

This Week in Virology

with Vincent Racaniello, Ph.D. and Dick Despommier

Episode 1: West Nile virus

September 12th, 2008

<http://www.twiv.tv/2008/09/24/west-nile-virus/>

Vincent Racaniello:

This is "This week in Virology", episode 1, September 12th, 2008. We're going to talk about West Nile virus. I'm Vincent Racaniello, I'm here with Dick Despommier, my colleague here at Columbia.

Dick Despommier:

That's right!

Vincent:

And we're going to tell you about West Nile, but first let's tell you about what "This Week in Virology" is, or "TWiV", do you like that abbreviation?

Dick:

TWiV is very good.

Vincent:

T-W-i-V.

Dick:

Yep!

Vincent:

We hope to have it out on a weekly basis to teach you about viruses, and how they make you sick.

Dick:

Exactly!

Vincent:

Does that sound like a good goal?

Dick:

Yeah, it does actually!

Vincent:

Alright. So, I am a Virologist at Columbia University, whatever we say is our opinion and not that of our employer.

Dick:

That's...

Vincent:

Correct?

Dick:

I believe that's true.

Vincent:

Alright. So I'm a Virologist at Columbia, and Dick where are you?

Dick:

Well, I'm also at Columbia!

Vincent:

[laughing]

Dick:

I'm in two places, actually. I'm with you part of the time in Microbiology, but mostly I'm in the School of Public Health in the Department of Environmental Health Sciences.

Vincent:

Are you a Virologist?

Dick:

I'm not a Virologist, actually.

Vincent:

What is your training?

Dick:

My training is in Parasitology. So, if you wanted to know what a parasite was, I would have to tell you that a parasite is any organism that can take advantage of another organism, to derive what it needs from that organism. And I don't mean predator-prey relationships, you know of lions and gnus, I mean a small organism taking advantage of a large organism. A typical example are head lice. Head lice are considered parasites because they are permanent residents in your hair, they don't always feed on you but when they do feed, they need what you have. So they take away from your... let's say biological mass in the way of sucking blood and they use that for their own metabolism and to make more lice.

Vincent:

Sounds a bit like a virus.

Dick:

Sounds a little bit like a virus, but viruses are parasites too!

Vincent:

They are parasites. What would be the one big difference between a virus and your parasites?

Dick:

Well, you know if you took a louse off my head, which I don't have by the way, because I'm sort of missing a lot of hair... [laughing]

Vincent:

[laughing]

Dick:

But if I had head lice you could actually pick one off and put it into a Petri dish and you could manage to feed that probably and it could make it on its own. If you took a virus particle, right..., out of a cell, and threw that into a Petri dish with everything you thought it needed, you're gonna still have some problems I think.

Vincent:

That's correct. A virus can't do anything on its own. It's the ultimate parasite.

Dick:

That's it.

Vincent:

It absolutely requires a cell in which to grow, in contrast to your parasites.

Dick:

My parasites are bigger than your parasites, but nonetheless...

Vincent:

Exactly, another defining feature of viruses: they're very small.

Dick:

Yep!

Vincent:

Completely dependent on host cells.

Dick:

Exactly.

Vincent:

So viruses are not living.

Dick:

Nuh uh.

Vincent:

Are parasites living?

Dick:

Well.... depends on how you define that term, doesn't it? [laughing]

Vincent:

Something living is able to reproduce itself in some way, so a parasite fits that definition.

Dick:

Parasites can do that... I mean we can get some parasites to reproduce *in vitro* as we call it, that is apart from the host, but for best reproduction, they still need their host species in order to reproduce, so there's a fine line that you can draw between absolute requirement for a host cell let's say for example for a virus, and the almost host requirement let's say for *Rickettsia*, that you can grow *in vitro* sometimes...

Vincent:

Yes.

Dick:

And then into the bacterial species that cause disease which don't require the host at all unless you, uhm... think about things like maybe Cholera for instance. Cholera is very difficult to grow outside of where it lives, but there are other organisms which we catch on a regular basis that can easily be grown outside, right? But then as you move up that scale and get into the protozoans, those are single cells with true nuclei, it becomes difficult again to grow these things, and we've had to work long and hard to produce things like the causative agent for maybe Dysentery for instance, and *Giardia*, uh... we've mastered Malaria we think, but it's still very difficult to get a lot of them to grow without the host, I think it's best to have a host, so everywhere you look at the relationship between the parasite and the host you have dependencies, alright, that are created by the biologies of these two organisms. I wouldn't call a virus an organism but anything up from that we would call an organism.

Vincent:

A virus is a chemical, isn't it?

Dick:

Yeah, it's a collection of chemicals, organized chemicals.

Vincent:

A quite complex chemical, on its own it can't do anything, but when it enters a host, it then can reproduce and cause problems as is the case for our virus today.

Dick:

That's right.

Vincent:

Now, this is why you're uniquely qualified to talk with me about viruses because what you worked on were similarly parasitic....

Dick:

Sure.

Vincent:

....and so the concepts are very similar. Do you work on parasites anymore?

Dick:

I do, but I do some work on their ecology rather than on the worm that I used to work on, or the West Nile virus, in fact I never worked with viruses in my life, but I'm aware of the environmental situations that are necessary for their transmission. So I've concentrated more on the environment that they exist in, rather than the Biology of the organism itself.

Vincent:

Is that important?

Dick:

Well... it is actually, it's extremely important... [laughing]

Vincent:

[laughing]

Dick:

... in fact, if you're not aware of the conditions under which these things are transmitted from person to person then you have no public health measure whatsoever to intervene with their life cycles.

Vincent:

So this is what you call Medical Ecology, is that correct?

Dick:

This is my definition, that's correct.

Vincent:

Perhaps that would be the topic of another "This Week in Virology".

Dick:

Yeah!

Vincent:

Especially how the Ecology influences virus infections.

Dick:

Absolutely.

Vincent:

It would be very interesting.

Dick:

You bet.

Vincent:

Now you've written a book, "West Nile Story".

Dick:

I have.

Vincent:

"A New Virus in the New World."

Dick:

That's right.

Vincent:

And why did you write this book?

Dick:

Hah hah hah!

Vincent:

[laughing]

Dick:

Well, there are many different reasons.

Vincent:

You did it to get rich. Ha ha!

Dick:

Yeah sure, and you can see how well that worked!

Vincent:

You have a very fancy office here.

Dick:

Ah yeah, but I'm not paying the overhead for this one probably. [laughing]

Vincent:

[laughing]

Dick:

I think the reason why I wrote the book was because I had some down time basically between my research projects and the virus infection had just blossomed in this country. In fact, before it came here I was totally unaware of the fact that there was a West Nile virus. Why would we have ever heard of this unless... it's a parasite in our own local area. So in fact, in this book that I've written you'll learn right away that we thought it was something else first, and we thought it was something that we do have in this country, namely the La Crosse virus, which is a relative of the West Nile virus, but it is not the West Nile virus.

Vincent:

So today, West Nile is all over the U.S....

Dick:

It is!

Vincent:

...West Nile virus. But originally it was not, before what year?

Dick:

1999.

Vincent:

And what happened in 1999?

Dick:

Well the summer of 1999, which..., we'll get back to this in our second presentation, was the hottest, driest summer on record for 100 years in New York City. Ah, it was also the year of a major outbreak of West Nile virus infection in Israel. And there's another book out, which I wish I'd written but I didn't, called "The Perfect Storm"...

Vincent:

Hmm.

Dick:

And in that book you can read what did in these Sword fishermen that ventured out too far and stayed out too long. Uhm, all of the storms came together at the same place and they lost their lives as a result of this. So if you create scenarios for outbreaks of disease, whether they're

infectious or not infectious, and you understand the conditions under which they arose, you can then rewrite that book and call it "The Perfect Storm for...". So I could have actually rewritten this book and called it "The Perfect Storm for West Nile Virus". Why was 1999 the perfect year for this virus? It turns out that there are a tremendous number of coincidental events which conspired together to allow the virus to escape from its Israeli origins, which, that's not where it's originally from, but that's....

Vincent:

Where is it from originally?

Dick:

Originally it's from the West Nile district of Uganda...

Vincent:

Ok.

Dick:

... that's why it's called the West Nile virus. It was originally mistaken for African sleeping sickness, which is in my Baileywick of parasites, that's a true parasite, that is to say, it has a true nucleus, and it's got a flagellum, and it's got a body, and it causes sleeping sickness, it's transmitted by the tsetse fly. The guys who originally were in Uganda looking for other cases of sleeping sickness, encountered this infection instead, and thought it was sleeping sickness until the patients developed further symptoms. And as a result of that they could distinguish it at least on a clinical basis from something that they already knew about. So they thought this was something new, so they took the blood back into their laboratories in England, and what they discovered was that they were dealing with these new filterable agents that we now come to call viruses. Uhm, the next time we heard about this was in the 1950s, in the Middle East, all throughout the Middle East, particularly in Israel, particularly in Palestine and even in Southern Russia, throughout the Mediterranean, now that we learned how to look for it, actually we're looking for the evidence that it was there, I guess we're looking for antibodies now, these were the newer technologies that were evolving through the 50s and 60s to look for evidence of infection, and the moment we could detect antibodies against the West Nile virus in patients' sera, we could then do what they call serosurveys and we could then look in places where we suspected the virus to be, but weren't sure, and if someone has an antibody titer - that is the amount of response that a patient engenders against an infectious agent - it's measured by the level of antibody molecules in their serum. Uhm, when you start using that technology to ask whether or not West Nile virus was there or not..., it's a pretty accurate way of measuring the presence or absence of an organism, other than trying to demonstrate the organism itself. So when they did serosurveys in Spain and Italy and France and the Camargue for instance, they found evidence that people had already encountered this virus infection, they got sick, or didn't get sick, maybe they were just infected, and then they got better. And so what's left afterwards are the antibodies that you can now detect and you use those to sort of paint a broad picture of where this organism really lives, and where..., by the way, we haven't mentioned this yet, but this is a mosquito-transmitted infection...

Vincent:

Yes, right.

Dick:

...so it also tells you where the mosquitoes live and what their biting habits are, what their feeding habits are, so you learn a lot by just investigating a little fact and it takes you through this maze of scientific investigation until pretty soon you've described an entire culture.

Vincent:

So before 1999 had there been serological surveys done in the United States looking for this virus?

