Healthy People Healthy Practice
Oklahoma State University
2023 Summer Seminar
Laurie Fonken, Ph.D., LPC

Introduction

Veterinary professionals are highly committed and dedicated individuals who work hard to care for their patients, clients, colleagues, and communities. For those who devote their lives to the service of others, the physical, emotional and spiritual demands of the work, while rewarding, can lead to exhaustion. Day to day work expectations and pressures can at times feel overwhelming and isolating and have detrimental effects on personal and professional well-being. The natural response may be to work harder, to give more, until there is nothing left to give. The good news is that as caring individuals you have the capacity to focus that care on yourself. With development of healthy practices, you can continue to effectively provide comprehensive and compassionate care for others, while taking care of yourself. This paper will address and define some of the main challenges to health and wellbeing and identify strategies and tools individuals can implement to address them.

Current Research Findings

The recently released Executive Summary of the 2021 Merck Animal Health Veterinary Wellbeing Study III and Veterinary Support Staff Study found 92% of the 2,493 veterinarian and 448 veterinary staff respondents rated increased stress at one of their top mental health challenges while 88% cited student debt and concerns about the risk of suicide as main stressors for veterinary professionals. Effects of the pandemic were seen in that more than 90% of respondents reported shortages of qualified veterinary staff and 68% highlighted the difficulty of providing services during the pandemic. Pandemic related concerns included difficulty finding enough staff, employees spending time away from work due to illness and family care and anxiety around the risk of increased exposure to Covid 19. For those who were able to work, increased hours were another contributor to stress. More than 90% of both veterinarians and veterinary support staff believe the shortage of qualified veterinary professionals to be among the most critical challenges facing the profession.

In this third of three studies completed by Merck, the first in 2017, the second in 2019, the number of veterinarians reporting serious psychology distress grew 3.3% from 2019 at 6.4% to 2 9.7% in 2021. 18.1% of veterinary staff reported being in serious psychological distress nearly twice the percentage reported in 2019. High burnout levels were reported at 30.5% for veterinarians and 49.6% for veterinary staff. Workload and excessive work hours continue to be among the main contributors to serious psychological distress and burnout. Veterinarians under 50 years of age had lower wellbeing. Only 56.5% or veterinarians and 50.2% of veterinary staff reported they were flourishing in their work. Food animal and equine practitioners had higher levels of wellbeing then mixed and companion animal practitioners.

Similar to the findings in 2019 only 47% of veterinarians said they would recommend the profession to others, citing cost of becoming a veterinarian compared to income level and stress of the profession as the main reasons. 18% of respondents said they regretted becoming a veterinarian. 1 in 5 said they were likely to leave the profession within the next 2 years.

Veterinary staff were more apt to leave the profession in the next 2 years with 31% stating plans to leave their employment.[1]

Trends and Challenges

In May of 2019, the World Health Organization added burn-out to the 11th Revision of the International Classification of Diseases (ICD-11) as an occupational phenomenon and defined it as "a syndrome conceptualized as resulting from chronic workplace stress that has not been successfully managed." It is characterized by three dimensions: "1) feelings of energy depletion or exhaustion; 2) increased mental distance from one's job, or feelings of negativism or cynicism related to one's job; and 3) reduced professional efficacy. Burn-out refers specifically to phenomena in the occupational context and should not be applied to describe experiences in other areas of life[2]."

Factors challenging the health and wellbeing of veterinary professionals are complex and interwoven. Compassion fatigue is a state experienced when one is feeling the impact of burnout, defined above, and secondary trauma. Secondary trauma is when exposure to others pain and suffering creates a sense that the trauma has happened to you. The combination of these factors leads to a reduced capacity for engagement as a consequence of exhaustion from being with suffering. Moral distress refers to feelings provoked by the real or perceived violation of one's moral or ethical beliefs and can include issues of fairness, respect, commitment to care[3]. Decision fatigue is "a psychological phenomenon surrounding a person's ability or capacity to make decisions[4]." When one experiences decision fatigue, the ability to make decisions can get worse as the brain will be more fatigued. This fatigue applies to all decisions, not simply the large or more difficult ones. Most strategies and tools for intervention exist at the individual and working group level. It is important to note that burnout, as a phenomenon directly relates to the workplace, must be acknowledged and dealt with by organizations and institutions as they have a primary role in creating the situational factors inherent in it.

Stress and the Stress Cycle

Stress and stressful events (stressors) are an inevitable and unavoidable part of life. Often we have no control over the events that lead us to the experience of stress, what we can control is our response to the stressor. Dealing with a particular stressor is different that dealing with our stress response. Stress is a neurological and physiological shift that happens in your body when you encounter what is perceived to be a threat. It can be an external threat (lion) or an internal threat (self-criticism, belief you are a failure) Stress is an evolutionary response meant to keep us safe from harm by triggering a physiological response which are meant to help us survive. A stressor is anything that activates a stress response in us. The hit by car that comes through the door initiates a response where we jump into action, our thinking mind starts to analyze the situation, assess, diagnose and make a plan of action. Our physiology kicks in hormones that helps us take physical action to deal with the situation, we move in a way that will help the patient. We focus in on what is necessary in that moment to deal with that situation. Once the stress response is triggered and the hormones and endorphins flood our body we are able to deal with the stressor. The issue comes when the stress response continues after the stressor is dealt with. The situation is handled and yet our physiology is still

in a stress response. Adrenaline, cortisol, and glycogen are still in the system, the body is still in action mode. It takes time to complete the stress cycle and it takes a conscious action.

Completing the stress cycle may bring up emotions, the threat is gone, the hit by car is in recovery and you are overcome with relief, tears, physiologically shaking, agitation, inability to relax or sleep. Going from 100mph down to 10mh you need time to decelerate.

We get stuck in the stress cycle when we are in an environment with chronic stressors, stuck in a stress activating situation. This is not necessarily bad unless the stress outpaces the capacity for one to process it. [5] What happens in veterinary medicine is we are faced with one stress after another and there is no time to complete one stress cycle before the next one is triggered. Once the stressor has passed having a plan for release of the physiological energy and emotion connected with it are necessary so you can continue on with what is ahead. Completing the stress cycle is not an intellectual process, it is a physiological one and involves actually doing something. This may be physical activity, walking, stretching, getting outside, or calling a debrief with the team, time set aside to share how things went, how people are doing and what they might need, or spending some time in a quiet space to do some deep breathing or writing. Whatever you choose it is important to know the stress will remain in your body until you have taken time to release it.

Boundaries

Have you ever heard good fences make good neighbors? A fence is a boundary. It delineates where one property ends, and another begins. Dr. Henry Cloud clearly and simply explains how fences are important for keeping things in one space and other things out of that space. Fences are functional. If your neighbor has a tree that falls over the fence into your yard it may become something you have to deal with[6]. Healthy boundaries, like good fences, help keep in what you would like and out what does not serve. By keeping the boundaries, you set for yourself it lets others know and see you value yourself and take responsibility for your wellbeing and that you trust them to do the same for themselves.

We teach people how to treat us by the way we treat ourselves. Others learn from watching us what is acceptable behavior toward us. If we continually stretch our boundaries to meet other's needs, they will see this. As we know actions speak louder than words. Every time we say one thing and do another, we teach others it is ok to do the same. Setting healthy boundaries is hard and yet if we say it, we must do it. The short-term default for many to unhealthy boundaries means that while the discomfort of asserting yourself and saying no is avoided, the negative feelings of frustration, resentment and ultimately exhaustion linger on. These situations and the feelings that go with them affect not only the relationships you have with others, but also contribute to your individual burnout.

Our relationships with people differ depending on the setting. We have professional relationships and personal relationship. Clearly identifying the type of relationship you have with another can help with boundary setting. Consider your role in the relationship. In professional relationships boundaries are expected and necessary for you to do the work you need to do in the manner consistent with your professional responsibilities[7]. Respecting professional boundaries is key to the structure and operation of your practice.

What are the barriers to setting healthy boundaries? These may vary from individual to individual and include internal as well as external barriers. Internal barriers are personal beliefs

about work and roles. We each have a work ethic and standards we set for ourselves. External barriers include the culture of the environment within which we work, and the spoken and unspoken expectations and norms set there. Understanding our personal work ethic and the cultural expectations can help us to assess if there is a match or mismatch. Awareness and open communication about these expectations and the impact they have on teams is essential.

Step one in setting healthy boundaries is believing we deserve to focus on our own health and wellbeing and to see ourselves with the same compassion we show others. Self-compassion includes self-kindness- we must eliminate the judgments and messages in our minds that put us down; common humanity- we must remember that just like me someone else would find this situation difficult; and mindfulness- we must separate the issue from self, we are not what we did or what happened, we are who we are[8]. "No." Is a complete sentence. Let's acknowledge that many of us have difficulty saying "No". Some of us can say the initial "no" and then feel compelled to explain, defend, rationalize or compromise the "no". For our boundaries to be respected we must respect ourselves by sticking with our "no" as is. We do not need to explain everything to everyone. "No." is a fine response.

Tips for setting healthy boundaries include acknowledging you are worthy of time off and self-care. Meeting your physical, emotional, mental, spiritual and social needs is important to your overall health and wellbeing. Setting limits is essential when we are in situations of ethical and moral stress, as well as at times we need to step back, renew and refocus. Clarity is a critical element in boundary setting. Make sure you are specific, confident and clear about your limits and expectations. Lack of clarity leads to misunderstanding which leads to different expectations and often negative outcomes. Finally, consistency is key, if you set a boundary and expect others to respect it, you also need to respect it. Remember we teach people how to treat up by the way we treat ourselves. Consistency is a sign of professionalism and respect for self and others[9].

Strategies Supporting Wellbeing

The Self Care Equation X≥Y

In this equation you and your health and wellbeing are the **X.** Everyone and everything else is the **Y.** Like the oxygen mask on the airplane you are responsible for placing your mask on first before assisting others. If you are not accountable to your own health and wellbeing the responsibility may fall to others. There will be times when the Y has to come first, these should be the exception not the rule.

Identifying and naming your challenges can help you find ways to deal with or overcome them. Common strategies for individuals include development of coping skills, setting boundaries, conflict and time management. Assessing the potential to change work patterns, working less, taking more breaks, job sharing, avoiding overtime work. In addition, building a strong community of support both at work and outside have been found to support wellbeing. Finally, utilizing relaxation techniques, promoting good health, eating, fitness and sleep provide a strong foundation of health, wellbeing and self-care which can be helpful when faced with the challenges of work.

Engagement has been identified as the positive counterpart to the challenges described above. Engagement with the meaning and purpose of your work, connection to the calling which brought you to veterinary medicine, involvement with colleagues, clients and patients,

giving back to the community and a sense of efficacy and connection to the deeper value in the work you do sets a foundation of protection when facing professional challenges. Fostering compassion satisfaction and self-compassion helps one focus on the positive aspects of working as a helper caring for others and oneself. Compassion makes us feel good and compassionate action activates pleasure circuits in the brain. In a 2015 article on sources of satisfaction in veterinary professionals, Martin Cake and colleagues found 7 elements contributed to a life of meaning: helping and healing animals, grateful clients, interesting and varied challenging job, lifelong learning, educating others, and financial rewards[10].

Conclusion

To practice effective and beneficial veterinary medicine, one must learn specific clinical skills and techniques and have the education, knowledge, and experience to implement them. The process of practice includes assessment, diagnosing, treatment planning and implementation, evaluation and possibly modification or additions to what was done. It is the same for our professional and personal health and wellbeing. Developing awareness of what we are experiencing, naming it, assessing the various elements involved, creating strategies and techniques to address and overcome challenges and taking action. These steps followed by evaluation and adjustments as necessary can support us in being whole, healthy human beings with the expertise, clinical skills, knowledge and ability to be competent and caring veterinary practitioners while maintaining our personal and professional health and wellbeing.

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Real World Stress Management: Principles in Practice

Elizabeth Brock, DVM, MS

Abstract

Veterinary practice is stressful and always will be. Stress is a natural animal adaptation that allows us to face challenges and survive. And yet, the thinking human brain gives us the unique opportunity to convert a physiologic mechanism meant to protect us into a chronic condition that causes us bodily harm. How then do we create coping strategies to stop our propensity for chronic, maladaptive stress? While there is excellent data that proper diet, exercise and sleep habits help, veterinarians often have time challenges that limit their ability to employ these practices routinely. Practicing techniques like meditation, gratitude, self-compassion and story-checking, all of which can be done in the truck between calls, or in small moments between patient rooms, can wake us up to our habits of thought and change the volume and channel on the chatter in our brains. Waking up to our thoughts is the first step to changing how we relate to stress as it arises in the moment and being more resilient in our ability to cope with it.

Introduction

As veterinarians, we are trained to evaluate presentations of disease, synthesize the data we collect with physical examinations and diagnostic tests, prepare a differential diagnosis list and treatment strategy and monitor for outcome. Four years of veterinary education, countless hours in practice and our propensity for Type A personalities, teaches us the following mantra: “See the problem and fix it”. We are good at this, except when it comes to our mental health and wellbeing. Veterinarians also, I would argue, suffer from a “tough guy” mentality. Our identity

in some respects revolves around our ability to work a physically difficult job, in trying weather (if you are ambulatory) and at all hours of the day. The mythology of the tough guy says that the signs of chronic stress and burn out – including sleep abnormalities, diet indiscretion, and irritability – are a normal part of the job and the treatment is to "suck it up". For some, this strategy could be successful. For me, it led to a humiliating moment in the emergency room when what I thought was a stroke, turned out to be a full-blown panic attack.

The Second Arrow

Stress is a normal animal adaptation that protects us from threats to our safety. When the gazelle on the plains senses the presence of the lion, her sympathetic nervous system activates to move her body effectively to safety. We, as veterinarians, know the exact physiologic mechanisms by which this occurs. However, once that gazelle is safe again, her sympathetic response shuts down and she returns to her peaceful existence grazing on the plain. She does not stand around worrying about the next lion attack, wondering if she has protected her offspring well enough, or doubting whether she will be fast enough to get away the next time[1]. Those responses to stress are uniquely human, for better or worse. Our brains often respond to stress by catastrophizing the next stressful event, doubting our abilities to respond, and using our inner cattle prods to condemn our response and "motivate" us to be better next time.

Buddhists call this phenomenon the "second arrow"[2]. In this parable, when we suffer misfortune, two arrows are shot our way. The first is the actual event which is undoubtably painful and very often out of our control. The second arrow we shoot at ourselves by creating a story around the event, berating ourselves with our response to it and reliving it repeatedly. Psychologists

describe this as the negativity bias of the brain. We dwell on the bad so that we will remember it and never, ever do it again.

Let's use an example to depict this concept. Imagine you arrive at a calving in your first few months of practice. It's 3 am and you've never been to this facility before. The client tried to get the calf out for 3 hours before finally calling you. When you arrive, the cow is down in lateral recumbency and all you see is a very swollen head of a dead calf protruding from a very swollen vulva. As you attempt to manipulate the head back into the uterus, it becomes clear that you cannot fix this dystocia in the manner in which you were taught: "repel and reposition". You start to panic because the client is watching you like a hawk and you don't know what to do. As you get lost in negative thought, your prefrontal cortex (the part of your brain that could come up with a solution to the problem) is hijacked by your amygdala (the part of your brain that is supremely unhelpful in this situation). You call your boss who arrives 45 minutes later, incredibly grumpy, works for 30 minutes and extracts the calf. As you drive away, your inner critic begins berating you for your lack of expertise, you tell yourself a story about how your boss and the client think you are an idiot and you start to wonder if you will ever succeed in this industry. Sound familiar?

The first arrow is the difficult dystocia. You did not cause this cow to attempt to deliver a calf head-first. It is not your fault the client worked at it for so long before calling you. You are not at fault for your inexperience. All these factors are a normal component of the stressful job of veterinary medicine. The second arrow is all the stories you will tell yourself about the event. Left unchecked, these stories will lead to decreased self-worth, increased imposter syndrome,

difficulty taking constructive criticism and ultimately poor job performance. How do you stop the second arrow?

Coping with stress

In my opinion, meditation is a super power. It has a bad rap as a touchy feeling thing one does on a pillow surrounded by incense and weird music. In reality, it is the ability to see the thought-stream that runs on continuous loop through our minds. The act of meditation is simply sitting still, trying to focus on one thing and inevitably failing over and over as your mind wanders. The moment you notice you have gotten lost in thought, the moment when you fail at focusing, is the entire point of meditation. Like going to the gym, each moment you notice you have gotten lost in thought is a bicep curl for your brain[3]. As you practice meditation, you get better at this "noticing" skill. This simple ninja move is the foundation for subsequent techniques to ease whatever stressful moment you face in practice.

Once you can wake up from your thoughts, you can begin to change your relationship to them. Three strategies are particularly good at this; gratitude, self-compassion and checking your story. The daily practice of gratitude – simply noticing three specific, unique good things from each day - has been shown to improve levels of optimism, satisfaction in relationships and job performance[4]. Psychology suggests gratitude practice subverts our negativity bias and instead gets us focused on the good.

Self-compassion is a powerful tool that physiologically downregulates the threat response and the sympathetic nervous system. The act of self-compassion has been shown to activate our mammalian care system, releasing oxytocin and endorphins, thereby lowering our stress levels[5].

Psychologist Kristin Neff describes a simple three step move that can be employed when you notice yourself struggling. First, simply acknowledge that whatever you are experiencing is difficult. Second, remind yourself that this moment is difficult for many people, that you are not alone in your feelings. Lastly, send yourself some kindness and warmth, just as you would for a friend who was struggling with something similar, in other words, put down the hotshot. Veterinary medicine has a variety of avenues to connect with others to realize this shared experience – from NOMV, Moms with a DVM, and mentorship programs through organized vet med. By sharing our rough times, we can remember that times can be hard for even the "toughest" of us.

Lastly, it is important to acknowledge the fallibility in the stories we tell ourselves. They will almost always be biased and at their worst, simply untrue. When you notice you are lost in a story, ask yourself, "is it demonstrably true?" or better yet, ask others to check your story for you[2]. Exposing the inaccuracy of our stories makes us believe them less and in turn, frees us from our self-critical minds.

Revisit our example

Let's return to the calving example to try out these strategies. The first step is to notice the thoughts that have carried you away while you are working the problem – their negativity is not helpful, and in fact physiologically shuts down the part of your brain that can find a solution. Secondly, send yourself some compassion in that moment. That calving was hard, it would be hard for lots of people – heck it was hard for the client who worked at it for three hours! Lastly, when the dust has cleared, talk to your boss that you had to call out to help. Brene Brown suggests beginning with the preamble "The story I'm telling myself is…"[2]. In this case, you

could try “The story I’m telling myself is that I am a burden on you and will never improve at bad calvings.” I would hazard to guess your boss will have a completely different story to share about that moment and the conversation will improve your connection and relationship to one another. From this space, you will be better able to learn from the moment, rather than beat yourself up about it, which will improve your performance for next time.

Conclusion

Veterinary practice will always be inherently stressful and our sympathetic nervous systems will be perpetually activated by moments in our careers. However, the practices of mediation, gratitude, self-compassion and story-checking can supercharge our ability to turn down the sympathetic response when it is no longer needed. Mastering these skills is not soft or feminine. In fact, they make us even tougher, more resilient and more competent veterinarians. They help us stop shooting the second arrow and go back to peacefully grazing on the plains.

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FOOD TRIALS FOR THE DERMATOLOGY PATIENT

2023 OSU / OVMA Virtual Summer Seminar

Jennifer Thomas, DVM
Diplomate, American College of Veterinary Dermatology

OBJECTIVES

At the end of this presentation, participants should be able to:

- Recognize the cutaneous pattern(s) of cutaneous adverse food reactions, canine atopic dermatitis, and feline atopic skin syndrome, and feline food allergy
- Recognize non-cutaneous symptoms that may be attributed to food allergy or food intolerance
- Recognize the differences and utility of novel protein diets, home-prepared diets, and hydrolyzed/ultra-hydrolyzed diets in a food trial for dermatological diseases
- Identify the gold standard for diagnosing adverse food reactions in dogs and cats, as well as recognize the limitations of other testing modalities for adverse food reactions
- Appreciate the systematic approach to planning and performing a diet trial

When should you suspect a cutaneous adverse food reaction (CAFR)? Why do you need to consider the role diet is playing in the workup of an allergic skin disease patient?

