Food Allergy Tips and Tidbits

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Food hypersensitivity, food intolerance and other adverse reactions to food (ARF) could be the subject of a carrier of study. Food hypersensitivity in the dog and cat can cause a myriad of effects on several different systems of the body, with the integument and digestive system being most commonly affected. This article will hopefully give insight into how ARF will affect the skin in dogs and cats.

Because food hypersensitivy can be the manifestation of a type I, III or IV hypersensitivity reaction, the onset of clinical signs can range from minutes to days after ingestion of the offending allergen. In humans the allergen usually has a molecular weight above 12,000 Daltons, although this has not been confirmed in domestic animals, where the offending allergen may be smaller. A number of studies published over the years have listed the most common food allergens in dogs and cats. Summarizing these reports has led many dermatologists to conclude that animals have the potential or ability to become allergic to any food stuff to which they are exposed, especially proteins. In a 1996 report (Jeffers) from the United States, the most common allergens were beef, chicken, chicken egg, cow milk, wheat, soy and corn. In this report 80% of the dogs reacted to just one or two items although there are reports of dogs allergic to as many as nine food items. Additional published reports will list fish, rice and potato as foods known to cause adverse reactions. The food items most commonly known to cause ARF in cats include chicken, fish and dairy products. A few minutes spent reading ingredient labels of most commercial cat foods will show these are the most common ingredients used in formulating the diets.

One common misconception by clients and many veterinarians is that food allergy is more likely to develop only after a recent diet change. In fact when food allergies develop the offending allergen has often been fed for over two years, and some patients will eat the same protein for many years before the allergy develops. To further complicate the workup of a suspect food allergic patient is the recognition that some patients will have cross reactions between related food ingredients. This phenomenon is well recognized in human medicine as well. Examples include patients allergic to chicken who will not tolerate duck or turkey. Some patients who are allergic to beef will cross-react or show clinical signs when exposed to other ruminants such as lamb or venison. Fortunately not all food allergic patients will have cross reactions, *but some will*, which further complicates the workup of these patients

Food hypersensitivity in dogs

No age or sex predisposition is known to exist regarding the development of food allergy in the dog, but as many as 50% of food allergic patients may exhibit clinical signs at less than a year of age. There may be a higher rate of food allergy in “allergic breeds” such as the Cocker spaniel, Springer spaniel, Labrador retriever, Miniature schnauzer, Shar Pei, West Highland white terrier, Wheaten terrier, German Shepherd, and Golden retriever. Three breeds of dogs this author associates with a higher rate of food allergy are German Shepherds, Rhodesian ridgebacks, and the Shar Pei dog. Clinical signs are variable but nonseasonal pruritus, otitis, and dermatitis are frequently seen in dogs suffering from a food allergy. Sometimes the clinical signs are as simple (or vague) as recurring pyoderma or a nondescript keratinization disorder (seborrhea). Food allergy should always be considered as a cause for any patient with recurring urticaria, and eosinophilic vasculitis has also been associated with ARF.

In general the clinical signs of food allergy are non-seasonal, although they could be episodic if due to sporadic treat administration. It is also possible for the effects of a food allergy to be low or subclinical (below a pruritic threshold) and only with the addition of environmental allergens will the patient flare.

Any dog with a non-seasonal pruritic dermatosis should have food allergy ruled out as a contributing cause of the skin disease. In addition there are several other clues which may raise the index of suspicion that a patient is suffering from a food allergy. One is the pattern of skin disease. Food allergies are known to commonly affect the “ears and rears” of the patient. Another potentially useful clue is the response to corticosteroids. Atopic dermatitis is usually responsive to corticosteroids at anti-inflammatory doses. While some patients with a food allergy will be very steroid responsive, some will not, and when the pruritus is not steroid responsive, food allergy should be considered. Nearly half of this authors patients will have gastrointestinal manifestations of their ARF. Dramatic GI signs include vomiting and diarrhea, but it may be as subtle as flatulence or frequent (more than 2/day) bowel movements. Rarely reported clinical signs of ARF include seizures and respiratory signs including bronchitis, rhinitis and chronic obstructive pulmonary disease, all of which have been recognized by this author.

Feline food allergy

No age or sex predisposition has been reported or recognized in food allergic cats. White (1989) reported the offending allergen had been fed on average over two years. Siamese and Siamese crosses may be a breed predisposed to food hypersensitivity. The classic or hallmark clinical sign for food allergy in the cat is pruritus, especially of the head. Others will manifest as “self induced alopecia”, or any manifestation of the eosinophilic granuloma complex.

Diagnostic tests

The diagnosis of food allergy in the dog and cat remains a challenge. Unfortunately as of 2012 the only method to accurately identify patients which suffer from food allergy is by performing an elimination diet trial for sufficient time while controlling all concurrent allergies and secondary infections. This is easier said than done. Both intradermal allergy testing and serology testing for food allergies remain unreliable with both false positive and false negative reactions occurring.

Three types of diets are available and useful in a veterinary dermatology setting. Novel protein and hydrolyzed protein diets are useful for the diagnosis and long-term management of a food allergic patient. Therapeutic diets are formulated with higher and "balanced" levels of omega 3 &6 fatty acids and are most useful for the atopic patient. They will not necessarily be formulated with novel proteins. Most of the major manufactures of prescription dog food now provide a line of "hypoallergenic" foods. There is no foolproof "works every time" test diet. Choosing the "best" diet to feed a suspected food allergic patient requires careful and detailed questioning of the client regarding previous and current diets, treats, and flavored medications. Once that information is known, the practitioner must choose a diet that 1) consists of proteins to which the patient has not had exposure 2) with minimal chance of cross reactions with previously fed proteins 3) that the patient will eat 4) and that the client is able and willing to feed. Because of all these factors, rabbit, kangaroo, and occasionally fish are the first diet of choice for the majority of our suspected food allergic patients. The clinician should also have confidence the manufacturer of the food has truly kept the food limited to what is stated on the label, and not allowed contamination with other feeds or proteins.

In addition to determining which novel protein is appropriate for the test diet, it is also necessary to counsel the owners on what to avoid feeding. We frequently deal with situations where the owners have fed an appropriate test diet, but continued to feed treats and protein based supplements. Some of our food allergic patients will flare, or continue to exhibit clinical signs simply from beef or pork based additives in chewable medications. Hydrolyzed diets are also available to be fed, with hydrolyzed chicken and soy based foods being the most common. Several published studies have reported the majority of patients fed hydrolyzed diets have improvement in clinical signs, even if they are allergic to the parent protein. Yet other studies show up to 50% of food allergic patients flare or fail to improve on a hydrolyzed diet. In 2010 Olivry summarized all of the various (and sometimes conflicting) articles on the subject and concluded hydrolyzed diets not be used if the patient could potentially be hypersensitive to the parent (non-hydrolyzed) protein. This author prefers novel proteins for the test phase. Occasionally a food allergic cat will refuse to eat novel proteins, and hydrolyzed chicken diets are the second choice.

There is a plethora of over the counter novel proteins which claim to be restricted in their protein sources. The veterinarian and client need to read labels closely to insure they are consistent with the goals of the food trial, or management of the food allergic patient. Because of price and convenience these OTC foods are often preferred by the client. Unfortunately close scrutiny and evaluation has revealed many of the OTC "novel protein diets" contain several ingredients not listed on the label. Raditic et al (2011) published an evaluation of four popular OTC venison diets which were tested for soy, beef and chicken. Three of the four diets contained soy, beef and/or chicken, and the fourth contained rice protein. Continued studies in both the United States and Europe confirm these findings. For this reason using prescription diets from reputable companies with stringent quality control remains the method of choice for determining if a patient is food allergic. Once the food allergic patient is stable one can always "work backwards" and challenge the patient with an OTC novel protein diet and monitor for a flare. Whereas improvement on a diet may require weeks, most dogs flare within days if not hours.

One will find variable recommendations regarding the length of time necessary to see improvement once the patient is placed on the hypoallergenic diet, with some recommending a twelve week diet trial. In this authors experience it is rare for a food allergic patient to not show measurable improvement within 4-6 weeks, therefore six weeks is our normal recommended length. Requiring a client and patient to struggle on for 12 weeks without seeing improvement in clinical signs can cause many owners to lose faith with the entire process, leading to abandonment of the food trial and possibly seeking out a different opinion. It may require more than six weeks for the maximum improvement to be seen, but at least the patient is improving during the process which provides encouragement to continue the trial.

During the food trial it is very important to minimize the other causes of pruritus which will interfere with the ability of the client and veterinarian to determine the success or failure of the food trial. Zealous flea control in flea endemic areas is necessary. Monitoring and treating secondary infections (pyoderma and Malassezia) are also necessary. These infections are often times the reason a food trial is being performed in the first place, so it is not uncommon to treat the patient with appropriate antimicrobial therapy for potentially the first half of the food trial. Further counseling is then needed to insure the medications are not administered in a "treat".

At times a client will desire to utilize a diet cooked at home. In these cases the challenge is to find a novel protein which fits the previously discussed criteria that is available and not cost prohibitive. I typically will utilize white or sweet potato as the carbohydrate. If the patient has not had exposure to fish, I might recommend tilapia as the protein source. We recommend a ratio of one part protein and 2 parts carbohydrate. Since this diet is intended to be used as a test diet and not long-term maintenance, we do not attempt to balance the diet with various micronutrients. If the patient is to be fed a home-cooked diet long-term then we will suggest a resource

such as www.balanceit.com for advice regarding a proper balance of nutrients. There are several new companies providing frozen or freeze dried novel exotic proteins for feeding dogs or cats which may provide alternative options for clients.

One last pitfall for successfully implementing an effective food trial is the "unbelievers" at home whom cannot comprehend the detriment a little snack can have. Small children who drop food and other dogs at home eating different diets can also provide challenges the owner will have to overcome. The cost of the prescription diets can also be an obstacle in performing a food trial. Supplementing the diet with home cooked ingredients which are already allowed (such as potato) can help buffer the cost of the food trial and is preferable to OTC foods. Flavored medications have become an increasingly common challenge to overcome when enforcing a food trial. Many flavored medications contain beef and pork protein. I have observed patients flare from their once monthly flavored heart worm preventative. Glucosamine chondroitin is another potential allergen commonly administered.

It is not uncommon for an atopic dog or cat to have multiple triggers for their disease, with both food and environmental allergens playing a role. The clinician trying to sort out these multiple triggers will also sometimes have to make compromises when developing a comprehensive treatment plan for the pruritic patient. Feeding a large dog such as a Labrador retriever a novel prescription diet long-term may leave nothing else in the budget for control of the environmental triggers. In such cases I will frequently recommend some of the OTC fish based diets in an attempt to find an OTC food that will not trigger the food allergy, and possibly provide some supportive care for the atopic dermatitis due to the omega three fatty acids. This of course assumes the patient is not allergic to fish, and that there are not other protein contaminants in the food but not on the label.

Even though we utilize handouts to help educate clients on the principles of the food trial, we do not rely on them alone. It requires time to properly educate a client on how to perform the food trial. We will schedule a follow up from one of our office staff after a few days of initiating the trial, as well as after 4-6 weeks of starting the trial to schedule a recheck so that progress, or lack thereof, can be assessed.

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Dermatology Emergencies: Yes They Do Exist

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Dermatology "emergencies" can range from irritated or inflamed skin which is disturbing the patients and owners quality of life, to truly life threatening dermatological disorders.

Pruritus/pyotraumatic dermatitis

One of the more common reasons for a patient to be presented on an urgent or critical basis is intense pruritus and/or pyotraumatic dermatitis (aka "hotspot"). Clinically the pruritus is often acute and may progress into secondary Staphylococcal or Malassezia dermatitis due to the self-trauma. Underlying causes of the pruritus are oftentimes flea allergy although mites, atopy and food allergy can also be a cause of the initial pruritus. Clinically these patients are pruritic or even painful with rapidly enlarging areas of erythema, alopecia and exudative dermatitis. Lesions are most common on the trunk, tail base, lateral thigh, neck and face. Lesions on the lateral face are known to be associated with a deeper bacterial folliculitis and furunculosis. Treatment includes finding the underlying cause of the pruritus, aggressive parasite control. It can be helpful to clip/clean lesion with dilute chlorhexidine or dilute betadine although pain control +/- sedation may be needed. Topical antibiotic/steroid products are indicated and usually systemic steroids. Systemic oclacitinib would also be indicated for 7-10 days. If lesions include papules, pustules or thickened skin, or if the lesions is on the lateral face, a 3-4 week course of oral antibiotics are indicated.

Otitis +/- aural hematoma

Otitis most commonly is due to a primary allergic trigger (parasite, food, atopy) and less commonly due to hypothyroidism, keratinization disorders and foreign bodies such as foxtails. Once the pinnae and ear canal are inflamed, they are often complicated by secondary bacterial or Malassezia infection. Factors which perpetuate the otitis include thickening of skin, stenosis of the canal and otitis media. Even though identification and treatment of the secondary infection gets much of the attention when dealing with otitis, it is more important for the emergency clinician to also deal with the inflammation and pain which is present. This usually requires topical and systemic steroids with the dose and duration based on the severity of the inflammation. Control of the secondary infections are always based on cytology (one cannot treat ear disease without a microscope) and not odor, texture of the exudate, or other factors. Ultimately identification and control of the underlying allergic disease will lead to successful prevention of recurring otitis but this may not be the focus of an emergency visit. Corticosteroids are also useful when dealing with an auricular hematoma. Some clinicians advocate immediate surgical intervention of an ear hematoma, but it is also possible in the short-term to drain the hematoma with an 18 or 20 gauge needle attached to an appropriate sized syringe and aspirate the fluid within the hematoma. Surgi-sox® Dogleggs head wrap can be useful in reducing trauma from head shaking and then surgical correction can be performed once the otitis externa is controlled.

Juvenile cellulitis

(aka puppy strangles, juvenile pyoderma, or juvenile sterile granulomatous dermatitis and lymphadenitis) is a granulomatous and pustular disorder of the face, pinnae and submandibular lymph nodes. The cause is uncertain although the favorable response to steroids suggests an immune mediated component, while breed predisposition suggests a heritable component may also be involved. Patients with juvenile cellulitis tend to be young (3 weeks to 6 months) and multiple members of a litter may be affected. Breeds which seem over represented include golden retriever, dachshund, Labrador retriever, Gordon setter, beagle and pointers. Patients present with facial swelling, pustules and papules on the eyelids, lips, muzzle, bridge of the nose and medial pinnae. Patients are frequently febrile, and often have submandibular lymphadenopathy. The lesions can fistulate, drain and produce crust. The diagnosis is based on the clinical features and ruling out other causes of folliculitis including demodicosis, deep pyoderma, dermatophytosis and drug reactions. Cytology of a pustule (or crust) show pyogranulomatous cellular infiltrate with no bacteria. Histopathology helps confirm the diagnosis, but the distinct presentation of this condition often makes histopathology unnecessary after the infectious causes mentioned above have been ruled out. Corticosteroids are essential in the treatment of juvenile cellulitis, with a starting dose of 1-2 mg/kg/day until lesions are inactive. A slow taper over the next 6-12 weeks is then indicated. Relapses are rare unless the prednisone is tapered to quickly. Doxycycline may have some steroid-sparring affects, but keep in mind the age of the patient and potential for staining of the teeth.

Urticaria and angioedema

It is not uncommon for patients to present on an emergency basis with acute swelling of the face. The pathogenesis is thought to be a Type I and orType III hypersensitivity disorder. Clinical signs include erythematous wheals (which disappear on diascopy),

edematous swelling of face and ventral neck, and variable pruritus. An extensive list of triggers should be explored including adverse reactions to foods, drugs, vaccines, insects, intestinal parasitism, skin parasites, infection and atopy. Treatment includes identification of triggering factor if possible, along with antihistamines IM, glucocorticoids IV, IM, SQ, PO and epinephrine in severe cases.

Post-grooming furunculosis

The pathogenesis is thought to be due to short coated breeds being predisposed with mechanical trauma from vigorous grooming. Other causes or in longer-coated breeds being due to contaminated shampoos applied at grooming. Patients typically present 24 to 48 hours post grooming with the dorsal midline being most severely affected. Lesions include marked erythema, induration, pustules (hemorrhagic), papules, furuncles, ulcers and draining tracts. Patients are usually febrile and initially may mimic spinal pain. The diagnosis is based on the history, physical exam and cytology findings showing a marked pyogranulomatous inflammatory response with intercellular rod-shaped bacterial organisms. If rods are seen, a culture for sensitivity testing is indicated. Histopathology reveals a deep pyogranulomatous to suppurative inflammation with folliculitis, furunculosis, panniculitis and cellulitis; bacteria may or may not be seen. Treatment is with systemic antibiotics based on culture, but fluoroquinolones are a good first empirical choice while results are pending. Pain management with Tramadol or NSAIDs may also be indicated.

Sterile pustular erythroderma of miniature schnauzers

(aka superficial suppurative necrolytic dermatitis, Schnauzer syndrome) is a rare cutaneous and visceral disease with an unknown etiology. It can be due to adverse drug reactions, or unusual allergens or immunogens, especially components of shampoos or other topical chemical products, especially "herbal" topical products. Even though usually seen in miniature schnauzers, other breeds have been recognized with similar clinical presentations. Patients present with localized erythematous macules and papules with coalescing edematous plaques with crust. Lesions usually spread rapidly, become painful, and the patients become obviously ill with fever, anorexia. Patients may have hypoalbumenemia and a neutrophilic leukocytosis. The prognosis can be poor and patients can die without aggressive supportive treatment as would be appropriate for a burn patient.

Erythema multiforme

(EM) is considered to be a host specific, cell-mediated hypersensitivity reaction induced by various antigens including drugs, chemicals, infections, neoplasia and even food allergy. Many are idiopathic. Toxic epidermal necrolysis (TEN) is considered to be a more severe manifestation of EM. As the name suggest, EM can present with a variety of cutaneous lesions ranging from erythematous macules to slightly raised papules which spread peripherally and clear centrally. Urticarial plaques, vesicles, bullae, ulcers can occur, and lesions most commonly affect the ventrum, mucocutaneous junctions, pinnae and footpads. With TEN lesions are even more extensive and can include full thickness necrosis of the epidermis. Both can be acute onset and life threatening and the presumptive diagnosis is based on history and physical examination and confirmed with histopathology. Treatment includes identifying and treating the underlying cause if possible. Any suspect drugs should be discontinued if possible. Mild cases may spontaneously resolve within 2-4 weeks but immunosuppressive treatment may be needed for severe or refractory cases. Corticosteroids, cyclosporine and pentoxifylline at immunosuppressive doses are this author's first treatment of choice, but keep in mind severe cases may require supportive therapy including hospitalization. Glucocorticoid use is controversial with TEN and patients should ideally be referred to a facility skilled with the treatment of intensive care.

Necrotizing fasciitis

(aka "flesh eating" infection, Toxic shock syndrome) is a fulminant, rapidly progressive, life threatening infection of fascial and SQ tissues which in dogs is usually caused by Streptococcus canis (Group G streptococcus). Fascial tissue infection may occur if the normal skin barrier is compromised such as with a penetrating wound or blunt trauma. Tissue destruction and extension occurs due to bacterial exotoxins and proteases, resulting in localized erythema, edema, swelling, heat, *marked* pain with subsequent sloughing. A malodorous discharge may develop in the SQ tissue leading to the term "Murky dishwater." The limbs and trunk are most commonly affected and patients are febrile, lethargic and tachycardic. The diagnosis should be suspected based on the clinical presentation combined with cytological findings of pairs or chains of gram positive coccoid bacteria. A positive "finger test" is where the SQ tissue is easily separated from fascia by blunt dissection. Early tissue culture and sensitivity is critical and successful treatment hinges on early and complete surgical debridement. Limb amputation may be required. Medical treatment alone is usually not successful due to poor antibiotic penetration of affected areas and continued production of bacterial exotoxins. It is recommended to start a combination of penicillin, aminoglycoside and clindamycin pending culture results, and also to avoid fluoroquinolones as they may induce bacteriophages encoding superantigen genes thus increasing bacterial virulence. Pain control with opioids is also important for these patients but one should avoid NSAIDS as they may enhance disease progression via neutrophils inhibition. Intensive supportive, nutritional and hemodynamic therapies similar to care for a severe burn patient are essential.

Thermal burn
Superficial burns affecting the epidermis only lead to painful erythematous desquamation which heals in 3-5 days via re-epithelialization. Partial to full thickness burns affects the epidermis and varying degrees of the dermis and sub cutis, resulting in blister, edema, and eschar formation if the entire dermis is involved. Burns can be caused by strong chemicals, electric currents, solar and microwave radiation and heat (fire, boiling liquids, heating pads, dryers). Damage from solar or heat can be hidden by fur and not become evident for a week post injury when necrotic skin appears, thus making history important with any necrotic lesion. Treatment is similar as for toxic epidermal necrolysis.

Vasculitis
An inflammatory disorder of blood vessels which is usually due to immune complex deposition in vessel walls, therefore any antigenic stimulation can trigger vasculitis. The clinical presentation consists of purpura, necrosis, punctate ulcers, alopecia, crusting and erosions most often on the ears, tail tip and footpad. The diagnosis is confirmed with histopathology. Therapy includes finding and treating the underlying cause when possible and immunosuppressive therapy. Pentoxifylline is an important immune modulating drug which is usually indicated with vasculitis.

Pemphigus foliaceus
May present in an emergency setting and the challenge is for the busy emergency clinician to not assume the lesions are due to a bacterial pyoderma since the primary lesion of pemphigus is a superficial pustule, which then leads to secondary crust, scale and alopecia. With generalized skin disease, fever, lethargy, depression, limb edema, lymphadenopathy may occur. Cytology of a pustule can be very helpful in distinguishing pemphigus (with acantholytic keratinocytes seen on cytology) vs pyoderma (which will reveal intercellular coccoid bacteria) but of course the diagnosis is confirmed with histopathology. On an emergency basis, treatment with oral or injectable corticosteroids would be indicated (after the biopsy) but if the diagnosis is confirmed, additional therapy with azathioprine, cyclosporine, or mycophenolate can have significant steroid-sparring affects.

Eosinophilic furunculosis of the face
Seen in dogs and is often suspected to be due to insect or arachnid envenomation although in practice, the cause in most cases remains speculative. Patients present with an acute onset erythematous papular eruption of the bridge of the nose which leads to alopecia, erosions and ulcers, with serous and hemorrhagic crusting. Differential diagnosis would be nasal bacterial furunculosis or pemphigus complex, but cytology should show eosinophils without bacteria or acantholytic keratinocytes. Treatment with systemic corticosteroids over 2-4 weeks usually leads to resolution.

Feline mosquito bite hypersensitivity
An uncommon, seasonal dermatosis in cats that predominantly affects the bridge of the nose, pinnal, and footpad areas. Initially after the bite a focal wheal may develop, which progresses to a popular eruption with serous crusting, alopecia and potentially erosions or ulcers. Black skin seems overly predisposed for unknown reasons, and is obviously seasonal and correlates with mosquito season. Treatment involves keeping the patient inside, especially dawn to dusk and topical and or systemic corticosteroids.

Equine Dermatology: What Triggers an Itch in Trigger- How to Work up and Treat a Pruritic Horse

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Pruritus is the most common manifestation of skin disease in the horse. Pruritus is exhibited in a number of ways including the obvious scratching, rubbing, chewing and biting, but also in more subtle fashion such as head shaking, foot stamping or "irritability". When a clinician begins the work up for a pruritic horse, the history should include questions such as length of time of the skin disease; does the condition appear to be contagious? Seasonal? Recurring? Are multiple horses affected? The most common causes of pruritus in horses include hypersensitivity reactions, bacterial and fungal infections, infestations with mites or lice, and irritation or hypersensitivity reactions caused by biting insects. This lecture will cover only some of the more common causes of pruritus in horses seen by this author.

Cutaneous infections (folliculitis)

Two common infections of the skin include bacterial folliculitis and dermatophytosis which may also involve hair follicles. Many different bacteria are known to infect or colonize the skin, and most infections will stimulate some degree of pruritus, however *Staphylococcus* species accounts for much of the true skin infections seen in horses. Clinically lesions can be localized or widespread and start as a papular to pustular dermatosis which can progress into serous our hemorrhagic crusting lesions. Alopecia is also common and may produce a "moth eaten" appearance to the coat. A Staphylococcal infection may be secondary to other underlying dermatopathies, particularly hypersensitivity reactions. Cytology of lesions (crust or pustules) revealing intracellular coccoid bacteria will confirm the diagnosis. Culture and sensitivity testing is normally only performed if the patient fails to respond to appropriate systemic antibiotics. Unfortunately methicillin resistant Staphylococcal infections are becoming increasingly common around the world in both veterinary and human medicine. At the Veterinary Microbiological Diagnostic Center, the Netherlands, the percentage of methicillin-*resistant Staphylococcus aureus* (MRSA) isolates found in equine clinical samples increased from 0% in 2002 to 37% in 2008. Their study found that nosocomial transmission occurs in equine clinics and that personnel played a role in the transmission. An increased awareness of this epidemic should motivate all veterinary personnel to utilize more complete sanitation practices between handling patients, especially hand sanitation with frequent washing and antiseptic rinses or gels. If a patient with folliculitis is failing to respond to appropriate, empirically chosen antibiotics, then a resistant strain should be suspected and cultures of an intact pustule, or fresh exudate underneath a crust should be obtained. Topical therapy is also useful when treating superficial skin infections. Chlorhexidene shampoos, mupirocin ointment and 0.4% stannous fluoride gel all have efficacy, especially for localized infections, or as adjunctive therapy with systemic antibiotics. The author commonly examines horses with bacterial folliculitis which have been treated with antibiotics for seven to ten days, instead of the necessary 21 days.

Dermatophytosis

Microsporum and Trichophyton are the two most common genus of ringworm in the horse. Clinically lesions are similar to bacterial induces lesions, although the sites affected are most commonly at points of friction or under saddle or tackle. Cytology (trichogram) of infected hairs is difficult to perform, and most patients are diagnosed with Dermatophyte cultures. Sabouraud's agar is required to recover some of dermatophyte species which infect horses, such as *Trichophyton equinum*. Sab-Duet™ (Hardy diagnostics) are ideal culture plates since they contain both Sabouraud's on one side, and a DTM on the other. Others advocate placing 1-2 drops of an injectable multi-B vitamin on the media. Due to the large number of saprophytic mold spores on the coat of horses, cleaning the hair coat prior to sampling is recommended. Wiping the coat clean with alcohol, or even washing the site with a gentle shampoo or detergent is recommended to minimize the numbers of contaminants on the culture. Because many cases spontaneously resolve, therapy may be conservative and limited to topical antifungal products, many of which are available in shampoo, spay, ointment and rinse formulations.

Parasites

One of the most common sources of pruritus in the horse is irritation or allergic reactions to parasites. Common mite infestations include *Chorioptes* which is most commonly found in the distal limbs of horses, especially those with heavily haired fetlocks. *Psoroptes* mites in horses will frequently affect the head/ears and or tail head and cause moderate or severe pruritus at these sites. Chigger mites (*Trombicula*) will affect lower limbs, and the head area of horses which graze grass. In all cases mites are recovered by skin scrapings. Lice (both biting and sucking) are another parasitic cause of pruritus, and can be diagnosed by visualization of eggs (nits) or adults on the skin or hair. The incidence of all these parasites has been reduced with the widespread use of avermectin drugs.

Culicoides can cause dermatitis in any horse simply due to frequent biting (especially ventral midline) resulting in an irritationreaction. When a horse develops a hypersensitivity reaction to Culicoides, a more severe dermatosis will develop. Culicoides feeds mostly at dawn or dusk, and different species prefer to feed on the dorsal vs. ventral midline region of the horse. The flanks and legs are usually spared, which can be a diagnostic clue. Papules and excoriations develop initially which might progress to widespread alopecia or pustules and crust, especially when complicated by a secondary pyoderma. The diagnosis is based on history (time of year associated with Culicoides), physical examination, response to insect control, and ruling out other causes of pruritus, although atopy can potentially mimic insect hypersensitivity. Intradermal testing for Culicoides is sensitive and specific for diagnosing Culicoides hypersensitivity. Ideal therapy includes insect control or insect repellants as well as control of the inflammatory response, usually with glucocorticoids. Treatment of a secondary pyoderma may also be necessary.

Atopy

The most common cause of pruritus in horses at Dermatology for Animals in Arizona is atopic dermatitis. This prevalence may partly be due to a lower parasite burden in the Southwestern United States. Two presentations are recognized, the pruritic horse, and the horse with urticaria (hives) which may or may not be pruritic. After ruling out other causes of pruritus, a tentative diagnosis of atopy should be considered. Other causes of hives include adverse drug reactions, vasculitis, and even folliculitis or pemphigus foliaceous which may mimic urticaria due to the hairs sticking straight out as opposed to lying flat on the skin.

The International Task Force on Atopic Dermatitis developed guidelines in 2010 for the treatment of atopic dermatitis which involve a multifaceted approach including

- Treatment of acute flares
- Attempt to ID and avoid all triggers of flare
- Improve skin & coat hygiene
- Treat ongoing pruritus with drug therapy
- Allergen specific immunotherapy should be offered when feasible

Even though this is directed towards atopic canines, the principles certainly apply to the atopic horse. The diagnosis of atopic dermatitis is not based on any laboratory or skin test but is based on a combination of signalment, history, clinical signs and the ruling out other causes of inflammatory skin. When attempting to effectively help a patient with atopic dermatitis it is necessary to understand the pathogenesis of the disease, and teach the client these basic concepts. Atopic dermatitis is known to be an inherited type 1 hypersensitivity reaction to ***percutaneously absorbed*** antigens. Research is also showing conclusively that epidermal barrier defects contribute to the pathogenesis. Bacterial and yeast infections provide additional antigens or mediators which exacerbate pruritus.

Treatment of acute flares usually requires systemic and possibly topical corticosteroids. Drugs such as antihistamines are often ineffective when dealing with an intense flare. When attempting to indentify and avoid the triggers of the flare, remember that multiple triggers may be present. The atopic horse is likely to be more sensitive or predisposed to developing hypersensitivity reactions to insects, therefore insect control is particularly important. Intradermal skin testing can identify reactions to both airborne allergens as well as insects such as *Culicoides.*

Improvement of skin and coat hygiene is multifaceted yet simple. Frequent baths or simply hosing down the coat on a frequent basis (weather permitting) is useful for removing allergens from the coat and skin. Several products have been developed for dogs which claim to restore intercellular lipids within the epidermis, thus enhancing the barrier function. They include ceramides with fatty acids (Virbac), Phytosphingosine (Solgenol) and EFAs (Dermoscent). Clinical trials are ongoing, but these products make sense if they are in fact able to restore the epidermal barrier, reduce transepidermal water loss, and reduce percutaneous absorption of allergens. For the horse prone to secondary bacterial folliculitis, the use of shampoos containing chlorhexidine can be useful in prevention o f these infections. Many clients (and veterinarians!) have the misconception that frequent baths will cause adverse reactions to the skin such as excessive drying, when in practice this is quite rare. Overall frequent baths are part of the solution, not part of the problem.

The use of allergy specific immunotherapy (ASIT) or desensitization is underutilized in the treatment of equine atopic dermatitis. In our practice, compared to dogs and cats, horses are easily the “best” responders to ASIT. The skin test tend to be easier to interpret since positive reactions can be more dramatic compared to other species. Improvement in clinical signs also tends to be much faster in an atopic horse compared to the other species, with many patients showing improvement within the first few months. Immunotherapy seems equally helpful for both the pruritic horse as is does for the atopic horse with hives. At our practice, the presence of hives is not a contraindication to administration of an allergen injection. For ASIT to be its most effective, three things need to be determined. The proper “recipe” of the allergen vial, the volume injected, and the frequency of the injections.

We rely on intradermal skin testing exclusively when we work up an atopic horse. The contents of the vial are based partially on the skin test results, but other factors must be considered. It is wishful thinking to expect formulating a vial based exclusively on test results will give maximum results. The correlation between results and the seasonality of the patient should “match”. For example a

horse which demonstrates the most clinical signs every fall, then weed pollens should be given a higher priority in the formulation of the extract. Another factor to consider is the likelihood of exposure. This requires the clinician, or whoever is formulating the recipe, to have knowledge of the local flora, their pollinating seasons and the bouncy of the pollens and spores. Consideration should be given regarding the quantity of pollen produced. If the clinician is relying on an outside source (such as a serology company) to formulate vials without vital historical and exposure data, the success of the immunotherapy program may suffer. For these reasons referral to a clinician who is trained and experienced in the diagnosis and management of allergic patients should be offered when available. If this specialized service is not available, then it is likely that serology (blood) testing is the only alternative. In such cases a complete history regarding seasonality of clinical signs, where and when the horse is symptomatic (and when not) should all be available to whoever is formulating the recipe.

The other critical components of ASIT which need to be determined is the injection schedule. Allergy specific immunotherapy is most definitely not a "one size fits all" but the optimal schedule needs to be determined for each individual patient. Normally we utilize a "rush" schedule for our immunotherapy where patients are administered 0.25 ml of concentrated (20,000 pnu/ml) extract weekly, with the volume increasing by 0.25 ml each week until a total volume of 1.0-1.5 ml is administered every 2-4 weeks. Through this process the owners are instructed to watch closely for patterns such as more, or less, pruritus. A horse which flares immediately after 1.0 ml of allergen should have the volume reduced. A patient flaring by the third week after an injection should have the frequency of the injections increased. Balancing this volume and frequency requires good communication and a hands-on approach, but will lead to improved success in the immunotherapy program.

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Allergen-Specific Immunotherapy: One Size Does Not Fit All

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Allergen specific immunotherapy (desensitization or "allergy shots") has been one of the mainstays of care in specialized dermatology practice for years. In the mid 1980s serology (RAST) testing was marketed to veterinarians, and since then numerous companies have developed their own RAST or ELISA tests. Intradermal allergy testing (skin testing) is the traditional test performed by most veterinary dermatologist. The number, purity, and specificity of extracts available for skin testing and immunotherapy have improved over the years. The diagnosis of atopy should be made based on history, clinical presentation and the ruling out of other hypersensitivities such as parasite and food allergy and not based on any type of allergy test.

Allergen specific immunotherapy is most definitely not a "one size fits all" program. If a veterinarian wants to become proficient at administering immunotherapy, she or he should first become familiar with the regional pollen producing plants, when they bloom, how long they bloom, and how prevalent the plant (and allergen) is in the area. An awareness of the prevalence of indoor, potentially year round allergens, such as house and storage mites, mold spores, animal and human dander and insect particles is also necessary. This knowledge will enable the veterinarian to more effectively determine or prioritize what each individual patient should be desensitized to. The first critical step in achieving success with immunotherapy is determining *accurately and completely* what the patient is allergic to. In our practice we utilize intradermal skin testing almost exclusively for defining what an atopic patient is allergic to. We find we get the most specific and sensitive results from intradermal testing. This also allows us to customize the list for which we are testing based on specific location, not just region. Does it really make sense to lump Southern Arizona in the same region as northern Montana when considering what allergens to test for? Intradermal allergy testing is expensive to set up and maintain, and requires practice and skill interpreting results and is therefore mostly performed only in a specialty setting. If intradermal testing is not available, then serology testing must be utilized.

It should be emphasized that the only reason to perform any type of allergy (blood or skin) testing is to follow up with immunotherapy. Once allergy test results are obtained, these results should *always* be critically analyzed to insure that the results are consistent with the patients' pruritus history. This determination will include historical information regarding seasonality. If allergy testing reveals positive reactions only to seasonal pollens in a patient which is pruritic year-round, then something is being missed! Choosing the allergens to be included in the extract is something the veterinarian should *personally* direct based on the specifics of each individual patient. This is where knowledge of the regional allergens is necessary. For the outdoor working dog that is pruritic only in the summer and fall, then positive reactions to grasses and weeds should be present, and they need to be emphasized or prioritized when formulating the extract. For the indoor Chihuahua which sleeps under the covers at night and who is pruritic year round, then indoor allergens such as dander, mold spores, house dust and house mites need a higher priority in the extract recipe. Yet another factor to consider when developing the "correct" mix or recipe is how long particular pollen is present. In our practice Bermuda grass is one of the dominant pollens, and Bermuda will bloom for over six months in our area. Most tree pollens are present for 2-6 weeks. Does it make sense to put equal levels of a tree pollen and Bermuda grass? Or equal levels of house mites and Ash tree pollen in the patient pruritic year round? One should not assume that the allergens in a vial all have to be equal quantity or volume. If Oak is a significant reaction in a dog living in central California who is the most pruritic in spring, why not double (or more) the quantity of Oak pollen compared to some of the other ingredients. Our current skin test panel includes 70 different allergens.

A number of our patients will have significantly strong skin test reactions to over twenty different positive allergens and some will have over 50 significantly positive reactions. In such cases we will often utilize two different vials of allergen to more fully incorporate all the allergens into the immunotherapy program. Another reason to utilize two different vials of allergens is when significant reactions to mold spores occur. Some molds may have proteolytic enzymes which have the potential to degrade pollen proteins when mixed in the same vial. In such cases, placing the molds in a second, separate vial can alleviate this concern.

The volume, concentration, and frequency of the allergen injections are additional variables which will affect the success of the immunotherapy program. At Dermatology for Animals we have utilized a "rush protocol" in over 5,000 patients over 20 years. With this schedule, patients receive therapeutically effective levels of allergen (10,000 pnu) within two weeks. We find patients respond more quickly to this program, which can be important for the suffering patient and impatient owner. Yet each patient will respond differently to immunotherapy so there is no "set in stone" protocol. Determining the most effective volume and frequency of injections requires close observations by the owners and the ability of the clinician to make proper adjustments of the protocol. Finding the minimum effective volume with the maximum duration of effect is our goal when administering immunotherapy. For patients under 20 pounds, we are especially careful as we increase the quantity of protein given, and will usually limit the maximum amount of protein to 10,000 pnu.

Occasionally during the course of immunotherapy, owners will observe a flare of pruritus after exposure to certain allergens such as a walk in the park, or a trip to the mountains. Such observations by the owner can be helpful in "fine tuning" the extract contents. For these patients we will make slight or moderate adjustments in the contents of the extract to specifically address the cause of the flare. For example, when an owner reports the patient flares after going outside and walking on the lawn, increasing the grass content in the extract of that particular grass would be indicated.

Immunotherapy continues to improve partly due to advances in allergen purification as well as isolation of specific allergen isotypes. We also continue to have additional allergens available for testing and treatment. Significant additions in the last several years include Malassezia allergen, human dander and storage mites.

Keep in mind that immunotherapy will never be effective if the wrong diagnosis has been made, or if additional concurrent allergies are present but not identified or treated. We find many of our atopic patients to have a concurrent food allergy or parasite (flea) allergy. It is not uncommon to have to repeat food trials, or reinstitute parasite control if or when immunotherapy has failed to help after an "adequate" amount of time. Many of our patients will respond favorably to the ASIT program within the first 2-5 months of starting injections, yet we recognize the occasional patient which requires over 18 months before improvement is seen. Obviously in such cases it is imperative that the diagnosis be accurate and complete.

Because ASIT requires some time before efficacy is seen, and because there is only partial improvement for some patients receiving ASIT, it is often appropriate to treat an atopic patient with concurrent medication, especially in the induction phase of the immunotherapy program. Fortunately there is no evidence that medications such as corticosteroids or cyclosporine interfere with ASIT. Therefore ASIT is rarely utilized as the single therapy for atopic dermatitis initially. Once the positive effects of ASIT are seen, the concurrent therapies are often reduced and then eliminated.

Management of adverse events or reactions to ASIT is also occasionally necessary. In our practice less than one percent of patients undergoing immunotherapy need to have the program discontinued do to adverse reactions. Potential adverse reactions include pain or swelling at the injection site, lethargy or increased pruritus immediately after an injection. More serious events include urticaria or hives after the injection. Signs of anaphylaxis or collapse are rare but could occur. Owners are instructed to always monitor the patient for at least one hour after an injection is given. If mild adverse events are observed, we simply reduce the volume of the injection to the previous, well tolerated level. If a serious event occurs, this is not an indication to discontinue the program, but closer monitoring is necessary. In these cases we will hospitalize the patient on the day the injection is due, and pretreat with diphenhydramine (2 mg/kg) orally 1-2 hours before the injection is given. We will administer 50% less volume of the quantity which triggered a reaction, and observe the patient for the day before discharging later that afternoon. Once a quantity of allergen is found which is tolerated by the patient we will not exceed that level. It may be necessary to adjust the frequency of the injections if it is determined the effects are "wearing off" before the next injection is due. Our clinical impression is these patients often time do very well with the ASIT program, which is why patients who have adverse events need their program modified, not discontinued.

For many atopic patients, immunotherapy is one of the more safe, cost effective and medically effective options for managing their disease. In general it is easy for most owners to administer. It is an excellent choice in large and or young patients where the long term lower maintenance costs are best realized. It is also an excellent choice for the non-seasonal patient where treatment with corticosteroids or cyclosporin on a long-term basis would have medical or financial drawbacks. Consequently it is not as good a choice for the geriatric patient, or patient with short-term seasonal disease. Immunotherapy does not lend itself to starting and stopping (using as needed) unlike the other medical options.

Below is an example of a one vial and two vial induction schedule which we would use for a patient in our office.

Immunotherapy: Induction schedule

It is very important that all injections be given subcutaneously (SQ) and that they be given on schedule. Side effects are rare but may include hives, difficulty breathing, vomiting and weakness. Animals should be watched closely for 1 to 2 hours after each injection. If any adverse reactions (side effects) occur, they should be treated as a potential emergency. Our office and your regular veterinarian should be notified

immediately. If a reaction does occur, it does not necessarily mean that desensitization must be stopped, although a change in the dose may be required and the next infection should be given under the direct supervision and observation of a veterinarian. Occasionally, a small lump may occur at the site of the injection. Since this is normal and will slowly resolve, it can be ignored unless it is warm or painful to your pet. If the animal develops recurring painful lumps, then our office should be notified.

Please keep allergens refrigerated at all times. Injections are given only once during the week and a new syringe and needle need to be used each time.

Week volume injected date given commentsEEK VOLUME INJECTED DATE GIVEN COMMENTS

1	0.25 cc			
2	0.50 cc			
3	0.75 cc			

4	1.00 cc
5	SKIP
6	1.0 cc
7	SKIP
8	SKIP
9	1.0 cc
10	SKIP
11	SKIP
12	1.0 cc
13	SKIP
14	SKIP
15	SKIP
16	1.0 cc

Booster injections of 1.0 cc are then given every 3-4 weeks although this can vary with each patient.

When you have finished the above schedule, please call for an appointment so that we may reevaluate your pet so that a maintenance program may be started. This usually involves a booster injection every 2 to 6 weeks, depending on the response of your animal. It occasionally requires over 12 months of desensitization before a good response is seen**.**

Immunotherapy: Induction schedule for 2 vial set

It is very important that all injections be given subcutaneously (SQ) and that they be given on schedule. Side effects are rare but may include hives, difficulty breathing, vomiting and weakness. Animals should be watched closely for 1 to 2 hours after each injection. If any adverse reactions (side effects) occur, they should be treated as a potential emergency. Our office and your regular veterinarian should be notified immediately. If a reaction does occur, it does not necessarily mean that desensitization must be stopped, although a change in the dose may be required and the next injection should be given under the direct supervision and observation of a veterinarian.

Occasionally, a small lump may occur at the site of the injection. Since this is normal and will slowly resolve, it can be ignored unless it is warm or painful to your pet. If the animal develops recurring painful lumps, then our office should be notified**.**

Please keep allergens refrigerated at all times LEASE KEEP ALLERGENS REFRIGERATED AT ALL TIMES.

Injections are given only once during the week and a new syringe and needle need to be used each time.

WEEK	VIAL	VOLUME INJECTED	DATE	COMMENTS
1	A & B	0.10 CC EACH		
2	A & B	0.20 CC EACH		
3	A & B	0.40 CC EACH		
4	A	0.60 CC		
6	B	0.60 CC		
8	A	0.80 CC		
10	B	0.80 CC		
12	A	1.00 CC		
14	B	1.00 CC		
16	A	1.00 CC		
18	B	1.00 CC		

Booster injections of 1.00 cc are then given every 2 weeks by alternating between vial A & B although this can vary with each patient.

When you have finished the above schedule, please call for an appointment so that we may reevaluate your pet so that a maintenance program may be started. It occasionally requires over 12 months of desensitization before a good response is seen.

Atopic Dermatitis: Treatment Recommendations of the International Task Force on Atopic Dermatitis

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Atopy or Atopic dermatitis continues to be one of the most common dermatological disorders afflicting both dogs and cats. At our referral dermatology specialty practice, 75% of our patients have atopic dermatitis as one of the final diagnosis. The problem is so common and severe that many drugs have been utilized in an attempt to offer relief to the suffering patient. The challenge for the clinician is to try and find the right balance between all of the therapy options, their cost, efficacy and safety. The disease continues to generate research, with new therapies being developed. The International Task Force on Atopic Dermatitis developed guidelines in 2010 for the treatment of atopic dermatitis which involve a multifaceted approach including

- Treatment of acute flares
- Attempt to ID and avoid all triggers of flare
- Improve skin & coat hygiene
- Treat ongoing pruritus with drug therapy
- Allergen specific immunotherapy should be offered when feasible

The diagnosis of atopic dermatitis is not based on any laboratory or skin test but is based on a combination of signalment, history, clinical signs and the ruling out other causes of inflammatory skin. Obtaining a certain and complete diagnosis for the pruritic patient can be challenging, but is a necessity if efficient and effective care is to be delivered.

When attempting to effectively help a patient with atopic dermatitis it is necessary to understand the pathogenesis of the disease, and teach the client these basic concepts.

- In dogs, atopic dermatitis is known to be an inherited type 1 hypersensitivity reaction to ***percutaneously absorbed*** antigens
- Epidermal barrier defects contribute to the pathogenesis
- Bacterial and yeast infections provide additional antigens which may exacerbate pruritus

I try and simplify options with clients and explain there are four groups of options for the treatment of atopic dermatitis. They include supportive therapy, corticosteroids, cyclosporine and allergen specific immunotherapy. The point of this lecture is how to minimize the corticosteroids and cyclosporine (C&C). Allergen specific immunotherapy is covered in more detail in a separate lecture. These options are frequently used in combination in order to obtain synergistic effects, which is an important concept to teach clients. In order to use less C&C clients must administer more intensive supportive therapy.

Supportive therapy is always a good place to start when treating a “mildly” affected atopic patient and includes antihistamines, essential fatty acids, bathing, restoration of the epidermal barrier, control of secondary infections, and potentially topical anti-inflammatory products.

A number of antihistamines have been utilized to control pruritus in dogs. Good clinical trials with placebo controls show the benefits of reducing pruritus ranging from zero to 30%. Many dermatologists will utilize antihistamines as part of the ongoing maintenance control of atopic dermatitis, but recognize their limited value when treating an acute or intense flare. Antihistamines which we currently recommend at our practice include cetirizine, amitrpytilline, clemastine, diphenhydramine, and chlorpheniramine. Most are available in generic formulation, and are over the counter, which helps keep the cost low. I usually try 2-3 different antihistamines, but expectations need to be realistic in understanding the value of these drugs may be in their steroid sparring effects. Remind owners to avoid formulas which contain decongestants and pain relief products.

