



TREATING RESISTANT SKIN INFECTIONS IN DOGS

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Ppyoderma is a common skin disorder in small animal practice. Now that the major canine pathogen, *Staphylococcus pseudintermedius*, has acquired methicillin resistance, treatment has become more challenging and more expensive. Keys to success in treatment and prevention require:

- Prompt identification and treatment of the underlying cause
- Use of culture and sensitivity to guide antibiotic use
- Increased reliance on topical therapy.

WHY ARE DOGS SUSCEPTIBLE TO SKIN INFECTIONS?

Of all the species with which we work, dogs seem uniquely predisposed to bacterial skin infections.^{1,5} Dogs are more susceptible to skin infections due to basic structural features, such as:

- Lack of a follicular lipid plug, which acts like a drain stopper
- Fragile skin barrier
- Alkaline pH.

Table 1 lists underlying skin disorders that predispose dogs to staphylococcal skin infections.⁶ Dogs with atopic dermatitis are especially susceptible due to:

- A defective skin barrier, which is represented by the stratum corneum and one of the first physical and chemical defenses against microbial infection⁷⁻⁹
- Potentially decreased levels of defensins—cationic antimicrobial proteins that defend against bacterial infections as part of the innate immune system.¹⁰

WHICH BACTERIA CAUSE PYODERMA IN DOGS?

The major canine skin pathogen is *S pseudintermedius*;¹¹ however, *Staphylococcus schleiferi*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* have also been identified in canine pyoderma.

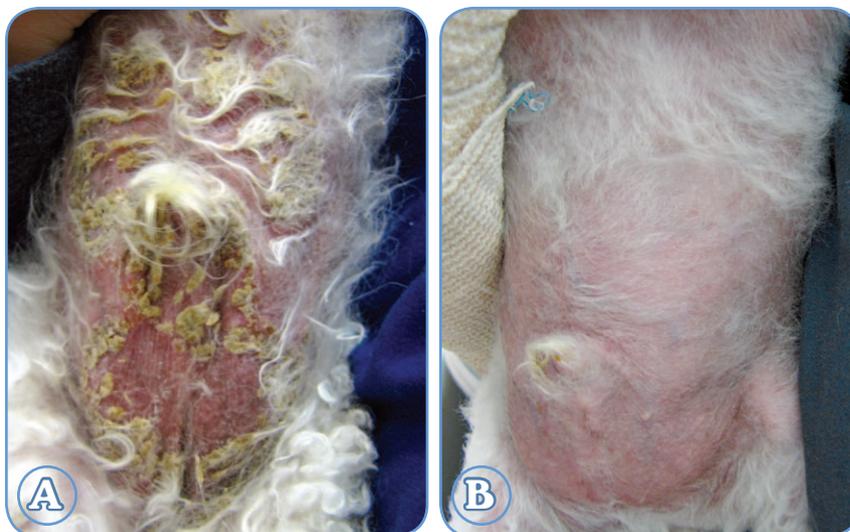


Figure 1. 10-year-old male neutered poodle with atopic dermatitis: Severe generalized crusting associated with superficial pyoderma failed to respond to amoxicillin-clavulanate and cefpodoxime; culture revealed methicillin-resistant *S pseudintermedius* sensitive to amikacin and rifampin (A). Three weeks after topical therapy, consisting of clipping and washing with chlorhexidine and twice daily topical application of amikacin (5 mg/mL) in Tris EDTA; no systemic antibiotics were used (B).

TABLE 1. Underlying Disorders in Staphylococcal Skin Infections

- Atopic dermatitis
- Other allergic skin conditions
- Disorders of keratinization
- Endocrinopathies
- Parasitic diseases

S aureus—a human pathogen—has been identified in a low percentage of dogs. However, this bacterium has received a great deal of attention due to its methicillin resistance in humans and potential role as a zoonotic agent—dogs infected with methicillin-resistant *S aureus* (MRSA) most likely acquired the infection from a human.

S pseudintermedius, while not as

virulent, shares many characteristics with *S aureus*, including:

- Enzyme and toxin production
- Ability to adhere to matrix adhesive proteins
- Ability to form biofilms.

Methicillin-resistant *S pseudintermedius* (MRSP) is unlikely to cause human infection, unless a person is very young, very old, or immunocompromised.

