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Protecting Public Health: The Role of Penn Vet

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PROTECTING PUBLIC HEALTH

THE ROLE OF PENN VET

Expanding the idea of what a veterinary school does to protect human and animal health

BY KELLY STRATTON

> The community as a whole has a stake in environmental protection, hygiene and sanitation, clean air and surface water, uncontaminated food and drinking water, safe roads and products and control of infectious disease.
>
> **Lawrence O. Gostin,** Public Health Law: Power | Duty | Restraint

In a continuing series of answering the question "What does a veterinarian do?" we focus this issue on three researchers at Penn Vet who are examining big-picture issues with the aim to find solutions for both human kind and animal kind. While two of our faculty members featured are not trained as veterinarians, their work speaks to the role of the veterinary school – and illustrates how Penn Vet is uniquely positioned to address such public health issues.

RABIES: A MODEL VIRUS

Ronald N. Harty, PhD, associate professor of microbiology, takes rabies seriously. Very seriously.

It's in his lab where he and his team work to better understand the virus, focusing on its individual proteins, with the ultimate goal of intercepting its budding activities.

While lab workers don't work with the live virus – instead they use Vesicular Stomatitis Virus (VSV) – this pathogen's proteins act similarly to those of rabies virus.

Researchers in Dr. Harty's lab are most interested in the molecular events that lead to virus assembly and budding and focus on the viral matrix proteins (M proteins) that serve as the building blocks of the virus particle. It's those M proteins that work to orchestrate the function of assembly and budding and therefore spread of the virus within a body.

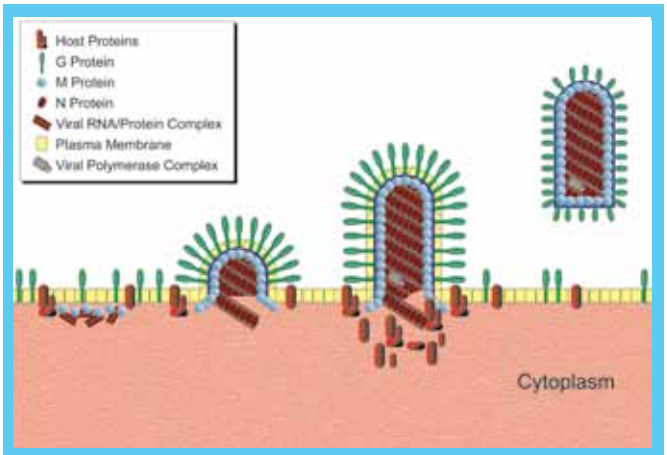

Diagram showing the sequential steps of rabies virus budding. The rabies virus M protein directs the early assembly process of viral RNA and associated proteins (N protein) at sites on the inner surface of the plasma membrane that are enriched for the G surface protein. Packaging of the helical viral RNA/protein complex into the virus particles begins as does bud protrusion through the plasma membrane. Host proteins recruited by the viral M protein help to facilitate the final step of virus-cell separation or pinching-off from cell surface, leading to the release and dissemination of mature, infectious virions. *(Figure designed and created by Deborah Argento).*

In addition to studying the relationship between how these viral M proteins interact with host proteins to facilitate the budding process, Dr. Harty's lab is also interested in understanding the host's innate immune response to virus infection and identifying antivirals that can inhibit the spread of the virus.

"Host proteins are hijacked by the virus to help with budding," said Dr. Harty. "But if we find an inhibitor to prevent that interaction, we could prevent the virus from spreading. It's called 'host-directed therapeutics.'"

But his lab isn't focused on rabies for rabies' sake.

Dr. Harty and colleagues are using what they learn from the rabies virus to apply it to other viruses that assemble and bud similarly, like Ebola and Marburg and other hemorrhagic syndrome viruses.

"Ebola and rabies viruses, they bud similarly," said Dr. Harty. "So if you find the inhibitor to block one, you could block many others."

Those others include HIV, Marburg and arenaviruses, such as Lassa fever.

Some of these viruses are considered likely bioterrorism agents and are on the high priority list of the Center for Disease Control and National Institutes of Health. High priority agents pose a risk to national security because they can be easily disseminated or transmitted, have potential for major public health impact and could cause widespread panic.

If Dr. Harty's lab can understand the mechanism of virus budding, then candidate drugs can be identified and presented to slow down the assembly/budding process and give the immune system an opportunity to begin fighting the pathogen.

"Vet schools are on the front line in terms of identifying and combating pathogens," said Dr. Harty. "Many diseases are zoonotic in origin so if we can understand how a virus works we can more quickly act if and when it jumps to the human population."

Dr. Harty at work in his lab.

SOLVING THE MRSA MYSTERY

Dr. Morris evaluating a patient at Ryan Hospital.

