

- **Positive Inotrope** increase cardiac M. contraction and little effect on the heart rate.

strength by making intracellular calcium available in muscle protein as:-

- 1- **Beta-adrenergic agonist** as Isoproterenol, Dobutamine  
**Dopamine, epinephrine**

### Role of Epinephrine in cardiopulmonary cerebral resuscitation (CPCR)

- Increase coronary circulation via peripheral vasoconstriction via its **effect on alpha adrenergic receptors**. This promotes a shift of the blood volume back to the heart which increases aortic and coronary blood flow
- There is no way to directly 'rest art' an arrested heart. Cardiac contractions resume when oxygen delivery is restored, and energy production is adequate
- Vasopressin also produces peripheral vasoconstriction via activation of V1 receptors on vasculature. It is often used in addition to or instead of epinephrine during CPCR.

- 2-**Cardiacglycoside** as Digoxin, digitoxine

- 3-**phosphodiesterase enzyme (PDE)** as Milrinone, amrinone, Pimobendane

**Pimobendane** is an **orally** administered "**inodilator**" (has both inotropic and vasodilator effects) approved for treatment of congestive heart failure due to dilated cardiomyopathy and degenerative valvular disease in **dogs**. **It is not approved in cats**

- 4-**Angiotensin converting Enzyme ACE Inhibitors** as enalapril

- 1- **Vasodilators** so **increase cardiac output**.
  - 2- Prevent formation of angiotensin II, prevent vasoconstriction
  - 3- Reduce retention of Na & water in animals
- Rx.** -Congestive heart failure  
 -with furosemide (diuretics)  
 -with Beta blockers in systemic hypertension

-**Angiotensin** converting enzyme formed in endothelial cell of lung

primary, and convert **angiotensin I** to **angiotensin II**

- **Angiotensin II** cause retention of Na & water, and in part of synthesis **Aldosterone** by adrenal cortex and is **vasoconstriction**

- **Aldosterone** is mineralocorticoid produced in the adrenal cortex, also acts on the distal tubules (and collecting ducts) to retain Na<sup>+</sup> and water, secrete K<sup>+</sup> and increase blood pressure.
- **Potassium-sparing diuretics (Spironolactone, amiloride):** are aldosterone **antagonists**
- **Negative Inotrope** decrease force of cardiac muscle contraction

**Calcium –channel blocker** is **antiarrhythmic** as Verapamil, amlodipine, diltiazem

**Rx.** Atrial fibrillation, supraventricular tachycardia, hypertrophic cardiomyopathy (**HCM**) and Hypertension.

- **Negative chronotrope** **decrease heart rate**
- Beta Adrenergic blockers** is negative inotrope & Negative chronotrop as **propranolol**, **atenolol**. **Propranolol** must be **gradually tapered**

**Rx.** Arrhythmias, systemic hypertension, HCM

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- **Sodium channel blockers** such as Lidocaine and quinidine
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- **Alpha 1 adrenergic antagonist:** as prazosin, **acepromazine**, Phenoxybenzamine which Decrease peripheral vasoconstriction & promote digital circulation. **vasodilatation**

## **Acepromazine** (Phenothiazine tranquilizers)

- It is a **sedative** used in many animals that **alpha-1 receptors antagonist** and Producing **vasodilation** and sometimes **hypotension**.
- **Antagonizes dopamine receptors in the brain**, which produces **sedative, anti-emetic**, and anti-arrhythmic effects, as well as causing muscle relaxation
- **Penis protrusion** in large animals

- No analgesic effect
- Contraindicated in **Organophosphate** (opp) toxicity
- **debilitating and Geriatric** animals need decrease dose
- **Sight hounds dog and Giant dog** overly sensitive

- Xylazine, Detomidine, Dexmedetomidine, and Medetomidine are **Alpha-2 agonists**.
- **Vasoconstriction** and **high blood pressure**, **slow heart rate (Bradycardia)** in response to the high blood pressure and **decrease cardiac output**

This is called a "**reflex bradycardia**" or a "**baroreceptor**" response as the cardiovascular system strives to keep blood pressure within a normal range. It is mediated via the parasympathetic input via the vagal nerve. It protects the heart from the increased work that would be required if it were to beat fast against high vascular tone

- potent **sedative** used in **horses**
- good **analgesics**
- This group inhibit release of **norepinephrine** at Presynaptic alpha-2 receptors both centrally and peripherally. They are a

There are 3 subtypes of alpha-2 receptors (2A, 2B, 2C). Alpha-2 agonists also

**Stimulate alpha-1 receptors at postsynaptic sites.**

Differences between specific drugs are due to their affinity for different alpha-2 subtypes and for alpha-1 vs. alpha-2 Receptor affinity.

