This Week in Virology

with Vincent Racaniello, Ph.D. and Dick Despommier, Ph.D.

Episode 3: Dengue

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Vincent Racaniello:
I'm Vincent Racaniello.

Dick Despommier:
And I'm Dick Despommier.

Vincent:
How have you been, Dick?

Dick:
I've been well, Vince. Did you have a good week?

Vincent:
Have you built any vertical farms?

Dick:
No. In my dreams.

Vincent:
Beautiful day. No rain today.

Dick:
Nope.

Vincent:
What are we talking about today?

Dick:
We had a little rain yesterday, though, so that might have jump started a few batches of mosquitoes. Yes, I think so.

Vincent:
Weather is hard to predict, isn't it?

Dick:
It's impossible.

Vincent:
Dick, I know we are talking about Dengue today but before we do I found a new news item which we should discuss because it's timely. Every day I scour the internet for articles on viruses. Do you know what most of the returns are about? Computer viruses.

Dick:
Hah, hah, hah.

Vincent:
Some of them are about the viruses that infect you which is what we talk about on this podcast. Listen to this headline: Researchers link home foreclosures to West Nile Virus outbreaks. So apparently you know we are having a financial crisis. Everyone seems to know except John McCain. We can't be political in this podcast otherwise people won't listen to us. In California, a study was done. This is published in the journal called "Emerging Infectious Diseases," which is a publication of the Centers for Disease Control and Prevention and we'll put the link in the show notes for this. It's an article coming out in the November issue. The article is entitled "Delinquent Mortgages Neglected Swimming Pools and West Nile Virus, California." The idea is that when people lose their houses, the pools, the swimming pools, the Jacuzzis, and the ornamental ponds become polluted because they have fences around them and no one can get in to spray them. As it says here, as chemicals deteriorate invasive algal blooms create swimming pools that are exploited rapidly by urban mosquitoes. So they did a study in the swimming pools and so forth in California and found many mosquitoes carrying West Nile Virus. Are you surprised by this at all?

Dick:
Actually I'd like to invoke a Yogi Berra quote here if you wouldn't mind. It's dejá vu all over again. Well, because in 1999, the exact same thing happened in Northern Queens and people, because of the increased electric bills that they were getting, if they had the option they went on vacation. They went somewhere else where it was nice and cool. But they turned off their pumps, which filtered the water in their swimming pools generating an ecosystem for *Culex pipiens*, which is a pollution-loving mosquito, as we discussed. That was the jump-start for the initial outbreak in Northern Queens. Here you are talking about 2008 and under the heading "Lessons Unlearned" or "Lessons Not Learned," with the same scenario happens in another place. Now, do we have to reinvent this wheel for every section of the country before everybody understands that polluted water, hot temperatures, and urban mosquitoes have the potential for jump-starting outbreaks of West Nile Virus in people?

Vincent:
No. I think when people lose their homes there's not much they can do.

Dick:
No there isn't.

Vincent:
A law states you have to lock fence around the pool. People who are doing spraying can't get in to spray, so what should be done?

Dick:
Well, empty the pool for one thing. If you're not going to use it, empty it.

Vincent:
The people who leave should empty it?

Dick:
Of course, but that doesn't avoid rainfalls filling it back up actually again, but it certainly limits the amount of ecosystem available.

Vincent:

The problem, Dick, is that certain kinds of pools—gunite concrete pools—you can't empty them or else they'll pop out of the ground from the hydrostatic pressure so you need to leave some water in.

Dick:
Well, then I would [crosstalk] covering them.

Vincent:
Would that keep the mosquitoes out?

Dick:
Depends on how tight the cover is. They should be covered anyway to keep little kids from wandering into them.

Vincent:
No. They have a fence around them.

Dick:
The fence is there. Okay. I would say a tight-fitting cover.

Vincent:
Would the cover stop the algal blooms?

Dick:
Yes, because you're sealing off the sunlight.

Vincent:
Would that reduce the mosquito infestation significantly?

Dick:
If there aren't any food, they're not going to have a habitat.

Vincent:
Now listen to this statement here which you might find interesting. During 2008, many of the pools previously positive for *Culex pipiens* are now positive for *Culex tarsalis*.

Dick:
A look-alike species.

Vincent:
It says a more competent vector of West Nile virus. Meaning the virus is spread more readily in this vector, grows better?

Dick:
All of the above.

Vincent:
So a change in mosquito populations is also a problem.