There are many published reports regarding efficacy of essential fatty acids (EFAs) for the treatment of atopic dermatitis. Unfortunately many of these studies failed to control, or account for the amount of EFAs in the diet which makes interpretation and comparison of these studies difficult. Most dermatologist support the use of EFAs in the treatment of chronic atopic dermatitis. Despite claims to the contrary, currently it is the position of the Task for on Atopic Dermatitis that there is no evidence of superiority of any particular EFA combination, dosage, ratio or formulation (including enriched diets) to improve skin and coat quality. As with antihistamines, EFAs are not adequate as a single therapy for atopic dermatitis except in mildly affected patients. I recommend minimizing other oils or fats such as olive oil or animal fat to minimize competition for absorption of the EFAs.

Improvement of the epidermal barrier has recently been getting more investigation and implementation. Simply bathing the atopic patients has many benefits including physical removal of antigens, reduction of bacterial and yeast populations, repair of epidermal barrier defects and the anti-pruritic effects of cool water cooling hot inflamed skin.

Despite the widespread belief that frequent baths will dry out the skin, it is this authors belief that a client cannot over bathe an allergic dog. The biggest drawback of frequent baths is the concern of washing away some of the flea control products. In such case recommendation of flea control products which are not washed off are appropriate.

A plethora of OTC and prescription antipruritic shampoos are available with ingredients including oatmeal, corticosteroids, diphenhydramine, pramoxine, lidocaine and coal tar just to name a few. It is the feeling of this author that the higher cost and short-term benefit of these products usually do not justify their use. Instead, at our practice we utilize products with antiseptic and epidermal restoration effects. Knowledge of any and all infections of the skin should influence the choice of antimicrobial shampoo. Chlorhexidene, triclosan with ethyl lactate, or benzoyl peroxide are chosen for most allergic patients prone to recurring pyoderma. If the skin is oily, or the infection is deeper than a superficial folliculitis, ethyl lactate or benzoyl peroxide is chosen since they are more potent "degreasers" and have follicle flushing activity. Shampoos with miconazole or ketoconazole are chosen if the skin is infected only with Malassezia, otherwise a shampoo with multiple ingredients may be needed for a mixed infection of bacteria and yeast. Recently we have utilized a shampoo and spray containing Tris EDTA with a 4% chlorhexidine, particularly when dealing with methicillin resistant Staphylococcal infections of the skin.

Formulations which extend or prolong the antimicrobial effects of the product include "Leave on" lotions/sprays/conditioners. Also the active ingredient can be formulated into "Spherulites™" or "Liposomes" which adhere to the skin and hair with a slow prolonged release

The final "goal" of shampoo therapy is to repair or restore the epidermal barrier. Products marketed for this function include L-Rhamnose and phytosphingosine, both of which also contain chlorhexidine . There are also a number of new topical "pour on" products available which attempt to mimic and replace the endogenous lipid barrier of the epidermis. They include ceramides with fatty acids (Virbac), phytosphingosine (Sogeval) and EFAs (Dermoscent). Clinical trials are ongoing, but these products make sense if they are in fact able to restore the epidermal barrier, reduce transepidermal water loss, and reduce percutaneous absorption of allergens.

Simple management techniques can be employed to reduce overall allergen load on the skin surface. In addition to frequent baths, the coat can be wiped down on a daily (or more often) basis in an attempt to wipe off allergens. Keeping the hair coat short can reduce the "dust mop" affect of a longer coat. Wearing T-shirts and boots or socks can act as a physical barrier to the allergens.

The advantages of the supportive care options outlined above include safety and benefits which are seen relatively quickly, although EFA supplementation may require two months before a benefit is seen. Another benefit is that no specific diagnostic testing is required once the diagnosis of atopic dermatitis has been made. There is no cost for monitoring of blood work, or even examinations if OTC products are used. Drawbacks include rather lower efficacy, moderate (or more) cost, and they are labor intensive.

Another significant therapy option for the control of atopic dermatitis is allergy specific immunotherapy (ASIT) or "desensitization" injections. With the increased "popularity" of drugs such as cyclosporine, it seems that ASIT is considered "only if Atopica fails." It is the opinion of this author and of the International Task Force on Canine Atopic Dermatitis that this is a mistake. For many atopic patients ASIT can become one of the easier, safer, more cost effective therapies. For ASIT to be its most efficacious, several factors should be considered. This subject is covered in more depth in a different lecture.

Other Nontraditional therapies which are frequently promoted for use in treating atopic dogs includes yucca extract, local bee pollen, biotin, herbs such as "Skin-eze" (Tang-Kuei; Articum; Calamus Gum; Salvia; Rehmannia; Forsynthia; Sophora Root; Cicada; Kochia; Schizonepta; Siler; Licorice). This author has utilized many of these products with no success, nor are there any published scientific studies to support their use. If effective, I would be one of the best customers of these products.

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Olivry T, DeBoer DJ, Favrot C et al Treatment of canine atopic dermatitis: 2010 clinical practice guidelines from the International Task Force on Canine Atopic Dermatitis. Veterinary Dermatology 2010; 21: 1-16

Folliculitis:
The Big 3 and How I Treat Them

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As all veterinarians know, the big three causes of follicle infections are demodicosis, dermatophytosis and bacterial pyoderma. It may be surprising to learn that I probably receive more telephone requests for advice for the up to date treatment options regarding demodicosis and dermatophytosis than any other topic. This fact plus the rise in incidence of methicillin resistant Staphylococcus makes this discussion timely.

Demodicosis

Without a doubt the number one telephone call received at Dermatology for Animals (D4A) from veterinarians is how to treat a refractory case of demodicosis. The short answer is usually ivermectin, but there are certainly cases where this is not an appropriate or acceptable therapy. Typically demodex is considered to be either generalized or localized, although the distinction in practice is not always obvious. If a patient, especially one under a year of age presents with just a few small patches of alopecia I will typically attempt topical therapy only. Products such as rotenone or benzoyl peroxide gel can be applied until skin scrapes are negative. Realize the alopecia will persist for a few weeks to months even after the mites are cleared.

If the mite infestation is more severe, with more numerous lesions present, then I will initiate some type of systemic therapy along with supportive topical treatment. Despite the fact amitraz dips are one of the few approved therapies for treatment of generalized demodicosis, I rarely utilize this product. In my *opinion* there are usually safer options for both the dog and the human household members. I usually recommend weekly (or more) bathing with a product designed to have follicle flushing and antibacterial properties. Benzoyl peroxide and ethyl lactate shampoo both are helpful adjunctive therapies for a patient with demodicosis. DermaBenSs™ from Dechra is a nice choice as it contains 2.5% benzoyl peroxide with ceramides which minimize the drying effects of benzoyl peroxide while repairing the epidermal barrier. If treatment includes amitraz dips, then prewashing with a benzoyl peroxide product is again recommended. Most patients with generalized demodicosis require several months minimum before control or "cure" is achieved, so owners need to be educated to expect this.

The majority of patients treated at D4A with generalized demodicosis receive ivermectin orally at a dose ranging from 0.4-0.6 mg/kg daily. This therapy is used because for most patients it is safe, inexpensive and effective. There are well known published list of dog breeds where ivermectin should not be used, or used with caution. The adage "white feet don't treat" while not a very precise screening process, is actually a consideration.

Ideally patients will be screened for a MDR1 gene defect which leads to cytochrome P450 liver enzymes unable to properly metabolize ivermectin. This results in higher blood levels of ivermectin, which may then cross the blood brain barrier and lead to side effects. Gingival swabs or blood may be submitted to the diagnostic lab at Washington State University. Forms and instructions for submission of samples can be downloaded from their website at www.vetmed.wsu.edu/VCPL Owners should still be aware of clinical signs of ivermectin toxicity and we always have owners sign consent forms for its usage. The clinician should also keep all the other drug interactions in mind. Concurrent use of cyclosporine might increase ivermectin blood levels and lead to toxicity in breeds not usually prone to such reactions.

Several options exist for a patient where ivermectin is not or cannot be used. Milbemycin oxime is safe in dogs which might not tolerate ivermectin. The orally given dose is 1.6-3.8 mg/kg and the main drawback of the drug is the expense. Another macrocylic lactone similar to ivermectin, but with perhaps fewer side effects is doramectin. The efficacy appears to be similar to ivermectin, and we have used this drug successfully both in ivermectin "failures" and in patients which did not tolerate ivermectin. However reactions can still occur in ivermectin sensitive breeds. The dose is 0.2 mg/kg given weekly by SQ injections although there are anecdotal reports of giving as much as 0.6 mg/kg weekly, or giving 0.3 mg/kg orally every other day. Another product approved for the treatment of generalize demodicosis contains a combination of metaflumizone and amitraz (Promeris®) and is applied every four weeks. This product is currently off the market although some practitioners may have product in stock. Efficacy in patients with naturally occurring demodicosis was 43% and 65% at three months in patients treated monthly or biweekly, respectively. Side effects included lethargy, temporary hyperglycemia, and an unpleasant odor and texture after application. There have also been many documented cases of a pemphigus foliaceus like drug reactions caused by this product. Finally one study of imidacloprid + moxidectin (Advantage Multi®) showed efficacy at killing demodex mites, especially with off label weekly dosing, although ivermectin at 0.5 mg/kg daily showed superior efficacy. As a final note, both lime sulfur and Selemectin are ineffective for the treatment of canine demodicosis

Dermatophytosis

Although some advocate that treatment of a local dermatophyte lesion, especially in a dog, is self limiting, due to the zoonotic potential of this disease I am usually uncomfortable treating to conservatively. I therefore prefer to treat dermatophytosis in dogs and cats with both topical and systemic therapies. Lyme dip remains one of the most effective and safe topical products available for the treatment of dermatophytosis, but due to the objectionable odor, many clients and veterinarians prefer alternative options. Various "azoles" are available in formulations including cream, shampoo, and leave on conditioner. Chlorhexidine is not effective in the treatment of dermatophytosis. I prefer the lyme dip or a shampoo with miconazole or ketoconazole to avoid simply "chasing the spots" and have owners apply terbinafine (OTC) to local lesions if they are few in number. The systemic options for treating dermatophytosis include ketoconazole, fluconazole, itraconazole, griseofulvin and terbinafine. I never use ketoconazole (to many side effects), or griseofulvin (to toxic *and* to expensive). Generic fluconazole (5-10 mg/kg daily) is inexpensive and many patients have responded favorably. Compared to itraconazole and terbinafine, fluconazole does not reach the same levels in the skin, and now that terbinafine is available in a generic form we have started using this drug more frequently. A dose of 30-40 mg/kg daily is our starting dose, and the pharmacokinetics of this drug suggest that pulse dosing will be effective. Several protocols have been used, and we have seen regiments of "one week on, one week off" succeed. Terbinafine may cause vomiting, diarrhea, or elevation in liver enzymes, so monthly monitoring of liver values is suggested. Itraconazole is also very effective for the treatment of dermatophytosis, but a generic option is unavailable. Itraconazole is frequently compounded from bulk drugs or the proprietary capsules, however, during compounding, inactivation may occur. Itraconazole is insoluble in water and cannot be formulated into aqueous vehicles. Itraconazole may also adsorb to plastic and glassware, decreasing product drug concentrations. For these reasons this author never uses compounded itraconazole. For small patients (especially cats) the brand name itraconazole is available in a liquid formulation, and we use this product frequently at 5-10 mg/kg daily. When multiple pets are in the home, it is wise to culture all in house pets, and segregate those positive from negative. Weekly prophylactic lyme dips or "azole" baths is also recommended for all pets. All positive pets are treated until two negative DTM cultures have been obtained, and we generally culture every four weeks. Since therapy may slow the growth of the dermatophyte, we hold all cultures three weeks before concluding they are negative.

Treatment of the environment is usually indicated as well, especially when multiple pets are involved. Effective but reasonable environmental control is usually the challenge. At a minimum we recommend frequent vacuuming of carpeted areas, and disinfection of hard surfaces with a diluted bleach solution. It is also recommended to discard all grooming instruments (brushes) and cat trees if they are present. In summary the optimum therapy for the treatment of dermatophytosis includes:

- Clipping the hair coat
- Twice weekly topical antifungal therapy
- Concurrent systemic antifungal therapy
- Environmental decontamination
- Fungal culture monitoring every 2–4 weeks until mycological cure

Therapies which have fallen out of favor and shown ineffective for the treatment of dermatophytosis include lufeneron, and dermatophyte vaccines.

Pyoderma

Over the last several years there has been a worldwide increase in cases of multidrug and methicillin resistant *Staphylococcus pseudintermedius* (MRSP) and *S. aureus* (MRSA) infections. While MRSA is the dominant infection in people, it is MRSP that is responsible for most of the drug resistant infections in veterinary patients. Some regions of North America are reporting that as many as 50% of skin infections treated are due to MRSP. The escalating incidence of both MRSA and MRSP are causing some medical and public officials to call for regulation and restriction of the usage of certain antibiotics in veterinary medicine. Veterinarians must become even more judicious in the usage of antibiotics in the future, and should employ some of the basic and reasonable methods to reduce the spread of MRSP and MRSA within their practice and facilities. Fortunately even though the incidence of MRSP has clearly increased, the virulence of these bacteria has not seemed to worsen in our dermatology patients. Much of the pathology that Staphylococcus causes is due to the various toxins these bacteria can produce.

For many of the "milder" forms of pyoderma in the dog, I have become much more of an advocate of topical therapy. Numerous chlorhexidine shampoos, sprays, and leave on conditioners are now available, with strengths from 2%-4% and combined with either Tris-EDTA (TrisChlor 4™ Dechra), or phytosphingosine, or formulated to "stick" to the epidermis and hair for as long as a week after bathing. If the skin is particularly greasy, then benzoyl peroxide is indicated (DermaBenSs™ Dechra). The clinician should utilize these products in all cases of pyoderma. Even dogs which are difficult to bathe can at least be sprayed with these products. Obviously not all clients are able to comply with a vigorous topical regiment, and not all patients will respond to topicals as the sole therapy, but with the rising rate of MRSP it should compel us to try. When antibiotics are necessary, it is more imperative than ever to utilize proper doses and treatment duration. We are not doing our patients, clients or society any favors by utilizing inadequate doses in an attempt to save clients money. Remember "Dead bugs don't mutate." The other issue which many times is overlooked is

investigation of the underlying cause of the pyoderma. Even with successful control of the active infection, if the underlying etiology is not identified and controlled, the patient is susceptible to further infections. There has been a true “paradigm shift” regarding our approach to the use of antibiotics. In previous years, it was “do everything reasonable” to avoid the chronic use of corticosteroids, but now we attempt everything reasonable to avoid the repeated use of antibiotics. Techniques such as “pulse dosing” are no longer utilized for our dermatology patients.

There are several studies to support the hypothesis that the frequent use of fluoroquinolone antibiotics has been one of the factors responsible for the rise in MRSP. Therefore they should be used for cases of pyoderma only when there are no other feasible or effective options. I still prefer the cephalosporins such as cephalexin or cefpodoxime as my first line of antibiotics, although clavulonic acid potentiated amoxicillin, Trimethoprim sulfas, and clindamycin all remain appropriate first line empirical choices. I am now much quicker to recommend a culture if a patient is not responding to an empirically chosen antibiotic. Simply choosing a different antibiotic empirically risks wasting more time and money, especially since most MRSP are resistant to many of the empirically chosen antibiotics. For patients who do have a MRSP infection, there still may be oral antibiotics to which the bacteria are sensitive. My preference in order that I will use is clindamycin, Trimethoprim/sulfa, doxycycline and chloramphenicol only as a last resort. Injectable aminoglycosides are only used in the most serious and refractory cases. Drugs such as vancomycin are not absorbed if given orally, and are used in life-threatening infections in people. Most feel they should not be used in veterinary patients to minimize the risk of this drug loosing efficacy in people.

Alopecia:
What to do when the Thyroid is Normal

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When a patient presents to a veterinarian with the complaint of hair loss, we have had it ingrained in us to investigate the thyroid and cortisol levels. When these tests reveal normal thyroid and adrenal gland function, a second tier of differential diagnosis needs to be considered.

There are normally several phases to the hair cycle. Anagen is when the follicle is in an active growing stage. Catagen is a transition phase between anagen and telogen which is the resting phase. Exogen is the shedding of the hair. Breeds in which anagen is the predominant phase will have minimal shedding but require regular grooming or cutting of the hair. Examples are poodles, Old English sheepdogs, Angora rabbits and humans. Breeds in which telogen is predominant will exhibit continuous or seasonal shedding. Labrador retrievers have continuous shedding while malamutes will be more seasonal with their shedding. Clients and others will use the term “blow the coat” to describe this dramatic shedding.

As with many dermatological abnormalities, the signalment and history can be important when determining the cause of hair loss. Questions regarding age of onset, sex of the patient, reproductive history, the medical history prior to onset of the alopecia are all potentially important.

When examining a patient with alopecia, the clinician should evaluate for the presence or absence of inflammation and look for lesions suggestive of pruritus with hair barbering. Changes in skin or coat color or texture might prove helpful diagnostically. Note the pattern, is the alopecia bilaterally symmetrical suggestive of hormonal or congenital abnormalities, or is there asymmetry or focal or multifocal lesions suggestive of inflammation of the skin or follicle. Lesions such as papules, pustules, crust or scale are also important to note and typically suggest an inflammatory cause to the hair loss, and/or secondary bacterial infection of the follicle.

Approach to hair loss diagnostics

A Trichogram, or hair pluck, is a vastly under-utilized diagnostic tool when evaluating a patient with hair loss. The technique involves plucking a group of hairs with a hemostat and placing the hair on a glass slide which has a drop of oil to hold the hairs in place. The microscope diaphragm should be closed. The hair shaft should be evaluated, is there breakage at the tip suggesting broken or barbered hairs? The presence of melanin clumping should be noted, as well as the shape of the hair bulb and the stage of hair growth. With practice a clinician can identify ectothrix hyphae of dermatophytes, and demodex mites can also be found with trichograms.

Congenital and heritable causes of alopecia

Examples of congenital or heritable alopecia include the well-known alopecic dog breeds such as the Mexican hairless (Xoloitzcuintle), Chinese crested, as well as the lesser-known American Hairless terrier and Inca hairless dogs. Cats with heritable alopecia include the Sphinx, Donskoy, Bramble cat, Dossow and Peterbald. In these breeds, the hairlessness is thought to have an autosomal dominant mode of inheritance, and some individuals may also have features of ectodermal dysplasia or may also exhibit abnormal dentition, glandular formation and/or function.

Black hair follicular dysplasia

An uncommon condition where the alopecia is confined to the black haired portions of the coat. The early clinical appearance may be broken or dull appearing hair which later develops more obvious alopecia and scaling. The condition is thought to be an autosomal recessive trait and susceptible breeds include Bearded collie, Saluki, Border collie, King Charles spaniel, Jack Russell terrier, Gordon setter and Yorkshire terriers. The diagnosis can be supported with a trichogram which reveals clumping of melanin in the hair shaft and confirmed with histopathology showing large clumps of melanin within the melanocytes of the hair matrix as well as atrophic or distorted hair follicles.

Color dilution alopecia

Affects blue, gray, fawn and red coats (aka “dilute coats) with clinical signs occurring between 3-24 months of age. These individuals typically have full hair coats as puppies and young adults. Alopecia is thought to be due to abnormal transfer of pigment into the hair which results in broken hairs and subsequent alopecia. Trichogram and histopathology findings are identical to that of black-haired follicle dysplasia, and no effective therapy exists for either condition.

Other even more uncommon or rare congenital or hereditary causes of alopecia will be shown during the lecture including melanoderma and alopecia in Yorkshire terriers, “Bald thigh syndrome” in greyhounds, and breeds with hair cycle abnormalities leading to alopecia such as Irish water spaniels and Portuguese water dogs.

Immune-mediated alopecia

One of the more common immune-mediated causes of alopecia is sebaceous adenitis. Breeds which are predisposed include the Standard poodle, Samoyed, Akita, Havanese, German shepherd, vizsla and dachshund. Clinically the condition may be generalized and symmetrical, or more focal or multifocal. There is often a change in both the color and texture of the skin and coat, and the clinicians should note the presence of follicular casts. Pruritus is variable. On histopathology the pathologist will see inflammation around sebaceous glands or even more commonly complete absence of these glands. Because the hair loss can be symmetrical, and dramatic in long-coat breeds, the disorder is frequently misdiagnosed as hypothyroidism.

Other rare immune-mediated causes of hair loss will be shown including alopecia areata, alopecia universalis, and canine familial dermatomyositis.

Hypothyroidism

The first test usually called for with symmetrical alopecia is resting thyroid. Thyroid hormone influences cell cycle kinetics of the hair bulb, and low thyroid levels leads to decrease proliferative activity. Thyroid receptors are found on sebocytes, cells of the outer root sheath and dermal papilla. With hypothyroidism the alopecia is a result of slower elongation of the hair shafts (prevention of anagen) and hair cycle arrest. Clinically the hair coat may appear dull and brittle, with *nonpruritic*, *non-inflammator*y and symmetrical truncal alopecia, although alopecia may be first noted in areas of wear or failure to regrow post-clipping. In some breeds such as boxers and Doberman pinschers, hair retention may lead to a "bleached out" appearance. Average age of onset is between 6-10 years of age, and dermatologic changes are seen in approximately 60-80% of cases. Other clinical signs include lethargy, weight gain, mental dullness and myxedematous changes (tragic facial expression). It is important to differentiate between true hypothyroidism and euthyroid sick syndrome, and to keep in mind the drugs that will interfere with thyroid levels when testing. An in depth discussion of thyroid testing is beyond the scope of these notes and lecture.

Hyperadrenocorticism

(Cushing's disease) is the second most common endocrine disorder resulting in alopecia in the dog. In addition to symmetrical alopecia, other cutaneous abnormalities can include thin skin, comedones, hair color changes (bleaching) and hyperpigmentation. Non-dermatologic clinical signs include PU/PD, polyphagia, muscle wasting and pot-belly formation, excessive panting and lethargy. The diagnosis and treatment of Cushing's disease is beyond the scope of this presentation.

Alopecia X

This is yet a different endocrine abnormality resulting in alopecia. The exact etiology is unknown, but thought to be related to imbalance of adrenal gland steroid hormone intermediates such as 17-hydroxyprogesterone. Plush coated breeds are predisposed such as Pomeranians, Alaskan malamutes, Chow chows, Keeshonds, Samoyeds, Siberian huskies. Age of onset can be younger than other endocrinopathies, often between 1-3 years of age. Initially loss of guard hairs results in a dry, dull coat which progresses to hair loss, especially in frictional areas, that becomes more wide-spread. The underlying skin may become scaly or hyperpigmented. The diagnosis is generally one of exclusion. Histopathology will show the classic changes of an endocrinopathy, but may also have features of follicular dysplasia or flame follicles. The sex-hormone stimulation test available at the University of Tennessee can also help rule out other sex-hormone disorders. Since this condition is not known to cause other systemic illness (unlike hypothyroidism or Cushing's disease), conservative therapy is called for. Melatonin and flax seed oil with lignans may cause regrowth in about 40% (caution with diabetics). Mitotane and Trilostain can cause hair growth but have a higher risk of side effects.

Transdermal absorption of topical sex hormones

A growing cause of alopecia in dogs is being recognized due to accidental or unintended, transcutaneous absorption of human topically applied hormone replacement cream. This is often a testosterone cream for males or more commonly a combination cream (progesterone and/or estrogen and/or testosterone) for female application. In our experience the affected dogs are usually smaller (less than 15 kg) and have direct exposure to the human skin where the sex hormone replacement has been applied. The resulting alopecia in dogs is usually "patchy" and hyperpigmentation may also be seen. Other clinic signs have included onset of sexual behavior, enlarged nipples, or estrous like behavior in females. The diagnosis is based on history and the University of Tennessee sex-hormone panel can also confirm abnormal sex hormone levels. It is critical to question owners about exposure to exogenous sex-hormone replacement products in dogs with abnormal blood levels, especially before expensive imaging or invasive exploratory surgeries.

Pattern alopecia

Aka pattern baldness, is a non-inflammatory, non-pruritic, slowly progressive alopecic dermatosis which most commonly affects the convex pinna, periaural areas, ventral trunk and caudal thighs, usually in a bilateral symmetrical pattern. Breeds most commonly affected include Boston terrier, boxer, Chihuahua, dachshund, Italian greyhound, miniature pinscher and whippet. No affected therapy is known, although there are anecdotal reports of melatonin having some efficacy.

Traction alopecia

Can develop after application of a hair clip or rubber band that is too tight, causing disruption of cutaneous blood flow and follicular atrophy. The alopecia is localized, typically on the dorsum of the head.

Flank alopecia

Aka seasonal flank alopecia, cyclic flank alopecia or recurrent flank alopecia is a localized, potentially seasonally recurring, non-inflammatory alopecia which is often accompanied with hyperpigmentation. Some consider this another variation of Alopecia X. It is often bilateral but not necessarily symmetrical. Melatonin and Flax seed oil with lignans is the normal recommended therapy, but this has variable and sometimes poor efficacy.

Post-vaccination panniculitis

Occur most commonly, but not limited to, a rabies vaccination. Lesions are most commonly alopecic patches at or near the injection site, but can be wide spread, and even multiple sites. Alopecia may be noted 2-4 months after an injection and small dogs (under 10 kg) are predisposed. Topical tacrolimus and systemic pentoxifylline are therapeutic options.

Chemotherapy induced hair follicle dystrophy

Is caused by chemotherapeutic agents which affect cell division, resulting in impaired mitotic and metabolic processes in actively growing hair follicles. Hair loss begins 7-10 days following initiation of treatment and is most dramatic within 1-2 months. Breeds with hair follicle in which anagen is the dominant stage (poodles, Old English sheepdogs and terriers) are at increased risk.

Post-clipping alopecia is

A term to describe failure of regrowth within 3 months of clipping. "Plush coated" breeds are at higher risk such as the Alaskan malamute, American eskimo, chow chow, pomeranian, samoyed, Siberian husky and keeshond. Because complete regrowth can occur within a year, it is also speculated these breeds normally have a very slow hair growth rate.

Paraneoplastic alopecia

A rare syndrome which is most commonly associated with pancreatic malignancy. The alopecia is generally acute with rapid onset spreading over the entire body and is accompanied with a characteristic shiny skin and large scale.

Telogen effluvium

Results from a stressful occurrence (pregnancy, shock, drugs and anesthesia) which results in abrupt premature cessation of growth and synchronization of hair follicles into catagen and then telogen. Hair loss typically occurs within 1-3 months of insult a trichogram may help identify large numbers of telogen follicles. The condition will spontaneously resolve.

Allergy Mimickers

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When a clinician is presented with a pruritic patient, it is correct to initially consider, and rule out, the more common hypersensitivity disorders. Atopic dermatitis, adverse food reactions, and parasite hypersensitivities (especially flea allergy dermatitis) are seen on a daily basis. The challenge is to not overlook other dermatological conditions which might cause pruritus. An overview of some of the "allergy mimickers" will be presented with emphasis on specific clinical changes which should alert the clinician to consider these mimickers.

Four common conditions misdiagnosed as allergic skin disease are sebaceous adenitis, folliculitis (specifically demodicosis and dermatophytosis), cutaneous epitheliotropic T cell lymphoma and pemphigus foliaceus

Sebaceous adenitis

(SA) is an inflammatory disease of the sebaceous glands which can lead to their destruction. An inheritance mode is suspected, especially in breeds such as the Standard Poodle. Breeds predisposed for development include the Akita, Standard poodle, Vizsla, Samoyed, German shepherd and Havanese. However SA is seen in many other breeds, as well as mixed breeds.

When sebaceous glands are damaged or destroyed by SA, resulting changes are predictable. Lesions include alopecia (patchy or generalized), scale and dry skin, follicular cast formation, variable amounts of erythema, and nodule or plaque formation in some patients. Occasionally the affected skin and hair will become discolored or hyperpigmented. Bacterial pyoderma is common in these patients as sebum from sebaceous glands is important for both barrier function of the epidermis and for the bactericidal properties.

Sebaceous adenitis is misdiagnosed as allergic skin because these patients can be pruritic, both because of the actual disease, and also because of the concurrent secondary infections. Keys to help distinguish SA from allergic disease is the amount of scale tends to be greater in SA, as well as the alopecia tends to be more dramatic compared to allergic skin. The skin is actually dry (hypohidrosis) where as in most allergic patients there is often *increased* amounts of sebum. Remember that scaly skin is not necessarily dry skin. Because the alopecia can be generalized and bilaterally symmetrical, SA can also be misdiagnosed an endocrine disorder. Finally, the presence of follicular casts are very suggestive of SA and warrants biopsy. Sebaceous adenitis is confirmed with histopathology.

Therapy basically attempts to replace sebum and its function, as well as potentially allow regeneration of sebaceous glands. Supportive care of the skin includes anti-seborrhea baths and rinses. If the shampoo also contains chlorhexidine, antibacterial benefits will be achieved which could reduce the need for systemic antibiotics. New products such as ceramides or phytosphingosine act as the mortar of a brick wall which improves barrier function and improves clinical signs and should be one of the foundations of treatment for an SA patient. Concurrent therapy with Vitamin A (600-1,000 IU/kg daily) and omega 3/6 fatty acid supplementation are also encouraged. Baby oil (or other oils) applied to the skin as a "soak' for 30-60 minutes are labor intensive, but many owners are pleased with the results. The oil is washed off with a gentle shampoo after the soak. Topical humectants such as Propylene glycol, urea, lactic acid, or glycerin can be applied daily or as desired by the owner. Cyclosporin (5-10 mg/kg daily) has been shown to cause improvement of clinical signs and there is documentation that sebaceous glands can regenerate when patients are receiving cyclosporin therapy. In my experience complete control or "cures" are uncommon, and balancing the therapy with clinical signs, patient comfort, and cost is the goal and challenge for the owner and clinician.

Other conditions which mimic allergic skin disease are two causes of folliculitis, namely Demodex and dermatophytosis.

Demodicosis

It is infestation by Demodex mites. In addition to *D. canis*, several additional Demodex mites have been described in the dog and include the large bodied *D. injai* which lives in sebaceous glands and the short-bodied *D. cornei* which is found in the superficial epidermis. Demodex injai is only present in low numbers and is associated more with a greasy or oily dermatitis on the dorsal neck and trunk. Because all species of Demodex can cause inflammation and subsequent pruritus, patients with Demodex are misdiagnosed as suffering from atopic dermatitis or other allergic diseases. The obvious and simple way to prevent this is to "*Always Scrape.*"

Clinical signs of demodicosis include alopecia, erythema, papules, comedone formation and potentially deeper bullae, fistulous tracts and pustules when secondary pyoderma develop. Serous and or hemorrhagic crust can also be present. With the follicular species, a subtle dark "sheen" may develop due to follicular plugging (less dramatic than a comedone). Two locations where demodex mites tend to be overlooked are when present in the feet or ears. When localized in the feet, a pruritic pododermatitis can develop which is frequently misclassified as allergic disease. Demodex mites can cause a dramatic ceruminous otitis and if patchy alopecia is not present elsewhere, the diagnosis is easily overlooked.

Diagnosis is usually made with skin scrapings. Shaving the hair, placing mineral oil on the site to be scraped, and gently squeezing the skin to promote extrusion of the mites to the surface can all enhance recovery of mites. In areas such as interdigital folds where it is difficult to scrape effectively, plucking hair and placing on a slide with mineral oil may yield mites. Swabbing or scraping

ceruminous material from the ear pinnae and placing in mineral oil is also indicated. Numerous treatment options are now available and are beyond the scope of these notes to discuss.

Dermatophytosis

It is the second cause of folliculitis which will occasionally present with significant pruritus and be misdiagnosed. The three species of dermatophytes commonly diagnosed in dogs and cats are *Microsporum canis, M. gypseum and Trichophyton mentagrophytes* with the latter being able to cause the most inflammation and most likely to mimic allergic skin disease.

Clinical signs include patchy or generalized alopecia, erythema and scale. The diagnosis is best made with fungal (DTM) cultures of the skin and hair. The toothbrush technique will increase the sensitivity of the testing. Remember *Trichophyton* species can be slower growing the *Microsporum* which is why we always hold our cultures a minimum of three weeks. *Trichophyton* may form macroconidia in low numbers which can make the correct speciation of the fungus difficult. In such cases if the color of the colony remains light (white, light tan or yellowish) it may be prudent to submit the culture to a commercial laboratory. Because treatment may require many months it is especially prudent the diagnosis be made correctly. Treatment involves both topical and systemic antifungal medications and is beyond the scope of these lecture notes.

Cutaneous epitheliotropic T-cell lymphoma

(CETL) or mycosis fungoides is defined as a spontaneous neoplasm of skin and mucous membranes in which neoplastic T lymphocytes infiltrate the epidermis and adnexal structures. The average age at onset is 9-11 years which should be the first clue when trying to distinguish from allergic disease. Several clinical forms or manifestations will occur in the dog and include an exfoliative erythroderma, plaques and nodules, ulcers or erythema of the oral mucosa and mucocutaneous lesions. An exfoliative erythroderma is defined as erythematous scaly skin along with alopecia and potential hypopigmentation. The pruritus can be variable but up to 50% of the patients with a CETL are pruritic which is why it is misdiagnosed as allergic disease.

Clinically because this is a neoplastic disorder there are often subtle (and not so subtle) physical changes of the skin which should raise the index of suspicion regarding CETL. The size of the scale itself is different with CETL. The scale is larger, even to the point of being described as “sheets” of scale and also appears more “shiny.” Many patients with CETL will exhibit hypopigmentation which would be unusual in allergic disease. Distribution of lesions can also be helpful. In some reports, up to 50% of patients had involvement of the mucosa. Foot pad lesions are not uncommon with CETL whereas in allergic disease the footpad is usually sparred (although interdigital skin is certainly affected with allergic disease). Patients with CETL may also develop plaques or nodules in the skin which would be unusual for allergic disease. Finally with close scrutiny the skin itself (even hypopigmented skin) reveals subtle thickening or swelling suggesting an infiltration process.

Diagnosis is based on histopathology although cytology of lesions will sometimes reveal numerous lymphocytes which raise the index of suspicion for CETL and further mandate biopsies. Biopsies of scale, plaques, hypopigmentation or significantly erythematous lesions are the best for sampling.

There are conflicting reports regarding correlation of chronic inflammatory skin disease with the development of CETL. Santoro et al (Vet Derm 2007) found that atopic dogs were 12 times more likely to develop CETL, however Fontaine et al (Vet Derm 2010) found no association between CETL and previous chronic dermatosis. The long-term prognosis of CETL is poor with an average survival time of six months after the diagnosis is made. Treatment is not known to extend the survival rate, but is known to improve the quality of life. Corticosteroids and lomustine are two of the drugs of choice when treating CETL but consultation with an oncologist is suggested, especially if the clinician is not familiar with the use of lomustine.

Pemphigus foliaceus

(PF) is one of the most common autoimmune skin diseases of dogs and cats and is the final allergy mimicker which can be misdiagnosed as allergic disease. Pemphigus is a bullous autoimmune skin disease that affects the epidermis and hair follicles. In dogs and cats, 5 forms of pemphigus have been recognized: Pemphigus foliaceus, pemphigus erythematosus, panepidermal pustular pemphigus, pemphigus vulgaris, and paraneoplastic pemphigus. Pemphigus foliaceus is the most common form and may be further divided into spontaneous forms and drug induced PF.

In dogs, breeds such as the Akita, Chow Chow, Doberman pincher, schipperke and others are predisposed to the development of spontaneous PF. Some of the drugs implicated in triggering drug-induced PF in humans include the Thiol compounds and sulph-hydryl (-SH) groups. In dogs, some of the drugs more commonly linked to a drug eruption include Trimethoprim/sulfonamides, other antibiotics such as penicillins and cephalosporins, Rifampin, captopril, enalapril, piroxicam, phenylbutazone, and phenobarbital. Doberman pinchers and Labrador retrievers may be predisposed to drug induced pemphigus foliaceus.

Cats can be especially challenging to make a correct diagnosis if pemphigus foliaceus. Pustules are not always as obvious or as stable (they quickly dry into crust). Crust on the dorsal nasal area, pinnae, digits (paronychia) and nipples or areola area should always prompt the clinician to consider PF and perform appropriate diagnostic tests to confirm or rule out this possibility.

The hallmark lesion of PF is a pustule which may be larger (bullous) and not necessarily centered around hair follicles. Because pruritus can also be present, these patients are frequently "assumed" to be allergic with a secondary pyoderma. If treated with anti-inflammatory doses of corticosteroids the disease can be partially subdued but not ideally controlled due to insufficient dose. The "classic" presentation of PF is for pustules to develop on the nasal planum, as well as the nasal bridge, pinnae, and then become generalized from there. When patients do not have the facial distribution of lesions, the disease is more likely to be overlooked or missed. The development of pustules can wax and wane (or "come in waves") and concurrent pruritus can be variable but may be intense. Affected patients may also be anorexic, febrile, lethargic, and may present with lameness if the footpads are affected.

The diagnosis is based on microscopic evidence. Cytology is helpful in distinguishing PF from a superficial pyoderma. The presence of acantholytic cells and absence of bacteria from cytology samples can help raise the index of suspicion regarding PF but confirmation should be based on histopathology of an intact pustule. If pustules are not present for sampling, then biopsy of crust can be diagnostic, but care should be taken to leave the crust attached to the underlying epidermis.

When treating a patient with PF the primary goal is to balance the drugs with their efficacy, cost, and tolerance (side effects) by the patient. The goal is not necessarily to prevent every pustule from forming. Corticosteroids are the mainstay of therapy for PF, but better control of the disease can be achieved when multiple different drugs are used, and it is possible to see synergistic effects between the drugs. Azathioprine and cyclosporine are two systemic drugs often combined with the steroid. Once control is achieved, the clinician should start to reduce the medication, and this will partially be based on any side effects from the drugs being used. Regular monitoring of a CBC and chemistry panel will be necessary. Most patients will start to improve and allow a reduction in dose after 2-4 weeks of initial therapy. Gentle shampoo therapy may be useful in crust removal, but caution owners to avoid intensive scrubbing of the skin.

The prognosis is variable, but most cases with PF respond reasonably well to therapy, especially when multiple therapies are utilized so that the corticosteroids can be minimized. Patients should be rechecked at least two times/year and monitoring parameters include physical exam, clinical signs, secondary skin infections, CBC, chemistry panel, urinalysis, urine culture and sensitivity. Long-term treatment is usually required, however some patients may remain in remission and discontinuing immunosuppressive therapy is a possibility. Long-term immunosuppressive therapy may lead to recurrent pyoderma, demodicosis, or dermatophytosis, which are more reasons to try and find the minimal amount of drug therapy necessary for acceptable control of the disease.

Guidelines for Diagnosing and Treating Superficial Bacterial Folliculitis

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Over the last several years there has been a worldwide increase in cases of multidrug and meticillin resistant *Staphylococcus pseudintermedius* (MRSP) *Staphylococcus schleiferi* (MRSS) and *S. aureus* (MRSA) infections. While MRSA is the dominant infection in people, it is MRSP and MRSS that is responsible for most of the drug resistant infections in veterinary patients. Some regions of North America are reporting that as many as 50% of skin infections treated are due to MRSP or MRSS. The escalating incidence of both MRSA and MRSP are causing some medical and public officials to call for regulation and restriction of the usage of certain antibiotics in veterinary medicine. Veterinarians must become even more judicious in the usage of antibiotics in the future, and should utilize basic and reasonable methods of reducing the spread of meticillin resistant Staphylococcus (MRS) within their practice and facilities.

Guidelines for the diagnosis and antimicrobial therapy of canine superficial bacterial folliculitis was developed and published by the International Society for Companion Animal Infectious Diseases (ISCAID) . The working group which developed the guidelines was chaired by Dr. Scott Weese and included veterinary dermatologist, microbiologist and pharmacologist. The guidelines were published in Veterinary Dermatology in 2014.

Fortunately even though the incidence of MRS has clearly increased, the virulence of these bacteria has not seemed to worsen in our dermatology patients. Much of the pathology that Staphylococcus causes is due to the various toxins these bacteria can produce. The toxins that cause disease with sensational headlines such as “flesh eating” disease are still fortunately rare even in our referral dermatology practice. It is vital veterinarians remember this when they are making treatment recommendations.

Resistance to meticillin is due to a mecA gene, which is present in both S. pseudintermedius and S. aureus. The mecA gene encodes for production of an altered penicillin binding protein (PBP2a or PBP2’) that has a low affinity for all beta-lactam antimicrobials such as the penicillins and cephalosporins. Therefore the bacteria are able to produce a normal cell wall despite the presence of these antibiotics.

Phylogenetic analysis of members of the Staphylococcus intermedius group (SIG) has revealed the existence of three closely related species (*S. intermedius, S. pseudintermedius* and *S. delphini*), and S. pseudintermedius turned out to be commonly misidentified as S. intermedius in the past.

For many of the “milder” and superficial forms of pyoderma in the dog, the guidelines and myself have become much more of an advocate of topical therapy. Three agents are commonly used by veterinary dermatologist include chlorhexidine shampoos, sprays, and leave on conditioners are now available, with strengths from 2%-4% and combined with either Tris-EDTA, or phytosphingosine, or formulated to “stick” to the epidermis and hair for as long as a week after bathing. If the skin is particularly greasy, then benzoyl peroxide is indicated. The clinician should utilize these products in all cases of pyoderma. Even dogs which are difficult to bathe can at least be sprayed with these products. Another topical product which is being used by some veterinary dermatologist is bleach, diluted 1:30 with water. Diluted bleach is unstable and should be mixed fresh each time it is applied. We will have owners sponge or spray on directly to affected skin, and it is surprisingly well tolerated. Mupirocin is a topical antibacterial agent that in humans is used both for the treatment of skin infections and for the suppression or elimination of nasal carriage of *Staphylococcus aureus*, including meticillin-resistant *S. aureus.* In veterinary patients it is ideal for the treatment of localized or focal lesions, and may be used when just a few lesions are present. Resistance to mupirocin is being documented in human medicine, and unfortunately sensitivity testing is not routinely available for our patients. Obviously not all clients are able to comply with a vigorous topical regiment, and not all patients will respond to topicals as the sole therapy, but with the rising rate of MRS we should be compelled to recommend more topical therapies.

The guidelines of the working group recommend a 3 tier classification when systemic antimicrobial drugs (AMDs) are necessary. The 1st tier AMDs are the first choice for empirical therapy, when no risk factors for resistance are present. Possibilities include clindamycin on lincomycin, first generation cephalosporins, amoxicillin-clavulanate, and trimethoprim and ormetoprim potentiated sulfonamides. 2nd tier AMDs are recommended when 1st tier choices and topicals are not appropriate or tolerated and should be based on culture and sensitivity. These drugs include doxycycline, minocycline and chloramphenicol. 3rd generation cephalosporins such as cefovecin and cefpodoxime require special consideration. Neither veterinary dermatologist nor the Antimicrobial Guidelines Working Group of the ISCAID could agree on 1st vs 2nd tier classification of these drugs. Fluoroquinolones should be considered a second tier group only when based on culture, and only when no other options exist. Other 2nd-tier options include aminoglycosides and rifampin, but do to their potential for toxicity, the recommendation was to refer prior to usage of these drugs.

The use of 3rd tier AMDs (linezolid, teicoplanin, vancomycin) is strongly discouraged, their use should be reserved for the treatment of MRSA in humans.

Prevention of superficial bacterial folliculitis

When antibiotics are necessary, it is more imperative than ever to utilize proper doses and treatment duration. We are not doing our patients, clients or society any favors by utilizing inadequate doses in an attempt to save clients' money. Remember the adage "Dead bugs don't mutate." Despite these recommendations, we continue to see patients with a pyoderma treated for less than the recommended three weeks for superficial infections and four weeks plus for the deeper infections. It has become imperative to educate owners if a positive response is not seen to an empirically chosen antibiotic, then a culture for sensitivity testing should be obtained before simply prolonging the use of an ineffective drug.

The other issue which many times is overlooked is investigation and treatment of the underlying cause of the pyoderma. Even with successful control of the active infection, if the underlying etiology is not identified and controlled, the patient is susceptible to further infections. The majority of the patients seen with recurring pyoderma suffer from an underlying allergy, or on occasion an endocrinopathy. There has been a true "paradigm shift" regarding our approach to the use of antibiotics. In previous years, it was "do everything reasonable" to avoid the chronic use of corticosteroids, but now we attempt everything reasonable to avoid the repeated use of antibiotics. Techniques such as "pulse dosing" of antibiotics to reduce recurrence of pyodermas are no longer utilized for our dermatology patients. There are some patients where the underlying cause of the pyoderma cannot be ascertained. Even more commonly we may know the patient is atopic but skin infections continue to recur despite our best attempts at treatment of the atopy. In such cases we have been quicker to recommend Staphage Lysate (SPL) ® injections. Staphage Lysate is useful for preventing new infections, not necessarily in treating an active infection. For a patient with recurring pyoderma, we will start SPL injections when we initiate antibiotic therapy, and then continue SPL injections on a weekly basis while monitoring for a relapse. It is still more effective to identify and deal with the underlying allergy more directly such as allergy specific immunotherapy for the atopic patient, and diet restriction for the food allergic patient, but SPL does offer an additional option when control of the underlying allergy is not effective.

Besides exposure to antibiotics, especially fluoroquinolones, the other notable risk factor for our patients acquiring a MRSP infection is veterinary visits which require hospitalization, especially surgery. Because of this, recommendations for prevention and control of bacterial resistance have been developed. Recommendations by the Canadian Committee on Antibiotic Resistance (2008) Infection Prevention and Control Best Practices for Small Animal Veterinary Clinics are available on the web at www.wormsandgermsblog.com and give more in-depth guidance for veterinary clinic and hospital policies. The highlights of these recommendations are as follows:

Summary of infection prevention and control best practices for small animal veterinary clinics

1. Infection prevention and control strategies are designed to protect patients, owners, veterinary personnel and the community. All veterinary personnel should play an active role in protecting every person and animal associated with the veterinary clinic.
2. Every veterinary clinic, regardless of type or size, should have a formal infection control program, a written infection control manual, and an infection control practitioner (ICP) to coordinate the program.
3. Some form of surveillance (either passive or active) should be practiced by all veterinary facilities. The keys to passive surveillance are to centralize the available data, and to have a designated ICP who compiles and evaluates the data on a regular basis.
4. Routine Practices that are critical to infectious disease prevention and control include:
    a. Hand hygiene,
    b. Risk reduction strategies, particularly those related to:
        i. Use of personal protective equipment (PPE)
        ii. Cleaning and disinfection
        iii. Laundry
        iv. Waste management
5. All **surgical procedures** cause breaks in the normal defensive barriers of the skin or mucous membranes, and therefore carry an inherent risk of surgical site infection (SSI). Good general infection control practices (e.g. hand hygiene, cleaning and disinfection) are important for prevention of SSIs, but there are also specific infection control measures pertaining to surgery that should be considered.
6. Every veterinary clinic should have an isolation area for caring for and housing animals with potentially contagious infectious diseases.
7. Proper wound care is critical to preventing transmission of bacteria, particularly multidrug-resistant pathogens, between animals, personnel and the environment.
8. Animals from shelters and similar facilities should be considered high risk from an infectious disease standpoint and managed appropriately to prevent transmission of disease.

9. Safety of personnel and animal owners should always be a priority. Personnel should take all necessary precautions to prevent animal-related injuries (e.g. bites, scratches), and all bite wounds should be taken seriously. Proper sharps handling practices should be emphasized to reduce the risk of needle-stick injuries.
10. Education of personnel and clients about zoonotic and infectious disease risks and prevention is crucial.