Dick:

There was no reason to do them, so the answer is no, but the moment we discovered what this organism really was, rather than being La Crosse virus, which we thought it was because, again, I have to describe something about antibodies, and so the listeners that know about this already will forgive me for simplifying the concept, but if you have three similar objects and each one happens to be called an antigen and you inject all of those into the same person, you will get antibodies specific for each of those three antigens, and if they're very similar, uhm, you will get a mild cross reactivity of antibody A against antigen B, and antigen A against antibody C. All those antibodies that are not directly against A, could still react with the antigen A if the antigen is very similar. Now there's a group of viruses that fall into that category, they're called the Flaviviruses, that's a Greek word for "yellow", and indeed it's derived from the concept of Yellow fever, and Yellow fever is the biggest virus that's part of this group.

Vincent:

Biggest in size, or...

Dick:

Biggest in terms of clinical significance.

Vincent:

Ok.

Dick:

... that it takes more lives away, almost, than Malaria in some cases, it's the thing that prevented the establishment of the Panama canal before we found out how it was transmitted...

Vincent:

Right.

Dick:

So Yellow fever we all know about. And the..., well we know about a few others too. Dengue fever is another virus-like infection, which uhm, I didn't mean to say "like", but it's like the Yellow fever virus in that it has a similar antigenic signature. So, if you were to take antibodies

made against Yellow fever and react those against these other groups of viruses that fall into the same category, you would find some, what they call cross-reactivity.

Vincent:

Right.

Dick:

So when this virus came to the United States, and we were trying to find out what it was, it began by expressing itself in two different directions, it infected people, which was fine, but it also infected birds. So the Ames group said "Great! Send them to us because we have great need for your antibodies because we need to look at this virus to find out which one it is." And the Centers for Disease Control reversed the tables and said "No no, please you send us the virus, and we'll tell you what you have". Now...., this brings up a little issue!

Vincent:

[laughing]

Dick:

The issue is..., the issue of the tissue. Who owns...

Vincent:

Who owns the virus?

Dick:

Who owns the virus? I mean if you know which virus you have you might own it, but it doesn't do you any good and if you have the antisera against all the viruses, but you don't have the virus, you're still not ahead of the game.

Vincent:

It sounds like everyone should get everything.

Dick:

It does, doesn't it?

Vincent:

I mean, shouldn't we collaborate to learn, rather than have our egos predominate?

Dick:

We should do this, and that's another show of course.

Vincent:

Of course. "Science and ego." Maybe a dozen shows!

Dick:

It's unfortunate that that did rear its ugly head at that particular moment in time though, because it prevented the Ames group from actually making the diagnosis. They reluctantly sent the virus

particles to the group in Fort Collins, and Fort Collins then identified clearly that it was West Nile virus.

Vincent:

How did they do that?

Dick:

They did it by a series of inhibition tests, using antibodies against a similar but different Flavivirus group, the only one that strongly reacted with the virus and could not be inhibited by the other antisera against the other Flaviviruses was the one specifically against the West Nile virus.

Vincent:

Ok, so they were the first to say "this is West Nile virus".

Dick:

That's exactly right. And not only were they the first to say it, they also got some sequence data from actually extracting the RNA from the virus itself and doing a sequence on the RNA molecule. They got a partial sequence.

Vincent:

And that confirmed that it was West Nile virus.

Dick:

It confirmed that not only was it West Nile but now they were still behind the eight ball because the laboratory in Fort Collins didn't have all the strains of West Nile, so....

Vincent:

Mhmm.

Dick:

... so while they knew it was West Nile, they didn't know which West Nile. So now, we have to talk more about viruses, so I'm going to turn it back over to you. What do you mean by a "strain"?

Vincent:

That's a very good question!

Dick:

[laughing]

Vincent:

A strain of a virus is something that's slightly different from all the other kinds of viruses of the same names, so West Nile virus occurs in strains, which differ by sequence. And the real question nowadays when we can generate a sequence in hours, is how much difference do you need to be a strain?

Dick:

I was just about to ask that.

Vincent:

In the old days before sequencing, strains were defined by antibody reaction. You would have antibodies made against different isolates of virus...

Dick:

Yup!

Vincent:

... and you would react them against each other, and if there was a little difference in the reactivity you would call it a strain. Nowadays, strains are being defined by sequence.

Dick:

Mhhmm!

Vincent:

And in some cases it turns out that to get a difference in antibody reaction with two different strains, it doesn't require many changes in nucleotide sequence. It's really quite amazing and I've heard.... I was at a meeting in May where..., the classification of viruses is overseen by the International committee on the Taxonomy of viruses, ICTV, and they have begun to define strains on sequence basis now.

Dick:

Oh wow! Great!

Vincent:

So yes, you could sequence different isolates, in this case the West Nile isolate, and say, is it different from strains that you see circulating in Israel, or other parts of Europe for example. So you would have to sequence it.

Dick:

So we're kind of lucky in one sense, in that we have this wonderful tool called the internet. Now the internet allows for the dissemination of knowledge overnight. In fact, it's instantaneous, as we know. And there is a wonderful web service called PubMed, which you can look things up on and find that literature on, and there is another one, which is called ProMED. Now ProMED is different from PubMed. PubMed is a literature search. ProMED is the Program for Monitoring Emerging Diseases, that's the acronym for ProMED, and it was established actually by one of our own faculty members here, Steve Morris, who is a Virologist by the way.... he got his training at Rockefeller University....

Vincent:

Is that right, he established ProMED?

Dick:

Oh yeah, he did! That's right!

Vincent:

By the way, all these websites that we mention, we will have show notes associated with these podcasts and we will put the links in the show notes.

Dick:

You bet!

Vincent:

That's going to be at twiv.tv. Twiv.tv.

Dick:

Cool.

Vincent:

So look for the show notes. So ProMED-mail and PubMed. What do you get out of ProMED-mail?

Dick:

So the moment the CDC group had a partial sequence they put it up on ProMED, to say "does anybody recognize this sequence?".

Vincent:

Fabulous.

Dick:

And, they got an answer almost immediately! There's a Virologist working at the Pasteur Institute in Paris. His name is Vincent Deubel. Vincent Deubel has been studying West Nile virus for 20 years. Vincent Deubel has got viral strains from all over the Mediterranean, into Africa, the Middle East, and parts of Russia. Now, Vince, I want to ask you another question here, because I'm confused myself about this. If there are so many different strains of this virus because it undergoes random mutation, and if the mutation doesn't interrupt the life cycle of virus because it's not a lethal mutation but it just alters the surface code, let's say of the proteins that it makes to hide its RNA, or it manufactures a different variant of an enzyme and it needs to take advantage of the host cell, why are these variants regional? Why is the strain of a virus, let's say for West Nile, because we're going to come to a point here, [laughing]... Vincent Deubel has made a map of where these strains are. There are actually twenty-three different strains of this virus, definable by their RNA sequence.

Vincent:

So these strains are geographically restricted.

Dick:

Apparently so!

Vincent:

Even in the era of travel...

Dick:

Yup!

Vincent:

... where viruses can go anywhere for free...

Dick:

This is very true.

Vincent:

... these strains of West Nile are restricted.

Dick:

It seems that way.

Vincent:

So, yeah, before travel I would say they were restricted because they can't go anywhere, but now that's not an issue anymore.

Dick:

It's not an issue.

Vincent:

It must be that in areas, people are different as you know...

Dick:

Yep!

Vincent:

Here, in New York versus even New Jersey!

Dick:

This is true.

Vincent:

And they're different from the U.S. versus Europe. And those differences may allow some viruses to grow better than others.

Dick:

Yes.

Vincent:

For a virus to maintain in a population it has to replicate in the host, it has to grow in the host, it has to spread from host to host.

Dick:

Yep!

Vincent:

It may have other non-human hosts that it has to grow in, and those may..., so animals for example. So we haven't talked about this at all, but West Nile is a mosquito-transmitted virus, but it doesn't actually grow in mosquitoes, correct?

Dick:

Mmmmm! Yes it does!

Vincent:

It does? But it's not the reservoir of the virus, meaning where does most of a virus grow, what animal host does it grow, is it the mosquito or is it a bird..., I think the host is going to be a reservoir..., is both?

Dick:

The answer is yes!

Vincent:

Ok, it's both mosquitoes and birds, so anyway, with respect to the question, it could be that the reservoir of this virus just differ, and those sequence differences in the strain that are geographically restricted have something to do with that..., a slightly different protein that works better in a North European vole than in a crow in the United States for example. To make it simple...

Dick:

Of course.

Vincent:

... we don't really appreciate the complexity. We're just beginning, but...

Dick:

Right, but the interesting part about West Nile as it turns out, is that these strains are maintained regionally. So if you find out the sequence of the virus that you're dealing with, and you match it up with any of these other twenty-three strains of viruses you can tell where it came from.

Vincent:

So Vincent in Paris said this is West Nile and you could ev..., did he know what strain it was by looking at the sequence?

Dick:

Not at that point.

Vincent:

Ok. He just said it was West Nile...

Dick:

He confirmed that it was West Nile.

Vincent:

And this by the way, is how science should work.

Dick:

That's right.

Vincent:

You have discovered something and you put it out for help. You don't hide it. I would like to just put forth a hypothetical situation: if that had been an academic lab instead of the CDC, perhaps they would have not sent it out and they would have tried to figure it out themselves.

Dick:

I think that's right.

Vincent:

Because of the ego issue.

Dick:

Or, well, your career. [laughing]

Vincent:

Well also, the problem is that we need grants to do our research.

Dick:

Exactly.

Vincent:

So, to do that we need to publish, and if you're the first to publish that this is West Nile, you have a better chance.

Dick:

Well guess what, one of those academic people did get a hold of this virus, but in the form of the brain tissue.

Vincent:

Was that Ian Lipkin?

Dick:

It was! And what did he do? What he did, was an *in situ* PCR reaction to get the complete sequence of the virus in three days. Based on the snippet of information that CDC released through ProMED. And when he did...

Vincent:

So the techniques will be difficult for some of our listeners, but the end result was in a very quick time for those days, he got the entire sequence of the genetic information of the virus, and this was just after the short sequence was obtained.

Dick:

That is correct.

Vincent:

And what did that tell us, having that whole sequence?

Dick:

It told us that it matched identically, except for one base pair substitution, for a virus which had been completely sequenced from a goose that had died on a kibbutz.

Vincent:

[chuckling] In Israel.

Dick:

In Israel.

Vincent:

In what year?

Dick:

In 1999.

Vincent:

Same year.

Dick:

So there was a big outbreak of West Nile virus in geese... hmmm, now this is starting to tell us something about the complexity of this virus. Not only is it a parasite of mosquitoes..., remember viruses can't make it on their own, so they have to replicate even inside the cells of...

Vincent:

Sure.

