Veterinary Medicine: Overview for Pharmacists

“Dogs, cats, horses and cattle are not four legged people.”

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Goals and Objectives

- Introduce human medications commonly used for animals.
- Calculate proper human medication dosages used for animals.
- Compare the similarities of select veterinary and human medications.
- Describe possible challenges and solutions of pet ingestion of medications.
- Investigate common disease states of small animals.
- Explain the process of compounding "pet friendly" dosage forms.

Veterinary Medicine: Overview for Pharmacists

Speaker: Peter A. Kreckel R.Ph. is a graduate of the University of Pittsburgh, Bachelor of Science in Pharmacy, Magna Cum Laude, Class of 1981. He served as the President of the Pharmacy School Class of 1981 for 3 years, and President of the Pharmacy School Student Council for 2 years. During this time he received the Upjohn Achievement Award for leadership and academic achievement.

Speaker Disclosure: Peter Kreckel, RPh has no actual or potential conflicts of interest in relation to this program.

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US Pet Ownership 2007

<table>
<thead>
<tr>
<th></th>
<th>Dogs</th>
<th>Cats</th>
<th>Horses</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of households</td>
<td>37.2%</td>
<td>32.4%</td>
<td>1.8%</td>
</tr>
<tr>
<td>Total number</td>
<td>72,114,000</td>
<td>81,721,000</td>
<td>7,295,000</td>
</tr>
<tr>
<td>Average #</td>
<td>1.7</td>
<td>2.2</td>
<td>3.5</td>
</tr>
<tr>
<td>Vet $ spent household</td>
<td>$356</td>
<td>$190</td>
<td>$360</td>
</tr>
<tr>
<td>Vet $ per animal mean</td>
<td>$200.00</td>
<td>$81.00</td>
<td>$92.00</td>
</tr>
</tbody>
</table>

Famous “First Pets”

1. Name of Franklin D. Roosevelt’s dog?
2. Name of Caroline Kennedy’s pony?
3. Name of Lyndon Johnson’s dogs?
4. Name of Amy Carter’s cat?
5. Name of the Clinton’s cat?
6. Name of the Clintons dog?
7. Name of George W. Bush’s dog?
8. Name of Barack Obama’s dog?

Answers to famous “First Pets”

1. Scottish Terrier: “Fala”
2. “Macaroni”
3. 2 beagles: “Him” and “Her”
4. Siamese cat: “Misty Malarky Ying Yang”
5. “Socks”
7. Scottish terrier: “Barney”
8. Portuguese waterdog: “Bo”

Vital Signs

<table>
<thead>
<tr>
<th>Animal</th>
<th>Temp (F)</th>
<th>Pulse rate (bpm)</th>
<th>Respiratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle</td>
<td>100-102.5</td>
<td>55-80 (calf 100-120)</td>
<td>10-30 (15-40)</td>
</tr>
<tr>
<td>Cat</td>
<td>100-103.1</td>
<td>100-120 old 130-140</td>
<td>20-30</td>
</tr>
<tr>
<td>Dog</td>
<td>99.5-102.5</td>
<td>80-120 old 110-120</td>
<td>15-30</td>
</tr>
<tr>
<td>Horse</td>
<td>99-101.3</td>
<td>28-40 old 40-80</td>
<td>10-14</td>
</tr>
</tbody>
</table>
Horses are described as “very low maintenance.”

- Require very little drug intervention. “Healthy as a horse.”
- Most care involves the hooves.
- Most often reported condition gastrointestinal symptoms. “Colic” due to lack of water.
- Lack of water especially in stalls without running water, and in the wintertime due to bucket freezing.
- Adequate hydration will overcome most gastritis in horses.

Source: David Hershey – Tyrone Milling

Cattle: Fatty Liver Disease

- Fatty liver is likely to develop concurrently with another disease, typically disorders that are seen at or shortly after calving.
- A single 100 IU IM dose of a 24-hr slow-release insulin immediately after calving may be prophylactic. (Usually Ultra-Lente)
- Insulin suppresses both adipose mobilization and ketogenesis, but should be given in combination with glucose or a glucocorticoid to prevent hypoglycemia.

