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Canine cutaneous autoimmune disease

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Introduction

Immune-mediated dermatoses are uncommon diseases in the dog and cat and may be subdivided into autoimmune and immune-mediated categories (1). Autoimmunity is considered to result from failure of the immune system to recognize "self", mounting an immune response composed of antibodies or activated lymphocytes against normal body structures and tissues, whereas immune-mediated conditions are triggered by a foreign antigen such as drugs (including vaccines) or infectious agents.

KEY POINTS

- **Autoimmune diseases result from failure of the immune system to recognize "self".**
- **There are numerous autoimmune and immune-mediated cutaneous diseases that have variable clinical presentations; they can often mimic other, more common, cutaneous disorders.**
- **Histopathologic evaluation is the gold standard in diagnosing a cutaneous autoimmune disease, but location and stage of the lesion can influence the diagnostic outcome.**
- **Use of immunomodulatory medications versus immunosuppressive medications is dependent on the type and severity of disease.**

There are numerous autoimmune and immune-mediated dermatoses, with the prognosis dependent on the type of disease. Some disorders affect only the skin and have minimal or mild systemic involvement; other diseases, such as lupus erythematosus and various forms of vasculitis, can affect other organ systems and have a serious systemic impact.

This article will focus on recognition of clinical signs, diagnostic options, therapeutic modalities, and avoidance of potential triggers for autoimmune dermatoses. With the proper approach, many of these diseases can be rewarding to treat.

Clinical signs and diagnosis

As with any skin disease, diagnosis is made utilizing a combination of history, clinical signs and routine dermatologic diagnostics, such as skin scraping, cytologic analysis, and biopsy with histopathology. It is not uncommon for some disorders, such as pemphigus, to have a waxing and waning history. Most autoimmune disorders occur in young to middle-aged animals, and many autoimmune dermatoses show a breed predisposition which can aid in formulating a differential diagnosis.

Clinical presentation may be variable and can mimic many other dermatoses due to the limited number of reaction patterns of the skin. With the wide diversity of cutaneous autoimmune dermatoses, there are multiple clinical signs; whilst there is no singular "pathognomonic" sign that conveys a cutaneous autoimmune disease, the clinician may identify alopecia, crusting (*e.g.*, pemphigus foliaceus), erythema and purpura (*e.g.*, vasculitis, erythema multiforme), ulcerations (*e.g.*, vasculitis,

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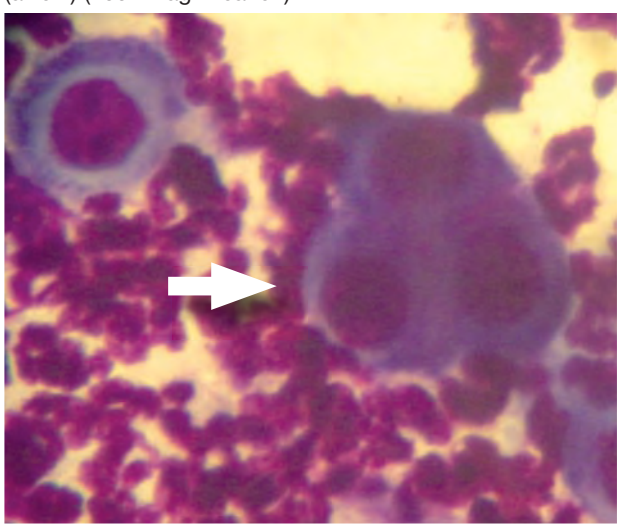
lupus/lupoid variants), and vesicles (*e.g.*, bullous skin diseases).

The gold standard for diagnosis of autoimmune dermatoses is biopsy with histopathologic evaluation by a dermatopathologist. Multiple punch biopsies should be obtained from representative lesions; if present, areas of crusting and pustules should be biopsied for examination. Additionally, individual crusts can be submitted for evaluation for such diseases such as pemphigus. Selected sites should not be clipped or scrubbed as this can remove crusts, possibly adversely affecting results. Ideally, animals should not be on corticosteroids when biopsied, and submission of only ulcerated tissue is discouraged, as the outcome may result in an obscure diagnosis of "ulcerative dermatitis". Special stains, including Periodic acid-Schiff (PAS), may be useful in evaluating for other mimickers, such as dermatophytosis.

Additional diagnostic considerations include cytology, dermatophyte culture, antinuclear antibody test (ANA), and tick titers. Cytology is invaluable in supporting or refuting a diagnosis of an autoimmune disease; *e.g.*, the presence of acantholytic keratinocytes surrounded by neutrophils is highly suggestive of pemphigus foliaceus ***(Figure 1)***. However, staphylococcal infections and dermatophytes, especially *Trichophyton spp.*, can also induce acantholysis (2). It is therefore important to evaluate for such agents and treat appropriately, if present. If bacteria are present, a 4-6 week course of systemic antibiotics should be instituted, and if resolution is noted, then a diagnosis of mucocutaneous pyoderma is supported. Note that for discoid lupus erythematosus, the clinical signs and histopathologic changes can very closely resemble mucocutaneous pyoderma of the nasal planum (3). ANA titers, as well as histopathologic analysis, can be helpful in supporting the diagnosis of systemic lupus erythematosus. Additional tests include immunofluorescence or immunohistochemical testing; direct immunofluorescence and immunohistochemical testing (often limited to specialist veterinary immunopathology laboratories) frequently requires special tissue handling, whilst indirect immunofluorescence testing on serum to detect the presence of circulating autoantibodies has shown more promise recently (1,4,5).

Figure 1. Impression cytology obtained below a crust on the nasal planum of a dog diagnosed with pemphigus foliaceus. Note the number of neutrophils surrounding clusters of large, basophilic acantholytic keratinocytes (arrow) (100x magnification).



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Treatment

With autoimmune/immune-mediated dermatoses, there are two therapeutic approaches that can be utilized for treatment: immunosuppression or immunomodulation ***(Table 1)***. Disease type and severity determines the approach. Most dogs with discoid lupus erythematosus, rabies vaccine-induced cutaneous vasculitis, pinnal margin vasculitis, and symmetric lupoid onychodystrophy will respond favorably to, and can be maintained on, immunomodulatory drugs. Other diseases such as pemphigus foliaceus, erythema multiforme, systemic lupus, and various other vasculitides will need immunosuppressive therapies.

Immunomodulatory drugs may take time to effect an improvement (generally seen within 3-4 weeks of starting therapy) so if the clinical signs are severe, a tapering course of high dose glucocorticoids can be utilized initially to obtain rapid control, along with a chosen immunomodulatory drug. Once remission is achieved the immunomodulatory drug can be continued as maintenance. Note that both the glucocorticoids and the immunomodulatory drug should be given initially since the latter class of drug can take time to be effective: this will help prevent relapse of the disease once steroids are tapered. The primary benefit of immunomodulatory drugs is that they have less serious adverse side effects and decreased health impact.

When immunosuppressive therapy is utilized, the most commonly used drug is a glucocorticoid. Initially, high doses are needed to achieve remission, and then tapered to the lowest possible dose that will maintain remission with minimal adverse systemic effects. In

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Table 1. Commonly used drugs for the treatment of cutaneous autoimmune and immune-mediated diseases.[1,24,25]

Drug	Dosage and notes	Mechanism of action	Side effects
Immunosuppressant drugs			
Glucocorticoids	Prednisone/prednisolone 2.2-4.4 mg/kg q24H Dexamethasone 0.2-0.4 mg/kg q24H Triamcinolone 0.2-0.6 mg/kg q24H The above are induction dosages that are then tapered to the lowest dose q48H (prednisone) – 72H (dexamethasone, triamcinolone) to maintain remission	Decreases circulating levels of T-lymphocytes; inhibits lymphokines; inhibits neutrophil, macrophage and monocyte migration; inhibits phagocytosis and chemotaxis; reduces production of interferon	Symptoms of hyperadrenocorticism, panting, vomiting, diarrhea, hepatic enzyme elevations, pancreatitis, GI ulceration, lipidemias, urinary tract infections, diabetes mellitus, muscle atrophy, behavioral changes
Cyclosporine	Induction: 5-10 mg/kg q24H Maintenance: 5-10 mg/kg q48H or less	Immunosuppressant: blocks IL-2 transcription and T-cell responsiveness to IL-2; inhibits IFN-α transcription, inhibits mononuclear cell function	Vomiting, diarrhea, anorexia, gingival hyperplasia, papillomatosis, hirsutism, bacteriuria, bone marrow suppression, nephropathy
Azathioprine	Induction: 1.5-2.5 mg/kg q24H Maintenance: 1.5-2.5 mg/kg q48H but can be tapered to as low as 1 mg/kg q72H	Affects rapidly proliferating cells Greatest effects on cell-mediated immunity and T-cell-dependent antibody synthesis	Anemia, leukopenia, thrombocytopenia, vomiting, hypersensitivity reactions, pancreatitis, elevated ALP and ALT, rashes, alopecia, diarrhea, hepatotoxicity, increased risk of infections
Mycophenolate mofetil	10-20 mg/kg q12H	Inhibits *de novo* purine synthesis and suppresses T and B lymphocytes and production of antibodies	Nausea, vomiting, diarrhea, bone marrow suppression, increased incidence of infections
Chlorambucil	Induction: 0.1-0.2 mg/kg q24-48H Maintenance: 0.1-0.2 mg/kg q48H or less	Cytotoxic effects via cross-linking of DNA	Anorexia, vomiting, diarrhea, myelosuppression
Cyclophosphamide	1.5 mg/kg q48H Due to side effects, often recommended for use in induction phase only; rarely used currently for cutaneous autoimmune diseases	Inhibits mitosis; immunosuppressive to humoral and cell-mediated systems, suppresses antibody production	Sterile hemorrhagic cystitis, bladder fibrosis, teratogenesis, infertility, alopecia, nausea, GI inflammation, increased infections, bone marrow suppression
Immunomodulatory drugs			
Tetracyclines	Doxycycline: 5 mg/kg q12H Minocycline: 5-10 mg/kg q12H Tetracycline: 500 mg for dogs >10 kg q8H 250 mg for dogs <10 kg q8H	Anti-inflammatory properties that affects chemotaxis, antibody production, complement activation; down-regulates cytokines; inhibits prostaglandin synthesis, lipases and collagenases	Vomiting, anorexia, lethargy, diarrhea, increased liver enzyme activity
Niacinamide	500 mg for dogs > 10 kg q12H* 250 mg for dogs < 10 kg q12H* *Given q8H if administered with tetracycline	Blocks antigen IgE-induced histamine release and degranulation of mast cells; photoprotectant and cytoprotectant that blocks inflammatory cell activation and apoptosis; inhibits phosphodiesterases; decreases protease release	Anorexia, vomiting, lethargy, occasional hepatic enzyme elevations
Pentoxifylline	10-30 mg/kg q8-12H	Inhibits erythrocyte phosphodiesterase and decreases blood viscosity, increasing erythrocyte flexibility, reduces negative endototoxic effects of cytokine mediators	Vomiting, anorexia, CNS excitement or nervousness
Topicals			
Tacrolimus 0.1%	Applied 1-2 times per day then taper down to less frequent use	Inhibits T-cell activation and proliferation via cytokine suppression	Localized erythema, irritation, pruritus Owners should wear gloves
Betamethasone 0.1%	Applied 1-2 times per day then taper down to less frequent use (ideally twice weekly for chronic use)	Similar effects as with systemic glucocorticoids; inhibit migration of lymphocytes and macrophages locally	Dermal atrophy; increased risk of induction of hypothalamic-pituitary-adrenal axis suppression; systemic glucocorticoid effects; development of milia and comedones; local skin reactions

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many autoimmune diseases, adjunctive therapies are necessary in order to permit the glucocorticoid dose to be lowered to a level which minimizes adverse side effects. In the more severe cases, it is not unusual to combine several different immunosuppressant drugs to achieve and maintain remission. As many of these medications can have adverse side effects on the liver and bone marrow, blood monitoring every 2-3 weeks for the first several months is recommended, with maintenance monitoring every 4-6 months. If significant changes in the blood parameters are noted, the offending drug should be discontinued and replaced with another medication. The most commonly utilized adjunctive medications include azathioprine, cyclosporine, mycophenolate mofetil, cyclophosphamide, and chlorambucil. In more severely affected dogs, supportive care for open wounds, fluid corrective therapy and monitoring of serum protein levels may be necessary. Use of human intravenous immunoglobulin (hIVIg) has shown promise in treating severe autoimmune dermatoses when other treatments are failing (6).

Topical therapies can be useful with more localized lesions or for sporadic flare-ups. The most commonly used topicals include betamethasone or tacrolimus. Betamethasone has the benefit of rapidly controlling inflammation and disease symptoms but can induce dermal atrophy with chronic use; therefore, transition to tacrolimus is prudent if a topical is needed for long-term use.

There are four phases to consider in the treatment of cutaneous autoimmune dermatoses: induction phase, transition phase, maintenance phase and determining cure (1). With the induction phase, the goal is to stop the inflammatory component as quickly as possible and suppress the immunologic response directed towards the skin. In this phase, higher doses of medications are normally necessary. If an acceptable response is not noted in a timely manner, another treatment regimen should be considered; *i.e.*, alternative medications chosen or additional medications added to the current treatment regimen. In the transition phase, drugs are tapered to minimize side effects and adverse reactions. When drug combinations are utilized, those with the greatest side effects – such as glucocorticoids – are the first to be tapered. Medications are slowly reduced, often over several weeks or months, until an acceptable maintenance dose of medications is achieved, or until signs recur. If this happens, the medications are increased until remission is again achieved, then tapered down to the last dose that maintained the patient's symptoms under acceptable control (the maintenance phase). A "cure" is considered for cases of immune-mediated dermatoses that have achieved remission and are successfully controlled with maintenance therapy but do not then recur after cessation.

Cessation of maintenance therapy in a patient that has been well-controlled is a difficult decision to make, especially if the initial disease was severe. This decision should be one that is mutually agreed between the clinician and owner; it is essential that the client is well-informed, with the realization that if the patient relapses, achieving remission a second time may be more difficult. When to discontinue maintenance therapy depends on the type of disease, whether or not a trigger was identified and removed, and the risk to the patient if therapy is discontinued. In many cases, maintenance therapy for 8-12 months is recommended before cessation (1). In animals where the risk of recurrence outweighs the benefit of discontinuing therapy, the drugs can be maintained life-long with appropriate lab work monitoring.

Future vaccinations are often discouraged in cases of autoimmune dermatoses, even in those where vaccination is not a known trigger. Concern lies with the idea that vaccination may stimulate a broad, non-specific immune response, possibly initiating recrudescence of the autoimmune disease (7).The author prefers to discontinue rabies vaccination and monitor titer levels for distemper and parvovirus. If titers are not sufficient to maintain proper immunity, a risk vs. benefit assessment should be performed before considering re-vaccination.

Specific diseases

Pemphigus foliaceus

The most common autoimmune skin disorder in the dog, pemphigus foliaceus (PF) is a pustular to crusting autoimmune dermatitis. PF affects the epidermis, targeting various adhesion molecules, especially desmosomes, which hold keratinocytes together. In human PF, the desmoglein-1 glycoprotein (DSG1) in the desmosome is the primary target of autoantibodies (8) and the same glycoprotein was previously suspected to be the primary target in dogs (9,10); however, it is now believed to be a minor autoantigen (11), with current evidence suggesting that desmocollin-1 is a major autoantigen in canine PF (12).

Genetic factors appear to play a role in the development of PF, with Akitas and Chow Chows the breeds considered most at risk (10). Triggers include chronic allergic

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Figure 2. Pemphigus foliaceus: **(a)** Honey-colored crusting involving the dorsal muzzle and nasal planum is depicted. Mild erosion of the nasal planum can be seen underlying the lifted crust. **(b)** A more generalized presentation of pemphigus foliaceus.

skin disease and drugs (antibiotics, NSAIDs, topical flea spot-ons), but the most important one is ultraviolet light (1,10). The initial lesion is a macule that rapidly progresses to pustules, which are often large and coalesce. The pustules are frequently fragile and easily ruptured, resulting in crusting. As a result, crusts are the most common clinical sign (1,9,10). Erosions may be noted; ulcerations are rare but can be present in cases complicated with a deep pyoderma. Canine PF is often characterized by crusting, initially involving the face (especially dorsal muzzle and nasal planum, peri-ocular region and pinnae), and subsequently progressing to a generalized form ***(Figure 2)***.

Cytology of an intact pustule or of the skin below a crust will often reveal the presence of numerous non-degenerate neutrophils surrounding individual or rafts of acantholytic keratinocytes, which appear as large, rounded basophilic nucleated keratinocytes ***(Figure 1)***. Histological evaluation reveals subcorneal pustules containing neutrophils and variable numbers of eosinophils, and acantholytic keratinocytes (13). Treatment often involves high doses of steroids with an adjunctive immunosuppressant and topicals for localized treatment.

Discoid lupus erythematosus

Also referred to as "collie nose" or cutaneous lupus erythematosus, discoid lupus erythematosus (DLE) is a benign ulcerative disease without systemic manifestations (1). DLE is generally localized to the nasal planum, but can involve the sun-exposed areas of the pinnae and peri-ocular region and there are reports of generalized variants (14). The most common clinical sign is initial loss of the cobblestone architecture of the nasal planum progressing to depigmentation and scaling ***(Figure 3)***. With chronicity, erosions, ulcerations and crusting occur. Annular to polycyclic hyperpigmented plaques involving the neck, trunk and extremities may be seen in the generalized variant cases.

