Chapter 3

Anesthetic Agents and Adjuncts

Anesthetic agent: any drug used to induce a loss of sensation with or without unconsciousness
Adjunct: a drug that is not a true anesthetic, but that is used during anesthesia to produce other desired effects such as sedation, muscle relaxation, analgesia, reversal, neuromuscular blockade, or parasympathetic blockade

Classification of Anesthetic Agents and Adjuncts

- Route of administration
  - Inhalant
  - Injectable
  - Oral
  - Topical
- Time of administration
  - Preanesthetic
  - Induction
  - Maintenance

Classification of Anesthetic Agents and Adjuncts (Cont'd)

- Principal effect
  - Local vs. general
  - Sedatives and tranquilizers vs. analgesics
  - Neuromuscular blockers
  - Anticholinergic agents
  - Reversal agents
- Chemistry

Anesthetic Agent and Adjunct Actions

- Pharmacokinetics
- Pharmacodynamics
- Drug distribution
- Target tissues and stimulation
  - CNS—depression or stimulation

Agonists

- Bind to and stimulate target tissue
- Most anesthetic agents and adjuncts

Antagonists

- Bind to target tissue but don’t stimulate
- Reversal agents

Partial Agonists and Agonist-Antagonists

- Opioids
- Partial agonists
- Agonist-antagonists
- Used to block pure agonists

Analgesia

- Most general anesthetics are not analgesics
- Must provide analgesic pre- and postoperatively
  - No pain perception while anesthetized
- True analgesics don't provide general anesthesia

Drug Combinations

- Don’t mix drugs in a single syringe unless they are compatible
- Don’t administer a drug combination if a precipitate develops when the drugs are mixed
- Most anesthetic agents and adjuncts are water soluble
  - Diazepam is not water soluble

Preanesthetic Medications

- Calm or sedate excited animal
- Minimize adverse drug effects
- Reduce dose of concurrent drugs
- Smoother anesthetic induction and recovery
- Analgesia
- Muscle relaxation

Preanesthetic Medications (Cont'd)

- Route of administration affects onset of action and duration of effects
  - SC—slowest onset, longest duration
  - IM—faster onset, shorter duration
  - IV—fastest onset, shortest duration

Preanesthetic Anticholinergics

- Parasympatholytic drugs—block acetylcholine
  - Prevent and treat bradycardia
  - Decrease salivary secretions
- Atropine and glycopyrrolate (dogs and cats)
  - IV, IM, SC, or IT
  - Atropine—faster onset, shorter peak, shorter duration
  - Glycopyrrolate—slower onset, longer peak, longer duration

Anticholinergic Effects

- CNS—limited effect
- Cardiovascular—prevent bradycardia
- Secretions—decrease
- Eye—mydriasis and corneal drying
- Bronchodilation

Anticholinergic Adverse Effects

- Cardiac arrhythmia
  - Contraindicated in animals with elevated heart rates or cardiac diseases
- Temporary bradycardia—atropine
- Thickened respiratory and salivary secretions
  - May lead to airway blockage—cats and ruminants
- Intestinal peristalsis inhibition
  - May lead to colic (horses) or bloat (ruminants)

Tranquilizers and Sedatives

- Phenothiazines
- Benzodiazepines
- Alpha$_2$-adrenoceptor agonists
- Alpha$_2$-antagonists

Phenothiazines—Acepromazine Maleate

- Also known as acepromazine or “ace”
  - Preanesthetic sedation
  - Decrease dose of general anesthetic
  - Ease induction and recovery
  - May be used with opioids for minor procedures
  - Approved for horses, dogs, and cats
  - Administered IV or IM
  - No reversal agent
  - Metabolized by liver
  - Will slowly cross the placenta

Effects of Acepromazine

- CNS
  - Calming, reluctance to move, decreased interest in surroundings
  - Sedation less pronounced in cats
  - Not an analgesic
- Cardiovascular System
  - Peripheral vasodilation that leads to hypotension, increased heart rate, and hypothermia
  - Protects against arrhythmias and decreases cardiac output

Effects of Acepromazine (Cont'd)

- Respiratory system
  - Worsens depressive effect of other drugs
- Gastrointestinal system
  - Antiemetic
- Prevents histamine release and decreases allergic response

Adverse Effects of Acepromazine

- CNS
  - Reduced seizure threshold
  - May produce aggression or excitement
- Cardiovascular system
  - Hypotension—dose dependent
- Penile prolapse
  - Seen in horses and other large animals
  - May lead to permanent injury
- Decreased PCV
  - Possibly due to splenic engorgement

Use of Acepromazine

- Dose and needle placement
- Increased potency and duration
  - Geriatrics, neonates, debilitated animals
- Breed considerations
  - Australian shepherds
  - Giant breeds, Boxers, Greyhounds
  - Terriers and cats
- Overdose treatment

Benzodiazepines

- Tranquilizers—controlled substances
  - Diazepam
  - Zolazepam
  - Midazolam
- Rapid onset of action
- Short duration of action

Effects of Benzodiazepines

- CNS
  - Calming and antianxiety only in old or ill patients
  - Not an effective sedative or analgesic
  - Anticonvulsant—use with animals having seizures
- Cardiovascular and respiratory systems
  - Minimal effect with a high margin of safety
- Skeletal muscle relaxation
- Potentiate general anesthetics
- Appetite stimulation (cats and ruminants)

Adverse Effects of Benzodiazepines

- CNS
  - Disorientation and excitement—young, healthy dogs
  - Dysphoria and aggression—cats
  - Muscle fasciculations—horses
  - Ataxia and recumbency—any large animal
- Diazepam must be given by IV slowly
  - Oral diazepam in cats can cause liver failure

Use of Benzodiazepines

- Diazepam
  - Not water soluble
  - Don’t mix with water-soluble drugs
  - Don’t store in plastic
  - Commonly used with ketamine to induce anesthesia in small animals and horses
  - Administer IV slowly

Use of Benzodiazepines (Cont'd)

- Midazolam
  - Water soluble
  - Can be administered IM or SC
  - Excellent sedative for swine, ferrets, rabbits, and birds
  - Used in combination with ketamine to induce anesthesia in dogs, small mammals, and birds

Use of Benzodiazepines (Cont'd)

