia-- 1/60,000 with succinylcholine to 1/260,000 without
 - halothane in 60%, succinylcholine in 77%
- Classic-- rapid rise in body temperature, muscle rigidity, tachycardia, rhabdomyolysis, acidosis, hyperkalemia, DIC
 - most common masseter rigidity
 - family history

Halothane Side Effects



- Malignant Hyperthermia (continued)
 - high association with muscle disorders
 - autosomal dominant inheritance
 - diagnosis--previous symptoms, increase CO₂, rise in CPK levels, myoglobinuria, muscle biopsy
 - physiology--hypermetabolic state by inhibition of calcium reuptake in sarcoplasmic reticulum

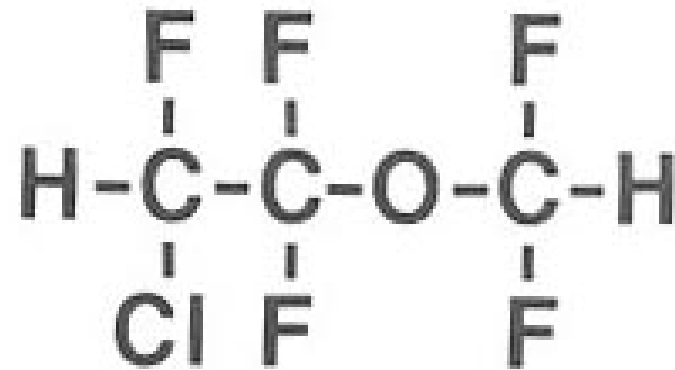
Halothane Side Effects



- Malignant Hyperthermia (continued)
 - treatment--early detection, d/c agents, hyperventilate, bicarb, IV dantrolene (2.5 mg/kg), ice packs/cooling blankets, lasix/mannitol/fluids. ICU monitoring
 - Susceptible patients-- preop with IV dantrolene, keep away inhalational agents and succinylcholine

Enflurane

- Developed in 1963 by Terrell, released for use in 1972
- Stable, nonflammable liquid
- Pungent odor
- MAC 1.68%



enflurane

Enflurane Systemic Effects



- Potent inotropic and chronotropic depressant and decreases systemic vascular resistance-- lowers blood pressure and conduction dramatically
- Inhibits sympathetic baroreflex response
- Sensitizes myocardium to effects of exogenous catecholamines-- arrhythmias

Enflurane Systemic Effects



- Respiratory drive is greatly depressed--
central and peripheral responses
 - increases dead space
 - widens A-a gradient
 - produces hypercarbia in spontaneously breathing patient

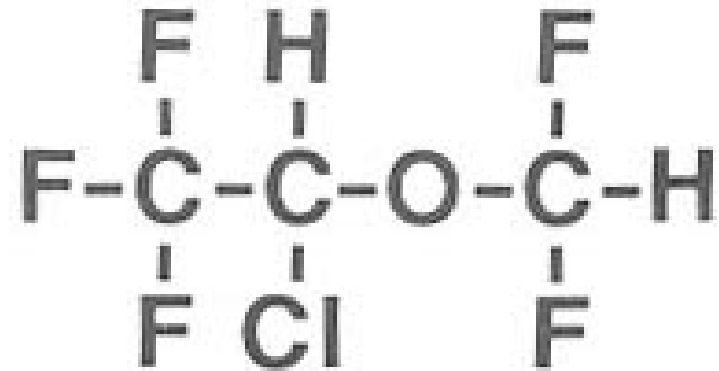
Enflurane Side Effects



- Metabolism one-tenth that of halothane-- does not release quantity of hepatotoxic metabolites
- Metabolism releases fluoride ion-- renal toxicity
- Epileptiform EEG patterns

Isoflurane

- Synthesized in 1965 by Terrell, introduced into practice in 1984
- Not carcinogenic
- Nonflammable, pungent
- Less soluble than halothane or enflurane
- MAC of 1.30 %



isoflurane

Isoflurane Systemic Effects



- Depresses respiratory drive and ventilatory responses-- less than enflurane
- Myocardial depressant-- less than enflurane
- Inhibits sympathetic baroreflex response-- less than enflurane
- Sensitizes myocardium to catecholamines -- less than halothane or enflurane