- Cutaneous manifestations of adverse food reactions (CAFRs)
    - Review of cutaneous reaction patterns in dogs and cats
- Non-cutaneous manifestations of adverse food reactions
    - Dogs
        - Increased frequency of defecation
        - Diarrhea and vomiting most common
        - Rare: Symmetrical lupoid onychodystrophy (SLO), sneezing, anaphylaxis
    - Cats
        - Vomiting and diarrhea most common
        - Other: conjunctivitis, salivating, flatulence, hyperactive behavior, respiratory signs
    - In both dogs and cats with AFRs, >20% presented with vomiting and/or diarrhea
- Signalment
    - Age of onset
        - Dogs: any age, though often polarized ages <1 yo (~40%) or >7 yo
        - Cats: any age, with ~25% by 1 yo
    - Breed predisposition
        - Dogs: GSDs, Labradors, Golden Retrievers, WHWT
        - Cats: DSH, Persians, Siamese, Burmese
- Non-seasonal pruritic dermatitis
- Pruritus is poorly or non-responsive to anti-inflammatory doses of glucocorticoids
    - IMPERATIVE that secondary infections are ruled-out when making this call

How common are CAFRs?

- variable, but must be considered in animals with non-seasonal pruritus and/or signs of allergic skin disease
- In dogs, sole CAFR is less common than environmental allergies
- In dogs with environmental allergies (canine atopic dermatitis), ~1/3 of dogs have some degree of concurrent AFR

What are our options for diagnosing CAFRs in dogs and cats?

- Elimination diet trials with subsequent challenges are uniformly recommended as the method for diagnosing AFRs – The GOLD STANDARD
- Though frequently offered, serum IgE testing is not reliable for diagnosis of AFRs
- Intradermal tests are not reliable for the diagnosis of AFRs
- Saliva and hair allergy tests are unable to distinguish allergic from non-allergic patients, and unable to distinguish patient samples from synthetic hair or saline

What types of diets are available for the elimination-challenge diet trial?

- Homemade Diets
- Commercial Diets
    - Novel protein
    - Prescription versus Non-prescription diets
    - Hydrolyzed and Ultra-Hydrolyzed Diets
- Commercial Diet Advantages
    - Easy to feed
    - In general, nutritionally balanced & bioavailable
- Commercial Diet Disadvantages
    - More than 1 source of protein or carbohydrate may be present
    - Discrepancies between ingredients and labeling
    - Cross-contamination
    - Many disadvantages minimized by utilizing prescription diets
- Most common ‘offending’ food allergens
    - Primarily proteins
    - Dogs in the United States: beef, dairy products, chicken, wheat, & lamb
    - Cats in the United States: beef, fish, chicken
- Beware of known cross-reactivity and potential cross-reactivity of protein sources

How do you choose which diet to use?

- Patient dietary history
- Patient age & size

- Concurrent medical conditions
- Ability to orally medicate the pet

How long does the elimination diet trial need to last?

- In general, at least 8 weeks
- By 3 weeks, approximately 50% of dogs had a marked reduction in clinical signs
- In patients with sole CAFR, complete remission of clinical signs can be appreciated in
    - approximately 80% of dogs by 5 weeks of the elimination diet trial;
    - > 90% of dogs by 8 weeks
    - approximately 80% of cats by 6 weeks of the elimination diet trial;
    - 90% of cats by 8 weeks
- It is ultimately up to the clinician's discretion of when and how to challenge the elimination diet trial

After dietary challenge, how long does it take to see signs of skin/ear flare in dogs and cats with CAFRs?

- Signs of cutaneous flare can occur within hours of oral challenge
- In general, >90% of pets will experience flare within 14 days

How do you conduct the elimination-challenge diet trial to set yourself, the client, and the pet up for success?

- Determine if a diet trial can successfully be performed
- Choose preventives that will not interfere with the trial
- Choosing medications, and routes of administration
    - Is the owner able to dry-pill if oral medications are needed?
- Timing of therapies, medications, and planned withdrawals
- Investigate and educate for complicating factors & strategize beforehand:
    - Treats, toothpaste, toys, bowls, food containers
    - Is the pet in training? Going to doggy day care? Dog parks? Does the pet hunt?
    - What other pets and food sources are in the environment?
    - Is the pet off-leash (non-fenced) or otherwise out of the owner's control?
    - Does the pet have a history of coprophagy?
- Don't forget storage mites!
- Client buy-in

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Non-healing corneal ulcers – now what?

Emily McCool, DVM, MS, DACVO

Outline

- Corneal anatomy
- Definition
- Clinical signs
- Types of corneal ulcers
  - Superficial, uncomplicated
  - SCCED
  - Infected
  - Other
- Treatment

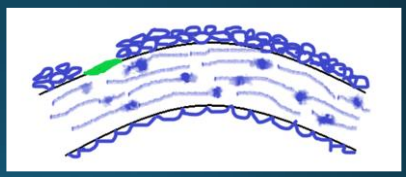
Sl

Normal corneal anatomy

- Total corneal thickness is 0.6 mm
  - Anterior most layer – corneal epithelium
  - Stroma – 90% of corneal thickness
  - Descemet's membrane
    - Basement membrane for endothelial cells
  - Endothelial cells
    - Single cell layer; maintain relative dehydration
- Avascular
- Highly innervated (ophthalmic branch of CN V)

Definition of corneal ulcer

- Erosion or loss of corneal epithelial cells
  - Exposure of corneal stroma
- Diagnosed with fluorescein stain
  - Hydrophilic corneal stroma
- Epithelial cells migrate to cover defect
  - 5-7 days



Clinical signs

- Superficial, uncomplicated ulcer
  - Blepharospasm
  - Elevated third eyelid
  - Pawing/rubbing at the eye
  - Epiphora
  - Conjunctival hyperemia
  - Mucoid discharge
  - +/- corneal edema
- Should not be able to visualize corneal opacity or defect with a superficial, uncomplicated ulcer
  - Diagnosed with fluorescein stain

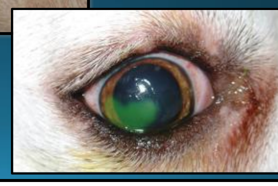
Causes of corneal ulcers

- Aberrant hairs
  - Ectopic cilia
  - Trichiasis
    - Entropion
  - Distichia
- Tear film disorders
  - KCS
  - Qualitative tear deficiency
- History of topical chemical exposure (i.e. shampoo)
- Infectious
  - Moraxella bovis
  - Feline herpesvirus-1
- Primary corneal disease
  - Corneal degeneration
    - Ca++ deposits
    - Endothelial degeneration – bullae
- Foreign body
- Facial nerve paralysis
- General anesthesia
- Exophthalmos
- Trauma

Recommended diagnostics

**contraindicated if ulcer is deep or perforated

- Must perform a complete ophthalmic exam
  - STT**
  - Fluorescein stain
  - +/- intraocular pressure**
    - Reflex uveitis
  - Palpebral reflex?
  - Examine behind third eyelid

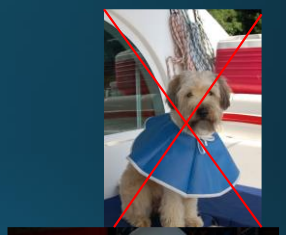


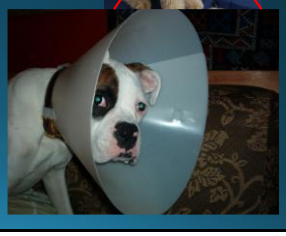
Treatment – superficial, uncomplicated ulcers

- Topical antibiotic to PREVENT secondary bacterial infection
  - Avoid fluoroquinolones (save for infected ulcers)
  - Avoid polymixin B in cats
  - Apply QID
- Topical atropine
  - Relieves ciliary body muscle spasm (reflex uveitis)
  - Every 12-24 hours
  - Pupil will remain dilated for up to 2 weeks
  - Bitter taste!
    - Ointment vs. solution
  - Contraindications: glaucoma, lens instability, dry eye disease

Treatment – superficial, uncomplicated ulcers

- Systemic analgesia
  - NSAIDs or opioids (systemic)
  - Topical NSAIDs do NOT provide analgesia
- Elizabethan collar
  - Must be hard plastic
  - Must be worn at all times
  - Self trauma can:
    - Delay wound healing
    - Increase risk of secondary bacterial infection





Recheck

- 5-7 days
- Client should report improved comfort
- Concerning signs to monitor for at home
  - Worsened squinting
  - Mucopurulent discharge
  - Divot or opacity on the surface of the eye

Types of non-healing corneal ulcers

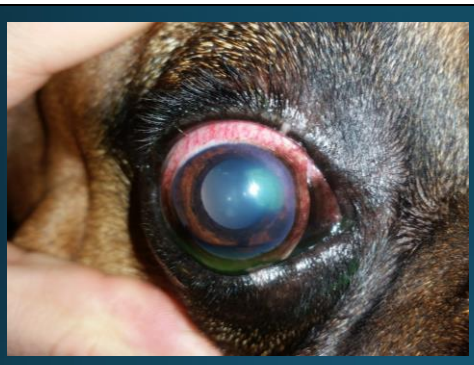
- SCCED
- Infected
- Other
  - Underlying cause not identified
  - Persistent underlying corneal pathology
  - Compliance?

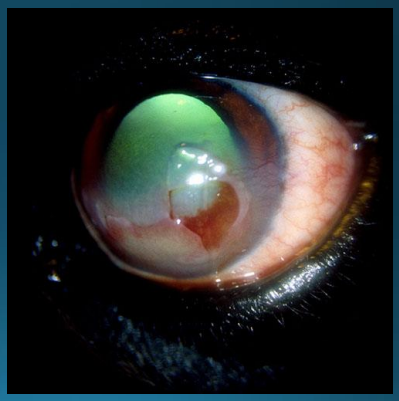
SCCED

- Spontaneous Chronic Corneal Epithelial Defect
  - AKA "indolent ulcer"
- DOGS only
- Signalment
  - Boxers, Corgis, Golden Retrievers
  - ANY middle-age or older dog (typically >8 yr)
  - Be skeptical of brachycephalic breeds
- Pathogenesis
  - Abnormal adhesion between the epithelial cells and the stroma
    - Acellular hyaline membrane noted histopathologically

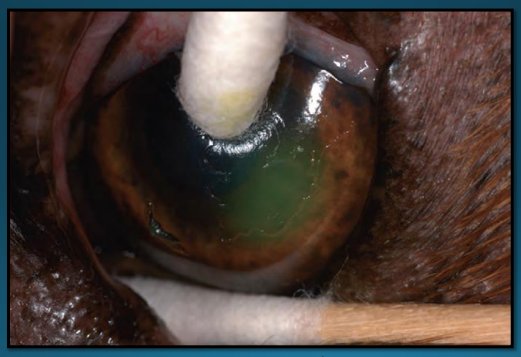
SCCEDs

- Clinical signs
  - Same as clinical signs of superficial, uncomplicated ulcer = ocular pain
  - "halo" pattern of fluorescein uptake
  - Loose lip of epithelium
    - May not be as obvious as you see in textbooks
    - Proparacaine → manipulate edges with CTA
  - +/- granulation tissue
    - Especially in Boxers
  - Must be a SUPERFICIAL ulcer





Corneal debridement



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SCCEDs - treatment

- Apply proparacaine
- Prep
  - Dilute betadine solution (1:50)
  - Eye wash
- Debridement
  - Cotton-tipped applicator debridement
    - Approx. 40% will heal with CTA debridement alone
    - Must be performed prior to grid or diamond burr keratotomy
  - Linear grid keratotomy
    - Use margins established by CTA debridement
    - 25 g needle with bevel up
      - From normal adhered epithelium across stroma to adhered epithelium
    - Success rates 75-100%
  - Diamond burr keratotomy
    - Use margins established by CTA debridement
    - Success rates 92.5%

Grid keratotomy

Veterinary Ophthalmology 5th Ed

Diamond burr keratotomy

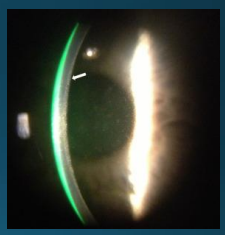
AJ Rankin

Treatment

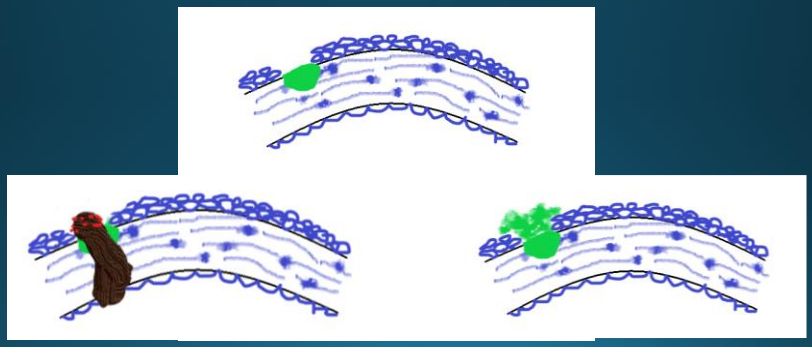
- Medications same as superficial, uncomplicated ulcer
  - Topical antibiotic QID
    - Topical tetracycline may help improve healing time
      - Terramycin®
  - +/- topical atropine
  - Systemic analgesia
    - NSAID
    - Opioid
  - Hard, plastic e-collar
  - +/- bandage contact lens
- Recheck in 2 weeks

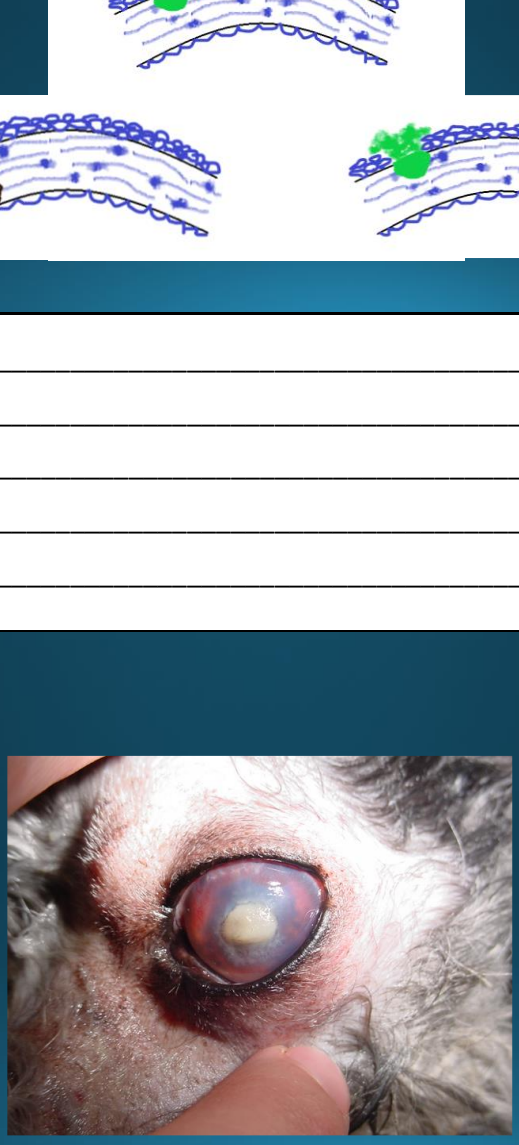
Infected corneal ulcer

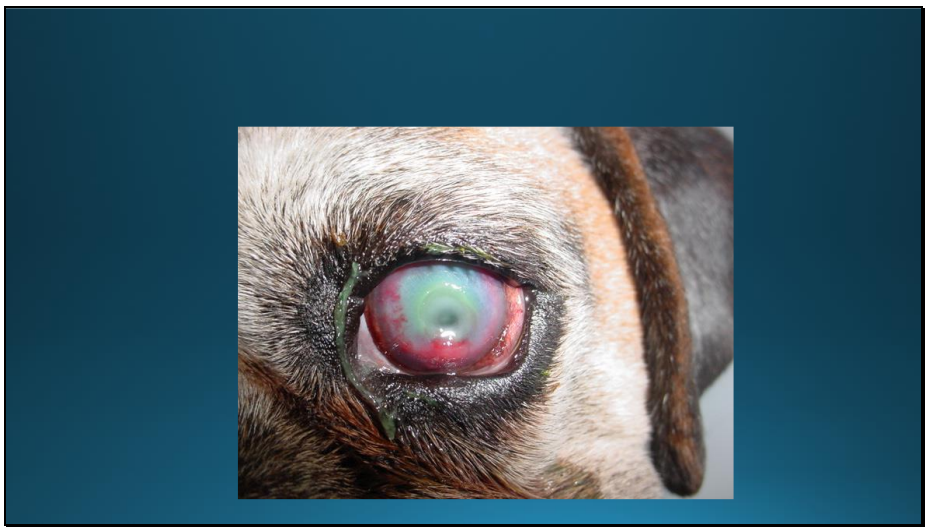
- ANY DEPTH
  - How do you gauge depth?
- Color change
  - White, creamy, tan
- Corneal melting
  - AKA keratomalacia
- Mucopurulent ocular discharge
- Severe reflex uveitis
  - Hypopyon
  - Flare
- Deep, 360º neovascularization