Dick:
Right. As I mentioned before the strain of the virus has changed, so now you got a brand new species of mosquito implicated in the outbreaks and you've got a brand new strain of this virus in the outbreaks. I think this is proof positive that the creationists just don't have it right.

Vincent:
That's right. It is evolution right in front of our eyes.

Dick:
Exactly.

Vincent:
It's unfortunate when you lose your home, the last thing on your mind is to take care of your swimming pool.

Dick:
That's true.

Vincent:
There has to be some system put in place especially in warm climates where we can take care of the pools; otherwise, we are going to have more human disease.

Dick:
No question about it. So another way to solve this problem is to use a larvacide which is non-toxic to anything else and just physically blocks their ability to breed because the larvae have these little snorkels that they use to stick up above the water surface but they feed under the water. There are many, many different substances which are inert, basically, like oils, for instance, that you could make as a thin surface over the top which would completely eliminate the possibility of mosquitoes breeding in those places. That's another approach that I just thought of as we are talking

Vincent:
Of course, if you chlorinate properly the mosquitoes won't breed.

Dick:
Yes. They don't like chlorine because of the implications for the ozone depletions in the stratosphere.

Vincent:
Yes. People use that to sanitize the pool.

Dick:
But of course they do.

Vincent:
Maybe we could select for a chlorine-resistant mosquito.

Dick:
Also possible.

Vincent:
What's the larvacide consist of?

Dick:
Actually, the chlorine would be inhibiting the food of the mosquito, not the mosquito itself, I think.

Vincent:
Okay. It inhibits the algae growth? Algaecides and chlorine. Well, if you don't have money for your mortgage, you're not going to have money for chlorine and algaecide.

Dick:
Certainly, the local public health officials should realize this too and as best they can triage this problem and identify the hot spots in the neighborhoods. Now anybody with a pool, its seems to me, that's fairly affluent people as far as I can see.

Vincent:
Not necessarily.

Dick:

Well, I understand this. I think there's a lot of borrowed money out there that just had to come home to the bank and there was no way for them to pay it, so you're right. People living way beyond their means and diseases take advantage of this, don't they?

Vincent:
Yes. If the house is not going to be sold for a while I think you're right. It needs to fall into the purview of the Public Health Department which means another burden for them. More costs for them to put the pool on their list and take care of it.

Dick:
California happens to be one of those enlightened states that has maintained a Mosquito Control Board throughout the entire state. Every county has a Mosquito Control Board so I don't think it's going to be that much of a burden to be honest with you. I think the same is true for states like New Jersey. They have twenty-one counties in New Jersey and every one of them has a Mosquito Control Board. The need to invent a wheel isn't there for these two states. These are two of the shining examples of the way public health should work to protect the citizens from outbreaks and here's one of the things they need to get on the stick about. It's back.

Vincent:
It's very interesting, isn't it?

Dick:
Yes. Thanks for pointing it out.

Vincent:
Dick, do any of these mosquitoes in the swimming pools in California carry the virus of dengue fever?

Dick:
The answer is no.

Vincent:
Is it in the US at all?

Dick:
Yes.

Vincent:
Let's talk about dengue.

Dick:
Sure. That's another flavivirus. That's a nice segué.

Vincent:
It's related to the West Nile. It's the same family: Flaviviridae or flaviviruses, very well. Should we put a picture in the enhanced podcast?

Dick:
I think it would be essential.

Vincent:
Very good. What do we know about dengue?

Dick:
What we know about dengue is that it is carried by the same mosquito species that carries yellow fever.

Vincent:
Which is?

Dick:
Aedes aegypti.

Vincent:
Different from *Culex,* now?

Dick:
Correct. Much different. In fact, it's as different as living in an apartment versus living in a free-standing home with lots of water around it. When you compare the lifestyles of those two people they are totally different. When you compare the lifestyles of *Culex* species and *Aedes* species you've got two completely different breeding strategies and biting strategies and host preferences, and biology. In fact, if you were to really do a complete description of mosquito biology, you would say that virtually every species has a unique lifestyle. Some have commonalities like all of the *Aedes* species are temporary water breeders. But as we'll describe the biology of this mosquito and to show you how difficult without knowing what its life cycle is like to get rid of it. We mention the fact it does transmit yellow fever as well as dengue fever. This was the species of mosquito they needed to identify in order to complete the Panama Canal project. Without knowing where this mosquito breeds, you would continue to die from massive epidemics of yellow fever during the digging of this very important man-made structure. So it has a rich history.