Histopathology reveals interface basal cell degeneration (apoptosis), with a moderate pleocellular lichenoid infiltrate of the dermis (13). As this disease can closely mimic mucocutaneous pyoderma both clinically and histopathologically, cytologic evaluation of the nasal planum below a crust can be useful; treatment of mucocutaneous pyoderma is recommended if bacteria are present.

Figure 3. A mild form of discoid lupus erythematosus in a dog with chronic sun exposure; note the loss of cobblestone architecture of the nasal planum with depigmentation and focal erosions.

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In most cases of DLE, the use of potent immunosuppressants are unnecessary; a systemic immunomodulatory approach utilizing a tetracycline (doxycycline, minocycline) and niacinamide coupled with topical therapy (topical steroids, tacrolimus) is often successful at controlling the disease. In refractory or severe cases, high doses of corticosteroids may be needed initially. In the reported generalized variants, hydroxychloroquine or cyclosporine were effective treatments (14,15). As sunlight plays a significant role in DLE, it is important that sun exposure be minimized with avoidance and use of sunscreens. Vitamin E supplementation (400 IU daily) may also be helpful.

Erythema multiforme

A rare immune-mediated dermatosis, erythema multiforme (EM) can be idiopathic in nature or triggered by numerous factors, including drugs, bacterial infections, parvovirus, food, vaccination and neoplasia (1,16,17). In one review of 44 dogs with EM, drugs were the trigger in 26 (59%) cases (16); the most commonly implicated drugs are antibiotics such as trimethoprim-potentiated sulfonamides, penicillins and cephalosporins. EM has been subclassified into major and minor forms. EM minor is mild, with acute onset of the typical target lesions most often involving the extremities, with no or slight mucosal involvement; if present, it is limited to the oral mucosa, and systemic symptoms are not noted. EM major is more severe, with significant mucosal involvement and often constitutional symptoms such as lethargy and pyrexia. The distinction between EM major and Stevens-Johnson syndrome (SJS) can be difficult, and it is possible that many cases diagnosed as EM may actually be a result of SJS (1). Skin lesions are variable ***(Figure 4)***, and this disease can mimic many other dermatoses; however lesions may have an acute onset and are often symmetrical, consisting of erythematous macules or elevated papules that spread peripherally, clearing centrally. Many can have an annular to arciform or serpiginous pattern. Additional lesions include urticarial plaques, and vesicles and bullae that progress to ulcers. Mucosal lesions are generally erythematous and can also progress to vesicular, bullous and ulcerative lesions; crusting may be associated with some lesions. The most commonly affected sites include the ventrum, axillae, mucocutaneous junctions, oral cavity, pinnae and footpads.

With such variation in clinical signs and a large differential diagnosis to consider based on clinical signs (bacterial folliculitis, demodicosis, dermatophytosis, urticaria, other vesicular and bullous disorders), biopsy with histopathology is needed for diagnosis. The most characteristic histopathologic feature with EM is panepidermal apoptosis with lymphocyte satellitosis and an interface dermatitis (13). Response to treatment and perhaps permanent remission is contingent upon identifying and eliminating a trigger where one can be found, as elimination of the etiology can result in spontaneous resolution within weeks of correcting and treating. A hypoallergenic elimination diet trial should be performed in cases with no identifiable trigger, as food hypersensitivity can be a potential cause (18). In more severe cases, and for those cases where a trigger cannot be identified, immunosuppressants such as corticosteroids, azathioprine, and cyclosporine have been effective. In life-threatening cases, hIVIg has been utilized to improve and expedite treatment outcome (1,19).

Cutaneous vasculitis

There are a variety of vascular diseases that affect dogs. Cutaneous vasculitis is a disease process whereby blood vessel walls are targeted by an inflammatory response, resulting in subsequent destruction of blood vessels and ischemic necrosis of the affected tissue. It is important to note that cutaneous vasculitis is more a cutaneous reaction pattern rather than a specific diagnosis, as there are multiple causes that trigger vasculitis. Cutaneous vasculitis has been associated with other co-existing diseases, including food hypersensitivity, insect bites, malignancies, and infectious diseases including tick-borne diseases (20-22). Additionally, numerous drugs

Figure 4. Erythema multiforme exhibiting various clinical lesions, including patchy alopecia, scaling, erythema, erosions and ulcerations. Note the lesional changes on the eyelids consistent with the mucocutaneous involvement found with this condition.

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have been implicated as causing vasculitis (21-23). In many cases, an underlying etiology is not readily identifiable and the disease is considered idiopathic. In most cutaneous vasculitides, the pathomechanism is suspected to be a type III hypersensitivity reaction, whereby immune complexes formed following antigen exposure are deposited in vessel walls. However, additional factors may be involved, including genetics, defects in immune complex clearance, and autoantibodies.

The skin may be the only organ involved with vasculitis, but other organs may also be affected, such as the kidneys in Greyhounds. Typical cutaneous lesions of cutaneous vasculitis include palpable purpura, erythemic to purpuric plaques, hemorrhagic bullae, with progression of the disease resulting in development of demarcated ulcers involving paws, pinnal apex, lips, tail and oral mucosa (20). Pitting edema may also be present. In some cases, the claws may be affected and exhibit signs of onychodystrophy, onychomadesis, petechiae, and exudate within the claw. Erosive, ulcerative or hyperkeratotic lesions may affect the pads. Often, the ulcerations or depressions will affect the center of the pad; however, lateral margins may also be affected. In rabies vaccine-induced vasculitis, an annular patch of alopecia with variable degrees of hyperpigmentation ***(Figure 5)***, erythema and occasional scaling occurs at the site of vaccination, usually within 2-6 months of vaccination. In these cases, additional areas may be affected, especially the apex of the pinnae.

Diagnosis is made by histopathologic evaluation; however, changes can often be subtle depending on the stage of the disease and the site selected for biopsy, making diagnosis difficult. Histological findings typical of vasculitis include variable degrees of neutrophilic, eosinophilic and mononuclear cell invasion of vessel walls with endothelial cell swelling, fibrinoid degeneration, red blood cell extravasation, and occasional leukocytoclasia noted within or near the vessel walls (13,20).

Figure 5. An alopecic, hyperpigmented patch consistent with ischemic dermatopathy following rabies vaccination.

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Other dermal changes include pale-staining collagen, follicular atrophy, and cell-poor interface dermatitis (1,13). In cases of vaccine-induced vasculitis, an amorphous basophilic material may be noted representing likely vaccine product (13). The type of cellular inflammation present may be indicative of the trigger; for example, an eosinophilic vasculitis is often associated with arthropod reactions, food hypersensitivity, mast cell tumors or canine eosinophilic dermatitis.

When a diagnosis of vasculitis is made, additional work up may be needed to determine the underlying cause. A thorough history should be taken and any recent drug or vaccine administration should be investigated. Tick titers should be performed. An elimination diet trial with a commercial novel protein or hydrolyzed protein diet may be useful if food hypersensitivity is suspected, especially in cases of urticarial vasculitis.

Treatment of vasculitis is dependent on the severity of disease and type of vasculitis. Treatment length is also variable, as some cases may resolve and go into permanent remission if an underlying trigger can be identified and eliminated. Other cases may require life-long therapy. In more severe cases, treatment with glucocorticoids (with or without an adjunctive immunosuppressant drug) may be necessary once infectious causes have been ruled out. In cases of vaccine-induced vasculitis, immunomodulatory therapy utilizing a combination of medications, including doxycycline/minocycline, niacinamide and pentoxifylline, is often successful. Topical therapies containing steroids, such as betamethasone, can be utilized short term for more localized lesions, with transition to tacrolimus if longer treatment is necessary for topical control.

Conclusion

In conclusion, cutaneous autoimmune and immune-mediated diseases are uncommon to rare in dogs, but are still likely to be encountered in general practice. As many disorders can mimic cutaneous autoimmune disease – and vice versa – a thorough history and diagnostic work-up is imperative to achieve an appropriate

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diagnosis and treatment regimen, with identifiable triggers eliminated. Where appropriate, immunomodulatory therapy, rather than immunosuppressant therapy, should be considered as there are perceived less systemic side effects, but life-long therapy may be necessary in many cases.

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HOW I APPROACH...

Demodicosis

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Introduction

The diagnosis and treatment of demodicosis has evolved since it was first described in 1842 (1). Indeed, as recently as 1979 one publication (2) noted: "Demodectic mange, particularly in the generalized form, may be one of the most persistent of diseases and often responds poorly to treatment," but times have changed; a recent dermatology textbook states "the prognosis for generalized demodicosis has improved dramatically since the mid-'90s…..with intense treatment, most cases, probably near 90%, can be cured, but it may take nearly a year" (3).

KEY POINTS

- **The diagnosis and treatment of demodicosis has evolved since it was first described. In the last few years, newly identified mites and new shapes of old mites have been reported.**
- **Demodicosis can be either localized or generalized, and may be juvenile or adult in onset, but the clinical appearance can vary markedly.**
- **The traditional diagnostic tests of skin scraping and trichograms are still valid, but good sampling technique can increase the chances of successfully identifying the mite.**
- **Appropriate treatment recommendations and prognosis will vary with the clinical presentation, the *Demodex* species and the life stages identified.**

Over the past few years, newly identified mites and new shapes of old mites have been reported. Before you can identify the mite, however, you first need to find it; missing the mite will certainly decrease your success rate! Knowing where to look is therefore critical. Appropriate treatment recommendations and prognosis will vary with the clinical presentation, the *Demodex* species and the life stages identified. As in all therapies, one must consider the risks associated with treatment; some former recommendations have been found to have no effect on speed of resolution, whilst adjunctive therapies may be helpful and necessary – but some could lead to fatal drug interactions. This article therefore reviews the various presentations of demodicosis and discusses the most effective diagnostic techniques, as well as considering treatment options and potential pitfalls.

Presentation

Localized versus generalized

Demodicosis in both dogs and cats can present as either a localized or a generalized form. The differentiation is important, as most localized cases generally have a very favorable prognosis and will usually resolve without specific miticidal treatment. There is no universally accepted definition that clearly specifies the differences between the two, but localized demodicosis has been defined as one where there are "6 or fewer lesions that are less than 2.5 cm in diameter" (3). Generalized demodicosis can be defined as one where there are more than 12 affected areas, or a presentation where a whole body region (*e.g.*, head and face) is affected (3). Pododemodicosis falls into the generalized category (3).

Unfortunately, this leaves a grey area between localized and generalized that requires clinical judgement (is it "multifocal localized" or generalized?) and it would be

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useful to have a diagnostic test that would separate the two. A recent paper looked at acute phase response in dogs with generalized versus localized demodicosis and found that the generalized form does indeed have biomarker changes which do not seem occur in the localized form (4). The parameters tended to normalize after treatment, and it has been suggested that measurements of serum C-reactive protein and haptoglobin may help to differentiate generalized from localized cases – and indeed that they may be used in future to monitor treatment efficacy, as the return to normal reference values could indicate a good response.

Juvenile versus adult onset

Demodicosis is also defined by the age of onset; I define "juvenile onset" where the disease presents at under 12 months in small breed dogs, 18 months in large breeds and 2 years in giant breeds. Many cases diagnosed between 2-4 years of age have had ongoing problems since puppyhood and so the time of onset may be less clear. Adult onset demodicosis (*i.e.*, no skin problems before 4 years of age) carries a poorer prognosis.

Clinical appearance

Successful treatment is dependent on recognizing that an animal could have *Demodex* in the first place; this is not always easy, as affected patients may present in a variety of guises: for example;

- Papulopustular dermatitis – easily confused with bacterial skin disease ***(Figure 1)***.
- "Moth eaten" appearance of the coat (alopecic macules or patches) – especially in short-haired dogs, and easily confused with bacterial skin disease, dermatophytosis and hair follicle abnormalities.
- Erythematous dermatitis – previously known as "red mange" ***(Figure 2)***.
- Hyperpigmented patches/comedones – owners sometimes complain that the skin is "turning blue" ***(Figure 3)***.
- Scales – easily confused with a scaling dermatosis or infection ***(Figure 4)***.
- Pododemodicosis – *Demodex* can be particularly challenging to diagnose in these cases.

Dogs with *Demodex injai* may present differently; such patients commonly present with a seborrheic dermatitis on the dorso-lumbar area ***(Figure 5)***. Dogs older than two years and Terrier breeds appear to be over-represented, although the parasite has been identified in other breeds including the Dachshund and Lhasa Apso. Excessive glucocorticoid therapy and hypothyroidism have been reported as predisposing causes, and secondary bacterial folliculitis and *Malassezia* dermatitis may also be present (5,6).

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Figure 1. Generalized demodicosis and secondary pyoderma. The comedones (one of the many presentations of demodicosis) are filled with *Demodex* mites. Note also the pustule; secondary pyoderma and bacterial folliculitis are commonly found in cases of demodicosis.

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Figure 2. *Demodex* can present as a severe erythroderma, earning it the title "red mange".

In the cat, localized *Demodex cati* is rare; signs are most often seen in the peri-ocular region, head, neck and eyelids, and the problem presents as a variably pruritic, patchy alopecia with scaling and crusting (3); it can also present as a ceruminous otitis externa. Localized lesions can self-heal, especially if an underlying cause can be identified and treated. Siamese and Burmese cats may be predisposed to the generalized form, although it is

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Figure 3. Ventral abdominal comedones; large numbers of *Demodex canis* mites were found on scrapings on this 2-year-old Giant Schnauzer. The dog had suffered from chronic skin problems since one year of age.

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Figure 4. A common presentation of pets with demodicosis is a scaling dermatosis.

usually associated with a significant underlying disease such as diabetes, hyperadrenocorticism, FIV or FeLV (6). *D. cati* infestation has been identified in lesions of multicentric squamous cell carcinoma (3,7). Differential diagnosis includes dermatophytosis (which can occur simultaneously), bacterial pyoderma, and allergic skin disease, although in fact all causes of seborrhea and crusting in cats should be considered (6).

Demodex gatoi dermatitis is a pruritic skin disease usually seen in young, short-haired cats with alopecia or broken hairs, erythema, scaling, excoriations and crusting, particularly on the head, neck, elbows and/or flanks, the ventrum and rear limbs. Hyperpigmentation can occur, and the disease may be symmetrical (3).This form of *Demodex* is contagious to other cats in the home. Note this parasite seems to be regional – I have only diagnosed three cases – so the case history may be suggestive; verify if the pet has lived in a geographical region that has reported the mite (*e.g.*, southern USA) and/or if there is a history of contagion. There may be also an association with allergic skin disease, although the reason for the link is as yet uncertain.

Pathophysiology

The parasite is a normal resident of the dog's skin, as shown by PCR studies demonstrating that small populations of the mite colonize most parts of the skin of healthy dogs (8). The mites transfer to the neonate by nursing contact with the mother within the first 2-3 days of life (3); puppies removed from the bitch by cesarean section and raised away from her do not have mites. The immune system of the host usually keeps mite numbers under control (9); dogs with generalized demodicosis have a genetic cell-mediated immunodeficiency associated with depressed T-cell function (actual T-cell numbers are typically normal) (3) and it is recommended that these dogs are not used in any breeding program. One paper notes that generalized juvenile demodicosis with *Demodex injai* has not been reported to date; it is postulated that the suspected genetic defect in the control of *Demodex* populations may be specific for *D. canis* (1). It is assumed that the mite colonizes the skin of healthy cats too, but to date there are no PCR studies to confirm this.

Figure 5. *Demodex injai* commonly presents in middle-age terriers as a greasy skin condition; the interscapular and lumbar regions are commonly affected.

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Important factors in the pathogenesis include cutaneous barrier rupture, inflammation, secondary bacterial infections and a type IV hypersensitivity reaction, which may explain the alopecia, pruritus, erythema and comedone formation associated with this disease (9).

Diagnostic testing

In humans, the prevalence of *Demodex* is close to 100% with a mean of 0.7 mites per cm^2 of facial skin, especially the chin (8). However, it seems that mites are more difficult to find in dogs and even very small numbers of mites found on scrape should be viewed as suspicious. If a single *D. canis* is found, this should not be considered as indicative of normality, and additional examinations are recommended before excluding demodicosis (10). Note that scrapes should always be considered before initiating corticosteroid treatment; one of the main causes of demodicosis in adult dogs is hyperadrenocorticism.

Skin scraping and trichograms (hair pluckings) are the traditional tests performed to diagnose demodicosis. Hair plucking is considered less sensitive than skin scraping when the number of mites is low (70% relative sensitivity) (11). However, one study found that there was no significant difference between skin scraping and hair plucking in the proportion of positive samples taken from 161 dogs suffering either from localized or generalized demodicosis. Squeezing the skin prior to scraping significantly improved the number of positive samples, but hair plucks should not be squeezed prior to sample collection to reduce extrusion of the follicular keratin during the procedure (12).

One diagnostic technique using acetate tape has been reported; tape is applied to the test area and the skin squeezed before lifting the tape ***(Figure 6)***. The study reported the technique allowed a significant increase in mite detection compared to deep skin scraping, both in the total number of mites and in the number of larvae and adults detected ($P < 0.05$) (13). No significant difference between the two methods was observed for the number of eggs or nymphs. Nevertheless, I still find that scraping and squeezing yields the greatest number of mites when compared to trichograms or the "tape and squeeze" collection technique, although tape is a great option in "hard-to-scrape" areas.

In general skin biopsy is not considered an appropriate diagnostic test to exclude demodicosis. The sample collected is generally small and the mites tend to shrink during histological preparations, making detection difficult (10). One exception may be pododemodicosis, where good scrapings are difficult to obtain ***(Figure 7)***. No matter what technique is employed, the following tips can increase the likelihood of a positive test:

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Figure 6. Acetate tape examination can be particularly helpful in finding *Demodex* in areas that are not amenable to scraping.