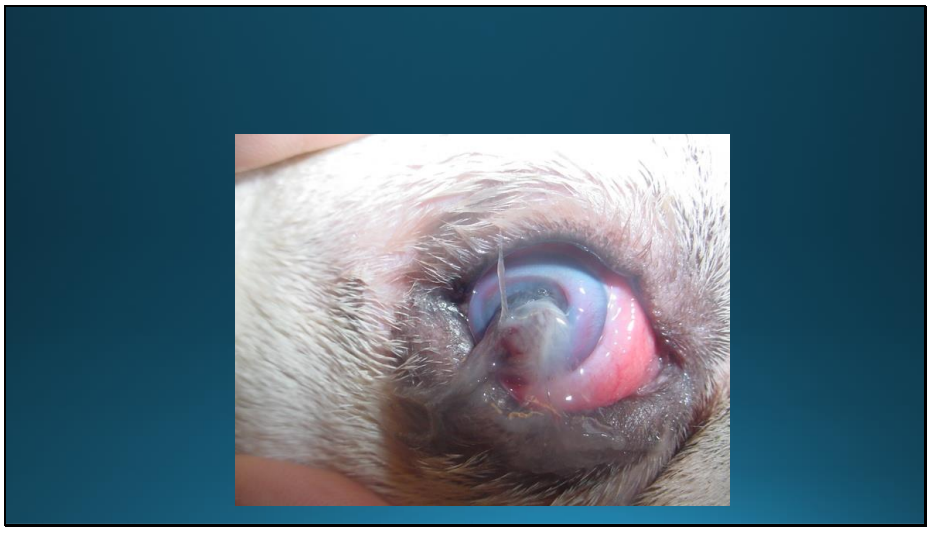


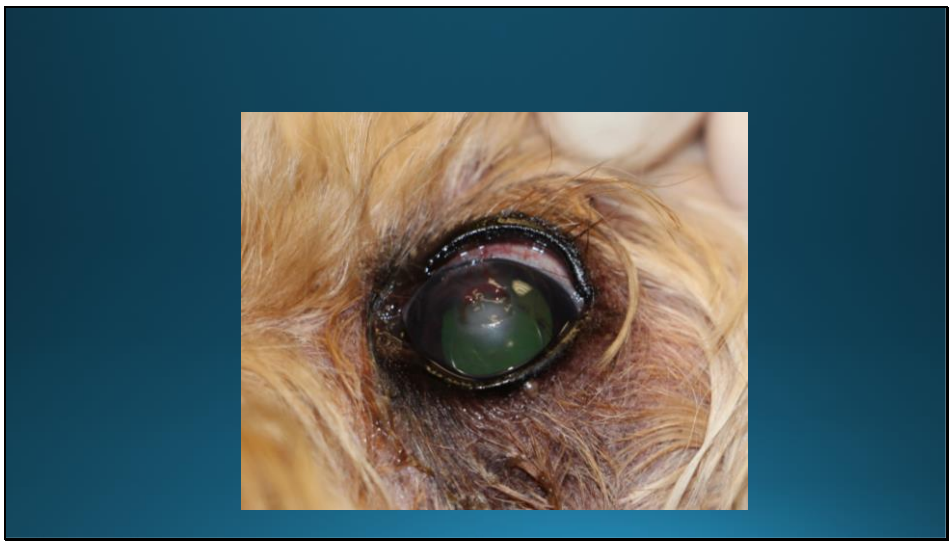
Infected corneal ulcer

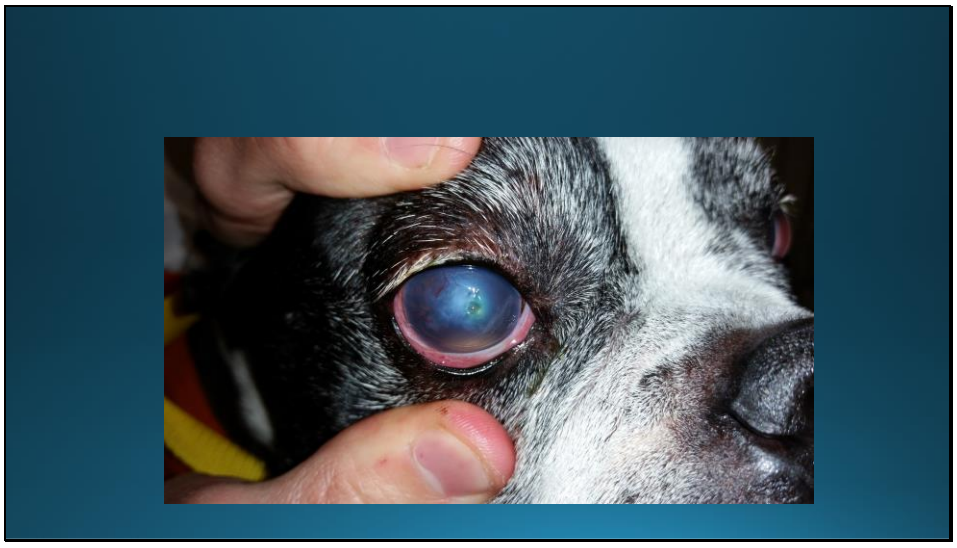


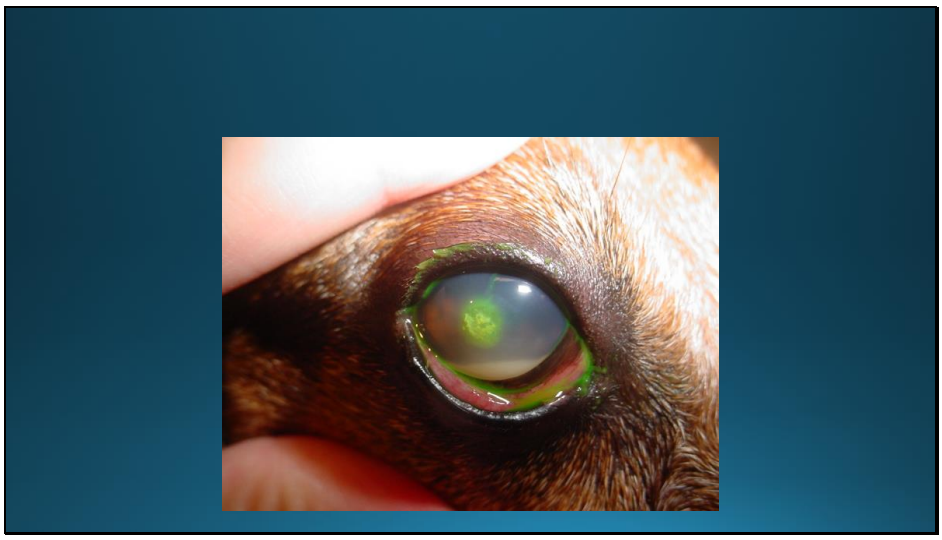


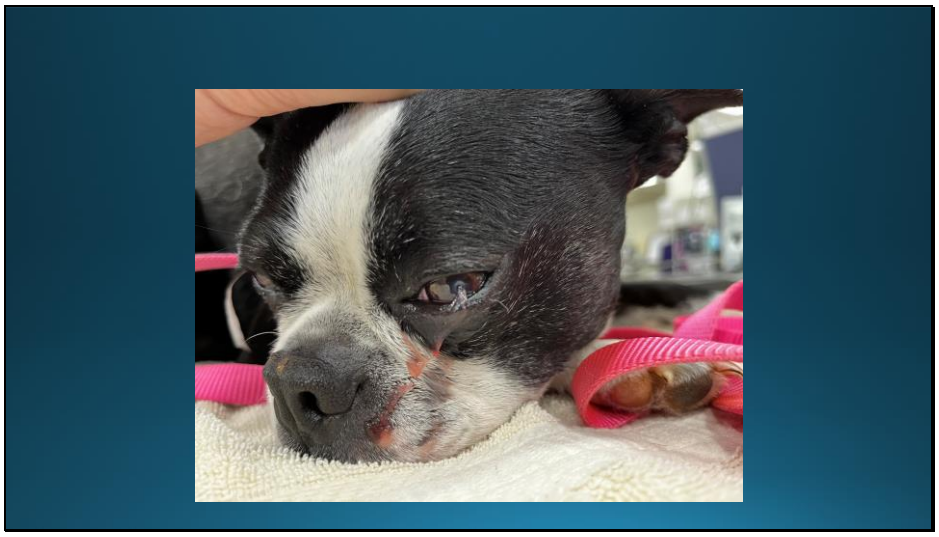


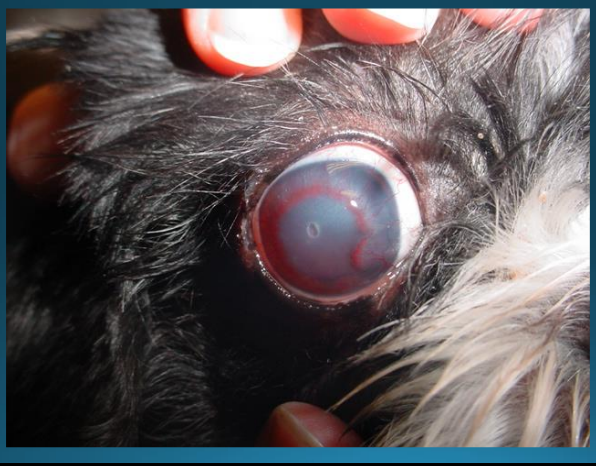












Infected corneal ulcer

- Diagnostics
  - No STT if concerned that there is depth!
    - Can address KCS later if present
  - Fluorescein stain
  - No intraocular pressure if there is depth or rupture!
  - Corneal cytology
    - Periphery of ulcer
  - Corneal culture
    - Aerobic
    - Periphery of ulcer

Infected corneal ulcer - treatment

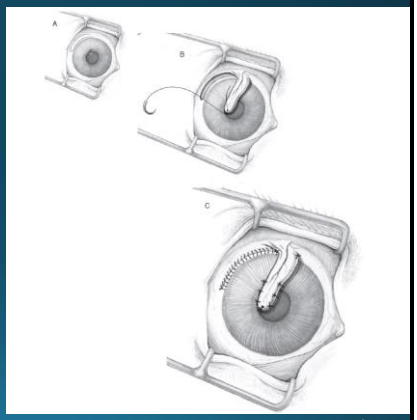
- Topical antibiotic (no ointments)
  - Broad spectrum: Fluoroquinolone q 1-2 hours
  - Gram positive: Cefazolin 50 mg/mL q 1-2 hours
    OR
  - Gram negative: Tobramycin (or gentamicin) q 1-2 hours
- Topical anticollagenase
  - Serum q 1-2 hours
- Topical atropine (no ointments)
  - Dilates pupil and relieves ciliary body muscle spasm
  - q 8-12 hours

Infected corneal ulcer - treatment

- Systemic antibiotic
  - Gram positive: Cefpodoxime, Clavamox®, Cephalexin
  - Gram negative: Enrofloxacin
- Systemic NSAID
- Systemic opioid
- Hard, plastic e-collar
  - FRAGILE eye
- No neck leads, activity restriction
- Recheck every 1-2 days

Surgical options

- Conjunctival pedicle graft
  - Blood supply
  - Tectonic support
  - Approx. 93% success rate for deep ulcers
  - Perforation lowers success rate
    - Could still be as high as 85%
    - Depends on
      - Chronicity
      - Size
      - Pupil present?
  - Cost: $2,000 (approximately)



Veterinary ophthalmology, 5th ed.

Infected corneal ulcer

- DEBRIDEMENT (grid or diamond burr) is CONTRAINDICATED in an infected corneal ulcer
  - Including cats!
    - Corneal ulcer in cat = feline herpesvirus
- Ulcer that has loose edges AND signs of infection?
  - INFECTED

Other?

- Catch-all category
  - Underlying cause not identified
    - Ex. Plant foreign body embedded in NM
  - Underlying cause not corrected
    - Ex. KCS that has not responded to therapy
  - Owner compliance
    - Persistent self-trauma (no e-collar)
- Must repeat a complete ophthalmic exam

Corneal endothelial degeneration

- Dachshund, Chihuahua, Boston terrier
  - Any geriatric dog
- Loss of corneal endothelial cells leads to fluid accumulation within corneal stroma
  - Corneal edema
- Severe corneal edema → bulla formation → ruptured bulla → corneal ulcer
- May be slow to heal due to "water-logged" stroma
- Treatment
  - Same as superficial, uncomplicated corneal ulcer
  - NaCl 5% ophthalmic ointment 3-4 times per day
- Referral options
  - Thermokeratoplasty
  - Superficial keratectomy with Gunderson inlay flap

Corneal degeneration

- Typically geriatric dogs
- Characterized by crystalline deposits in the cornea and corneal neovascularization
- Sloughing of crystalline deposits → corneal ulcer
- Treatment:
  - Same as superficial, uncomplicated corneal ulcer
  - EDTA 1% ophthalmic solution (compounded)
    - 2-3 times per day

Questions

VETERINARY MEDICINE

Complex Spay/Neuter SX

Kimberly Carter, DVM, MS

1

1

Outline

Females
- Estrus
  - Pseudo pregnancy
  - OE
- Pregnant
  - Fetal euthanasia
- Pyometra
- Ovarian Remnant Syndrome

Males
- Cryptorchidism
  - Paramedian, midline surgical approach

2

2

Learning Outcomes

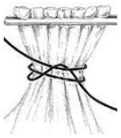
At the end of this presentation viewers will be able to:
- Describe why intrauterine fetal euthansia is not necessary
- Name the most common species for pyometra and most common organism isolated
- Name the most common species and occurrence of ORS
- Name the most common species and occurrence for cryptorchidism
- List common post op complication of Complex OHE
- List common post op complications of cryptorid OC

3

3

Estrus

- Bleed more due to estrogen influence on tissues
- Ovarian/uterine vessels enlarged
- Tissue is more fragile
- Double ligate!
- Your Best Friend is the Miller's Knot – a friction binding knot
- May consider doing an OE



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RH Miller's

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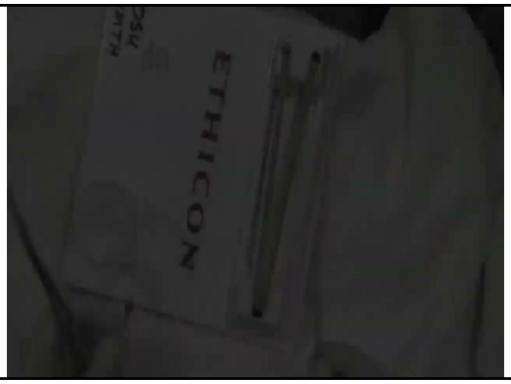
LH Millers



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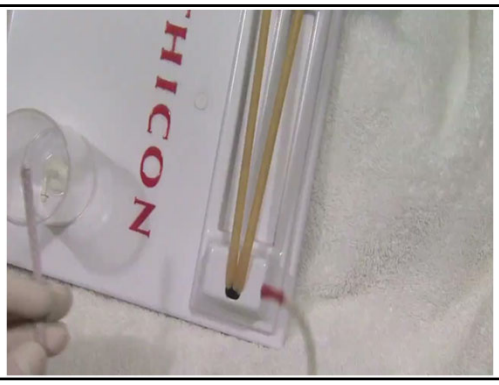
RH Modified Millers



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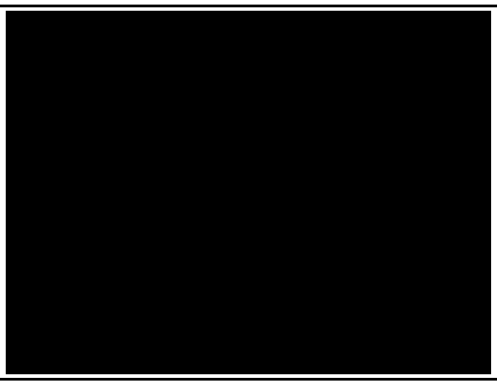
Left handed Modified Millers



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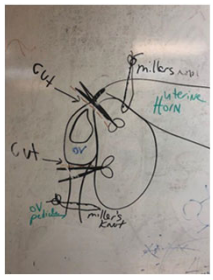
OE

- Remove only the ovaries to avoid an enlarged, toned uterus
- No disadvantages except perhaps using a spay hook twice
- Incision can be moved cranially to allow easier access to ovaries (must avoid spleen)



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Making a rational choice between ovariectomy and ovariohysterectomy in the dog: a discussion of the benefits of either technique

https://pubmed.ncbi.nlm.nih.gov/16472293/

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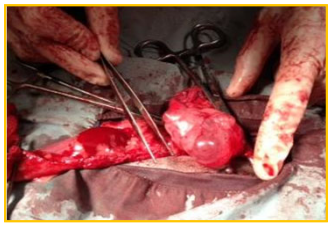
In Heat Ovary - Normal



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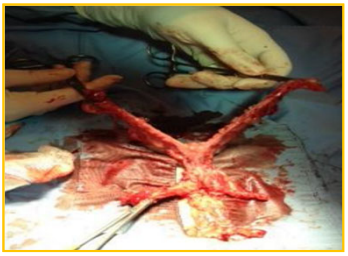
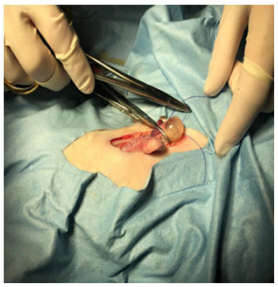
Cysts – Not Normal





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Estrus Cont.

- One can induce Pseudo-Pregnancy (pseudocyesis) in the bitch if spayed at the time of estrus
- **NOT A COMMON SQUELLA**
- Breed and individual variation (some influence of nutrition) for the development of mild to overt pseudocyesis

Note: Pseudocyesis can be seen in intact bitches 45-60 days post Estrus when endogenous P4 concentrations naturally decrease

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Treatment for Pseudopregnancy/Lactation after Spay

- Time – Often resolves on own in 4-8 weeks
- Reduce stimulation for the behavior
  - Take away bedding
  - Change nesting area
  - Take away “babies” – toys being “mothered”

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Treatment for Pseudopregnancy/Lactation after Spay

- Stop lactation
  - E-collar/t-shirt-to stop stimulation of nipples by licking
  - Cool compresses (not warm)
  - Cabergoline 5ug/kg P.O. SID for 4- 6 days
    (or 10-14 days if aggressive behavior noted)
  - Benadryl 2-4 mg/kg P.O.
  - Raw green cabbage leaves (hold in place with bandage until wilted, do for 2 days)

Canine pseudopregnancy: an evaluation of prevalence and current treatment protocols in the UK
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5968611/#CR16

Treatments for breast engorgement during lactation https://pubmed.ncbi.nlm.nih.gov/32944940/

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Pregnant

- Spay can be safely done up until parturition starts
- IV or SQ fluid should be administered to late term pregnant animals to compensate for volume loss
- May see a drop in blood pressure when a late term pregnant uterus is removed

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Why Should We Spay Pregnant Animals?

1. Number one cause of Death for domestic dogs and cats is euthanasia due to unwanted/overpopulation
2. Causes no suffering for feti
3. No guarantee of normal parturition and any birth is stressful.
4. Dystocia rate for dogs* 8.3%

*Dystocia after Unwanted Mating as One of the Risk Factors in Non-Spayed Bitches—A Retrospective Study https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7552611/

Dystocia rate for cats* 3-6%

*Root Kustritz MV. Feline reproduction FAQs. Clinical Theriogenology 2010;2:230-232. https://www.dvm360.com/view/feline-reproduction-faqs-proceedings

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Do We Need to Euthanize Feti?

(Intrautero/Neonatal Euthanasia)

NO!

Simply do not open the horns or uterus

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Concerns with Fetal Euthanasia

1. Respiration
   - Normal fetuses "breathe" move fluid in and out of lungs from midterm on, but this is never mechanism for O2 exchange; thus the presence of breathing movements in a fetus is a normal occurrence and should not on its own accord be an indication of stress or distress

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Concerns with Fetal Euthanasia

2. Fetal Heartbeat is not a good measure of fetal death since effective blood circulation and brain activity may have ceased long before the heart ceases to contract
   - PEA (Pulseless Electrical Activity) the coordinated electrical activity of the heart muscle without peripheral pulses
   - PEA is not considered to be a conscious state

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Concerns with Fetal Euthanasia

3. Fetal pain/distress:
   - The ability for the brain to perceive pain cannot occur before the third trimester
4. Fetal Movement:
   - Majority of medications we administer (opiates, diazepam, ketamine, medetomidine, barbarities) achieve same serum levels in the fetus that are achieved in dam

Periods and Stages of the Prenatal Development of the Domestic Cat https://pubmed.ncbi.nlm.nih.gov/11841356/

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All That Leads to This:

FETI WITHOUT injection of barbiturates are deeply sedated and bathed in drug saturated amnion. Since they receive minimal external stimulation, they become hypoxic and die as oxygen in their closed system (removed uterus) get used up.

https://olaw.nih.gov/policies-laws/avma-guidelines-2020.htm

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Surgical Tips:

- A Longer incision may be necessary to expose a large uterus in the bitch
- An Extra set of sterile hands can be useful
  (part time to help lift the weight of a late term canine uterus and remove it from the field)
- Miller's Knots on pedicles with Stick ligatures for the uterine body

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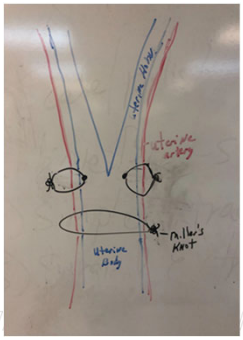
Stick ligatures "bite" a small amount of uterine body and tie off each vessel



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Stick ligatures in a queen

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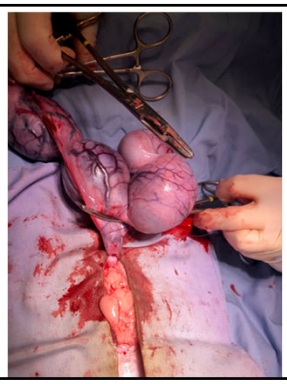

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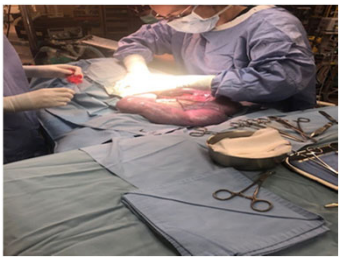
Normal



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Complex S/N: Pyometra

More common in dogs than cats*

- Incidence rate is 199 per 10,000 dog-years at risk.
- Incidence rate of 17 cats per 10,000 cat-years at risk.

*Pyometra in Small Animals.Veterinary Clinics of North America: Small Animal Practice, Volume 48, Issue 4, July 2018, Pages 639-661. https://www.sciencedirect.com/science/article/pii/S0195561618300263?via%3Dihub#bbib2

- "Closed": cervix closed = sicker animal
- "Open": cervix open = pus can drain out of vagina
  *E coli most often isolated
- IV fluids and IV antibiotics should be administered followed by oral antibiotics after surgery

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Surgical Tips

- DO NOT transfix uterine body-Miller's Knot
- Have lap sponges available
- May need larger incision due to increased size of uterus
- A change of gloves and instruments is recommended (definitely if any leakage occurs- and lavage abdomen with warm electrolyte solutions)

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Canine

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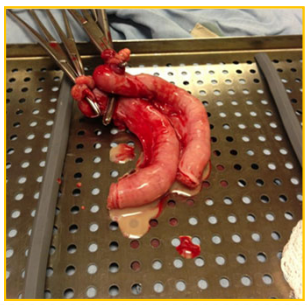
Feline



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Complex S/N: Ovarian Remnant Syndrome (ORS)

- ORS – presence of functional ovarian tissue accompanied by signs of estrus following routine OHE
- More common in cats than dogs

The ovarian remnant syndrome in the bitch and queen, Vet Clin North Am Small Anim Pract. 1991 May;21(3):501-7. https://pubmed.ncbi.nlm.nih.gov/1858245/

- More common in the right ovary than left in dogs

•Ovarian remnant syndrome in dogs and cats: 21 cases (2000-2007) J Am Vet Med Assoc. 2010 Mar 1;236(5):548-53. doi: 10.2460/javma.236.5.548. https://pubmed.ncbi.nlm.nih.gov/20187819/

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Causes of ORS

1. Surgical failure to remove all of normal ovary
1. Presence of “accessory ovary” (NOT Common)
1. Ovarian tissue that re-vascularizes after being dropped back into abdomen after removal (NOT Common)

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Diagnosing ORS

1. Signs of Estrus Post OHE
2. History –make sure no exogenous hormones are being used
3. LH test – sometimes hard to interpret

   LH is high >24hr in spayed animal = positive test

   LH is low = negative=intact animal or ORS

3. Vaginal cytology
4. Serial serum progesterone levels - hormone challenge

Anti Mullerian Hormone Test***

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Treating ORS

To Cut Is To Cure:

- Make sure to do surgery when patient is exhibiting signs of estrus, makes the tissue easier to see
- Always Submit removed tissue for histopathology

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Most Common Post OP Complications of OHE

1. Hemorrhage
2. Dehiscence
3. Recurrent estrus
4. Ligation of ureter
5. Urinary Incontinence

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Cryptorchidism

One or both testicles do not descend into the scrotum by 6 months of age

35

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Cryptorchidism

More common in Dogs than Cats

Dogs: Incidences up to 13%. Certain breeds are predisposed Chihuahuas, Miniature Schnauzers, Pomeranians, Poodles (miniature, toy, and standard), Shetland Sheepdogs, Siberian huskies, and Yorkshire terriers have increased prevalence.