Isoflurane Systemic Effects



- Produces most significant reduction in systemic vascular resistance-- coronary steal syndrome, increased ICP
- Excellent muscle relaxant-- potentiates effects of neuromuscular blockers

Isoflurane Side Effects



- Little metabolism (0.2%) -- low potential of organotoxic metabolites
- No EEG activity like enflurane
- Bronchoirritating, laryngospasm

Sevoflurane and Desflurane



- Low solubility in blood-- produces rapid induction and emergence
- Minimal systemic effects-- mild respiratory and cardiac suppression
- Few side effects
- Expensive
- Differences

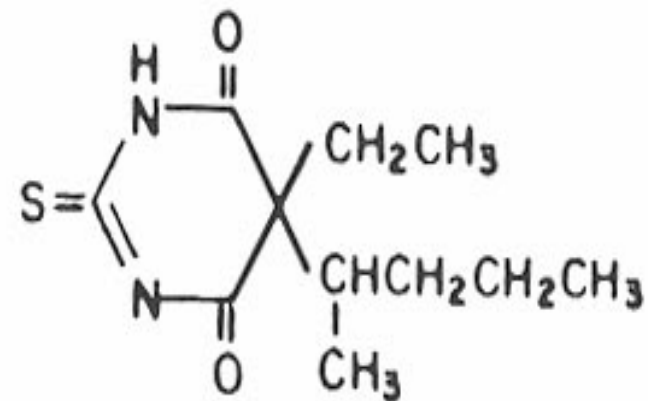
Intravenous Anesthetic Agents



- First attempt at intravenous anesthesia by Wren in 1656-- opium into his dog
- Use in anesthesia in 1934 with thiopental
- Many ways to meet requirements-- muscle relaxants, opioids, nonopoids
- Appealing, pleasant experience

Thiopental

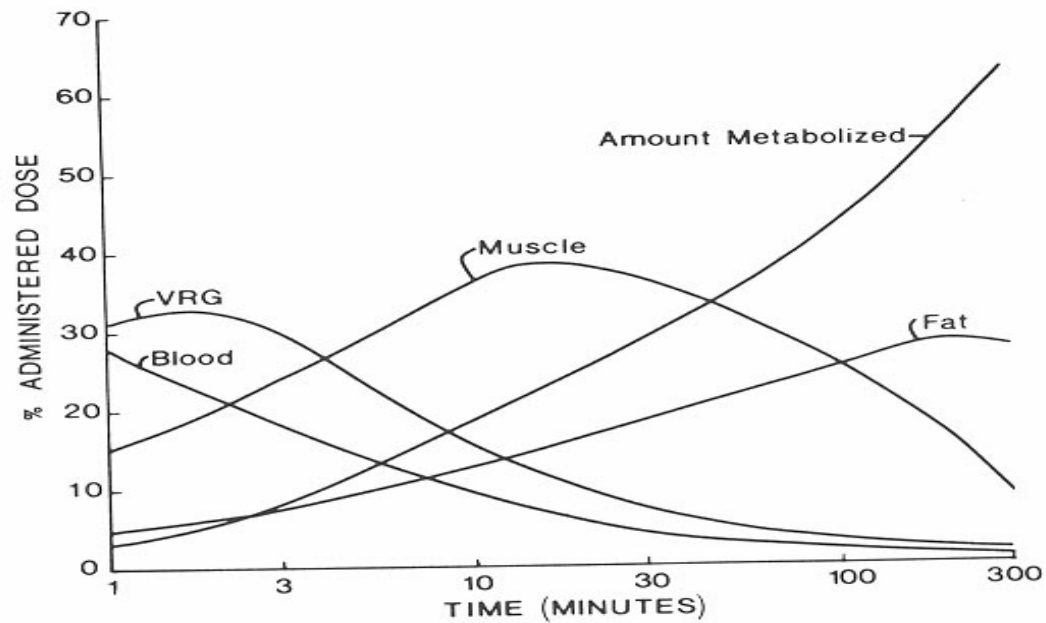
- Barbiturate
- Water soluble
- Alkaline
- Dose-dependent suppression of CNS activity--decreased cerebral metabolic rate (EEG flat)