Choosing the test site:

- Take your time; look closely at the skin and choose the most appropriate sites (and choose a technique suitable for the chosen area). Good places to test include:
  - red scaly areas
  - comedones/hyperpigmented regions (these can look "blue" but with magnification nearly coalescing comedones are apparent)
  - regions of follicular casts (these can also be good for hair plucks in hard-to-reach areas such as the interdigital region)
- Cats may ingest the mites due to overgrooming, which can make identification difficult; however

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Figure 7. Pododemodicosis can be very uncomfortable, making deep scrapings difficult. Biopsy may be required to make the diagnosis when it is the only clinical finding, but hair plucking and tape tests may aid in the diagnosis.

D. gatoi may be found at the base of neck on superficial scrapings (as the cat cannot reach this area); sometimes the parasite can be found on tape preps, or it can be worthwhile scraping another cat in the household that is less affected.

- *D. cati* is most commonly found around the head and neck, whilst superficial interscapular scrapings may identify *D. gatoi*, but do deep scrapes as well – it is possible to have dual *D. cati/gatoi* infections.
- Deep skin scrapings under sedation or biopsy may be needed with pododemodicosis.

When scraping:

- Advise the owner that the lesion may look worse after sampling than before.
- Dull the blade (*e.g.*, by using a tongue depressor) before scraping; experience is required to get the correct degree of sharpness.
- Squeeze the skin before and during the procedure.
- Hold the blade at right angles to the skin; this reduces the likelihood of cutting the pet.
- Scrape deep enough to get a significant amount of capillary bleeding and collect samples from multiple sites.
- The sample needs to be of sufficient quantity to make the procedure worthwhile.

When taping:

- Use tape that will not be visible under the microscope.
- Place the tape on a suitable lesion and squeeze the skin under the tape.
- Remove the tape and apply to a microscope slide.

Trichogram (hair plucks)

- Pluck in the direction of hair growth to increase the likelihood that the base of the hairs are included in the sample.
- Do not squeeze; aim for 100 hairs per sample.

Examining the slides

- Smear the sample onto a microscope slide, add enough mineral oil and a cover slip to minimize oil slicks and aid visualization.
- Lower the condenser to help look for motility and aid identification of mite skeletons.
- Be sure to look at all fields using 10x power.
- Look for all the different life stages and record the number of mite and life stages. This will allow comparison with future scrapings, and assist assessment of response to therapy.

Ancillary tests

Localized demodicosis

Demodex mites (and also *Cheyletiella*, scabies mites and fleas) can be found on SAF* fecal exams. It may be wise to remind the lab to report external as well as internal parasites! Anecdotally a higher success rate in diagnosing *D. gatoi* in fecal exams compared with skin scrapings has been reported.

Close scrutiny of adult onset cases may be indicated as this presentation may be a harbinger of things to come. Factors to consider include verifying any concurrent medication (*e.g.*, steroids, including chronic use of potent topical steroids) and hematological and biochemical profiles, including a heartworm test if indicated. Endocrine studies may be indicated (based on results and patient's history). In all cases dietary assessment (to ensure that the pet is on a complete and balanced diet) is essential.

Generalized demodicosis

In juvenile onset generalized *Demodex* cases both good nutrition and parasite control play very important roles in recovery, and a general health assessment (including hematological and biochemical profiles and a urinalysis) is warranted to rule out congenital disease. Heartworm

*SAF: Sodium acetate-acetic acid-formalin solution

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Figure 8. *Demodex injai*. Note the long body in this species (40x magnification).

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Figure 9. *Demodex gatoi*. This short-bodied mite is contagious to other cats (40x magnification).

testing (in endemic areas) is indicated before avermectin treatment and an MDR1 screening test should be performed in breeds known to be predisposed to this genetic problem (see below).

For the adult dog with generalized demodicosis all the preceding considerations should be part of the standard workup. In addition, a detailed hunt for a possible sinister disease affecting the immune system is recommended, including thyroid evaluation, hyperadrenocorticism tests, and screening for tumors using abdominal ultrasound and thoracic radiography.

Workup in the cat for generalized demodicosis is similar, paying special attention to the possibility of steroid-induced disease. Hematological and biochemical profiles should be performed to assess for diabetes and FIV/FeLV tests are certainly indicated.

The "Players" – identifying the "cigars with legs"

Demodex in the dog

1. *Demodex canis* inhabits the hair follicle. The cigar-shaped adult measures approximately 170-225 µm and has 4 pairs of legs (5). *D. canis* nymphs have a shorter body but the same number of legs. Larvae only have 3 pairs of stubby legs and the eggs look like "pregnant bananas".

2. *Demodex injai* is a relative newcomer ***(Figure 8)***. It can be found most commonly in the sebaceous glands, and all life stages are much longer than the equivalent *D. canis* stages – the adult is 330-370 µm long (approximately twice the size of *D. canis*) (5).

A short-bodied *Demodex* mite that may be more of a surface (*stratum corneum*) dweller, similar to *D. gatoi* in cats, has been described in the dog (6) and has been unofficially named *Demodex cornei*. It measures half the length of *D. canis* and is often found at the same time (14). However, recent studies have questioned the novel nature of this mite. The relationship between *D. canis*, *D. injai*, *D. cornei* and the human mite, *D. folliculorum*, has been assessed using mitochondrial rDNA (1). This study concluded that *D. canis* and *D. injai* are two different species, but that the short-bodied mite *D. cornei* is a morphological variant of *D. canis*. *D. injai* appeared to be closer to *D. folliculorum* than to *D. canis*.

Demodex in the cat

1. *Demodex cati* is similar to *D. canis* – the adult mite is about 200 µm in length (6). The ova are more oval than the eggs of *D. canis*.

2. *Demodex gatoi* is the short-bodied *Demodex* mite of cats ***(Figure 9)***.

Unlike the situation in the dog, *D. cati* and *D. gatoi* have been shown to be different species (15).

Treatment

Localized demodicosis

Systemic antiparasitic therapy is not appropriate for localized demodicosis. There is no evidence that failure

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to treat localized cases results in generalized ones and in fact this treatment may fail to identify the patients that become generalized. That is not to say that there are no treatments. In juvenile dogs with localized demodicosis, it is essential to ensure a "stress-free" lifestyle. Poor nutrition will certainly play a role in the pet's immune competence, and close evaluation of the diet and proper dietary recommendations are important factors; I typically recommend balanced, high quality, commercial diets from reputable companies. Fecal evaluation and appropriate de-worming is also important. Products containing benzoyl peroxide are often recommended by dermatologists as they are said to aid "follicular flushing" – although the owner should be advised that manipulation of the lesion could initially increase loss of hairs that were about to be shed. Benzoyl peroxide does dry the skin and should be followed with a moisturizer.

Generalized demodicosis

The owner must be aware that once treatment for generalized demodicosis is commenced, the pet should be monitored by repeat scraping every 4 weeks. The life stages and numbers of parasites should be recorded to monitor progress, and advise the owners that treatment will continue for two months after a negative scrape – typically 3-7 months in total. If one form of treatment is unsuccessful, try a different one, but some patients are "control versus cure" (especially the adult onset cases).

Amitraz is licensed in many countries for the treatment of demodicosis. There is good evidence of efficacy using the drug at 250-500 ppm every 7-14 days (possibly better with shorter time intervals) (16). Long- and medium-haired dogs should be clipped before application, and treatment should only be performed in a well-ventilated area (respiratory problems have been observed in humans) by veterinary personnel wearing protective clothing; dogs should remain in the veterinary hospital until dry and should not become wet between rinses. Treated animals should not be subjected to stress for a period of at least 24 hours post-treatment (16,17). Amitraz is a monoamine oxidase (MAO) inhibitor and it is important to remember the potential for drug interactions; as an α2-adrenergic agonist, side effects can be treated (pre- or post-treatment) with yohimbine or atipamezole.

Avermectins (ivermectin, doramectin) are macrocyclic lactones. They bind selectively and with high affinity to glutamate-gated chloride channels resulting in increased cell permeability and neuromuscular blocking resulting in paralysis and death of the parasite. They interact with gamma-aminobutyric acid (GABA) sites (17). GABA is a CNS neurotransmitter and these drugs are kept out of the nervous system by the P-glycoprotein pumps of the brain capillary endothelial cells (blood-brain barrier). It is important to remind the owners that using such products at the doses recommended for demodicosis is considered off-label use.

Numerous breeds have members that are homozygous mutants for the MDR1 (multi-drug resistant) gene which are very sensitive to the effects of ivermectin. Although Collies have the highest allelic frequency for the mutant, other affected breeds include the Longhaired Whippet, Shetland Sheepdog, Miniature Australian Shepherd, Silken Windhound, McNab, Australian Shepherd, Wäller, White Swiss Shepherd, Old English Sheepdog, English Shepherd, German Shepherd and Border Collie (18). Since this genetic defect has been identified in many mixed breed dogs testing could be recommended in all dogs before using an avermectin.

Remember that some other drugs (*e.g.*, ketoconazole, erythromycin) can also tie up P-glycoprotein and increase risk of neurotoxicosis when co-administered with a macrocyclic lactone.

Ivermectin (the injectable product given orally) is the most common treatment for generalized demodicosis used in my practice. I routinely recommend a slowly increasing dosage protocol with the drug given with food. A suggested schedule is to start at a trial dose of 0.05 mg/kg daily, then increase to 0.1 mg/kg for the next week. If all is well, increase to 0.2 mg/kg the next day, and 0.3 mg/kg the following day, and finally maintain on 0.4 mg/kg daily, although some patients may require doses as high as 0.6 mg/kg. Continue treatment for two months past negative scrapings. Advise the owner to discontinue immediately if there is evidence of toxicosis (especially lethargy, ataxia, mydriasis and gastrointestinal signs); in this situation, I will usually revert to a lower dose – typically 0.3 mg/kg – on an alternate day treatment schedule (if the dog does not show adverse signs at this dose), while monitoring closely for adverse events.

Note that ivermectin has a relatively long half-life and with daily administration serum concentrations continue to increase for weeks before reaching equilibrium; adverse effects have been reported as long as 10 weeks following institution of treatment (17). Neurotoxicosis can be induced in "normal" (*i.e.*, MDR1(-/-)) dogs after

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administration of ivermectin or doramectin equal to or greater than 100 µg/kg (18). Clinical signs are dose-dependent and can range from mild depression and ataxia, as well as disorientation and mydriasis within 12 hours of dosing (at 0.1-0.12 mg/kg), to more severe ataxia, stupor, recumbency, head bobbing, apparent blindness, facial twitches, hypersalivation, episodes of hyperventilation and bradycardia (at doses up to 0.17 mg/kg). Severe neurotoxicosis signs can be seen with doses around 0.2-0.25 mg/kg or more, and include depression, ataxia and apparent blindness as early onset symptoms, as well as vomiting, paddling movements, tremor and excessive salivation, followed by stupor, feeble attempts to crawl, recumbency, and finally non-responsiveness and coma within 30-50 hours after application, often resulting in death (18).

Doramectin has been recommended with apparent efficacy for the treatment of demodicosis in MDR1 (+/+) dogs at weekly subcutaneous injections of 0.6 mg/kg (14), although the author has no personal experience with this product and further investigation has been recommended (17).

Milbemycins can be successful in treating demodicosis. Milbemycin oxime given orally (0.5-2 mg/kg q24H) is reported, with a better success rate at the higher dose (17,18). I usually do not suggest "step-up" dosing of these cases but there will be the rare "sensitive" patient that develops neurological adverse effects. Moxidectin has also been evaluated for canine generalized demodicosis (0.2-0.5 mg/kg q24H PO) and again careful monitoring is recommended (19). Moxidectin is available in some countries as a 2.5% spot-on formulation (in combination with 10% imidacloprid) and can be used to treat demodicosis when applied weekly; the spot-on formulation has a markedly higher success rate in dogs with milder disease.

Lime sulfur dips (2%) used weekly for 4-6 weeks can be useful in treating feline demodicosis (6).They are very safe, and may be used as a parasiticide response trial to rule out *D. gatoi* in a pruritic cat; most affected cats will improve after three treatments. All in-contact cats should be treated when following this regime, and owners must be cautioned that this product can turn white cats yellow and may discolor jewellery; they should also be warned about the odor associated with treatment. A protective collar should be applied to the cat until it is dry, as many cats will vomit if allowed to groom while the product is wet.

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Figure 10. Generalized demodicosis pre **(a)** and post **(b)** treatment; this dog was rescued and successfully treated for its demodicosis and now leads a happy, healthy life. It was virtually bald on initial presentation.

Finally, follicular demodicosis is associated with bacterial furunculosis, and I have significantly reduced the population of *Demodex* using benzoyl peroxide (BPO) shampoos (followed by a conditioner) and antibiotics without antiparasitic drugs. Clipping the animal may improve contact with the shampoo. It is important to treat concurrent pyoderma/furunculosis as bacteria have been implicated in the immunosuppression of affected patients; however, the infection is considered secondary. Recent studies have shown that the use of systemic antibiotics did not change the treatment duration of dogs with generalized demodicosis when administered

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in addition to oral ivermectin and BPO shampoo; there was no significant difference in duration until the first negative scraping. One can presume that antibiotics can be discontinued once the pyoderma is clinically resolved (20).

In summary, one can conclude that with appropriate diagnostic skills and aggressive therapy, the success rate for this most challenging disease can be quite good. The response to treatment can be dramatic and very satisfying ***(Figure 10)***.

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Malassezia dermatitis and otitis in dogs

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Introduction

Malassezia, a genus of fungi, is frequently found as a commensal organism in the skin, ear canals, nose, oral surfaces, perianal surfaces, anal sacs, and vagina of normal dogs and cats (1-4), and has even been identified on the epidermis of puppies as young as three days old (5). However it can also be involved with dermatological disease; common clinical manifestations include hyperpigmentation, seborrhea oleosa, erythema, and variable degrees of pruritus ***(Figure 1)***.

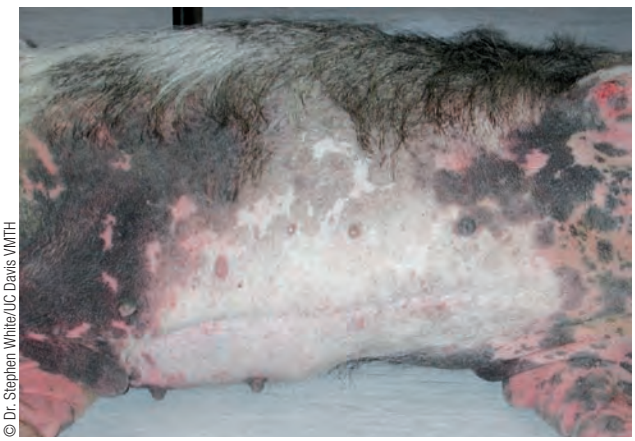
The most common species of yeast isolated in the dog is *Malassezia pachydermatis* (also known as *Pityrosporum canis*, *Pityrosporum pachydermatis*, and *Malassezia canis*). This non-mycelial organism is a non-lipid dependent, lipophilic, saprophytic yeast that reproduces asexually by sympodial or monopolar budding. *Malassezia obtusa*, *M. restricta*, *M. sloofiae*, *M. furfur* (also known as *Pityrosporum ovale*), and *M. sympodialis* are all lipid-dependent lipophilic species that have also been isolated from the skin and ears of dogs and cats, but less commonly (6).

Malassezia pachydermatis has significant genetic diversity; seven sequevars or strains (1a through 1g) of the organism have been identified (7); sequevar type 1a was the most prevalent and found in all host species, while type 1d was found solely in dogs. None of the sequevar types have been specifically associated with either healthy or lesional skin at this time, and more than one sequevar may colonize a single host (8,9).

KEY POINTS

- ***Malassezia pachydermatis* is a common cause of dermatitis and otitis in dogs.**
- **The clinical signs are due to release of virulence factors from *Malassezia* organisms and the resultant inflammatory cascade within the skin.**
- **Typical clinical signs include pruritus, erythema, scaling, waxy exudation, and lichenification.**
- **Cytological examination is the most beneficial and convenient method for diagnosis of *Malassezia* dermatitis.**
- **Treatment must be focused on resolving the underlying cause of the *Malassezia* dermatitis; topical therapy is the mainstay for both treatment and management, while systemic therapy may be utilized in severe or refractory cases.**

Figure 1. A mixed-breed dog with severe lichenification, erythema, and alopecia due to *M. pachydermatis*.



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Pathogenesis

Multiple factors are involved in the pathogenesis of *Malassezia* dermatitis, such as the host's corneocyte adherence mechanisms and the prevalence of concurrent symbiotic organisms, as well as the host's immune response.

Adherence to canine corneocytes may be an important factor in the pathogenesis of *Malassezia* dermatitis in some dogs. Yeast cell walls, which consist of chitin, glucan, chitosan, and mannan (1), contain trypsin-sensitive proteins or glycoproteins that contribute to adherence to canine corneocytes. *M. pachydermatis* also specifically expresses adhesins that bind to mannosyl-bearing carbohydrate residues on the canine corneocyte. This adherence mechanism, however, does not apparently play a role in the pathogenesis of *Malassezia* dermatitis in Basset Hounds (which are prone to *Malassezia* overgrowth) but seems to be significant in other breeds (10).

