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VETERINARY PRACTITIONER PROGRAM

PROCEEDINGS

February 1-3, 2019
Results of the Merck Animal Health Veterinary Wellbeing Study

Terms like “burnout,” “depression,” “compassion fatigue,” and “stress” have been appearing with increasing frequency in veterinary journals. Some articles have suggested that veterinarians have an elevated risk of mental health problems and suicide.

To more fully understand the mental health status of veterinarians and what, if anything, could be done to address it, Merck Animal Health engaged Brakke Consulting, in collaboration with the American Veterinary Medical Association, to conduct a major study of US veterinarians. The goals of the Merck Animal Health Veterinary Wellbeing Study were: (1) To definitively quantify the prevalence of mental illness in the veterinary profession; (2) identify at-risk segments and contributing factors; and (3) suggest interventions or remedies that individuals and organizations could take to address any problems identified.

To design the research, Brakke and Merck Animal Health assembled a team with expertise in psychology, social work, veterinary medicine and survey research. AVMA provided a sample of 20,000 names and email addresses from its database of working veterinarians. A survey was conducted in November 2017. As an incentive, participants were invited to enter a drawing for twenty $100 gift cards. In addition, researchers offered to contribute $1 to the American Veterinary Medical Foundation for each response. The study generated 3,540 completed surveys, for a response rate of 17.7%. Margin of error at the 95% confidence level was 1.62%. Respondents represented owners and associates in all types of practice, as well as employed veterinarians working in positions other than practice.

Mental health of respondents was measured using the well-established Kessler Psychological Distress Scale. Kessler determines the presence or absence of severe psychological distress, or mental illness, using a numeric score. Wellbeing was measured using an index based on three questions widely used to measure wellbeing. Wellbeing goes beyond the presence or absence of mental illness and measures how people feel about their lives compared with the best or worst they can imagine. Results for veterinarians were compared to the US general population of employed adults using data from the University of Michigan’s Panel Study of Income Dynamics (PSID) and the National Institutes of Health. Begun in 1968, PSID is the longest-running longitudinal study in the world and consists of a nationally representative sample of 18,000 adults in 5,000 US households.

The Merck Animal Health Veterinary Wellbeing Study explored the impact of various factors that can influence mental health or wellbeing, including student debt, overall financial health, work hours, social and marital status, attitudes towards job, work-life balance, participation in healthy activities, personality and other attributes.

Key Findings

• An initial question in the survey established that veterinarians consider student debt, stress and suicide as the three most critical issues facing the profession.

• Veterinary medicine is a stressful profession. Two thirds of veterinarians, including 79% of associate veterinarians in practice, reported experiencing feelings of depression, compassion fatigue or burnout, and/or anxiety, within the last year.
• Overall, 5.3% of veterinarians experienced severe psychological distress, or mental illness, within the past 30 days. This is consistent with the 4.7% reported in PSID for the general population. However, the 5.3% is lower than that reported for veterinarians in other, non-representative studies.

• Younger veterinarians (<45yr) were much more likely to suffer severe psychological distress than older veterinarians (Figure 1). The prevalence of serious psychological distress was generally consistent across practice types except for food animal practice, where it was low to non-existent.

Fig. 1. Prevalence of serious psychological distress among veterinarians and the general population

• Work-related factors most often associated with severe psychological distress included working long hours, having student debt, working as a relief veterinarian, and working more – or fewer – hours per week than desired. Interestingly, it was the presence of student debt, not the amount of it, that was most associated with serious psychological distress.

• Only half of veterinarians with severe psychological distress were receiving treatment. In addition, only 16% of those psychologically distressed were taking advantage of resources available from professional organizations, most commonly AVMA and Veterinary Information Network (VIN).

• 25% of veterinarians had thought about suicide at some time in their lives. This was higher than seen in other studies. However, only 1.6% of respondents had attempted suicide, lower than in the general population (5.1%).

• Veterinarians score somewhat lower in wellbeing than the general population. However, older veterinarians scored much higher than their counterparts in the general employed adult population, and younger veterinarians much lower. Owners scored higher in wellbeing than associates in practice (Figure 2). To demonstrate the difference between mental health and wellbeing, only 28% of those who were “suffering” from a wellbeing perspective were also experiencing severe psychological distress as measured by the Kessler scale.
Fig. 2. Wellbeing of male and female practice owners and associates

- Work-related factors most often associated with high levels of wellbeing included higher income, working fewer hours, not working evenings, having little or no student debt, and being owner of a practice.

- Of concern, only 41% of veterinarians would recommend a career in veterinary medicine to a friend or family member; 33% would not recommend it, and 26% were unsure. That compares to 70% in the general population who would recommend their career, and 51% of physicians (Figure 3). Only 24% of veterinarians <35 years of age would recommend the profession. The reasons most often given for not recommending the profession include low compensation (54%), high student debt (54%) and the personal toll the profession takes (44%)

Fig. 3: Likelihood of veterinarians to recommend a career in their field vs. general population and physicians

Reducing Severe Psychological Distress and Improving Wellbeing

Those veterinarians without severe psychological distress, as well as those with high wellbeing, were much more likely to participate in healthy activities (Figure 4).

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Non-work factors contributing most to high wellbeing and sound mental health included:

- Spending time with family
- Socializing with friends
- Traveling and reading for pleasure
- Having a hobby
- Exercising
- Being married or in a relationship.

The study also found that spending more than one hour a day on social media was negatively associated with good mental health and a high level of wellbeing. In fact, those with severe psychological distress were more than twice as likely to spend more than two hours a day on social media. Limiting time on social media such as Facebook or Instagram – or taking a periodic sabbatical from such activities – seems prudent.

Given the high level of stress inherent in the profession, it would behoove veterinarians to consult with a mental health professional to develop a stress management plan. Likewise, working with a certified financial planner could assist in developing a plan to manage student debt and living expenses within the limits of one’s income.

It is important that employers recognize the issues common in the profession and acknowledge it to employees. Providing time off for appointments with mental health professionals, financial planners and similar counselors is important. Offering an Employee Assistance Program with mental health counseling benefits would be particularly valuable.

Ultimately, it is important that professional veterinary organizations and veterinary colleges work to reduce the cost of veterinary education through scholarships, low-cost loans, loan forgiveness and other support. In addition, colleges of veterinary medicine could make the services of on-campus counselors available to alumni. College and professional organizations should also explore novel alternatives such as online or tele-behavioral health counseling to improve the availability and lower the cost of mental health services.

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DEA Requirements for DVM's for Controlled medications

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Drug Abuse

• According to the Centers for Disease Control and Prevention, the #1 cause of death in 17 U.S. states is prescription drug abuse, surpassing motor vehicle accidents.
• Approximately 70,000 Americans died from overdose last year
  • Half of which were due to improper use of legally owned prescriptions
  • 56% of teens believe it is easier to get prescription drugs than illicit substances
  • Could be twice this amount since unless drugs are suspected no autopsy
• Approximately 1 in 6 Americans have admitted to abusing prescription drugs

Drug Abuse

The United States makes up only 4.6% of the world’s population, but it consumes 80% of its opioids – and 90% of the world’s hydrocodone supply

Hydrocodone, Oxycodone, Morphine, Fentanyl, Buprenorphine(Suboxone), Methadone, Hydromorphone (Dilaudid), Codeine
Signs of drug abuse

- How do you know if a client may be abusing opioids
- While these may all be ordinary occurrences, some warning signs that a client is potentially abusing opioids may include:
  - Suspect injuries in a new patient
  - Asking for specific medications by name
  - Asking for refills for lost or stolen medications
  - Pet owner is insistent in their request

Signs of employee abuse of diversion

- Some warning signs that veterinary staff may be abusing opioids include:
  - Mood swings, anxiety, or depression
  - Mental confusion and an inability to concentrate
  - Making frequent mistakes at work
  - Not showing up for work
  - Combating opioid addiction and addressing misuse of pain medication continues to be one of FDA’s highest priorities. Veterinarians as medical professionals have an opportunity to partner with FDA and others to take on this deadly epidemic, and the agency encourages them to continue to work with their clients and both local and national organizations to join in the fight.

Abuse by humans cause restrictions on Veterinary Practice

- Human abuse of controlled medications cause regulations that affects veterinary practice.
  - Gabapentin now a CIV.
  - Tramadol is now a CIV.
  - Both of these medications are used in veterinary practice, but because of abuse on the human side we have to follow the same requirements.
State regulations for controlled medications

- Each state creates its own regulations for the practice of veterinary medicine within its borders. These include regulations about secure storage of controlled substances, like opioids, and under what conditions veterinarians can prescribe them to patients.

DEA RECORD KEEPING REQUIREMENTS

- According to federal regulations, all Drug Enforcement Administration (DEA) applicants and registrants shall meet the following record keeping requirements:
  - Your records must show the flow of controlled substance into and out of the practice – including any time a controlled substance is acquired, dispensed, administered, distributed, stolen, lost, disposed of and inventoried;
  - You must keep two physically separate files – one for Schedule II substances, and one for Schedule III-V substances (the files can be stored together);
  - Your controlled substance records must be readily retrievable;
  - You must store all copies of DEA Form 222* (the form used for ordering Schedule I and II controlled substances) in a substantially constructed, securely locked cabinet and you must immediately report to the DEA any change in a copy (or copies) of the form’s status (used/unused, lost, stolen);

DEA RECORD KEEPING REQUIREMENTS

- Each registrant who maintains an inventory of controlled substances must maintain a complete and accurate record of the substances in possession and the date a new inventory was conducted. A new inventory is required whenever a control change occurs such as being acquired, dispensed, administered, distributed, stolen, disposed of, lost, inventoried, or destroyed.
  - Each inventory must contain the following information:
    - Whether the inventory was taken at the beginning or close of business
    - Names of controlled substances
    - Each finished form of the substances (e.g., 100 tablets per bottle)
    - The number of dosage units of each finished form in the commercial container (e.g., 100 tablets per bottle)
    - The number of commercial containers of each finished form (e.g., one 100 tablet bottle)
  - It is important to note that inventory requirements extend to controlled substance samples provided to practitioners by pharmaceutical companies.
DEA RECORD KEEPING REQUIREMENTS

• Each practitioner must maintain inventories and records of controlled substances listed in Schedules I and II separately from all other records maintained by the registrant. Likewise, inventories and records of controlled substances in Schedules III, IV, and V must be maintained separately or in such a form that they are readily retrievable from the ordinary business records of the practitioner. All records related to controlled substances must be maintained and be available for inspection for a minimum of two years.

Inventory

• Each registrant who maintains an inventory of controlled substances must maintain a complete and accurate record of the controlled substances on hand and the date that the inventory was conducted. This record must be in written, typewritten, or printed form and be maintained at the registered location for at least two years from the date that the inventory was conducted. After an initial inventory is taken, the registrant shall take a new inventory of all controlled substances on hand at least every year.

• Each inventory must contain the following information:
  • Whether the inventory was taken at the beginning or close of business
  • Names of controlled substances
  • Each finished form of the substances (e.g., 100 milligram tablet)
  • The number of dosage units of each finished form in the commercial container (e.g., 100 tablet bottle)
  • The number of commercial containers of each finished form (e.g., four 100 tablet bottles)
  • Disposition of the controlled substances
  • It is important to note that inventory requirements extend to controlled substance samples provided to practitioners by pharmaceutical companies.

Disposal of Controlled Substances

• A practitioner may dispose of out-of-date, damaged, or otherwise unusable or unwanted controlled substances, including samples, by transferring them to a registrant who is authorized to receive such materials. These registrants are referred to as “Reverse Distributors.” The practitioner should contact the local DEA field office (See Appendix E) for a list of authorized Reverse Distributors. Schedule I and II controlled substances should be transferred via the DEA Form 222, while Schedule III–V compounds may be transferred via invoice. The practitioner should maintain copies of the records documenting the transfer and disposal of controlled substances for a period of two years.
<table>
<thead>
<tr>
<th>Schedule II</th>
<th>Schedule III &amp; IV</th>
<th>Schedule V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Registration:</td>
<td>Required</td>
<td>Required</td>
</tr>
<tr>
<td>Receiving Records:</td>
<td>Order Forms (DEA Form 222)</td>
<td>Invoices, Readily Retrievable</td>
</tr>
<tr>
<td>Prescriptions:</td>
<td>Written Prescription</td>
<td>Written, Oral, or Fax</td>
</tr>
<tr>
<td>Refills:</td>
<td>No</td>
<td>No more than 5 within 6 months</td>
</tr>
<tr>
<td>Distribution Between Registrants:</td>
<td>Order Forms (DEA Form 222)</td>
<td>Invoices</td>
</tr>
<tr>
<td>Security:</td>
<td>Locked Cabinet or Other Secure Storage</td>
<td>Locked Cabinet or Other Secure Storage</td>
</tr>
<tr>
<td>Theft or Significant Loss:</td>
<td>Report and complete DEA Form 106</td>
<td>Report and complete DEA Form 106</td>
</tr>
</tbody>
</table>

**DEA RECORD KEEPING REQUIREMENTS**

- You may transfer controlled substances to another DEA registrant but all transfers must be recorded and cannot comprise more than 5% of all the dosage units you distribute and dispense;
- You must report thefts or significant losses within one business day to the DEA, the state controlled substance authority, and local police. The occurrence must be recorded on DEA Form 106;

**DEA RECORD KEEPING REQUIREMENTS**

- You may issue prescriptions for controlled substances in writing, verbally, or electronically (using systems meeting DEA criteria), or by fax (note that a paper prescription is needed before any pharmacy can dispense a Schedule II substance). Prescriptions must include the following:
  - Date;
  - Signature of registrant;
  - DEA registration number;
  - Patient’s name/address;
  - Practitioner’s name/address;
  - Drug name, strength, dosage form and quantity;
  - Directions for use (frequency and route of administration); and
  - Number (if any) of refills authorized
- Note that Schedule II drugs cannot be refilled.
- Note that state law may restrict the ability to refill or the number of refills.
Your usage logs will be your biggest source of frustration. They must include:

1. The controlled substance type
2. Bottle number
3. Lot number
4. Expiration date
5. Beginning balance
6. Balance forward on:
   a. The end of every completed page
   b. The beginning of every new page
7. Remaining balance after each draw
8. Date bottle placed into use
9. Page number
10. For each draw
    a. Date
    b. Patient
    c. Person who made the draw
11. All errors/corrections require:
    a. A single line out (no scribbling over)
    b. Accompanying initials of the person recording the correction
12. Remember, these are legal documents!!
State regulations for controlled medications

- Not only are states changing reporting requirements, some are also setting limits on the number of pills that can be prescribed at one time and some are even limiting the duration of a patient’s treatment with opioids. States such as Colorado and Maine require veterinarians to look at a pet owner’s past medication history before dispensing opioids or writing an opioid prescription.
- To ensure that they are in full compliance with current state laws, veterinarians can contact their State Board of Veterinary Medicine and their State Board of Pharmacy for updated regulations.

Tennessee new requirements for opiate prescriptions

- The biggest change has to do with how much of a drug you can get and when. Under the new law, pharmacists can only partially fill a prescription for no more than half of the number of days it’s written for. And there are limits on prescriptions, too: General prescriptions are limited to a 10-day supply (and no more than 500 cumulative morphine milligram equivalents). Prescriptions after surgery are limited to a 20-day supply (maximum 850 cumulative MMEs). “Medical necessity” prescriptions are limited to a 30-day supply (maximum 1,200 cumulative MMEs).
- DVM’s are exempt from this, but pharmacist may not fill prescriptions unless they follow these requirements.

FDA and DEA requirements for controlled medications

- FDA approves controlled drugs and monitors reported adverse events associated with these drugs. The Drug Enforcement Administration (DEA), however, creates and enforces the regulations regarding controlled substances. Veterinarians should contact their local DEA office if they have questions about the federal regulations regarding controlled substances.
- Practitioners are required to store stocks of Schedule II thru V controlled substances in a secured locked, substantially constructed cabinet.
- When controlled substances are stolen from the clinic, veterinarians must report the theft to DEA and to their local police department as soon as possible.
- Diversion is going to be an increased emphasis by the DEA.
FDA and DEA requirements for controlled medications

- Prior to March 2018, there had been two FDA-approved opioid products approved for use in animals. Wildlife Laboratories, the sponsor of a potent analog of fentanyl called carfentanil (marketed as Wildnil), voluntarily relinquished the approval for this drug in March 2018, as it hadn’t been marketed in at least five years, and because the sponsor wanted to avoid the possibility of diversion of the drug if marketed in the future.
- Recuvyra (fentanyl), now the only FDA-approved opioid for use in animals, is not being marketed. Therefore, veterinarians who need to use an opioid to control pain in their patients use products approved for use in humans.
- FDA has pre-approval (abuse potential review) and post-approval safeguards in place for these drugs, and requires Risk Evaluation and Mitigation Strategies (REMS) for some products to ensure that the benefits outweigh certain risks.
- While veterinarians using approved human opioids extra-label in animals do not have to follow the human drug’s risk mitigation requirements, they do have to follow the regulations for extra-label use in animals. FDA also strongly encourages veterinarians to read the label information for human opioid drugs and take any associated training. Veterinarians can find a list of FDA-approved human drugs marketed under REMS programs on FDA’s website.

DEA, FDA and State inspections

- How to be ready for a DEA, FDA or State inspection for controlled medications?
  1. Documentation
  2. Documentation
  3. Documentation—Document ever time a controlled drug is used. Do not write that 5 bottles of ketamine was used for a heard of 100 cows. Document how much was used on each cow.
- Document how much was used on each animal. (even mice for research)

Owners storage of controlled medications

- Pet owners may be unaware that pet opioid prescriptions in the home pose a risk for accidental or intentional misuse by family members or guests. Whenever pets are actively receiving opioids, veterinarians should advise pet owners to secure the opioids and store themout of sight. When the pet owner has unwanted opioids, disposing of the medication should be a priority. Because of their inherent risks, FDA has specific recommendations for opioid disposal.
Pet overdose on opiates.

- Not only can people overdose on opioids, but so can pets. Working dogs, like narcotics detection dogs, are particularly susceptible because they may inhale the powdered drug. Because fentanyl and fentanyl-related drugs are potent, it only takes a tiny amount of drug to cause an overdose. Veterinarians can contact the University of Tennessee College of Veterinary Medicine’s for suspected cases of canine opioid overdoses.
- Narcotic detection dog handlers should have naloxone with them.

Prevention is the most cost effective way to treat addiction

- 1. Deceasing the supply of controlled medications on the street is a very effective way of decreasing drug abuse.
- 2. This is one of the reasons that the DEA and other enforcement agencies are looking for drug diversion.

Q: What are the requirements for writing veterinary prescriptions?
- A: The AVMA’s Principles of Veterinary Medical Ethics require a Veterinarian-Client-Patient Relationship (VCPR) before a veterinarian can write a prescription for an animal patient. In addition, most states have laws that specifically require a VCPR for a veterinarian to be able to write a prescription. Each state’s veterinary medical board regulates how prescriptions must be written – specifically, what information must be included on the prescription. Although this is not a requirement, a third resource is the FDA’s “A Microgram of Prevention is Worth a Milligram of Cure: Preventing Medication Errors in Animals” document, which provides additional guidance on writing prescriptions.
Prescription Requirements

- Name, address, and telephone number of veterinarians
- Name of clients
- Identification of animal(s) treated, species and numbers of animals treated, when possible
- Date of treatment, prescribing, or dispensing of drug
- Name, active ingredient, and quantity of the drug (or drug preparation) to be prescribed or dispensed
- Drug strength (if more than one strength available)
- Dosage and duration
- Route of administration
- Number of refills
- Cautionary statements, as needed
- Expiration date if applicable
- Slaughter withdrawal and/or milk withholding times, if applicable

Q: Do I have to give my client a written prescription?

A: As a veterinarian, when you determine that a medication is needed for a patient, you can discuss with your client the benefits of having the drug dispensed directly from your clinic. If your client still wants the prescription filled elsewhere, you should comply with their wish and provide a written prescription. For more information about this, see the AVMA’s Principles of Veterinary Medical Ethics. Most pharmacist and very little if any veterinary pharmacy training. Make sure you are aware of your state’s rules and regulations regarding prescriptions. Some states require veterinarians to write prescriptions for clients to have filled elsewhere if requested by the client, while some are less strict about prescriptions; in addition, specific guidance on ways the prescription can legally be filled (via a written prescription, telephone or fax) might be offered by your state.

Q: Whom should I contact to report a problem with a drug obtained from a pharmacy?

A: The state boards of pharmacy oversee the practice of pharmacy within the state and ensure state rules are followed. Contact your state board of pharmacy if you suspect that the pharmacy’s dispensing practices may be in violation of the law. Also, if the pharmacy is based out of another state, call that state’s board of pharmacy.
Q: Can I enter an agreement with a pharmacy that will give me a commission based on drug sales?

- A: Gaining an undisclosed commission through an agreement with a pharmacy could be viewed as a deceptive business practice by your state board and thus might be a violation of your state’s practice act. You should check with your state veterinary medical board for rules and requirements about disclosure of business relationships and advertising guidelines.
Common mistakes in managing epilepsy

Dr. William Thomas  wthomas@utk.edu | University of Tennessee College of Veterinary Medicine

Events that can mimic seizures

The diagnostic evaluation is designed to answer two questions: (1) Is the patient having seizures, and (2) If so, what is the cause of the seizures. Seizures are recognized by their spontaneous onset, stereotypic signs, self-limiting time course and exclusion of common imitators. The client's description of the seizures, their frequency and duration, and the dog's behavior between seizures should be recorded. Ask about any focal signs at the start of the seizure, such as turning the head to one side or jerking of one limb. Any abnormalities before and after the seizure should be characterized. It is also important to determine if the events occur at a certain time of day or in association with situations such as feeding or exercise. Since the veterinarian will usually never see the seizure, the client's observations are extremely important. In some cases it helps if the client videotapes the episodes.

<table>
<thead>
<tr>
<th>Paroxysmal event</th>
<th>Distinguishing Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syncope</td>
<td>Partial or complete loss of consciousness</td>
</tr>
<tr>
<td></td>
<td>Often associated with exercise or excitement</td>
</tr>
<tr>
<td></td>
<td>Lack of violent motor activity</td>
</tr>
<tr>
<td></td>
<td>Short duration</td>
</tr>
<tr>
<td></td>
<td>Lack of postictal signs</td>
</tr>
<tr>
<td>Narcolepsy/cataplexy</td>
<td>Flaccid paralysis and loss of consciousness</td>
</tr>
<tr>
<td></td>
<td>Precipitated by excitement, feeding</td>
</tr>
<tr>
<td></td>
<td>Lack of postictal signs</td>
</tr>
<tr>
<td>Myasthenia gravis</td>
<td>Stiffness, tremor, weakness</td>
</tr>
<tr>
<td></td>
<td>Precipitated by exercise</td>
</tr>
<tr>
<td></td>
<td>Normal consciousness</td>
</tr>
<tr>
<td></td>
<td>Lack of postictal signs</td>
</tr>
<tr>
<td>Vestibular dysfunction</td>
<td>Nystagmus, head tilt, ataxia</td>
</tr>
<tr>
<td></td>
<td>Normal consciousness</td>
</tr>
<tr>
<td>Normal or abnormal movements during sleep</td>
<td>Twitching, vocalization, paddling</td>
</tr>
<tr>
<td></td>
<td>Occur only during sleep</td>
</tr>
<tr>
<td></td>
<td>Can be interrupted by waking</td>
</tr>
<tr>
<td></td>
<td>Lack of postictal signs</td>
</tr>
<tr>
<td>Behavior disorders (stereotypy)</td>
<td>Sterotypic pattern of abnormal behavior</td>
</tr>
<tr>
<td></td>
<td>Event can usually be interrupted</td>
</tr>
<tr>
<td></td>
<td>Normal consciousness</td>
</tr>
<tr>
<td></td>
<td>Lack of postictal signs</td>
</tr>
<tr>
<td>Pain (e.g. cervical disk disease)</td>
<td>Crying, muscle tremor/rigidity</td>
</tr>
<tr>
<td></td>
<td>May be associated with movement</td>
</tr>
<tr>
<td></td>
<td>Normal consciousness</td>
</tr>
</tbody>
</table>

Underlying causes of seizures

The clinician should ask about familial history of seizures, significant injuries or illnesses, vaccination status, diet, and potential exposure to toxins. Ask about any prescription or nonprescription medications. Any interictal abnormalities are noted, such as changes in behavior, gait, appetite, weight, or sleep habits. Perform a complete neurologic examination to detect any persistent neurologic deficits. Cerebral lesions often cause focal, relatively subtle deficits such as delayed proprioceptive positioning on one side or blindness in one visual field. Be careful when interpreting the examination shortly after a seizure. Any generalized deficits, such as ataxia, depression or blindness may be due to postictal disturbances and not necessarily indicate underlying brain disease. Repeating the examination in 24 to 48 hours may be necessary to determine if any deficits persist.

A complete blood count and serum chemistry profile are indicated in any patient with one or more seizures. Bile acids are a good idea in young animals with clinical features suggestive of a portosystemic shunt. Blood lead determination should be performed in patients with possible exposure to lead, patients from areas with a high incidence of lead poisoning, and in animals less than one year of age.
Idiopathic epilepsy is a clinical diagnosis based on the typical age of onset, lack of interictal abnormalities, and exclusion of other causes. Symptomatic epilepsy should be suspected when: (1) seizures start before one or after five years of age, (2) there is a sudden onset of multiple seizures, or (3) there are interictal abnormalities detected on history, examination, or laboratory tests.

Cerebrospinal fluid (CSF) analysis and magnetic resonance imaging are indicated in patients with:
- interictal neurological deficits
- onset of seizures at less than 1 or greater than 5 years of age.
- Any cat

<table>
<thead>
<tr>
<th>Disease category</th>
<th>Examples</th>
<th>Clinical features</th>
<th>Diagnostic tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic</td>
<td>Portosystemic shunt, hypoglycemia, hypocalcemia, polycythemia</td>
<td>Waxing and waning</td>
<td>CBC, chemistry, bile acids</td>
</tr>
<tr>
<td>Toxic</td>
<td>Lead</td>
<td>Older house, remodeling</td>
<td>Blood lead</td>
</tr>
<tr>
<td>Brain lesion</td>
<td>Tumor, encephalitis, stroke</td>
<td>&lt;1 or &gt;5 years age, Deficits on neuro exam</td>
<td>MRI, CSF</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>Idiopathic epilepsy</td>
<td>1-5 years of age, normal in between seizures</td>
<td>Clinical features, rule out other causes</td>
</tr>
</tbody>
</table>

**Initial choice of drug therapy**

Based on clinical experience and pharmacokinetic information, phenobarbital, zonisamide or levetiracetam are acceptable as initial therapy. In dogs, bromide is commonly used but has the highest rate of side effects. There is little evidence of a synergistic action among antiseizure drugs and polytherapy has several potential disadvantages, including increased cost, the need to monitor and interpret serum concentrations of multiple drugs, potential drug interactions, and more complicated dosing schedules.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Cost*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenobarbital</td>
<td>2.5 mg/kg BID</td>
<td>Effective, familiarity</td>
<td>High risk of side effects, drug interactions</td>
<td>$62**</td>
</tr>
<tr>
<td>Bromide</td>
<td>20-30 mg/kg KBr daily</td>
<td>Once daily dosing, least expensive</td>
<td>Highest rate of side effects, long time to steady state</td>
<td>$11**</td>
</tr>
<tr>
<td>Zonisamide</td>
<td>10 mg/kg BID (daily in cats)</td>
<td>Low rate of side effects</td>
<td>Rare liver, kidney and KCS</td>
<td>$51</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>20 mg/kg TID XR 30 mg/kg BID</td>
<td>Lowest rate of side effects</td>
<td>TID dosing necessary for small dogs</td>
<td>$30 $56</td>
</tr>
</tbody>
</table>

*Cost is based on 30 kg dog for 1 month of therapy. **Cost does not include therapeutic monitoring

**Monitoring therapy**

Any drug used should be given an adequate chance to work and should not be discarded prematurely. Commonly used antiseizure drugs often must be administered for several weeks or longer before obtaining maximum antiseizure effects. Furthermore, it may take several months or more to adequately evaluate seizure control in a dog that has seizures separated by long periods of time. A common cause of poor seizure control is failure to maximize the dose before discarding.
a particular drug. This may lead to the need to backtrack at a later date for a second, more aggressive trial. This can be difficult, however, because once a client is convinced a particular drug is ineffective, they are often reluctant to agree to a second trial.

**Client education**

The client should be fully informed about the nature of the disease and its treatment. They should understand the goals of therapy and potential side effects. Mild side effects are common when first starting treatment with antiseizure drugs. These will often resolve or diminish after a few weeks of treatment. If the client understands this, they are less likely to become alarmed and prematurely stop treatment if they notice side effects.

The client must appreciate the need for regular administration of medication. They need to know what to do if a dose is missed (in general, the missed dose is given as soon as the mistake is recognized, then the next dose is given on schedule). Maintaining an adequate supply of medication is important and the client should know how to obtain refills if medication is lost or runs out during travel. Suddenly stopping antiseizure medication may precipitate seizures and should be avoided at all costs. Having the client keep a log of the time, date, and characteristics of each seizure and any side effects is very helpful in assessing therapy. Finally, clients must not alter treatment without the advice of the veterinarian. Some clients are tempted to alter the dose based on a short-term assessment of seizure control or side effects, but frequent dose changes are detrimental and make interpretation of therapeutic monitoring difficult.

**Ketogenic diets**

The beneficial effects of fasting in people with epilepsy have been recognized for centuries, probably because the ketosis and acidosis resulting from minimal caloric intake produced an antiseizure effect. The medium chain triglyceride (MCT) diet can produce ketones more easily than other carbohydrate restricted diets. Law et al published a randomized, double-blind study comparing a MCT ketogenic diet with a standard diet in dogs with idiopathic epilepsy refractory to treatment with phenobarbital and/or bromide. The study diet was associated with a statistically significant lower number of seizures compared to the placebo diet (2.7 seizures/month and 2.3 seizures/month, respectively). One third of the dogs (n=10) were removed from the study before completion. This diet is commercially available. (NC NeuroCare, Purina).

**Cannabidiol (CBD)**

Several placebo-controlled studies show CBD reduces the frequency of convulsive seizures among children and young adults with the Dravet syndrome and Lennox-Gastaut syndrome, but is associated with adverse events including somnolence and elevation of liver enzyme activity. These studies led to the FDA approval of a CBD oil product (Epidiolex) for these patients. In veterinary medicine, we don't have good data and safety and efficacy in dogs with epilepsy. Several studies are ongoing. We also need more/better pharmacokinetic studies, as some products have poor bioavailability when given orally in dogs. Epidiolex is Schedule 5, so could be prescribed off label in dogs. Unfortunately it is quite expensive. What is most commonly being used in dogs are unapproved and poorly regulated products, some of which have no CBD or less than advertised and in some cases enough THC to be potentially toxic.
The Down Dog: Management of Acute Paralysis

Dr. William Thomas  wthomas@utk.edu  | University of Tennessee College of Veterinary Medicine

Intervertebral Disc Disease

Although severe trauma can cause extrusion of a normal, non-degenerated disk, most disk disease is secondary to underlying degeneration of the disk. The normal disk maintains spinal stability while allowing flexible movement and dissipation of stress applied to the spine. With degeneration of the disk, there is a loss of water, the nucleus becomes less flexible, and stress is born primarily by the annulus fibers. This can damage and weaken the annular fiber, which can eventually tear, allowing protrusion or extrusion of the disk.

Hansen type I extrusion is extrusion of the nucleus pulposus through the annular fibers. This is most common in chondrodystrophic breeds with calcification of the disk. This predisposes to sudden extrusion of large amounts of disk material that causes acute, severe spinal cord compression. Hansen type II protrusion is shifting of the nucleus that causes protrusion of the annulus. This is most common in non-chondrodystrophic dogs, cats, and people in which the disk undergoes fibrous degeneration with age. These slowly progressive changes tend to cause gradual protrusion resulting in chronic compression of the spinal cord.

Displacement of the disk can cause compression of a nerve root (pain) or the spinal cord (myelopathy). The severity of the spinal cord damage is related to the degree and duration of compression, and the velocity at which the disk strikes the cord (Table 1). Mild spinal cord damage is manifested as loss of proprioception because the proprioceptive fibers are the most susceptible to compression. With more severe damage, there is progressive loss of motor function as the motor fibers are damaged and finally, loss of deep pain perception because the fibers that convey deep pain sensation are the most resistant to compression. Acute, severe spinal cord injury can result in progressive necrosis that spreads cranial and caudal to the site of initial injury, called ascending/descending myelomalacia.