Thiopental

Thiopental

■ Redistribution



Thiopental Systemic Effects



- Varied effects on cardiovascular system in people-- mild direct cardiac depression-- lowers blood pressure-- compensatory tachycardia (baroreflex)
- Dose-dependent depression of respiration through medullary and pontine respiratory centers

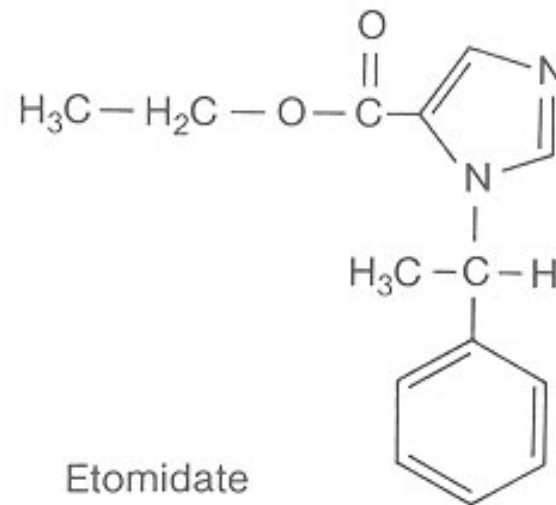
Thiopental Side Effects



- Noncompatibility
- Tissue necrosis--gangrene
- Tissue stores
- Post-anesthetic course

Etomidate

- Structure similar to ketoconazole
- Direct CNS depressant (thiopental) and GABA agonist
- Redistribution



Etomidate Systemic Effects



- Little change in cardiac function in healthy and cardiac patients
- Mild dose-related respiratory depression
- Decreased cerebral metabolism

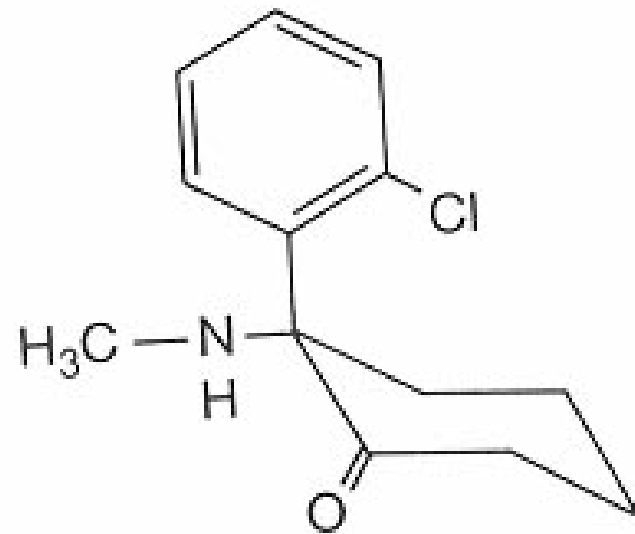
Etomidate Side Effects



- Pain on injection (propylene glycol)
- Myoclonic activity
- Nausea and vomiting (50%)
- Cortisol suppression

Ketamine

- Structurally similar to PCP
- Interrupts cerebral association pathways -- “dissociative anesthesia”
- Stimulates central sympathetic pathways



Ketamine

Ketamine Systemic and Side Effects



- Characteristic of sympathetic nervous system stimulation-- increase HR, BP, CO
- Maintains laryngeal reflexes and skeletal muscle tone
- Emergence can produce hallucinations and unpleasant dreams (15%)

