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Chikungunya Virus: A Look at Prevention Strategies and Vaccine Innovations

Dr. Turck:

You're listening to *VacciNation* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss a novel vaccine for the increasingly prevalent chikungunya virus and how we can protect our patients traveling abroad is Dr. David Hamer. He's a Professor of Global Health and Medicine at the Boston University School of Public Health, and he specializes in infectious diseases with a particular interest in tropical ones. Dr. Hamer, welcome to the program.

Dr. Hamer:

Thank you very much for having me.

Dr. Turck:

Well, to start us off, cases of chikungunya have risen significantly in recent years, so what do we need to know about this disease, and what's causing these rising numbers?

Dr. Hamer:

Well, it's complicated. Chikungunya was first identified in the 1950s in an outbreak in Tanganyika, which is now part of Southern Tanzania, and it has occurred sporadically and over time; but really, I think around 2005, there was a focal outbreak in the Indian Ocean amongst some of the islands there, and since then, there have been sporadic outbreaks in India. In 2013, roughly, it came to the Western Hemisphere and caused a massive outbreak in Latin America, probably started somewhere in the Caribbean—we don't know exactly—and then spread throughout the Caribbean into Central America and South America, and then it sort of fizzled out, although it keeps flaring. When I say it flares, there's a large intense focal outbreak. Paraguay had one last year, and there have been a few smaller ones since then. Actually, Minas Gerais in Brazil had a fairly big outbreak earlier this year, and the context was sort of hidden within a dengue outbreak. We don't understand what causes it to flare like that and then fade away.

But the disease itself can be very nasty. It's a virus that leads to high fever, a lot of joint pains, muscle aches, but the joint pains are really prominent. Sometimes there's a mild rash, and then rarely neurologic complications may occur, but it's really the joint pains that are the cardinal manifestation, and these can be both arthralgias that we call them, technically sort of painful joints, but they also can be actual arthritis where there's tender, red, swollen joints. And the challenge is that this can be very disabling during an acute episode or acute illness, but then in a subset of people, this lasts for many months and can interfere with their ability to work, go to school, and their activities of daily living. And with time, we've learned that as many as 10–30 percent of people have arthritis that can last for several years, and that can be crippling and can really greatly interfere with the ability to do usual activities.

Dr. Turck:

Now as I understand it, the FDA approved a chikungunya vaccine not long ago, so how effective is it against chikungunya? And to which patients should we consider giving this vaccine?

Dr. Hamer:

So the FDA approved the first vaccine. There's another one coming that's probably another year or two away from being approved. This vaccine is a live attenuated strain of chikungunya vaccine. They allowed both of these vaccines to go through the approval process based on immune response, on the development of neutralizing antibodies against the chikungunya virus. So we know that this induces

very high concentrations of antibodies. We know in animal models that it protects against disease, but we don't have a lot of human data to show that it's going to protect humans. We think it will because we think that the presence of antibodies equates to protection from the disease, but because this disease tends to flare and then disappear very quickly, it's been hard to find a location to be able to do a randomized controlled trial to assess the protective efficacy of the vaccine. The company that developed it is working on that, and each time there's an outbreak, I think they want to try to get in early and see if they can use it to test the protective efficacy, but so far, we don't have data on how well it protects.

The ACIP came out with specific recommendations for use of the vaccine, and their key recommendation is to use it only if there's an epidemic of chikungunya. But then how do we define when there's an epidemic? Well, in some places, if there's one case, that's an outbreak because it just doesn't exist there, but other places have had intermittent disease, and so you really need to have a lot of cases to have an epidemic. And as of now, at least in the United States, the CDC says that they will be the ones to define where there's an outbreak and that the primary use would be for travelers going to a place where there's an active outbreak. The other group where they're recommending it is longer-term travelers, six months or more, to countries where there's been chikungunya in the last few years, especially travelers that are higher risk: older individuals or those with underlying multiple medical morbidities or underlying immunocompromising disorders. I think the tricky part is that we need good surveillance systems in place to be able to identify chikungunya outbreaks early so we can protect travelers to those locations with the vaccine.

Dr. Turck:

And as a follow-up to that, what kinds of adverse effects should travelers getting the chikungunya vaccine be aware of?