- Zolazepam
  - Available only as a component of Telazol®
  - A powdered product
  - Reconstituted with sterile water

Alpha$_2$-Adrenoceptor Agonists

- Also written alpha$_2$-agonists or α_2-agonists
- Noncontrolled agents
- Sedation, analgesia, and muscle relaxation
- Large and small animals—IM or IV
- Administered prior to minor procedures
- Readily reversed with alpha$_2$-antagonist

Alpha$_2$-Agonists

- Xylazine (Rompun, Anased)
- Detomidine (Dormosedan)
- Romifidine (Sedivet)
- Dexmedetomidine (Dexdomitor)

Alpha$_2$-Agonists (Cont'd)

- Stimulates alpha$_2$ receptors of the sympathetic nervous system (SNS)
  - Decrease release of norepinephrine
  - No "fight-or-flight" response
- Sedation, analgesia, bradycardia, hypotension, and hypothermia
- Metabolized in liver; excreted in urine
- Rapid sedation; 1-2 hour duration

Effects of Alpha$_2$-Agonists

- CNS
  - Dose-dependent sedation
  - Analgesia—short-acting
- Cardiovascular system—early phase
  - Dose-dependent vasoconstriction and hypertension
  - Bradycardia
  - Cardiac arrhythmias
- Cardiovascular system—late phase
  - Decreased cardiac output
  - Hypotension and further bradycardia

Effects of Alpha$_2$-Agonists (Cont'd)

- Respiratory system
  - Dose-dependent depression
- Other effects
  - Muscle relaxation
  - Increased effect of other anesthetic agents
  - Vomiting—immediate response (dogs and cats)
  - Hyperglycemia—transient
  - Hypothermia

Adverse Effects of Alpha$_2$-Agonists

- CNS
  - Change in behavior—varies with species
- Cardiovascular system
  - Bradycardia, hypotension, decreased output
- Respiratory system
  - Depression—varies from animal to animal
  - More severe if given with other drugs

Adverse Effects of Alpha$_2$-Agonists (Cont'd)

- Increased urination
- Gastrointestinal effects
  - Bloat—dogs, cattle, and horses
  - Salivation and regurgitation—cattle
- Premature parturition—cattle (last trimester)
- Sweating—horses
- Absorbed through skin abrasions and mucous membranes
  - Wash off immediately

Use of Alpha$_2$-Agonists

- Use with caution; monitor patients closely
- Avoid use in geriatric, diabetic, pregnant, pediatric, or ill patients
- Administer anticholinergics 10-20 minutes prior

Alpha$_2$-Agonist—Xylazine

- 2% solution (small animals)
- 10% solution (horses)
- Use 1/10 horse dose in cattle
- Used mostly in large animals

Alpha$_2$-Agonist—Dexmedetomidine

- Dexdomitor®
- Most commonly used in dogs and cats
- Produces sedation and analgesia
- More potent and safer than xylazine
- Antagonist—atipamazole (Antisedan®)
- Preanesthetic in low doses
- Can be mixed with other drugs

Alpha$_2$-Agonists—Detomidine and Romifidine

- Detomidine
  - Used in horses
  - Sedation, analgesia, muscle relaxation
  - Two times the duration of xylazine
  - Standing sedation with butorphanol
- Romifidine
  - Produces less ataxia

Alpha$_2$-Antagonists

- Reverse all effects of alpha$_2$-agonists
  - Beneficial effects—for example, analgesia and sedation
  - Detrimental effects—for example, bradycardia
- Wide margin of safety
- Effects of overdose
  - Neurological—excitement and muscle tremors
  - Cardiovascular—hypotension and tachycardia
  - Gastrointestinal—salivation and diarrhea

Use of Alpha$_2$-Antagonists

- Dose is expressed as a ratio
  - Agonist to antagonist
  - 10:1 means the dose of the antagonist is 1/10 of the dose of the agonist
- Administer slowly by IV
- Reduce dose if more than 30 minutes has elapsed since the agonist was administered

Alpha$_2$-Antagonist—Tolazoline

- Nonspecific alpha$_2$-antagonist
- Used in ruminants at a 1:10 dose ratio with xylazine
- Reverses cardiovascular and sedative effects

Alpha$_2$-Antagonist—Yohimbine

- Used in dogs, cats, horses, and exotic species
- Reverses cardiovascular and sedative effects of xylazine
- Dose ratio is species dependent
  - Dogs and horses—10:1
  - Cats—2:1

Alpha$_2$-Antagonist—Atipamezole

- Antisedan®
- Specific antagonist for dexmedetomidine
- IM injection (IV in emergencies)
- Use ½ the dose in cats compared to dogs
- Reversal—5-10 minutes after IM injection

Opioids

- Derivatives of opium
- Opiates—naturally derived compounds
- Produce analgesia and sedation
- Anesthetic induction when combined with other drugs
- Classified as agonists, partial agonists, agonist-antagonists, or antagonists

Commonly Used Opioids

- Agonists
  - Morphine, hydromorphone, oxymorphone, fentanyl, and meperidine
- Partial agonist
  - Buprenorphine
- Agonist-antagonists
  - Butorphanol and nalbuphine
- Antagonists
  - Naloxone, etorphine, and carfentenil

Opioids

- Controlled substances
  - Except for antagonists and nalbuphine
- Administered IV, IM, SC, oral, rectal, transdermal, subarachnoid, and epidural
- Wide margin of safety

Opioids—Pharmacodynamics

- Mimic endogenous opioid peptides
  - β-Endorphins, dynorphins, enkephalins
- Analgesia and sedative effects
  - Result of action on the receptors in the brain and spinal cord
  - Types of receptors
    - Mu (μ), kappa (κ), and delta (δ), plus many subtypes
    - Each opioid has a different action at each receptor

Opioids—Pharmacodynamics (Cont'd)

- Agonists
  - Bind to and stimulate mu and kappa receptors
  - Best for moderate to severe pain
- Partial agonists
  - Bind to and partially stimulate receptors
- Agonist-antagonists
  - Bind to mu and kappa receptors, but stimulate only kappa receptors
- Antagonists
  - Bind to but don't stimulate mu and kappa receptors

