

Challenges & New Developments in CANINE PYODERMA

Disease Overview & Diagnosis

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- Canine pyoderma is a bacterial skin disease usually caused by *Staphylococcus pseudintermedius* (previously known as *Staphylococcus intermedius*).¹
- *S. pseudintermedius* is a gram-positive, coagulase-positive cocci bacteria, which is considered part of the normal canine mucosal flora and cultured from 37% to 41% of normal dogs.^{2,3}
- Less common bacterial species found in canine pyodermas include *S. aureus* (4.7%–8.3% of cases, usually human origin) and *S. schleiferi* (19%–28% of cases).⁴⁻⁶

DISEASE PROFILE

Transmission

The perineum and nasal mucosa are primary colonization sites, and bacteria can be transferred to other body sites via licking and grooming.²

- *S. pseudintermedius* can be an opportunistic pathogen and create infection in dogs with underlying conditions that compromise the normal skin barrier or immune function.
- Similar to *S. aureus*, *S. pseudintermedius* produces virulence factors to enhance infection, such as coagulase, proteases, thermolysin, and toxins (ie, haemolysins, exfoliative toxins, enterotoxins). It also has the ability to bind to fibrinogen, fibronectin, and cytokeratin, as well as form biofilms.¹

Underlying Conditions

Types of Conditions

Chronic or recurrent canine pyoderma is usually associated with an underlying cause; idiopathic pyoderma is rare. The most common underlying conditions include (Table 1, page 33).⁷

This is the first article in a 3-part series discussing the latest information available regarding canine pyoderma. Future articles will discuss treatment as well as methicillin-resistant infection.

THE THREE Ms: MIC, MPC, & MSW

Mean inhibitory concentration (MIC) is usually based on blood levels of an antibiotic, and is the **minimal antibiotic concentration needed to inhibit bacterial growth**. When the MIC exceeds the concentration of drug that can be safely achieved in the bloodstream, then the organism is deemed resistant.

Bacterial Mutation & Resistance

MIC is based on standardized bacterial inoculums (10^5 CFU/mL) exposed to varying drug concentrations in a test tube, and it varies with both the drug and the bacterial species targeted.

- Since MIC does not equal complete killing of all bacteria, bacterial mutation and resistance is a concern.
- *Patients with normal intact immune systems:* Inhibition of the susceptible bacterial population allows immune clearance of infection, including resistant mutants.
- *Immunocompromised patients, those with prior infection or previous exposure to antibiotics, or those in which therapy for acute infection fails:* Continued proliferation of resistant mutants may occur.
- When a high-density bacterial population is exposed to an antimicrobial agent, it only requires one spontaneous mutation to the exposed agent for the culture to become a $> 10^{12}$ population of resistant bacteria following overnight incubation.¹

Measuring Mutant Prevention

Recently, the mutant prevention concentration (MPC) has been described as a novel measurement of *in vitro* bacterial susceptibility or resistance. **MPC defines the lowest drug concentration required to block the growth of the least susceptible bacterium present in the tested population.**

MPC is based on the testing of a larger bacterial inoculum ($\geq 10^9$ CFU/mL), which:

- More closely approximates bacterial load in actual infections
- Takes into account the probability of mutant subpopulations being present in high-density bacterial populations.^{1,2}

Dosing based on MPC drug concentration may reduce overall bacterial numbers as well as prevent the selective amplification of the resistant subpopulation. As with MIC, MPC varies with both the antimicrobial and bacterial species targeted.

Minimizing Mutation Development

The mutant selection window (MSW) defines the danger zone for therapeutic drug concentrations, and is bordered by the MIC and the MPC values. Minimizing the length of time that an antibiotic concentration remains in the MSW may reduce the likelihood for development of resistance during therapy.

