

Tickborne and Arboviral Diseases Jodi Reber, RN

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Hi. My name is Jodi Reber. I am the vectorborne nurse epidemiologist and a regional communicable disease nurse consultant. My presentation today is on reportable tickborne and arboviral diseases in North Carolina.

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First off, when you hear the word arboviral, think mosquito. Now, why do we care about ticks and mosquitoes ? In general, tickborne and arboviral diseases cannot be spread from human to human, but, if a person is infected with a mosquito-borne illness, like malaria, they may be able to pass it on to another mosquito – if the mosquito bites them while they are sick – thus allowing the potential spread of the illness to continue from mosquito to human. Individual illness caused by ticks and mosquitoes can range from mild to severe and even death. Some people will completely recover while others will have life-long complications. When we monitor for tickborne and arboviral disease, we must consider what species are present in a particular region. North Carolina and California do not have the same ticks and mosquitoes, and not all species of ticks and mosquitoes carry the same disease-causing organism. So, for example, California rarely sees Rocky Mountain Spotted Fever (RMSF) cases as compared to North Carolina. That is because the tick that transmits Rocky Mountain Spotted Fever is much more prevalent here.

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The learning objectives for this presentation are to identify the reportable tickborne diseases in North Carolina; to understand the difference between neuro-invasive and non neuro-invasive arboviral disease; to distinguish between viral, arboviral, bacterial, and other causes of meningitis/encephalitis; and lastly, to identify key surveillance criteria for tickborne and arboviral illness that will help you during your case investigations.

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Let's start with tickborne disease. First off, let me tell you that the tickborne terminology has changed over the years. You may want to be aware of this since you may hear others refer to some different diseases by different names. Previously, we kept statistical information on one of the specific diseases caused by the bacteria *Rickettsial rickettsii*, and that was Rocky Mountain Spotted Fever. The CDC has determined that it may not be certain that all of the events actually reported to them as Rocky Mountain Spotted Fever in the past were actually Rocky Mountain Spotted Fever – that some of these events could be another tickborne disease altogether – that a different bacteria, although from the same bacterial family, actually caused the disease. So, to better define what is actually being reported, there was a change made to incorporate all the potential diseases caused by all of the different bacteria in the Rickettsial family. So, we now refer to the group as a whole...the Spotted Fever Group. One other change is with Anaplasmosis. Anaplasmosis used to be considered a type of Ehrlichiosis, and referred

to as Human Granulocytic Anaplasmosis. However, it is now considered its own distinct disease and not within the same bacterial genus and species as Ehrlichiosis. So, the current tickborne diseases of interest in North Carolina are: Spotted Fever Group, Ehrlichiosis, Anaplasmosis, Lyme disease, and Babesiosis.

Let me tell you a story. This is based on real events that occurred here in North Carolina. Imagine one day that your normally active child starts complaining that they do not feel well and comes down with a sudden fever. Soon afterwards he starts complaining of a horrible headache. You realize that your child is pretty sick, so you take him to the doctor. At the office, the doctor states that he has seen a lot of the same signs and symptoms lately and quickly assesses the child and diagnoses him with a viral infection. The doctor then provides instruction on how to treat the fever, headache, and general discomfort your child is experiencing. You go home with the understanding that your child should feel better in a few days. Unfortunately, your child isn't getting better. After another 2 days, he starts having abdominal pain, and nausea and vomiting, and a rash is beginning to appear and spread all over his body. You take your child back to the doctor. After the doctor sees the child again, he quickly realizes that he may have not assessed the patient fully on the first visit. He asks the mother "Has your child been bitten by a tick recently?" And the mother replies, " Oh yes, he plays outside a lot and comes in every now and then with a tick on him". Then the doctor's new assessment is that the child is now extremely ill, so he sends the child to the hospital. At the hospital, it is determined that the child has Acute Respiratory Distress Syndrome and his kidneys are failing. They now suspect that the child has Rocky Mountain Spotted Fever and immediately start him on Doxycycline. However, after a few days, the child dies. One important fact to remember is that some tickborne diseases come on quite quickly and can progress to severe illness within a matter of a week. Rocky Mountain Spotted Fever is the most serious of the tickborne illnesses, and North Carolina reports about 1/3 of all the cases in the United States. In general, when we talk about the tickborne diseases of interest in NC, three of the five tickborne diseases, Spotted Fever Group, Ehrlichiosis, and Anaplasmosis have similar clinical features. In these diseases, after an incubation period of 5-10 days, there is usually a sudden onset of fever. Severe headaches are also a common sign and symptom, as well as malaise and muscle aches. Most people will seek medical treatment for these signs and symptoms. As you see, these signs and symptoms are pretty vague and could represent many disease processes. It is imperative that the doctor assesses to see if there was a known tick exposure. However, there are many cases where a person does not remember a tick bite at all. This may be because the ticks can transmit disease when they are smaller, before they become an adult. So, it is also important to assess if the patient has been in an environment where ticks are present.