Cats: Incidences up to 4%, with an increased prevalence in Persians.

Cryptorchidism. Nappier M. Birchard SJ, editor. Compend Contin Educ Vet. 2008
Yates D, Hayes G, Heffernan M, et al: Incidence of cryptorchidism in dogs and cats. Vet Rec 2003.

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Cats

High incidence of concurrent conditions: patellar luxation, tetralogy of Fallot, tarsal deformities, microphthalmia, and upper eyelid agenesis

- The failure of testicular descent in cats tends to be unilateral without a bias to one side or the other.
- Inguinal cryptorchidism predominated in one study.

Richardson EF, Mullen H: Cryptorchidism in cats. Compend Contin Educ Pract Vet 15:1342–1345, 1993.
- Yates D, Hayes G, Heffernan M, et al: Incidence of cryptorchidism in dogs and cats. Vet Rec, 2003.

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Cryptorchidism

- Cats testicles usually totally descend by 6-8 weeks, dogs may take a little longer, but may be present at birth in both
- Surgical LANDMARK - Bifurcation of vas deferens
  - » "under" - Dorsal to the bladder
- Palpate!!! Palpate!!! Palpate!!!- Where can they be??
  - Abdominal cavity, subcutaneous (inguinal area) or trapped in the inguinal canal

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Diagnosis

Physical examination and palpation!

- Dogs and cats presenting with only one testicle should be considered cryptorchid until proven otherwise as monorchidism is rare in both dogs and cats.
- Bilateral cryptorchidism = Neutered - Very Rare
- Physical features (penile barbs in cats, undeveloped penis in dogs)
- X-rays- (generally only if testis is enlarged can it be visualized)
- Ultrasound -Felumlee AE, Reichle JK, Hecht S, et al. Use of ultrasound to locate retained testes in dogs and cats. Vet Radiol Ultrasound. 2012;53(5):581-585
- Hormonal testing – Anti Mullerian Hormone , LH or GnRH stimulate testosterone secretion

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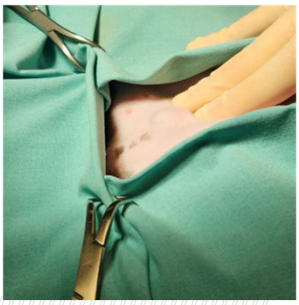
External Subcutaneous Inguinal Ectopic Testicles

- Locating ectopic testes can be difficult

Incise directly over stabilized skin
With the trapped testicle held firmly

Small testicles are sometimes difficult to distinguish from regional lymph nodes and inguinal fat



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Midline or Paramedian approach for K9

Midline
larger skin incision deviated around penis- allows for greater exposure, can retroflex bladder

Paramedian
Smaller incision, spay hook used to retrieve vas deferens
Blunt incision used to enter the oblique abdominal muscle layers, must correctly decide which testes is retained to place incision on that paramedian side

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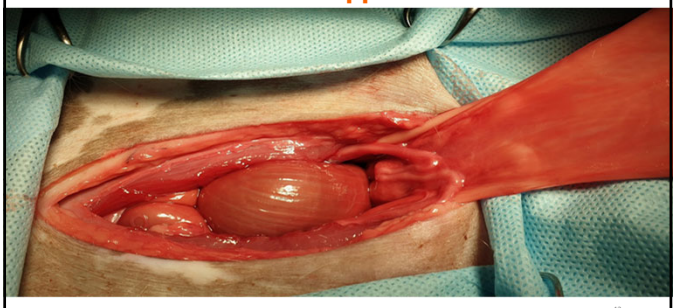
Midline Approach



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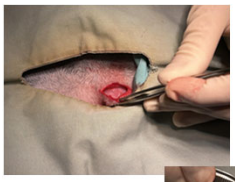
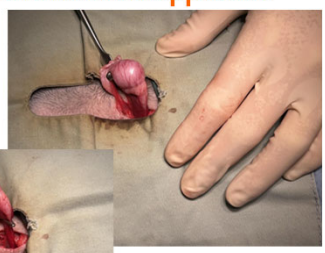
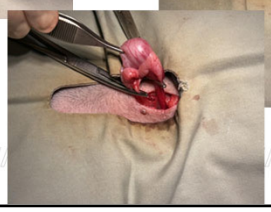
Paramedian Approach







- Blunt thru external and internal obliques

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Most Common Post OP Complications in Males

- Prostatectomy
- Partial prostate, urethral, and ureteral avulsions
- Swelling, bruising

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How to Avoid Post OP S/N Complications

1. Aseptic technique
2. Short sx times
3. Gentle tissue handling
4. Careful ligation
5. Adequate suture placement
6. Adequate exposure

IF in doubt of what you are seeing- extend your incision-get good exposure!

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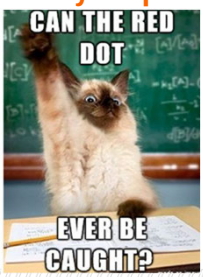
Thank you for your participation

QUESTIONS??



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KIMBERLY CARTER

OSU COLLEGE OF VETERINARY MEDICINE

O | 405.744.8374
E | Kimberly.carter@okstate.edu

vetmed.okstate.edu

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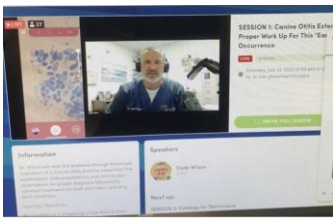
It's Not Just A Dental!

Dr. Cade M. Wilson

Carter County Animal Hospital /Skoped Micro/ CMW Consulting LLC

Who the heck is Cade Wilson??

Who the heck is Cade Wilson??



Who the heck is Cade Wilson??

SKOPED MICRO

CCAH CARTER COUNTY ANIMAL HOSPITAL

CMW Consulting, LLC

Why this topic?

"We need to schedule a dental."

- Office/Client Conflict
- Decreasing burn out by decreasing conflict
- Taking the time to explain what we truly observe during an exam and what our expectations are
- Easier to take 5 minutes to educate than 10 minutes to calm clients down
- We do a lot of things in our head that owners can not comprehend
- "Set your table"

Educating your clients!

Take the time to educate clients what they can do at home

Brushing teeth

Food changes

Food Sensitivities/Allergies

A lot of issues systemically can start with a terrible mouth!!

It's Not Just A Dental!

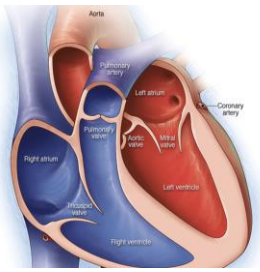
Taking the time to educate about oral health is not just for the mouth!

Take your time

Increase the client's knowledge

Increase your patient's longevity

Improve your client/clinic relationship



How common is this in your work life?

Let's walk through how to talk with our clients…

How do we explain it all??

- Gingivitis
- Plaque Build Up
- Infections and Plaque under the gum line
- Cavities

How do we explain it all??

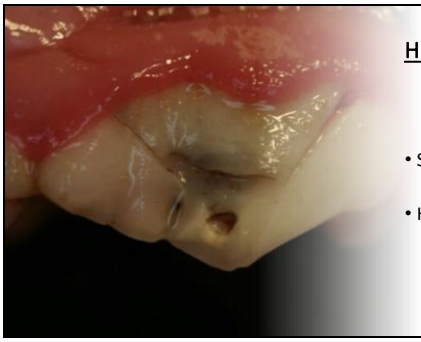
- **Deciduous Teeth!!**
- **Explain early in life**
- **Document when owners decline removal**

How do we explain it all??

- Malalignment
- Will need prophylactic dental procedures more often.
- Multiple dental specials per year

How do we explain it all??

- Oral Nasal Fistula
- How is your gingival flap game?



How do we explain it all??

- Slab Fractures
- Hiding under plaque

How do we explain it all??

- Glad this isn't a scratch and sniff picture!
- "Plaqued in" teeth
- Slab fracture?
- Gravity is going to take these
- Tooth Fairy is going to be busy
- Don't tell them they "need a dental"!!

Scenarios…

- Talking through some real-life examples

1-Great client/Does what you recommend

- The Good…
- Mild plaque build up
- Mild gingivitis
- No loose teeth
- Does yearly dental cleanings
- Praise them! You are extending this pets life!

2-Double Trouble

- 6-month-old Lab in for a neuter
- Bilateral upper deciduous canines in place
- What do you do?

3 -Most Common "Dental"

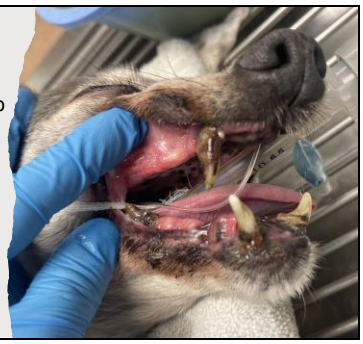
- Severe Calculus
- Gingivitis
- Oral infections
- Antibiotics and NSAIDslikely needed
- Known in exam room
- Prophy more often

4- Repeat Offender

- The Ugly….
- Wish this wasn't common…
- Needed help 6 months ago
- Incisors have steadily fallen out
- Likely slab fracture on 3rd Premolar
- If you only said a dental was needed… you're in trouble

5- Surprise "Dental"

- Owner called and set up "Dental Cleaning" without prior exam
- What do you do?



Client relations are like building good fences…

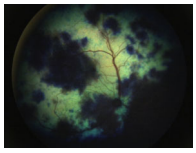
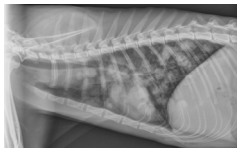
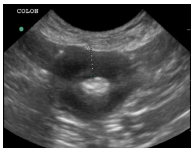
- Take your time
- Do it right from the beginning
- Done properly, it saves you time

QUESTIONS?

Dr. Cade M Wilson

- 315 North Rockford Road
  Ardmore, OK 73401
- Office- 580-226-1001
- Email- wilson.dvm30@gmail.com
- www.ardmorevet.com
- www.skopedmicro.com

Histoplasmosis: Everything You Need to Know

Andrew Hanzlicek, DVM, MS, DACVIM (SA)
Director, Veterinary Medicine
MiraVista Diagnostics
16May2023

1

Speaker Disclosure

Histoplasmosis: Everything You Need to Know
Andrew Hanzlicek

DISCLOSURE:
Employed by MiraVista Diagnostics which commercially offers biomarker tests discussed in this lecture.

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OUTLINE

1. Background
2. Clinical findings
   - Signs, PE, Imaging studies
3. Pathology
4. Culture
5. Biomarkers
   - Antigen, Antibody, DNA
6. Treatment & Monitoring

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IMPORTANCE: INVASIVE FUNGAL INFECTIONS

>13 million infections / year[1]

≥1.5 million deaths / year[1]
Like TB and 3x malaria

$7.5 billion direct Medical Costs (U.S.)[2]
Only includes acute care

Growing Incidence and Geographic range[3]
Climate change, Increasing population w risk factors

Antifungal Resistance increasing[4]
Candida auris, *Aspergillus* spp.
Agrichemical use, co-infections, changing microbiota, climate change

1. American Society for Microbiology; 2. Bongomin F et al. J Fungi 2017; 3. World Health Organization; 4. Fisher M, et al. Nature 2022.

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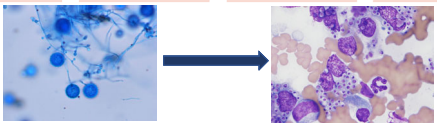
CLASSIFICATION: INVASIVE FUNGAL INFECTIONS

Molds	Dimorphs	Yeasts	Oomycetes
• *Aspergillus* • Hyaline molds • Pigmented molds • Mucorales • Entomophthorales	• *Blastomyces* • *Histoplasma* • *Coccidioides* • *Sporothrix* • *Paracoccidioides* • *Talaromyces*	• *Cryptococcus* • *Candida*	• *Pythium* • *Laganedium* • *Paralagenidium*



1. American Society for Microbiology; 2. Bongomin F et al. J Fungi 2017; 3. World Health Organization; 4. Fisher M, et al. Nature 2022.

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PREDICTIVE VALUES

➢Example: 93% Sensitivity & 98% Specificity

Probability	(+) Predictive Value	(-) Predictive Value
1%	23.8%	99.9%
5%	➡ **62.0%**	99.6%
10%	77.5%	99.2%
20%	88.6%	98.2%
30%	93.0%	97.0%
40%	95.4%	95.4%
50%	96.9%	93.3%
60%	97.9%	90.2%
70%	98.6%	85.6%
80%	99.2%	77.6%
90%	99.6%	60.6%
95%	99.8%	➡ **42.2%**
100%	100.0%	0.0%

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GEOGRAPHY

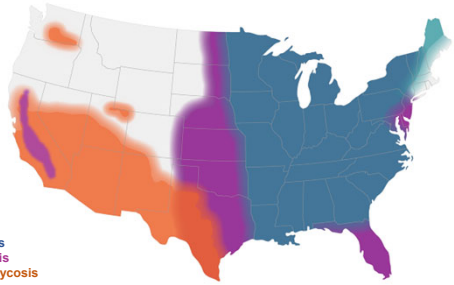

Image: CDC, modified

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CLINICAL PRESENTATION – WHEN TO BE SUSPICIOUS

1. Fever unresponsive to antibiotics
2. Multisystemic disease
3. Nodular / ulcerative skin disease
4. Lung disease
5. Lymphadenopathy (incl. TB nodes)
6. Inflammatory Ocular (incl. periocular) disease
7. Osteomyelitis & Arthropathy
8. Discospondylitis
9. Infiltrative GI disease
10. Orchitis / Prostatitis
11. Hepatopathy / Splenomegaly
12. Cytopenia(s)

Image: https://www.judson-group.com

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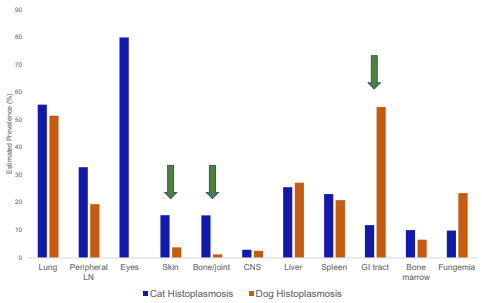
ORGANS INVOLVED



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RISKS

- No consistent breed / sex predilections
  - OSU predisposed: miniature schnauzer and Siberian husky
  - Poorer prognosis: Great Pyrenese[1]
- Anything that aerosolizes up dust
- 1/3 of cats are indoor only
- Exposure to chicken coops or out-buildings
  - Cycle of wet-dry conditions
  - Soil contaminated w bird or bat droppings

1. Wilson AG, et al. JAVMA 2018

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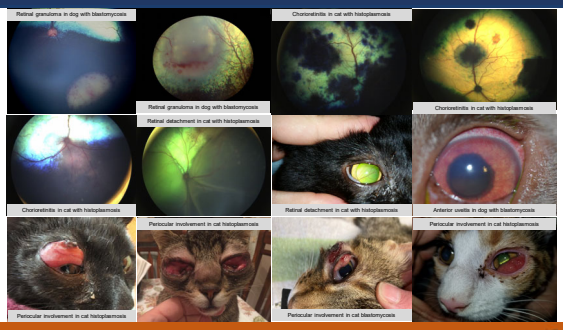
EYES!



Images courtesy Dr. Emily McCord, Dr. Rachel Allbaugh, Dr. Jonathan Packett

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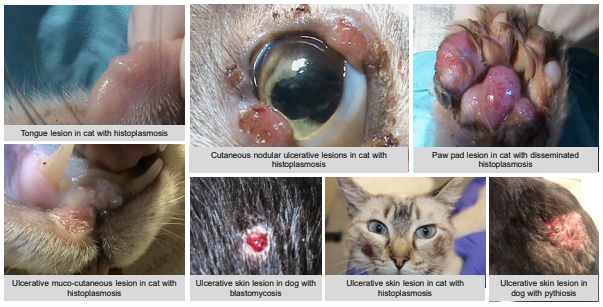
SKIN, SQ, MUCOSAL



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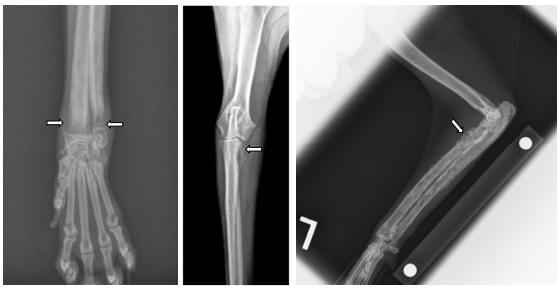
BONE



Bone involvement with histoplasmosis and blastomycosis.

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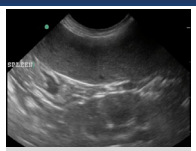
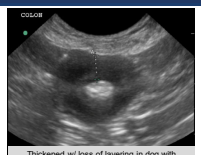
ABDOMINAL VISCERA

Large hyperechoic liver in dog with histoplasmosis.



Large hypoechoic spleen in cat with histoplasmosis.



Thickened w/ loss of layering in dog with histoplasmosis.

Infiltrative GI disease in a dog with pythiosis.

Infiltrative GI disease in a dog with pythiosis.

Kidney image courtesy of Dr. Laura Nofs

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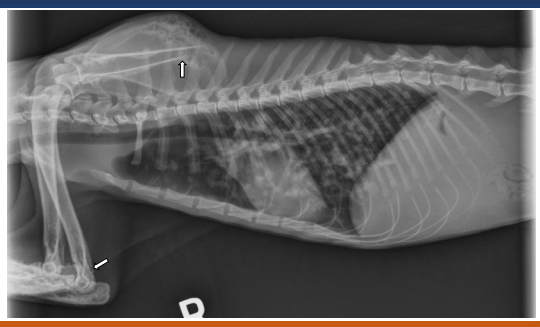
Histo - Diffuse structured interstitial pattern in cat. Bone lesions also present



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Histo - Diffuse unstructured interstitial pattern in cat

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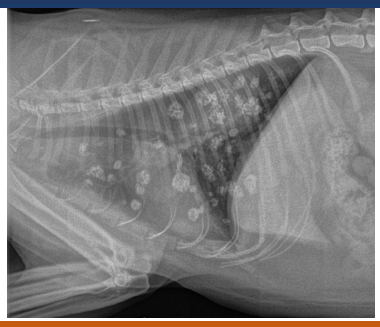
Histo - Diffuse structured interstitial pattern with mass-like lesions in cat

17

Histo – Calcified nodules post treatment in cat



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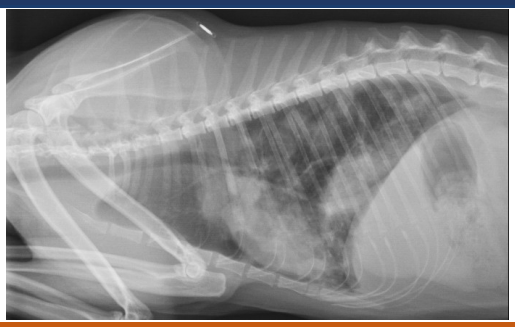
Histo - Unstructured interstitial to patchy alveolar pattern in cat



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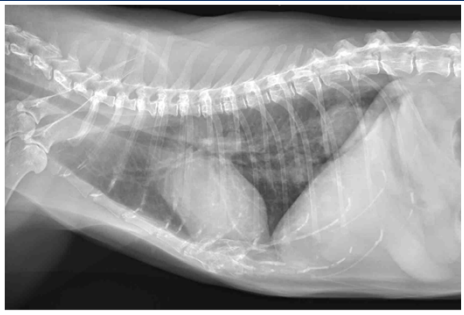
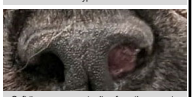
Crypto - Unstructured interstitial w/ mass-like lesion in a cat



Facial deformity and nasal discharge in cat with cryptococcosis.