Dick:

... the mosquito. So that's a fact that you have to keep in mind about these things. A mosquito just doesn't pick it up and give it to something else, the mosquito picks it up, the virus invades its

cells, and it starts to replicate. And in fact, it replicates at a rate dependent on the ambient temperature. And we're going to come back to this because..., it's not always a parasite of people, it's mostly a parasite of birds...

Vincent:

Mhmm.

Dick:

... and other wild life.

Vincent:

Ok.

Dick:

So being a parasite of mosquitoes and birds means, you would use this term, "promiscuous", because there isn't a single species of birds that's not susceptible to the infection.

Vincent:

How do we know that?

Dick:

Because we can randomly infect any kind of a bird you want and they will develop a viremia.

Vincent:

At least the ones we've tested are susceptible.

Dick:

That's right!

Vincent:

I'm sure we haven't tested every species of birds, right?

Dick:

Well we've tested right about every song bird in the United States now.

Vincent:

Is that right?

Dick:

How have we done that? We've collected them, because they die, and we've done the Virology on one side, and we've done the antibody testing on the other side, so...

Vincent:

Mhmm.

Dick:

... there is now a species list for a host species that is about 150 different species.

Vincent:

And how about aquatic birds, are they also susceptible?

Dick:

Oh yeah!

Vincent:

Because they travel long distances...

Dick:

Absolutely.

Vincent:

... so you could imagine that the virus could readily spread that way, correct?

Dick:

This is true. There's no bird species that isn't susceptible, but some are more susceptible than others, and it turns out that the most susceptible to the ill effects of a virus infection are domesticated water fowl...

Vincent:

Why is that, do we know?

Dick:

... ducks and geese. I think because we've bred them for their breast meat contents rather than their ability to respond to a natural infection.

Vincent:

Sure, right.

Dick:

So they're going to lose...

Vincent:

The birds who died in '99 were American birds...

Dick:

Wild birds, that's right.

Vincent:

... and not from Africa, in the zoo anyway.

Dick:

Correct.

Vincent:

Is that because they had antibodies to the virus, or they're genetically resistant for some reason? Yes, they were resistant. You're nodding...

Dick:

I'm nodding my head to the latter of those two choices because it brings up another huge issue of infection versus disease. Mortality versus mild infection...

Vincent:

Mhmm.

Dick:

... and mild disease. Uhm, we know of many instances, in human history as a matter of fact, where a modern infection was introduced into an isolated community. Anthropologists are very much aware of this situation and they hate to be the first one into an undiscovered..., let's say small tribe of Native Americans living in the South American jungle for instance. Those people have remained genetically isolated for thousands of years, perhaps.

Vincent:

Sure.

Dick:

And their immune systems are absolutely tailored to the local setting. They're not going to get sick from Malaria, they're not going to get sick from Leishmaniasis, but they will get sick from the common cold, or they'll die from Smallpox. And we know what happened when the Spanish conquistadors came to this part of the world.

Vincent:

Sure.

Dick:

There were 50 million people living here when they came. When they left, 200 years later, there was 5 million left.

Vincent:

And it wasn't because of their military prowess.

Dick:

It certainly wasn't! They ran out of bullets really early.

Vincent:

[laughing] It was the pathogens that they brought in. Exactly, sure.

Dick:

That's exactly right. So if you are evolving, and your immune system is evolving, and the infections are evolving with you, it's sort of like a spy versus spy, or an arms race..., we've likened it to an arms race, but it really is an attempt at symbiosis. The attempt at symbiosis is: "I don't want to hurt you. I want you to spread me from one bird to the next...", and the bird says "as long as you don't hurt me, come on in!". And so, the bird gives up a little something for this, in the beginning, all the birds die except for a few.

Vincent:

Correct.

Dick:

And you know why the ones that don't die, didn't, because they were pre-adapted to this virus.

Vincent:

Yes.

Dick:

Ok so, it's strictly an evolutionary...

Vincent:

I mean it doesn't make sense for the virus to kill its host.

Dick:

No, not at all!

Vincent:

So this is often...

Dick:

Another clue is that it's never been in this country before, because domestic birds are dying like crazy...

Vincent:

Exactly.

Dick:

... we're losing jays, we're losing crows...

Vincent:

Now here we are, we're nine, we're ten years down from the original isolation...

Dick:

That's right.

Vincent:

Are birds any more resistant, the wild birds anyway, or is it the same level of susceptibility?

Dick:

Well, if you were a population geneticist and I'm not, and you can say you are, but I'm not ...

Vincent:

I'm not, I'm not either.

Dick:

No, I'm not but there are mathematical formulae that you can apply to this setting.

Vincent:

Mhmm.

Dick:

To say how long it would take for..., in a random mutation fashion for the right genes to come up, which would allow these birds to resist dying from the infection even. And there haven't been enough generations of birds yet, you only get two generations a year out of these things and we've lost 90% of our crows.

Vincent:

Well, there is a...

Dick:

They haven't come back.

Vincent:

There is an incident, a related incident, that shed some light on this. You may know that some years ago a European rabbit was introduced into Australia...

Dick:

Yeah I know this one. [chuckling]

Vincent:

And it bred uncontrollably.

Dick:

Right.

Vincent:

There were rabbits everywhere, and the Australians said "we have to get rid of these rabbits".

Dick:

That's right.

Vincent:

So they introduced a rabbit virus to kill them off.

Dick:

Dr. Fenner as a matter of fact.

Vincent:

And the first year after the initial introduction I believe 90% of the rabbit population died, but then the following year they were almost uniformly resistant to infection.

Dick:

That's right.

Vincent:

It was only within a year, so perhaps rabbits maybe quicker than crows do... [laughing]

Dick:

Ha ha ha! There are more offspring per litter also.

Vincent:

... or other birds. But eventually you would suspect...

Dick:

That's right.

Vincent:

And humans being..., reproducing so slowly, take forever..., but you would imagine that eventually any viral disease in humans would reach a level where it is less pathogenic..., you evolve to a level.

Dick:

Take influenza. I mean that was in 1918, we had a huge outbreak of influenza, around the world, right? It was a pandemic.

Vincent:

Correct. That's correct, yeah.

Dick:

We lost something like 1% or 2% of the world's population. That's all. But it happened in a very narrow age group, from like age 10 to age 30.

Vincent:

Right.

Dick:

Which wiped out an entire generation of young people. That wouldn't happen anymore with that particular virus, but it would happen again with something else, in plague for instance, which is not a virus, it's a bacterium, but it's still a good example, when it was first introduced in the 1300s, it wiped out like, two thirds of Europe. But one third wasn't wiped out. The next time it came back, which was another 100 years from that, it only wiped out about 20% of Europe, and the next time it came back, which was 100 years later than that, it only wiped out 1% of Europe.

Vincent:

Of course, there were other things going on besides population there, sanitation is improving and so forth, but yes, your point is well taken.

Dick:

That's it, so...

Vincent:

So we have now in 1999 West Nile viruses here, and what I wanted to...

Dick:

And proof where it came from.

Vincent:

Proof where it came from. Now is this amazing that the virus that was isolated from New York City was only one base different from one from an outbreak from Israel. As a Virologist I can tell you that this is amazing. And why is that amazing?

Dick:

Uhm, well, from my perspective it's amazing that it wasn't identical. I think it was a mistake on the base pair. [laughing]

Vincent:

So you think it was even the same exact virus.

Dick:

Yeah it wasn't a big enough difference...

Vincent:

So what does that imply about how it got here?

Dick:

Ok so that opens up a whole subject area of speculation, right? As to..., ok so now everybody wants to know if this was never here before and we have serum banks of all kinds of human sera collected for different reasons, the bank at the Centers for Disease Control and at the NIH in Bethesda, that you can go back and search, to make sure that this actually wasn't there, and for

sure we haven't found any positive evidence that West Nile virus was in the United States prior to 1999...

Vincent:

Ok.

Dick:

... there were no big bird die-offs..., I want to come back to the weather though because the weather was the trigger on this, but the perfect storm that created the opportunity for this virus, was so fortuitous, that you could not depend on being able to predict this ever happening again, alright? There was a huge outbreak in Israel, remember that.

Vincent:

Same year. '99?

Dick:

The same year, and that's how they know what that goose strain was because...

Vincent:

Ok.

Dick:

... they lost over a million geese. Now you're going to have to ask me the question. [chuckling] What's Israel doing raising geese?

Vincent:

That's a good..., I wouldn't have thought of it, but what is Israel doing raising geese? [laughing]

Dick:

Thank you, because you don't only learn about the parasite, you learn about the habits of people, and you learn about economies, and you learn about, uhm, sociological differences and similarities and eating habits and sexual habits, and you know the moment you start investigating an outbreak of an infectious disease it leads you down so many different paths, that you tend to get lost along those paths until they converge back again. So I'm trying to paint an economic picture. So let's start with some disparate facts and let's try to sew them together into a story because really what we have to do is try to figure out the best possible scenario for how this thing actually got to the United States.

Vincent:

This thing meaning...

Dick:

West Nile virus.

Vincent:

... West Nile virus.

Dick:

It had never been here before...

Vincent:

Did it go first class, or coach?

Dick:

Hah hah hah! I think coach because it actually came over in a little kid.

Vincent:

[chuckling]

Dick:

So, let's set the stage. First of all, there was a series of outbreaks of West Nile virus throughout the Middle East. And in fact, one of them was occurring at the moment that it occurred in New York City, almost simultaneously in Israel.

Vincent:

This was in people.

Dick:

No.

Vincent:

In animals.

Dick:

Interestingly enough, not. It was in domestic geese. In fact, millions of domestic geese in Israel had to be culled in order to get rid of the West Nile virus in that country.

Vincent:

Is it fatal in geese?

Dick:

Ahh, domestic geese, yes.

Vincent:

It is, alright.

Dick:

So...

Vincent:

Why do they grow geese in Israel? [laughing]

Dick:

[laughing] Thank you, that was the question I was hoping for. Ha ha ha! So, when you explore infectious diseases, you learn about everybody's eating habits, sexual habits, travel habits, everything. Because a lot of these diseases depend on distribution, our habits and their habits have to mesh, in order for us to create the conditions necessary for an outbreak. So in this case, West Nile virus being a promiscuous virus, as we've already talked about, it not only infects birds, it infects mosquitoes, it infects amphibians, it infects cold blooded vertebrates, you name it. And the West Nile virus seems to find its way into that host. Now, just as an aside Vince, you're the Virologist here, what does that tell you about how this virus gains entrance into host cells?

Vincent:

Well it probably uses a receptor that's present on many different cell types and many different species of animals, and we haven't talked about such things yet...