Effects of Opioids

- CNS
  - Effect depends on many factors
  - Dogs
    - Causes sedation
    - Narcosis
  - Cats, horses, and ruminants
    - Causes CNS stimulation
    - Bizarre behavior patterns or dysphoria
    - Use lower dose
  - Analgesia
    - Pure agonists are most effective against severe pain
    - Used as a premedication for painful surgery

Effects of Opioids (Cont'd)

- Cardiovascular system
  - Bradycardia
- Respiratory system
  - Minimal decreased rate and tidal volume

Other Effects of Opioids

- Miosis in dogs
- Mydriasis in cats, horses, and ruminants
- Hypothermia in dogs
- Hyperthermia in cats
- Increased responsiveness to noise
- Sweating in horses
- Decreased urine production with urine retention

Adverse Effects of Opioids

- CNS
  - Anxiety, disorientation, excitement, dysphoria
- Cardiovascular system
  - Pronounced bradycardia
- Respiratory system
  - Decreased respiration and tidal volume
  - Decreased PaO_2 and $PaCO_2$
  - Dose dependent with some agents
  - Ceiling effect with some agents

Adverse Effects of Opioids (Cont'd)

- Gastrointestinal system
  - Salivation and vomiting—small animals
  - Initial diarrhea, vomiting, and flatulence
  - Pretreat with atropine or acepromazine
  - GI stasis follows initial GI stimulation
    - May predispose to colic in horses
    - Avoid administration to any animal with a GI obstruction

Other Adverse Effects of Opioids

- Addiction (physical dependence)
- Facial swelling and hypotension
- Increased intraocular and intracranial pressure
- Drug interactions
  - Meperidine and MOA inhibitors or tricyclic antidepressants (human)

Use of Opioids

- Preanesthetic
  - Agonists, partial agonists, or agonist-antagonist
  - May be used alone or in combination with
    - Tranquilizers
    - Anticholinergics
- Analgesia
  - Prevent and treat postoperative pain
  - Used with tranquilizer to produce neuroleptanalgesia

Neuroleptanalgesia

A profound state of sedation and analgesia induced by simultaneous administration of an opioid and a tranquilizer

Neuroleptanalgesia (Cont'd)

- Opioids
  - Morphine
  - Buprenorphine
  - Butorphanol
  - Hydromorphone
- Tranquilizers
  - Acepromazine
  - Diazepam
  - Midazolam
  - Xylazine
  - Dexmedetomidine

Use of Neuroleptanalgesics

- Sedation for minor procedures
- Induction of general anesthesia—dogs
  - Not in young, healthy dogs
  - Not in cats

Opioid Antagonists

- Reverse undesirable effects
  - CNS and respiratory depression
- Wake up patient following sedation
- Naloxone hydrochloride
  - IM or slow IV administration
  - Dogs, horses, cats, exotic mammals
- Naltrexone
  - Used in wild animals
  - Longer lasting

Naloxone Hydrochloride

- Mechanism of action is unknown
- IM—5 minutes to reversal
- IV (slowly)—2 minutes to reversal
- Duration of action 30-60 minutes

Effects of Opioid Antagonists

- Reversal of effects of opioid agonists, partial agonists, and agonists-antagonists
- Reversal can be complete in a few minutes
- Adverse effects are rare
  - Sudden analgesia loss can cause excitement, anxiety, and sympathetic nervous system stimulation
  - Prevent by using an agonist-antagonist

Use of Opioid Antagonists

- Emergencies
- Overdose
- Reverse neuroleptanalgesia
- Reviving neonates delivered by C-section
  - If dam received opioids
  - One drop placed under the tongue

Injectable Anesthetics

- Can produce unconsciousness
- Don’t provide analgesia or muscle relaxation
- Used with other agents
- Administered “to effect” IV
- Barbiturates, propofol, and etomidate

Barbiturates

- Subclasses based on duration of action
  - Ultrashort
    - Thiopental sodium, methohexital, and thiamylal
    - Dogs, cats, and horses
    - Induce general anesthesia
  - Short
    - Pentobarbital
    - Laboratory animals
    - Induce general anesthesia
    - Treat epilepsy in small animals
  - Intermediate
  - Long-acting

Barbiturates (Cont'd)

- Subclasses based on chemical structure
  - Oxybarbiturates
    - Phenobarbital, pentobarbital, and methohexital
  - Thiobarbiturates
    - Thiopental and thiamylal

Action of Barbiturates

- Not fully understood
- Mimics the inhibitory neurotransmitter GABA
- Causes CNS depression and loss of consciousness
- Termination of effect
  - Agent leaves brain
  - Is metabolized, excreted, or redistributed

Pharmacodynamics of Barbiturates

- Affect potency, onset, and duration of action
- Ionization
  - Polar (ionized) and nonpolar (nonionized) forms
  - Nonpolar forms pass through the cell membranes
  - Acidosis (blood pH <7.4)
    - Increased nonpolarization
    - Increased drug amounts to brain
    - Exaggerated patient response
    - Lower dose to anesthetize an acidotic animal

Pharmacodynamics of Barbiturates (Cont'd)

- Protein binding (plasma proteins)
  - Free (unbound) drug enters the brain
  - Hypoproteinemia results in more free drug
  - Increased drug amounts to brain
  - Normal drug dose may produce prolonged unconsciousness or death