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DOI: 10.1111/vde.12118

Useful Websites

www.wormsandgermsblog.com

www.cdc.gov

Donkey, Draft Horse, and Mule Practice: Overview

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Mules are the offspring of a male donkey (Jack or Jackass) and a female horse (mare). Their size, shape and use are often determined by breed characteristics of both the sire and dam. Thus, mules can come in all statures, colors, and types of conformations, etc. They once were used primarily as riding, packing and/or working animals. Today, mules are used for the previously described purposes, as well as for guards (eg small ruminants), shows, recreation, and pets. The female mule is traditionally referred to as a female, mare mule, Molly or Molly mule, whereas the male mule is traditionally referred to as a male, gelded/stud mule or John mule. Mules are considered more sure-footed, patient, hardier, and slower than horses, and less obstinate than donkeys. As donkeys have 62 chromosomes and horses have 64, the mule hybrids are rarely fertile. The cross between a stallion and a Jenny is a Hinny, which tend to be more donkey-like and much less common than mules

There are approximately 30 breeds of draft or draft horses found in the world today. These horses (1400 -2600 lbs) are utilized in farming and logging industries, blood/plasma donation, biological and pharmaceutical production, advertising campaigns, as carriage horses, show horses and pets. Of the most popular breeds of draft horses used in the United States, the Belgians, Clydesdales, Percherons, and Shires all originated in Western Europe. These breeds were selected for their overall tall stature, heavy bone/frame structure, muscular hindquarters and patience in order to haul large loads. Traditionally, these working animals are thought to have a similar nutrient metabolism as pony breeds.

Donkeys or asses (Equus africanus asinus or Equus asinus) traditionally have also been considered working animals. In North America, donkeys or "burros" are used for work, show, cart and/or carriage pulling, competitive riding, drug smuggling, as guard animals, training animals and pets. There are 15 to 20 breeds of donkeys, including miniatures, standards, large standards, and mammoth stock, which vary greatly in size (32-62 in). The female is commonly referred to as a Jenny or Jennet, and the intact male is commonly called a Jack or Jackass. These animals characteristically have longer ears and make loud vocal noises ("bray"), as ompared to horses. quality.

Geriatric care

Whenever presented with the geriatric Draft horse/Donkey/Mule, a complete physical examination, including but not limited to a thorough oral, lamness/orthopedic/ophthalmic, skin, etc examination, should be performed. Although ill health and disease may exist, the practice of geriatric medicine in most instances should emphasize: 1) dentistry, 2) medical maladies, 3) arthritic conditions, 4) dietary modification to accommodate existing problems, and 5) general health maintenance/husbandry. As behavior, competition for feed, arthritis, failing eye sight may decrease feed intake in the geriatric, the clinician should help the owner maintain adequate feeding space, safe feeding areas, and that water supplies, mineral container/feeders and feed bunks are designed for adequate nutrient intake.

On the initial visit, blood should be collected for a complete blood count and serum biochemistry panel in order to help identify medical or metabolic conditions that may be present. Aging Draft Horse/Donkey/Mule nutrition may be similar to that of young growing horses, as more digestible protein, energy, and mineral/vitamins may be required.

Supplemental reading & references

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Donkey, Draft Horse, and Mule Practice: Herd Health

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Parasite control

Small strongyles (cyathosomes, cyathostomins) are the most significant pathogenic internal parasite of Draft Horses, Donkeys, and Mules in North America. Small strongyle resistance to anthelmintics by cyasthastomes has occurred due the over and inappropriate use of anthelmintics. When a horse is administered an anthelmintic, it is unlikely that it will be 100% efficacious, and the parasites not killed by the deworming agent survive and breed. This results in the modification to the parasite gene pool within that horse, as well as on the farm. The more frequently the animal is dewormed with a particular class of anthelmintic, the greater potential for survival of an increased number of parasites that are not killed by that particular agent, resulting in a genetic shift or selection for parasites not killed by the particular class of anthelmintic occurs. On a farm, if all animals are dewormed frequently then parasite resistance in all or most horses on a particular farm may occur. Resistance has now been documented to all classes of anthelmintics by small strongles in north American horse populations.

Parasites should be controlled when they negatively affect the horses health. But the formulas of the past (monthly or bimonthly administration of anthelmintics), have contributed to the level of anthelmintic resistance that now threatens modern horse production.

In order to help reduce the continued onset of anthelmintic resistance, programs which reduce the frequentcy of deworming or using anthelmintics only on a portion of the horse population on any given farm or facility.

By performing fecal egg counts (McMasters), horse/donkey/mules can usually be placed into one of three categories: high (>500 eggs), moderate (200-500 eggs), and low (<200 eggs). By identifying low shedders and reducing the number of treatments in this group, another source of refugia may be created. The clinician can then apply a more aggressive parasite control program on horse/donkey/mules in the higher shedding categories. Treating adult horse/donkey/mules in this low egg shedding group minimally should result in effective parasite control and allowing for a source of refugia on the farm. Conversely, treating horse/donkey/mules in the high egg count class (>500 epg) more aggressively should result in effective parasite control and reduced pasture contamination.

Good practices for manure and other waste disposal, in order to eliminate breeding habitats is the most effective method of fly control. Removing manure twice weekly, avoiding straw as a stall bedding material, removal of spilled feedstuffs, using tightly closed garbage containers, regularly cleaning all garbage cans or dumpsters, and placing garbage/manure holding sites or containers as far as practical from the stable or horse/donkey/mules facilities are all critical points in reducing fly breeding sites.

Waste materials can be disposed of by proper composting, spreading over pastures in a manner that allows drying, or by hauling away, burying, or storing in properly maintained lagoons. Compost piles should be properly managed to allow heat production and/or covered with a fly barrier material such as plastic. Cropland, hay fields, and non-horse/donkey/mules grazing areas should be used for spreading manure. Mowing or removing plants in these areas may reduce fly activity will reduce fly 'harborage areas'. Fly traps or baits may be of value in reducing numbers of adult house flies, and to a lesser extent, face flies, but work poorly for stable fly control. Insecticidal baits should be kept away from domestic animals and children. All fly traps should be cleaned 1-2 times per week. Stabling horse/donkey/mules during peak fly activity may also be of benefit if barns or stalls have fans and/or are equipped with fly proof screens.

Application of insecticides to horse/donkey/mules has minimal long term fly control value. Sprays or whips applied to the abdomen and legs of horse/donkey/mules can help reduce stable fly bites, and can be very effective in reducing face fly feeding when applied around the eyes nose, and mouth.

Residual insecticides used in fly resting areas (ceiling beams, and also to cracks or crevices), tends to be more effective than spraying the animals. Spraying should begin in the early spring, and should be repeated as necessary.

Mange mites are best controlled by clipping and/or shaving the long hair or 'feathers' on the pasterns of affected horse/donkey/mules. Removing this hair will enhance the contac ttime for mite controlling chemicals time and further improve the efficacy of mite control chemicals. Cleaning of the affected areas with keratolytic shampoos will aid in mite removal and the control of secondary fungal or bacterial infections, and can help minimize the clinical signs or symptoms.

Feeding

These large work animals are thought to have a similar nutrient metabolism as pony breeds and are usually fed as if they require slightly less feed per kg of body weight than do light breed horses. The NRC suggests that idle, mature, healthy draft horses could subsist on 30.3kcal of digestible energy (DE)/kg of body weight, which is slightly lower than recommendations for light horse breeds. The mature draft horse should be fed a minimum of 1.5% of their body weight in roughage daily. The draft breeds should be fed by using many of the general guidelines applicable to lighter breeds of horses. Good quality grass-legume mixed pastures or hay will

usually suffice for maintenance animals, while feeding to maintain a body condition score of 5-6 (BCS 1-9 scale). Supplemental feeds should be added in order to help maintain optimal BCS.

The amount of fed energy required will depend on the type of work, duration of the work, and weight of loads or amount of force required to do the work. Draft horses may be prone to Polysaccharide Storage Myopathy, Exertional Rhabdomyolysis, metabolic Syndrome, and other diet related conditions. Therefore energy supplementation should be done very

The large size of draft horses and amounts of feedstuffs required present many management problems.. The author has observed a more feed related founder and a more difficult time handling heat stress in obese draft horses as compared to lighter breeds

The donkeys or asses (Equus africanus asinus or Equus asinus) appear to readily adapt to new environments and feedstuffs. They are commonly fed less than horses on a body mass basis., They are selective browsers, and appear to consume higher quality portions of available forages., Donkeys appear to have a lower dry matter intake than do ponies, on poor quality forage diets., Dry matter intakes of between 1.75 and 2.25 % of body weight of moderate to good quality forage will support maintenance in mature donkeys. When offered moderate to good quality forages, donkeys will readily adapt to consume complete diets.

Donkeys may have higher apparent digestibility's for dietary DM and fiber portions of diets than ponies and horses particularly, when fed poor quality forages, which may be due to a greater gut retention time, as compared to ponies or horses.

Donkeys also appear to be efficient in dietary protein utilization. Dietary programs that are applicable to light breed horses should meet requirements for donkey, with respect to protein intake.

Donkeys fed to obesity will develop fat deposits on their neck, back and sides; and like ponies are prone to hyperlipemia. A body condition scoring systems for donkeys have been described.by Pearson and by Vall; and are: is a 1 to 4 scale from emaciate, (score of 1) to good (score of 4). Diets useful and practical for horses can usually easily be applied to donkeys, as long as obesity is avoided. Enough energy fed to maintain fit, non obese animals, enough dietary protein offered at a rate of 6 and10% of the diet for maintenance, free access to fresh clean water and a good quality mineral mixture designed for horses.

Mules are commonly fed less than horses on a body mass basis, yet more than similar sized donkey. Feeding practices should be designed to take this in to account that genetically, the mule is more closely related to the horse. Like donkeys, obesity can be a major problem when feeding mules, thus caution should be exercised when offering high energy supplements. Energy, protein, mineral requirements are similar to that of the horse, but mules may be more efficient.

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Donkey, Draft Horse, and Mule Practice: Reproduction

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Draft horse reproduction is quite similar to light horse breeds. There appears to be a greater incidence of dystocia and twin births, however the clinician with ability in routine equine theriogenology can easily practice this art and science to the larger, draft horses. There are approximately 30 breeds of draft or draft horses found in the world today. These horses (1400 -2600 lbs) are utilized in farming and logging industries, blood/plasma donation, biological and pharmaceutical production, advertising campaigns, as carriage horses, show horses and pets. Of the most popular breeds of draft horses used in the United States, the Belgians, Clydesdales, Percherons, and Shires all originated in Western Europe. The draft breeds should be fed by using many of the general guidelines applicable to lighter breeds of horses. Good quality grass-legume mixed pastures or hay will usually suffice for maintenance animals, while feeding to maintain a body condition score of 5-6 (BCS 1-9 scale). Supplemental feeds should be added in order to help maintain optimal BCS. The amount of fed energy required will depend on the type of work, duration of the work, and weight of loads or amount of force required to do the work

Donkey reproduction is similar to that horse reproductive medicine, with some noted differences. In North America, donkeys or “burros” are used for work, show, cart and/or carriage pulling, competitive riding, drug smuggling, as guard animals, training animals and pets. There are 15 to 20 breeds of donkeys, including miniatures, standards, large standards, and mammoth stock, which vary greatly in size (32-62 in). The female is commonly referred to as a Jenny or Jennet, and the intact male is commonly called a Jack or Jackass The jenny reaches puberty in 1-2 years, which appears to be associated with body size. This author prefers to breed females after they have are 60-70% of their mature body weight, with a body condition score of no more than 6-7 (1-9 scale). The jennies reproductive life will rarely exceed 16-18 years. Donkeys display less seasonality than that of the horse. The jenny's cervix is longer than the mare’s, with a smaller diameter, and protrudes into the vagina. The cervix of older females undergoes less estral modified softening than young jennies. Because of cervical size, artificial insemination appears more difficult and the incidence of post-dystocia cervical adhesions are greater than that seen in horses. The estrous cycle ranges from 20 to 40 days, but is usually 23-30 days. Estrus behavior has been characterized by mouth opening and closing or chomping with salivary dribbling, (occasionally with the neck extended with ears back), winking, urinating, tail rising and lowering the hind quarters. Diestrual behavior includes running away and/or trying the kick the jack, and clamping the tail. Estrus averages between 6 and 9 days, with ovulation 5-7 days after the onset of estrus. Approximately 80% of jennies will ovulate within a 48 hour period prior to the end of estrus with a 25-35 mm or greater follicle. Follicles > 25-30 mm should be considered potentially ovulatory. Multiple ovulations is of higher incidence in mammoth jennies. If natural breeding systems are used, the jenny should be mated the second day of estrus, and then at 48 hour intervals until the end of "standing heat.

Pregnancy diagnosis is very similar to the mare, both from a palpation (when possible) and ultrasonographic standpoint. The embryonic vesicle may be detected as early as day 9 to 11 post-ovulation. Embryo mobility in the jenny occurs up until day 13 to day 18 post-ovulation.

The author prefers to vaccinate on the 3rd, 5th, 7th, and 9th months of gestation for EHV type 1 (Pnheumnobort K) and one month prepartum for tetanus, EEE, WEE, WNV, and influenza. In the pregnant jenny, secondary corpora lutea are formed from day 39 to 46, and hormonal profiles are similar to mares. Gestational length has been reported to be 372 to 374 days. Prepartum behavior is similar to a horse in that the jenny may become restless, have engorged teats, and a lengthened vulva. She will usually lay down to deliver the foal. Foal heat usually occurs between 5 and 13 days postpartum. Metritis, endometritis, retained fetal membranes, etc. are less common than in the horse. Vaginal prolapse in a 'molly' mule is not an uncommon medical condition. This author performs an epidural, carefully replaces the vagina, and places a modified Buhner or deep Caslick’s suture to close to the vulva.

The jack (jackass), like the jenny, has many reproductive similarities to the horse. The testes, epididymis, ampullae, and penis of the jack are larger than that of comparably sized horses. The jack takes a longer time to tease, achieve an erection, and ejaculate as compared to the stallion. The jack will vocalize to all the females, he may also sniff or nibble the female’s' vulva and perineal area, nibble at her head, neck, flank or legs, exhibit a flehmaen, and mount the female prior to achieving an erection; and may usually require 5-30 minutes (compared to 10-11 minutes in the stallion) from teasing to completion of ejaculation. Ejaculation will take ~30 seconds, and is accompanied by 4-9 ejaculatory urethral waves, with an average volume of 25-45 ml. Jack ejaculates usually have higher concentrations and lower volume when compared to stallions. The Clinician can use the same principles when assessing semen quality for the jack as they do with the stallion. Donkey semen should be handled using the same temperature, light, and cleanliness techniques employed to ensure stallion semen quality.

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Vaccines for Happiness:
Ten Tips to Take Home Today for Practice Positivity

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In order to work on the 40% of our happiness we have under our control, there are tools. These tools can be used to increase the positivity ratio, to tip towards and over that 3:1 barrier and to lift us past our genetic set point and circumstances into that area where WE are controlling our own destinies, WE are controlling our mind and WE are choosing positivity, happiness and success. When we do this we improve our emotions, our health, our minds and our businesses. These tools work, as simple as they are, because our minds are plastic and we can change them.

Here is a little reminder of what we already know: "Feelings 101 – in order to have a feeling or emotion, it must be preceded by a thought – a good thought will create a good feeling, a bad thought will create a bad feeling – these thoughts can be real or imaginary, conscious of subconscious, but the feelings that result are very real. In order to change your feelings, you must change the thought".

1.Gratitude has been shown to increase positivity

I think that is one of the reasons why we felt so good visiting the seniors. Clearly they were grateful to us. There are 2 gratitude exercises that have been studied extensively and work well.

Martin Seligman, the founder of positive psychology describes the 'gratitude visit ': write a 300 word letter thanking someone who has been influential in your life, specifying what they did to influence you and why it was important. Meet with this person, and read the letter to them in person. There will probably be tears. Not only will you feel better but they will too and the effects of this single exercise can last months because gratitude expressed is a powerful catalyst to happiness. Take a moment to think about an influential person in your life that you may like to thank. Can you write down a name or 2? How did they affect you? What was the result? What would it take to conduct a gratitude visit to this person? How might you both benefit? What is stopping you?

Also in this category is the Gratitude Journal, also called Three Blessings. It is most beneficial to keep journals on our nightstand because what we write before we sleep will go into our subconscious mind more effectively. Write down 3 things for which you are grateful. It can be as simple as your comfortable bed, good health, the ice cream you ate or something deeper, like a nice thing someone said or did at work today or the safe return of a group of hostages. To maintain this journal for at least 30 days will cause positivity and happiness to increase significantly over that of control groups. Some people have found that maintaining this daily becomes boring for much longer than 30 days although this has not been the case for me. A suggestion for this is after a couple of weeks perhaps start entering their 'gratitudes' every other day or perhaps every third day. Regardless it is scientifically proven that honing our recollection of things to be grateful for will sharpen our mind to look for other things to be grateful for. Gratitude is a very powerful form of positivity and to seek it out is very effective. Here's why:

Tetris effect

Have you ever played a video game for so long that the pattern in the game was all you could see? Of course psychologists have studied this effect called 'cognitive afterimage'. They did this with the addictive video game Tetris where the goal is to fill all the gaps with tiles. Participants played as much as they could non-stop for 3 days; afterwards all they could see were patterns with gaps and would search for something to fill the gap, like looking at a city skyline, and moving a skyscraper to fill the gap between 2 buildings. Harvard psychologist Shawn Achor describes this as the 'Tetris Effect'. Now imagine you are in a profession that constantly scans for errors/mistakes/loopholes, like a tax accountant, a lawyer or a medical person scanning for abnormalities. This constant scanning for WHAT IS WRONG, makes it very hard to see WHAT IS RIGHT! In fact, this behaviour can spill into their everyday life so they are spending their time looking for what is wrong with their spouse, their kids, their life; it's no wonder these professions have high levels of depression, lawyers at 4 times the rate of the general population. They have high levels of pessimism where they are more apt to see things as permanent, pervasive and beyond their control. The very same traits that make them good lawyers or doctors can make them prone to depression. Achor calls this the negative Tetris effect. This is exactly WHY exercises like gratitude journals can be effective to retrain the brain to look for what is Right, what is Good, correcting the negative Tetris Effect and trying to create a positive Tetris effect.

2.Positive events journal/what went well and why (W4)

This is another strategy to retrain the brain to scan for the positive events that have happened. On those days when not writing about 3 things for which one could be grateful, try writing about something that went well today and ***why*** it went well. This takes a bit more work and can be quite fulfilling. The extra thought to determine ***why*** things went well bolsters positivity significantly. According to the research the positive effects of maintaining a Positive Events Journal for 30 days can last for months.

3. Kindness

Studies show that intentionally boosting our kindness will increase our positivity. Everyone has likely heard about random acts of kindness where gestures such as paying for another's highway toll, or cup of coffee makes both the giver and receiver feel good. Studies have shown exactly this. What is wonderful is that it has now been proven by research that kindness is a sure-fire positivity booster. Kindness is a self-fulfilling prophecy because as we think about what nice, kind thing we may do next for someone, we are actually performing a kindness on yourself, scanning for a good thing, a kind of Positive Tetris Effect, increasing your own positivity. When you perform a kindness, your levels of oxytocin and progesterone, the bonding hormones, increase, in the same way that makes you feel good to be hugged and the stress hormone cortisol lowers, in both giver and receiver. The latest findings in neuroscience show that when we connect with others in a positive fashion there is a neural synchrony where both the giver and receiver have similar brain wave patterns. In fact kindness and positivity feed on each other to create a positive upward spiral.

It's suggested and Seligman determined that boosts in your positivity are most profound when we create a "kindness day" each week where the plan is to perform a number of kindness acts, such as helping at a shelter, delivering meals and so on. Volunteerism is strongly linked to positivity. I would highly recommend regular volunteer work as an integral part of everyone's life. Seligman showed that participating in even one kindness day would have lasting positive effects for participants, up to months. Clearly a constant focus towards kindness is not only a pretty good strategy for the health of this planet but also is a wonderful self-help tool to grow positivity.

4. Positivity ratio.com

There is a 20 question brief positivity questionnaire created by Fredrickson on –line which will rapidly calculate our positivity ratio. Not only does it create awareness of our current status but we can also track our own progress as we work to improve our positivity ratio. Fredrickson also suggests a great way to boost your ratio is to "TRIPLE YOUR PLEASURE/SAVOUR THE GOODNESS". I like this idea. Remember that we want to improve our positivity so the ratio of positive emotions to negative emotions we experience is 3 to 1 or greater. With this strategy we anticipate a positive event with great enthusiasm, we experience it well, and then we savour it, remembering it fondly, sharing it with our friends, reminding ourselves with pictures or memorabilia. It is too easy to quickly forget a positive event, a vacation, a family outing. Squeeze all the positivity juice possible out of every good event and triple the pleasure; anticipate eagerly, enjoy enthusiastically and savour frequently. There are four kinds of savouring, **basking** in it if it was congratulatory**, thankfulness** if it was a blessing, **marvelling** if it was something to awe and **luxuriating** if it was a sensory experience.

5. Commune with nature

Studies out of the University of Michigan showed that spending time outside in good weather increased positivity – as little as 20 minutes per day increased positivity, increased the openness of their thinking and expanded working memory. Isn't it great that something physically healthy is also emotionally healthy. That's why looking at glaciers and hiking all feel so good. It feels good to get physically close to the earth by walking barefoot, getting our hands in the soil gardening, laying on a beach, floating in a lake or river or ocean, sleeping on the ground, anything that puts us in contact with Mother Earth. These feel good mentally, may also have physical benefits such as better oxygenation and may possibly be linked with a grounding effect and a flow of electrons into the earth. Regardless science shows it is good for us to get outside. What a great way to improve memory!

6. Connect with people

Be social! Psychologist George Vaillant study of Harvard Men was a longitudinal study of hundreds of Harvard men beginning in the 1930's. The study showed very clearly that social connections, good relationships and friendships were a key factor in health, longevity, marital success and business success. Subsequent studies have duplicated these results. While people can be also a source of stress, surrounding one with good, successful, loving people will contribute dramatically to positivity. Other studies have shown that social interactions increase one's resiliency and lateral thinking. Make the extra effort to connect and re-connect with loved ones, pick up old friendships and stretch out to make new friendships. Social connections can help keep us happy, healthy and alive for a long time. It may seem pretty obvious yet the science shows we are a social species who are at our best when we are with others.

7. Flow

The state of Flow is the "mental state of operation in which a person performing an activity is fully immersed in a feeling of energized focus, full involvement, and enjoyment in the process of the activity". In essence, flow is characterized by complete absorption in what one does. Proposed by Mihály Csíkszentmihályi, this positive psychology concept has been widely referenced across a variety of fields. Everyone has at least one thing they do well that is difficult and requires concentration, be it surgery, fly-fishing, needlepoint, playing a musical instrument or bridge. It was said that Edison was in a state of flow when he developed the light bulb and Michaelangelo when he painted the Cistine Chapel. They went for days with very little sleep or food, completely absorbed in their

work. When truly in flow it is impossible to think of something else because the task at hand requires complete focus and time stands still.

There is great deal of literature showing a direct correlation between experiencing flow and having a positive effect. A very successful happiness strategy, is to be certain to incorporate into most days something that allows one to go into flow. If we can incorporate it into our job, even better!

Take a moment to write down one or several things that you do that put you into flow. Is it singing, surgery, a musical instrument, fishing, running, flying? What do you need to do to incorporate flow into your life regularly? Find a way to make it easy to access the opportunity, schedule it and have the equipment or whatever you need nearby and ready☺

8. Mindfulness

To quote the founder of MBSR Jon Kabat-Zinn, ' to be mindful is to be in the present moment, on purpose, by choice and without judgement'. That can be quite a tall order. In the early 80's at the University of Massachusetts Medical School, Kabat -Zinn volunteered to take on a group of patients that conventional medicine could not treat. There were chronic pain patients, psychiatric patients with depression and anxiety disorders and medicine patients including cardiac patients, hypertensives and so on. He taught them to meditate and to be mindful, developing an 8 week course that is taught to this day. It involves a weekly 2.5 hour class and daily homework. Involvement in this course was found to significantly improve pain scores, psychological scores and other medical parameters over the control group. In simple terms learning to be mindful and in the present moment was more beneficial controlling medical symptoms for these patients than pharmaceuticals. This same course has now been taught to tens of thousands over the past 30 years.

There are now over 1300 peer-reviewed papers which chronicle the medical, physical and psychological benefits of meditation. It has been shown that daily meditation is correlated with a better sense of well-being, less anxiety. Meditation increases compassion, forgiveness and self-forgiveness. It improves working memory, improves executive decision- making and task performance – pretty important stuff for a vet – and a myriad of other mental functions.

The thing about mindfulness, is simply this; when we are in the present moment it is not possible to think about other things. This by definition is a very sublime form of happiness (serenity); the concept is elegant in its simplicity. Just let the nervous system have a rest, just let it be, instead of functioning in overdrive all the time. Mindfulness may be more important now than ever before in a world of constant distraction where our phones have us on an endless treadmill of information and interruptions.

Those who meditate feel more positive and optimistic. In Fredrickson's study, **meditation alone** was able to shift the positivity ratio from less than 3:1 to greater than 3:1 in a few short months. The most powerful meditations are modifications of ancient Buddhist teachings of loving kindness and compassion. In my view this single tool, the loving kindness meditations that are freely available on-line, are the most effective positivity tools.

This is the same loving kindness meditations the Tibetan monks did in the Stanford study. With loving kindness meditation the purpose is to imagine the warm feelings you have towards a loved one and to send these same feelings towards everyone in your sphere starting with your immediate loved ones and extending into friends, community and even the entire world. A mantra such as 'may they be safe, may they be healthy, may they be happy, may they live with ease' is traditionally used.

There are countless websites, books and apps on learning how to meditate. It requires discipline and a small amount of time each day but the rewards are immeasurable.

Breathing, learning to breathe properly, fully and deeply will lower stress and increase positivity. This is a form of 'mini-meditation', as all meditations have a focus on the breath as a component. When you are feeling stressed, stop and take in 10 deep breaths, inhalations and exhalations. It will lower your heart rate and blood pressure, release oxytocin, improve your vagal tone, lower cortisol and you will feel better after.

9. Signature strengths

www.authentichappiness.org signature strength – Martin Seligman at the University of Pennsylvania, has made available a website with a large number of questionnaires and it includes one which can determine your strengths. This is a 240 question survey to determine which of the 24 strengths are more predominant for an individual and in what order. These 24 strengths include social intelligence, bravery, diligence, kindness and many others. The 5 for which one is rated highest are that person's signature strengths. Studies show that to incorporate our signature strengths into our job and into our daily life is very satisfying and fulfilling. In fact just completing a single task using our signature strengths fully will have a lasting positive effect for a couple of months. If we can incorporate these into our job, our marriage, our family, we can have a dramatic positive effect that can be very long lasting and even permanent.

10. Positivity portfolios

Fredrickson devised the strategy of creating a portfolio or memorabilia to demonstrate how any of the 10 aspects of positivity, such as joy, gratitude or love, play a role in one's life. It might be a series of photos, a screensaver, a collection of paraphernalia, a montage or

any of a number of possible ways to commemorate positivity that is meaningful to the person. These portfolios should be built with care and consideration. It is suggested to take up to a week to build one. After all it is designed to be a testimony to a particular element of positivity in your life. Fredrickson describes how to build positivity portfolios in more detail in her book, ‘Positivity’.

Positivity has been documented to contribute to help build better physical and mental health as well as business success. Almost half of the positivity or happiness we experience is within our control. We can modify the way we think and create lasting patterns of happiness and positivity using a large number of well researched positivity tools. It is not for the faint-hearted; it takes work and dedication in the same way one would embark on a weight-loss or exercise program or learn to play a musical instrument, yet is well worth the effort. I challenge you to take on the task of improving your own personal positivity. Leadership starts at the top. What can you do to improve your own positivity? What effect could it have on your business, your happiness, your health? I encourage you to explore the work of the authors discussed above, look at their websites, do your own research and find the strategies that work best for you.

The Evidence-Based Power of Mindfulness

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The purpose of this article and accompanying discussion is to share some of my own experiences with happiness and positivity, look at the evidence-based science that shows the benefits of positivity in the workplace and in our personal lives, and then offer some research based strategies that have worked for thousands, including me. While we enjoy this conference it is an opportune time for reflection. Modern life has created a hectic treadmill where the demands of commerce and technology have torn us mercilessly in many directions. Everyone wants to be happy yet excessive, destructive stress is prevalent for many members of our profession. I believe the pursuit of happiness and positivity is important for many reasons. In no particular order here are a few:

1. Clients gravitate to a pleasant environment – people want to do business with happy, positive people
2. A positive business environment is conducive to higher profitability, higher client satisfaction and greater team productivity and performance
3. Happiness and positivity are clearly linked to physical, mental and emotional health and any efforts to improve this for ourselves and our loved ones is an effort well-spent
4. The evidence –based strategies for developing positivity work not only to help someone who is languishing lift themselves from depression and negativity, but also to help someone who is already doing well do even better and flourish.
5. Happiness and positivity are contagious to the point that we can become an 'epi-center ' of positivity, radiating and infecting those around us, creating a ripple effect to help make the world a better place

My vet school visits to nursing homes with dogs back in 1980 were heartwarming and humbling. The most memorable thing for me was a woman who was bed-ridden and seemed catatonic to me. My dog started nuzzling her hand and she started moving and talking, even though incoherently. Her caregiver was brought to tears as she said the woman hadn't moved for weeks. Two things dawned on me later. First that it was better to give than to be selfish, but more importantly it was then I realized we weren't just in the business of animal health but we were in the business of happiness. If we could keep animals healthy so they could bring this much joy to people then what we did was exceedingly important.

I used this new found knowledge to support me in vet school. I knew I would graduate because I had a higher calling, to keep animals healthy so they could help make people happy. What could be more important than helping people be happy?

As a young veterinarian and business owner I became intrigued with happiness and positivity because I noted that business success seemed to be intricately linked with happiness. The positive owners I met were more likely to have successful businesses and they had cheerful team members. The ones who were negative or sour just didn't seem to be as successful, plus they seemed miserable. I took a Dale Carnegy course, then helped teach it, and read positive motivational literature by authors like Norman Vincent Peale, Napolean Hill, Dale Carnegie – How to Win Friends and Influence People, The Amazing Results of Positive Thinking, Think and Grow Rich. And the results were pretty good. Diane and I had 3 veterinary clinics by the time we were 27 and by most measures were pretty successful. In hindsight our clinics exuded positivity and attracted positive employees and clients.

Fast forward 25 years and I became so consumed by life, family, practice and veterinary association work that I forgot all the positivity I had learned and the success it had helped create. Eventually I became burned out and retired from active practice. It turns out I was not alone. Surveys in our profession report very high levels of stress. The suicide rate for veterinarians is 4-7 times that of the general population. In a large Harvard study people reported being unhappy 47% of the time.

For the past 6 years I have been a consultant relying on my business skills to help clients. Perhaps it was because of the experience I had been through, but I found I was spending more time helping the owners deal with their unhappiness than their business. During this time I have studied positive psychology, how to work on one's happiness and how to cope with stress. Seeking more tools, I became a certified life coach and attended a number of courses on stress reduction through mindfulness. In my studies I uncovered lots of work showing how deliberate efforts to improve positivity created happiness, but also improved business success.

Whereas the early positive thinking that I had read about in the 80's was anecdotal and opinion-based, the new positive psychology and business literature was rigorously evidence based. There are many people in veterinary medicine talking about how stressed we are, but very few talking about what we can do about it. There is plenty of work on positivity in the workplace but few are talking about how critical this is to the success of a veterinary team.

Harvard researcher Shawn Achor describes research about the relationship between positivity and success. A team of researchers studied 60 business teams for several years. Research assistants were trained to code every single statement made during business meetings as to whether they were positive or negative. Positive statements (P) tended to be more uplifting, other-focused and based on inquiry whereas negative statements (N) were deflating, self-focused and self-advocating. It was determined the high-performing successful teams had significantly higher P/N ratios vs those low performance teams.

In one specific example, a mining company was losing 10% per year and the ratio was 1.15:1 The researchers trained the executives to increase their praise and positive comments. The company profits improved by over 40% when the ratio increased to 3.56:1. It was shown there was a direct correlation between positivity and current and future business success in not only this company but many others. Companies with low ratios also had very few resources to cope with adversity. One major business hurdle like an economic turndown, a new competitor or loss of a key client may be all it would take to topple these companies with low positivity.

Studies show positive teams make higher sales, have better customer satisfaction and perform better on 360 degree reviews. Negotiators are more successful when trained to be positive. It's not all that surprising when you think of it. Subsequently it has been shown in studies at numerous business schools that positivity fuels creativity, energy, motivation, resiliency, engagement and productivity, all precursors to success. Efforts of management to foster positivity using techniques such as Appreciative Inquiry are successful not only in team-building but financially as well.

University of North Carolina positive psychologist Barb Fredrickson has studied positivity extensively for almost 20 years. She defined, quantified and has been able to create in the laboratory 10 positive states, namely: joy, gratitude, serenity, hope, interest, pride, amusement, inspiration, awe, and love. She is renowned for her 'broaden and build' theory which proves that positivity broadens ones mental, psychological, physical and social resources and that positivity enables one to create/build a better future life.

She sought to determine the relationship between positivity and negativity and whether a higher P/N would separate those who are truly flourishing from those who are merely existing (languishing)? First she conducted a survey with participants to determine their baseline psychological state. Next, over a period of several months she tallied the ratio between the number of positive and negative emotions participants experienced each day. She found a similar phenomenon to that of the successful companies. In order to flourish emotionally, one must experience at least 3 times as many positive emotions as negative. She then worked with those participants with scores lower than 3:1 to increase their positivity using a number of tools described below and was successful in doing so. Other researchers have duplicated these results and provided additional information regarding the relationship between positivity and mental well-being.

Positivity and happiness are terms that are often used interchangeably. What is happiness? Wikipedia calls it a state of positive well-being ranging from contentment to intense joy. According to University of California psychologist Sonja Lyubomirsky , author of "The How of Happiness", about 50% of our happiness is genetically predetermined , 10% is due to current circumstances and about 40% by intentional activities. Some of us are genetically pre-programmed to have higher dopamine and serotonin levels than others and therefore be more positive than others. There is nothing we can do about this 50% genetic set point.

The next portion of our happiness is the 10% of our happiness related to our current circumstances. I find this work fascinating. As one might imagine it's easier to be happy while on holiday than while un-plugging the toilet. But all the studies have shown that happiness OR unhappiness, related to circumstances, is temporary. The most telling study as described by Harvard psychologist Dan Gilbert compared mega-lottery winners with acute paraplegics. While understandably there was a large increase in the happiness of the lottery winners and a large decrease in the happiness of the paraplegics, within 6 months each group settled back to their original genetic set point of happiness. In other words, adversity or good fortune had no lasting effect! Other studies have shown that age, health, education, geography, sex and many other variables have no lasting effect on happiness. To say, I'll be happy when, I get that job, if I was more beautiful, younger, more intelligent or lived in a better climate, is only true temporarily – one will revert back to the basic level of happiness. That's why people fall madly in love only to separate a few months later. A change in circumstance will only buy a few months happiness at best. One study showed that the thrill obtained from buying something may only last for as little as 11 minutes. This can be seen perfectly at holiday resorts. In the beginning people are delighted to be there and to be waited on and have delicious food and beverages…….. but within a few days we see righteous indignation while waiting a few extra seconds for a beer, or IMAGINE forgetting our dessert fork, or the maid did not leave a mint on the pillow!

To recap 50 % of our happiness is predetermined genetically and 10% is circumstantial. This leaves 40% that we CAN do something about . We CAN intentionally increase our happiness, by using the large number of evidence-based tools that have been proven to improve happiness and positivity, help people to feel fulfilled and improve well-being . We can change how our brain works and new findings in neuroscience substantiate this.

NEUROSCIENCE: it is very well evidenced now that our nervous system is plastic and the term neuroplasticity is recognizable. It used to be thought that once we reached adolescence our intelligence and reasoning abilities were cast in stone; we could only look forward to diminishing capacity with aging. This is not true. This is the very reason why brain training companies like Luminosity exist. Extensive research has shown that we absolutely can modify our nervous system, our thought processes, and subsequently our feelings and emotions.

If one considers that when we multiply the number of neurons times the number of synapses and interneuronal microtubules there are 10 x 27th possible interneuronal connections. That's more than the 10 x 23rd stars that Google estimates are in the universe. There are so many possible firing sequences and each time we learn a new thing and habitualize it , be it piano or a surgery technique or learning to appreciate things more often, new neural pathways are being created that can be documented by fMRI. My analogy is this is like creating a new trail through deep snow. Each time we pass through this trail the path becomes easier to traverse.

It is now known we can and do grow new brain cells. Just as we replace skin and blood cells, there are neural stem cells in the hippocampus and lateral ventricles that differentiate into neurons as required. Essentially we replace all the cells in our body every 3 months so that we become a ‘new person’! Some people have hypothesized as we retrain the brain we are essentially training new cells?

We can train new pathways for our emotions just as we can for motor skills. Functional magnetic resonance imaging/fMRI shows different areas of the brain lighting up after training . The best example of this is the Stanford Tibetan monk study where monks laid in MRI machines and meditated on loving kindness. They had 4 standard deviations greater left pre-frontal cortex activity than is normal or average, suggesting that thinking about love and compassion will forge a new neural pathway. It is said in neuroscience, ‘neurons that fire together, wire together’.

It is now known that happiness activates the vagus nerve which controls and calms heart rate and respiration ie improves ‘vagal tone’. Vagal activation triggers the secretion of oxytocin, the ‘bonding hormone’ which creates warm feelings of attachment and inclusiveness. Oxytocin dampens the amygdala, the trip switch that enables our brain to flip from cool logical thinking into panicked flight and fright and as a result cortisol production is reduced. A happy person, one with a strong positivity ratio, has better health, is calmer and is able to think more clearly.

Neuroscience says and researchers have proven that positivity and happiness can become a habit. Because we have developed and worked on them, we have created new neural pathways to support them, and the benefits to us are greater contentment, better health and greater success in our life and business.

The Sometimes Tricky Art of Diagnosing Hyperadrenocorticism in Dogs

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1. Introduction

A. Cushing's syndrome refers to all causes of hyperadrenocorticism with overproduction of cortisol.
   a. ACTH-dependent
      i. Cushing's disease: Pituitary hypersecretion of ACTH which results in bilateral adrenal hyperplasia (90% of cases)
      ii. Ectopic ACTH production: Non-pituitary tumors secreting ACTH resulting in bilateral adrenal hyperplasia. Has not been completely documented in dogs or cats.
   b. ACTH independent
      i. Adrenocortical adenoma or carcinoma: Hypersecretion of cortisol with atrophy of normal adrenal and suppressed ACTH concentrations (10% of cases).
   c. Iatrogenic
      i. Excessive or prolonged administration of glucocorticoids. Clinically indistinguishable from natural disease. Results in adrenal atrophy and suppressed ACTH levels.

2. Signalment

A. Poodles, Dachshunds, Schnauzers, Boston Terriers, Boxers.
B. Middle to old age. Average 12 years; range 6 months to 17 years.
C. No sex predilection.
D. Rare in cats. Usually seen with insulin resistant diabetes mellitus and/or cats with severe dermal atrophy/ulceration.

3. Clinical signs

A. PU / PD
B. Pendulous, "pot-bellied abdomen": Due to muscle catabolism by glucocorticoids and hepatomegaly.
C. Bilaterally symmetric alopecia: Head and extremities spared.
D. Thin skin
E. Muscle weakness and muscle atrophy; cruciate ruptures
F. Mineralization of skin (calcinosis cutis)
G. Hyperpigmentation: ACTH similar to MSH, co-existing hypothyroidism, chronic skin irritation.
H. Reproductive abnormalities
   a. Anestrus
   b. Clitoral hypertrophy
   c. Testicular atrophy
   d. Perianal adenomas in females and neutered males.
I. Respiratory signs
   a. Panting: Pulmonary hypertension and decreased compliance, primary CNS disturbance, pulmonary mineralization.
   b. Dyspnea: Rare; seen with pulmonary thromboembolism and concurrent congestive heart failure.
J. Central nervous system
   a. Seen with large pituitary tumors (macroadenomas). Present at time of diagnosis or following therapy for Cushing's disease as microscopic pituitary tumors enlarge into macroadenomas.
   b. Signs due to compression/invasion of pituitary and/or hypothalamus:
K. Seizures
   a. Pacing
   b. Lethargy
   c. Inappetence
   d. Behavior change
   e. Head pressing
   f. Circling

4. Diagnosis of Hyperadrenocorticism

A. History and clinical signs

B. R/O iatrogenic disease with questions concerning current or past medications. These medications can include oral, ophthalmic, otic, and topical medications. Make sure the owner tells you about everything and anything that went on or in their pet.

C. Laboratory data

- a. Hemogram
  - i. Polycythemia (PCV 45-55%)
  - ii. Stress leukogram
    1. Lymphopenia
    2. Eosinopenia
    3. Neutrophilia (mature)
- b. Biochemistry profile
  - i. Elevations in:
    1. Serum alkaline phosphatase (SAP)
    2. Cholesterol
    3. Serum alanine aminotransferase (ALT)
    4. Fasting blood glucose: Diabetes in 5-10%.
- c. Thyroid function tests
  - i. T3 and T4 basal levels are generally decreased.
  - ii. Response to TSH parallels normal.
  - iii. Secondary to negative feedback of cortisol on pituitary.
  - iv. 80% have a normal fT4ED
  - v. Does not require thyroid supplementation.
- d. Blood pressure: 50 – 80% are hypertensive, cause unknown.
  - i. Recent study demonstrated normal or decreased levels of atrial natriuretic factor (ANF) in dogs with hyperadrenocorticism. Argues against hypervolemia as the etiology of the hypertension.
- e. Urinalysis
  - i. Decreased urine specific gravity.
  - ii. Proteinuria

D. Radiographic abnormalities

- a. Thoracic films
  - i. Bronchial calcification
  - ii. Metastases from adrenal adenocarcinoma
- b. Abdominal films
  - i. Hepatomegaly
  - ii. Osteopenia
  - iii. 50% of adrenal tumors are visualized as soft tissue or calcified masses.
  - iv. Subcutaneous calcification

E. Adrenal function tests

- a. Three tests used to diagnose hyperadrenocorticism. They do not differentiate between PDH or AT.
  - i. ACTH stimulation test
    1. Look for exaggerated cortisol response in response to ACTH.
    2. See protocols at the end of this discussion.
    3. Diagnostic in 85% of pituitary-dependent cases (PDH)
    4. Diagnostic in 70% of adrenal tumors (AT)
    5. Overall accuracy 80-85 %
    6. A suppressed response to ACTH in animals with clinical signs of hyperadrenocorticism suggests iatrogenic disease.
- b. Low-dose dexamethasone suppression test
  - i. Low doses of dexamethasone inhibit ACTH release from the pituitary via negative feedback and decrease plasma cortisol concentrations in normal dogs.

ii. Dogs with Cushing's are more resistant to steroid suppression. Therefore, lack of suppression following dexamethasone = hyperadrenocorticism.
iii. Diagnostic in 95% of PDH
iv. Diagnostic in 100% of AT

c. Overall 90-95%
i. May also be used to distinguish PDH from AT (see below)
ii. See protocols

d. Urine cortisol/creatinine ratio
i. Assessment of cortisol production and excretion rate.
ii. Sensitivity of this test is greater than that of the LDDS (some animals with clinical signs of hyperadrenocorticism may have normal LDDS response tests but elevated urine cortisol to creatinine ratios). Used as a screening test.
iii. Test is easy to perform.
iv. As with all adrenal function tests, elevated results may occur in animals with non-adrenal disease.
v. Positive tests confirmed with a LDDS.
vi. Must be performed on urine obtained at home, preferably in the AM

e. Tests to differentiate PDH from AT (performed after confirming diagnosis of hyperadrenocorticism).
i. High-dose dexamethasone suppression test
1. With PDH, a high dose of dexamethasone results in a decrease in ACTH release from the pituitary and a decrease in plasma cortisol.
2. With AT, the tumor secretes cortisol autonomously thereby suppressing ACTH production. With low ACTH concentrations already present, dexamethasone has no effect on plasma cortisol.
3. 70% of patients with PDH suppress plasma cortisol to less than 50% of the pre-treatment value.
4. 100% of patients with AT do not suppress.
5. Therefore: Suppression = PDH; Lack of suppression = Inconclusive
6. See protocol

f. Endogenous ACTH concentration
i. PDH: Levels normal or high
ii. AT: Levels low to undetectable
iii. Contact lab regarding sample handling and collection. Use of the preservative (Aprotinin) allows for greater utilization of this test.
iv. Excellent method to differentiate PDH from AT.

Testing protocols

These are suggested protocols that are used in the evaluation of patients with hyperadrenocorticism. You must use the protocol and normal values from the laboratory to whom you are submitting samples to properly evaluate endocrine tests.

A. ACTH Stimulation Test
a. Synthetic ACTH (Cortrosyn) 5 ug/kg IV or IM; collect serum at 0 and 1 hour, or
b. ACTH gel (Acthar) 2.2 U/kg IM; collect serum at 0 and 2 hours.
c. Hyperadrenocorticism if post-cortisol > 20 ug/dl (530 nmol/L)

B. Low-Dose Dexamethasone Suppression Test
a. 8 A.m: Baseline serum cortisol. Administer 0.01 mg/kg dexamethasone sodium phosphate (0.015 mg/kg dexamethasone) IV.
b. 12 p.m: Collect 4 hour post-dexamethasone cortisol.
c. 4 p.m: Collect 8 hour post-dexamethasone cortisol.
d. In normal animals cortisol suppresses to less than 1.0 ug/dl (27.5 mmol/L) at 8 hours.
e. 50% or greater suppression at either 4 or 8 hours together with lack of suppresion at 8 hours is diagnostic for PDH and additional tests are not necessary.

C. Urine Cortisol/Creatinine Ratio
a. First morning urine sample is preferred. Sample should be obtained at home. Requires 1 – 2 mls.
b. Stable at room temperature or refrigerated for 3 days.

c. Normal range 2.8 - 4.8. A normal result effectively rules-out hyperadrenocorticism, an abnormal result should be confirmed with a LDDS or ACTH stimulation test.

Differentiating PDH From AT

A. Low-Dose Dexamethasone Suppression Test
   a. See above.
B. High-Dose Dexamethasone Suppression Test
   a. 8 a.m: Obtain serum cortisol. Administer 0.1 mg/kg dexamethasone sodium phosphate (0.15 mg/kg dexamethasone) IV.
   b. 4 p.m: Collect post-dexamethasone cortisol.
   c. Suppression defined as greater than a 50% reduction of cortisol.
   d. Suppression = PDH, non-suppression = Inconclusive
C. Endogenous ACTH Concentration
   a. Check with lab on sample collection and handling.
   b. Normal: 20-100 pg/ml (4.4-22.0 pmol/L)
   c. PDH: 40-500 pg /ml (8.8-110 pmol/L)
   d. AT: < 20 pg/ml (<4.4 pmol/L)

Exploring Treatment Options for Canine Hyperadrenocorticism

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Treatment options

A. Pituitary-dependent hyperadrenocorticism

1. Surgical management
    a. Bilateral adrenalectomy
        i. Technically difficult
        ii. Poor surgical/anesthetic risk
        iii. Permanently hypoadrenal and require lifelong replacement therapy
    b. Hypophysectomy
        i. See discussion at the end of this section
        ii. Lifelong therapy with thyroid hormone and prednisone necessary.
2. Medical therapy

Prognosis

Most dogs with PDH live normal lives (average 2.2 years, but remember most are geriatric to begin with.)