Top Reasons for Trips to the Vet

**CATS**
- Urinary tract infection
- Gastritis/vomiting
- Chronic renal failure
- Enteritis/diarrhea
- Diabetes mellitus

**DOGS**
- Ear infections
- Skin allergies
- Pyoderma/hot spots
- Gastritis/vomiting
- Enteritis/diarrhea

Over the Counter Antihistamines

- Benadryl (diphenhydramine)
  - For antihistaminic effects, also for prevention of motion sickness, sedative, anti-emetic
  - Dog: 2-4 mg/kg q 8-12 hours
  - Cat: 0.5mg /kg q12hrs (liquid taste awful)
Over the Counter Analgesics

- Acetaminophen (Tylenol®)
  - Contraindicated in cats in ANY doses!
  - In most species, excluding cats, a majority of administered acetaminophen is excreted in the urine as glucuronide and sulfate conjugates which are essentially nontoxic metabolites.
  - Cats are relatively deficient in activity of the enzyme glucuronyl transferase which conjugates acetaminophen. Cats can only conjugate 3% of APAP doses, while dogs and humans can excrete 50-60%. Toxic metabolites accumulate.

For Animals That Can Take Acetaminophen......

- Dogs: 10-15mg/kg (similar to human dose) but every 8-12 hours
  - Pocket pets, Rabbits and Rodents:
    - Use 1-2 mg per ml in drinking water.
    - APAP/codeine for rabbits: 1ml in 10-20ml of drinking water.

Aspirin Therapy

- Cats are relatively sensitive to Aspirin. Dogs are sensitive to GI bleeding. Recommend buffered aspirin
  - CATS: Dose carefully at 10mg/kg PO every OTHER day.
  - DOGS: Analgesia:10-25mg/kg every 8-12 hours. Fever: 10mg/kg BID. Platelet aggregation: 0.5mg/kg BID

Aspirin Therapy: Large Animals

- Mature cattle: two to four 240grain boluses BID
- Calves: one or two 240 grain boluses BID
- Horses: two to four 240grain boluses BID
- Swine: 10mg/kg every 4 hours 300lb=2 boluses

- 240grain bolus= 15.552 grams
- Source: Drugs.com veterinary
Case study: Casey and Her Dog

Casey is a 9 year old female who weighs 57lb (26kg). She has a Husky/Shepherd mix named “Bree,” that weighs 115 lbs (52kg).

- Calculate each patient's dose of ibuprofen.
- Calculate each patient's maximal daily dose of ibuprofen.

INTERACTIVE QUESTION

Who gets the largest dose of ibuprofen???

- CASEY (26kg)
- BREE (her 52kg dog)
- THEY take equal doses

TYPE your answer in the chat box!

Ibuprofen Toxicity in Dogs

- Ibuprofen has a narrow margin of safety in dogs. One recommended dosage is 5 mg/kg/day, divided. However, signs of toxicosis have been seen with a dosage of 8 mg/kg/day for 30 days. (an 88lb dog = 200mg ibuprofen per day)
- Toxicity due to gastrointestinal, renal CNS effects.
- Most sources say to avoid ibuprofen in small animals.

Back to Casey and Her Dog

Pediatric Dosing of Ibuprofen.

- 5mg/kg if fever under 102.5 °F q6h
- 10mg/kg if fever 102.5 °F q6h

CASEY's dose: 10mg/kg every 6 hours x 26kg
260mg q6h = 1040mg/day

Casey's dog: (5mg/kg/day)x 52kg divided
130mg BID = 260mg per day

Even though Casey weighs half that of her dog, she can take 4 times as much ibuprofen in one day!
So...What do we give “Old Yeller” for arthritis pain?

Rimadyl® (carprofen) by Pfizer
- 24-hour, non-steroidal anti-inflammatory drug (NSAID) that is administered once a day. Dose: 4.4mg/kg daily (or divided). Approved for dogs.
- Available as: 25, 75, 100mg scored tablets and chewable tablets. Cost 100mg chew= $1.10 ea

Deramaxx® (deracoxib) by Novartis
  - Dose: 1-2mg/kg per day
  - Available as 25mg and 100mg beef flavor tablets

Other Human Meds— Novel Veterinary Uses

- Naltrexone: treatment of self mutilating or tail chasing behaviors in dogs and cats.
- Nizatadine (Axid): prokinetic effects- treat delayed gastric emptying, constipation.
- Ethanol: treatment of methanol or ethylene glycol toxicity. Percutaneous EtOH for feline hyperthyroidism.
- Baclofen: treatment of urinary retention in dogs.
- Amitriptyline: generalized anxiety or separation anxiety in dogs.
- Pentoxifylline: reduces indirect lung injury in dogs after fresh water drowning.

