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Skin Deep: Exploring the Hidden World of Dogs (and Humans)

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Above: Penn Vet dermatologists use an instrument to measure pH levels on the pinna of a dog's ear.

Below: A device quantitates the sebum on the skin.

skin deep

Exploring the Hidden World of Dogs (and Humans)

BY MANASEE WAGH

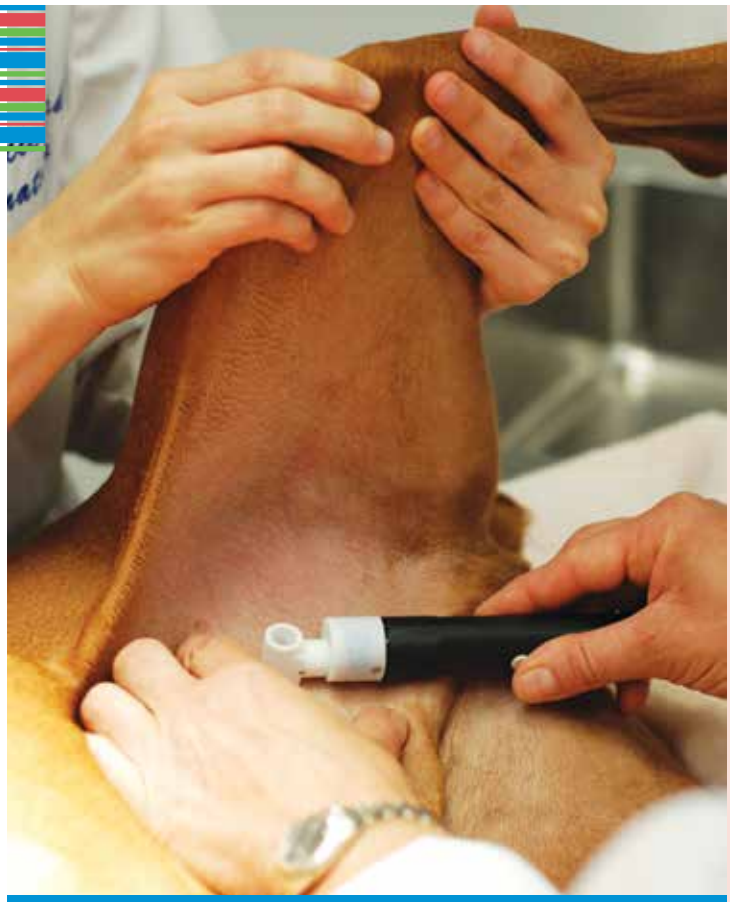
By current estimates, the human body contains 10 times more microbial cells than human cells. Acting in ways both beneficial and harmful, the microorganisms living on the surface of the skin, as well as in the gut and other organs, constitute a complex ecosystem known to influence digestion, allergies, and a variety of diseases.

Scientists are more interested in the microbiome than ever. At Penn Vet, researchers are crossing disciplines to seek greater understanding of how these diverse populations of "friendly" bacteria inhabit and interact with their host. Penn Vet's new Center for Research on Microbes in Health and Disease is currently funding pilot projects that explore the microbiomes of both human beings and animals.

"There's increasing evidence that the microbiome is important in regulating many diseases, and it may be something we can control or manipulate, either through dietary intervention, such as prebiotics or probiotics, or by medical means," said Dr. Dan Beiting, Research Assistant Professor in Penn Vet's Department of Pathobiology.

One of the collaborative studies the Center is funding is a one-year, $50,000 project bringing together scientists from Penn Vet and the Perelman School of Medicine. Researchers will peer into the microbial world of dogs that have atopic dermatitis, a common allergic skin condition.

Precipitated by allergens such as pollen, dust, and molds, the disease is similar to human atopic dermatitis and commonly occurs spontaneously in about 10 percent of



Penn Vet dermatologists measure transepidermal water loss on the inside of a dog's leg.

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dogs. In both humans and dogs, atopic dermatitis is treated with a wide array of interventions, some of which may include antibiotics and corticosteroids. Veterinarians at Penn Vet's Ryan Hospital treat dogs that present with typical symptoms such as itching and then progress to scabs, hair loss, and secondary bacterial infections that can often be resistant to antibiotic treatments.

Veterinary researchers will examine the bacterial population on the dogs' skin and follow changes in the microbiome of each dog during treatment. The goal is to understand the role of resistant microbial organisms in the innate resistance to infection, the onset of infection, and the development of antimicrobial resistance once infection does occur.

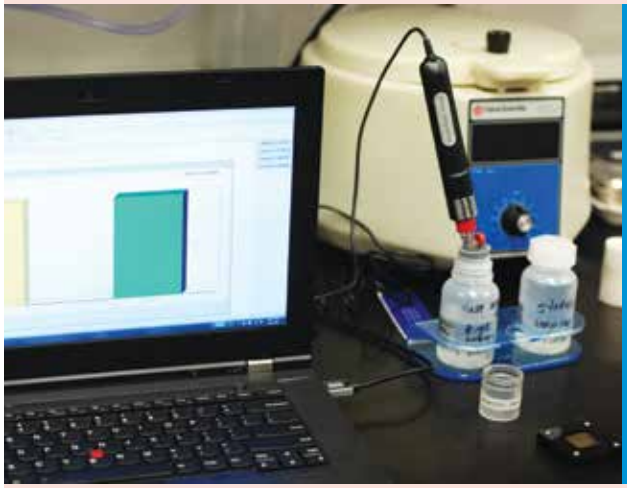
"The skin is a wall between the body and the world. We're looking at the relationship between the bacteria and the skin, and the different components of the dog's skin that affect its barrier function," said Dr. Charles Bradley, a Pathobiology Lecturer at Penn Vet. Dr. Bradley is part of the research team, which brings together the knowledge of people that specialize in human medicine and veterinary dermatology, pathology, and microbiology.