Dick:

No.

Vincent:

... since this is the first episode...

Dick:

That's right.

Vincent:

... but a receptor is a portal on a cell surface that a virus can attach to and get into the cell, so it can begin to grow.

Dick:

Right! So, in order to grow, it has to attach first, correct?

Vincent:

Correct, always.

Dick:

That's the first stage of a virus infection, so in this case this virus seems to have found a universal receptor, in the sense that every cell in your body is susceptible to this virus, although when it gets in your brain it causes more problems. But it is distributed throughout your body, and by the way the same thing happens in birds. So it develops into a dissimilar disease in humans, in fact it almost seems like a hemorrhagic disease, rather than an encephalitis for the birds. So I'm going to take you back to Israel in the summer of...

Vincent:

The geese were infected.

Dick:

The geese were infected, so you have to ask me another question then.

Vincent:

Did the geese..., did one of the geese fly to New York, is that what happened?

Dick:

Ha ha ha, well you can't fly very far when you've got West Nile virus inside your body.

Vincent:

In an airplane, why not?

Dick:

It could come in an airplane, that's one...

Vincent:

Do these geese get shipped to the U.S.?

Dick:

Actually they don't.

Vincent:

Alright, so we can rule that out.

Dick:

So you were asking me what the geese were doing in Israel...

Vincent:

I'm sorry, what were the geese doing in Israel?

Dick:

They were busy raising foie gras for France.

Vincent:

Correct? Is that right?

Dick:

That is exactly right.

Vincent:

Fascinating.

Dick:

Well now you made a connection between two disparate countries, they both have West Nile virus, by the way. France gets it as well, but mostly in the southern part in the Camargue, and

mostly in wild horses..., suffer from this. But in Israel, because they're on the fly way from Africa, throughout the...

Vincent:

Right.

Dick:

... breeding zones for these African birds, the African birds are flying along, they look down, they see nothing but Mediterranean Ocean, and then the next thing they see is this green zone...

Vincent:

Right, in Israel...

Dick:

... and the green zones, they've greened up the deserts. So here they go, they fly down to these kibbutzes...

Vincent:

Mhmm.

Dick:

... they start eating goose food, and they start...

Vincent:

... drinking the goose water...

Dick:

... goose water, and the goose water is a little bit...

Vincent:

... and they leave viruses behind...

Dick:

... sure, well the mosquitoes are there, the mosquitoes see a new host, they start to bite these new invaders...

Vincent:

Right.

Dick:

... basically, and they pick the virus up from the African birds that are carriers for the virus, but they don't suffer from it.

Vincent:

Mhmm.

Dick:

It's more or less the same concept that you'd have for bats and rabies. So here are these African birds, totally adapted to the virus, transporting it to a zone that's not adapted to the virus.

Vincent:

Yeah. Right.

Dick:

So the big thing that happens there if you're a goose, you die. And if you're an Israeli goose farmer, you lose your entire crop of geese.

Vincent:

Right.

Dick:

So in order to prevent the epidemic from spreading...

Vincent:

You kill all the geese.

Dick:

... they cull...

Vincent:

Culling, yes.

Dick:

Just like what's happening now with the H5N1 strain of influenza virus in Southeast Asia.

Vincent:

In birds, yeah. Mhmm.

Dick:

It's the same deal! So to prevent something, you either quarantine, or you cull around the outbreak and hope it hasn't spread beyond that perimeter.

Vincent:

Right.

Dick:

So that's what they did in Israel. And in doing so of course, then they had to type that virus strain. They took that virus strain to a laboratory in..., probably in Tel Aviv, at the University, ah, either one of those two places there are very very good, the Weizmann Institute has a wonderful virus department, they did the complete sequence of the virus, and they said, "this year's virus strain is..." By the way, this also affects the training of Israeli soldiers.

Vincent:

How so?

Dick:

They train in the desert.

Vincent:

Yes.

Dick:

And every now and then there's an outbreak of West Nile virus in the soldiers that are training.

Vincent:

Mhmm.

Dick:

And..., we'll come back to that because it's a desert that they're training in, so you're going to have to ask a question: how can a mosquito-borne infection survive in the desert?

Vincent:

Right.

Dick:

Alright, but that's an aside, we'll come back to that. So, the outbreak in Israel apparently was unrelated to the new outbreak in the United States in northern Queens, and in the South Bronx.

Vincent:

How..., what do you mean by unrelated?

Dick:

Well, we never connected the dots, because frankly speaking, when the outbreak occurred in northern Queens and resulted in three deaths, those samples were sent to the Centers for Disease Control in Atlanta, which then relayed them to Fort Collins Centers for Disease Control, which is actually where the vector-borne diseases are analyzed. And because they didn't detect anything in the samples that were sent to them at the CDC Atlanta, they figured it probably is an encephalitis virus, the Arbovirus group is located in Fort Collins, we'll send it to them. And Duane Gubler was in charge of that group at that time, a world expert on Dengue fever, which is another Flavivirus of course, and lo and behold, when they ran the serology, it weakly cross reacted with antisera from St. Louis encephalitis. So the initial diagnosis was new strain of St. Louis encephalitis because we've had it here already. That sort of threw everybody off, because what was happening at the same time in the South Bronx, namely at the zoo, was that crows were dying outside the compound...

Vincent:

Mhmm.

Dick:

... and exotic birds were dying inside the compound.

Vincent:

Right.

Dick:

And Tracey McNamara was the veterinarian pathologist at the time...

Vincent:

Right.

Dick:

... and what she noticed was of course that, if this is St. Louis encephalitis, this can't be right, because exotic birds might die from it, because they're not adapted to that virus in this country, you know from African birds, or South American birds, but crows don't die from it. Crows are highly adapted to St. Louis encephalitis, and in fact, it's a silent infection in these birds, that's how it goes from place to place without us knowing it.

Vincent:

Right.

Dick:

So, what she suggested was that this is a new virus, which is killing both the people and the birds, and of course nobody listened to her, because at that time, and probably it still is true, there was not a lot of cross-talk between the medical community and the veterinarian community, which is a tragedy because if you look back from 1976 to the present, about 60% of all the new entities in the world that are considered emerging infections, are zoonotic, meaning they come from other animals rather than humans. And then they infect humans also. Veterinarians play a huge role in identifying these outbreaks. So, they have become the new medical community that we look for in terms of what diseases are here, and which ones are possible. That having been said, it gets complicated now because the birds from the zoo were then sent to Iowa, and that's when you find out that the veterinarians have a national laboratory, set up expressly for this purpose, to diagnose unknown diseases, basically. And they have a virus lab, and in the virus lab, they did the postmortems on these exotic birds, and I might add another aside here, if Tracey McNamara had kept track of where the exotic birds had come from, in the world, she would have noticed right away that no African exotic birds were dying.

Vincent:

Right.

Dick:

Only birds from either South America, North America, or Asia.

Vincent:

It probably wasn't her job to keep track of that. But if you were a virus hunter...

Dick:
Right!

Vincent:
... you would have to take that information into account.

Dick:
Or Dr. House. [laughing] That's right, so at any rate, that point was later on added to the story sort of as a hind sight event. Ah, but what the veterinarian's laboratory out in Iowa did discover was that the birds died from a Flavivirus-like infection.

Vincent:
Right.

Dick:
And they thought that if the Centers for Disease Control in Fort Collins were kind enough to send them all of the antisera that they were in control of, they could identify which Flavivirus this was.

Vincent:
Right.

Dick:
But it actually turned out to be the other way around. The Centers for Disease Control in Fort Collins said "no no, you send us the virus, and we'll tell you what you have". So the more powerful of the two groups turned out to be the Centers for Disease Control, and by that I mean they had more political clout, they were able to demand that the Iowa laboratories send them the virus, and so they ended up getting credit for identifying the fact that what they were really dealing with was not St. Louis encephalitis, but rather, the West Nile virus. And for the very first time then, they discovered an infection that had emanated from somewhere across the Atlantic that had found its way into people and into birds, and this explained the death of the birds in this country because our birds are not adapted to that particular virus.

Vincent:
Right.

Dick:
So here we have..., so now what we have to do is account for how it got here.

Vincent:
So we talked previously that the sequence showed that it was virtually identical to the goose virus.

Dick:
This is correct. We were lucky that there was a first rate Virology lab in Israel, and it was set up by the way in 1951, as a result of the original discovery of the West Nile virus in the West Nile

district of Uganda. That initial discovery in 1937 led to the establishment of a Virology lab in the newly established country of Israel, when it first started.

Vincent:

Why would that have an effect in Israel?

Dick:

Because it affects not just birds, but it also infects people as well.

Vincent:

Ok.

Dick:

So every year they have major outbreaks. Almost every year, not every year, I wouldn't say.

Vincent:

So how long after the first cases here in New York did we understand that this was very similar to the goose virus in Israel, a few months?

Dick:

No actually it was..., it was actually..., the goose virus isolate was, uhm, somewhere in March or April, and the outbreak here did not occur until mid July or early August. So there was a big delay as to how this thing came about.

Vincent:

But the sequence..., the aligning of the two sequences happened within a few months of the beginning of the New York outbreak.

Dick:

It happened within a few months, that's correct, and in fact, it happened in a few days once it was learned that it was West Nile virus.

Vincent:

Ok.

Dick:

So the group in Fort Collins actually did a little bit of the sequence work on the virus just to make sure that that's what they were dealing with. And indeed, they put up, on the internet, on an information blog called ProMED the beginning sequence of this virus... and said, "this looks like West Nile virus to us", and they got an instant response from a guy in Paris at the Pasteur Institute, his name was Vincent Deubel. Vincent Deubel had all twenty-three strains sequenced down to the last base pair. And indeed, this little snippet that they sent and put up on the internet said "yes, it's West Nile virus, and so far, it matches identically with a strain isolated from a goose in Israel in that year". Now that wasn't the end of the story of course, because other groups were interested in this virus too, and namely, there was a group in California, led by Ian Lipkin, who had requested samples from both the veterinarians and the medical community, and

the only responders were the state pathology lab in New York state. What they did, is they sent him little pieces of brain tissue from the three victims who had died from this infection in northern Queens.

Vincent:

Mhmm.

Dick:

Once Ian Lipkin had the beginning sequence of the virus, he, by using a technique called polymerase chain reaction, he elicited the rest of the sequence from the brain sections. The viral RNA is all throughout the tissue, infecting all the cells as we've discussed before. So what he was able to do for the very first time in the history of any infection, was to get a complete sequence of the genome of this organism from a tissue section.