Dr. Hamer:

Yeah, I think like any vaccine, there's going to be some local site pain and tenderness and maybe a little redness or swelling, but those are usually relatively mild and transient. A subset of patients are developing arthralgias, basically painful joints, that can last weeks and maybe even months after the vaccine. Now that's only a limited number of cases in the trials that led up to approval of the vaccine, but because of this potential risk for a chikungunya-like syndrome, the FDA has requested that the company do a phase 4 study to assess the safety of the vaccine to see how common those sort of persistent arthralgias occur and whether there's certain groups that are at higher risk for that.

Dr. Turck:

For those just tuning in, you're listening to *VacciNation* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. David Hamer about chikungunya vaccination.

So in addition to this vaccine, Dr. Hamer, how else can providers better prepare travelers about the risks of chikungunya and other infectious diseases?

Dr. Hamer:

So chikungunya, like dengue, which is an even bigger risk in many parts of the world, is carried by mosquitos: mosquitos of the Aedes aegypti family primarily, but also Aedes albopictus, the Asian tiger mosquito. Basically, anti-mosquito measures are very important for travelers to be aware of to try and limit their likelihood of being bitten by a mosquito, and those include wearing long-sleeve clothing, which is, unfortunately, not always practical in hot, tropical, humid environments, and using effective insect repellents. And there's several different options that the CDC has recommended: DEET picaridin, oil of lemon eucalyptus, IR3535. There's several different options. Some of them have age restrictions, but most of them have very good safety profiles and are very effective at repelling mosquitos.

The other important part of this is that these mosquitos tend to be daytime-biting mosquitos. They're often active early in the morning and late afternoon, but they may be active during the middle of the day. This is in contrast to malaria-carrying mosquitos, which tend to be active at night. So really daytime anti-mosquito measures are very important for providers to emphasize to their patients.

Dr. Turck:

Now you mentioned another vaccine in development, so if we look ahead for just a moment, what additional research is needed to improve our understanding of chikungunya and its prevention?

Dr. Hamer:

One is we need to understand how well the vaccines prevent the disease. The other vaccine also is very effective at inducing neutralizing antibodies. It's a virus-like particle vaccine, so it's not an active vaccine; that reduces the safety concerns of persistent

arthralgias that have been seen with the first vaccine, but we need more information on that before it needs to go through the FDA review and ACIP review.

I think we need to better understand the factors that lead to explosive outbreaks of chikungunya, why they occur, and whether there's anything we can do to try and limit their occurring, and some of that requires good surveillance systems, which unfortunately, many low- and middle-income countries do not have in place. Higher-income countries do, and I say that because the tiger mosquito you can find all the way up in Massachusetts in the United States. It's worked its way into Ontario as well. It's moved up so that it's almost on the Canadian border and in Canada and several parts of the United States. It's also done the same in Europe, so it was introduced and then spread up from the Mediterranean, and you now find it in the Paris region and even north of Paris. And the risk is if you have somebody that has chikungunya and they're acutely ill and they fly into that country while they still have virus in their system and you have the right local mosquitos, you can have onward transmission. In the last 10 years, there have been increasing numbers of local outbreaks of both dengue and chikungunya in France and Italy and also a few foci in the United States, so one of my worries is that we need to understand how this is happening and have stronger surveillance systems in place so we can identify it and try and control these outbreaks before they grow.

Dr. Turck:

And before we wrap up, Dr. Hamer, is there anything else you'd like to share with our audience today?

Dr. Hamer:

Chikungunya can be a very devastating disease on an individual basis, and certain groups—actually, women seem to be more prone to have symptomatic persistent disease than men, older individuals, and so I think we need to understand more about who's at risk and really make a focus to make sure that population is most well protected.

Dr. Turck:

Well, with those final thoughts in mind, I want to thank my guest, Dr. David Hamer, for joining me to discuss the prevention of chikungunya infection. Dr. Hamer, it was great having you on the program.

Dr. Hamer:

My pleasure. Thank you.

Dr. Turck:

For ReachMD, I'm Dr. Charles Turck. To access this and other episodes in our series, visit *VacciNation* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.