S schleiferi was first identified from human clinical specimens in 1988, and has now been identified as a cause of pyoderma and otitis externa in dogs.¹²⁻¹⁴

P aeruginosa—while not common—has been identified on the skin of dogs, particularly in lip fold pyodermas and postgrooming folliculitis.^{15,16}

Identifying the particular *Staphylococcus* species in-

volved in skin infections, and its antimicrobial sensitivity, is important with regard to determining whether the dog is infected with a methicillin-resistant strain.

WHAT ARE THE CLINICAL MANIFESTATIONS OF PYODERMA?

Pyoderma can be classified many ways, but categorizing it by depth of skin affected is particularly useful because it can help determine type and duration of therapy.

Surface pyodermas are bacterial infections confined to the surface of the skin. These bacteria produce toxins, resulting in inflammation. The best examples include fold pyodermas of the face, lips, tail, and axilla.

Superficial pyodermas are bacterial infections that present beneath the stratum corneum layer of the epidermis, and include impetigo, folliculitis, and bacterial overgrowth syndrome.

- **Impetigo** is a subcorneal pustular disease seen frequently on the abdomen of puppies; it may, or may not, be pruritic, but is often self-limiting.
- **Bacterial folliculitis**—infection and inflammation of the hair follicles—is the most common pyoderma seen in dogs. It has many clinical forms, the features of which may be unique to the individual dog breed. The earliest form is a follicular papule—the lesion progresses as bacteria spread into surrounding hair follicles. The classic lesion is the epidermal collarette, characterized by a circular area of hair loss with variable redness, crusting, and hyperpigmentation. These lesions may, or may not, be pruritic; however, pruritus is usually quite profound in atopic dogs and pyoderma is a factor that escalates itch.
- **Bacterial overgrowth syndrome** is a superficial cutaneous disorder, associated with an overgrowth of *S pseudintermedius* and characterized by large numbers of bacteria, erythema, pruritus, and malodor.¹⁷

Deep pyodermas are less common, and occur as either focal, or localized, furunculosis or generalized furunculosis and/or cellulitis. Furunculosis is caused by bacterial infection that affects the hair follicles and causes small abscesses under the skin.

- **Localized forms of furunculosis** occur on chins of short-coated dogs (eg, English and French bulldogs, boxers, pugs, Boston terriers, Doberman pinschers, Great Danes, pitbulls and related breeds/crosses), on lateral stifles and other pressure points, and between the digits (interdigital pyoderma or interdigital cyst). Golden retrievers develop furunculosis that has many features of acute pyotraumatic dermatitis; however, it is an acute and deep bacterial skin infection. These dogs will often have fever, loss of appetite, and malaise prior to the eruption of the lesions.⁶ Likely these infections represent an individual host–pathogen interaction.
- **Generalized furunculosis and cellulitis** are not common, but often accompany demodicosis. Inflammation is quite severe, and dogs are often systemically ill when infection is deep. German shepherd dogs develop a severe ulcerative pyoderma that is generalized and painful. Hemorrhagic bullae and ulcers often result in the mistaken notion that affected dogs have an autoimmune disease.

Any of the bacteria listed previously can cause surface, superficial, or deep pyoderma.

HOW DO WE DIAGNOSE PYODERMA?

Pyoderma is diagnosed by history and clinical examination, and supported by cytologic findings.

Cytology is important for several reasons; it:

- Identifies coexistent staphylococcal and *Malassezia* infections; in order to resolve the infections, both need to be treated
- Confirms the presence of bacteria and white blood cells
- Helps to differentiate pyoderma from other cutaneous diseases that mimic, or may coexist with, pyodermas, such as pemphigus foliaceus.

Samples can be obtained for cytology in several ways.

- **Clear tape** is an excellent way to collect materials from feet and skin folds, as well as from collarettes. See **Step by Step: Using Clear Tape for Cytologic Evaluation of Pyoderma**.
- **Direct impression smears** can be obtained from moist lesions and pustule exudate, allowed to dry, and then stained.
- **A dry #10 blade** can collect crusts from very dry lesions, which are then placed on a slide and minced into sterile saline. Once dried, the slide can be stained and examined.

Culture and sensitivity is recommended for all generalized deep pyodermas and if treatment with 2 different classes of oral antibiotic, repeated courses of a previously effective antibiotic, or one injection of cefovecin¹⁸ fail to resolve any superficial or deep infections (**Figure 1**, page 44).