Severity of clinical signs

<table>
<thead>
<tr>
<th>Spinal pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ataxia</td>
</tr>
<tr>
<td>Ambulatory paresis</td>
</tr>
<tr>
<td>Non-ambulatory paresis</td>
</tr>
<tr>
<td>Paralysis</td>
</tr>
<tr>
<td>Paralysis with loss of deep pain perception</td>
</tr>
<tr>
<td>Ascending/descending myelomalacia</td>
</tr>
</tbody>
</table>

In chondrodystrophic breeds there is usually an acute onset of back pain and/or neurologic deficits. Caudal lumbar disk extrusion can cause pelvic limb lameness, due to nerve root or spinal nerve compression (nerve root signature). Careful palpation of the spine usually allows identification of a focal site of pain. Spinal reflexes are normal to exaggerated (T10-L2 disks) or weak or absent (L3-S1 disks). In dogs with substantial paresis, assessment of the cutaneous trunci (panniculus) reflex also allows localization. In dogs that are unable to walk, it is important to test for deep pain. A behavioral response such as turning the head or vocalization indicates conscious perception – withdrawal of the limb indicates only an intact reflex arc.

Definitive diagnosis is based on imaging. Radiographic signs include:
1. a narrowed or wedge-shaped disk space,
2. a small intervertebral foramen,
3. narrowing of the space between the articular facets,
4. calcified disk material within the vertebral canal.

A calcified disk confined to the disk space indicates disk degeneration but not extrusion. Survey radiographs are accurate in about 70% of cases. Myelography shows extradural compression of the cord dorsal to the affected disk space. Computed tomography and magnetic resonance imaging are also helpful in diagnosis.
Nonsurgical treatment

Nonsurgical treatment is indicated in dogs with no or mild neurologic deficits and when surgery is not an option. The most important aspect of nonsurgical management is strict cage rest. In dogs with persistent pain, analgesics are appropriate (for example, prednisone at 0.5 mg/kg daily for 3-5 days), but only in conjunction with cage rest. The patient is reevaluated frequently for response to therapy. If the dog does well, the cage rest is continued for at least 2 weeks. Approximately 80% of dogs with back pain or mild neurologic deficits due to thoracolumbar disk extrusion will improve with nonsurgical therapy. The recurrence rate is 30-40%. The prognosis is guarded for dogs with nonambulatory paraparesis (50% recovery rate) and very poor for dogs with absent deep pain perception.

Surgery

Indications for surgery are substantial neurologic deficits (e.g. unable to walk), mild signs that persist despite appropriate nonsurgical therapy, and recurrent attacks. The results of hemilaminectomy (removal of the pedicle and articular facets on one side) are superior to those for dorsal laminectomy (removal of the lamina on both sides), probably because it provides for safer and more complete removal of disk material. Prophylactic fenestration (removing the nucleus from the disk space) at the time of decompressive surgery may decrease the rate of recurrence. Approximately 90-95% of dogs with intact deep pain perception recover neurologic function when surgery is performed in a timely fashion. For dogs with absent deep pain perception, the prognosis for recovery is about 50% if surgery is performed within 24-48 hours of losing pain perception. The prognosis is poor if surgery is delayed for more than 48 hours.

Fibrocartilaginous Embolic Myelopathy

Fibrocartilaginous embolic myelopathy (FCEM) is an acute infarction of the spinal cord caused by a vascular embolus of fibrocartilage, probably originating from the intervertebral disk. Adult large- or giant-breed dogs and miniature schnauzers are most commonly affected. This disease is less common in small dogs, chondrodystrophic dogs, and cats.

The onset is sudden and often associated with activity such as running or playing. Neurologic deficits rarely progress beyond the first few hours. Although patients sometimes yelp as if in pain at the onset of signs, spinal pain is rarely evident by the time of examination. This lack of focal spinal pain is helpful in ruling out other causes of acute spinal diseases, such as fracture/luxation and disk extrusion. Any region of the spinal cord may be affected, and the spinal cord segments involved dictate the specific neurologic deficits. Ataxia, paresis, or paralysis may affect the pelvic limbs or all limbs. Asymmetric or unilateral deficits are common. Lower or upper motor neuron deficits may result. In severe cases there is loss of deep pain perception caudal to the lesion.

Diagnosis is based on the clinical features and exclusion of other causes. Essential features of FCEM are the signalment, sudden onset, nonprogressive course, lack of focal spinal pain, and often the asymmetry of deficits. The differential diagnosis includes intervertebral disk disease, trauma, neoplasia, and inflammatory disease. Radiographs and myelography are typically normal, although myelography occasionally shows focal spinal cord swelling. Cerebrospinal fluid analysis is nonspecific. Magnetic resonance imaging is the best imaging modality and usually shows signal changes suggestive of focal spinal cord infarction.

There is no specific treatment for this condition. Corticosteroids are sometimes used although there is little evidence that any drug is beneficial. Nursing care and physical therapy play an essential role in promoting recovery and preventing complications. About 85% of patients recover, depending on the severity of the deficits and owner’s commitment.

Trauma

Major trauma can result in various spinal lesions, depending on the anatomic location. A thorough history usually documents the presence and mechanism of trauma, although the cause is sometimes unknown or surmised by concurrent findings if the accident is not witnessed. Automobile accidents, gunshot wounds, falls, and dog fight injuries are common. Spinal injuries may consist of vertebral luxation, vertebral fracture, vertebral fracture/luxation, or traumatic IVD herniation.

In any trauma patient, full assessment of all body systems is essential to diagnose and treat shock and any other injuries. A neurologic examination is performed to localize the injury and determine the severity of the deficits. It is vital that the examination be carefully performed, minimizing movement of the patient to avoid further damage to the spinal cord as a result of instability of the spinal column. Assessment of mentation, cranial nerves, voluntary movement, and spinal reflexes, as well as head and spine palpation, is performed, but moving the patient to test gait and postural reactions is avoided until unstable spinal injuries are ruled out with radiographs.
The presence or absence of deep pain caudal to the injury is the most important prognostic sign; lack of deep pain sensation after spinal trauma carries a poor prognosis for neurologic recovery. Following initial assessment and stabilization, appropriate analgesics are administered. A lateral-view radiograph of the affected region of the spine is obtained when the patient is stable. If dorsoventral views are necessary, a horizontal beam view is safest. The purpose of radiography is to confirm the localization, classify any fracture/luxation as stable or unstable, and try to determine if there is any persistent spinal cord compression that may require surgery. The two components of the spine that maintain stability are (1) the dorsal compartment, consisting of the articular facets and lamina, and (2) the ventral compartment, consisting of the vertebral bodies and intervertebral disk. Damage to one of these components usually does not result in severe instability, whereas damage to both the dorsal and ventral components usually requires fixation to prevent further displacement. Myelography or CT is indicated if survey radiographs are normal or inconclusive. Routine chest and abdominal films also may be indicated to determine other body systems affected by the trauma.

The decision to treat the patient is based on the severity of the neurologic deficits, the type of vertebral injury, the severity of any concurrent injuries, and the owner’s understanding of the risk, prognosis, and expense of the injury and treatment. Animals with mild neurologic deficits caused by cervical injuries or stable thoracolumbar injuries often recover with nonsurgical therapy. This consists of 4 to 6 weeks of complete cage rest, with very cautious movement of the animal to assist it with posturing to urinate and defecate. Weight bearing is generally not encouraged, unless the vertebral column is stable. Sometimes an external splint is used in conjunction with cage rest.

Indications for surgery include:
(1) unstable fracture/luxation, usually evident on imaging by disruption of the dorsal and ventral components of the vertebrae;
(2) persistent compression of the vertebral canal, evident as a substantially displaced fracture/luxation or extradural compression of the spinal cord on myelography, CT, or MRI; and
(3) progressive deterioration in neurologic status despite conservative treatment, usually owing to an unstable fracture/luxation or progressive spinal cord compression from hemorrhage or disk extrusion.

Surgery usually involves decompression of the spinal cord and fixation of unstable vertebrae. The choice of fixation technique depends on the size of the animal, the type and location of the injury, and the surgeon’s preference and experience. In general, dorsal techniques (spinal staples, dorsal spinal plates, and modified spinal instrumentation) are indicated if the ventral components of the vertebrae are intact. Ventral techniques (vertebral body plates, pins/screws, and bone cement) are stronger and can be used with dorsal and ventral component injuries. A laminectomy to decompress the spinal cord from intervertebral disk material, ligament, or bone may be necessary before fixation. External splints of light casting material or moldable thermoplastic materials provide some stability and are most applicable to thoracic, cranial lumbar, and cervical regions. Splints may create sores and have the potential for creating complicated wounds that require additional care. Splints may also be used as an adjunct to internal fixation.

Diffuse lower motor neuron disease
These diseases are characterized by paresis with decreased to absent muscle tone and spinal cord reflexes. In some cases the paresis involves the motor cranial nerves (facial, jaw, pharyngeal weakness). Sensory function is often preserved (proprioception, pain perception).

Acquired myasthenia gravis is failure of neuromuscular conduction due to reduction in number of acetylcholine receptors at the neuromuscular junction. It is caused by the development of circulating antibodies directed against the acetylcholine. It is fairly common in mature dogs and is uncommon in cats. The classic presentation is exercise-induced stiffness, tremors, and weakness that resolve with rest. However, weakness is not always associated with exercise. Facial, pharyngeal, or esophageal weakness is common and in many cases there is megaesophagus without generalized weakness (focal myasthenia). Regurgitation and aspiration pneumonia are frequent complications. Generalized weakness often resolves quickly after the intravenous administration of edrophonium chloride (0.1-0.2 mg/kg), which is often used as a diagnostic test. Definitive diagnosis is based on the detection of antibodies in serum. Treatment consists of anticholinesterase drugs, such as pyridostigmine (1-3 mg/kg PO BID, TID) or neostigmine (0.04 mg/kg SQ QID). Immunosuppressive dosages of prednisone are recommended in animals that do not respond to anticholinesterase therapy. The prognosis is generally good and many dogs will undergo spontaneous remission, evident by a decrease in antibody titer. The prognosis is guarded for animals with aspiration pneumonia or persistent weakness.

Acute idiopathic polymyeloneuritis is a common inflammatory disease primarily affecting the ventral nerve roots and peripheral nerves. It is common in dogs and rare in cats. Clinical signs often develop 7–14 days after a raccoon bite or scratch (Coonhound paralysis); however, other affected animals have no exposure to...
raccoons. A similar syndrome can occur in dogs and cats within 1--2 wk of vaccination. An immune-mediated reaction to raccoon saliva or other antigen is suspected. Typically, flaccid paresis begins in the pelvic limbs and progresses within 1--2 days to tetraparesis and, in some cases, facial and laryngeal weakness. Occasionally the thoracic limbs are initially affected. Death from respiratory paralysis can occur in severe cases. Spinal cord reflexes are weak to absent and severe muscle atrophy is evident within 10--14 days. Pain perception is intact and some dogs may appear hyperesthetic. Mentation and appetite are not affected. Urination, defecation and tail movement usually remain normal. Analysis of CSF collected from the lumbar subarachnoid space shows increased protein with a normal cell count. Electromyography shows denervation and nerve conduction studies show marked dispersion and prolonged latency of F-waves, indicative of slowed conduction in the ventral roots. There is no effective treatment other than nursing care, and corticosteroids are not helpful. Most affected animals begin to improve spontaneously within 3 wk, with complete recovery by 2--6 mo. Patients with severe signs and marked muscle atrophy may recover incompletely. Relapses can occur, especially in hunting dogs that frequently encounter raccoons. Pathologically there is inflammation, demyelination, and varying degrees of axon degeneration in the ventral nerve roots and peripheral nerves.

Tick paralysis is characterized by rapidly progressing paralysis caused by several species of ticks. Some female ticks produce a salivary toxin that interferes with acetylcholine release at the neuromuscular junction. In North America *Dermacentor variabilis* and *Dermacentor andersoni* are most often incriminated, with dogs, sheep, and cattle being the domestic animals most commonly affected. In Australia, *Ixodes holocyclus* commonly causes an especially severe form of tick paralysis in dogs, cats, and sheep. In Africa, the major tick associated with paralysis is *Ixodes rubicundus*, with cattle, sheep, goats, and, rarely, dogs, being affected. A wide variety of ticks affect animals in Europe and Asia. Clinical signs consist of paraparesis that progresses within 24--72 hr to flaccid tetraplegia, with weak to absent spinal cord reflexes. Sensory perception and consciousness remain normal. Dysphagia, facial paralysis, masticatory muscle weakness, and respiratory paralysis may occur in severe cases. Treatment consists of removal of the tick. Application of a topical acaricide is used to kill any hidden ticks. In general, prognosis is good and recovery occurs within 1--2 days.
VERIFICATION OF THE ELEMENT POC BLOOD GAS INSTRUMENT FOR USE WITH CAMELID BLOOD, WITH DETERMINATION OF REFERENCE INTERVALS.

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Clinical Pathology Laboratory Director  

Department of Biomedical and Diagnostic Sciences  
College of Veterinary Medicine, University of Tennessee  
Knoxville, TN

This presentation provides an overview of the following published study:  

Authors wish to thank the Department of Biomedical and Diagnostic Sciences Fund for Education, Advancement, and Research for funding this study. Additionally we thank Dr. Andrea Lear, Dr. Stephanie Davenport, Dr. Kristen Judy, Ms. Celia Hurley, and staff of the UTVMC Clinical Pathology and Parasitology laboratories for their technical support of this project.

Method Validation and Verification

Method validation and verification are a series of experiments designed to prove that an analytical method:

- Measures what it is intended to measure
- Meets instrument or assay manufacturer’s claims for analytical performance (“verification”)
- Meets the laboratory’s analytical quality goals
- Performs properly in the target species

Method validation is important because you cannot assume that a method that works well in one species will work equally well in another. This is true for all assays but is especially important for any assays involving reagent antibodies.

Method verification is important because instrument and assay operators should verify that the instrument or test kit they have purchased performs according to manufacturer performance claims (in other words, verify it works and you got what you paid for!).

Considerations for method validation/verification study design include:

- Intended use of the test
- Complexity of the assay
- Stability of the measured substance (a.k.a. measurand or analyte)
- Type of sample (whole blood vs. plasma vs. serum vs. other)
- Species of interest
- Health and safety considerations (e.g., toxic or biohazardous reagents?)
- What is known about the method (published literature, experience of other users)
- Whether any governmental regulations apply

An analytical quality goal is a “yardstick” against which analytical performance is assessed. Goals can be based on expert consensus or biological variation data and are often expressed in units of percent. Goals can be established for for imprecision, bias, and total analytical error (which is calculated from imprecision and bias). The basic idea is that if observed performance metrics (imprecision, bias, and/or total error) are numerically less than the corresponding quality goal, performance is considered acceptable.

Analytical properties that can be studied scientifically as part of method validation/verification include:
<table>
<thead>
<tr>
<th>Property</th>
<th>Explanation</th>
<th>Represented by (all are calculated from the study data)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precision (repeatability)</td>
<td>Dispersion of data resulting from repeated measurement of the same sample</td>
<td>Standard deviation (SD)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Coefficient of variation (CV)(^a)</td>
</tr>
<tr>
<td>Accuracy</td>
<td>Difference between a measured value and some representation of “true” analyte concentration</td>
<td>Mean difference (e.g., between results from two methods)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Percent bias</td>
</tr>
<tr>
<td>Linearity</td>
<td>Range of concentrations over which the mathematical relationship between analyte concentration and measured result is linear</td>
<td>Usually same as the instrument’s reportable range (i.e., minimum to maximum concentration that the instrument will report)</td>
</tr>
<tr>
<td>Analytical specificity</td>
<td>Whether the method is subject to interfering substances in the sample (e.g., lipemia, hemolysis, icterus)</td>
<td>Percent interference</td>
</tr>
<tr>
<td>Recovery</td>
<td>Whether there is an effect of potential competing reactions in the sample matrix</td>
<td>Percent recovery</td>
</tr>
<tr>
<td>Analytical sensitivity</td>
<td>Smallest concentration that the method can detect(^b)</td>
<td>Detection limit</td>
</tr>
</tbody>
</table>

\(^a\) SD expresses imprecision in measurand units, whereas CV expresses it in units of percent. CV is useful for comparing imprecision across various analytes that may have differing units. CV is SD expressed as a percentage of the mean of the data, or CV = (SD/mean)*100.

\(^b\) Most important for drug tests, hormone assays, and other tests measuring very low concentrations of analyte.

**What are the basic steps of method validation/verification?**

1. **Acquire & set up instrument or test kit**
   - Company field engineer may help here

2. **Personnel learn operation**
   - Writing an SOP for your particular setting is recommended!

3. **Evaluate basic analytical performance:**
   - a. Imprecision (repeatability study)
   - b. Bias (method comparison study)
   - c. Compute observed total error & compare to a quality goal

4. **If needed, additional studies:**
   - Linearity, reportable range
   - Interferents
   - Recovery
   - Detection limit

5. **Generate new (or validate imported) reference intervals for target species**

When performance deemed satisfactory

Ready for clinical use!

ASVCP = American Society for Veterinary Clinical Pathology; SOP = standard operating procedure.
Verification and validation of point-of-care instruments (those designed for in-clinic or “cage-side” use) is inherently challenging due to the cost of consumable supplies, limited ability of the instrument operator to manipulate the testing process, and the labile nature of samples (often whole blood) and measurands (e.g., blood gases).

---

### Alpaca reference intervals for the Heska Element POC instrument (EPOC).

Established using a non-parametric statistical method. Reference limits and confidence limits were rounded to the number of significant figures reported by the EPOC instrument for that measurand.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Units</th>
<th>Distribution Gaussian?a</th>
<th>Lower Limit (90% CI)</th>
<th>Upper Limit (90% CI)</th>
<th>Based on (sample)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>None</td>
<td>No</td>
<td>7.310 (7.296 to 7.372)</td>
<td>7.514 (7.500 to 7.564)</td>
<td>Ven/mix</td>
<td>79</td>
</tr>
<tr>
<td>pCO2</td>
<td>mmHg</td>
<td>Yes</td>
<td>25.7 (25.5 to 27.7)</td>
<td>50.5 (47.3 to 53.3)</td>
<td>Ven/mix</td>
<td>79</td>
</tr>
<tr>
<td>pO2</td>
<td>mmHg</td>
<td>No</td>
<td>16.3 (13.1 to 19.8)</td>
<td>60.0 (52.8 to 172)</td>
<td>Ven/mix</td>
<td>79</td>
</tr>
<tr>
<td>HCO3</td>
<td>mmol/L</td>
<td>Yes</td>
<td>17.3 (15.7 to 18.1)</td>
<td>32.7 (31.3 to 35.2)</td>
<td>Ven/mix + arterial</td>
<td>96</td>
</tr>
<tr>
<td>BE(b)</td>
<td>mmol/L</td>
<td>No</td>
<td>-6.5 (-8.9 to -5.8)</td>
<td>8.3 (7.0 to 10.0)</td>
<td>Ven/mix + arterial</td>
<td>96</td>
</tr>
<tr>
<td>BE (ECF)</td>
<td>mmol/L</td>
<td>Yes</td>
<td>-7.3 (-10.0 to -6.4)</td>
<td>9.0 (7.8 to 11.2)</td>
<td>Ven/mix + arterial</td>
<td>96</td>
</tr>
<tr>
<td>SO2</td>
<td>%</td>
<td>Yes</td>
<td>23.8 (15.9 to 30.8)</td>
<td>91.6 (88.8 to 99.7)</td>
<td>Ven/mix</td>
<td>79</td>
</tr>
<tr>
<td>Na</td>
<td>mmol/L</td>
<td>No</td>
<td>140 (139 to 145)</td>
<td>156 (154 to 158)</td>
<td>Ven/mix + arterial</td>
<td>96</td>
</tr>
<tr>
<td>K</td>
<td>mmol/L</td>
<td>Yes</td>
<td>4.0 (3.8 to 4.2)</td>
<td>5.8 (5.7 to 7.2)</td>
<td>Ven/mix + arterial</td>
<td>96</td>
</tr>
<tr>
<td>Ca</td>
<td>mmol/L</td>
<td>Yes</td>
<td>1.12 (1.11 to 1.14)</td>
<td>1.43 (1.38 to 1.44)</td>
<td>Ven/mix + arterial</td>
<td>96</td>
</tr>
<tr>
<td>Cl</td>
<td>mmol/L</td>
<td>Yes</td>
<td>104 (103 to 107)</td>
<td>119 (118 to 120)</td>
<td>Ven/mix + arterial</td>
<td>96</td>
</tr>
<tr>
<td>TCO2</td>
<td>mmol/L</td>
<td>Yes</td>
<td>18.1 (16.6 to 19.0)</td>
<td>34.1 (32.6 to 36.8)</td>
<td>Ven/mix + arterial</td>
<td>96</td>
</tr>
<tr>
<td>AG</td>
<td>mmol/L</td>
<td>No</td>
<td>14 (14 to 15)</td>
<td>21 (20 to 24)</td>
<td>Ven/mix + arterial</td>
<td>96</td>
</tr>
<tr>
<td>Hct</td>
<td>%</td>
<td>Yes</td>
<td>15 (15 to 18)</td>
<td>31 (30 to 32)</td>
<td>Ven/mix + arterial</td>
<td>96</td>
</tr>
<tr>
<td>Hgb</td>
<td>g/dL</td>
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<td>5.1 (4.9 to 6.0)</td>
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<td>Glucose</td>
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<td>Yes</td>
<td>91 (87 to 95)</td>
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CI = confidence interval; n = number of samples.
Based on Anderson-Darling test for normality.

Five outliers having high lactate concentrations (from 6.36 to 9.57 mmol/L) were omitted following discussion by the authors. Subjective impression during blood collection was that stress impacted this analyte significantly; unfortunately, study records did not permit retrospective identification of all animals deemed "stressed" during collection. See published article for additional details.

Llama data for the Heska Element POC instrument (EPOC).
Measured values are given as reported by the instrument. Calculated values are rounded to the number of significant figures reported by the EPOC instrument for that measurand.

**THESE ARE NOT STATISTICAL REFERENCE INTERVALS – RATHER, MINIMUM AND MAXIMUM VALUES REPRESENT A SINGLE, SMALL LLAMA POPULATION. THESE ARE INTENDED AS A GUIDELINE ONLY. APPLY TO OTHER LLAMAS WITH CAUTION.**

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Units</th>
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<td>BE(b)</td>
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<td>BE (ECF)</td>
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<tr>
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<td>AG</td>
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<tr>
<td>Hct</td>
<td>%</td>
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<td>30</td>
<td>25 ± 3.0</td>
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<tr>
<td>Hgb</td>
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<td>6.6</td>
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<td>Glucose</td>
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<td>108 ± 9.51</td>
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<td>2.16 ± 0.298</td>
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<td>17</td>
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</tbody>
</table>

Additional suggested resources, if you are interested in quality assurance of in-clinic laboratory testing:
3. American Society for Veterinary Clinical Pathology (ASVCP) guidelines (various), available for free at [www.asvcp.org](http://www.asvcp.org) (see “Publications” and then “QALS Guidelines”).
Meniscal Tips and Tricks

Kyle Snowdon, DVM, DACVS-SA
University of Tennessee, Knoxville, TN

Key Points:
- The medial and lateral menisci have different attachments.
- Stifle instability leads to damage of the medial meniscus.
- Early CrCl diagnosis and treatment may spare the meniscus.
- The medial meniscus is firmly attached to the tibial plateau by the medial collateral ligament.
  - Less mobile than the lateral collateral ligament.
- Damage is most common to the caudal pole of the medial meniscus.
- When using a meniscal probe to inspect the menisci it is important to recognize that the capsule should be firmly attached to the entire periphery of the medial meniscus (besides the meniscotibial ligament).

A healthy meniscus is crucial to the biomechanics and overall health of the canine stifle joint. Damage results in pain, inflammation and ultimately osteoarthritis. Therefore, it is crucial to accurately diagnose and develop a treatment plan for meniscal pathology in our patients.

The meniscus is a C-shaped disc of fibrocartilage between the condyles of the femur and tibia. The canine stifle joint contains two menisci located medially and laterally in the femorotibial joint space. It has an important role in load transmission, shock absorption, joint stability, proprioception, lubrication, and prevention of synovial impingement. Of particular importance is load transmission, where the menisci transmit a portion of the axial forces across the knee joint by converting this load into “hoop stresses.” Failure of any part of the meniscus or its attachments may lead to loss of hoop stress, which leads to concentration of the forces in the femorotibial joint and development of articular cartilage wear and subsequent osteoarthritis.

It’s important to understand not only the anatomy of the meniscus, but how damage to other structures in the joint may contribute to meniscal pathology. The menisci are anchored to the tibia and femur by five meniscal ligaments (cranial tibial and caudal tibial ligaments of the lateral and medial menisci and the lateral meniscofemoral ligament) and to each other by the intermeniscal ligament. The medial collateral ligament (MCL) remains taught in both flexion and extension, while the lateral collateral ligament (LCL) is taught in extension only. Laxity of the LCL during flexion allows normal internal rotation of the tibia and caudal displacement of the lateral femoral condyle. The lateral meniscus moves with the femoral condyle because of the attachment of the lateral meniscofemoral ligament. However, the medial meniscus has limited mobility due to a firm attachment to the MCL and absence of a meniscofemoral ligament.

In conditions such as cranial cruciate ligament (CrCl) rupture, increased cranial tibial translation may result in damage to the medial meniscus, which has been identified in 50-70% of cases at the time of CrCl surgery. Several types of meniscal pathology are possible due to crushing or tearing during tibial translation (radial, "bucket-handle", and caudal peripheral detachment with folding). The meniscus has a poor capacity to heal, due to a limited blood supply, which is isolated to its outer one-third, which limits treatment options available to the surgeon. The most common methods for treating meniscal tears include: complete meniscectomy, caudal pole meniscectomy, partial meniscectomy (removal of the torn portion only) and meniscal release. Each one of these treatments will provide pain relief and return to function, though they compromise meniscal function and will lead to the development of osteoarthritis.
The risk of medial meniscal tears increases 12.9-fold with complete rupture of CrCl. Therefore, it is important to diagnose partial or incomplete CrCL disease early before cranial drawer is present. Common methods of diagnosis when drawer is absent include: pain on hyperextension of the stifle joint, stifle effusion and medial buttress. The presence of medial buttress points to the chronicity of the condition, ruling out acute trauma to the animal’s knee. Modalities such as physical therapy may lead to short term improvement in these cases, but they are unlikely to change the progression of the disease to a complete rupture. A common case presentation to our institution includes waxing and waning mild – moderate weight bearing lameness of several months’ duration. These patients often develop a more severe lameness following normal activity (running in the backyard) from complete rupture of the ligament. Preservation of the meniscus may be helped by early diagnosis and treatment of CrCl disease before complete rupture of the ligament occurs.

Stifle evaluation products:

- Stifle distractor (multiple sizes)
  - JorVet $210
- Ventura Stifle Thrust Levers
  - JorVet $150
  - IMEX
  - Arthrex
- Meniscal probe
  - JorVet $23 (1mm small dog, 2 mm large dog)
- Micro Hohman Arthroscopic
  - JorVet $39.00
- Meniscal Clamp
  - JorVet: Micro-toothed Meniscus Clamp $36
Background & Significance:
- Monitoring of patients’ vital parameters under anesthesia is a standard of care
- Specialized monitoring equipment has improved in quality, sensitivity, and affordability during the last 25 years
- Subjective and objective patient monitoring should be supported with appropriate continuous monitoring systems
- Vigilant anesthetic monitoring improves early recognition of problems, and decreases the risk of mortality and morbidity

Minimum Recommendations for Patient Monitoring:
- Cardiac rate and rhythm
- Ventilation and oxygenation
- Anesthetic depth, muscle relaxation, and analgesia
- Body temperature

Types of Anesthetic Monitors:

ELECTROCARDIOGRAM (ECG; EKG)
- Uses: assessment of cardiac rate and rhythm; detection of rhythm disturbances, changes in cardiac conduction system
- Advantages: continuous and real-time information allowing immediate interpretation; non-invasive; available on most multi-parameter commercial monitors; may also be used in the pre- and post-anesthetic periods
- Limitations: may receive interference from other electrical devices (cautery, power supply, supplemental heating devices, etc.); lead placement locations; lead contact interference or inadequate signal; requires skilled interpretation; pulseless electrical activity (PEA) may be present in cardiac arrest

DOPPLER FLOW DETECTOR
- Uses: assessment of peripheral (or cardiac) pulsation rate and rhythm; detection of rhythm disturbances; may be used to determine blood pressure if placed over a distal artery
- Advantages: continuous and real-time information allowing immediate recognition of issues or changes; non-invasive; low to moderate cost; may be used during pre- and post-anesthetic periods; provides audible monitor of pulse quality; provides systolic blood pressure estimate (dogs) or systolic/mean arterial pressure estimate (cats)
- Limitations: audible pulse quality may be affected by drugs that affect peripheral perfusion (alpha-2 agonists), blood viscosity (anemia, dehydration, etc.); movement or disruption of probe; limited ability to interpret arrhythmia; blood pressure must be obtained manually

OSCILLOMETRIC (NON-INVASIVE) BLOOD PRESSURE
- Uses: measurement of blood pressure; some monitors concurrently provide a pulse rate
- Advantages: non-invasive; automated blood pressure measurements (every 3-5 minutes); minimal interference with placement of cuff on distal limb or tail base; accurate measurements of mean
arterial pressure, algorithm calculates systolic and diastolic pressures; may be included in some multiparameter monitors

- Limitations: delay in readings (3-5 minutes between measures); may be difficult to select appropriate cuff sizes for all size/shape patients; too large cuff will result in decreased blood pressure reading, too small cuff results in overestimation of blood pressure; should not be positioned over bony structures, joints, matted hair, non-perfused limbs; cuff position should be level with the heart or falsely high/low readings may be obtained; may be more useful in observing trends; inaccuracy at severe hypo- or hypertensive states

**ARTERIAL (DIRECT) BLOOD PRESSURE**

- Uses: measurement of blood pressure, most accurate
- Advantages: continuous measurement, shows immediate changes; accuracy with systolic, diastolic, and mean arterial pressures at any cardiovascular status; allows assessment of arterial pressure waveform and pulse pressure variability
- Limitations: invasive – requires placement of an arterial catheter; specialized transducer required, and additional cost on multiparameter monitors

**CAPNOGRAPHY**

- Uses: measurement of partial pressure of end-tidal carbon dioxide; confirmation of correct endotracheal tube placement; assessment for airway obstructions, leaks, or tube disconnections; assessment of ventilation and systemic perfusion
- Advantages: non-invasive; simplicity of use; continuous measurement with numerical and graphical representation; typically good agreement with PaCO₂ in small animals; often included in multiparameter monitors; portable models available for low-moderate cost
- Limitations: may increase dead space, depending on type of connection, with small size patients; accuracy depends on tidal volume and respiratory rate (depends on patient size), may see artifactually low values with small patients, high respiratory rates

**PULSE OXIMETRY**

- Uses: estimates percent saturation of hemoglobin with oxygen (SpO₂), and pulse rate; some models include plethysmography
- Advantages: non-invasive; simplicity of use and interpretation; rapid function, real-time values; low-moderate cost with additional options available (plethysmography, combined with capnography); portable models available; may be used in pre- and post-anesthetic periods; plethysmography can be used to assess pulse pressure variations non-invasively
- Limitations: differing technologies between models require specific probes/placement on tissues; probes measure light wavelength, errors common (excessive ambient light, motion, poorly perfused tissues with low pulsatile flow; pigmentation; loss of signal when distal to blood pressure cuff; arrhythmias; etc.); inaccuracy possible with other species, severe anemia, carboxyhemoglobinemia, methemoglobinemia

**References:**

Small Animal Reproductive Surgery
Karen Tobias, DVM, MS, DACVS

Notes about Routine Procedures:

Scrotal versus prescrotal castration: Scrotal castration can be performed in any size dog. Prescrotal castration is difficult in young dogs because the testicles slide into the inguinal rings, making them hard to find. Dogs undergoing prescrotal castrations and an intradermal closure have greater incidence of self-trauma and shorter surgical times than those castrated through a scrotal incision and with a single simple interrupted subcutaneous stitch for closure (Woodruff et al, Vet Med 2015). Caudal scrotal incisions are also no more likely to cause complications than prescrotal incisions (Snell et al, New Z J 2015).

Ovariectomy vs. OHE: Ovariectomy without hysterectomy is becoming more common, particularly with laparoscopic spays. Ovariectomy alone does not increase the risk of pyometra, since endometritis, pyometra, and stump pyometra require progestagens to develop. Ovariectomy may be less traumatic because incision size is smaller and tissues are handled less; the only increased risk compared to OHE is future development of uterine tumors, which are rare in dogs (0.03%). Most of these tumors (90%) are benign leiomyomas; therefore, the true overall incidence of malignant uterine tumors is 0.003%.

In a recent study comparing dogs undergoing ovariectomy or ovariohysterectomy, there was no significant difference in surgical time, pain scores, or wound scores.