M. pachydermatis appears to have a symbiotic relationship with commensal staphylococci species, although suggestions that *Malassezia* dermatitis is associated with prior antibiotic therapy have not been substantiated. The two organisms produce growth factors and micro-environmental alterations that are mutually beneficial; thus there are increased numbers of *Staphylococcus pseudintermedius* or *S. intermedius* on dogs with concurrent *Malassezia* (1,4,8). In fact, 40% of dogs with *Malassezia* overgrowth are diagnosed with staphylococcal pyoderma due to the symbiotic relationship between the two organisms (3,11).

The yeast may elicit a spectrum of immunological responses in the host. The humoral response is stimulated, exemplified by higher numbers of antibodies found against more antigens in dogs with *Malassezia* versus healthy dogs (12,13). However, the elevated IgA and IgG levels found in dogs with *Malassezia* dermatitis does not appear to offer any additional protection against infection with the yeast. Cell-mediated immunity may play a larger role in protection against disease than humoral immunity. For example, Basset Hounds appear to have decreased lymphocyte responses to *Malassezia* versus healthy dogs which do not get overgrowth of the yeast (14).

Another type of immunological response that can occur in dogs is a hypersensitivity or inflammatory reaction. The preceding reactions to yeast products and antigens appear to be the main culprit in the pathogenesis of *Malassezia* dermatitis, since the yeast itself remains in the upper level of the epidermis (4,8). As the yeast adheres to the canine corneocytes, it secretes various substances including zymosan, urease, proteases, phosphohydrolase, phospholipases (especially phospholipase A2), lipoxygenases, phosphatases, glucosidase, galactosidase, and leucine arylamidase. These virulence factors cause alteration of the local pH, proteolysis, lipolysis, complement activation, and eicosanoid release in the skin, thus inciting the inflammatory response and pruritus (1,4,8). Furthermore, higher levels of *Malassezia*-specific IgE to allergens of 45, 52, 56 and 65 kDa have been found in atopic dogs compared to normal dogs, further substantiating the hypersensitivity potential of yeast (15).

Factors that predispose to pathogenicity

Factors that may predispose *M. pachydermatis* to become pathogenic, rather than remain commensal, may include any of the following: increased humidity, skin folds, endocrine diseases, keratinization disorders, genetic predisposition, immunologic dysfunction, hypersensitivity diseases, and increased numbers of symbiotic staphylococci.

Humidity may be important as *Malassezia* organisms appear to be more common in otic canals and skin folds and prevalence increases in humid climates (1). Endocrine diseases, such as hypothyroidism, primary and iatrogenic hyperadrenocorticism, and diabetes mellitus may allow increased availability of nutrients and growth factors for the yeast. This may be due to changes in cutaneous fatty acid concentrations, abnormal keratinocyte lipogenesis, and alterations in sebaceous gland function (16,17). American Cocker Spaniels, Shih Tzus, English Setters, West Highland White Terriers, Basset Hounds, Toy and Miniature Poodles, Boxers, Australian and Silky Terriers, Cavalier King Charles Spaniels, Dachshunds, and German Shepherd dogs appear to be at a higher risk for *Malassezia* dermatitis, suggesting a genetic component to the disease (4,6,8). Dysfunction in secretory IgA or cell-mediated immunity may also contribute to pathogenicity in some dogs (2,4). For example, Basset Hounds with *Malassezia* dermatitis have decreased *in vitro* lymphocyte blastogenic response to *M. pachydermatis* antigen when compared to healthy Bassets, indicating a cell-mediated immune dysfunction (14). Hypersensitivity diseases, such as flea allergy dermatitis, cutaneous adverse food reaction, and atopic dermatitis, may also predispose dogs to *Malassezia* dermatitis due to incitation of the inflammatory cascade and resultant pruritus.

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In summary, any dermatoses that produces disruption of the *stratum corneum* barrier, whether mechanical (due to pruritus), or biochemical (due to endocrinopathies, keratinization or immunologic disorders), may potentially allow *Malassezia* virulence factors to gain exposure to the subcorneal immune system, resulting in pathogenicity of the yeast.

Diagnosis

Clinical presentation

Dermatological lesions of *Malassezia* dermatitis may be localized ***(Figure 2)*** or generalized. They commonly manifest in warm, moist areas such as lip folds, otic canals, axillae, groin, ventral neck, medial thighs, interdigital skin, perianal and perivulvar regions, and other intertriginous areas ***(Figure 3)***. Concurrent dermatoses, such as staphylococcal pyoderma, allergies, or keratinization disorders, are seen in 70% of affected dogs (1,4). Appearance of the lesions commonly starts in the humid summer months – which is also the peak time for seasonal allergies – and may persist through the winter months. Historically, patients lack a response to glucocorticoids.

A consistent clinical sign is pruritus, which can be mild to severe (1). Physical examination findings may vary, but most commonly consist of erythema ***(Figures 4 and 5)***, yellow/gray adherent or non-adherent scaling, and occasionally adherent crusting. Other manifestations include a papulocrustous dermatitis, interdigital cysts, reddish-brown discoloration of the claw beds and claws ***(Figure 6)***, erythematous macules and patches, and malodor. Secondary lesions, such as waxy or greasy exudation, lichenification, hyperpigmentation, and excoriations, may also be detected.

Figure 2. A dog with peri-ocular *Malassezia* dermatitis.

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Figure 3. A dog with *Malassezia* dermatitis and accompanying lichenification, erythema and alopecia.

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Figure 4 shows a dog with diffuse *Malassezia* dermatitis whilst **Figure 5** depicts a dog with *Malassezia* pododermatitis. Erythema is a common finding in dogs with *Malassezia*.

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Figure 6. A Shih Tzu dog with *Malassezia* paronychia.

Differential diagnoses for *Malassezia* dermatitis may include one or more of the following: superficial staphylococcal folliculitis, demodicosis, scabies, dermatophytosis, fleabite hypersensitivity, cutaneous adverse food reaction, contact dermatitis, atopic dermatitis, seborrheic dermatitis, epitheliotropic lymphoma, and acanthosis nigricans. It is important to rule out each differential possibility by specific diagnostic methods in order to achieve successful patient management.

Cytology

Cytological examination is the most beneficial and convenient method for diagnosis of *Malassezia* dermatitis (1). There are multiple modalities to obtain the cytological sample, including superficial skin scraping, clear acetate or cellophane tape stripping, direct impression smears, and cotton swab smears (1,4). Tape stripping can be quite effective in many anatomical locations, including dry and greasy lesions. Cotton swab impressions, while effective for otic samples, appear to be significantly inferior to direct impression, tape stripping, and superficial scraping methods in recovering yeasts from the skin (18). The sample is affixed to a glass slide, heat-fixed (if not tape), and stained with a commercial Romanowsky-type stain. Tape samples may be prepared by introducing a stain such as new methylene blue under the tape, and then placing immersion oil on top of the tape for microscopic evaluation.

Under the microscope, yeasts are usually round to oval, but may resemble a “bowling pin” or “peanut” shape either as single organisms, in clusters, or adhered to keratinocytes ***(Figure 7)***. *M. pachydermatis* yeasts are 3-8 µm in diameter, with monopolar budding from one side of the cell wall and formation of a bud scar or collar at the site of daughter cell development (8). An exact number of organisms is not required to make a diagnosis, as there may be different yeast numbers at different body sites, and normal numbers of yeasts may vary between breeds. However, some studies support a diagnosis of *Malassezia* dermatitis if one of the following are met: greater than two organisms per high power field (400x) seen with any sampling technique (4), four or more yeasts visible per oil-immersion microscopic field (OIF, 1000x) (3), greater than ten organisms seen in fifteen different OIF using a tape strip method (2), or one or more yeasts visible in ten OIF (11). However, in patients with a suspect hypersensitivity response to yeast-derived antigens, the recovery of even a small number of yeasts may prove significant.

Culture

The utility of culture for diagnosis of *Malassezia* dermatitis is debatable for purposes other than research. *M. pachydermatis* is relatively easy to culture on Sabouraud dextrose agar at 32-37ºC, since it is non-lipid dependent. A few strains may be difficult to culture, so creating an atmosphere of 5-10% carbon dioxide usually results in increased isolation frequency and colony counts (19). Media that will grow lipid-dependent as well as non-lipid dependent *Malassezia* include modified Dixon agar and Leeming’s medium (5,19). Detergent scrub methods or contact plates may be utilized for quantitative culture if necessary (6). Again it is prudent to remember that regardless of even quantitative culture results, *Malassezia* remains a commensal organism and results may have little or no practical diagnostic value.

Biopsy

Biopsy is not specific for diagnosis, as *Malassezia* yeasts are only seen histologically in 70% of cases ***(Figure 8)***. Histological characteristics include parakeratosis, superficial perivascular to interstitial dermatitis with irregular hyperplasia, spongiosis, prominent exocytosis of lymphocytes (CD3-positive) and a subepithelial accumulation of mast cells (4). Since the organisms reside in the superficial keratin, they may be removed during biopsy processing. Yeast may also be seen in the superficial keratin with many dermatoses and be non-pathogenic; however, follicular yeast organisms should always be considered pathogenic (20).

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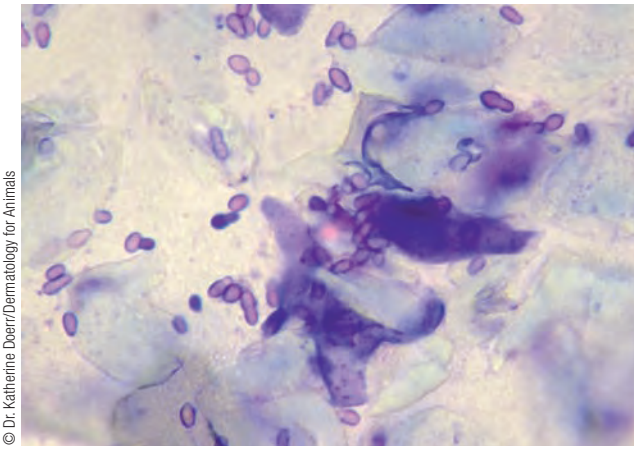
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Figure 7. Acetate tape cytology demonstrating *M. pachydermatis*, stained with a commercial preparation (100x magnification).

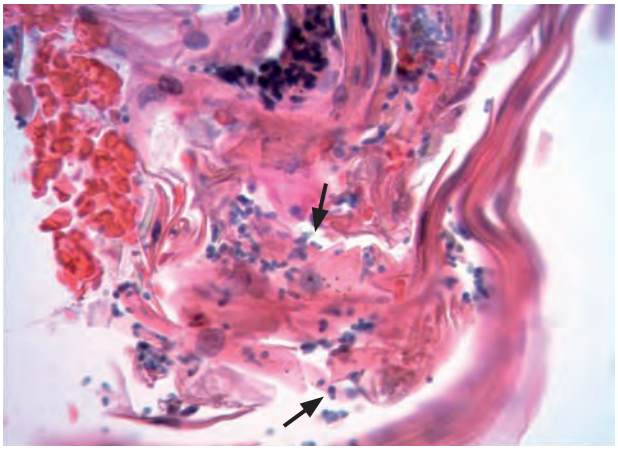
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Figure 8. A skin biopsy demonstrating the histopathological appearance of *Malassezia* otitis (40x magnification).

Intradermal allergy testing

M. pachydermatis reactivity is commonly evaluated during intradermal allergy testing (IDAT). One study noted that healthy dogs and atopic dogs without *Malassezia* dermatitis show no reaction to the appropriate antigen, while positive reactivity to *M. pachydermatis* was seen in all atopic dogs with concurrent *Malassezia* dermatitis and 30% of forty-six dogs with seborrheic dermatitis (21). Results of the IDAT may be taken into account for formulation of allergen-specific immunotherapy; however, it should not be utilized to diagnose *Malassezia* dermatitis.

Response to therapy

The diagnosis of *Malassezia* dermatitis may be established when a dog with an abnormally high population of *M. pachydermatis* on lesional skin responds to antifungal therapy (1). Some dogs may have very little yeast cytologically but may respond well to antifungal therapy. As mentioned previously, yeast-derived antigens may incite a hypersensitivity response in some dogs, so relatively low numbers of organisms may be pathogenic.

Treatment

Therapy for *Malassezia* dermatitis and/or otitis should be individualized given the patient's severity of clinical signs, any accompanying diseases, owner compliance, and other varying factors. Most therapies for yeast target the cell wall components of the organism. Thus far, resistance mechanisms to therapy have not been characterized for *M. pachydermatis*. Note that the use of some or all of the following drugs, both topical and systemic, may be off-label in some countries.

Topical therapy

Topical therapy is usually effective if patient and owner compliance are high. However, in large breed dogs, dogs with long hair coats, fractious dogs, or with elderly or physically disabled clients, topical therapy may not be a viable option. Topical therapy may be utilized focally in otic canals, facial and tail folds, and interdigital spaces with topical creams, lotions, ointments, and wipes. Generalized dermatitis may be treated with total body applications of shampoos and/or rinses (4).

Ingredients that are effective against *Malassezia* topically are shown in ***Table 1*** (1,3,4,22). Therapy should be applied twice daily to every other day until resolution. However, the most recent evidence-based systematic review concluded that there was good evidence supporting use of a 2% miconazole-2% chlorhexidine shampoo twice weekly for three weeks as sole therapy, while there was insufficient evidence for endorsing use of other topical therapies for sole use (22). Furthermore, using a keratolytic, degreasing shampoo prior to the medicated shampoo can assist in removing excess

Table 1. Topical ingredients effective against *Malassezia*.

• Nystatin • Amphotericin B 3% • Clotrimazole 1% • Miconazole 2% • Ketoconazole • Thiabendazole 4%	• Enilconazole 0.2% • Chlorhexidine 3-4% • Lime sulfur 2% • Acetic acid/boric acid • Acetic acid 2.5%

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Table 2. Oral drugs commonly used for the treatment of *Malassezia* dermatitis in dogs.

Drug	Class	Dose	Monitoring
Ketoconazole	Imidazole	5-10 mg/kg q24H	Check liver enzymes and total bilirubin every 2 weeks
Itraconazole	Triazole	5-10 mg/kg q24H *	
Fluconazole	Bis-triazole	2.5-5 mg/kg q24H	
Terbinafine	Allylamine	20-30 mg/kg q24H *	

* - Pulse dosing may be possible.

oils and scale on the patient, resulting in increased efficacy of the medicated shampoo. Otic preparations for *Malassezia* otitis externa, consisting of either miconazole, clotrimazole, ketoconazole, or thiabendazole, should be applied twice daily for a minimum of 2-4 weeks for resolution.

Systemic therapy

If topical therapy is ineffective or not practical for the patient or client, systemic therapy may be utilized ***(Table 2)***. Azole derivatives are often used as they impair ergosterol synthesis in fungal cell walls by inhibiting lanosterol 14-demethylase, the cytochrome P450 enzyme, thus stopping the conversion of lanosterol to ergosterol in the organism. Furthermore, they inhibit cell wall chitin synthesis and intracellular triglyceride and phospholipid biosynthesis (1). Ketoconazole is the most frequently used therapy and should be given with a fatty meal to maximize absorption (1,6). This drug may also be anti-inflammatory and is a general inhibitor of mitochondrial P450 enzymes (1). If the patient has contraindications to receiving ketoconazole or failed therapy, a triazole may be suitable (1,22). Another option includes the allylamine antifungal, terbinafine, again given with a fatty meal (23). Both the triazoles and allylamines persist in the skin due to their lipophilic and keratinophilic properties; pulse therapy regimens may therefore be possible. In fact, two consecutive days per week pulse therapy regimens with itraconazole or terbinafine has been shown to be effective in some dogs (6,24). Improvement should be seen within a week of therapy; however, treatment should continue for at least one week past clinical cure, with an average duration of four weeks required (1). It is important to note that the antifungal griseofulvin is ineffective for *Malassezia* dermatitis.

With any systemic antifungal, serum hepatic enzymes and total bilirubin should be monitored prior to and every two to four weeks during the course of therapy (1). General potential side effects include vomiting, diarrhea, anorexia, abdominal pain and hepatotoxicity; if any adverse events are noted, the drug should be discontinued.

Prevention

Relapse is common in patients with *Malassezia* dermatitis if the underlying cause is not well controlled; weekly or bi-weekly maintenance with topical shampoos/rinses may be necessary for some patients. Pulse therapy regimens using oral antifungals should only be utilized if absolutely necessary due to potential side effects. Most importantly, the underlying cause of the recurrent *Malassezia* dermatitis should be diagnosed and treated appropriately. If allergies are suspected, strict flea control and/or a novel or hydrolyzed protein diet trial should be utilized to rule out flea and/or food allergies respectively, while patients with atopic dermatitis should be managed utilizing hyposensitization or medical management. Underlying keratinization disorders, endocrinopathies, and neoplasias should be treated as required by the condition. For patients with significant skin folds, surgical remediation may be required for patient comfort and prevention of infection.

Zoonotic potential

There are rare zoonotic implications of *M. pachydermatis* in humans. The yeast has been cultured from CSF, urine, and blood of low-birth-weight neonates in a neonatal intensive care unit that was staffed by a health care worker whose dog had *Malassezia* dermatitis (25); resolution of the infections occurred once hand-washing procedures were imposed. Dog owners with inflamed skin have the potential of carrying the organisms from their dogs, and so discussing and enforcing precautionary hygiene measures is important when managing patients with *Malassezia* dermatitis (1).

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Conclusion

Malassezia is a common cause of pruritus, dermatitis, and otitis in dogs. Virulence factors secreted by the yeast can induce a hypersensitivity response in some dogs, even those with very few organisms. The diagnosis is reached by the presence of appropriate clinical signs and supportive cytological analysis, along with clinical and mycological response to antifungal therapy. Successful management of *Malassezia* dermatitis and otitis requires individualized combinations of topical and potentially oral therapy, as well as treatment of the underlying inciting cause.