- Methicillin resistance is increasing in canine skin infections, and sensitivity results are required to select the correct antibiotic.
- Currently, we do not have validated methods for empirically selecting antibiotics for methicillin-resistant staphylococcal infections in dogs.

HOW DO WE TREAT PYODERMA IN DOGS?

Specific to Type of Pyoderma

Surface infections are often best treated topically. They are not considered curable because the moisture and occlusive nature of folds predisposes toward recurrence. Surgical excision may be curative in some cases of vulvar fold pyoderma and tail fold pyoderma in English bulldogs.

Superficial pyodermas can often be treated exclusively with topical therapy (which is preferred to systemic antibiotic administration in my opinion), but frequent bathing is required (daily or every other day). Bathing frequency can be reduced by the use of chlorhexidine leave-on conditioners, sprays, wipes, and mousses in between. The use of topical therapy seems to speed the rate of recovery, and we suspect topical therapy reduces the length of time a dog requires systemic antibiotics.

Deep pyodermas usually require prolonged (several weeks) courses of antibiotic therapy. While topical therapy alone is unlikely to resolve a deep pyoderma, it is an invaluable tool in the dog's recovery. Bathing helps to remove adherent crusts and sticky exudates, promoting drainage and drying.

Step by Step: Using Clear Tape for Cytologic Evaluation of Pyoderma

1. Press the tape—sticky side down—onto the lesion, then stain with a modified Wright’s Giemsa stain, such as Diff-Quick. Do not fix the tape with methanol as it will cloud the tape.
2. After staining, rinse with water and lay—sticky side down—onto a glass slide.
3. Press out excess water with a paper towel; then examine the slide.
4. While the slide can be scanned at lower powers, the oil immersion lens is recommended for examination of bacteria and yeast.

Topical Treatment

Most of the veterinary dermatologic literature supports the use of 2% to 4% chlorhexidine as the most effective topical antiseptic agent against *S pseudintermedius*, *P aeruginosa*, and *Malassezia* species.

One of the most critical aspects of pyoderma treatment is bathing (see **Step by Step: Bathing as Topical Therapy for Pyoderma**), which is beneficial because it:

1. Helps clean the skin, removing scaling and crusts that contain bacteria
2. Makes the dog look, feel, and smell better
3. Frequently helps compress the course of antibiotics, reducing the time for selection of resistant strains.

If bathing is combined with systemic antibiotics, minimal bathing frequency should be once weekly. However, if owners are willing and able to bathe more frequently, they should be encouraged to do so. They can augment their bathing with the use of rinses, sprays, leave-on conditioners, mousses, and wipes in between baths.

Systemic Antibiotics

Modern recommendations for antibiotic selection suggest that we:

- Consider efficacy, safety, and compliance
- Use those that are best in class.

Traditionally, we have been taught to select older generation, less active antibiotics based on the belief that if the antibiotic fails, we can then use newer, more active compounds. However, this principle can no longer be applied in the age of staphylococcal methicillin resistance—once the less active, beta-lactam antibiotics become ineffective, the entire class is useless for systemic therapy.

CHALLENGES OF COMPLIANCE

- Compliance is likely a bigger problem in veterinary medicine than we have realized,²¹ and lack of compliance is a common factor in treatment failure and/or recurrence of pyoderma.
- A component that is often ignored, but very important, is whether the antibiotics are administered correctly and for the full course of therapy.
- Poor compliance may allow for selection of more resistant bacteria, contributing to the potential for development of a methicillin-resistant infection.