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For the most severe of these tickborne diseases, Rocky Mountain Spotted Fever affects 50% - 60% of adults and 90% of children. They all then develop a rash. The red, spotted petechial rash of Rocky Mountain Spotted Fever is usually not seen until the sixth day or later after onset of symptoms. The rash may involve the palms or soles of the feet. In contrast to Rocky Mountain Spotted Fever, rash is relatively uncommon in adult patients with ehrlichiosis, however, is seen in children about 60% of the time.

Rarely do we see a rash in anaplasmosis. The rash is actually considered a late sign....meaning that a patient who develops a rash is at much greater risk of developing very serious, even life-threatening, illness. Therefore, treating a patient quickly for these suspected tickborne diseases is important. Rocky Mountain Spotted Fever has a mortality rate of 5-10%, and for those who survive, there can be long-term effects. These health problems following Rocky Mountain Spotted Fever infection include partial paralysis of the lower extremities, gangrene requiring amputation of fingers, toes, arms or legs, hearing loss, loss of bowel and bladder control, movement disorders, and language disorders. These complications are most frequent in people recovering from severe, life-threatening disease, often following lengthy hospitalizations. There are fewer deaths and long-term complications associated with Ehrlichiosis and Anaplasmosis.

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If a physician chooses to obtain serology, a person with Rocky Mountain Spotted Fever, Ehrlichiosis, or Anaplasmosis may show signs of anemia, thrombocytopenia, leukopenia, and elevated liver enzymes. And again, this will be a sudden onset of anemia, decreased levels of platelets, decreased levels of white blood cells, or elevated liver enzymes.

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When you look at the case definitions for tickborne diseases, you will see that a variety of tests can be used to meet laboratory surveillance criteria. Physicians are not required to perform testing for surveillance purposes, however doing so helps us to characterize disease and disease burden in North Carolina. In regard to obtaining laboratory data to assist with surveillance collection, let me first tell you that there are many types of tests that a physician may order to diagnose the illness. But, there is a difference between diagnostic tests and tests needed for surveillance purposes. For surveillance, there are only a few tests that we accept as appropriate indicators of disease. The most commonly used of these tests measure how the patient's immune system is acting toward the suspected organism. This is an indirect way of determining if the organism is responsible for the illness. Getting the most accurate picture of how the immune system is responding requires obtaining a serologic sample and getting a second specimen 2 – 4 weeks later. When the results of the two specimens are compared, it can be determined if the organism appears to be responsible for the patient's clinical illness. If only one specimen is obtained, then it may appear that the organism is responsible for disease, but we do not know for sure, so we cannot say the event is a confirmed case. There is more to know and understand about these labs, but that material will be covered at a future date.