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Prevalence of canine atopy

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Introduction

Atopy can be challenging to diagnose accurately and therefore to treat effectively. Pets with this condition typically present with pruritus, a signalment that can also be caused by other dermatologic conditions such as food allergy and sarcoptic mange; secondary skin infections (*e.g.*, yeast or bacteria) also add to the confusing presentation. Although atopy is commonly associated with IgE antibodies to various environmental allergens (as demonstrated through diagnostic laboratory testing), it is not a universal finding, and this can make definitive diagnosis (and development of allergen-specific immunotherapy) difficult, if not impossible; the diagnosis is sometimes made by ruling out other dermatologic conditions (1-3). These factors, as well as the varying degrees of severity in clinical presentation, make estimating the prevalence of atopy in the pet population difficult. Previously reported prevalence of canine atopy ranges between 3-30%, depending on the study and the population represented (*e.g.*, primary care vs. specialty practice) (3-4), and breed predisposition has been reported. This article reviews the prevalence of atopy in dogs seen at a network of primary US veterinary hospitals.

Methods of analysis

The health records of all dogs presented at Banfield Pet Hospitals from 2009 through 2013 (a total of 5,716,821 dogs) were screened to identify those with a recorded diagnosis of atopy or atopic dermatitis. The appropriate records were then screened to identify season(s) of diagnosis and geographical region where the diagnosis* was made; the seasons and regions are defined in ***Figure 1***. Prevalence was calculated overall and by region and season. The 2012 and 2013 prevalence and relative risk estimates for more common breeds (*i.e.*, at least 500 patients of that breed were seen) were also calculated, and those 10 breeds with the highest prevalence levels are presented. The risk of atopy in each of these breeds is compared to that in "mixed breed" dogs. The relative risk is estimated by a prevalence ratio or the prevalence of atopic disease in each breed divided by the prevalence of atopic disease in mixed breeds.

Results

The annual prevalence of atopic dogs slowly increased from 2.4% in 2009 to 2.8% in 2013, as shown in ***Table 1***. A total of 187,689 unique cases were seen during this period (some dogs were diagnosed with the condition in more than one year), giving a 5-year prevalence of 3.3%. The seasonal and regional prevalences are shown in ***Figure 2***; notable peaks can be seen in the spring and

*Diagnosis was by intradermal testing, lack of response to food elimination trials, referral to a specialist dermatologist, and/or by clinical judgement.

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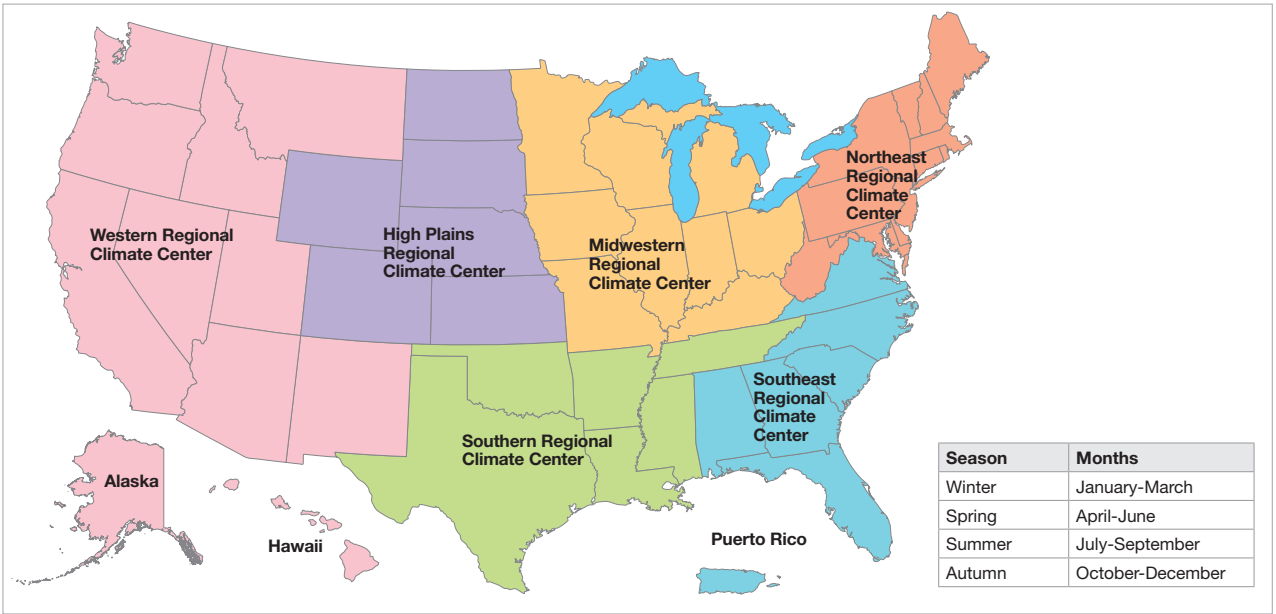

Figure 1. Seasons and regions. The regions are based on climate regions as defined by the National Oceanic and Atmospheric Administration (5).

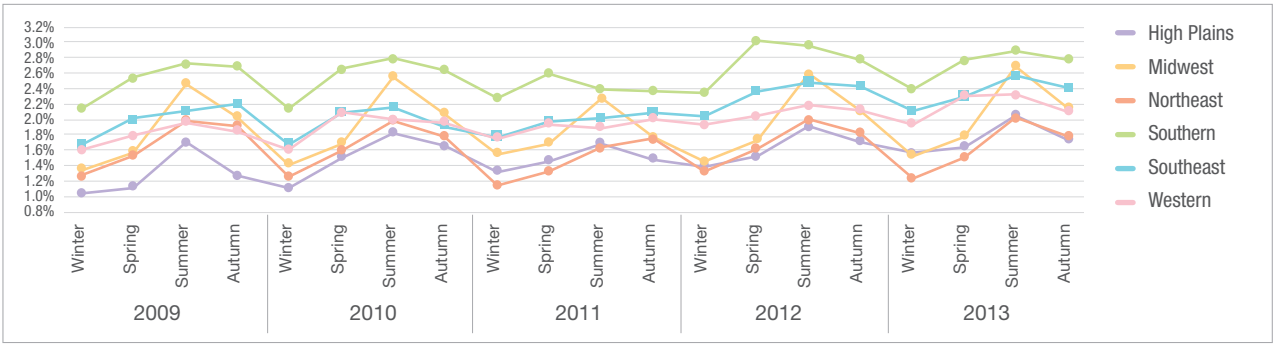

Figure 2. Prevalence of canine atopy in the United States (2009-2013).

summer months, depending on the region, with a slightly higher prevalence in the south central region. As can be seen in ***Table 2***, the West Highland White Terrier had the highest prevalence (9.6%) for 2012 and 2013. With the exception of the Scottish Terrier (2012) and the Welsh Terrier (2013), the remaining eight breeds were in the "top 10" list for both years. When compared to mixed breed dogs, each of the breeds on the list had almost double the risk (prevalence) of atopy.

Discussion

The prevalence of atopy in the Banfield canine patient population was found to be similar to the lowest prevalence level (approximately 3%) previously reported (3-4). The variation in reported incidence may be due to several factors, including global/regional differences and the actual pet population studied (*i.e.*, primary veterinary practice vs. veterinary dermatology specialty clinic or teaching hospital). In addition, it is possible that atopy is either under- or over-diagnosed in the Banfield population because diagnosis can be cumbersome (*e.g.*, food elimination diet to rule out food allergy, referral to dermatology specialist). Given that there is no obvious reason to suspect that diagnosis may have occurred more or less frequently in any year during this 5-year span, it is unlikely to have affected the interpretation that the prevalence has only slightly increased in that time. As expected, regional and seasonal differences were found. Among the commonly seen breeds of dogs, a number had significantly higher risk of atopy when compared to mixed breeds. Because some of the dogs included in the breed categories may actually have been

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Table 1. Annual prevalence of canine atopy or atopic dermatitis diagnosis (2009-2013).

	Total number of affected dogs	Prevalence	# Cases per 10,000 patients
2009	44,297	2.4%	238.2
2010	48,687	2.5%	250.7
2011	47,955	2.4%	237.2
2012	60,274	2.8%	275.2
2013	64,026	2.8%	279.4
2009-2013	187,689*	3.3%	328.3

*An overall total of 187,689 dogs were recorded with atopy; some dogs were diagnosed in more than one year.

Table 2. The top 10 breeds with atopy (among those breeds where at least 500 pets of that breed were seen during that year), based on prevalence. Relative risk is estimated by the prevalence ratio, the prevalence of atopic disease in each breed relative to the prevalence in those recorded as "mixed" breed.

2012				2013			
	# of dogs	Prevalence	Relative risk		# of dogs	Prevalence	Relative risk
West Highland White Terrier	12,173	9.6%	3.9	West Highland White Terrier	12,177	9.6%	3.7
French Bulldog	6,677	8.3%	3.3	Welsh Terrier	658	9.0%	3.5
Bull Terrier	2,418	7.4%	3.0	French Bulldog	7,986	8.5%	3.3
Soft-Coated Wheaten Terrier	3,887	6.2%	2.5	Bull Terrier	2,648	6.9%	2.7
Staffordshire Bull Terrier	1,877	6.0%	2.4	Soft-Coated Wheaten Terrier	3,952	6.8%	2.6
English Bulldog	25,798	5.8%	2.3	Staffordshire Bull Terrier	1,980	6.3%	2.4
Shar-Pei	6,409	5.6%	2.3	English Bulldog	27,308	6.1%	2.4
Scottish Terrier	3,385	5.3%	2.1	Shar-Pei	6,578	6.0%	2.3
American Bulldog	13,705	5.1%	2.0	American Bulldog	14,471	5.5%	2.1
American Staffordshire Terrier	6,104	5.1%	2.0	American Staffordshire Terrier	6,451	5.4%	2.1
Mixed breed	75,321	2.5%	1	Mixed breed	77,835	2.6%	1

mixed breed rather than purebred, and assuming the genetic benefits of crossbreeding for some health conditions, the relative risks calculated may be viewed as conservative estimates of the true risk of that breed relative to mixed breed dogs.

These findings provide additional evidence to the veterinarian about the epidemiology of atopy. It would benefit the practitioner to understand not only the basic biology and epidemiology of the disease, but also the regional and seasonal trends specific for their patient base, including learning from veterinary dermatologists the more common environmental allergens affecting pets in his/her area and recommended diagnostic and therapeutic protocols. These data may enable the practitioner to more effectively diagnose and treat pruritic patients.

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Canine pyoderma: the problem of meticillin resistance

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Introduction

Before the emergence of meticillin resistance, *Staphylococcus pseudintermedius* was susceptible to most of the antibiotic drugs available for animals. More recently, the bacterium has acquired genetic material and developed meticillin resistance; indeed a multi-drug resistance pattern has emerged, limiting treatment options and highlighting the need for responsible antibiotic use. This paper gives an overview of our current knowledge of meticillin-resistant *Staphylococcus pseudintermedius* (MRSP) as a causative pathogen of canine pyoderma and considers diagnosis of the disease, treatment options, prevention and zoonotic aspects.

S. pseudintermedius – a pathogen?

Staphylococci bacteria are normal commensals of the skin and mucosae of healthy dogs, but they are also opportunistic pathogens. The most frequent clinical presentation of canine staphylococcal infections is pyoderma, followed by otitis externa. *Staphylococcus pseudintermedius* (formerly misidentified as *S. intermedius*) is the most common pathogen, and since 2007 has been classified within the *S. intermedius* group along with *S. delphini* and *S. intermedius* (1). Other coagulase-positive staphylococci that are considered pathogenic include *S. aureus*, *S. hyicus* and *S. schleiferi* subspecies *coagulans*. Coagulase-negative species, namely *S. schleiferi* subspecies *schleiferi*, have also been recognized as a cause of pyoderma (2).

KEY POINTS

- **Canine bacterial pyoderma is caused mainly by *Staphylococcus pseudintermedius*.**
- **Meticillin-resistant *S. pseudintermedius* (MRSP) has a worldwide distribution. The bacteria is resistant to beta-lactam antibiotics and is also frequently resistant to other drugs commonly used to treat canine pyoderma.**
- **Bacterial culture and antibiotic sensitivity is strongly recommended if MRSP is suspected.**
- **Veterinary practices need to implement strict hygiene protocols to prevent dissemination of this pathogen.**

What do we mean by meticillin resistance?

Meticillin (formerly known as methicillin) was introduced in 1959 and is a semi-synthetic penicillinase-resistant penicillin. The antibiotic was developed to overcome the resistance mediated by the enzyme beta-lactamase, which destroys the β-lactam ring of the penicillins. Meticillin resistance was first documented in *S. aureus* in 1961 (3). Meticillin-resistant *S. aureus* (MRSA) evolved to produce a defective penicillin-binding protein mediated by the acquisition of the *mecA* gene; this is part of a larger mobile genetic element known as the "staphylococcal chromosomal cassette", which can integrate into the staphylococcal chromosome. Nowadays, meticillin is no longer used clinically, and oxacillin has become the substitute for *in vitro* MRSA testing ***(Figure 1)***; resistance to oxacillin represents virtually total non-susceptibility to all β-lactams, including drugs that are commonly used to treat canine pyoderma (4) such as:

- Cephalosporins (*e.g.*, cefalexin, cefpodoxime proxetil, cefovecin).
- Potentiated amoxicillins (*e.g.*, amoxicillin-clavulanate).
- Penicillins (*e.g.*, ampicillin, amoxicillin).

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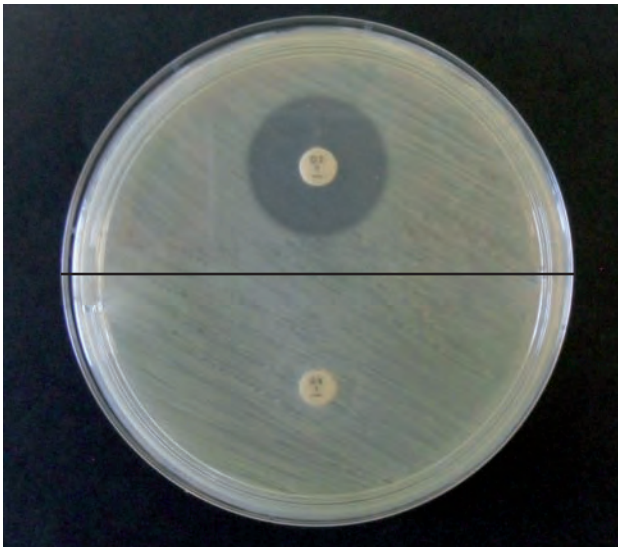

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Figure 1. Oxacillin has become the preferred antibiotic for *in vitro* MRSA testing; here the upper isolate is sensitive to oxacillin but the lower one is resistant, indicating virtually total non-susceptibility to allβ-lactams.

Cefoxitin can be used in human medicine to screen for MRSA, but it is not appropriate to determine non-susceptibility to β-lactams in *S. pseudintermedius* (5).

Meticillin-resistant *S. pseudintermedius* (MRSP) was first reported in 1999 in North America and is now recognized as having a worldwide distribution (6-8). Referral practices, which commonly receive cases of pyoderma that are chronic or recurrent (and therefore have had previous antibiotic therapies) frequently report high levels of MRSP (6). Due to the zoonotic impact of MRSA, less attention has been paid to MRSP and meticillin-resistant *S. schleiferi*.

Is MRSP a challenge?

Historically, pyoderma has been treated empirically with beta-lactams, macrolides or potentiated sulfonamide antibiotics. The problem with MRSP is not only β-lactam resistance but also resistance to other antibiotics such as clindamycin, erythromycin, fluoroquinolones, gentamicin and tetracycline (9). The multi-resistant phenotype is associated with genetic changes due to transposable mobile elements which encode for antibiotic resistance (10). Two clonal MRSP lineages developed simultaneously in Europe and US with different resistant patterns; the North America clone is still susceptible to chloramphenicol, rifampicin and amikacin, whilst the European clone reveals susceptibility to fusidic acid and doxycycline/minocycline (9).

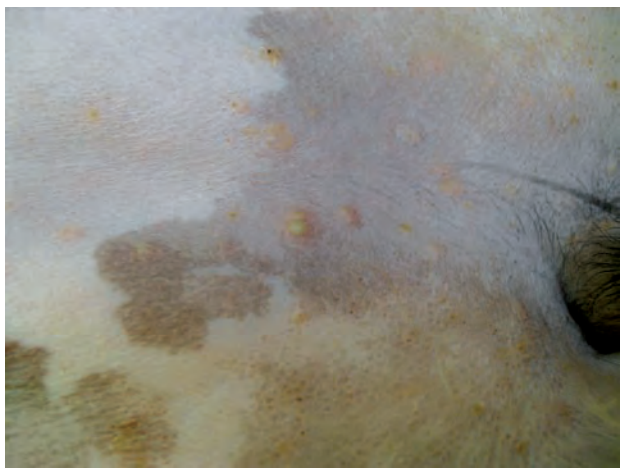
S. pseudintermedius with resistance to three or more classes of antibiotic is classified as a multidrug resistant staphylococcus, and it is therefore not advisable to empirically switch from one antibiotic class to another if treatment fails with the first-line antimicrobial. These cases should be cultured and sensitivity tested before a second antibiotic is prescribed (11). Differentiation between susceptible and resistant *S. pseudintermedius* strains based on the clinical picture is not possible, as MRSP is not more virulent compared to meticillin susceptible *S. pseudintermedius* (MSSP) (6).

