

Climate Driven Vector Creep

Transcript

Dr. Clancy

Welcome to Rounding@IOWA, continuing medical education podcast developed by and for healthcare teams. I'm your host, Dr. Gerry Clancy, Senior Associate Dean of External Affairs for the Carver College of Medicine here at the University of Iowa. Today we'll delve into climate-driven vector creep and the associated infectious diseases that can creep into new territories. A few years ago, I was invited by the World Health Organization to visit and give a talk in the Amazon. It was a complicated visit because going into the Amazon requires that you prepare for months ahead of time, particularly around what vaccinations you'll need and how you will schedule out those vaccine schedules. I would also need to take protection from mosquitoes to a new level. When I visited the county health department to begin my course of vaccines, the public health nurse was so excited. I recall her saying in a gleeful voice, wow. I've heard about all the vaccines you need to visit the Amazon, yellow fever, typhoid, rabies, and more, but I've never had a real patient going there. This is going to be great. You're going to experience many versions of these infectious diseases with each vaccine and will need to wash your clothing in special deep products. And of course, you can't have any water from the faucet or the shower touch your lips. And at that moment, I again realized how many deadly infectious diseases are out there. And as we will learn today, some of them are on the move. In a previous Rounding@IOWA podcast, we discussed tick-borne illnesses and the impact of climate change on several infectious agents and diseases carried by ticks. As we record this episode, we are finishing up a super El Nino summer with record temperatures across the globe, so stay tuned as this topic evolves over time. Today, we will go much further discussing how other vectors and the associated infectious agents are expanding their territories driven by global climate change. For our learning objectives, by the end of this podcast, participants will be able to first, identify emerging vectors and pathogens shifting into new geographic regions. Second, recognize clinical presentations and diagnostic considerations in emerging vector-borne diseases and in other parts of the globe that we may not think about. And third, apply prevention strategies and early management principles for climate-sensitive vector-borne infections. We have the great advantage today to have back on Rounding@IOWA two infectious disease experts, Dr. Benjamin Appenheimer and Dr. Jason Barker, to help us sort through all of this. Dr. Appenheimer is a Clinical Associate Professor of Internal Medicine in the Infectious Disease Division here at the University of Iowa. He is Assistant Director of

the Infectious Disease Fellowship. and the Associate Clinical Director of the Infectious Diseases Division. He earned his MD at the University of Illinois College of Medicine at Peoria. He completed his internal medicine residency at the University of North Carolina Hospitals, and then Dr. Appenheimer came to the University of Iowa for his infectious diseases fellowship. Dr. Barker is an Associate Professor of Internal Medicine in Infectious Diseases here at the University of Iowa. He earned his MD degree from Baylor College of Medicine. He completed internal medicine residency at University of Texas Southwestern in Dallas. Dr. Barker also came to the University of Iowa for his fellowship in infectious diseases. Dr. Appenheimer and Dr. Barker, welcome to Rounding@IOWA.

Dr. Barker

Thank you. Yeah, thanks. It's good to be back.

Dr. Clancy

I'm glad to have you guys back as well. When we use the term climate-driven vector creep, and that's something that I made-up, what does that actually mean in practical clinical terms, just as kind of a setting the stage for today?

Dr. Barker

I think that one thing to do is to sort of set the stage a bit just generally for vector-borne diseases that they've been evolving for a while. If you wanted to just tell the story of Lyme disease, it's an interesting story of the spread of the deer tick from the Southeast throughout the United States in the 20th century, but then cycles of forestation and deforestation. So if we can talk about climate-driven, I think you're talking about what are the effects of climate change on top of these already quite complex dynamics that affect how we interact with the vectors. It's not just about the vectors. If you want to talk about the vector-borne disease, it's about do humans interact with the vectors that are carrying the agent of interest? And are those interactions more frequent, more intense, and so forth? When we talk about climate, we're just having to layer an entire new set of challenges on top. And it can frankly be hard to disentangle, just like we think with climate generally.

Dr. Clancy

Sure. Ben, anything to add there?

Dr. Appenheimer

Yeah, I think the other thing that's at play with that makes these interactions even more complex is that it also affects the reservoir host. So just to kind of give a definition there, you know, reservoir host is the animal where the infection propagates and how these

vectors that we're speaking of get infected in the 1st place. And so for most of these infections, with the exception of malaria, humans are not the main reservoir and they require the presence of other animals like mice or deer or things like that. And so that's another feature that factors into the geographic locations of these infections and also where climate can factor in as well.

Dr. Clancy

Both of you, when you answered that, I thought back to Ebola and how growth of major metropolitan areas in Africa into the jungle and into areas that are deforested have changed the pattern of the bats that carry the Ebola virus as well. So I see what you mean as far as it's not just climate change because people are on the move as well and deforestation is on the move and all that. So what are the major environmental drivers then that are changing this vector behavior and distribution? What are you seeing as far as those multiple layers?