Ovarian sparing surgery: Hysterectomy alone as a method for preventing pyometra and avoiding the inconvenience of vaginal discharge during heat cycles is offered as an option to other. There are no studies on short or long-term outcome of the procedure. When ovarian-sparing hysterectomy is performed as an open surgical technique, the incision must be large enough to see the ovaries and the cervix (https://www.parsemus.org/projects/ovary-sparing-spay/). The vessels to the uterine horns (including those between the ovary and uterine horn) are ligated, and the cervix is clamped at either end, ligated, and transected. The entire uterus must be removed to remove the risk of stump pyometra, so the distal ligation must be at or beyond the cervix. There is a risk of vaginal rupture if hysterectomized dogs are allowed to copulate.

Greyhounds: Greyhounds have an unusually high risk of subcutaneous hemorrhage after ovariohysterectomy and castration. In fact, 26% of retired racing greyhounds had significant subcutaneous hemorrhage. Potential bleeding tendencies are not identifiable on preoperative blood work or coagulation panels. Administration of fresh frozen plasma decreases the prevalence of hemorrhage, but not all dogs respond. While the cause of the bleeding disorder has not been identified, it is thought to be a result of abnormal fibrinolysis. Administration of aminocaproic acid on the day of surgery and for 4 days thereafter may decrease the risk.

Pedicle ties: In high volume spay practices, ovarian pedicles in cats are often “tied on themselves” (pedicle tie), similar to cat castration. Complication rates are low, with hemorrhage noted in 0.28% and usually detected in surgery. Surgery times are about 2 minutes faster when pedicle ties are used.
Female Reproductive Surgeries: Beyond Pyometra and C-section

Unusual Uterine Diseases:
While congenital uterine anomalies are rare, the veterinarian must be prepared for these conditions. Congenital anomalies are identified in 0.09% of female cats and 0.05% of female dogs. The most common anomaly is unicornuate uterus. Other anomalies include segmental agenesis of one uterine horn and uterine horn hypoplasia. Ipsilateral renal agenesis is present in 29% of cats and 50% of dogs with uterine anomalies. Both ovaries are usually present in animals with unilateral uterine abnormalities and are often farther cranial than normally expected. When segmental agenesis is present, the remaining cranial segment of the affected horn is usually fluid filled. In cats, uterine anomalies have also been associated with presence of ectopic, mummified fetuses.

Uterine prolapse is rare and is usually associated with prolonged parturition. One or both horns may prolapse into the cranial vagina or through the vulva. Animals may develop hemorrhagic shock, pain, perineal bulging, or excessive grooming. Diagnosis is by digital evaluation- an index finger can be slipped between the prolapsed tissue and vestibular wall. After stabilization, manual reduction with temporary vulvar suture closure can be attempted, but surgical amputation and OHE may be required.

Uterine torsion usually occurs with uterine distension from pregnancy, dystocia, pyometra, or a mass (e.g. an endometrial polyp). Clinical signs are those of “acute abdomen”, including abdominal pain, pyrexia, anorexia, and vomiting and dystocia in pregnant animals. If torsion involves only one horn, fetuses can be successfully passed from the unaffected horn.

Uterine rupture can occur with parturition or in association with pyometra. Small tears associated with dystocia can be repaired or treated by unilateral ovary and horn removal, but OHE is required for large tears, severe hemorrhage, or pyometra. The abdominal cavity must be thoroughly flushed to remove any contamination.

Of uterine masses, the most common in dogs is endometrial polyps, which are often associated with cystic endometrial hyperplasia. These polyps can be large enough to compress abdominal viscera, predispose the bitch to pyometra, or even lead to uterine horn torsion or rupture. Uterine tumors are uncommon, with leiomyoma being reported most often in bitches. The most common uterine tumor in cats is endometrial adenocarcinoma, which can develop in cats less than one year of age. Other reported tumors include lymphoma, hemangiosarcoma, fibroma, mast cell tumor, leiomyosarcoma, poorly differentiated sarcoma, and squamous cell carcinoma. Some animals are asymptomatic, while others present with pyometra or hydrometra. In most cases, treatment is ovariohysterectomy, with resection including the cervix.

Vaginal Hyperplasia and Prolapse: Vaginal hyperplasia is an exaggerated response to estrogen. Affected vaginal tissue become edematous, and the mucosal folds of the vaginal floor enlarge and protrude (prolapse) from the vulva. This is usually seen in intact, typically young bitches. Vaginal prolapse is a circumferential prolapse of tissue, including the urethral orifice. It can be associated with dystocia, tenesmus, or forced separation during mating, but its occurrence is rare. In a true prolapse of the vagina, the cervix is visible. Signs may include dysuria, excessive grooming, and a protruding mass that may bleed from trauma. Differentiation from uterine or bladder prolapse is by digital exam- with vaginal prolapse, a fornix (blind end recess) can be felt between the margins of the prolapsed vaginal tissue and the vaginal wall in dogs with vaginal prolapse. Hyperplastic and edematous tissues will usually regress when the bitch enters diestrus; until then, tissues should be kept lubricated and a retention suture can be placed temporarily across the vulva in valuable breeding dogs. Episotomy may be necessary for tissue reduction. Ovariohysterectomy is the treatment of choice for prevention. Dogs with necrotic or nonreducible tissue may require surgical excision.

Vulvar/Vaginal Tumors: The most common tumors of the canine vagina and vulva are leiomyomas and fibromas. Leiomyomas may be either intra- or extra- luminal and are often pedunculated. Clinical signs include vaginal discharge or bleeding, mass protrusion, excess grooming, dysuria, dyschezia,
constipation, or perineal swelling. They are diagnosed by visual or digital examination and vaginoscopy. Cytology is usually not helpful since these tumor types do not exfoliate easily. Treatment is surgical resection, which often requires an episiotomy; a urinary catheter should be placed during the procedure. Vulvar adenocarcinoma has been reported in dogs and cats and, in dogs, has been associated with hypercalcemia.

**Male Reproductive Surgeries: Beyond Cryptorchid Castration**

**Phimosis:** In dogs with phimosis, the preputial orifice is too small to allow extrusion of the penis. Causes can be congenital or acquired (e.g. inflammation, infection, neoplasia, trauma). Severely affected dogs may get urine retention or dribbling or secondary infections. The opening can be enlarged by making a midline incision on the craniodorsal aspect of the prepuce; some dogs may require removal of a full thickness, V-shaped wedge. Excision size should be large enough to prevent urine pooling without causing permanent exposure of the glans penis. The preputial mucosa is apposed to the ipsilateral skin edge with a simple interrupted or continuous pattern. In cats, phimosis is usually reported in kittens, with clinical signs of stranguria, pollakiuria, and vocalization when urinating. Diagnosis is made on physical exam by demonstrating inability to manually extrude the penis. Repair is similar to that in dogs.

**Paraphimosis:** Paraphimosis is the inability to retract the penis into the preputial cavity. Etiologies include a congenitally small preputial orifice with subsequent penile entrapment, ineffective preputial muscles, hypoplastic prepuce, trauma, infection, neoplasia, persistent erection from inability to drain the venous cavernous tissue, and sexual excitement. Swelling and engorgement of the penis makes retraction impossible, resulting in dryness, irritation, and even ischemic necrosis and urethral obstruction. Bands of preputial hairs may also encircle and cause or contribute to the condition. Treatment for a hypoplastic opening is surgical widening, with apposition of the preputial lining to the skin.

Paraphimosis can be a surgical emergency because it can result in ischemic necrosis of the penis and urinary obstruction. Treatment includes heavy sedation, reduction of swelling (cold compresses, hyperosmolar solutions such as sugar or mannitol), lubrication, and manual reduction. If retraction into the prepuce is impossible, the preputial opening may need to be temporarily or permanently enlarged (see phimosis, above). If the penis is necrotic, amputation may be required. If the muscles are weak, advance the prepuce cranially and shorten the muscles: remove a crescent-shaped piece of skin cranial to the prepuce; transect, excise, and reappose the muscles with horizontal mattress sutures; and close the skin. Phallopexy or partial penile amputation can also be used. For phallopexy, incise through the skin and subcutis at the junction of the prepuce and body wall. Cut through the preputial mucosa to expose the penile shaft. Make a superficial (epithelial) incision into the ventral aspect of the penile shaft and a second incision in the ventral preputial mucosa. Suture the preputial and penile mucosal epithelial edges together with simple interrupted sutures. Confirm that the penile shaft is sufficiently restrained before closing the remaining incision site.

**Hypospadias:** Hypospadias is a developmental anomaly characterized by abnormal location of the urinary orifice which, in a male dog, can be located anywhere along the ventrum of the glans penis to the perineum. Animals may have concurrent congenital defects such as cryptorchidism, penile hypoplasia, penile deviation, and preputial defects. Affected dogs should be castrated. Asymptomatic animals may require no other treatment; severely affected animals may require reconstructive surgeries or penile amputation.
URINE TROUBLE: CHRONIC KIDNEY DISEASE
Joe Bartges, DVM, PhD, DACVIM, DACVN
The University of Georgia
Athens, GA, USA

Overview of the Issue
CKD implies irreversible renal failure that remains stable for a period of time, but ultimately progresses. Although many things can cause chronic kidney disease, by the time chronic kidney disease is diagnosed the cause(s) is/are not present and not treatable. Kidneys are involved with whole body homeostasis; therefore, CKD affects general well-being. CKD is ultimately progressive. The cause(s) of progression of CKD is not completely known. It is likely that in typical situation, CKD results from repeated insults over time that result in sequential loss of nephrons. The compensatory response is an increase in single nephron GFR in the surviving nephrons. This results in maintenance of total GFR despite loss of functional renal tissue (renal reserve). There is dilation of the afferent arteriole and an increase in intraglomerular pressure resulting in increase in GFR and renal blood flow. There are trade-offs, however. The increase in GFR due to increase in renal blood flow and intraglomerular pressure increases likelihood of increased protein loss. Increased intraglomerular pressure is transmitted distally. There is activation and release of growth factors that promote tubulointerstitial fibrosis and glomerulosclerosis. Eventually, these adaptations result in loss of further nephrons and the cycle continues. Over time, renal reserve is lost as the threshold of nephron mass loss is surpassed resulting in progression of CKD to end stage.

Objectives of the Presentation
The objectives of the presentation are to:
• Outline the etiopathogenesis of CKD and mechanisms of progression
• Describe diagnostic testing for CKD
• Outline a management plan for patients with CKD including serial monitoring

Key Clinical Diagnostic Points
Clinical signs involve primarily change in water balance: polyuria / polydipsia (PU / PD), gastrointestinal signs (vomiting, hyporexia / anorexia, halitosis), and signs of chronic disease (weight loss, loss of body condition, unkempt appearance). Laboratory evaluation may reveal: azotemia, inappropriately dilute urine, hyperphosphatemia, metabolic acidosis, hypokalemia, non-regenerative anemia, bacterial UTI, systemic hypertension (occurs in 65-80% of patients), proteinuria.

International Renal Insufficiency Society (IRIS) Staging: The International Renal Insufficiency Society (http://www.IRIS-kidney.com) has developed staging system for animals with CKD and treatment based on staging. The staging system is designed for use with dogs and cats with CKD. A diagnosis of CKD is made first and staging is accomplished by evaluating. CKD is staged by magnitude of renal dysfunction and further modified (sub-staged) by presence or absence of proteinuria and/or hypertension. Proteinuria ONLY refers to renal proteinuria and not pre-renal (e.g. hyperglobulinemia) or post-renal (e.g. urinary tract infection, hematuria, etc), and is based on UPC.

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### UPC value

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<th>Dogs</th>
<th>Cats</th>
<th>Substage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.2</td>
<td>&lt;0.2</td>
<td>Non-proteinuric (NP)</td>
</tr>
<tr>
<td>0.2 to 0.5</td>
<td>0.2 to 0.4</td>
<td>Borderline proteinuric (BP)</td>
</tr>
<tr>
<td>&gt;0.5</td>
<td>&gt;0.4</td>
<td>Proteinuric (P)</td>
</tr>
</tbody>
</table>

### Systolic BP mm Hg

<table>
<thead>
<tr>
<th>Diastolic BP mm Hg</th>
<th>Adaptation when breed-specific reference range is available *</th>
<th>Substage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;150</td>
<td>&lt;10 mm Hg above reference range</td>
<td>AP0: Minimal Risk (N)</td>
</tr>
<tr>
<td>150 – 159</td>
<td>10 – 20 mm Hg above reference range</td>
<td>AP1: Low Risk (L)</td>
</tr>
<tr>
<td>160 – 179</td>
<td>20 – 40 mm Hg above reference range</td>
<td>AP2: Moderate Risk (M)</td>
</tr>
<tr>
<td>≥ 180</td>
<td>= 40 mm Hg above reference range</td>
<td>AP3: High Risk (H)</td>
</tr>
</tbody>
</table>

No evidence of end organ damage/complications   No complications (nc)
Evidence of end organ damage/complications       Complications (c)
Blood pressure not measured                      Risk not determined (RND)

#### Tests of Renal Function:
Renal function testing for CKD has conventionally relied on assessing azotemia (increased BUN and/or creatinine) and urine specific gravity (USG). While BUN and creatinine are biomarkers and creatinine tends to be a better test of renal function, they are influenced by non-renal situations such as hydration, diet, and muscle mass. Additionally, they do not tend to increase until a substantial (> 75%) of nephron mass is lost. It is possible to determine GFR by measuring reduction of an injected substance in the blood over time such as creatinine, iohexol, or DTPA (a radiopharmaceutical). There are other biomarkers that have and are being evaluated. Symmetric dimethylarginine (SDMA) is available. SDMA is a small molecule that originates from hydrolysis of methylated proteins and appears to be exclusively eliminated by glomerular filtration with minimal extra-renal influence although anything that alters renal blood flow and GFR (such as hydration status) can influence SDMA levels. In dogs with rapidly progressing CKD, SDMA correlated strongly with GFR estimated using iohexol clearance and tends to increase with loss of approximately 40% of nephron mass. In cats with CKD, SDMA appears to have similar benefits to dogs and changes approximately 17 months earlier than the increase in serum creatinine.

#### MANAGEMENT OF CKD.
The goal of management is to minimize excesses and deficits induced by CKD in order to improve quality and quantity of patient’s life

**NUTRITION.** The goal of nutritional support is to maintain optimal body condition and lean muscle mass. Anorexia and nausea occur commonly with CKD. Treatment involves feeding a highly palatable diet, modifying feeding patterns, and treating uremic gastroenteritis. Treatment of uremic gastroenteritis involves decreasing dietary protein (stimulates gastric acid production), decreasing gastric acidity with H2 blockers, proton pump inhibitors, and/or sucralfate. Mirtazoamine, a noradrenergic and serotonergic antidepressant stimulates appetite and is an anti-emetic. Maropitant is a neurokinin-1 (NK-1) antagonist that is used for motion sickness and is an anti-emetic. Capromorelin is a growth hormone secretagogue that stimulates appetite in dogs. If necessary feeding tubes may be used to facilitate nutritional and fluid support and provides a means to administer medications. One theory of progression of CKD involves intraglomerular hypertension in the remaining nephrons. This is beneficial in that it keeps GFR up; however, the intraglomerular hypertension may ultimately result in loss of surviving nephrons and progression. Feeding diets or administering omega-3 fatty acids has been shown to be beneficial in dogs by reducing intraglomerular hypertension and inflammation. An omega-6 to omega-3 fatty acid ratio of 3:1 to 5:1 appears to be a reasonable intake and is present in many renal failure diets. Other treatments such as a medicinal rhubarb extract (Rubenal) and a proprietary mixture of amino acids and peptides (RenAvast, AminAvast) have not been shown to be beneficial.

**ELECTROLYTES.** Hypokalemia may occur especially in cats due to anorexia, excessive losses, transcellular shift due to metabolic acidosis, and activation of the renin-angiotensin-aldosterone system. Clinical signs include polymyopathy, worsening of renal failure, and anorexia. Treatment is aimed at maintaining the serum potassium.
Mineral and bone disorder in CKD (MBDCKD) occurs, in part, because of phosphorous retention and of shortened survival. Treatment is decrease serum phosphorous concentration to normal. Serum phosphorous concentration may be decreased by: feeding a low phosphorous diet, administering phosphate binders with food (e.g. aluminum hydroxide, calcium acetate, sevelamer hydrochloride, lanthanum carbonate, or chitosan + calcium carbonate), and/or administering vitamin D. When administering vitamin D, dietary phosphorous should be restricted and serum phosphorous concentration should be normalized because of risk of hypercalcemia and increasing calcium x phosphorous solubility product. To date, only dogs in stage III or IV IRIS CKD that documented worsening azotemia with increased dietary sodium intake; however, other studies have not shown this and dietary sodium has not been shown to be correlated with hypertension.

**PH OF BLOOD (ACID-BASE STATUS).** Metabolic acidosis occurs commonly with CKD because of retention of organic acids, decreased renal ability to regenerate and reclaim bicarbonate, decreased ammoniagenesis (ammonia is a buffer and is renally excreted with acid), and generation of acids from catabolism. Treatment involves feeding a diet that is low protein = as dietary protein is a main source of organic acids and alkalinizing (most contain potassium citrate).

**PROTEINURIA.** Proteinuria is not just a marker of glomerular disease but is also associated with progression of CKD as it stimulates renal fibrosis and activates inflammation. Treatment is indicated with IRIS CKD stage 1 and UPC > 1.0 to 2.0 and IRIS CKD stages 2-4 when UPC > 0.4 in cats and 0.5 in dogs. Treatment involves feeding a renal diet, administering an ACE-I and/or ARB, and omega-3 fatty acids.

**HYDRATION.** Polyuria due to CKD is offset by compensatory polydipsia but dehydration may occur if this is inadequate. Provide clean and fresh water daily. Supplemental SQ fluids may be administered if needed, which appears to be more common in cats than in dogs. In a hospital situation, IV fluids should be administered.

**RETENTION OF WASTES.** Elimination of wastes particularly nitrogen-containing compounds is an important function of the kidneys. Reduction of dietary protein seems logical but results of studies are contradictory as to whether dietary protein restriction alters progression of CKD. Dietary protein restriction may be associated with: decreased azotemia, decreased hyperphosphatemia, decreased metabolic acidosis, and decreased gastric acid secretion. Three studies, two in cats and one in dogs, of spontaneously occurring CKD, demonstrated a beneficial effect from feeding a renal failure diet when compared with feeding a maintenance diet. Level of dietary protein found in renal failure diets is adequate for maintenance of adult animals is not likely to be associated with protein malnutrition.

**Prebiotics:** Feeding diets that contain soluble fiber may redistribute a small amount of nitrogen into the gut for elimination thus decreasing the amount required by the kidneys to eliminate (“nitrogen trapping”)

**Probiotics:** involve administering live bacteria. One formulation, Azodyl, is marketed as “enteric dialysis”. In one study of cats with CKD, there was no benefit and administration of Azodyl was not associated with decreasing the degree of azotemia.

**OTHER RENAL INSULTS – AVOID.** Dehydration may precipitate an acute renal failure episode making the chronic kidney disease worse. Certain situations and drugs may be directly nephrotoxic or may worsen renal failure including: aminoglycosides, urinary acidifiers, catabolic drugs (e.g. immunosuppressive drugs), and non-steroidal anti-inflammatory drugs, and UTI. NSAIDs may be nephrotoxic if given in high enough dose but at low doses may be beneficial in CKD by decreasing inflammation while maintaining renal vasodilation.

**NEUROENDOCRINE FUNCTION.** There are 3 neuroendocrine changes occurring with CKD, renal secondary hyperparathyroidism, hypoproliferative anemia, and systemic arterial hypertension.

**Mineral and bone disorder in CKD (MBDCKD)** MBDCKD occurs, in part, because of phosphorous retention and decreased calcitriol (vitamin D3) metabolism by the failing kidneys. Hyperphosphatemia may result in renal mineralization and loss of nephrons. Hyperphosphatemia is associated with progression of chronic kidney disease and of shortened survival. Treatment is decrease serum phosphorous concentration to normal. Serum phosphorous concentration may be decreased by: feeding a low phosphorous diet, administering phosphate binders with food (e.g. aluminum hydroxide, calcium acetate, sevelamer hydrochloride, lanthanum carbonate, or chitosan + calcium carbonate), and/or administering vitamin D. When administering vitamin D, dietary phosphorous should be restricted and serum phosphorous concentration should be normalized because of risk of hypercalcemia and increasing calcium x phosphorous solubility product. To date, only dogs in stage III or IV IRIS benefit from calcitriol therapy; however, no study has documented benefit of vitamin D in cats with any stage.

**Hypoproliferative anemia.** Normocytic, normochromic non-regenerative anemia occurs in many animals with chronic kidney disease. It may induce progression of disease due to decreased blood flow, stagnation of blood, oxidative stress, decreased oxygen diffusion, and induction of fibrosis. Causes of anemia include decreased erythropoietin production, nutritional imbalances, and blood loss due to uremic gastroenteritis. Treatment includes maintaining a good nutritional status, minimizing GI blood low, and stimulating red blood cell production.
While anabolic steroids have been used, they are associated with heptatoxicty. Recombinant human erythropoietin (rHuEPO) and its synthetic analog darbepoetin have been used successfully in dogs and cats with chronic kidney disease that are severely anemic. Many patients receiving rHuEPO feel better even if their anemia does not improve. Darbepoetin may be associated with fewer incidence of antibody production and is administered weekly and is the hormone replacement of choice. Darbepoetin should be started when even mild anemia is present with the goal of hormone replacement therapy being a PCV of 35-40%. Supplemental iron dextran should be given.

**Systemic arterial hypertension (SAH).** SAH occurs commonly and is due, in part, to activation of RAAS, activation of sympathetic nervous system, increased ADH due to hypovolemia. End-target organ damage due to SAH include eyes (retinal hemorrhage and detachment, blindness), kidneys (proteinuria, progression), heart (left ventricular hypertrophy), and brain (encephalopathy, seizures, death). The greater the degree of SAH the higher the likelihood of hypertensive-related complications. The goal of treatment is a systolic blood pressure (sBP) < 150 mmHg. Treatment involves feeding a renal diet and administering anti-hypertensive drugs. Calcium channel blockers are most effective and lower sBP by an average of 50 mmHg. ACE-I are less effective and lower sBP by an average of 10 mmHg but are more effective for treating proteinuria. Benazapril does not slow progression in animals with CKD unless UPC is > 1. Angiotensin receptor blockers (ARB) may be used alone or in conjunction with an ACE-I and/or CCB.

**OTHER POTENTIAL TREATMENTS.** Renal transplantation has had success in cats and dogs but more so in cats. In one study, 50% survival time was over 500 days. Intermittent hemodialysis may be performed in patients with IRIS CKD stage 4 disease. Mesenchymal stem cells (MSCs) have been proposed as a novel treatment option for the management of CKD although there are no conclusive data.

**SERIAL MONITORING.** Chronic kidney disease is progressive and thus a dynamic disease. Serial monitoring of body condition, body weight, thoracic auscultation, blood pressure, CBC and serum biochemical profile, urinalysis, and urine culture are necessary to adjust treatment. Dietary modification can offset many deficiencies and excesses that occur with chronic kidney disease. Dietary modification includes more than just dietary protein restriction as renal failure diets are more calorically dense, may contain omega-3 fatty acids, may contain soluble fiber, low phosphorous, low sodium, potassium replete, alkalinizing, and water soluble vitamin replete.
### Key Therapeutic Points

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Dosage for dogs (D) or cats (C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H2 blocker</td>
<td>Famotidine</td>
<td>D, C: 1-2 mg/kg PO q12h</td>
</tr>
<tr>
<td></td>
<td>Ranitidine</td>
<td>D, C: 1-2 mg/kg PO q12h</td>
</tr>
<tr>
<td>Gastroprotectant</td>
<td>Sucralfate</td>
<td>D: 0.5-1 gm PO q8-12h; C: 0.25-0.5 gm PO q8-12h</td>
</tr>
<tr>
<td>Proton pump inhibitor</td>
<td>Omeprazole</td>
<td>D, C: 0.7-2 mg/kg PO q12-24hr</td>
</tr>
<tr>
<td></td>
<td>Esomeprazole</td>
<td>D, C: 0.7 mg/kg PO q12-24hr</td>
</tr>
<tr>
<td>Serotonin antagonist</td>
<td>Mirtazapine</td>
<td>D: 15-30 mg PO q24h; C: 1.875-3.75 mg PO q72h - can give q48h with CKD</td>
</tr>
<tr>
<td></td>
<td>Ondansetron</td>
<td>D, C: 1) 0.5 mg/kg IV; then 0.5 mg/kg/hr constant rate infusion 2) 0.1-0.2 mg/kg IV slowly q6-12h prn 3) 0.5-1 mg/kg PO q12-24h</td>
</tr>
<tr>
<td>NK-1 inhibitor</td>
<td>Maropitant</td>
<td>D, C: 2-4 mg/kg PO q24h</td>
</tr>
<tr>
<td>PGE2 analogue</td>
<td>Misoprostol</td>
<td>D: 2-7.5 mcg/kg PO q8-12hr; C: 5 mcg/kg PO q8hr</td>
</tr>
<tr>
<td>Medicine rhubarb</td>
<td>Rubenal</td>
<td>D: &lt; 3kg: 37.5 mg; 3-6kg: 150 mg; 6-12kg: 150 mg; 13-25kg: 300mg; 26-45kg: 600mg; &gt;45kg: 900 mg PO q12h C: &lt;2kg: 37.5mg; &gt;3kg: 75mg PO q12h</td>
</tr>
<tr>
<td>Amino acids / peptides</td>
<td>RenAvast, AminAvast</td>
<td>C: 1 capsule with food</td>
</tr>
<tr>
<td>Potassium</td>
<td>Potassium citrate</td>
<td>D, C: initial: 75 mg/kg PO q12h</td>
</tr>
<tr>
<td>Probiotics</td>
<td>Azodyl</td>
<td>D, C: &lt; 2.5kg: 1 capsule PO q24h; 2.5-4.5 kg: 1 capsule PO q12h; &gt; 4.5kg: 2 capsules PO in AM and 1 capsule PO in PM with food</td>
</tr>
<tr>
<td>VSL#3</td>
<td></td>
<td>D: 1/10 packet per 4.5kg PO q24h with food</td>
</tr>
<tr>
<td>Phosphate binder</td>
<td>Aluminum hydroxide</td>
<td>D, C: 15-45 mg/kg PO q12h with food</td>
</tr>
<tr>
<td></td>
<td>Calcium acetate</td>
<td>D, C: 60-90 mg/kg PO q12h with food</td>
</tr>
<tr>
<td></td>
<td>Sevelamer hydrochloride</td>
<td>D, C: 400-1600 mg PO q12h with food</td>
</tr>
<tr>
<td></td>
<td>Lanthanum carbonate</td>
<td>D: 5-20 mg/kg PO q12h C: 1 ml (1 pump) PO q12h (Renalzin)</td>
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<tr>
<td></td>
<td>Chitosan + calcium carbonate</td>
<td>D, C: 1 g/kg PO q12h 3-5kg: 1 scoop; 10kg: 2 scoops; 15kg: 3 scoops; 20kg: 4 scoops PO q12h (Ipakitine)</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Erythropoietin</td>
<td>D, C: initial:2-2.5 ng/kg PO q24h; maximum: 5 ng/kg PO q24h</td>
</tr>
<tr>
<td>Erythropoietin</td>
<td></td>
<td>D, C: 100 ug/kg SQ 3X/week initially</td>
</tr>
<tr>
<td>Darbepoetin</td>
<td></td>
<td>D, C: 1.5-1.0 ug/kg SQ 1X/week initially</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>Amlodipine</td>
<td>D: 0.1-0.4 mg/kg PO q24h; C: 0.625-1.25 mg PO q24h</td>
</tr>
<tr>
<td>ACE-I</td>
<td>Enalapril</td>
<td>D, C: 0.25 mg/kg PO q12h initially</td>
</tr>
<tr>
<td></td>
<td>Benazepril</td>
<td>D, C: 0.25 mg/kg PO q12h initially</td>
</tr>
<tr>
<td>Angiotensin receptor blocker</td>
<td>Losartan</td>
<td>D, C: 1 mg/kg PO q12h</td>
</tr>
<tr>
<td></td>
<td>Azilsartan</td>
<td>D: 0.1-1.0 mg/kg PO q12h</td>
</tr>
<tr>
<td></td>
<td>Irbesartan</td>
<td>D: 5 mg/kg q12-24h</td>
</tr>
<tr>
<td></td>
<td>Telmisartan</td>
<td>D, C: 1 mg/kg PO q24h</td>
</tr>
<tr>
<td></td>
<td>Valsartan</td>
<td>D: 80-160 mg PO q24h</td>
</tr>
<tr>
<td>Aldosterone receptor blocker</td>
<td>Spironolactone</td>
<td>D, C: 1-4 mg/kg PO q12h-24h</td>
</tr>
</tbody>
</table>

### Summary including KEY “TAKE HOME” POINTS

1. CKD occurs commonly and is progressive over some length of time in dogs and cats
2. Early diagnosis may aid in early intervention with potential of slowing progression
3. Treatment is aimed at correcting excesses and deficiencies induced by CKD including nutrition, electrolytes, acid-base, proteinuria, hydration, and neuroendocrine imbalances
4. Serial monitoring is vital to successful management of patients with CKD

### Summary

CKD implies irreversible renal failure that remains stable for a period of time, but ultimately progresses. Although many things can cause chronic kidney disease, by the time chronic kidney disease is diagnosed the cause(s) is/are not present and not treatable. Treatment is aimed at correcting excesses and deficiencies induced by CKD including nutrition, electrolytes, acid-base, proteinuria, hydration, and neuroendocrine imbalances. Serial monitoring is important and aids in altering treatment in order to maximize response.
References/Suggested Reading
URINE PAIN: URINARY TRACT INFECTIONS
Joe Bartges, DVM, PhD, DACVIM, DACVN
The University of Georgia
Athens, GA, USA

Overview of the Issue
Bacterial urinary tract infection occurs commonly in dogs, but is uncommon in young adult cats; however, older cats have a higher incidence. UTI occurs when there is a break in host defenses and an urovirulent organism is present. Treatment involves identifying whether the UTI is uncomplicated or complicated. In patients with recurrent UTI where predisposing factors cannot be corrected, prophylactic therapy should be undertaken.

Objectives of the Presentation
The objectives of this presentation are to:
• Describe etiopathogenesis of bacterial urinary tract infection
• Describe diagnostic testing for bacterial urinary tract infection
• Outline treatment plan for uncomplicated and complicated urinary tract infections
• Describe prophylaxis of urinary tract infections

Key Etiologic and Pathophysiologic Points
The urogenital tract is in contact with the external environment and bacteria normally reside in the distal part of the tract. Urinary tract has many defense mechanisms to prevent bacterial urinary tract infection including anatomic barriers (length of urethra, presence of high pressure zones, peristalsis, vesicoureteral flaps, and extensive renal blood supply and flow), mucosal defenses (glycosaminoglycan layer, secretory antibody, intrinsic antimicrobial properties, exfoliation of cells, and commensal nonpathogenic bacteria), composition of urine (osmolality, high urea nitrogen concentration, organic salts, low molecular weight carbohydrates, and Tamm-Horsfall mucoprotein), cell-mediated and humoral-mediated immunity, and micturition (frequent and complete voiding of urine). For a urinary tract infection (UTI) to occur there must be one or more temporary or permanent breaks in host defenses and colonization by a uropathogenic organism. For UTI, bacteria must possess 1 or more urovirulence factors for motility, adherence, invasion, production of enzymes, and production of toxins. Most UTI originate from ascension of bacteria from the lower urogenital tract. However, the presence of bacteria in urine (bacteruria) is not necessarily an indication to administer antimicrobial agents. Asymptomatic bacteruria (ABU) is defined as isolation of a specified quantitative count of bacteria in an appropriately collected urine specimen from an individual without symptoms or signs of urinary tract infection or other consequences of the presence of the bacteria. In one study of 109 dogs, ABU was identified in approximately 9% by culture. After 3 months, half had cleared the organism while 4.5% maintained the ABU with the same organism and antimicrobial sensitivity pattern. ABU does not require treatment.

Key Clinical Diagnostic Points
PHYSICAL EXAMINATION FINDINGS AND CLINICAL SIGNS – UTI may be symptomatic or asymptomatic. Bacterial infection of the lower urinary tract is often associated with signs similar to other lower urinary tract (LUT) diseases including hematuria, pollakiuria, dysuria, stranguria, and inappropriate urination. Bacterial infection of the upper urinary tract may be associated with hematuria, but may also be associated with systemic illness. Two to three
percent of dogs present with a UTI, which is more common in females than in males. In cats, less than one percent of cats less than 10 years of age have a UTI while greater than 40% of cats older than 10 years have a UTI with signs of LUT disease. It is important to evaluate the patient for temporary or permanent breaks in host defenses whether localized (e.g. recessed vulva, urocystoliths, etc) or systemic (e.g. diabetes mellitus, hyperadrenocorticism, thyroid diseases, etc).