Vincent:

Without ever growing the virus?

Dick:

Without ever growing the virus. He amplified the RNA molecule, converted it to cDNAs, did the sequence, and in three days of working around the clock, said "not only is this West Nile virus, this is the West Nile virus from those geese in Israel...

Vincent:

... geese in Israel.

Dick:

... of the same year's outbreak". Now..., that's a startling finding, because it pinpoints the origin of this virus. But how do you handle that situation?

Vincent:

How..., how did it get here? Do you know..., do you know how it got here?

Dick:

Well, not only do I not know... [laughing]

Vincent:

No one knows.

Dick:

... but nobody knows! But there are some cogent hypotheses. And some believable hypotheses and some very unbelievable hypotheses. The first unbelievable one is that a mosquito "hitchhiked", or crossed the Atlantic...

Vincent:

Crossed the Atlantic.

Dick:

... on an airplane, got off at Kennedy Airport, or LaGuardia, and then somehow bit somebody, and then, you know, that's....

Vincent:

It's not unreasonable...

Dick:

It's not unreasonable.

Vincent:

I've seen flies in trans-Atlantic airplanes. Right?

Dick:

Oh! And I know you can get...

Vincent:

No problem.

Dick:

... you can get, uhm, Malaria this way and if you've ever flown on Qantas airlines you'll know that when you land, you don't get off the airplane until they come through with the insecticides...

Vincent:

They spray it.

Dick:

Oh they do spray it, they're very very aware of this.

Vincent:

[chuckling]

Dick:

But West Nile virus has been around the Middle East for a long, long time. And it's transmitted to birds all the time, and there are mosquitoes all the time. Why now?

Vincent:

Why now? Ok, why now?

Dick:

Ok, so the mosquito hypothesis, although valid, is not high on my list.

Vincent:

Because it could have happened anytime.

Dick:

It should have happened way before this.

Vincent:

Twenty, thirty years..., of air travel, right?

Dick:

Yeah, exactly, but it didn't.

Vincent:

Ok.

Dick:

The second hypothesis involves the blowing off of course of migratory birds out of Africa. An even more..., uhm, less likely hypothesis...

Vincent:

These birds would have come to the US in some way.

Dick:

Right!

Vincent:

Ok.

Dick:

Right, now this does happen with exotic fish species. I'll give you an example. Tarpon are native to the south coast of the United States and the Caribbean, they're tropical fish, basically.

Vincent:

Mhmm.

Dick:

But when there's an enormous warm spell, the gulf stream actually allows tarpon to come up as far north as Long Island, before the currents start to lose their temperature on their way over to the British Isles.

Vincent:

Hmm.

Dick:

So people have actually caught tarpon off the beaches of Long Island, on unusual weather events, which allowed them migrate north...

Vincent:

... which normally you don't catch tarpon...

Dick:

No, normally you don't, you have to spend a lot of money to go to Belize to catch tarpon, basically. So, the point is that birds being blown off course would have been noticed, an exotic bird from Africa would have instantly been noticed by somebody, you know a stork, or a flamingo, or I mean what kind of bird are we talking about here? And those are the kinds of birds that actually do the migration.

Vincent:

Right.

Dick:

Alright, the third hypothesis is the most likely hypothesis, and that's the one that Vincent Deubel actually adheres to, and it's the one which I had developed independent of him, we had met at a meeting in Westchester the year after the outbreak and we exchanged ideas, and I think the reason why we did this..., he didn't know who I was, but I did know who he was, we sat together because we both have French last names, [chuckling], so there are some interesting reasons why people get to know each other, and as I was discussing my forthcoming book with him, and in it I discussed this hypothesis, he says "I thoroughly agree with you, because I think this is exactly how it got here". So what he told me, was what I will now tell you. During this outbreak of West Nile virus in the geese, little kids and adults can also become infected, as the virus amplifies through the hosts and becomes more prevalent, the farmers and their children and their relatives can also become infected with the West Nile virus. And this happens on a regular basis. It just so happened that this year was an unusual year in many respects: A) it was very very hot, and very dry, so it favored the outbreak, because it's transmitted by a mosquito that actually thrives under those conditions.

Vincent:

So that particular host, which mosquito is it?

Dick:

It's a *Culex* mosquito.

Vincent:

It likes hot weather.

Dick:

It loves it, and it..., well...

Vincent:

It needs water to reproduce, correct?

Dick:

It does, and it actually seeks out polluted water, so there's no better source of polluted water than during a hot spell, because as the water dries down, it gives off these organic odors, which attract the mosquitoes to them...

Vincent:

Ok.

Dick:

... and that's where they find these polluted bodies of water.

Vincent:

So it was hot not only in Israel, but here as well in the summer.

Dick:

That's correct, and in fact if you look at the records on the weather channel, or you go back to the national weather service and look it up, this was the hottest, driest summer in 100 years in New York City. And so by July, the conditions were absolutely perfect for introducing this virus into this country. So, just the big question is, "how was it introduced?", and Vincent Deubel and I share the same view that it was introduced by a small child who had a viremic infection, but was asymptomatic.

Vincent:

Why not an adult?

Dick:

Adults don't get asymptomatic infection [laughing], and the reason for it is that if you're an adult - well I wouldn't say that adults don't get, uhh..., they don't, uhm..., let me back up. For every case of West Nile virus in an adult, there are 100 inapparent infections, but in none of those adult cases does the viremia reach a level which would allow the transmission of virus to the mosquito. The number of viral particles circulating in the blood are not high enough to infect a mosquito. Whereas, it's already been shown that little children that acquire this infection particularly in southern Egypt, which is the hottest, driest place I can think of, or northern South Africa, which is another hot, dry place, next to the Namib desert, it's a disease of children, and how do we know this, because there isn't a single adult case recorded in those areas. And when you do serosurveys you find everybody is positive, so they must have caught it as a child. Now, there's a lot of records out there that when this disease was first discov..., described, I should say..., there were some deaths in children, particularly in places like India and throughout the Middle East.

Vincent:

Hmm.

Dick:

It's got about a 2-5% mortality rate even in children, but the rest of the infections in children, even though they may reach viremic levels necessary to transmit this from one person to another by mosquitoes..., never results in clinical disease, and the reason for that is very simple. An encephalitis is a swelling of the outer membranes, and also of the brain tissue itself. And in an adult, the brain case is solidly shut, all the bones are actually fused, and you've got the sawtooth joints holding everything together, there's nowhere for the brain to go. So as it swells up, that's

where the symptoms start. And in fact, one of the treatments for West Nile virus right now is just to give them steroids. To keep the swelling down. You can save lives this way. A child's brain case is still growing, and until we reach about age 5, the brain case can still spread apart as the brain swells to accommodate the new volume of brain tissue, then once the encephalitis has fought off, the brain tissue goes down, the brain closes and from that point on there's permanent immunity as a result. So a lot of these intricate facts have to be brought into play in order to account for this if this is still going to be a viable hypothesis.

Vincent:

But most likely the child who was infected that brought virus into the U.S. didn't have any symptoms of encephalitis.

Dick:

That's correct. This is exactly right.

Vincent:

The child wouldn't be able to travel...

Dick:

Exactly! Exactly. But, nonetheless it was still infected, so the hypothesis goes further than this, however. Because there was another event occurring, which attracted a crowd, as they would say.

Vincent:

Mhmm.

Dick:

And that is at the Bronx zoo they had opened a new exhibit. They called it "The Congo Exhibit". And in the Congo exhibit they had 19 lowland gorillas, on display. It was as though a family of gorillas had gone on vacation and come to the United States. At the Bronx zoo, in the Congo exhibit there were 19 lowland gorillas, that throughout the summer months of the year 1999 attracted 3 million visitors. My hypothesis includes the visitation of a small child, a viremic small child, visiting relatives in northern Queens, who then said, "wait till I take you to the Bronx zoo, you're not gonna believe what you'll see". They stood in line for an average of three hours. Now, why would you stand in line for three hours unless there was really something spectacular to see? Remember, three million people saw this exhibit.

Vincent:

Is that a big number for the Bronx zoo?

Dick:

That's an enormous number.

Vincent:

Ok, unusual.

Dick:

This was the highest number of visitors to a single exhibit that they've ever had.

Vincent:

Ok.

Dick:

And the average wait on line was three hours.

Vincent:

Was it a hot day?

Dick:

It wasn't just a hot day, it was a hot, dry day. [laughing] As those novels open, you know, "it was a dark and stormy night...", it was a hot, dry summer day. And there was one other factor here that you can throw into the equation, which was absolutely essential. And that is that the Congo exhibit was situated adjacent to the Egyptian pond..., they called it the Egyptian pond because it was loaded with Egyptian geese..., this is a wild animal now. The Egyptian geese were kept on this little pond, just to the side of the Congo exhibit. Now, the pond itself was essentially, the most polluted body of water at the Bronx zoo at that point.

Vincent:

And let me guess..., it had mosquitoes breeding in it. Yes.

Dick:

[laughing] Now that was a good guess Vince. In fact, everyone recalls how annoying it was to stand on line for three hours and be bitten alive by mosquitoes waiting to see...

Vincent:

There are records of this...

Dick:

Yeah, everybody showed up in shorts and short sleeved shirts, and everybody said how intense the mosquitoes were..., now I must tell you that *Culex* is not a day biter, by definition. It is not a day biting mosquito, they prefer to bite at night. But, when there are so many people around, and where there are so few other things around to bite, namely, what they really prefer is birds. It's hot, dry, if you're a bird, you go to where it's cool and wet, leaving people as the only victim. So here's this little kid waiting on line for three hours, giving his blood to the mosquitoes, which then turned around and on a second bite...

Vincent:

Passed it on.

Dick:

...could pass it on to all the birds.

Vincent:

Did any of the Egyptian geese die?

Dick:

None!

Vincent:

Because they were from Egypt, they were actually imported birds, so they...

Dick:

Yeah!

Vincent:

... were immune or resistant to...

Dick:

Yeah, no African bird died at the zoo! None of them. The Kori Bustard didn't die...

Vincent:

Mhmm.

Dick:

... the African flamingoes didn't, but the South American flamingoes did, so you even have those differences, [laughing] there with two species of flamingoes, it was a very very interesting tapestry of facts after the fact of course.

Vincent:

And there always has to be a coincidence for a new infection like this to emerge.

Dick:

That's correct.

Vincent:

And maybe at some future point when we talk about SARS we'll explore similar tapestries as well.

Dick:

Yup!

Vincent:

So now the virus is introduced into New York, and it finds its way to three victims.

Dick:

More than that actually, there were five sick people..., nope, six.