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Now let's briefly discuss investigating these types of tickborne illness. When you look at the case definitions, there seem to be a lot of requirements or choices for meeting clinical and lab criteria and it can seem very confusing. It may take you a while to feel comfortable investigating these cases. Do not hesitate to call your communicable disease regional nurse consultant to review the case definitions as you begin

investigating these types of events. Right now, here are a few key points to remember. For all tickborne disease, in order to meet confirmed or probable case definition, specific clinical and laboratory criteria must be met. A physician's diagnosis of the tickborne disease can substitute for lack of clinical criteria. We do see events where the patient may have few, if any, clinical signs of illness, but the physician decides to diagnose the disease. We accept that diagnosis; just remember that specific laboratory criteria must also be present. When no diagnosis has been made, look at the clinical symptoms. It's important to remember that these illnesses generally have a sudden onset of fever. Thus, fever is considered a required clinical symptom. If there is no fever, either objective or subjective, then clinical criteria are not met and you don't have a case. It does not matter if there are any other clinical signs or laboratory criteria present.

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Confirming an event in NC EDSS can be challenging because you must have specific clinical criteria present and the required two serum tests taken 2-4 weeks apart that show a four-fold change in the titer level. We mostly see physicians ordering only one lab, and not a follow-up lab. The single positive lab can be used as supportive evidence, and, along with the clinical criteria, can be classified as a probable case.

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There may be times that you do not get all the information you need from the provider to complete your investigation. Your health department should have policies in place to clarify how many times you should try to obtain information from the physician. If you have followed your local health department policy, then for tickborne diseases, you may submit the event to the state, even though it is incomplete. Select the classification of Suspect. You will need to write a note in the administrative package, to explain why you are selecting the Suspect case classification.

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Now let's talk about the emerging tickborne disease in NC. It is Lyme disease. This disease was first identified in 1975 in Lyme, Connecticut, by pediatricians who were seeing a lot of unusual arthritis cases in their patients. Since then, Lyme disease has become endemic in the North Atlantic States and parts of the Midwest. The ticks that transmit Lyme disease have been slowly moving south and we have just started seeing acquired Lyme disease cases here in North Carolina. In 2009, we established our first endemic county for Lyme disease, and that was Wake County. Once a county has been able to prove, by case definition, that two persons have acquired the disease in that county, we can then call the county *endemic*. In 2009, there were also four other counties with a single acquired Lyme disease event. Once any of those counties can demonstrate another Lyme disease event that is acquired in their county, it will become known as an endemic county. When a county becomes endemic, the case definition rules change, and the surveillance criteria lessen, making it easier to consider events confirmed.

Now I want to tell you another story. First, let's talk about the great outdoors. We all know what happiness we feel when we see children go outside to explore the world. I

am sure we can all remember the first time a child picked a flower, which really may have actually been just a weed. Then we watched as that child proudly brought their new discovery to us so we could share in the joy. I am sure this brings a smile to your face just thinking about it. In this day and age of computers and video games, most of us encourage our children to spend more time outdoors. We want to have a balance between modern society and nature. In many areas of NC, people have chosen to live closer to nature. Often, the woods are literally in their backyards. This is great for exploring, but often times there is an unrealized risk. We all know that it's not unusual to get a summertime cold, but what if the achy pains didn't go away? What if it turned out that it was so much more? This happened just recently to one North Carolina child. Let's call her Stacey. Stacey could not wait until it was warm enough to go outside and play. Stacey loved playing with her friends outside in the neighborhood. One day Stacey didn't feel well enough to go outside and play. She told her mom that she was tired and hurting a bit in her arms and legs. When Stacey was getting out of the bath that evening, mom noticed a red spot on her back near her right armpit. It wasn't that large, so she decided to see if it was better in the morning. When Stacey got up the next morning, mom looked at the spot. It had gotten bigger and started to appear to have rings. Mom looked up "rashes" on the internet. She realized that Stacey could have been bitten by a tick while outdoors and could have a tickborne illness – specifically, Lyme disease. Mom called the pediatrician and took Stacey in. Mom explained how Stacey was outdoors a lot in the neighborhood, and that the neighborhood was woody in areas. She explained that Stacey had complained of tiredness and achy arms and legs and showed the doctor the spot on her back. After the doctor examined Stacey fully, he explained to Stacey's mom that Lyme disease cannot be acquired in North Carolina and that he thought she was having an allergic reaction to something that was causing the rash. He advised her to get some creams to help the rash go away. It took several weeks, but the rash did go away and Stacey did feel better. That is, until a month or so later. Then Stacey started complaining about her left knee. Mom noticed that it looked like it was starting to swell. Mom figured Stacey must have landed wrong after jumping so many times out of the trees. And, it did go away after several days. After another month passed, Stacey again wasn't feeling well and her knee started to swell again. This time it was even larger--2-3 times its normal size. Mom took Stacey to the Emergency room. Stacey was admitted to the hospital because the doctors were concerned that she had a septic knee. Stacey went to surgery several times for incision and debridement of the knee. After talking with the doctors, Stacey's mom reviewed the entire summer's events. The doctors decided to run Lyme disease testing. The results came back a strong YES. Stacey's mom was beside herself. Stacey had gone through so much suffering. If only the doctor had acknowledged that it could have been Lyme disease (or any other tickborne illness) when she had the rash; the treatment was a simple course of antibiotics. Not only would that have most likely prevented the later issues of massive joint swelling, but she really did not have a septic knee now. She did not need the surgeries! She just need appropriate antibiotics. Once Stacey was home and recovering, Stacey's mom talked with other parents in the neighborhood about the risk of tickborne illness. They all admitted that they did not realize the dangers in their own backyard, that they had not been properly protecting their children, and that they