Achieving Optimal Antibiotic Dosing

MPC values, when considered with antimicrobial pharmacology, may allow more accurate prediction of probability of resistance when bacteria are exposed to antibiotics during therapy for infectious diseases. With the increasing emergence of resistant infections, resistance prevention should be an important goal of antimicrobial therapy.¹⁻³

Hopefully, MPC and MSW values may eventually become more widely available from reference laboratories and allow for optimal antibiotic dosing, reducing antimicrobial resistance.

CFU = colony forming units; MIC = mean inhibitory concentration; MPC = mutant prevention concentration; MSW = mutant selection window

1. Blondeau J. New concepts in antimicrobial susceptibility testing: The mutant prevention concentration and mutant selection window approach. *Vet Derm* 2009; 20:383-396.
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Table 1. Underlying Causes for Recurrent Canine Pyoderma

Endocrinopathy	<ul style="list-style-type: none"> • Hyperadrenocorticism (Cushing's disease) • Hyperestrogenism • Hypothyroidism
Follicular Dysplasia	<ul style="list-style-type: none"> • Color-dilution alopecia • Congenitally alopecic breeds
Hypersensitivity Dermatitis	<ul style="list-style-type: none"> • Atopic dermatitis • Flea allergy dermatitis • Food allergy
Keratinization Abnormalities	<ul style="list-style-type: none"> • Ichthyosis • Primary seborrhea • Sebaceous adenitis • Zinc-responsive dermatosis
Parasites	<ul style="list-style-type: none"> • Fleas • <i>Demodex</i> mites • Sarcoptic mange (scabies)

Table 2. Clinical Signs of Superficial or Surface Pyoderma

Superficial or Surface Pyoderma	Clinical Signs
Bacterial Folliculitis	<ul style="list-style-type: none"> • Primary lesions: Papules (1–2 mm raised and/or crusted, pink or red bumps) and pustules • Secondary lesions: Expanding areas of alopecia; surrounding scaling (epidermal collarettes), crusts, hyperpigmentation, and lichenification^{1,2}
Bacterial Overgrowth Syndrome	<ul style="list-style-type: none"> • Erythema, scaling, lichenification, hyperpigmentation, odor, pruritus, and eventual alopecia • Often present on ventral trunk, axillary, and inguinal areas • No papules, pustules, or epidermal collarettes present³
Impetigo	<ul style="list-style-type: none"> • Nonpruritic pustules not associated with follicles • On sparsely haired areas of the skin, such as inguinal area • Pustule results in epidermal collarettes and scaling • Often seen in young puppies^{1,2}
Intertrigo (Fold Dermatitis/Pyoderma)	<ul style="list-style-type: none"> • Dermatitis occurs in areas of skin folding, such as face, lip, and tail folds and vulvar area • Lesions are areas of moist, inflammatory dermatitis with surface bacterial overgrowth^{1,2}
Mucocutaneous Pyoderma	<ul style="list-style-type: none"> • Dermatitis occurs on lip margins, eyelids, nares, or anus² • Erythema, inflammation, and crusting +/- depigmentation
Pyotraumatic Dermatitis (Acute Moist Dermatitis)	<ul style="list-style-type: none"> • Areas of acute, painful, moist, exudative, inflammatory dermatitis created by self trauma • Often occurs in thick-coated dogs with underlying flea allergy or atopic dermatitis • Peripheral papules/pustules or thickened lesions indicate pyotraumatic folliculitis^{1,2}

See Table 3 (page 35) for references.

- Hypersensitivity dermatitis
- Parasitic skin infestations
- Endocrinopathies
- Follicular dysplasia
- Keratinization disorders.

In one prospective study of 30 cases of canine recurrent pyoderma:⁸

- Atopic dermatitis was found in 60% of cases. Atopic dogs are prone to recurrent skin infections due to increased adherence of staphylococcal bacteria to atopic canine skin cells,⁸⁻¹⁰ alterations in normal skin barrier function,¹¹ and altered skin immune system function.^{12,13}
- Food allergy, flea allergy, and hypothyroidism each accounted for 7% of cases.
- Hyperestrogenism, demodicosis, and zinc-responsive dermatosis each accounted for 4% of cases.
- In only 2 dogs were underlying causes unidentified.