Soft tissue mass protruding from the nares in cat with cryptococcus.

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Large tracheobronchial lymph nodes in dog

21

Large tracheobronchial lymph nodes compressing mainstem bronchi in dog

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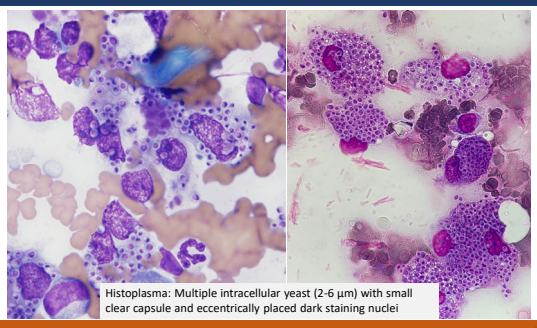
22

Histoplasma



Histoplasma: Multiple intracellular yeast (2-6 µm) with small clear capsule and eccentrically placed dark staining nuclei

Image courtesy Dr. Jim Meinkoth, Dr. Steven Hodges

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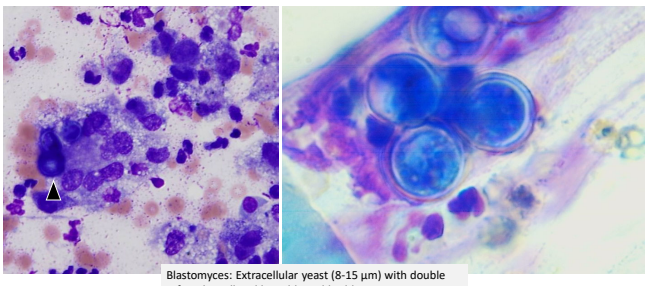
Blastomyces



Blastomyces: Extracellular yeast (8-15 µm) with double refractile wall and broad-based budding

Image courtesy Dr. Jim Meinkoth, Dr. Jeff Powers

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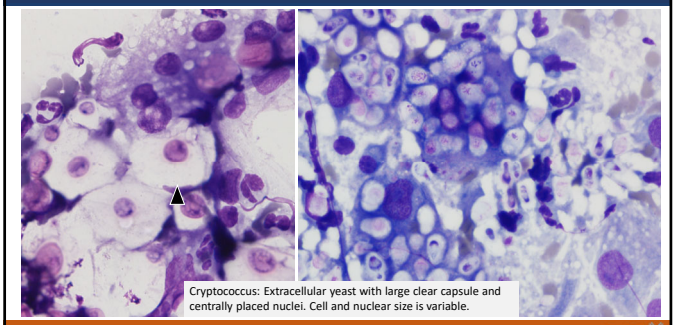
Cryptococcus



Cryptococcus: Extracellular yeast with large clear capsule and centrally placed nuclei. Cell and nuclear size is variable.

Image courtesy Dr. Jim Meinkoth

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Aspergillus

Aspergillus: Narrow, septate, acute angled branching, with round ends.

Image courtesy Dr. Jim Meinkoth

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PATHOLOGY – DIAGNOSTIC PERFORMANCE

- Pathology-proven cases overrepresented in published research
  - Pulmonary forms underrepresented
  - Include probable cases
- High diagnostic specificity
  - Some look-alikes
- Diagnostic sensitivity
  - Special stains – GMS, PAS
- Samples
  - LN, rectal scrape, skin, liver, spleen, bone, bone marrow

Host-Species	Diagnostic Sensitivity [1] (cyto for Histo)
Dog	18/19; **95%** (81-100)
Cat	30/33; **91%** (10-100)

1. Hanelloek AK, et al., JVIM 2022.

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HEMOPHAGOCYTOSIS

CASE SERIES

WILEY

Hemophagocytosis and *Histoplasma*-like fungal infection in 32 cats

Deanna M. W. Schaefer[1] | Theresa E. Rizzi[2] | Angela B. Royal[3]

[1]Department of Biomedical and Diagnostic Sciences, University of Tennessee, Knoxville, Tennessee

[2]Department of Veterinary Pathobiology, Oklahoma State University, Stillwater, Oklahoma

[3]Department of Veterinary Pathobiology, University of Missouri, Columbia, Missouri

Correspondence
Deanna Schaefer, Department of Biomedical and Diagnostic Sciences, University of Tennessee, Knoxville, TN.
Email: dschaefe@utk.edu

Abstract

Histoplasmosis is one of the most common systemic fungal diseases in cats from the United States. It commonly causes respiratory or disseminated disease and is often associated with one or more cytopenias. Here, we describe 32 cats in which a *Histoplasma*-like fungal infection was associated with concurrent hemophagia in at least one sample site, commonly spleen, bone marrow, liver, and/or lymph node. The degree of hemophagia was characterized as moderate or marked in the majority of cases, and in all cases, there was a predominance of phagocytized mature erythrocytes. A few cases also had macrophages with phagocytized erythroid precursors, platelets, and/or neutrophils. Complete blood count results were available for 25 cats, and cytopenias were common (20/25), including solitary anemia (10), anemia and thrombocytopenia (5), solitary neutropenia (2), pancytopenia (2), and anemia and neutropenia (1). Bone marrow samples were only available in a small subset of cases, preventing the further assessment of the causes of the cytopenias. Hemophagocytosis has been previously reported in cats with neoplastic diseases and a cat with calicivirus infection, and likely occurs with other conditions as well, such as hemorrhage or hemolysis. Results of this report suggest that systemic fungal disease is an additional differential to consider when there is hemophagia in a feline cytology sample.

KEYWORDS
bone marrow, feline, hematology, hemophagocytic lymphohistiocytosis, hemophagocytic syndrome

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CULTURE

- Long TAT
  - Up to 6 weeks
- Marginal Sensitivity
  - 15-60%
- Susceptibility testing
  - Minimal utility unless using fluconazole
  - More useful molds/yeasts

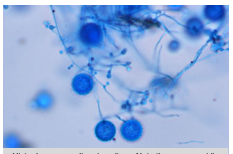
Host Species	Sensitivity Fungal Culture[1]
Cat	17/33; **51%** (34-69%)
Dog	15/19; **79%** (34-69%)

STANDARD ARTICLE

Journal of Veterinary Internal Medicine ACVIM

Clinical utility of fungal culture and antifungal susceptibility in cats and dogs with histoplasmosis

Andrew S. Hanzlicek[1,2] | Kate S. KuKanich[2] | Audrey K. Cook[2] | Steven Hodges[2] | John M. Thomason[2] | Rupika DeSilva[2] | Akhilesh Ramachandran[2] | Michelle M. Durkin[2]



Histoplasma mycelium in culture. Note the macroconidia and microconidia.

1. Hanzlicek, JVIM 2022.

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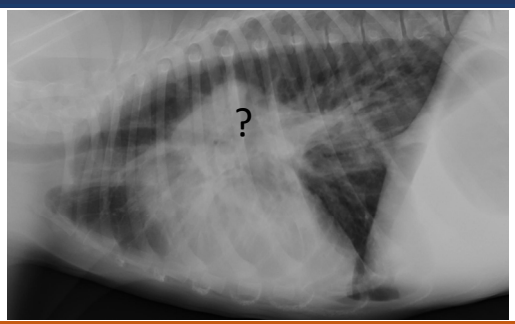
OPTIONS?



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ANTIBODY & ANTIGEN DETECTION

- Immunodiffusion (ID or AGID)
  - Clear agarose gel
  - Visual inspection
    - line of immunoprecipitation
  - Low complexity
  - "Fungal Serology Panels"
- Enzyme immunoassay (EIA)
  - Higher analytical sensitivity (than ID)
  - More efficient
    - Scalable
    - Shorter TAT
- Lateral flow assay (LFA)
  - Point-of-care device

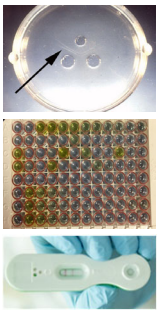

image: https://phines.org/glossary/agid-agar-gel-immunodiffusion-assay/

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BIOMARKERS HISTOPLASMOSIS

- Antigen eia (MVD)
  - Galactomannan (GM)
    - Soluble fungal cell wall polysaccharide
      - continuously shed then replenished
  - **Urine**
  - Serum
    - Lower GM concentration = lower dSens

Histo Ag Study	# Dogs	Sens (%) urine	Spec (%) urine
Cunningham, JAHAA 2015 (dog)	60	89	100
Clark, JVIM 2020 (dog)	110	95	98
Cook, JFMS 2012 (cat)	18	94	NA
Rothenburg, JVIM 2019 (cat)	105	94	97
TOTAL	**293**	**93**	**97**

- IgG Antibody eia (MVD)
  - If urine antigen (-) & still suspicious (5-10% cases)
  - If urine antigen <0.5 ng/ml and clinical suspicion was low
  - If localized disease
  - Histo:
    - 77-81 sensitivity
    - 92-95 specificity

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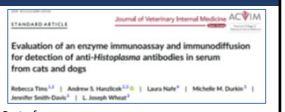
HISTOPLASMA ANTIBODY DETECTION

CATS - Test(s)	Positive/Number Animals (Sensitivity, %)		
	Proven	Probable	Total
Antibody AGID	0/30 (0%)	0/7 (0)	**0/37 (0)**
IgG EIA	24/30 (80%)	6/7 (86)	30/37 (81)
Antigen EIA	28/30 (93%)	7/7 (100)	35/37 (95)
IgG or Antigen EIA	30/30 (100%)	7/7 (100)	**37/37 (100)**

Part of:
"Fungal Serology Panels"

DOGS -Test(s)	Positive/Number Animals (Sensitivity, %)		
	Proven	Probable	Total
Antibody AGID	3/21 (14%)	0/1 (0)	**3/22 (14)**
IgG EIA	17/21 (81)	0/1 (0)	17/22 (78)
Antigen EIA	19/21 (91%)	1/1 (100)	20/22 (91)
IgG or Antigen EIA	21/21 (100%)	1/1 (100)	**22/22 (100)**

Part of:
"Fungal Serology Panels"



STANDARD ARTICLE

Journal of Veterinary Internal Medicine ACVIM

Evaluation of an enzyme immunoassay and immunodiffusion for detection of anti-*Histoplasma* antibodies in serum from cats and dogs

Rebecca Tims[1,2] | Andrew S. Harclerode[1,2,3] | Laura Nafe[4] | Michelle M. Durkis[4] | Jennifer Smith-Davis[4] | L. Joseph Wheat[4]

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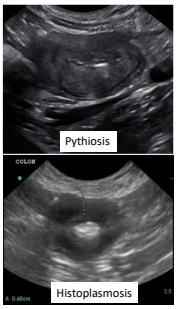
NEW: PYTHIUM TEST at MVD

Successful management of 3 dogs with colonic pythiosis using itraconzaole, terbinafine, and prednisone

Krystle L. Reagan[1] | Stanley L. Marks[2] | Patricia A. Pesavento[3] | Ann Della Maggiore[1] | Bing Y. Zhu[1] | Amy M. Grooters[4]



- GI disease like histoplasmosis
- New: *Pythium* IgG test (MVD)
  - Dog & Cat
  - Diagnosis
    - Sensitivity > 99%
    - Specificity > 98%
  - 0.25 ml serum
  - Next day results
  - Treatment Monitoring

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ANTIGEN CONCENTRATION AS PROGNOSTICATOR

STANDARD ARTICLE

Journal of Veterinary Internal Medicine ACVIM

Retrospective analysis of the effects of *Blastor* concentration in urine and radiographic findin in dogs with blastomycosis

Laura O. Motschenbacher | Eva Furrow | Aaron K. Rendahl | Kari L. Anderson | Lindsay K. Merkel | Edward E. Patterson

Pretreatment *Histoplasma capsulatum* urine enzymatic immunoassay concentrations do not correlate with outcome but may be influenced by renal function in cats with histoplasmosis

Jennifer E McGill[1], Andrew S Hanzlicek[2], Kate S Kukanich[3], Gary D Norsworthy[4] and Audrey K Cook[5]

SAGE

- Blasto antigen urine (dogs)
  - <5 ng/ml = 100% survival
  - >5 ng/ml = 68% survival
- Histo antigen urine (cats)
  - No correlation to outcome

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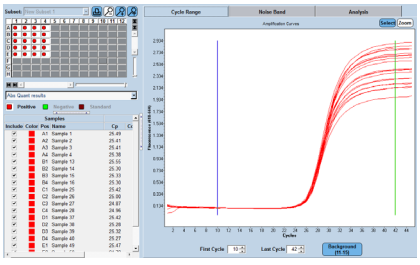
MOLECULAR ASSAYS

- Real-time PCR (qPCR)
  - Semi-quantitative
  - Cycle threshold (Ct value)
  - Fluorescent probes
- Small sample volumes
- Multiple pathogens
  - Multiplex assays



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BEWARE OF THE PCR PANELS!

- Laboratory v Clinical Validation
  - Is DNA expected in sample type?
    - Blood, urine, BALf, CSF, aqueous, other
  - Performance for sample type in naturally occurring disease?
- Commercially available panels
  - Fever of Unknown Origin Panel, Systemic Mycoses Panel, Uveitis Panel
  - Diagnostic performance data???
- Variability
  - Laboratory / Platform
  - Sample type - inhibitors
  - Purification / concentration
  - Single vs. Multi-copy gene
  - Many others

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TREATMENT GUIDELINES

- Itraconazole = First choice
  - FDA Generic, Itrafungol®, or Sporanox®
  - **NOT COMPOUNDED!!**
  - **Therapeutic Drug Monitoring**
    - 3-week steady state, Near-Trough (within 4 hours of next dose)
    - MVD Itraconazole Bioassay
- Fluconazole = Second choice
- Amphotericin-B = Life-threatening Disease
- Posaconazole, Voriconazole, +Terbinafine
  - Salvage (Rescue Therapy)

https://www.vetsupplysource.com/itrafungol-oral-solution-52ml.html

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TREATMENT MONITORING* or WHEN TO STOP ANTIFUNGAL*

Monitoring Tool	Criteria	Notes
Treatment Duration	Minimum of 6-months	▪ Required duration is often much longer.
History	≥1-month past resolution of signs	▪ Mild exercise intolerance might persist, most notable in working or performance animals. ▪ Persistent tracheobronchial lymphadenopathy can cause cough, requiring concurrent corticosteroid treatment.
Physical Examination	≥1-month past resolution of abnormalities	▪ Differentiating active ocular disease from permanent inactive change is important.
Imaging Studies	≥1-month past resolution abnormalities	▪ Pulmonary scarring can be permanent and can cause static focal unstructured interstitial lung disease. ▪ Radiographic bone lesions should improve but might never return to normal.
Histoplasma Antigen EIA (urine)	≥1-month past negative urine antigen OR <0.4 ng/ml on 2 occasions at least 3 months apart (dogs only)	▪ Submit urine for antigen testing at diagnosis, every 3 months during treatment, and at 6 months then every 12 months after treatment.

*Meet all criteria before stopping antifungal drug.

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TAKE-HOMES

1. Histoplasmosis looks different in cats vs dogs
2. Signs overlap with other IFIs
3. Multiple biomarkers might be needed
4. Some commercially available tests are not recommended
   - "Fungal Serology Panels" = immunodiffusion
   - Blood PCR
5. Itraconazole = Avoid compounded drug & use TDM
6. Amp-B = life-threatening disease
7. Treatment Monitoring is multi-modal

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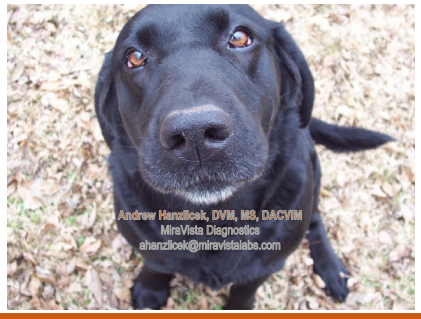
QUESTIONS?



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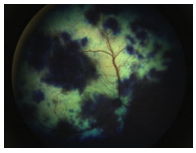
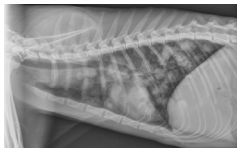
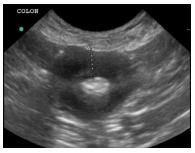
ANTIFUNGAL THERAPY

Andrew Hanzlicek, DVM, MS, DACVIM (SA)
Director, Veterinary Medicine
MiraVista Diagnostics

16May2023

1

DISCUSSION

1. Brief history of Antifungals

2. Clinical considerations for:
   - Azoles
   - Terbinafine
   - Amphotericin-B

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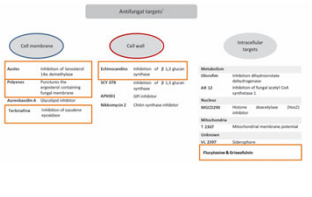
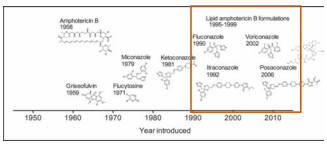
HISTORY OF ANTIFUNGALS





Van Daele R, et al. Antifungal drugs: What brings the future? MED MYC 2019;57:S328-S343.
Lewis RE, et al. Current concepts in antifungal pharmacology. MAYO CLIN PROC. 2011.

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CONSIDERATIONS

1. Organism sensitivity
2. Tissue permeation
3. Adverse-effects
4. Formulation
5. Cost

https://healthypets.mercola.com/sites/healthypets/archive/2015/08/01/cat-pill-medication.aspx

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TREATMENT GUIDELINES

Disease	Out-patient	Life-threatening	Salvage (Rescue)
Histoplasmosis			
Blastomycosis			
Coccidioidomycosis (Valley fever)			
Cryptococcosis* Candidiasis*			
Aspergillosis* (other molds)			

Dimorphs | Yeasts | Molds

* Sensitivity varies and some molds and yeasts are resistant. Base treatment on culture and sensitivity

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TRIAZOLES

- First generation
  - Itraconazole (Sporanox®, Itrafungol®)
  - Fluconazole (Diflucan®)
- Second generation
  - Posaconazole (Noxafil®)
  - Voriconazole (Vfend®)

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MECHANISMS OF ACTION

- Inhibit fungal ergosterol synthesis
  - Lanosterol 14α-demethylase = CYP450
  - Fungal p450 > human p450
- Drug-to-Drug interactions
  - ↓ Drug Metabolism = ↑ Drug Concentrations
  - Keto > Flu > Itra
  - ❖Ivermectin, benzodiazepines, cyclosporine, macrolide antibiotics, corticosteroids, amitriptyline, digoxin
- Inhibit adrenal cortical function
  - Cholesterol → Cortisol (p450 enzymes)
  - Keto > Flu > Itra

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- Which is the first-choice treatment for mild/mod histoplasmosis?

Q1

A. Fluconazole
B. Itraconazole
C. Voriconazole
D. Posaconazole

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ITRA- VS FLU-

Itraconazole	Fluconazole
• Absorption ↓ w antacid	• Absorption not affected by antacid or food
• Capsule w food	• Blasto, Histo, Cocci = less sensitive
• Blasto, Histo, Cocci = more sensitive	• Acquired resistance
• No acquired resistance	• 4 tablet sizes
• 1 capsule size	• Cost =
• Cost =	

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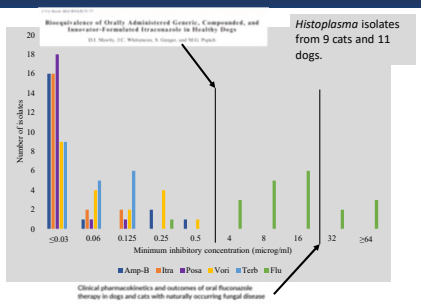
MIC VS BLOOD LEVELS



Histoplasma isolates from 9 cats and 11 dogs.