TABLE 2. Antibiotics for Treatment of Canine Pyoderma

ANTIBIOTIC	DOSE
AMINOGLYCOSIDES	
Amikacin	15 mg/kg SC Q 24 H
AMPHENICOLS	
Chloramphenicol	50 mg/kg PO Q 8 H
CEPHALOSPORINS (FIRST GENERATION)	
Cephalexin*	22–30 mg/kg PO Q 8 or 12 H
CEPHALOSPORINS (THIRD GENERATION)	
Cefovecin (Convenia)*	8 mg/kg SC; repeat in 2 weeks if necessary
Cefpodoxime (Simplicef)*	5–10 mg/kg PO Q 24 H (higher doses best)
LINCOSAMIDES	
Clindamycin	11 mg/kg PO Q 12 H
Lincomycin	20 mg/kg PO Q 12 H
PENICILLIN COMBINATIONS	
Amoxicillin–Clavulanate (Clavamox)*	20 mg/kg PO Q 8–12 H
QUINOLONES/FLUOROQUINOLONES (SECOND GENERATION)	
Ciprofloxacin (not recommended)†	30 mg/kg PO Q 24 H
Enrofloxacin (Baytril)	10–20 mg/kg PO Q 24 H
QUINOLONES/FLUOROQUINOLONES (THIRD GENERATION)	
Marbofloxacin (Zeniquin)	5.5 mg/kg PO Q 24 H
RIFAMYCINS	
Rifampin‡	5–10 mg/kg PO Q 24 H
SULFONAMIDES	
Ormetoprim–Sulfadimethoxine (Primor)	27.5–30 mg/kg PO Q 24 H
Trimethoprim/Sulfamethoxazole	20–30 mg/kg PO Q 12 H
TETRACYCLINES	
Doxycycline (if sensitive)	10 mg/kg PO Q 12 H
Minocycline (if sensitive)	5–10 mg/kg PO Q 12 H

* For methicillin-sensitive infections only

† Ciprofloxacin, while inexpensive, is a second generation fluoroquinolone with less activity against gram-positive bacteria than desired. In 2 separate studies, it has been very inconsistent in absorption, potentially leading to lack of efficacy and resistance.^{19,20}

‡ Keep dose at maximum of 10 mg/kg/day to reduce risk of hepatic damage, including necrosis and death; avoid use with other hepatotoxic drugs.

Most dermatologists believe that the most appropriate first-choice antibiotic for canine pyoderma is a cephalosporin and, in most patients, treatment with cephalosporins may be empirical. If a pyoderma fails to resolve with a cephalosporin, it is important to step back and re-evaluate the diagnosis and treatment plan.

If cytology from lesions of pyoderma identifies rods, suspicion is raised for a *Pseudomonas* or other gram negative pyoderma. The empirical choice of antibiotic in these patients is a fluoroquinolone. However, infections with rod-shaped bacteria should be cultured to verify:

1. What bacteria are present
2. Which antibiotic (if any) is indicated.

Table 2 (page 46) contains a list of antibiotics and doses used to treat canine pyoderma.

WHAT IS METHICILLIN RESISTANCE, AND HOW DO WE RECOGNIZE IT?

Genetic Development

Methicillin resistance in *Staphylococci* is associated with acquisition of a gene, *mecA*, that is incorporated into the bacterial genome and subsequently passed on to all daughter cells.²²⁻²⁴

- *MecA* encodes for a mutated form of penicillin-binding protein on the bacteria's surface.
- This mutant protein cannot bind any beta-lactam antibiotic; therefore, all penicillins and cephalosporins are ineffective.
- The genetic element on which the *mecA* gene resides can also carry other antibiotic-resistant genes, and some *S pseudintermedius* will be resistant to all antibiotics tested.
- This genetic element is retained within the *Staphylococcus* as long as antibiotic pressure is present. If antibiotic pressure is removed, the bacteria have the potential to excise the incorporated genetic element and become sensitive again.
- For this reason, it may work best to avoid systemic antibiotic therapy for dogs with surface or superficial pyoderma caused by methicillin-resistant staphylococci (MRS) and, instead, focus on aggressive topical therapy.

Diagnosis

To diagnose methicillin resistance, culture and sensitivity testing is needed. It is no longer acceptable for a laboratory to report coagulase-positive *Staphylococcus* species as the final diagnosis—the *Staphylococcus* species should be determined to allow clinicians to appropriately counsel clients as to risk of contagion.

It is very important to provide precise terminology:

- MRSA refers specifically to methicillin-resistant *S aureus*, the human pathogen.
- MRSP is not more contagious or virulent than methicillin-susceptible *S pseudintermedius* (MSSP); just simply harder to treat.

HOW DO WE TREAT METHICILLIN-RESISTANT PYODERMA IN DOGS?