**Here is a list of potency and cost, from highest to lowest, and ratio of alpha-1 to Alpha-2 receptor action:**

Medetomidine	..... ..	1:1620
Romifidine	..... ..	1:340
Detomidine	.. .. .	1: 260
Xylazine	.... ..	1:160

- **Yohimbine, atipamezole, or tolazoline** is an **alpha-2 receptor antagonist** is used to **reverse** alpha-2 Agonists with **analgesic and sedative effects**.
- **Amitraz** is used to **treat** generalized **demodicosis** as a dip with **caution** in TOY breeds. The **side effect** is **SEDATION**

## **Reversal by Yohimbine** atipamezole, or tolazoline

**When you hear organophosphate toxicity, think 3 things**

1. Sedative for seizures (diazepam (Valium®), phenobarbital or pentobarbital)
2. Atropine
3. Pralidoxime chloride (Protopam®)

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- **Ketamine and tiletamine**
    - It is an **antagonist** at N-methyl-D-aspartate (**NMDA**) receptors.
    - **Dissociative anesthetics** can cause **seizures at high doses**
    - It **is not recommended** for routine use in patients with **head trauma** because it **increase intracranial pressure (ICP)**.
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- **Atropine** an **anticholinergic** agent. It **blocks** **parasympathetic** tone in the heart, which results **tachycardia (increases the heart rate)**
    - **Used for:**
      - ✚ **Organophosphate toxicity**, bradycardia, and sinoatrial arrest
      - ✚ Preanesthetic to **reduce respiratory secretions**
      - ✚ treat other **toxicities** (e.g., blue-green algae, muscarinic mushrooms, carbamates)
    - **CONTRAINDICATIONS**
      - ✚ **when** dexmedetomidine is used in dogs and cats p 80
      - ✚ **Tachyarrhythmias**
      - ✚ **Narrow-angle glaucoma**
      - ✚ **Ileus or GI obstruction**
      - ✚ **Urinary obstruction**
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- **Opioids**
- are the most effective **analgesics** available for treatment of acute pain in many animals, including **dogs and cats**
- **Mu receptor opioid agonists:** (**morphine, oxymorphone, hydromorphone**, etc.) are the most potent and effective, especially for short term therapy

**Side effects** such as sedation, **dysphoria**, and constipation limit long term use in most patients.

- **Kappa receptor agonists:** such as **butorphanol**, have fewer adverse side effects but the analgesic effect is weaker, and duration is short
- **Butorphanol** is an **opioid** used in many animals; it **activates kappa receptors**, but **inhibits the mu receptor**

- pure Opioid **Antagonist:** **Naloxone** is the most commonly used
- It is effective at all the opioid receptors (mu, kappa, and delta) but has a **greater** activity at the **mu** receptor. **Nalmefene** is similar but it is longer lasting.
- At **very low doses**, side effects may be reversed while preserving the **analgesic effects**.
- **Propofol** is a general anesthetic that **enhances** the activity of the **GABA** receptor
- **Benzodiazepine (BZ) as Diazepam, Alprazolam and midazolam:**
- It is an **agonist** at the gamma-amino butyric acid (**GABA**) receptors
- Binding of a benzodiazepine (BZ) to the gamma-amino butyric acid (GABA) receptor **enhances** the binding of the **inhibitory neurotransmitter GABA**. A chloride channel opens, the cell membrane becomes **hyperpolarized**, and **neuronal activity is inhibited**
- They have Sedation, muscle relaxation, and anti-seizure effects. **A calming effect is seen from inhibition** in the

limbic and reticular formations in the brain.