Identification of Conditions

Depending on clinical presentation, age of onset, seasonality, and other clinical signs, identification of underlying disorders includes:

- Stringent flea control
- Deep skin scrapings for *Demodex*
- Trial treatment for scabies
- Hypoallergenic diet trial
- Intradermal allergy testing and desensitization
- Screening for endocrinopathies
- Skin biopsy for keratinization disorders.

Outcomes

- **In dogs without compromising disease**, treatment of pyoderma will likely result in complete cure.
- **In patients with relapsing infection** (recurs within 1–2 weeks), inadequate duration of treatment or bacterial resistance is likely.
- **In patients with recurrent infection** (recurs within 3 months), identification/treatment of underlying disorders must be undertaken.⁷

Differential Diagnosis

The following differential diagnoses should be considered for any dog presenting with signs of pyoderma:

- Demodicosis (**Figure 1**, page 34)
- Dermatophytosis



Figure 1. Demodectic pododermatitis



Figure 2. Dog with sebaceous adenitis, resulting in patchy hypotrichosis and scaling



Figure 3. Dog with cutaneous lymphoma, resulting in erythema, scaling, and alopecia

- *Malassezia* dermatitis
- Noninfectious skin diseases (**Figures 2 through 4**), such as sebaceous adenitis, cutaneous lymphoma, and pemphigus foliaceus.

Clinical Signs

Canine pyoderma can be nonpruritic or minimally to markedly pruritic. Clinical signs can vary with the:

- **Depth of infection** (superficial versus deep)
- **Location of infection** (ie, haired versus non-haired skin, mucocutaneous junctions, skin folds)
- **Breed of dog** (in some cases).

The variable manifestations of pyoderma are listed in **Tables 2**, page 33, and **3**, page 35. These tables will be repeated in the next article and will include figures and treatment recommendations.

Lesion Distribution & Appearance

Lesion distribution in cases of canine pyoderma:

- May be localized or generalized
- Can depend on the underlying cause
 - » In pruritic dogs, lesions commonly occur in areas of self trauma and then spread
 - » In dogs with endocrinopathies, lesions commonly begin on the trunk, then spread and

become pruritic *after* development of infection.⁷

Clinical recognition of pyoderma can be complicated by differences in disease presentation, including area of the body affected and variations in coat length and breed of dog.

Identification

- Mucocutaneous or nasal pyoderma can present as a crusting inflammatory disease similar to discoid lupus erythematosus (**Figures 5–7**, page 36).
- Pyoderma on the thinly haired inguinal area may be easy to identify, but the same lesions on the thickly haired dorsal and lateral trunk may be harder to notice.
- Short-coated dogs with folliculitis can present with raised tufts of hair on the trunk that can be confused with urticaria; however, lesions are not evanescent as occurs in urticarial lesions, and eventually hair is lost, leaving a moth-eaten appearance of the hair coat (**Figure 8**, page 36).
- Long-coated dogs with pyoderma may initially demonstrate a dull coat with scaling +/- odor, easily epilated hair, and pruritus (**Figure 9**, page 36).
- In chronic lesions of pyoderma, lichenification can develop that may appear identical to *Malassezia* infection (**Figure 10**, page 36).

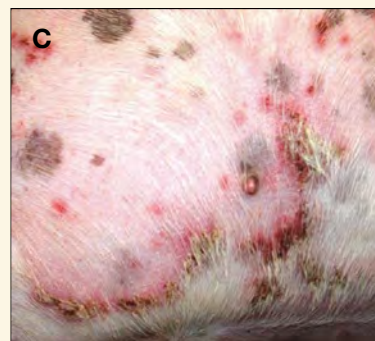
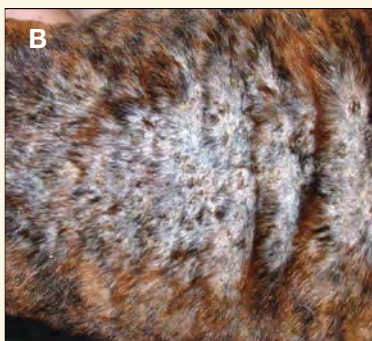