How is pyoderma diagnosed?

It is possible to diagnose a pyoderma based on previous history and clinical signs. Minimal diagnostic tests include cytology, bacterial culture and antibiotic sensitivity testing. The differential diagnosis includes demodicosis and dermatophytosis and, more rarely, sterile pustular diseases. Other diagnostic procedures, such as skin scrapings, dermatophyte culture and histopathology, should be applied on a case by case basis.

S. pseudintermedius colonizes the skin and mucosa (nose, mouth and anal mucosa) of healthy dogs and around 80% of the infections originate from the patient carriage sites (12). Canine skin infections caused by *S. pseudintermedius* include superficial and deep pyoderma. The most common form of canine superficial pyoderma is bacterial folliculitis; typical lesions include small pustules and erythematous papules that are associated with hair follicles ***(Figure 2)***. Epidermal collarettes and target lesions are also frequently observed, whilst crusts, alopecia, erythema and hyperpigmentation

Figure 2. Typical lesions of folliculitis include small pustules and erythematous papules.



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may also be seen. In short-coated breeds the clinical presentation may be characterized by multifocal circular areas of alopecia (giving a "moth-eaten" appearance). Signs of deep pyoderma include hemorrhagic bulla, draining sinuses, ulcers, edema and severe inflammation ***(Figure 3)***. A hemorrhagic and/or purulent discharge may be observed with associated pain. It is crucial to distinguish between bacterial folliculitis and deep pyoderma; the latter is more penetrating, with hair follicle rupture and involvement of the dermis and subcutis, and therefore requires a longer treatment duration (13).

Cytology is a reliable, fast, and minimally invasive in-house test to confirm the presence of a bacterial infection. The presence of neutrophils with intracytoplasmic phagocytosed cocci confirms a pyoderma ***(Figure 4)***. Where there is deep pyoderma, the inflammatory pattern is characterized by the presence of degenerate neutrophils, macrophages and sometimes eosinophils. Rods can also appear in rare cases. Lack of microorganisms in skin cytology does not rule out an infection, and whilst cytology is the first diagnostic test to be performed, it cannot replace bacterial culture or histopathology (14). Culture and sensitivity can be performed for any case, but is strongly recommended in the following situations:

- If clinical signs and cytological findings are not consistent with each other, *e.g.*, if no microorganisms are seen with cytology but the clinical signs are still suggestive of pyoderma.
- If rod-shaped bacteria are seen on cytology, as antibiotic susceptibility for bacilli is difficult to predict.
- For any case of deep pyoderma, as it requires a longer treatment duration.
- Any life-threatening infection.
- If MRSP infection is suspected.

Table 1. Risk factors associated with MRSP.

1) New lesions appear after two or more weeks of antibiotic therapy
2) Poor clinical response to empirical therapy
3) Recurrent or relapsing bacterial pyoderma
4) The patient has had a previous MRSP infection
5) The patient lives with an MRSP affected dog
6) Recent antibiotic use
7) Recent hospitalization

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Figure 3. Signs of deep pyoderma can include draining sinuses, ulcers, edema and severe inflammation.

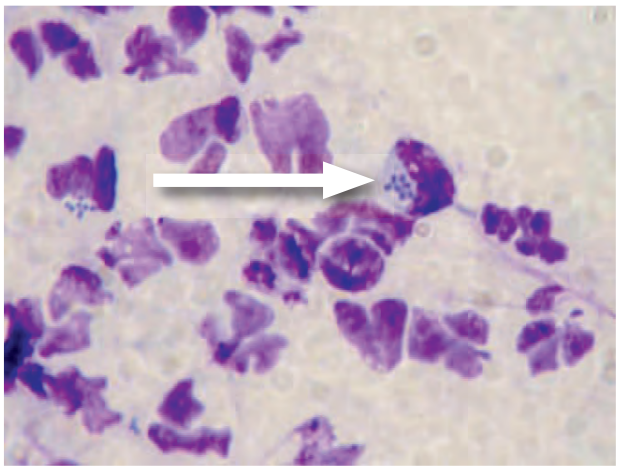

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Figure 4. The presence of intracytoplasmic cocci phagocytosed by neutrophils (arrowed) confirms a pyoderma (1000x magnification).

When should MRSP infection be suspected?

MRSP should be suspected if one or more risk factors ***(Table 1)*** are recognized (4,11,14-16). Clinicians should be aware that MSSP infections, confirmed by culture, can turn into MRSP infections during antibiotic treatment. This can either be due to transmission of genetic factors, or because although multiple clones of both MSSP and MRSP were present in the patient, only MSSP was cultured at the first attempt (17).

How should material for bacterial culture be collected?

Several types of lesions can be cultured but contamination of the samples must be avoided. The skin should

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firstly be wiped with alcohol and left to air dry. Intact pustules, papules and furuncles are suitable lesions and can be carefully opened with a sterile needle before collecting the content with a sterile swab ***(Figure 5)***. If no intact lesions are present, it is still possible to collect material by swabbing an epidermal collarette or from under a recently formed crust. Recently, three sampling techniques (dry cotton swab, saline-moistened cotton swab and surface skin scraping) were reported to deliver similar results when used for bacterial culture (18). In the case of draining tracts, the lesion should be squeezed gently to collect fresh material. For nodular lesions, obtain material by puncturing the nodule with a needle and aspirating the content with a syringe. Skin biopsy is helpful to collect material from deeper tissues and can be done using a biopsy punch or a scalpel blade for a full-thickness wedge biopsy; this allows examination of subcutaneous or deeper tissues. The material is sent to a microbiological laboratory in a sterile container using appropriate transport media.

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Figure 5. Intact pustules, papules and furuncles are suitable lesions for sampling and can be carefully opened with a sterile needle before collecting the content using a sterile swab.

What tests should a microbiological laboratory perform?

The laboratory will identify the micro-organism and perform appropriate antibiotic testing. It is advised that *S. aureus* is discriminated from other coagulase-positive staphylococci for two main reasons; *S. aureus* bacteria have zoonotic implications, and antibiotic sensitivity breakpoints differ between *S. aureus* and *S. pseudintermedius*. Recently published guidelines (11) recommend initial antibiotic testing should include erythromycin, clindamycin, amoxicillin-clavulanate, tetracycline (for testing susceptibility to doxycycline), trimethoprim-sulfamethoxazole, gentamicin, cephalothin (or cefazolin, as a first generation cephalosporin), cefpodoxime proxetil (as a third generation cephalosporin) and enrofloxacin. Oxacillin is included to detect meticillin resistance in *S. pseudintermedius*. Inclusion of other fluoroquinolones (difloxacin, marbofloxacin and orbifloxacin) may be considered if enrofloxacin is not the fluoroquinolone of choice. The results should be compared with breakpoints as defined by the Clinical and Laboratory Standards Institute* (CLSI). Antibiotics with "intermediate susceptibility" should be reported as resistant, as they are unlikely to achieve therapeutic concentrations in the affected sites (11). Finally, the D-zone test for inducible clindamycin resistance is performed if *in vitro* results reveal resistance to erythromycin and susceptibility to clindamycin, as 2% of clindamycin inducible resistance was reported in MRSP (9). If a meticillin-resistant staphylococci is identified, additional testing susceptibility for amikacin, chloramphenicol, minocycline and rifampicin can be performed by the laboratory (11).

*The CLSI standards include information from the Subcommittee on Veterinary Antimicrobial Susceptibility Testing and the European Committee on Antimicrobial Susceptibility Testing.

How is *S. pseudintermedius* pyoderma treated?

Systemic therapy is frequently employed for the treatment of canine superficial and deep pyoderma. Before starting antibiotic therapy it is important to determine if the pyoderma is deep, severe or/and generalized enough to require systemic antibiotics (13). The treatment of MRSP and MSSP follows the same basic principles, with recognition of the pathogen and susceptibility pattern (19). Patient factors, such as the underlying cause, immunosuppression and concurrent disease, all need to be addressed. Owner compliance and drug availability, cost, and side effects should also be taken in consideration. Some drugs may be unlicensed for animal use in certain countries, and if off-label use is proposed the clinician should first discuss implications with the owner.

A recent systematic review identified good evidence for high efficacy of subcutaneously injected cefovecin in superficial pyoderma and for oral amoxicillin-clavulanate in deep pyoderma (20). A fair level of evidence was identified for moderate to high efficacy of oral amoxicillin-clavulanate, clindamycin, cefadroxil, trimethoprim-sulphamethoxazole and sulfadimethoxine-ormetoprim

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in superficial pyoderma and oral pradofloxacin, oral cefadroxil and subcutaneously injected cefovecin in deep pyoderma (20). A recent publication provides clinical guidelines for the diagnosis and treatment of canine superficial bacterial folliculitis (11).

How is first-occurrence superficial pyoderma/folliculitis treated?

A first occurrence of superficial pyoderma/folliculitis can be treated empirically or after bacterial culture and sensitivity. The recommended antibiotics for empirical use are amoxicillin-clavulanate, cefadroxil/cefalexin, clindamycin, lincomycin, trimethoprim- or ormetoprim-sulfonamides, and these options are licensed for veterinary use in most countries (11). If compliance is poor, cefovecin and cefpodoxime proxetil can also be considered for first occurrence pyoderma. It is important to keep in mind that these latter antibiotics have a broader spectrum of activity, including some gram-negative bacteria, and should only be used when appropriate and after culture and sensitivity tests (13).

How should MRSP be treated?

Systemic antibiotic options for MRSP or multi-drug resistant staphylococci are more limited. It is recommended that suitable drugs are selected after culture and susceptibility and when there are no alternatives. When choosing a treatment plan, it is important to consider that there is a risk that further resistance of the infective strain may develop (4). Another consideration is that MRSP can be treated only with diligent topical therapy. The drugs available for MRSP are tetracyclines (*e.g.*, doxycycline and minocycline), fluoroquinolones (*e.g.*, enrofloxacin, marbofloxacin, orbifloxacin, pradofloxacin and ciprofloxacin), chloramphenicol, rifampicin and aminoglycosides (*e.g.*, gentamicin and amikacin). The use of drugs such as linezolid, teicoplanin, or vancomycin is strongly discouraged, regardless of the susceptibility, as these drugs are reserved for the treatment of serious MRSA infections in humans (11).

Some of the drugs used for MRSP have potentially serious side effects. Chloramphenicol is a bacteriostatic antibiotic which must be handled with gloves due to possible irreversible aplastic anemia in humans. Side effects in the dog include vomiting, hepatic toxicity and (reversible) bone marrow suppression. More recently, hind limb weakness has been also reported (21). Aminoglycosides can cause nephrotoxicity and ototoxicity and are best avoided in animals with renal insufficiency. Monitoring of renal function for prevention of aminoglycoside-induced acute kidney injury is advised**. Rifampicin can cause hepatoxicity and requires hepatic function monitoring before starting therapy and then at weekly intervals during treatment; other side effects include anemia, thrombocytopenia, anorexia, vomiting, diarrhea and orange discoloration of body fluids. It has been reported for *S. aureus* that rifampicin resistance can be prevented

**According to the International Renal Interest Society (IRIS) guidelines (www.iris-kidney.com).

Table 2. Recommended antibiotics and dosages for superficial bacterial folliculitis in the dog (11).

Category	Comments	Drug	Suggested dose
First tier	Primary choice for empirical therapy based on suspected sensitivity or if susceptibility proven by culture and sensitivity	Clindamycin	5.5-10 mg/kg PO q12H
		Lincomycin	15-25 mg/kg PO q12H
		Amoxicillin-clavulanate	12.5-25 mg/kg PO q12H
		Cefadroxil/cefalexin	15-30 mg/kg PO q12H
		Sulfonamide-trimethoprim	15-30 mg/kg PO q12H
First or second tier	Third generation cephalosporins	Cefovecin	8 mg/kg SC every 2 weeks
		Cefpodoxime proxetil	5-10 mg/kg PO q24H
Second tier	Reserve to use after proven susceptibility and if first tier drugs are not an option	Doxycycline	5 mg/kg PO q12H or 10 mg/kg PO q24H
		Minocycline	10 mg/kg PO q12H
		Enrofloxacin	5-20 mg/kg PO q24H
		Marbofloxacin	2.75-5.5 mg/kg PO q24H
		Pradofloxacin	3 mg/kg PO q24H
Third tier	Use after proven susceptibility; should be used with caution due to potential severe side effects	Chloramphenicol	40-50 mg/kg PO q8H
		Amikacin	15-30 mg/kg IV/IM/SC q24H
		Rifampicin	5-10 mg/kg PO q12H

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by association with certain antibiotics like clindamycin and cefalexin. It is unknown if this also occurs with MRSP, since development of resistance has been reported even with association with another antibiotic (22).

The recommended drugs and dosages for treating superficial folliculitis are shown in ***Table 2***. Deep pyoderma with extensive scarring and necrosis may limit drug penetration in the tissues, therefore antibiotics that penetrate sites of inflammation such as clindamycin, cefovecin and fluoroquinolones can be used in these cases (13). In general, for uncomplicated superficial pyoderma, therapy is given for 3-4 weeks plus one week after clinical resolution. In recurrent cases, deep pyoderma or concomitant immunosuppression, treatment should be given for 6-8 weeks plus 10-14 days after clinical resolution. Failure to diagnose and control the underlying cause can also prevent complete resolution of the infection and predispose to future infections. Longer treatment regimes might be necessary for MRSP in many cases (23). Rechecks are usually rescheduled every 2-4 weeks until clinical remission is achieved.

Topical therapy – does it help?

Topical treatment for pyoderma hastens recovery and/or reduces the need for systemic therapy. Topical agents may be the only treatment required in some cases, or can be adjunctive to systemic antibiotics. Topical products may be divided into antimicrobial products and topical antibiotics; both may be used for generalized or localized lesions.

Topical antibacterials include chlorhexidine, benzoyl peroxide, ethyl lactate and sodium hypochlorite based products. 2-4% chlorhexidine concentration has been reported to be effective as a sole therapy, and chlorhexidine shampoo revealed more efficacy when compared to benzoyl peroxide shampoo (24). These products can be used in the form of shampoos, conditioners, sprays, wipes or diluted in the bath water. No biocide resistance has been reported for chlorhexidine in MRSP (25). For localized lesions, other topical antibacterial alternatives include honey-based ointments, which have an antibacterial effect against MSSP and MRSP (26). Nisin is an antimicrobial peptide, available as wipes to treat localized pyoderma and bacterial surface colonization (27).

When necessary, topical antibiotics can be used for focal lesions. They include fusidic acid, silver sulfadiazine, gentamicin, fluoroquinolones and mupirocin, and may be useful even when resistance is reported by the laboratory. Fusidic acid is a concentration-dependent antibiotic and high concentrations can be achieved locally, and may be an effective option for MRSP even when *in vitro* testing reveals non-susceptibility. Mupirocin is used for topical nasal infection and decolonization of MRSA in humans, but some countries restrict its use in animals.

What are the zoonotic implications of MRSP?

With the emergence of MRSP there has been a renewed interest in zoonotic implications of *S. pseudintermedius*. It has been shown that nasal colonization can occur in humans, and owners with dogs affected by deep pyoderma can carry the same genetic MRSP strain that occurs in their pets, which supports inter-species transmission (28). Veterinarians in contact with infected animals also seem to have a higher risk of being MRSP nasal culture positive when they share the environment (29). Humans are not natural hosts for *S. pseudintermedius*, which explains the lower impact of MRSP compared to MRSA, but it is unknown if *S. pseudintermedius* strains containing mobile genetic elements could represent a reservoir for the spread of resistant genes to the human commensal skin flora (4).

How can MRSP dissemination in the practice be prevented?

Guidelines are available on how to maintain high standards of clinical practice and hygiene in order to reduce the risks of MRSA and MRSP and manage infected patients (30). Prevention of MRSP is based on responsible antibiotic use, strict hand hygiene and environment disinfecting measures. All surfaces and equipment must be effectively cleaned and disinfected between patients; if surfaces are soiled, detergent and water must be used first as soiling can compromise the efficacy of disinfectants. All surfaces should be easily cleanable (*e.g.*, by using washable computer keyboards) and team involvement is crucial, with cleaning and disinfection procedures displayed at appropriate places and recording of the protocol tasks. One MRSP hospital outbreak has been reported with colonized and infected canine and feline patients (31). The report suggested that rigorous control measures are needed to control an outbreak, and recommends the implementation of a search-and-isolate policy and standard precautions including hand disinfection, barrier nursing, environment and clothing hygiene to prevent MRSP transmission between patients.

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What conclusions can be drawn?

Small animal clinicians often encounter dogs with bacterial pyoderma, and most first occurrence cases can be treated empirically. However, an MRSP infection should be suspected if there is a poor response to previous antibiotherapy or other risk factors are present, and culture and antibiotic sensitivity should be performed as MRSP offers limited systemic antibiotic options. Topical treatment is advised as a sole or adjunctive therapy to systemic antibiosis to hasten recovery. MRSP has zoonotic implications and practices should implement protocols to avoid dissemination of this pathogen.

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Perianal pruritus in the dog

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Introduction

Perianal pruritus, or *pruritus ani,* has been recently defined as "itchiness in the region around the anus, ranging from the ventral tail base to (but excluding) the genitalia" (1). Dogs try to alleviate their discomfort by "scooting" along the floor, and/or by licking or chewing the area. Despite the fact that it is a common problem in practice, there has been little in the way of research; indeed, only one published study to date specifically considers canine perianal pruritus (1), and notes that 37% of dogs presented to a dermatological specialist had this clinical sign. The aim of this review is to address the etiologies of the condition, discuss the diagnostic work-up, and review current medical treatments.