needed to do better. This is based on a true story that happened in the summer of 2009 in North Carolina, and unfortunately, Stacey and her family are not alone.

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Let's talk a bit about Lyme disease. Lyme disease is caused by a bacteria from the spirochetes, or corkscrew-shaped family, called *Borrelia burgdorferi*. There can be multiple stages to Lyme disease. In general, the person infected progresses through these stages because the disease is not diagnosed and antibiotic treatment is not initiated. The good news is that 95% of people will fully recover from Lyme disease if they do receive treatment, no matter what stage they have reached. Let's briefly look at the stages. The first stage is called Early Localized Lyme disease. The symptoms generally start to appear, on average, 7-10 days after a tick bite. The first manifestation in around 60%-80% of patients is an Erythema migrans (EM) rash. This rash develops at the site of the tick bite and expands over several days. Sometimes this rash can look like a bull's-eye with alternating red and clear rings, but not always. The rash is not normally painful. If present, this rash is of great significance for surveillance purposes. This rash is the only symptom we know that develops right after a tick has bitten. So it provides the only opportunity to be able to know when and where the tick bite occurred. If there is a physician-diagnosed Erythema Migrans rash, greater than 5cm in size, and the patient has not traveled outside his home county 1 month prior to the onset of the rash, then we can say with certainty that the tick bite occurred in the home county. As stated before, Lyme disease is emerging in North Carolina and it is important to try and locate any newly acquired North Carolina cases. If you discover a patient with a physician-diagnosed EM rash, greater than 5cm, and there was no history of travel 30 days prior to the tick bite, you should notify your CD nurse consultant to discuss the case.

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If Lyme Disease was not treated in the early localized phase, some cases, weeks to months later, could develop systemic manifestations of Lyme Disease. This stage is referred to as Early Disseminated Lyme disease. Patients may feel well for a period after the acute phase resolves and may not recall any acute symptoms, or this phase of illness can overlap with the acute phase. Systemic manifestations of fever, headache, malaise, fatigue, achiness, and regional lymphadenopathy begin to occur. The organs usually involved in Early Disseminated Lyme Disease infection include the skin, nervous system, heart, joints, and eyes. Disseminated skin lesions may develop and differ from the primary Erythema Migrans. These lesions tend to be multiple, light, salmon-colored macules of varying sizes. These lesions usually fade within a month. In about 15% of untreated patients, frank neurologic disease develops. Classic unilateral or bilateral Bell's palsy can occur. Aseptic meningitis, encephalitis, cranial neuritis, ataxia, and motor and sensory abnormalities may also occur. Some patients develop cardiac involvement resulting in varying degrees of AV block, sometimes requiring temporary pacing. Some patients have evidence of more diffuse heart disease compatible with acute myopericarditis. Cardiac disease is brief, lasting from three days to six weeks. Other symptoms may include migratory musculoskeletal pain in joints, tendons, bursae, muscle, and bones, as well as conjunctivitis to the eyes.