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ANTIFUNGAL MICs

Fungus	No. Isolates	Antifungal Agent	MIC range (µg/ml)	MEC range (µg/ml)	MIC_{50}/ MEC_{50} (µg/ml) (MIC_{90}/ MEC_{90})	References
Dimorphic fungi						
Blastomyces dermatitidis	34	Anidulafungin	2-8->8	NR	(4)/NR	71,77
	5	Caspofungin	0.5-8	NR	(2)/NR	77
	6	Micafungin	>8/<0.01-0.03*	NR	NR	63
	35	Amphotericin B	≤0.03-0.25*	NR	0.25/NR	63,71
	35	Fluconazole	1.0-32*	NR	16/NR	63,71
	6	Itraconazole	≤0.01-0.03*	NR	NR	63
	5	Posaconazole	≤0.03-0.06	NR	(0.05)/NR	77
Coccidioides immitis	4	Micafungin	0.01	NR	NR	63
	25	Caspofungin	≥8	NR	>8/NR	74
	29	Amphotericin B	0.06-0.5	NR	0.5/NR	63,74
	29	Fluconazole	4-64	NR	64/NR	63,74
	4	Itraconazole	0.06-0.12	NR	NR	63
Histoplasma capsulatum	5	Anidulafungin	2-4	NR	(3.6)/NR	77
	5	Caspofungin	0.5-4	NR	(1.3)/NR	77
	4	Micafungin	>8/0.03-0.06*	NR	NR	63
	4	Amphotericin B	0.06-0.5*	NR	NR	63
	4	Fluconazole	1.0-16*	NR	NR	63
	4	Itraconazole	≤0.01-0.03*	NR	NR	63
	5	Posaconazole	≤0.03-0.06	NR	(0.04)/NR	77

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Flu- Guidelines

- Diflucan® or FDA Generic
  - 50, 100, 150, 200 mg tablets
  - 10, 40 mg/ml solution
- Dose
  - Cat = 20 mg/kg/day
  - Dog = 20 mg/kg/day
- First-choice
  - cryptococcosis, coccidioidomycosis
  - lower urinary tract infections
- Second-choice
  - histoplasmosis, blastomycosis
- NOT effective against molds (*Asper)*

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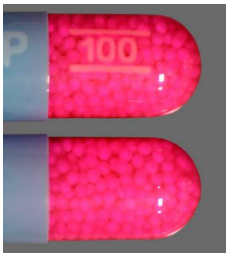
ITRACONAZOLE

- Solution = ↑ bioavailable
  - Cats NOT dogs
  - Solution NOT affected by meal
- Hydroxypropyl-β-cyclodextrin (HPβCD)
  - Not in compounded solutions
- Coated beads
  - Not in compounded drugs from bulk chemical



https://www.cvs.com/drug/itraconazole

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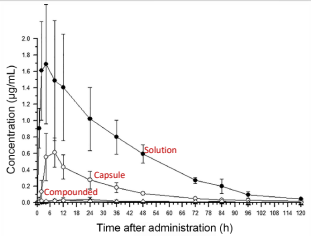
PK STUDY HEALTHY CATS

Comparison of absorption characteristics of oral reference and compounded itraconazole formulations in healthy cats



Nowby et al. Comparison characteristics of oral reference and compounded itraconazole formulations in healthy cats. JAVMA 2018;252:595-200.

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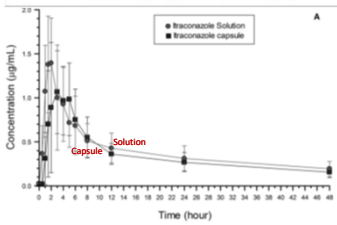
PK STUDY HEALTHY DOGS

Standard Article

Pharmacokinetics and Relative Bioavailability of Orally Administered Innovator-Formulated Itraconazole Capsules and Solution in Healthy Dogs

A.E. Hasbach, D.K. Langlois, E.J. Rosser Jr, and M.G. Papich



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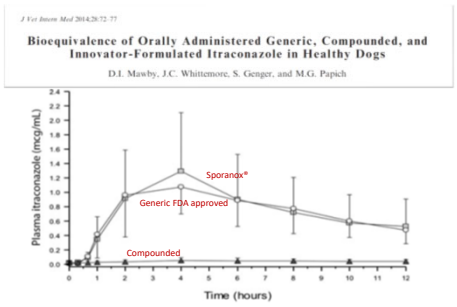
PK STUDY HEALTHY DOGS



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Q2

➢This Golden is receiving 10 mg/kg/day of itra for blasto has improved clinically but after 2 mos. of treatment developed skin lesions. What's the most likely underlying cause?

A. Bacterial pyoderma
B. Progressive blasto
C. Food allergy
D. Itra toxicity

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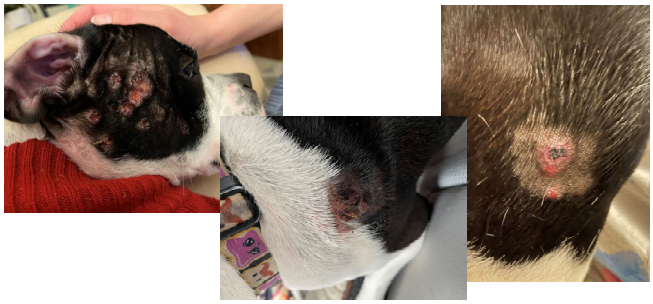
CUTANEOUS LESIONS DUE TO ITRA- TOXICITY



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1-MONTH AFTER D/C ITRACONAZOLE

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PHASES OF ITRA- TOXICITY

1. Vague/Non-specific
   - Hyporexia
   - Lethargy
2. Hepatotoxicity*
   - 60% ↑ ALT w mean itra 13 ug/ml
   - 12% ↑ ALT w mean itra 3 ug/ml
3. Vasculitis - ulcerative skin lesions*
   - 7.5% of dogs w mean itra 13 ug/ml
   - 0% of dogs w mean itra 3 ug/ml

*Legendre AM, et al. Treatment of blastomycosis with itraconazole in 112 dogs. J Vet Int Med. 1996;10:365-371.

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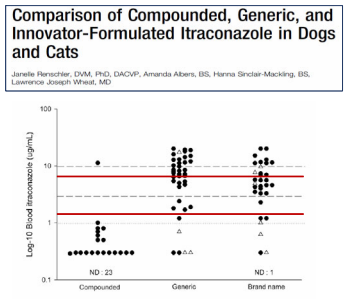
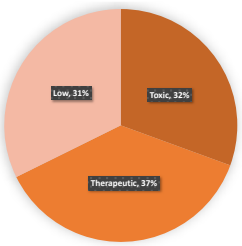
POPULATION PK STUDY DOGS AND CATS



Renschler J, et al. Comparison of compounded, generic, and innovator-formulated itraconazole in dogs and cats. JAVMA 2018;54:192-200.

21

MVD BIOASSAY BLOOD ITRA LEVELS (N=2000)



22

THERAPEUTIC DRUG MONITORING OPTIONS

Bioassay (MVD)

- Pharmacodynamic
  - Inhibition of fungal growth
- Itra + metabolites
- Lower cost ($40)
- Affected by other antifungal drugs
- Target trough level:
  - 2-7 mcg/ml

LC-MS

- Pharmacokinetic
  - Direct measurement
- Parent drug only
- Higher cost ($120-500)
- Not affected by other antifungal drugs
- Target trough level:
  - 0.5 – 1 mcg/ml itra
  - 0.5 – 1 mcg/ml OH-itra

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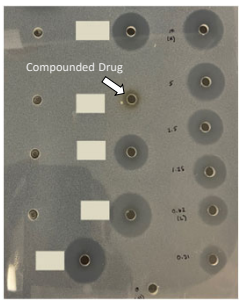
MVD BIOASSAY



24

ITRAFUNGAOL™ FOR INVASIVE FUNGAL INFECTIONS

- FDA approved
  - Dermatophytosis in cats
- Identical ingredient list to Sporanox®
  - 10 mg/ml
  - Cyclodextrin
  - Flavoring
- ≈1/3 cost

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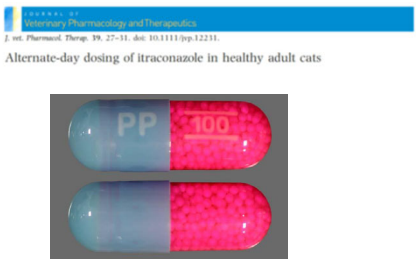
CAT OR SMALL DOG OPTIONS

- Divide FDA capsule
  - Smaller capsule
  - Open place over food
- EOD dosing in cats*
  - 100 mg EOD
  - Monitor blood levels


Journal of Veterinary Pharmacology and Therapeutics
J. vet. Pharmacol. Therap. 39, 27–31. doi: 10.1111/jvp.12231.

Alternate-day dosing of itraconazole in healthy adult cats

*Middleton SM, et al. Alternate-day dosing of itraconazole in healthy adult cats. J VET PHARMACOL THERAPEUT 2015;39:27-31; https://www.vin.com/drug/itraconazole

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ITRACONAZOLE GUIDELINES

- FDA Generic, Itrafungol®, or Sporanox®
  - **NOT COMPOUNDED!!**
- Give capsule w/ food
- Avoid concurrent antacid
- Dose:
  - D = 5 mg/kg/day
  - C = 4-5 mg/kg/day (solution)
  - C = 10 mg/kg/day (capsule)
- Therapeutic Drug Monitoring
  - Steady-state: >=3 weeks after starting
  - Near-Trough (within 4 hours of next dose)

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TISSUE DRUG CONCENTRATIONS

Drug	Mol Wt.	Protein Binding	Lung	Liver	Spleen	Skin	CSF	Bone	Synovium
FLU	305	12	1.1-1.6 (1.2 cat)[2]	3.4	6.1	11-40	1.0-2.3 (0.9 cat)[2]	0.3	0.88
ITRA	706	99.8	0.9-7 (5 dog)[4]	3-12 (12 dog)[4]	1.0-3.1	0.5-10 (10 dog)[4]	0-12	4.7	0.5-5
VORI	349	51	0.3-3.2	1.1-7.4	0.4-3.5	NA	0.2-1 (0.2 dog)[3]	5	0.25 (0.2 dog)[3]
POSA	700	97	>5	NA	NA	0.5-5	<0.5	NA	NA

1. Felton T, et al. Tissue penetration of antifungal agents. CLIN MICRO REVIEW 2014;27:68-88.
2. Vaden SL, et al. Fluconazole in cats: pharmacokinetics following intravenous and oral administration and penetration into cerebrospinal fluid, aqueous humour, and pulmonary epithelial lining fluid. J VET PHARMCOL THERAP 1997;20:181-186.
3. Lemetayer JD, et al. Pharmacokinetics and distribution of voriconazole in body fluids of dogs after repeated oral dosing. J VET PHARMACOL THERAP 2015;38:451-456.
4. Heykants J, et al. The pharmacokinetics of itraconazole in animals and man. REC TRENDS DISC DEV EVAL ANTIFUNGAL AGENT. 1987;32Supp:223-249.

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ITRA- SUPERIOR TO FLU- FOR VALLEY FEVER WITH BONE INVOLVEMENT

Comparison of Oral Fluconazole and Itraconazole for Progressive, Nonmeningeal Coccidioidomycosis

A Randomized, Double-Blind Trial

John N. Galgiani, MD; Antonino Catanzaro, MD; Gretchen A. Cloud, MS; Royce H. Johnson, MD; Paul L. Williams, MD; Laurence F. Mirels, MD; Faris Nassar, MD; Jon E. Lutz, MD; David A. Stevens, MD; P. Kay Sharkey, MD; Vipul R. Singh, MD; Robert A. Larsen, MD; Kathy L. Delgado, LPN; Cynthia Flanigan, BS; and Michael G. Rinaldi, PhD, for the National Institute of Allergy and Infectious Diseases–Mycoses Study Group

Background: In previous open-label noncomparative clinical trials, both fluconazole and itraconazole were effective therapy for progressive forms of coccidioidomycosis.

Objective: To determine whether fluconazole or itraconazole is superior for treatment of nonmeningeal progressive coccidioidal infections.

Design: Randomized, double-blind, placebo-controlled trial.

Setting: 7 treatment centers in California, Arizona, and Texas.

Patients: 198 patients with chronic pulmonary, soft tissue, or skeletal coccidioidal infections.

Intervention: Oral fluconazole, 400 mg/d, or itraconazole, 200 mg twice daily.

Measurements: After 4, 8, and 12 months, a predefined scoring system was used to assess severity of infection. Findings were compared with those at baseline.

Results: Overall, 50% of patients (47 of 94) and 63% of patients (61 of 97) responded to 8 months of treatment with fluconazole and itraconazole, respectively (difference, 13 percentage points [95% CI, −2 to 28 percentage points]; $P = 0.08$). Patients with skeletal infections responded twice as frequently to itraconazole as to fluconazole. By 12 months, 57% of patients had responded to fluconazole and 72% had responded to itraconazole (difference, 15 percentage points [CI, 0.003 to 30 percentage points]; $P = 0.05$). Soft tissue disease was associated with increased likelihood of response, as in previous studies. Azole drug was detected in serum specimens from all but 3 patients; however, drug concentrations were not helpful in predicting outcome. Relapse rates after discontinuation of therapy did not differ significantly between groups (28% after fluconazole treatment and 18% after itraconazole treatment). Both drugs were well tolerated.

Conclusions: Neither fluconazole nor itraconazole showed statistically superior efficacy in nonmeningeal coccidioidomycosis, although there is a trend toward slightly greater efficacy with itraconazole at the doses studied.

Ann Intern Med. 2000;133:676-686. www.annals.org
For author affiliations, current addresses, and contributions, see end of text.

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- What to do if first-line treatment fails (salvage therapy)?

Q3

A. Check Itra- blood level
B. Switch to Posaconazole
C. Switch to Voriconazole
D. Add terbinafine
E. All of the above could be appropriate

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POSA- VS VORI-

Posaconazole	Voriconazole
▪ Next generation itra-	▪ Next generation flu-
▪ Noxafil®	▪ Vfend®
▪ FDA generic	▪ FDA generic
▪ Approved:	▪ Approved:
▪ Prevent *Aspergillus*	▪ Treat *Aspergillus*
▪ *Histo, Blasto, Cocci*	▪ *Histo, Blasto, Cocci*
▪ Formulations:	▪ Formulations:
▪ 100 mg ER tablet	▪ 50 & 200 mg tablets
▪ 40 mg/ml solution	▪ 40 mg/ml solution
▪ Higher cost	▪ Lower cost

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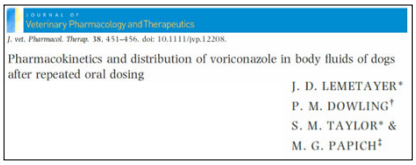
VORI- PK STUDY IN HEALTHY DOGS

➢Repeated dosing dogs

➢Drug concentrations:
- CSF:Plasma = 0.20
- Synovial:Plasma = 0.22
- Aqueous:Plasma = 0.19

➢BID dosing is required


JOURNAL OF Veterinary Pharmacology and Therapeutics

J. vet. Pharmacol. Therap. **38**, 451–456. doi: 10.1111/jvp.12208.

Pharmacokinetics and distribution of voriconazole in body fluids of dogs after repeated oral dosing

J. D. LEMETAYER*
P. M. DOWLING†
S. M. TAYLOR* &
M. G. PAPICH‡

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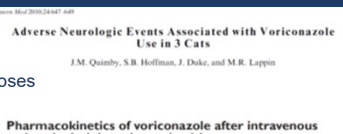
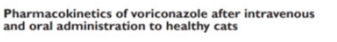
VORICONAZOLE FOR CATS


J Vet Intern Med 2010;24:647–649

Adverse Neurologic Events Associated with Voriconazole Use in 3 Cats

J.M. Quimby, S.B. Hoffman, J. Duke, and M.R. Lappin

➢Neurotoxicity seen with higher doses
- 10 mg/kg/day


Pharmacokinetics of voriconazole after intravenous and oral administration to healthy cats

➢No neurotoxicity seen w lower doses
- Suggests 12.5 mg (total dose) q 72 h
- Achieved target blood levels

1. Quimby JM, et al. Pharmacokinetics of voriconazole after intravenous and oral administration to healthy cats. J VET INT MED 2010;24:647-649.
2. Vanhoozer P, et al. Pharmacokinetics of voriconazole after intravenous and oral administration to healthy cats. AM J VET RSC 2014;75:569-578.

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VORICONAZOLE GUIDELINES

- Dog:
  - 5 mg/kg BID
- Cat:
  - 12.5 mg (total dose) q 72 hours
    - more info needed
- Consider therapeutic drug monitoring
  - Auto-induction of metabolism
- Clinical Uses
  1. Invasive molds (*Aspergillus*)
  2. Salvage therapy if itra- or flu- fails
     - *Blasto, Histo, Cocci, Crypto*

https://www.californiapetpharmacy.com/voriconazole-200mg-per-tablet.html

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POSACONAZOLE GUIDELINES

- Dogs
  - ER tablet = 5 mg/kg EOD
  - Solution = 5 mg/kg BID
- Cats
  - Solution = 7.5 mg/kg SID
- Clinical Uses
  1. Invasive molds (Aspergillus)
  2. Salvage therapy if itra- or flu- fails
     - Blasto, Histo, Cocci, Crypto

J Vet Intern Med 2010;30:1703–1707

Posaconazole Pharmacokinetics in Healthy Cats after Oral and Intravenous Administration

D.I. Mawby, J.C. Whittemore, L.E. Fowler, and M.G. Papich

Posaconazole pharmacokinetics after administration of an intravenous solution, oral suspension, and delayed-release tablet to dogs

Jennifer Kendall DVM
Mark G. Papich DVM, MS

https://www.clinicaltrialsarena.com/projects/noxafil-posaconazole-for-treatment-of-fungal-infections/

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TERBINAFINE

- Inhibits squalene epoxide reductase
  - ↓ production ergosterol = damage fungal cell membrane
- Well-tolerated & inexpensive
  - GI upset and hepatotoxicity are possible
- Single oral dose 30-35 mg/kg
  - Healthy large breed dogs
  - Cmax = 3.5-4 ug/mL
  - ≥ 18h MIC for Blastomyces & Histoplasma

1. Sakai M-R, et al. Terbinafine pharmacokinetics after single dose oral administration in the dog. VET DERM 2011;22:528-534.
2. Williams MM, et al. Pharmacokinetics of oral terbinafine in horses and Greyhound dogs. VET PHARM THER 2011;34:232-237.

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TERBINAFINE IS SYNERGISTIC WITH AZOLES

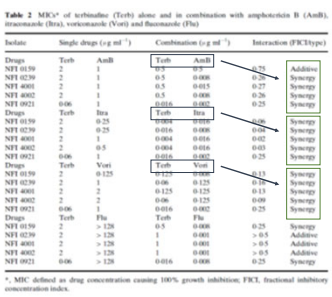

Table 2 MICs* of terbinafine (Terb) alone and in combination with amphotericin B (AmB), itraconazole (Itra), voriconazole (Vori) and fluconazole (Flu)

Isolate	Single drugs (μg ml⁻¹)		Combination (μg ml⁻¹)		Interaction (FICI/type)
Drugs	Terb	AmB	Terb	AmB	
NFI 0159	2	1	0·5	0·5	0·75 Additive
NFI 0239	2	1	0·5	0·008	0·26 Synergy
NFI 4001	2	1	0·5	0·015	0·27 Synergy
NFI 4002	2	1	0·5	0·008	0·26 Synergy
NFI 0921	0·06	1	0·016	0·002	0·25 Synergy
Drugs	Terb	Itra	Terb	Itra	
NFI 0159	2	0·25	0·004	0·016	0·05 Synergy
NFI 0239	2	0·25	0·016	0·008	0·08 Synergy
NFI 4001	2	1	0·004	0·016	0·02 Synergy
NFI 4002	2	0·5	0·004	0·016	0·03 Synergy
NFI 0921	0·06	1	0·016	0·002	0·25 Synergy
Drugs	Terb	Vori	Terb	Vori	
NFI 0159	2	0·125	0·125	0·008	0·13 Synergy
NFI 0239	2	1	0·06	0·125	0·56 Synergy
NFI 4001	2	2	0·125	0·125	0·13 Synergy
NFI 4002	2	2	0·06	0·125	0·09 Synergy
NFI 0921	0·06	1	0·016	0·002	0·25 Synergy
Drugs	Terb	Flu	Terb	Flu	
NFI 0159	2	> 128	0·5	0·008	0·25 Synergy
NFI 0239	2	> 128	1	0·001	> 0·5 Additive
NFI 4001	2	> 128	1	0·001	> 0·5 Additive
NFI 4002	2	> 128	1	0·001	> 0·5 Additive
NFI 0921	0·06	> 128	0·016	0·008	0·25 Synergy

*, MIC defined as drug concentration causing 100% growth inhibition; FICI, fractional inhibitory concentration index.