Globally, researchers study the microbiome primarily in humans and in mouse models of disease, but very little is known about the dog microbiome. Since dogs develop spontaneous and complex diseases, much like humans, they serve as ideal models for understanding how both animals and humans can go from being healthy one day to dealing with a chronic or recurring disease the next day.

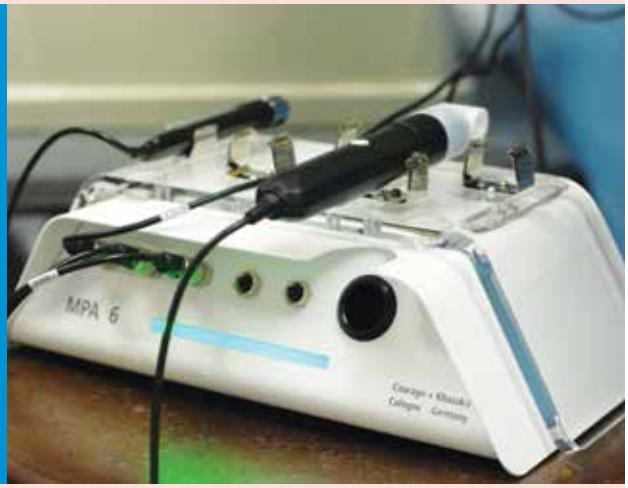
Because culturing bacteria and other microbes in a lab can be time consuming, and may be biased and error prone, today's researchers prefer genomic approaches such as directly sequencing bacterial DNA from skin swabs to identify the microbes that are present.

Dr. Elizabeth Grice, Assistant Professor of Dermatology at Penn's Perelman School of Medicine, is devoted to studying the skin microbiome of humans. Instead of growing bacteria in cultures, her approach to identifying bacteria starts with observing them directly from a skin sample. She has teamed up with Penn Vet researchers who will use her lab's methods to investigate atopic dermatitis.

"We'd normally use bacterial cultures, but those don't capture the full diversity of bacteria present on the skin. Now we can target bacterial genes and identify the types of bacteria present with greater precision than before," Dr. Grice said.



New diagnostic equipment and software allow Penn Vet researchers to measure the efficacy of the skin barrier directly on the skin.



This is a less biased method than growing bacteria by microbiologic culture, because cultures are highly selective for particular environments, nutrient sources, temperature, and other growth conditions that may favor some types of bacteria over others. By using genomic, culture-independent approaches, researchers see a more precise picture of the microbes.

"A whole-community analysis allows you to see that many different organisms are present at time zero, and after antimicrobial therapy, the population may have shifted to two or five or 10 organisms that dominate the skin. We'd recognize those as causing the infection, because those are the ones that have overgrown," said Dr. Shelley Rankin, Associate Professor of Microbiology at Penn Vet and a member of the project team.

In addition to assessing the dog microbiome, the veterinary group will also be measuring the integrity of the skin barrier, which is provided by the stratum corneum – the topmost, non-porous layer that is the body's first line of defense against the environment.

"In humans with atopic skin disease, that skin barrier is defective and allows allergens to penetrate the skin and cause allergic reaction," said Dr. Elizabeth Mauldin, Associate Professor of Pathology and Dermatology at Penn Vet and another researcher involved in this interdisciplinary study. "We want to know what role the barrier plays in dogs with allergic skin disease. Are they losing too much water through their skin? What's the pH, and is it different from normal? In people, these characteristics could have a genetic basis. We don't really know that much about dogs yet."

A major complication following the treatment of atopic dermatitis and similar skin infections that compromise the natural defense mechanisms of the skin is that antibiotic therapy can lead to the development of antibiotic-resistant bacteria. Dogs that start with a mild case of itching may progress to a drug-resistant staph infection.

Is the skin's resident population of *Staphylococcus* becoming resistant to antibiotics during antibiotic therapy? According to Dr. Rankin, it may be that there are small numbers of drug-resistant staphylococci already present on the skin, and because antibiotics kill the susceptible bacteria, those antibiotic-resistant bacteria get the chance to propagate – unhindered.

"One of the goals of the study is to determine the character of the skin's microbiome during the development of these complications," said Dr. Dan Morris, a member of the research team and Chief of the Section of Dermatology and Allergy at Penn Vet.

The researchers will selectively look for genes associated with drug-resistant strains of bacteria such as methicillin-resistant *Staphylococcus*, before and after therapy.

"We see a shift toward resistant populations during antimicrobial therapy, but we don't have a good grasp right now of how that occurs. Are we amplifying an existing population? We're spending a lot of time considering this question," Dr. Rankin added.

Scientists believe that the answers they find in the canine microbiome will provide a better understanding of human medical dilemmas such as drug-resistant bacterial infections and the role of microorganisms in normal skin functioning. Encouraged by the Center for Research on Microbes in Health and Disease, this unique collaboration will bring researchers closer to finding answers to these important questions.

"Hopefully, what we discover will be used by dermatologists in the human medical field, and lead to prevention and treatment for people as well as for our canine patients," Dr. Rankin concluded.