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The last stage of illness occurs in about 60% of untreated patients and is referred to as Late Lyme disease. This stage can occur months after the initial exposure. Patients experience attacks of joint swelling and pain. Large joints, especially the knees, are affected. Attacks last from weeks to months with periods of complete remission. In about 5% of untreated patients, recurring, long lasting neurologic disease develops months to years after initial infection, sometimes following long periods without symptoms.

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As with the other tickborne diseases, reading the case definition for Lyme Disease may be a little confusing. Again, contact your CD regional nurse consultant if you have any questions when working on an investigation. For now, keep in mind these few points. Both clinical criteria and lab criteria must be present to meet overall case classification of confirmed or probable. A physician's diagnosis of the tickborne illness can substitute for a lack of clinical criteria. As I stated above, we do see events where the patient may have few, if any, clinical signs of illness, but the physician decides to diagnose the illness. We accept that diagnosis; just remember that specific laboratory criteria must also be present. The case definition may require more than one type of lab to be performed.

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Look closely at the lab criteria for surveillance. In the early course of the illness, there are 2 different labs that must be positive to meet case definition. If the illness has been ongoing for over a month, a different, single lab test is acceptable. As mentioned before, you may use the suspect case classification for all tickborne disease. Utilize this if you are unable to obtain medical records. Just remember to follow your local health department policy and put a note in the administrative package as to why you classified the event as Suspect.

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I want to mention one quick note about the treatment of tickborne disease. The recommended drug of choice for all tickborne disease is Doxycycline. The North Carolina Department of Public Health recommends that all physicians treat tickborne disease immediately if it is clinically suspected and not wait for laboratory confirmation.

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Just a few words about a newly reportable tickborne illness--Babesiosis. Babesiosis is a common tickborne illness in the North Atlantic states. However, it is not currently known to be transmitted through ticks in NC. However, there have been many cases of Babesia discovered after receiving blood transfusions. Currently, there is no blood test to check for babesiosis in donor blood. To help monitor this situation Babesiosis will be made reportable in the United States starting in 2011. NC also plans to change the current administrative code to require Babesiosis to be reportable in NC. Training on Babesiosis will come at a later date.

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Now let's change pace and talk a bit about Arboviral or mosquito-borne illness. Arboviral illness is a leading killer throughout the world. Most people have heard of the mosquito-borne illness called Malaria. Did you know that in 2008, an estimated 863,000 people died of malaria --and these were mostly young children in sub-Saharan Africa. Lucky for us, we live in the US, where malaria has been eradicated. And, in general, we do not have the arboviral morbidity and mortality rates that other countries do, but we are not free from disease and death caused by the transmission of infection from the mosquitoes around us. As we all well know, mosquitoes bite every chance they get. But what you may not know is that many of us are often infected by microorganisms they inject into us; we just don't get that sick. Most of us may be asymptomatic or just suffer a mild flu-like illness. However, some individuals may have fever, headache, myalgias, malaise and occasionally collapse from complete exhaustion. And others, unfortunately, when the virus has invaded the central nervous system, may suffer with problems such as encephalitis, which is inflammation of the brain, and aseptic meningitis, which is inflammation of the lining of the brain, which can lead to seizures, coma, and even death. And also remember one fact that I briefly mentioned earlier in this presentation. Although we cannot give a mosquito-borne illness to another human, we can give it to another mosquito. In fact, between 1957 and 2009, in the United States, 63 outbreaks of locally transmitted mosquito-borne malaria have occurred. In such outbreaks, local mosquitoes become infected by biting persons carrying the malaria parasite (which they acquired in endemic areas outside of the US) and then transmit malaria to local residents. So, in order to help keep the public safe from these potentially deadly infections, we do keep surveillance information on them. For those arboviral illness that can be acquired here in North Carolina, we conduct surveillance on those that are considered neuro-invasive, meaning the virus has gotten into the central nervous system and is causing severe disease. We do not collect surveillance data on milder illnesses that have occurred outside of the central nervous system, which is referred to as non neuro-invasive disease. And, just a quick note, about 1,500 cases of malaria are diagnosed in the United States each year. The vast majority of cases in the United States are in travelers and immigrants returning from countries where malaria transmission occurs, many from sub-Saharan Africa and South Asia.