Dr. Appenheimer

The biggest ones that we think about are temperature, rainfall, and then urbanization. And also along with that, humidity I think plays in a role as well. These are not linear relationships and they're very complex. A lot of times I kind of think of this as like a Goldilocks situation where it's not like rising temperatures increase activity completely. They do to a point and then at a certain point it drops off. So there's kind of this middle ground that a lot of these vectors like to live in. Temperature affects ticks and mosquitoes by causing faster development and shorter life cycle and increased activity. So they're more likely to seek out hosts, they're more likely to bite humans and things like that in specific temperatures. I mentioned rainfall. When you think about that, this affects ticks and mosquitoes a little bit differently. With mosquitoes, they require standing water to breed, and so they need enough rainfall and enough moisture to have standing water in order to survive and in order to propagate. Whereas for ticks, precipitation at a certain level is helpful. It increases tick survival and their activity, but at a certain level, if it gets too high, then they kind of seek shelter and don't do as much activity in seeking hosts and things like that. So there's really this kind of middle ground when it comes to rainfall. And then urbanization, when you think about that, it's a really complicated variable. Some vectors may thrive in urban settings, so certain mosquitoes. When you think about standing water in pipes or in gutters or things like that, this can set up locations where they can live and thrive. Whereas for ticks, the thought is that the expansion of the urban and suburban development into rural areas really kind of closes the gaps to where ticks and humans live and increases that interaction between the vector and the humans.

Dr. Clancy

Great, great answer. Go ahead, Jason.

Dr. Barker

I was just going to add, I think you can think of urbanization as part of a broader category of just human adaptation. For instance, one observation made is that even droughts counterintuitively can lead to waterborne diseases or mosquito-borne diseases because it drives people in desperate conditions to sort of ad hoc collect water and keep them in buckets or in large vats and so forth. Even more broadly, if you think about humans responding to disaster conditions, there's a whole setup. We could do a podcast on post-flood infections because of what happens with water being exposed to people and the various kinds of things that you can see. And then of course, just the general disruption to infrastructure, meaning that if we're gonna talk about climate and we're gonna talk about extreme weather events, to the extent that these are more frequent, that's another aspect of the climate-driven infectious diseases even generally, but even specifically with vectors.

Dr. Clancy

Great, great. Well, you two are command of probably thousands of different infectious disease agents. It's amazing how much territory you have to be able to know in infectious disease. But What's kind of your top list of pathogens here? What's your top 10 or top 20 on your list of vector-borne diseases?

Dr. Barker

I would start with thinking about where we're practicing and where maybe most of our listeners are in the Midwest. The #1 vector-borne disease in the United States is Lyme disease. We're not in one of the sort of most hyperendemic areas. We have those areas around us in Wisconsin and Minnesota, certainly on the Atlantic Seaboard, East Coast. In the last 20 years, this is probably in part due to, some extent, perhaps due to climate change, have seen more and more Lyme in Iowa proper. Both I and dermatologists in the community I've spoken with have said it used to be that all the Lyme I saw was in people, you know, getting back from Minnesota or Rhode Island, what have you. But then in the last 15 years, we've all seen honest to goodness Lyme where someone never left. So I would start with that as something that we see here. Anaplasmosis and ehrlichiosis, we're kind of stuck between those and those are of course are tick-borne infections and the distribution of those has been changing. So those would be the top three. There's some less frequent ones that are dangerous that we talked about on the tick-borne disease talk. I think the ones then that you think about being more associated with climate change and temperature changes and rainfall changes would be some of the mosquito-borne stuff,

right? So we had a huge Zika outbreak in South America and the Caribbean not that long ago. So we were having to deal with thinking about that. I'm old enough that I remember St. Louis encephalitis in Texas back in the 70s and 80s. It was kind of a realization that this was spreading. So we see these waves, but I would say that I would put those tick-borne infections as the main ones for us to think about as far as stuff you can get here. And then thinking about these outbreaks of mosquito-borne disease, which are probably going to be more frequent.

Dr. Clancy

You both have been practicing for a while. Tell me how the US map of infectious disease predominance has changed over the past decade or so.

Dr. Appenheimer

Yeah, I think when you look specifically at these vector-borne diseases and the maps associated, they seem to be expanding. And I would say they seem to be becoming more dense in most endemic areas as well. So these infections that we used to rarely see, at least here in Iowa, are becoming more common. I think Jason mentioned that when he was referring to Lyme disease. If you look at the incidence of Lyme disease in Iowa over the last 10 to 15 years, 15 years ago there were very few cases that we would see here in Iowa. And over the last 10 to 15 years, they have had a steady increase to where we're seeing them more frequently. The other thing that has increased in incidents in the United States is West Nile virus. And so those are probably the two biggest ones that I think of. Internationally, it's a different story. I know most of our focus will probably be on the United States here, but internationally, both malaria and dengue have increased over that same time span. So it's hard to know how much of this, as we've talked about, it's a really complex interplay, so it's hard to know how much of this is directly related to climate change versus other factors, but certainly it's part of it. And I would say that partly because if you think about, and we'll get into this I think in a little bit about, how climate change should affect the distribution of the vector for Lyme disease like the Ixodes tick. You would think based strictly on climate change that it should be going northward into Canada and things like that, which it is, but here we're also seeing expansion southward from Minnesota and Wisconsin into Iowa. So that just goes to show you that there's more factors at play than just climate change.

Dr. Clancy

Sure. almost passively, I've become much more protective of my skin when I'm outdoors. I just don't think about it. It's almost natural to me now to make sure I'm covered up, make sure I've got spray on if I'm going to be out and about long enough. You both mentioned mosquitoes and ticks. Are there other vectors that we need to be considering? I got bit by a

deer fly right in the back of the neck a week ago, and it hurt and it bothered me. But I thought to myself, is that more than a deer fly that just got me? So are there other bugs we need to worry about?