Systemic antibiotic therapy for dogs with MRS should not be selected empirically—culture and sensitivity is required to identify the antibiotic most likely to be effective. Given that systemic antibiotic therapy drives retention of resis-

Step by Step: Bathing as Topical Therapy for Pyoderma

Advise owners to:

1. Bathe using tepid water.
2. Massage the shampoo gently in by hand, first onto the areas most affected (rather than pouring it down the back).
3. Wash the rest of the dog and leave the shampoo on the skin for 10 minutes before rinsing.
4. Soak crusts that are tightly adherent, which helps loosen them gently.

tance factors, clinicians should consider topical antiseptic therapy for superficial pyoderma.

Topical Therapy

It has been hypothesized that topical therapy may give bacteria time and opportunity to eject the resistance genes and become susceptible again (see **Topical Therapy: A Stand-Alone Treatment?**).

Shampoos containing 2% to 4% chlorhexidine are best,²⁵⁻²⁸ and use of only shampoos produced by quality veterinary pharmaceutical companies is recommended, as careful formulation is critical to maintain the activity of chlorhexidine.

Shampoos improve skin and coat quality as infection is resolved, and are considered superior to other topical therapies because many shampoos contain:

- Lipids, such as ceramide complex or phytosphingosine, that help repair the skin barrier when used over time
- Emollients that help prevent drying of the skin, which can happen with other products, such as scrubs.

Topical antibiotics can be used in some cases to help resolve MRS-associated pyodermas.

- Mupirocin topical ointment is effective against most strains of MRSP and can be used to resolve focal lesions.
- Topical amikacin spray can be used twice daily in some patients; it can be made by mixing amikacin (5 mg/mL) in Tris-EDTA. This spray is preferable to commercial products containing gentamicin and betamethasone.

Note: Betamethasone is a potent steroid that can induce severe cutaneous atrophy if overused; its use should be restricted to less than 14 days, particularly on thin skin such as that on the abdomen.

Systemic Therapy

Not all dogs with MRS will respond to topical therapy, particularly if the infection is severe, generalized, or a deep pyoderma. For these dogs, systemic antibiotic therapy is required, and culture and sensitivity mandatory. **Table 2** contains a list of antibiotics, with doses to be considered.

Sulfonamides: If the organism is sensitive, potentiated sulfonamides can be used. While side effects are possible, most dogs tolerate these drugs quite well. Sulfamethoxine/ormetoprim is useful, as it can be administered once daily.

Lincosamides: If reported as sensitive, clindamycin can also be used, but only if the bacteria are sensitive to all macrolides.²⁹ A resistance factor, termed the *clindamycin-inducible resistance factor*, can be found in *Staphylococ-*

cus species. One indicator that this gene may be present is reported resistance to erythromycin, but sensitivity to clindamycin. Treatment with clindamycin will rapidly induce the resistance factor, and antibiotic therapy will fail.

Tetracyclines: Although use of tetracyclines is not advocated for most *S pseudintermedius* infections—because most isolates are resistant to tetracyclines and penicillins—MRSP may revert to tetracycline sensitive. However, considering that tetracycline is no longer available, doxycycline or minocycline may be used instead. However, the breakpoints for determining sensitivity to doxycycline are changing: if the minimum inhibitory concentration is greater than 0.5 to 1 mcg/mL, then failure of therapy is more likely even if a culture indicates sensitivity.³⁰

The majority of MRSP are sensitive to chloramphenicol, rifampin, and amikacin:

Amphenicols: Chloramphenicol must be given at 30 to 50 mg/kg Q 8 H, which can result in poor compliance.

- After 30 days of treatment, most dogs become nauseated or develop vomiting and diarrhea, and some dogs develop a poorly understood hindlimb paresis that resolves upon cessation of antibiotic use.
- Chloramphenicol is a health risk for humans, with the potential to induce aplastic anemia. If dispensed to clients, advise clients to handle the medication carefully.

Aminoglycosides: Amikacin is well tolerated by most dogs but must be given by subcutaneous injection (15 mg/kg once daily) and does present the risk for renal toxicity.

- Frequent monitoring of urine for casts and repeated

blood analysis of blood urea nitrogen (BUN) and creatinine can make this an expensive option.

- For a healthy dog, weekly urinalysis can evaluate cast formation, proteinuria, and a drop in specific gravity.
- Urinalysis is more sensitive than BUN or creatinine to amikacin-induced renal toxicosis.

