Good afternoon. I'm Commander Ibad Khan, and I'm representing the Clinician Outreach and Communication Activity (COCA) with the Emergency Risk Communication Branch at the Centers for Disease Control and Prevention. I'd like to welcome you to today's COCA Call, "What Clinicians Need to Know about Dengue in the United States. " All participants joining us today are in listen-only mode. Free continuing education is offered for this webinar.

Instructions on how to earn continuing education will be provided at the end of the Call.

In compliance with continuing education requirements, all planners and presenters must disclose all financial relationships, in any amount, with ineligible companies over the previous 24 months, as well as any use of unlabeled product or products under investigational use. CDC, our planners, and presenters wish to disclose they have no financial relationships with ineligible companies, whose primary business is producing, marketing, selling, reselling, or distributing healthcare products used by, or on, patients. Content will not include any discussion of the unlabeled use of a product or a product under investigational use. CDC did not accept financial or in-kind support from ineligible companies for this continuing education activity.

At the conclusion of the session, participants will be able to accomplish the following: Describe current dengue epidemiology and the populations who are at greatest risk for dengue and severe dengue in the United States. Recognize the three phases (febrile, critical, convalescent) and the three severity levels of symptomatic dengue (dengue, dengue with warning signs, severe dengue) based on a patient's clinical and laboratory findings, and identify the indicated treatment group (A, B, or C), including hospital admission and intravenous fluids management recommendations based on dengue phase and severity.

After the presentations, there will be a Q&A session. Please submit questions at any time during today's presentation. To ask a question using Zoom, click that Q&A button at the bottom of your screen. Then type a question in the Q&A box.

Please note that we often receive many more questions than we can answer during our webinars.

If you are a patient, please refer your questions to your healthcare provider. If you are a member of the media, please contact CDC Media Relations at 404-639-3286 or send an email to media@cdc.gov.

I would now like to welcome our presenters for today's COCA Call. We are very pleased to have with us Dr. Laura Adams and Dr. Liliana Sanchez-Gonzales, both of whom are epidemiologists in the Dengue Branch in the Division of Vector-Borne Diseases at CDC's National Center for Emerging and Zoonotic Infectious Diseases. It is my pleasure now to turn it over to Dr. Laura Adams. Dr. Adams, please proceed.

Thank you, Dr. Khan. Next slide, please.

We'll start with the background on dengue epidemiology. Next slide and next slide.

Dengue is caused by dengue viruses 1 through 4, sometimes called serotypes, all of which can cause disease. Infection with the dengue virus leads to lifelong type-specific immunity against the infecting dengue virus and short-term cross-protective immunity to the other dengue viruses, usually for about one to three years. Next slide.

There's also genetic variation within dengue virus types, with some variants showing higher levels of virulence. You can see an example of this in the image on the right, which shows different variants and genotypes within each of the four dengue viruses. However, it can be difficult to ascertain the role of virus-specific factors, as additional factors such as age and the time between infections, has also been shown to play an important role in the risk for severe disease. Next slide.

Dengue is primarily a mosquito borne disease spread through the saliva of infected mosquito bites. Aedes aegypti is the most common vector shown in the image on the top right. However, Aedes albopictus, shown on the bottom, can also sustain transmission.

Other modes of transmission for dengue virus are less common but include vertical transmission from a mother to a baby, blood transfusion or organ transplantation, needle stick, mucocutaneous exposure, or hospital or laboratory accidents, breast milk, and rarely, sexual transmission. Next slide. Many factors can affect an individual's risk for severe dengue. There is a known risk by age, with particularly higher risk among infants born to seropositive mothers, as well as elderly populations. The number of dengue infections, and the time between those infections, can also play a role. Although severe dengue can occur during any dengue infection, there's a higher risk on the second dengue infection compared to the first, third, or fourth infection, and last but not least, underlying comorbidities can also be associated with worse outcomes, including asthma, diabetes, obesity, hypertension, and sickle cell disease. Next slide.

Next, among people infected with dengue virus, most, up to 60 to 80%, will be asymptomatic.

Next, of the 20 to 40% that develop symptoms, 1 to 5% will develop severe dengue. Next.

Among people with severe dengue, more than 95% will survive. However, dengue can be fatal with higher rates if untreated or with inappropriate treatment. Next slide.

