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## CHRONIC RECURRENT PYODERMA

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### INTRODUCTION

This information is designed to offer a practical approach to dealing with the frustrating diagnosis of recurrent superficial bacterial pyoderma due to *Staphylococcus intermedius*.

In order to be brief, emphasis will be placed on understanding the causes of this problem as well as diagnostic and therapeutic options. The widely available veterinary dermatology literature that covers the specifics of diagnosing and treating single episodes of pyoderma should be consulted as background information.

### CLINICAL APPROACH

An appropriate clinical approach requires an appreciation of the cutaneous defense mechanisms. A functional cutaneous defense mechanism relies on both skin specific defenses as well as "general immunologic defenses." Our formal didactic veterinary training, typically emphasizes the latter, while in practice, most cases of recurrent bacterial pyoderma are due to the former. It is extremely important to consider disorders of the "general immunological defenses" in order to avoid overlooking diagnoses with the potential to affect more than the skin.

"General immunologic defenses" can be compromised by either primary or acquired immunodeficiencies. Two of most common diseases that lead to an acquired immunodeficiency and pyoderma include hypothyroidism and hyper-adrenocorticism. Other diseases that can lead to an acquired immunodeficiency are typically associated with symptoms that would likely be more troublesome than symptoms associated with pyoderma. Except for German shepherd pyoderma, primary immunodeficiencies are typically congenital and inherited. German shepherd pyoderma may not manifest until maturity. Selective IgA deficiency is one of the better known primary immuno-deficiencies. IgA deficiency tests are best performed by an experienced laboratory that has developed its own reference range of values. Cell-mediated immunodeficiencies are the second most common primary cause. (Bull terrier, Weimaraner, others).

The skin associated defense mechanisms rely on both an intact "general immune system" as well as skin specific defenses. The three components to the skin defenses are physical, chemical and microbial. The stratum corneum is the most significant contributor to the physical barrier. Seborrhea disrupts this barrier. In its healthy state, it is composed of tightly packed keratinized epidermal cells and a rich emulsion of sebum, sweat and intercellular cement substance. The intercellular emulsion also acts as a chemical barrier. Fatty acids, especially linoleic acid, inorganic salts and proteins inhibit bacteria. The emulsion also contains immunoglobulins (IgA, IgG, IgM, IgE), cytokines and complement. Normal skin's normal microflora has "squatters rights" and makes it difficult for pathogenic organisms to multiply. Heat, pH, salinity, humidity and fatty acids may affect the microenvironment. The skin associated defense mechanism is complex. Any disruption (such as with seborrhea or allergy induced inflammation) may lead to the potential for pyoderma.

The patient's history and physical examination augmented by diagnostic tests will assist the clinician in determining the etiology. Unfortunately, a thorough history acquisition and physical examination may be bypassed or buried in the medical record as a dermatological problem progresses from an originally mild dermatitis to a chronic condition. This is particularly true with a "middle aged" to older patient. Obtaining a proper history and thorough physical examination are of paramount importance.

### HISTORY

In most patients, the likely underlying cause of the recurrent pyoderma can be ascertained by obtaining an accurate and complete history. Routine questions regarding diet, water consumption, exercise, appetite, urination and defecation are crucial and should not be overlooked when a dermatological problem is present. They can give clues as to potential systemic diseases and food allergy. The presence of lethargy, exercise intolerance, increased appetite or increased water consumption suggests various endocrine diseases. Both weight gain or weight loss are important historical findings. An improper diet may compromise the general immune system or the specific skin defenses.

If pruritus or otitis is present historically, airborne or food allergies may be present. Quantification of the level of pruritus can be aided by asking the question: "Does the itching/licking/ biting/chewing wake you up at night?" Dogs with food allergy may defecate more often than normal or have a "loose stool." While most atopic patients will exhibit some degree of pruritus in the absence of pyoderma, food allergy may occasionally manifest as only a recurrent pyoderma. Either allergy can lead to an inflammatory otitis that will likely become infected with either bacteria or yeast. Otitis is perhaps the most overlooked symptom of allergic disease.

An accurate history of previous veterinary care is equally important. Due to the chronic and often frustrating nature of dermatological problems, many clients may not accurately recall or relay information. They understandably may have seen more than one veterinarian, further complicating the issues. While I prefer that clients utilize a "history form," to help ensure that the history is complete, most clients appreciate the bonding experience of an oral history or at least confirmation of the most troublesome symptoms and pertinent historical information.

The age of onset of the first pyoderma may reveal the true chronic nature of the problem. Many clients somewhat inaccurately report the onset of the problem as being when the pyoderma quickly returned after therapy or when it became poorly responsive. Actually, there may be a several year history of an intermittent pyoderma that responded to treatment. Past episodes of otitis may also be present. Confirmation of medications used and duration may help differentiate between a true recurrent pyoderma and inadequate treatment duration. The use of steroids (such as to treat atopy) may predispose a patient to pyoderma. The early history may also hint towards a seasonal nature of the symptoms. While it is true that seasonality points to an allergic cause, there are also non allergic environmental factors (humidity, swimming) that may lead to seasonal recurrences.