Ryder NS, et al. Synergistic interaction of terbinafine with triazoles or amphotericin B against Aspergillus species. MED MYC 2001;39:91-95.

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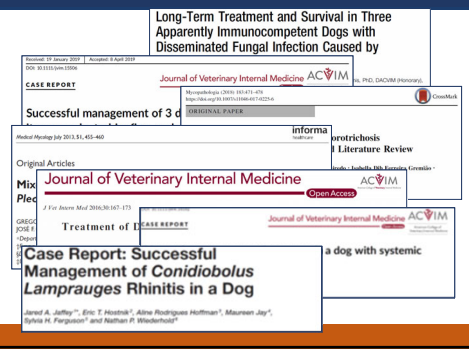
TERBAFINE IN THE LITERATURE



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Q4

➢What's the most effective antifungal for life-threatening invasive fungal infections?

A. Amphotericin-B
B. Fluconazole
C. Terbinafine
D. Flucytosine

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AMPHOTERICIN - B

- Original formulation
  - Deoxycholate (Fungizone®)
- Complexed Amp-B
  - Lipid complex (Abelcet®)
  - Liposome encapsulated (AmBisome®)
  - Colloidal dispersion (Amphotec®)

https://www.mims.com/drug/info/ambisome?type=full

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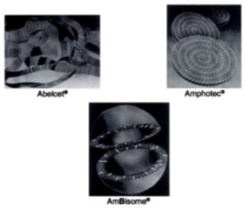
ABELCET® & ABMISOME®

- Less entry into renal tubule
  - 8-10 x less nephrotoxic
- Concentrates liver, spleen, & lungs
- Macrophage activator
  - Potentiates phagocytosis & fungicidal activity
- Released @ sites inflammation (lipases)



Boswell GW, et al. AmBisome (liposomal amphotericin B): a comparative review. J Clin Pharmacol.38:583-592.

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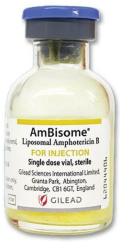
AMBISOME

- D: 1–2 mg/kg EOD IV over 2-4 h
- C: 0.5–1 mg/kg EOD IV over 2-4 h
- Max cumulative dose:
  - D: up to 24 mg/kg
  - C: up to 12 mg/kg
- IV fluids = 2 x maintenance rate
  - 30 m before - 2 h after infusion
- Kidney values + electrolytes
  - Delay dose if kidney values are increasing
- Handling and Administration



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AMPHOTERICIN – B GUIDELINES

- Any life-threatening IFI
- IV Ambisome or Abelcet
  - SQ Amp-B deoxycholate – less expensive option
- Monitor kidney values + electrolytes
- Step-down therapy w/ azole
  - Dimorphic
- Concurrent therapy w/ azole
  - Mold or Yeast
- Concurrent corticosteroid
  - Inflammation from drug and dying fungal organisms

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SUB-CUTANEOUS AMPHOTERICIN - B

- Deoxycholate formulation
  - 0.5-0.75 mg/kg in 350 ml 0.45% NaCl
  - 2-3 times / week
  - Tissue irritation possible
  - <20 mg/L concentration


SMALL ANIMALS

Long-term outcome of therapy for 59 cats and 11 dogs with cryptococcosis

CR O'BRIEN,* MR KROCKENBERGER,† P MARTIN,‡ DI WIGNEY§ and R MAUR*

O'Brien CR, et al. Long-term outcome of therapy for 59 cats and 11 dogs with cryptococcosis. AUS VET J 2004;84:384-392.

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TREATMENT GUIDELINES

Disease	Out-patient	Life-threatening	Salvage (Rescue)
Histoplasmosis	Itraconazole > Fluconazole	Amphotericin-B	Posaconazole > Voriconazole Terbinafine + azole
Blastomycosis	Itraconazole > Fluconazole	Amphotericin-B	Posaconazole > Voriconazole Terbinafine + azole
Coccidioidomycosis (Valley fever)	Fluconazole = Itraconazole	Amphotericin-B	Posaconazole > Voriconazole Terbinafine + azole
Cryptococcosis* Candidiasis*	Fluconazole > Itraconazole	Amphotericin-B	Posaconazole > Voriconazole
Aspergillosis* (other molds)	Posaconazole + terbinafine Voriconazole + terbinafine	Amphotericin-B	Amphotericin-B + Azole +Terbinafine +/- Echinocandin

Dimorphs | Yeasts | Molds

* Sensitivity varies and some molds and yeasts are resistant. Base treatment on culture and sensitivity

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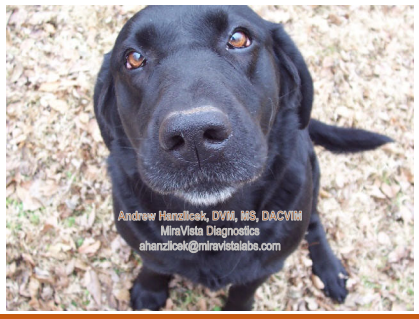
QUESTIONS?



Andrew Hanzlicek, DVM, MS, DACVIM
MiraVista Diagnostics
ahanzlicek@miravistalabs.com

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Identification and treatment of sepsis in the small animal patient
Summer Seminar 2023
Allison Biddick, DVM, MS, DACVECC

Definitions:

1. Sepsis

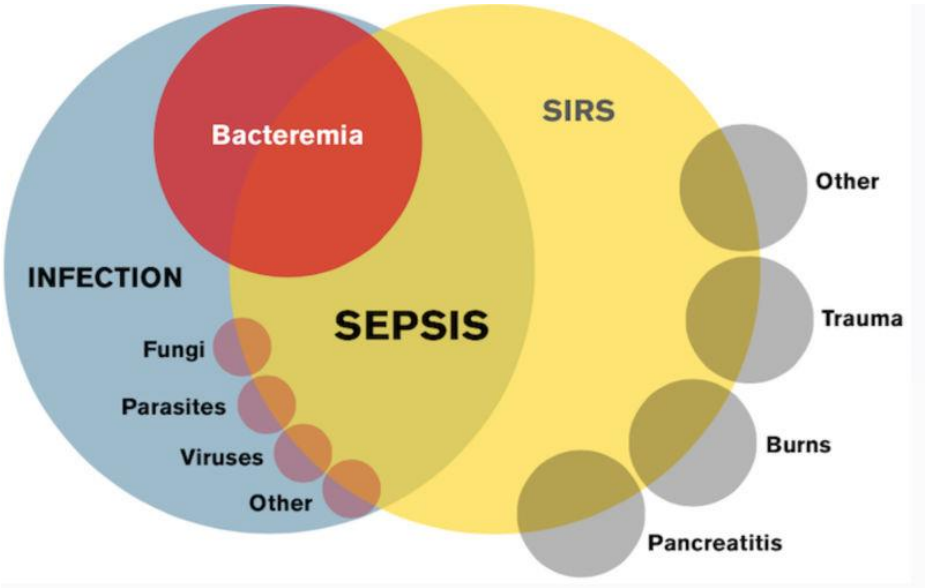
Life-threatening organ dysfunction caused by dysregulated host response to infection.

2. Septic shock

More severe form of shock that requires vasopressors to maintain MAP > 65 mm Hg; associated with higher mortality

3. SIRS

Systemic inflammatory response syndrome; exaggerated host response of body to stressor; may or may not be infectious (i.e. neoplasia, trauma, inflammation, immune-mediated, ischemia, etc)



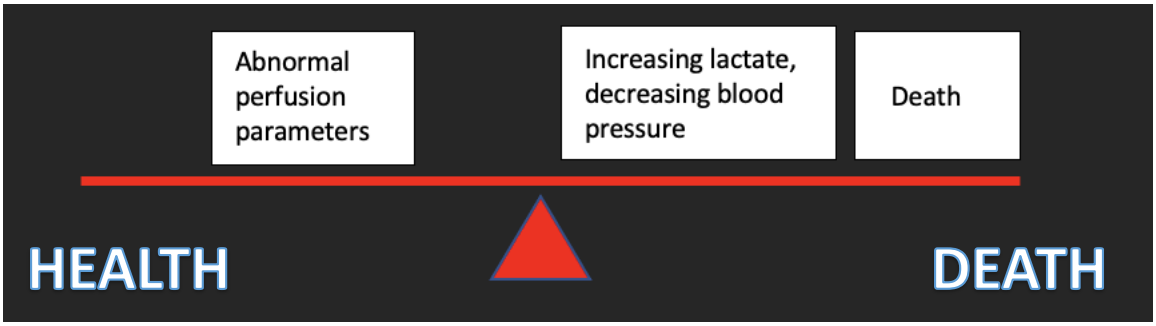
SIRS criteria

	Dogs Must have >/= 2 abnormalities	Cats Must have >/= 3 abnormalities
Temperature	<100.6 or >102.6F	<100 or >104F
HR	>120 bpm	<140 or >225 bpm
RR	>20 brpm	>40 brpm
WBC count	<6 or >16 x 10^3/uL OR >3% bands	<5 or >19 x 10^3/uL

Identification and treatment of sepsis in the small animal patient
Summer Seminar 2023
Allison Biddick, DVM, MS, DACVECC

Perfusion parameters (deficits may indicate abnormal perfusion/oxygenation BEFORE lactate/blood pressure become abnormal)

MM color – often injected/brick red with sepsis
CRT – often rapid (<1 second) with sepsis
Mentation
Pulse rate – most often increased in dogs/decreased in cats
Pulse quality – may be bounding/hyperdynamic in sepsis
Distal extremity temperature



Common causes of sepsis in small animals:

- GI bacterial translocation (parvo, AHDS, enteritis, PLE, severe endoparisitism, etc)
- Pneumonia
- Infected bite wounds/trauma
- Surgical site infections/nosocomial infections
- Dental/oral infections
- Pyelonephritis
- Pyometra

Misc findings associated with sepsis:

- CBC
  - White blood cells- commonly decreased in decompensated sepsis; may be normal or increased
  - Platelets- decreased if in DIC or having consumption from bleeding
  - Red blood cells- often increased from dehydration, but may be decreased if chronic disease or hemorrhage is present
- Chemistry
  - Glucose- commonly decreased in decompensated sepsis; may be increased from stress/steroid response
  - ALT- increased from hepatocyte leakage
  - Bilirubin- increased from abnormal processing of bilirubin secondary to cytokines and hepatic dysfunction

    - Albumin- most commonly decreased (negative acute phase protein), may be increased or normal if severe dehydration is also present
    - Renal values- often increased from pre-renal or renal azotemia
- Blood pressure
    - May be normal in decompensated shock, but will become low if not recognized and treated promptly
    - If hypotension is not responsive to IV fluid resuscitation, vasopressors are indicated
- Lactate
    - May be normal or high, lactate clearance more important than absolute lactate value
    - Use as resuscitation end-point
- Body temperature
    - Dogs and cats may be febrile when they have an infection but they are often hypothermic once sepsis occurs. A normal or low body temperature does NOT rule out an infection/sepsis.

<u>Antimicrobial administration</u>

Antimicrobial choice should always be based on culture & susceptibility results when possible. Hospital patterns should also be noted/tracked via routine cultures of the environment and recognition of an increase in surgical site or other nosocomial infections. Each environment will have its own types of antimicrobial resistance patterns based on caseload, types of cases seen, disinfectants used for cleaning, and patient prepping/antiseptic use.

If a patient is presenting with sepsis, especially if they are leukopenic, hypoglycemic, or hypotensive, it is wise to start with broad-spectrum antimicrobial coverage (typically 2 antibiotics- I use Unasyn/Baytril* in dogs and Unasyn/Veraflox in cats). Once the patient is more stable, one or both antimicrobials may be discontinued based on the underlying disease process. There are high rates of antimicrobial resistance to all commonly used antimicrobials. If a patient is not showing signs of clinical improvement within 24 hours then switching antimicrobial classes should be considered. If Unasyn/Baytril do not seem to be working, I will escalate to an aminoglycoside or carbapenem such as Meropenem. Aminoglycosides such as amikacin or gentamicin are great broad-spectrum antimicrobials that are usually efficacious against E coli, Klebsiella, Staphylococcus and Enterobacter spp. I typically avoid aminoglycoside use in animal with AKI, severe hypotension or kidney insufficiency if possible. The patient's history should also be taken into account- for example, if a patient has been treated with Clavamox multiple times over the past few months and still has sepsis I assume that Clavamox or Unasyn may not be a wise choice and may not be efficacious against the organism in question.

*Baytril/enrofloxacin is a concentration dependent antimicrobial, which means it works best at higher doses. It should never be given at doses <10 mg/kg. I typically give 12-15 mg/kg IV q24h in DOGS. For cats, avoiding baytril is recommended because it can cause blindness. Veraflox/pradofloxacin comes in a liquid formula for cats and is my preference for broad spectrum antimicrobial in this species.

"Hit hard, exit fast" – Dawn Boothe, DVM, PhD, DACVIM, DACVCP

VETERINARY MEDICINE

Emergencies in Exotic Companion Mammals

Julianne McCready, DVM, DVSc
Assistant Professor, Zoological Medicine
Oklahoma State University
College of Veterinary Medicine

Summer Seminar 2023
June 16, 2023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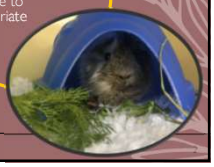
VETERINARY MEDICINE

INTRODUCTION

- Majority of exotic companion mammal (ECM) pets are prey species
  - Tend to hide signs of illness
  - Often very sick by the time they present
- Although there is a perception that some of these species "always die," they may be able to recover from significant illness with appropriate diagnostics and treatment





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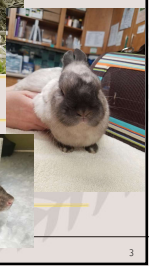
VETERINARY MEDICINE

Topics for Today

1. Gastrointestinal stasis
2. Vestibular signs
3. Dyspnea
4. Urolithasis and urinary obstruction
5. Insulinoma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VETERINARY MEDICINE

Gastrointestinal Stasis

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VETERINARY MEDICINE

Who Gets Gastrointestinal Stasis?




RABBITS
Hindgut Fermenter

CHINCHILLAS
Hindgut Fermenter

GUINEA PIGS
Hindgut Fermenter

HAMSTERS
Nonglandular forestomach similar to ruminants

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VETERINARY MEDICINE

Symptoms of GI Stasis

- LETHARGY
- ANOREXIA
- SMALL/IRREGULAR FECES
- LACK OF FECAL PRODUCTION
- ABDOMINAL PAIN

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VETERINARY MEDICINE

Etiology of GI Stasis

GI stasis is a SYMPTOM, not a disease!

CAUSES

- Dietary: inadequate fiber, excessive sugar, rapid change
- Stress
- Liver lobe torsion
- Dental disease
- Bladder stones
- Essentially any disease that causes stress or pain

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VETERINARY MEDICINE

Diagnostic Work-Up

BLOODWORK

- Blood gas analysis
- Electrolytes
- Complete blood count
- Biochemistry

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VETERINARY MEDICINE

Diagnostic Work-Up

BLOODWORK

- Blood gas analysis
- Electrolytes
- Complete blood count
- Biochemistry

Blood Gas & Electrolyte Analysis

- Hypochloremic metabolic alkalosis: suggests obstruction
- Hyponatremia: poor prognostic indicator; obstruction
- Lactate: higher in rabbits than other species

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VETERINARY MEDICINE

Diagnostic Work-Up

BLOODWORK

- Blood gas analysis
- Electrolytes
- Complete blood count
- Biochemistry

Complete Blood Count

- Anemia: r/o liver lobe torsion
- Leukocytosis: uncommon even with significant inflammatory disease
- Thrombocytosis: indicator of inflammation in rabbits

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VETERINARY MEDICINE

Diagnostic Work-Up

BLOODWORK

- Blood gas analysis
- Electrolytes
- Complete blood count
- Biochemistry

Biochemistry

- Azotemia: pre-renal vs renal
- Elevated urea: ↑ risk death
- Elevated liver enzymes: r/o liver lobe torsion
- Hypercholesteremia: inflammation/severe disease
- Hyperglycemia: poor prognosis if severe (>360 mg/dL); obstruction

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VETERINARY MEDICINE

Diagnostic Work-Up

IMAGING

- Radiographs
- Ultrasound
- Advanced imaging

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VETERINARY MEDICINE

Diagnostic Work-Up

ADDITIONAL DIAGNOSTICS

- Fecal flotation
- Fecal culture
- Blood culture if concern for sepsis
- Sedated/anesthetized oral exam

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VETERINARY MEDICINE

Diagnostic Work-Up

ADDITIONAL DIAGNOSTICS

- Fecal flotation
- Fecal culture
- Blood culture if concern for sepsis
- Sedated/anesthetized oral exam

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VETERINARY MEDICINE

Treatment of GI Stasis

Core Treatment
- Analgesia
- Fluids
- Syringe-feeding

Additional Treatments
- Heat support
- GI protectants
- Toxin binders
- Antibiotics

Questionable or Not Recommended Treatments
- Enzymes
- Pro-motility agents

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VETERINARY MEDICINE

Treatment of GI Stasis

Analgesics
- Meloxicam
  - Only if mild stasis and patient well-hydrated and non-azotemia
  - HIGHER dose than dogs/cats
    - 1 mg/kg/day
- Opioids:
  - buprenorphine, hydromorphone, methadone, fentanyl
- Tramadol? Efficacy questionable
- Lidocaine CRI
- Maropitant
- Gabapentin

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VETERINARY MEDICINE

Treatment of GI Stasis

Fluids
- SQ fluids
  - If mild
- IV fluids
  - If moderate to severe
  - IVC sites: cephalic, lateral saphenous, marginal ear vein
- Norepinephrine if hypotensive

Syringe-Feeding
- Oxbow Critical Care
- EmerAid Herbivore

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VETERINARY MEDICINE

Treatment of GI Stasis

Fluids
- SQ fluids
  - If mild
- IV fluids
  - If moderate to severe
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Syringe-Feeding
- Oxbow Critical Care
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VETERINARY MEDICINE

Treatment of GI Stasis

Fluids
- SQ fluids
  - If mild
- IV fluids
  - If moderate to severe
  - IVC sites: cephalic, lateral saphenous, marginal ear vein
- Norepinephrine if hypotensive

Syringe-Feeding
- Oxbow Critical Care
- EmerAid Herbivore

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VETERINARY MEDICINE

Treatment of GI Stasis

Additional Treatments
- Heat support
  - Hypothermia is negative prognostic indicator
  - Do not warm too rapidly
  - Rehydrate while rewarming
- GI protectants
  - Anorexia → gastric ulcers
- Toxin binders
  - Cholestyramine
- Antibiotics
  - Dysbiosis, sepsis, confirmed infection
- Mirtazapine?

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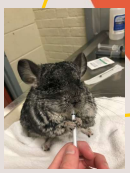
VETERINARY MEDICINE

Treatment of GI Stasis

Antibiotics
- Certain antibiotics unsafe for hindgut fermenters
  - Flora mainly G+
  - Abx that target mainly G+ may be unsafe
- Generally well-tolerated:
  - Fluoroquinolones
  - Trimethoprim-sulfamethoxazole
  - Metronidazole
  - Azithromycin
- Chinchillas prone to anorexia with antibiotics
  - Pradofloxacin
  - Metronidazole
  - Tinidazole (high dose)



Antibiotics UNSAFE in Herbivores
- P: penicillins
- L: lincosamides
- A: ampicillin, amoxicillin
- C: cephalosporins
- E: erythromycin

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VETERINARY MEDICINE

Treatment of GI Stasis

Questionable or Not Recommended Treatments
- Enzymes
- Metoclopramide
- Cisapride
  - Rabbits: no effect on fecal output and food/water intake
  - Chinchillas: slight but not clinically relevant improvement
- Trocarization
  - Risk of gastric perforation
  - Orogastric tube can be passed to decompress stomach if needed

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VETERINARY MEDICINE

Treatment of GI Stasis

Surgery?
- Surgery rarely indicated for GI stasis
  - Poorly tolerated
  - Even cases that appear obstructive can often be managed medically
- Surgery is the preferred treatment for liver lobe torsion
  - Survival rates of 43-80% with medical vs 72-100% with surgery (varies with study)
  - Longer MST (4 y vs 1.5 y)
- GDV?

