JON ABRAMSON: So dengue and Zika viruses are RNA viruses of the family of flaviviruses. They also include viruses such as West Nile, yellow fever, Japanese encephalitis virus, and tick-borne encephalitis viruses. Some of these are bad actors. Yellow fever, for instance, has a mortality rate of about 30%, and is particularly bad in pregnant women, as far as mortality and their babies.

So they're transmitted by the bite of the Aedes mosquito infected with these viruses. And though we are-- we have these viruses even in North Carolina, we're less likely to go through what Puerto Rico, for instance, right now, is going through, where 25% of its population is already infected by Zika virus. Hadn't been there until either early this year or late last year. 25%. That's how explosive Zika virus transmission is.

The mosquito becomes infected when it bites a person with dengue or Zika virus, and then spreads it. So this is where-- I think this is the dengue slide. It is. This is where dengue is now. And as I say, it is clearly coming up. And as I'll show you in a following slide, how fast dengue is spreading across the world.

And dengue, also, like Zika virus, has a very low mortality rate. The dengue, have you get it a second time, cause substantial problems with bleeding and shock. We'll talk a little bit about that.

So the instance of dengue virus has increased dramatically during the last several decades, in conjunction with a substantial change in the number of countries with endemic disease. Current estimates are that 3.9 billion people in 128 countries are now at risk for dengue. Before 1970, only nine countries had severe dengue.

390 million dengue infections occur per year, of which 96 million manifest clinically. So it's approximately 25% rate of clinical illness, sort of like Zika, which looks like it's about 20% of clinical illness. Approximately 1% to 2% of patients reported to have clinical dengue develop severe disease. Again, there are four serotypes.

Zika virus. Zika virus was not in the Americas in 2014. It first arrives probably on a plane as a mosquito carries itself along as somebody's infected with it and comes into the United States a lot like-- and comes into South America or Brazil a lot like West Nile came into the United States. And then it spreads, and it's spread very rapidly. There are countries in South America that now have 60% of the population infected. Remember, most of those are not-- do not develop clinical disease, though we'll talk about the microcephaly in a few minutes.

So Zika virus was first detected in monkeys in Africa in 1947, and there's been relatively small number of cases in humans in Africa and Asia along a narrow geographic equatorial belt. The first human case that was known about was in Nigeria in the '60s, and the first outbreak of Zika occurred in the Micronesia, in Asia, in 2007.

The presence of the Zika virus in Brazil, as I said, only started in 2015, and has now spread to 28 countries. Brazil estimated 440,000 to 13-- I mean, 1,300,000 cases in 2015. And as I said, it was rapidly spreading.

So let's go back to the clinical points that I think are very important for you to know. And there's more in your slide set.

There are four distinct dengue virus serotypes, 1, 2, 3, 4. And the first infection is usually, if it's clinical, it's mild. It's the second infection that you have to worry about.

And it causes a lot of havoc across the world, because people are scared of it and worried about it, and rightfully so, because they see the hemorrhagic and shock disease that can occur. And so when the severe disease occurs, we still don't have any treatment for it. And so all of the support is supportive care.

And there is a vaccine. We will be making a decision on a vaccine in April of 2016, in two months, about whether we recommend it for all countries. There are some problems with this vaccine, and this vaccine is not the right one.

And in two or three years, there's another one coming along. This vaccine that we have, actually only effective against three of the four. And any country, at any time-- Mexico, for instance-- has all four in different places. But in one place it could come in, go away, and it will be replaced by another serotype.

Pregnant women, as I noted, are severe-- much-increased risk of severe disease. And that's a big problem, from our standpoint, because every death you have in a pregnant woman is essentially a death in a child, too.

Zika virus, for most people, is asymptomatic. 80% of those who are-- I'm sorry, 20% of those who get it and have clinical symptoms develop fever, rash, and arthralgias, usually about a week's duration.

There are now two major morbidities that appear to be associated, and in fact, I would take away the word "appear." Clearly the microcephaly in infants is associated. When I just came back from a meeting in Ethiopia, where [AUDIO OUT] that we talked about, and clearly the data are now overwhelming that it causes microcephaly.