**PHYSICAL EXAMINATION**

A thorough physical examination is necessary to evaluate the likelihood of a pyoderma and to evaluate for the possibility of an underlying or coexisting disorder that may be affecting more than the skin.

Both hypothyroidism and hyperadrenocorticism have classic physical presentations, but their more subtle symptoms can be overlooked in an older patient or in certain breeds. Some patients with recurrent pyoderma due to these diseases may not have any "classic physical examination findings."

The presence of otitis, salivary staining or excoriations may be suggestive of allergies. As a pyoderma can be pruritic and lead to excoriations, it is often necessary to reevaluate a patient/repeat the physical examination after the pyoderma has been resolved. Many moderately pruritic patients will not exhibit evidence of self trauma and an accurate history is necessary.

Excessive scaling or "dandruff," may be a symptom of pyoderma. However, it can also be suggestive of seborrhea, a keratinization defect, which can disrupt the normal physical cutaneous defense mechanism. Excessively dry or oily skin may accompany this symptom. Seborrhea may be either primary in nature or secondary. Common causes of seborrhea include allergies, endocrine disease and pyoderma. It is often necessary to reevaluate a patient after the pyoderma has been addressed to assess the remaining symptoms.

Thorough initial and follow up physical examinations help document the history and narrow the list of differential diagnoses. Clients should be educated that these are true diagnostic tools that require time and should be prepared in advance that multiple visits will likely be necessary to evaluate and confirm the patient's response to medications. Veterinary dermatology is not a particularly high tech field. Busy clients may not be aware of the importance of their participation in helping to identify the problem. The use of a journal or "Daily Doggie Dermatological Diary" can be quite useful. It also can help emphasize the need for a veterinary reevaluation at the end of the course of therapy. Good communication skills, patience and common sense can be used to identify those chronic recurrent pyoderma patients that may have contributing, coexisting or causative diseases.

The diagnostic dilemma begins after the diagnosis of pyoderma has been confirmed, a thorough history and physical examination have tentatively eliminated potential contributing factors and no other microorganisms appear to be complicating the assessment. It is in this stage that many clients require articulation of the diagnostic and therapeutic plan. Proper client communication is paramount. The diagnostic plan should be discussed in a step by step manner along with when referral is advisable. Otherwise, the client may become a "vet hopper" and begin to see different veterinarians. While understandable, "vet hopping" can actually delay a proper work up and treatment for the patient.

**DIAGNOSTIC TESTS****(to supplement a complete history and physical examination)**

In addition to the history and physical examination, three basic tests should be considered in most cases of recurrent pyoderma. They include; multiple deep skin scrapings, cytologies and a dermatophyte culture. With these tests, we are attempting to confirm the presence of pyoderma and exclude mites, yeast and dermatophytes as differential

diagnosis or contributing factors. All of these diseases can mimic bacterial infections or be present concurrently. It is essential that these tests be performed correctly to ensure that important differentials have been ruled out.

**ADDITIONAL DIAGNOSTIC TESTS**

At this stage, a client's expectations and concerns regarding their pet's skin problems should be discussed. Many are willing to accept the infrequent use of antibiotics if they feel comfortable that a more insidious internal medical or immune system dysfunction is not likely. After a thorough history and examination, a CBC/Chemistry may be appropriate. If more specific tests for hypothyroidism and hyperadrenocorticism do not seem necessary, the client should be made aware of what symptoms to look for and the possibility that these diseases may manifest with only dermatological abnormalities. Unfortunately, a normal CBC/Chemistry does not entirely rule out the possibility of hyperadrenocorticism or other diseases. Concurrent or prior medications can alter the results of a CBC/Chemistry and thyroid tests. I like to explain to clients that while we primarily perform a CBC/Chemistry to ensure that "nothing bad" is obviously detectable, we perform thyroid testing in hopes that a relatively easily treated disease is the cause of the recurrent pyoderma.

A bacterial culture and sensitivity is seldom indicated when the pyoderma adequately responds to therapy, but returns. It is indicated when the symptoms appear to be poorly responsive to appropriate antibiotic use. As in ear cultures, different strains of the same organism may be present with different antibiotic susceptibility patterns and all results should be correlated with the patient's response to therapy.

A skin biopsy is useful in confirming the diagnoses of many diseases, but is seldom necessary in most cases of recurrent pyoderma. Primary seborrhea may be present if a patient has seborrhea that does not entirely improve with antibiotics, the above-mentioned test results are normal and allergies are unlikely. A skin biopsy can help confirm the suspected keratinization defect. Proper biopsy site selection, timing and reading by a trained dermatohistopathologist will improve the interpretation of the findings.