Vincent:
In order to complete the canal it was necessary to have mosquito control in the region, in the Canal Zone. This was specifically for the *Aedes* mosquito.

Dick:
That's right. They knew it was mosquito-borne at the time but they didn't know which mosquito.

Vincent:
Who figured out what mosquito? Was that Walter Reed?

Dick:
It was Walter Reed but he had a lot of help from his gibbon friends.

Vincent:
How were the mosquitoes wiped out eventually, with DDT?

Dick:
Actually no. They were wiped out environmentally.

Vincent:
Environmental controls?

Dick:
That's correct. Once you know where these mosquitoes were breeding, in temporary bodies of water associated with discarded items like tin cans for instance that people were using, like K-rations, for instance. You'd open a can of beans. You'd eat the beans and throw the can away. This was the workers, all right? When it rained, of course, often in the tropics, these cans would fill up with water and then they would start to empty. When they are about half-empty, they start to give off an odor which attracts the white mosquito too, namely, *Aedes aegypti. Aedes aegypti* then, unlike *Culex*, lays its eggs near the edge of water. *Culex* lays their eggs on the water. Anopheles on the water. So the rafts of eggs are easy to identify. You don't see the eggs of the *Aedes aegypti* because they stick to the sides of the can, or the turned-over boat or the tire that's discarded. What happens as the water continues to evaporate the eggs dry out, so almost like freeze-dried eggs but they're alive.

Vincent:
They're preserved. Yes, they're still alive.

Dick:

Which is a miracle because everybody thinks of mosquitoes and water, with *Aedes aegypti* what they think about is the next rain. The first rain supplies the water level that they need to start with and then as the water evaporates the eggs just sit and they wait. Now when it rains again, if the rainwater exceeds the level of the eggs, the eggs are now submerged in water. They revive. They hatch. They know there's enough water to carry out their life because they judged how much water was there to begin with. They got enough water to complete about 1½ weeks' worth of biology which is what it takes to go from the egg to the adult.

Vincent:
Now in a jungle where there aren't cans or boats where would the mosquitoes breed?

Dick:
Well, the other name for this mosquito is "tree hole-breeding mosquito." There are tons of tree holes. Birds make holes, like woodpeckers and hornbills and all these other wonderful tropical birds. Not necessarily woodpeckers, but hornbills and other animals also burrow down into the bark of trees and make their nests there. When they abandon them after the breeding season, these become breeding sites for *Aedes aegypti*.

Vincent:
So during the construction of the canal, these were presumably the problematic sites. Then as workers moved in they left their cans around and that added to the problem?

Dick:
No question.

Vincent:
They got rid of the cans by diligence. What about the tree holes? Did they have to address those as well?

Dick:
They did not in fact. All they had to do was police the area. It's essentially the same problem, we just pointed out for West Nile in California. If you police the area and look for the breeding sides and you identify them, the best approach is to eliminate the environment rather than spraying or vaccines and stuff like that. It was actually quite simple once they determine which species of mosquito was at fault here. There were some tragedies associated with determining that which violates current IRB regulations.

Vincent:
IRB is Institutional Review Board.

Dick:
There's a lot of unethical—we would consider it unethical behavioral now—by actually subjecting human beings to clinical trials where mosquitoes that were deemed yellow fever-free were allowed to feed on patients suffering from yellow fever and then each species of mosquito was allowed to feed on a group of volunteers. Some of those volunteers actually went to medical school here, Vince, here at Columbia University.

Vincent:
Yes. Some of them were also scientists who subjected themselves to and they died. Didn't Clara Maass died from such experiment at least being bitten by an infected mosquito?

Dick:
That's correct.

Vincent:
So it's the same species of mosquito that carries dengue virus?

Dick:
It is.

Vincent:
Should we worry about dengue in the US?

Dick:
Well, it depends on how much you like to worry. We've had outbreaks in the southern part of Texas in recent past. There are sporadic outbreaks. They are not permanent outbreaks. We used to have dengue fever here a lot.

Vincent:
Maybe we should say first what dengue fever is. What does "dengue" mean, the word?

Dick:
I wish I could tell you.

Vincent:
Is it the name of a city?

Dick:
I don't know the origin of that. I'm sorry.

Vincent:
Well, we'll have to look it up. We'll put it on our show notes.

