INSIGHTS IN DERMATOLOGY

The Canine Skin and Ear Bacterial Microbiota

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Like humans, dogs and cats are natural hosts to an array of cutaneous microorganisms (e.g., bacteria, fungi, viruses, mites). Collectively, these organisms compose the host's skin microbiota. Changes in cutaneous microbiota composition are currently being studied for their role in health and disease states in skin diseases in humans and animals.

Presently, most veterinary microbiota research focuses on identifying bacteria using high-throughput sequencing techniques. As in humans, the skin bacterial microbiota of dogs is more diverse than previously believed.[1-4] This article reviews the bacterial microbiota of the canine skin and ear canal in health as well as in 4 dermatologic diseases.

FACTORS THAT INFLUENCE THE SKIN'S BACTERIAL MICROBIOTA

Changes in the composition of the bacterial microbiota have been described in association with canine skin diseases.[2-8] Other factors, such as environment and lifestyle, can also influence the skin's bacterial composition. The interactions between the environment, microbes, and immune system are not fully understood; however, living in an urban environment is associated with higher rates of allergy in both dogs and humans.[9,10] One recent study showed that lifestyle—urban versus rural—influenced both the canine skin microbiota and the risk of allergic disease.[9]

Cohabitation with members of the same or other species also plays a role in microbiota composition. Humans living with pet dogs have a more diverse skin bacterial microbiota and share their microbiota with

Abstract

The skin microbiota plays an important role in canine atopic dermatitis (CAD). Compared with healthy dogs, dogs with CAD exhibit bacterial dysbiosis of the skin and the ear, with reduced bacterial diversity, concomitant domination of *Staphylococcus pseudintermedius*, and significantly different bacterial community composition. Research into skin microbiota in veterinary dermatology is in its infancy, and published data regarding microbiota-based therapies in dogs are scarce.

Take-Home Points

- Alterations of the skin's bacterial community composition are associated with canine atopic dermatitis (CAD), pyoderma, mast cell tumor, and otitis in dogs. It remains unclear if these alterations are a result or a consequence of the underlying disease.
- *Staphylococcus pseudintermedius* plays a major role in canine pyoderma and CAD.
- Flares of CAD are associated with abundant *S pseudintermedius*. Future studies are needed to develop and validate microbiota-based therapeutic approaches such as topical probiotics.
- Current treatment of CAD is multimodal. Treatment regimens should target normalizing the microbiota and restoring the skin barrier function.

their pets.[11] Similarly, dogs that live together strongly influence each other's skin bacterial microbiota.[3]

The age of the individual dog also plays an important factor in shaping the skin's bacterial microbiota. Puppies have different bacterial community compositions than adult dogs.[12] A recent study suggested that diet can influence the diversity of the skin's bacterial microbiota as well.[13] Future studies in larger populations are needed to validate this result.

BACTERIAL MICROBIOTA OF HEALTHY SKIN AND EAR CANALS

Actinobacteria, Proteobacteria, Firmicutes, and Bacteroidetes are the most dominant bacterial phyla in healthy canine skin and ear canals.[2,3,5] However, bacterial composition is highly variable across body sites, such as mucosae versus haired skin, as well as between dogs.[2,7] Data regarding the stability of the canine cutaneous microbiota over time are very scarce; however, 1 study showed that the bacterial community composition of the healthy canine ear canal was stable for the duration of the study (28 days).[5]

DISEASE-ASSOCIATED CHANGES IN CUTANEOUS BACTERIAL MICROBIOTA

Canine Atopic Dermatitis

Canine atopic dermatitis (CAD) is an important disease due to its high prevalence and severity[14] and because it is a natural homologue to atopic dermatitis in humans.[15] A major clinical feature is pruritus, which can manifest as scratching, rubbing, chewing, or licking the skin; scooting; and/or head shaking. While the skin of atopic dogs may be alesional, pruritus is commonly associated with erythema and papules. In patients with chronic disease, secondary skin lesions (e.g., crusts, excoriations, lichenification, hyperpigmentation) may be present. Lesions are typically found in the concave ear pinnae and axillae and on the abdomen, perineum, and distal aspects of the legs (**FIGURE 1**).[16] Variations of this phenotype have been documented among breeds.[17]

Role of Microbiota

Skin barrier dysfunction, inflammation, and changes in the skin microbiota are involved in the pathogenesis of CAD. Although early-life skin microbiota is believed to play an important role in the pathogenesis of atopic dermatitis in humans, the first canine birth cohort study did not find that individual early-life microbiota predisposed to later development of CAD.[12]

FIGURE 1. French bulldog with typical distribution of canine atopic dermatitis skin lesions. Note the symmetrical erythema on the muzzle, around the mouth, in both axillae, on the flexor sites of the elbows, and on the abdomen. Multifocal, erythematous papules are also present.