Airborne allergies are perhaps the most common underlying reason for recurrent pyoderma. The symptoms of food allergy are indistinguishable from those of atopy. Patients with food allergy may occasionally present with additional gastrointestinal symptoms. **THERE ARE NOT ANY ACCURATE TESTS CURRENTLY AVAILABLE FOR FOOD ALLERGY.** While positive food allergy test results can encourage a patient to pursue a limited diet, it can give a false sense of security as well. A stringently performed

8-10 week hypoallergenic diet based on the patient's dietary history (or an "ultra" hydrolyzed diet) while eliminating flavored treats and medications is the best means of determining if food allergy is present. In many patients, this should be pursued during the low point of the airborne allergy season because of the potential for concurrent airborne allergies to complicate the assessment. Many clients are willing to pursue a hypoallergenic dietary trial before being referred to a dermatologist for further evaluation and work up including allergy testing for airborne allergies. The work up and management of patients with airborne allergies is complex and variable. The finding of positive reactions on an allergy test do not mean that atopy is present or a contributing factor to recurrent pyoderma. Immunotherapy can be very effective in managing atopy, but has a variable

success rate and can take up to one year for full improvement is noted. Client education is extremely important. Modification of the standard protocol is common. Immunotherapy is best performed under the guidance of an individual with training and experience.

### THERAPEUTIC OPTIONS

Treatments for single episodes of pyoderma have covered in the dermatology literature. With recurrent or persistent episodes, it is important to distinguish between treatment failure and incomplete duration of therapy. In general, therapy should be continued for 1-2 weeks after clinical resolution or three weeks total (whichever is longer). Inadequate treatment duration or inappropriate antibiotic dosages are more common reasons for apparent treatment failure than antibiotic resistance to *S. intermedius*.

Obviously, if an underlying etiology has been identified, it should be addressed to prevent recurrence of a pyoderma. In situations where an underlying problem has not been identified or while waiting for therapy for the underlying problem to become effective, topical and systemic antimicrobial therapy can be utilized.

Proper topical therapy has also been extensively covered in the literature, but is often overlooked as a sole or adjunct therapy in cases of recurrent pyoderma. Baths play an important role in cleansing the skin of debris and limiting microenvironments where bacteria can multiply. Leave on conditioners, sprays or rinses offer alternatives to the more time consuming task of frequent baths. Excessive use of topical therapy can actually harm the integrity of the epidermal layer. Chlorhexidine, ethyl lactate and benzoyl peroxide are common shampoo ingredients. While seldom effective as the sole treatment for superficial pyoderma, appropriate topical therapy can help delay its recurrence. Good controlled studies are lacking to ascertain which products are best in most patients.

Systemic antimicrobial therapy for simple pyoderma has also been covered in the literature. In general, most dermatologists choose a cephalosporin, fluoroquinolone or amoxicillin clavulanate. These drugs are generally very effective and offer a wide margin of safety. A minimum of three weeks (or 1-2 weeks past resolution) of therapy is appropriate in most cases of uncomplicated pyoderma. The nuances of an individual patient's recurrent pyoderma dictate how maintenance or pulse antibiotics are utilized while investigating and addressing the underlying problem. The same general rules apply to patients whose pyoderma has been determined to be idiopathic. If a patient's pyoderma typically returns within a week of antibiotic discontinuation, the course of antibiotics should be utilized until the infection has been controlled for a period of several weeks after clinical resolution. Then the option of a lower dose or less frequent maintenance administration is suggested. Mostly client and patient factors determine the decision. If the pyoderma does not typically return for several weeks or months, then antibiotics may be reinitiated several days before the expected onset.

They are then discontinued after a minimum period of approximately one-week. Some patients require the use of antibiotics "on a week on, week off" basis, while others may do well if antibiotics are utilized for one week out of the month. Fortunately, the development of antibiotic resistance with the use of the above classes of antibiotics for *S. intermedius* infections in dogs is really quite rare. Appropriate topical therapy may further delay the onset of the pyoderma.

### IMMUNOMODULATION

As an alternative to chronic antibiotic use, immunomodulation can be considered in patients with recurrent pyoderma. Many varied agents have been utilized in an attempt to "boost" a weak immune system in a patient with no other known abnormalities. They are not indicated in patients with an uncontrolled underlying etiology for the pyoderma. Levamisole, cimetidine and IFN- $\alpha$  have been utilized, but good studies are lacking to prove their efficacy. Side effects have been reported even with low doses of levamisole and cimetidine can be rather expensive. Bacterial products such as autogenous staphylococcal bacterins, *P. acnes* (Immunoregulin: Immunovet) and *S. aureus* phage lysate (Staphage Lysate: Delmont Labs) have been the subject of various non-comparative studies. Anaphylaxis can occur with the autogenous products. *P. acnes* is licensed for IV use only and can cause problems if given SQ or IM. The *S. aureus* phage lysate is the one most commonly used by dermatologist, but even then it is rarely needed because in most cases, an underlying cause can be identified and treated. It is typically given SQ at a dose of 0.5cc twice weekly for 10-12 weeks, then tapered to effect.

### SUMMARY

Patient and client considerations play a significant role in determining a diagnostic plan. I generally recommend pursuing diagnostics if indications of a systemic disease are present, antibiotics are needed more than 3-4 times a year, the patient is frequently uncomfortable or pruritic or has reached an age that leads me to be concerned that an insidious disease may be present. Obtaining a proper history and thorough physical examination are of paramount importance as is appropriate client communication.

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