Figure 4. Pemphigus foliaceus can mimic pyoderma, with lesions such as: (A) patchy alopecia and scaling; (B) truncal crusting; (C) inflammatory papules and serpiginous crusts

Table 3. Clinical Signs of Deep Pyoderma

Deep Pyoderma	Clinical Signs
Acral Lick Dermatitis	<ul style="list-style-type: none"> • Alopecic, firm, raised, thickened plaque or nodule that may become ulcerated • Often found on the dorsal carpus or dorsolateral metatarsus • Multifactorial, self-inflicted (by licking) disorder often associated with underlying atopic dermatitis, food allergy, trauma, endocrinopathy, bone pain, neuropathy, or behavioral causes • Perpetuated by secondary deep pyoderma^{1,2}
Bacterial Furunculosis	<ul style="list-style-type: none"> • Focal to multifocal areas of thick crusting, alopecia, inflamed bullae, and/or ulcerative draining skin lesions, often pruritic and/or painful • Often associated with underlying atopic dermatitis, food allergy, endocrinopathy, demodicosis, etc^{1,2}
Callus Furunculosis	<ul style="list-style-type: none"> • Inflammation, swelling, ulceration, and draining tracts affecting pressure points, such as lateral elbows/ hocks or sternal callous in deep-chested breeds • Most commonly affects giant breeds^{1,2}
Canine Acne	<ul style="list-style-type: none"> • Nonpainful, nonpruritic papules, pustules, bullae +/- draining tracts on the chin or muzzle • More common in large, young, short-coated dogs • May be induced by friction or trauma to the chin, which pushes the short hairs under the skin^{1,2}
Pedal Folliculitis/ Furunculosis	<ul style="list-style-type: none"> • Interdigital erythema, pustules, bullae, nodules, fistulas, alopecia, & swelling; variably painful and pruritic • Often seen in large, short-coated dogs • May be associated with regional lymphadenopathy and/or swelling of associated metacarpus or metatarsus • Often associated with underlying atopic dermatitis, food allergy, endocrinopathy, demodicosis, etc^{1,2} • In some cases isolated lesions are associated with abnormal weight bearing and formation of interdigital cysts, often between P4 and P5⁴
Post-Grooming Furunculosis	<ul style="list-style-type: none"> • Usually occurs within 24 to 48 H after grooming • Areas of intense localized erythema and swelling that evolve into punctuate foci of erythema, erosion, painful hemorrhagic bullae, and drainage • Lesions are usually on the dorsal trunk and occur more commonly in short-coated dogs. Affected dogs may be lethargic or febrile. • <i>S pseudintermedius</i>, <i>Pseudomonas</i>, <i>Proteus</i>, and <i>Escherichia coli</i> have been grown in pure or mixed culture from lesions • Causal factors include contaminated shampoos or grooming apparatus and over-zealous scrubbing of short hairs “against the grain”^{5,6}

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Dog Breeds

Breed differences with regard to pyoderma manifestations are not uncommon (**Figures 11–13**, page 37).

- **Bulldogs** often develop localized areas of plaque-like hyperkeratosis or papillomatous appearing dermatitis (**Figure 11**).
- **Dalmatians** can develop small areas of brownish, discolored fur associated with papules (“dalmatian bronzing syndrome,” **Figures 12 and 13**).
- **Shar-peis** often diffusely lose hair due to folliculitis, with minimal to no associated skin inflammation or visible papules.

- **Cocker spaniels** may present with crusted plaques and follicular casting as a manifestation of pyoderma that can be mistaken for idiopathic or primary seborrhea (a far rarer diagnosis) and lead to inappropriate diagnosis and therapy.
- **Shetland sheep dogs** often develop large superficial spreading areas of alopecia, erythema, and scaling.