Studies have shown that up to 91.7% of CAD patients are predominantly colonized by *S pseudintermedius* versus only 39.5% of healthy dogs.[19,20]

Staphylococcus pseudintermedius may induce flares of CAD.[18] Studies have shown that up to 91.7% of CAD patients are predominantly colonized by *S pseudintermedius* versus 39.5% of healthy dogs.[19,20]

Bacterial Diversity Findings

Dogs with pyoderma (erythema, scaling, papules, pustules, crusts) secondary to CAD,[8] as well as CAD patients without pyoderma,[2,3] have lower skin bacterial diversity (alpha diversity) and different bacterial community compositions compared with healthy dogs.

One study showed that allergic patients with pyoderma have an increased relative abundance of *Staphylococcus* bacteria (predominantly *S pseudintermedius)*, correlating with the reduced diversity in bacterial community composition.[8] *S pseudintermedius* dominated all other bacteria, contributing to dysbiosis. Skin barrier function in these patients was found to be abnormal. After 4 to 6 weeks of systemic antimicrobial treatment, diversity was restored, the relative abundance of *Staphylococcus* bacteria was reduced, and skin barrier function was normal. However, 1 month after discontinuation of antimicrobial treatment, bacterial diversity decreased again.[8] These findings emphasize that even when the skin of animals with CAD appears macroscopically normal, dysbiosis can be present.

Glossary

Alpha diversity A measure of microbiota diversity within a community/sample

Dysbiosis An "imbalance" of the microbiota, associated with disease

High-throughput (or next-generation) sequencing Modern technologies that can sequence DNA or RNA

Microbiome The entire community of microbes (bacteria, fungi, viruses, and their genes) that naturally live on and inside a human or animal

Microbiota A gene-based collection of microorganisms

Treatment

In this study, the skin barrier exhibited increased transepidermal water loss and altered pH during disease flares, highlighting the importance of correcting dysbiosis to restore skin barrier function as part of CAD treatment.[8] However, it is well established that treatment with systemic antibiotics comes with the risk of antimicrobial resistance. Therefore, in human medicine, where similar findings have been documented, new studies focus on microbiota-based therapy of atopic dermatitis. Topical treatments such as dilute bleach baths and emollients can reduce atopic dermatitis lesions and severity.[21] Other potential treatment options include probiotic treatments, which promote enrichment of the skin flora with beneficial commensals, and phage therapies.[22]

Currently, very few data exist regarding microbiota-based treatment of CAD in veterinary dermatology. One study investigated the effects of an antimicrobial shampoo in 3 dogs with CAD without pyoderma or *Malassezia* skin infection and 3 healthy dogs.[23] Bathing with this shampoo led to improvement in CAD severity in the CAD group, but without significantly changing the skin microbiota in either group.[23]

A preliminary, noncontrolled, prospective clinical trial evaluated the effects of a novel veterinary spray product (Linkskin spray; DRN, drnpet.com) containing heat-killed lactobacilli (*Lactobacillus rhamnosus* and *Lactobacillus reuteri*) in patients with CAD.[24] Although there was no significant change in the cutaneous bacterial microbiota after daily use for 28 days, a significant, rapid decrease in clinical signs associated with CAD was documented.[24] Larger randomized, controlled, blinded studies are needed to further investigate the effect of topical probiotic formulations in CAD patients; nevertheless, this preliminary study is very promising.