1. Complications
    a. Recurrence of disease.
    b. CNS signs.
    c. Pulmonary thromboembolism.
    d. Infections.
    e. Hypertension.
    f. Congestive heart failure.
2. Adrenal tumors:
    a. Adenomas: Good if no evidence of local invasion.
    b. Carcinomas: Guarded to grave with metastases.

Trilostane therapy of canine hyperadrenocorticism

The efficacy and safety of trilostane in the treatment of canine PDH were evaluated in a multicentre study at the Royal Veterinary College in London, the Veterinary Teaching Hospital in Dublin and Small Animal Hospital in Glasgow. Seventy-eight dogs with confirmed PDH were treated with trilostane for up to 3 years. The starting dose varied from 1.8 to 20 mg/kg (mean = 5.9 mg/kg).

Trilostane appeared to be well tolerated by almost all dogs with only 2 dogs developing signs and biochemical evidence of hypoadrenocorticism. One of these dogs recovered with appropriate therapy. The other died despite withdrawal of trilostane and administration of appropriate therapy. A further two dogs died within one week of starting trilostane but in neither case could a direct link with the trilostane therapy be established. The low prevalence of side effects compared favourably to those reported with mitotane.

Trilostane was found to be nearly as effective as mitotane in resolving the signs of hyperadrenocorticsm. Polyuria, polydipsia and polyphagia had dissipated in 40 dogs within 3 weeks after starting trilostane. Within 2 months, a further 20 dogs showed decreases in their water and food consumption. These improvements were maintained as long as the dogs remained on adequate doses of trilostane. Skin changes resolved in 24 out of 39 (62%) of dogs that initially presented with dermatological signs. All of these improvements were maintained as long as the dogs remained on adequate doses of trilostane. Only 8 dogs that were treated with trilostane for more than 2 months showed poor control of clinical signs. In contrast, mitotane is effective in about 80% of cases of pituitary dependent hyperadrenocorticism (PDH).

Trilostane caused a significant ($p<0.001$) reduction in both the mean basal and post-ACTH stimulation cortisol concentrations after 10 days of treatment. The post ACTH cortisol concentration decreased to less than 250 nmol/l (9 µg/dl) in 81% of dogs within one month and in another 15% at some time whilst on treatment. These improvements were also maintained in the study population for the duration of the trial.

Thirty-five dogs had at least one dose adjustment over the treatment period. The dose was increased in 23 dogs up to four times the starting dose. In one dog the dose was increased nine fold over a period of six months. The dose was decreased in nine dogs to as low as a quarter of the starting dose.

The mean survival of all trilostane treated dogs was 661 days. Direct comparison with mitotane was difficult as 65% of the dogs were still alive at the time of censor and therefore the mean survival may still increase.By comparison, the mean survival of mitotane treated dogs has been reported to be 810 to 900 days.

Dosage and administration

The current suggested initial starting dose range for dogs with PDH is 1-2 mg/kg once daily. This needs to be adjusted according to clinical signs and serum cortisol values (see below). Doses up to 40-50 mg/kg (divided twice daily) have been given with no unwanted side effects. In some dogs twice daily dosing may be necessary. The drug is given with food.

Transsphenoidal hypophysectomy

A variety of treatments are available for PDH. Medical treatment options include drugs that chemically destroy the adrenals (lysodren or op-DDD) inhibit enzymes in the adrenal leading to the synthesis of cortisol (ketoconazole, trilostane) or inhibit the release of ACTH from the pituitary gland (Anipryl or selegiline). While these treatments can improve the clinical signs in 40-80% of patients they need to be chronically administered, necessitate frequent monitoring and do not cure or address the primary cause of the disease (the pituitary tumor). In humans, surgery to remove the tumor is the most successful long-term therapy. The most common approach used is the transsphenoidal method, in which a passage way is made in the sphenoid sinus, an air space behind the back of the nose, which is just below the pituitary gland. Surgical cure rates for PDH are reported to be in the range of 65-85%, although more recent long-term follow up data suggest that the recurrence rate is as high as 25 % within 5 years. When no discrete adenoma can be identified, remission of hypercortisolism is observed in only about 40%. Surgery has also been used to treat PDH in dogs. Several groups, most notably in the Netherlands have performed these surgeries with success rates paralleling those reported for humans. However, these surgeries have generally not been performed in the US. Veterinarians at VCAWLAAH, in collaboration with human neurosurgeons that regularly perform transsphenoidal surgery in humans have developed the methods to perform these surgeries in the US and are conducting a research study to determine how effectively these surgeries can be performed.

How I Treat Diabetes in Cats

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Diabetes mellitus is a common endocrine disorder in dogs and cats. Recent data has shed light on the pathogenesis of the disorder in dogs and cats and has highlighted the role of diet, insulin and novel hypoglycemic therapies. In the majority of cases, the most appropriate therapy in both dog and cats includes the administration of insulin.

The key to successful management of the diabetic patient lies in close communication with the pet owner and prompt recognition and treatment of concurrent disorders.

Key facts

1. Insulin is still the mainstay of therapy in the majority of dogs and cats with diabetes mellitus.
2. Diet is an important part of diabetic management especially in obese patients and cats.
3. Auto-immune disease, pancreatitis and amyloidosis are the most common causes of diabetes in dogs and cats.

Successful management of the diabetic patient involves many factors. An understanding of dietary therapy, insulin preparations, oral and novel hypoglycemic agents and management of concurrent illness, are all required to optimize glycemic control. The goals of therapy are to control clinical signs, prevent or slow the progression of cataracts, avoid hypoglycemia and maintain ideal body weight. An additional goal in cats is to obtain remission. The challenge is to address these concerns while attempting to help the owners deal with what they may consider a time consuming, expensive and chronic medical condition.

Diabetes Mellitus in dogs and cats results from a decrease in insulin secretion from the beta cells of the pancreas and/or a decrease in insulin action. There are three classifications of diabetes:

Type I diabetes is comparable to insulin dependent diabetes mellitus (IDDM) in humans. It results in low basal insulin concentrations with impaired insulin secretion following a glucose load. Treatment requires insulin injections. It is the most common form of diabetes in dogs.

Type II diabetes is similar to non-insulin dependent diabetes (NIDDM) in humans and is managed with dietary therapy and oral hypoglycemics. It causes normal to increased basal insulin concentrations with decreased secretion following a glucose load. Insulin may or may not be required for animals with Type II diabetes.

Type III diabetes is seen most commonly in *hormonally-induced* diabetes in dogs and cats and is similar to impaired glucose tolerance (IGT) in humans. Diabetogenic hormones (epinephrine, cortisol, glucagon and growth hormone) or medications interfere with insulin action and cause glucose intolerance, which can lead to diabetes.

Etiology and signalment

Feline

The most common causes of diabetes in cats are obesity, pancreatitis and most commonly, amyloidosis of the pancreatic beta cells. There appears to be very little gender predisposition to this disease in cats, although it is slightly more common in males than females. As with dogs, the onset of diabetes in cats occurs most often in middle age.

Clinical signs

The clinical signs of diabetes include PU/PD (polyuria and polydipsia) from hyperglycemia, resulting in glycosuria and a resultant osmotic diuresis. Polyphagia and weight loss is common although many animals will still be obese upon presentation. In addition to the polyphagia, there may be variable degrees of dehydration especially in the cat. Cataract formation is very common in dogs with diabetes, but rare in cats. Cats often present with icterus as a result of concurrent hepatic lipidosis and/or pancreatitis. Icterus is not common in dogs unless they have pancreatitis. Cats may also exhibit a plantigrade stance (peripheral neuropathy) that is directly related to the severity and duration of hyperglycemia. Clinical neuropathies do occur in dogs, but are extremely rare.

Differential diagnoses include: hyperthyroidism (in cats), gastrointestinal lymphoma, hepatic disease, renal disease, pancreatitis, hyperadrenocorticism, and acromegaly.

Diagnosis

Diagnosis involves testing for persistent fasting hyperglycemia, with fasting blood glucoses greater than 200mg/dl. Clinicians also will need to rule out transient hyperglycemia that may be due to: post-prandial hyperglycemia; diabetogenic hormones (endogenous or exogenous); and stress hyperglycemia. Stress hyperglycemia can be a problem in cats due to the release of epinephrine when stressed or handled.

Laboratory abnormalities include:

- Hemogram
  - non-specific
  - signs of dehydration
- Biochemistry profile
  - hyperglycemia
  - increases in SAP and ALT
  - increases in bilirubin (usually in cats)
    - hepatic lipidosis
    - pancreatitis
- Urinalysis
  - glycosuria
    - renal threshold for glucose
      - canine 180-220mg/dl
      - feline 240-300 mg/dl
  - ketonuria
  - up to 40% of patients will have positive urine cultures in the absence of an active urine sediment.

Treatment

The number one cause of death in diabetic dogs and cats is not the disease itself, rather, it is the owner's frustration with the disease. This is an extremely important point to remember when treating diabetic animals. Good communication with the pet owner is perhaps the most important component of managing the disease.

It is recommended that clinicians schedule a 30-minute appointment with the client at the time of discharge before sending the diabetic patient home for the first time. During this appointment, clinicians should thoroughly discuss the care required for the patient. Include the following instructions in that discussion: how to give the animal injections; how to store insulin, what types of food to feed and how often; how to recognize the signs of hypoglycemia and how t react to this condition. Also include information on what clinical signs to look for in terms of monitoring water intake and urine production. The client should be give written instructions for use as a reference once they are caring for the patient at home. It is essential that the clinician and veterinary staff strive to educate the caregiver and motivate them to get involved in the care of their diabetic pet.

The goals of treatment include elimination of the clinical signs of diabetes, prevention or slowing of cataract formation and resulting blindness, prevention of potentially dangerous hypoglycemia, and prevention and/or treatment of concurrent illness.

Therapy for diabetes centers on three main areas: Treatment of concurrent illness (i.e., urinary tract infections, pydermas, etc.), insulin therapy, and dietary management.

Concurrent illness

Monitoring for concurrent illness is very important in effectively managing diabetic dogs and cats. Clinicians must effectively recognize and treat the other disorders because the concurrent illness will impact the diabetic regulation and many common diseases have similar clinical signs to diabetes mellitus. Even simple problems such as UTI's and pyodermas can result in activation of stress hormones and result in insulin resistance.

Insulin therapy

There has been a considerable amount of confusion over the various insulin preparations that are available. In general, animal origin insulins are being discontinued as the desire and ability to treat people with human derived insulin preparations has progressed.

There is concern that animals receiving human insulin will develop antibodies resulting in decreased insulin activity and/or effectiveness. Dogs receiving any insulin product that is not derived from pork may make antibodies. However, studies have shown that those antibodies do not interfere with the glucose control. In fact, dogs that made antibodies against insulin had a longer duration of insulin action, which actually enhanced the effect of the insulin rather than decreased its efficacy. A recent study in cats should that 13% developed anti-insulin antibodies. None of the cats should signs of insulin resistance.

The options with human insulin include ultra short acting, short acting, intermediate acting, and long-acting insulins. The short acting insulins are primarily used for ketoacidosis, and therefore, are not covered in this article. The intermediate acting insulins are classified as either NPH or Lente. It is important to note however, that even though they are classified as intermediate, they do not behave the same way in the dog or cat. Lente is actually a mixture of two different insulin preparations, which results in a bimodal onset of actions. This is helpful in some patients because is helps block post- prandial hyperglycemia. Conversely, a lente insulin is not recommended for use in an animal that does not develop post prandial hyperglycemia. It is recommended that NPH be used in the majority of dogs and cats with diabetes and it is also understood that most patients will require two injections a day to achieve glycemic control.

Feline patients

Newly diagnosed patients

1. Insulin glargine (Lantus): Glargine is a modified, recombinant, long acting insulin analog. A study presented at ACVIM in 2005 showed a very high rate of remission (8/8 in remission within 4 months with 6/7 still in remission at 1 year) in feline diabetics with the use of glargine and a low carbohydrate-high protein diet. The recommended starting dose is 0.5 units/kg BID if the fasting blood sugar is greater than 360 mg/dl and 0.25 units/kg BID if the initial fasting blood glucose is less than 360 mg/dl. For additional product information see: www.lantus.com. Glargine highlights:
    a. Should not be diluted or mixed as this will affect pH
    b. Should be kept refrigerated. Once open the vial has a shelf life of 4 weeks at room temperature. I would discard any remaining insulin after 8 weeks of refrigeration pending further clinical data.
2. PZI: As with dogs we only recommend the use of PZIR from BI.
3. Humulin N and Novolin N: Similar to PZI with remission rates of 40-50 % when used with a low carbohydrate-high protein diet. Starting doses are generally 1-3 units/cat once a day.
4. Vetsulin: Again similar to PZI and Humulin N with remission rates of 40-50 % when used with a low carbohydrate-high protein diet. Starting doses are generally 1-3 units/cat once a day.

Transitioning feline patients

If you have patients currently taking either Humulin L or Humulin U, I would switch them to either Vetsulin or Humulin N. The initial starting dose will remain the same with re-assessment of clinical signs and a serial blood glucose curve performed 1 week after changing insulin preparations. If you wish to transition them to glargine, I would follow the dosage recommendations as outlined above under newly diagnosed patients. It is important to note that remission rates will be much lower with glargine and a low carbohydrate-high protein diet in long standing diabetic patients (cats with diabetes for more than 6 months) than in newly diagnosed patients.

With the recent introduction of the AlphaTrak Blood Glucose Monitoring System (Abbott) we have the ability to very accurately measure blood glucose concentrations in both dogs and cats using very small quantities of blood. This will allow both veterinarians and pet owners to obtain very reliable results in both the hospital and home setting. This information can then be used to make informed decisions regarding the management of diabetic patients. These decisions impact the type and dose of insulin selected, the frequency of insulin administration, aid in the assessment of glycemic control, help in preventing hypoglycemic episodes and monitor for remission of diabetes especially in feline patients.

Glycemic control can be evaluated in a numbers of ways. Owner assessment of clinical signs (polyuria, polydipsia, weight gain or loss), progression of diabetic cataracts (dogs), presence of peripheral neuropathy (cats), and episodes of hypoglycemia are often the best indicators of glycemic control. Changes in insulin dosage or documenting remission of diabetes, is best determined by blood glucose measurement. Recognizing that the measurement of blood glucose concentrations can be problematic in the hospital setting (especially in cats as a result of stress induced hyperglycemia) recent work has evaluated the practicality and value of at home blood glucose monitoring in dogs and cats. At home blood glucose monitoring is essential in the management of human patients with diabetes given that a number of the complications associated with long term diabetes are directly related to persistent hyperglycemia. While diabetic retinopathy, nephropathy, painful neuropathies and cardiovascular disease are rare in our veterinary patients, adequate glycemic control is required to eliminate clinical signs and decrease morbidity and mortality in dogs and cats. Control of clinical signs does not require the restoration of euglycemia but rather involves keeping the blood glucose levels below renal threshold for the majority of the day. Renal threshold for glucose is 180 mg/dl in the dog and approximately 280 mg/dl in the cat. It is very important that we remember the owners of diabetic dogs and cats are being asked to do a great deal to help in the management of their pet's chronic illness and we need to do whatever we can to make the clients job easier while at the same time taking steps to assure maximal diabetic control.

Using the information derived using at home or in hospital glucose monitoring

The data obtained with at home blood glucose monitoring in conjunction with clinical signs is used to adjust the dose of insulin and to monitor for remission of diabetes. We will look at scenarios for both cats and dogs. The recommendations for cats are based on our experience as well as the data generated by Dr Jacquie Rand at the University of Queensland.

Cats

1. Cats on Glargine and PZI Insulins
    a. If the preinsulin blood glucose concentration is > 360 mg/dl and/or the nadir blood glucose (PZI) or 4 hour (glargine) post blodd glucose concentration is > 180 mg/dl the dose of insulin is increased by 0.5 to 1 unit BID.
    b. If the preinsulin blood glucose concentration is 270 to 360 mg/dl and/or the nadir glucose (PZI) or 4 hour (glargine) post blood glucose blood glucose concentration is 90 - 180 mg/dl the dose of insulin is maintained.

c. If the preinsulin blood glucose concentration is 190 - 270 mg/dl and/or the nadir glucose (PZI) or 4 hour (glargine) post blood glucose blood glucose concentration is 54 - 90 mg/dl use the nadir, clinical signs and the next preinsulin glucose concentration to determine if the dose is decreased or maintained.
d. If the preinsulin blood glucose concentration is < 180 mg/dl and/or the nadir blood glucose (PZI) or 4 hour (glargine) post blood glucose glucose concentration is < 54 mg/dl the dose of insulin is decreased by 0.5 to 1 unit BID. If the total insulin dose is already 0.5 – 1 unit BID, stop the insulin and check for diabetic remission.

2. Cats on NPH, Lente or Ultralente Insulins
   a. If preinsulin blood glucose is < 210 mg/dl withhold insulin and check for diabetic remission.
   b. If preinsulin blood glucose is 234 - 288 mg/dl total insulin dose should not be higher than 1 unit BID.
   c. If nadir blood glucose is < 54 mg/dl insulin dose should be reduced by 50%.
   d. If nadir blood glucose is 54 - 90 mg/dl dose should be reduced by 1 unit BID.
   e. If nadir blood glucose is 91 - 162 mg/dl insulin dose should remain the same.
   f. If nadir blood glucose is > 180 mg/dl insulin dose should be increased by 1 unit BID.

Diet

There is a considerable amount of reliable research data showing that diets high in carbohydrates, low in fat and high in fiber are helpful in regulating diabetic dogs. These types of diets lower the average insulin dose, the average blood sugar, the amount of urine being produced and glycosolated hemoglobins and fructosamine levels.

The carbohydrates in these diets are complex carbohydrates. It is important to avoid diets high in simple sugars, which includes any commercial semi-moist food, primarily those packaged in foil packets. Diets high in simple sugars are absorbed very rapidly before the insulin has time to work. The goal with diet is to balance the absorption of sugar with the onset of action of the insulin. A high carbohydrate/low fat diets also decreases plasma free fatty acid and cholesterol concentrations, and increases the number and activity of insulin receptors.

High fiber diets reduce insulin resistance. The fiber acts to decrease post prandial hyperglycemia, primarily because it delays gastric emptying. A high fiber diet also decreases absorption of glucose and increases insulin action at the receptor.

It has recently been suggested that diabetic cats be fed a high protein/low carbohydrate diet. This can be accomplished with several commercially available canned diets (Hill's M/D, IVD Development, Purina DM, many other canned kitten diets). These diets may result in remission of the diabetes and elimination of the need for exogenous insulin and/or oral hypoglycemic agents. High protein/low carbohydrate diets more closely resemble the diet of felines in the wild and may help reduce glucose intolerance, insulin resistance and obesity.

Feeding

Ideally, the feeding schedule should be coordinated with the onset of action of the insulin. With dogs, this is fairly easy to regulate, but with cats, it is nearly impossible due to their "grazing" style of eating. For cat owners who may not be able to follow a strict feeding schedule or those with multiple pet households, insulin therapy will have to be adjusted to meet the owner's needs. The most important component of the dietary plan is to stress consistency in the diet. The following feeding schedule can be used for dogs and some cats. With insulin given once a day, feed three meals a day (of equal calories) at six-hour internals. Give the first meal at the time of the insulin injection. For animals receiving insulin twice a day, feed four meals a day. Schedule them to coincide with the insulin injections and feed mid-afternoon and late evening.

If the owner is unable to follow this schedule, advise them to feed twice a day, at the time of injection and 8-10 hours later (for once a day insulin patients); or at the times of insulin injections (for twice a day insulin patients).

Home management

1. Instruct owner on proper injection techniques, injection locations, storage and handling of insulin.
2. Instruct owner on how to monitor clinical signs.
3. Continue feeding schedule and dietary therapy.
4. Instruct owners to initially monitor urine glucose/ketone levels daily, usually in the morning or evening prior to feeding. If persistent glycosuria or ketonuria is observed, ask owner to contact the veterinary hospital.
5. Advise owners of the signs of and treatment for hypoglycemia. Have owners keep a bottle of Karo syrup on hand if signs occur (i.e., weakness, ataxia, seizures) so they can rub syrup on the gums immediately. Instruct them to call the veterinary hospital.
6. Home monitoring of a diabetic cat is frequently based on observance of clinical signs only.
7. Serial sugars after the first week of home management.

Re-check evaluations

1. Obtain owner assessment of clinical signs.
2. Serial blood sugars are helpful due to:

a. Variability of insulin action in a given patient.
b. Inaccuracy of random blood or urine sugars in monitoring the degree of glycemic control.
c. Not particularly helpful as a routine procedure in animals that are well controlled clinically.

3. Body weight
4. Physical examination/ophthalmic exam
5. Discuss urine log book with owner
6. Laboratory work as clinically indicated
7. Role of glycosylated hemoglobin and frustosamine:
8. Fructosamine may be helpful in distinguishing stress-induced hyperglycemia from diabetes in cats. These tests can be used every 3 – 4 months as an indicator of long term (2-3 weeks fructosamine; 4-6 weeks glycosylated hemoglobin) glucose control. Rising values indicate the need for further evaluation.

Problems with insulin therapy

1. Insulin induced hyperglycemia (Somogyi phenomenon)
   a. Hypoglycemia (<65mg/dl) followed by hyperglycemia (>300mg/dl) within 24 hours of insulin injection.
   b. Suspect when insulin requirements exceed 2 U/kg and clinical signs persist.
   c. Suspect when animal has signs of hypoglycemia in afternoon.
   d. Diagnosis with serial sugars.
   e. Treat by decreasing insulin dose 25-50% and review insulin administration with the owner to rule out management problems.
   f. Re-check serial sugars in one week.
2. Rapid insulin metabolism
   a. Duration of insulin less than 18 hours.
   b. Signs return in the evening.
   c. Diagnosis is with serial sugars. Hyperglycemia (>250) within 18 hours of insulin injection without previous hypoglycemia.
   d. Treatment:
   e. -Review management with owner
   f. -Switch to twice daily insulin administration. Most dogs and cats require insulin twice a day to achieve adequate glycemic control. Consider switching to PZI in cats.
3. Insulin Resistance
   a. Hyperglycemia (>300) throughout the day, despite insulin dosages > 2 U/kg.
   b. Diagnosis based on serial sugars.
   c. Potential causes of insulin resistance:
   d. Management problems
   e. Hyperadrenocoticism
   f. Steroid or Ovaban administration
   g. Diestrus or pregnancy
   h. Acromegaly
   i. Concurrent illness, infection
   j. Anti-insulin antibodies
   k. Hypothyroidism (dogs), hyperthyroidism (cats)
   l. If insulin dose exceeds 2U/kg, the animal should be evaluated for one of these causes of resistance.
4. Hypoglycemia
   a. Insulin overdosage
   b. Suspect if animal shows weakness, shaking, ataxia, seizures at time of insulin's peak effect.
   c. Therapy (instructions for owners)
   d. Mild signs - give food and call veterinarian
   e. Moderate signs - apply Karo syrup to the mouth, offer food when alert and then notify veterinarian.
   f. Comatose - apply Karo syrup to mouth and take animal to hospital.
   g. When hypoglycemia occurs, serial sugars should be performed to re-assess insulin dose

Insulin-Resistant Diabetes: What to do When Your Insulin Therapy Stops Working

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Insulin resistance is a condition in which a normal amount of insulin produces a suboptimal biologic response. Insulin resistance may result from problems occurring before the interaction of insulin with its receptor (e.g., insulin-binding antibodies), at the receptor (e.g., altered insulin receptor binding affinity or concentration), or at steps distal to the interaction of insulin and its receptor. Post-receptor problems are difficult to differentiate clinically from receptor problems, and both often coexist. In dogs and cats, receptor and post-receptor abnormalities are usually attributable to obesity, inflammation (such as occurs with pancreatitis or gingivitis), a disorder causing excessive secretion of a potentially insulin-antagonistic hormone (such as cortisol in dogs and cats or growth hormone and T4 in cats), or a disorder that causes a deficiency of hormone necessary for insulin action (such as thyroid hormone).

No insulin dose clearly defines insulin resistance. For most diabetic dogs and cats, control of glycemia can usually be attained using 1.0 U or less of NPH, lente insulin or glargine (cats) per kilogram of body weight given twice daily. Insulin resistance should be suspected if control of glycemia is poor despite an insulin dosage in excess of 1.5 U/kg, when excessive amounts of insulin (i.e., insulin dosage >1.5 U/kg) are necessary to maintain the blood glucose concentration below 300 mg/dL, or when control of glycemia is erratic and insulin requirements are constantly changing in an attempt to maintain control of glycemia. Failure of the blood glucose concentration to decrease below 300 mg/dL during a serial blood glucose curve is suggestive of but not definitive for the presence of insulin resistance. An insulin resistance-type blood glucose curve can also result from stress-induced hyperglycemia (cats), the Somogyi response, and other problems with insulin therapy, and a decrease in the blood glucose concentration below 300 mg/dL can occur with disorders causing relatively mild insulin resistance. Serum fructosamine concentrations are typically greater than 500 µmol/L in animals with insulin resistance and can exceed 700 µmol/L if resistance is severe.

Two diseases that have the potential to cause the most severe insulin resistance are hyperadrenocorticism and hypersomatotropism (acromegaly), although insulin resistance may also be mild or variable. Approximately 80% of cats with hyperadrenocorticism and nearly all cats with hypersomatotropism will develop diabetes mellitus. Hyperadrenocorticism is rare: 75% to 80% of cats have pituitary-dependent disease and 20% to 25% have cortisol secreting adrenocortical tumors. In rare circumstances, adrenocortical tumors secrete other steroid hormones (e.g.,progesterone). However, clinical signs are identical to those of hypercortisolism, and diabetes mellitus may develop as well.In addition to PU/PD and weight loss, which are usually due to concurrent diabetes mellitus, typical clinical signs are abdominal enlargement, an unkempt seborrheic hair coat, thinning of the hair coat, failure of hair to regrow, or alopecia and muscle weakness. Severe cases may have thin, fragile skin that tears easily. Cats with large pituitary masses may have CNS disturbances. However, clinical signs may also be mild and hyperadrenocorticism is often not suspected until it becomes evident that the diabetes is difficult to regulate. The dexamethasone suppression test is the preferred screening test. Whether poorly regulated diabetics do indeed have hyperactivity of the hypothalamus-pituitary-adrenal gland axis that leads to abnormal test results is controversial. Based on recent studies, the dexamethasone test (0.1 mg/kg dexamethasone IV with a pre, 4 and 8 hour post) appears to be a suitable part of the diagnostic workup in diabetic cats suspected of having hyperadrenocorticism and should be carried out only after insulin therapy has been instituted for 6-8 weeks to mitigate the effects of poor glycemic control on the HPA axis.

Hypersomatotropism in cats is caused by a growth hormone (GH)-producing tumor (usually an adenoma) in the pars distalis of the pituitary gland. GH has catabolic and anabolic effects; the latter are in part mediated by insulin-likemgrowth factor-1 (IGF-1). The catabolic effects are mainly due to insulin antagonism and are the reason for the diabetes mellitus. The anabolic effects include proliferation of bone, cartilage, soft tissue, and organs resulting in a large body size, broad head and large paws, weight gain, prognathia inferior, respiratory difficulties because of thickening of pharyngeal tissues, degenerative arthropathy, and organomegaly with potential organ dysfunction. Growth of the tumor may lead to signs of CNS disease. As previously mentioned for hyperadrenocorticism, clinical signs may also be very subtle or even absent. Acromegaly has long been considered a rare disorder. However, it was recently suggested that acromegaly occurs more frequently than previously thought and is most likely underdiagnosed. Because the availability of a validated GH assay for cats is inconsistent, diagnosis is usually based on the finding of high IGF-1 concentration. Two important points should be kept in mind. First, circulating IGF-1 is bound to proteins, which must be removed before measurement. Not all assay methods are equally effective, and intra assay inference of binding proteins may lead to false high IGF-1 levels. Therefore, only assays validated for the cat should be used. Second, IGF-1 concentrations are often low in newly diagnosed diabetic cats and increase markedly after initiating insulin therapy. Low IGF-1 levels have also been seen initially in untreated diabetic cats with acromegaly. This observation is explained by the fact that relatively high insulin concentrations are required in the portal vein for the expression and function of GH receptors on hepatocytes, and this mechanism is impaired in insulin-deficient states. IGF-1 is therefore measured 6 to 8 weeks after initiating insulin therapy.

Problems with insulin therapy

- Inactive insulin
- Improper insulin syringe
- Diluted insulin
- Improper administration technique
- Inadequate dose
- Somogyi response
- Inadequate frequency of insulin administration
- Impaired insulin absorption
- Anti-insulin antibody formation (rare)

Caused by concurrent disorder

- Diabetogenic drugs
- Hyperadrenocorticism
- Diestrus (intact female dogs)
- Infection, especially of skin, oral cavity and urinary tract
- Chronic inflammation, especially pancreatitis and oral cavity
- Severe obesity
- Hyperlipidemia
- Hypothyroidism
- Hyperthyroidism (cat)
- Acromegaly (cat)
- Renal insufficiency
- Liver insufficiency
- Cardiac insufficiency
- Pancreatic exocrine insufficiency
- Neoplasia
- Glucagonoma
- Pheochromocytoma

Many disorders can interfere with the effectiveness of insulin therapy. The most common disorders causing insulin resistance in dogs include severe obesity, use of diabetogenic drugs (glucocorticoids), hyperadrenocorticism, diestrus, chronic pancreatitis, renal insufficiency, oral and urinary tract infections, hyperlipidemia, and antiinsulin antibodies in dogs receiving beef source insulin. Obtaining a complete history and a thorough physical examination are the most important steps in identifying these concurrent disorders. Abnormalities identified on the physical examination may suggest a concurrent insulin-antagonistic disorder or infectious process, which will give the clinician direction in the diagnostic evaluation of the dog. If the history and physical examination are unremarkable, a CBC, serum biochemical analysis, serum progesterone concentration (intact female dog), abdominal ultrasound, and urinalysis with bacterial culture should be obtained to further screen for concurrent illness. Additional tests will be dependent on results of the initial screening tests.

Diagnostic tests to consider for the evaluation of insulin resistance in diabetic dogs and cats

- Complete blood count, serum chemistry profile, UA and UMIC
- cPLI (pancreatitis)
- TLI (if suspect EPI)
- Adrenal Function Testing
    - Dexamathsone suppression test (cats)
    - ACTH stimulation (likely less affected by concurrent diabetes in dogs)
- Thyroid Function Testing
    - TT4
    - fT4 (if TT4 is less than 1.5 ug/dl in a dog or between 2.5 – 4.0 ug/dl in a cat)
- Serum progesterone levels (diestrus in dogs)
- Serum IGF-1 concentrations (cats with suspected acromegaly)
- Fasting triglycerides and cholesterol
- Abdominal ultrasonography (pancreatitis, neoplasia, adrenal masses or enlargement)
- Thoracic radiographs (cardiopulmonary disease, neoplasia)
- MRI (if document PDH or acromegaly)

A Fool-Proof Method for Managing Hypothyroidism in Dogs

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Canine hypothyroidism, while a common endocrinopathy in the dog, may be over diagnosed due to confusion/inconsistencies in establishing a definitive diagnosis.

Etiology/pathophysiology

Hypothyroidism is due to decreased thyroidal production of the thyroid hormones thyroxine (T4) and triiodothyronine (T3). Greater than 90% of cases are primary and are due to acquired immune mediated destruction of the thyroid gland which is preceded by thyroiditis, idiopathic atrophy or less commonly neoplasia. Secondary forms of the disease include thyroid stimulating hormone (TSH) deficiency, pituitary neoplasia, and cystic Rathke's pouch, are uncommon clinical entities. Tertiary hypothyroidism with thyrotropin releasing hormone (TRH) deficiency has not been documented in dogs. Congenital cases have been reported in both dogs and cats.

Signalment/history

Hypothyroidism most commonly occurs in young to middle aged dogs with an average age of 7 years. Dogs with autoimmune disease tend to develop hypothyroidism at a younger age. While thyroid values decrease within the reference range in senior dogs, hypothyroidism is very uncommon and other factors (see below) are likely responsible for the observed decreased thyroid concentrations in euthyroid older patients. Spayed females and neutered males are at an increased risk when compared to sexually intact animals. Breed predispositions have been reported for golden retrievers and Doberman pinschers. Thyroiditis is heritable in the beagle, Borzoi, golden retriever, great Dane, Irish setter, Doberman pinscher, and old English sheepdogs.

Risk factors

No known environmental factors have been identified. Breed predispositions as outlined above.

Historical findings

As thyroid hormone regulates the metabolic rate and influences the functions of many organs, clinical signs are often non-specific and insidious in onset. Many other diseases can have similar clinical signs to hypothyroidism, which may lead to an incorrect diagnosis. As such laboratory testing of thyroid function is often performed as part of the diagnostic work in animals with non-thyroidal illness.

Clinical features

Common clinical signs include lethargy, mental dullness, weight gain, exercise intolerance, alopecia, and obesity.

Differential diagnosis

Many metabolic, infectious, neoplastic, congenital, degenerative, and inflammatory diseases can cause similar clinical signs and biochemical abnormalities seen with hypothyroidism.

Diagnostics

Laboratory diagnosis

Thyroxine is the major secretory product of the thyroid while the majority of T3 is derived from extra-thyroidal sources. Both T4 and T3 are highly protein bound to serum carrier proteins such as thyroid binding globulin, transthyretin and albumin. Only unbound (free) hormone is able to penetrate cell membranes, bind to receptors and result in biologic activity. Protein bound hormone acts as a reservoir to maintain steady concentrations of free hormone in the plasma despite rapid alterations in release and metabolism of T3 and T4 and changes in the plasma protein concentrations.

Serum total T4

Serum T4 is a sensitive (>90-95%), but not specific test (70-75%) for the diagnosis of canine hypothyroidism. The vast majority of dogs with hypothyroidism have a serum T4 below normal, but some normal dogs and those with a variety of other problems may have a low serum T4. A diagnosis of hypothyroidism can be ruled out if the T4 is in the upper 50% of the reference range. Autoantibodies to T4 occur in about 15% of hypothyroid dogs, and these antibodies may falsely increase the serum T4 concentration from below normal into or above the normal range. In house testing of TT4 is not recommended.

Serum total T3

Serum T3 concentration is an unreliable test for evaluation of thyroid function.

Serum free T4 (fT4)

Thyroxine is highly (99.9%) protein bound in the circulation. Protein binding can be altered by many nonthyroidal illnesses and by certain drugs. Measurement of the unbound or free hormone can provide a more accurate assessment of thyroid function in these cases (sensitivity > 95%, specificity > 97%). The sensitivity of fT4 is equivalent to or slightly better than total T4 in diagnosing hypothyroidism in routine cases. More importantly, fT4 is more specific, particularly when non-thyroidal factors that can influence

total T4 are present. Free T4 is less affected by most non-thyroidal illness and drugs, but still can be altered in cases of moderate to severe illness. In addition, fT4 by equilibrium dialysis is not affected by the presence of T4 autoantibodies that will falsely elevate total T4. Measurement of fT4 by equilibrium dialysis should be performed when uncommon clinical signs of hypothyroidism are present, the dog is being treated with a drug that may affect thyroid function, when non-thyroidal illness is present, and if autoantibodies to T4 are detected.

Serum TSH

Primary hypothyroidism results in a decrease in T4 and thus decreased negative feedback on the pituitary gland. In response, the pituitary secretes more TSH and plasma TSH levels increase. In man, TSH is elevated prior to any decrease of T4 or fT4 outside the normal range. In the dog, TSH concentration is elevated in only 65-75% of cases of hypothyroidism, as such it lacks sensitivity for use as a screening test. The combination of decreased total T4 or fT4 with an elevated serum TSH is diagnostic of hypothyroidism (specificity > 95%). Therefore, a normal TSH does not rule out hypothyroidism, but an elevated TSH combined with a low T4 or fT4 provides a definitive diagnosis.

Diagnosis of thyroiditis

Antibodies against either T4 or T3 or both are sometimes present in dogs with thyroiditis with or without hypothyroidism. The presence of these antibodies does not indicate that the dog is hypothyroid, but suggests that autoimmune thyroid disease is present. These antibodies frequently cause false elevation of T4 or T3 concentrations that can result in marked elevation of the hormones. Autoantibodies to T4 are present in about 10-15% of hypothyroid dogs.

Dogs with autoimmune thyroiditis may have circulating antibodies to thyroglobulin, the primary protein in the colloid of the thyroid gland. This is not a test of thyroid function, but rather a marker for the presence of autoimmune thyroiditis. In one long-term study at Michigan State University, 20% of asymptomatic, antithyroglobulin positive dogs with normal thyroid function progressed to hypothyroidism in 1 year. The presence of these antibodies in a dog with borderline laboratory evidence of hypothyroidism and clinical signs supports a diagnosis of hypothyroidism.

Additional considerations

Breeds

Certain breeds have normal ranges of thyroid hormones that are different from most other breeds. Few have been evaluated, but greyhounds have serum total T4 and fT4 concentrations that are considerably lower than most other breeds. Scottish deerhounds, Saluki's and whippets also have total T4 concentrations that are well below the mean concentration of dogs in general. Alaskan sled dogs have serum T4, T3, and fT4 concentrations that are below the reference range of most pet dogs, particularly during periods of intense training or racing.

Time of day

In one study 50% of normal dogs had a low serum T4 concentration at some time during the day.

Medications

The drugs that are known to commonly alter thyroid function tests are glucocorticoids, phenobarbital, sulfonamides, clomipramine, aspirin, and some other NSAIDs. Glucocorticoids suppress total T4 and sometimes fT4 as well. Phenobarbital causes decreased total T4 and mild increases in TSH. Sulfonamides can induce overt primary hypothyroidism with clinical signs and thyroid function tests that support the diagnosis. The changes may be reversible when the medication is discontinued. There are dozens of drugs that affect thyroid function and thyroid function tests in man, so many others likely affect the dog as well.

Nonthyroidal illness

Illness not involving the thyroid gland can alter thyroid function tests and has been labeled "non-thyroidal illness" or "euthyroid sick syndrome". Any illness can alter thyroid function tests, causing a fairly consistent decrease in total T4 and T3 concentrations in proportion to the severity of illness. Serum TSH concentration is increased in 8-10% of dogs with non-thyroidal illness. Serum fT4 measured by equilibrium dialysis is less likely to be affected, but can also be increased or decreased. However, in dogs with substantial non-thyroidal illness, the fT4 is likely to be decreased. It is recommended that testing of thyroid function be postponed until the non-thyroidal illness is resolved. If this is not possible, measurement of T4, TSH and fT4 are indicated.

Ancillary testing

Thyroid gland ultrasound

Although rarely necessary, ultrasound of the thyroid glands (by an experienced ultrasonographer) can be used to aid in differentiating dogs with primary hypothyroidism from those with non-thyroidal illness. Thyroid glands of hypothyroid dogs tend to be smaller, less homogeneous, and hypoechoic than those of euthyroid dogs. There is considerable overlap with the ultrasonographic appearance and size of the thyroid glands of euthyroid and hypothyroid dogs. Thyroid ultrasound can only be used to help support a diagnosis of hypothyroidism if the thyroid glands are quite small.

Therapeutics

Drugs

Levothyroxine is the only hormone that appears necessary for treatment of hypothyroidism. The frequency of levothyroxine dosing is controversial, and the only study to closely evaluate the response to treatment showed that once daily treatment is adequate. However, in clinical practice some dogs seem to respond better to twice-daily treatment.

The initial starting dose is 0.02 mg/kg PO q 24 h. In general you will never have to exceed exceed 0.8 mg as an initial daily dosage even in very large dogs. If the dog has significant cardiovascular disease, diabetes mellitus, or hypoadrenocorticism, treatment should be instituted at 25% of the standard dose, with the dosage increased by 25% every 2 weeks based on clinical response and post-pill testing. Most dogs show improvement within the first 1-2 weeks, with increased activity, improved attitude, and partial or complete resolution of neurologic signs. The cutaneous manifestations of hypothyroidism may take several weeks to months to resolve. Post treatment monitoring may be carried out but clinical response is the most important monitoring tool. Peak T4 concentrations generally occur 4-6 hours after administration of levothyroxine and should be in the high normal to slightly above normal range (40-70 nmol/L). However, the bioavailability of thyroxine ranges from 13 to 87% in the same dog from day to day bringing into the question the utility of random post pill monitoring of TT4. It is likely more meaningful (though more expensive) to measure TSH (especially if the TSH concentration was elevated pre-treatment) or fT4 concentrations after replacement therapy has been started, especially in animals that show a poor clinical response to therapy. Serum TSH concentrations should be in the normal range or undetectable and fT4 concentrations should be in the normal range. Serum concentrations of TSH and fT4 should not be performed until the patient has been on supplementation for at least 2 weeks. If the patient was initially started on twice daily therapy, treatment can be reduced to once daily treatment when a good clinical response has been obtained.

Hyperthyroidism is the most common complication of treatment with levothyroxine, but it is rare in dogs. Clinical signs are similar to those of hyperthyroidism in cats and the diagnosis is confirmed by documenting a substantial elevation of serum T4. Treatment consists of stopping levothyroxine treatment for 2-3 days, then instituting treatment at a lower dose.

Comments

Expected course and prognosis

Response to therapy should be observed in the first 4- 8 weeks post treatment. Improvements in mentation and physical activity may be noted within the first week though some abnormalities, especially dermatologic signs, may take several months to resolve. An absent or incomplete response to therapy may be due to an incorrect diagnosis, poor owner compliance, inadequate dosing, or poor absorption.

Feline Hyperthyroidism: Management and Options for Treatment

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Hyperthyroidism is recognized as the most common endocrinopathy of older cats. Despite worldwide occurrence, the pathogenesis of feline hyperthyroidism remains unclear. Traditional methods of managing feline hyperthyroidism include thyroidectomy, anti-thyroid medications, and radioactive iodine. Recent studies document that another option now exists for hyperthyroid cats; feeding a limited-iodine food normalizes thyroid hormone concentrations and alleviates clinical signs of hyperthyroidism. Surgery and radioactive iodine are designed to provide permanent solutions, whereas, oral anti-thyroid drugs and nutritional management control hyperthyroidism and are needed daily to achieve/maintain their effect. All management options are effective and each has its pros and cons. It's important to discuss all options with pet owners so the appropriate management can be selected for each hyperthyroid cat.

Diagnosis

Diagnosis most often is based on the presence of one or more typical clinical signs and increased serum total thyroxine (T_4) concentration. However, up to 10% of all hyperthyroid cats and 40% of those with mild disease have serum T_4 values within reference range [1,2] The diagnosis of hyperthyroidism should not be excluded on the basis of a single normal serum T_4 value, especially in a cat with typical clinical signs, a palpable thyroid nodule and serum T_4 in the upper half of the normal range.[3] In these cases, serum free T_4 (fT_4), measured by equilibrium dialysis, may provide an alternative means of diagnosing hyperthyroidism in cats with normal serum total T_4 values. Studies document that up to 20% of sick euthyroid cats can have increased fT_4 concentration.[4] Therefore, it is most appropriate and reliable to interpret the two values together. Mid-to-high reference range total T_4 and increased fT_4 concentration is consistent with hyperthyroidism. In contrast, low total T_4 and increased fT_4 values are usually associated with non-thyroidal illness.

Management options

Once hyperthyroidism has been diagnosed, all management options (thyroidectomy, radioactive iodine, anti-thyroid drugs, nutritional management) should be discussed with pet owners. All options can be ≥ 90% effective for controlling hyperthyroidism when used appropriately. The selected management option will differ for each cat based on several considerations **(Table 1)**. Radioactive iodine therapy is considered the gold standard for treatment of hyperthyroidism; however, most pet owners currently opt for medical management. Until recently, this included oral or transdermal anti-thyroid drugs. Now nutritional management using a limited-iodine food is another option for cats with hyperthyroidism.

Radioactive iodine

Radioiodine treatment is often considered the best option for many hyperthyroid cats because:

- It has the potential to eliminate a benign thyroid tumor or abnormal thyroid tissue with a single treatment
- It treats extra-thyroidal thyroid tissue, which may occur in 10 to 20% of hyperthyroid cats
- No general anesthesia is required
- Reported side effects are minimal

Cats should be stable prior to radioiodine therapy; those with clinically significant cardiovascular, renal, gastrointestinal, or endocrine (e.g., diabetes mellitus) disease may not be very good candidates, especially because of the time necessary for boarding after treatment.[5]

After administration, radioactive iodine is actively concentrated by the thyroid gland and has a half-life of 8 days. It emits both ß-particles and γ-radiation; the ß-particles are responsible for the majority of tissue destruction, but are only locally destructive, traveling a maximum of 2 mm. Therefore, no significant damage to adjacent parathyroid tissue, atrophic thyroid tissue, or other cervical structures is expected. The main limitation to widespread use of radioactive iodine is the requirement for special licensing and the isolation of the cat for variable periods after treatment. This can range from several days to several weeks depending on state or local radiation regulations and the dose administered.[6]

The goal of treatment is to restore euthyroidism with the smallest possible single dose of radioactive iodine, while avoiding development of hypothyroidism.[6] Controversy exists as to the best method of calculating the optimum dose for individual cats. [5,6] Based on the majority of reported cases, post-treatment hypothyroidism is transient and generally uncommon (2 to 7% of cases); even fewer cats have clinical signs or appear to require thyroid hormone replacement. [7-11] However, up to 30% (50 of 165 cats) were hypothyroid 3 months after radioactive iodine therapy in one study; of these, 56% (19 of 34 hypothyroid cats with available information) had clinical signs of hypothyroidism and 52% (23 of 44 cats) were given thyroid hormone supplementation.[12] Thyroid hormone replacement may be needed in some cats, especially those with concurrent kidney disease, since hypothyroidism has been

associated with azotemia and decreased survival time in previously hyperthyroid cats.[13] Owners should be advised of this possibility, particularly if their motivation is to avoid long-term oral medication.

Anti-thyroid drugs

Anti-thyroid drugs (e.g., methimazole, carbimazole) are commonly used for treatment of hyperthyroidism in cats. [14-21] If administered appropriately, they reliably inhibit the synthesis of thyroid hormones and thereby lower serum thyroid hormone concentrations. These drugs do not affect the thyroid gland's ability to trap inorganic iodide or release preformed hormones. They are widely recommended to stabilize hyperthyroid cats prior to surgery and are the only drugs that can be used chronically for management of hyperthyroidism.[6] Almost all cats are potential candidates unless thyroid carcinoma is suspected.