Dick:
Does anyone out there know what the origin of dengue is? It's probably a place because most viruses are named after the place they were first isolated from. You can do this for Hantavirus. That's the Hantan River in Korea. You can do it for Ebola. That's a town in West Africa. The Lassa…

Vincent:
Now how do we get to yellow fever, Dick? Because you look yellow when you're jaundiced, when your liver is infected, right?

Dick:
Correct. That's exactly right.

Vincent:
There are two kinds of dengue. There are four serotypes. In terms of disease, right.

Dick:
There are just the two kinds.

Vincent:
So there are four serotypes of the virus, which is important. You need antibodies against all of them to protect you. There are two kinds of illness. Tell us about that.

Dick:
Well the first kind is a fever, obviously, that's created by a viremia that you develop but it's usually a mild fever followed by what you would call "arthritic like syndrome."

Vincent:
Joint pain.

Dick:
Yes. The name for this is "breakbone fever." You feel as though your joints are going to come apart and you are in pain constantly throughout your whole body. It lasts for about two weeks. Then you recover and you are all better. That's disease number one.

Vincent:
That's called "dengue fever," is that correct?

Dick:
That's dengue fever. Then there's another form of this which is the most unfortunate form of this. It's the lethal form called "dengue hemorrhagic fever."

Vincent:
Okay, DHF, as it's referred to in the literature.

Dick:
That's exactly right. It's usually associated with dengue strain number three. And they've had lots of deaths from this thing. It usually is a disease of children and young adults. It's very unfortunate because when you encounter that particular strain of dengue virus, not only do you get the breakbone fever-like syndrome, you also develop hemorrhagic lesions throughout your body and eventually you bleed to death. That is a very horrible disease indeed.

Vincent:
So apparently being infected once increases your chances of developing haemorrhagic fever on a second infection?

Dick:
So the literature suggests.

Vincent:
We don't really understand the mechanism of that at all?

Dick:
We do not. I think anybody listening to this would wonder - there's a great vaccine already for yellow fever—and that's a flavivirus. In fact, I think it's one of the best vaccines that's ever been devised. Dengue fever seems to be related very closely to yellow fever. Why don't we have a similar vaccine for dengue fever that we have already for yellow fever? Why haven't we been able to reengineer the yellow fever virus with the missing parts from dengue virus to allow a super-virus to be created that covers yellow fever, dengue fever? We could even make one for West Nile because that's related too. What's the stumbling block on this thing do you think?

Vincent:
Well, I think it is being worked on. One of the issues is that preexisting immunity is not protective against hemorrhagic fever. The vaccine has to protect you against all four serotypes immediately because if you were inoculated and only developed immunity against one, then you would have a high risk of getting hemorrhagic fever especially in areas of the country where mosquitoes prevalent. You could be infected within a week of being immunized, for example.

Dick:
As an interested listener from last week's program, I learned that there are three different strains of polio and we've got a vaccine against all three. So here's just one more to add on to that. Why haven't we done that?

Vincent:
Well, in the case of polio, when you're infected with one serotype and then you're subsequently infected with the second, say, there's no increased risk of a more severe disease or a disease of another kind, as there is with dengue. It's a very unusual pathogen in that the second infection seemed much worse than the original. That is a bit frightening in terms of a vaccine, which is not to say there is not research going on. It's quite active. As you know, huge numbers of people, we're talking about, [are] infected and susceptible to dengue in the world.

Dick:
Exactly. So that raises the question of where do you find dengue?

Vincent:
Where do we find dengue?

Dick:

Where could you possibly travel to avoid dengue, first of all. I would think dengue fever classifies as one of those true tropical diseases. If you look at the distribution maps that the Centers for Disease Control and Prevention have on their web sites you see that this is a disease that centers around the equator

Vincent:
South of the equator?

Dick:
That's around the equator, actually. If you draw the equator and go above and below it, you've got about equal numbers of cases above and below it.

Vincent:
Where's the equator there, Dick?

Dick:
On this map it goes right through Brazil.

Vincent:
Okay. Yes, I see.

Dick:
The point is that here we have a tropical disease but it's being introduced into subtropical regions. The southern part of the United States is classified as a subtropical region. We have *Aegis aegypti* within the continental United States, as we speak, although as we just discussed, if you just police up the area and get rid of these temporary standing bodies of water you can greatly reduce the incidence of mosquito; however, there is a little nuance here that we need to discuss. That's another species of *Aedes* that's been introduced recently into the United States which has become a competitor species for *Aedes aegypti* and that is *Aedes albopictus*; otherwise know known as the "Asian Tiger mosquito." This brings us to a very interesting point in terms of environmental control. How did Aedes albopictus get introduced into the United States, do you think?