- **Diazepam** in Cat P 43 part 3
  - **Flumazenil** reverses the effects of benzodiazepines.
  - **Zolazepam** (Telazol®) is **combined** with **tiletamine** in the general anesthetic
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- **Firocoxib** is a COX-2 selective
    - lower ulcerogenic and renal risk than the other nonselective NSAIDs listed
    - is the **least likely to cause gastrointestinal ulcers and renal disease in horses**
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## Lots of toxic effects

**1-Trimethoprim Sulfate (TMS) (sulfonamide)** a lot of toxic effects:

-In high dose cause **bone marrow suppression**, Type I, III **hypersensitivity**, **urticarial**, **KCS**, Hemolytic anemia, Hematuria, and hypothyroidism. **Sulfamethazine should not be administered to dairy cattle over 20 months of age** page 227

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**2-Tetracycline** lots of toxic effects (adverse effect in multiple organs)

1-**Hepatoatotoxicity**, **potentiate nephrotoxicity** (so contraindicated in renal insufficient)

2-Disrupt gastric and rumen micro-flora

3-**Swelling, discoloration at injection site**, so **this part of food animal carcass should discard**

4-**Chelate calcium** in teeth and bone

- **Doxycycline** may cause **esophageal strictures** in **feline** patients and is best administered with food or followed with 6 cc of water
- **Quinolones** like enrofloxacin (Baytril®) : associated with **damage to articular cartilage** in young growing animals and with neurotoxicity (like convulsions) at higher doses
- **Cephalosporins**: like cephalexin (Keflex®), ceftriaxone (Rocephin®), and ceftiofur (Naxcel®) are relatively **nontoxic**, but there may be **pain at injection site**
- **Aminoglycosides**: like gentamicin and amikacin are most often associated with **NEPHROTOXICITY**, **ototoxicity**, and **neuromuscular blockade**
- **Macrolides**: like erythromycin **do not have many side effects**. One particular macrolide, **TILMICOSIN** (Micotil®), is **contraindicated in pigs**, and should not be used in an automatically powered syringe because an accidental self-injection can

kill humans

- **Lincosamides:** like clindamycin (Antirobe®) may be associated with **GI upset**. **DO NOT (but not contraindicated)** use clindamycin in rabbits, guinea pigs, chinchillas, hamsters, horses, and ruminants. **CONTRAINDICATED** IN **HORSES** because a **severe, even fatal colitis** can occur.

remember **ETC** (**Enrofloxacin** (Baytril®), **Trimethoprim Sulfa** (TMS), **Chloramphenicol**). These 3 "ETC" antibiotics are **ok** in **rabbits, guinea pigs, hamsters and other rodents**

**Sulfonamides. Lincosamides. Macrolides:** GI disturbances (ie: vomiting, nausea, diarrhea, colitis, colic)

**3-Chloramphenicol:** cause Aplastic anemia, bone marrow suppression, **contraindicated in food animals**

**Acute equine laminitis:** should **NOT** be treated with corticosteroids like **triamcinolone**

or with ACTH, because these drugs decrease protein synthesis and promote tissue insulin resistance. Hyperinsulinemia can be a primary or contributing factor to laminitis.

Remember, "AVOID the 'ROIDS" in laminitic horses.

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- **Oral sulfonylurea (Glipizide):**

Is **a human oral hypoglycemic agent** and used in manage **cats** with **uncomplicated type 2 diabetes mellitus** and **NO history** of **ketoacidosis**

- **Cyclosporine** (Atopica): acts as an **immunosuppressant**, is **CONTRAINDICATED** in **cats** infected with **feline leukemia, feline immunodeficiency virus and Toxoplasma**. used in the management of **canine and feline** atopic dermatitis.
- **Azathioprine:** is a **chemotherapeutic** agent, contraindicated in feline patients due to the likelihood for **bone marrow suppression**
- **Phenobarbital** is usually the first-line **anticonvulsant** administered to **dogs**. **However**, it can cause **hepatotoxicity**, so it may **not be selected** in animals with underlying liver disease (i.e., hepatopathy).
- **Potassium bromide** is second-most commonly used **anticonvulsant in dogs**. **It is NOT use in cats**.
- **carprofen** (Rimadyl ®)
  - is a non-steroidal anti-inflammatory (NSAID) incidence of **hepatopathy**
  - **contraindicated** in animals with **bleeding disorders**, like von Willebrand's disease
- **Flunixin meglumine:** is labeled for use in dairy and beef cattle in the U.S.
- **Polymyxin B** is a **polypeptide** antibiotic that, at low doses, has been shown **to bind endotoxin in horse's circulation**, thus