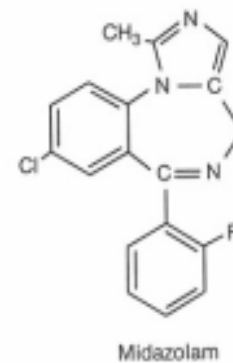
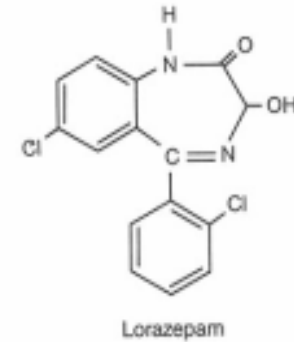
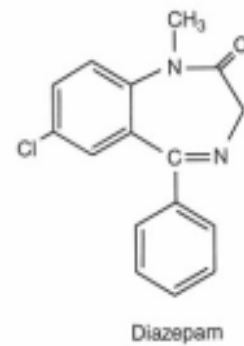
Propofol



- Rapid onset and short duration of action
- Myocardial depression and peripheral vasodilation may occur-- baroreflex not suppressed
- Not water soluble-- painful (50%)
- Minimal nausea and vomiting

Benzodiazepines

- Produce sedation and amnesia
- Potentiate GABA receptors
- Slower onset and emergence



Diazepam



- Often used as premedication or seizure activity, rarely for induction
- Minimal systemic effects-- respirations decreased with narcotic usage
- Not water soluble-- venous irritation
- Metabolized by liver-- not redistributed

Lorazepam



- Slower onset of action (10-20 minutes)-- not used for induction
- Used as adjunct for anxiolytic and sedative properties
- Not water soluble-- venous irritation

Midazolam



- More potent than diazepam or lorazepam
- Induction slow, recovery prolonged
- May depress respirations when used with narcotics
- Minimal cardiac effects
- Water soluble

Narcotic agonists (opioids)

- Used for years for analgesic action-- civil war for wounded soldiers
- Predominant effects are analgesia, depression of sensorium and respirations
- Mechanism of action is receptor mediated

Receptor-Mediated Effects of Narcotics

Receptor	Effects
μ (mu)	Analgesia, respiratory depression, euphoria, physical dependence
κ (kappa)	Analgesia, respiratory depression, sedation, miosis
σ (sigma)	Dysphoria, hallucinations, tachypnea, tachycardia

Narcotic agonists (opoids)



- Minimal cardiac effects-- no myocardial depression
- Bradycardia in large doses
- Some peripheral vasodilation and histamine release -- hypotension
- Side effects nausea, chest wall rigidity, seizures, constipation, urinary retention

Narcotic agonists (opoids)



- Meperidine, morphine, alfentanil, fentanyl, sufentanil are commonly used
- Naloxone is pure antagonist that reverses analgesia and respiratory depression nonselectively-- acts 30 minutes, effects may recur when metabolized

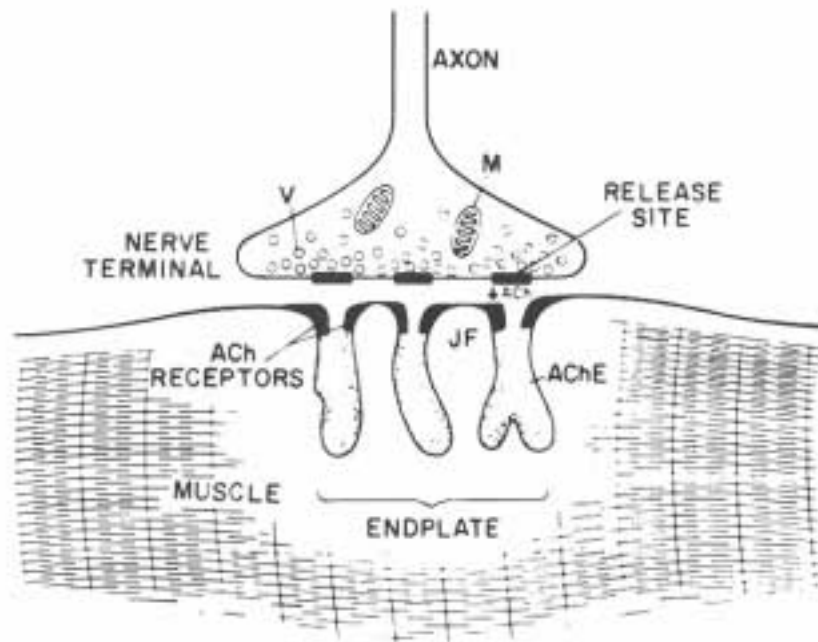
Muscle Relaxants



- Current use of inhalational and previous intravenous agents do not fully provide control of muscle tone
- First used in 1942-- many new agents developed to reduce side effects and lengthen duration of action
- Mechanism of action occurs at the neuromuscular junction