Methods of dengue prevention are historically based on preventing mosquito bites and include the use of EPA registered insect repellants and wearing long-sleeve shirts and long pants. Additionally, controlling mosquitoes around the home can reduce exposure, including having screens in windows and doors, staying in locations with air conditioning, and regularly emptying and cleaning water-holding items that can serve as breeding sites for mosquitoes. Next slide.

In 2021, a dengue vaccine was recommended for use by the ACIP in dengue-endemic areas of the United States. This vaccine, called Dengvaxia, includes three doses, and is recommended for people 9 to 16 years old, with evidence of laboratory-confirmed previous dengue infection and living in dengue-endemic areas. It is not recommended for travelers to endemic areas. Next slide.

Let's talk briefly about global dengue epidemiology. Next slide.

Dengue is the most important and most common virus transmitted by mosquitoes worldwide. Dengue occurs in tropical and subtropical areas, as shown on the map. The countries shown in dark blue are considered to have frequent or continuous dengue transmission. The areas in light blue have sporadic, or uncertain, dengue transmission, and the areas shown in tan have no evidence of risk. Next slide.

One of the concerns with dengue is that dengue incidence is likely to increase as global temperatures increase, as shown by the growing areas with environmental suitability for dengue transmission shown on the bottom figure, compared with the figure on the top. This occurs because of the expanded range of the mosquito vector, as well as other factors promoting increased transmission. Next slide.

During 2022, multiple countries have reported dengue outbreaks, shown by the areas in blue on the map. The colors by each country represent the dengue viruses or serotypes circulating in those areas. As you can see, many endemic areas report circulation of multiple dengue virus types. Next slide.

Next, let's take a look at dengue epidemiology in the United States.

First, it's important to know that dengue is endemic in six US territories and freely associated states shown on this slide. These include Palau, the Federated States of Micronesia, the Marshall Islands, and American Samoa in the Pacific, in Puerto Rico, and the US Virgin Islands in the Caribbean. Next slide.

Dengue cases in US states are usually associated with travel to endemic areas, although locally-acquired cases have been reported in some states, including Florida, Texas, and Hawaii. However, there's a risk for local transmission of dengue because the mosquito vectors are present in multiple states, particularly in the southern United States, as you can see in the maps on the right side of the slide. Next slide.

In recent weeks, there's been an increase in travel-associated dengue cases in the United States. This figure shows a number of travel-associated dengue cases reported to ArboNET, the National Arboviral Surveillance System, by week of symptom onset shown on the X axis. The height of the bar represents the total number of cases by week, and the color indicates the location of travel. During case investigations, public health officials found that the majority of the recent cases reported travel to Cuba, shown in purple, travel to all other locations, as shown in gray. Clinicians should have a high level of suspicion for dengue among febrile patients reporting recent travel to Cuba or the Caribbean region, and I'll now pass the microphone to Dr. Liliana Sanchez, who will talk more about dengue clinical presentation and recommendations for case management. Next slide.

Okay, thank you, Dr. Adams, and good afternoon. Next slide.

During the next 30 minutes, I will present an overview of the general concepts and recommendations for the clinical classification, the clinical course and assessment, laboratory aspects, and management of dengue. Next slide.

During this section, I hope to be able to give you some tools to be prepared to, one, recognize, and two, manage dengue, as not recognizing this disease continues to be one of the main causes of death among dengue patients, and if you have clinical suspicion, you should monitor and manage patients as dengue, as appropriate and timely management with IV fluids can be lifesaving. Next slide.

Let's start with the clinical classification and course of dengue disease. The clinical classification of dengue was updated by the World Health Organization in 2009. This classification by severity aims to be more useful to guide clinicians' decisions as to where and how intensively the patient should be observed and treated. There are three clinical categories, dengue, dengue with warning signs, and severe dengue. Next.

You should suspect dengue in a patient who lives in or has traveled to -- previous, please. Previous, please. Thank you.

Or in a patient who lives in or has travel to an endemic area and presents with fever and two or more criteria in this list. Nausea and vomiting, rash, aches and pains that include headache, retroorbital pain, myalgia and arthralgia, a positive tourniquet test, and leukopenia. Next.

If the patient also presents with any of the criteria in this list, then the clinical classification corresponds to dengue with warning signs: PAbdominal pain or tenderness, persistent vomiting defined by WHO is three or more episodes in an hour or four or more episodes in six hours. Clinical fluid accumulation. Mucosal bleeding. Lethargy or restlessness. Postural hypotension. Liver enlargement of more than 2 centimeters, and a progressive increase in hematocrit. These warning signs are very helpful to identify patients who might progress to severe disease, and it's very important that we assess them in all patients that we suspect dengue. Patients with warning signs should undergo medical observation or hospitalization. Next.