Vincent:

And probably many more infected who didn't have symptoms.

Dick:

Correct. In fact, we'll get to that in a moment, but actually seven people ended up dying from this infection. Six were from the United States. One was from Toronto, Canada. Now, how did a person from Toronto, Canada catch West Nile virus? He made a stop in New York City.

Vincent:

He died while in Toronto.

Dick:

He flew from Europe, stopped in New York, got off the airplane...

Vincent:

Mhmmm.

Dick:

... probably went to the zoo. I don't know the facts involved in this, but if I were a tourist and I had a day to do something, and I heard about this lowland gorilla exhibit, I might have been tempted to go for just a day, and wait on line, and somehow this man encountered this virus either in northern Queens or in southern Bronx. One of those two places. Now if you're from Toronto it's unlikely that you'd visit southern, uh..., northern Queens, or any other reason unless you had a relative that lived there. And perhaps he did. Because he was now..., actually the focus of the infection, actually two foci of infection. So you have to say why that is true also, and I think this little kid's relatives lived in northern Queens and took him to the Bronx zoo. That's exactly what I think happened. But there's virtually no way to prove this. So, that makes the best sense. Now, of course, you're going to ask another question then, ok, so how many people from Israel come to the United States during the summer months?

Vincent:

I would guess very many, right?

Dick:

300,000 a month. [laughing]

Vincent:

Yeah. So it probably wasn't possible to trace any particular..., among those there were many children I presume.

Dick:

Correct. And so...

Vincent:

But what about children who live on goose farms? Maybe you could narrow it down even further.

Dick:
Maybe!

Vincent:
Was that attempted, or not even? They don't have the records.

Dick:
Ahh, if it was, I'm not aware of any of those explorations, but it's likely that at least one of them had been from the farm, there aren't that many people living in Israel altogether, it seems like almost everybody from Israel comes to the United States at one time or another during the year.

Vincent:
Well it's a plausible hypothesis.

Dick:
Yep!

Vincent:
And what we learned from it is that next time there is an unusual outbreak, we need to pay attention to the details.

Dick:
This is all true.

Vincent:
Always.

Dick:
It's..., the devil, as they say, is in the details. And in this case you won't have an outbreak of West Nile in people unless it's hot and dry. Let's take this fast forward now.

Vincent:
Sure.

Dick:
So 1999 to the present. This is 2008 and the virus has been here for nine years.

Vincent:
What has it done in nine years?

Dick:
Aahhhh! It's infected birds in every single state.

Dick:
It's infected people...

Vincent:

In every state.

Dick:

... in every single state except Alaska. And Hawaii!

Vincent:

It's gone to Canada.

Dick:

Yes, it's all throughout central Canada...

Vincent:

Mexico...

Dick:

Mexico, Central America...

Vincent:

South America?

Dick:

Not to my knowledge, but it's throughout the Caribbean, and remember, this is a parasite of birds, mostly. I'm worried about exotic birds. I'm even worried about the California condor recovery program out in Utah, those birds will be highly susceptible to this virus if they ever encounter it.

Vincent:

So they're every..., what is the season now, the summer, the warm months?

Dick:

It's interesting, uhm, the season starts early now, because this virus overwinters in *Culex pipiens*. The mosquito species that transmits it in the United States is primarily *Culex pipiens* and *Culex tarsalis*, those are two pollution loving mosquito species that are closely related and they're found throughout the United States. The one in Europe..., is..., there are two other species, *Una vetadas* in Africa and *molestus* in the Middle East and Africa. So..., but those, still, those two species of mosquitoes breed in temporary bodies of water that are actually polluted. So, once we create those situations, let's say you're an army on bivouac in the middle of the desert, you still have to drink, and you do your shaving in the morning, and you brush your teeth, and somehow that water gets deposited, maybe there's a receptacle that everybody has to spit into because they want to sanitize..., well, that's where the mosquitoes find their breeding sites.

Vincent:

And that's why in the desert in Israel the soldiers get infected.

Dick:

That's correct, and in fact there are no records of human outbreaks that are not associated with hot dry weather except one. And that was in Romania.

Vincent:

Mhmm.

Dick:

And that had an unusual set of circumstances, which you could interpret as a hot, dry situation, but it actually was not. It's the only one that doesn't fit that epidemiologic pattern. It's..., it's not unusual for the Camargue region in France, this is the swampy lower region along the Mediterranean, to have outbreaks of West Nile virus, but mostly in the horses. So, remember it's so promiscuous that it'll infect every mammal, right? Horses are 40% mortality rate oriented with regards to this virus. That's an enormous number...

Vincent:

That's why we have a vaccine for horses.

Dick:

Well that's exactly right, that's...

Vincent:

Because you don't want your race horse to be infected.

Dick:

That's exactly right [laughing]..., exactly right.

Vincent:

Now when it's spread in the U.S., can we tell from the pattern of spread whether it was mainly birds...

Dick:

Mmmm.

Vincent:

... or people travelling that spread the virus, or is it not possible?

Dick:

Good question. Well, it's possible to guess, but again, you're going to have to guess because I think once this outbreak established itself in this country, and I met the EIS officer at CDC Atlanta who was in charge of the whole program, I'm blocking on his name right now..., but uhm, but he told me confidentially that he got a call from the White House, that once they realized this virus was here, and the potential for disease was real, they ordered him to get rid of it. They said "just get rid of it". That's an interesting order coming from the White House, isn't it, because we've only gotten rid of one thing in our entire history as a human species, and that's Smallpox. And the only reason we got rid of Smallpox, is because it only infects human beings

and nothing else. I know we're close to getting rid of polio also, which is your specialty, but we haven't done that yet, so for the White House to tell somebody at the CDC to "just get rid of it", reflects an enormous ignorance on the part of that person.

Vincent:

It's perfect... the perfect word. I would pick the same word.

Dick:

Whoever said that...

Vincent:

Did they listen? At the CDC...

Dick:

Well, you know, they tried their best to understand what was going on, but another subterfuge that arose out of this meeting that was held the year afterwards was..., so someone at this meeting got up and said "we don't know anything about the West Nile virus". With Vincent Deubel sitting in the audience, with all twenty-three strains sequenced. "What do you mean we don't know anything about this virus, I know everything about this virus. I know all its proteins, I know what the host ranges are, I know...", but the one thing that we didn't pay attention to, was the ecological setting under which the virus switches from birds to humans. That's the key. To understand what causes human outbreaks, means that you can predict in advance, whether there will be a human outbreak or not. If you could determine what those factors are. So let me just give you my take on this, which has by the way been borne out by nine years of history with this virus in this country.

Vincent:

Mhmm.

Dick:

But, if you went back to the literature that was established back in the 50s and 60s, you could have predicted this, based on that literature. Every one of the outbreak that's big, there was one outbreak in the south of..., in the northern part of South Africa, which involved 3000 cases. And I remember you were asking me this just recently before, like, if you have one case that's clinical, how many sub-clinical, or inapparent...

Vincent:

Mhhmm. Right.

Dick:

... infections do you have? And the answer is about 150-200 inapparent infections...

Vincent:

Mhmm.

Dick:

... or people that had a headache, but didn't get worse...

Vincent:

Right.

Dick:

... the immune system fought it off, I guess they threw up a lot of interferon and turned off the virus replication cycle...

Vincent:

Mhmm.

Dick:

... whatever the reasons, you have one times 200, so in South Africa there were 3000 cases, now you multiply that times 200 and you get 600,000...

Vincent:

Infections.

Dick:

... infections.

Vincent:

Huge. Right?

Dick:

That's huge. And the next year they had none! That brings up the concept of herd immunity, and indeed that's probably why there were none the next year, because everybody got infected this year in that region, and there was no peer person left who was susceptible after that.

Vincent:

Mhmm.

Dick:

The same thing happens in massive epidemics for other things too.

Vincent:

Sure.

Dick:

So, uhm..., in the United States, after 1999, I began tracking the weather patterns to see whether there was a correlation between hot, dry periods...

Vincent:

Mhmm.

Dick:

... and the switch of the virus from birds, which was rampant, during the cool, wet periods, to people during the hot, dry periods. Birds are highly susceptible to this virus, it takes very little virus to kill a bird. Why? Because the birds' temperature is higher than ours, and it adds a little bit of zip to the viral replication cycle. So we've got a temperature of 37 degrees, the bird has a temperature of 41, 42 degrees, but that big difference..., that doesn't sound like much of a difference, but it's so big, that the virus..., even a single particle introduced into a crow, in three days the crow is dead. You do the same thing to a person, the virus slows down. What does this tell you about the virus? I think that..., what it tells me is that it's a virus of birds, not people, and we're the incidental host. The virus doesn't do as well in us, so it takes a bigger injection dose to get us started. Now...

Vincent:

So...

Dick:

... to get a bigger injection dose started requires the mosquito living at a higher temperature for a while.

Vincent:

Mhmm.

Dick:

Because the Israelis did a wonderful set of studies on this. They infected mosquitoes artificially, and then held them at various temperatures, and then measured the viral titer inside each mosquito. And you know for every 10 degrees increase you get a doubling of biochemical reaction. That's also true for the viral replication cycle. And that's what they exactly showed. If it's 80 degrees it's this, if it's 90 degrees it's twice as much, if it's 100 degrees, it's twice as much as that or four times that of 80 degrees. So, what you've really got here is an amplification process that's temperature-dependent. That's number one, so, the viral dose per mosquito is higher at hotter temperatures.

Vincent:

Ok.

Dick:

And in fact, as far as I know there's never been an outbreak in humans, where the temperature never exceeded 90 degrees. I've looked at this now for 7 years in a row, and there hasn't been one single incident of an infection where the ambient temperature in that region has not exceeded 90 degrees. So it needs 90 degrees or more in order to hyper infect the mosquitoes enough to infect people. That's number one.

Vincent:

Mhmm. Ok.

Dick:

Number two, is that when it's hot and dry..., you're a bird, hot and dry for a day, that's not a problem, hot and dry for three days..., still not a problem. Hot and dry for a week, we're starting to get hungry, remember birds eat about ten times their weight every day in food...

Vincent:

Mhmmm.

Dick:

... just to keep them alive because of their high rate of metabolism. The seed eating birds, the insect eating birds, they all have the same metabolic requirements. During hot, dry spells, what happens? The number of plants drops off, and the number of insects drop off, because the number of plants drop off, because that's what the insects are eating. The ecology changes. You have three weeks of hot, dry weather, you have a month, you have two months..., take New York City back in 1999, the hottest, driest summer. Starting on May 21st, it didn't rain until August 13th, I believe the day was. A whole two and a half months without rain!