Muscle Relaxants

■ Neuromuscular Junction



Nondepolarizing Muscle Relaxants



- Competitively inhibit end plate nicotinic cholinergic receptor
- Intermediate acting (15-60 minutes):
atracurium, vecuronium, mivacurium
- Long acting (over 60 minutes):
pancuronium, tubocurarine, metocurine
- Difference-- renal function

Nondepolarizing Muscle Relaxants



- Tubocurarine-- suppress sympathetic, mast cell degranulation
- Pancuronium-- blocks muscarinics
- Reversal by anticholinesterase-- inhibit acetylcholinesterase
 - neostigmine, pyridostigmine, edrophonium
 - side effects muscarinic stimulation

Depolarizing Muscle Relaxants



- Depolarize the end-plate nicotinic receptor
- Succinylcholine used clinically
 - short duration due to plasma cholinesterase
 - side effects-- fasciculations, myocyte rupture, potassium extravasation, myalgias
 - sinus bradycardia-- muscarinic receptor
 - malignant hyperthermia

Techniques



- History and physical examination
- Induction
- Maintenance
- Emergence

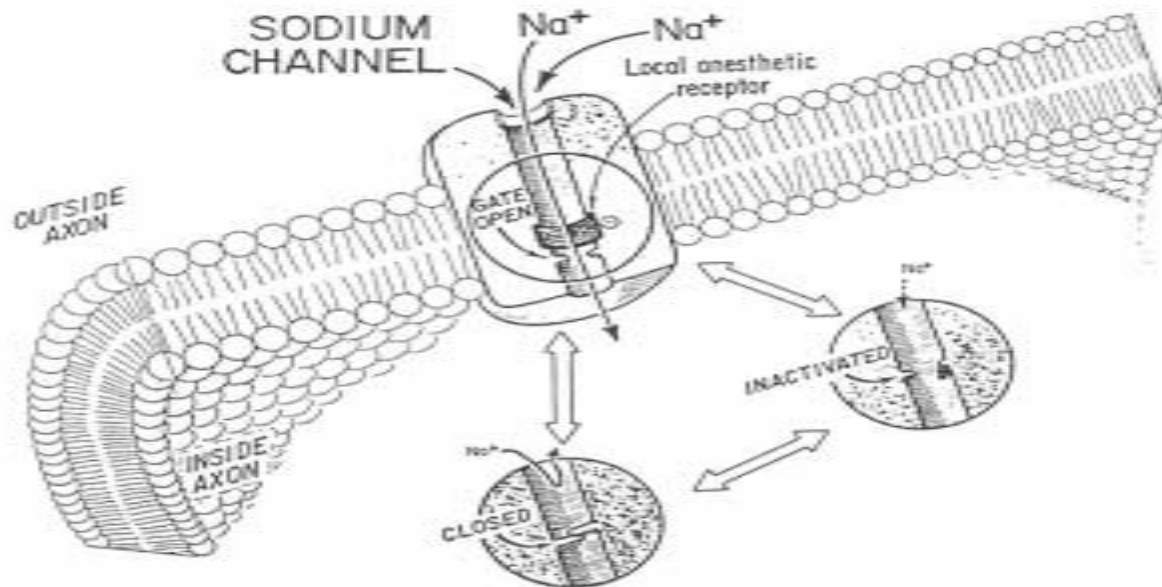
Local Anesthetics



- Followed general anesthesia by 40 years
- Koller used cocaine for the eye in 1884
- Halsted used cocaine as nerve block
- First synthetic local-- procaine in 1905
- Lidocaine synthesized in 1943