Dr. Barker

I would say that they're not nearly as frequent. So I think that really, I think you can focus your prevention practically on ticks and mosquitoes and that helps you decrease the tick-borne infection incidence, but also with respect to mosquitoes, West Nile and other causes of encephalitis, which although rare are devastating, and there's certainly many of these viral encephalitis are much more dangerous for older people. And so that could be relevant to someone making decisions about that. So I think as a practical matter, when you talk about, okay, which products would I want to use, really focus on ticks and mosquitoes. And that's really most useful. The West Nile story is interesting because it was introduced, we think, in roughly the late 90s, first appreciated out near Long Island, New York City area in 99. And once introduced, spread across the country. It was really amazing. You could look at the year to year. And actually in 2002, that summer was the first summer that we had it here in Iowa. I was a fellow and one of my first rotations, I actually was on TV. My faculty was like, I'm going out to dinner with my wife tonight, can you do this? And I was like a brand new fellow and yeah, I got to do the press conference talking about the first case of West Nile at the university. And so we've seen the emergence of a vector-borne disease. So from 1999 to 2005, we see it go across. The first years are the worst and then you kind of hit this sort of background now where we have several thousand cases reported every year of West Nile. It's an interesting bit of history that we unfortunately got to see a pandemic too. I wish we hadn't had that opportunity, but we've also had the opportunity to see the establishment of a new vector-borne disease right in front of our eyes.

Dr. Clancy

Yeah, well, we've talked a lot about ticks. Let's talk a little bit more about mosquitoes. Personally, to me, a mosquito is a mosquito, but for you folks, there's differences. And so which mosquitoes and which pathogens are we worried about with the mosquitoes? You mentioned West Nile, but what are the other ones we're worried about now?

Dr. Appenheimer

So when I think of the different genera of mosquitoes that can transmit infections, I think there's three probably that come to mind most frequently. The Aedes mosquitoes, the Anopheles, and the Culex that Jason mentioned recently. The Aedes mosquitoes are mostly associated with different arboviruses. Those are the ones that carry things like dengue and chikungunya. The Anopheles mosquitoes are famous for carrying malaria. I

believe they also transmit filariasis as well, not something we see here in the US. And then the Culex mosquitoes are West Nile and St. Louis encephalitis and other encephalitis. You can get more species specific, but the way my brain works is kind of more of a higher-level view. And that's how I group things in my mind, thinking about the different types of mosquitoes.

Dr. Clancy

Yeah. So, you know, kind of coming back to the map a little bit, are there examples of pathogens and diseases showing up in places where clinicians may not expect them? Are we getting malaria in different parts of the US that previously we hadn't? and other infectious diseases? Are they, it's not happening very often, but is it happening to some extent?

Dr. Barker

The one I can think of, we had some local transmission of malaria where there was, I think about 8 cases, I want to say in Florida and Texas in the summer of 23. And it's thought that what happened was these are anopheles transmitted. And in these areas, we have these genera and people, travelers returned with Plasmodium vivax. And then in the next couple of months later, we don't know for sure if those cases were the cause, but then we saw locally acquired vivax malaria. Seven of those folks were hospitalized. So, you know, that was a situation where, and that's sort of like analogous to the classic airport malaria, right, where someone literally gets off a plane and then there's mosquitoes on the ground there and they can get passed around a bit. Now, the good news is they don't end up getting established in the human population for a variety of reasons. Probably just, we have a lot of air conditioning. And then we have just less overall mosquito exposure. And that's one of the ones we think about the reservoir, it's humans practically. So if it doesn't get established in the human population, you don't have people getting bit frequently, you won't see it. But specifically with respect to some of these infections surprising clinicians, that'll do it. And then the question is, so what do you, what do you do? Because, 99.9% of the time it's not going to be airport malaria. But I do think that we can think about certain things that might trigger our thinking. If you pick up on a bunch of hemolysis, if, you know, a blood smear can be helpful for a lot of conditions. In some of the tick-borne stuff, you might trip over a CM or Babesia or something. And of course, if you have the picture right, just put that in your list. There's even sort of point-of-care antigen kits for malaria that aren't perfect, but they're pretty good, and you still need a smear, but that can be done faster. So I think what are some clues? Okay, I had this infectious syndrome. It's not quite localizing for me obviously yet. How do I cast the net widely? I will still say we're always as clinicians pressed for time. I think you can very quickly ask someone, so what do you do for a living?

And I think you can very quickly ask someone, have you been outside where we are now any time in the last two months? You could sort of work in some question just to say, am I going to have to worry about something associated with travel or more exotic exposures? That's still going to be more frequent, I think, than things like airport malaria.

Dr. Appenheimer

I think when people hear about locally acquired malaria, it makes them nervous because they think, okay, it's here. They've seen how other diseases can spread. And so they start to think, okay, what's going to happen when this becomes endemic in the US and it's just something that we have to deal with on a daily basis, which would be a really big deal just based on the severity of malaria. But there's several factors, and Jason hit on a few of these that I think are reassuring and make the likelihood of this happening extremely, extremely unlikely. First, we've talked about how humans are the main reservoir. In the United States, most humans have not been exposed to malaria before, so when they get exposed, they're highly symptomatic. And so when people are symptomatic, they go to the hospital, they seek treatment, and they get the medications, and they get cured. And because there's no reservoir outside of humans, there's no other way for this to propagate within the population. It's not like it can get into deer or mice or lizards and then become more prevalent within those hosts, allowing it to get transmitted to humans. The other thing is, when things happen locally, there are things you can do to decrease the local mosquito population. And the other factor is things, as Jason mentioned, like air conditioning. So window screens, air conditioning, all those sorts of things are preventative. And so The likelihood of anything getting into the United States and then expanding quickly to become endemic as far as malariality goes is highly, highly unlikely.