Those patients who present with any of these manifestations, severe plasma leakage, that is the hallmark of severe dengue, that is leading to shock or respiratory distress, severe bleeding defined by the clinician, usually corresponding to gastrointestinal bleeding, and severe organ involvement that most commonly manifests with hepatitis, encephalitis, and myocarditis. These patients are classified as severe dengue. Next.

So, every time dengue is suspected in a patient, we should use this classification to determine severity of disease. As you see, the case definition for dengue is broad, and that is the intention of this classification to have a sensitive case definition with which the majority of the dengue patients can be identified. The majority of dengue patients will be in the first group. You can still see and find sometimes the old classification that included the very well-known term dengue hemorrhagic fever, but this current classification here tries to take away the focus from platelet counts and bleeding and put into the severe dengue manifestations. Patients with severe dengue don't necessarily present with bleeding, and shock is usually the most common severe manifestation. Next.

Besides the classification of severity, we need to be aware of the clinical course of dengue. After the patient is bitten by the mosquito, the incubation period is usually short, four to seven days,

but it can go as long as 14 days. Remember that most dengue infections will be asymptomatic, or will result in mild disease. In symptomatic patients, the typical clinical course of dengue has three phases, febrile, critical, and convalescent. Next slide.

Starting with the febrile phase, when the patient presents with the common symptoms of dengue, and they usually last two to seven days. Note that the patient is viremic during this phase, even a couple of days before the symptoms start, which means that a mosquito that bites them can become infected and continue transmission. This is important if you're living in a place with dengue vectors. During the febrile phase, the most common clinical problems include dehydration and febrile seizures and neurological disturbances in young children. Defervescence, this is the abatement of fever to less than 38 Celsius or 100. 4 Fahrenheit degrees occurs on day three to eight. After the febrile phase, most patients will start to improve. Next slide.

But some patients will enter the critical phase. That starts with the defervescence. It lasts one to two days and is characterized by an increase in capillary permeability. It is when extravasation of fluid into the interstitial space, or plasma leakage, usually occurs. Some patients might progress to this phase without the abatement of fever, and then, besides defervescence, this phase can be identified by increasing the hematocrit or hemoconcentration, because there is plasma leakage, but the red blood cells are too large to pass into the interstitial space. Warning signs that we all have memorized by now occur in this phase, and the most common clinical problems correspond to the progression, to severe manifestations of the disease. Next slide.

The last phase of dengue is the convalescent phase that lasts about three to five days. In this phase, the extravascular fluid is reabsorbed in a gradual manner, and the clinical problems in this phase include hypervolemia and pulmonary edema, many times caused by excessive IV fluids administered to the patient during the previous phases. Next slide.

Some important things to remember here, the presentation of dengue can change quickly. The clinical phase usually lasts only 24 hours. It is very important to monitor and identify warning signs and severe criteria to classify your patients and then be able to manage them appropriately. Plasma leakage and progression to severe disease usually happens in the critical phase, and it's very important that we're able to identify, and shock, not bleeding, is the most common severe dengue manifestation. Next slide.

Now let's talk about clinical assessment. Next slide.

When we have a febrile patient, with a potential exposure to dengue, the overall assessment should include several criteria. The diagnosis, is it dengue? Does it meet the key definition criteria? Was exposure within 14 days? Do you have another diagnosis for this patient? The classification that we see that corresponds to the severity of disease. Does your patient have warning signs? Is the patient already in the severe dengue? The phase, that's knowing which phase of disease the patient is, febrile, critical, or convalescent, will help you determine how often you want to monitor your patient. Comorbidities or other conditions that increase the risk of severe disease in your patient, and then, based on those four things, you assign an intervention category, A, B, or C.

I want to emphasize that the assessment and the management of dengue patients usually doesn't require very specialized tests or interventions, especially if you suspect the disease early and intervene in an opportune manner. Dengue clinical presentation is dynamic and complex, but the treatment is relatively simple, inexpensive, and very effective. We are able to successfully manage dengue patients in low-resource areas and in primary care facilities. Dengue beds are preventable, and clinicians who are trained in recognition and early treatment with IV fluids are the most important resource we have to prevent them. Next slide.