Methicillin-resistant Staphylococcus aureus (MRSA) infections are caused by a strain of staph bacteria that does not respond well to the kinds of antibiotic drugs normally used to treat them. Because of that, they can be particularly challenging to the human doctors trying to treat a patient and frustrating and painful for the patient.

If left untreated, superficial MRSA infections (of the skin and soft tissues) can progress to cause potentially life-threatening infections in a person's bones, joints, bloodstream and lungs.

So, when a MRSA scare strikes, public health experts and human physicians are called in to contain hysteria. People are told to wash their hands well and often, keep wounds covered, shower after working out and keep sheets on their beds clean.

But in some cases, the cycle – and the infection – continues, leaving patients and doctors confused and concerned.

And it's when he hears about cases like these that Daniel O. Morris, DVM, MPH, section chief of dermatology and allergy at Ryan Hospital and professor of dermatology, brings a different point of view to the table.

"When a person has contracted a drug-resistant staph infection, you have to look at the entire household," said Dr. Morris. "You have to ask the human patient, 'Do you have any pets?'"

Pets are, according to Dr. Morris, a potential link in the cycle of infections within a household. Although pets typically carry a different species of Staph bacteria than do people, they are still capable of becoming silent carriers of the MRSA bacteria, just like their human counterparts. They can also develop MRSA infections, but their role in passing infections back to people is poorly characterized at the present time.

It's that potential link – of pets passing infections back to people – that Dr. Morris, in conjunction with the Perelman School of Medicine and Johns Hopkins, is looking at in a recently launched study. In it, Dr. Morris and his human medicine colleagues are specifically examining the prevalence of MRSA bacteria on pets and their bedding in households where a family member has a recurring MRSA infection. The study will also assess the persistence of Staph carriage by the pet, when the household and family members undergo a treatment intervention. It's an important step in understanding the relationships between people and their pets and the appropriateness of how close we should allow our best friends to be.

In the case of a recurring infection, is the person living with a pet? And is the pet sleeping in the bed? Giving kisses? Is the pet a dog that serves in a therapy capacity and goes on hospital visits, where the likelihood of contracting MRSA is greater? If so, and the pet is a "silent carrier," the recurring infection of a household member could potentially be related to close pet contact, and this relationship will need to be adjusted to put an end to the cycle.

But just the simple question of "Do you own a dog?" isn't often in a medical doctor's repertoire.

"Veterinarians need to be involved when a physician suggests a pet-to-person link," said Dr. Morris. "It's what they do. They're trained to ask different questions and they understand the human-animal bond a little better than a medical doctor might. The pet is the member of the family – they're sleeping in the same bed, licking people's faces. It's what's in the journals we read and it's what we talk about as part of our daily practice."

DEFINING DISEASE BIOMARKERS

Cutaneous leishmaniasis is an ugly disease. A protozoan parasite transmitted by sand flies, *leishmaniasis* may not sound familiar to many in the U.S., but for the people of Brazil and across the Middle East and Afghanistan, the disease is much more prevalent. In Corte de Pedra, Brazil there are approximately 1,000 new cases annually.

Phillip Scott, PhD

And it is there that Phillip Scott, PhD, associate dean for research, professor of microbiology and immunology, focuses his research.

There are two types of the parasite – cutaneous and visceral. Dr. Scott's lab focuses on the cutaneous disease, which causes skin lesions, hair loss and dermatitis. The parasite affects people, as well as dogs.

"It's similar to leprosy," said Dr. Scott.

(The visceral type leads to swollen lymph nodes, weight loss, decreased appetite, nose bleeds and, eventually, kidney failure.)

What is interesting about the cutaneous disease is that some individuals have a severe reaction to infection while others have more mild reactions.

In his laboratory, Dr. Scott and his colleagues are working to define biomarkers to understand this discrepancy in reaction. Based on an individual's immune response, his lab may be able to successfully fight infection with the help of a drug, while others may need repeated treatments.

When early lesions are identified, an individual goes through a 21-day treatment of receiving the drug intravenously.

If however, within the first 15 days of infection, a biomarker is identified that shows a person will not respond to that treatment, the attending physician can jump straight to the second treatment option, which involves a stronger, more expensive drug.

"There's no vaccine, treatment isn't great," said Dr. Scott, "but if we can identify the biomarkers of those people who don't respond well with the traditional first round of treatment, we can go straight to the second option – a better, more expensive drug."

In a recent paper published in *The Journal of Immunology*, Dr. Scott and co-investigators point out a probable link between the relationship of T cell response and the likelihood of the cutaneous lesions returning. That is, the inability of lymph nodes to recruit lymphocytes may mean a greater likelihood of a chronic, recurring condition in certain individuals.

"Understanding how these parasites circumvent generating a strong immune response allows us to design new therapies to enhance immune responses in patients, and thus promote more rapid cure of the disease," said Dr. Scott.