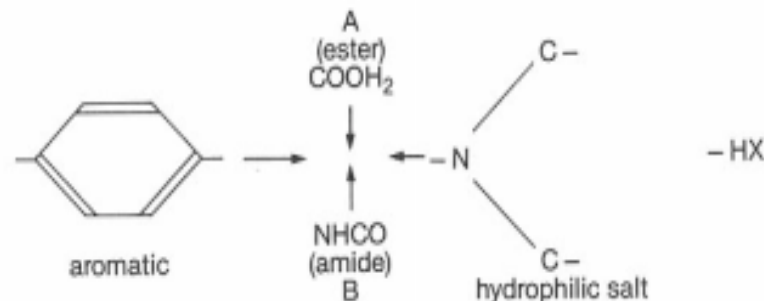
Local Anesthetics

- Mechanism of action is by reversibly blocking sodium channels to prevent depolarization
- Anesthetic enters on axioplasmic side and attaches to receptor in middle of channel



Local Anesthetics

- Linear molecules that have a lipophilic and hydrophilic end (ionizable)
 - low pH-- more in ionized state and unable to cross membrane
 - adding sodium bicarb-- more in non-ionized state



Local Anesthetics

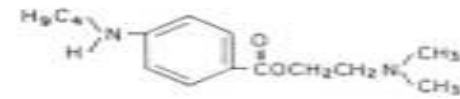
- Two groups: esters and amides
 - esters metabolized by plasma cholinesterase
 - amides metabolized by cytochrome p-450



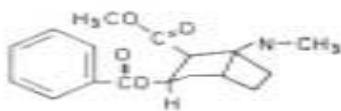
Procaine



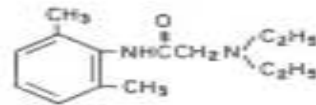
Chlorprocaine



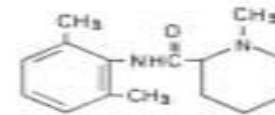
Tetracaine



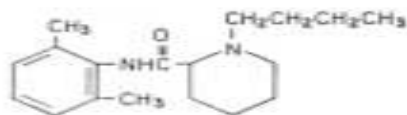
Cocaine



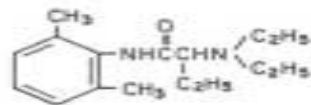
Lidocaine



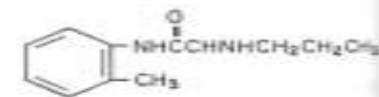
Mepivacaine



Bupivacaine



Etidocaine

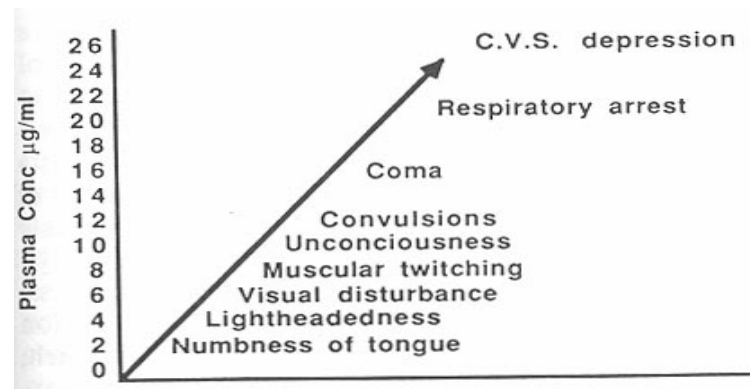


Prilocaine

Local Anesthetic Toxicity

■ Central nervous system

- initially-- lightheadedness, circumoral numbness, dizziness, tinnitus, visual change
- later-- drowsiness, disorientation, slurred speech, loss of consciousness, convulsions
- finally-- respiratory depression



Local Anesthetic Toxicity



- Cardiovascular
 - myocardial depression and vasodilation-- hypotension and circulatory collapse
- Allergic reactions-- rare (less than 1%)
 - preservatives or metabolites of esters
 - rash, bronchospasm