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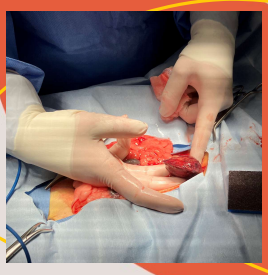
VETERINARY MEDICINE

Liver Lobe Torsion

Treatment
- Removal of affected liver lobe
  - Caudate > right > left lateral
- May require blood transfusion depending on severity of anemia
- Pain management



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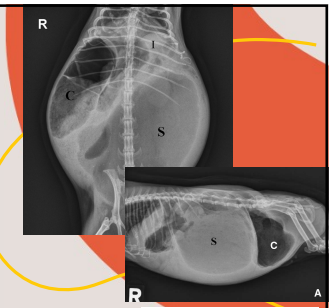
VETERINARY MEDICINE

Gastric Dilatation & Volvulus

- Guinea pigs
- Anorexia, lethargy, abdominal distension, lack of feces, lack of gut sounds, dyspnea, hypothermia, brady/tachycardia, cyanosis
  - NOT retching
- Spleen can be affected
- Tx: analgesia, stomach decompression, fluids, sx
- High mortality rate
  - Both with sx and medical mgmt.



Gastric Dilatation-Volvulus in a Guinea Pig (*Cavia porcellus*)

J Am Anim Hosp Assoc 2010;46:174-180

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VETERINARY MEDICINE

GI Stasis: Further Care and Prevention

- Syringe-feed until appetite normalized
- Dental care
  - May need dentals lifelong
  - Appropriate interval to prevent further GI stasis
- Appropriate diet
  - 80% grass hay
  - 15-20% medium leafy greens
  - 5% timothy hay-based pellets
- Brushing
- Keep cool in summer
- Education
  - What is an emergency?

Not eating for 8-12 hours

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VETERINARY MEDICINE

Vestibular Signs

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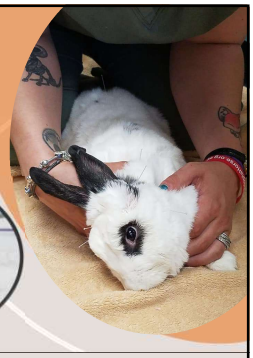
VETERINARY MEDICINE

Common Causes of Vestibular Signs

- Otitis media
  - Rabbits: *Pasteurella*, lop anatomy-related
  - Guinea pigs: *Bordetella*
  - Rats: *Mycoplasma*
  - Chinchillas: *Pseudomonas*
- *Encephalitozoon cuniculi*
  - Rabbits, rarely guinea pigs
- Pituitary tumors
  - Rats



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VETERINARY MEDICINE

Clinical Signs

- Head tilt
- Nystagmus
- Circling
- Rolling
- Rats: holding food w/ 1 paw in rats with pituitary tumors
- May see concurrent facial nerve deficits in rabbits with otitis media

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VETERINARY MEDICINE

Signalment

- Breed:
  - Lop rabbits: otitis media very common due to anatomy
  - Other breeds – otitis media more likely to be from spread through Eustachian tube secondary to URI
- Age:
  - Pituitary tumors in older rats
  - Younger rat – may be more concerned for otitis media

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VETERINARY MEDICINE

Diagnostic Work-Up

- Imaging
  - Radiographs
  - CT
- *E. cuniculi* testing
  - IgG, IgM, CRP
- Routine bloodwork
  - Evaluate for systemic illness
  - Pre-treatment baseline

Otitis media in a rabbit

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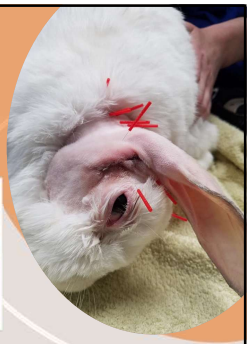
VETERINARY MEDICINE

Treatment

- Soft, padded enclosure
- Midazolam PRN for rolling/anxiety
- Meclizine?
- Otitis media
  - Antibiotics
  - Eye lubrication PRN
  - May require surgery
- Pituitary tumor
  - Cabergoline
  - Steroids



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VETERINARY MEDICINE

E. Cuniculi Treatment

- Fenbendazole x 28 d
- CBCs should be performed weekly
  - At least PCV
- Bone marrow suppression can occur and can be severe enough to necessitate transfusion
  - STOP fenbendazole if anemia develops

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VETERINARY MEDICINE

Dyspnea

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VETERINARY MEDICINE

Common Causes of Dyspnea

- Rabbits
  - *Pasteurella* pneumonia
  - Thymomas
- Guinea pigs
  - *Bordetella* pneumonia
- Rats
  - *Mycoplasma* pneumonia
  - Lymphoma
- Ferrets and hamsters
  - Cardiovascular disease

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VETERINARY MEDICINE

Rabbits

- *Pasteurella*
  - Common and can affect numerous organs including lungs
  - Rhinitis, conjunctivitis, tracheitis, otitis, pneumonia, pleuritis, abscessation
- Other common respiratory infections:
  - *E. coli, B. bronchiseptica, P. Aeruginosa, Moraxella, Pseudomonas*

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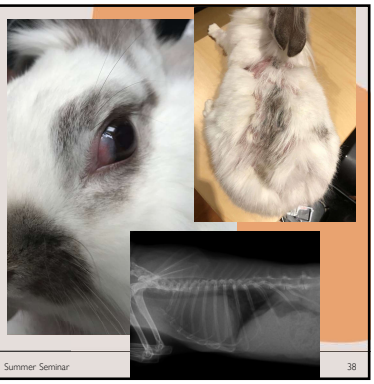
VETERINARY MEDICINE

Rabbits

- Thymoma
  - Common mediastinal mass in rabbits
  - Dyspnea, exophthalmos, third eyelid elevation
  - ± Lymphocytosis
  - Rarely exfoliative dermatitis



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VETERINARY MEDICINE

Rabbits

- Cardiovascular disease:
  - Prevalence 2.6%
  - Males, lops
  - Diagnoses:
    - Degenerative valve disease
    - Cardiomyopathy
      - DCM > unclassified > RCM > HCM
    - Myocarditis
    - Arteriosclerosis
  - Treatment:
    - Furosemide, enalapril, pimobendan commonly used
    - May need higher pimobendan dose than dogs/cats
    - DO NOT pill pimobendan with pill gun – risk of aspiration

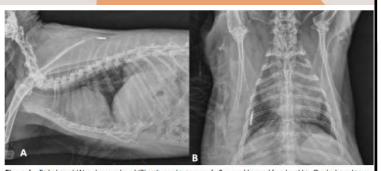

Figure 1—Right lateral (A) and ventrodorsal (B) radiographic images of a 9-year-old spayed female rabbit. On the lateral image, there is severe cardiomegaly with dorsal deviation of the trachea and a diffuse bronchointerstitial lung pattern. On the ventrodorsal image, there is cardiomegaly and a diffuse bronchointerstitial lung pattern.

Clinical and pathological findings in rabbits with cardiovascular disease: 59 cases (2001–2018)

JAVMA | OCT 1, 2021 | VOL 259 | NO. 7

Sarah Ozawa DVM
David Sanchez-Migallon Guzman DVM, MS
Kevin Keel DVM, PhD
Catherine Gunther-Harrington DVM

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VETERINARY MEDICINE

Guinea Pigs

- *Bordetella* common
- Other causes: *Streptococcus pneumoniae, Streptococcus equi* subsp. *zooepidemicus, Pseudomonas aeruginosa*
- Avoid contact with rabbits and dogs
  - Asymptomatic carriers

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VETERINARY MEDICINE

Rats

Most common causes of dyspnea in pet rats

- *Mycoplasma pulmonis*
- *Filobacterium rodentium* (formerly CARB)
- *Streptococcus*
- *Corynebacterium kutscheri*
- Lymphoma/round cell neoplasia

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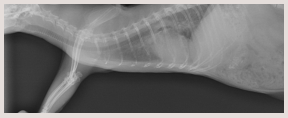
VETERINARY MEDICINE

Ferrets

Cardiovascular Diseases

- Valvular regurgitation
- Dilated cardiomyopathy (DCM)
- Restrictive cardiomyopathy (RCM)
  - Rare
- Heartworm



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VETERINARY MEDICINE

Diagnostic Work-Up

- Thoracic radiographs
- Thoracic ultrasound
- Echocardiogram
- CT Scan
- Complete blood count
- Serology
- Cytology and culture
  - BAL
  - Pulmonary aspirate


Positioning a rat for DV chest radiographs


BAL from a rabbit

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Murine respiratory mycoplasmosis with concurrent *Filobacterium rodentium* in a rat

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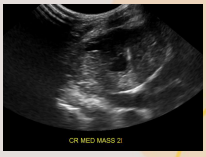
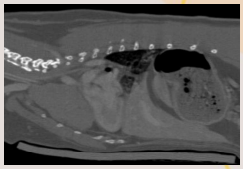
Thymomas in rabbits





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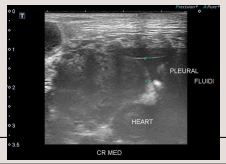
Mediastinal lymphoma in rats



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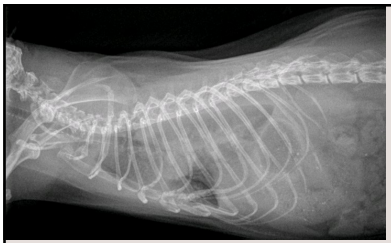

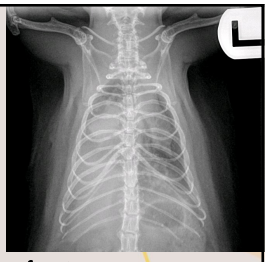

Lymphocytic leukemia in the lungs of a rat

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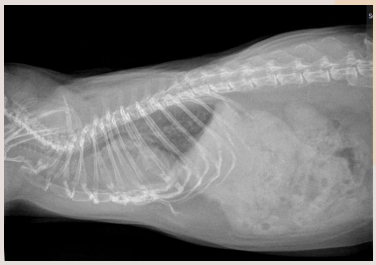

Dilated cardiomyopathy in a rat

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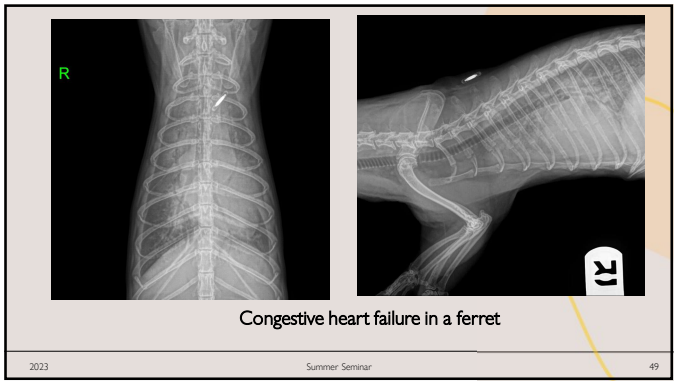

Congestive heart failure in a ferret

2023 Summer Seminar 49

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VETERINARY MEDICINE

Treatment

General Treatment

- Oxygen
- ± Sedation if distressed
  - Sedation highly recommended for imaging
- Antibiotics if infectious
- CHF tx: similar to dogs and cats
- Thoracocentesis if pleural effusion
- Steroids ± chemotherapy if round cell neoplasia
  - Limited data

2023 Summer Seminar 50

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VETERINARY MEDICINE

Treatment

Thymoma

- Aspiration of cystic parts of mass
- Radiation therapy is ideal treatment
  - MST 1.7 y (range 1-3 y) with palliative RT x 5 weekly sessions
  - Steroids if owners decline RT
    - MST 9 months
    - Risks: hepatopathy, infections, GI ulcers
- Surgery carries very high mortality (50-70%) rate and is not recommended

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VETERINARY MEDICINE

Treatment

Respiratory Infections in Rats

- Antibiotics
  - *Mycoplasma*: enrofloxacin + doxycycline, azithromycin, chloramphenicol
  - *Filobacterium*: sulfondamides, chloramphenicol
  - *Corynebacterium*: ampicillin, chloramphenicol, tetracycline
  - Streptococcus: amoxicillin-clavulanate
- Bronchodilators
- Nebulization
  - Saline, aminophylline, antibiotics, acetylcysteine
- Sildenafil
- ± Steroids

2023 Summer Seminar 52

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VETERINARY MEDICINE

Urolithiasis & Urinary Obstruction

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VETERINARY MEDICINE

Common Cause of Urinary Obstructions

- Uroliths
  - Rabbits, guinea pigs, chinchillas: calcium carbonate
  - Ferrets: cystine
- Adrenal disease → prostatomegaly
  - Ferrets

2023 Summer Seminar 54

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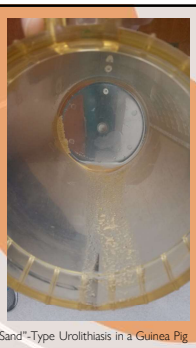
VETERINARY MEDICINE

Common Cause of Urinary Obstructions

- Uroliths
  - Rabbits, guinea pigs, chinchillas: calcium carbonate
  - Ferrets: cystine
- Adrenal disease → prostatomegaly
  - Ferrets



"Sand"-Type Urolithiasis in a Guinea Pig

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VETERINARY MEDICINE

Diagnostic Work-Up

- Abdominal radiographs
  - Most uroliths in ECM show up on radiographs
- Abdominal ultrasound
- Urinalysis
- Urine culture
- Stone analysis

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VETERINARY MEDICINE

Uroliths in Rabbits & Guinea Pigs

- Possible factors:
  - Diet (alfalfa hay, high calcium greens, mineral block)
  - Inadequate water intake
  - Inactivity
  - Obesity
- Treatment:
  - Unblocking if obstructed
  - Surgery
  - Manual removal with Lonestar retractor if very distal
  - Fluids
  - PAIN MANAGEMENT
  - Antibiotics based on culture results
    - Often sterile but *Corynebacterium* common in guinea pigs

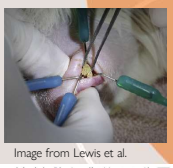
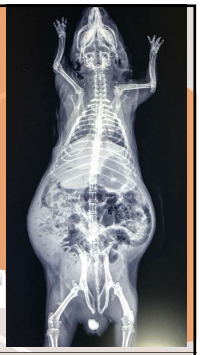


Image from Lewis et al.



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VETERINARY MEDICINE

Uroliths in Rabbits & Guinea Pigs

- Prevention:
  - Only grass hay once 1 yo (no alfalfa)
  - Low calcium greens
  - No mineral block
  - Multiple water sources (bowls & bottles)
  - Exercise
  - Lean body condition
  - K citrate?

Low Calcium	High Calcium
Romaine	Parsley
Leaf lettuce	Kale
Cilantro	Mustard greens

https://www.guinealynx.info/diet_vegs.html

https://rabbit.org/care/fruits-vegetables/

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VETERINARY MEDICINE

Urolithiasis in Ferrets

- 2011: 67% struvite
- 2021: 90% cystine
- Genetics?
- Treatment:
  - Unblocking if obstructed
  - Surgery
- Prevention:
  - Limited info
  - Low protein diet?
  - Fluids
  - K citrate?

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VETERINARY MEDICINE

Adrenal Disease in Ferrets

- Early neutering? Indoor housing?
- Overproduction of sex steroids
- Alopecia, pruritus, stranguria, vulvar swelling
- Urinary obstruction may occur in males due to prostatomegaly

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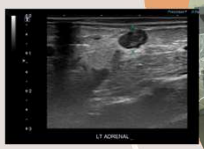
VETERINARY MEDICINE

Adrenal Disease in Ferrets

- Diagnostics:
  - Adrenal hormone panel (UTenn)
  - Abdominal ultrasound
- Treatment:
  - Unblocking if obstructed
  - GnRH agonist: leuprolide or deslorelin
  - Antibiotics if concern for prostatitis
  - ± Androgen receptor blockers
  - Adrenalectomy?
    - Lower MST than medical mgmt.
    - Risk of hemorrhage



Estradiol	466* (30-180)	pmol/L
17 OH Progesterone	<0.1 (<0.1-0.80)	nmol/L
Androstenedione	1.5 (<0.1-1.5)	nmol/L

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VETERINARY MEDICINE

Insulinoma

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VETERINARY MEDICINE

Insulinomas

- Very common in ferrets (20-25%)
- Rarely metastasize
- Lethargy, stargazing, pawing at mouth, ptyalism, seizures

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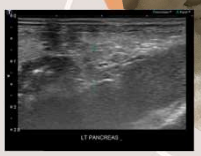
VETERINARY MEDICINE

Insulinomas

Diagnostics

- BG < 60 mg/dL after 3-4 h fast
  - Ensure spun down & plasma separated ASAP
  - Benchtop preferred over glucometer
  - If glucometer used, AlphaTrak dog setting preferred
- Insulin level
- Fructosamine NOT helpful
- Abdominal ultrasound



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VETERINARY MEDICINE

Insulinomas

Emergency Treatment

- Feeding if alert and able to swallow
- Dextrose
  - Avoid if possible – rebound hypoglycemia
- Glucagon CRI

Long-Term Treatment

- Frequent feeding of high-protein, low-carb diet
- Steroids
- Diazoxide
- Monitor BG weekly until normalized, then q 2 wks, then q 4 wks long-term
- Surgery?
  - Older studies (1990s) show longer MST with surgery
  - Risks: recurrence, diabetes mellitus

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VETERINARY MEDICINE

Case Example

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VETERINARY MEDICINE

Case Example

2-year-old neutered male mixed breed rabbit

- Intermittent periods of anorexia, lethargy, and decreased fecal production over the past few months
- Has not been evaluated by a vet for these episodes and they resolve on their own
- Now presenting for anorexia and decreased fecal production x 12 h

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VETERINARY MEDICINE

Case Example

Physical Examination

- T 101.5 F, HR 300 bpm, RR 100 brpm
- MM light pink and tacky
- Slight discomfort on cranial abdominal palpation
- Stomach and cecum more empty than normal

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VETERINARY MEDICINE

Case Example

Diagnostics

What diagnostics would you recommend for this rabbit?

- Blood gas and electrolytes
- Complete blood count
- Biochemistry profile
- Abdominal radiographs
- Abdominal ultrasound

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VETERINARY MEDICINE

Case Example

Diagnostics

Owner elects to start with bloodwork

Complete Blood Count
Hct 30%
Hgb 8 g/dL
Platelets 400 x 10^3/uL
WBC 7 x 10^3/uL
40% heterophils, 50% lymphocytes, 6% monocytes

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VETERINARY MEDICINE

Case Example

Diagnostics

Owner elects to start with bloodwork

Biochemistry
Creatinine 1.8 mg/dL
Urea 40 mg/dL
Glucose 175 mg/dL
ALT 563 U/L
AST 213 U/L
ALP 114 U/L
CK 700 U/L

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VETERINARY MEDICINE

Case Example

Diagnostics

Owner elects to start with bloodwork

Biochemistry
Creatinine 1.8 mg/dL
Urea 40 mg/dL
Glucose 175 mg/dL
ALT 563 U/L
AST 213 U/L
ALP 114 U/L
CK 700 U/L

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VETERINARY MEDICINE

Case Example

Diagnostics
What is your next recommended step?

Abdominal ultrasound:
Caudate lobe of liver is hypoechoic and lacks blood flow on Doppler

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VETERINARY MEDICINE

Case Example

Treatment
What is your diagnosis and recommended treatment?

Live lobe torsion

Surgery is recommended due to longer MST but medical management with pain medications and supportive care can be considered if client cannot afford surgery

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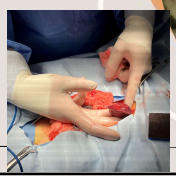
VETERINARY MEDICINE

Case Example

Outcome
Client agrees to surgery
- Because anemia is mild, blood transfusion not performed
- Premedicated with midazolam/hydromorphone IM, induced with midazolam/ketamine IV, intubated, maintained on sevoflurane
- Midline ventral abdominal incision
- Liver lobectomy
- Post-op: lidocaine CRI, meloxicam, hydromorphone, IVF, syringe-feeding until eating
- Discharged 3 d after surgery



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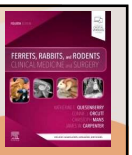

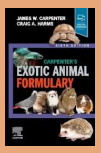

Further references available upon request

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Any Questions?

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Thank You!

Julianne McCready, DVM, DVSc
Zoological Medicine, Oklahoma State University
Julianne.mccready@okstate.edu
vetmed.okstate.edu

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