DIAGNOSIS

Consideration of clinical signs and lesions is taken together with evaluation of microscopic cytology, skin scrapings, and possibly dermatophyte culture to eliminate other possible causes of folliculitis.

Cytology

Collection

- **Impression cytology:** Impression cytology of an exudative or lichenified lesion or a ruptured pustule directly onto a slide is easy to obtain.
- **Skin scrapings:** Drier lesions, such as scaly areas or epidermal collarettes, can be sampled by collecting skin debris on a dull dry scalpel blade or spatula, smearing the debris on a slide, and then staining it with Diff-Quik or similar stain.
- **Tape preparation:** Clear acetate tape preparation of an affected area can be applied onto a slide over a drop of blue stain.

Microscopic Evaluation

- Slides are first scanned under 10× to identify areas of interest; then examined under 40× to 100× to evaluate inflammatory cells and organisms.
- **Bacterial folliculitis** can be confirmed by identification of inflammatory cells and intracellular cocci (Figure 14).
- In **bacterial overgrowth syndrome**, numerous extracellular bacteria are seen, which can include mixed flora with rod-shaped bacteria with or without *Malassezia* (Figures 15–16).
- In cases of **deep pyoderma**, marked pyogranulomatous inflammation is usually seen, and organisms may be few in number (Figure 17).

Culture & Sensitivity

When to Culture

Culture and sensitivity of skin lesions associated with pyoderma is recommended if:

- There is no clinical response and bacteria persist cytologically despite empiric antibiotic therapy (especially if a patient with recurrent pyoderma has been treated with multiple antibiotics) or if there is a history of multidrug- or methicillin-resistant infections
- If primarily rod-shaped bacteria are found on cytology of lesions
- In cases of deep pyoderma.⁷

Culture Techniques

Culture can be obtained with a sterile culturette via:

- Swabbing contents of a freshly ruptured pustule
- Swabbing debris or exudate under an intact crust or under the rim of an epidermal collarette
- Obtaining a 4- to 6-mm punch biopsy of a papule or pustule for macerated aerobic tissue culture (the biopsy sample is placed in a red top tube with 0.25 mL sterile saline).

Since lidocaine has antibacterial activity, biopsies for culture should ideally be collected under sedation or general anesthesia.⁷



Figure 5. Mucocutaneous pyoderma in dog



Figure 6. Nasal mucocutaneous pyoderma secondary to atopy

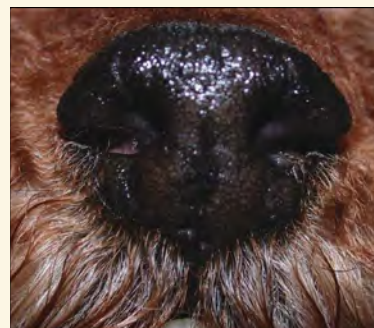


Figure 7. The same dog in Figure 6 after 3 weeks of oral and topical antibiotic therapy



Figure 8. Bacterial folliculitis in a short-coated dog secondary to food allergy; note the subtle areas of raised hairs and hypotrichosis



Figure 9. Pyoderma in an atopic dog, resulting in patchy hypotrichosis and scaling

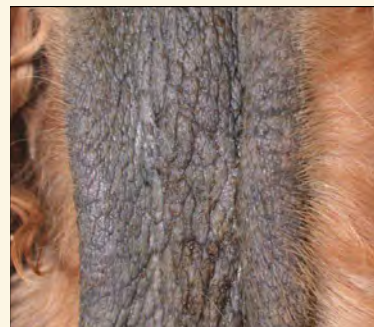


Figure 10. Chronic pyoderma can create lichenification similar to *Malassezia* dermatitis