**DIAGNOSIS** – Diagnosis may be made on urinalysis, but urine culture of urine collected by cystocentesis is best. UTI may be associated with pyuria (> 5 WBC/hpf); however, not always. Hematuria may or may not be present. The nitrate and leukocyte esterase test pads on a urine dipstick do not provide reliable results for ruling in or ruling out a bacterial UTI or inflammation. There is a system that is basically a urine dipstick mounted to the underside of a urine specimen collection lid to which the owners add voided urine and invert the closed specimen cup. The urine then reacts with the dipstick and the owners take a photograph of the dipstick and use an app to acquire results. This may be useful in identifying changes in urine pH and presence of blood; however, as with standard urine dipsticks it is less useful for ruling in or ruling out bacterial UTI due to the lack of usefulness of the nitrite and leukocyte esterase test pads and due to contamination of the urine with bacteria from the distal urogenital tract. Staining the urine sediment with a modified Wright’s stain increases the positive and negative predictive value (unstained urine sediment examination: sensitivity = 82%, specificity = 76%, positive predictive value = 40%, negative predictive value = 96%; stained urine sediment examination: sensitivity = 93%, specificity = 99%, positive predictive value = 95%, negative predictive value = 99% when compared with aerobic bacteriological culture). Additionally, urine sediment examination may reveal struvite crystalluria or casts. Urine culture is the most definitive means of diagnosing a bacterial urinary tract infection. If processing is delayed, refrigerate the sample. Alternatively, a blood agar plate can be streaked and later submitted for identification and antimicrobial susceptibility pattern if bacteria grow. If bacteria grow on initial agar, then organisms are transferred to agar plates and agar gel antimicrobial diffusion testing is performed to determine the organism’s susceptibility to antimicrobial agents.

**POINT-OF-CARE BACTERIOLOGICAL TESTING.**

**In-house culture plates.** Blood agar and MacConkey’s agar plates may be inoculated and incubated for 24-48 hours. A calibrated bacteriologic loop or a microliter mechanical pipette that delivers exactly 0.01 or 0.001 mL of urine to the culture plates should be used to estimate cfu/mL, and urine should be streaked over the plates by conventional methods. Blood agar supports the growth of most aerobic bacterial uropathogens, and MacConkey’s agar provides morphologic information that aids in the identification of bacteria and prevents “swarming” of *Proteus* spp. Plates are incubated or placed under an incandescent light. If bacterial growth is noted within 48 hours, the plates may be submitted for identification and determination of antimicrobial sensitivities.

**Flexicult.** An agar plate with one compartment for quantitative analysis using a chromogenic substrate allowing for bacterial identification and 5 antibiotic impregnated compartments: ampicillin, amoxicillin plus clavulanate, cephalothin, enrofloxacin, and trimethoprim-sulfamethoxazole. Accurately excludes urinary tract infection but less reliable for diagnosing infection, especially with Gram-positive cocci. Most of the antimicrobial susceptibilities had only fair concordance with standard microbiological culture technique.

**EZ-PZ.** A rapid catalase based urine-screening test. Screens for bacteriuria, hematuria, pyuria and the presence of other somatic cells. A positive result indicates that urine requires further diagnostic evaluation.

**Indicator RX.** This is a 24 hour test that detects the presence of bacteria in canine or feline urine samples. Identifies bacteria as one of the primary gram-negative uropathogens (i.e., *Escherichia coli*, *Klebsiella*, *Enterobacter* spp., and *Proteus* spp.) that are responsible for feline and canine urinary tract infections (UTI). Predicts the antibiotic resistance pattern for the UTI-related gram-negative bacteria found in canine and feline urine samples. Device is composed of 5 test wells, labeled “BAC” (bacteria), “GM(+)” (Gram negative), “FO” (fluoroquinolone), “AMO” (amoxicillin), “CEP” (cephalosporins – first generation) and 2 control wells labeled “POS” (positive) and “NEG” (negative).

**Uriform Vet.** A UTI screening by providing a semi-quantitative colony count along with a presumptive identification of many common uropathogens. Product consists of a two sided paddle containing selective and non-selective media that fits securely into a screw cap plastic vial to maintain sterility. One side contains C.L.E.D. agar that changes color in the presence of various organisms including E. coli, Proteus, Pseudomonas, Enterobacter, and others. The opposite side contains EMB (Eosin Methylene Blue) agar, a selective medium that will support the
growth of most Gram negative organisms while providing additional information regarding the suspected pathogen

**RapidBac Vet**: A 20 minute test using monoclonal antibodies to detect as few as 1,000 cfu/ml of bacteria in a urine sample. Reported to have 97.4% sensitivity, 98.8% specificity, 98.5% overall accuracy, with a 95% positive predictive value and 99% negative predictive value.

**COMMON BACTERIAL ISOLATES** – Over 75% of UTIs are due to a single organism, with approximately 20% being associated with 2 organisms, and 5% associated with 3 or more organisms. *Escherichia coli* is most common in dogs and cats accounting for 1/3 to 1/2 of infections. Gram positive organisms are second most common cause with *Staphylococci* and *streptococci* account for 1/4 to 1/3 of infections. Other bacteria accounting for remaining 1/4 to 1/3 of infections include *Proteus spp.*, *Klebsiella spp.*, *Pasteurella spp.*, *Enterobacter spp.*, *Pseudomonas spp.*, *Corynebacterium spp.*, and *Mycoplasma spp.*

**Key Therapeutic Points**

Treatment of bacterial urinary tract infection is dependent on whether the breech in host defenses is temporary or persistent. Bacterial urinary tract infections can be classified as simple/uncomplicated, or complicated

**Simple/uncomplicated bacterial urinary tract infection** – Bacterial urinary tract infection with no underlying structural, neurologic, or functional abnormality is considered a simple infection. This occurs in many dogs. Usually it is successfully treated with a 10-14 day course of the proper antimicrobial administered at appropriate dose and frequency. A recent study demonstrated effectiveness of a 3-day course of once-a-day, high dose, Enrofloxacin (20 mg/kg PO q24h for 3 days). Trimethoprim-sulfa has also been shown to be effective in a 3 day course when compared with a 10 day course of cepahlexin. Clinical signs should resolve and urinalysis results should improve within 2 days. There is evidence that treating for 7 days may be adequate in most patients with simple urinary tract infections.

**Complicated bacterial urinary tract infection** – Bacterial urinary tract infection associated with a structural, neurologic, or functional abnormality. Reproductively intact dogs, all cats, and animals with predisposing causes for bacterial urinary tract infections (e.g. renal failure, hyperadrenocorticism, diabetes mellitus) for example. In addition, animals that have bacterial urinary tract infections that are relapses, reinfections, or superinfections. Pyelonephritis and prostatitis are examples of complicated bacterial urinary tract infections. Complicated infections are often treated for 3-6 weeks, although there is some evidence that treating for 7-14 days may be adequate. Complicating factors for recurrent UTIs include breaks in host defenses or bacterial factors. Breaks in host defenses may be local (e.g. recessed vulva, anatomic defects, indwelling urinary catheter) and breaks in systemic host defenses include complicating diseases (e.g. diabetes mellitus, hyperadrenocorticism, hypothyroidism, hyperthyroidism). Complicating bacterial factors include an unusual organism (e.g. *Corynebacterium*) and multi-drug resistance.

**RESISTANT URINARY TRACT INFECTIONS**

*Resistant E coli* – Several options may exist depending on results of culture and sensitivity including flouroquinolones, aminoglycosides, potentiated beta-lactams, carbaminopenems, 3rd generation cephalosporins, and Cefovecin.

*Staphylococcus (methicillin resistant)* – These appear to be more difficult to treat. With resistance to methicillin, beta lactam antibiotics even potentiated ones will not be effective. *Staphylococci* are inherently resistant to flouroquinolones (as are most Gram positive cocci) even with a favorable sensitivity pattern. Treatment may include chloramphenicol, trimethoprim-sulfa, linezolid, and vancomycin.

*Enterococcus* - Oftentimes *Enterococcus* UTI is not associated with clinical signs and there is suggestion that not treating may be better than treating. In some animals without clinical signs or urinalysis changes (pyuria, hematuria), no treatment with re-culture in 2 weeks may reveal eradication of the organism. Treatment should be considered for animals with active clinical infection or in those that are immunocompromised and may include penicillins with or without amikacin. Enterococci are inherently resistant to cephalosporins, flouroquinolones, trimethoprim-sulfa, erythromycin even if favorable sensitivity results.
PREVENTION
Minimize bacterial contamination of the urinary tract and avoid or minimize conditions that impair host defenses.
Catheterization and endoscopy of the urinary tract always carries a risk of inducing a bacterial urinary tract infection
PROPHYLACTIC TREATMENT - This may be indicated in animals with relapses or frequent reinfections.
*Antimicrobial agents – Prophylactic antimicrobial therapy may be undertaken with either pulse therapy (agent is administered one week out of every four weeks) or by administering the agent at 1/3 to ½ of the dose once a day typically at night. If a “break through” infection does not occur during a 6 month period, then antimicrobial treatment can usually be discontinued. Disadvantages of this approach include development of resistant bacteria and side effects of the antimicrobial agent
*Methenamine – An effective preventative in select cases that is a cyclic hydrocarbon that is hydrolyzed to formaldehyde at pH < 6.0. It is effective against many organisms, but may cause systemic acidosis because it has acidifying properties. Methenamine is combined with an acid (mendalic or hippuric) to induce an acidic urine pH; however, some patients require additional acidification with Vitamin C or d,l-mehtionine or ammonium chloride to achieve a urine pH < 6.0. The main adverse effect of Methenamine is GI upset; however, it should not be administered patients with pre-existing metabolic acidosis related diseases (e.g. CKD) or in situations where alkaluria is desirable (e.g. with calcium oxalate urolith prevention). Additionally, cats do not typically tolerate Methenamine.
*Nitrofurantoin – Nitrofurantoin is a urinary antiseptic that has activity against many organisms. It is not used much in veterinary medicine; therefore, susceptibility is high; however, complications include GI upset, hepatopathy, peripheral neuropathy when used at therapeutic dosages (3-4 mg/kg PO q6-8hr) but are less likely to occur when used at prophylactic dosages (3-4 mg/kg PO q24h)
*Estrogens – Estrogens may be helpful in female dogs with recurrent vaginocystitis. Estrogens promote vaginal and urothelial cell turnover and so may help decrease bacterial load in the distal urogenital tract. They also promote increased secretions in the distal urogenital tract that may be useful in decreasing bacterial adherence. Dose is same as used with urinary incontinence.
*Urinary acidifiers – Urinary acidifiers do NOT work for prevention of bacterial UTI in dogs and cats. It is not physiologically possible to acidify a dog or cat urine to < 5.5 and bacterial can live in urine pH range of 4.0-10.0.
*Ecotherapeutics - Ecotherapeutics include probiotics (live bacteria) and probiotics (fiber sources that select for certain strains of bacteria), which may populate the GI tract and thus the distal urogenital tract. There is minimal evidence that this aids in preventing UTI’s; however, it does seem to help some dogs. It is thought that probiotics alter the GI tract flora and is associated with immune system modulation. When using probiotics, more is better – more numbers and more types. I typically use VSL#3 (http://www.vsl3.com) as it contains 450 billion organisms of 8 strains per packet of unflavored powder. I will give 1/10 packet per day to a cat and small dog and 1/4 to 1/2 packet per day to larger dogs.
*Cranberries - The active ingredient in cranberries are proanthocyanidins, which bind to adhesins, primarily PapG pili that are virulent factors involved with binding of the bacteria to uroepithelial cells. PapG pili are found on 25-50% of canine E coli, but not with most other bacteria. Therefore, proanthocyanidins might be helpful in preventing certain strains of E coli from binding to uroepithelia, but not all E coli and not all bacteria. There is evidence in human medicine (nearly 2 dozen positive randomized, controlled clinical trials), but one study in dogs failed to show benefit; nonetheless, some dogs may benefit from proanthocyanidins found in cranberry extract.
*D-mannose – D-mannose is a sugar that may prevent bacterial adherence. It is also incorporated into the glycosaminoglycan layer and may prevent bacterial invasion into uroepithelial cells.
Live biotherapeutic products – Live biotherapeutic products such as strains of E coli and vaccines have been studied. Intravesicular administration of E coli ASB 83972 in humans with recurrent UTI has been reported to reduce symptoms of UTI and protect some patients. E coli ASB 2-12 has been shown to be effective in a mouse model of recurrent E coli UTI.
* Herbs - Evaluation of herbs and herbal extracts are lacking in medicine, but use of such compounds may decrease antimicrobial resistance by uropathogens. Two extracts prepared from Agropyron repens L. and Zea mays decreased bacterial adhesion by interacting with bacterial outer membrane proteins in vitro. Three herb extracts: Betula spp., Orthosiphon stamineus, and Urtica spp. showed anti-adhesive effects. Arctostaphylos Uva-ursi folium (bearberry leaf) has traditionally been used for medicinal purposes in Europe and America for the treatment of
UTIs and may have direct antibacterial effects. In a study of *Aframomum melegueta*, bacteriocidal activity was evaluated against *E. coli*, *L. monocytogenes*, methicillin resistant *Staphylococcus aureus* (MRSA) and *S. aureus*. Two exhibited more potent antibacterial activity compared to current clinically used antibiotics. Other plant extracts have been evaluated for use in UTIs with the bioactive compound berberines including *Mahonia aquifolium* (Oregon Grape), *Hydrastis canadensis* (goldenseal), and *Coptis chinensis* (goldthread).

**Summary including KEY “TAKE HOME” POINTS**

1. A bacterial UTI occurs when there is a temporary or permanent break in host defenses and a urovirulent bacterial organism is present
2. UTI may be uncomplicated or complicated depending on whether there are pre-existing breaks in host defenses or if the organism is highly urovirulent or there is recurrent infections
3. Correction of identifiable breaks in host defenses is important in prevention of recurrent UTI
4. Prophylactic measures may be required to prevent recurrent UTI

**Summary**

Bacterial UTI may be categorized as uncomplicated or complicated. In patients with recurrent UTI, urine culture should be performed in order to direct therapy and prophylactic measures should be undertaken.

**References/Suggested Reading**

URINE AGONY: UROLITHIASIS
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Objectives of presentation:
Following this presentation, the attendee should be able to
- describe minerals that form uroliths in dogs and cats
- describe mechanism(s) of urolith formation
- describe management of urolithiasis including medical dissolution, minimally invasive procedures, and preventative measures

EVOLVING UNDERSTANDING OF UROLITH FORMATION AND ASSESSMENT
Formation of uroliths is not a disease, but rather a complication of several disorders. A common denominator of urolithiasis is that urine can from time to time be oversaturated with one or more crystal precursors resulting in formation of crystals. Urolith formation, dissolution, and prevention involves complex physical processes including: 1) supersaturation resulting in crystal formation, 2) effects of inhibitors of crystallization and inhibitors of crystal aggregation and growth, 3) crystalloid complexors, 4) effects of promoters of crystal aggregation and growth, and 5) effects of noncrystalline matrix. Assessment of urolith formation risk and response to therapy is difficult and has been based on results of epidemiological studies, measurement of urinary mineral concentrations, and urinary pH. Because supersaturation of urine with stone-forming substances is necessary for stones to form, measurement of urine saturation is a more accurate means of assessing risk of stone formation, Determining the relative supersaturation (RSS) of a urolith-forming substance in urine is one technique. RSS values are limited by the fact that the constants used for these calculations have not been measured in the patient's urine and it may overestimate activity of different minerals, and tend to underestimate risk of urolith formation. Activity product ratios (APR) are another method although an exact measurement of supersaturation is not obtained. APR does not eliminate errors associated with effect of unknown factors; however, since the same urine sample is analyzed before and after equilibration with seed crystals, the same type of error occurs in evaluation and errors cancel. APR overestimates undersaturation, underestimates supersaturation, and correctly measures saturation. One limitation of APR determination is the assumption that urine has reached the stability for the salt following incubation. Limited studies utilizing urine saturation testing have been performed in veterinary medicine, and few have been performed in dogs or cats that are urolith-formers and no studies exist that compares estimates of urinary saturation with recurrence rates of uroliths. Urinary supersaturation represents a risk for urolith formation, but there is overlap between urolith-forming animals and healthy, non-urolith-forming animals.

CLINICAL APPLICATION TO DOGS AND CATS
- Urinary saturation is the most important, but not the only, driving force for crystallization and urolith formation
- Several methods exist for estimating urinary saturation; however, none of them adequately describe what is occurring naturally in the biological system (urinary tract)
- Determination of RSS and APR give different results and information. Determination of RSS is a valuable and reasonably reliable technique for estimating urinary saturation; however, it (a) is influenced by concentration of analytes measured, which, in turn, is influenced by urine volume, and (b) it does not account for urinary constituents that are not measured including the influence of inhibitors. Because it is influenced by urine volume, methods designed to increase urine volume (e.g. feeding canned foods, administration of diuretics, and stimulating water consumption by increased levels of dietary sodium) would be expected to lower the relative supersaturation; however, clinical studies in urolith-forming dogs and cats are lacking. APR does not give an exact estimation of the supersaturation; however, because a patient’s urine is used pre- and post-incubation with seed crystals, this technique does account for unmeasured urinary constituents and the influence of inhibitors.
- Medical dissolution of uroliths is accomplished by inducing a state of undersaturation of urine with the minerals that formed the uroliths
- Medical prevention of uroliths is accomplished by inducing a state of undersaturation of urine or at least a state of saturation at the lower end of the metastability limit.
- Despite use of estimates of urinary saturation, there are no published studies in urolith-forming dogs and cats that validate their prediction of urolith recurrence.
- Means to decrease urinary saturation include increasing urine volume thereby decreasing concentrations of calculogenic substances and decreasing dietary intake of calculogenic substances. Despite these measures, they do not guarantee prevention of urolith recurrence in all patients demonstrating that urolith formation is a complex process and many questions remain unanswered.

**EVOLVING MANAGEMENT OF UROLITHIASIS**

In 2016, the ACVIM released a consensus on management of urolithiasis in dogs and cats, which is available as an open source document at http://www.acvim.org and summarized.8

**LOWER URINARY TRACT UROLITHS**

Struvite uroliths (ie, moderately radiopaque uroliths in dogs with alkaline urine and a urinary tract infection caused by urease-producing bacteria (such as Staphylococcus spp), and moderately radiopaque uroliths in cats with approximately neutral urine pH) should be medically dissolved unless (1) medications or dissolution foods cannot be administered or are contraindicated, (2) uroliths cannot be adequately bathed in modified urine (eg, urinary obstruction, large solitary urocystoliths occupying almost all of the urinary bladder), or (3) uncontrollable infection despite appropriate medical management and owner compliance. Medical dissolution for struvite uroliths is highly effective and infection-induced struvite usually dissolve in 8 weeks while sterile struvite dissolve in less than 2–5 weeks.9,10 Urocystoliths small enough to pass through the urethra should be removed by medical dissolution, voiding urohydropropulsion, basket retrieval, or other extraction procedures that do not involve surgical intervention. Urocystoliths too large to pass through the urethra should be removed by medical dissolution, intracorporeal laser lithotripsy, or percutaneous cystolithotomy.11,12 Consider medical dissolution of urate uroliths before removal. Hyperuricosuria, concentrated urine, and acidic urine are the predominant factors driving urate urolith formation.11 In most dogs and cats, uric acid is transported to the liver where it is metabolized by uricase to allantoin. A defective uric acid transporter (ie, SLC2A9 genetic mutation) and hepatic porto-vascular anomalies are common causes for hyperuricosuria and urate urolithiasis.14 However, for some animals, especially cats, the cause(s) for hyperuricosuria and urate urolith formation remains idiopathic. Dissolution of urate uroliths in dogs usually is accomplished within 4 weeks by feeding a purine-restricted, alkalinizing, diuretic diet, and administering a xanthine oxidase inhibitor (ie, allopurinol: 15 mg/kg PO q12 h).13 Dissolution has not been possible in cats or in dogs and cats with uncorrected liver disease. Cystine uroliths form, in part, because of decreased proximal tubular reabsorption of cystine. Consumption of a decreased protein, urine-alkalinizing, canned food with a 2-mercaptopropionylglycine at a dosage of 15–20 mg/kg PO q12 h successfully dissolves cystine stones.15 Cystine solubility increases with increasing urine pH. In vitro studies that achieved a urine pH > 7.5 increased efficacy of thiol-binding drugs to solubilize cystine in the urine. Administration of 2-mercaptopropionylglycine without modifying the diet is associated with dissolution.15,16 Dissolution should be attempted cautiously in cats because of intolerance of 2-mercaptopropionylglycine. Dogs and cats without clinical signs but with nondissolvable uroliths too large to pass into the urethra or too irregular to cause urethral obstruction need only periodic monitoring and appropriate client education. With the onset of clinical signs (eg, hematuria, dysuria, UTI, urolith removal should be considered. Educate clients about clinical signs of urinary obstruction. In order to minimize patient discomfort and unnecessary damage to healthy tissues, nonsurgical removal methods (eg, dissolution, basket retrieval, lithotripsy, percutaneous cystolithotomy) should be considered for nonclinical urocystoliths that are likely to cause urinary obstruction. Urethroliths should be managed by intracorporeal lithotripsy and basket retrieval.17 In male dogs and cats urethroliths can be urohydropropulsed retrograde back into the bladder and retrieved by percutaneous cystolithotomy or cystotomy.18 Urethrostomy can be considered to minimize future urethral obstruction in highly recurrent stone-forming animals. Rigid adherence to strategies to prevent urolith recurrence, however, should be considered first. Because of the high frequency of morbidity and adverse effects associated with urethral surgery, urethral surgeries are discouraged except under few circumstances.
UPPER URINARY TRACT UROLITHS

Only problematic nephroliths require treatment such as outflow obstruction, recurrent infection, pain, and those enlarging to the point of causing renal parenchymal compression, should be considered for removal in dogs and cats. Dissolution only should be considered for nonobstructive nephroliths or if the obstruction can be concomitantly alleviated or bypassed (eg, urethral stenting). The presence of nephroliths in cats with chronic kidney disease did not significantly affect the progression of renal disease. Treatment for other nephroliths potentially amenable to dissolution should be addressed on a case-by-case basis considering the stability of kidney function and the likelihood of complete removal or dissolution. Approximately 20–30% of upper urinary tract uroliths in dogs are suspected to be struvite for which dissolution should be effective. Rapid control of infection while avoiding surgical urolith extraction should maximally preserve kidney function. Dissolution should not be attempted in cats with obstructive upper urinary tract uroliths. Over 90% of nephroliths and ureteroliths in cats are composed primarily of calcium oxalate. Delaying appropriate care may contribute to an irreversible decrease in kidney function. Problematic nephroliths should be removed by (1) dissolution, (2) endoscopic nephrolithotomy (ie, for nephroliths too large for extracorporeal shock wave lithotripsy and for nephroliths in cats), and (3) extracorporeal shockwave lithotripsy (for nephroliths in dogs only). Extracorporeal shockwave lithotripsy has minimal effects on renal function, but is reserved for nephroliths ≤1.5 cm in diameter. Nephroliths >1–1.5 cm often require concurrent ureteral stent placement. A diagnosis of a ureteral obstruction should be based on ultrasonographic findings of hydronephrosis and associated hydrourerter proximal to an obstructive ureterolith regardless of the degree of the renal pelvic dilatation. If renal pelvic dilatation is <5 mm, careful imaging is needed to confirm obstruction unless it is associated with concurrent hydrourerter proximal to an obstructive ureterolith. If no obstructive lesion is seen on ultrasound examination, abdominal radiography should be performed concurrently to evaluate for the presence of nephroureteroliths. If ureteroliths are not visualized, a ureteral obstruction is not necessarily excluded, because ureteral strictures are common (>25% of cats). In a study evaluating the causes of hydronephrosis, all renal pelves >13 mm were associated with ureteral obstruction and those >7 mm were likely associated with ureteral obstruction. Partial and complete ureteral obstructions should be managed as an emergency regardless of whether the obstruction is partial or complete. Interventional procedures, such as ureteral stents and subcutaneous ureteral bypass, have a lower morbidity and mortality rate for ureteral obstruction than do traditional surgical options in both dogs and cats, respectively. Medical management of stable obstructive ureterolithiasis can be considered for 24–72 hours. Medical treatment should include fluid diuresis and mannitol continuous rate infusion treatment, if tolerated. Alpha adrenergic antagonists and tricyclic antidepressants also have been used with anecdotal reports of improvement in some cases. Medical treatment should not be continued in animals that are persistently oliguric or anuric, hyperkalemic, have progressive azotemia and progressive renal pelvic dilatation; minimally invasive urolith extraction or bypass is needed. Fluid treatment should be closely monitored to prevent overhydration. In dogs, in addition to propulsive treatment for uroliths, broad-spectrum antimicrobials IV (ideally for at least 24 hours before intervention) should be administered. Ureterolith-induced ureteral obstructions should be monitored rather than decompressed when renal pelvic dilatation is ≤3–5 mm, and renal function is stable. Medical management for the treatment of cats with ureteral obstructions is only reported to be effective in 8–13% of cases. Because over 25% of ureteral obstructions in cats are associated with concurrent ureteral strictures, success of medical management often is limited. Subcutaneous ureteral bypass or ureteral stenting for ureteral obstructions in cats should be considered the first choice for the best possible outcome. Interventional options such as ureteral stent placement, extracorporeal shockwave lithotripsy, or both for the treatment of ureteral obstructions in dogs always should be considered and offered to clients. Ureteral stents are associated with the lowest short- and long-term morbidity and mortality rates when compared to all other reported treatment options. Careful assessment of urinalysis (eg, crystals, urine pH), urine culture results, radiographic appearance, and when possible, quantitative urolith analysis should always be performed. In dogs, suspected struvite ureteroliths should be stented and then dissolved. Suspected obstructed calcium oxalate ureteroliths should be either stented for long-term treatment or stented with concurrent or subsequent extracorporeal shockwave lithotripsy, if necessary. Cystine and urate ureteroliths should be treated by a ureteral stent and concurrent medical and dietary treatment. Ureteral stents in dogs often can be placed endoscopically. Owners should be aware of reobstruction risks that are most often associated with concurrent ureteral stricture. Knowing the urolith composition will help by employing appropriate medical and dietary treatment to prevent stent encrustation and future urolith formation. If stenting fails, other options such as extracorporeal shock wave lithotripsy and subcutaneous ureteral bypass device placement, or traditional
surgery, can be considered. Dogs with ureteral obstruction should have their urine cultured and should be given antimicrobial treatment at the time of diagnosis because of the high incidence of concurrent UTI and pyonephrosis.

PREVENTION OF UROLITHS
Removal or bypass of uroliths will not alter the underlying conditions responsible for their formation. The most effective prevention strategies are those that eliminate the underlying cause. For cases in which a cause remains elusive or cannot be altered, minimize pathophysiologic risk factors associated with formation. Nutritional treatment remains a subject of much clinical interest and debate because of epidemiological and pathophysiologic data associating nutrient intake with urine saturation and lithogenicity. For all mineral types (except infection-induced struvite), feeding diets high in moisture is one of the cornerstones of urolith prevention strategies. Primary treatment for preventing infection-induced struvite uroliths, which is the most common struvite urolith in dogs, is early identification and elimination of UTI. Eliminating these infections will prevent recurrence of infection-induced struvite uroliths. Foods marketed to treat struvite urolithiasis will not prevent their recurrence but may delay or minimize, urolith burden in the presence of unrecognized UTI. Calcium oxalate urolithiasis in dogs and cats appears to be driven primarily by hypercalciuria in association with either hypercalcemia (eg, primary hyperparathyroidism, idiopathic hypercalciemia in cats) or normocalcemia. Selection of effective preventative treatment is challenging because (1) properly designed clinical trials evaluating urolith recurrence have not been published, (2) the exact mechanisms underlying calcium oxalate urolith formation are not completely understood, (3) associative factors identified in epidemiological studies have not been proven to result in disease, and (4) surrogate endpoints of therapeutic efficacy such as relative supersaturation are mathematical models that may not correlate well with calcium oxalate urolith formation. The high recurrence rate of calcium oxalate uroliths warrants a comprehensive approach and regular monitoring. High-moisture (>75% water) foods or adding water to dry food should be recommended. Strive to achieve a urine specific gravity ≤1.020 in dogs and <1.030 in cats. Increasing dietary protein from 35% to 57% (dry matter) increased urine calcium concentration by 35% and decreased urine citrate concentration by 45% in cats. In dogs and cats with hypercalciemia, correcting or controlling hypercalciemia aids in preventing calcium oxalate urolith recurrence. Doing so is difficult in cats with idiopathic hypercalciemia and no single treatment has been shown to be effective, including glucocorticoids, bisphosphonate administration, or dietary modification using a high-fiber diet with potassium citrate administration. Feeding high-sodium (>375 mg/100 kcal) dry foods should not be a recommended as a substitute for high-moisture foods. High-sodium foods increase urinary water excretion, but the effects appear to be short-lived (ie, 3–6 months). Potassium citrate is an alkalinizing salt that when administered PO and metabolized promotes the excretion of more beneficial alkaline urine. Alkaline urine enhances urinary citrate excretion, which is a chelator of calcium ions. Consider thiazide diuretics for frequently recurrent calcium oxalate uroliths as they enhance the renal tubular reabsorption of filtered calcium. Some recommend the concomitant administration of potassium citrate because thiazide diuretics contribute to urine acidification. A 55% decrease in urinary calcium concentration was reported in urolith-forming dogs that were treated with hydrochlorothiazide at a dosage of 2 mg/kg q12h. A 65% decrease in urinary calcium oxalate relative supersaturation was reported in clinically normal cats receiving hydrochlorothiazide at a dosage of 1 mg/kg q12h. In order to minimize urate urolith recurrence, decrease urine concentration, promote alkaline urine, and limit purine intake. For dogs with the SLC2A9 mutation, urate urolith recurrence can be minimized by increasing fluid intake, promoting alkaline urine (pH ≥ 7), and limiting purine intake. In cats and dogs with porto-vascular anomalies, correcting of the vascular anomaly should also be considered, if appropriate. Data in cats are limited, but purine restriction and urine alkalization are recommended. High-moisture (>75% moisture) foods or adding water to dry food is recommended. Strive to achieve a urine specific gravity ≤1.020 in dogs and <1.030 in cats. Additional water consumption to achieve lower urine concentrations of uric acid provides more effective prevention. Urate solubility increases with increasing urine pH. Decreasing dietary protein has been shown to decrease urinary saturation with ammonium urate in dogs. Selecting an effective food may be difficult because properly controlled studies evaluating urate urolith recurrence are rare. Consider xanthine oxidase inhibitors for dogs homozygous for genetic hyperuricosuria that have failed therapeutic diet prevention. Use a dosage of 5–7 mg/kg q12–24 h to safely prevent urate uroliths. Administration of xanthine oxidase inhibitors should be avoided in dogs that are not receiving decreased purine diets to minimize the risk of xanthine urolith formation. Xanthine oxidase inhibitors have not been formally investigated in cats. In order to minimize cystine urolith recurrence, decrease
urine concentration, limit animal protein intake, limit sodium intake, increase urine pH, and neuter. Newer classification systems for cystinuria have been published recently.26 High-moisture (>75% moisture) foods or adding water to dry food is recommended. Strive to achieve a urine specific gravity ≤1.020 in dogs and <1.030 in cats. Cystine solubility increases with increasing urine pH. In vitro studies that achieved a urine pH > 7.5 increased the efficacy of thiol drugs to solubilize cystine in the urine of cystinuric humans. Therefore, potassium citrate or other alkalinizing citrate salts should be administered to dogs and cats with persistently acidic urine. The dosage should achieve a urine pH of approximately 7.5. Diets for the prevention of cystine uroliths should be low in methionine and cystine precursors with adequate amounts of taurine and carnitine. Feeding high-protein diets, particularly those rich in methionine, a cystine precursor, should be avoided in cystinuric dogs. In some forms of cystinuria, neutering has been associated with decreases in cystine concentration because of a suspected androgen-dependent effect, but this effect is not universal. In recurrent cystine urolith formers, add 2 mercaptopropionylglycine to prevention strategies to further lower cystine concentration and increase cystine solubility. Dosages are 15 mg/kg PO q12h.

REFERENCES
URINE A MESS: DISORDERS OF MICTURITION
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Overview of the Issue
Micturition refers to the process of storing and periodically voiding urine. Disorders of urine storage usually lead to urinary incontinence, whereas disruption of urine voiding leads to incomplete emptying, dysuria, or urine retention. Micturition is a complex integration of central, sympathetic, parasympathetic, and somatic nervous systems, with resultant muscular activity. The two functional units of the lower urinary tract include the reservoir/pump (urinary bladder) and the continence/conduit (urethra). The urinary bladder and proximal urethra are composed of smooth muscle and are thus under autonomic nervous system control while the distal urethra is composed of skeletal muscle and thus under somatic nervous system control.