Anti-thyroid drugs used most often in cats include methimazole and carbimazole; both can be given orally or formulated for transdermal application. Custom formulation of transdermal products may increase expense of therapy and stability of the product is not guaranteed. Results of a recent prospective study conducted in New Zealand showed that once daily treatment for 12 weeks with transdermal methimazole in a novel lipophilic vehicle was as effective as twice-daily carbimazole administered orally.[14]

While many cats have been successfully managed long-term with anti-thyroid drugs, it's important to monitor for potential side effects that have been associated with their use.[15,18,19,21] In the study with the largest number of cats, 18% had side effects associated with methimazole; a more recent study revealed that 44% of 39 cats had side effects.[15,19] In 44 cats receiving carbimazole for 1 year, 44% had associated side effects with gastrointestinal signs (decreased appetite, vomiting, diarrhea) being most common. In another study, 13% of 39 cats treated with carbimazole experienced side effects.[18] It's difficult to determine what % of side effects are caused by the drug versus something else such as concurrent disease.[21]

Most adverse reactions occur within the first few weeks to months after beginning therapy and include depression, inappetence, vomiting, and self-induced excoriations of the head and neck (facial pruritus). Gastrointestinal signs are less common with transdermal administration of methimazole.[16] Mild to serious hematological complications, including agranulocytosis and thrombocytopenia either alone or concurrently, and more rarely immune-mediated hemolytic anemia may also occur. Hepatic toxicity with marked increases in bilirubin concentration and hepatic enzyme activities has been described in less than 2% of cats treated with methimazole. Cessation of therapy is required if either serious hematologic or hepatic reactions develop. Serum antinuclear antibodies develop in approximately 50% of cats treated with methimazole for longer than 6 months, usually in cats on high-dose therapy (> 15 mg/day). Although clinical signs of a lupus-like syndrome have not been reported, decreasing the daily dosage is recommended.[6]

Nutritional management

Production of thyroid hormone requires uptake by the thyroid gland of sufficient amounts of iodine, which is provided by dietary intake. The only function for ingested iodine is for thyroid hormone synthesis.[5] This observation led to the hypothesis that limiting dietary iodine intake could be used to control thyroid hormone production and potentially manage hyperthyroidism in cats. After more than a decade of research and development, a limited-iodine therapeutic food (Hill's® Prescription Diet® y/d™ Feline) containing < 0.3 ppm (mg/kg) iodine on a dry matter basis (DMB), is now available as an option for managing cats with hyperthyroidism.

Iodine content of commercial cat foods

Iodine occurs naturally in many ingredients typically used in the manufacture of commercial pet foods (particularly fish, shellfish and fresh meats) and unless steps are taken to strictly control the iodine content of ingredients, the final iodine concentration in pet foods varies widely.[22-25] Commercial cat foods in New Zealand had iodine amounts ranging from 0.19 to 21.2 ppm in one study whereas in Germany a range of 0.22 to 6.4 ppm was reported.[22,26] Evaluation of 28 canned cat foods in the US revealed an iodine content ranging from 1.09 to 52.3 ppm (mean = 7.83) and 14 dry cat foods contained iodine amounts ranging from 1.34 to 5.94 ppm (mean = 2.77). [25] Based on these studies, the amount of iodine is much higher in many canned foods compared with dry foods and variability of iodine content is much greater in canned food. [22,25-26]

Multiple feeding trials have been conducted in a research colony using over 100 cats with naturally occurring hyperthyroidism to determine the safety and effectiveness of limited dietary iodine in the management of the disease. The results of all studies support that a therapeutic food with dietary iodine ≤ 0.3 ppm iodine (dry matter basis) provides a safe and effective management option for cats with naturally occurring hyperthyroidism. Serum total thyroxine concentrations return to the normal range within 4 to 12 weeks of initiating nutritional management and 90% hyperthyroid cats maintained on the limited-iodine food as the sole source of nutrition become euthyroid.

Three studies were designed to determine the magnitude of iodine control necessary to return newly diagnosed cats to a euthyroid state;[27] the maximum level of dietary iodine that maintains cats in a euthyroid state;[28] and the effectiveness of a therapeutic food formulated based on the previous studies to control naturally occurring hyperthyroidism in cats.[29] In summary, results of these studies demonstrated that a food with 0.17 or 0.32 ppm iodine (DMB) maintained normal thyroid hormone concentrations in hyperthyroid cats, helping to further define the range of iodine effective for managing hyperthyroidism.

We have treated 22 cats to date with feline y/d with follow-up data for at least 6 months. All of the cats found at least one form of the diet (dry or canned) to be palatable. Nineteen of 22 (86%) cats experienced clinical improvement with normalization of their TT4 concentrations. Of the three cats that failed to achieve remission, 2 cats were discovered to be eating foods other than y/d and when the owners switched them to y/d exclusively remission of hyperthyroidism was achieved. One cat (5%) failed to respond to dietary therapy and was subsequently treated with 131-I.

We are currently conducting a prospective study evaluating the efficacy of feline y/d in managing feline hyperthyroidism to include monitoring of thyroid function (TT4, fT4ED, TSH), clinical signs, body weight, renal function and blood pressure pre and post-treatment. The study should be completed in 2015.

Newly diagnosed patients

After confirming the diagnosis and performing a thorough patient evaluation, nutritional management should be discussed along with other options for managing hyperthyroidism. If selected as the management option, gradual transition to the limited-iodine food (Hill's® Prescription Diet® y/d™ Feline) over at least 7 days is recommended. It is very important to counsel owners so they understand that success of nutritional management depends on the limited-iodine food being the sole source of nutrition for their cat.

The first recheck evaluation should be done 4 weeks after completing the transition to y/d Feline (i.e., once the cat has eaten y/d exclusively for 4 weeks) and as a minimum should include physical examination and measurement of T_4, BUN, serum creatinine, and urine specific gravity. All cats should have decreased T_4 concentrations compared with baseline and many will have returned to normal by the 4-week evaluation. Clinical improvement including weight gain, improved hair coat and decreased tachycardia/cardiac murmur also may be noted by the first evaluation. Clinical signs should continue improving by the next re-evaluation at 8 weeks and most cats will be euthyroid. Some cats require slightly longer to become euthyroid; however, it's expected that 90% will have normal T_4 concentrations if the limited-iodine food is their sole source of nutrition.

If euthyroidism is not achieved within 4 to 12 weeks, a thorough history is indicated to confirm that only the limited-iodine food is being fed.

Managing hyperthyroid cats with concurrent kidney disease

Chronic kidney disease (CKD) and hyperthyroidism are more likely to be diagnosed in older cats so it's not surprising that many hyperthyroid cats have CKD. Untreated hyperthyroidism complicates the diagnosis of CKD because it's associated with increased glomerular filtration rate (GFR) and therefore often masks biochemical markers of CKD. Regardless of the therapeutic modality (methimazole, surgical thyroidectomy, or radioiodine), decreased GFR, increased serum urea and creatinine concentrations and development of overt clinical signs of kidney disease have been reported after successful treatment of hyperthyroidism.[4,33-36] The presence of underlying CKD may affect the prognosis - one study documented a shorter survival time in hyperthyroid cats with azotemia.[7] However, two recent studies comparing survival of cats that developed azotemia with those that did not after treatment of hyperthyroidism found no significant difference between the two groups if cats did not become hypothyroid post-treatment.[38,39]

The reported occurrence of azotemia after treatment of hyperthyroidism ranges from 15 to 49%. [31,35-37,40] Iatrogenic hypothyroidism has been reported to decrease GFR in human patients.[41] Post-treatment iatrogenic hypothyroidism has been reported in cats after radioiodine therapy and bilateral thyroidectomy, which constituted the predominant therapeutic modalities in previous studies.[40] In one recent study, cats with iatrogenic biochemical hypothyroidism were almost twice as likely to develop azotemia post-treatment as euthyroid cats.[38] The hypothyroid cats with azotemia had shorter survival times than cats without azotemia, whereas, consistent with previous reports, there was no difference in survival times of euthyroid cats with or without azotemia.

It's not possible to consistently predict which cats will develop overt CKD after treatment of hyperthyroidism or have progression of their kidney disease. This should be considered when deciding on treatment options, particularly those that are irreversible (thyroidectomy, radioactive iodine). Regardless of the option selected for managing hyperthyroidism, it's important to remember that the only intervention shown to improve quality of life and prolong survival time in cats with naturally occurring CKD is feeding a therapeutic renal food.[42,43] Until recent availability of limited-iodine food, nutritional recommendations have not generally been considered for hyperthyroid cats without azotemia. In cats with compromised renal function, but without azotemia (IRIS Stage 1), the decrease in GFR associated with normalizing serum T_4 levels may be sufficient to prevent effective clearing of protein metabolic by-products (BUN and creatinine) when dietary intake of protein and phosphorus is high. This could contribute to the occurrence of post-therapy azotemia in hyperthyroid cats.

In our work with 22 cats with hyperthyroidism treated with feline y/d, 4/22 cats (18%) were azotemic (IRIS Stage 1 and 2 CKD) prior to starting the diet. All 4 cats experienced normalization of their BUN and creatinine within 30-150 days along with normalization of their TT4's. One potential explanation is that the expected decrease in GFR associated with normalizing serum T_4 may be offset by the nutrient profile of the limited-iodine food which is similar foods for mature adult cats or cats with early CKD. Additional study is needed to better understand the effects of using limited-iodine food on hyperthyroid cats with concurrent kidney disease.

Conclusions/summary

Hyperthyroidism is the most common endocrine disease of older cats worldwide. While the pathogenesis is unclear, several effective management options are available. All should be discussed with pet owners, including pros/cons, so that the best option can be selected for individual patients and their owners. Feeding a limited-iodine food is now available as an option for effective management of hyperthyroid patients. When fed as the sole source of nutrition, approximately 90% of hyperthyroid cats become euthyroid within 4 to 12 weeks. To date, over 150 cats with naturally occurring hyperthyroidism have been managed successfully by feeding a limited-iodine food, most for 2-3 years and some cats for as long as 6 years.

Getting to the Bottom of Polyuria and Polydipsia

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Introduction

A. Polyuria and polydipsia (PU / PD) refer to excessive water consumption and urine production respectively. These are common clinical signs in both dogs and cats.

B. Water consumption exceeding 100 ml/kg or urine production exceeding 50 ml/kg body weight per day is considered abnormal and should be pursued. These numbers have been established in laboratory reared dogs and may not reflect "normal" water consumption in pets. They are to be used only as guidelines.

C. Water consumption can vary greatly from day to day so it is important to have owners subjectively assess water consumption in the home environment for several consecutive days in order to obtain an accurate picture before beginning unnecessary and expensive diagnostic tests. Actual quantification of water consumption can be very difficult and may not be practical for the majority of pet owners.

Normal water homeostasis

A. Extracellular fluid volume is maintained by regulation of fluid intake and urine production.

B. The thirst center is stimulated by an increase in plasma osmolality (sodium concentration) and/or a decrease in blood volume (hypovolemia) resulting in an increase in water consumption.

C. Increasing plasma osmolality and hypovolemia also stimulate osmoreceptors in the anterior hypothalamus and baroreceptors in the aortic arch resulting in the release of antidiuretic hormone (ADH) from the anterior pituitary.

D. ADH circulates and binds to receptors on the renal tubular cells of the distal tubules and collecting ducts resulting in the production of cAMP. This causes the opening of pores in the luminal membrane of the tubular cells and allows for reabsorption of water from the glomerular filtrate resulting in a concentrated urine. In order for water to be pulled out of the tubule it must move along a concentration gradient maintained by the hypertonic renal medullary interstitium. Loss of this gradient (medullary washout), will result in an inability to concentrate urine even in the face of normal ADH activity. Urea and sodium are largely responsible for maintaining the hypertonicity of the interstitium.

E. The sensation of thirst and secretion of ADH are suppressed when plasma osmolality and blood volume are returned to normal.

Differential diagnosis: Mechanisms of PU/PD

A. Renal disease:
   a. Chronic renal failure: A decrease in the number of functional nephrons causes an increase in tubular flow in the remaining nephrons and leads to a solute diuresis. A decrease in urine concentrating ability may be the only laboratory abnormality indicating renal disease (especially in feline patients) presented for PU/PD.
   b. Pyelonephritis: Bacterial induced tubular destruction and an increase in renal blood flow cause a decrease in medullary hypertonicity.
   c. Primary renal glycosuria (Fanconi's Syndrome): A proximal tubular defect results in renal glycosuria leading to an osmotic diuresis. The blood glucose is normal.
   d. Post-Obstructive diuresis: May be seen in previously blocked cats. Due to osmotic diuresis from loss of large amounts of sodium and urea into the urine following relief of urethral obstruction.

B. Diabetes mellitus:
   a. Hyperglycemia results in glycosuria and an osmotic diuresis. Threshold for renal glycosuria is a blood glucose of 180 – 220 mg/dl (dog) and 240 – 300 mg/dl (cat).

C. Liver disease:
   a. PU/PD may occur as the result of: (1) decreased production of urea which is a major component of the hypertonic medullary interstitium, (2) increased renin and cortisol levels due to a lack of hepatic degradation, (3) increased aldosterone concentration leading to increased sodium concentration, and (4) hypokalemia (see hypokalemic nephropathy).

D. Hyperthyroidism:
   a. Increased total renal blood flow reducing the tonicity of the medullary interstitium.
   b. Psychogenic polydipsia or primary polydipsia is reported in humans with hyperthyroidism.

E. Hypercalcemia:
   a. Interference with cAMP activation by ADH,damage to ADH receptors, and mineralization of renal tubular

cells.

F. Hyperadrenocorticism:
   a. Glucocorticoids interfere with the action of ADH at the renal tubule and decrease
   b. ADH secretion by reducing osmoreceptor sensitivity to rising plasma osmolality.

G. Hypoadrenocorticism:
   a. Renal sodium wasting leads to decreased medullary hypertonicity.

H. Pyometra:
   a. coli endotoxins interfere with sodium reabsorption and damage ADH receptors and may result in an immune-complex glomerulonephritis.

I. Hypokalemia:
   a. Degeneration of renal tubular cells, (2) decreased medullary hypertonicity, stimulation of thirst, and (4) stimulation of renin release.

J. Polycythemia:
   a. Mechanism unknown; may be related to sluggish blood flow in kidney or hypothalamus.

K. Medications:
   a. Exogenous steroids, diuretics, salt supplementation, primidone, phenobarbital, KBr and vitamin D.

L. Pituitary or central diabetes insipidus (CDI):
   a. Due to inadequate production, storage or release of ADH. May occur as a congenital defect or secondary to trauma, mass lesions, infection or infarction of the pituitary or hypothalamus.

M. Nephrogenic diabetes insipidus (NDI):
   a. Congenital structural or functional defects in ADH receptor. Rare in dogs and cats.

N. Primary polydipsia or psychogenic polydipsia:
   a. Underlying cause unknown (possible CNS lesion); results in increased renal blood flow and a decrease in medullary hypertonicity. Extremely uncommon in dogs and cats and is largely a diagnosis of exclusion.

Diagnostic approach to PU / PD

A. Document PU/PD actually exists. Recommend assessment of water consumption in the home environment. Hospitalized animals frequently do not drink as much as they would in their natural surroundings.

B. Quick evaluation of urine specific gravity and glucose is cheap, easy, and very helpful in evaluating animals for possible pathologic PU/PD. If the urine specific gravity of a non- glycosuric sample, obtained from a dog or cat without signs of dehydration, is greater than 1.030 (dog) or 1.035 (cat), the likelihood of pathologic PU/PD is small and further work-up may not be required.

C. Most causes of PU/PD will be identified following a good history, physical examination, and an initial data base consisting of a CBC, chemistry profile, and urinalysis with bacteriologic culture.

D. If a cause has not been discovered after step C, the most likely diagnoses are hyperadrenocorticism (dog only, cats with Cushing's are usually overtly diabetic), central and nephrogenic diabetes insipidus, and primary polydipsia. As hyperadrenocorticism is far more common than either of the other causes, an ACTH stimulation test, urine cortisol/creatinine ratio or low-dose dexamethasone suppression test should be performed before proceeding to the modified water deprivation test (See Canine Hyperadrenocorticism).

Modified water deprivation test (MWDT)

A. This test is designed to help differentiate CDI, NDI, and primary polydipsia. It is not very helpful unless other causes of PU/PD have been ruled out.

B. The test is designed to determine whether ADH is released in response to dehydration and whether the kidneys can respond to the circulating ADH.

C. VERY IMPORTANT !! THE TEST SHOULD NEVER BE PERFORMED ON AN ANIMAL WITH PRE-EXISTING AZOTEMIA OR OBVIOUS DEHYDRATION. DOING SO IN ANIMALS WITH RENAL INSUFFICIENCY MAY RESULT IN DECOMPENSATION AND THE DEVELOPMENT OF OLIGURIC RENAL FAILURE OR ANURIC RENAL FAILURE.

D. Severe dehydration can occur very rapidly (4-6 hours) especially in animals with diabetes insipidus. Leaving them unattended without water for several hours or overnight may result in severe hyperosmolality, coma, and death.

E. Gradual water restriction should be instituted at home for 2-3 days prior to performing the MWDT in order to help minimize medullary washout from long-standing PU/PD.

Phase one

1. Animal is weighed, bladder emptied and urine saved for specific gravity and osmolality (if available).

2. Blood is obtained for BUN and osmolality.
3. Water is withheld. BUN, plasma osmolality and body weight are obtained hourly. The bladder is emptied every hour and a sample is saved for specific gravity and osmolality.
4. Test concluded with either a 5% loss in body weight, azotemia (BUN > 30), or urine specific gravity > 1.030 (1.035 cats). The bladder is emptied and urine is saved for specific gravity and osmolality, and plasma is obtained for osmolality.

Phase two

1. Aqueous vasopressin (Pitressin) 2 - 3 units (dog) or 0.25 U/# (cat) is given SQ. Alternatively DDAVP may administered into the conjunctival sac (1 – 2 drops for dogs and 1 drop for cats).
2. Urine and plasma osmolality and urine specific gravity are obtained every 30 min for 90 minutes.
3. Bladder must be emptied at every 30 minute sampling period.
4. Water is withheld throughout the test.

Interpretation of the MWDT

A. Normal Animals: Following water deprivation will concentrate urine to > 1.030 (dog) or 1.035 (cat). Urine osmolality in excess of 1,200 mOsm/kg.
B. CDI: Unable to concentrate urine in excess of 1.008 (< 300 mOsm/kg). After ADH administration, urine specific gravity should increase to greater than 1.012 with a 50 - 500 % increase in urine osmolality.
C. NDI: Similar to CDI following water deprivation. No further response following ADH injection.
D. Partial CDI: Results depend on how much ADH is available. Following water deprivation urine specific gravity between 1.008-1.019 and urine osmolality between 300 to 1,000 mOsm/kg. Urine specific gravity and osmolality increase after ADH administration. Similar response seen with hyperadrenocorticism and a number of the other causes of PU/PD. This is why it is important to rule-out these processes prior to a MWDT.
E. Primary polydipsia: Depends on degree of medullary washout. With minimal washout results are similar to normal animals. More severe washout gives results similar to partial diabetes insipidus.

Treatment of polyuria and polydipsia

A. Treat the underlying disorder !
B. Treatment of CDI
    a. DDAVP (Desmopressin acetate) 1-2 drops into the conjunctival sac or 0.01 to 0.05 mls subcutaneously SID or BID. May also dose orally with 0.1 to 0.2 mg once or twice a day.
        i. 1 drop = 1.5 to 4.0 ug. Can use TB syringe to dose.
        ii. Duration 8 - 24 hours.
        iii. Redosed when polyuria returns.
        iv. Most commonly used treatment today.
        v. Use the intranasal preparation.
    b. Chlorpropamide (Diabenese)
        i. Oral hypoglycemic. Stimulates ADH release and potentiates ADH action. Hypoglycemia is the limiting factor.
        ii. 25 - 40 mg once or twice a day (cat). Limited experience.
C. Treatment of NDI
    a. Salt restriction
    b. Thiazide diuretics:
        i. Natriuresis results in a decrease in blood volume and increased sodium reabsorption in the proximal tubule.
        ii. Hydrochlorothiazide 12.5 - 25 mg once or twice a day (cat).
        iii. Chlorthiazide 20 - 40 mg/kg BID (dogs).
        iv. May also help with partial CDI.
D. Treatment of Primary Polydipsia
    a. Treatment to restore hypertonic renal medullary interstitium.
    b. Gradual water restriction over several days.
    c. Behavioral modification or referral to a behaviorist may be needed.

Diabetes Mellitus in Dogs: Acute Care and Long-Term Management and Helping Clients Pay for it

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Diabetes mellitus is a common endocrine disorder in dogs and cats. Recent data has shed light on the pathogenesis of the disorder in dogs and cats and has highlighted the role of diet, insulin and novel hypoglycemic therapies. In the majority of cases, the most appropriate therapy in both dog and cats includes the administration of insulin.

The key to successful management of the diabetic patient lies in close communication with the pet owner and prompt recognition and treatment of concurrent disorders.

Key facts

1. Insulin is still the mainstay of therapy in the majority of dogs and cats with diabetes mellitus.
2. Diet is an important part of diabetic management especially in obese patients and cats.
3. Auto-immune disease, pancreatitis and amyloidosis are the most common causes of diabetes in dogs and cats.

Successful management of the diabetic patient involves many factors. An understanding of dietary therapy, insulin preparations, oral and novel hypoglycemic agents and management of concurrent illness, are all required to optimize glycemic control. The goals of therapy are to control clinical signs, prevent or slow the progression of cataracts, avoid hypoglycemia and maintain ideal body weight. An additional goal in cats is to obtain remission. The challenge is to address these concerns while attempting to help the owners deal with what they may consider a time consuming, expensive and chronic medical condition.

Diabetes Mellitus in dogs and cats results from a decrease in insulin secretion from the beta cells of the pancreas and/or a decrease in insulin action. There are three classifications of diabetes:

Type I diabetes is comparable to insulin dependent diabetes mellitus (IDDM) in humans. It results in low basal insulin concentrations with impaired insulin secretion following a glucose load. Treatment requires insulin injections. It is the most common form of diabetes in dogs.

Type II diabetes is similar to non-insulin dependent diabetes (NIDDM) in humans and is managed with dietary therapy and oral hypoglycemics. It causes normal to increased basal insulin concentrations with decreased secretion following a glucose load. Insulin may or may not be required for animals with Type II diabetes.

Type III diabetes is seen most commonly in hormonally-induced diabetes in dogs and cats and is similar to impaired glucose tolerance (IGT) in humans. Diabetogenic hormones (epinephrine, cortisol, glucagon and growth hormone) or medications interfere with insulin action and cause glucose intolerance, which can lead to diabetes.

Etiology and signalment

Canine

There are some distinct differences in the etiology of canine and feline diabetes. In dogs, it is generally thought to be an immune mediated disease with gradual destruction of beta cells. The progression from normal, to glucose intolerant, to diabetes, is generally slow so that most islets (over 90%) are lost before diabetes occurs. Other causes of diabetes in dogs include genetic predisposition, chronic pancreatitis and medication-induced diabetes (*glucocorticoids* and *megestrol acetate*).

Genetic predisposition to diabetes is most common in the following breeds: German Shepherd dogs, Schnauzers, Beagles, and Poodles. Golden Retrievers and Keeshonds are more prone to juvenile diabetes.

Gender is a factor in dogs with females being three times more likely to develop diabetes than males. Generally, diabetes occurs in dogs in middle age (6-9 years) but can also present earlier for specific breeds, particularly the Golden Retriever and Keeshond.

Feline

The most common causes of diabetes in cats are obesity, pancreatitis and most commonly, amyloidosis of the pancreatic beta cells. There appears to be very little gender predisposition to this disease in cats, although it is slightly more common in males than females. As with dogs, the onset of diabetes in cats occurs most often in middle age.

Clinical signs

The clinical signs of diabetes include PU/PD (polyuria and polydipsia) from hyperglycemia, resulting in glycosuria and a resultant osmotic diuresis. Polyphagia and weight loss is common although many animals will still be obese upon presentation. In addition to the polyphagia, there may be variable degrees of dehydration especially in the cat. Cataract formation is very common in dogs with diabetes, but rare in cats. Cats often present with icterus as a result of concurrent hepatic lipidosis and/or pancreatitis. Icterus is not common in dogs unless they have pancreatitis. Cats may also exhibit a plantigrade stance (peripheral neuropathy) that is directly related to the severity and duration of hyperglycemia. Clinical neuropathies do occur in dogs, but are extremely rare.

Differential diagnoses include: hyperthyroidism (in cats), gastrointestinal lymphoma, hepatic disease, renal disease, pancreatitis, hyperadrenocorticism, and acromegaly.

Diagnosis

Diagnosis involves testing for persistent fasting hyperglycemia, with fasting blood glucoses greater than 200mg/dl. Clinicians also will need to rule out transient hyperglycemia that may be due to: post-prandial hyperglycemia; diabetogenic hormones (endogenous or exogenous); and stress hyperglycemia. Stress hyperglycemia can be a problem in cats due to the release of epinephrine when stressed or handled.

Laboratory abnormalities include:

- Hemogram
  - non-specific
  - signs of dehydration
- Biochemistry profile
  - hyperglycemia
  - increases in SAP and ALT
  - increases in bilirubin (usually in cats)
    - hepatic lipidosis
    - pancreatitis
- Urinalysis
  - glycosuria
    - renal threshold for glucose
      - canine 180-220mg/dl
      - feline 240-300 mg/dl
  - ketonuria
  - up to 40% of patients will have positive urine cultures in the absence of an active urine sediment.

Treatment

The number one cause of death in diabetic dogs and cats is not the disease itself, rather, it is the owner's frustration with the disease. This is an extremely important point to remember when treating diabetic animals. Good communication with the pet owner is perhaps the most important component of managing the disease.

It is recommended that clinicians schedule a 30-minute appointment with the client at the time of discharge before sending the diabetic patient home for the first time. During this appointment, clinicians should thoroughly discuss the care required for the patient. Include the following instructions in that discussion: how to give the animal injections; how to store insulin, what types of food to feed and how often; how to recognize the signs of hypoglycemia and how t react to this condition. Also include information on what clinical signs to look for in terms of monitoring water intake and urine production. The client should be give written instructions for use as a reference once they are caring for the patient at home. It is essential that the clinician and veterinary staff strive to educate the caregiver and motivate them to get involved in the care of their diabetic pet.

The goals of treatment include elimination of the clinical signs of diabetes, prevention or slowing of cataract formation and resulting blindness, prevention of potentially dangerous hypoglycemia, and prevention and/or treatment of concurrent illness.

Therapy for diabetes centers on three main areas: Treatment of concurrent illness (i.e., urinary tract infections, pydermas, etc.), insulin therapy, and dietary management.

Concurrent illness

Monitoring for concurrent illness is very important in effectively managing diabetic dogs and cats. Clinicians must effectively recognize and treat the other disorders because the concurrent illness will impact the diabetic regulation and many common diseases have similar clinical signs to diabetes mellitus. Even simple problems such as UTI's and pyodermas can result in activation of stress hormones and result in insulin resistance.

Insulin therapy

There has been a considerable amount of confusion over the various insulin preparations that are available. In general, animal origin insulins are being discontinued as the desire and ability to treat people with human derived insulin preparations has progressed.

There is concern that animals receiving human insulin will develop antibodies resulting in decreased insulin activity and/or effectiveness. Dogs receiving any insulin product that is not derived from pork may make antibodies. However, studies have shown that those antibodies do not interfere with the glucose control. In fact, dogs that made antibodies against insulin had a longer duration of insulin action, which actually enhanced the effect of the insulin rather than decreased its efficacy. A recent study in cats should that 13% developed anti-insulin antibodies. None of the cats should signs of insulin resistance.

The options with human insulin include ultra short acting, short acting, intermediate acting, and long-acting insulins. The short acting insulins are primarily used for ketoacidosis, and therefore, are not covered in this article. The intermediate acting insulins are classified as either NPH or Lente. It is important to note however, that even though they are classified as intermediate, they do not behave the same way in the dog or cat. Lente is actually a mixture of two different insulin preparations, which results in a bimodal onset of actions. This is helpful in some patients because is helps block post- prandial hyperglycemia. Conversely, a lente insulin is not recommended for use in an animal that does not develop post prandial hyperglycemia. It is recommended that NPH be used in the majority of dogs and cats with diabetes and it is also understood that most patients will require two injections a day to achieve glycemic control.

Canine patients

Newly diagnosed patients

1. Vetsulin (porcine origin lente): A zinc, porcine, intermediate acting insulin. Canine and porcine insulin have an identical amino acid sequence thereby eliminating the theoretical complication of anti-insulin antibodies and their effect on glycemic control. The suggested, initial starting dose is 0.5 units/kg BID. This insulin is only available at a concentration of 40 iu/ml (U-40) so please make sure that proper insulin syringes are provided to the owner. Re-assessment of clinical signs and a serial blood glucose curve should be performed 1 week after starting therapy. This insulin must be thoroughly shaken before administration. For additional information see: www.vetsulin.com.
2. Humulin N or Novolin N; These are both intermediate acting, human origin insulins. Suggested starting doses are 0.5 units/kg BID. Re-assessment of clinical signs and a serial blood glucose curve should be performed 1 week after starting therapy. I would avoid NPH insulins from Wal Mart due to product inconsistencies.
3. Glargine:
4. Detemir:
5. PZI:

Transitioning canine patients

If you have canine patients currently taking Humulin L lente insulin, I would switch them to either Vetsulin or Humulin N. The initial dose of Vetsulin or Humulin N will remain the same with re-assessment of clinical signs and a serial blood glucose curve performed 1 week after changing insulin preparations.

With the recent introduction of the AlphaTrak Blood Glucose Monitoring System (Abbott) we have the ability to very accurately measure blood glucose concentrations in both dogs and cats using very small quantities of blood. This will allow both veterinarians and pet owners to obtain very reliable results in both the hospital and home setting. This information can then be used to make informed decisions regarding the management of diabetic patients. These decisions impact the type and dose of insulin selected, the frequency of insulin administration, aid in the assessment of glycemic control, help in preventing hypoglycemic episodes and monitor for remission of diabetes especially in feline patients.

Glycemic control can be evaluated in a numbers of ways. Owner assessment of clinical signs (polyuria, polydipsia, weight gain or loss), progression of diabetic cataracts (dogs), presence of peripheral neuropathy (cats), and episodes of hypoglycemia are often the best indicators of glycemic control. Changes in insulin dosage or documenting remission of diabetes, is best determined by blood glucose measurement. Recognizing that the measurement of blood glucose concentrations can be problematic in the hospital setting (especially in cats as a result of stress induced hyperglycemia) recent work has evaluated the practicality and value of at home blood glucose monitoring in dogs and cats. At home blood glucose monitoring is essential in the management of human patients with diabetes given that a number of the complications associated with long term diabetes are directly related to persistent hyperglycemia. While diabetic retinopathy, nephropathy, painful neuropathies and cardiovascular disease are rare in our veterinary patients, adequate glycemic control is required to eliminate clinical signs and decrease morbidity and mortality in dogs and cats. Control of clinical signs does not require the restoration of euglycemia but rather involves keeping the blood glucose levels below renal threshold for the majority of the day. Renal threshold for glucose is 180 mg/dl in the dog and approximately 280 mg/dl in the cat. It is very important that we remember the owners of diabetic dogs and cats are being asked to do a great deal to help in the management of their pet's chronic illness and we need to do whatever we can to make the clients job easier while at the same time taking steps to assure maximal diabetic control.

Using the information derived using at home or in hospital glucose monitoring

Dogs

- Dogs on NPH or Lente Insulins
    - If the preinsulin blood glucose concentration is > 360 mg/dl and/or the nadir blood glucose concentration is > 180 mg/dl the dose of insulin is increased by 25%..
    - If the preinsulin blood glucose concentration is 270 to 360 mg/dl and/or the nadir blood glucose concentration is 90 - 180 mg/dl the dose of insulin is maintained.
    - If the preinsulin blood glucose concentration is 190 - 270 mg/dl and/or the nadir blood glucose concentration is 54 - 90 mg/dl use the nadir, clinical signs and the next preinsulin glucose concentration to determine if the dose is decreased (50%) or maintained.
    - If the preinsulin blood glucose concentration is < 180 mg/dl and/or the nadir blood glucose concentration is < 54 mg/dl the dose of insulin is decreased by 50%.

The use of the AlphaTrak Blood Glucose Monitoring System both in the clinic and at home will greatly improve our ability to assess glyemic control and improve insulin therapy. In conjunction with close observation of clinical signs, at home glucose monitoring should go a long way towards improving the quality of life of diabetic pets and their owners.

Diet

There is a considerable amount of reliable research data showing that diets high in carbohydrates, low in fat and high in fiber are helpful in regulating diabetic dogs. These types of diets lower the average insulin dose, the average blood sugar, the amount of urine being produced and glycosolated hemoglobins and fructosamine levels.

The carbohydrates in these diets are complex carbohydrates. It is important to avoid diets high in simple sugars, which includes any commercial semi-moist food, primarily those packaged in foil packets. Diets high in simple sugars are absorbed very rapidly before the insulin has time to work. The goal with diet is to balance the absorption of sugar with the onset of action of the insulin. A high carbohydrate/low fat diets also decreases plasma free fatty acid and cholesterol concentrations, and increases the number and activity of insulin receptors.

High fiber diets reduce insulin resistance. The fiber acts to decrease post prandial hyperglycemia, primarily because it delays gastric emptying. A high fiber diet also decreases absorption of glucose and increases insulin action at the receptor.

It has recently been suggested that diabetic cats be fed a high protein/low carbohydrate diet. This can be accomplished with several commercially available canned diets (Hill's M/D, IVD Development, Purina DM, many other canned kitten diets). These diets may result in remission of the diabetes and elimination of the need for exogenous insulin and/or oral hypoglycemic agents. High protein/low carbohydrate diets more closely resemble the diet of felines in the wild and may help reduce glucose intolerance, insulin resistance and obesity.

Feeding

Ideally, the feeding schedule should be coordinated with the onset of action of the insulin. With dogs, this is fairly easy to regulate, but with cats, it is nearly impossible due to their "grazing" style of eating. For cat owners who may not be able to follow a strict feeding schedule or those with multiple pet households, insulin therapy will have to be adjusted to meet the owner's needs. The most important component of the dietary plan is to stress consistency in the diet. The following feeding schedule can be used for dogs and some cats. With insulin given once a day, feed three meals a day (of equal calories) at six-hour internals. Give the first meal at the time of the insulin injection. For animals receiving insulin twice a day, feed four meals a day. Schedule them to coincide with the insulin injections and feed mid-afternoon and late evening.

If the owner is unable to follow this schedule, advise them to feed twice a day, at the time of injection and 8-10 hours later (for once a day insulin patients); or at the times of insulin injections (for twice a day insulin patients).

Home management

1. Instruct owner on proper injection techniques, injection locations, storage and handling of insulin.
2. Instruct owner on how to monitor clinical signs.
3. Continue feeding schedule and dietary therapy.
4. Instruct owners to initially monitor urine glucose/ketone levels daily, usually in the morning or evening prior to feeding. If persistent glycosuria or ketonuria is observed, ask owner to contact the veterinary hospital.
5. Advise owners of the signs of and treatment for hypoglycemia. Have owners keep a bottle of Karo syrup on hand if signs occur (i.e., weakness, ataxia, seizures) so they can rub syrup on the gums immediately. Instruct them to call the veterinary hospital.
6. Home monitoring of a diabetic cat is frequently based on observance of clinical signs only.
7. Serial sugars after the first week of home management.

Re-check evaluations

1. Obtain owner assessment of clinical signs.
2. Serial blood sugars are helpful due to:
    a. Variability of insulin action in a given patient.
    b. Inaccuracy of random blood or urine sugars in monitoring the degree of glycemic control.
    c. Not particularly helpful as a routine procedure in animals that are well controlled clinically.
3. Body weight
4. Physical examination/ophthalmic exam
5. Discuss urine log book with owner
6. Laboratory work as clinically indicated
    a. Role of glycosylated hemoglobin and frustosamine:
    b. Fructosamine may be helpful in distinguishing stress-induced hyperglycemia from diabetes in cats. These tests can be used every 3 – 4 months as an indicator of long term (2-3 weeks fructosamine; 4-6 weeks glycosylated hemoglobin) glucose control. Rising values indicate the need for further evaluation.

Problems with insulin therapy

- Insulin induced hyperglycemia (Somogyi phenomenon)
    - Hypoglycemia (<65mg/dl) followed by hyperglycemia (>300mg/dl) within 24 hours of insulin injection.
    - Suspect when insulin requirements exceed 2 U/kg and clinical signs persist.
    - Suspect when animal has signs of hypoglycemia in afternoon.
    - Diagnosis with serial sugars.
    - Treat by decreasing insulin dose 25-50% and review insulin administration with the owner to rule out management problems.
    - Re-check serial sugars in one week.
- Rapid insulin metabolism
    - Duration of insulin less than 18 hours.
    - Signs return in the evening.
    - Diagnosis is with serial sugars. Hyperglycemia (>250) within 18 hours of insulin injection without previous hypoglycemia.
    - Treatment:
        - Review management with owner
        - Switch to twice daily insulin administration. Most dogs and cats require insulin twice a day to achieve adequate glycemic control. Consider switching to PZI in cats.
- Insulin Resistance
    - Hyperglycemia (>300) throughout the day, despite insulin dosages > 2 U/kg.
    - Diagnosis based on serial sugars.
    - Potential causes of insulin resistance:
        - Management problems
        - Hyperadrenocoticism
        - Steroid or Ovaban administration
        - Diestrus or pregnancy
        - Acromegaly
        - Concurrent illness, infection
        - Anti-insulin antibodies
        - Hypothyroidism (dogs), hyperthyroidism (cats)
    - If insulin dose exceeds 2U/kg, the animal should be evaluated for one of these causes of resistance.
- Hypoglycemia
    - Insulin overdosage
    - Suspect if animal shows weakness, shaking, ataxia, seizures at time of insulin's peak effect.
    - Therapy (instructions for owners)
        - Mild signs - give food and call veterinarian
        - Moderate signs - apply Karo syrup to the mouth, offer food when alert and then notify veterinarian.
        - Comatose - apply Karo syrup to mouth and take animal to hospital.
    - When hypoglycemia occurs, serial sugars should be performed to re-assess insulin dose

Rectal Tears:
Act Now!

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Clinical signs

Most rectal tears occur in association with rectal palpation and should be suspected when a sudden decrease in the resistance to palpation is felt or when fresh blood is observed on the palpation sleeve. With grade three or four tears the horse will begin to sweat, develop an increased heart rate, fever, abdominal pain and splinted abdomen in 2-3 hours consistent with signs characteristic of septicemia, endotoxic shock, and peritonitis. Most rectal tears occur dorsally, in a longitudinal direction 25 to 30 cm cranial to the anus in the intra peritoneal portion of the rectum and dissect obliquely for a variable distance along the lateral wall. In this region there is a decrease in the circular muscle thickness that corresponds with the increase in thickness of the mesenteric taenial band of the small colon. The decrease in circular muscle thickness along with a lack of serosal surface of the bowel enclosed in the mesorectum could contribute to the inherent weakness at this site. Rectal tears that occur caudal to the peritoneal reflection may lead to a retroperitoneal abscess that could extend into the abdominal cavity or require draining into the rectum, vagina, or perineum.

Diagnosis

Rectal tears have been classified on a four-grade system. Grade one tears are restricted to the mucosa and submucosa and palpate as a small roughening or defect in the rectal wall associated with bleeding. Grade two tears involve only the muscular layers of the rectal wall while the mucosa and serosa remain intact. No blood is seen on the rectal sleeve and these are considered to be incidental findings. Grade three lesions involve all tissue layers except the serosa or mesorectum. There are deep defects that are often filled with feces. Grade 3A tears have the serosal covering of the intact bowel, whereas Grade 3B tears occur dorsally into the fat filled mesorectum. Grade four tears involve a perforation of all layers of the rectal wall which permit direct communication between bowel contents and the abdominal cavity. Palpation of the abdominal organs directly is possible through a Grade 4 tear. Circumferential retroperitoneal rectal tears have been reported but are infrequent.

When a rectal tear occurs, prompt action will often improve the patient's chance of survival and the veterinarian's defense against litigation. An epidural anesthetic and sedation (xylazine 0.4 mg/kg intravenously and butorphanol tartrate 0.05 mg/kg IV) will help facilitate a careful examination of the rectum. Careful determination of the extent and exact location of the tear can be facilitated by bare arm palpation or cutting the fingers off a normal rectal sleeve and using a latex exam glove over the exposed fingers. The feces should be carefully removed from the rectum before beginning the rectal examination. The tear may then be located by sequentially inserting a hand into the rectum further each time until blood is observed. A vaginal speculum can help to visualize the tear; however the rectal mucosa usually folds around the speculum, making direct visualization difficult. Careful palpation will determine the severity of the tear once it is located. The tear should be very gently felt for position, distance from the anal sphincter, size and depth. Any feces in or around the tear should be very carefully removed. The improper healing of grade one or two rectal tears can lead to abscess and/or fistula formation. Grade two tears may be felt upon subsequent rectal palpations as a variable-sized diverticulum that is more accurately described as a mucosal-submucosal hernia. These tears are usually incidental findings, as luminal bleeding is not associated with these tears. Grade 3A tears usually form a diverticulum lined by serosa, which fills with feces shortly after the injury. The 3B tears allow fecal contamination of the mesocolon. Fecal contamination of Grade 3 tears may progress to a Grade 4 tear. Grade four tears are easily detected with direct palpation of abdominal organs. Peritoneal fluid changes occur quickly in horses with Grade 3 and 4 rectal tears with nucleated cell counts exceeding 50,000 cells/μl in 30 minutes.

Treatment

Accurate and early treatment has a marked influence on case survival. Horses with Grade 1 tears are amenable to either medical treatment alone or can be treated using epidural anesthesia with direct suturing techniques in the standing animal. Broad-spectrum antibiotics should be administered with serial hemograms and peritoneal fluid analysis to aid in monitoring the patient. The horse should be monitored closely for one week and fed a laxative diet such as water-soaked alfalfa pellets, combined with regular administration of mineral oil by nasogastric tube. Oral or intravenous fluid replacement may be required to restore circulating volume, ensure tissue perfusion, and prevent bowel stasis and possible colon impaction.

Grade two tears are discovered as an incidental finding on subsequent rectal palpations as a variable-sized diverticulum that is commonly described as a mucosal-submucosal hernia. Horses with Grade 2 tears may present with signs of tenesmus or with rectal impactions. The hernia or diverticulum is usually detected after manual evaluation of the rectum. These tears occasionally lead to the formation of a pararectal abscess. These tears are frequently manageable with conservative measures such as dietary control aimed at keeping the feces soft. Horses with Grade 3 rectal tears require prompt and aggressive medical and surgical intervention. Early recognition of the condition, along with aggressive precautionary measures to arrest the further development of the tear are indicated.

Surgical intervention should be instituted immediately, for delaying repair only increases the mortality rate associated with the disease.

The immediate goal is to prevent enlargement and development of a Grade 4 tear. This is accomplished by tranquilizing the horse, providing epidural anesthesia to eliminate straining, manually removing feces from the rectum, and packing the rectum to prevent fecal contamination and diverticulum formation. Epidural anesthesia should be maintained to prevent the horse from straining against the pack. A combination of xylazine and carbocaine may be useful to provide a long-acting effect. All feces within reach are removed from the rectum and small colon, and the rectum is packed with moist cotton inside a well lubricated 3 inch stockinette. The purpose of the packing is to fill, but not distend, the rectum. The pack should extend from the anus to approximately 10 cm cranial to the site of the tear. No material should be packed into the tear itself. The anus is then closed with towel clamps or a purse string suture to prevent the packing from exiting. Vigorous medical management should be instituted. Atropine, a parasympatholytic drug, has been recommended by some clinicians to depress intestinal motility. When used correctly as a single dose (0.044 mg/kg IM or subcutaneously [20 mg for a 450-kg horse]), atropine will decrease intestinal motility for up to 12 hours. This can be a safe and excellent way to depress intestinal motility. Broad-spectrum systemic antimicrobials, tetanus toxoid, and fecal laxatives such as mineral oil should also be administered. Balanced polyionic fluids should be administered to rehydrate the horse in anticipation of an extensive surgical procedure and to counter the hemodynamic effects of endotoxins.

Several surgical techniques have been described to repair rectal tears. These include direct surgical repair via a rectal approach, partial prolapse of the rectum, placement of a temporary diverting colostomy, placement of a temporary rectal liner and direct surgical approach and repair via a celiotomy. The technique chosen to repair the rectal injury depends largely on the location of the tear, the preference and expertise of the surgeon, and the availability of specialized surgical equipment.

Techniques used to repair Grade 3 tears also apply for Grade 4 tears. Because there is more direct contamination of the abdomen in Grade 4 tears, there is an increased expense due to the likelihood of multiple postoperative complications. As a result, a poorer prognosis is associated with Grade 4 tears so the value of the animal in perspective to the expense incurred should be taken into consideration.

Direct closure of Grade 3 tears can be done in the standing animal if the tear is less than 15 cm from the anus. The horse must be cooperative and have a rectum that is easily dilated. The surgeon must have good patience and the manual dexterity to close the wound without further damaging the edges of the tear or incorporating nearby mucosal folds into the tear that would reduce the rectal diameter.

An interrupted cruciate pattern utilizing size 0 or 1 absorbable suture material with a swaged-on taper point, half-circle needle incorporating all layers is the method of choice. The tear can be repaired blindly with the sewing hand inserted into the rectum. Incomplete suturing of the tear, however, will allow for continual packing of the defect with feces and eventual breakdown or submucosal dissection. The use of an expandable rectal speculum or wire basket (Robert A. Roland, Davis, CA) and long-handled instruments can facilitate closure of these tears for individuals inexperienced with the blind suturing method. Transection of the anus will improve access to the tear and facilitate defecation after surgery. Contraction of the wide muscular bands and circular smooth muscle increases the risk of dehiscence of the sutured tears. With proper patient selection (Grade 3-A tears), primary closure of the tear with sutures has yielded excellent results in six of 7 patients.

Direct suturing of the tear can also be achieved by prolapsing the small colon until the tear is exposed outside the anus. A hand is passed through the rectum to grasp the colon wall with a gauze sponge placed by an assistant through a laparotomy incision. Surgical stapling equipment (TA 90 premium, United States Surgical Corporation, Norwalk, CN) has been successfully used to repair rectal tears exteriorized via suture traction of the rectum and wound edges. This procedure is more easily accomplished in thin horses as less pressure is applied on the mesenteric vessels during traction of the small colon.

Placement of a temporary rectal liner via a ventral midline celiotomy has been described for the treatment of Grade 3 or 4 tears. Each end of a 5 x 10 cm plastic rectal ring (Rectal Ring, Regal Plastic Co, Detroit Lakes, MN) is trimmed to form a 5 x 7-cm ring. Holes are drilled 1.5 cm apart in one edge of the central groove around the circumference of the ring and #5 Dacron suture material is laced through the holes, forming a continuous anchor suture. The rectal ring is inserted into the small end of an arthroscopy camera sleeve (Video Camera Cover, Surgical Resources, Inc. Darlington, MD). Modern rectal palpation sleeves have proven too unreliable creating the need to use the more durable camera sleeve. A rubber band is placed around the sleeve and over the center groove in the ring at the opposite end from the anchor suture. The sleeve is fastened to the end of the ring with cyanoacrylic and the sleeve is inverted over the ring and fastened to itself. Inversion of the sleeve protects the intestine against irritation by the rubber band, the cut edges of the sleeve, and the cyanoacrylic. An assistant passes the plastic rectal ring and sleeve through the anus and small colon until it can be surgically placed oral to the tear. Number 3 surgical catgut is passed around the colon and over the groove on the ring and is tied to constrict the serosal surface. Four interrupted retention sutures are placed equidistant through the colon wall to include the circumferential catgut suture and the Dacron suture in the rectal ring. Absorbable retention sutures (2-0) in a Lembert pattern are then oversewn over all previous sutures so as to infold the wall.

