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The Potential Threat of Dengue Fever

POTENTIAL PUBLIC HEALTH THREAT TO THE US OF DENGUE FEVER

Change and challenge is in the wind as 2008 comes to an end. The same is true when examining this month's ReachMD XM160 special series - Focus On Global Medicine. We take a look at both the changes and the challenges impacting global medicine.

Dengue fever, the new West Nile virus. You are listening to ReachMD, the Channel for Medical Professionals. Welcome to The Clinician's Roundtable, I am your host, Dr. Gary Cohen and joining me is Dr. David Morens who is a senior advisor to the National Institute Of Allergy and Infectious Diseases of the NIH in Bethesda, Maryland. Dr. Morens is a trained epidemiologist, an academic PhD Department Chair and has published and spoken extensively on the epidemiology and pathogenesis of the viral hemorrhagic fevers. Dr. Morens comes to us from his office in Maryland and we are going to be talking about the potential public health threat to the US of dengue fever.

DR. GARY COHEN:

David, thanks for joining us today. We appreciate it.

DR. DAVID MORENS:

It's good to be here.

DR. GARY COHEN:

Let's maybe before we get into the meat of the matter, may be you can tell us little bit about your own medical background and what got you interested in this little corner of epidemiology.

DR. DAVID MORENS:

Yeah, it's kind of a round about story, but that's the way it works in tropical medicine. I went to medical school at the University of Michigan and got an M.D. degree and did residencies in Pediatrics and then Preventive Medicine and I went to CDC, the Centers for Disease Control, in Atlanta as an epidemiologist and while there just got really interested in tropical infectious diseases and had, you

know, around the time I went there about 1976, there was a lot of activity of dengue in the Caribbean and I got involved in that and was involved in a number of outbreak investigations and just really got interested in the disease dengue as well as a number of other viral diseases that were prevalent or occurring in other parts of the world, Rift Valley fever in Egypt and it's just an interest had stuck.

DR. GARY COHEN:

Well, I saw your article in JAMA last month. I was taken aback as I suspect many of our audience were that you talked about this as a potential public health threat in United States because I think many of them, most of us, learned about dengue as you did it in tropical areas and of some academic interest, but not an immediate interest to us. I want to give us the lay of the land with dengue and where it is now in the world and how it fits into your concerns about the United States?

DR. DAVID MORENS:

Well, dengue is a disease and it is caused by any one of 4 dengue viruses and these are arthropod-1 viruses, mosquito viruses that have been prevalent in much of the tropical and subtropical world for several centuries and in fact we have had dengue in the United States before. We have had major epidemics and we have had, you know, pretty big ones mostly as far back as the colonial times, there was an epidemic in Philadelphia, not a tropical city, Philadelphia in 1780 and the physician signer of the Declaration Of Independence, Benjamin Rush, was very much involved in that epidemic. So, yes, it's a tropical disease in the sense that it is prevalent in the tropics pretty much worldwide every year, but because it's a mosquito disease, it can appear wherever the mosquitoes go and those mosquitoes are able to breathe in the summer of the United States temperate areas like Philadelphia and other places. So, essentially, although we can call it a tropical disease, it has the potential to occur at virtually any place where the mosquitoes occur and in recent decades, some of the mosquitoes have been extending their geographic range. So, that's one of the things that puts the United States at risk.

DR. GARY COHEN:

Has it changed or expanded its vectors or is that the vectors that are expanding their reach?

DR. DAVID MORENS:

I think it's both. Classically, the dengue is caused by a mosquito vector called in the Aedes aegypti, the same vector that causes yellow fever and for those of you listeners, who really follow this kind of news, there is another unrelated disease called chikungunya, which also can be carried by that mosquito. The Aedes aegypti has a number of related species such as Aedes albopictus, which are different mosquitoes, but also capable of transmitting dengue viruses and it's 80s albopictus that has over the recent decade spread alarmingly geographically to the point where it now is found in a number of the United States, most of the Southern United States and some of the northern ones as well. It's capable of causing dengue fever epidemics. It has in other parts of the world and I believe it's been involved according to the news reports in the chikungunya epidemic in Italy. So, a lot of this stuff is happening. The mosquitoes are moving, the viruses are adapting. This seems to be a broad trend in mosquito-borne diseases and dengue is just a one notable and bad example of it.

DR. GARY COHEN:

Given that, where would you fit dengue in terms of other emerging infectious diseases and how they are potential threat to the United States? For example, you mentioned in your article that a decade ago, we didn't know much about West Nile and now it's a member of

the same family, how would you compare this to that?

DR. DAVID MORENS:

Well, I mean, I think it depends on what the parameters you are interested in are. In terms of likelihood of spreading in the United States, I put it very high. We had an epidemic in Hawaii in 2001. We have had cases in Southern Texas along the border off and on for 20 or so years and I think the chance we will have epidemics is in continuing one is probably very large, but on the other hand, it's a very different virus than West Nile. It doesn't get into birds and gets spread all over the place. So, its geographic range is going to be limited and seasonal and sort of geographically fixed. It's not going to move around with bird migrations like West Nile does. The other thing you can say about it is generally dengue is not a fatal disease and I would expect that if we have epidemics in the United States in the future, which we will, we are not likely to see many fatal cases, but we are likely to see an awful a lot of illness and you know, when you have dengue, I believe I had it once and I have certainly known friends who have had it and seen many patients, you almost wish you were dead. It's like having the flu, but worse.

DR. GARY COHEN:

Got it, got it.