Objectives of the Presentation
The objectives of the presentation are to:
- Describe the neurophysiology of micturition
- Describe disorders associated with urine retention and their management
- Describe disorders associated with urine leakage and their management

Key Etiologic and Pathophysiologic Points
There are several different ways of classifying including problems with storage vs. voiding, if the urination problem occurs with a full bladder vs. empty bladder, and whether the urination problem is neurogenic vs. myogenic in origin. It is important to establish status of urinary bladder contractile force and patency of urethral outlet, determine whether disorder is primarily neurogenic or myogenic, and determine underlying etiology or contributing factors. In addition to routine collection of historical information and performing a complete physical examination, a complete neurological examination and rectal palpation should be performed. Have the owners describe what the pet is doing and whether there is a good urine stream or not. If possible observe urination or have the owners’ video record the pet urinating. Depending on the underlying disorder of micturition additional diagnostic testing should always include a urinalysis and urine culture. Laboratory evaluation may include a CBC, biochemical analysis, and infectious disease testing. Abdominal imaging by survey radiography and possibly ultrasonography or contrast radiography should be considered. Cystoscopy or exploratory laparotomy may also be considered.

Key Clinical Diagnostic Points
PROBLEMS WITH STORAGE
Bladder overactivity – Bladder overactivity occurs due to hyperexcitability of the storage phase. This results in inability to permit adequate bladder filling because of urgency. Patients have increased frequency of urination, pollakiuria, inappropriate urination. Often urethral irritation or spasm is present. Examples of bladder hyperactivity include cystitis, urocrystolithiasis, chemical stimulation (cyclophosphamide). The treatment is to RELAX bladder using antimuscarinic agents (propantheline, oxybutynin, tolterodine) and antispasmodic agent (oxybutynin, flavoxate, tolterodine). These drugs decrease detrusor activity and have urethral anti-spasmodic effects. Other drugs may help with refractory incontinence by increasing urine storage including tricyclic antidepressants such as imipramine, amitriptyline. These may improve bladder storage by several mechanisms including anticholinergic, alpha-adrenergic, and beta-adrenergic effects.

Bladder atony – Bladder atony may be due to neurogenic or myogenic causes. Bladder atony is associated with bladder overdistention but the patient does not posture to urinate. The treatment is to STIMULATE bladder contraction. This should only be done if the urethra is relaxed pharmacologically as well. Manage large overdistended bladder with urinary catheterization. Pharmacologically, bethanechol is a parasympathomimetic with direct cholinergic activity that stimulates or augments smooth muscle contraction. Metoclopramide has been shown to stimulate canine ureteral smooth muscle in vitro and anecdotally to stimulate bladder contraction in
human beings with bladder atony associated with diabetes mellitus. It appears to stimulate bladder contraction in some dogs and cats.

PROBLEMS WITH VOIDING

*Increased outlet resistance* – Inability to void due to increased outlet resistance may occur because of mechanical problems (e.g. urethral obstruction from a stone or mass) or functional problems (e.g. urethral spasm or neurogenic). The treatment is to relieve the urethral obstruction or relax the urethra if neurogenic.

- Relieve the obstruction – The urethral obstruction should be relieved by inserting a urethral catheter that may be left in place or performed intermittently or by repeated cystocentesis.
- Relax the urethra - Urethral relaxation is accomplished by administering sympatholytic agents that antagonize alpha adrenergic receptors (e.g. phenoxybenzamine, prazosin, tamsulosin). Tamsulosin is an effective drug that is administered once a day and builds up in prostatic and urethral smooth muscle tissue. Skeletal muscle relaxants (e.g. diazepam, dantrolene, baclofen) may relax the urethral skeletal muscle (external urethral sphincter); however, they have less effect than alpha adrenergic blockers.
- Urethral stent – In patients with urethral obstruction due to neoplasia, a urethral stent may be placed. Usually self-expanding metallic stents composed of nitinol are used. These are placed with fluoroscopic guidance. Most dogs are incontinent after placement as many transitional cell carcinomas involve the entire length of the urethra.
- Low profile cystostomy catheter – A low profile cystostomy catheter is a mushroom-tipped catheter that is surgically implanted into the urinary bladder through the ventral abdominal wall lateral to midline. A cystotomy is also performed. The catheter sits just above the skin surface and contains 1 or 2 valves to prevent leakage. It provides urinary diversion; however, owners must empty the urinary bladder 2 to 3 times per day.

*Paradoxical incontinence* – Paradoxical incontinence occurs when there is outflow obstruction resulting in bladder overdistention. The increased bladder pressure results in “leaking” of urine through or around obstruction. Usually the patient dribbles urine with a full bladder and is unable to void. It may be due to functional or mechanical outflow obstruction and is often associated with bladder atony.

*Reflex dyssynergia* – Reflex dyssynergia refers to a dyssynergia or lack of coordination between bladder contraction and urethral relaxation during micturition. Typically it is seen in large breed male dogs. Dogs begin urination normally with a good stream, but the stream decreases to dribbles or spurts or stops midway through the micturition process even though the urinary bladder contains urine. This may be seen with prostatic disease or upper motor neuron disease; however, in many cases it is idiopathic. Treatment involves decreasing urethral tone with alpha-adrenergic agents and possibly skeletal muscle relaxants. Some dogs also require a parasympathomimetic due to urine retention. In dogs that fail medical therapy, intermittent urethral catheterization, an indwelling cystostomy tube, or a urethral stent may be considered.

*Decreased outlet resistance* – Decreased urethral tone and outlet resistance results in incontinence, which may be neurogenic, myogenic, or anatomic in origin. The most common cause is urethral sphincter mechanism incompetency in female dogs.

- Ectopic ureters – Normally, the ureters enter at the trigone; however, occasionally they may terminate distally. They may either be extramural (where the ureter bypasses its normal insertion and inserts into the urethra or vagina at a distal point) or, more commonly, intramural (where the ureter enters the bladder at the trigone but tunnels in the wall before opening). Extramural ectopic ureters are surgically corrected. Intramural ectopic ureters may also be surgically corrected; however, laser ablation of the medial wall results in better continence (85% vs. 65%).
- Urinary incontinence – Urinary incontinence refers to the unconscious release of urine and is most often due to urethral sphincter mechanism incompetency (USMI). It is uncommon in male dogs and male and female cats, but may occur in up to 20% of spayed female dogs. Usually urination while awake is normal.

  Treatment: Pharmacologically – The treatment of urinary incontinence is to stimulate the urethral smooth muscle resulting in increased tone of the internal urethral sphincter. Administration of sympathomimetics (e.g. alpha agonists: phenylpropanolamine) results in continence in 85-90% of patients. Once a day treatment may be as effective as three times a day administration and is associated with fewer side effects. Estrogen replacement
therapy (estriol, diethylstilbesterol, Premarin) may increase alpha adrenergic receptor responsiveness and improve urethral vascularity and other mucosal characteristics. They are safe and reasonably effective (40-65%); however, estriol (Incurin) is reported to have a 93% excellent response rate. Gonadotropin releasing hormone (GnRH) analogs have also been used. In ovariectomized dogs, chronically unsuppressed FSH and LH release (due to lack of negative feedback) may contribute to urinary incontinence. Administration of GnRH analogs paradoxically reduces FSH and LH over time. It was found effective in 12/13 dogs in one study and in another study 9/23 dogs were continent from 70-575 days with another 10/23 having partial response; however, the 23 dogs also responded to PPA.

Treatment: Non-pharmacologically – In patients with USMI that are unresponsive to pharmacological therapy, there are several potential treatments. Urethral bulking involves injection of an agent submucosally in the proximal urethra via cystoscopy. It is thought to create artificial urethral cushions improving urethral closure (coaptation). It may also function as central filler volume increasing length of smooth muscle fibers and closure power of internal urethral sphincter. There are no bulking agents available for use in veterinary medicine. Historically, glutaraldehyde cross-linked collagen was used, but has been withdrawn from market. A study with polydimethylsiloxane has promising results. Artificial sphincter/urethral occluding device is similar to a blood pressure or vascular cuff that is placed surgically around proximal urethra with a loose fit. A tube connects the device with a subcutaneously implanted injection port providing a means to increase pressure within the device and therefore urethral pressure in area of internal urethral sphincter. Continence rates are high; however, they may require adjustment with time. Although surgical techniques (e.g. slings, plication, culposuspension) are available, long term continence rates are low.

Summary including KEY “TAKE HOME” POINTS
1. Micturition is a reflex with conscious control involving the sympathetic, parasympathetic and somatic nervous systems in addition to smooth and skeletal muscle
2. Pharmacologic treatments stimulate or inhibit these parts of the nervous system or the musculature
3. Disorders of micturition associated with urine retention may be either mechanical or functional in nature
4. Disorders of micturition associated with urine leakage may also be mechanical or functional in nature

Summary
Disorders of micturition occur commonly and involve urine retention or leakage due to mechanical or functional causes. Treatment is aimed at inhibiting or stimulating micturition or relieving mechanical causes of urine retention and leakage

References/Suggested Reading
<table>
<thead>
<tr>
<th>Agent</th>
<th>Mechanism of action</th>
<th>Recommended dosage</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Agents used to increase urinary bladder contractility</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bethanechol</td>
<td>Parasympathomimetic; direct cholinergic activity</td>
<td>D: 5-25 mg PO q8h</td>
<td>Nausea, vomiting, salivation</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Prokinetic; sensitizes to acetylcholine</td>
<td>C: 1.25-7.5 mg PO q8h</td>
<td></td>
</tr>
<tr>
<td><strong>Agents used to decrease urinary bladder contractility</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propantheline</td>
<td>Parasympatholytic; acetylcholine blockade</td>
<td>D: 7.5-30 mg PO q8h</td>
<td>Nausea, vomiting, constipation, sedation, increased ocular pressure</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Prokinetic; sensitizes to acetylcholine</td>
<td>C: 1.25-7.5 mg PO q8-12h</td>
<td></td>
</tr>
<tr>
<td><strong>Agents used to increase urethral resistance</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estriol (Incurin)</td>
<td>Reproductive hormone</td>
<td>D: 0.5-2 mg PO q2-3d</td>
<td>Signs of estrus, bone marrow suppression</td>
</tr>
<tr>
<td>DES</td>
<td>Reproductive hormone</td>
<td>D (females): 0.1-1 mg PO q4h for 5 days [approximately 0.02mg/kg do not exceed 1mg] followed by 0.1-3mg PO q7d</td>
<td></td>
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<tr>
<td>Premarin</td>
<td>Reproductive hormone</td>
<td>D: 20 mg/kg q2-3d</td>
<td></td>
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<tr>
<td>Testosterone propionate</td>
<td>Reproductive hormone</td>
<td>C (males): 2.2 mg/kg SQ or IM q2-3d</td>
<td>Aggression, prostatic disease, perineal hernia</td>
</tr>
<tr>
<td>Testosterone cypionate</td>
<td>Reproductive hormone</td>
<td>D (males): 2.2 mg/kg IM q30d or 200 mg IM q30d</td>
<td></td>
</tr>
<tr>
<td>Phenylpropanolamine</td>
<td>Alpha agonist; urethral smooth muscle contraction</td>
<td>D: 12.5-50 mg PO q8h; 1-2 mg/kg PO q8h</td>
<td>Anxiety, cardiac arrhythmias, anorexia, hypertension</td>
</tr>
<tr>
<td>Ephedrine</td>
<td>Alpha agonist; urethral smooth muscle contraction</td>
<td>C: 1.0-1.5 mg/kg PO q8h</td>
<td>Anxiety, cardiac arrhythmias, hypertension</td>
</tr>
<tr>
<td><strong>Agents used to decrease urethral resistance</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenoxybenzamine</td>
<td>Alpha antagonist; urethral smooth muscle relaxation</td>
<td>D: 5-15 mg PO q12h</td>
<td>Hypotension, tachycardia, vomiting, diarrheea, increased intraocular pressure</td>
</tr>
<tr>
<td>Prazosin</td>
<td>Alpha antagonist; urethral smooth muscle relaxation</td>
<td>C: 2.5-10 mg PO q24h</td>
<td></td>
</tr>
<tr>
<td>Tamsulosin</td>
<td>Alpha antagonist; urethral smooth muscle relaxation</td>
<td>D: 0.25 mg/kg PO q12h</td>
<td></td>
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<tr>
<td>Doxazosin</td>
<td>Alpha antagonist, urethral smooth muscle relaxation</td>
<td>C: 0.02-0.04 mg/kg q12-24h</td>
<td></td>
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<tr>
<td>Terazosin</td>
<td>Alpha antagonist; urethral smooth muscle relaxation</td>
<td>D, C: 0.5-5 mg PO q12-24hr</td>
<td></td>
</tr>
<tr>
<td>Terazosin</td>
<td>Alpha antagonist, urethral smooth muscle relaxation</td>
<td>D: 0.1-1.0 mg/kg PO q24h</td>
<td></td>
</tr>
<tr>
<td>Fidoxosin</td>
<td>Alpha antagonist, urethral smooth muscle relaxation</td>
<td>D: 0.1-3.0 mg/kg PO q24h</td>
<td></td>
</tr>
<tr>
<td>Diazepam</td>
<td>Striated muscle relaxation; central nervous system depressive effect</td>
<td>D: 0.2 mg/kg PO q8h or 2-10 mg PO q8h</td>
<td>Sedation, paradoxical excitement</td>
</tr>
<tr>
<td>Dantrolene</td>
<td>Striated muscle relaxation; direct action</td>
<td>C: 2.5-5 mg PO q8h or as needed or 0.5 mg/kg IV</td>
<td></td>
</tr>
<tr>
<td>Acepromazine</td>
<td>Urethral muscle relaxation by neuroleptic effect; alpha antagonism</td>
<td>D: 0.1-2 mg/kg PO q8-12h</td>
<td>Sedation, hypotension, seizures</td>
</tr>
<tr>
<td>Acepromazine</td>
<td>Urethral muscle relaxation by neuroleptic effect; alpha antagonism</td>
<td>C: 0.1 mg/kg IV or 1.1-2.2 mg/kg PO q12h</td>
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</table>
URINE FOR A SURPRISE: FELINE LOWER URINARY TRACT DISEASE
Joe Bartges, DVM, PhD, DACVIM, DACVN
The University of Georgia
Athens, GA, USA

Overview of the Issue
Prevalence of lower urinary tract disease is more common in cats between 1 and 10 years of age; whereas in dogs, the prevalence increases with advancing age. In cats greater than 10 years of age, bacterial urinary tract infection is most common. In young cats, idiopathic lower urinary tract disease occurs most commonly. Urinary tract infections and urolithiasis has been discussed previously in this conference; therefore, this discussion will focus on feline idiopathic cystitis (FIC).

Objectives of the Presentation
The objectives of this presentation are to:
- Outline causes of lower urinary tract disease in cats
- Describe proposed etiopathogenesis of feline idiopathic cystitis
- Outline diagnostic and therapeutic plans for cats with idiopathic cystitis
- Compare and contrast treatment options for cats with idiopathic cystitis

Key Etiologic and Pathophysiologic Points
By definition, FIC is an idiopathic disease and therefore the underlying cause is unknown. It is entirely possible (and perhaps even probable) that FIC is not a single entity, but rather a syndrome that may have more than one underlying cause. Nevertheless, in a number of different studies, both local bladder abnormalities and/or neurohormonal changes have been observed in at least a proportion of cats affected by FIC. While these changes are hard to interpret, and again it can be difficult to differentiate cause from effect (and sometimes even incidental observation), they do support the concept of complex underlying abnormalities and predispositions that may contribute to the development of FIC.

There are several proposed local bladder abnormalities in the pathogenesis of FIC. Studies in cats with idiopathic cystitis have shown that as in humans with interstitial cystitis, there is a decreased concentration of glycosaminoglycans (GAGs) in the urine of affected cats. Other local bladder factors have also been identified that may have a role to play in the pathogenesis of FIC. These include: an altered tissue or and/or urine concentration of inflammatory or other bioactive molecules such as complement c4a, thioredoxin, NF-kB p65, galectin-7, I-FABP, fibronectin, and trefoil factor 2; mucosal muscarinic receptors have been reported to have increased sensitivity in cats with FIC, which could potentially enhance smooth muscle spontaneous contraction, although evidence of an overactive bladder has not been found in association with FIC; increased bladder tissue concentrations of norepinephrine and an increase in maximum urethral pressures and urethral closure pressures in affected cats; histological changes in the bladder wall including oedema, haemorrhage, vasodilation, occasionally ulceration, and a variable increase in the number of mast cells; there is evidence to support the presence of neurogenic inflammation and mediators of pain and inflammation in the bladder, with evidence of increased expression of transmitters such as ATP and nitric oxide, altered expression of purinergic receptors, increased numbers of substance P containing neurons, increased expression of high affinity substance P receptors, and increased excitability of afferent bladder neurons, with evidence that urothelial cells themselves may be involved in the process.

As in humans with interstitial cystitis, a number of neuro-hormonal abnormalities have been detected in cats with FIC that might have a role to play in the pathogenesis of the condition. These observations include: an increase in plasma norepinephrine and dihydroxyphenylalanine in FIC cats compared with normal cats, but without a concomitant increase in cortisol or adrenocorticotropic hormone (ACTH); an increase in tyrosine hydroxylase immunoreactivity in the locus coeruleus of the brain of cats with FIC (during apparent quiescent periods), further supporting a role for increased sympathetic activity in cats with FIC; potential adrenal insufficiency in cats with FIC evidenced by significantly reduced responses to ACTH compared with healthy cats, and reduced volume of their adrenal glands; differences in responses to the α2-adrenergic agent medetomidine in FIC cats compared with normal cats. Collectively, these findings (although performed in a limited number of cats)
lend support to the fact that FIC appears to be associated with a stress response in many cats, but also suggests an uncoupling of the normal stress responses with increased sympathetic stimulation but suppressed adrenocortical responses.

Key Clinical Diagnostic Points

**CLINICAL SIGNS OF LOWER urinary tract disease** — Causes of lower urinary tract disease in cats present with similar clinical signs including, but not limited to pollakiuria, hematuria, stranguria, and inappropriate urination.

**WHAT ARE RISK FACTORS FOR FIC?** — Some studies show a higher risk in males while others show no gender predisposition. Most studies do not show a breed predilection; however, one study did show a predisposition in long-haired cats. In another study, the following factors were found to be associated with development of FIC: being more fearful than other cats in the same household, being more nervous than other cats in the household, having a lower water intake, partaking in less hunting activity, having lower activity levels, using a litter box, moving house, hiding when unknown visitors are in the house, having a higher body condition score, and having less access to an outdoor environment. Additionally, it is not uncommon for cats with FIC to have one or more other chronic diseases such as inflammatory bowel disease, respiratory disease, and behavioral disorders.

**DIAGNOSTIC TESTING WITH LOWER urinary tract SIGNS** - CBC and biochemical analysis are normal unless urethral obstruction is present. Urinalysis reveals hematuria; however, pyuria and bacteriuria may be present with UTI. Urine culture is negative unless UTI is present. Abdominal radiography and ultrasonography may be normal unless uroliths are present. In cats with FIC, cystoscopy reveals small pin-point hemorrhages called glomerulations and bladder wall biopsy often reveals submucosal edema, mucosal ulceration, possible submucosal inflammation, and possible fibrosis. FIC is a diagnosis of exclusion.

**Key Therapeutic Points**

**URETHRAL OBSTRUCTION** — Urethral obstruction may occur from uroliths or urethral plugs. Matrix-crystalline urethral plugs are found only in male cats and approximately 84% of matrix-crystalline plugs contain a mineral component with struvite being the most common mineral present. Uroliths have been discussed previously. Urethral obstruction results in dehydration, azotemia, metabolic acidosis, hyperphosphatemia, hyperkalemia, and eventually death. Treatment involves rehydration, relieving the urethral obstruction, and managing hyperkalemia. After relieving urethral obstruction, an indwelling urinary catheter may be required. If inserted, use a closed collection system, do not administer antimicrobial agents, and do administer urethral relaxants (alpha adrenergic blockers).

**NON-OBSTRUCTIVE IDIOPATHIC LOWER urinary tract DISEASE** - There have been dozens of proposed treatments for cats with lower urinary tract disease; very few have undergone evaluation in a randomized controlled clinical trial.

- **Antimicrobial agents** — The role of microbial agents in feline lower urinary tract disease is controversial. In young adult cats evaluated at university referral hospitals, the incidence of bacterial urinary tract infection is 1% or less; however, approximately 1 in 3 cats seen at primary care facilities in Norway had bacterial urinary tract infection. Furthermore, older adult cats are more likely to have a bacterial urinary tract infection and as many as 50% of older cats with lower urinary tract signs have a bacterial urinary tract infection. Unless a UTI is present, administration of an antimicrobial agent is not warranted.

- **Urinary tract antiseptics and analgesics** - Methenamine and methylene blue are not indicated in cats as they may induce metabolic acidosis and Heinz body anemia. Phenazopyridine is an over the counter preparation available for use by women with recurrent vaginitis/cystitis that causes Heinz body anemia in cats.

- **Smooth muscle and skeletal muscle relaxants** - Many cats with FIC have urge incontinence and inappropriate urination. Propantheline, an anticholinergic agent, minimizes force and frequency of uncontrolled detrusor contractions and may be beneficial in some cats; however, one study did not document a benefit. Phentolamine and prazosin are sympatholytic agents that decrease urethral tone and spasm and may help some cats. Cats with FIC have been found to have a dysregulation in their stress response with an increase in sympathetic autonomic nervous tone and a decreased hypothalamic-pituitary-adrenal response. Prazosin has more systemic effects than phentolamine and; therefore, may have benefit in cats with FIC to decrease the
increased sympathetic nervous system activation. Diazepam and dantrolene are skeletal muscle relaxants that may decrease tone and spasm of the distal urethra.

**Anti-inflammatory and analgesic agents** – Glucocorticoids have been used to decrease inflammation; however, studies have shown no benefit in cats with FIC. They are contraindicated in cats with urethral obstruction or those that have indwelling urinary catheters because they increase risk of UTI. Nonsteroidal anti-inflammatory drugs (NSAID) may decrease inflammation and pain; however, they are contraindicated with azotemia and dehydration. Buprenorphine and Torbugesic do not have anti-inflammatory properties, but do decrease pain and appear to make cats with FIC more comfortable.

**Amitriptyline** – Amitriptyline is a tricyclic antidepressant that may have analgesic properties, stabilize mast cells, and decrease inflammation. In one uncontrolled study, 9 of 15 cats with idiopathic lower urinary tract disease improved with amitriptyline. One controlled study of cats with active lower urinary tract disease showed no benefit and cats receiving amitriptyline had a higher incidence of recurrence of lower urinary tract signs. The goal is to find a dose that will have a calming effect.

**Glycosaminoglycans (GAGs)** - Cats with FIC have decreased concentrations of GAGs in their urine. GAGs may have a protectant role at the mucosal-urine interface. Two controlled studies, failed to show a difference in clinical signs between a GAG and placebo in cats with idiopathic lower urinary tract disease. There is one pilot study of intravesical instillation of a GAG (A-CYST) in cats presenting with urethral obstruction that showed reduction in repeated urethral obstruction (0% recurrence in GAG treated cats versus 43% in placebo treated cats); however, it was not statistically different.

**Dietary modification** - In cats with matrix-crystalline plugs or with struvite crystalluria, feeding a struvite preventative diet may have some benefit. In one study of cats with idiopathic lower urinary tract disease, cats fed a canned diet had fewer recurrences than those fed a dry diet. In a more recent randomized controlled clinical trial, cats with FIC had an 89% reduction in recurrences when fed a diet enriched with omega-3 fatty acids and anti-oxidants also containing L-tryptophan and alpha-casozepine.

**Maropitant** – Maropitant is used as an anti-emetic because it is a neurokinin inhibitor. It has been suggested that may aid in treating cats with FIC by reducing spasticity; however, no studies have been performed to validate this hypothesis.

**Stress reduction and multi-modal environmental modification (MEMO)** – The role of stress in eliciting clinical signs in cats predisposed to FIC is well documented. Decreasing stress by modifying environment may be beneficial. Cats do not respond to force, are territorial, and like to be in control of their environment. Minimizing stress and conflict may help some cats with FIC. Litter boxes and food should be away from noise and distractions. Cats like to climb, hide, scratch, and hunt; therefore, vertical and horizontal space should be provided. One food dish, water bowl, and litter pan should be available for each cat in the household with one additional of each. Additional information can be found at the Indoor Cat Initiative: [http://www.vet.ohio-state.edu/indoorcat.htm](http://www.vet.ohio-state.edu/indoorcat.htm). Additionally, the ‘urinary stress’ diet that was shown to decrease recurrences by 89% is formulated to not only be anti-inflammatory but to also have a calming effect.

**Clomipramine and Fluoxetine** – These drugs are used for urine spraying / marking behavior. They appear to modify behavior may have some analgesic effects.

**Pheromones** – Feline facial pheromones may calm a cat; however, in one study of cats with FIC, no benefit was found.

**Key Prognostic Points**

Over 90% of cats with idiopathic cystitis will have resolution of clinical signs in 4 to 7 days regardless of treatment; approximately 10% of cats with idiopathic cystitis will experience persistent or highly recurrent clinical signs. If clinical signs do not resolve in 4 to 7 days then additional diagnostic testing should be undertaken to rule out urolithiasis, infection, etc. Recurrence of clinical signs is highly variable and unpredictable.

**Summary**

Over 90% of cats with idiopathic cystitis will have resolution of clinical signs in 4 to 7 days regardless of treatment; approximately 10% of cats with idiopathic cystitis will experience persistent or highly recurrent clinical signs. The cause(s) of feline idiopathic cystitis is/are unknown but viral infection and dysregulation of the sympathetic nervous system are the current theories. Only feeding a diet enriched with omega-3 fatty acid and antioxidants have been shown in a controlled clinical trial to benefit cats with idiopathic cystitis. Other treatments...
such as anti-inflammatory drugs, stress reduction, feeding canned food, glycosaminoglycans, neurokinin-1 inhibitor administration, in addition to other treatments are worth considering.

HOW DO I TREAT CATS WITH LOWER URINARY TRACT DISEASE?

<table>
<thead>
<tr>
<th>YOUNG CAT, FIRST EPISODE</th>
<th>OLD CAT, FIRST EPISODE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Urethral obstruction</strong></td>
<td></td>
</tr>
<tr>
<td>Unobstruct</td>
<td>Unobstruct</td>
</tr>
<tr>
<td>Radiographs, UA (other lab work?)</td>
<td>Radiographs, UA (other lab work?)</td>
</tr>
<tr>
<td>Indwelling catheter?</td>
<td>Indwelling catheter?</td>
</tr>
<tr>
<td>Torbugesic?</td>
<td>Torbugesic?</td>
</tr>
<tr>
<td>Diet change (likely)?</td>
<td>Diet change (likely) - Stones or plug?</td>
</tr>
<tr>
<td>Antibiotics (peri-catheterization)</td>
<td>Others?</td>
</tr>
<tr>
<td>MEMO?</td>
<td>Antibiotics (peri-catheterization)</td>
</tr>
<tr>
<td>If persists or recurs, diagnostics</td>
<td>If persists or recurs - diagnostics</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No urethral obstruction</th>
<th>No urethral obstruction</th>
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</thead>
<tbody>
<tr>
<td>Urinalysis (minimum)</td>
<td>Diagnostics</td>
</tr>
<tr>
<td>MEMO</td>
<td>MEMO</td>
</tr>
<tr>
<td>Torbugesic?</td>
<td>Torbugesic?</td>
</tr>
<tr>
<td>Diet change? Likely – usually stones or plugs)</td>
<td>Diet change? Likely –calcium oxalate urolith</td>
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<tr>
<td>If persists or recurs</td>
<td>If persists or recurs</td>
</tr>
<tr>
<td>Do additional diagnostics</td>
<td>Do additional diagnostics</td>
</tr>
<tr>
<td>Diet?</td>
<td>Torbugesic as needed</td>
</tr>
<tr>
<td>Amitriptyline?</td>
<td>Diet?</td>
</tr>
<tr>
<td>Glycosaminoglycans?</td>
<td>Amitriptyline?</td>
</tr>
</tbody>
</table>

References/Suggested Reading


VETERINARY TECHNICIAN PROGRAM

PROCEEDINGS

February 2, 2019
SAY NO TO NPO: FEED PARVO PUPPIES RIGHT AWAY

Kenichiro Yagi, MS, RVT, VTS (ECC, SAIM)
Cornell University College of Veterinary Medicine
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Canine parvovirus (CPV) infections cause severe gastroenteritis, lead to dehydration, shock, disseminated intravascular coagulation, bacterial translocation and sepsis when left untreated. With aggressive treatment, the mortality rate can be reduced to between 0% and 30% from 90%. Therapeutic options in addition to fluid and pharmacologic therapy speeding gastrointestinal recovery is desirable to reduce patient mortality and morbidity, as well as financial strain to the clients for prolonged aggressive treatment. Use of elaborate treatment options such as oseltamivir (Tamiflu), interferon omega, recombinant bactericidal proteins, equine lipopolysaccharide antitoxin, human recombinant factors, and antibody rich plasma have not shown promising results. One simple to implement, therapeutic option that makes a significant difference in survival chance is enteral feeding started within hours of admission, even when vomiting.

Feeding When Vomiting

Feeding a patient when they are vomiting goes against most traditional approaches to nutrition in a patient suffering from gastrointestinal ailments. A typical approach in such a case is to withhold food, designating an NPO (nil per os, or no food or water from the oral route) to prevent nausea from introduction of food and distension of the stomach. Small amount of easily digestible food is introduced, being increased to a normal amount gradually.

There are several reasons why withholding of food is thought to be beneficial. These include the idea of resting the bowel, as it is irritated and has a reduced ability to absorb the nutrients. Vomiting is also thought to be reduced in frequency when the stomach is empty, giving decreased chances of vomiting and potential aspiration in a critically ill animal. In addition, food contains fat and fibers that are difficult to digest potentially increasing the chances of vomiting even further. In a patient with dysfunctional gastrointestinal systems, food will pass into the intestines undigested, leading to bacterial proliferation and osmotic diarrhea by pulling water into the intestinal lumen. All of these reasons combined, it may seem reasonable to withhold food in a patient with gastrointestinal issues. However, many of these beliefs actually might not be true.

One argument for feeding early, is that the guts are actually not able to rest when being fasted. Fasting causes a phenomenon called "hunger pains", which arises from intense peristaltic contractions migrating down from the pylorus to the ileum. The peristaltic activity is decreased when nutrients are present in the intestinal lumen, allowing for better rest of the guts, and nutritional absorption. If fasting leads to less rest and pain to the patient, feeding is the better option.

Does feeding actually lead to more vomiting? A study evaluating this with patients with hemorrhagic gastroenteritis indeed did observe an increased frequency of vomiting upon feeding when compared to fasting. However, they also saw that the frequency of vomiting decreased below the fasted dogs by day 2. Feeding creates a prokinetic effect, and reduces emesis, leading to an overall shortening of the time before the patient stops vomiting. The presence of food in the gastrointestinal lumen also decreases insult to the mucosa from toxins, reducing vomiting. The concept behind food minimizing chances of vomiting when certain medication is given along with it applies here as well. Feeding causes more vomiting initially, but leads to a quicker subsiding of vomiting.

Food high in fat and soluble fibers and large volume feedings can indeed increase chances of vomiting. Mal digestion and gastrointestinal distention stimulates vomiting. Small, frequent feedings are recommended to reduce gastric acid release, leading to reduced vomiting. In many cases, employment of antiemetic drugs help in preventing vomiting, allowing earlier enteral nutrition. Adequate antiemesis is especially important for inappetant patients requiring placement of NE or NG tubes.

Undigested food being present in the intestinal lumen does increase nutritional resources for microorganisms leading to bacterial proliferation. However, feeding increases levels of volatile fatty acids such as butyrate and porprionate, reducing the population of bacteria sensitive to acidic environments (Campylobacter and Clostridium spp.). The presence of food helps maintain enteric barriers, preventing bacterial translocation (movement of bacteria from the guts into the blood stream) and subsequent sepsis. Diarrhea in dogs is attributed to unabsorbed nutrients and endogenously derived osmotic elements instead of osmotic pressure created by undigested food. Insult to the intestinal mucosa preventing absorption of water and increased effusion through leaky blood vessels (increased vascular permeability) is alleviated with enteral nutrition, which helps reduce diarrhea when compared to a fasted state.
Fasting causes a plethora of negative effects that outweigh the small benefits it may have. Fasting causes reduced expression of digestive enzymes, impairing digestive function when food is reintroduced. Presence of nutrients reduces inflammation by inhibiting expression of adhesion molecules, preventing activation of neutrophils which contribute to mucosal damage and impair immune response. Malnutrition leads to protein, essential fatty acid, mineral and vitamin deficiencies preventing healthy turnover of gastrointestinal mucosa. Feeding leads to faster intestinal recovery, even when compared to parenteral nutrition, indicating benefits of passive luminal nutrition. Feed those guts!