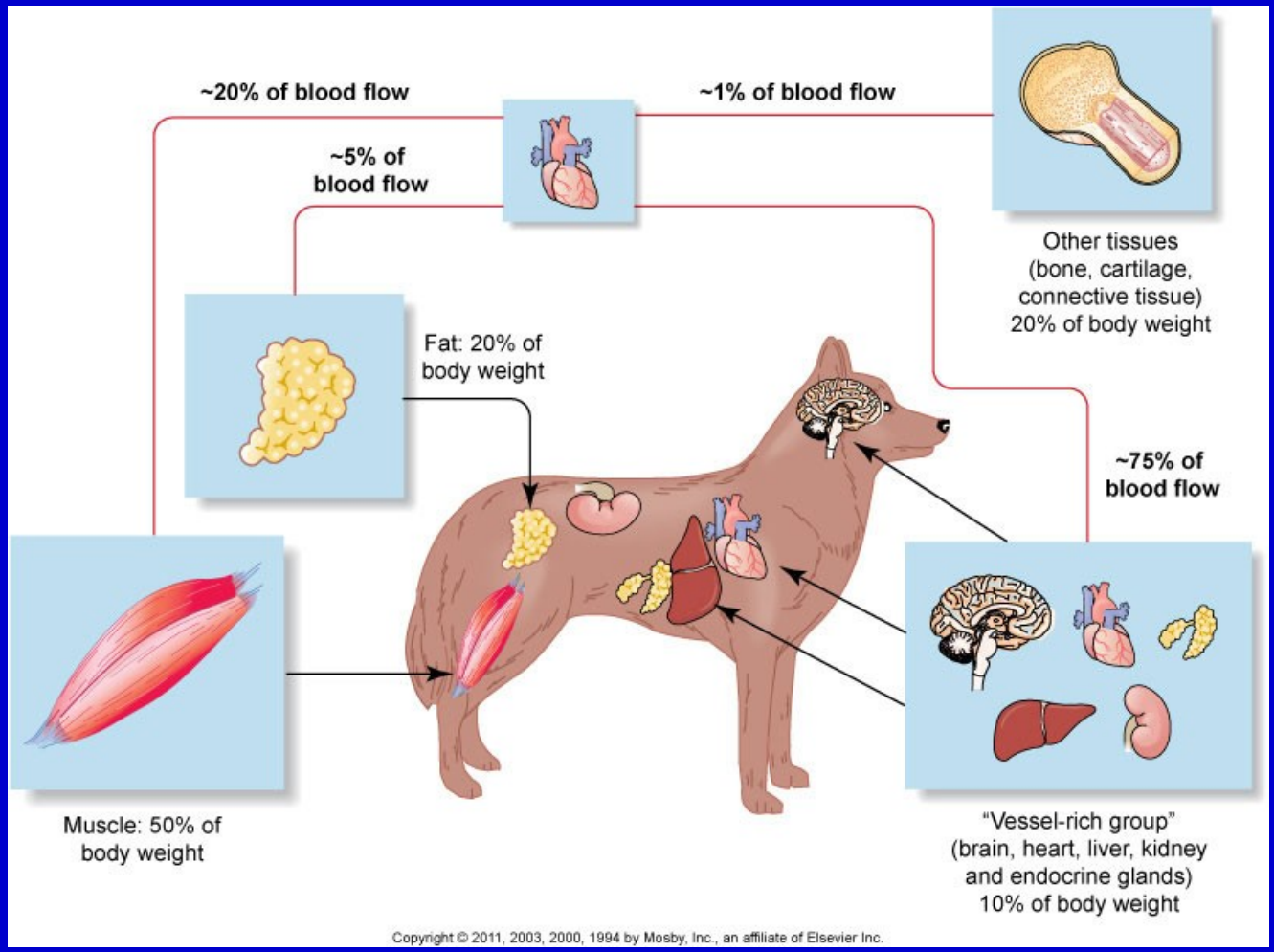
Pharmacodynamics of Barbiturates (Cont'd)

- Lipid solubility (partition coefficient)
  - Tendency of the drug to dissolve in fats, oils, and lipids
  - Affects the ability to penetrate the cell membrane fatty layer
  - High solubility results in ultra–short-acting drug
  - High solubility results in rapid tissue redistribution
  - Short-acting drugs are moderately lipid soluble
  - Long-acting drugs have low lipid solubility

Pharmacodynamics of Barbiturates (Cont'd)

- Redistribution
  - Drug is administered by IV
  - Drug is distributed fastest to vessel-rich tissues
  - Drug enters tissue based on lipid solubility
  - Effect occurs when drug is in the tissue
  - Drug leaves the tissue when blood level drops
    - Animal recovers
  - Blood carries drug to other tissues
  - Drug is released by tissues and eliminated

Barbiturate Redistribution



Variations of Barbiturate Redistribution

- Thiopental—ultra–short-acting
  - Redistributed to muscle and fat and slowly released
  - Continuous or repeated dosing may lead to “full” muscle and fat and prolonged recovery
- Methohexital—ultra–short-acting
  - Redistributed to muscle and fat but released faster
  - Muscle and fat don’t get “full” so there is no prolonged recovery with continuous or repeated doses

Variations of Barbiturate Redistribution (Cont'd)

- Phenobarbital—long acting
  - Sustained effect caused by slow uptake and release from the brain
  - Release is dependent on kidney excretion, which is slowest
- Pentobarbital—short acting
  - Brain levels decrease based on liver metabolism
  - Faster than kidney excretion

Use of Barbiturates

- Rapid anesthetic induction
  - To allow intubation (thiopental and methohexital)
  - Sustain with inhalation anesthetic (thiopental)
  - Sustain with repeated doses or continuous infusion (methohexital)
  - Use alone for short procedures
  - Always intubate

Effects of Barbiturates

- CNS
  - Mild sedation to unconsciousness
  - Possibly excitement at low dose
- Cardiovascular system
  - Cardiac depression
  - Thiopental
    - Autonomic nervous system imbalances
    - Increased cardiac sensitivity to epinephrine
    - Cardiac arrhythmias

Effects of Barbiturates (Cont'd)

- Respiratory system
  - Decreased respiratory rate and tidal volume
  - Brief apnea (thiopental)
  - Shallow breaths (pentobarbital)
    - Respiratory acidosis
    - Poor tissue oxygenation

Other Effects of Barbiturates

- Sneezing, larynospasm, coughing
  - Due to salivation
  - Prevent with anticholinergics
- Initial decreased GI motility
  - Later increased GI motility
- Incomplete muscle relaxation

Adverse Effects of Barbiturates

- Cardiovascular system
  - Cardiac arrhythmia with VPCs
  - Bigeminy
  - Minimize with slow administration and dilute concentration
  - Preoxygenization—3-5 minutes
  - “Bag” the patient two or three times after intubation

Adverse Effects of Barbiturates (Cont'd)

- Respiratory system
  - Related to dose and rate of administration
  - Initial apnea (<1-2 minutes)
  - Neonate respiratory depression
    - C-section using barbiturates