There's a lot of things we don't know, and these are questions I get all the time. If someone has travelled in 2015 down there, and now comes back-- say, travelled in October, November, December, down to Honduras, and now comes back. Didn't have any clinical symptoms. Could their baby be infected and develop microcephaly?

We don't know that answer yet. We will relatively soon. But we don't know that answer. If you develop symptoms, it means it was in the bloodstream at one point, and therefore it could develop. We don't know the percentage. If you're clinically infected-- if you have clinical symptoms, and you're infected with Zika virus-- I'm sorry, with Zika virus, what percent develop microcephaly? We don't know.

Third of all, we now know, and there's six or seven cases that we know about, that it can be sexually transmitted from a male to a female. We do not know the other way around, but we certainly know male to female. But there's six or seven cases in the United States where we know that's occurred.

So again, you have to be cautious if you're pregnant. You certainly have to use condoms if you're pregnant. And if you're thinking about pregnancy, you have to be cautious about it, with all the same things.

There is-- appears to be an increased incidence of Guillain-Barre disease. Now remember, there are many viruses and many bacteria, at least until this one, campylobacter, was probably the number one single organism that caused Guillain-Barre syndrome. So we know-- it looks like-- and again, this is more now at this point, an association rather than causal proof. But it looks like it can cause Guillain-Barre syndrome.

All right. So there's some important questions. Besides the things that we know already, there are a lot of things we don't know. Has the Zika virus mutated in a way that allows it to rip through South America, in a way that it didn't rip through Africa? You'd say, well, why would you even think that? And the answer is the environment in South America is really a lot like the environment in Africa, with lots of mosquitoes, lots of places the mosquitoes hang out, and yet, we really don't know if it's mutated or not.

We know, as I said, that it affects a baby's brain. If you have microcephaly, they appear to be significantly developmentally delayed. We know that some women in the United States who traveled there and then came back and know they were infected actually decided to have abortions. I'm not recommending that or saying anything about it. I'm just telling you the fear that's out there.

And we don't know how long Zika virus can stay in the semen of males. So these are just some of the things that we do not know at this point.

I think that will-- so how can you avoid it? Well, the CDC does something differently. The CDC makes recommendations for the United States. So CDC has flat out said, warned against going down, if you're pregnant or thinking about a pregnancy, getting pregnant, to the countries that are infected. So that list is growing all the time.

The WHO has called it a global emergency, but has not recommended travel restriction. It's a very complex equation that goes into that. I'm not saying the CDC is right and the WHO is wrong or vice versa. It's just a complex equation.

There will-- there is now being ramped up rapidly-- I was at the CDC a few weeks ago. They have-- it looks like NASA. It was like you're looking at the NASA board and watching a rocket go off.

And they're following four diseases. They're following influenza. They're following Ebola. They're following Zika. And they're following Flint, Michigan. And there's 600 people, literally, standing at-- working at computer screens, following various aspects of this. So we are gathering information very quickly.

So we can, as-- Tom Frieden was down in Ethiopia, and he said the CDC has been trying to affect the mosquito so it doesn't do what it does for about three decades now, and it's failed. Every single attempt has failed. But he said maybe this time, with genetic engineering or radiation, maybe they're on to something. So we can genetically, you know, alter the mosquito, and not allow it to mate, and kill off a lot of the mosquito population.

And then I told you about the vaccines, where we stand. They are unlike Ebola, where they knew Ebola was a terrible disease, and they'd been working on it for over a decade. There are no studies with Zika virus vaccine.

But what we've learned about Ebola is important. And the backbone for the Ebola virus, and different techniques we've learned, will be applied to Zika. I say the earliest, the earliest, there'll be a phase 3 study would be late 2017. But remember, that's unbelievably fast compared to what it usually takes a new vaccine to get through.

So I'll leave you with that. I'm happy to answer questions after Larry gives you his quiz. If you fail, you have to leave the room, though. So I can't help it.

LAURENCE GIVNER: So this is a quiz. These are simple words that all of us use all the time. But let's see who knows what they mean.

All right. What is the difference between elimination and eradication of an organism or disease? This is something we talk about all the time-- smallpox, polio, measles. So what is the difference between elimination and eradication of one of these diseases? Anybody?

