Beth Bamford:

Research is really important because by definition it's the only way to get new knowledge. There's so much that isn't yet known that it's just a cool time to be in science.

Cole Cullen:

I think at the end of the day, what really gets us out of bed in the morning is just the curiosity, trying to understand things we didn't understand the day before.

Beth Bamford:

Welcome to Reach, the podcast that tells the stories of researchers, their studies, and how their work impacts you and the world you live in. I'm Beth Bamford ...

Cole Cullen:

... and I'm Cole Cullen. Today we're going to tell you about viruses, more specifically, the research being done at Penn State with ticks, mice, bats, and the viruses they carry.

Beth Bamford:

None of those things are my favorite.

Cole Cullen:

No, they're all kind of gross.

Here in the Northeast, we need to worry about ticks and Lyme disease, especially if you're outside a lot, but it turns out ticks can also be used in research of viruses.

Beth Bamford:

We talked with Dr. Kurt Vandegrift about ticks and emerging epidemics. He even took us into the field to show us how he collects ticks to take back to the lab.

Kurt Vandegrift:

I'm dragging a white corduroy sheet through the forest in hopes of ticks attaching to this sheet. This is what we call drag sampling for ticks. They mistake it for a host, a squirrel or a raccoon or a woodchuck. There we got one. This is an adult female. You can tell because she's got red on her back right here. We have such high exposure. The ticks, they're feeding on our blood, right? They're out taking their first blood meal from all the different wild animals, and then they come to us for their second blood meal. They're essentially like little syringes running out and poking all this wildlife biodiversity, and then taking a blood meal from us next.

Beth Bamford:

It's really scary when you compare it to a bloody syringe or-

Kurt Vandegrift:

I'm terrified by them. I have thousands of them on me per year and so do most of the other people that venture too far off the path here in the Northeast of the US.

Hi, my name is Kurt Vandegrift. I'm from the biology department at Penn State University, associated with the Center for Infectious Disease Dynamics. I am an assistant research professor. I have sort of a dual responsibility in teaching students and in doing research.

We work at the forefront of the fight against emerging infectious diseases, SARS, HIV, Ebola, Lyme disease, West Nile virus, these sorts of pathogens that spill over into the human population and can cause mass morbidity and mortality.

I think these emerging infectious diseases are really scary and they're dangerous. We don't know where they come from, we don't know why they jump from animal species into humans, and we don't have any preventative measures designed. There's no vaccine for a pathogen that you didn't know existed. Ebola is a terrifying one that's going on right now. Ebola, that's very similar to Lyme disease, in that they're both emerging infectious diseases. One is occurring in East Africa, one is occurring in the Northeast of the US. One causes you to bleed out your eyes and die immediately, the other causes you to get a rash and then suffer various neurological and arthritis symptoms.

Here in the Northeast of the United States, we have the resources and the knowhow to be able to identify other potential pathogens that very well could have symptoms more similar to Ebola than does Lyme disease have, and so we're being more proactive about it in that we're looking for them before they've started to cause us to bleed from our eyes.

Beth Bamford:

You're researching in central Pennsylvania and the diseases and the carriers, the animals or mammals that are carrying these diseases, could prevent an outbreak from spreading around the world?

Kurt Vandegrift:

Yeah. We went with an odds on approach. We ask of the pathogens that have emerged, where did they come from? What type of pathogens are they? Most of them are viruses. Most of those are zoonotic viruses, meaning they go from animal to man. If you say what animal, most of them are coming from rodents, but not just rodents, the rodents that live in our house. We have very high exposure to these rodents that live in our houses. With the ticks, they're sampling all of that wildlife biodiversity and then sampling us. These ticks are a bridge to transmission.

We're interested in how these viruses accumulate in the hosts. In the ticks, they might get some viruses from their mother, vertically transmitted viruses, but after that, they're probably going to pick it up during their first blood meal. Then they might get more viruses during their second blood meal. They might drop some off in that second host. They might get more viruses in their third blood meal. The same thing with the mice. We catch them and we put PIT tags in their back, the same thing that you put in your dogs and cats, so we can scan them, they have an eight digit number, and we release them. We take blood, urine, feces, saliva and skin from every mouse every three weeks, and we release them where we caught them, and then we come back and we catch them again.