During the history taking and the physical exam, these are some of the main criteria we want to assess. For fever, we want to know when the fever started, if it was measured. Dengue fever is abrupt, it can be very high 104 Fahrenheit or 40 centigrade. If the fever has already started to decrease, or if the patient is no longer febrile or in defervescence. Besides the case of finding symptoms of dengue, patients can also present with respiratory symptoms or the gastrointestinal symptoms like anorexia and other symptoms like lymphadenopathy or conjunctival injection.

To assess hydration status, you need to know if the patient is able to drink fluids, and how is the diuresis. Are other things affecting the hydration status like diarrhea or vomiting? Of course, warning signs, you should always ask and assess about them, and there is the list again. Examine the skin for rashes, including the abdomen, the back and limbs, and examine mucosa for bleeding. Sometimes, minor bleeding can be missed in the nose and gums. Ask for changes in colors of stools and urine that can indicate bleeding, too. Assess changes in mental status, especially in children, and assess chronic and social conditions that can put your patient at high risk for severe disease. Another important aspect to assess in dengue patients, of course, next, is plasma leakage that deserves its own slide.

Severe plasma leakage is the most serious complication that distinguishes dengue from severe dengue. Signs of plasma leakage include hemoconcentration that you can identify if the patient's hematocrit is 20% or higher than their baseline. It is very important always obtain a baseline hematocrit in the first medical encounter with a suspected dengue, because this will be your baseline, and will allow you to identify hemoconcentration later. Or if after administering IV fluids, the patient's hematocrit drops 20% or more, which indicates that the patient was hemoconcentrated, and you're diluting the intravascular fluid. Other important sign of clinical plasma leakage is clinical accumulation that you can suspect and assess through the clinical presentation with respiratory distress or abdominal discomfort or flank pain, and you can confirm with imaging, including chest x-rays and abdominal ultrasound. Next slide.

Shock is the main manifestation of severe dengue, and unrecognized shock is another common cause of death among dengue patients. It's very important to remember to always look for early signs of shock, not only decompensated or hypertensive shock. Look for narrowing pulse pressure. This is when the difference between the systolic and the diastolic pressure is 20 or less. For delayed capillary refill, more than two seconds, or for tachycardia in the absence of fever. Next slide.

Now let's see the different types of rashes that present in dengue patients, as their presence can help us guide our clinical suspicion. With the abrupt onset of fever, next, right here, next, dengue patients can present with marked flushing of the neck, face, and chest. In this period, they can

also present with red lips and injected pharynx, and sometimes patients are diagnosed as pharyngitis in this period and just sent home. Next slide.

During the febrile phase, this is days two to six, next, patients may present with a maculopapular rash that usually starts in the trunk and spreads to face and limbs. It is blanchable, as you can see in the bottom picture, and it may become scaly.

The second picture corresponds to the patient in the previous slide. She presented with both rashes. Next slide.

During the convalescent phase, next, patients can present with a very characteristic rash known as islands of white in a sea of red, the islands being the normal skin, and usually presenting in the lower limbs. Their rash can be very pruritic, and we have seen cases were patients have mild symptoms during the febrile phase and normally come to see physicians during the convalescent phase because of the discomfort with this pruritic rash. Next slide.

Regarding bleeding in dengue, only about 1/3 of patients with non-severe dengue will present with minor hemorrhagic manifestations. The occurrence of severe bleeding, that is, usually gastrointestinal bleeding, has been associated with prolonged shock, another reason to identify shock early, and metabolic acidosis. Gastrointestinal bleeding might occult. It's important to ask patients about stool characteristics.

The first picture here is showing a petechial rash, and the second picture is showing skin bleeding manifestations after the use of a blood pressure cuff in a dengue patient. Next slide. The clinical diagnosis of dengue can be challenging, as many other illnesses can present similarly early in the disease course. In general, the top three differential diagnoses in returning travelers to the tropics with fever are malaria, dengue, or typhoid fever. Dengue patients are often tested for malaria because the two diseases can look very similar.

Other considerations should include influenza; other arboviruses like Zika and chikungunya; measles; leptospirosis; yellow fever; and now, of course, COVID-19. We should obtain a detailed history of immunizations, travel, and exposures that guide the differential diagnosis. We don't have time to go in depth on the many differential diagnoses and the fascinating topic of fever in the return traveler, but I want to highlight here a couple of things. During the critical phase, dengue and preeclampsia can be challenging to distinguish, as both can present with thrombocytopenia, plasma leakage, impaired liver function, among other common signs. Dengue, then, should be also suspected in pregnant women. Abdominal pain in dengue can mimic acute abdomen, and this is usually due to collections of retroperitoneal fluid, the result from excessive vascular leakage. Next slide.