Dr. Clancy

Sure. So you bring up really good points about being outdoors, being in other parts of the world. Are there other populations or other situations that make you more vulnerable to picking up some of these diseases? Anything else on the list? Age or immune status or anything like that?

Dr. Appenheimer

And I think these are, they kind of differ depending on which disease we're talking about, but there are certain types of immunocompromised status that increases risk of acquisition and severity of some of these infections. A specific one that I'm thinking of is when we think of something like babesia, people who have had a splenectomy or are functionally splenic have significantly increased risk of infection and severe disease. Pregnancy tends to be a risk factor for severe disease in a lot of these things as well. And

really though, any other immunocompromised status, malnutrition, a lot of those things can also affect people's risk of both getting these and also how severe the infections are.

Dr. Barker

And one other specific immunocompromising conditions, we have a lot of patients now in biologics, right? So, and the one that's been associated particularly with relapsing a more severe Babesia requiring really long courses of therapy and sometimes retreatment is the anti-CD20 type, so the anti-B cell drug, so Rituxan. and its cousins, that babesiosis can be really tough. First of all, you have to think about it to make the diagnosis in the 1st place. You know, because when we're thinking about immunocompromising conditions, our brains will tend to go other places, but that's one. And then the other thing is that the diagnosis of later Lyme disease can be challenging in folks whose B cells don't work because your serology has become unreliable. You know, we've seen patients on a anti-CD20 drug and have some cryptic presentation, and in some senses, we've been fortunate to sort of trip over it or I guess the serology wasn't that bad. We still were able to catch it and catch these things, but that's another specific one that you'll see pretty frequently.

Dr. Clancy

So you both are specialists and you receive referrals primarily from internists and family medicine physicians. If you could talk to the internists and the family medicine docs through this podcast, what would you want to let them know as far as being a frontline clinician and being aware of what might be a presenting set of symptoms for these patients? You mentioned fatigue, but what else is on the list?

Dr. Barker

I think one way to think about it is that these conditions are remarkable in the way they don't localize. And in fact, therefore, I think the bucket that you can kind of put in mentally is, okay, I have an infectious syndrome that's not localizing. Now, sometimes it's not localizing yet, right, because you haven't scanned or you haven't picked up a transaminitis or what, you know, something might actually end up focusing it. But that is, it's a lack of localization is a kind of localization, right? It's a kind of So I think that when you have that and you haven't been able to sort of pin down where is this coming from, that is what a lot of these look like. And that's why then there's so many things that can do that. It's why the exposure history becomes so important. It's like, oh, I need to think about tick-borne diseases because they often don't present with something obvious on the first presentation. So I think that having, and it's actually what I teach our students and residents and fellows and everyone is like, with infectious diseases, we think about localizing. Okay, does it localize for us or not? And if so, where? And together with context,

like where are we? Where's the patient? Who is the patient? What's their age? Are they immune suppressed, like we talked about? You put together context and localization, that's kind of how I think about it. So if you've got a kind of non-localizing, maybe non-specific liver stuff, what have you, aches and pains, but then a potential exposure, then that kind of opens up your mind. Oh, right. Okay, so now I think about some tick-borne things. I might think about some travel things and be extra careful with my travel history. So that's what I As far as just the overall syndrome recognition, that's what I would say.

Dr. Appenheimer

It's difficult because a lot of these can present differently. And so it's a really heterogeneous mix of infections. And so I think what Jason said is key and when I was kind of thinking about this, anytime fever without an explanation and especially without localization. And then I think you can add into the context of things that you take into consideration is things like travel history and potential outdoor exposure. And so I think when you're seeing someone, not every patient you see requires an extensive travel history, but if you have someone who's coming in with what looks like an unspecified infectious process that doesn't localize, I think that is a start asking those questions, and that can help you narrow in what you're thinking about. The other, I think, initial clues that I think of, especially for specific tick-borne diseases like Ehrlichia and Anaplasma and things like that, is someone who's coming in with a fever and then leukopenia, maybe some mildly elevated AST and ALT, and that can kind of go with things like dengue as well. So when you're thinking about some of these vector-borne diseases, those are also things that I take into consideration and that we get for a lot of these patients.

Dr. Barker

Following up on that, it's a great point because low platelets are even not super specific, of course, because anything that makes you septic can make you septic enough can drop your platelets. But that's also really a feature of the tick-borne diseases, the many Borrelia, many rickettsial illnesses, no matter how you acquire them, and certainly the red blood cell parasites. Babesia and malaria can cause that activation of all the white blood cells all throughout your body in a particular way that they seem to just, you just kind of consume the platelets. That's another one that when you see that, think, okay, could this be severe sepsis and so forth, but also maybe that's something else that can make you in that moment think more broadly about your differential. And I will say that in the sepsis criteria, if we were doing a talk on sepsis, low platelets is one of the markers of organ failure. It's something that generally speaking, if someone has an acute drop in their platelets with an acute illness, it makes me nervous. So that's another potential clue.

Dr. Clancy

Again, you both have practiced for a while. How you take the travel history, has that changed at all? We have a lot of people in the US go to Mexico and they go to the Caribbean or they go to Canada. How in-depth and what questions you ask as far as travel history, has that evolved some?