Specifically for parvoviral enteritis, early enteral nutrition reduced the time for patient to have normal attitude, appetite, ceasing of vomiting and diarrhea, increased body weight, and improved muscular permeability when compared with fasting.

**Nutritional Tubes**

Nutritional interventions are a vital part of successful treatment of critical care patients, but often overlooked. An animal who is anorexic for as short as 3 days can develop nutritional deficiency related detrimental effects (metabolic derangements, depressed immune system, catabolic wasting, and deteriorating GI system, to name a few), and should receive nutritional support at latest by 5 days into anorexia. While enticing voluntary eating is most comfortable and beneficial for patients, this is not always sufficient to meet nutritional and caloric needs. When a patient is anorexic, there are several methods at which nutritional supplementation can be performed, divided into enteral and parenteral routes.

The least invasive of tubes utilized in nutrition are nasoenteral tubes. Nasoenteral tubes are inserted through the nares and down into the GI tract. Tubes terminating in the esophagus are called nasoenteral (NE) tubes, while nasogastric (NG) tubes terminate in the stomach. Nasoenteral tubes are used for short term feeding and are able to be used immediately after placement and typically no longer than 10 days. The tubes are typically too narrow to feed blended canned foods, and require a liquid diet to be infused. When a nasogastric tube is in use the gastric content may be evacuated and measured to determine the degree of functional gastric motility. The placement is typically well tolerated with none to minimal sedation.

Contraindications include patients with intractable vomiting, poor mentation, respiratory distress, facial trauma, or nasal diseases. One of the most important aspects of nasoenteral tube placement lies in prevention of tracheal placement. Food infused into the trachea can very easily turn into life-threatening respiratory compromise. Radiographic confirmation of appropriate placement should always be performed to prevent this. Other complications include epistaxis, rhinitis, and vomiting. If vomiting occurs, the placement of the tube should be rechecked make certain the tube did not come up the esophagus and inhaled into the trachea. The tube can also clog due to its narrowness, and requires constant infusions or flushing after bolus feedings.

Esophagostomy tubes may be opted to be placed through the side of the neck in a surgical procedure for patients requiring longer term nutritional intervention. Esophagostomy tubes can be used immediately upon placement and for up to 20 weeks when cared for properly. The larger diameter when compared to nasoenteral tubes allow for feeding of blended canned foods, providing the ability to meet nutritional needs more easily. It is also useful in patients with facial trauma or nasal diseases as it bypasses the muzzle into the GI tract. The procedure does require anesthesia to perform. Another significant advantage is the ability for an owner to take a patient home with an esophagostomy tube for long term care and relieving the need for hospitalization for nutritional management. The tube should be flushed with 5-10mL of water after feeding to prevent the tube from being clogged. Main complications include blocked tubes, displacement of the tube by vomiting or intentional removal by the patient, and stoma site infections. The stoma site (insertion site) of the tube requires regular monitoring for redness, swelling, and signs of infections.

Gastrostomy tubes (G tubes) are another surgically placed enteral feeding tube. G tubes extend from the skin on the side of the abdomen and into the stomach. G tubes are used for long term enteral feeding, capable of providing nutrition for years after placement. Polyurethane or silicone based G tubes are required for long term use as they are resistant to loss of integrity from digestive enzymes. Fibrin sealing of the stoma site will occur within 12-24 hours after placement, and feeding should not be started until this seal is formed to avoid contamination and infection of the site. This option may be taken when the patient has esophageal disorders, facial or oral trauma. There is a higher cost associated with the procedure, which may make it cost prohibitive. As this is a more invasive surgical procedure, there is a higher anesthetic risk involved, and should be avoided with patients with healing impairments. Patients vomiting consistently should be held off for the procedure until vomiting is under control. G tubes require similar attention to the stoma site as esophagostomy tubes. Complications include vomiting, aspiration pneumonia, peritonitis, accidental tube removal, pressure necrosis, and stoma site infection.

Jejunostomy tubes are more rarely placed, bypassing the stomach and into the jejunum. The tube may be used from week to months, and is used when resting of the upper GI tract is necessary. These include patients with pancreatitis, uncontrolled vomiting, gastroparesis, and recent gastric surgery. Feeding can
commence 12-24 hours after placement. Liquid diets are necessary since the tube diameter is narrow. Constant infusions alleviate the risks of cramping and diarrhea. Patients with jejunostomy tubes require close monitoring and will need to be hospitalized. Complications include osmotic diarrhea and vomiting. Obstruction of the tube is a common complication, and can be best avoided through periodic flushing (every 4 hours). If there is leakage of GI tract content, a peritonitis can develop and is a serious complication. When the GI tract is dysfunctional all together, parenteral nutrition should be used, and can be provided through a dedicated sterile port through a central line.

Enteral nutrition is very important in mainlining a healthy GI tract and mucosa. Many of the traditional thoughts of benefits to withholding food does not hold up to be as detrimental when compared to the benefits of early enteral feeding. Because of this, knowledge of use and maintenance of enteral feeding tubes will allow one to help influence a positive patient outcome. In the case of parvovirus gastroenteritis, anything more invasive than nasoenteral tubes are rarely used.

Nutritional Plan

When the decision is made to feed the patient, there are a few key points to consider. What will we feed? How much of it will be fed and how fast?

Current recommendations include oral rehydration over 3-4 hours, and then introducing food. It is unreasonable to attempt feeding their full maintenance energy requirement for patients suffering from acute diarrhea or frequent vomiting. The amount that can be reasonably be fed initially should be targeted for 1/4 resting energy requirement (RER), as a highly digestible, low-fat diet in order to ensure healthy gut recovery and minimal stimulation of vomiting and diarrhea.

An animal’s RER can be calculated by the formula: \( \text{RER} = 70 \times (\text{BW in kg}^{0.75} \text{ kcal per day}) \). As an example, a patient that is 15kg would have a RER of 70 x 15^{0.75}, or 533.5 kcal per day. ¼ of this will be 133.4 kcal, leading to a feeding rate of 5.6 kcal per hour. Depending on the energy density of the diet being fed, the volume will differ.

The type of food fed in these cases ideally should be highly digestible. There are many commercial diets available which are highly digestible (gastrointestinal diets). The diet should also be low in fat content, with less than 20% of metabolizable energy coming from fat. Excessive fiber content should be avoided since it can cause delayed gastric emptying, diarrhea, flatulence, and abdominal pain. The recommended level is no more than 8% dietary fiber.

In critical care, especially for feeding through a nasoenteral tube, liquid diets are employed. Products such as Clinicare has been a commonly used diet due to the simple calculation of the volume required to fulfill RER through its caloric density of 1 kcal/mL. The product also comes readily made as a liquid in a can, making preparation simpler. There are newer products on the market such as Emerald Critical Care HDN specifically formulated for dogs and cats and being highly digestible. This product is formulated for critical care patients at a higher default caloric density of 1.5-2.4 kcal/mL (concentration is adjustable as it is mixed with water on preparation), allowing for lower volume feeding. The choice of liquid diet may vary depending on clinician preference.

Regardless of what product is used, early implementation of nutrition is the key element to encouraging swift recovery of patients with parvoviral enteritis, providing passive nutrition for the enterocytes which prevents mucosal breakdown and bacterial translocation. Technicians play a large role in advocating for patients and their proper nutrition to influence patient outcomes.

Outpatient vs Inpatient Strategies for Parvoviral Enteritis

When a patient presents with parvoviral enteritis and the client is given the choice of hospitalized care for their pet, the cost of hospitalization commonly become a point of concern, especially when multiple animals in a litter is considered. In these situations, the question of whether parvoviral enteritis can be managed through an outpatient protocol can provide a significant chance of survival.

A study comparing outpatient protocol and inpatient protocol for treatment of canine parvoviral enteritis which utilized IV crystalloids, replacement of ongoing loss, KCl supplementation, IV antibiotics and IV antiemetics for the inpatient protocol and subcutaneous fluids ignoring ongoing loss, no potassium supplementation, long duration subcutaneous antibiotics, and subcutaneous antiemetics saw that there was no significant difference in survival chance and hospitalization time between patients in the two groups.

The one common intervention both groups received was the providing of a canine convalescence diet via syringe until the appetite regained, which likely highlights the importance of early enteral nutrition in survival chance. The authors commented that early enteral nutrition leads to earlier clinical improvement and syringe feeding is realistic for an outpatient protocol.
Oral Recuperation Fluids as a Supplement

An additional tool that has been added to our toolbox are oral recuperation fluids (ORFs). Oral recuperation fluids typically contain prebiotics, omega 3 and 6 fatty acids, and amino acids such as glutamine, arginine, and taurine and is provided to assist animals to recovery from illness. The intended effect of the fluid is to improve immune function and aid in regaining of normal mucosal morphology and permeability, as well as encouraging early regaining of voluntary appetite. The data associated with studies on ORFs shows significant decrease in time to regaining voluntary appetite and an increase in percent of RER consumed the first 24 hours after return of appetite. The ORF can be provided in place or, or alongside a bowl of water, fed via syringe, or through feeding tubes.

With the clear evidence of better patient outcome with institution of early enteral we should do everything we can to advocate for it to improve patient outcome in the GI patients.

References:
MYTHBUSTERS: THE BLOODY TRUTHS OF TRANSFUSION MEDICINE
Kenichiro Yagi, BS, RVT, VTS (ECC, SAIM)

Can RBCs Be Given Through an Infusion Pump?

Whether there is an optimal method of red blood cell transfusion administration has been a point of discussion. Studies evaluating the effect of various administration methods on the integrity of blood cells exist, focused on the in vitro effect of infusion pumps, measuring the degree of free RBC content (free hemoglobin, potassium, lactate dehydrogenase, bilirubin) and osmotic fragility. The results vary from observing significant increases to insignificant increase in values, while transfusions with red cells with longer storage time resulting in a larger increase of hemolysis markers than those with shorter storage times. The variability in results, in addition to the anecdotal evidence of patients benefiting from RBC transfusions administered with infusion pumps are a cause for varying opinions.

A study assessing in vivo survival time of RBCs infused with various infusion methods, compared the use of gravity flow, volumetric peristaltic pump, and syringe pump in autologous transfusions in dogs. Blood was collected from 9 healthy dogs, washed, and separated into 3 portions labeled with different densities of biotin. These labeled red cells were transfused through either gravity flow with a 170-260 µm filter, volumetric peristaltic infusion pump with a 170-260 µm filter, or a syringe infusion pump with an 18 µm aggregate filter at 2mL/kg/hr. Blood was sampled from test subjects at day 1, and every 7 days until day 49, measuring the proportion of red cells with biotin labels through flow cytometry. Additional in vitro testing was conducted, measuring plasma hemoglobin and osmotic fragility testing.

Labeled RBCs infused through gravity flow, volumetric pump, and syringe pump were detectable in 100% (8/8), 50% (4/8), and 14.3% (1/7) samples, respectively post-transfusion. The quantity and half-life between RBCs infused by gravity flow and volumetric pump that were detectable (4/8) were not different. The RBCs infused via syringe pump detected at 24 hours post transfusion was no longer detectable at 7 days, indicating complete removal of those cells from circulation sometime between 24 hours and 7 days post transfusion. No differences were seen in in vitro values examined.

The study concluded that delivery of RBCs with a syringe pump and microaggregate filter is associated with significant decrease in in vivo survival time. Volumetric pump delivery was associated with a 50% probability of loss of transfused RBCs within the first 24 hours, and gravity flow allowed for highest chance of RBC survival. The reason behind this difference is speculated to be the mechanical shear damage to the RBC membranes when transfused through the microaggregate filter, causing preferential removal of damaged cells upon entry into the circulation and exposure to the mononuclear phagocytic system. Though unconfirmed, there is a potential for microclots to have formed in the blood during resuspension in sub-room temperature plasma, which placed a higher degree of shearing stress on the RBCs going through the filter, causing this effect. Early denaturation and oxidation of hemoglobin due to the mechanical stress induced by syringe pump and volumetric pump methods, leading to IgG binding to the red cell surface and removal from circulation, is another possible cause for early removal.

Small sample sizes limiting the power of the results is a common limitation in the veterinary field, and this study is no exception. The results are most relevant to exact methods used in the study, and we can only make speculations on alternate setups to remove the use of microaggregate filters with the syringe pump (use of an in-line pediatric 170-260 µm filter or extraction of blood through a 170-260 µm filter administration set into a syringe, for example).

The authors of the study recommended against using a syringe pump with 18 µm aggregate filters in the light of the results of their study, though considering the limitations, drastic changes to clinical protocols was not stated to be necessary. The current best practice considering this evidence would be to administer blood products via gravity flow for larger volume, higher flow rate transfusions as long as consistency in flow rate is monitored closely (as it can be influenced by catheter patency, positioning and motion by the patient, and amount of blood left in the bag). The syringe pump method is particularly useful when performing small volume transfusions such as in felines. A similar study performed with feline blood stated their observation of RBC survival time being unaffected by the syringe pump method.

There are a couple of infusion pumps approved for blood product, one of which is an internal approval, and the other of FDA approval for human blood products. These pumps could be the next best solution and validation with veterinary blood products is warranted.

PRBC Has an Expiration Date of 42 Days?
Current practices in blood banking involve the usage of APS and additive nutrient solution which are labeled for 42 days of storage. Other studies have observed significant changes in degree of hemolysis, ATP level, and 2, 3 DPG concentrations by 31 days. More recent evidence gathered over the past decade indicates stored red blood cells to have impaired RBC survival, reduced efficacy as an oxygen carrier, and even incite adverse effects in the recipient causing mortality and morbidity. These changes are seen as early as 7 to 14 days into storage, and involve a collection of biochemical, biomechanical, and oxidative changes to the RBC and storage solution, all collectively referred to as “storage lesions”.

Mature RBCs lack mitochondria and rely on glycolysis for ATP production, leading to a lowered pH. ATP production is reduced by the acidic environment, combined with depletion, leads to decreased RBC membrane integrity. Lowered pH also affects 2,3 diphosphoglycerate (2,3 DPG) level reducing hemoglobin’s effectiveness as oxygen carriers, though this effect is reversible and not significant in cats. Hemoglobin in longer stored RBC products contain free hemoglobin and microparticles that scavenge nitrous oxide (NO) upon transfusion and cause a vasoconstrictive effect impairing blood flow, stimulate coagulation, induce oxidative damage, and cause proinflammatory effects. Microparticles, which are vesicles that have budded off of cellular components, induce proinflammatory and procoagulant effects. Stored RBCs show morphologic changes to echinocytes and spheroechinocytes leading to a loss of deformability and impairment in normal flow through capillaries. Oxidative damage leads to increased hemolysis and methemoglobin formation decreasing viable RBC count and oxygen carrying capacity.

There are many complicated mechanisms in play during RBC storage. To summarize the effects, storages lesions can lead to impaired RBC survival, reduce the efficacy of RBCs as oxygen carriers, and induce adverse effects such as arrhythmias, thrombosis, systemic inflammation, transfusion-related acute lung injury (TRALI), acute respiratory distress syndrome (ARDS), hypotension, and multiple organ dysfunctions. These changes occur as early as 7-14 days into storage, making supplying our patients with safe transfusion products a realistic challenge. Clinical impact of storage lesions is a topic of ongoing investigation while blood banks strive to balance provision of fresher products and minimizing wasting.

First Transfusions Are “Free”?

Compatibility testing for canine blood transfusions has traditionally been omitted in the interest of swift transfusions and financial considerations. This comes from the a widespread notion that the “first transfusions are free for dogs”, intended to state that canine RBC transfusions can be given without blood type matching (without typing the donor or recipient) or cross matching yet be performed without signs of immunologic complications, namely acute hemolytic transfusion reactions or anaphylaxis. This statement is made with the understanding that the most clinically significant dog erythrocyte antigen (DEA) is DEA 1, responsible for inciting acute hemolytic transfusion reactions when preexisting alloantibodies for the antigen is present. In 98% of the population, these antibodies are not present, so the first mismatched transfusion will only result in sensitization of the immune system to the antigen, leading to the development of antibodies over a course of approximately 4 days. This leads to a delayed hemolytic transfusion reaction, often asymptomatic as long as the patient has overcome the initial incident of anemia, or clinical symptoms of anemia as well as bilirubinemia and bilirubinuria may arise.

Given the asymptomatic or mild nature of clinical signs, many have accepted this reason to forgo compatibility testing. However, the sensitization will lead to an acute hemolytic transfusion reaction in subsequent mismatched transfusions, resulting in hemolysis of transfused cells and likeliness of anaphylaxis. By omitting compatibility testing, we run the risk of priming a patient for such reaction in the next transfusion which may be handled similarly if the patient’s transfusion status is not noticed. A medical team may be placed in a situation where the transfusion status of the patient may be unknown (pet brought in by pet sitter who thinks there had been no transfusions, or adopted dogs who “probably” has not had a transfusion). In the case a patient presents with risk of imminent death from anemia, this practice may be justified with the knowledge of the risk. Blood typing of all blood donors and stocking of DEA 1 negative blood is highly recommended for use in these situations to avoid sensitization of the patient to DEA 1. If there is any uncertainty in the transfusion history of the patient, cross matching is appropriate as erythrocyte antigens aside from DEA 1 exist with limited knowledge on consequences from patients sensitized for these miscellaneous antigens (some reports of AHTR exist). Transfusions of canine RBCs without compatibility testing are not “free”, and certainly have the hidden costs of DHTR and sensitization. Cats possess alloantibodies for the RBC antigens foreign to them (aside from the very rare type AB cats), leading to hemolytic transfusion reaction even with first exposure.

DEA 1 Negative is the Universal Blood Type?

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The concept of “universal” blood type indicates a blood type that can be given to any member of the same species without expectation of an immunologic reaction related to blood type mismatches. Because DEA 1 is the one
antigen we know most about and leads to AHTR when mismatched for the second time, blood from DEA 1 negative
dogs can be given without sensitization of DEA 1 negative and DEA 1 positive recipients, and often is considered as
“universal”. There are, however, other RBC antigens such as DEA 3 through 8, dal, and other less known antigens
confirmed to exist which can lead to sensitization when mismatched transfusions occur. Therefore, a donor should be
tested negative for every RBC antigen we are capable of testing in order to truly considering it “universal”. This creates
a challenge as 98% of the canine population is positive for DEA 4, and a donor negative in DEA 4 is virtually
impossible to find. Fortunately this is not a clinical issue since the recipient is likely DEA 4 positive as well, allowing
the blood types to match. Another challenge lies in our current inability to routinely test for DEA other than 1, 4, and 7
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the blood types to match. Another challenge lies in our current inability to routinely test for DEA other than 1, 4, and 7
through a reference lab due to a lack of testing anti-sera (and anything aside from DEA 1 not available as in-house kits),
preventing complete typing of our donors and timely testing of our recipients. Given our knowledge of additional RBC
antigens, we should consider DEA 1 negative, 4 positive, 7 negative blood type as the “least antigenic”, and type our
donors for all DEAs we are capable of, given finances permit it. DEA 1 negative can be considered safe blood to use
from anecdotal evidence as reports of hemolytic transfusion reactions are rare, and cross matches should detect
incompatibility issues arising from repeated exposure to the less known erythrocyte antigens. Cats have no universal
donors, though type AB cats may receive transfusions from both type A and B donors.

Are Blood Transfusions between Different Species Possible?

Despite common knowledge that blood product transfusions should be between members of the same species
to prevent immunologic consequences, there is ongoing research to test interspecies transfusions, or xenotransfusions.
Early experiments in blood transfusion in the 1600’s document a human patient receiving sheep blood, and showing no
signs of reaction (at least on first exposure). Porcine red blood cells with modified antigens have been a topic of
research in compatibility as human blood substitute. In the veterinary field, feline blood is consistently in short supply,
especially for patients with the rare blood type of B. Type B cats can only be transfused with type B blood as
introduction of a small volume of type A blood will result in an acute hemolytic reaction and anaphylaxis. In addition,
even for type A patients, blood supply may be short causing delays or inability to obtain blood products in a timely
manner as the patient suffers life-threatening anemia. In these situations, veterinarians have attempted to use canine
blood as a source of blood as it is more readily available, and can easily tolerate the small volume donations.

There is limited amount of evidence available from a few studies conducted on canine to feline transfusions. The results of the studies concluded felines do not possess naturally occurring alloantibodies against canine
erythrocytes. Compatibility testing methods such as slide-agglutination test and cross-matching only revealed
agglutination on the minor-crossmatch. Of the total of 62 transfusions performed between the various studies, 5 cats
showed signs of mild reactions, with tachypnea and pyrexia within 24 hours of the start of transfusion. Development of
antibodies against canine RBCs were seen 4 to 7 days after the transfusion, indicating the transfusion led to sensitization
of the immune system to the foreign antigens. Because of this, the life span of the transfused RBCs was approximately 4
days due to delayed hemolytic transfusion reactions while feline to feline transfusions allow RBCs to last 30 days. Subsequent transfusions resulted in anaphylaxis and were fatal in 66% of documented cases.

While transfusion of dog blood to a feline patient is not the best solution to supplementing oxygen carrying
capacity, it may be justifiable when faced with imminent death of the feline patient and without blood. A responsible medical team would discourage dog to cat transfusion and consider the method only when the patient 1) has no source of
compatible cat blood (Type B cat with no stocked blood, donor, or nearby hospital with stock, for example) or
hemoglobin based oxygen carrier solutions, 2) is imminently going to pass away without a transfusion or compatible
blood will not be obtained soon enough (truly dying animal), 3) is expected to benefit from a short term oxygen carrying
capacity gain, and 4) the owner understands risks and consequences. Xenotransfusions should not become a common
practice and maintaining a good source of cat blood should always be pursued without considering canine blood as
“backup”.

Premedication Reduce Chances of Reactions?

Premedication, or administration of antihistamines, glucocorticoids, or antipyretics in anticipation of
immunologic complications to counter histamine and inflammatory mediators and suppress the effects, have been a
traditional practice in transfusion medicine. There are a number of human studies observing no difference in incidence
of type I hypersensitivity reactions (allergic reaction) or febrile non-hemolytic transfusion reactions (FNHTR). Some
clinicians reason that administration of premedication potentially masks early symptoms of immunologic complications
delaying required interventions for treatment, advocating against it. Evaluation of the difference in severity between
recipients with premedication or without premedication has not been performed, and remains a question whether this
reasoning is valid. Human evidence is unfortunately not always directly translatable into veterinary practice, though
expectations of similar physiological mechanisms exist. A recent veterinary retrospective study evaluating the effect of premedication on acute transfusion-related reactions saw no beneficial effect. There might be a beneficial effect to administration of diphenhydramine in decreasing chances of acute allergic reactions, though further studies were recommended by the authors since the incidence of allergic reaction in the non-premedicated group was already low (2.6%). Studies evaluating effects of premedication and efficacy in prevention of hemolytic transfusion reactions are not apparently available, and the theoretical benefit is no justification for forgoing proper compatibility testing.

Is Warming of Blood Products Necessary?

Warming of blood products in the interest of prevention hypothermia in the recipient is a consideration during blood product administration. Concerns for hemolysis of erythrocytes when warming during transfusion exist, and studies point towards little to no difference in markers for hemolysis in vitro when blood is warmed to typical body temperature. However, at non-emergent administration rates, blood reaching the patient through the line placed in a room temperature environment is easily at room temperature upon reaching the patient, and will not contribute to a significant decrease in body temperature. In the case of rapid transfusions of large volumes into small patients, warming of the blood may be indicated with care taken to be evenly warmed to 35-37°C and not exceed 42°C close to the patient to minimize loss of heat. Hypothermia is also a documented complications related to massive transfusions. Aside from these situations, in many cases warming effort directed at the patient is most effective in treating hypothermia.

Is Plasma Indicated for Use in Hypoproteinemia? Parvoviral Enteritis?

Plasma contains many proteins of interest, namely hemostatic proteins, albumin, and immunoglobulins. Hypoproteinemia, specifically hypoalbuminemia, occurs in many critically ill patients with protein-losing disorders including protein-losing enteropathies, protein-losing nephropathies, liver failure, trauma, burn wounds, etc. This leads to a loss of intravascular colloid osmotic pressure (COP), and subsequent consequences. Administration of plasma products (fresh frozen plasma, frozen plasma, or cryosupernatant) have been used as a method in supplementing albumin for COP. However, the amount of plasma required to raise the patient’s albumin level by 1g/dL is approximately 40-50mL/kg. This is equivalent to 1.1L of plasma (9.5 units) for a 50# patient. The amount of plasma required to make a significant difference in the measurable level of albumin is both cost prohibitive and pose a large immunologic risk to the patient. Whether increasing the albumin level to a normal value (>2g/dL) will lead to increased chances of a positive outcome is still unclear, and difficult to advocate.

Similar concepts can be applied to the usage of plasma products derived from survivors of parvovirus infection. Clinicians have theorized that transfusion of plasma containing antibodies against canine parvovirus (CPV) will aid in recovery from CPV infections. A study evaluating use of a single dose of plasma containing CPV antibodies in its efficacy versus saline placebo saw no significant difference in reducing clinical signs, viremia, or speeding recovery. The volume used in this study (12mL) may be a limitation to the efficacy of the compared treatment, though the amount of plasma required for an adequate dosage of antibodies is unknown, and is likely to be at similar or higher levels of dosage for albumin supplementation. Thus, same concerns prevent use of plasma in this manner.

References:

**Keywords:** Transfusions, Evidence-based Medicine, Premedication, Transfusion reactions, Blood pump
Transfusion medicine and the use of blood products have become extremely valuable treatment options in emergency and critical care situations. Our knowledge and ability in selecting and administering suitable blood components for specific disorders and conditions have advanced. Some examples of these advancements include using red blood cells (RBCs) for anemia to supplement oxygen carrying capacity, plasma and its contents to provide coagulation factors in coagulopathies, platelets to aid in hemostasis in patients with life-threatening hemorrhaging due to thrombocytopenia. In addition, supportive evidence is emerging for canine specific albumin to positively affect the outcome in hypoalbuminemic patients. Less commonly, intravenous immunoglobulin (IVIG) is administered for its immunomodulatory effect in immune-mediated hemolytic anemia (IMHA), immune-mediated thrombocytopenia (ITP), and sudden acquired retinal degeneration syndrome. Furthermore, specific immunoglobulins are utilized as antitoxins for snake envenomation and tetanus. Providing these products poses a realistic challenge as the supply is limited by donor availability and our ability to process the blood into its components. Commercial blood banks have increasingly available supply and variety of blood products, though are not exempt from resource limitations. Veterinary practices would benefit from making a conscious choice about how to supply and administer blood products in a practical manner.

Practical Banking
Equipped with the knowledge of the various blood products available, a veterinary practice must decide the most practical and reasonable way to provide patients with the best course of treatment. The method of supplying blood products will be strongly influenced by the type and size of the practice. Historically, it has not been uncommon for a practice to have a “hospital cat/dog” or the pets of the staff members donate their blood (whole blood) for the patients. While many lives have been saved this way, it is difficult, with current knowledge and availability of blood products, to recommend this method except in dire circumstances. If caught in a situation where blood products are unavailable, seeking help from a nearby practice with an in-house blood bank to obtain blood products or referring the patient may be available options.

In-house Banking
The next logical step is to store blood products at the practice as an in-house blood bank. Larger practices or emergency specialty practices are more likely to have an in-house blood bank as need for blood products arise more frequently. This can be accomplished with a blood banking specific storage system or a simple household refrigerator and freezer. A variety of blood products can be purchased from commercial blood banks.

Since blood products have limited shelf lives, financial viability is a real concern. In an ideal situation, every blood product should find its way into a patient in a helpful manner prior to its expiration, without ever having a patient wait for the product any longer than necessary for appropriate testing. After all, the purpose of an in-house bank is to have our blood components available to us swiftly when needed. By maintaining transfusion logs or reports, usage of these products can be tracked and help the practice fine-tune their supply based on historic demand. Unfortunately, even with the most diligent planning, it is unlikely we will prevent all situations of blood component unavailability.

Donor Selection
It is at this point, the practice should evaluate taking the next large step in blood banking, which is to set up and maintain a blood donor program. While this may feel like a huge endeavor, donor programs can vary in scope and size. If the decision is made to move in this direction, a practice can start at a smaller scale to supply their basic needs while products requiring more investment can be purchased from commercial banks. There are some minimal requirements of a donor program, regardless of its size, noted below:

<table>
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<th>Canine</th>
<th>Feline</th>
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<tr>
<td>• Between the age of 1 and 8 years</td>
<td>• Between the age of 1 and 8 years</td>
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<td>• Body weight greater than 55 lb or 25kg</td>
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<td>• Not currently on any drugs aside from above</td>
<td>• Not currently on any drugs aside from above</td>
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<tr>
<td>• Screened free of bloodborne pathogens</td>
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<td>• Conformation and suitable jugular vasculature for repeated venipuncture</td>
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<tr>
<td>• A good temperament, without being overly</td>
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General Screening
A blood donor must be screened based on multiple criteria. First and foremost, the healthiness of the donor is determined so the donor is not harmed by donating. A veterinarian will conduct a full physical and health exam on the potential donor. Complete blood chemistry, urinalysis, and complete blood counts should be run on each potential donor prior to admittance into the donor program. This helps rule out any underlying systemic disease which will make the donor unsuitable to donate.

Blood Typing
Ideal canine blood donors possess blood which will not cause an immunologic reaction when transfused to any random canine recipient (the concept of a “universal” donor). In canines, 98% of populations have been reported to be positive for DEA 4. Because of this, potential donors that are negative in all but DEA 4 (“DEA 4 positive only”) is considered to be ideal for donation. Dogs that are DEA 1 positive but still negative in every DEA aside from DEA 4 can be considered to enter the donor pool. They will provide blood for patients that are DEA 1 positive and stable enough to be blood typed prior to transfusion. Extensive DEA typing is offered by commercial laboratories (though DEA other than 1, 4, 5, and 7 are unable to be typed due to antisera being unavailable) and is recommended for canine donors entering a donor program. Typing for DEA 1 with a point-of-care typing kit as the only blood typing for canine donors may be the protocol implemented by banks because other DEAs rarely cause clinically significant transfusion reactions. Other antigens such as Dal and Kai are known to exist, though typing is not readily available.

Feline donors of both type A and B blood are necessary. Majority of felines are type A, but a small portion of the population are type B, or on very rare occasions type AB. An antigen called Mik (though currently unable to test in-house) has been described, and may be responsible for hemolytic transfusion reactions in type-matched blood transfusions. Naturally occurring antibodies against different AB blood group antigens in cats leading to severe transfusion reactions require blood banks to keep both type A and type B feline blood on hand. The rarity of type B poses a difficulty in having blood components of the type on hand, making type B donors very valuable to have in your donor pool. Point-of-care blood typing kits for felines are reported to be accurate and are inexpensive, allowing for typing solely in-house.

Bloodborne Pathogen Screening
Canine blood is to be screened for heartworm, and other pathogens. The ACVIM consensus statement issued in 2016 recommends screening for babesiosis, leishmaniasis, ehrlichiosis, brucellosis, anaplasmosis, neorickettsiosis, trypanosomiases, and bartonellosis. Feline blood is to be screened for FeLV and FIV, as well as other pathogens. The ACVIM consensus statement issued in 2016 recommends screening for hemoplasmosis, bartonellosis, cytauxzoonosis, ehrlichiosis, anaplasmosis, and neorickettsiosis. Feline donors should be kept strictly indoors to eliminate interactions with potentially infected cohorts. Commercial blood banks and veterinary teaching institutions such as Antech Laboratories, Animal Blood Resources International, and UC Davis provide blood screening services (some offer blood typing and screening with a single submission). This screening should be repeated at least on an annual basis and the donor removed from the donor program if positive results are seen.

Other factors
Any previous transfusions will exclude the candidate from becoming a donor. While we are unclear how long antibodies produced from previous transfusions remain, currently accepted recommendation is to remove them from the donor pool. In the past, pregnancies were thought to induce production of antibodies against fetal blood in the mother, making their blood unsuitable for transfusions. A study in 2009 has shown there is no significant antibody production through pregnancy, allowing previously pregnant dogs to stay in the donor pool. Donors of both species should also be selected for their level of cooperation. While blood components are valuable, it is hard to justify collecting blood from a “volunteer” donor who gets extremely stressed in the process. Many blood banks are successful at building a canine donor pool solely on donors who willingly donate without the need of sedation. Every canine donor program should aim to do so, as donating stress-free without any sedation is a good sign our canine donors are “volunteering” their blood. The use of sedation in feline donors still seems necessary, however, in order to have a stress-free donation.