Vincent:
In tires that are filled with water?

Dick:
That's correct and where did those tires come from?

Vincent:
Somewhere else.

Dick:
Correct. Why were they being brought to the United States?

Vincent:
I don't know why we're importing tires. I thought we sold tires.

Dick:
Yes, we do. We do, actually. If you were a tire maven and you live in a place where you can set up an industry of recovering old tires and turning them into new tires, then you can reestablish the tire industry in any place you want. So the United States, it turns out - and this is what the interesting part of infectious disease is for me - it shows you how interconnected everything it is and it tells you about human behavior as well. The United States sends huge numbers of worn-out tires to Japan. Japan then retreads the tires and then sends them back to the United States for resale. Now you might want to ask why don't we just retread these tires ourselves? If we did, of course, then we would have avoided the introduction of a temporary body of water breeding mosquito, namely, *Aedes albopictus*.

Vincent:

Where was the origin of the Aedes albopictus? Asia?

Dick:
Japan. We know this. Because, why? Because you can do the genetics on the mosquito and, because there are varieties of species, you can pin down exactly where this mosquito came from and it came from Japan.

Vincent:
Albopictus is all over the US now, is that correct?

Dick:
So it is. *Aedes aegypti* isn't.

Vincent:
You mentioned that *albopictus* is a competitor of *aegypti*. Does that mean that it is driving out *aegypti* from parts of the United States?

Dick:
It actually does. Now you've got an ecological setting for measuring whether or not *Aedes aegypti*, the older tree-hole breeder can outbreed and introduce the new species that requires the same niche. So an ecological concept that's worth keeping in mind here is that no two different species can occupy the same niche and here's proof positive.

Vincent:
It's sort of like matter, right?

Dick:
Yeah. You have energy or you have that energy, both at the same time, that's right. What you have here is—we're fortunate, by the way, that *Aedes albopictus* has been introduced and has pushed out *Aedes aegypti*, because it's not as competent a vector for dengue. So now you have an advantage of having *albopictus* hanging around. However, it's a much better vector St. Louis encephalitis, for Lacrosse virus and maybe even perhaps for West Nile because those are other flaviviruses that are ordinarily found in the environment where the mosquito now lives. So we still have a worry but it's not as severe if we were worried about dengue.

Vincent:
The reason that dengue is sporadic in the US is that it's imported in some way, probably in a tire or travelers. It spreads a bit, but then it burns out because it's not carried well by the mosquito population.

Dick:
That's correct. So there's a big lookout for *Aedes aegypti* and there's a recent lookout for *albopictus* as well, and that's when they discovered that all these old breeding sites for *aegypti* are now breeding sites for albopictus.

Vincent:
Okay. Now why in countries near the equator, why is it persistent? Why is it endemic in these areas? It has to do with the fact that there are so many mosquitoes they breed so well in these regions?

Dick:
One is that. Two is the presence of humidity all the time and temporary rain. It rains almost every day in the tropics during the rainy season and then in the non-rainy season it rains sporadically. Now, just after the rainy season is when you'd expect dengue outbreaks not during the rainy season, after rainy season because the water has to dry down a bit. They lay their eggs around. Then it rains again and back up they come. I want to tell you about one introduction which I think I mentioned the first time we talked of dengue fever. It was in Bangladesh, of all places. In Bangladesh, prior to the introduction of dengue fever back in the 1990's, they had none. You wonder how a country so unfortunate to have so many endemic infectious diseases had avoided

dengue fever. The fact is that they had none, and then something horrible happened. A cyclone came through and cyclones in the northern hemisphere have a counter-clockwise rotation. What this cyclone did was it picked up *Aegis aegypti* from the Malaysian peninsula and dumped it into Bangladesh. From that point on they've had endemic dengue fever in Dhaka.

Vincent:
Yes. as we talked about that spreading West Nile after a hurricane in the US.

Dick:
That's right. Hurricane Floyd. That's exactly right.

Vincent:
Now I'm looking at a chart here: "Dengue since 1955," which is a very nice article which I'll post the link too on the web site. In the 1950's less than a thousand cases globally and then suddenly increasing to where we have almost a million cases a year in over fifty countries. What's the reason for that? Why the increase? Is it the tire trading increasing essentially spreading the mosquito?