Vincent:

So the bird population during this time is reduced.

Dick:

After the first week it's reduced!

Vincent:

Ok, and what's the effect on West Nile virus?

Dick:

Well, if you're a mosquito infected with West Nile virus and your imperative biologically is to reproduce...

Vincent:

Now you'll bite some people.

Dick:

You'll bite anything, so I like to say that the bird is the steak equivalent for the mosquito, and we, unfortunately are the hot dog, but when you're hungry and there's no steak and hot dog..., you eat that hot dog, even though you'd rather have a steak. The mosquito species in this case can feed on human beings, but prefers birds. So, when they have a choice, they pick bird every time. So, the only time that there are no birds around human populations is when it gets very hot and very dry!

Vincent:

Mhmm.

Dick:

And of course, remember, this is a pollution loving mosquito, so we're good at doing that as well. So, it's sort of...

Vincent:

The absence of West Nile in Alaska, is that because the temperature rarely goes above 90 degrees?

Dick:

Yeah, I don't think it's ever gone above 90 degrees in Alaska... [laughing]

Vincent:

But they do have mosquitoes there.

Dick:

They have tons of them!

Vincent:

Do we know if there's any virus, any West Nile virus in Alaska, has anyone looked?

Dick:

Ahh, well of course they've looked, I'm sure they have, I don't know of any records of Alaskan mosquitoes harboring West Nile...

Vincent:

I would guess not, otherwise we'd see infections, right?

Dick:

Correct. So what has been the consequence of West Nile virus in the United States, apart from human infection? Crow populations are 90% reduced.

Vincent:

Is that right?

Dick:

90%.

Vincent:

I didn't know that.

Dick:

Blue Jay populations, robin populations, the corbies are reduced...

Vincent:

Mhmm.

Dick:

Greatly reduced.

Vincent:

In all states.

Dick:

In all states. So, the question that I'm going to ask is, what good is a crow? What good is a robin, and what good is a Blue Jay, because we can now know, because we don't have them anymore to speak of. So, are these birds species important in disease control for humans, because they're eating things that would ordinarily transmit diseases to us, like other insect species, other mosquito species. If I was worried, really worried about this whole situation, I'd worry about the bat die-offs that we've been having recently, bats eat tons of mosquitoes. Are they dying...

Vincent:

Why are they...

Dick:

... because they're eating West Nile virus laced mosquitoes? Are they?

Vincent:

We should be able to find out.

Dick:

I don't know that answer, but I'm just raising it as a question. And by the way, bat body temperatures are much higher than humans' also.

Vincent:

So is West Nile here to stay? In the U.S.?

Dick:

West Nile is now an endemic infection in the United States.

Vincent:

And the reservoir is..., many things, most animals...

Dick:

Everything. [laughing] And the mosquito, the mosquito species that transmit it are ubiquitous, they're found wherever humans are found, and they're found throughout the United States.

Vincent:

So let's say if I went on a summer vacation in a remote area, where there are a lot of mosquitoes, would I worry about acquiring West Nile infection?

Dick:

Tell me what the temperature regime is first. [laughing]

Vincent:

If it's not above 90 I don't have to worry.

Dick:

Right, and if you go to the White River plateau in Colorado, or if you go down into the Grand Canyon, hmm....

Vincent:

The Adirondacks...

Dick:

The Adirondacks, as long as the temperature..., oh, it can exceed 90 degrees in those areas, it can, actually.

Vincent:

It can, not often though.

Dick:

Not often, but sometimes, I remember a summer up there, I was there and it did exceed 90.

Vincent:

Ok.

Dick:

But if you track this now, there are two places in the country that always exceed 90. Every year. One of them is the Imperial Valley of California...

Vincent:

Mhmm.

Dick:

... and the other is the entire southern region of Texas. And the southwest, but the southwest region of Texas has got a lot of people living in it. So that you have the option here for this ecology to develop, and Texas and California, regardless of the weather conditions in any other place, will always have a number of cases for West Nile...

Vincent:

Mhmm.

Dick:

Some years they had a tremendous number of cases and other years they have had reduced numbers, but they still lead the country.

Vincent:

Well I happen to have a map here of cases in 2008...

Dick:

Ok.

Vincent:

It's a map of the U.S....

Dick:

Alright!

Vincent:

... and under each state we have the number of cases.

Dick:

Right.

Vincent:

The state with the most cases is....

Dick:

Uhm, I would guess California. [laughing]

Vincent:

You were right. 155...

Dick:

Aha!

Vincent:

There were, uh..., I don't know the total for 2008, but in 2007...

Dick:

It was higher than that.

Vincent:

... there were 35,000 cases of fever...

Dick:

That's right.

Vincent:

... 1200 of encephalitis, and 117 deaths. Anyway, 155 so far this year in California, 23 in Texas...

Dick:
Right.

Vincent:
... how about New York state, six?

Dick:
Six.

Vincent:
Not very many.

Dick:
If you go to North Dakota and South Dakota...

Vincent:
Twenty-three, thirty-four...

Dick:
Unpredictable, but yet there it is.

Vincent:
Colorado, thirty-seven...

Dick:
Yup!

Vincent:
Arizona and New Mexico not many, eighty-three.

Dick:
That's right.

Vincent:
And that would be because there's not much standing water?

Dick:
Yeah, I would guess that's the reason.

Vincent:
It's too dry.

Dick:
Because in California, remember it's mostly agricultural community throughout the Imperial Valley. They flood irrigate there.

Vincent:

And there are some states that have no human cases yet this year.

Dick:

That's right. That's right, it's been cool and dry in this country this year.

Vincent:

Could you guess which states might be included in those? Just take a guess.

Dick:

Well I would guess Maine... [laughing]

Vincent:

Maine is one of them. Washington.

Dick:

Ok!

Vincent:

But interestingly, Florida...

Dick:

Aha!

Vincent:

... is also one of them.

Dick:

Probably if it..., you know, if you have a lot of rain..., here's what rain does. It has to be hot and dry, remember I said, not just hot, it has to be hot and dry, because if it's not dry, and it's hot, that still allows the plants to survive and it allows the insects to survive and it allows the birds to stick around and still feed. So you're not going to drive them off with hot, wet weather, you're going to drive them off with hot, dry weather.

Vincent:

Mhmm.

Dick:

I would say that Florida is a pretty stormy state during the summer months, I mean, the Marlins..., the Florida Marlins have difficulties attracting evening crowds to their baseball games because they're almost daily interrupted by thunderstorms.

Vincent:

So it's hot, but it's too wet in Florida.

Dick:

That's right!

Vincent:

It's not the good condition.

Dick:

That's exactly right.

Vincent:

Now I'm interested to know whether, in the nine years the virus has been circulating in the U.S., is it changed, so that it's now better able to infect the people that are here, or the animals that are here, as opposed to where it came from.

Dick:

Right.

Vincent:

Do we know?

Dick:

Uh, we do know, actually, that's a very good question because it does point out the fact that we live in an evolving world. Ah..., and, so let's look across the world first, and let's take Vincent Deubel's twenty-three strains, and ask the question: can you determine the geographic range of each of those strains? Are they overlapping, are they found together, are they individuals, what is the distribution of these twenty-three strains? And the answer is, you could take those twenty-three strains and divide them into two sub-groups: pathogenic, and less pathogenic. The death rate in humans from the group that's pathogenic is very high compared to the group that's considered non-pathogenic, or at least mildly pathogenic. None of them are non-pathogenic. So, you can tell where they're from by looking at the death rates. And there's a very pathogenic strain of this virus that lives in the Volga Basin in Russia. Now the Volga Basin, if you look at the ecology of that, it's desert. This goes through a very dry, hot region, and almost every year they have an outbreak of West Nile virus there, and it's of the strain that's highly pathogenic, and it stays there, it has not moved, it has not..., if you allow this..., it has not mutated to become less pathogenic. Whereas, the West Nile virus from Israel, that was introduced in the United States, remained the same strain up until the year 2002. In 2002 it underwent antigenic change, which was reflected of course in its genome as well. So now it's considered to be a separate strain from the Israeli strain that was introduced to begin with. And maybe it's because this virus has had the opportunity to infect so many different kinds of hosts. And the influences on this virus in terms of its rate of replication and transmission to mosquitoes, and then transmission back into more hosts, this recirculating of the virus, again and again and again through the wild life, may have resulted in the selection for strains of the virus which are more suited for a more robust biodiversity than exists in, let's say, the kibbutz of Israel, or the dry desert of the Volga region of Russia. And so what you see here now is probably strain number twenty-four. Vincent is now going to add this one to his list, and, by the way, lucky for us, the robust pathology associated

with the original strain of West Nile..., by the way, part of it is due to the fact that we failed to recognize it until it was too late in those people, if we had recognized it as West Nile virus immediately, we would have put them on steroid therapy. And I know this is counter-intuitive, because steroid therapy inhibits the immune response, but it also inhibits swelling.

Vincent:

Swelling of the brain. Sure.

Dick:

That's the pathology of this infection, so today, when someone comes in with the following signs and symptoms, they are assumed to have West Nile. They have to have muscle pain, they have to be confused, and they have to have a headache. If you have those three things together, they immediately start you steroids.

Vincent:

I have those often.

Dick:

Ha ha ha! Yeah, so do I! [laughing] But interestingly enough, during the transmission season, which you can start from May in some cases and go all the way through October..., and by the way, I think we should go back to the original outbreak and say, why didn't it continue? You know, what stopped it?

Vincent:

Did it rain?

Dick:

Ahhh! It didn't just rain... [laughing]

Vincent:

It poured.

Dick:

It poured! Hurricane Floyd came in over North Carolina...

Vincent:

Mhmm.

Dick:

... and completely rearranged the landscape in September...

Vincent:

And that was in September. So August 13th was...

Dick:

I guess it shut it down.

Vincent:

... you said before it rained on August 13th and thereafter.

Dick:

That's right. It was a mild rain. But in September it really rained, and it flooded as a matter of fact, and there was lots of environmental damage.

Vincent:

Mhmm.

Dick:

But what those hurricanes do too though, remember, they have counter clockwise circulation...

Vincent:

Mhmm.

Dick:

... they could have picked mosquitoes up from the coast that were infected and put them farther inland. So that might have been one mechanism for jump starting this thing.

Vincent:

Would mosquitoes survive those winds? Yeah?

Dick:

Oh yeah! I'll give you a specific example of that, uh..., Bangladesh never had Dengue fever before a typhoon came into Southeast Asia, and picked it up from some other place and put it right down into Dhaka.