KEY POINTS

- **Perianal pruritus may be defined as itchiness in the region around the anus, ranging from the ventral tail base to (but excluding) the genitalia.**
- **Typical presentations of perianal pruritus are scooting, licking or chewing at the anal/perianal region and/or under the tail. Secondary signs are common and may include erythema, excoriations, alopecia, hyperpigmentation and lichenification.**
- **There are various etiologies of perianal pruritus, including inflammatory (mainly allergic), parasitic, infectious and neoplastic diseases; a diagnosis requires a methodical approach, as successful identification and treatment of the underlying cause is essential in order to effect a cure.**

Etiology

Perianal pruritus is not found in healthy dogs (2), and may be the result of a number of different causes. These can be broadly subdivided into non-dermatological and dermatological problems, and each is discussed briefly below.

Non-dermatological causes

Intestinal parasites

Intestinal parasites of dogs have a worldwide distribution, although the prevalence varies geographically from 12.5-34.4% (3). Whilst deworming is regularly done for puppies, it is less common in adults. The most common intestinal parasites are roundworms, hookworms, whipworms and tapeworms; of these, only whipworms and tapeworms have been associated with anal pruritus (3).

Trichuris vulpis is a whipworm commonly found in dogs. The life cycle is direct, with transmission being via ingestion of the eggs, followed by larval migration to the

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cecum and colon where they penetrate into the mucosa and mature. Eggs are laid into the gut lumen and released into the environment via the feces. Clinical signs depend on the degree of infestation, the presence of other diseases and the nutritional condition of the dog. Although chronic diarrhea is the most important clinical sign, some dogs scoot or lick the perianal area (4).

Dipylidium caninum is a tapeworm distributed worldwide. It has an indirect life cycle, with fleas as the intermediate host. The dog is the definitive host and is infected by ingestion of the adult flea containing the cysticercoid. These worms reside in the small intestine and produce proglottids, which contain eggs. Gravid proglottids may pass intact via the feces or leave the host spontaneously, emerging from the anus and crawling onto the perianal skin; this migration can cause pruritus. The life cycle is continued by ingestion of the eggs by a flea.

Anal sac disease

Anal sacs are cutaneous diverticula of the anus, lined by keratinized, stratified squamous epithelium. Apocrine anal sac glands secrete a mixture of fatty and serous materials and cellular debris; the secretion may vary in amount, color and consistency (1,5). Perianal pruritus can be associated with anal sac disease (ASD) (2); dogs scoot, lick and chew the perianal area to alleviate the discomfort caused by distension of the anal sacs and/or irritation secondary to inflammation or infection. The anal sacs may be affected by the following conditions:

- **Impaction:** One study documented anal sac impaction in 2.1% of all dogs presenting in small animal practice (6). Although the exact etiology is unknown, over-secretion or changes in secretion consistency may make passive emptying of the sacs more difficult (7). Furthermore, changes in muscle tone due to aging or obesity, or even the presence of soft feces, may cause the sacs to over-fill (8).

- **Infection:** Anal sac infection can occur as a consequence of chronic fecal impaction or contamination, incomplete emptying of the colon, obesity, chronic bowel disease, allergy, endocrinopathies, and iatrogenic damage when the sacs are expressed. Infection is characterized cytologically by the presence of inflammatory cells as well as bacteria or yeasts (9), but the presence of bacteria and neutrophils within anal sac contents does not always indicate infection, as they can also be found in healthy dogs (2). Indeed, dogs with pyoderma but no ASD have much higher levels of intracellular bacteria and inflammatory cells in their anal sacs than dogs with ASD (5).

- **Abscessation:** Abscesses are well circumscribed masses containing suppurative exudate ***(Figure 1)*** that can develop as a consequence of impaction and infection. However rupture of the abscess can lead to exudate spreading into the surrounding tissue, causing cellulitis and pain, or formation of a perianal fistula.

- **Neoplasia:** Adenocarcinoma is the most common neoplasm affecting the anal sacs, and is often accompanied by hypercalcemia. Although older females were once believed to be over-represented, this is now questionable, and at least one study which looked at apocrine gland carcinoma of the anal sac in dogs reported an equal gender distribution (10). Squamous cell carcinoma (11) and malignant melanoma (12) have also been described.

Perianal diseases

- **Perianal furunculosis:** Also known as perianal fistulae, this is a chronic, debilitating, painful and progressive condition affecting the anus, peri-rectal tissues and perianal skin characterized by inflammation, ulceration and sinus tract formation ***(Figure 2)***. The etiology of the disease is still unknown, but an immune-mediated process has been suggested, although since the disease mainly affects German Shepherd dogs there may be a genetic predisposition. Affected dogs may show significant anal discomfort, manifested as pain, tenesmus and licking; hemopurulent discharge may leak from the fistulae. Although furunculosis is not typically considered a primarily pruritic disease, in the

Figure 1. Anal sac abscessation: Yellow purulent exudate is visible when the nodule is lanced.

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initial phases sometimes scooting may be the only presenting sign.

- **Neoplasia:** Hepatoid glands, also called circumanal or perianal glands, are modified sebaceous glands present in the perianal region; hepatoid gland adenoma is a common neoplasm, accounting for 8-10% of all canine skin tumors (13). It is especially common in aged intact male dogs ***(Figure 3)*** and whilst the etiology is unknown, testosterone may be involved in the development of the condition. Perianal gland carcinoma (including perianal gland epitheliomas) (14) is by comparison rare in the dog. Adenomas and well-differentiated carcinomas are characterized by nodules around the anus; poorly differentiated carcinomas are not well circumscribed and often ulcerate. Common signs include tenesmus, constipation, pain, anorexia, and weight loss. Secondary infection is likely and is often associated with pruritus.

Other non dermatological causes

Other less frequent conditions have been associated with perianal pruritus, including rectal diseases, gastrointestinal conditions (*e.g.*, colitis) (15), psychological and metabolic factors (7) and drug reactions (including diarrhea related to medications).

Dermatological causes

Allergies

A recent study investigated the association between perianal pruritus and skin diseases in dogs without gastroenteric, anal/perianal or rectal diseases (1). 92 out of 250 (37%) dogs presented to a dermatological specialist had perianal pruritus and it was found significantly more often in cases with atopic dermatitis (52% of affected dogs) and/or adverse food reactions (51% of affected dogs) than in all other skin diseases, in line with a previous study (16). Flea bite hypersensitivity has also been associated with perianal pruritus, with a prevalence ranging from 9-67% (1,17).

Other skin diseases

Although less common than allergies, other skin disorders such as sarcoptic mange, demodicosis, keratinization defects, sebaceous adenitis and contact dermatitis can be associated with perianal pruritus. Furthermore, immune-mediated diseases, such as pemphigus foliaceus and mucocutaneous lupus ***(Figure 4)***, and neoplasias, such as epitheliotropic lymphoma and mast cell tumor, can also affect the anal and perianal skin and occasionally cause itching.

Diagnostic approach

To determine the correct diagnosis a methodical work-up should be initiated: it is important that all differentials are considered during the collection of the history and the clinical examination. The diagnosis is achieved by excluding other possible etiological factors.

Signalment and history

Breed, age and sex can give important clues for the diagnosis. Some diseases may have a breed predisposition, such as perianal furuncolosis in the German Shepherd dog or allergic dermatitis in the West Highland White Terrier and Labrador Retriever. Onset of clinical signs at an early age (< 1 year of age) is suggestive of parasitoses or food allergy. Anal sac carcinoma may be more often diagnosed in females, and hepatoid gland tumors are more frequent in intact male dogs.

It is important to collect information on the clinical presentation of the pruritus. Recurring pruritus in the warmer

Figure 2. A dog with perianal furunculosis; note the severe ulceration and coalescing fistulae.

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Figure 3. Multiple perianal hepatoid gland tumors in an old entire male dog.

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months may suggest seasonal atopy or flea bite hypersensitivity. If the itch improves after the anal sacs are squeezed, anal sac impaction is the more probable cause. If other areas of the body are itchy, such as paws, groin, axillae or ears, atopy or food allergy could be to blame, while if pruritus is localized mainly on the back and tail base fleas and/or flea bite hypersensitivity may be the most likely diagnosis. The clinician should also accurately assess the dog's behavior: it has been speculated that licking or chewing at the anal region without scooting may be more indicative of an allergic disease than of ASD (1).

Establish if there are concomitant gastroenteric abnormalities. If the dog has a history of excessive bowel movements alone or with chronic flatulence, and if signs such as vomiting, diarrhea, constipation, tenesmus and/or dyschezia are present, then gastrointestinal problems such as colitis, intestinal parasites, adverse food reactions and intestinal bowel diseases (IBD) should be considered. To highlight concurrent food-related disorders such as adverse food reactions, colitis and IBD, the history should also consider the current diet and any previous modifications. In humans, contact dermatitis (from soap, toilet papers or creams) is a common cause of perianal pruritus. In dogs this is less frequent, but it is always worth asking if topical products, such as cleansing wipes, have been used. Previous administration of drugs, including anti-parasitic products, should be also investigated and the pharmacological history should be detailed.

Examination

A general clinical examination, checking for systemic signs, should be followed by a full dermatological evaluation, looking for evidence of skin lesions and/or parasites in all areas of the body. Finally the clinician should focus on the perianal area, looking for both primary and secondary lesions. Perianal erythema ***(Figure 5)*** and excoriation, as well as alopecia, hyperpigmentation and lichenification ***(Figure 6)*** are common sequelae of acute and chronic inflammation respectively. Presence of such lesions in the perianal region is strongly associated with perianal pruritus (1).

The anal orifice and the surrounding skin may be affected by fistulae ***(Figure 2)***, swelling ***(Figure 1)*** or nodules ***(Figure 3)***, as seen in perianal furuncolosis or neoplasia. Emerging proglottids, indicative of tapeworm infestation, may be present. A digital anorectal examination should follow, to assess the presence of indurations, nodules or purulent or hematogenous exudate. The anal sacs should

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Figure 4. A dog with mucocutaneous lupus; note the severe perianal ulceration.

then be gently squeezed to evaluate the presence, color and consistency of the secretion, and cytological evaluation of the contents should be undertaken. If the perineal area is highly inflamed and painful, it is advisable to apply a local anesthetic cream, or even sedate the patient, before doing any physical examination.

Ancillary testing

Cytology is useful for diagnosing infection or neoplasia. In the perianal skin the presence of *Malassezia* dermatitis or pyoderma can be best assessed by tape imprints, stained and examined under light microscopy. A small amount of anal sac secretion from each side should be placed on a glass slide, allowed to dry and then stained: the presence of neutrophils may indicate an anal sac infection or a pyoderma (5).

Cytology is indicated to investigate nodules and palpable lymph nodes; the presence of degenerate neutrophils together with phagocytosed bacteria suggests infection, *e.g.*, an anal sac abscess, whilst neoplasia may be suspected when cytology shows a monomorphic population of non-inflammatory cells.

Biopsy is indicated when cytological examination is suggestive of neoplasia or immune-mediated disease, or

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Figure 5. A dog with atopic dermatitis; note the intense erythema of the perianal region.

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Figure 6. Chronic skin lesions secondary to food allergy; there is severe hyperpigmentation and lichenification of the perianal area and ventral tail.

when lesions do not respond to an apparently appropriate therapy. Fecal examination and broad-spectrum antiparasitics will be useful in the diagnosis of intestinal parasites. Blood sampling may be useful in some cases, *e.g.*, hypercalcemia can be indicative of anal sac carcinoma.

Strict flea control can help identify a flea bite allergy, while an 8-week long elimination food trial, followed by provocative challenge, can help to diagnose a food allergy. Elimination food trials can be performed by feeding a home-cooked or limited antigen diet with ingredients novel to the dog, or by feeding a hydrolyzed diet. If all previous tests prove negative, then the dog most probably has atopic dermatitis. A symptomatic, non-sedating treatment for pruritus (*e.g.*, oclacitinib) can be used to discriminate atopic dermatitis from behavioral disorders.

Therapy

Etiological treatment

For a successful, long-term cure, it is necessary to control and treat the underlying etiology responsible for the perianal pruritus. A detailed description of all therapeutic interventions for the various cited underlying etiologies is beyond the scope of this article, but it is appropriate to focus on the most typical or frequent causes of pruritus affecting the anal and perianal area.

Anal sac impaction is best treated by frequent manual expression of the sacs (7); a finger is introduced into the anus and the sac is expressed with delicate pressure between the finger and thumb. This method permits the complete emptying of both sacs. Alteration of the diet, *e.g.*, integration with prebiotics to improve the consistency of the stools may promote natural emptying.

Anal sac infection is treated by emptying and flushing the sacs; this can be painful and may require sedation. The sacs are catheterized using a round-ended catheter (*e.g.*, a cat urinary catheter) and flushed with isotonic saline (7); a suitable antibiotic solution (based on culture results if available) is then introduced. Various antibiotic combinations can be employed but chloramphenicol has been shown to have a broad spectrum of activity against the common pathogens. Corticosteroids may also be infused if appropriate. If *Malassezia* is present then the use of nystatin or an imidazole derivative (miconazole, clotrimazole) is indicated.

When an anal sac abscess is present, there is a risk of rupture with drainage to the perianal skin or into the rectum. In this case systemic antibiotics are indicated, preferably based on sensitivity testing, although topical treatment (drainage and lavage with 0.5% chlorhexidine or 10% povidone iodine and instillation of an antibiotic solution) can also be useful. Surgical removal of the sacs is advised in cases of frequently recurring anal sacculitis or abscesses (7).

Perianal furunculosis is best treated with oral antibiotics, cyclosporine (5-10 mg/kg q12-48H (18)) and/or topical 0.1% tacrolimus (19) given until 4-8 weeks after resolution. Administration of ketoconazole (2-10 mg/kg q12-24H) improves the efficacy of cyclosporine and can reduce its dose (and possibly cost) by up to 50% (20). Relapses and incomplete resolutions are frequently seen,

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and alternate day permanent maintenance therapy may be necessary in some cases (21).

Flea infestation and flea bite hypersensitivity require a strict flea control program. Food allergy is best controlled by avoidance of the specific offending food, preferably by means of a complete well-balanced commercial limited-antigen or hydrolyzed protein diet (15). Causative factors responsible for contact dermatitis or allergy may be identified by patch testing and further avoided if possible. Atopic dogs can be controlled with allergen-specific immunotherapy (21) or symptomatic treatments against pruritus (see below).

Symptomatic treatment

In many cases, in order to decrease pruritus and improve the quality of life for both dogs and owners, symptomatic treatment of pruritus may be necessary. Topical antipruritic therapy is usually based on corticosteroid cream or solution. Several studies have confirmed the efficacy of a commercial hydrocortisone spray (22) which is easy to administer and is indicated for managing both acute and chronic pruritus (22). It is well tolerated and safe: skin thinning, which is a side effect often associated with prolonged topical corticosteroids, has not been reported with daily application of this product (23).

Systemic antipruritic drugs, such as cyclosporine (5 mg/kg q24H given for one month, then tapered to every other day (24)), or oclacitinib (0.4-0.6 mg/kg q12H for two weeks, then tapered to q24H (25)), can be the best options for long-term management in many cases.

Conclusion

Perianal pruritus is a complaint commonly reported by dog owners and a distressing condition for the pet. Although there are many different etiologies, it is most often linked to anal sac disease or allergic dermatitis; however, the clinician should always perform a systematic diagnostic approach to identify and, when possible, remove the cause.

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Alternatives to corticosteroids in treating canine pruritus

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KEY POINTS

- **Pruritus is the most common presentation for skin disease in the dog; the cause of the pruritus should always be determined, as this will allow a prognosis to be given and the selection of appropriate treatments.**
- **Corticosteroids are very effective antipruritic drugs but may produce intolerable side effects, particularly if used over prolonged periods of time.**
- **Where prolonged, or lifelong, treatment of pruritus is likely then alternatives to chronic glucocorticoid treatment should be explored.**
- **In the majority of cases multimodal treatment is likely to be required for satisfactory control of chronic pruritus; this is especially so when managing canine atopic dermatitis.**
- **A number of effective treatments are available as alternatives to corticosteroids. These are mainly licensed for, and used in the management of, canine atopic dermatitis.**
- **Several other treatments with poor to moderate efficacy are also available and may be considered for alternative or additional use where the more efficacious treatments have failed to achieve satisfactory control of pruritus.**

Introduction

Pruritus is considered to be the most common presentation for skin disease in the dog. It requires prompt and effective management in order to prevent self-trauma and the development of chronic inflammatory lesions. Whilst corticosteroids are excellent drugs to control inflammation and pruritus, they have potential unwanted side effects that can be serious when used over a prolonged period of time. In the short term, the major adverse effects are polydipsia and polyuria, which may prove intolerable for owners; more serious side effects, including the development of iatrogenic hyperadrenocorticism, may arise with prolonged use (1). Corticosteroids are most useful for short-term use to gain rapid control of acute pruritus and a break in the itch-scratch cycle. Where prolonged antipruritic treatment is required, alternatives to corticosteroids may be sought to avoid the potential for side effects. This paper will explore the alternatives to chronic glucocorticoid treatment.