Other Adverse Effects of Barbiturates

- Exaggerated potency in sighthounds, critically ill patients, hypoproteinemic or acidotic patients
- Tissue irritation and sloughs
  - Perivascular injection
  - Treat with saline, with or without lidocaine
  - Use dilute barbiturate solutions
- Intraarterial injection
  - Thiopental
  - Vasoconstriction, pain, tissue necrosis

Excitement During Induction

- Perivascular injection
- Very slow rate of administration
- Stage II excitement
- Insufficient concentration in brain to induce Stage III
- Administer more drug

Excitement During Recovery

- Pentobarbital
- Paddling and vocalization
- IV diazepam
- Preanesthetic medications

Barbiturate-Drug Interactions

- Enhance muscle relaxants
- Increase hepatic enzyme activity
  - Prolonged use
  - Shorter duration of activity of drugs metabolized in the liver
    - Opioids and diazepam
  - Administration with chloramphenicol
    - Enhanced effects of pentobarbital and phenobarbital

Thiopental

- Ultra–short-acting
  - Small animals and horses
  - Rapid onset, but brief duration of action
  - Complete recovery in 1-2 hours
- Crystalline powder in multidose vials
  - Reconstitute with sterile water, normal saline, or 5% dextrose in water
  - 2.0-2.5% solution (small animals)
  - 5% solution (horses)
  - Shelf life: 1 week refrigerated or 3 days at room temperature
  - Don’t use if a precipitate is present

Thiopental (Cont'd)

- Dose
  - Varies with protocol and procedure
  - Reduced up to 80% in debilitated animals
  - Reduce dose in heavily sedated animals
  - Give to effect
  - Repeat doses are cumulative leading to prolonged recovery
  - Don't use for anesthetic maintenance
  - Various protocols for administration

Methohexital

- Ultra–short-acting
- Similar to thiopental
- Can be useful on an unfasted animal
  - Rapid induction and intubation
  - Decreased risk of vomitus aspiration
- A powder that must be reconstituted (sterile water)
  - 1-2.5% solution (small animals)
  - Shelf life—6 weeks without refrigeration
  - More expensive than thiopental

Methohexital (Cont'd)

- Dosage
  - 1/2 to 1/3 calculated dose IV over 10 seconds
  - Should allow intubation
  - Give needed additional drug within 30 seconds
- Can be used in sighthounds
- Can cause profound respiratory depression
- Excitement and seizures during induction and/or recovery
  - Premedicate with tranquilizer
  - Control postoperative seizures with diazepam IV
  - Don't use in animals with epilepsy

Pentobarbital

- Short acting
- Used to treat status epilepticus
- Largely replaced with propofol
- Administered IP to rodents for general anesthesia
- Status epilepticus
  - Administer IV to stop seizure and produce heavy sedation
  - Narrow margin of safety

Pentobarbital (Cont'd)

- Provided as a 5% solution
- Onset of action 30-60 seconds IV
  - Initially unable to raise head
  - Jaw and tongue relaxed; pedal reflex is present
  - Pedal reflex absent—intubate and provide respiratory support
- Duration of action
  - 30 minutes to 2 hours
  - Repeated doses can be given
    - Recovery time may be prolonged with associated excitement

Propofol

- Ultra–short-acting, nonbarbiturate anesthetic
- IV for anesthetic induction and short-term maintenance
- Small animals, small ruminants, exotic animals, neonates of all species
- Other use
  - IV bolus and CRI to treat status epilepticus in dogs and cats

Propofol (Cont'd)

- Minimally water soluble
- Available in an egg lecithin/glycerine/soybean oil aqueous solution—10 mg/mL
- Milky appearance—OK to give IV
- Unknown how it affects GABA receptors
- Highly fat soluble
- Onset of action—30-60 seconds
- Duration of action—5-10 minutes
- Complete recovery
  - 20 minutes—dogs 30 minutes—cats

Effects of Propofol

- CNS
  - Dose-dependent depression from sedation to general anesthesia
  - No analgesia
- Cardiovascular system
  - Cardiac depressant
  - Transient hypotension
- Respiratory system
  - Depressant with possible apnea
  - Administer slowly to effect
  - Monitor patient carefully

Other Effects of Propofol

- Twitching during induction—dogs
- Muscle relaxation
- Safe to use in animals with liver disease or kidney disease
- Appetite stimulant (low dose)
- Antiemetic
- Decreases intraocular and intracranial pressure

Adverse Effects of Propofol

- CNS
  - Transient excitement and muscle tremors (induction)
  - Paddling, muscle twitching, nystagmus, opisthotonus (resembles seizures)
- Cardiovascular system
  - Hypotension—transient
- Respiratory system
  - Apnea (rapid injection; high dose)
    - Intubation if necessary

Other Adverse Effects of Propofol

- Seizure-like signs (induction)
  - Treat with diazepam
- Pain with IV injection
  - Perivascular injection does not produce tissue damage
- Cats with repeat doses
  - Heinz body formation on red blood cells (RBCs)
  - Diarrhea and anorexia
  - Prolonged recoveries
- Sighthounds—prolonged recovery
  - Also other breeds
  - If maintained on propofol >30 minutes

Use of Propofol

- IV slowly over 1-2 minutes to effect
- IM produces mild sedation and ataxia only
- Dose depends on premedications
- Highly protein bound
  - Don’t use in hypoproteinemic animals
- May cause excitement if given too slowly

Use of Propofol (Cont'd)

- Administration
  - Boluses repeated every 3-5 minutes for 20 minutes
  - CRI with syringe pump or through IV line
    - Can maintain anesthesia for several hours
    - Use a low dose
    - Can control depth of anesthesia
- Recovery
  - Dogs—complete in 20 minutes Cats—in 30 minutes
- Premedication with tranquilizers
  - Decrease propofol dose
  - Facilitates IV injection in unruly animals

Propofol Handling and Storage

- Poor storage characteristics
  - Egg lecithin, glycerol, and soybean oil support bacterial growth
  - Use aseptic technique
  - Discard unused drug within 6 hours of opening
  - 3-year shelf life if unopened
- more expensive than ketamine-diazepam or thiopental

Dissociative Anesthetics

- Phencyclidine and ketamine hydrochloride
- Only ketamine is used in veterinary medicine
- Used alone
  - Cats—for minor procedures or to facilitate restraint
- Used with other drugs
  - Tranquilizers and opioids to induce general anesthesia
- Subanesthetic dose
  - CRI for analgesia