Figure 11. Chronic pyoderma in a bulldog, resulting in raised, thickened lesions

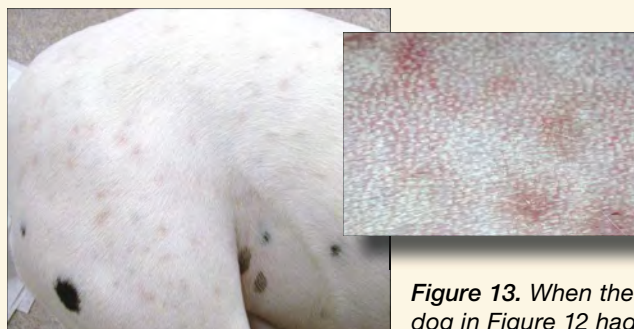


Figure 12. Bacterial folliculitis in a dalmatian, resulting in multifocal areas of brownish, discolored hair ("dalmatian bronzing")

Figure 13. When the dog in Figure 12 had its lesions shaved, the underlying papular dermatitis was revealed

Sensitivity Testing

Sensitivity is usually tested by either:

- **Agar diffusion and disk process** (ie, Kirby Bauer, which may be more indicative of topical antibiotic concentrations achievable at surface infections, such as otitis)
- **Broth diffusion technique**, resulting in determination of the mean inhibitory concentration (MIC).

Antimicrobial susceptibility or resistance is then determined by comparing the measured MIC value to previously established breakpoints that take into account the drug's *in vitro* activity, achievable and sustainable drug concentrations in the host, drug pharmacokinetics, and drug toxicity.¹⁵ See **The Three Ms: MIC, MCP, & MSW** (page 32) for further information.

Histopathology

Biopsy of lesions is recommended if:

- There is a poor response to antibiotics based on culture
- No organisms are identified on cytology or culture
- There is an unusual distribution (ie, facial, pinna, or footpad lesions are suggestive of immune-mediated disease) or appearance of skin lesions.

Canine demodicosis can sometimes be difficult to find in very scarred, fibrotic areas, such as the feet or in the shar-pei breed, and may require biopsy for diagnosis. ■

The second article in this series will be published in our next issue and will focus on topical and systemic treatment of canine pyoderma.

MIC = mean inhibitory concentration

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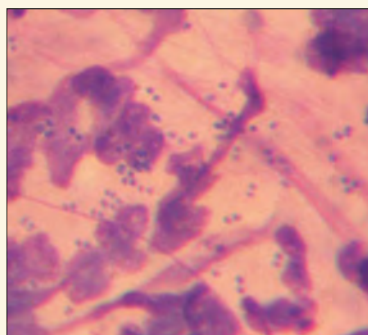


Figure 14. Pyoderma cytology, demonstrating intra- and extracellular cocci

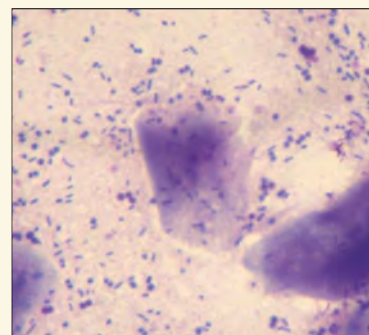


Figure 15. Cytology of bacterial overgrowth, demonstrating mixed cocci and rods

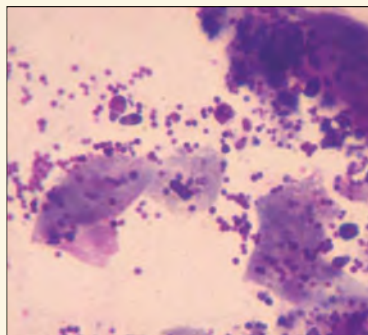


Figure 16. Cytology of bacterial and yeast overgrowth

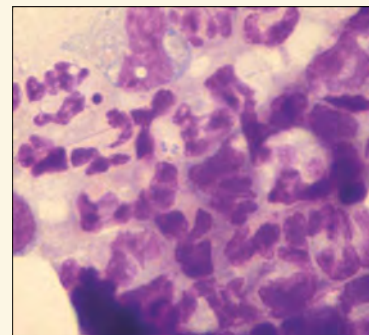


Figure 17. Cytology of deep pyoderma; pyogranulomatous inflammation with intracellular cocci



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