Blood Donation

On the day of the donation
Prior to each donation, the donor should be evaluated for their eligibility to donate. Each donor should undergo a physical exam and have bloodwork (PCV or Hemoglobin minimally) performed prior to donation to detect any health issues. A CBC may be performed to ensure an adequate HCT (>40% canine, >30% feline), hemoglobin (>13g/dL canine, >10g/dL feline), and platelet count (>200 x 10³/µL). Paying close attention to any sudden changes to these values is also important. As an example, if a greyhound that normally has a 55% HCT comes in to donate and has a 40% HCT on the day of donation, the greyhound should be examined further to determine a cause. If none is found the HCT should be rechecked at a later date (and pass on the donation this time around).

Canine donors can donate 19-22mL/kg of blood once every 6-8 weeks (though many programs often give a longer recuperation time in between). Donors weighing greater than 55 lb will be able to donate 450mL of blood; the required amount for commercially available multi-bag collection systems. The term blood “donation” implies a voluntary giving of the blood. In reality, our donors, at least initially, are volunteered by their owners to donate blood and usually require restraint. However, many of our canine donors will tolerate donating without sedation and with gentle handling and proper training, will learn to willingly donate. Blood donation will become a pleasant and routine experience. A quiet, secluded room should be set aside and regularly used as the donation room. Effort should be made to habituate the donor to the room by providing ample praise and treats. The collection process will require 2-3 people (one person for restraint, one person for the venipuncture, and an optional person to handle items surrounding the collection). The involvement of the owner should be gauged on an individual basis as some donors do well in the owner’s presence while others may not.

The donor can be placed in lateral or sternal recumbency during the donation process. If a vacuum collection setup is used, the donor will be able to stay on the floor. If gravity assisted collection is chosen, the donor will be placed on higher surface (table, for example). The venipuncture area is gently clipped and prepped to minimize irritation. The venipuncture is performed with the blood tubing clamped to prevent entry of air into the bag. The clamp is removed once the needle enters the jugular vein. The progress of the collection is monitored with a gram scale. The goal is to collect 450mL (474g), though 405-495mL (426-521g) is allowable. If flow is disrupted, troubleshoot by adjusting the needle or working out occlusions. Gently rock the blood bag intermittently if using gravity assisted collection. Once the desired amount is collected, re-clamp the blood line close to the needle, and remove the needle from the donor. Pressure should be applied to the venipuncture site and should be monitored until hemostasis is achieved. Donors typically will be able to get up and walk around the donation room. Complications such as hypotension, bruising or extravasation, and irritation of the clipped and prepped area may occur. Food and water should be offered. Donors should be restricted from exercising for at least 24 hours. Placing pressure on the jugular with neck leads should be avoided.

Feline donations are performed similarly, though sedation is almost always required for a stress-free collection. A ketamine/benzodiazepine or ketamine/opioid combination is commonly used. Great effort should be made in making the donation process as pleasant as possible. This effort starts with the owners making trips to the veterinary clinic a non-threatening process, and the medical staff being conscious of stress points during the cats’ stay and donation. Feline donors can donate 11-15mL/kg of blood once every 6-8 weeks (though many programs often give a longer recuperation time in between). Donors weighing greater than 10 lb will be able to donate 50mL of blood. Similar steps as canine donations are followed, with the major difference being the collection system used. Feline donations are collected through a “semi-closed” system; a sterilized assembly of a 19ga butterfly catheter, 60ml syringe, and a 60-100ml collection bag, connected through a three-way stopcock. An anti-coagulant preservative solution (7-8ml CPDA-1 for a 50ml collection, for example) is added to the syringe just prior to the collection, leading to a “semi-closed” system, causing a compromise to the sterility. Administration of a crystalloid fluid through the subcutaneous or intravenous route is often performed for cats, as hypotension is more common in comparison to dogs.

**Component Separation**

Because component therapy is overall beneficial due to the ability to provide targeted therapy for specific diseases, eliminating unnecessary risks of transfusions, and efficiently using limited biological resources, component separation should be considered by any practice supplying themselves of blood products through donations. Component separation requires additional equipment and is a significant financial investment for a practice, but will allow a practice to be in better control of blood component supply, providing better care for their patients.

**Storage**

Blood components have different storage requirements depending on the product. Blood refrigerators are equipped with efficient and fast cooling mechanisms that control the temperature at desired levels. Plasma freezers easily maintain temperatures of -40ºC or less. These storage devices can have built in thermometers with history recording and alarm settings with remote notifications, allowing blood bank personnel to constantly keep tabs on the bank. Storage is another large financial investment for a blood bank, and in veterinary settings, many use a household refrigerator/freezer unit for their needs. This practice, while not completely ideal, is a realistic solution and viable as long as the storage units are used solely for blood products (preventing loss of temperature due to frequent opening and potential contamination) and temperature levels are monitored.
**Centrifuge**
A variable speed, large volume capacity, and temperature controlled centrifuge is necessary as standard equipment for processing blood components. A couple of prominent manufacturers of these centrifuges include Beckman-Coulter and Sorvall (Thermo Scientific). Benchtop and Floor Model centrifuges are available. Benchtop models are compact and have a smaller footprint, but typically require a higher rotation per minute (RPM) to create the required relative centrifugal force (RCF). Floor models have a larger footprint, but require lower RPM for the RCF required, improving stability. These centrifuges cost thousands of dollars, making purchasing of second-hand centrifuges not uncommon in veterinary applications. Depending on the model, controls may be quite simple; dial settings for temperature, RPM, and spin duration, allow computerized programmed pre-sets for spin settings.

**Plasma Extractor**
A spring loaded plasma extractor is used to gently squeeze the blood bag after centrifugation in order to push the plasma out of the blood collection bag into a satellite bag. The even gentle pressure this device provides makes plasma extraction more reliable without disturbing the centrifuged red blood cells. Plasma extractors cost $100-140, making them a relatively inexpensive investment.

**Tubing Sealer**
Aluminum sealing rings and a hand sealer can be used to crimp the tubing on the blood bag, pinching the plastic together, creating a barrier within the tubing where the crimps are applied. Aluminum seals are inexpensive to acquire, and the crimping mechanism is built in with the tubing stripper, making this a financially light option. Thermal tubing sealers replace aluminum rings, physically fusing the plastic to form a true seal, which is more certain in its ability to prevent contamination. Benchtop and hand-held thermal tubing sealers are available on the market for a few thousand dollars, though acquiring one second-hand for far less may be possible.

**Platelet Agitator**
Platelet concentrate requires storage at room temperature and under constant agitation. This is achieved with a piece of equipment called the platelet agitator, which rocks the contents of the bag back and forth in a gentle side to side motion. A practice’s decision to purchase a unit will depend on whether the demand for platelet concentrate is high enough to justify the cost of regular processing and storage, given its short shelf life of 5 days.

**Component Separation Process**

**Fresh Whole Blood (FWB)**
FWB is simply blood collected that has not been altered and used within 8 hours of collection. FWB contains RBCs, platelets, labile and stable coagulation factors, albumin and other plasma proteins. No processing or storage equipment is required for use of blood in this manner, and is the most traditional method of use in a veterinary practice. Bags should be stored upright and rotated twice a week to allow mixing of nutrient poor portions of the plasma with nutrient rich portions through storage.

**Stored Whole Blood (SWB)**
If the collected blood is not due to be used within 8 hours, it can be stored at 1-6ºC for 21-28 days depending on the anticoagulant-preservative solution (APS) used. SWB contains RBCs, stable coagulation factors, albumin and other plasma proteins. The amount of labile coagulation factor decreases as time passes on. A temperature controlled storage unit dedicated to blood products is necessary for SWB storage. Bags should be stored upright and rotated twice a week to allow mixing of nutrient poor portions of the plasma with nutrient rich portions through storage.

**Packed Red Blood Cells (PRBC)**
In order for packed red blood cells to be separated from plasma, blood should be collected into a collection system with a satellite bag. The bag undergoes centrifugation at 5000 x g RCF for 5 minutes (plus spin down time) for canine blood at 4 ºC. The plasma portion is transferred into one or two satellite bags with a plasma extractor, leaving a dense RBC portion. If no additive solution (AS) will be added to the RBC, the PCV must remain lower than 80% by leaving 50mL of plasma within the bag. If an AS is used, the maximum amount of plasma possible is removed. In canines, a donation of 450mL blood typically yields 220-260mL of RBC/AS solution mixture. This volume is typically divided into two separate bags to yield approximately 125mL units. In felines, a donation of 50mL of blood typically yields 15-20mL of pRBC after centrifuging at 3000 x g for 10 minutes. 10mL of AS solution is added to yield a 25-30mL mixture, which is considered a feline pRBC unit. Special equipment required for this process includes a plasma extractor and a temperature controlled centrifuge. Bags should be stored upright and rotated twice a week to allow mixing of nutrient poor portions of the plasma with nutrient rich portions through storage.
Fresh Frozen Plasma (FFP) and Frozen Plasma (FP)
The extracted plasma, which is placed in one or two satellite bags and frozen within 8 hours from collection (placed in the freezer before 6hrs to allow for freezing by 8hrs), is considered as FFP. FFP contains both labile and stable coagulation factors. FFP can be stored for 1 year at lower than -20ºC. If the plasma is not frozen within 8 hours, FFP is left unused for 1 year, or FFP is thawed but not opened, it can be stored as FP at -20ºC for 5 years total. Frozen plasma products should be handled with care and storing them in storage cartons protecting the frozen plastic bags from cracking is recommended. The plasma can be stored vertically to allow visualization of any thawing that may have occurred during storage, especially if a household freezer is used (which achieve the minimal temperature needed for plasma product storage, and may have an auto-defrost cycle).

Cryoprecipitate and Cryosupernatant
Plasma can be separated into cryoprecipitate and cryosupernatant. The plasma is frozen as usual, except with an empty satellite bag attached to it. The plasma is then placed in a refrigerator at 1-6ºC to slowly thaw until it reaches a slushy consistency (10% frozen). It is then centrifuged at 5000×g for 7 minutes, and the supernatant is transferred to the empty satellite bag. The 10-15mL of precipitate remaining is called cryoprecipitate, containing von Willebrand factor, coagulation factor VIII, fibrinogen, fibronectin, and factor XIII. The supernatant removed is called cryosupernatant. Both cryoprecipitate and cryosupernatant should immediately be refrozen and has an expiration date of 1 year. Administering desmopressin at 0.6µg/kg diluted in 15ml saline IV 30-60mL prior to donation will result in an increased yield in vWF. The plasma can be stored vertically to allow visualization of any thawing that may have occurred during storage, especially if a household freezer is used (which achieve the minimal temperature needed for plasma product storage, and may have an auto-defrost cycle). Production of cryo-products for felines is typically not performed.

Platelet Rich Plasma (PRP) and Platelet Concentrate (PC)
Platelets can be separated out from fresh whole blood through a two-step process.
1. Fresh whole blood is centrifuged at a “light spin” setting. Settings are variable depending on blood bank protocols. Protocols utilizing 1000 x g for 4-6 minutes or 2000-2500 x g for 2.5-3 minutes at 20-24ºC are seen. The platelets above the buffy coat are extracted into a satellite bag along with the plasma, referred to as PRP.
2. PRP can be centrifuged further with varying protocol such as 2000 x g for 10 minutes or 5000 x g for 5 minutes at 20-24ºC and have all but 35-70mL of platelet-poor plasma removed, to produce PC. This second spin creates platelet pellets, which is allowed to rest undisturbed for 1 hour to promote disaggregation of platelets. The pellets are gently broken down and resuspended through manual agitation. Once the platelets are resuspended, it is stored under continuous gentle agitation in a platelet agitator at 20-24ºC. The required room temperature storage makes platelet products more prone to bacterial contamination, making them viable for only 5 days.

Platelet products are not typically processed with feline blood, though feline PRP has been observed to contain platelets with in vivo efficacy. Special equipment necessary for platelet processing and storage include a platelet agitator and possibly a blood tubing welder to add additional satellite bags for processing.

Donor Programs
If commitment in proper screening and simple forms of component separation can be made, there are various possibilities in acquiring your donor pool. An immediate option may be the hospital cat/dog and pets of the staff. Staff members may also have close friends or family members who are just as enthusiastic about canine or feline blood donation, aiding in the creation of an in-house donor program. Rescue organizations and various breed groups in the area could prove to be great allies in finding potential donors. A well-established blood bank may choose to operate a completely community based blood donor program, taking volunteers from the public.

It is important to take to heart that a donor program (in-house or community) is based fundamentally on altruistic intentions of providing a life-saving resource to the critically ill. This makes our donors and their owners very special, and they should be treated as so. Donor programs often provide small tokens of appreciation and “goodie bags” to give to their donors at each donation, while others have “The Wall of Heroes” displaying photos of long-term donors. Some may consider providing a retirement gift after a dedicated career in blood donation. There are multitudes of methods as gestures of appreciation, showing our donors some gratitude.

Finally, a community program is an excellent way to make an additional positive connection and raise awareness of our increasing blood component needs. After all, the veterinary medical community, along with the pet-loving community is made up of individuals who share the passion of providing the best care for our furry (or sometimes non-furry) friends.

References
1. Weiss DJ, Wardrop KJ, Schalm’s Veterinary Hematology 2010;Ch.94:p731-737.
The Right Tool for the Right Job: Blood Component Therapy
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Traditionally, whole blood transfusions were the most common form of blood products administered. Component therapy has become more common as separated components became more widely available. A higher standard of medicine involves replacement of components required in specific patient situations, eliminating unnecessary risks from administration of extraneous foreign blood components for treatment. Component separation allows us to produce multiple components from a single donation, potentially treating more than one patient. Administration of components at ratios differing from what is ordinarily found in whole blood is also possible. Finally, the blood components can be stored by different methods which are optimal for each component, maximizing the effectiveness and shelf-life.

BLOOD COMPONENTS

Whole Blood

Whole blood is considered Fresh Whole Blood (FWB) for 6-8 hours after collection, and Stored Whole Blood (SWB) when stored at 4ºC for longer than 8 hours, up to 21-35 days (shelf life is anticoagulant dependent). Whole blood contains red blood cells, platelets (functional in FWB), coagulation factors, albumin, and other plasma proteins, from which all separated components are derived. Whole blood is useful when a patient needs both red blood cells and plasma, such as in acute and/or severe hemorrhaging due to trauma or coagulopathy. Whole blood may also be given if appropriate blood components are not available to the patient in a timely manner to meet the urgency. In most general practice settings FWB may be the most easily available source of platelets, indicating its use in thrombocytopenia or thrombocytopathia with accompanied bleeding.

Packed Red Blood Cells

When plasma is removed from whole blood through centrifugation, packed red blood cells (pRBC) is the component which remains (with a minimal amount of plasma), stored at 4ºC for 21-42 days depending on the anticoagulant used. pRBC is used primarily to provide oxygen-carrying capacity for patients showing signs of hypoxia due to a deficiency in circulating RBC mass. Such a situation may arise from loss of RBCs (trauma, coagulopathy, surgical complications, ectoparasites, gastrointestinal disease, etc), destruction of RBCs (immune-mediated hemolytic anemia, mechanical injury, biochemical insult, cellular parasites, etc), or decreased erythropoiesis (renal disease, viral diseases, bone marrow dysfunction, etc.). The most common cause of anemia in dogs and cats is hemorrhaging. In cats, the second most common cause is impaired erythropoiesis.

“Transfusion triggers” or “transfusion thresholds” have been suggested in which a patient’s need for a RBC transfusion would be determined by lab values assessing anemia (PCV, hematocrit, or hemoglobin). However, basing decisions to transfuse based solely on these lab values is not recommended, and clinical assessment of the patient is still important to prevent unnecessary transfusions. With that said, a PCV of less than 20% (Hgb of less than 7g/dL) is very likely to result in clinical signs of anemia. Lactate levels can be a good indicator of tissue hypoxia, and can be an indicator of inadequate oxygen carrying capacity, given that perfusion is not impaired.

In addition to provision of oxygen carrying capacity, RBC transfusions have a couple of less recognized benefits. Evidence supports better hemostasis in patients with a higher HCT, independent of platelet counts. The mechanism behind this phenomenon is currently under investigation, but could be related to RBCs stimulating thromboxane production by platelets, ADP release from RBCs acting as platelet agonists, displacement of platelets by RBCs towards the endothelium promoting platelet adhesion, and reduction of free nitric oxide (an inhibitor of platelet adhesion and aggregation) through binding to Hgb. RBC transfusions can also serve to provide available iron for anemia caused by iron deficiency, making RBC transfusions an excellent treatment option by providing oxygen carrying capacity and building blocks for new hemoglobin.

Plasma

Plasma is called Fresh Frozen Plasma (FFP) if frozen under -18ºC for storage within 8 hours from collection, and Frozen Plasma (FP) if taken longer. The distinction is due to the diminished amount of labile coagulation factors (V, VIII, IX, vWF) contained after 8 hours. The labile factors will last for 1 year while frozen, at which point the FFP can be relabeled as FP and stored for another 4 years. Liquid plasma is thought to go through most of its labile
factor loss in the first 24 hours, but may contain clinically significant amount of coagulation factors for up to 7 days when stored at 4°C. Plasma is primarily used for coagulation factor replacement due to the hemostatic proteins contained within plasma, categorized by their function (The hemostatic system and mechanisms involved is complex, and is beyond the scope of this lecture).

- Coagulation proteins – Factors II, V, VII, VIII, IX, X, XI, XII, XIII, von Willebrand’s Factor (vWF), fibrinogen
- Anticoagulants – Antithrombin, protein C, and protein S.
- Fibrinolytic proteins – plasminogen, antiplasmin, plasminogen activator inhibitor-1.

Inherited coagulopathies (hemophilia A and B, von Willebrand’s disease) and acquired coagulopathies (anticoagulant rodenticide toxicity, hepatic dysfunction) are indications of use. Alternative uses may be for protein (albumin) replacement in cases like protein losing enteropathy or nephropathy, and hepatic dysfunction. Supplementation of albumin through plasma requires approximately 45ml/kg to increase the albumin level by 1g/dL, and can be unrealistic from a patient intravascular volume, blood bank supply, and/or financial perspective.

**Cryoprecipitate/Cryosupernatant**

Factor VIII, vWF, and fibrinogen can be separated out of plasma to create concentrates of these factors through centrifugation of a partially thawed plasma unit. This is called cryoprecipitate, and is useful to specifically replace these factors (hemophilia A, von Willebrand’s disease). Advantage in its use is the provision of a therapeutic level of these factors with a small volume transfusion, reducing the risk of intravascular volume overload. Administering desmopressin at 0.6µg/kg diluted in 15ml saline IV 30-60mL prior to donation will result in an increased yield in vWF. Cryoprecipitate can be stored for a year, frozen. Lyophilized (freeze-dried) forms are also commercially available.

The left over plasma is called cryosupernatant (may also be referred to as cryo-poor plasma), containing remaining factors and proteins (II, V, VII, IX, X, XI, XII, XIII, albumin, immunoglobulins). It is useful in treating specific factor deficiencies like hemophilia B (factor IX deficiency) and vitamin K antagonism (factor II, VII, IX, and X deficiency). Cryosupernatant can be stored for 1 year, frozen.

**Albumin**

Albumin serves in the vasculature to provide colloid osmotic pressure, functioning to retain blood volume. Albumin also functions as carriers for chemicals, drugs, and hormones, scavenges toxins and free radicals, and plays a role in regulating coagulation. Indications for use include protein losing enteropathy, protein losing nephropathy, hepatic dysfunction, peritonitis, polytrauma, and any other causes of hypoproteinemia (specifically albumin). Human serum albumin (HSA) has been used in canine patients with hypoalbuminemia. However, these infusions have a significant chance of an immunologic reaction due to the antigenic nature of human albumin, especially when repeat doses are necessary. Canine specific albumin has been recently produced as a commercial product, observed to increase serum albumin levels in the recipients with a low chance of immunologic complications. However, a connection between an improvement in serum albumin level and ultimate survival is currently under investigation.

**Immunoglobulins**

The use of human intravenous immunoglobulin (hIVIG) has gained some attention in the veterinary field for its use as immune-suppressants in refractory immune mediated diseases. Immune-mediated hemolytic anemia (IMHA), immune mediated thrombocytopenia (IMT), pemphigus foliaceous or other immunologic dermatologic disorders, and sudden acquired retinal degeneration syndrome are some of the conditions IVIG has been used on. The immunoglobulin content of plasma solutions are not observed to be sufficient to provide a immunosuppressive dose, and a concentrate derived via fractionation from thousands of blood donors is required. The concentrate consists mostly of biologically active IgG, though other Ig types are present. The mechanism of immunosuppression is thought to involve an inhibition of phagocytic activity of mononuclear lymphocytes, inhibition of cytotoxic T-cell function, and blunting of damage caused by complement activation and pro-inflammatory cytokines.

**Platelets**
Platelets are indicated for hemostasis of current hemorrhaging secondary to thrombocytopenia (low platelet count) or thrombocytopathia (dysfunctional platelets). Transfused platelets are rapidly destroyed in patients with IMT, and be of little benefit for disseminated intravascular coagulation (coagulopathy induced platelet consumption). Prophylactic administration of platelets is not seen in veterinary medicine, given the short supply.

Separation of platelets from plasma is possible, and practiced to provide fresh platelet concentrate and cryopreserved (frozen) platelet concentrate. Viability of cryopreserved platelets are significantly lower (60-70%), though significant shelf life is gained. Fresh platelet concentrate is stored at room temperature under constant gentle agitation for up to 5 days. Cryopreserved concentrate is stored less than -20°C for up to 6 months.

FWB, as mentioned previously, is likely the most immediately obtainable source of platelets for most veterinary practices. A significant change in platelet count may not be observed with usual dosages of FWB, but has been seen to provide adequate hemostasis in many cases.

TRANSFUSION ADMINISTRATION AND MONITORING

RBC Transfusions

Preparation of Red Cell Product: The blood pack should be determined by visually inspecting for any abnormalities. Changes in color of blood, such as brown or purple could indicate bacterial contamination, formation of methemoglobin, and deoxygenation of hemoglobin. Formations of clots could be indications of bacterial contamination or compromise to the red cells due to storage lesions. The product type, species, blood type, and expiration date should be doubled checked by the medical staff to ensure no mistake in the pack being transfused.

Warming of the blood is not recommended as it promotes growth of any bacterial contaminants and the loss of integrity to the red cells. In the cases where hypothermia is a concern, as with relatively large volume transfusions to small sized patients, pre-warming to 22-37°C immediately before transfusion can alleviate it. While different devices for warming are available, passing the tubing through a warm water bath during the transfusion is the simplest and most available method in veterinary medicine. It is important to warm blood ONLY when absolutely necessary, and if decided to warm the blood, the temperature must be very carefully controlled.

Dilution of pRBC with saline is recommended if pRBC was prepared without any additive nutrient solution (AS) to reduce the viscosity and density of the solution. Addition of 50mL 0.9% NaCl to 200mL will achieve a similar dilution as with a standard AS addition during processing, yielding ~60% PCV of the solution. Because diluting the product will add to the transfusion volume, care should be taken when transfusing patients at risk of fluid volume overload. WB or pRBC with AS added will not require any dilution.

Blood Administration: Blood products require filtration when being administrated in order to remove cells, cellular particles, and microclots that may have formed. Administration sets with filters are available for these transfusions with pore sizes ranging from 170µm to 260µm. Microaggregate filters with pore sizes 18-40µm have also been used for smaller volume transfusions to eliminate the larger priming volume an administration set has. However, the use of 18µm filters along with a syringe pump have recently come into question through a study which observed a severely short in vivo viability of red cells transfused with this setup.

Red blood cells should be administered through an IV catheter (central or peripheral), though IO administration is a viable alternative. A dedicated line is recommended as infusion of blood products provide for a good bacterial growth medium if infused through contaminated IV sites. In addition, a dedicated line will allow for administration of blood products without potential incompatibilities with other fluids being administered. 0.9% NaCl is the safest fluid to use in dilution, as it is both isotonic and free of substances that may cause any issues. Calcium containing crystalloids such as LRS can promote clotting of the blood product by activating the clotting cascade. Hypotonic solutions can lead to hemolysis due to fluid movement into the red cells.

There are various formulas used for RBC transfusion dosages. Through a recent study, two formulas were observed to be the most accurate in predicting the actual PCV increase (in dogs).
1. Dogs:
\[ \frac{90\text{mL}}{\text{kg}} \times \frac{\text{Desired PCV} - \text{Patient PCV}}{\text{PCV of Donor Blood}} = \text{mL to transfuse} \]
\[ \frac{90\text{mL}}{\text{kg}} \times \frac{\text{BW (kg)}}{\text{Desired PCV} - \text{Patient PCV}} \times \frac{\text{PCV of Donor Blood}}{\text{BW (kg)}} = \text{mL to transfuse} \]

2. Cats:
\[ \frac{70\text{mL}}{\text{kg}} \times \frac{\text{Desired PCV} - \text{Patient PCV}}{\text{PCV of Donor Blood}} = \text{mL to transfuse} \]
\[ \frac{70\text{mL}}{\text{kg}} \times \frac{\text{BW (kg)}}{\text{Desired PCV} - \text{Patient PCV}} \times \frac{\text{PCV of Donor Blood}}{\text{BW (kg)}} = \text{mL to transfuse} \]

1.5ml x %PCV increase x BWkg (pRBC only)

The first set of equations applies to both WB and pRBC, as the PCV of the donor blood is considered in the calculation. The degree of ongoing loss of red cells will affect the post transfusion PCV. A typical target PCV would be 25-30%, though many patients tolerate a much lower PCV if they have compensated for a low PCV due to its chronicity.

Administration rate will be influenced by several factors. Red cell products, once taken out of storage, must be transfused within a total of 4 hours as the chances of bacterial growth from contamination are higher and red cell viability is significantly lower after this timing. Considerations of intravascular volume overload should be made to determine the transfusion rate. Patient with a positive fluid balance or cardiac diseases require a slower transfusion rate to avoid transfusion associated circulatory overload. In these cases, transfusion of pRBC over WB will also alleviate the volume introduced (2-4mL/kg/hr). The lowered rate will require splitting of full transfusion volumes into smaller portions, leaving amounts more than 4 hours at a time left under refrigeration. Patients that are hypovolemic due to ongoing hemorrhaging will tolerate, and may even require, a higher transfusion rate to keep up with the losses. In normovolemic patients, a typical rate is within the range of 10-20ml/kg/hr to reduce likeliness of circulatory overload.

Monitoring During Administration: Administration of blood products has chances of causing transfusion related complications, vigilant monitoring during the transfusion is necessary. A staff member should be dedicated to monitoring the transfusion for the earliest detection of complications if any is to occur. The patient will be monitored throughout the transfusion and recorded on a transfusion monitoring sheet as a part of the patient’s medical record.

Before a transfusion is started, a baseline set of vitals are obtained on the patient. This includes heart rate, respiratory rate and effort, pulse rate and quality, mucus membrane color, capillary refill time, mentation/attitude, temperature, and blood pressure. Existence of external symptoms such as vomiting and diarrhea prior to the transfusion should also be noted. Measurement of baseline vitals serves as a point of reference to compare further measurements during transfusion to, in case changes occur. Once the transfusion is started, the same parameters are monitored intermittently throughout the transfusion (details on frequency are described below). Other external signs such as facial swelling, urticaria, pruritis, are monitored as well.

Initial Rate: The transfusion is initially started very slowly in order to prevent a large volume to have been delivered if a reaction does occur. If an acute immune reaction is to occur, signs are likely to manifest in the beginning stages of the transfusion. While various protocols in gradual introduction of blood products exist, all have a slow initial rate in common. Blood products can be started at a rate of 0.25-1mL/kg/hr, or 25-50% of the calculated target rate for the first 15-30 minutes. During this time, the patient is closely monitored, having transfusion monitoring parameters obtained every 5 minutes. If any changes to the parameters occur indicating a transfusion related complication, the transfusion is stopped and the veterinarian notified immediately.

Intermediate Rate: Some protocols may include an intermediate rate, increasing the administration to 50-75% of the target rate, and closely monitoring for another 15-30 minutes. This is done with the intent of detecting possible transfusion reactions due to an increased administration rate.
**Target Rate:** After the initial and intermediate (if part of the protocol) stages go by without any signs of reactions, the rest of the blood product is transfused within a total of 4 hours. Patient monitoring is continued every 30 minutes to an hour during the rest of the transfusion.

The following table summarizes clinical manifestation to transfusion related complications.

<table>
<thead>
<tr>
<th>Clinical Signs</th>
<th>Timing</th>
<th>Complication</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever, facial swelling, pruritis, urticarial, vomiting, diarrhea, anaphylaxis</td>
<td>Minutes to hours</td>
<td>Type I hypersensitivity; Allergic Reaction</td>
<td>IgE complex leading to mast cell degranulation and inflammatory mediator release</td>
</tr>
<tr>
<td>Intravascular hemolysis: Fever, vomiting, dyspnea, hypotension, hemoglobinemia/uria</td>
<td>Minutes to hours</td>
<td>Type II hypersensitivity; Acute Hemolytic Transfusion Reaction</td>
<td>IgG and IgM mediated cytotoxic reaction to RBC surface antigens</td>
</tr>
<tr>
<td>Extravascular hemolysis: Hyperbilirubinemia/bilirubinuria, decline in PCV</td>
<td>3-21 days post transfusion</td>
<td>Type II hypersensitivity; Delayed Hemolytic Transfusion Reaction</td>
<td>IgG mediated cytotoxic reaction to RBC surface antigens</td>
</tr>
<tr>
<td>Fever, vasculitis, arthralgia, myalgia, lymphadenopathy, glomerulonephritis</td>
<td>1-3 weeks</td>
<td>Type III hypersensitivity; Serum sickness</td>
<td>Immune complexes induced complement activation and inflammation</td>
</tr>
<tr>
<td>Increased respiratory effort, dyspnea, crackles, often accompanied by hypertension</td>
<td>Minutes to hours</td>
<td>Transfusion associated circulatory overload</td>
<td>Increased hydrostatic pressure leading to pulmonary edema</td>
</tr>
<tr>
<td>Increased respiratory effort, dyspnea, crackles; no signs of circulatory overload. May include fever, hypotension.</td>
<td>Minutes to hours, up to 6 hours post transfusion</td>
<td>Transfusion related acute lung injury (TRALI)</td>
<td>Endothelial activation leading to neutrophil adherence, and subsequent neutrophil activation by transfused biological (not fully understood)</td>
</tr>
</tbody>
</table>

**Post Transfusion:** The patient should be continued to be monitored post transfusion for signs of transfusion related complications. A PCV or Hb should be taken at a minimum right after the transfusion and 24 hours later. Monitoring for delayed hemolytic reactions through evaluation of plasma and urine is also recommended. The patient should be monitored for any respiratory signs.

**Plasma Transfusion**

**Compatibility Testing:** In dogs, there are no naturally occurring alloantibodies for DEA 1, the most clinically significant antigen. Therefore, plasma from donors that are both DEA 1 negative or positive will be unlikely to cause any immune responses. In cats, due to the existence of naturally occurring antibodies and their antigenic nature, type matching is required for plasma transfusions.

**Preparation of Plasma:** Plasma should be handled with care when being handled out of the freezer. The plastic bags when frozen can be more brittle and be broken if hit against hard surfaces. The bag is submerged in warm water not exceeding 98.6°F (37°C) to facilitate thawing of the plasma. Higher temperatures may denature the proteins within the plasma. The plasma bag should be placed in a plastic bag closed off from the water to prevent contamination of the spike port. The thawing process may take 15-30 minutes.
**Plasma Administration:** Plasma products also require filtration when being administered in order to remove cells, cellular particles, and microclots that may have formed. The administration sets used for red cell transfusion are also used for plasma transfusions. As with red blood cells, plasma can be administered through an IV catheter (central or peripheral), though IO administration is a viable alternative. A dedicated line is recommended as infusion of plasma products provide for a good bacterial growth medium if infused through contaminated IV sites.

A typical plasma dosage for replacement of coagulation factors is 10-20mL/kg. Doses may be repeated if the coagulopathy still exists. While fresh frozen plasma (FFP) or stored frozen plasma (FP) is not commonly used to replace albumin, a 40-50mL/kg dose is thought to increase a patient’s plasma albumin level by 1g/dL. The large volume required poses a greater risk for transfusion related complications and is cost prohibitive. Administration rate of plasma should be initially started at 1-2mL/min while the patient is closely monitored for the first 15-30 minutes. The rest of the transfusion is typically completed within 1.5-2hrs.

**Albumin Transfusion**

**Preparation of Albumin:** Canine serum albumin is provided in lyophilized (freeze dried) form, and requires reconstitution with 0.9% NaCl. A 5 gram vial can be reconstituted with 30mL of 0.9% NaCl to provide a 16% (166mg/mL) solution for use as a hypertonic volume expansion fluid, or with 100mL 0.9% NaCl to provide a 5% (50mg/mL) solution. The solution should be swirled gently for approximately 15-30 minutes until reconstitution is completed. Vigorous shaking will foam up the solution. The diluent can be warmed to no higher than 90ºF (32ºC) prior to being added to aid reconstitution.