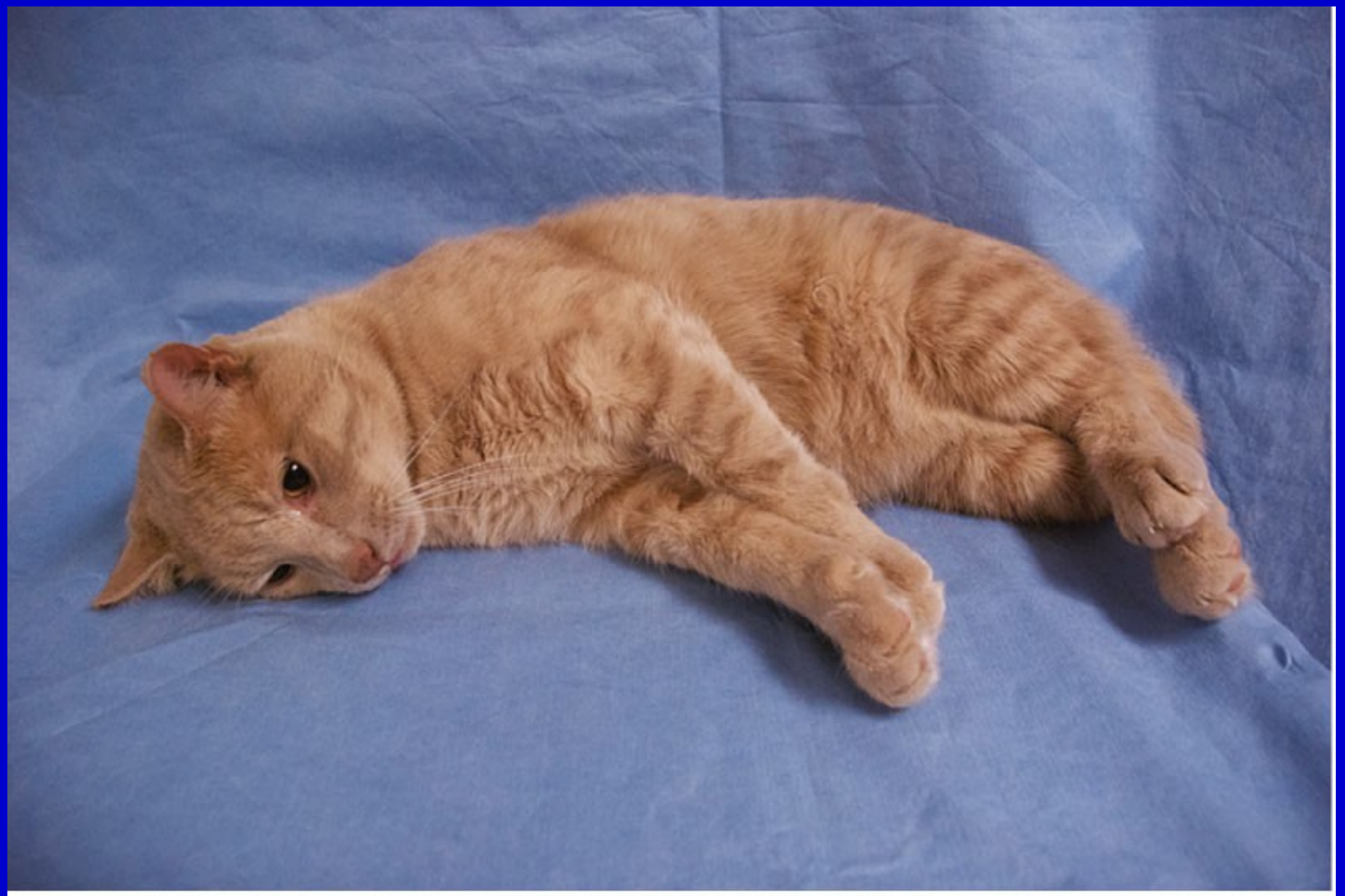
Dissociative Anesthetics (Cont'd)

- Tiletamine hydrochloride
  - Combined with benzodiazepine zolazepam
  - Telazol®
  - IM or IV to produce sedation and anesthesia
  - Used alone or in combination with other drugs
  - A controlled substance

Mode of Action

- Disrupts nerve transmission in some brain sections
- Selective stimulation in parts of the brain
- Decreases windup through NMDA inhibition
- Trancelike state
  - Animal appears awake
  - Immobile and unaware of surroundings

Dissociative Anesthetic Trancelike State



Ketamine

- Peak action
  - 1-2 minutes after IV injection
  - 10 minutes after IM injection
- Duration of effect
  - 20-30 minutes
  - Increased dose prolongs duration but doesn't increase anesthetic effect
- All dissociatives are either metabolized in the liver or excreted unchanged in the urine
  - Avoid use in animals with liver or kidney disease

Dissociative Effects on the CNS

- Cataleptoid state
- Intact reflexes
  - Palpebral, corneal, pedal, PLR, laryngeal, swallowing
- Ocular effects
  - Eyes remain open
  - Central dilated pupil
  - Use ophthalmic ointment

Dissociative Effects on the CNS (Cont'd)

- Muscle tone
  - Normal to muscle rigidity
  - Counteract with concurrent tranquilizer
- Analgesia
  - Somatic analgesia
  - Visceral analgesia
- Amnesia (humans)
- Sensitivity to sensory stimuli

Dissociative Effects on the Cardiovascular System

- Increase in heart rate
- Increased cardiac output
- Increased mean blood pressure
- Effects due to stimulation of the SNS

Dissociative Effects on the Respiratory System

- Respiratory rate and tidal volume may change
- Respiratory depression usually insignificant
- Apneustic respiration at higher doses

Adverse Effects of Dissociatives on the CNS

- Response to sensory stimulation
- Avoid in animals with seizure disorders
- Avoid in animals that have ingested CNS stimulants
- Avoid in animals undergoing neurological system procedures
- Hallucinations and personal injury
- Personality change
- Nystagmus

Adverse Effects of Dissociatives on the Cardiovascular System

- Decreased inotropy
- Cardiac arrhythmias in response to epinephrine release
- Screen patients for preexisting heart disease