Vincent:

Fascinating.

Dick:

And now it's endemic.

Vincent:

Maybe there is something to this medical ecology.

Dick:

[laughing] Maybe! It's possible.

Vincent:

Maybe, we'll see. Strain number twenty-four is in the U.S.

Dick:

It is.

Vincent:

Have we found it anywhere outside of the U.S?

Dick:

I don't know, I actually don't know the answer to that, I think it hasn't been looked for anywhere else, but...

Vincent:

You would think it could spread out just as it came in.

Dick:

You would. Or I think this is the strain that they're seeing down in Central America and in the Southern Tier of Canada, I think that is the strain, it's the 2002 strain.

Vincent:

Yeah, I'd like to see it cross an ocean. Or perhaps I should rephrase, I don't...

Dick:

You mean go back.

Vincent:

I don't want to see it. But, I'm curious to see whether it would go back or cross the Pacific.

Dick:

And if it does, would it revert back to its older pattern, because of the wildlife influencing the outcome of the infection.

Vincent:

Sure. Yeah, wonderful question. That's why...

Dick:

The interesting part..., go ahead.

Vincent:

Virology is fascinating, because it's an ongoing experiment...

Dick:

It's an amazing world, isn't it?

Vincent:

... it's, it's dynamic...

Dick:

Here's one of those science news magazines, this is a pretty good one, and they featured on their cover in the August 30th/September 5th edition the following statement:

Vincent:

"Vive le virus", or "viva the virus - evolution's most creative force".

Dick:

Evolution's MOST creative force. MOST creative force.

Vincent:

Absolutely! There's no question it's influenced evolution. This is something we've only realized recently.

Dick:

Correct!

Vincent:

Do you know Luis Villarreal?

Dick:

I know the name, I do not know the individual.

Vincent:

He wrote a Scientific American article...

Dick:

Aha...

Vincent:

... a few years ago, asking the question "why aren't viruses on the tree of life?"

Dick:

Ahhh!

Vincent:

Even though they may not be living, they certainly have influenced it.

Dick:

Absolutely.

Vincent:

Same idea.

Dick:

Well, if I was a bird living in this country, United States, and if I was a crow, I would be scared. I would absolutely be scared.

Vincent:

Is this a good magazine, New Scientist?

Dick:

I like it, I think it's a little bit newsy...

Vincent:

Yeah...

Dick:

... ah, but they don't skimp on facts either, they give you the references to the articles, so I think that you can depend on the information in there. Yeah! I think it's a good one.

Vincent:

“Welcome to TheVirusphere: we hardly notice them unless we get sick, but without viruses we'd be up the primordial creek without a paddle.”

Dick:

[chuckling]

Vincent:

Excellent, I'll have to have a look at this.

Dick:

You're good. That just came out, I thought you'd like it.

Vincent:

Excellent.

Dick:

So the effects of West Nile virus in the New World, that is our part of the world, are totally unpredictable, and in that sense I think Duane Gubler was correct in that we don't know anything about West Nile virus in the United States, except that human outbreaks are always associated with hot, dry spells.

Vincent:

Mhmm.

Dick:

That's the one fact we do know. So, so Vince, from a control standpoint, without the use of vaccines, without the use of drugs, you're the public health officer in charge of the West Nile virus surveillance program, and monitoring, and alert network, what would be your advice, now that you know what the weather patterns are like...

Vincent:

Hmm...

Dick:

... for a warning at least, to the general public.

Vincent:

Absolutely. If the temperature is going above 90 for an extended period, you issue a warning, a West Nile virus alert. So what should we do, what would the warning constitute? Stay home, don't go outside? That's not practical, people are going to go out.

Dick:

Of course they are.

Vincent:

What would you do, use mosquito repellent if you're going to go outside for recreation?

Dick:

Number one.

Vincent:

Get rid of standing water?

Dick:

Number two.

Vincent:

Hmm..., don't do things at night when the mosquitoes are more likely to feed?

Dick:

Number three!

Vincent:

That means stay inside, right?

Dick:

Yeah, number three!

Vincent:

Anything else?

Dick:

No! And that's why...

Vincent:

Does that happen? Are there people who issue such alerts?

Dick:

There are, and in fact when the CDC explained to the residents of northern Queens what was going on, and why the year that the people with in-ground swimming pools got so frustrated with Con Edison, and this is another confounding factor that increased the likelihood that this would stick around..., ah..., during the summer months of course, everybody would like to go into their pool...

Vincent:

Mhmmm.

Dick:

... and cool off, right? It got so hot that people were uncomfortable even swimming in their swimming pools, and by the way, if you've got a swimming pool, it's probable that you have enough money to escape from that heat and go someplace where it's nice and cool for a while until things cool down again. So in fact, that's exactly what happened. There was 150 some odd in-ground swimming pools in northern Queens at the time of this outbreak, and about half of the owners of those pools vacated the premises to go off to, let's say, Zermatt Switzerland, or, I can name some other nice cool places to go to...

Vincent:

[chuckling]

Dick:

... you know, some of those cool places are hot, actually... [laughing]

Vincent:

When they were gone, they didn't chlorinate the pool!

Dick:

No, here's what happened: Con Edison, in its infinite wisdom, to try to save on electricity, upped the rates. Now, if you're a middle class person...

Vincent:

Mhmm.

Dick:

... and you're hot as heck during your work day and you go home, what's the first thing you do? You turn on your air conditioner. So Con Edison says "too much electricity, you're going to brown out the city, we're going to charge you more". Are you going to turn off your air conditioner just because...

Vincent:

No.

Dick:

... of course you're not!

Vincent:

You'll turn your pool off.

Dick:

Yeah, well that's exactly what happened, so they did, they..., you know they turned it off, they left. So the pools began to stagnate. And as the summer progressed, the water got lower, and more stagnant, and now these late night parties starting at ten and ending at three or four in the morning would..., the absolute perfect storm for transmitting this disease. They did a serosurvey on the community the year afterwards to find out how many might have been involved in the outbreak. You'll never guess how many people they said were involved in this outbreak. Eight thousand people living in northern Queens had inapparent infections. That's how many seropositivities they estimated from their random sampling of northern Queens.

Vincent:

Mhmm. It's an estimate though, it's not an actual number.

Dick:

It's an estimate, but it's a pretty good estimate.

Vincent:

Ok.

Dick:

So 8000 people got bitten and infected, during that outbreak. The residents of northern Queens have never stopped turning off their pumps.

Vincent:

Mhmm.

Dick:

They keep them on no matter what. [laughing] Because now they know that stagnant water encourages the spread of this disease. So the lessons are learned, but I don't know for how long. You know, that's another question of course.

Vincent:

Yeah these memories are short, unfortunately.

Dick:

They are. They are. The next big crisis forces you to focus on something else, right?

Vincent:

Has there been an outbreak of a similar size since then, in New York City?

Dick:

No. There has not. There has not.

Vincent:

It probably has not been as hot.

Dick:

That's correct! In fact I will give you something even more remarkable to think about and that is, the next year, the year 2000, was the coolest, driest..., I'm sorry, it was the coolest, wettest summer on record for 100 years. Here you have the hottest, driest, 1999, the coolest, wettest in the next year, it almost shut it down completely. The only outbreak we had was on Staten Island.

Vincent:

How many infections in that outbreak?

Dick:

Ten.

Vincent:

Less than ten?

Dick:

Something like that. Other parts of the country however did have more.

Vincent:

Right.

Dick:

But 2000 was a bad year for West Nile in this country for people. It was a great year for West Nile in birds. And this absolutely spread the infection. Now, you're going to ask me, how does a virus infection that's spread by mosquitoes and birds primarily, make it from the east coast to the west coast in three years, because that's exactly what happened. That's very fast.

Vincent:

Do you think so?

Dick:

And there's only a transmission cycle in the summer time. Ok well, the original hypothesis that we rejected out of hand was that a mosquito hitchhiked a ride from Israel on an air plane. It's not unlikely that could happen, but...

Vincent:

Well that's probably what's happening in the U.S....

Dick:

Ha ha ha, but every day you could have mosquitoes in cars and in trucks and on produce...

Vincent:

Absolutely.

Dick:

Going back and forth, so, but there's another thing here. Crows are the primary host for this infection. Crows are roadside feeders.

Vincent:

Mhmm.

Dick:

The ditches on main major highways accumulate water in the summertime...

Vincent:

And the crows get bitten...

Dick:

... and that's stagnant water, the crows..., and the drafts from cars could actually by wind alone spread this mosquito infection...

Vincent:

Sure.

Dick:

... down that main highway until you get to the desert primarily.

Vincent:

So, uhm, I think we should wrap this up soon.

Dick:

Perfect.

Vincent:

But one more thing I'd like to just bring up. Clearly there's a human vaccine being worked on.

Dick:

Yep.

Vincent:

And I assume at some point it will work and be tested and be licensed by the FDA so, I assume this will be a voluntary use vaccine, not mandatory. So who should take it?

Dick:

If I lived in Scottsdale Arizona, and I was over the age of 50, I would take it.

Vincent:

Anywhere where there are sustained high temperatures.

Dick:

And a lot of old people...

Vincent:

Yeah.

Dick:

... because, basically it's a disease of old people, it's not an inf..., it's an infection of all of us, but it's a disease of old people. Old meaning beyond the age of 55 let's say. All of the deaths, maybe 90% of the deaths in this country were in people over the age of 55.

Vincent:

So I also assume that if there were West Nile conditions as we've talked about before, high temperatures predicted for a while, that would be a good time to get immunized.

Dick:

Or avoid. [laughing]

Vincent:

Or go away..., to Zermatt?

Dick:

Or just take avoidance precautions. Don't stay out on the lawns late at night, or what you just said before, that's right. That's exactly right.

Vincent:

Alright, anything else you want to bring up? That was a good discussion, I think it sets the tone for future TWiVs.

Dick:

Right.

Vincent:

The whole interaction between the environment and viruses, which was a big factor in the emergence of West Nile is equally important for other viruses, and I think we can explore that when we talk about other types of viral infections in the future. So this has been "This Week in Virology", our first episode. Go to our website, twiv.tv, and we have some links about the things we've mentioned here, uhm, go and buy...

Dick:

[laughing]

Vincent:

... Dick's book, *The West Nile Story*, we'll put a link for that on the website as well, if you have any questions, if you want us to discuss things on the show, send us an email, twiv@twiv.tv, and we'll be happy to do that. And do subscribe and come back another time!

Dick:

Great!

Vincent:

Goodbye!

Dick:

So long!

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Transcribed by Gertrud Rey