Elimination is regional or local. Eradication is global. So we have eradicated smallpox. We've eliminated polio and measles from certain areas-- endemic disease, anyway-- but we haven't yet eradicated them, because they're still seen throughout the world, or in some parts of the world. So that's the difference between elimination and eradication.

All right, here we go. There are the answers for you. And these slides are going to be posted on the website. I know you're excited about that.

OK. What is the difference between isolation and quarantine? This one's easier. What's the difference between isolation and quarantine? Anybody? These we use all the time, especially on the inpatient units. They need to be put in isolation, and their contacts need to be this and that, and they need to be all this and-- this is how you do it. What's the difference?

So it's simple. Isolation is for sick people. Quarantine is for well people. The answer is usually like, quarantine is more strict, or stuff like that. But it's very simple.

What's the difference between efficacy and effectiveness? So you often read about this vaccine had blah, blah efficacy. And another article said this vaccine had such and such effectiveness. What's the difference between these two terms?

Efficacy is a prospective, controlled trial. So it's often done to license the vaccine or the drug. And then effectiveness is what happens in the real world.

You know, so-and-so elementary school had an outbreak of such-and-such. Let's compare those who were vaccinated, those who didn't, and see the incidence of disease in those two groups. And that gives you the effectiveness. So effectiveness is real world, and efficacy is well-controlled prospective trials.

What percent of reptiles excrete salmonella? And you have to be plus or minus 5%. Salmonellosis in reptiles, up to 90% are infected by salmonella. 90%. They're asymptomatic. And of course, few of them seek medical care.

[LAUGHTER]

In 1996 to '97, it caused 74,000 cases of human disease associated with reptiles. And I know that's old data, but if you look at the-- one reason I presented this, if you look at this month's *Pediatrics,* there are a series of outbreaks in this country due to salmonella because of pet turtles.

And amphibians-- for example, frogs-- 21% are infected. So these, especially reptiles, commonly carry these things. So when your patients come in and say, oh, I love my little lizard at home. Their lizard doesn't love them.

[LAUGHTER]

So here's a high risk for invasive salmonella disease. Of course, this is the kind of list you see everywhere for high-risk patients. Immunocompromised hosts, pregnant women, and especially young children, in part because they like to kiss the turtle. And I've kissed a lot of turtles in my life, I'll say that. Before I was married. They're more likely to put turtles in their mouth, if you can imagine that.

But you don't need direct contact. If you live in a household with a turtle, you're exposed to the turtle and its excretions, and you may well get infected, regardless of what age you are. But it's the young kids who are most at risk, not only to acquire it, but also to have serious invasive disease.

So don't have them as pets. That's pretty simple. In 1975, the sale of turtles with less than a four-inch shell length was outlawed, in part because it's easier for kids to stick them in their mouths.

But in 2006, there are still almost 2 million turtles in United States households. So it's still widely out there. And these kids are being infected, and coming in to see you guys and us. So when you see this guy along the highway, don't stop. You want to drive right by the turtle man.

All right. Last serious-- last question. If you've given a drug for an off-label use, you must-- document the reason in the medical record, notify the patient or family, notify your institutional review board if you're in an institution, notify the FDA, all of the above, or none of the above.

All of the above? None of the above. Families.

All right. Let's go through this one. The FDA approval and indications are based on studies presented to the FDA, usually at the time of licensure, but often later on, if they want to get other indications for that drug or vaccine. The indications speak only to the pharmaceutical company, regarding what they can advertise or speak about to health care professionals when they talk to you about their drugs.

And if you been reading the editorials, medical literature, whatever you look at-- I'm sure you're reading them. I shouldn't say "if." But when you read them, you'll see fines have been levied against these companies in the billions of dollars, because they continue to be noted to be talking to health care practitioners about things that the FDA has not approved.

But this does not-- these indications do not in any way limit the physician. Not in any way does it limit what you talk about, does it limit your use of the drug, that at least half of the drugs we use for half of the diseases we use them has no FDA indication. And it's totally irrelevant to a physician whether or not there is an approved FDA indication.

Like I said, the slides will be posted on the website. There's a bulletin board right outside. Your final grades will be posted by 3 o'clock this afternoon. And I hope you all did well. Thank you.