**Albumin Administration:** Albumin requires filtration when being administrated in order to remove microaggregates. Filtration can be accomplished by the use of blood administration sets or with in-line filters like the hemonate filters. Albumin can be administered through an IV catheter (central or peripheral), though IO administration is a viable alternative. A dedicated line is recommended.

Albumin dosage is calculated with the following formula:

\[
BW(kg) \times \frac{90mL}{kg} \times \frac{\{Target\ Albumin - Patient\ Albumin\}}{5\ gram/dL} = mL\ of\ 5\%\ solution
\]

More simply put, 450ml/kg should be given for a desired increase by 0.5g/dL in albumin.

**Monitoring:** As with any blood product transfusion, a baseline set of vitals and perfusion parameters, blood pressure, and temperature is taken prior to transfusion. The patient is closely monitored and given a reduced administration rate during the first 30 minutes of transfusion, and the rest transfused over a total of 4-8 hours. Acute allergic and anaphylactic reactions are possible. The hyperoncotic nature of albumin solutions poses a volume overload risk to the patient, requiring close monitoring of respiratory status.

**SUMMARY**

As blood component transfusions became more common, development in methods of donor selection, blood screening and collection, component therapy, patient risk assessment, and blood product administration has made blood component transfusions a much safer treatment than ever before. Despite these advances, blood component transfusions are not a benign process and carries inherent risks and potential for various reactions. Patient monitoring during blood component transfusion is very important to uphold a high standard of care, as every blood component transfusion has a potential for complications from the transfusion. Patients receiving blood component transfusions should ideally have a dedicated technician monitoring, and being ready to react to, signs of reactions.

**REFERENCE**

VET MED FEUD: THE PATIENT ASSESSMENT GAME
Kenichiro Yagi, MS, RVT, VTS (ECC, SAIM)

As our capability in emergency and critical care medicine becomes more sophisticated we can treat patients with more debilitated conditions. Conditions once thought to be difficult to treat are steadily coming within reach with advancements in diagnostics and therapy. Ability to treat such complicated diseases and severely compromised patients is accompanied by the expanding multitude of considerations one must keep in mind on a continuous basis to maximize therapeutic effects and prevent potential complications. In the realms of critical care, there are a series of daily assessment points evaluated through both subjective and objective methods to help assess progress and optimize further care, referred to as Kirby’s Rule of 20. Each point can be assessed with low to high tech and non-invasive to invasive methods in obtaining subjective and objective measures. The methods chosen will be influenced by consideration of benefits gained in return for the risks posed to the patients, as well as financial considerations, leading the medical team to selectively implement monitoring orders. The obtained monitoring parameters in turn are interpreted given current clinical conditions and further therapy is formulated. By applying the rule of 20, the medical team will have a complete picture of the patient’s status and evaluate any emergence of new problems. The rule of 20 serves as a checklist for the complicated process of critical care, improving the efficacy and efficiency in the ever changing and sophisticated field.

The rule of 20 includes considerations in fluid balance, oncotic pull, glucose status, electrolyte and acid-base balance, oxygenation and ventilation, mentation, perfusion and blood pressure, cardiac function, albumin level, coagulation, red blood cell and hemoglobin level, renal function, immune system, gastrointestinal system, drug dosages and metabolism, nutrition, pain control, nursing care and patient mobilization, wound care and bandage change, and tender loving care.

**Patient Assessment Points (Rule of 20)**

**Fluid Balance:** Fluid within a patient is distributed into the intracellular and extracellular compartments, shifting between them to maintain equilibrium. The extracellular compartment consists of the interstitial space (between cells) and intravascular space. Patients receiving fluids at a rate higher than required or can eliminate (due to physical limits or compromise in elimination due to disease) will develop a positive fluid balance and fluid overload leading to effusion of fluid into third spaces. When fluid requirements are not met or intravascular volume is unable to be maintained due to loss of colloid osmotic pressure, perfusion is compromised. Fluid balance can be assessed through physical assessment of mucous membrane (MM) color, capillary refill time (CRT), heart rate, pulse quality, and extremity to core temperature gradient, representing intravascular volume with abnormalities seen in hypovolemia. Interstitial fluid balance can be assessed through physical parameters such as body weight, skin turgor test, MM moistness, and presence of external signs of edema (pitting edema, chemosis), or laboratory tests including packed cell volume (PCV) and total protein (TP).

**Oncotic Pull:** Colloid osmotic pressure (COP) is exerted by colloids (large molecules that do not cross vascular walls) contained within the intravascular space favoring movement of free water into the intravascular space instead of out. The net effect results in maintenance of intravascular volume which leads to better cardiac output through retention of adequate plasma volume and preload. Natural colloids (albumin) or synthetic colloids such as hydroxyethyl starch (hetastarch) provide COP, ideally maintained at greater than 15mmHg to prevent peripheral edema. Assessment of COP in veterinary medicine is primarily performed through patient evaluation for signs of edema along with clinical reasons for hypoalbuminemia (protein-losing enteropathy/nephropathy, liver dysfunction, severe trauma, and any other source of plasma loss). Colloid osmometers are available as equipment with the ability to quantify COP, however is not very common due to the expense and labor intensiveness in maintenance.

**Glucose:** Hypoglycemia can manifest in a variety of critical illnesses, warranting regular measurement of blood glucose levels. Particularly of interest is the tendency for hypoglycemia to develop in patients with sepsis. The bacteria within the blood stream when numerous consumes glucose for their metabolism and the body is unable to take in or produce enough glucose to meet the overall demands. Hypoglycemia prevents adequate energy production for body systems, leading to physiologic abnormalities. Blood glucose may be supplemented through intravenous fluids, but maintenance of blood glucose may be difficult without resolution of the underlying cause. The effect of
hyperglycemia is largely unknown, but is observed to be associated with higher morbidity and mortality rate in human patients, leading veterinary medical teams to attempt maintenance between 3.9-8.0 mmol/L or 70-144mg/dL (Lv et al 2017; Mesotten et al 2015).

**Electrolyte and Acid-Base Balance:** Sodium, chloride, phosphate, potassium, calcium, and magnesium are electrolytes commonly affected by abnormalities in critically ill animals. Hyper- and hyponatremia result in central nervous system dysfunction, and should be gradually corrected to prevent abnormal fluid shifts due to neurologic damage induced by changes in osmolarity between the intravascular space and cerebrospinal fluid at a rate exceeding adaptive mechanisms. Hyperkalemia can lead to cardiac dysfunction and arrest if uncontrolled, and hypokalemia can lead to metabolic, neuromuscular, renal, and cardiovascular consequences. Hypercalcemia may lead to neurologic dysfunction such as ataxia and dulled mentation, as well as muscle twitching, seizures and coma. Hypocalcemia is commonly associated with muscle tremors, muscle cramping, and seizures. Hypomagnesemia is commonly seen in the critically ill, and result in cardiac arrhythmias and neuromuscular dysfunction. Laboratory testing for electrolytes are readily available and patients may require very frequent sampling depending on the cause and severity of the electrolyte abnormality.

Acid-base balance is important in the maintenance of a normal pH (7.35-7.45), as acid-base abnormalities have cardiovascular, neurologic, respiratory, and metabolic consequences. Disturbances arise from either a respiratory (inability to control normal CO2 levels) or metabolic (accumulation of acidic metabolites or loss of protons) cause, or both (mixed acid-base disorders). Readily available patient side or laboratory acid-base chemistry analyzers provide indirect measures of oxygenation and ventilation status. Venous sampling will give a more direct CO2 measurement, allowing for measurement without the need of endotracheal intubation of specialized ETCO2 sampling tube. An arterial blood gas analysis, less commonly performed due to technical skill requirement and potential patient morbidity will provide the most accurate measurement of oxygenation (partial pressure of oxygen in the arteries, PaO2) and ventilation (partial pressure of oxygen in the arteries, PaCO2). A patient exhibiting signs of respiratory compromise and less than normal oxygenation (SpO2 < 95%, PaO2 < 80mmHg) should receive higher oxygen supplementation. A patient exhibiting signs of respiratory compromise and higher than normal CO2 levels (ETCO2 > 60mmHg, PaCO2 > 60mmHg) despite treatment of underlying causes may require assisted breathing (manual or mechanical ventilation).

**Mentation:** Alteration of mentation is indicative of inadequate oxygen delivery to the brain related to blood oxygenation or cerebral perfusion. Primary neurologic dysfunction through neurologic disorders, toxins, drug overdose, and brain injury may also be possible. Mentation should be monitored throughout the day with changes, especially if sudden, warranting swift intervention to assess the cause and provide therapy.

**Perfusion and Blood Pressure:** A compromise in the cardiovascular system leading to hypotension and poor perfusion is common in critical care. Hypovolemia due to fluid losses through hemorrhage and gastrointestinal or urinary losses as well as relative hypovolemia from severe vasodilation is a cause for lowered preload and cardiac output, leading to hypotension. The six physical parameters used to evaluate appropriate perfusion include heart rate, pulse quality, MM color, CRT, core-to-body temperature gradient, and mentation. Blood pressure measurement is possible through Doppler, oscillometric, high definition oscillometric, and direct arterial measurement through an arterial catheter and pressure transducer line. Blood pressure measurement is especially important and performed frequently on patients with hemodynamic instability. A mean arterial pressure (MAP) of greater than 60mmHg is required for proper perfusion of the kidneys and brain (the first organs to be affected with a lower BP). While blood pressure provides a typically non-invasive method of evaluation of circulation, in cases of severe vasoconstriction maintenance of normal blood pressure may not provide sufficient perfusion due to the narrowed vessels and reduced blood flow. Evaluation of markers for anaerobic metabolism such as lactate measurements and acid-base analysis will provide further insight on oxygen delivery. A patient with a MAP of greater than 145mmHg is considered to be hypertensive and can be a result of renal, hyperthyroidism, hyperadrenocorticism, neoplasia, or pain.
Heart Rate, Rhythm, and Contractility: Another cause for inadequate perfusion relates to function of the heart. Reduced oxygen delivery can in turn affect myocardial function leading to arrhythmias. Tachycardia is a sign of hemodynamic compromise, while bradycardia can be a sign of impending arrest. Heart rate and rhythm can be monitored regularly through auscultation, or equipment such as electrocardiogram. An echocardiogram may be considered if a primary cardiac disease is suspected. When tachycardia is observed, the cause should be evaluated to rule out compensatory tachycardia from compromised perfusion. Pain and anxiety may cause tachycardia as well. Arrhythmias observed through auscultation or ECG should prompt alerting of the veterinarian and treated if perfusion is compromised as a result. Poor contractility associated with cardiac disease or dysfunction will lead to further perfusion compromise, requiring inotropic therapy.

Albumin: Albumin is the main source of colloid osmotic pressure in the plasma, along with other proteins. Hypoproteinemia (and hypoalbuminemia) is a common finding with various critical illness such as protein losing enteropathy (hemorrhagic gastroenteritis, paroviral enteritis), protein-losing nephropathy, liver disease, severe trauma, burn wounds, etc. As mentioned previously, hypoalbuminemia leads to inability to maintain intravascular volume and edema since albumin serves to maintain COP. In addition, albumin’s ability to deliver drugs through circulation, aid in elimination of toxins, maintain endothelial integrity, mediate coagulation, and scavenge reactive oxygen species is lead to consequences in hypoalbuminemia. Albumin levels can be measure through serum chemistry, with a value lower than 20g/L (2g/dL) qualifying as hypoalbuminemia associated with increased mortality rate, though a clear association between albumin concentrate administration to raise albumin level to normal values and improved survival rate has not been established (Craft et al 2012; Mazzaferrro et al 2002).

Coagulation: Animals may be critically ill due to hemostatic diseases, or develop hemostatic disorders during a disease process. Coagulopathies can be acquired through ingestion or administration of anticoagulants, impaired coagulation factor synthesis from liver failure, increased fibrinolysis from neoplasia, immune-mediated platelet destruction, or toxin or drug related platelet inhibition. Dilutional coagulopathies can occur when high volume fluid infusions are performed diluting coagulation factors and platelets in circulation to an ineffective level, commonly occurring with severely hemorrhaging patients. Consumption of coagulation factors and platelets through consistent hemostatic demand is possible as well. Hypercoagulable states can result from reduction of antithrombosis or fibrinolysis, associated with protein-losing nephropathy, neoplasia, immune-mediated hemolytic anemia, acute pancreatitis, hypercortisolism (iatrogenic or disease), and sepsis, leading to thromboembolism at a macroscopic or microscopic level leading to tissue ischemia (Park et al 2014; Kitrell et al 2012). Hypercoagulability also have been reported to be associated with the degree of inflammation and hematocrit, with patients with higher C-reactive protein and interleukin-8 level and hematocrit resulting in hypercoagulable TEG tracings (Marchner et al 2018). Disseminated intravascular coagulation (DIC) is a development of a hypercoagulable state leading to formation of microthrombi within the vasculature leading to microvascular thromboembolism and consumption of coagulation factors and platelets. Once the procoagulants are depleted, a coagulopathy sets in with blood loss leading to further consequences of organ dysfunction through development of anemia and hypovolemia. Coagulation status may be monitored through evaluation of the patient for external signs of coagulopathy and its progression, as well as laboratory testing such as PT/PTT. Hypercoagulable states are difficult to diagnose through laboratory testing, with thromboelastography being an option in larger scale practices and has been reported in dogs, cats, foals, and adult horses (McMichael et al 2011).

Red Blood Cell and Hemoglobin: Provided there is adequate intravascular volume and tissue perfusion, DO2 is dependent on the oxygen level contained in the blood (arterial oxygen content, CaO2) and how quickly the body can circulate the blood to the tissues (cardiac output, CO). The resulting mathematical expression of DO2 is: DO2 = CaO2 x CO. Oxygen contained within blood exists in two forms; dissolved in the plasma and bound to hemoglobin. The amount of oxygen dissolved in plasma depends on the partial pressure of oxygen (PaO2), with 1 mmHg creating enough tension to result in 0.0031mL of dissolved O2 per dL of plasma. Each gram of hemoglobin can theoretically carry 1.39mL of O2 when fully bound with oxygen, making up a significant portion of oxygen content of blood. In reality, there are portions of dysfunctional hemoglobin lowering this to approximately 1.34mL. In addition, not every hemoglobin molecule will be fully bound to oxygen in every situation (SaO2, or arterial oxemoglobin saturation) adding some variability. With these considerations in mind, the resultant formula to quantify DO2 is the following, expressing the impact lowered hemoglobin concentration and saturation of the hemoglobin will have on overall delivery of oxygen: DO2 = [(1.34 x Hgb x SaO2) + (0.0031 x PaO2)] x CO. Hemoglobin levels can be measured with a hemoglobinometer, though measurement of PCV is much more common to be measured. PCV of 25-30% is thought to
make preemptive analgesia imperative in any patient, especially the critically ill. Patient should be evaluated for the healing, immune system, cardiovascular function, and more. Pain is much easier to prevent than to catch up with, and therefore providing adequate oxygen carrying capacity in most all situations. Manifestation of clinical signs of anemia (tachycardia, weakness, altered mentation, pale MM) or marker for anaerobic metabolism (lactate, pH, HCO3) pointing to metabolic acidosis thought to be related to reduced oxygen carrying capacity is an indication to provide a RBC transfusion (Kisielewicz et al 2014).

**Renal Function and Urine Output:** Reduced urine output (<1ml/kg/hr in a hydrated patient) is indicative of renal dysfunction, whether it may be a pre-renal (poor perfusion) or intrinsic renal (renal disease) cause. Patients with low urine output should have their perfusion status re-evaluated, and any nephrotoxic drugs to be adjusted if renal damage is suspected. Measurement of urine output is most conveniently evaluated through the placement of a urinary catheter with an attached collection bag. Placement of a urinary catheter increases risks of hospital acquired infection, and should be implemented after consideration of the risks and benefits. Performing diagnostics such as urinalysis, BUN, and creatinine will also give insight to renal function.

**Immune Status:** Bacterial infections are common causes of critical illness, and can be acquired while hospitalized. Antimicrobial therapy is instituted when infections are suspected, and should be evaluated for its effectiveness. Cultures being obtained prior to initiation of antimicrobial therapy are advised, if possible without delaying antimicrobial treatment. The various catheters, as well as any gastrointestinal compromise can become sources of sepsis. White blood cell counts and differentials will help monitor the immune system’s response to said infections. Patients considered to be immunocompromised should have aseptic technique utilized around them with hand washing, disinfection of equipment and surrounding area, and wearing gloves a common practice.

**Gastrointestinal Motility and Mucosal Integrity:** Problems with emesis and gastric motility is common in critical illness. Administration of gastric protectants, antiemetic, and gastric motility agents are commonly performed to help prevent or resolve motility issues. A nasogastric tube may be placed to gauge gastric motility through quantification of accumulated fluid after set intervals. The same tube may be used to provide enteral nutrition as well. Preventing emesis and gastric motility issues is helpful in minimizing chances of dehydration and electrolyte imbalances.

**Drug Dosages and Metabolism:** As drugs are primarily metabolized by the liver and excreted by the kidneys, patients with suspected hepatic and renal dysfunction should have extra attention in drug dosages. Drug dosages should be adjusted as needed to achieve a desired effect, and their pharmacology considered. The signs evaluated in the patient will be dependent on the type of drug being administered, its effects, side effects, and elimination pathway.

**Nutrition:** In most cases, early nutritional intervention is ultimately beneficial for positive patient outcomes. One of the most common causes of sepsis and decline of a critically ill patient is bacterial translocation from breakdown of gastrointestinal barriers from a lack of passive nutrition to the enterocytes. In addition, absence of nutritional intake will lead to visceral organ atrophy, immunocompromised, electrolyte imbalance, muscle atrophy, and more. At the very latest, nutritional intervention at the 3rd day of anorexia is recommended and can be provided through various methods such as nasogastric or nasoesophageal, esophagostomy, gastrostomy, and jejunostomy tubes. Syringe feeding is not recommended unless the patient willingly takes amounts meeting energy requirements.

**Pain Control:** The pathophysiology of pain is often underestimated and contributes to negative effects to healing, immune system, cardiovascular function, and more. Pain is much easier to prevent than to catch up with, making preemptive analgesia imperative in any patient, especially the critically ill. Patient should be evaluated regularly for comfort, and signs of pain such as awkward posturing, tachycardia, tachypnea, hypertension, restlessness, mental depression, and irritability should be evaluated consistently through standardized methods. Analgesic interventions should subsequently be assessed in their effectiveness.

**Nursing Care and Patient Mobilization:** Critically ill patients are often recumbent from weakness and inability to move. A patient should be turned at least every 4 hours to prevent pressure sores and atelectasis of the alveoli. Catheter insertion sites and cleanliness should be evaluated regularly to minimize chances of nosocomial infections. Any fecal, urinary, or salivary soiling should be tended to in prevention of irritation to the skin which also serves as means for bacterial organisms to cause issues.

**Wound Care and Bandage Change:** Incision sites and any wounds should be inspected regularly throughout the day for any signs of bleeding, irritation, dehiscence, and infections. Bandages that are wet for any reason should be replaced. Marking the outer edges of bruises, or taking photo images of wounds will allow for a more objective comparison for progress.
Tender Loving Care: In addition to appropriate medical care, attention to the mental health of the patient is invaluable in aiding the healing process for our patients. Making sure our patients have comfortable, dry, clean bedding is a minimal requirement. Providing a stress-free (as much as possible) with regards to noise, lighting, movement, and smells around the patient contributes to a healing environment. Taking time, when the patient feels well enough, to provide the caring, gentle touch, attention, soothing voices, occasional toys, and other forms of enrichment of the mind is one of the most important aspects of our care.

Oxygen in Energy Production

Regular monitoring and assessment of patients ultimately are directed at ensuring there is no compromise to vital systems and functions that allow proper delivery of oxygen (DO2) to tissue systems. The importance of maintaining adequate DO2 lies in the difference of the amount of adenosine triphosphate (ATP) produced in the presence and absence of oxygen. ATP is considered the “currency of cellular energy”, providing energy for cellular processes required to maintain life as phosphate groups are cleaved off resulting energy release and formation of adenosine diphosphate (ADP) or adenosine monophosphate (AMP). ATP is involved in cellular signaling, DNA and RNA synthesis, muscle contraction, cytoskeletal maintenance, active transporting, and many other cellular functions. There is a finite amount of ATP available within a body, and a constant recycling of ADP and AMP into ATP is required to keep up with energy demands. In the presence of oxygen, 38 ATP molecules are generated from metabolism of a single glucose molecule undergoing oxidative phosphorylation occurring in the mitochondria. In contrast, a single glucose molecule yields two ATP molecules through anaerobic metabolism. The presence of oxygen is imperative in efficient energy generation.

In animals without disease, DO2 is significantly above oxygen consumption (VO2), supplying a very comfortable buffer of available oxygen for energy production. This buffer allows for sudden changes in oxygen demand through changes in cellular metabolic rate or reduction in CaO2. When DO2 is significantly compromised (termed critical oxygen delivery), tissue hypoxia results and increased lactate levels and lowered pH are seen. The oxygen extraction ratio can also be used to express the level of oxygen consumed in relation to DO2 (\(O_2\)ER = \(VO_2/DO_2\)). Higher oxygen consumption or lower DO2 leads to a higher ratio. The normal \(O_2\)ER value is approximately 0.2, though different organ systems have varying \(O_2\)ER (normal \(O_2\)ER of the heart is 0.6, making it more sensitive to hypoxemia). A normal DO2, VO2, and \(O_2\)ER in dogs were observed to be 790ml/min/m2, 164ml/min/m2, and 0.205, respectively in one study. Another couple of studies cite a normal DO2 of 20-25ml/kg/min and observed critical oxygen delivery levels of 8-11ml/kg/min regardless of the cause (anemia, hypoxemia, and cardiac tamponade). A patient is said to be in hypoxemic shock when Hgb, SaO2, or PaO2 levels are low enough for DO2 to reach this critical oxygen delivery level. In clinical settings, measurement of specific values such as CO and VO2 (though can be estimated) are rather difficult, and we utilize this concept in determining when a patient is suspected to be in hypoxemic shock rather than making direct comparisons.

Tissue Perfusion

The maintenance of normal blood pressure and tissue perfusion depends on adequate CO, and systemic vascular resistance (SVR). The most common form of reduced DO2 and shock occurs secondary to reduction in CO or SVR. CO is can be reduced through a loss of intravascular volume, leading to hypovolemic shock. Hypovolemic shock can be caused by many situations leading to hypovolemia, such as internal or external hemorrhaging, fluid loss through vomiting, diarrhea, polyuria, exposed subcutaneous surfaces (burns, bit wounds) and/or reduced water intake. A loss in circulating blood volume leads to a diminished venous return and preload to the heart, reducing the stroke volume (SV). A significant degree of reduced CO due to decreased SV is compensated for through an increase in heart rate (\(CO = SV \times HR\)). SV itself is improved through increased contractility, or a more forceful contraction of the heart to eject a larger volume of blood. Reduced blood flow to the kidneys stimulates the renin-angiotensin-aldosterone system, increasing production of aldosterone leading to sodium retention, increasing plasma osmolarity and encouraging shifting of fluid to the intravascular compartment. Increased antidiuretic hormone (vasopressin) also promotes water retention, reducing urinary fluid loss. While vasoconstriction does not directly add to intravascular volume, its occurrence increases systemic vascular resistance, improving blood pressure and circulation of the reduce blood volume.

Patients faced with hypovolemia initially show signs of compensatory shock, involving tachycardia, normal prolonged capillary refill time (CRT), normal to pale mucous membranes, tachypnea, and cool extremities. Pulse
Patients suffering from gastric dilatation-volvulus (GDV) will have a distended stomach compressing the intra-abdominal vessels (caudal vena cava, portal veins, and splanchnic vessels), impeding venous return to the heart leading to a reduced CO. This is considered obstructive shock by many (while many others consider it a form of distributive shock), where major blood vessels are occluded or carry reduced blood flow contributing to poor CO. The cause of shock in GDV is multi-faceted, since the occlusion of major vessels leads to portal hypertension and splanchnic pooling, leading to effusion of intravascular fluid into the abdominal cavity and interstitium, contributing to hypovolemia. Additional fluid loss may also occur due to vascular injury to gastric vessels as it is stretched, and repeated vomiting. Many disease processes involve different causes of shock occurring in varying in degrees, leading to the cumulative effect of reduced CO and DO₂.

**Initial Respiratory Assessment and Treatments**

Assessment of a respiratory patient starts from external physical signs. Patients presenting with signs such as tachypnea, increased respiratory effort, and open-mouth breathing are clearly in trouble. Exaggerated movement of parts of the body surrounding the physical construct of the airway such as flaring nostrils, lip movement with respiration, sucking in and out of the skin under the chin and thoracic inlets, and paradoxical abdominal movement are all signs of severe respiratory distress. An orthopneic position, characterized by open-mouth breathing, extending of the head and neck, sitting up sternal, and abduction of the elbows in the effort to open up the airway as much as possible, is another common external sign of respiratory distress. If the patient progresses to being unable to hold themselves up, going into lateral recumbency with no improvement in respiratory signs, the patient may be experiencing respiratory fatigue and facing imminent arrest.

Assessment and treatment of a patient in respiratory distress poses a dilemma, as swift determination of the patient’s problem is required, yet they may be compromised such that the stress of diagnostics and treatment may push them into respiratory and cardiac arrest. These patients are in a very fragile state, and initial efforts are aimed at improving the patient’s ability to breathe while minimizing stress and deterioration in respiratory status. Providing oxygen supplementation through flow-by, mask, induction chamber, or cage would be one of the first lines of therapy to alleviate distress.

Patients in respiratory distress are often very anxious, which often makes the patient even more dyspneic. A light sedation with small doses of benign sedative such as butorphanol may be beneficial to help ease anxiety. The staff working on the patient should conduct themselves in a calm and quiet manner yet maintaining swiftness. A calmer environment will not only benefit the patient, but may benefit a worried owner. The presence of the owner can either be beneficial or detrimental to the patient, and staff directing attention to calming a panicked client (and successfully doing so) may also help the patient.
Diagnostics and treatment such as physical examination, radiographs, blood work and IV catheterization may have to be held off until the patient is more relaxed and breathing better. Evaluation of a patient’s respiratory problem begins with external visualization of their breaths. The manner in which a patient breathes is adapted to the method requiring the least work of breathing. An obstructive breathing pattern, involving a prolonged inspiration (upper airway) or expiration (intrathoracic lower airways), will be observed in patients with narrowed airways. A restrictive breathing pattern, involving shallower but tachypneic breathing, will be observed in pleural disease or reduction of lung compliance. Abdominal effort may be seen with patients with compromised lungs. Certain conditions (anemia, metabolic acidosis, and pain, for example) can cause “non-respiratory look-aliases”.

Auscultation is a valuable skill in early detection and detection of change in lung states. Stertor (snoring), wheezes (whistling), and stridor (high pitched noise) can indicate different upper airway issues. Crackles indicate fluid in the alveoli, such as in pneumonia or pulmonary edema. The location lung sounds are present or absent in helps indicate causes as well. Cardiogenic pulmonary edema often begins near the heart (perihilar region), and aspiration pneumonia often originate in the cranoventral lobes. Absence or decrease in lung sounds in the caudal and ventral fields may indicate pleural effusion, while dorsal fields may be due to pneumothorax. While abnormalities in auscultations do not lead to a diagnosis, it serves as an indication for further diagnostics.

If pleural space issues like pleural effusion or pneumothorax is suspected, performing thoracocentesis to evacuate the fluid or air can provide diagnostic information and therapeutic treatment simultaneously. The staff should be prepared to perform endotracheal intubation and provide positive pressure ventilation (PPV) if the patient does not stabilize with initial treatment and progressively gets worse.

**Respiratory Patient Monitoring**

During the treatment of patients with respiratory compromise, the patient should be closely monitored on three different aspects; oxygenation, ventilation (carbon dioxide elimination), and the degree of respiratory effort. In addition to the visible respiratory effort and auscultation, different instrumentation and blood analysis can give insight to the progression of the patient’s recovery.

**Oxygenation**

A physical sign seen in patients with severe hypoxemia is cyanosis, or a blue color to the mucous membranes. Cyanosis becomes apparent when there is more than 5 g/dL of deoxyhemoglobin present in the blood. An average hemoglobin level in dogs is approximately 13-17 g/dL, and in cats is approximately 10-14 g/dL. This means the oxygen saturation of hemoglobin will be a significantly decreased level on average of 61 -70% for dogs and 50 -64% for a cat before cyanosis is seen. Patients presenting with cyanosis is severely compromised in their DO2 and requires immediate attention.

Oxygenation can be better gauged through measurement of PaO2, serving as an indicator of pulmonary function. PaO2 can be measured through blood gas analysis of arterial blood, requiring arterial blood sampling and a blood gas analyzer. A patient with normal respiratory function breathing room air will have a PaO2 of 80-100mmHg. PaO2 of less than 80mmHg qualifies as hypoxemia, and 60mmHg is considered severe hypoxemia.

Pulse oximetry allows non-invasive measurements of the percentage of oxygenated functional hemoglobin in the arterial bloodstream, utilizing the concept of light absorption. The saturation of oxygen measured by pulse oximetry (SpO2) closely reflects SaO2 and can be used to estimate the PaO2 level. The oxygen-hemoglobin dissociation curve expresses the relationship between SaO2 and PaO2. A SaO2 of 95-98% corresponds to a PaO2 of 80-100mmHg. A SaO2 below 90% indicates a PaO2 of less than 60mmHg. Pulse oximetry has its limitations, including false reading in the presence of significant levels of dysfunctional hemoglobin species (methemoglobin, carboxyhemoglobin), inconsistent readings with movement, poor perfusion, anemia, and pigmented skin. Interpretation of oxygenation and pulmonary function can performed by calculated values called the PaO2:FiO2 Ratio (PF ratio) and alveolar-arterial (A-a) gradient.

**Carbon Dioxide Elimination**

CO2 is produced by tissues as a metabolic byproduct of energy production. The body normally maintains control of CO2 levels in order to control the pH level of the body. An accumulation of CO2 causes an increase in levels of carbonic acid, leading to higher levels of dissociated hydrogen ions, leading to a more acidic environment (lower
pH). A reduction in CO2 level will lead to a decrease in hydrogen ions, leading to a more basic environment. This effect is called respiratory acidosis and respiratory alkalosis, respectively.

The amount of CO2 eliminated by the body depends on the movement of air in and out of the alveoli to perform gas exchange, or ventilation. Room air contains about 0.04% CO2 (0.3mmHg), and the replacement of gas within the alveoli with fresh room air will promote diffusion of CO2 out of the blood stream into the gas within the alveoli, which in turn gets expired out of the lungs and airway. A normal CO2 levels within the blood is approximately 35-45mmHg in dogs, and 30-40mmHg in cats, and can be measured by blood gas analysis (PaCO2 if arterial or PvCO2 if venous). The difference in PCO2 in the pulmonary capillaries and alveoli create a pressure gradient required for gas exchange (high to low; high in the capillary, low in the alveoli).

PCO2 is largely influenced by the amount of air that can be moved in and out of the alveoli, or alveolar ventilation. The value will increase with hypoventilation (>45mmHg) in cases of respiratory depression (suppression of respiration due to drugs, neuromuscular disease, CNS disease), inability to expand the lungs (pleural space disease, compromise to chest walls), or increased resistance to breathing (narrowed airway). Hyperventilation and subsequent low PaCO2 can be seen in patients with increased RR due to anemia and hypoxia. In metabolic acidosis, compensatory increase in respiratory effort and hyperventilation is often seen, countering the metabolic acidosis effect with respiratory alkalosis. This occurs because the presence of hydrogen ions will stimulate the respiratory center of the brain to increase respiratory efforts.

The PaCO2 can be estimated by measurement of End-tidal CO2 (ETCO2). The CO2 content in the gas present at the probe at the end of expiration is measured to obtain this value. The ETCO2 in normal cardiovascular and respiratory situation, is within 5mmHg of the PaCO2. The ETCO2 is most easily measured when an endotracheal tube is placed in a patient (anesthetic procedure or mechanically ventilated patients, for example).

**Veterinary Technician’s Role in Patient Assessment**

A veterinary technician plays a vital role in the veterinary team to monitor patients and obtaining the parameters necessary to assess the patient’s status. In many cases in a critical care setting, the veterinary technician is the first line of team members that can detect the changes seen in a patient which leads to the appropriate interventions. The status of the patient and priority body system in need of monitoring may change depending on the progression of the patient’s disease process during the course of care, and a veterinary technician well versed in patient assessment is invaluable to influence a positive outcome.

**References**


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