Adverse Effects of Dissociatives on the Cardiovascular System (Cont'd)

- Respiratory depression
- Respiratory arrest
- Significantly increased salivation and respiratory tract secretions
- Aspiration

Other Adverse Effects of Dissociatives

- Pain after IM injection due to tissue irritation
- Increased intracranial and intraocular pressure

Use of Dissociative Anesthetics

- Administration: IM or IV
- Wide margin of safety
- Useful in cats and horses
- Used in combination with tranquilizers
  - Short procedures
  - Anesthetic induction for intubation
  - Chemical restraint—cats
  - Immobilization—large and exotic animals
  - Pain control
- No effective reversal agent

Ketamine

- Approved for use in cats and subhuman primates
- Also used in dogs, birds, horses, and exotic species
- Schedule III drug (United States) prescription drug (Canada)
- Rapid onset of action—high lipid solubility
- Administer IV or IM or orally (cats)

Ketamine (Cont'd)

- Avoid repeated injections
- Recovery in 2-6 hours
- Elimination
  - Hepatic metabolism—dogs
  - Renal metabolism—cats
- Often used in combination with tranquilizers

Ketamine and Diazepam Combination

- IV induction in dogs and cats
- Equal volumes of diazepam and ketamine
- Can be mixed in one syringe
  - Watch for possible precipitate
- Onset of action—30-90 seconds
- Duration of action—5-10 minutes
- Recovery—30-60 minutes
- Alternative combination for IM injection: midazolam and ketamine

Tiletamine

- Similar to ketamine
- Sold only in combination with zolazepam (Telazol®)
- Telazol®—sold as a powder to reconstitute
  - Stable for 4 days at room temperature, or 14 days if refrigerated
  - A class III drug
  - Can be used in combination with other tranquilizers or with ketamine
    - Possible long and difficult recoveries
    - Metabolized in liver and excreted via the kidneys

Advantages of Telazol® (as compared to Ketamine)

- Decreased apneustic respiratory response
- Can be administered SC
- Used effectively in some wildlife

Etomidate

- Noncontrolled, sedative-hypnotic imidazole drug
- Used for induction—dogs, cats, exotics
- Minimal effects on the cardiovascular and respiratory systems
- Expensive
- Pain with IV injection
- Nausea and vomiting possible

Etomidate Mode of Action

- Similar to barbiturates and propofol
  - Increased GABA inhibitory action
- Short duration of action
  - Rapid redistribution away from brain
  - Rapid metabolism
- Wide margin of safety

Etomidate Effects on the CNS

- Hypnosis
- Very little analgesia
- Decreased brain oxygen consumption
- Brain perfusion maintained
- Anticonvulsant

Effects of Etomidate

- CNS
  - Initial hypotension
  - Heart rate, rhythm, blood pressure, and cardiac output minimally affected
- Respiratory system
  - Initial apnea
  - Crosses placental barrier
- Musculoskeletal system
  - Muscle relaxation
  - Spontaneous muscle twitching and movement

Adverse Effects of Etomidate

- Painful IV injection
- Perivascular sterile abscesses
- Hemolysis with rapid administration (cats)
- Decreased adrenal cortex function
  - Decreased cortisol levels
- Nausea, vomiting, involuntary excitement during induction and recovery

Use of Etomidate

- IV administration
- Premedicate with opioid or diazepam
- Premedicate with dexamethasone
- Repeated boluses to maintain anesthesia

Guaifenesin (GG)

- Previous name—glyceryl guaiacolate ether (GGE)
- Noncontrolled muscle relaxant
- Common use in large animals
  - Muscle relaxation
  - Facilitate intubation
  - Ease induction and recovery
- Not an anesthetic or an analgesic
- Mode of action is not understood

Effects of Guaifenesin

- Skeletal muscle relaxation
  - Minimal effect on diaphragm
- Minimal effect on the cardiovascular and respiratory systems

Adverse Effects of Guaifenesin

- Few adverse effects at therapeutic doses
- Overdose
  - Muscle rigidity
  - Apneustic respiration
- Perivascular tissue irritation
- Hemolysis (ruminants and horses) in high concentrations

Use of Guaifenesin

- Used with ketamine in anesthetic induction protocol
  - Premedicate with alpha$_2$-agonist or acepromazine
- Triple drip: GG, ketamine, xylazine
  - Used in horses
  - Maintain anesthesia for less than an hour
- Administered IV rapidly until animal is ataxic
  - Following premedication
  - Induce when patient is ataxic
  - Smooth recovery

Use of Guaifenesin (Cont'd)

- Not a sedative or analgesic
  - Must premedicate
  - May cause excitement if there is no premedication
  - Increased risk of side effects if there is no premedication

Inhalation Anesthetics

- Classes of inhalation anesthetics
- Isoflurane and sevoflurane (halogenated compounds)
- Nitrous oxide and desflurane
- Enflurane
- Halothane
- Methoxyflurane
- Diethyl ether

Diethyl Ether

- No longer used as an anesthetic agent
- Classic stages and planes of anesthesia described using ether
- Desirable characteristics
  - Stable cardiac output, rhythm, and blood pressure
  - Stable respirations
  - Good muscle relaxation

Diethyl Ether (Cont'd)

- Undesirable characteristics
  - Tracheal and bronchial mucosal irritation
  - Prolonged induction and recovery
  - Postoperative nausea and vomiting
  - Flammable and explosive

Halogenated Organic Compounds

- Isoflurane and sevoflurane are the most commonly used agents in this class
- Liquid at room temperature
- Stored in a vaporizer on an anesthetic machine
- Vaporized in oxygen that flows through the vaporizer

Uptake and Distribution of Halogenated Organic Compounds

- Liquid anesthetic is vaporized and mixed with oxygen gas
- Mixture is delivered to the patient via a mask or endotracheal tube (ET tube)
- Mixture travels to lungs (alveoli) and diffuses into the bloodstream
- Diffusion rate is dependent on concentration gradient (alveoli/capillary) and lipid solubility
- Concentration gradient is greatest during initial induction

Uptake and Distribution of Halogenated Organic Compounds (Cont'd)