The large colon should be evacuated by a pelvic flexure enterotomy, and a stomach tube is passed retrograde from the anus up the sleeve to thoroughly flush the small colon with water and to infuse 4 L of mineral oil into the right dorsal colon. Feces that enter the ring are contained within the liner until passed through the anus. The anastomosis maintains continuity of the intestinal tract until the ring and circumferential suture slough nine to 12 days after surgery. The temporary indwelling liner effectively protects Grade 3 tears during healing, unless the tear converts to a Grade 4 tear. The horse is kept standing until the rectal tear heals because the sleeve could retract into the rectum if the horse becomes recumbent. Mineral oil and a pelleted ration are fed until the ring and liner detach.

Diverting colostomies can be performed with the horse standing, using sedation and local anesthesia or with the horse under general anesthesia. Advantages of the standing procedure include the elimination of risk of damage to the stoma during recovery from anesthesia, less expense and the elimination of possible complications incurred during general anesthesia. Advantages of performing the colostomy with the horse under general anesthesia include the greater ease of tissue handling with the horse in lateral or dorsal recumbency. In the presence of peritoneal inflammation, the un-anesthetized horse may be reluctant and unwilling to permit any traction and manipulation of the bowel.

Ileus is a common complication after repair of a rectal tear. Peritonitis from the tear and surgical manipulation of the small colon, as well as postoperative anesthetic depression of bowel motility contribute to this complication. Although these concerns will subside with time, neostigmine can be administered early to prevent ileus and decrease patient morbidity and mortality. It is generally administered intravenously via a slow-drip system (Travenol infusor, Deerfield, IL) at 2 ml per hour (0.01 mg/kg/hour) connected to the IV catheter. If the horse shows signs of discomfort, the rate of neostigmine administration can be decreased. Neostigmine administration is stopped in horses that continue to be painful. The drip is used for 48-96 hours postoperatively to enhance propulsive activity of the large colon. Metaclopromide, which enhances gastroduodenal motor activity, may be used separately or in combination to prevent or treat ileus. Correcting all electrolyte disturbances, walking the horse routinely, feeding a diet of lush green grass, administration of analgesics and control of peritonitis all play equally critical roles in minimizing occurrence of ileus. Waiting for the bowel to become severely distended or for other metabolic problems to arise impairs the intestinal motility and jeopardizes survival of the patient.

A warm water enema to keep the lumen open and to prevent reimpaction may be necessary as the colostomy site becomes edematous within the first 24 hours after surgery. It is important to treat local abscesses as they arise at the stoma by drainage and lavage so as to allow the tissues to heal before it is time for the reanastomosis procedure. Serial peritoneal fluid analysis can be used to assess the abdominal response to the tear, and peritoneal lavage can be performed as an adjunct to control inflammation. Serious consideration should be given to the treatment of peritonitis if the patient is febrile, depressed, anorectic, or has ileus. Further evidence of peritonitis would be indicated by increased quantities of peritoneal fluid with a nucleated cell count exceeding 150,000 cells per mm^3, karyolysis of the neutrophils or the presence of bacteria and a high total protein concentration in the fluid. A large bore (30 French) mushroom catheter may be inserted through the linea alba into the cranial abdomen and used to infuse three to 10 L of warmed lactated Ringers solution into the abdomen. After an hour, the fluid is allowed to drain out the same catheter.

The method of closure for the loop colostomy involves taking down the stoma. The attachments to the skin and external abdominal oblique muscles are carefully dissected free from the edge of the small colon. The antimesenteric band is closed with double-inverting layers, utilizing 2-0 absorbable suture, and the small colon is vigorously cleaned and replaced in the abdomen. If the small colon is excessively traumatized in this dissection, the effected small colon should be brought through the incision and a resection and end-to-end anastomosis performed. The flank incision is then closed in a routine manner.

Loop colostomy may be of benefit to horses with rectal tears provided it is done soon after the tear occurs. In two retrospective studies of 13 horses with grade 3 rectal tears, seven survived. Complications after loop colostomy include septic peritonitis, laminitis, incisional infections of the colostomy site, peristomal hernia and prolapse. Complications associated with colostomy include stoma abscesses, prolapse, dehiscence, disuse atrophy of the distal portion of the small colon and intra-abdominal adhesion formation.

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Reproductive Emergencies in Stallions and Mares (Parts 1 and 2)

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Castration is one of the most common surgical procedures performed in equine practice. Although an elective and routine procedure, surgical complications of castration constitute the most common cause of malpractice claims against equine practitioners. Evisceration through the vaginal ring and open scrotal incision is uncommon and potentially fatal. Evisceration generally occurs within 4 hours, but may occur up to 6 days after castration. Evisceration of the small intestine makes up 67% of cases while omental prolapse compromises the remainder. A survival rate of 85 to 100% can be expected where appropriate treatment is carried out.

Post-castration evisceration is always a risk following open castrations, but the risk is increased in certain breeds with large inguinal rings, or after castration of an adult stallion. Standardbreds, Tennessee Walking Horses and Belgians are at greater risk because they have larger inguinal rings. Other predisposing factors include a pre-existing undetected inguinal hernia, presence of visceral structures adjacent to the internal inguinal ring, and increased abdominal pressure after surgery. Palpation of the scrotum and inguinal structures for hernias prior to castration is recommended.

Evisceration of omentum or small intestine can occur and must be appropriately identified prior to treatment. The main objective is to clean and protect the intestine and return it to the abdomen before it is excessively traumatized or contaminated. Prior to the veterinarian's arrival it is important to instruct the owner to keep the horse quiet. The structure should be supported by a moistened towel in a sling fashion to support the eviscerated structure to avoid further stretching or damage. Examination will quickly reveal what structure is involved so that treatment can be initiated.

Excessive hemorrhage is usually the result of an emasculator that is improperly applied or is in imperfect working order. Reversing the emasculator by placing the cutting edge toward the abdomen usually results in severe hemorrhage because the cord is crushed distal to the site of transection. The emasculator should be applied perpendicular to the cord because transection of the cord other than at a right angle increases the diameter of the severed ends of the testicular vessels. The blade of the emasculator should not be so sharp that the testicular vessels are severed before they are crushed properly. A blade that is too sharp can be dulled by using it several times with a cotton rope.

The testicular vessels may be insufficiently crushed if scrotal skin is inadvertently included in the emasculator jaws. The thick cord of a mature stallion may require double emasculation to sufficiently crush the vessels. Using this technique, the parietal tunic and cremaster muscle are crushed and transected separately from the testicular vessels and ductus deferens.

Treatment

Omental evisceration

Prolapse of the omentum through the scrotal incision after castration generally is not an immediate emergency but signals the possibility for potential evisceration. A rectal palpation should be performed to ensure that there is no associated small intestinal involvement. Prolapse of the omentum through the inguinal ring can usually be managed using sedation and transecting the prolapsed omentum as far proximal as possible. In more severe cases a short-term general anesthetic is given. The omentum and scrotum are cleaned and prepped, and the omental segment is emasculated. The scrotum is packed with gauze and closed, and the horse is given systemic antibiotics. The packing can be removed after 2 days, and antibiotics are continued for 24 hours after removal of the pack.

Small intestinal evisceration

It is important to replace the intestine within the abdomen as soon as possible after evisceration. Delay in repair of the evisceration puts undue stress on the mesenteric vessels leading to avulsion of the mesenteric vessels, thrombosis, and further damage to the intestine proper. In the field the intestine should lavaged and where possible placed back within the scrotum which is then sutured.

The horse should be anesthetized immediately to minimize contamination and damage to prolapsed intestine. Intravenous fluids and hypertonic saline should be administered to minimize hypotension. The intestine is copiously lavaged and examined for damage. If avulsion of mesenteric vessels or strangulation has occurred, requiring intestinal resection, the scrotum is sutured closed containing the intestine and the horse is referred to a surgical facility.

If the intestine is clean and appears healthy, it is replaced in the abdomen. To replace the intestine in the abdomen, the internal inguinal ring often must be dilated. Care must be made that the intestine is replaced within the abdomen through the inguinal canal, and not through a separate iatrogenic opening. If the herniation cannot be reduced confidently, or if there is avulsion of mesenteric vessels or strangulation requiring resection the intestine is replaced in the scrotum, packed with gauze and the horse is referred to a surgical facility. The horse is placed in dorsal recumbency under general anesthesia. A ventral midline celiotomy is used to expose the abdomen for the presence of further damage to the intestine and associated mesenteric structures. To replace the intestine into the abdomen, dilation of the vaginal ring and traction on the intestines through the abdominal incision are usually necessary. Devitalized intestine outside the abdomen is resected and healthy intestine anastomosed prior to replacing the intestine through the vaginal canal and into the abdomen. Lesions involving the ileum may require resection of the ileum and jejunocecostomy.

If the herniation can be reduced successfully, the fundus of the vaginal sac is identified if it has not been shredded during the initial castration or reduction of the prolapse. The fundus of the vaginal sac is ligated with absorbable suture and transfixed to the edge of the superficial inguinal ring. This procedure seals the exit of the intestine. The superficial inguinal ring is then closed with double absorbable suture in a continuous pattern. The superficial layers of the wound are left unsutured if the wound is grossly contaminated. Sterile gauze can be packed into the inguinal canal and scrotum rather than suturing the superficial inguinal ring. Care must be taken to avoid introducing gauze into the abdomen. A short segment of gauze is left exposed through the scrotal closure. . If the horse progresses well, the gauze packing can be removed in 48 hours, and the antibiotics discontinued 24 hours after removal of the packing. The deep inguinal ring should be palpated per rectum before the packing is removed to confirm that intestine is not adhered to the pack.

Broad spectrum antimicrobial therapy should be initiated, analgesic doses of flunixin meglumine (1 mg/kg IV) administered and the horse immediately referred to a surgical facility to be monitored closely for development of colic or ileus, indicating intestinal devitalization has occurred requiring immediate exploratory celiotomy

Hemorrhage

A ligature placed around the entire spermatic cord or around the testicular vessels can be used alone or in conjunction with an emasculator, to prevent hemorrhage. Although a ligature, with or without an emasculator may be more effective than the emasculator alone in preventing hemorrhage, the use of a ligature may increase the incidence of infection at the surgery site. The increase risk of infection associated with the use of a ligature is likely to be the result of reduced resistance of tissue contaminated with bacteria to infection in the presence of foreign material, especially if nonabsorbable suture is used.

Dripping of blood from the wound for several minutes after emasculation is expected and should cause no concern. Continuous streaming of blood for 15 to 30 minutes is abnormal and an indication for concern. The testicular artery is the usual source of severe hemorrhage. Because the testicular veins are valved, hemorrhage from these vessels is usually mild. Hemorrhage form scrotal vessels is usually not serious and soon ceases spontaneously. If, the horse horses to stand quietly for 15 to 30 minutes, hemorrhage does not diminish, the end of the cord can be grasped using fingers and stretched to allow application of a crushing forceps or an emasculator. A crushing forceps with curved jaws, such as a kidney clamp, is easier to apply and maintain in position than a strait forceps. If the horse is castrated while standing, the end of the cord is likely to be desensitized, and the forceps or emasculator can usually be applied without causing serious discomfort to the horse. The forceps is removed the next day. If the horse is castrated while recumbent, the cord is not desensitized, so to safely grasp and crush the end of the cord the horse may need to be reanaesthetized.

If the end of the cord is inaccessible through the scrotal incision, hemorrhage can be stopped by ligating the testicular vessels intra-abdominally using the procedure described for laparoscopic removal of an abdominal testis. Laparoscopic surgery to stop hemorrhage after castration can be performed with the horse standing or anesthetized and positioned in dorsal recumbency. The testicular artery can be coagulated using electrocoagulation, or occluded with a laparoscopic suture loop or vascular clip.

If the end of the cord is inaccessible, and if intra-abdominal ligation of the testicular vessels using laparoscopy is not an option, sterile gauze can be packed tightly into the inguinal canal and scrotum, the scrotum closed with sutures or towel clamps. The pack is removed the next day.

Ten percent formalin (1 part 37% formaldehyde and 9 parts water) has been used with questionable success to stop hemorrhage. In one study, 8-16 ml of a 4%-12% formaldehyde solution administered intravenously to average size horses decreased time of coagulation by 67% in 24 hours. However, another study demonstrated no variation in time of coagulation after intravenous administration of formaldehyde solution.

Formaldehyde solution is pyretogenetic and accelerates pulse and respiration. Other side effects include restlessness, lacrimation, salivation, elevation of the tail, nasal discharge, increased peristalsis with frequent defecation, sweating, quivering of muscles, signs of severe abdominal pain and tenesmus. Physical reaction is minimal when 10 ml of 4% formaldehyde solution (i.e., 10% formalin) diluted in a liter or more of physiological saline administered intravenously. Although empirical evidence clearly demonstrates its clinical effect in decreasing hemorrhage minutes after administration convincing scientific evidence of the safety and efficacy of formaldehyde solution in reducing hemorrhage is lacking.

Vaginal lacerations secondary to breeding

Vaginal lacerations incurred during breeding most commonly involve the cranial dorsal vaginal wall close to the cervix. They are generally less than 5 cm long and are accompanied by minor transient hemorrhage. Minimal hemorrhage in maiden mares may result from perforation of a persistent hymen, does not require treatment, and must be differentiated from vaginal laceration. If not for the presence of fresh blood on the penis of the stallion after dismounting most of these lesions would go unnoticed. These lacerations have been attributed to the disproportionate size of the stallion's penis and mare's vagina or may be related to the copulatory technique of some stallions. The associated hemorrhage mixed with semen could have the same effect as hemospermia, which has been associated with reduced fertility. With minor lacerations spontaneous healing is rapid and complete as most lesions are usually undetectable by the next estrous cycle.

Extreme lacerations to the vagina after breeding can result in rupture of the vaginal wall. Evisceration of bowel or urinary bladder may present as bulging of these structures from the vulvar lips. Most commonly this affects the dorsal aspect of the cranial vagina. Unless the mare is examined after detection of fresh blood at the vulva or on the stallion's penis, the possibility of vaginal rupture and contamination of the peritoneal cavity may be overlooked. A manual examination with a sterile glove and sleeve can help determine whether the peritoneal cavity is penetrated. Peritoneal centesis may reveal the presence of peritonitis or spermatozoa. Discovery of the injury warrants prompt preventive antimicrobial therapy. If a vaginal rupture is overlooked, the mare becomes depressed in 2 to 3 days after breeding and shows signs of acute peritonitis. The peritoneal cavity is contaminated with bacteria from the stallion's penis and mycolic acid from sperm cells.

For wounds not entering the peritoneal cavity the vagina should be gently lavaged with a sterile saline solution and infusion of a local antibiotic (Furacin). An epidural anesthetic may be indicated if tenesmus is present (5-8 ml 2% lidocaine). Systemic antibiotics are indicated for 7 days (procaine penicillin 22,000U/kg IM q12h; gentamicin, 6.6 mg/kg q24h)

For wounds entering the peritoneal cavity, local and systemic antibiotics should be initiated as described with the addition of metronidazole (15 mg/kg PO q8h). If a portion of the bowel eventrates through the rent, it should be washed with normal saline solution containing non irritating antimicrobials before replacement in the abdominal cavity. The vagina should be flushed with normal saline solution. Unless surgical repair of vaginal damage can be easily achieved it is not indicated. Peritoneal lavage with large volumes of sterile saline solution is indicated if severe inflammation of the peritoneum is present. Vaginal lacerations heal by second intention in 7 to 10 days. However, to prevent the evisceration of abdominal viscera, it is wise to keep the mare from lying down for 5 days with close observation during this time.

If extensive trauma to the herniated small intestine or gross contamination of the peritoneal cavity has occurred, the mare should be referred to a surgical facility. Triage prior to referral is indicated. The herniated intestine should be cleansed and replaced in the abdomen with interim suturing of the vaginal lips for transport. Intravenous fluids should be administered prior to and during shipment if the mare is showing signs of shock

Acute septic metritis

Septic metritis occurs most commonly when there is extensive trauma and resulting contamination of the reproductive tract during a difficult dystocia. Because of the severe consequences, this condition must be managed rapidly and aggressively. Clinical signs may begin as early as 12 to 24 hours after foaling, with the mare becoming severely depressed, anorectic and painful. Signs of septicemia include increased temperature, pulse, and respiration, injected mucous membranes, dehydration, and cool extremities. Clinical signs of laminitis may become evident 12 hours to 5 days after the onset of acute septic metritis. Vaginal discharge is usually not copious but a thin watery discharge with a variable smell may be seen. Closer examination within the uterus reveals an enlarged thin-walled uterus distended with a chocolate colored, fetid fluid.

The treatment goals for acute septic metritis are directed at reducing the bacterial growth and eliminating toxins by supportive systemic therapy and removing the fluid accumulating in the uterus. Intravenous fluids are needed to correct shock and dehydration. Flunixin meglumine (0.3 mg/kg IV q8h) is indicated to lessen the effects of endotoxemia. Aggressive systemic therapy should be initiated. Penicillin, gentamicin, and metronidazole are indicated until blood culture and sensitivities are reported. The predominant anaerobic bacteria cultured is *Bacteroides fragilis* and frequently is resistant to penicillins and aminoglycosides but is inhibited by systemic administration of metronidazole.

Large volumes of a warm 38^0 C saline solution or dilute povidone iodine solution can be infused into the uterus by gravity flow using a large bore nasogastric tube and funnel. Before lavage, the uterus should be palpated per rectum to evaluate the amount of fluid accumulating in the lumen between treatments. The uterine contents are then siphoned and repeated until the fluid drained out of the uterus is similar to the fluid being pumped into the uterus. The procedure is repeated 2 to 3 times daily, depending on the severity of the condition. Uterine involution can be evaluated by rectal palpation after lavage. Mares responding to treatment, with uterine involution, have a thickened corrugated uterine wall, whereas mares not responding have a thin, flaccid uterine wall. Uterine lavage is discontinued when intrauterine fluid is clear to slightly cloudy and the systemic WBC count is greater than 5000 cells/ *u*l. Removal of the toxic uterine fluid should resolve systemic signs. Because the uterine fluid may continue to accumulate with fluid and cause toxemia, careful monitoring is needed until the infection is controlled.

Mares with acute septic metritis typically have severe leucopenia with WBC counts less than 2-3,000 cells/*u*l. There is usually a left shift, with toxic neutrophils and fibrinogen levels in excess of 600 mg/dl. As the acute toxemia resolves with therapy, the WBC count will return to normal levels. The fibrinogen with become normal 2 to 3 days after WBC count becomes normal.

Laminitis is an aggravating and infrequent complication with acute septic metritis. Laminitis can develop suddenly with acute septic metritis and frequently has dire consequences. Laminitis should be treated with soft footing, caudal heel support, aspirin (90 grains /450-kg horse PO q48 h), acepromazine (0.02-0.05 mg/kg q 8h), pentoxyfylline (8.4 mg/kg PO q12h), nitroglycerine cream (topically q12h) and supportive therapy. Severe rotation of the third phalanx frequently results necessitating euthanasia.

Uterine torsion

Aggressive rolling or trauma may play a role in the onset of uterine torsion. The exact cause, however, is not known. Suspension of the equine uterus from the broad ligament attached to the dorsolateral body wall makes torsion of the gravid uterus uncommon. Signs of abdominal discomfort in mares late in pregnancy suggest uterine torsion as a differential diagnosis. Colic signs may be mild to severe and related to tension on the broad ligaments or pressure on the uterine wall. Secondary gastrointestinal disturbances may result from altered position of the displaced uterus. Necrosis of the uterus, with subsequent rupture, may occur spontaneously.

The most diagnostic findings on transrectal examination are those related to tension and position of the broad ligaments. For a clockwise torsion of the uterus, the left broad ligament is stretched across the dorsal aspect of the uterus from left to right and the right broad ligament disappears ventrally down the right body wall. The fetus usually is displaced cranially by torsion in the uterine body. Occasionally this twisting can be palpated just cranially to the cervix. Vaginal signs of uterine torsion are inconclusive. For torsions less than 180 degrees the cranial vagina may have signs of twisting to the point where the cervix cannot be palpated readily or observed through a speculum.

The foremost approach to correction of uterine torsion in the mare is surgical although they can be corrected with rolling in a manner similar to that used for cows. In cases of uterine torsion without uterine tissue necrosis the objective is to return the uterus to a normal position and allow pregnancy to continue to term. Most cases treated in this manner result in a normal delivery. Correction of uterine torsion in mares at term often results in the immediate delivery of a normal foal.

A standing flank laparotomy is the best approach for correction of uterine torsion. Torsion of 180 degrees or less can often be corrected through this approach simply by rolling the twisted uterus back into a normal position. The torsion is reduced by elevation from beneath and repulsion of the fetus rather than by grasping and pulling the fetus through the uterine wall. Pulling on the uterus and fetus incurs a greater risk of uterine rupture. Attempting to correct uterine torsions from a ventral midline approach in the gravid mare is counterproductive since the weight of the uterus prevents the safe and proper correction of the torsion.

The prognosis is grave when uterine rupture and escape of the fetus into the peritoneal cavity has occurred. If the laceration is small with only partial exposure of the fetus, these cases are occasionally successfully managed by removing the fetus and closing the defect in the uterus. Formation of adhesions or other damage to the peritoneal cavity and abdominal viscera typically result in loss of the mare.

Uterine prolapse

Uterine prolapse may follow dystocia, retained placenta or normal delivery particularly in multiparous mares and should be treated as an emergency situation because mares are particularly predisposed to shock and hemorrhage under such circumstances. Treatment of shock associated with uterine prolapse is as essential as replacing the prolapsed uterus. Immediate attention at the time of injury includes elevating and covering the prolapsed uterus in a moistened towel to avoid further trauma or dehydration and to reduce edema of the uterine tissues until veterinary assistance is available.

Cleansing and replacement of the prolapsed uterus should be attempted as soon as possible. Epidural anesthesia (xylazine, 0.25 mg /kg, mixed in 8 ml saline solution) greatly facilitates replacement by reducing straining. Minimizing trauma to the exposed endometrium reduces straining. Large volumes of warm, mild antiseptic solution should be employed to cleanse the endometrial surface thoroughly. Carefully palpate to confirm that the bladder is not within the prolapsed uterus prior to attempting to replace the uterus. A distended bladder must be drained before attempting to replace the uterus by passing a soft rubber stallion catheter through the urethra or placing a 5 cm 14-gauge needle through the uterine wall into the bladder.

Replacing the uterus is achieved by applying pressure first near the cervix and gradually working the everted uterus back through the cervix. Elevating the uterus with the help of an assistant greatly facilitates replacement of the uterus. It is important to be sure that the tips of the uterus are not inverted once the uterus is passed through the cervix. Using a long arm or extending the arm with the flat base of an empty clean wine bottle to elongate the tip of each uterine horn will facilitate this process. General anesthesia may be indicated in fractious mares.

Once the uterus is replaced, infusing 2 to 3 liters of warm saline solution should be repeated two times a day for 3 days using the siphoning technique previously described for acute septic metritis. Systemic treatment includes oxytocin (20 units IM) to involute the uterus and systemic antibiotics (gentamicin, 6.6 mg/kg IV SID and procaine penicillin, 44,000 IU/kg IM BID) along with flunixin meglumine (0.30 mg/kg IV TID) to prevent metritis and laminitis.

Hemorrhage can occur as a result of stretching of the broad ligaments after uterine prolapse. The combination of shock, hemorrhage, contamination, and/or uterine trauma warrants a poor prognosis in most cases.

Ruptured uterine arteries

Hemorrhage from the uterine artery or external celiac artery is common in multiparous broodmares older than 11 years of age and is a significant cause of death. Postpartum hemorrhage may occur in young mares as well. Once the mare has a history of periparturient hemorrhage, she is more likely to bleed in future pregnancies.

Hemorrhage can occur into the abdomen or into the broad ligament and is not always fatal. The hemorrhage may slowly dissect into a broad ligament between the myometrium and the serosa of the uterus, forming a hematoma. The resulting clot stops the arterial

bleeding and the mare may not exsanguinate. If the broad ligament ruptures or the serosal surface of the uterus tears during the formation of the hematoma, the mare quickly bleeds to death.

As the tension in the broad ligament increases and uterine serosa stretches, the mare shows sign of colic with sweating, an increase in the pulse rate and pale mucous membranes. Transrectal examination reveals hemorrhage into the broad ligament. Palpation causes severe discomfort and the degree of enlargement of the uterus indicates the extent of the hemorrhage. Mares may not exhibit signs of colic if parturition was normal. The post foaling pain is mistakenly thought to be due to uterine contractions. It is not uncommon that many mares with post foaling hemorrhage are not discovered until they are weak or dead.

Confining the mare to a dark, quiet stall, using mild sedation usually results in the most successful treatment. Acepromazine, (0.01–0.02 mg/kg) should be administered only if the mare is anxious. It is important to allow for "permissive hypotension" to allow the systemic blood pressure to fall between 70 to 90 mm Hg until it is clear that the bleeding has stopped. Therefore, crystalloids and colloid fluid therapy should be used with caution during this initial episode.

Administer fluids only if the mare is hypotensive. Such indicators would include tachycardia, poor pulse quality, cold extremities, or systolic blood pressure less than 70 mmHg measured with an indirect blood pressure cuff applied to the tail. Aminocaproic acid (Amicar, 10-20 mg/kg IV) is administered slowly in the fluids or by means of slow infusion if fluids are not being administered. Blood transfusions, plasma volume expanders and fluid therapy are controversial and may even be contraindicated if the mare becomes excited by the procedures. Other treatments that have been used include naloxone, formaldehyde and hypertonic saline solution.

The foal should be moved to an adjoining stall if the mare appears weak and a danger to the foal. Oxytocin decreases bleeding from the myometrium and intraluminal bleeding only. Since it does not affect bleeding form the external iliac or uterine artery it should not be used if a hematoma is present in the broad ligament. Surgical correction is unlikely to be successful because of the acute and rapid ongoing bleeding. The prognosis is poor with any treatment if there is uncontrolled bleeding into the abdominal cavity.

Hydrops of fetal membranes

Excessive fluid accumulation in either the amniotic (hydramnios) or allantoic (hydroallantois) cavity is not a common occurrence in mares but can be fatal if not diagnosed and managed quickly. Hydramnios occurs most often in pregnancies with congenitally abnormal foals. Hydroallantois is caused by an abnormal chorioallantois and more commonly affects multiparous mares. Hydroallantois occurs more commonly than hydramnios in the mare. Distinguishing the two conditions does not alter the therapeutic regime.

Clinical signs generally become apparent at 7 – 10 months of gestation. The pregnant uterus is grossly distended with fluid, filling the abdominal cavity dorsally, sometimes into the pelvic inlet. This distention can be so severe as to prevent the successful ballottement of the fetus on transrectal examination. The sudden increase in abdominal distention usually occurs over a 10 to 14 day period. Severe ventral edema develops with associated abdominal pain. The mare is often reluctant to move, has an altered gait with dyspnea on recumbency. Inguinal herniation, rupture of the abdominal muscles, prepubic tendon or uterus can develop.

Abortion should be induced by means of gradual dilation of the cervix over 15 to 20 minutes. Intravenous fluids should be provided as the uterine fluid is removed to prevent cardiovascular collapse. A total of 120 to 220 L of allantoic fluid may be expelled on rupture of the chorioallantoic membrane. Hypertonic saline solution and hetastarch is generally indicated to stabilize the cardiovascular system. Forced extraction of the fetus is often necessary because uterine inertia is often present.

Induction of parturition with oxytocin (20-40 IU) is effective in some but not all cases. It is more effective if the fetus is near term. During parturition, the abdominal contractions are weak and assistance with delivery is often necessary. Following delivery, affected mares may develop hypovolemic shock and need to be treated accordingly.

Placental edema and cystic changes of the allantoic membrane have been observed on examination of the placenta. The prognosis for the future ability of the mare to have foals varies depending on uterine involution. Since most cases of hydramnios are caused by congenital abnormalities of the foal, it is necessary to breed the mare to a different stallion.

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It's Not the End:
What's New in Ileal Impactions

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Etiology

Ileal impaction is the most common cause of non-strangulating obstruction of the small intestine in the adult horse. In the southeastern United States these impactions are associated with consumption of coastal Bermudagrass hay, which is often dry, fine, and has a high lignin content and thus poor digestibility. Poor digestibility is especially the case in hay cut either late in summer or stored in round bales. The disease has been associated with *Strongylus vulgaris* infection and, more commonly, *Anoplocephala perfoliata* infection. Ileal impaction occurs in other parts of the United States and in Europe where coastal Bermudagrass hay is not fed. The disease appears to be more common in the United States from June to November, especially in the fall, although a seasonal effect is not consistent. The risk for impaction is not generally reduced by combining costal Bermudagrass hay with other hay, however, appears to be increased by the recent introduction of feeding poor quality hay, limited water usage associated with cooler weather, and appears to be lowered by feeding a pelleted-concentrate feed in addition to hay. The disease has been reported in a wide range of horses, including newborn and older foals. In a large series of cases, mares and Arabian horses were significantly over represented. A study of 78 horses reported that feeding coastal Bermudagrass hay and failure to administer an anthelmintic effective against tapeworms placed horses at risk for ileal impaction. Orbatid mites are the intermediate hosts for *Anoplocephala perfoliata* and their preference for humid regions such as the southeastern United States could contribute to the geographic distribution of ileal impaction in the United States.

Clinical findings and clinical pathology

Abdominal pain, which is a result of small intestinal distension and spasm at the site of the impaction, is moderate to severe and intermittent. Distended small intestinal loops are usually palpable on trans-rectal examination. Sometimes the impaction of the ileum can be palpated in the right dorsal abdominal quadrant, at approximately the 1 o'clock position, as a sausage-shaped, firm structure which can be tracked to the medial aspect of the cecum. Gastric reflux can be absent in the very early phase of the disease, but upon initial evaluation, most horses have a moderate volume of yellow-green reflux that has a gastric odor. Pain is not alleviated by gastric decompression. By comparison horses with proximal enteritis or with strangulating lesions, horses with ileal impactions will maintain better cardiovascular function and not deteriorate systemically as rapidly. Signs of mild to moderate dehydration, i.e., CRT 2-3 seconds, prolonged skin tenting and tacky, dry mucous membranes; are common and become more obvious if the impaction persists. Hematology and serum chemistry abnormalities, if any, are secondary to the level of dehydration. These can include high PCV and total protein, high BUN or creatinine values, mild metabolic acidosis, mildly elevated lactate, or increased anion gap.

Diagnostic testing

Abdominocentesis yields straw-colored to clear fluid with normal (<2.0 g/dL) to mildly increased protein and normal nucleated cell count and distribution (< 5,000 cells/µL). Compared to horses with strangulating lesions, the changes in peritoneal fluid occur later in the course of the disease, when the ileum becomes compromised.

Treatment

Medical treatment is the preferred course of therapy in horses diagnosed with ileal impaction. Treatment consists of intravenous fluid therapy, anti-inflammatory and analgesic drugs (flunixin meglumine 1.1 mg/kg IV), and spasmolytics (Buscopan™, 0.3 mg/kg IV). Horses should be closely monitored and no food or water allowed while gastric reflux is present. In this instance, a degree of hyper-hydration is beneficial because fluids will cross into the intestinal lumen which will help soften the impaction and allow its transit. Balanced polyionic fluids should be administered intravenously at twice to three times maintenance rate (120-180 mL/kg/day). Repeated doses of sedatives such as xylazine (0.2 to 1 mg/kg IV) or detomidine (0.01-0.02 mg/kg IV), with or without butorphanol (0.01-0.02 mg/kg IV), are usually needed during the early spasmodic portion of the intestinal obstruction.

Most ileal impactions resolve medically, and surgery is performed only in horses with signs of progressive abdominal disease and unrelenting pain, in which instance a strangulating lesion of the small intestine rather than ileal impaction becomes of concern. If surgery is required, the impaction is broken down by manual massage, added by mixing it with fluid from the proximal bowel and intraluminal injection of carboxymethylcellulose while manipulations are being conducted. Several techniques have been used to relieve the impaction if manual reduction is not successful such as enterotomy, ileocolostomy and jejunocecostomy with or without ileal resection. The surgical latter techniques reduce the successful long term prognosis.

Prognosis

Aggressive medical treatment is typically uncomplicated and successful if started early. Medical treatment reduces hospital stay, cost of treatment, and expense of lost time for recuperation and hastens return to athletic activity as compared to surgical intervention. Resolution of small intestinal distension and gastric reflux are good indicators of successful response to medical treatment.

After resolution of the impaction, horses should be started gradually on low bulk, easily digestible feed such as grass or mashes. Poor quality coastal Bermudagrass hay should be avoided. Because tapeworms are thought to play a role in this disease, anthelmintics are recommended, such as a pyrantel pamoate (double dose 13.2 mg base/kg) combined with praziquantel to provide a more complete treatment in the fall and again in late spring. Three combination deworming products: Equimax, Quest Plus, and Zimectrin Gold all three contain praziquantel, a dewormer effective against tapeworms as well.

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Equine Wounds:
Triage to Treatment

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Exposed bone

Exposed or denuded bone is a common complication of wounds of the distal aspect of the limb. Exposed cortical bone in which the periosteum has been removed, is prone to desiccation of the superficial layers of the cortex, which may result in infectious superficial osteitis and sequestrum formation. Exposed bone within a wound can delay wound healing directly if the bone becomes infected, or indirectly because its rigid structure can delay the formation of granulation tissue and wound contraction.

Distal limb avulsion wounds with exposed bone increase in wound size for 14 to 21 days. Wound expansion is due predominantly to the distraction forces applied across the wound during the inflammatory and debridement stages of wound healing, and the lack of a granulation tissue bed in the center of the wound to neutralize the tensile forces exerted on the wound margins from the surrounding skin. Wounds with a small amount of exposed bone, or wounds without exposed bone, expand for a shorter period because less time is required for granulation tissue to seal the wound. Larger wounds with exposed bone take longer to form a granulation bed and subsequently wound contraction is postponed.

Periosteal insults from blunt trauma, tendon/joint capsule strain, surgical manipulation, or laceration/degloving injuries may result in extensive periosteal exostosis. Injuries involving bones in horses stimulate more periosteal new bone growth than similar wounds in other species and ponies. More extensive periosteal reaction in young compared to adult horses has been attributed to a more active osteoblastic activity of the periosteum in young horses. The extensive periosteal new bone growth seen in adult horses is poorly understood. Deferred collagen lysis compared to other species may be a contributing factor. The more extensive periosteal new bone formation in horses compared to ponies is alleged to be the result of a slower onset and longer duration of the periosteal response and prolonged extensive limb swelling in horses, as compared to ponies.

Despite the common occurrence of exposed bone associated with trauma to the distal aspect of the limb, there has been little investigation into methods of stimulating coverage of granulation tissue over exposed bone in horses. Granulation tissue development is a very important role in second-intention healing because it provides a barrier to infection and mechanical trauma for the underlying tissues. Healthy granulation tissue is resistant to infection and provides a moist surface for epithelialization. The delay in wound healing caused by exposed bone has prompted the search for different methods to promote granulation tissue coverage of bone in other species.

Head trauma, thermal injury, and surgical oncology often results in exposed bone of the cranium in humans. In these cases the outer cortex of the uncovered portion of the cranium is fenestrated with drill holes, burrs, or lasers to expose the medullary cavity from which granulation tissue grows to cover the exposed bone. Similarly, exposed cortices of long bones in humans have been fenestrated with drill holes to promote granulation tissue formation. It has been suggested that the drill holes promote healing by allowing osteogenic factors from the medullary cavity access to the wound, or by the enhancement of healing of bone and soft tissue by a nonspecific response known as “the regional acceleratory phenomenon”. Cortical fenestration combined with drugs that promote topical granulation tissue may accelerate granulation tissue coverage compared to control wounds, but further investigation is needed.

Cortical fenestration of 1.6 mm drill holes in the cortex of the second metacarpal bone in experimentally created wounds in dogs resulted in clot formation over the bone that promoted granulation tissue formation and may have protected the bone’s outer layers from desiccation. The effects of cortical fenestration with 3.2 mm drill holes were evaluated in experimentally created wounds of the distal aspect of the limb of horses. Cortical fenestrated wounds became covered with granulation tissue earlier than control wounds, and fenestration had no significant effect on sequestrum formation. The granulation tissue growing directly from the bone surface also contributed to granulation tissue formation. If the wounds are not large (< 6 x 6 cm) it may be difficult to realize a significant contribution from the granulation tissue growing from the cortical fenestration sites alone. Cortical fenestration may also be advantageous if it is used with other methods of promoting granulation tissue. Splinting of the limb is usually not necessary for the recovery from general anesthesia unless there are associated traumatic injuries to the limb that would suggest instability.

Degloving injuries

Degloving or avulsion injuries are not uncommon in equine practice, and their management can be challenging because of prolonged treatment, cost, and sometimes unknown outcome. The body that becomes entrapped in hazards or a limb that becomes intertwined in fencing or can quickly sustain tissue damage. The most common sites for this type of trauma are the hemi thorax, dorsal aspect of the metacarpus and/or metatarsus and the cranial aspect of the tarsus. Vascular, soft tissue and bone damage is directly proportional to the length of time and effort the horse uses to free itself. Some injuries that seem to be superficial and innocuous on the surface may involve vital structures surrounding the wound and/or later develop cutaneous and internal abscesses and/or ulcerative cellulitis. Local

wound care should be an integral part of the initial treatment. The severity and duration and location of the laceration determines the best approach to the treatment of degloving injuries as healing of wounds involving the distal limb is often delayed when compared with other areas of the body, further complicating the healing process.

Primary repair of the wound is the preferred treatment for wounds that involve detachment of skin with maintenance of an intact blood supply. Complications such as sequestrum formation are lessened and healing is improved when the exposed bone and tendons are covered with skin and soft tissue in the immediate post trauma period. Closing as much of the wound as possible improves the cosmetic and functional outcome and lessens the amount of healing having to occur by second intention.

Delayed closure of a degloving injury is preferred when there is significant contamination, swelling and trauma of the wound without loss of skin. Initial treatment for the first 2-3 days after injury include debridement and lavage of the wound followed by wet to dry bandages to facilitate further debridement. Pressure bandaging is indicated to remove edema associated with the injury. Debridement of the wound edges and appropriately applied tension sutures facilitate closure of the wound as skin retraction is a complication of delayed closure.

Second intention healing is indicated for degloving injuries in which there is a considerable loss of skin immediately at the time of injury or in which a closed degloving injury has developed avascular necrosis of the skin with subsequent sloughage. The wound is sharply debrided until only healthy tissue remains. A hydrogel Carradress®, Carrington, Irving, TX) dressing is applied to the region of the wound that remains open. These dressings are able to contribute moisture to dehydrated tissue, augment autolytic debridement and absorb some moisture from an exudating wound. The dressing is applied to the wound bed followed by application of a conformable absorptive dressing (Kerlix®, Kendall, Mansfield, MA). A firm cotton bandage is used to provide warmth, support and to minimize excessive movement of the limb and associated wound area. Depending on the size and location of the wound, skin grafting may be indicated to facilitate complete healing. Grafting should be delayed to permit maximum wound contraction which, depending on the location and size of the wound, may be 4-8 weeks after injury.

Dorsal knuckling of the fetlock and an inability to extend the digit is a common complication of distal limb wounds that is usually associated the loss of the extensor tendon of the distal limb. Supporting the dorsal aspect of the limb to counteract the pull of the flexor tendons on the palmar and/or plantar aspect of the limb is the premise for management of extensor tendon disruption. The wound and extensor tendon laceration is managed by second intention healing without suturing the extensor tendon. A rigid polyvinyl chloride (PVC) splint is applied to the dorsal or palmar and/or plantar aspect of the distal limb after wound bandaging. The bandage and splint, which maintains the limb in extension and prevents dorsal knuckling of the fetlock, are retained until normal limb function returns which may vary from 7 days to 6 weeks.

Excessive skin tension

Skin sutured with excessive tension is likely to have complications of healing due to local ischemia with pressure necrosis of the surrounding skin and the pull through of sutures at the skin edge with subsequent wound disruption. Undermining the surrounding skin, relief incisions, and appropriately applied tension sutures are the most common methods that can be used to lessen tension along the skin margins.

The surrounding skin can be undermined up to 4 cm from the wound edge without associated complications. Relief incisions can be closed after the primary incision is closed or left to heal by second intention.

In order not to interrupt the blood supply to the primary suture line, tension sutures are positioned well away from the wound margin. Once the tension suture is in place, the primary incision line is sutured to close the wound edges. Tension suture patterns include vertical mattress, horizontal mattress, far-far-near-near, and far-near-near-far patterns. Vertical mattress sutures with or without skin support to prevent laceration of the wound edges such as polyethylene or rubber tubing, are useful in reducing tension on the primary suture line. This tension suture support method is used in areas that cannot be bandaged well such as the upper limb, body and neck region. It is contraindicated to use tension suture supports under a limb cast or heavy bandage as these supports may cause tissue necrosis and suture line failure. Tension sutures are not effective after 7 to 10 days and should be removed in a staggered fashion with one-half removed initially followed by the remaining sutures later.

Movement

The extent of movement of the skin relative to the underlying bed of granulation tissue is usually much higher in the limb regions than in the trunk. This is possibly exacerbated by the relative lack of skin elasticity as well as the obvious proximity of the limb skin to structures with a high degree of motion such as joints and tendons. Trunk wounds have a better available reparative blood supply than those of the distal limb.

An injury to the distal limb metacarpal or metatarsal region of a horse which involves the flexor tendons and/or their sheaths requires healing by the ingress of blood vessels from adjacent structures. However, as healing attempts to progress, repeated tendon contraction and limb movement moves the injury away from the site of the skin wound leaving the damaged tissues with no effective mechanism for healing.

Rigid limb casting of a distal limb wound is very effective in facilitating wound contraction and epithelialization if the tissues are initially sharply debrided and lavaged. The mechanisms for this may be more complex than merely controlling movement. Although movement of the limb and wound is limited, added surrounding pressure applied to the wound may also facilitate the healing process. Warmth, restriction of movement and the presence of a moist healing environment in conjunction with a cast are probably significant factors that contribute to wound healing. Which aspects of the exudate are desirable and enhancing of wound healing and which are inhibitory is not known in the horse. Heat, pain, swelling, or lameness created by the cast indicate attentive reevaluation of the wound and the consideration of cast removal and or cast change.

Self-mutilation

Significant self-mutilation of wounds through rubbing, biting, and pawing can occur if the horse is not adequately restrained or medicated. Usually the most intense pruritic episodes occur in the first weeks of wound healing during the inflammatory phase of repair and during eschar sloughing but can be a later complication associated with burn wounds. To prevent extreme self-mutilation, the horse should be cross tied and/or sedated at this time and use of a neck collar may be considered. Delayed healing, poor epithelialization, and complications of second intention healing may limit return of the animal to their previous use.

Skin grafting

Skin grafting decreases healing time and is one of the best techniques for covering a wound that has been chronically affected by exuberant granulation tissue. Skin grafting of lower limb wounds should be considered to cover the granulating wound bed if contraction has ceased and the wound bed is large. Frequently, however, wounds in horses are treated for several weeks before skin grafting is initiated. At this point granulation tissue is mature, fibrous and has less of a blood supply than newly formed granulation tissue. Other complications of graft acceptance and healing are wound infection and sequestra formation.

Chronic inflammation, inherently present during second intention healing of wounds on the distal portion of limbs of horses may be at least as important as infection because it reduces the quality of the granulation bed and results in the production of a moderate amount of purulent exudate, both of which negatively influence acceptance of grafts. As a result the ability of a wound bed to accept a graft is lessened. It is therefore imperative that chronic granulating wounds be debrided to a level below the skin surface down to a level of healthy granulation tissue prior to graft application.

To increase the success of graft acceptance wound bacteria must be minimized. Beta hemolytic Streptococcus spp., Proteus spp., and Pseudomonas spp. are capable of producing destructive proteolytic enzymes and excessive purulent discharge which breakdown fibrinous attachments between the graft and recipient bed. Topical antiseptics have better efficacy than antibiotics in reducing bacterial wound load as the latter increase the risk of patient sensitization and the development of resistant organisms especially when used routinely over prolonged periods in uninfected wounds. Infected wounds, however, should be treated with broad-spectrum antibiotics while awaiting culture results. The bone underlying the wound should be radiographed for evidence of sequestra and excessive pericortical dystrophic mineralization. Large wounds often develop healthy granulating tissue around the perimeter before a sequestrum completely defines itself.

Donor site is influenced by the method of grafting, color, and texture of the donor hair, cosmesis of the donor site, and ease of obtaining skin. Common sites for obtaining donor skin include pectoral, dorsal neck region, perineum, ventral midline, ventral lateral abdomen and sternal region caudal to the girth area.

Pinch grafts

Pinch grafts are distinct pieces of skin (3 mm in diameter) produced by excising an elevated cone of skin. Graft acceptance is as high as 75% using pinch grafts partially due to the fact that the pockets of granulation tissue hold the graft in contact with the wound. Complications include necrosis of the graft, slower wound healing, improper orientation of hair, and thin skin coverage of the wound.

Necrotic spots along the top of the granulation pockets normally occur during healing, after which the graft epithelializes circumferentially. Because pinch grafts are small, complete epithelialization of the wound often requires greater than 70 days. Improper orientation of hair growth is a complication of pinch graft application despite repeated efforts to properly align the hair to match that of the recipient area. A cobblestone appearance with thin subcutaneous tissue is sequelae of pinch graft applications that may not be cosmetically acceptable for show horses.

Punch grafts

Punch grafts are circular pieces of skin that are directly removed from the locally anesthetized donor site or by obtaining biopsies from an excised piece of donor skin. Common complications of punch graft failure are incomplete removal of the underlying subcutaneous tissue from the graft, recipient site hemorrhage, and motion.

As punch grafts are full thickness they must have the subcutaneous tissue and fascia removed from the dermis with a surgical blade before implanting as these layers will prevent revascularization and subsequent graft failure. Placing grafts in saline soaked sponge gauze for a short period of time minimizes graft desiccation while recipient beds are created. Accumulation of blood and serum beneath the graft displaces the grafts from the recipient site. Hemorrhage can be avoided by ensuring that it is controlled before grafting. Displacement of the grafts can also be minimized by using a biopsy punch a size smaller than used to obtain donor graft to

ensure a snug fit in the recipient bed. Displacement of the graft by motion can be minimized by securing the wound under a heavy bandage. Displacement of grafted tissue at wrap changes can be reduced by soaking the primary bandage prior to removal. Casting is not indicated for punch graft techniques as punch grafts are not indicated for grafting over moveable areas of the body.

Tunnel grafts

Tunnel grafts are useful for healing of wounds that are hard to immobilize or bandage as on the dorsal surface of the hock or fetlock. Graft survival rates of 80% have been reported with excellent cosmetic results. Complications of tunnel grafting include the placement of tunnel grafts too close to one another, failure of the graft to become exposed and accidental removal of the tunnel graft when removing the overlying granulation tissue.

This technique requires harvesting of full-thickness or spit-thickness strips of skin 2 to 5 mm wide and slightly longer than the length of the wound's edges. These grafts are placed in granulation tissue that has been allowed to develop 4 to 8 mm above skin level. These tunnels can be created using a cutting needle, flattened K-wire with a trocar point, or malleable alligator forceps. The graft is then tunneled approximately 6 mm below the surface of the granulation tissue at the recipient site ensuring that the epidermal side of the graft faces the surface of the wound. Tunnel grafts should not be placed closer than 2 cm apart to prevent excessive necrosis of granulation tissue. The cut ends of the skin strips are sutured to the skin on either side of the granulation bed. A tourniquet may be useful to control hemorrhage and improve visualization of the strips for procedures that involve grafting on a limb. If placed the correct depth, the granulation tissue overlying the graft should slough in 7 to 10 days. If this does not occur, it should be excised at this time. Adjacent granulation tissue that is raised should be excised at this time. Most tunnel graft failures are attributable to accidental removal of the graft during removal of the overlying granulation tissue or failure of the graft to become exposed. Exposure of the graft if necessary may be facilitated by placing malleable probes or wires through the tunnels to cut through the overlying granulation tissue.