Dick:
A lot of international trade. A lot of container shipping. They invented this Sea-Land system.

Vincent:
I see.

Dick:
The Sea-Land, you know it's…

Vincent:
Massive shipping of tires.

Dick:
That's correct. That's exactly right.

Vincent:
Okay. Previously, in the 1930's, actually, there was quite a bit more dengue especially in South America. I'm looking at another map from the same article.

Dick:
It remained endemic in that area.

Vincent:
Then concerted eradication efforts to get rid of the vector, the mosquito.

Dick:
I can speak about that in a minute, too, because they didn't just tried to get rid of the *Aedes aegypti* mosquito but they were really trying to get rid of *Anopheles gambiae*. That was an introduced species from Africa.

Vincent:
What's the problem with *Anopheles gambiae*? What is it carrying?

Dick:
That is the world's best vector for malaria.

Vincent:
Malaria, okay.

Dick:
So long as they were getting rid of that one, they elected to get rid of this one too and they got two for the price of one.

Vincent:
We should point out that malaria is not a virus but it is a parasite.

Dick:
That's correct. It is a protozoan.

Vincent:
One of the biggest infectious disease on the globe.

Dick:
More people have died from that one than all the wars put together.

Vincent:
That effort ended up reducing dengue by 1970 and then it reemerged because of the tire trade.

Dick:
That's right, another trade too. I would say the breakdown of the public health systems in countries that were in conflict with—civil unrest and war and the drug trade, the illicit drug trade, I should say. These are ways of introducing things throughout the world that we are not in great control of unfortunately.

Vincent:
According to the World Health Organization there are 50 million dengue infections globally every year: 500,000 cases of hemorrhagic fever and 22,000 deaths mainly among children. The number at risk is in the billions because many people have been infected already once. The number at risk, I should say, for hemorrhagic fever is in the billions. This is obviously an urgent problem that needs a vaccine or some other approach. There is a lot of research on this. Now why is it mainly in children? Do you know?

Dick:
Well, these little kids are outside all the time. They play in the environment where the temporary bodies of water are.

Vincent:
They get bitten.

Dick:
That's correct. They're easy victims.

Vincent:
This brings up a thorny issue. There is some research on dengue in the US, but since it's not a problem here maybe there is not as much as we should need, correct?

Dick:
Well, you are right and you are 95% correct. There is a group down in Galveston, Texas. They are the remnants of the Arbovirology group that was originally at Rockefeller University, moved to Yale University, and then finally relocated down in Galveston when the offer was made thru the University of Texas. They've had a remarkable success rate down there. They were the ones that identify the first outbreaks of dengue within the United States just before 2000. It was about 1999, 1998 that they had their first outbreaks. They worry about it periodically being introduced and it is being driven by weather events.

Vincent:
Do you think it would be safe to say that at some point in the near future that we will have more dengue in the US?

Dick:
Sure. Look what happened in Galveston just recently. A hurricane that went through, hurricane Ike, caused the complete evacuation of the city. They weren't allowed back in there for two weeks. All of that water just sat around and attracted who?

Vincent:
Mosquitoes.

Dick:
There's no question about it. As a result it altered the ecology. Try to clean up after a hurricane sometimes. See what that's like. I know. I have some personal experience. I'm from New Orleans originally so I went back after Katrina to try to do some work during our spring break the year afterwards. All I ended up doing was demolishing a home down in Chalmette. To see the devastation that something like that can bring to an entire region is just absolutely depressing. Of course, even with maximum help that you get from government agencies, in this case, we had none. In other cases, for this latest outbreak of the hurricane that swept thru and hit Galveston, there was lots of aid and lots of programs in place and still you can't prevent these things from devastation. Disease outbreaks are just part and parcel of this. Now imagine what it would be like if you lived in, let's say, south Asia like the southern part of India, for instance, and a cyclone comes through there as happened when the tsunami hit and then afterwards. Now you've got breeding sites, and people that are disoriented, no public health in place, no vaccines, no drugs, no water. You've got outbreaks of salmonella. You've got outbreaks of vector-borne diseases of various kinds. It's a horrible, horrible, legacy.

Vincent:
Perhaps the hurricane in Galveston is the beginning of the real establishment of dengue in the US. Who knows? We'll see in the coming weeks and months perhaps we'll begin to see some infections there.

Dick:
Do you know what the tropical disease people say about the best control measure for tropical diseases?

Vincent:
What's that?

Dick:
Winter.