Veterinary Meds- How Similar They are to Human Meds.
- Rimadyl (carprofen): NSAID, safe for puppies down to 6 weeks old.
- Deramaxx (deracoxib) : NSAID coxib class
- Felimazole (methimazole) for hyperthyroid cats (2.5mg and 5mg)
- Cerenia (maropitant) : antiemetic for dogs.

Flavor Preferences for Veterinary Meds
- Birds: grape, molasses, orange, pina colada, tutti-frutti
- Cats: Beef, butterscotch, cheese, chicken, liver, molasses, peanut butter, salmon, sardine, tuna
- Dogs: beef, cheese, chicken, liver, marshmallow, peanut butter, raspberry, strawberry
- Horses: alfalfa, apple, caramel, cherry, clover, molasses
- Swine: anisette, corn, cherry, meal, milk, sarsaparilla, licorice

Source: Paddock Labs, Secundum Artem
Dealing with Those Finicky Cats!

- Cats are very picky
- They love to play with things
- Administration may be difficult because they have sharp claws

Solutions
- Make a compound that smells good and looks like food but they can’t play with it. Fish flavor works best.
- A common dosing form for cats is a PLO gel that can be applied to your cat’s ear and absorbed through the skin.
- Make a paste and apply to cat’s paws. Will lick it off because they don’t like to have messy paws. (Keep cat confined until paws are clean)

“Pill Pockets®” for Dogs and Cats

- Insert the pill into the Pill Pocket, pinch the end to close, and feed to your dog or cat. No more forcing a pill down your pet’s throat.

Feline hyperthyroidism

- Most common endocrine disease in cats
- Seen in middle age to older cats.
- Signs: hyperactivity, weight loss, increase appetite, increase water consumption and urination.
- Vomiting and diarrhea. Increase HR, arrhythmias and CHF.
- Treatment: drug therapy; surgery; I-131
- Drug of choice: Methimazole (Tapazole®) start 2.5mg/day. Increase by 2.5mg every 2 weeks until T4 levels are normal.

Diabetes in Dogs

- Symptoms
  - Increased urination. (may be confused for incontinence or bladder infection).
  - Drinks frequently / excessively.
  - Weight loss.
  - Dog is often tired, lethargic or sleeps more often.
Insulin Therapy for Dogs

- Vetsulin: is a lente insulin, (intermediate-acting insulin). Is U-40 pork insulin. Dogs are dosed at 0.5 unit per kg. Must use U-40 syringes.
- NPH (human) 0.25 units/kg BID. Evaluate every 7 days.
- Lantus® (glargine) (total NPH bid dose reduced by 20%)
- Administer the injection subcutaneously, 2 to 5 cm (3/4 to 2 in) from the dorsal midline, varying from behind the scapulae to the mid-lumbar region and alternating sides.
- Glucose levels very similar to humans 100-150mg/dl.

SelzUrs DiSoRdErS in DoGs

- Phenobarbital: 2-5mg/kg PO BID. Adjust dose based on serum levels. May use IV loading dose (20mg/kg) to achieve steady state faster. Increase dose by 50% to 100% in puppies due to increased metabolic rate. P-450 inducer.
- Primidone: metabolized to PEMA and phenobarb. Second line treatment. 10-30mg/kg/day. Divide to BID or TID.
- Clorazepate
- Potassium Bromide
- IMPORTANT: Seizure failure due to Non compliance. Owner must be counseled on importance of giving doses regularly

Clorazepate (Tranxene®)

- Is an anxiolytic, sedative-hypnotic and anticonvulsant used in dogs and cats.
- Dose: 1-2 mg/kg po q12h

We could give Casey’s dog (52kg) between 50-100mg po q12h! Obviously we would not give Casey (26kg) 25-50mg of Clorazepate!!! We’d start her on 3.75mg BID.

Clonazepam: dogs: 0.5mg/kg PO BID (26mg!)
Diazepam: dogs: 0.5-2mg/kg (26-104mg)

Potassium Bromide

- Primary or adjunctive therapy in dogs. 2nd or 3rd line in cats. Becoming first choice for dogs. Has been around since late 1800’s, and never got FDA approval.
- Depresses neuronal excitability and activity. Bromides compete with chloride resulting in membrane hyper polarization, and decreased seizure activity.
- Very long half life 25 days in dogs. About 10 days in cats. Takes 5 half lives to reach steady state. Could take 4-5 months for steady state concentration.
INTERACTIVE QUESTION

• What is the name of a commonly used HUMAN medication that requires almost a year to achieve steady state?