Full thickness sheet graft

Full thickness or split thickness grafts can be applied as a sheet or expanded before transplantation. The full thickness sheet graft is the most cosmetic type of free sheet graft as it contains all the properties of the surrounding skin, provides maximum piliation, and can withstand pressure and friction. Full thickness grafts are not as readily accepted because there are less exposed blood vessels available for imbibition of plasma and for inosculation.

No specialized equipment is needed for harvesting, and the procedure can often be performed in the standing sedated horse using local anesthesia. Donor sites of full thickness grafts should be sutured. The graft should be cut slightly larger than the recipient bed to allow for shrinkage after the graft is excised because of recoil of elastic fibers in the deep dermal layers of the of the graft. The full thickness graft should be sutured to the donor site with some tension to prevent occlusion of the dermal vessels that may occur if the graft is allowed to fully contract.

A high oxygen gradient between the wound and the graft is essential for neovascularization of the graft and graft acceptance. Full-thickness grafts treated with hyperbaric oxygen therapy developed less granulation tissue, edema, and neovascularization, but more inflammation. The superficial portion of these full-thickness grafts was also less viable than the superficial portion of those not treated with hyperbaric oxygen therapy.

Full thickness sheet grafts are often considered compromised because they often require more nourishment than can be supplied by the granulating recipient wound. As a result full thickness grafts are usually reserved for fresh uncontaminated wounds. The upper layers of a full thickness graft are more likely to slough because full thickness grafts require more nourishment and have fewer exposed vessels for this purpose. Because of the lack of abundant donor skin in the horse, the graft often must be meshed and expanded to achieve coverage of the wound larger than the donor area.

Split thickness grafts

Split thickness grafts are more readily accepted than full thickness grafts, and may be used to cover granulation beds that are less than ideal. Since blood vessels branch as they become more superficial in the dermis more vessels are cut and exposed with split thickness grafts. The greater the number of exposed vessels the better the absorption of nutrients will be from the granulation bed. A split thickness sheet graft is more cosmetic than a pinch or punch graft because the thickness of the graft and orientation of the hair are uniform and coverage by the graft is more complete.

A mechanical dermatome or a free hand knife (Watson Skin graft knife, Down's Surgical, Sheffield, England) is used to split the dermis. The latter is preferred as it is easy to use and economical to employ. General anesthesia is necessary to obtain the graft as split thickness donor sites are very painful to the horse, since many nerve endings are exposed. Grafts less than 0.5 mm thickness in the horse lack strength, durability, and have sparse or no hair follicles or exocrine glands which results in less sebaceous secretion. Grafts harvested between 0.63 mm and 0.75 mm have good coverage of hair and greater durability than do thinner grafts. Unlike full thickness grafts suturing of the donor site is not required and primary graft contraction is minimal since a portion of the dermis remains intact and heals with a scarred appearance.

The grafts can be applied to the wound after the horse has recovered from general anesthesia. This reduces anesthesia time and the possibility of damage to the graft during the recovery process. The graft can then be affixed to the wound with the horse standing

without using local anesthesia by overlapping and gluing the graft with cyanoacrylate to the skin surrounding the wound. To increase graft success in an area that is difficult to immobilize, such as the fetlock or hock, the graft can be further secured by suturing the graft to its recipient bed with simple interrupted absorbable sutures. Meshing grafts greatly enhances graft acceptance by preventing mechanical disruption of the graft from its vascular supply by exudate. Fenestration of the graft also enables topically applied antimicrobial agents to contact the graft bed and allow for the escape of fluid produced by the wound.

Although proper graft bed preparation and grafting techniques are important for successful graft application, successful graft acceptance depends greatly on attention to postoperative care. During the initial 4-10 days the graft may become edematous and pale. These changes are from a loss of blood supply due to vessel constriction and the expulsion of erythrocytes while the graft is nourished by passive imbibing nutrients onto its open vessels from the granulating bed via plasmatic imbibition. By day 10 the graft typically has a complete union to the graft bed. The epidermis might necrose and slough in some regions of the graft. Generally only the superficial areas of the graft have been lost and small areas of dermis surrounded by granulation tissue are present. The epidermis will regenerate from migration of epithelial cells present in the remaining sebaceous glands, sweat glands and hair follicles.

Periodic bandage changes allow for a clean environment and recognition of graft failure. For many horses frequent bandage changes aid in comfort. Soaking the inner bandage with sterile saline for 5 minutes and the carefully removing the bandage prevents destruction of many grafts. The presence of purulent material on the initial bandage change does not have a detrimental effect on acceptance of individual grafts. Silver sulfadiazine in a 1.0% water-miscible cream is effective against most Gram-positive and Gram-negative organisms and may enhance wound epithelialization. Additional immobilization gained with a cast is usually unnecessary to facilitate acceptance of grafts after 10-14 days. Immobilization may, however, lessen edema and decrease the possibility of self-mutilation. Persistence in re-grafting on horses that self-mutilate wounds has resulted in satisfactory wound healing in the majority of cases.

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The Icteric Equine: Diagnostic and Treatment Options

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The liver is the largest organ in the horse comprising 1% of body weight. Despite its importance in metabolism, detoxification, and elimination of substances, liver disease is relatively rare in the horse. Liver disease can be insidious and is often unrecognized until later in its course. This lecture will focus on etiologies, diagnosis, and treatment options for the horse with liver disease.

Liver function

The liver is important for nutrient metabolism. The majority of nutrients pass through the liver by way of the portal vein. The liver is the primary site of gluconeogenesis, storage, and release of glucose. It is also the site of synthesis of the majority of plasma proteins: clotting factors, fibrinogen, albumin, transport proteins, and acute phase proteins. Hepatocytes are also capable of transamination and deamination to synthesize or metabolize amino acids for gluconeogenesis in times of glucose unavailability. Ammonia is a by-product of amino acid catabolism which is transformed in the liver into glutamine or urea for excretion by the kidneys. The liver esterifies free fatty acids into triglycerides for transport to the remainder of the body and is capable of oxidation of free fatty acids into the tricarboxylic acid cycle for ATP production. Kupffer's cells, tissue macrophages, phagocytose bacterial products such as endotoxin and other particulate debris from portal circulation prior to entrance into systemic circulation.

The liver is the primary source of detoxification of foreign substances such as medications, toxins, insecticides, and mercaptans. The mechanism of removal of foreign substances is by biotransformation through the cytochrome P-450 system. These transformed compounds are then conjugated by glucuronate or sulfate prior to excretion.

Bilirubin metabolism occurs primarily in the liver. Bilirubin is the end-product of hemoglobin degradation. It is released unconjugated into systemic circulation where it binds albumin. The albumin-bound bilirubin enters the liver through systemic circulation where the bilirubin enters the hepatocyte. It is then conjugated to glucuronide and is excreted into the bile canaliculus. The conjugated bilirubin then is reduced to urobilinogen and stercobilin in the GI tract and excreted in feces.

Clinical signs of liver dysfunction

Common Signs	Less Common Signs	Uncommon Signs
Icterus	Photosensitization	Pruritus
Weight loss	Diarrhea	Injected mucous membranes
Colic	Ventral edema	Polydipsia
Depression	Bilateral laryngeal paralysis	Pigmenturia
Anorexia	Bleeding diatheses	
Hepatic encephalopathy	Ascites	
	Fever	

The clinical signs of hepatic dysfunction are often non-specific. Identification of clinical signs is usually sudden despite duration of disease. Greater than 80% of the liver must be affected before clinical signs are identified. Clinical signs are usually identified in a single animal however multiple horses may be affected if disease is caused by toxin ingestion.

Diagnostic testing

Liver enzymes

The mainstay of diagnosis of liver disease is the measurement of plasma or serum concentrations of liver enzymes. The liver enzymes that are specific for the liver in the horse are gamma-glutamyltransferase (GGT) and sorbitol dehydrogenase (SDH). Other enzymes that may be increased in plasma or serum with liver disease but are not specific for the liver are lactate dehydrogenase (LDH), alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST). Hemolysis and lipemia may affect accurate evaluation of some of these enzymes (SDH, AST, ALT). When evaluating any laboratory test, it is important to pay attention to the units and reported laboratory reference range. It is also important to note that foals have higher activities of all liver enzymes than adult horses.

GGT is a microsomal membrane protein found in epithelial cells of the biliary tract, renal tubules, mammary gland, and pancreas. An increase in blood GGT is specific for cholestasis. Damage to renal tubular epithelial cells leads to increases in urinary GGT. Pancreatic disease may result in increases in blood GGT but these diseases are rare in horses. GGT is considered to be the most sensitive indicator of liver disease in the horse. The half-life of GGT is 3 days and it is stable in blood at room temperature for 2 days. GGT may increase following hepatocellular necrosis and may increase for days to weeks despite clinical improvement. GGT is more persistently increased in chronic hepatic disease especially with cholestasis. GGT increases have been reported secondary to large colon displacement.

SDH is a cytosolic enzyme that is released during acute hepatocellular necrosis or changes in hepatocyte membrane permeability. It is not inducible and is specific for hepatocellular necrosis. The half-life of SDH is 12-24 hours and values return to normal within 3-5 days after single hepatic insult. SDH is stable for 4 hours at room temperature and loses 1 or 3.5% of activity per day when stored in the freezer or refrigerator respectively. It is therefore important for this enzyme to be measured within hours of sample collection making it an impractical test to perform in the field unless a laboratory is nearby or there is capability to separate and freeze the serum. Other liver-specific enzymes indicating hepatocellular necrosis are arginase and glutamate dehydrogenase. Arginase and glutamate dehydrogenase both have short half-lives in blood.

ALP is a mitochondrial membrane enzyme that increases following induction. It may increase with cholestasis and drug administration. ALP is also found in bone, intestine, kidney, placenta, and leukocytes therefore increases in ALP are not specific for liver disease in the horse but can be suggestive with increases in other liver-specific enzymes. Evaluation of this enzyme should be done in light of other specific indicators of liver disease.

AST (also known as SGOT) is a cytosolic enzyme present in all cells in the body. Highest concentrations are in skeletal muscle and hepatocytes however cardiac myocytes, erythrocytes, and enterocytes also contain sources of AST. The half-life of AST is 2 weeks. Increases in AST are not specific for liver disease and evaluation should be made in light of other specific indicators of liver disease.

LDH is a cytosolic enzyme located in the liver, muscle, erythrocytes, intestinal cells, and kidney. Increases in LDH are not specific for liver disease unless isoenzyme is specified. LDH-5 is suggestive of hepatocellular necrosis but LDH-5 is also present in skeletal muscle. In the absence of increased creatine kinase, increases in LDH-5 are specific for liver disease. LDH-5 is stable for 36 hours at room temperature making it a more useful test in the field.

ALT is a cytosolic enzyme that is not specific for liver disease in the horse.

Other tests

Bilirubin is an insensitive indicator of liver disease. Total bilirubin is composed of conjugated and unconjugated fractions. Bilirubin is a product of hemoglobin metabolism. The liver is responsible for conjugation and excretion of bilirubin into the GIT where it is further transformed and eliminated. A small amount enters the enterohepatic circulation. There are many causes of hyperbilirubinemia including anorexia, hemolysis, and liver disease. With acute hepatic necrosis, bilirubin conjugation is impaired and with cholestasis, excretion of conjugated bilirubin is impaired. An increase in conjugated bilirubin is specific for liver disease but both conjugated and unconjugated bilirubin may be increased in liver disease. Both hemolysis and anorexia may cause hyperbilirubinemia in the adult horse and should be considered when evaluating bilirubin concentrations.

Bile acids are synthesized and excreted solely by the liver. The hepatocyte produces bile acid from cholesterol which is then excreted through the bile duct into the duodenum. Bile acids are reabsorbed in the ileum. The liver removes 90% of bile acids from circulation. Measurement of bile acids the best test indicating liver function. An increase indicates reduced hepatic blood flow, failure of the liver to remove bile acids from enterohepatic circulation, failure of the hepatocyte to conjugate bile acids for excretion, or failure of excretion. Short term fasting does not affect serum bile acids concentration. Bile acids are stable frozen for one month.

Ammonia is a toxic by-product of amino acid metabolism. It is made in all tissues and by the microflora of the GIT. Ammonia is absorbed by the hepatocyte and used to synthesize nonessential amino acids from □-keto acids and ammonia. A key amino acid produced is glutamate which can convert ammonia into a non-toxic transport form, glutamine. Glutamine and ammonia are converted into urea within the hepatocyte mitochondria through the Krebs-Henseleit cycle forming urea. Urea is released by the liver to become blood urea nitrogen and is excreted by the kidneys. Decreases in blood urea nitrogen rarely occur during chronic hepatic failure.

Changes in blood *glucose* rarely occur in horses with liver disease. Hypoglycemia may occur in cases of severe acute hepatic failure. Hyperglycemia may develop secondary to catecholamine release or tissue insulin resistance.

Triglyceride concentrations rarely change in horses resulting from liver disease as a result of a greater clearance capacity for triglycerides as compared with other species. Anorexia is the most common cause of increased triglycerides in plasma. Exceptions include obese miniature horses, ponies, or donkeys that develop hyperlipidemia syndrome (see Hepatic Lipidosis). Increases in triglyceride concentrations are not specific for liver disease.

Albumin is synthesized solely in the liver. The half-life of albumin in the horse is 19-20 days therefore hypoalbuminemia occurs rarely with chronic liver disease. Other differentials for hypoalbuminemia must be considered as well.

Vitamin K-dependent clotting factors and *fibrinogen* are synthesized in the liver. The clotting factor with the shortest half-life is factor VII therefore abnormalities in the prothrombin time (PT) will be identified before abnormalities in the activated partial thromboplastin time (APTT). Clotting times are prolonged in 50% of horses with liver disease. Evaluation of coagulation parameters is not specific for liver disease; abnormalities should be viewed in light of other specific laboratory indicators of liver disease.

The majority of *lactate* produced in the tissues is converted to pyruvate in the liver. Other sites of lactate metabolism include the kidney and muscle. Hyperlactatemia may occur in liver disease as a result of inappropriate hepatic metabolism of lactate. Hepatic failure is a rare cause of hyperlactatemia in horses.

CBC may be helpful in diagnosis of liver disease. Increases in *WBC* and *fibrinogen* may suggest infectious causes of liver disease. Absolute *erythrocytosis* has been reported as a paraneoplastic syndrome secondary to hepatocellular carcinoma in a horse.

Preliminary data from a recent study evaluating the prevalence of erythrocytosis in horses with liver disease found erythrocytosis in 8/19 of horses with liver disease and liver biopsy presenting to a referral hospital. These data suggest that erythrocytosis may be more common in horses with liver disease than previously reported. The mechanism by which it develops is unknown.

Urinalysis is a simple, useful and practical procedure for evaluation of hepatic disease in horses. Bilirubinuria without the presence of hemolysis is suggestive of liver disease. Bilirubinuria causes a brown discoloration of urine like that seen with myoglobin. These two substances can be differentiated by simple dipstick analysis. Some horses with liver failure may develop an intravascular hemolytic syndrome with a subsequent hemoglobinuria. Because of the grave prognostic indications of this complication, routine evaluation of urine for the presence of bilirubinuria and hemoglobinuria is recommended.

Ultrasound

The liver can be seen using a 3 MHz sector probe. It is located primarily on the right side of the abdomen caudal to the diaphragm and can also be seen on the left cranioventral abdomen caudal to the diaphragm and cranial to the spleen. Size cannot be determined as a large portion remains behind the diaphragm. The liver should have homogeneous echogenicity and should be hypoechoic when compared to the spleen on the left side. Color-flow Doppler is used to distinguish blood vessels from bile ducts. Ultrasound is useful for determination of *echogenicity, identification of masses* and *cholelithsi*. Cholelithsi appear as hyperechoic structures within hepatic parenchyma that cast acoustic shadows. Enlarged bile ducts are suggestive of a cholelith within the common bile duct. Unfortunately, definitive diagnosis of hepatic disease cannot be made on ultrasound.

Liver biopsy

Liver biopsy is used to make a definitive diagnosis and prognosis for liver disease in the horse. A liver biopsy can be performed from the right 9-14th intercostal space at the intersection of a line between the wing of the ilium and the mid humerus. Some horses have atrophy of the right hepatic lobe and there is risk of biopsy of the colon or lung from that location. For those reasons, ultrasonographic guidance is preferred. Any identified masses or areas of abnormal echogenicity should be biopsied if possible. If abnormal areas are identified but in unsafe areas (ie next to the heart, colon, behind lung), a sample should be taken from an area that is safe. If the disease is diffuse (enough to cause increases in liver enzymes), a definitive diagnosis will most likely be made. PT/PTT should be performed prior to performing a liver biopsy and will alert the clinician to potential for hemorrhage resulting from the procedure. A recent paper described abnormal clotting test results in 58% of cases undergoing liver biopsy but no association between abnormal coagulation tests and bleeding. In that study, only 5% of cases had evidence of hemorrhage, none of the severity to warrant treatment.

In a lightly sedated patient, a sterile preparation is performed, the skin and underlying muscle blocked with lidocaine, and a stab incision made through the skin. In the absence of an identifiable mass, I choose a space on the right side where the liver is the largest. I prefer to use a Tru-Cut 14g biopsy instrument under ultrasonographic guidance to obtain the largest piece of liver possible. I usually take 3-4 pieces from the same skin incision. Two to three pieces are taken for histopathology and one piece for aerobic and anaerobic culture.

Liver biopsy is the best means of determining a definitive diagnosis and prognosis for horses with liver disease. A scoring system has been created for evaluation of liver histopathology and determination of prognosis. Factors evaluated included fibrosis, irreversible cytopathology (megalocytosis, necrosis), inflammatory infiltration, hemosiderin accumulation, and biliary hyperplasia. As the degree of each factor increased, the prognosis worsened. Reversible cytopathology (hydropic degeneration) was not associated with poor prognosis for survival.

Etiologies of liver disease

ACUTE	CHRONIC
Theilers Disease	Pyrrolizidine alkaloid toxicity
Hepatic Lipidosis	Cholelithiasis
Ascending bacterial cholangiohepatitis	Chronic active hepatitis
Tyzzers Disease	Clover toxicity
Infectious necrotic hepatitis	Hepatic Abscess
Viral hepatitis	Hepatic neoplasia
Parasitic hepatitis	
Aflatoxicosis	
Toxic hepatopathy	

Treatment

Treatment of liver disease is generally supportive. Therapy is aimed at reducing clinical signs associated with hepatic encephalopathy, systemic anti-inflammatory therapy, appropriate nutrition, intravascular fluid support, and antimicrobial therapy. Treatment should be undertaken while awaiting results of biopsy. Regardless of cause, *bridging fibrosis* represents a poor prognostic indicator and treatment will largely be unsuccessful.

Specific treatment for hepatic encephalopathy includes reduction in ammonia levels and controlling signs of cerebral dysfunction. Lactulose may be administered orally to create an acidic environment within the colon, decrease ammonia production, increase

bacterial utilization of ammonia, and trap ammonia within the lumen. Lactulose may cause an osmotic diarrhea as well. Neomycin has been used in the horse to alter enteric microflora. This may predispose to Salmonella overgrowth as Salmonella species are resistant to neomycin. However, neomycin reduced signs of HE in horses better than lactulose. If sedation is required, benzodiazepines should be avoided as high GABA activities in the central nervous system likely contribute to signs of HE. GABA antagonist flumazenil has not been highly successful in treatment of people with HE.

Intravenous fluid support with balanced polyionic solutions is important to reduce hepatic workload while supporting the vascular space. Fluid therapy may decrease the viscosity of bile and reduce biliary stasis. Administration of a 5% dextrose solution at 50 mL/kg/day will provide modest calories that are easily utilizable without hepatic metabolism. This does not provide a significant source of calories. In patients that are inappetent, partial parenteral nutrition or indwelling feeding tubes should be considered. Oral and intravenous formulations of branched chain fatty acids are commercially available.

Appetent patients should be fed diets high in branched chain amino acids. An example diet is 2 parts beet pulp mixed with one part cracked corn in molasses fed at a rate of 2.5 kg/100 kg body weight per day. It is optimal to divide the feed into 6 feedings per day because of impaired gluconeogenesis. Oat hay is best followed by grass hay. Legumes should be avoided due to high protein content. However, if the horse will only eat alfalfa or peanut hay, some intake is better than none. Oats, soybean meal, and high fat feeds should be avoided.

Any cholangial proliferation will result in mild cholestasis and potential secondary bacterial infection. Horses suspected of having liver disease with mild clinical signs can be treated with a short course (14 day) of *trimethoprim-sulfamethoxazole.* This should be continued even if the horse has a biopsy suggesting a lymphohistiocytic infiltrate. If a horse presents with fever, clinicopathological evidence of infection, or more severe clinical signs, a combination of a β-lactam (*penicillin, ceftiofur*) and either an aminoglycoside (*gentamicin, amikacin*) or floroquinolone (*enrofloxacin*) should be used. *Metronidazole* should be considered as anaerobes are often isolated in cases of ascending cholangiohepatitis. Metronidazole may also act against enteric flora producing ammonia.

Anti-inflammatories are an important component of treatment of hepatic diseases. Inflammation may cause signs of colic and may worsen cholestasis if bile ducts are involved. Non-steroidal anti-inflammatory agents (flunixin meglumine, phenylbutazone, or firocoxib) may reduce pain and inflammation associated with hepatic disease. Kupffer's cells are required to remove endotoxin and other bacterial by-products from systemic circulation. Therefore, endotoxemia is often a component of liver diseases. Anti-inflammatories including flunixin meglumine and pentoxifylline will reduce systemic effects of endotoxin (See Dr. MacKay's notes on endotoxemia). Pentoxifylline is an inhibitor of fibrosis and may be beneficial to reduce further fibrosis in the liver although no studies exist on its efficacy. It does not seem to be effective to reduce fibrosis in people with cirrhosis of the liver. Corticosteroids are the mainstay of therapy for chronic active hepatitis when an autoimmune cause is suspected. Corticosteroids also inhibit fibrosis.

Suggested Doses for Select Therapeutic Medications	
Amikacin	25 mg/kg IV, IM, SQ, q 24h (foal)
	10 mg/kg IV, IM, SQ, q 24h (adult)
Ceftiofur	2.2-4.4 mg/kg IV, IM, q12-24h
Dexamethasone	0.04 to 0.1 mg/kg, IV IM or PO, q 24h
Dextrose (50%)	2.5 - 5.0% of fluids IV as CRI
Enrofloxacin	5 mg/kg IV or 7.5 mg/kg PO q 24h
Gentamicin	6.6 mg/kg IV, IM, q 24h
Heparin	100-250 U/kg IV, q 12h
Insulin (Humulin-R)	0.01-0.1 U/kg IV as CRI
Lactulose	0.2 ml/kg PO, q 12h
Metronidazole	25 mg/kg PO, 35 mg/kg PR q 12h
Neomycin	5.0 mg/kg PO, q 12h
Prednisolone	1 mg/kg, PO, q 12-24 h
Potassium Penicillin	22,000 U/kg IV, q6h
Procaine Penicillin	22,000 U/kg IM, q 12h
Trimethoprim-Sulfa	30 mg/kg PO, q 12h

Emerging Equine Infectious Diseases

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Equine infectious diseases continue to emerge and re-emerge, infecting horses across the US and beyond. Infectious disease identification and treatment remain a cornerstone of equine practice. This lecture will discuss infectious disease updates and will review pigeon fever, piroplasmosis, MRSA, and others. The clinical syndromes, diagnostic techniques, and therapy will be included.

Equine piroplasmosis

Piroplasmosis is caused by the protozoan parasites *Babesia caballi* and *Theileria equi* (formerly called *Babesia equi*). It also can affect donkeys, mules, and zebras; but clinical disease in those equids is rare. The disease is transmitted by ticks and other biting insects; however, shared needles and/or blood contamination has been implicated in several disease outbreaks. Once horses are infected with *T. equi*, carrier status may be lifelong. Carrier horses are also capable of transmitting the disease to ticks—vectors that can transmit it to other horses. The disease is considered endemic in Africa, Central and South America, Asia, the Middle East, the Caribbean, and the Mediterranean. The U.S. has not been considered an endemic region. When infection occurs, *T. equi* tends to be the most common agent, rather than *B. caballi*. However, infection with both parasites can occur simultaneously.

Once horses become infected with the parasite, it usually takes between 5 and 30 days for any signs of the disease to appear. As previously stated, infected horses may not have any signs of EP at all. Generally, affected horses display nonspecific signs that can look similar to other diseases. Fever, depression, anorexia, pale or icteric mucous membranes, and edema of the limbs or along the ventral abdomen have been commonly reported. Reddish-brown or discolored urine may also be observed. Laboratory abnormalities typically include anemia and thrombocytopenia.

Several laboratory tests are available for diagnosis of EP. Occasionally, the parasite can be seen on microscopic examination of a blood smear. The U.S. Department of Agriculture (USDA) standard test is the cELISA (competitive enzyme-linked immunosorbent assay). Specific laboratories (the National Veterinary Services Laboratories, Texas Veterinary Diagnostic Services Laboratories, Florida's State Diagnostic Laboratory) have been identified to run the tests and report the results. The National Veterinary Services Laboratories is still testing all international transport samples.

Horses that test positive for equine piroplasmosis MUST be quarantined. Local veterinarians can work with state and federal veterinarians to ensure that manageable quarantine guidelines are being followed and are in place. Although there are several drugs (imidocarb, etc) that have been identified for treatment of piroplasmosis, the organisms can be refractory to treatment, and the carrier state is difficult to clear. Euthanasia for positive horses is not required, nor is it being recommended in every case by the USDA, especially since so many positive horses are asymptomatic. State and USDA veterinarians are working in conjunction with local veterinarians and owners to determine the best recommendations for each positive horse. Some owners elect to transport positive horses out of the country—to countries that have endemic piroplasmosis—but that is not a palatable option for most. In addition to quarantine, there is a treatment research program available for positive horses. This program is in conjunction with Washington State University and Dr. Don Knowles. Owners and their local veterinarians work with the USDA and Dr. Knowles to determine if they have a horse that is eligible for enrollment. Recent published research out of that program is showing promise for clearing infection in horses treated with imidocarb.

Fortunately, it does not appear that tick transmission has been significantly involved in EP transmission outside of the affected premises in Texas. However, people can spread this disease from horse to horse, and we can prevent that mode of transmission. All dental, surgical, and tattoo equipment must be thoroughly disinfected between horses. Horses have contracted the disease though the use of shared needles and/or syringes, as well as from blood transfusions. A new sterile needle and syringe should be used for each injection, whether into a muscle or a vein. Additionally, a previously used needle should never be inserted into a drug or vaccine multidose vial—and owners/trainers should be reminded of these infection control measures. Work with your veterinarian to ensure that all equipment is thoroughly cleaned and disinfected between horses. EP is still a very uncommon disease in the U.S., but it is critical to be vigilant and follow preventative measures.

Pigeon fever

This disease is caused by Corynebacterium pseudotuberculosis, which is a gram positive rod shaped bacteria. Horses and small ruminants typically get different strains of the infection, but cattle can get both types. In goats, the disease is known as caseous lymphadenitis, and affected animals will have external abscesses (the head, behind the ears, on the neck, shoulder or flank are some typical locations). Abscesses also occur in horses and cattle infected with this bacteria. Natural transmission from horses to goats or vice versa is not thought to commonly occur. Corynebacterium pseudotuberculosis is a soil organism that can survive for months to even years in direct sun. The largest numbers of cases are typically reported in the dry months of fall and winter.

Many things about this disease in horses are still not completely understood, such as the incubation period. The incubation period is the time it takes to develop clinical symptoms of the disease after being infected with the bacteria, and can be variable…. from weeks to even months. The bacteria can enter the horse through the skin, wounds, or abrasions in the mucous membranes. Horses with pigeon fever may have a poor appetite, fever, lethargy, swelling along the chest or ventral abdomen, and/or lameness. Three forms of the disease can occur in the horse: external abscesses, internal abscesses, and ulcerative lymphangitis. The most common form of pigeon fever is the development of external abscesses. These occur in about 90% of the cases. The disease got its name because abscesses will commonly occur in the pectoral region which becomes swollen and painful. In addition to the pectorals, abscesses may form on the prepuce, mammary gland, axilla, limbs, inguinal region, head, and other areas. There is no breed or sex predisposition for acquiring the infection, although young horses may have some increased risk. The second form of the disease is internal abscessation, which has been reported in about 8% of cases. The most common site of internal abscesses is the liver, although they can be associated with other organs as well. The third form, ulcerative lymphangitis, is a severe cellulitis that occurs in the fewest number of cases. Clinical cases of ulcerative lymphangitis have severe lameness and swelling of the limb.

Definitive diagnosis of pigeon fever is made by culturing the bacteria from an abscess or draining wound. There is a blood test available (called the synergistic hemolysis inhibition test) but the results depend on the severity and length of infection. This means that a negative blood test (titer) does not rule out the disease. In fact, early in the disease horses may have a negative blood test. The blood test is helpful in horses with internal abscesses, as the titers are typically very high (>1:512). Ultrasound examination may be a helpful diagnostic tool in these cases as well, especially for identifying internal abscesses in the abdominal cavity.

Treatment of pigeon fever is accomplished with drainage of external abscesses. The primary veterinarian should always be consulted about treatment. Abscesses should be allowed to mature and then drained. They should be flushed with antiseptic solutions. Purulent material drained from abscesses is highly infectious and must be carefully handled and disposed of. Collecting as much purulent material as possible into a waste bag for disposal is critical to reduce the risk of other horses being exposed. Bedding of infected horses should be properly disposed of as well. Pain medication may be indicated for horses with severe or deep abscesses or lameness. Topical fly treatment around wounds and draining areas is critical to reduce the possibility of biting insects transmitting the infection. Systemic antibiotics may be utilized for treatment on a case by case basis. In routine cases with external abscesses, antibiotics may prolong the course of the disease and are typically not required. However, antibiotics are appropriate in cases with severe disease or reoccurrence of infection. Long term systemic antibiotics are required for treatment of horses with internal abscesses. Fortunately, Corynebacterium pseudotuberculosis is usually sensitive to most antibiotics (including penicillin), but culture and sensitivity of a sample of purulent material is recommended to direct therapy.

A conditionally licensed vaccine was released and then removed from the veterinary market this past spring. It is recommended to isolate infected animals, especially if draining wounds/abscesses are present. Stalling affected horses will help reduce contamination of the pasture environment with infectious material. Horses should be treated in an area ideally with concrete or rubber flooring that can be disinfected. Although no reports exist of humans being infected from horses, there are reports of humans being infected with the sheep strain of the disease. Infection in people has occurred from the consumption of infected unpasteurized milk or milk products, close contact with infected animals, handling contaminated equipment, or exposure of wounds with infected material. Therefore, wearing gloves when handling infected horses is recommended. Fly sprays and feed through fly control may both be beneficial for insect control. If you suspect your horse is exhibiting signs of pigeon fever, contact your veterinarian for a thorough examination.

MRSA

The prevalence of Methicillin-resistant *Staphylococcus aureus* (MRSA) in routine infections in people and hospital outbreaks has initiated world-wide concern. *Staphylococcus aureus* is a common bacterium that colonizes the skin and has been found to cause disease in many species. *Staphylococcus aureus* began developing resistance to antibiotics almost as soon as they were introduced, beginning with penicillin, and progressing to methicillin resistance. MRSA is typically resistant to all beta-lactam antibiotics (penicillin and cephalosporin families) and often many other antibiotics as well. This antimicrobial resistance can make MRSA infections a challenge to treat. The percentage of community-associated infection (milder, outpatient type illness like skin infections/abscesses) from MRSA had risen from 35.1% in 2003 to 50.0% in 2006 in Florida.

Methicillin-resistant *Staph aureus* infections in the horse have manifested as wound and surgical site infections, cellulitis (soft tissue infections, typically of the limb), catheter-site infections, pneumonia, septic arthritis, and skin infections, among others. Historically, equine MRSA infections were uncommonly reported, and began to increase in prevalence in the late 1990s. More recent studies have demonstrated that MRSA is an important emerging pathogen in horses and can be zoonotic. It is also possible for humans to transmit the bacteria to horses as well. Approximately 25% of healthy children and adults can carry the *Staphylococcus aureus* bacteria in their nose or on the skin. For most people and horses, carrying the bacteria in the nose or on the skin causes no ill-effects. Certain circumstances such as a wound or an illness requiring hospitalization can result in active infection.

Studies done in horses have found that approximately 0-5% of horses carry the MRSA bacteria in their nasal passages, which is the most common site for colonization (Weese et al, 2005). Horses can also have the bacteria on their skin or in their intestinal tract. Although generally very few horses carry the bacteria, some farms with a history of MRSA infections in horses have demonstrated carrier rates of 0-45% (Weese et al, 2005). Horses that carry the bacteria in their nasal passages may not ever develop a clinical MRSA infection. However, these horses may transmit MRSA to other horses or people, and will sometimes develop active infections under certain conditions. People who work with horses seem to have a higher carrier rate of MRSA. Studies of equine veterinarians have reported colonization rates ranging from 10-14%, with predominantly the equine strain of the bacterium. This provides further evidence that carrier horses can transmit MRSA to humans.

Clinical infection with MRSA is certainly concerning. Fortunately, a multicenter study reported that 83% of horses with MRSA infections survived (Anderson et al, 2009). Many horses with clinical infections such as pneumonia or wound infections required prolonged hospital stays and needed additional surgeries. However, acceptable antibiotic options exist in most cases, especially when infection is identified early. In this author's experience, catheter site infections with MRSA, while uncommon, result in the highest mortality rates if the infection spreads through the bloodstream and into the lungs or other sites. Early detection and treatment is certainly critical for the best outcome for the horse. Currently, there is no evidence that horses that carry MRSA need to be treated with antibiotics. Farms with documented MRSA prevalence have successfully eradicated MRSA with good hygiene and infection control practices.

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Practical Approach to Coughing Horses

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Cough and poor performance are common complaints among pleasure and sport horses in equine practice. This lecture will discuss a practical diagnostic approach to the horse with a cough, and treatment of non-infectious lower respiratory disease.

History and examination

A complete history and physical examination are critical for evaluating the patient with cough. Duration, severity, nasal discharge, presence or absence of fever, and inciting causes can all be helpful in determining the underlying etiology. A rebreathing examination should be performed as part of a complete respiratory examination. Horses with inflammatory, non-infectious lower airway disease may have a prolonged recovery and the presence of crackles and/or wheezes on examination. Horses with infectious pneumonia may have abnormal adventitial sounds as well, and as such, this examination will not point to a specific etiology. A complete blood cell count may be beneficial to determine whether evidence of infection is present, but can be normal in horses with pneumonia. Changes in the white blood cell count or fibrinogen concentration should prompt further diagnostic consideration.

Horses with a history of fever and changes on the CBC should be suspected of having infectious lower airway disease/pneumonia. Definitive determination of a bacterial etiology is best accomplished with a percutaneous trans-tracheal aspiration sample submitted for cytology and culture/sensitivity. Pneumonia is often characterized cytologically with degenerative neutrophils (with or without the presence of intracellular bacteria). Broad spectrum antibiotics should be initiated if cytology is suggestive of pneumonia, while culture results are pending. Tracheal aspiration cytology can also be suggestive of inflammatory lower airway disease, when non-degenerative neutrophils are the predominant cellular population. Thoracic ultrasound examination and radiographs can be helpful in the evaluation of the horse with lower airway disease. Practically speaking in a field setting, ultrasound examination of the thorax can be accomplished with a trans-rectal probe. This technique is most useful to determine if pleural fluid or pulmonary infiltrates are present.

RAO (heaves, equine asthma)

Recurrent airway obstruction (also known as heaves, equine asthma, broken wind, and chronic airway reactivity) is a common respiratory disease of horses characterized by periods of reversible airway obstruction caused by neutrophil accumulation, mucus production, and bronchospasm. The classic clinical syndrome includes chronic cough, nasal discharge and respiratory difficulty. The term COPD is no longer used to describe this condition in horses, because the pathophysiologic and morphologic aspects of the disease are different from human chronic obstructive pulmonary disease.

Most evidence suggests that RAO is the result of pulmonary hypersensitivity to inhaled antigens, although multiple theories exist regarding the exact pathophysiology. The most common antigens are mold, organic dust, and endotoxin present in hay and straw. Periods of reversible small airway obstruction are caused by bronchoconstriction and accumulation of mucus and neutrophils. RAO occurs worldwide, with the highest prevalence in stabled horses fed hay in the northeastern and midwestern United States. A similar condition that can occur in horses in the southeastern United States is termed summer pasture associated obstructive disease (SPAOD). However, horses with SPAOD typically improve when stabled. RAO is a common respiratory disease of mature horses (typically > 7 years old). The average age of onset in RAO affected horses is 9-12 years, and both genders are commonly affected. Winter and spring appear to be the most common seasons for exacerbation of RAO. There does appear to be a heritable component to the etiology of this condition. The incidence of RAO in horses with healthy parents is approximately 10%, which increases to 44% if two parents are affected.

Clinical signs

Clinical signs of RAO typically include a chronic cough, nasal discharge and a prolonged labored phase of expiration. The classic “heave line” is due to hypertrophy of the abdominal muscles which are assisting in respiration. Flared nostrils and tachypnea are frequently observed. On thoracic auscultation, wheezes, tracheal rattles, and over-expanded lung fields may be present. Crackles may also be heard secondary to excessive mucus production in the lower airways. Severe cases may also exhibit weight loss, cachexia, and exercise intolerance. Horses are typically afebrile with normal complete blood cell count and serum biochemical profile, unless a secondary bacterial pneumonia has occurred.

Diagnostic evaluation

Diagnosis of RAO can be done on the basis of history and characteristic clinical examination findings in the majority of horses. Additional diagnostics to confirm and characterize the pulmonary inflammation include transtracheal aspiration (TTA), bronchoalveolar lavage (BAL), thoracic radiographs and ultrasound examination.

Transtracheal aspiration can be done to characterize inflammation in the lower airways and to determine if sepsis is present. The presence of degenerative neutrophils and intracellular bacterial organisms suggests sepsis, and warrants culture as well as appropriate antimicrobial therapy. Typical RAO cases have no evidence of sepsis, and TTA results are consistent with mucopurulent (neutrophilic) inflammation.

Bronchoalveolar lavage is indicated in horses with poor performance and coughing, and is not compulsory in horses with severe disease and suggestive clinical signs. Neutrophilic inflammation (with 20-70% of neutophils in total cell count, normal neutrophil count is <5-10%) confirms the presence of lower airway inflammation and is suggestive of RAO. Curschmann's spirals may be present on cytologic evaluation of TTA and BAL samples, and represent inspissated mucus plugs from the obstructed small airways.

Thoracic radiographs will often demonstrate an increased broncho-interstitial pattern throughout the lung fields. These changes may be difficult to differentiate from normal ageing changes in older adults. Radiographs are recommended for horses that fail to respond to standard therapy, or to further characterize pulmonary inflammation. Horses that have more respiratory difficulty on inspiration rather than expiration may have interstitial pneumonia or pulmonary fibrosis, and radiographs are indicated to better characterize lung disease in these cases. Ultrasound may be utilized if primary or secondary infectious pulmonary disease is suspected.

Lung function tests in horses with RAO typically demonstrate hypoxemia without hypercarbia, due to V/Q mismatch. Function abnormalities will often include high resistance and poor compliance of the lungs, with increased dead space ventilation. Lung function testing is not widely available, but can be performed at The University of Florida. It is beneficial in more subtle cases of poor performance and inflammatory airway disease (IAD).

Treatment

The most important treatment for RAO is environmental management to reduce exposure to organic dusts and mold. As previously mentioned, the most common antigens are organic dusts, mold, and endotoxin present in hay and straw. Round bale hay is high in endotoxin and organic dust content, and the presence of round bale hay is a potential cause of treatment failure in horses on pasture. Maintaining horses on pasture full-time is generally recommended. Horses that must be stalled should be kept in a clean, well-ventilated environment and ideally be transitioned to a complete pelleted feed. Straw is not recommended as bedding for RAO affected horses. Soaking hay (for at least 2 hours) and feed may alleviate the signs in mildly affected individuals, however, soaked hay may still exacerbate RAO in more severely affected cases. It is important to remember that although medications will alleviate the clinical signs of disease, respiratory disease will return if the horse remains in a mold/dust-filled environment once the medications are discontinued.

Systemic corticosteroids and aerosolized bronchodilators are the most immediately helpful therapy for a horse in respiratory distress. Intravenous administration of Dexamethasone (.1 mg/kg) should improve lung function within 2 hours of administration. Dexamethasone has an oral bioavailability of about 60%, and will improve pulmonary function within 6 hours if given by this route. Dexamethasone may be continued for one to several weeks at a tapering dose (usually quarter the dose every 3-5 days) for severe cases. Isoflupredone acetate (.03 mg/kg IM every 24h for 14 days) and a single dose of triamcinolone acetonide (0.05-0.09 mg/kg IM) have also been utilized in horses with significant respiratory difficulty and acute airway obstruction. For management of less severely affected cases of RAO, prednisolone is generally considered to be less potent and less toxic than the previously mentioned drugs. Prednisolone should be administered at 1-2.2 mg/kg orally once daily for a week and then gradually tapered. Oral prednisone is poorly bioavailable, and not recommended for treatment of RAO in horses.

Corticosteriods will not provide immediate relief of acute, severe airway obstruction, and rapidly acting β_2-adrenergic bronchodilators (such as albuterol sulfate) are indicated for treatment in those cases. Aerosolized albuterol sulfate (.8-2 µg/kg in MDI, metered-dose inhaler; typically 5-10 puffs/500kg of 100 µg/puff MDI every 4-6h) improves pulmonary function by 70% within 5 minutes of administration; however, the beneficial effects last only 1-3 hours. Administration of albuterol will improve the pulmonary distribution of other aerosolized medications, such as aerosolized corticosteroids, and speed mucociliary clearance. Salmeterol (210 µg dose, 1-3 times daily) may also be used as an inhaled bronchodilator. Ipratroprium bromide (20 µg/puff, 5-10 puffs/500 kg every 6-8 hours) has also been utilized for inhaled bronchodilator therapy.

Clenbuterol (.8-3.2 mcg/kg PO every 12 h), a β_2-adrenergic agonist, provides long-acting bronchodilation in horses with moderate to severe RAO. Side effects include tachycardia and sweating, which are more common at higher doses and with intravenous administration. The clinical efficacy of clenbuterol is inconsistent at lower dosages if exposure to a dusty environment is maintained. However, it does appear to improve the objective parameters of pulmonary function. Down-regulation of β_2-receptors has been documented in horses after administration of clenbuterol for 12 days (.8 µg/kg IV, every 12h). Administration of corticosteroids prevents clenbuterol-induced desensitization when administered concurrently. Since β_2-agonists have minimal to no anti-inflammatory activity, they should not generally be used alone for the treatment of RAO.

Systemic anti-cholinergic drugs are not recommended for long-term management of RAO due to their potentially severe side effects (CNS toxicity, ileus, mydriasis, tachycardia, etc). Atropine (5-7 mg IV/450 kg) can be administered as a rescue medication

during a severe airway obstruction episode. Ipratroprium bromide is a synthetic anti-cholinergic drug that is administered via inhalation and produces bronchodilation, inhibits cough, and protects against bronchoconstrictive stimuli. Its duration of effect is 4-6 hours and it is administered at 90-180 µg/horse in an MDI (AeroHippus and the Equine Haler).

Aerosolized corticosteroids are effective in horses with mild-moderate RAO, and can be used in conjunction with systemic therapy in severe cases. The two aerosolized preparations for administration to horses via the Equine Haler™ are beclomethasone diproprionate (3500 µg/horse every 12h via MDI) and fluticasone propionate (2000 µg/horse every 12 hours via MDI; typically 8-10 puffs/500 kg of a 220 µg/puff MDI twice daily). Fluticasone is the most potent and most expensive inhaled corticosteroid, and due to its low oral bioavailability, it has the least potential for adrenal suppression. In affected horses, fluticasone proprionate reduces pulmonary neutrophilia, improves parameters of pulmonary function, reduces responsiveness to histamine challenge, and speeds clinical recovery. Although the therapeutic effect is not immediate, pulmonary function typically begins to improve within 24 hours after administration of aerosolized corticosteroids. Additionally, horses in apparent "remission" from RAO may benefit from low dose, long term, aerosolized corticosteroid treatment.

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Strategic Parasite Control: A Reality?

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Strategic parasite control through targeted deworming programs based on fecal egg count testing is currently the recommended approach for equine parasite management. This lecture will review equine parasites and the use of a basic targeted deworming program. This lecture will be based on the AAEP's Parasite Control Guidelines, which can be accessed free online at: http://www.aaep.org/custdocs/ParasiteControlGuidelinesFinal.pdf

Foal Diarrhea: What Next?

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Foal diarrhea can be very concerning for owners as well as a diagnostic challenge for veterinarians. This lecture will review the most common etiologies, diagnostic, and treatment options for diarrhea in the foal. This lecture is based on the publication co-authored by the speaker:

Mallicote M, House AM, and Sanchez C (2012). A Review of Foal Diarrhea from Birth to Weaning. Equine Veterinary Education, April 2012, 24(4): 206–214. doi: 10.1111/j.2042-3292.2011.00358.x

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Hemorrhage in Field Situations

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Severe, acute hemorrhage can be a life-threatening situation that requires immediate. The practitioner must first identify the source of bleeding, arrest further blood loss if possible, and ensure adequate tissue perfusion. While the causes of acute bleeding are numerous, treatment can be focused with this step-wise plan for resuscitation.

Pathophysiology of hemorrhagic shock

Hemorrhagic shock is technically a subset of hypovolemic shock, defined separately from hypovolemia by a loss of oxygen carrying capacity as a result of loss of red blood cells. As blood volume decreases due to the loss of both plasma and cells, cardiac output and total oxygen delivery to the tissues decreases. In response, cardiac output is increased by autonomic responses that result in tachycardia, vasoconstriction, improved cardiac contractility, and redistribution of blood flow to the vital organs. In time, the oxyhemoglobin dissociation curve is shifted to the right, and tissue oxygen extraction increases from the red blood cells that remain. Severe or sustained blood losses eventually overwhelm these compensatory mechanisms and the body can no longer meet the needs of systemic oxygen demand. This stage of hemorrhagic shock is called the critical total oxygen delivery point, and is consistent whether it is caused by anemia, hypoxemia or hypovolemia.[1]

Clinical signs of dysoxia are related to the organ systems affected and the stage of hemorrhagic shock.[2] The respiratory, hepatic and gastrointestinal systems are the first organs affected, due to redistribution of the circulating blood to the heart, brain and kidneys. For the respiratory system, clinical manifestations of lung injury can include tachypnea and signs of pulmonary edema (dyspnea, frothy mucous from the lower airways), due to intrapulmonary shunting and reduced compliance. Hepatic injury may be identified by elevations of both bilirubin and alkaline phosphatase on serum chemistries. In the gastrointestinal tract, ischemia is characterized by signs of abdominal pain. Compromise of blood flow resulting in mucosal ischemia may allow for ulceration, bacterial translocation to the venous circulation and, ultimately, sepsis.