- Distribution to tissues is dependent on blood supply
  - Lipid solubility determines entry into tissues through cell walls
- Depth of anesthesia is dependent on partial pressure of anesthetic in the brain
  - Partial pressure in the brain is dependent on partial pressure of the anesthetic in blood and alveoli
- Maintenance of anesthesia is dependent on sufficient quantities of anesthetic delivered to the lungs

Elimination of Halogenated Organic Compounds

- Reducing amount of anesthetic administered reduces amount delivered to the alveoli
- Blood level is initially higher than alveolar level
- Concentration gradient now favors anesthetic diffusion from blood into the alveoli
- Blood levels drop quickly as patient breathes out anesthetic from the alveoli
- Brain levels drop as less anesthetic is delivered by blood
- Patient wakes up

Effects of Halogenated Organic Compounds

- CNS
  - Dose-related reversible CNS depression
  - Hypothermia
- Cardiovascular system
  - Depress cardiovascular function
  - Effects on HR variable
- Respiratory system
  - Dose-dependent ventilation depression

Adverse Effects of Halogenated Organic Compounds

- CNS (Cont'd)
  - Increased intracranial pressure in patients with head trauma or brain tumors
  - Considered safe for epileptic animals
- Cardiovascular system
  - Decrease blood pressure and may decrease renal blood flow
- Respiratory system
  - Hypoventilation
  - Carbon dioxide retention and respiratory acidosis

Physical and Chemical Properties of Inhalant Anesthetics

- Important properties to consider
  - Vapor pressure
  - Partition coefficient
  - Minimum alveolar concentration (MAC)
  - Rubber solubility

Vapor Pressure

- The tendency of an inhalation anesthetic to vaporize to its gaseous state
- Determines how readily an inhalation anesthetic will evaporate in the anesthetic machine vaporizer
- Temperature and anesthetic agent dependent

Vapor Pressure (Cont'd)

- Volatile agents
  - High vapor pressure
  - Isoflurane, sevoflurane, desflurane, and halothane
  - Delivered from a precision vaporizer to control the delivery concentration
  - All precision vaporizers are made to deliver only one specific halogenated agent
- Nonvolatile agents
  - Low vapor pressure
  - Methoxyflurane
  - Delivered from a nonprecision vaporizer

Blood:Gas Partition Coefficient

- The measure of the solubility of an inhalation anesthetic in blood as compared to alveolar gas (air)
- Indication of the speed of induction and recovery for an inhalation anesthetic agent
- Low blood:gas partition coefficient
  - Agent is more soluble in alveolar gas than in blood at equilibrium
  - Agent is less soluble in blood
  - Faster expected induction and recovery

Blood:Gas Partition Coefficient (Cont'd)

- High blood:gas partition coefficient
  - Agent is more soluble in blood than in alveolar gas at equilibrium
  - Agent is less soluble in alveolar gas
  - Agent is absorbed into blood and tissues (sponge effect)
  - Slower expected induction and recovery

Blood:Gas Partition Coefficient (Cont'd)

- Blood: gas partition coefficient determines the clinical use of the anesthetic agent
  - Induction: Can a mask be used?
  - Maintenance: How fast will the anesthetic depth change in response to changes in the vaporizer setting?
  - Recovery: How long will the patient sleep after anesthesia?

Minimum Alveolar Concentration (MAC)

- The measure of the potency of a drug
  - Used to determine the average setting on the vaporizer that will produce surgical anesthesia
- The lower the MAC, the more potent the anesthetic agent and the lower the vaporizer setting
  - MAC may be altered by age, metabolic activity, body temperature, disease, pregnancy, obesity, and other agents present
- Every patient must be monitored as an individual

Isoflurane

- Most commonly used inhalant agent in North America
- Approved for use in dogs and horses; commonly used in other species

Isoflurane (Cont'd)

- Properties
  - High vapor pressure: need a precision vaporizer
  - Low blood:gas partition coefficient: rapid induction and recovery
  - Good for induction with mask or chamber
  - MAC = 1.3% to 1.63%: helps determine initial vaporizer setting
  - Low rubber solubility
  - Stable at room temperature; no preservatives needed

Effects and Adverse Effects of Isoflurane

- Maintains cardiac output, heart rate, and rhythm
  - Fewest adverse cardiovascular effects
- Depresses the respiratory system
- Maintains cerebral blood flow
- Almost completely eliminated through the lungs
- Induces adequate to good muscle relaxation
- Provides little or no analgesia after anesthesia
- Can produce carbon monoxide when exposed to a desiccated carbon dioxide absorbent

Sevoflurane

- High vapor pressure: need a precision vaporizer
- Blood:gas partition coefficient: rapid induction and recovery
- Good for induction with a mask or chamber
- High controllability of depth of anesthesia
- MAC = 2.34% to 2.58%

Effects and Adverse Effects of Sevoflurane

- Minimal cardiovascular depression
- Depresses respiratory system
- Eliminated by the lungs, minimal hepatic metabolism
- Maintains cerebral blood flow
- Induces adequate muscle relaxation
- Some paddling and excitement during recovery

Desflurane

- Closely related to isoflurane
- Expensive
- Lowest blood:gas partition coefficient: very rapid induction and recovery
- Used with a special precision vaporizer
- MAC = 7.2% and 9.8%
  - Least potent inhalant agent
- Eliminated by the lungs

Effects and Adverse Effects of Desflurane

- Strong vapors cause coughing and holding the breath
- Other effects are similar to isoflurane
- Transient increase in heart rate and blood pressure (humans)

Other Halogenated Inhalation Agents

- Halothane (Fluothane)
  - Not commonly used anymore
  - Being replaced by isoflurane and sevoflurane
- Methoxyflurane
  - No longer available in North America
- Enflurane
  - Used primarily in human medicine
- Nitrous oxide
  - Used primarily in human medicine; some veterinary use
  - A gas at room temperature; no vaporizer is required

CNS and Respiratory Stimulants

- Doxapram
  - Analeptic agent
  - Stimulates respiration and speeds recovery
  - Used in neonate puppies and kittens after C-section
  - IV administration or sublingual drops (neonates)

Adverse Effects of Doxapram

- Wide margin of safety
- Lowers seizure threshold
- CNS damage

Use of Doxapram

- Repeat injections may be necessary
- Reverses respiratory depression from inhalant agents and barbiturates