I want to give you one last story; this one regarding arboviral disease. This story, like the others, is based on true events and occurred in the summer of 2009. A brother and sister were having fun on their summer break. Within a day of each other, they both started feeling bad with fever, headache, muscle aches and fatigue. The boy soon started vomiting, showing signs of altered mental status, and having seizures. He was taken to the hospital with uncontrollable seizures. By the next day, his sister was also admitted to the hospital with similar symptoms. The physicians tested for multiple issues, and even included testing for mosquito-borne illness. The initial testing for mosquito-borne illness did not show a clear positive for mosquito-borne illness. Although the physicians were doing everything they could do, within 5 days, the boy died. Luckily, his sister survived. Upon further investigation and follow-up testing with

the sister, it was determined by the Centers for Disease Control that in fact, they both had LaCrosse encephalitis.

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Specifically, In North Carolina, we report neuro-invasive arboviral illness for West Nile Virus, LaCrosse encephalitis, Eastern Equine Encephalitis, Western Equine Encephalitis, and St. Louis Encephalitis. Different arboviral diseases affect different parts of North Carolina. This is because the mosquito vector that transmits a certain disease may only be present in certain parts of the state. For example, the mosquito that transmits LaCrosse encephalitis is generally only found in the western part of our state. In general, the signs and symptoms of neuro-invasive arboviral disease are the same. We can determine the exact causative agent by performing laboratory tests. Let me clarify a few things. Encephalitis and meningitis can be caused by many different microorganisms and toxic substances. Arboviral neuro-invasive disease is specifically caused by different viruses. Bacterial causes for CNS diseases are not arboviral. Also, to distinguish between a bacterial cause of meningitis and a viral cause of meningitis, different terms may be used. If a bacteria is the causative agent of the disease, it will be referred to as meningitis or bacterial meningitis. If the causative agent is viral, it will be referred to as aseptic meningitis or viral meningitis. Keep this in mind when you are looking at physician's notes. When we think of aseptic meningitis (inflammation of the lining of the brain) and encephalitis, consider the swelling that is occurring and the pressure being put on different parts of the brain and even the blood flow to the brain. The swelling could be mild and so the person only has fever and headache, or it could become more severe and include symptoms such as stiff neck, confusion, personality changes, paralysis, seizures, coma, and death. And unfortunately, some of the people who recover from a more severe form of arboviral illness will suffer long- term problems, such as problems with mobility, speech, and memory. There are 2 arboviral diseases not normally acquired in North Carolina, which are Malaria and Dengue. We want to ensure that any citizen of North Carolina who might come down with these diseases did not acquire it here. We are also interested in ensuring we know the exact organism causing these illnesses. You may be asked at times to help facilitate getting lab samples to the North Carolina State Laboratory for Public Health and the Centers for Disease Control for evaluation.

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When you investigate these types of cases, please keep these things in mind. Understanding the case definitions for arboviral disease, just like tickborne disease, might seem quite confusing. Do not hesitate to contact your CD regional nurse consultant for help. And remember these few tips: for neuro-invasive disease, both clinical criteria and laboratory criteria must be met. It is not good enough to have positive labs – we must know the patient's clinical symptoms. Always remember to assess a patient's travel history. We try to monitor where the disease-causing mosquitoes are located. For example, if people on the east coast of North Carolina started coming down with LaCrosse encephalitis, and there was no history of travel outside their home counties, that would alert us to the possibility that the mosquito has now traveled to the eastern part of the state. And if people started coming down with

Malaria or Dengue fever and did not have a history of any travel to any area endemic for these diseases, we could have another local outbreak on our hands.

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A quick word about prevention. There are many things that can be done to prevent tick and mosquito-borne disease. You'll learn about these things as you complete the activities for this unit. Thank you and have a great day.

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References