Here are some clinical clues that can help you increase your clinical suspicion. If your patient doesn't have these, they still can have dengue, but these might be helpful. Facial flushing has been identified as predictor of dengue infection in some studies, and headache with retroorbital pain is very characteristic of patients with dengue.

A positive tourniquet test during the febrile phase can help you suspect dengue, and if your patient has warning signs, especially abdominal pain in the presence of fever and typical symptoms of dengue, this might help guide your diagnosis, too. After defervescence, if you have a patient with pleural effusions, bradycardia, or shock, this also can be a good sign that your patient has dengue, although if you are seeing your patient after shock, it might be too late. Next slide.

Now I want to do a self-knowledge check for all of you. This is a 17-year-old female from Puerto Rico who was visiting relatives in New York. She presents with fever for four days, the highest measured yesterday at 103 Fahrenheit. She has headache, myalgia, and arthralgia, sore throat, and five episodes of vomiting this morning. Here are the vital signs: The blood pressure is normal. I'll let you calculate the pulse pressure. She's tachycardic. She has a normal respiratory rate, and she's febrile with 38 Celsius.

We want to choose a true statement. A) patients with dengue do not present with respiratory symptoms. Therefore, this patient does not have dengue. B) It is more likely that this patient has malaria than dengue. C) This patient is in the febrile phase, given the temperature. Hence, we are not concerned with progression to severe disease yet. D) Dengue should be considered, as the patient is from a dengue-endemic area. This patient has warning signs for severe dengue and should be hospitalized. I will give you a couple of seconds to think about this. Next slide.

I hope you all chose the correct answer. That is D) and let's see why the other three are false. Less common symptoms of dengue include respiratory symptoms, like cough, sore throat, and runny nose.

B) there is no malaria in Puerto Rico, but there is dengue and it's endemic.

C) Defervescence can occur gradually as we discussed before, and the critical phase can start when the patient still has low fever, and D is correct. Persistent vomiting is a dengue warning sign, and this patient should be under medical observation or hospitalized. Next slide. Now regarding lab diagnosis and workup. Next slide.

Most likely, you won't be able to confirm the diagnosis during your patient's febrile and critical phase, and the management of this patient should be based on clinical suspicion and evaluation. Next slide.

Here is the course of disease that you are already familiar with. In dengue, we can detect the presence of the virus with molecular tests and determine if the patient was exposed recently or in the past using serological tests to detect antibodies against the virus. It is important to remember to obtain a sample for molecular testing as early as possible during the febrile phase. Next.

A real-time RT-PCR assay that can detect the virus RNA is also used to determine which of the four dengue types is causing infection. Patients are most likely to be positive during the first five days of disease, but we test during the first week, since the virus can be detected for a longer period. Next.

NS1 is another molecular test that looks for the nonstructural protein of the virus and is usually positive during the first phase of disease. For serological testing, IgM usually becomes detectable around day four or five, and this is important, because if you test for IgM before this time, you can obtain a negative result even if the patient really has dengue. IgM can stay positive for several weeks to around three months, sometimes longer. A convalescence specimen is needed to make a diagnosis of dengue when you're initial IgM is negative, and disease was not confirmed with a molecular test. Next.

An IgG is detectable around day eight to 10 and proceeds for years, even for life. IgG alone does not indicate active dengue infection. A convalescence sample showing a four-fold increase can confirm dengue diagnosis but is rarely used. Next slide. Next slide.

It is important to remember that dengue is a national notifiable disease, and if you suspect dengue, you should report the case to your local health departments. Rapid diagnostic testing is not available for RT-PCR and NS1. IgM testing can be arranged through your health department, and they can help you determine the recommended test based on your patient's symptom onset. Some private labs also have dengue testing available. Next slide.

As we mentioned before, it is recommended that during the first encounter with a suspected dengue patient, you obtain a complete blood cell count so that you have a baseline hematocrit, and most important, a platelet count, and leukocytes count.