Before considering the use of any anti-pruritic medication it is important to determine the cause of the patient's pruritus (*e.g.*, skin scrapes, elimination diet, etc.). Many pruritic dermatoses, including ectoparasitic infestations and microbial overgrowths/infections, require short-term use of anti-pruritic agents to prevent self-trauma, but

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ultimately respond to medications that target the etiological agents involved. Conversely, incurable pruritic dermatoses require the clinician to select anti-pruritic drugs that will be safe and well tolerated long term. In dogs the three most common groups of diseases that cause pruritus are parasitic skin disease, infectious skin diseases and allergies (most commonly canine atopic dermatitis) ***(Figure 1)***. There are, of course, various other skin diseases that may cause pruritus, for example epitheliotropic lymphoma. When deciding on a treatment plan for the pruritic patient it is therefore essential to have a diagnosis in order to select the most appropriate anti-pruritic agent for either short- or long-term use. Given that topical or systemic corticosteroids will be appropriate for most diseases requiring short-term anti-pruritic therapy, this paper will focus on anti-pruritics for the long-term management of canine atopic dermatitis.

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Figure 1. A five-year-old West Highland White Terrier suffering from atopic dermatitis. Secondary bacterial and *Malassezia* infections should be looked for in such cases.

Alternatives to corticosteroids

There are various treatments available as alternatives to corticosteroids. Perhaps the easiest classification is to divide them by efficacy, and each will be briefly considered below. ***Table 1*** summarizes the drugs, dosages and efficacy. Note that the data sheet recommendations (when available) should be followed wherever appropriate.

Products with good efficacy

- **Cyclosporine,** a calcineurin inhibitor, is available in many countries as a licensed treatment for canine atopic dermatitis (CAD) in both capsule and liquid form. Cyclosporine's principal mode of action is to inhibit T cell activation; its immunosuppressive activity is achieved by binding to the intracellular receptor protein cyclophilin-1. The overall effect of cyclosporine is a reduction in the number and activity of pro-inflammatory cells at sites of inflammation (2). The recommended initial dosage is 5 mg/kg every 24 hours, and in cases that respond well after four to six weeks of treatment it may be possible to reduce the amount of drug administered. Either reducing the daily dosage or increasing the interval between doses can be trialed (3). Several high-quality, randomized, controlled trials have shown cyclosporine to have good efficacy and safety, apart from minor reversible adverse effects (4). The most common side effect is transient gastrointestinal disturbances, although other rare side effects have been reviewed (5). Its efficacy is similar to that of oral corticosteroids, but it has a slower onset. Although cyclosporine's main use is in the control of atopic dermatitis, it has been successfully used in a number of other skin problems (2).

- **Oclacitinib** is a product now licensed in many countries for use in the control of CAD and canine allergic dermatoses. It has been shown to safely and effectively reduce pruritus, inhibiting key pathways involved in the itch and inflammation associated with allergy. Oclacitinib selectively inhibits Janus kinase 1-dependent cytokines; in particular it has been shown to strongly inhibit IL-31 cytokine function in dogs, a major cytokine involved in allergic skin disease, and thus may significantly reduce pruritus. The initial dose is 0.4-0.6 mg/kg bodyweight, administered orally, every 12 hours for 14 days. For maintenance therapy, the same dose is then given once daily. Occasional diarrhea, vomiting and anorexia have been noted in a small number of dogs undergoing treatment. Studies have shown that oclacitinib has similar antipruritic effects to both prednisolone and cyclosporine, with oclacitinib having a rapid onset of action which is comparable to prednisolone (*i.e.*, quicker than cyclosporine) (6, 7).

- **Allergen-specific immunotherapy:** In dogs diagnosed with CAD and where sensitization to environmental allergens has been identified via serum or intradermal allergy testing, allergen-specific immunotherapy (ASIT) can be included in the management plan. The mechanism of action of ASIT is unknown, but has been reviewed for both human and veterinary medicine (8). Numerous open, uncontrolled studies have implied that ASIT is efficacious in the treatment of CAD (9, 10), although in fact the success rates vary; most uncontrolled studies report "good to excellent" improvement in about 60% of cases (11, 12). There is no standardized protocol for the administration of ASIT and generally the protocol recommended by the

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Table 1. Summary table for alternative anti-pruritic agents.

	Dose	Comment
High efficacy		
Cyclosporine	5 mg/kg PO q24H. Can try to taper dose after 4-6 weeks if response is satisfactory	Generally safe. Gastrointestinal signs are the most common side effect
Oclacitinib	0.4-0.6 mg PO q12H for 14 days then the same dose to be given once daily	Occasional diarrhea, vomiting and anorexia
ASIT	Various treatment regimes	For use in CAD. Slow to act but appears to be a safe treatment
Medium efficacy		
Misoprostol	2-7.5 µg/kg PO q8-12H	Occasional mild diarrhea and vomiting. This drug should not be handled by pregnant women
Low efficacy		
Antihistamines	Dose varies depending on antihistamine use; see **Table 2**	Safe
Pentoxifylline	10 mg/kg PO q24H	Appears to be safe
Essential fatty acids	Various dose regimes dependent on type used	Safe. Available as diet supplements, topical treatments and skin support diets

vaccine supplier is undertaken. The main concern with the use of ASIT is the low risk of anaphylaxis at the beginning of therapy; animals commencing ASIT should therefore do so under the close supervision of a veterinary surgeon. Treatment response is slow and usually assessed over 6-9 months, and treatment for the other areas of pathogenesis must therefore be addressed whilst ASIT is taking effect.

Products with moderate to poor efficacy

- **Oral antihistamines:** Several antihistamine products ***(Table 2)*** have been used for the control of canine pruritus. To the authors' knowledge, none of the oral preparations are licensed for use in the dog in any country, and there is very little in the way of good quality, controlled clinical trials to prove the efficacy of these drugs. While a few studies have reported up to 30% improvement, the majority of trials show an efficacy of around 10% (4). In one study diphenhydramine and hydroxyzine were considered to be more effective than chlorpheniramine and clemastine (13). Despite their poor efficacy, antihistamines can be a beneficial adjunctive treatment; it has been suggested that the use of some antihistamines with glucocorticoids will have a steroid-sparing effect. Side effects of antihistamines are generally very low, with occasional dogs showing drowsiness.
- **Essential fatty acids (EFAs):** EFAs are necessary for good skin health, and although multiple studies have been conducted on the efficacy of EFAs for pruritic dogs, the studies have generally been of poor quality. In CAD there is evidence for the presence of skin barrier defects that result in increased trans-epidermal water loss; EFAs may help to correct these defects. EFAs are available as direct diet supplements and there are also a number of commercial diets available with a high EFA content. EFAs may be of benefit in reducing pruritus indirectly by improving skin barrier function, and they may also have a direct effect in controlling pruritus through their anti-inflammatory action on keratinocytes, dendritic cells, T lymphocytes and mast cells (14). One high-quality study suggests EFAs may help to reduce glucocorticoid usage (15). EFAs appear to be very safe but occasionally may cause minor digestive disturbances.

Table 2. Selected oral antihistamines.

Chlorpheniramine	4-8 mg per dog q8H
Hydroxyzine	2 mg/kg q8-12H
Clemastine	0.05-0.1 mg/kg q12H
Diphenhydramine	1-2 mg/kg q8-12H

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- **Misoprostol** is a prostaglandin-E1 analogue. Prostaglandin E elevates cyclic adenosine monophosphate which blocks secretion of cytokines produced by T helper 1 cells; this is thought to be responsible for the anti-inflammatory effect of the drug. Two clinical trials have shown this drug to have some efficacy in the management of inflammation and pruritus associated with atopic dermatitis (16, 17). The dosage is 2-7.5 µg/kg orally every 8 to 12 hours. Mild intermittent vomiting and diarrhea have been reported in some dogs. Note that this drug should not be handled by pregnant women or women who are trying to conceive.

- **Pentoxifylline** is a phosphodiesterase inhibitor. Its anti-inflamatory effect is due to the fact that it induces decreased leukocyte responsiveness to cytokines, decreased production of cytokines, and inhibition of T and B cell lymphocyte activation. It would appear that that the efficacy in controlling pruritus is low but this drug appears to be generally safe; very few published trials on the use of this drug are available (18). The dose is 10 mg/kg every 24 hours.

- **Recombinant interferon treatment:** A very limited number of clinical trials suggest that recombinant feline interferon-Ω and recombinant canine interferon-γ may be useful in the management of inflammation and pruritus associated with canine atopic dermatitis (4). Treatment protocols and overall safety have yet to be determined however.

Topical treatments

Certain topical treatments may prove useful in the management of the pruritic dog, including the following;

- **Tacrolimus** is a topical calcineurin inhibitor which is licensed for human use in atopic dermatitis but not animals. A small number of clinical trials have been conducted, with a 0.1% ointment for localized skin lesions showing the highest efficacy (19) . There is limited use for the treatment of generalized lesions but overall this treatment appears safe, apart from application-induced licking.

- **Topical corticosteroids:** Several different preparations are widely available, but special mention should be made of hydrocortisone aceponate (HCA). HCA is a diester glucocorticoid licensed in some countries for topical use in dogs as a 0.0584% spray which achieves high local activity with minimal systemic effects ***(Figure 2)***. HCA spray has been shown to be effective in the treatment of CAD (20, 21) and in one study efficacy was comparable to cyclosporine (21). The spray appears to be safe, with studies reporting no evidence of adrenocortical suppression. HCA can be used once daily for seven days for the management of acute flare-ups of CAD, and there is evidence to suggest that a single daily treatment on two consecutive days each week reduces the frequency of disease flares; this intermittent use appears to avoid the problem of skin thinning.

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Figure 2. A six-year-old German Shepherd dog with acral lick granuloma. Topical treatment may be sufficient to control the clinical signs in this case, but it is important to look for a primary skin disease and check for secondary infections.

- **Skin lipid supplements** are available as spot-on products in many countries; products vary in their constituents, and may contain substances such as fatty acids and essential oils, or are composed of ceramides, cholesterol and fatty acids. In CAD these products may be useful in improving skin barrier function and so help to indirectly reduce pruritus (22, 23).

- **Shampoos and emollients:** In dogs prone to pyoderma and/or *Malassezia* dermatitis the regular use of antimicrobial shampoos to combat these infections will help control pruritus. Shampooing can initially be as frequent as 2-3 times a week (depending on the severity of the condition) and the frequency can then be tapered to an interval between shampoos that is beneficial. Anti-pruritic shampoos are generally those with emollient properties; these will help alleviate pruritus and are useful “add in” treatments for use alongside more targeted anti-pruritic agents. Emollient sprays are also available and may prove useful as part of a treatment plan to control pruritus, especially in dogs with dry and scaly skin.

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Conclusions

Pruritic skin disease is common in the dog. The pruritic patient should undergo investigations to determine a diagnosis in order to select the most appropriate drugs for management of the pruritus. A major cause of chronic pruritus is allergic skin disease, and in particular atopic dermatitis. Canine skin that is inflamed or damaged is very prone to secondary infection with *Staphylococcus pseudintermedius* and/or *Malassezia pachydermatis*, and both of these infections will contribute to the level of pruritus in an individual patient; identification and treatment of these infections will therefore allow better overall control of pruritus. Long-term management of the chronically pruritic patient is likely to require the development of a multimodal treatment and management plan that suits both the patient and the owner, and a protocol to avoid chronic corticosteroid use should be considered wherever possible.

Although systemic corticosteroids are very effective in controlling pruritus and are useful for short-term control of acutely pruritic dermatoses and for managing flares in pruritus experienced by patients suffering from chronic pruritic conditions, in some animals (*e.g.*, those with diabetes mellitus or hyperadrenocorticism), systemic corticosteroids are contraindicated. In addition some patients will not tolerate corticosteroid treatment, even at low doses. In all patients with chronic pruritic dermatoses, corticosteroids have the potential to produce significant unwanted side effects if used for prolonged periods of time. A number of non-steroidal treatments are available to control pruritus, particularly that associated with canine atopic dermatitis. Cyclosporine, oclacitinib and ASIT have been shown to have good efficacy in the management of pruritus associated with CAD. Other less effective treatment, such as antihistamines and essential fatty acids, may be useful as adjunctive treatments in the overall management of the chronically pruritic patient and, when used in conjunction with corticosteroids, may also have a steroid-sparing effect, reducing the overall dose of corticosteroid needed for pruritus control.

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CUT-OUT AND KEEP GUIDE...

Ear infection: what the owner needs to know

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Introduction

Otitis externa is a common condition in dogs and cats, with a reported incidence of 10-20% in dogs and 2-6% in cats (1-3). Predisposing, primary, secondary and perpetuating factors should be identified wherever possible in order to control the condition. Predisposing factors include anatomical conditions such as a stenotic ear canal, excess hair within the canal, increased moisture (*e.g.*, in certain breeds with pendulous pinnae or in dogs that swim), and over-treatment. There are various possible primary factors; the most common are skin allergies, although foreign bodies, hypersecretory conditions (*e.g.*, primary seborrhea, hypothyroidism, or increased ceruminous gland activity), neoplasia and parasites are also common (4). Secondary factors include bacterial and yeast infections, whilst the main perpetuating factors are otitis media and chronic pathological changes in the ear canal secondary to inflammation (*e.g.*, stenosis, fibrosis and calcification of tissues). The correct techniques for ear examination, sampling and cleaning are key points in treating, diagnosing and managing otitis externa in dogs. The primary cause must be identified and treated, and any secondary factors must be eliminated. If there are chronic pathological changes present these must be properly controlled for satisfactory long-term management.

Ear examination

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The ear examination begins with careful observation and evaluation of the pinna.

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The vertical and horizontal canals are then examined using a good otoscope. Correct placement of the otoscope will avoid discomfort; this is particularly important in patients with inflamed ear canals.

Ear cytology sampling

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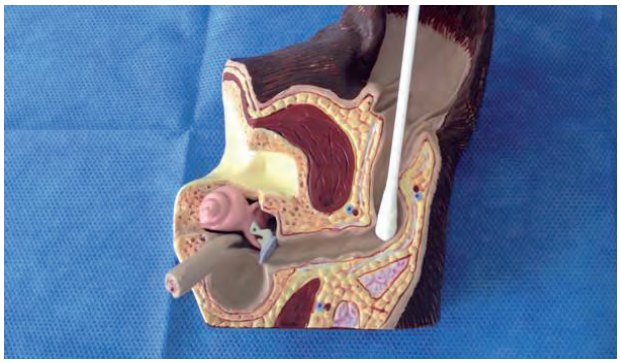
Secondary factors can be evaluated by cytology. Bacteria (cocci, rods), yeasts (*Malassezia spp.*) (5) and inflammatory cells may be observed microscopically by sampling and staining.



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Samples may be obtained with a sterile cotton swab at the point where the vertical and horizontal ear canals meet.

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Ear cleaning

Superficial ear cleaning does not require anesthesia or sedation in the majority of patients, and owners should be instructed as to how to perform this procedure properly at home. In most cases of otitis externa, epithelial migration, the self cleaning mechanism of the ear canal, is affected adversely, leading to cerumen accumulation (6,7).

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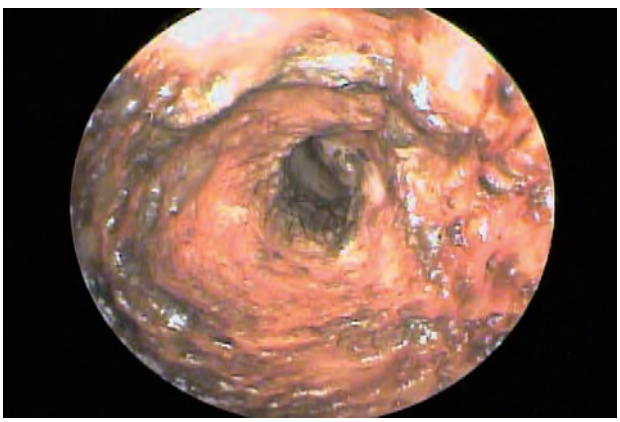
Ear cleaner should be installed into the ear canal and the ear massaged externally. The cerumen may be removed from the external part of the ear using a cotton swab, but excessive use of swabs inside the ear canal should be avoided. Cleaning helps reduce the amount of cerumen exudate and facilitates the penetration of topical treatments; it also decreases the bacterial and yeast biofilm, which assists in elimination of infectious agents.



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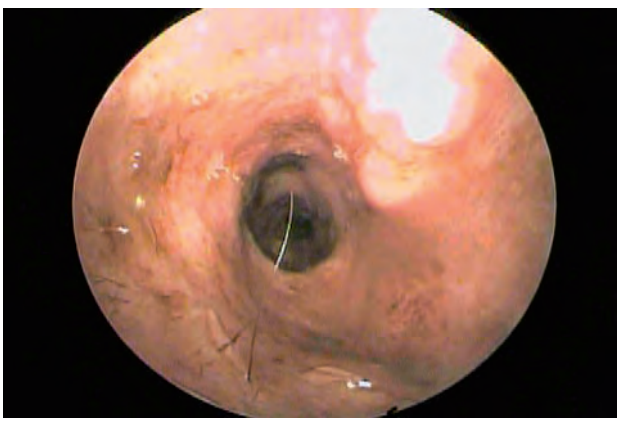

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An otoscopic view of the external ear canal pre (left) and post (right) cleaning. In the consultation room reducing or eliminating the ceruminous debris is important, as it allows a full examination to be performed; the structures of the ear, such as the epithelium of the external canal, can be evaluated, and the tympanic membrane integrity assessed. A correct balance between treatment and control of ceruminous debris is the main goal; excessive use of cleaning agents may damage the ear canal epithelium; this may be seen as white ceruminous debris and inflammatory cells with no micro-organisms detected on cytology.

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ROYAL CANIN