Rifamycins: Rifampin can be used as monotherapy for staphylococcal infections, but can be hepatotoxic; therefore, monitoring liver enzymes is important. Side effects can be minimized if the daily dosage is kept at 10 mg/kg/day or less.

- In an otherwise healthy dog, blood analysis should occur before administration, then 10 to 14 days into therapy.
- Owners should be warned to stop administration if dogs have any loss of appetite or vomiting.
- Urine may look red or orange due to the drug's color, but is not a reason to stop therapy.

IN SUMMARY

Pyoderma management in the age of methicillin resistance is an ongoing challenge in veterinary medicine. My mani-

Many methicillin-resistant staphylococcal infections are also multi-drug resistant—in these types of infections, the bacteria have acquired resistance factors to antibiotics other than beta-lactams, complicating treatment and limiting therapeutic options.

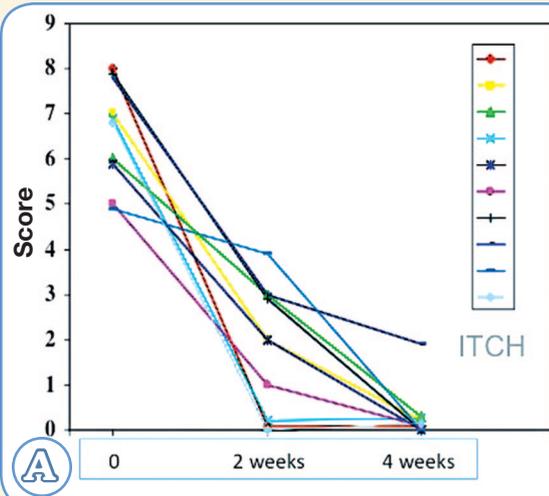


Figure 2. Results of daily washing with 3% to 4% chlorhexidine shampoo in 10 dogs with superficial pyoderma: A scoring system consisting of pruritus, erythema, crusting, and hair loss was used, with each component graded from 0 to 3 based on severity; at 2 weeks, all dogs showed 50% or more improvement, with 3 dogs demonstrating complete resolution, and at 4 weeks, all pyoderma lesions were resolved except for 1 dog, which was still pruritic due to uncontrolled atopic dermatitis (A). Image of patient with superficial pyoderma prior to treatment with daily baths (B), and at the end of treatment, with all pyoderma resolved and hair regrowth seen (C).



festus for pyoderma is to:

1. **Utilize frequent bathing** with chlorhexidine shampoos and/or other topicals instead of systemic antibiotics whenever possible.
2. **Be aggressive when systemic antibiotics** are required, treating with the appropriate dose until the pyoderma is completely resolved. Always combine systemic antibiotics with topical therapy.
3. **Avoid empirical use of fluoroquinolones** for staphylococcal pyodermas. Fluoroquinolones, particularly the early generations, are more effective against gram negative bacteria than gram positive bacteria.
4. **Utilize topical therapy** to prevent recurrence.
5. **Diagnose and treat** the underlying cause.

A very useful resource for current information about MRS, particularly zoonotic potential, is the Worms and Germs blog, coordinated by Dr. Scott Weese and Dr. Maureen Anderson (wormsandgermsblog.com/promo/services). At this site, you can download PDF files for your clients that explain these infections and how to handle them. ■

BOG = bacterial overgrowth syndrome; BUN = blood urea nitrogen; MRS = methicillin-resistant *Staphylococci*; MRSA = methicillin-resistant *S aureus*; MRSP = methicillin-resistant *S pseudintermedius*; MSSP = methicillin-susceptible *S pseudintermedius*

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Topical Therapy: A Stand-Alone Treatment?

In 2010, a randomized, double-blinded, controlled study tested the hypothesis that **topical therapy alone could treat dogs with methicillin-resistant superficial pyodermas**.²⁸

- Ten dogs with MRSP were bathed daily with a surgical scrub containing 2% chlorhexidine.
- A scoring system graded the following components—based on severity—on a scale of 0 to 3: pruritus, erythema, crusting, and hair loss.
- At 2 weeks, all dogs demonstrated 50% or greater improvement, with 3 dogs experiencing complete resolution.
- At 4 weeks, pyoderma lesions had resolved in all dogs but one, whose pruritus was due to uncontrolled atopic dermatitis.
- All dogs were cleared of clinically observable infection within 30 days (**Figure 2**).



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