**ameliorating** (improve) its effects. **higher doses** polymyxin B can be nephrotoxic and neurotoxic.

- **Pentoxifylline** is a xanthine-derivative **phosphodiesterase inhibitor** with anti-tumor Necrosis factor (**anti-TNF**) activity (among other anti-inflammatory and rheologic properties) also used to manage endotoxemic horses
- **Misoprostol**: a synthetic prostaglandin E1 analog, may be given concurrently with nonsteroidal anti-inflammatory drug-2 (NSAIDs) to **decrease** gastric acid secretion
- **drugs can depress T3/T4 hormones. Think of:**

Glucocorticoids, anabolic steroids, Anticonvulsants (phenytoin, phenobarbital). Phenylbutazone Ipodate (radiographic contrast agent), Furosemide, Anesthetics (thiopental, methoxyflurane, halothane), and Mitotane (o,p DDD)

- **Mibolerone and megestrol**: acetate are both used to delay or suppress estrus in dogs
- **Finasteride**: for benign prostatic hypertrophy (BPH)
- **Oclacitinib**: a Janus kinase inhibitor, is frequently used to control pruritus in dogs with

allergic/atopic dermatitis. **Side effects** include gastrointestinal upset (vomiting, inappetence, diarrhea), lethargy, and polydipsia.

- **The crash cart**: has **Epinephrine, atropine, dobutamine, vasopressin** for emergency (cardiac arrest or in shock).

**Endotracheal tubes, intravenous catheters and fluids, syringes and needles, clippers, tape, and other supplies needed for emergency**

- **Phenylpropanolamine**: is used to treat **urinary incontinence** associated with **urethral sphincter** mechanism incompetence (USMI) in dogs and cats
- **Metoclopramide**: crosses the **blood-brain barrier**, where **dopamine antagonism** at the medullary chemoreceptor trigger zone (CTZ) causes an **antiemetic effect**. This dopamine antagonism can also cause **adverse extrapyramidal signs**, like. Involuntary muscle spasms, motor restlessness and inappropriate aggression
- **Ivermectin**: works by inhibiting neuronal activity and muscular contractility in invertebrate parasites in two ways: binding to glutamate gated and GABA gated chloride ion channels

**Mammals** are normally protected from toxicity because they do not have neuronal glutamate gated chloride channels, and only have GABA-gated chloride channels in the central nervous system, which is protected by the blood brain barrier and the presence of functional P-glycoprotein.

- **Xylazine** is used as an **EMETIC** in CATS, causes vomiting.

diphenhydramine (Benadryl®), Maropitant, and metoclopramide: **ANTI-emetics** in cats

**Cisapride and metoclopramide**: are prokinetic drugs, they **stimulate gastrointestinal motility**.

- **Doxorubicin**: one of the most commonly used **antineoplastic** drugs. **Cardiac toxicity** is adverse effects
- **Amitriptyline HCL**: is a tricyclic **antidepressant** used for **behavior disorders** like self

mutilation, neuropathic pruritus.



- **Fomepizole (4-MP):** is used to treat **ethylene glycol toxicity**. primarily in DOGS but appears to be effective in cats if used at higher dosages.
- **P 29, 31 Part 3- Idiosyncratic reactions:** are uncommon and occur **for no known reason**, and **They do not occur in all members** of a type of animal. They are **not dose-dependent** and typically **occur after several days of treatment**. To deal with idiosyncratic reactions is avoidance or cessation of the drug once it has been identified as a problem. Therapeutic drug monitoring, dose reduction, and brief withdrawal do not help prevent or treat idiosyncratic drug reactions

**Dose-dependent drug reactions:** **affect all members of a type of animal** (or many animals) and are **predictable**. The **risk increases with increasing dose**. Renal disease and aminoglycosides is an **example**

- **P 37 Part 3- Avoid administration of phosphate-containing enemas to :**
- **P 64 part 3 RX of Cushing, Addison, and Hyperthyroidism in horse, dog, and cat**