The most we ever caught a mouse was 36 times. We get to know who has what, where they are and what they had last time too, and so we should be able to watch a pathogen spread through the community. The same thing with ticks. We go to the places where they process your deer to cut it into steaks and things, and we take the adult engorged ticks off of those deer. We raise them in humid vials, allow them to lay their eggs. When they lay their eggs, the mom dies, we subsample the eggs and we freeze mom. We test those, find out what viruses they have, then we allow the eggs to hatch into larvae. We subsample those larvae, we freeze those. Knowing what's in mom and what's in the larvae tells us which are the vertically transmitted pathogens, the ones that go from mom to offspring. Anything else

that we've seen is horizontally. They're picking that up from the host blood meal or from the environment maybe, but now we know what's in the rest of those brothers and sisters. We have larvae that have known viruses.

I can take a mouse that has known viruses and a tick that has known viruses and put the ticks on the mouse, then collect those ticks after they've fell off, sample them, see what did the ticks give to the mice, what did the mice give to the ticks. We still have lots of those engorged ticks. We put them in humid vials, we allow them to molt into the next stage, which is the nymph, which is the one that gives us Lyme disease. They presumably not only picked up viruses from the mice, but they picked up bacteria too. Then we say, which of those things persist through that molt? Then I take that nymph that's fed on a wild mouse and we put it on a pathogen-free lab mouse, and we say what that it picked up from that mouse, is it able to transmit onward to the lab mouse, and is that influenced by the viruses that were present?

Then we can put those on the lab mice. We collect those ticks off of the lab mice, then we test the lab mice by putting xenodiagnostic larval ticks on them, and then we kill the lab mice and we take blood samples and we see who gave what to who, when and how.

It's really pretty common sense. You'd think somebody would have done this before, given that the ticks are giving us lots of pathogens. It's not rocket science, is it? It's what we should do.

Beth Bamford:

It does seem complex. It seems like there's a lot of steps and a lot of things you're looking for down this sort of logical path.

Kurt Vandegrift:

Right, and so what we've done is sort of taken control so that we can sample these things and we can follow the progression of the pathogens and see what's picked up when and who's infected from whom.

Beth Bamford:

You're proactively trying to avoid some sort of epidemic, some sort of disease epidemic?

Kurt Vandegrift:

That's correct. I'd like to identify the next emerging infectious disease before it emerges and stop it from happening. In fact, the title in the grant was a proactive approach to emerging infectious diseases, because as we saw from the influenza pandemic that we recently had, the 2009 AH1N1, it made it halfway around the world in 6 months. Identifying them after they emerge can be too late.

I think at the end of my career, what I'd like is to have gotten a bunch of other students interested in the scientific method and the pursuit of knowledge, and generating data, testing hypotheses, getting to the next questions, and doing things in a very organized way that allows us to learn about the world that we live in. It's amazing to me how many courses students have, and we bang scientific method into their heads and we make them memorize it, and they just don't get it until they're actually out there in the field with dirt under their fingernails, sweating, getting bit by mosquitoes and ticks. They just don't get it until they start to use their hands and they actually do things. I think that if we had more students that had a grasp of where that can take us, that's what I'd really like. I think it's a unique opportunity to get more students involved in science.

Cole Cullen:

Little brown bats are disappearing.

Beth Bamford:

Which means we're going to have an insect problem.

Cole Cullen:

That's what they say. I don't like bats, so I trust when they say that bats are good for the environment.

Beth Bamford:

I might not like bats, but I like them a heck of a lot more than mosquitoes, ticks and any other little thing that will bite me.

Cole Cullen:

Yeah, I guess.

Beth Bamford:

We talked to Dr. Marilyn Roossinck about little brown bats and what can save them from extinction.

Marilyn R.:

My name is Marilyn Roossinck and I'm a Professor of Virus Ecology at Penn State. We study how viruses interact with their hosts and how that impacts the hosts' interactions with the broader environment.

Beth Bamford:

What types of things are you currently researching?