The labs listed here are also recommended to be performed in the workup for patients with possible dengue, especially those who need inpatient management. The metabolic panel can help determine electrolyte imbalances and kidney function. Serum protein and albumin levels are important to determine in the context of plasma leakage. A liver panel, specifically transaminases, AST and ALT, and a coagulation panel. According to the clinical presentation, patients will require additional tests, like cardiac enzymes. Next slides.

Common lab findings in the CDC include leukopenia, hemoconcentration, and thrombocytopenia. During the febrile phase, patients can have normal lab results, and at the end of the febrile phase, beginning of the critical phase, leukopenia with neutropenia and lymphocytosis can be present. For hematocrit, the increase also happens at the end of the febrile phase, beginning of the critical phase, and starts to recover as the critical phase ends. Platelets might take longer to decrease, and normal platelet count during the febrile phase doesn't rule out dengue.

The lowest platelet count usually coincides with the highest hematocrit during the clinical phase. Platelets can also take longer to improve, and patients can have thrombocytopenia well into the convalescent phase. Other common findings include elevated liver enzymes, AST, and ALT that is very common in dengue cases, even in nonsevere dengue cases. Next slide.

Now for dengue treatment, next slide, it is important to remember that the standard of care is supportive management. There is no curative treatment or antiviral available for dengue, but proper treatment with IV fluids can reduce case fatality rate to less than 1%. Next.

Depending on clinical manifestations, patients will be assigned to Group A and managed as outpatients; Group B and require observation or hospitalization, and Group C for emergency treatment. Next slide.

CDC has a dengue pocket guide available that can guide you to the classification of patients in these treatment groups and the algorithms for management. Next slide.

The pocket guide looks like this. It is available in English and Spanish and can be very helpful to quickly follow the current treatment guidelines. We are currently reviewing this pocket guide to make it, to improve it, to modernize it, to make it more friendly and more comprehensive. So, stay tuned, because we should have an updated pocket guide soon. Next slide.

The majority of patients will be assigned to Group A and can be managed as outpatients. These include patients who don't have warning signs, can tolerate oral fluids, and have a normal urine output. Ideally, with these patients, you should follow them every day, and you should obtain a daily CBC, too, until they are out of the critical phase. This is 48 hours after fever disappears or after defervescence.

Very detailed instructions should be given to your patient, so that they can recognize warning signs and they can come back if the warning signs appear, and you should look for warning signs and other things like signs of dehydration during your daily assessment. Febrile patients should be placed under a mosquito net, rest in bed, drink abundant oral fluids, and paracetamol for managing fever. I want to emphasize here that oral fluid intake has been associated with lower rates of hospitalization among children, and oral fluids intake should be encouraged in outpatients. Patients should not receive aspirin or NSAIDs, as these can increase the risk of bleeding. Next slide.

Patients with warning signs, coexisting conditions, are at increased risk of severe dengue or social circumstances that prevent them to be able to quickly return to hospital if needed, are assigned to Group B. These patients should be under observation. In countries where dengue's endemic and there are ongoing outbreaks, this observation usually happens in dengue units, but in the context of the US, it most likely would correspond to hospitalization instead. For these patients, they also should be under bed rest and under a mosquito net. You should obtain baseline laboratories, start an IV line, monitor ins and outs, and if the patient has warning signs or inadequate oral fluids intake, you should start isotonic crystalloids solutions in a stepwise manner. The hematocrit should be monitored every four to six hours if you started IV fluids. Next slide.

If you remember our patient from Puerto Rico, this patient would be included in Group B of treatment. The guide will give you instructions on taking a baseline hematocrit. Next.

Here, and start IV fluids in a stepwise manner. This is key in dengue. We might need to increase or decrease the IV fluids rates, always based in the clinical response of the patient. In this case -- that was the previous? In this case, for example, we start with 5 to 7 mL per kilogram per hour for a couple of hours, and we follow with 3 to 5 mL per kilogram per hour for the next four hours. Next.

Then we reassess the response, both clinically and with a hematocrit, to determine the next steps. The guide will tell you to, next, either decrease IV fluid rates, in this case to 2 to 3 mL per kilogram per hour if there is an adequate response or, next, increase the IV fluid rates if their response is not adequate. As you can see, dengue management requires frequent monitoring of vital signs, clinical response to IV fluids, and hematocrit changes. It can be very timeconsuming, especially in the context of dengue outbreaks, and you can see why health systems can collapse if there is a sharp increase in the number of dengue cases. So, next slide.