Vincent:
Yes. In Texas the winter isn't terribly severe.

Dick:
They can get snow down there.

Vincent:
It's cold enough to keep the mosquito but mosquitoes over winter as [crosstalk]. So that's the problem, they never go away.

Dick:
Another feature of this is the same for all the flaviviruses. These are vertically transmitted as well as horizontally transmitted. By that, I mean the mosquito eggs from infected adult mosquitoes can have the virus.

Vincent:
Yes, and then the next mosquito born will have the virus.

Dick:
So why don't these viruses kill the mosquitoes?

Vincent:
They've evolved in the mosquito for many years and they're exquisitely adapted. That's the ultimate strategy: to grow in a host without killing it.

Dick:

Yes, these are sneaky little beasts.

Vincent:
Is there another host for dengue besides mosquitoes and humans? Are there any other animals that harbor it?

Dick:
No. I think we're fortunate in the sense that dengue does not have reservoir hosts

Vincent:
That may make it more difficult for it to become established in the US where we have a winter that really dampens the mosquito population.

Dick:
This is one of the few exceptions though. The flavivirus group, in general, have lots of reservoir hosts including yellow fever. They've got monkey host. That's the way we introduced yellow fever from the jungle back into the human population. Whereas dengue fever, as far as we know, there are no reservoir hosts except - we're it.

Vincent:
The *albopictus* mosquito is not terribly good host for dengue but the virus could change so that it could adapt to this mosquito so that it is a better host.

Dick:
Yes. If we're unlucky enough to have an introduction of dengue in an area which has been displaced by *albopictus* and they are the recipients of this virus rather than *aegypti*, you could very well see a new version of this in the future. So emerging infections…

Vincent:
Well, that's what might happen in Galveston. *Albopictus* is already in Galveston, correct?

Dick:
Oh, yes. It's all over the sites.

Vincent:
So maybe we'll see more infections in the coming month. Now last thing perhaps we can talk about is climate change and dengue. What is the story with that, Dick? I have another picture and this lovely article, "Will Climate Change Affect the Spread of Dengue in Coming Years?"

Dick:
I presume the answer is "yes."

Vincent:
It seems to be getting warmer.

Dick:
So let's take two factors from mosquito breeding that are absolutely essential and that is temperatures above freezing and water You got to have both of those things. So as the rapidity of the climate changes, I think we worry about not climate change but the rapid climate change. So by that if I were an *Aedes aegypti* mosquito I'd be overjoyed at what's happening right now. I'd be absolutely jumping out of my six little legs trying to figure out how best I can grow myself in terms of the advantage that nature is now offering me. The advantage is that there are places throughout the tropics that will receive more water and therefore more rain events and therefore more breeding sites will be available for a longer period of time and those areas will be warmer. So that my breeding season will be longer. Now, in the tropics itself that's not a problem because the temperature never goes down below a certain level. As the tropics extend itself both towards the Tropic of Capricorn and the Tropic of Cancer, you can understand now the zone of tropics now increases. This is a tropical disease, a tropical disease. As the tropics increases, so do their diseases. Dengue is not the only thing to worry about here. There's a lot of other things out there waiting for us.

Vincent:
Sounds like I should work on dengue virus.

Dick:
Well, if you could find a cure or at least a vaccine for hemorrhagic fever I would be shaking your hand.

Vincent:
You know what the problem is, Dick? There's not a good animal model for haemorrhagic fever to do experiments in. A small animal in which you can infect and get the same kind of disease that we see in people just doesn't exist. If someone could make that, it would help a lot.

Dick:
What would be the steps that you would—let's say you are starting from scratch here. You know nothing about dengue. You know nothing about the vectors and you know nothing about its replication cycle. What would be your first questions to ask to develop an animal model?

Vincent:
Well, I'd like to use mouse because a mouse in the laboratory is very convenient. Try to get the virus to grow in mice.

Dick:
Why don't you think it can grow now?

Vincent:
Well I think it can grow in certain strains but it's not a very typical infection. The receptor may not be present for the virus. There may be other proteins inside the cells of the mouse that are not appropriate for dengue replication. You really need to understand better what the virus needs and what's missing in a mouse and that could take some time but its research worth doing because if you can get the virus to infect then perhaps you can start to work on getting the hemorrhagic fever part duplicated.

Dick:
Have they identified at least in human cell lines the receptor that the virus uses to get in?

Vincent:
Yes, the receptor is known. It's certainly present in mouse cells so there must be other blocks to infection besides the receptor.