Marilyn R.:

We've been working on this virus that infects a fungus. The fungus is a pathogen of bats. In about 2006, people noticed that little brown bats, and tri-colored bats particularly, were dying in New York, first in upstate New York, and later this disease spread around the Northeast and it's continuing to spread. What they noticed on these bats was that their noses were white and fuzzy. They found that they had a fungus growing on their noses. Later, they found it grew also on their wings and their tails. The disease is called White Nose Syndrome. It's very lethal to bats.

Normally bats go to sleep, they go into this torpor where their body temperature drops really low, and they stay that way through the cold months of our winters here. Then in the spring they wake up, but when they have this fungus, they wake up throughout the winter. By the end of the winter, they have no reserves left. Their body fat is all gone and they die.

It has killed about 99% of our little brown bats here in Pennsylvania, and the tri-colored bats. There are a few survivors. There are a few little brown bat survivors and it's possible that they have some kind of resistance in that they will repopulate over a long period of time. What we've noticed about them is that they tend to be bigger. If they weigh like 10 grams in the fall, they might make it through the winter. We're selecting for fat bats, I guess.

People aren't always so aware of bats because they're active at night and we don't see them that much, but they are very critical to our environment. They eat lots of mosquitoes and other insects. The

estimate in the US is that bats save the farmers about $4 billion worth of pesticides every year by the insects that they eat. It's something we all need to be concerned about.

People that were working on this disease in bats actually approached me and said, "Could you see if there's any viruses in this fungus? Maybe that would be a way that we could study the fungus better or maybe we could manipulate it." We found a virus very quickly. Many fungi have viruses. In fact, probably most fungi are infected with viruses. We've been using the virus to study how the fungus is moving.

Beth Bamford:

What does that mean, how the fungus is moving?

Marilyn R.:

Well, so the fungus was first found in upstate New York in a cave, and then later in Pennsylvania. Then over the years it's been spreading from the Northeast towards the South and West. Two years ago, I guess three years ago now, it was isolated in Washington state. It moved all the way across to the West coast.

Bats travel, especially in the summer. They fly like sometimes hundreds of miles. Some of our Pennsylvania bats go all the way to Kentucky in the summer. They are moving the fungus around, but we don't really have a very good handle on how that's happening yet. We're using the variation in the virus to look at how the fungus is moving.

These wildlife people, they go out and survey the bats and see if they have any symptoms of the disease. They take a little swab of the bat, and then we culture that when we get it back to the lab. We grow it in culture.

Now we're starting another project and it's called virus-induced gene silencing. You know that if you get sick, you get an immune response, you make antibodies to the virus. Well, plants and fungi, they don't make antibodies. They do something different. They have a way of recognizing RNA from a virus. Then they have a whole set of enzymes and genes that are turned on and they target the virus RNA and they degrade it. What we're trying to do in this next phase of the project is to use that as a way to actually destroy the RNA of the fungus. We're going to trick the fungus into thinking that some RNA is viral in it, and we hope that it will then destroy it.

We're just taking very specific genes in the fungus and then we use this system to try to make them be turned off or silenced. It's called RNA silencing. The idea is that we can study the genes of the fungus by turning those genes off or suppressing those genes and then see what happens to the fungus.

Beth Bamford:

Okay, so hopefully it would be eliminating the fungus.

Marilyn R.:

We're not necessarily going to destroy the fungus, but we're going to ... We hope that we will be able to understand how it causes the disease, because we don't know that. In order to try to figure out how we can do something for these poor bats, we really have to understand how the disease works. This is a way to look at how the fungus causes disease by turning off genes.

This will be a tool that can be used in other fungi as well. We think that it will be useful for a broad array of fungi, including plant pathogens and human pathogens and animal pathogens, so that people can understand those genes. Now a lot of fungi are also beneficial, especially in plants. It's another area

where we don't really understand always how that works. This tool could maybe be used in that too. There's broad applications for this tool, but we're just focusing on this particular fungus right now.

I like bats a lot, but it's the viruses I really love. I have a deep affection for viruses. In fact, I have a colleague who likes to say viruses make life worth living, and I have to agree with her. They're the most amazing, cool, biological entities on the planet, in my opinion.

Beth Bamford:

Thank you for listening to Reach, and a special thanks to Doctors Kurt Vandegrift and Marilyn Roossinck.

Cole Cullen:

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