Prevention and Treatment of Toxicity



- Primarily from intravascular injection or excessive dose -- anticipation
 - aspirate often with slow injection
 - ask about CNS toxicity
 - have monitoring available
 - prepare with resuscitative equipment, CNS-depressant drugs, cardiovascular drugs
 - ABC's

Treatment of Toxicity



All cases:

assure adequate ventilation
administer supplemental oxygen

Seizures:

diazepam (Valium)

Hypotension

Trendelenburg position (head down, legs up)
IV fluid bolus (isotonic saline or LR)
vasopressors (dopamine) (if refractory to above)

Dysrhythmias

as per ACLS protocol (but do not administer further
lidocaine)

Cocaine



- South American Indians used to induce euphoria, reduce hunger, and increase work tolerance in sixth century
- Many uses in head and neck-- strong vasoconstrictor, no need for epinephrine
- Mechanism is similar-- blocks sodium channel, also prevents uptake of epinephrine and norepinephrine

Cocaine



- May lead to increased levels of circulating catecholamines-- tachycardia, peripheral vasoconstriction
- Safe limits (200-400 mg)-- use with epinephrine clinically

Challenges in Anesthesiology

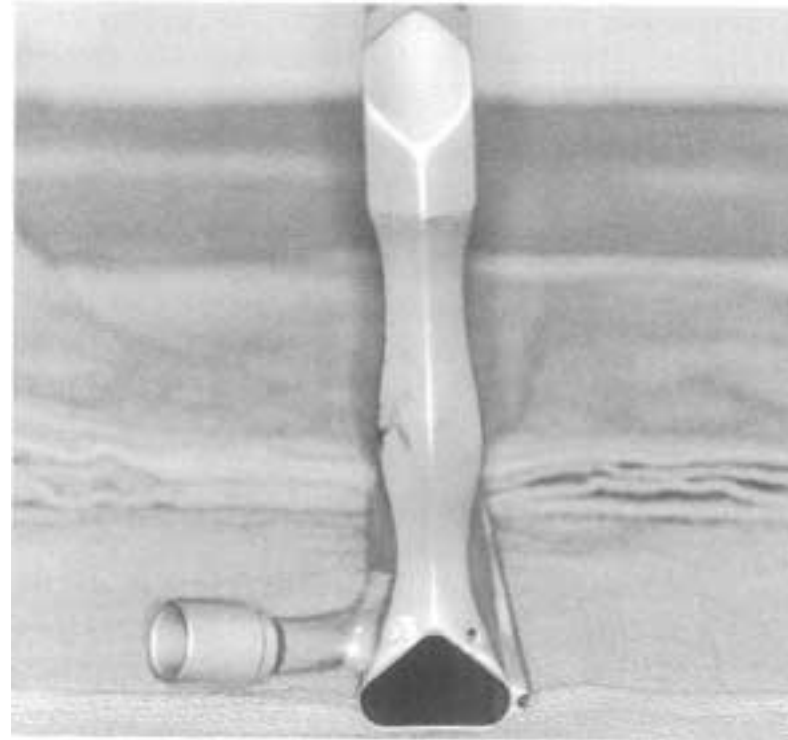


- Tonsillectomy
 - postoperative bleeding

- Ear surgery
 - bloodless operative field
 - nitrous oxide
 - muscle relaxants

Challenges in Anesthesiology

- Laryngeal surgery
 - ventilation, oxygenation, exposure
 - topical anesthesia
 - general anesthesia
 - small diameter cuff
 - intermittent apnea
 - Venturi injection
 - spontaneous respiration



Challenges in Anesthesiology



- Laryngeal surgery
 - Carbon dioxide laser
 - | no polyvinyl tubes
 - | Rusch or Xomed tubes
 - | Mixture of gases
 - | Tube cuff consideration
 - | Pulse mode
 - Management of fire

Challenges in Anesthesiology



- Acute airway problems post extubation
 - Laryngospasm
 - Postobstructive pulmonary edema
 - Postintubation croup
 - Aspiration pneumonitis
 - Recurrent nerve palsy
 - Massive subcutaneous emphysema