• Because of this, this drug is “loaded” in the hospital setting.

• Half life is approximately 63 days

DOSING OF POTASSIUM BROMIDE

• May consider loading dose to reach steady state sooner (still controversial).

•Loading dose: 120mg/kg/day for 5 days, then reduce to 30mg/kg/day. Check serum levels.

• If GI upset is a problem, consider switching to sodium bromide.

• If using sodium bromide, reduce dose by 15%

• Be sure to provide an accurate measuring device.

POTASSIUM BROMIDE

• Must be compounded in a pharmacy.

• Solubility KBr: 1gm in 1.5ml water.

• Soluble NaBr: 1gm in 1.2ml water

• Use USP or American Chemical Society (ACS) reagent grade.

• 25gm of KBr or NaBr qs ad to 100ml, yields 250mg/ml. Flavoring agents are usually not necessary.

DEATH OF POLO HORSES

Sunday, April 20, 2009 at Wellington FL

• Unable to legally bring a supplement into the U.S. called Biodyl, to make their horses more resilient, a Venezuelan polo team had a compounding pharmacy mix up that formulation.

• Biodyl is a supplement that contains vitamins and minerals made in France by Duluth, Ga.-based animal pharmaceutical firm Merial Ltd.

• According to a Biodyl website, this supplement contains vitamin B12 (cyanocobalamin), adenosine triphosphoric acid (ATP), potassium, magnesium and selenium. It is administered either in drinking water or by injection into either (IM) or (IV).
Death of Polo Horses- What Happened???

- FDA spokeswoman Siobhan DeLancey said compounding pharmacies cannot legally recreate existing drugs or supplements under patent. In most cases, they are also not allowed to recreate a medication that is not approved for use in the U.S. ([CBS.com](http://www.cbs.com))
- Florida’s state veterinarian, Dr. Thomas J. Holt, said toxicology tests on the dead horses showed significantly increased selenium levels. ([source: Newsvine.com](http://www.newsvine.com/4/28/09))

And the FDA Says…..

- However, FDA is greatly concerned about veterinarians and pharmacies that are engaged in manufacturing and distributing unapproved new animal drugs in a manner that is clearly outside the bounds of traditional pharmacy practice and that violates the Act (e.g., compounding that is intended to circumvent the drug approval process and provide for the mass marketing of products that have been produced with little or no quality control or manufacturing standards to ensure the purity, potency, and stability of the product).

Regulations for Veterinary Compounding

*Source: American Veterinary Medical Association*

- Must be used only by or on the order of a licensed veterinarian.
- Must be used only within the confines of a valid veterinarian/client/patient relationship
- May be used or dispensed only for the treatment or prevention of disease or to improve health and welfare of an animal
- Used only when a need has been established, and FDA approved products are not available or clinically effective.

Stability Guidelines

*Source: USP23/NF18 (Secundum Artem Vol 7 No.2)*

- For non-sterile compounded drug preparations packaged in tight, light resistant containers and stored at controlled room temperatures.
- **Non aqueous liquid and solid formulations** (manufactured drug product is source of active ingredient): Beyond use date is not longer than 25% of the time remaining of the products original expiration date or 6 months, whichever is earlier.
Stability Guidelines
Source: USP23/NF18 (Secundum Artem Vol 7 No.2)

- Where USP or NF substance is source of active ingredient: The beyond use date is not later than 6 months.
- Water containing formulations (prepared from ingredients in solid form): beyond use date is not later than 14 days when stored at cold temperatures.

Pharmacist Practice Pearls for Veterinary Medicine

- Don’t “shoot from the hip” on questions asked about veterinary dosages.
- Buy a reputable reference when advising owners about pet dosages.
- If compounding be sure to “brush up” on existing FDA regulations concerning compounding of medications.
- If dispensing medications for food production animals, be aware of drug residues with respect to date of slaughter.

Resources for the Pharmacist

- Merck Veterinary Manual- www.merckvetmanual.com
- http://www.flavorx.com/vet/
- www.paddocklabs.com
- FDA website: CPG Sec. 608.400 Compounding of Drugs for Use in Animals(CPG 7125.40) Page 345
- Plumbs Veterinary Drug Handbook
  - By Donald C. Plumb  6th edition

QUESTIONS??