Dick:
Once it gets in.

Vincent:
Once it gets in, yes. But I have never worked on dengue as you know. I work on picornaviruses. It is a fascinating virus. It's very important. The number of potential people who could get sick from this virus is huge and it certainly warrants more research than we do at the moment.

Dick:
Would you need a special lab to work on this, do you think?

Vincent:
No. I could work on dengue in my laboratory. The containment that we have, we could use—we could work on dengue.

Dick:
I happen to have been associated with the gentleman at the University of Notre Dame who actually championed the genetics of *Aedes aegypti*. His name was George Craig. George Craig actually has a book that he used as his foil written by a guy by the name Christopher. It was the complete biology of the *Aedes aegypti*. In this book, believe it or not, there was the blatant statement that there are no mutants of the *Aedes aegypti*. Right, exactly. Here was a whole book

about the biology and right there in print said, “There are no mutants. Don’t worry about looking for them.” So George Craig knowing this and laughed at the statement enlisted a bunch of his undergraduates at the University to look for mutants just like they did for fruit flies at Columbia. That's where genetics began. We sit at the seat of the beginning of modern genetics, right? So they used fruit flies first. Then George Craig picked up *Aegis aegypti* and son-of-a-gun if he didn’t find tons of mutants, of course.

Vincent:
Of course. There's always mutants.

Dick:
Yes. So the point is that every time you went up to George Craig’s laboratory you made sure you had your DEET with you because some of those escapees, they would feed on the students. That’s why I was asking you about a special laboratory. If you ever decided to do this for vector competency you’ll need a P2 facility.

Vincent:
For working with mosquitoes then you need more but just for the virus itself. So if I'm an American traveler and I'm going to a tropical zone should I worry about dengue? Yes. If so, what can I do to prevent being infected?

Dick:
Well, all you do the same thing that you do to prevent yourself from being infected with malaria from another vector that feeds. All right, you have to know the feeding zone for this mosquito. You have to know the time during the day or night that it feeds. Most malaria vectors feed at night. This is a day-feeding mosquitoes, so how do you avoid being bitten by a mosquito, period? You smear DEET all over yourself and hope for the best.

Vincent:
If I go to San Paolo, Brazil, in the city walking around do I need to take precautions?

Dick:
It depends on the season. All right, these are seasonal outbreaks. If this is during the rainy season, no; if it's just after the rainy season? Absolutely. That’s the absolute critical time for this. So you have to know what's going on there. So therefore surveillance is everything. You have to check with the local health authorities. Now how could you do that? Go to the CDC site.

Vincent:
They have information on the diseases.

Dick:
They do. They have a sort of like an emergency line or a hot line that you can call. You tell them where you are going and the next thing you know they’ll say, “Well, we have no recent reports of outbreaks from there.” By the way, just as an aside, wouldn't it be great if some service like—let me think—like Google has Google Disease Earth?

Vincent:
Absolutely.

Dick:
You have a big menu on one side. You have the globe on the other side. You click on dengue fever and all the hot zones light up as recent as yesterday. Then you can zoom in on the city and find out where they isolated the mosquito. Wouldn’t that be a great service?

Vincent:
Fabulous. They have Google Earth already which has photographs of the whole globe. That would be very good to integrate this with it. I think they are very interested in doing this already. I'd be interested in being a part of that though.

Dick:

Yes. So would I actually.

Vincent:
OK, so anything else you like to say about dengue, Dick?

Dick:
No. Just that it will continue to be a problem and we should pay attention to it. So have you thought about next week's topic?

Vincent:
I haven't yet. We'll have to surprise everyone because there's so many things. We may just do news things because there are plenty of virus infection in the news, but there are many things we can do.

Dick:
I'd like to discuss rabies next time if that's possible.

Vincent:
We could do rabies. You know why I'd like to discuss rabies? Actually, on Sunday, the New York Times, there was a short article about an outbreak where some people ate an infected cow. So we'll talk about rabies. Great idea, Dick! What a pair!

Dick:
Hey and everybody out there I'm not a virologist. Vince is.

Vincent:
Dick is a smart guy. That's why he is here. I don't know why I'm here. Send us your questions and comments to twiv@twiv.tv. Subscribe in iTunes. We're on iTunes now. Thanks for listening. See you next time.

Dick:
Okay. See you, Vince.

Transcribed by Jim Vandiver, corrections by Raphael Fernandez, MD.