Human medicine is a couple steps ahead in this area. A first-in-human topical microbial transplantation (*Roseomonas mucosa*) alleviated atopic dermatitis

symptoms in adults and children through a tumor necrosis factor–related epithelial pathway.[25,26] Despite promising initial data, another topical formulation with 3 strains of *R mucosa* failed to meet statistical significance in a more extensive trial, and development of the product was discontinued.[27]

Current treatment of CAD is multimodal. Flare factors should be identified, addressed, or avoided if possible. Topical and/or systemic medication should be used to reduce pruritus and inflammation. Allergen-specific immunotherapy can induce tolerance to the allergens and prevent or reduce allergy flares. Treatment regimens should target normalizing the microbiota and restoring the skin barrier function.

Pyoderma

Pyoderma is one of the most common reasons dog owners seek veterinary advice. Superficial pyoderma (bacterial infection of the epidermis and hair follicles) is most commonly secondary to an underlying disease (e.g., hypersensitivity, mites); primary pyoderma is rare. Canine pyoderma typically manifests in 3 forms: superficial bacterial folliculitis (**FIGURE 2**), bullous impetigo, and epidermal collarettes (**FIGURE 3**).[28] These forms can coexist in the same patient.

A recent study evaluated the bacterial microbiota of bacterial folliculitis lesions and epidermal collarettes.[28] As expected, the abundance of *Staphylococcus* species (predominantly *S pseudintermedius*) was increased in both forms. The bacterial community composition of the bacterial folliculitis lesions was significantly different from the epidermal collarettes, and both were significantly different from healthy control samples.[28] Further studies could elucidate differences among pyoderma forms, which could lead to targeted antimicrobial treatments to restore the microbiota.

Mast Cell Tumor

Another study evaluated and compared the skin bacterial microbiota in dogs with spontaneous mast cell tumors (MCTs) versus healthy control animals.[29] The bacterial community composition was significantly different between the 2 groups. MCT skin samples showed lower bacterial diversity with increased numbers of Firmicutes. This study could provide a starting point for further research into modifying the skin microbiota–host immunity response in MCT patients, with potential clinical applications.

Otitis

Otitis is a very common dermatologic disease in dogs, accounting for up to 20% of visits to small animal practices.[30] It manifests as head shaking, head/ear scratching, head tilt, and sometimes pain. Diagnosis is based on otoscopy (visualization of inflammation in the ear canal). Cytologic examination of an ear canal sample is then used to identify a secondary bacterial or yeast infection to determine appropriate treatment. Culture can be performed if systemic antibacterial treatment is indicated.

FIGURE 2. Symmetrical multifocal to coalescing erythematous papules and follicular pustules on the ventrum and inner thighs of the same dog as in **FIGURE 1**, typical of superficial bacterial folliculitis (form of superficial pyoderma) secondary to atopic dermatitis.

FIGURE 3. Epidermal collarettes **(arrows)** on the skin of the same dog as in **FIGURE 1**. An epidermal collarette is a secondary skin lesion consisting of a thin layer of scales that expand peripherally and form a ring.

However, in 1 study, cytology and culture of samples from ear canals with *Pseudomonas* infection were not as successful for identification of bacterial microbiota diversity as a next-generation sequencing technique.[4] Next-generation sequencing techniques therefore provide a better method for understanding potential opportunistic microorganisms in the canine ear, thereby driving more efficient treatment of otitis. For example, using next-generation sequencing, *Finegoldia magna*, a gram-positive anaerobic bacterium that is considered pathogenic in some mammals, but not in dogs, was recently found in otitis patients with significantly higher relative abundance than in normal canine ears.[31] However, aerobic cultures that are routinely used to screen otitis patients cannot detect this anaerobic bacterium. Based on the results of this study, further studies are needed to evaluate whether veterinarians should screen otitis patients for anaerobic bacteria as well. Next-generation sequencing techniques have also been used to show that, compared with healthy dogs, CAD patients have significantly different bacterial community compositions in uninfected ear canals and on the skin.[3,5] Future studies should focus on treatments that can normalize the bacterial community composition to prevent flares.

SUMMARY

Research of skin and ear canal bacterial microbiota in veterinary medicine is still in the beginning stages; however, even with limited data, it is commonly accepted that the bacterial microbiota of the skin and ear canal are pertinent to common dermatologic diseases. Further studies are needed to elucidate the microbiota and its interaction with host immunity to help develop future therapeutic strategies. TVP

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