Dr. Appenheimer

Yeah, I think it's evolved slightly in both how I take it and also how I think about it. and how I take that information back when I'm forming a differential diagnosis. one of the first things I ask, a lot of these, especially vector-borne diseases, have a pretty short incubation period. And so you don't necessarily have to ask, where have you traveled in the last two, three, four years? There are some infections that travel history throughout life. matters, and that includes things like tuberculosis. But for most of the things we're talking about today, really the incubation period is on the span of one to two weeks. And so the first question I'll often ask is, have you traveled anywhere in the past one to two months? And then not only do I ask internationally, but I also ask, where have you traveled in the United States or outside of Iowa? And that can give you a sense for, are they at risk for other things across the country? As we mentioned, now that we have had some locally acquired vector-borne diseases that we used to not have, things like malaria, and then there have been a in Florida and Texas of things like dengue and chikungunya. So I don't necessarily use travel history to rule out the possibility of things, but it certainly highly affects my pre-test probability and how likely I think a particular infection might be.

Dr. Clancy

You both are on a service that actually is very much across our hospital as well. You're in the intensive care units A lot. What are some of the really significant serious signs and symptoms that you may be called in on as far as a differential for some of these vector-borne illnesses.

Dr. Barker

So I think the first is just sepsis care, right? We learn how to recognize sepsis. We learn how to recognize organ failure and then to appropriately triage folks. And there's a whole world of literature from the critical care folks and how to manage perfusion and various aspects of critical illness. So I think first things first is just first principles. that's the first thing to say. I would say that a couple of, I guess maybe pearls, since we're talking about the sort of vector-borne stuff, anaplasmosis or ehrlichiosis can put people in the ICU. Babesia can do it certainly when you don't have a spleen. The other thing is that people who are not immune to malaria and get it, so for travelers, right, or expats who've been out of the

malaria area for many years lose that sort of booster effect. And so when people with inadequate, low amounts or no immunity to malaria get it, especially falciparum malaria, that is one of the things that will have a very high mortality rate. And the specific signs there, again, it's sepsis, severe hemolysis, organ failure. But I would say, you know, one of the criteria in our SOFA analysis, sepsis, organ failure, you know, assessment is mental status. So once again, we talk about cerebral malaria as a particular condition that requires us to think differently. And so I think, again, this is just general care, but generally if someone's sick enough to get altered, they're pretty darn sick. So I think as far as the sort of initial presentation, and then of course, I think certain things can drive you, but if you are seeing a lot of hemolysis, then okay, think about a red cell pathogen. Yeah, that's what I would start.

Dr. Clancy

You know, there's some overlap of some of these symptoms and so any diagnostic tricks or any diagnostic pitfalls that are common?

Dr. Barker

There is one thing, and I alluded to it earlier, and it's actually one that even as a specialist, I kick myself that I didn't think of it sooner. It's just if you're puzzled, sometimes a blood smear can be really helpful. I mean, just as a different kind of context, but one that you can see is like sometimes someone comes in super sick and before you've gotten back anything else, the blood, the lab might, if you're lucky, and they pick up on it as a human looking at it, they'll say this forms or something in the white blood cells. And it's histo and they have disseminated severe histo and they have HIV AIDS and histo and that's your first clue. Before you even have the serology or maybe the person wasn't even thinking AIDS. That's sometimes what you do. So if you want to think about like what is a pearl, again, have a person look at a smear. So I think that's one thing that I've found can be helpful.

Dr. Clancy

Great. I find this question very helpful as a specialist as well. When should you two be involved? When do you call infectious disease?

Dr. Appenheimer

So I think this varies again, probably based on which specific illness we're talking about. But in general, most of the time we get involved with these is the diagnostic stage. And that is because these patients end up hospitalized, they can get sick, they have fevers. And most of the testing that we've talked about or that you do to really firmly establish a diagnosis for these takes time. The exception to that is malaria. We could get a malaria

diagnosis back pretty quickly. But things like Ehrlichia and Anaplasma, we haven't talked about Rocky Mountain spotted fever, things like that, West Nile, all of those take a long time to get back. So most of the time what happens is there's a patient that's not getting better, not responding to the routine antibiotics that we give in the hospital. And so we get called to help with the diagnosis. And I think that's entirely appropriate. The other time I have gotten involved in these situations is in the outpatient setting. Fever and returning traveler, especially in something that doesn't have an obvious diagnosis right away, I think is a very reasonable time to get an infectious disease specialist involved. Just because there is such a nuance in thinking about location, duration, what type of prophylaxis they did before traveling, and things like that.

Dr. Clancy

Let's say they've traveled to Africa. They're having fever of unknown origin, some fatigue. What would be the first layer of labs you would recommend? I know Jason's going to say smear.

Dr. Barker

No, there is a couple before that. If you're getting the blood, if you're getting anticoagulated blood, go ahead and get the cell count differential. So is there evidence of myolysis potentially on there? Is it low platelets? What's the white count doing? And then plus the other things in your comprehensive metabolic can pick up on Hemolysis AST will often be elevated with enough hemolysis LDH you can use if you want a little more specific marker haptoglobin and what have you. But I think if you did a comprehensive metabolic CBC with diff, you're going to get a lot of the organ failure information you need, which is just first principles. But then I think that'll give you a chance to maybe trigger further investigations based on what some of those numbers show you.

Dr. Appenheimer

And then I think a lot of the next steps too would depend on additional symptoms they may be having. I think of someone who's returning with diarrhea very differently as someone who has a non-localizing infection and things like that. The other thing, if the patient is sick, consider blood cultures. Typhoid is on the differential as well. And that can be relatively nonspecific in the symptomatology at times.