As the compensatory mechanisms for hemorrhagic shock begin to fail subsequent to continued blood loss, the function of the brain, heart and kidneys begins to deteriorate. Clinical signs of hypoxia affecting the central nervous system are seen initially as agitation, followed by a lack of response to simple commands, depression, coma and death. While the cardiovascular system may attempt compensation early in the course of hemorrhage by tachycardia and increasing stroke volume, continued hemorrhage results in hypoperfusion of the myocardium, causing cardiac ischemia and eventually cardiac failure. Cardiac murmurs and arrhythmias may be noted in the late stages of hypovolemic shock. Activation of the renin-angiotensin-aldosterone system by the kidneys provides some support to the cardiovascular system early on. Urine specific gravity is initially increased, but as renal perfusion decreases, oliguria is noted as compensation fails. The goals for treatment of acute hemorrhage are limit further organ damage and prevent multi-organ failure. The method of treatment is to restore an adequate circulating volume and oxygen carrying capacity with fluids, plus or minus cells.

Treatment of hemorrhagic shock

The first step in treatment of acute blood loss is to classify the type of hemorrhage involved. Hemorrhage is defined as controlled if it is caused by blood loss from a vessel or organ that can be stopped using physical means. In situations of controlled hemorrhage, the solution is fairly straightforward in the form of applied pressure, bandages, or ligation of the bleeding vessel. In contrast, the source of bleeding in uncontrolled hemorrhage is either difficult to access, or so extensive that continued blood loss is expected. If bleeding is internal, inaccessible, or the source cannot be identified, mitigation is the key.

Medications that have been evaluated in horses to inhibit uncontrolled hemorrhage are aminocaproic acid, formalin, and yunnan baiyao. Aminocaproic acid, a lysine derivative, may reduce clot disruption through inhibition of fibrinolysis. In horses, administration can result in a reduction in partial thromboplastin time (PTT), which is the measure of the efficacy of the intrinsic and common coagulation pathways.[3] Due to its short half-life, this medication is currently recommended as a constant rate infusion, and has been shown to provide adequate circulating plasma levels using 3.5 mg/kg/min for 15 minutes, followed by 0.25 mg/kg/min.[4] This dose was based on efficacy of this medication in humans, and recent research in horses has identified that this dose may be twenty times too high, based on the sensitivity of the equine clotting system to this medication.[5] Further evaluation of the efficacy of this dose in a live animal model will be required, but its use should be cautioned if an underlying coagulopathy is suspected. In a field situation, a bolus dose of 30 mg/kg of aminocaproic acid may provide some benefit if a CRI is not possible. An alternative anti-fibrinolytic medication, called tranexamic acid, may be substituted for aminocaproic acid, and has been recommended by one manufacturer at an anecdotal dose of 5-25 mg/kg IV.[6]

Intravenous formalin has also been assessed in the horse to mitigate hemorrhage, due to its ability to activate platelets and enhance primary hemostasis when tested in other species.[7] A low dose (0.37% formaldehyde; 37ml of 10% buffered formalin in 1000 mL

balanced electrolyte solution) had no negative effects on bleeding times, PTT, activated partial thromboplastin time (APTT), fibrin degradation products, or activated clotting times in the horse. However, higher doses of formalin (0.74% formaldehyde) resulted in numerous side effects including muscle fasciculations, agitation, tachycardia, and tachypnea.

Finally, the Chinese hemostatic medication Yunnan baiyao (or paiyao), purported to contain a mixture of progesterones, saponins, and alkaloids, has been anecdotally documented to mitigate hemorrhage. The mechanism of action is unknown, but a study in ponies showed an prolongation of template bleeding time, which may indicate stimulation of platelet activation.[8] The dosage for Yunnan baiyao is 8 mg/kg 2-4 times daily, per os.[9] In all of these studies, the effects of these medications on hemorrhage were not directly assessed, only their effects on measures of clotting times and activation of the clotting cascade in the normal horse. At this time, aminocaproic acid would be the recommended medication for uncontrolled hemorrhage in the horse based on its safety documented in these experimental models.

Once hemorrhage has stopped, or attempts at reducing further blood loss have been made, fluid resuscitation should be instituted to improve tissue perfusion. There are important considerations for fluid therapy based on whether the bleed is classified as controlled or uncontrolled hemorrhage.[10] For horses where blood loss has been controlled, the goal of resuscitation is to restore the circulating blood volume to a level that normalizes arterial blood pressure and cardiac output. Objective measures of adequate fluid resuscitation in controlled hemorrhage include normalization of blood pH (7.35-7.4), blood lactate (<2.0 mmol/L), central venous pressure (7.5-12 mmHg), and urine output. To monitor resuscitation clinically, the practitioner should observe the horse for urine production and an improvement in peripheral pulses, temperature of the extremities, and mentation.

Fluid choices include crystalloids (Normasol R, Plasmalyte 148, Plasmalyte A, lactated Ringer's), colloids (Hetastarch) and 7.5% hypertonic saline. Crystalloids are preferred over colloids and hypertonic saline due to the fact that crystalloids can restore interstitial losses. Approximately 60-75% of the administered volume redistributes to the interstitium within 60 minutes of infusion, leaving approximately 30% in the vasculature. While a potential advantage, it is important to remember that approximately 3 liters of crystalloids will be required to replace each liter of lost blood. Colloids provide an advantage over crystalloids in that they can remain in the vascular space for up to 3 days, and can more rapidly improve cardiac output. Side effects of colloids include the possibility of coagulopathies at high doses (for Hetastarch, >10 ml/kg/day) due to dilution of clotting factors, and the inhibition of clotting factor 8 and von Willibrand's factor. In addition, colloids must be followed immediately by crystalloids administration to replace interstitial losses. Alternatively, hypertonic saline can be used in controlled hemorrhage to rapidly expand the extracellular fluid volume. While hypertonic has anti-inflammatory, anti-oxidant and anti-apoptotic effects, its effects on arterial pressures are short lived (<45 minutes). Hypertonic saline must be followed by crystalloid replacement to maintain the circulating volume. The dose for hypertonic saline is 2-4 ml/kg (approximately 1-2 liters per 1000 lbs. or 500 kg.). After restoring the intravascular fluid volume with fluid administration, blood products can be administered, if needed, to ensure a circulating hematocrit >12% and a platelet count of greater than 50,000/uL. Clinically, if the horse is still showing signs of tissue hypoxia (lactic acidosis, signs of colic), a transfusion may be required. It is important to remember that cardiac output cannot be significantly increased with blood products alone, due to their viscosity. Therefore crystalloids are still required for the initial volume resuscitation, and may prolong or prevent the need for a transfusion.

In uncontrolled hemorrhage where blood loss cannot be controlled, fluid therapy should be provided to maintain only the minimum circulating volume that will support the vital organs. This treatment, termed permissive hypotensive resuscitation, supports an adequate circulating volume to reduce further organ damage by hypoxemia, but prevents disruption of fragile clots or excessive dilution of clotting factors that could increase blood loss.[11] Initial therapy in uncontrolled hemorrhage should be provided by administration of crystalloids at a maintenance fluid rate (2.5 ml/kg/hour). Rapid plasma expanders, such as hypertonic saline and colloids, should be avoided. The goals of hypotensive resuscitation are to maintain a mean arterial blood pressure of 60-70 mmHg, with improvement in the other outcome measures, including a lactate <4 mmol/L, blood pH >7.25 and serum creatinine <3 mmol/L. Clinical parameters can be used to guide resuscitation, including improvement in mentation and peripheral pulses. In these horses, blood products should be administered as soon as practical to improve oxygen carrying capacity if hemorrhage cannot be contained.

Considerations for transfusion

Transfusions should be considered in horses that have been estimated to have lost >30% of their circulating blood volume. Estimating blood losses is often a difficult task. Urinary fluid losses, splenic contraction, water intake and fluid resuscitation all can alter packed cell volume by diluting or concentrating the remaining blood cells. Hematocrit, in the absence of iatrogenic fluid resuscitation, will not reflect the volume of blood lost until 8-12 hours after hemorrhage has stopped, when fluid from the interstitium and water intake have equilibrated with the circulating blood volume.[6] Once equilibration has occurred, blood loss can be estimated by the following formula:

liters blood lost = (normal PCV-patient PCV)/(normal PCV) x 0.08 x patient's weight in kg.

Because of the time it takes for equilibration, clinical findings are often more accurate than calculations early on for estimating blood loss, and can be based subjectively on pulse, respiratory rate, urine output and mental status. The overall clinical picture to

estimate blood lost by classifying hemorrhage into one of four groups, to estimate blood lost. (**Table 1**) More sensitive measures of acute blood loss may be serum lactate and central venous pressure (CVP), which is a measure of the systemic blood volume.[12]

Table 1: Classification of acute hemorrhage (adapted from Gutierrez, 2004)

	Classification of Hemorrhage			
	I	II	III	IV
Estimated Blood Loss	<15%	15-30%	30-40%	>40%
Clinical Parameter				
Pulse rate (beats/min)	<48	>50	>60	>80
Respiratory rate (breaths/min)	<20	>24	>30	>40
Mucous membrane color	pink	pale pink	white	white
Capillary refill time (seconds)	<2	<2.5	>3	>4
Pulse pressure	normal	decreased	decreased	decreased
Mentation	normal	agitated	depressed	stupor

To further guide the decisions for therapy, objective guidelines have been suggested for transfusion in the horse, including measurement of hematocrit, lactate and the oxygen extraction ratio. While hematocrit is variable, for the reasons stated previously, a hematocrit of <12%, or hemoglobin between 6-8 g/dl, is usually below the critical oxygen delivery level, and warrants transfusion. Lactic acidosis may result from anaerobic metabolism secondary to perfusion deficits or inadequate hemoglobin after hemorrhage. Lactate measurements are easily obtained using a hand held meter, and are relatively accurate for clinical purposes. Blood lactate levels should improve rapidly with fluid resuscitation if hemoglobin concentrations are adequate. Lactate measurements that persist above 2 mmol/L after fluid resuscitation may indicate the need for transfusion. While often less practical, the oxygen extraction ratio (arterial oxygen saturation minus central venous oxygen saturation, divided by arterial oxygen saturation) can be obtained by blood gas analysis. This calculation determines the oxygen extraction by the tissues, and a ratio >50% indicates tissue hypoxia. Central venous samples are difficult to obtain, therefore jugular sampling for PvO_2 levels as an estimate of oxygen extraction may provide some insight into tissue perfusion. The cutoff value indicative of inadequate oxygenation in the normovolemic horse is <31 mmHg, but must be interpreted with caution.[13] Finally, transfusions are warranted in any horse with uncontrolled hemorrhage with clinical signs of tissue hypoxia.

To select a blood donor, horses should be chosen to minimize the risk of transfusion reactions in the recipient. Geldings are preferred, and donors should be current on their vaccinations, and tested for blood borne pathogens. Because the blood types Aa, Qa and Ca are the most common to cause transfusion reactions, donors should be blood typed and tested for anti-erythrocyte antibodies (UC Davis VMTH Clinical Diagnostic Laboratory). In an emergency, when testing is not possible, a breed least likely to have these blood types (Standardbred or Quarter horse) should be selected. Fortunately, naturally occurring erythrocyte antibodies are rare, and the immune system takes up to 2 weeks to form antibodies after a transfusion. Up to 18 ml/kg (20% of blood volume) may be harvested from an individual donor, without harm, every 30 days. If clinical signs of hypovolemia are noted in the donor during blood collection, a crystalloid bolus (20-30 ml/kg) may be administered to counter blood loss. Often, the donor may show signs of agitation, and sedation may be administered (ie. detomidine, 0.01 mg/kg, IV) without affecting the recipient.

The blood from the donor should be collected into plastic bags to preserve the platelets. Because equine blood is rarely stored, short term anti-coagulants such as acid citrate dextrose (ACD) are typically used, at a 1:9 dilution with blood (400 ml ACD in a 4 liter bag of whole blood). Heparin should not be used, because it may remain active in the recipient, and can cause platelet activation.[14] The bag should be gently rocked during collection to mix the blood and anti-coagulant, and the bag can be weighed to determine the appropriate dilution has been met (1 ml blood = 1 mg).

Replacement of the total volume of blood lost is not usually required, due to the initial resuscitation by replacement fluids. The dilution caused by crystalloid administration supports cardiac output and improves microcirculation and tissue oxygenation by decreasing blood viscosity. A persistent anemia also allows the body to respond through an increase in erythropoietin production by the kidneys. The amount of blood required is estimated to be approximately 30% to 40% of blood lost. As an example, for a 1000 lb. (450 kg.) horse, a transfusion would typically be needed when blood loss reaches >40%. If the total blood volume is normally 36 liters (8-10% of body weight), a transfusion would be required after a loss of 14 liters of blood, and ~6 liters of blood would provide adequate oxygen carrying capacity by replacing 40% of the blood lost.

When administering a blood transfusion, a blood administration set is required to filter out microclots that form in the collected blood, despite the anticoagulent. The initial infusion rate should be slow, approximately 0.1 ml/kg over 15 minutes, which equates to 50 ml of blood for a 1000 pound horse. During the initial infusion, the heart rate, respiratory rate, mentation, and rectal temperature should be noted every 2-5 minutes to monitor for transfusion reactions. Common reactions include urticaria, tachypnea, and agitation, and are seen in approximately 16% of cases. If a reaction is noted, the transfusion should be stopped, and the horse should be administered either a non-steroidal anti-inflammatory (ie. flunixin meglumine 1.1 mg/kg, IV), a steroid (ie. dexamethasone 0.08-0.17

mg/kg, IV) or an antihistamine (ie. hydroxazine 0.5-0.1 mg/kg, PO). If anaphylaxis is noted, epinephrine (0.01-0.02 mg/kg, IV) and fluid bolus is immediately required to restore blood pressure. The transfusion may be restarted in horses with minor reactions after the reaction has resolved, but if it reoccurs, or anaphylaxis developed, a new donor will be required. If no adverse reaction is noted after the initial slow infusion, the blood may be bolused in controlled hemorrhage (up to 20 ml/kg/hr),[13] or increased to up to 3.75 ml/kg/hr for horses with uncontrolled bleeding. If large volumes of blood are administered, or if you are unsure of your dilution of the anticoagulant, serum ionized calcium should be monitored, due to the risk of citrate toxicity. In addition, crystalloids containing calcium must be stopped during the transfusion. The transfused red blood cells can survive from 4 to 20 days.[15]

Post-transfusion considerations

Broad spectrum antibiotics are indicated after severe hemorrhage, due to the risk of sepsis from the translocation of bacteria across the compromised gastrointestinal mucosa. Erosions of the gastrointestinal tract (the stomach specifically) due to hypoxia, can be addressed by the administration of gastroprotectants, including omeprazole.

Vital signs, mental status, and urine production should be reassessed throughout fluid resuscitation and after restoration of the circulating volume. Venous access would be indicated for horse with ongoing losses due to uncontrolled hemorrhage, or if the response to therapy was less than expected. Serum chemistries would ideally be performed daily to assess electrolytes, organ function and evidence of metabolic changes. Finally, tissue oxygenation can be estimated by the oxygen extraction ratio and serum lactate, to assess the response to therapy and if tissue hypoxia is persistent.

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Lefts and Rights:
Medical Management of Colonic Displacements

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Pathophysiology of large intestinal displacements

Displacement of the large, or ascending, colon is defined by the abnormal position of the large bowel in the abdominal cavity. A predisposing factor for this displacement is the normal anatomy of the equine gastrointestinal organs. The large colon of the horse is only affixed to the body wall at the junction of the right dorsal and transverse colon, and to the cecum by the cecocolic fold. Therefore the majority of this section of intestine can move freely about the abdomen. A displaced colon may be found in a number of different positions at surgery, and four typical presentations for a displacement have been described: 1) retroflexion of the pelvic flexure towards the diaphragm, 2) left dorsal displacement where the colon is positioned lateral to the spleen, or trapped over the nephrosplenic ligament (nephrosplenic entrapment), 3) right dorsal displacement where the colon lies between the cecum and body wall, and 4) a non-strangulating volvulus of <180 degrees.[1] Although displacements are not technically described as a strangulating lesion, they may cause intestinal compromise if significant bowel distention occludes venous outflow, or if the colon continues to twist into volvulus of >180 degrees.

While the lack of anatomic attachment to the abdominal wall allows the colon to displace, the cause of this type of colic is still unknown. One theory is that gas distention may cause the colon to become lighter than the surrounding viscera and alter gastrointestinal motility, resulting in movement of the colon out of its normal position. One cause of gas production includes the fermentation of carbohydrates in the colon that are allowed to pass through the small intestine undigested. Carbohydrate loads that reach the large intestine may be secondary to a sudden change in diet or a large meal of carbohydrates (>0.4% of body weight) that does not allow for adequate production of pancreatic amylase.[2] The result is fermentation by lactic acid-producing bacteria, luminal acidosis and gas production. A second cause of displacement may be due to changes in microbial flora of the colon secondary to oral antibiotics, resulting in a similar pathologic overgrowth of acid-producing bacteria. Gas distention may also result secondary to obstruction caused by impactions or foreign bodies, such as enteroliths or sand, both of which may complicate the treatment of a simple colon displacement. For right dorsal displacements, specifically, it has been proposed that aberrant gastrointestinal motility patterns at the pelvic flexure are involved.[1] Finally, medications or disease that directly impact gastrointestinal motility, including anticholinesterase medications (atropine), can alter the normal flow of ingesta, and predispose to displacement.

Clinical findings and diagnosis

Large colon displacement can present with variable signs of abdominal pain, depending on the degree of obstruction of the intestinal lumen that the displacement causes. While it is typically an acute disease, the owners in some cases may have noted intermittent discomfort in the days prior to presentation. Abdominal distention is commonly observed, and fecal production is reduced to absent. Horses with displacements may produce net nasogastric reflux, which may confound the diagnosis; the cause of reflux is suspected to be secondary to ileus, compression of the duodenal outflow tract, or tension on the duodenocolic ligament.

On rectal palpation, a tight band is often noted if the colon is within reach, and gas distention or a concurrent impaction may be palpated within the colon. If the band courses over the nephrosplenic ligament, between the caudal pole of the left kidney and the head of the spleen, the diagnosis of a nephrosplenic entrapment can be made. If the band traverses horizontally, between the cecum and body wall, a right dorsal displacement should be suspected. Characteristic rectal exam findings may not be present if the pelvic flexure is retroflexed, and horses with this type of displacement will be described as feeling “empty” when palpating in the caudal abdomen. However, it is important to note that false positives are common when diagnosing displacements by rectal examination; about 20% horses are incorrectly diagnosed with a displacement.[3] Differentials to consider for rectal findings consistent with displacement include cecal impaction, cecal or colon tympany, simple large colon impaction, enteroliths, or large colon volvulus.

Advanced diagnostics to consider should include transabdominal ultrasound for both right and left dorsal displacement. Left dorsal displacement has been described as a gas shadowing of the dorsal border of the spleen, ventral displacement of the spleen, presence of the colon lateral to the spleen, or failure to identify the left kidney medial to the spleen when imaged through the flank in a lateral plane.[4,5] Sensitivity of ultrasonography for identification of left dorsal displacement is around 89%.[5] Right dorsal displacement may also be identified on ultrasound, but has a lower sensitivity, between 56% and 67.7%.[6,7] A tentative diagnosis of right dorsal displacement may be made by identification of the vessels that normally lie on the medial surface of the colon incorrectly positioned against the right lateral body wall. If the colon is malpositioned, these vessels can be located by ultrasound between intercostal spaces 10 to 16, and dorsal to the costochondral junction.[6] The vessels of the colon should be differentiated from the cecal vessels, that are normally located by ultrasound in the right flank.

Bloodwork is not necessarily required for diagnosis, but may be helpful for identification of electrolyte abnormalities and hypovolemia that may affect choice of treatment. On serum chemistries, right dorsal displacements have commonly been described to have a distinctive increase in gamma glutamyltransferase activity (GGT), due to compression and obstruction of the bile duct.[8] These changes in serum chemistry have not been associated with an incidence of hepatic insufficiency or failure, and do not require additional therapy. However, there have been cases of left dorsal displacement with elevated serum GGT, which cautions its use as the definitive diagnosis for a right dorsal displacement.[8,9]

Treatment of colon displacements

Large intestinal displacements are treated similarly, regardless of the position of the colon in the abdomen. If the horse is hemodynamically stable, it is held off feed, and administered fluids to both correct deficits and to hydrate the ingesta if an impaction is suspected. Fluid therapy may be provided orally or intravenously. Oral fluids are preferred, due to the fact that they can directly rehydrate an impaction, when present. They are also cost effective compared to intravenous administration. Contraindications to oral fluids would be if the horse is significantly dehydrated, or if the horse is producing net reflux (>2 liters every 2 hours). In addition to fluids, therapy should include analgesics (non-steroidal anti-inflammatory medications), antispasmodics, and low doses of sedation. Providing light exercise (jogging for 10-20 minutes x times a day) may be helpful to improve gastrointestinal motility and return the colon the correct position.[3]

In addition to these treatments, horses with a left dorsal displacement are often treated with phenylephrine and exercised on a lunge line for 15 to 25 minutes to displace the colon from the nephrosplenic space. Phenylephrine is an alpha-1 adrenergic sympathomimetic that causes vasoconstriction, resulting in splenic contraction by up to 28%.[10] The dosage for phenylephrine is 0.04 mg/kg, or 10-20 mg per 1000 lb (450 kg) horse, administered as an intravenous infusion over 15 minutes. Once administration is complete, phenylephrine has a relatively short duration of action, with splenic contraction lasting only 25 minutes.[10] It is currently unknown if phenylephrine actually improves the odds of resolving a left dorsal displacement. A recent publication noted a 96.5% survival rate in horses treated conservatively with only fluids, anti-spasmodic medications, and analgesics.[11] Of these horses, only 9 out of the 114 were administered phenylephrine, which calls into question the effects, if any, of this medication for therapy of a nephrosplenic entrapment. Treatment with phenylephrine is not benign, and side effects include increased pulmonary artery and right atrial pressures, second degree heart block, hypertension, bradycardia, bradyarrythmias, and decreased cardiac output.[10] Phenylephrine should also be used with caution in older horses (>15 years), where severe and fatal hemorrhage into the thorax or abdomen has been reported.[12]

An alternative medical therapy to consider for nephrosplenic entrapment would include rolling under general anesthesia. This technique involves anesthetizing the horse in right lateral recumbency, rolling the horse over its back into left lateral, and continuing on into right lateral again to evaluate progress with either rectal palpation or ultrasound. If possible, it is preferred to lift the horse into the air by the hind limbs while in dorsal recumbency to allow for agitation of the abdomen before rolling into left lateral recumbency, to help dislodge the colon from the nephrosplenic space.[13] While rolling is considerably cheaper than surgery, it has similar anesthetic risks, and should be approached with caution if surgical facilities are not readily available. Reasons for treatment failure can include a second problem or the wrong diagnosis. The rolling procedure was initially described in conjunction with administration of phenylephrine, however, a recent publication noted no improvement in success rates in horses administered this drug.[4,14]

If the colon or cecum is moderately distended, trocarization may allow for medical management in cases where surgery is not an option. Decompression will improve blood flow to the abdominal organs and can provide the colon space within the abdomen to return back to its normal position. Trocarization is typically performed high in the right flank to decompress the cecum, however, decompression can also be performed on the left if a significant gas cap is present in the displaced colon. Ultrasound should be used to identify the position of the gas filled viscous subcutaneously, and to avoid large vessels or the spleen that may be between the skin and the colon. After routine sterile preparation, a 14 gauge, 5 inch (12 cm) catheter is placed percutaneously perpendicular to the skin, and advanced until gas is noted exiting an attached extension set. If the end of the extension set is placed in a cup of water, it is easier to determine if gas is still exiting the lumen of the bowel. Redirection of the catheter should be avoided to prevent laceration of the intestine, but the catheter can be slowly advanced if needed. Successful trocarization should take 30-45 minutes to significantly reduce gas distention if gas is evacuated passively. As the catheter is removed, an antibiotic may be injected to prevent subcutaneous abscess. Complications of this procedure include hemorrhage and peritonitis, and the horse should be monitored closely after this procedure for pyrexia, that could indicate a developing infection.

Indications for surgery in horses diagnosed with a large colon displacement include the presence of significant abdominal pain or distention on initial exam that is unresponsive to sedation and analgesics, or increasing distention and discomfort despite medical therapy. Horses with significant gastric reflux are also often taken to surgery.[11] Horse that will respond to medical therapy should require only low doses of sedation, and repeated administration may indicate the need for surgery or reevaluation of the diagnosis. Clinical signs consistent with endotoxemia including hyperemic mucous membranes, tachycardia, increasing hematocrit with a concurrent hypoproteinemia, and cold extremities are also often indicative of a surgical lesion. In addition, an abnormal

abdominocentesis or gas distention that severely limits rectal examination of the abdomen may suggest that medical management will not be successful.

Horses suspected to have a right dorsal displacement, 180 degree volvulus, or retroflexion of the pelvic flexure require a ventral midline or paramedian laparotomy to allow for correction of the displacement and concurrent enterotomy for lavage of an impaction may be needed. While ventral midline is preferred by the author to allow for full exploration of the abdomen, it is possible to perform a flank procedure to remove the colon from the nephrosplenic space, as well as simultaneously allow for ablation in horses with a left dorsal displacement.[15] However, standing procedures should not be attempted in horses exhibiting intractable pain, significant feed impactions or if there is a suspicion of a second intestinal abnormality.

Prognosis after colon displacement

The success of medical and surgical therapy for left dorsal displacement or nephrosplenic entrapment is excellent, between 90% and 100% for all treatments combined.[4,13] When the success of individual treatments are examined individually, the rolling procedure has a success rate between 33% and 90%,[4,13] exercise has a success rate between 33-100%,[13] and surgical management is from 80% to 95.9%.[11] As mentioned previously, palliative therapy including fluids, anti-inflammatory medications and antispasmodics has a success rate of 96.5%.[11] For right dorsal displacements, success rates overall are around 94%. Success of medical management is 64% whereas surgical success rates between 80 and 93%.[3]

Prevention of displacements

Client education is important in horses that have been diagnosed with a large colon displacement. Because of the link with management strategies, a thorough assessment of the feeding and exercise protocols of these horses should be performed. Of the 4 types of displacement, horses with right dorsal displacement have been noted to be more likely to present with a second episode of colic. In one publication, approximately 42% of horses with a right dorsal displacement experienced an additional episode of abdominal pain within 6 months of surgery, with 10% of those requiring relaparotomy.[16] Retroflection of the pelvic flexure was also noted to have a high incidence of recurrent colic in this study (46%), but these horses were unlikely to need a second surgery. Horses with left dorsal displacement and non-strangulating volvulus had a recurrence rate of 8% and 21%, respectively.[16] It is important to warn owners that horses with this diagnosis may be at a higher risk for colic in the future.

Recurrence of left dorsal displacement and nephrosplenic entrapment is much less common (about 8%), but some reports note a recurrence rate of up to 21%.[16,17] The risk of left dorsal displacement can be reduced by surgical ablation of the nephrosplenic space, but this procedure does not prevent other types of colic, likely due to the management issues surrounding displacements or an underlying motility disorder.[17,18] In addition, body type may predispose a horse to this type of colic, which appears to be more common in large, barrel-chested breeds.[11] The incidence of colic after this procedure is around 11-21%.[17,18]

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Equine Wounds:
Triage to Treament

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Exposed bone

Exposed or denuded bone is a common complication of wounds of the distal aspect of the limb. Exposed cortical bone in which the periosteum has been removed, is prone to desiccation of the superficial layers of the cortex, which may result in infectious superficial osteitis and sequestrum formation. Exposed bone within a wound can delay wound healing directly if the bone becomes infected, or indirectly because its rigid structure can delay the formation of granulation tissue and wound contraction.

Distal limb avulsion wounds with exposed bone increase in wound size for 14 to 21 days. Wound expansion is due predominantly to the distraction forces applied across the wound during the inflammatory and debridement stages of wound healing, and the lack of a granulation tissue bed in the center of the wound to neutralize the tensile forces exerted on the wound margins from the surrounding skin. Wounds with a small amount of exposed bone, or wounds without exposed bone, expand for a shorter period because less time is required for granulation tissue to seal the wound. Larger wounds with exposed bone take longer to form a granulation bed and subsequently wound contraction is postponed.

Periosteal insults from blunt trauma, tendon/joint capsule strain, surgical manipulation, or laceration/degloving injuries may result in extensive periosteal exostosis. Injuries involving bones in horses stimulate more periosteal new bone growth than similar wounds in other species and ponies. More extensive periosteal reaction in young compared to adult horses has been attributed to a more active osteoblastic activity of the periosteum in young horses. The extensive periosteal new bone growth seen in adult horses is poorly understood. Deferred collagen lysis compared to other species may be a contributing factor. The more extensive periosteal new bone formation in horses compared to ponies is alleged to be the result of a slower onset and longer duration of the periosteal response and prolonged extensive limb swelling in horses, as compared to ponies.

Despite the common occurrence of exposed bone associated with trauma to the distal aspect of the limb, there has been little investigation into methods of stimulating coverage of granulation tissue over exposed bone in horses. Granulation tissue development is a very important role in second-intention healing because it provides a barrier to infection and mechanical trauma for the underlying tissues. Healthy granulation tissue is resistant to infection and provides a moist surface for epithelialization. The delay in wound healing caused by exposed bone has prompted the search for different methods to promote granulation tissue coverage of bone in other species.

Head trauma, thermal injury, and surgical oncology often results in exposed bone of the cranium in humans. In these cases the outer cortex of the uncovered portion of the cranium is fenestrated with drill holes, burrs, or lasers to expose the medullary cavity from which granulation tissue grows to cover the exposed bone. Similarly, exposed cortices of long bones in humans have been fenestrated with drill holes to promote granulation tissue formation. It has been suggested that the drill holes promote healing by allowing osteogenic factors from the medullary cavity access to the wound, or by the enhancement of healing of bone and soft tissue by a nonspecific response known as “the regional acceleratory phenomenon”. Cortical fenestration combined with drugs that promote topical granulation tissue may accelerate granulation tissue coverage compared to control wounds, but further investigation is needed.

Cortical fenestration of 1.6 mm drill holes in the cortex of the second metacarpal bone in experimentally created wounds in dogs resulted in clot formation over the bone that promoted granulation tissue formation and may have protected the bone’s outer layers from desiccation. The effects of cortical fenestration with 3.2 mm drill holes were evaluated in experimentally created wounds of the distal aspect of the limb of horses. Cortical fenestrated wounds became covered with granulation tissue earlier than control wounds, and fenestration had no significant effect on sequestrum formation. The granulation tissue growing directly from the bone surface also contributed to granulation tissue formation. If the wounds are not large (< 6 x 6 cm) it may be difficult to realize a significant contribution from the granulation tissue growing from the cortical fenestration sites alone. Cortical fenestration may also be advantageous if it is used with other methods of promoting granulation tissue. Splinting of the limb is usually not necessary for the recovery from general anesthesia unless there are associated traumatic injuries to the limb that would suggest instability.

Degloving injuries

Degloving or avulsion injuries are not uncommon in equine practice, and their management can be challenging because of prolonged treatment, cost, and sometimes unknown outcome. The body that becomes entrapped in hazards or a limb that becomes intertwined in fencing or can quickly sustain tissue damage. The most common sites for this type of trauma are the hemi thorax, dorsal aspect of the metacarpus and/or metatarsus and the cranial aspect of the tarsus. Vascular, soft tissue and bone damage is directly proportional to the length of time and effort the horse uses to free itself. Some injuries that seem to be superficial and innocuous on the surface may involve vital structures surrounding the wound and/or later develop cutaneous and internal abscesses and/or ulcerative cellulitis. Local

wound care should be an integral part of the initial treatment. The severity and duration and location of the laceration determines the best approach to the treatment of degloving injuries as healing of wounds involving the distal limb is often delayed when compared with other areas of the body, further complicating the healing process.

Primary repair of the wound is the preferred treatment for wounds that involve detachment of skin with maintenance of an intact blood supply. Complications such as sequestrum formation are lessened and healing is improved when the exposed bone and tendons are covered with skin and soft tissue in the immediate post trauma period. Closing as much of the wound as possible improves the cosmetic and functional outcome and lessens the amount of healing having to occur by second intention.

Delayed closure of a degloving injury is preferred when there is significant contamination, swelling and trauma of the wound without loss of skin. Initial treatment for the first 2-3 days after injury include debridement and lavage of the wound followed by wet to dry bandages to facilitate further debridement. Pressure bandaging is indicated to remove edema associated with the injury. Debridement of the wound edges and appropriately applied tension sutures facilitate closure of the wound as skin retraction is a complication of delayed closure.

Second intention healing is indicated for degloving injuries in which there is a considerable loss of skin immediately at the time of injury or in which a closed degloving injury has developed avascular necrosis of the skin with subsequent sloughage. The wound is sharply debrided until only healthy tissue remains. A hydrogel Carradress®, Carrington, Irving, TX) dressing is applied to the region of the wound that remains open. These dressings are able to contribute moisture to dehydrated tissue, augment autolytic debridement and absorb some moisture from an exudating wound. The dressing is applied to the wound bed followed by application of a conformable absorptive dressing (Kerlix®, Kendall, Mansfield, MA). A firm cotton bandage is used to provide warmth, support and to minimize excessive movement of the limb and associated wound area. Depending on the size and location of the wound, skin grafting may be indicated to facilitate complete healing. Grafting should be delayed to permit maximum wound contraction which, depending on the location and size of the wound, may be 4-8 weeks after injury.

Dorsal knuckling of the fetlock and an inability to extend the digit is a common complication of distal limb wounds that is usually associated the loss of the extensor tendon of the distal limb. Supporting the dorsal aspect of the limb to counteract the pull of the flexor tendons on the palmar and/or plantar aspect of the limb is the premise for management of extensor tendon disruption. The wound and extensor tendon laceration is managed by second intention healing without suturing the extensor tendon. A rigid polyvinyl chloride (PVC) splint is applied to the dorsal or palmar and/or plantar aspect of the distal limb after wound bandaging. The bandage and splint, which maintains the limb in extension and prevents dorsal knuckling of the fetlock, are retained until normal limb function returns which may vary from 7 days to 6 weeks.

Excessive skin tension

Skin sutured with excessive tension is likely to have complications of healing due to local ischemia with pressure necrosis of the surrounding skin and the pull through of sutures at the skin edge with subsequent wound disruption. Undermining the surrounding skin, relief incisions, and appropriately applied tension sutures are the most common methods that can be used to lessen tension along the skin margins.

The surrounding skin can be undermined up to 4 cm from the wound edge without associated complications. Relief incisions can be closed after the primary incision is closed or left to heal by second intention.

In order not to interrupt the blood supply to the primary suture line, tension sutures are positioned well away from the wound margin. Once the tension suture is in place, the primary incision line is sutured to close the wound edges. Tension suture patterns include vertical mattress, horizontal mattress, far-far-near-near, and far-near-near-far patterns. Vertical mattress sutures with or without skin support to prevent laceration of the wound edges such as polyethylene or rubber tubing, are useful in reducing tension on the primary suture line. This tension suture support method is used in areas that cannot be bandaged well such as the upper limb, body and neck region. It is contraindicated to use tension suture supports under a limb cast or heavy bandage as these supports may cause tissue necrosis and suture line failure. Tension sutures are not effective after 7 to 10 days and should be removed in a staggered fashion with one-half removed initially followed by the remaining sutures later.

Movement

The extent of movement of the skin relative to the underlying bed of granulation tissue is usually much higher in the limb regions than in the trunk. This is possibly exacerbated by the relative lack of skin elasticity as well as the obvious proximity of the limb skin to structures with a high degree of motion such as joints and tendons. Trunk wounds have a better available reparative blood supply than those of the distal limb.

An injury to the distal limb metacarpal or metatarsal region of a horse which involves the flexor tendons and/or their sheaths requires healing by the ingress of blood vessels from adjacent structures. However, as healing attempts to progress, repeated tendon contraction and limb movement moves the injury away from the site of the skin wound leaving the damaged tissues with no effective mechanism for healing.

Rigid limb casting of a distal limb wound is very effective in facilitating wound contraction and epithelialization if the tissues are initially sharply debrided and lavaged. The mechanisms for this may be more complex than merely controlling movement. Although movement of the limb and wound is limited, added surrounding pressure applied to the wound may also facilitate the healing process. Warmth, restriction of movement and the presence of a moist healing environment in conjunction with a cast are probably significant factors that contribute to wound healing. Which aspects of the exudate are desirable and enhancing of wound healing and which are inhibitory is not known in the horse. Heat, pain, swelling, or lameness created by the cast indicate attentive reevaluation of the wound and the consideration of cast removal and or cast change.

Self-mutilation

Significant self-mutilation of wounds through rubbing, biting, and pawing can occur if the horse is not adequately restrained or medicated. Usually the most intense pruritic episodes occur in the first weeks of wound healing during the inflammatory phase of repair and during eschar sloughing but can be a later complication associated with burn wounds. To prevent extreme self-mutilation, the horse should be cross tied and/or sedated at this time and use of a neck collar may be considered. Delayed healing, poor epithelialization, and complications of second intention healing may limit return of the animal to their previous use.

Skin grafting

Skin grafting decreases healing time and is one of the best techniques for covering a wound that has been chronically affected by exuberant granulation tissue. Skin grafting of lower limb wounds should be considered to cover the granulating wound bed if contraction has ceased and the wound bed is large. Frequently, however, wounds in horses are treated for several weeks before skin grafting is initiated. At this point granulation tissue is mature, fibrous and has less of a blood supply than newly formed granulation tissue. Other complications of graft acceptance and healing are wound infection and sequestra formation.

Chronic inflammation, inherently present during second intention healing of wounds on the distal portion of limbs of horses may be at least as important as infection because it reduces the quality of the granulation bed and results in the production of a moderate amount of purulent exudate, both of which negatively influence acceptance of grafts. As a result the ability of a wound bed to accept a graft is lessened. It is therefore imperative that chronic granulating wounds be debrided to a level below the skin surface down to a level of healthy granulation tissue prior to graft application.

To increase the success of graft acceptance wound bacteria must be minimized. Beta hemolytic Streptococcus spp., Proteus spp., and Pseudomonas spp. are capable of producing destructive proteolytic enzymes and excessive purulent discharge which breakdown fibrinous attachments between the graft and recipient bed. Topical antiseptics have better efficacy than antibiotics in reducing bacterial wound load as the latter increase the risk of patient sensitization and the development of resistant organisms especially when used routinely over prolonged periods in uninfected wounds. Infected wounds, however, should be treated with broad-spectrum antibiotics while awaiting culture results. The bone underlying the wound should be radiographed for evidence of sequestra and excessive pericortical dystrophic mineralization. Large wounds often develop healthy granulating tissue around the perimeter before a sequestrum completely defines itself.

Donor site is influenced by the method of grafting, color, and texture of the donor hair, cosmesis of the donor site, and ease of obtaining skin. Common sites for obtaining donor skin include pectoral, dorsal neck region, perineum, ventral midline, ventral lateral abdomen and sternal region caudal to the girth area.

Pinch grafts

Pinch grafts are distinct pieces of skin (3 mm in diameter) produced by excising an elevated cone of skin. Graft acceptance is as high as 75% using pinch grafts partially due to the fact that the pockets of granulation tissue hold the graft in contact with the wound. Complications include necrosis of the graft, slower wound healing, improper orientation of hair, and thin skin coverage of the wound.

Necrotic spots along the top of the granulation pockets normally occur during healing, after which the graft epithelializes circumferentially. Because pinch grafts are small, complete epithelialization of the wound often requires greater than 70 days. Improper orientation of hair growth is a complication of pinch graft application despite repeated efforts to properly align the hair to match that of the recipient area. A cobblestone appearance with thin subcutaneous tissue is sequelae of pinch graft applications that may not be cosmetically acceptable for show horses.

Punch grafts

Punch grafts are circular pieces of skin that are directly removed from the locally anesthetized donor site or by obtaining biopsies from an excised piece of donor skin. Common complications of punch graft failure are incomplete removal of the underlying subcutaneous tissue from the graft, recipient site hemorrhage, and motion.

As punch grafts are full thickness they must have the subcutaneous tissue and fascia removed from the dermis with a surgical blade before implanting as these layers will prevent revascularization and subsequent graft failure. Placing grafts in saline soaked sponge gauze for a short period of time minimizes graft desiccation while recipient beds are created. Accumulation of blood and serum beneath the graft displaces the grafts from the recipient site. Hemorrhage can be avoided by ensuring that it is controlled before grafting. Displacement of the grafts can also be minimized by using a biopsy punch a size smaller than used to obtain donor graft to

ensure a snug fit in the recipient bed. Displacement of the graft by motion can be minimized by securing the wound under a heavy bandage. Displacement of grafted tissue at wrap changes can be reduced by soaking the primary bandage prior to removal. Casting is not indicated for punch graft techniques as punch grafts are not indicated for grafting over moveable areas of the body.

Tunnel grafts

Tunnel grafts are useful for healing of wounds that are hard to immobilize or bandage as on the dorsal surface of the hock or fetlock. Graft survival rates of 80% have been reported with excellent cosmetic results. Complications of tunnel grafting include the placement of tunnel grafts too close to one another, failure of the graft to become exposed and accidental removal of the tunnel graft when removing the overlying granulation tissue.

This technique requires harvesting of full-thickness or spit-thickness strips of skin 2 to 5 mm wide and slightly longer than the length of the wound's edges. These grafts are placed in granulation tissue that has been allowed to develop 4 to 8 mm above skin level. These tunnels can be created using a cutting needle, flattened K-wire with a trocar point, or malleable alligator forceps. The graft is then tunneled approximately 6 mm below the surface of the granulation tissue at the recipient site ensuring that the epidermal side of the graft faces the surface of the wound. Tunnel grafts should not be placed closer than 2 cm apart to prevent excessive necrosis of granulation tissue. The cut ends of the skin strips are sutured to the skin on either side of the granulation bed. A tourniquet may be useful to control hemorrhage and improve visualization of the strips for procedures that involve grafting on a limb. If placed the correct depth, the granulation tissue overlying the graft should slough in 7 to 10 days. If this does not occur, it should be excised at this time. Adjacent granulation tissue that is raised should be excised at this time. Most tunnel graft failures are attributable to accidental removal of the graft during removal of the overlying granulation tissue or failure of the graft to become exposed. Exposure of the graft if necessary may be facilitated by placing malleable probes or wires through the tunnels to cut through the overlying granulation tissue.

Full thickness sheet graft

Full thickness or split thickness grafts can be applied as a sheet or expanded before transplantation. The full thickness sheet graft is the most cosmetic type of free sheet graft as it contains all the properties of the surrounding skin, provides maximum piliation, and can withstand pressure and friction. Full thickness grafts are not as readily accepted because there are less exposed blood vessels available for imbibition of plasma and for inosculation.

No specialized equipment is needed for harvesting, and the procedure can often be performed in the standing sedated horse using local anesthesia. Donor sites of full thickness grafts should be sutured. The graft should be cut slightly larger than the recipient bed to allow for shrinkage after the graft is excised because of recoil of elastic fibers in the deep dermal layers of the of the graft. The full thickness graft should be sutured to the donor site with some tension to prevent occlusion of the dermal vessels that may occur if the graft is allowed to fully contract.

A high oxygen gradient between the wound and the graft is essential for neovascularization of the graft and graft acceptance. Full-thickness grafts treated with hyperbaric oxygen therapy developed less granulation tissue, edema, and neovascularization, but more inflammation. The superficial portion of these full-thickness grafts was also less viable than the superficial portion of those not treated with hyperbaric oxygen therapy.

Full thickness sheet grafts are often considered compromised because they often require more nourishment than can be supplied by the granulating recipient wound. As a result full thickness grafts are usually reserved for fresh uncontaminated wounds. The upper layers of a full thickness graft are more likely to slough because full thickness grafts require more nourishment and have fewer exposed vessels for this purpose. Because of the lack of abundant donor skin in the horse, the graft often must be meshed and expanded to achieve coverage of the wound larger than the donor area.

Split thickness grafts

Split thickness grafts are more readily accepted than full thickness grafts, and may be used to cover granulation beds that are less than ideal. Since blood vessels branch as they become more superficial in the dermis more vessels are cut and exposed with split thickness grafts. The greater the number of exposed vessels the better the absorption of nutrients will be from the granulation bed. A split thickness sheet graft is more cosmetic than a pinch or punch graft because the thickness of the graft and orientation of the hair are uniform and coverage by the graft is more complete.

A mechanical dermatome or a free hand knife (Watson Skin graft knife, Down's Surgical, Sheffield, England) is used to split the dermis. The latter is preferred as it is easy to use and economical to employ. General anesthesia is necessary to obtain the graft as split thickness donor sites are very painful to the horse, since many nerve endings are exposed. Grafts less than 0.5 mm thickness in the horse lack strength, durability, and have sparse or no hair follicles or exocrine glands which results in less sebaceous secretion. Grafts harvested between 0.63 mm and 0.75 mm have good coverage of hair and greater durability than do thinner grafts. Unlike full thickness grafts suturing of the donor site is not required and primary graft contraction is minimal since a portion of the dermis remains intact and heals with a scarred appearance.

The grafts can be applied to the wound after the horse has recovered from general anesthesia. This reduces anesthesia time and the possibility of damage to the graft during the recovery process. The graft can then be affixed to the wound with the horse standing

without using local anesthesia by overlapping and gluing the graft with cyanoacrylate to the skin surrounding the wound. To increase graft success in an area that is difficult to immobilize, such as the fetlock or hock, the graft can be further secured by suturing the graft to its recipient bed with simple interrupted absorbable sutures. Meshing grafts greatly enhances graft acceptance by preventing mechanical disruption of the graft from its vascular supply by exudate. Fenestration of the graft also enables topically applied antimicrobial agents to contact the graft bed and allow for the escape of fluid produced by the wound.

Although proper graft bed preparation and grafting techniques are important for successful graft application, successful graft acceptance depends greatly on attention to postoperative care. During the initial 4-10 days the graft may become edematous and pale. These changes are from a loss of blood supply due to vessel constriction and the expulsion of erythrocytes while the graft is nourished by passive imbibing nutrients onto its open vessels from the granulating bed via plasmatic imbibition. By day 10 the graft typically has a complete union to the graft bed. The epidermis might necrose and slough in some regions of the graft. Generally only the superficial areas of the graft have been lost and small areas of dermis surrounded by granulation tissue are present. The epidermis will regenerate from migration of epithelial cells present in the remaining sebaceous glands, sweat glands and hair follicles.

Periodic bandage changes allow for a clean environment and recognition of graft failure. For many horses frequent bandage changes aid in comfort. Soaking the inner bandage with sterile saline for 5 minutes and the carefully removing the bandage prevents destruction of many grafts. The presence of purulent material on the initial bandage change does not have a detrimental effect on acceptance of individual grafts. Silver sulfadiazine in a 1.0% water-miscible cream is effective against most Gram-positive and Gram-negative organisms and may enhance wound epithelialization. Additional immobilization gained with a cast is usually unnecessary to facilitate acceptance of grafts after 10-14 days. Immobilization may, however, lessen edema and decrease the possibility of self-mutilation. Persistence in re-grafting on horses that self-mutilate wounds has resulted in satisfactory wound healing in the majority of cases.

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