DR. DAVID MORENS:

Second thing that can be said is that one of the mysteries of dengue that you may or may not want to get into, but because it doesn't have an answer yet is that in recent decade, dengue has begun to cause fatal illness and to kill thousands of people every year and we don't really know why. It's a complicated, perhaps immunologic issue, but whatever, it's not possible to say anymore that dengue is a mild flu-like disease. It has almost the potential of fatal cases. That's said, I don't think there is anything about the epidemiology that would suggest to scientist that we are going to see major fatal epidemics with high numbers of death in the United States, but this was a disease that can really alarm a community when it gets in and I have seen it all over the world cause, if not panic, mass public and civil alarm. If everybody gets sick at once and they are very sick and the town or the city or even the country, in case of small countries, can almost literally shut down when a dengue epidemic occurs.

DR. GARY COHEN:

Yeah, I imagine it gets your attention. David, give some perspective on the attention and resources that are being focused on this disease. You have been around the CDC and the NIH and academia. Do you think it's getting the appropriate attention and resources at this point?

DR. DAVID MORENS:

I guess to answer that question, I would have to say for the United States and for domestic science such as the science that we funded NIH and that is funded and done by CDC, it's getting quite a bit of attention and has for a long time. Most of the death and most of the morbidity from dengue occur in an international setting and occur in developing countries and you can make an argument about to what extent we as Americans should be involved in that. I would say and it's our position here at NIH that we are very involved in international diseases because we know that they can and in many cases will come here. So, it's been one of those diseases, it's not as a bigger threat as cancer and heart disease and HIV and some of those things, but on the other hand, it's always a potential threat. It has been in the United States before and the federal agencies, you mentioned NIH and CDC have long been interested in dengue and have long

been doing things to research it, to better understand it. You know, as I mentioned 30 some years ago, CDC at that time had and still has an extensive operation, has a major laboratory in Puerto Rico with access to the Caribbean and to South America and has been involved in activities in other countries as well and a third federal player in this that shouldn't be forgotten is United States Military, particularly the Army, but also the Navy has long been involved in dengue research and you know, this goes way back to the turn of the last century, you know the 1800s to the 1900s when US military physicians were some of the major scientists investigating and trying to solve some of the problems of dengue. So, you know, this is below the radar screen of most Americans, I know, but United States scientists and civilian scientist and military scientists have been involved in dengue in a major way for over 100 years and I do think that's appropriate. Now, private companies are getting involved and there a number of vaccines and development, both federal vaccines. For example, the US military and also private companies are developing vaccines that could be used. It's not clear at this point what value those vaccines would be to American citizens other than those who live in the endemic areas, American citizens such as Puerto Ricans and people in the US Virgin Islands and people in Hawaii may be and travelers abroad, but certainly such vaccines are greatly needed in the developing worldwide. In many countries, dengue is one of major childhood causes of death.

DR. GARY COHEN:

You know, it's interesting as you talk about vaccines and the military. I can't help but think about yellow fever and how certainly it's a member of the same viral family. Why is it yellow fever has some immunization potentials and dengue does not? It's obviously been of interest for at least as long a time. What's different about it?

DR. DAVID MORENS:

That is a tough question. You know the yellow fever vaccine was one of the first effective viral vaccines made by Max Tyler in the United States many decades ago. You know, why that vaccine was successful, I don't know. You know, the general history of vaccinology for viral diseases is decades ago, we made a lot of good ones and it seems now we made them very easily and now we have a lot of trouble, so I don't know what Max Tyler knew that none of the rest of them know, but one of the things is we have a lot of safety concerns now that were not known to be concerns then such as making vaccines in mouse brains, which we essentially can't do any more and Tyler didn't have those restrictions, those theoretical safety restrictions on. The second thing about it, I think its difficult is that yellow fever is 1 virus. It's largely clonal, which is to say that although they are like the evolved viruses, there are variations of them, there are no major branches of the family, it's all 1 virus. So, the vaccine works against every yellow fever virus that is out there as far as we know. Dengue has 4 different viruses that are closely related, but not the same and so it would not be possible to make 1 vaccine against 1 dengue virus. You would have to make 4 vaccines against 4 dengue viruses and combine them and this has proved to be a big challenge for whatever reason, it's not clear, but we scientists talk about it as if these 4 viruses when put into a vaccine compete with each other or the immune responses to them compete with each other, so if you want to raise a high level of immunity to each of the 4 viruses, you tend to get may be 3 of them, but not the other one and then the person is not protected fully. The third thing which is really a mysterious thing is that there is much circumstantial evidence that severe dengue disease, which can be fatal, it's called dengue hemorrhagic fever or the severe form dengue-shock syndrome occurs on a second infection rather than a first or third or fourth with 4 dengue viruses, as you could theoretically have 4 infections, but dengue hemorrhagic fever and the fatalities seem to occur not exclusively, but pretty much on the second infection, not the first, third, or fourth and one of the prevailing theory about why that is a phenomenon called antibody-dependent enhancement, where a little bit of immunity to one of the viruses actually potentiate the next one you see. So, if that's true and we don't know it's true, that circumstance is consistent with the evidence, but it's not proven. If that's true, than there is the theoretical concern that a vaccine could raise enough immunity to potentiate the disease when you meet the real virus, the live one in an endemic setting or an epidemic setting, but not enough to protect you.

DR. GARY COHEN:

Well, you have given us a lot to cue on <_____> and we appreciate that. I wanna thank Dr. David Morens for being our guest. We have been talking about the potential US threat of dengue fever.

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