Dr. Clancy

All right, let's talk about a more frequent issue that is happening because of urgent care centers. You have a clinician in an urgent care center who is really time limited. They really do have 10, 15 minutes with the patient. Let's say you as a specialist get a call from urgent

care saying, hey, I'm wondering about this patient. They traveled somewhere. I'm a little worried about them. Is there a next step for them as well? Is it important for them to refer the patient to the emergency room to keep going with this eval? What would be your recommendations?

Dr. Barker

I would point out that yes, many of these tests, actually some of the sort of anti-malarials aren't stocked at most places. Some places when I talk to people on the phone, they won't get their CBC back for a couple of hours. And if someone's sick enough with a recent, say, exposure, so that often will trigger the call to us as, hey, this person returned from this place and they're sick and they don't look good. And that's 100% appropriate. There will be situations where the turnaround time and testing is just too long and therefore they need expedited care that you can get in an emergency room. Plus in the event that you do find a malaria, it's not as if Coartem is just sitting on most shelves for the initial treatment for falciparum malaria or even Malarone and some of the other second line agents. So there are definitely going to be situations where you do just need to get someone to where they can do this diagnosis much faster and where the turnaround times are much shorter. Your average urgent care is not going to have someone reviewing a blood smear anytime promptly, right? In some sense, the role is going to be a sort of triage role. And I think it's appropriate then to, you know, whatever your backup is that you have is to try to get someone to help you triage them to the right spot. Some things you don't want to wait on. They're not outpatient consults, right?

Dr. Clancy

Exactly. Great. Let's move on to early management and treatment. Let's talk about malaria a little bit. What's kind of the state-of-the-art right now as far as early steps in treating malaria once you've suspected?

Dr. Appenheimer

I would say the first step, and this probably goes without saying, is just confirming the diagnosis. there's a broad differential a lot of times when we're thinking about malaria, but obtaining the travel history, making sure that there's some epidemiologic risk, getting that CBC with differential, kidney function testing, doing a blood smear. There's a specific type of blood smear that's more helpful with malaria. It's called a thick and a thin smear. And then ideally, if they're available, you would want to send off a rapid diagnostic test. So we have this available here. It detects plasmodium specific proteins and it comes back very quickly. And in times it can differentiate between falciparum and vivax or other species. And so I think that's the first step is confirming the diagnosis. Second step is evaluating the

severity. There are circumstances where you can treat malaria as an outpatient once they've had a full evaluation, but a lot of times they do require hospitalization because they can progress very quickly. So once you confirm the diagnosis, you look for severity. Things that we look at, one, and Jason alluded to this earlier, what species is it? So falciparum tends to be more severe, so that's one thing that raises our concern. When they do the blood smear, they actually look for the percentage of red blood cells that have the parasite in them. So they call it the degree of parasitemia. And that gives us a sense if there's anything like altered mental status, hypotension, respiratory distress, just the usual things I think that would make us be concerned for severe illness or sepsis, AKI, anemia, those would all probably require hospitalization and more quick evaluation. Then once you've established severity, the question is, can you start off with an oral anti-malarial or do they need to be admitted for monitoring an IV? These are, as Jason also alluded to earlier, can be difficult to find, especially in rural locations. And so sometimes it does require coming to a place like an academic center where they may have these on hand or have ways to get them very quickly. Most of the treatments are artesunate based, both the orals, it's a combination pill, or if they're admitted to the hospital, it's IV. But yeah, not something that's just kind of you can call a local pharmacy and get these prescribed.

Dr. Barker

That's one of the consults that I've had on the phone from, let's say, a local community urgent care or hospital even. that they say, look, I can't get a new drug until Monday. And what we end up doing in ID with some of these malaria cases is there are phone calls you can make to various companies to try to get the Artemisinin shipped and so forth. And then there's also decisions you make about like you don't delay therapy because you can't get the number one therapy. You will often say, okay, well, if all we have is Malarone, we'll do Malarone. I mean, we used to use doxy and quinine. And those decisions are really specialist level. And the CDC even has malaria resources that we'll sometimes use if there's a weird situation or drug interaction or a particular kind of host that we'll have to get help with. So by then, by the time you're thinking about treating malaria, unless you have a lot of experience, we're probably involved to help navigate acquisition of the drug. It's a little easier than it used to be, but it's still, every time we do it, seems like there's new wrinkles in how to acquire it.

Dr. Clancy

When they do get the right drug, how quickly do they improve? Is it within days they start getting better?

Dr. Barker

Yes, the artemisinin drugs, so do artemether and some of the other cousins of that one, these are very potent. It's a very rapid decrease. In fact, it used to be that we talked about having to do exchange transfusions with much better drugs. It doesn't really make sense to use those because the drug will kill the organism pretty rapidly, that the percentage should decrease quite a bit within 24 hours. Patients will typically start to feel better. Now, anytime you have someone who's already in the ICU already with established organ failure, that's another problem because sometimes the, as you might, you've seen this with severely ill patients, the horse is out of the barn, right? So you have organ failure, you're now dealing with supporting a patient through that organ failure, even if you manage to kill what started it. That's a different situation. But yes, we're typically involved in the early stages of diagnosis and treatment of malaria.

Dr. Clancy

So with Dengue and West Nile and Zika, those arboviral diseases, how does treatment differ for those patients?

Dr. Appenheimer

Differs in mostly that it's supportive. So we don't have direct acting medications that kill the organism specifically. And so it really is. First assessing severity, similar to what I mentioned in malaria. Does this patient require hospitalization or can they be monitored closely as an outpatient? And then if they do need additional hospitalization, looking for or just managing them kind of with supportive care, similar to how we would manage other patients that are severely ill with sepsis or in the ICU and things like that.

Dr. Clancy

It's support their own immune system enough that their own immune system can knock it off.

Dr. Appenheimer

And support their organs enough if they're sick enough that gives their body time to fight off the illness and recover from the organ damage.

Dr. Barker

I will note that we still try to get a specific diagnosis. I mean, it is a bit limited. You know, we have some serologic testing. That's not perfect. Turns out the viremia for many of these things is quite brief. And so even if you try to do a PCR, you might miss it. But it certainly can be helpful because the different So even these different flaviviruses are not common, but Zika had important ramifications for people of child, women of childbearing age, a West

Nile virus and the neuroinvasive disease that has sort of prognostic clues. It's hard to predict how people are going to do after that, but it can be helpful to, okay, at least it's this. So even if we didn't have a specific antiviral, it's, I mean, part of our care, of course, is providing prognostic, information to scared patients and their families and of course scared providers who we want them to do well. So we will still send these things off even if like, oh, we can't treat it. Well, we can use that information in their care.

Dr. Appenheimer

I'll add to that a little bit too. I think it also helps establish the diagnosis so that we don't keep looking for other things necessarily. So A lot of these, there is a broad differential when patients return with these. And so if we could say, oh, this is dengue, then as long as everything is consistent with how we would expect dengue to be behaving, we don't have to worry about doing a bunch of other diagnostic workup or evaluation. And the other thing is a lot of these do have specific things we look out for once we know the diagnosis. So for example, with dengue, if it's a second exposure, patients can get really, really sick and it can be fatal and there are warning signs. And so if I have someone that I know has dengue, they're not sick yet, they can be managed or followed as an outpatient. you can warn them, if you start having severe abdominal pain or vomiting or notice any bleeding, like that is the time to get into the hospital right away. And so I agree that even though we don't have specific ways for treatment of these things, establishing a diagnosis is hugely important, both in helping us focus our thoughts and not worry about additional infections or other entities. and also helping people know what to look out for so that they can seek the appropriate care if things are getting worse.

Dr. Clancy

Well, you both have done a really good job of describing how, in general, the humans are not the host of these illnesses. And so the prediction that we're going to have, go ahead, Jason.

Dr. Barker

No, it kind of varies, right, the reservoir, right? So for malaria, we are the reservoir. some of the tick-borne stuff for dengue, for sometimes it's primates too, but yellow fever, there are some where it does have to get established in humans versus a reservoir. But unfortunately, nature didn't make it easy on med students or us practitioners, right? So it's like, each organism kind of has its own story, kind of what it does. And so it's like, yeah, you have to kind of figure out, all right, so to establish malaria, yes, you need ongoing dense transmission among humans with a certain density of monophylies and stuff. And it turns out we are the reservoir. in an important way, our ability to get rid of malaria in the United

States and North America was to some extent was using insecticides and perhaps overusing some of them. But a lot of it was air conditioning, right? So it's just a matter of just changing the way we interact with the vector, the world, you know?

Dr. Clancy

Brings me to an area that I think I'd like to touch on at least is when is public health involved? When do you call the county health department and say, hey, something's going on here?

Dr. Barker

I opened up in one of my browser tabs a list of reportable conditions in Iowa. I said I'll miss one. The mosquito-borne illnesses, that's another reason to make the diagnosis. Talked about prognosis, Ben appropriately brought up, yeah, you want to stop searching for other stuff once you have a good explanation and not expose the patient to unnecessary investigations. But then the other thing is like once you know, you then want to take the information and let public health know because if you do, the way you find out if you have airport malaria is you start to say, hey, wait a minute, what are we doing seeing this condition in someone who hadn't recently traveled themselves, what, if you do have a mosquito-borne virus starting to establish a self or find whether it has a human as reservoir or something else, that's important information for public health. So there's a long list, just Google, you know, Iowa and reportable conditions. You go to the HHS site and there's a nice page that has all of them listed, tells you kind of how many days you have to report it and so forth. Sometimes a lab, if you get a lab test back, the lab will actually trigger a warning to you. But then I would make sure that someone's following up with public health because we don't want those things falling through the cracks.

Dr. Clancy

So let's move on to prevention and risk reduction. What prevention strategies should physicians be discussing with their patients? For those people that work outdoors all day long and maybe for those people that are traveling and my travel nurse who gets so excited about all my vaccinations for the Amazon.

Dr. Appenheimer

It's easier to give direction on prevention for travelers where it's a short amount of time and they can do these really, you know, intense and labor some things for a week or two or a month versus kind of the people who may be exposed every single day. The things that we talk about, one is using DEET to help prevent ticks or mosquitoes from coming close. And the other thing you can do is treat your clothes with permethrin. So that is also a good way.

Things that you can do just on a day-to-day basis, especially with things like ticks or mosquitoes even, is one, wear light-colored clothing when you're out for hikes. that can make it a lot more obvious when there is a tick or a mosquito and can kind of bring that to your attention. I don't know that this is really evidence-based and my daughters make fun of me for this, but when I'm out for a hike, if there's a lot of ticks, I will put my socks outside my pants and that makes it so that ticks can't get in because a lot of times they get onto your sock and then they can climb up your leg and you don't see them. I found one on the back of my knee before and it had been a day or two since I'd hiked just because it got to a spot that you know I don't see every day. And so by doing that, you can just make it so that if ticks do get on your clothing, you can see them easier and it's harder for them to get to your skin. And also, when you're out walking, stay in the center of a trail, things like that. Just try not to be around brush. Those are kind of some basic things you can do. If you're traveling to a place where malaria is highly endemic and there's not air conditioning or window screens, using mosquito net I think is one of the best interventions that you can do. And also for mosquitoes, trying to eliminate standing water by your house, just being aware of where they might be able to breed and where they might be able to set up.

Dr. Clancy

So if traveling to a malaria endemic area, is there prophylactic medications now recommended?

Dr. Barker

Yes, we have a travel clinic here and there's a whole sort of database that sort of keeps up with CDC recommendations because a lot of countries in the world and things are changing. And I don't do travel clinic anymore, but when we do, we do refer to that to understand, okay, where do we have which agents and specifically with malaria, which malaria do they have and is it resistant? And there are regimens that we can recommend that are safe and they're less expensive than they used to be when I was doing this back in 2005. But like, yes, there are definitely things that we recommend for people going to areas with malaria transmission to prevent disease. And again, when you're not immune, the disease is from falciparum particularly is severe life-threatening.

Dr. Clancy

And in general, your recommendations around vaccines ahead of time, if you have time?

Dr. Appenheimer

Yeah, so when it comes to the vector-borne diseases, there aren't really great vaccines for the most part. There is a malaria vaccine that's available in endemic areas, but not for

travelers. It requires, three shots initially and then twice a year kind of ongoing for boosters. So it's not a, it does not provide long-term protection. And for the other vector-borne diseases we've mentioned, there's not great vaccine options, even if you're traveling. They looked into one for dengue. I don't think that's even commercially available anymore and it was not highly effective. We do recommend vaccines for other things. Yellow fever is one that you mentioned that is vector borne that yes, if you're going to a place, some places even require it for entry or if you're leaving from a place where there is a lot of yellow fever. Typhoid vaccines, the routine stuff, hep A, hep B, COVID, influenza, all of those things. And sure, I'm blanking on some. I'm just trying to run through the list quickly.

Dr. Barker

Yeah, there's one for very particular heavy exposures, Japanese encephalitis in Central and East Asia, particular areas. Again, we always kind of use the latest data that we have that people with heavy exposures, we would recommend that it's a flavivirus also. And that's another one that's kind of on the little bit more exotic list, but one that would be important for particular areas for people with heavy exposure to the outdoors.

Dr. Clancy

And how about on the bacterial side, anything typhoid or typhus and those?

Dr. Barker

The typhoid vaccines, that's a more sort of typical one that we do. And we also make sure people are updated on their hepatitis A. Most of us in North America, United States will not have been immune to that. And unfortunately, if you get hep A when you're older, tends to, like some other viral infections, when you get it when you're older for the first time, it can be much more severe. So we'll often make sure, and because it's spread the same way as typhoid, that kind of put that in the same bucket. When there is that potential exposure risk, we do recommend people get vaccinated. And I will say that some of these vaccines, it's one or two shots, or it may take time to take effect. So you want to do this ahead of time. During this week before, you may not be able to complete the vaccination, and it may be the case that the vaccination is not even fully effective for all the time that you're there. so that you do want to sort of try to plan ahead.

Dr. Appenheimer

The other thing I'll add for just completion's sake, another one that we do sometimes is rabies, depending on where people are going and what type of exposures they might have. And then just making sure they're up to date on other things like pneumonia vaccines and

meningitis vaccines. That's kind of like the comprehensive evaluation that you get when you go to the travel clinic.

Dr. Clancy

All right. Well, you guys have been great as always. I learned A lot. Any take-home points you'd like to kind of summarize for our listeners as we think about this changing world of vectors and infectious diseases?

Dr. Barker

One thing I would say before the blood smear is being helpful, no, is that I think it is important, and this is actually more broadly important, figure out a way, I think, to trigger a very quick exposure history, both recent travel and workplace, because some people have very heavy outdoor exposures that might change the way you think, working agriculture, certainly. So, I would say that figure out a way that you feel like you can shake loose those bits of history in a very rapid way. I think this is really important for folks in as an urgent care, so much pressure on your time, but it really can be useful that once you've triggered, okay, could this be vector borne? Do I need to think about this kind of syndrome and this kind of infection? Is learn a way to do that efficiently?

Dr. Clancy

Ben, how about you?

Dr. Appenheimer

I think, and we hit on this a little bit before, but I just think keeping these things in the back of your mind is important because if you're not thinking about them, they are easy things to miss because they don't localize, they require specific testing, and oftentimes won't respond to the usual empiric antibiotics that people might get if they're sick. And so even if you don't remember exactly what they are or what their geography is or things like that, just keep in the back of your mind that for these non-localizing febrile illnesses, thinking of vector-borne infections. And then you can always go back and look up, okay, what's here? This patient hasn't left Iowa. What should I be thinking about? Or, oh, this patient just returned from Florida. What has been going there? Just keeping them in mind and connecting that with your travel history to try to decide how concerned to be and what next steps to work up.

Dr. Clancy

Well, again, thank you both, Dr. Appenheimer, Dr. Barker, for your expertise and for joining us today. Again, you've been great guests with great knowledge and great guidance for us.

To our listeners, thank you for joining us for this session of Rounding@IOWA. You can access show notes and instructions for CEUs and CME credits in the show notes and look forward to you joining us again on Rounding at Iowa.