Those patients who have shock, either compensated or decompensated, are assigned to Group C and require emergency treatment. The IV fluids management in these patients is more aggressive using boluses of 10 to 20 mL per kilogram in short periods, and they require more frequent monitor of hematocrit. As we are giving these patients higher quantities of IV fluids, we should monitor for signs of fluid overload, including tachypnea, low oxygen saturation, increasing liver size, and peripheral edema, among others. Details on a specific IV fluids doses are included in the current WHO and CDC guidelines, and you can easily access them online. Next.

And here, I want to show you some of the guiding principles of fluid management of dengue, some of which we already know and we already saw, but it's important to have in mind every time you start IV fluids in a dengue patient that you should limit IV fluids in the febrile phase. If your patient is not dehydrated or there is no other reason to administer IV fluids, these are not needed during the febrile phase. You usually only need IV fluids for 24 to 48 hours, the time that the critical phase lasts. Give only isotonic solutions, and it's key to give only the minimum IV fluids required to restore intravascular volume, maintain good perfusion, and a urine output of at least 0. 5 mL per kilogram per hour.

Every time you implement an intervention, you should monitor signs of fluid response and reassess. If the patient is responding, you may want to decrease the rate of IV fluids. Next slide.

You should use the ideal body weight to calculate maintenance fluids in overweight or obese patients, and remember that extravasated fluids remain in the body and will need to be reabsorbed in the convalescent phase. You should monitor for fluid overload.

Although crystalloids are the first choice for fluid replacement in dengue, and most evidence do not show advantages of using colloids or crystalloids for initial IV fluid therapy, there are some situations where WHO contemplates the use of colloids, including when three boluses of crystalloids have been administered without response. Next.

Or when the blood pressure needs to be restored urgently. Previous, please. Blood transfusions should be given as soon as severe bleeding is suspected or recognized, but blood products should be used with caution because of the risk of fluid overload. Next.

Some don'ts in dengue management include do not use corticosteroids. They have not been demonstrated to have a benefit in dengue severity or dengue progression. Do not use NSAIDs, as they can increase the risk of bleeding. Do not give intramuscular injections, and do not give prophylactic platelet transfusions.

These have also not demonstrated any benefit in dengue patients. Next slide. Dengue patients can go home when they have been afebrile for more than 48 hours, when there is an improvement in their clinical status, when the platelet count has an increasing trend. As we saw before, the platelets don't need to completely recovered in order for the patient to go home. If they are going into an increasing trend, the patient can go home, and when the hematocrit is stable without the use of IV fluids. Next slide.

And to conclude, I hope that we can continue to think dengue in all the patients that have been exposed, have been potentially exposed, to dengue in the previous two weeks and present with fever. Remember that unrecognized disease is a common cause of death, and the earlier recognition of disease and the appropriate clinical management with IV fluids can be lifesaving. If you have ever listened to me before talking to dengue, you might know this picture, and I like it very much, because it's a child who came for a post-hospitalization checkup after dengue, and his most important problem at the time was that his dinosaur was broken. So, the physician at the hospital fixed it, and all his problems dengue-related and non-dengue-related were solved. This is what we can do when we recognize dengue early and we treat it the right way. Dengue-appropriate treatment can be lifesaving. Next slide.

Here is the dengue branch contact information, in case you have any questions regarding dengue epidemiology or dengue clinical management. We're always happy to receive any question or concern that you might have.

And now, I'll pass it back to our moderator for the Q&A session.

Presenters, thank you so much for providing this timely information to our audience. We will now go into our Q&A session. And for our audience, please remember to ask a question using Zoom, click the Q&A button at the bottom of your screen and type your question. So, our first question asks, is there a difference in the prevalence of the four dengue virus types based on geographical location?

Yes. Thank you for the question. There are differences in dengue seroprevalence by location, and that really depends on the specific location. In many places across the Americas and in Southeast Asia where dengue is endemic, all four dengue viruses circulate, and it really depends on the age of the population, and the trends in recent dengue circulation of the viruses in that area as to what the specific seroprevalence is by dengue virus type. Thank you.

Thank you. We have quite a few questions about treatment. So, here's one. The question asks is albumin useful in dengue cases in the situation of shock?

There are a couple of very specific situations that the guideline accepts the use of colloids, but it's -- their main recommendation is to always start resuscitation with crystalloids and to continue the treatment with crystalloids unless there is no response to them. But yes, there is a place where the use of albumin and dextran in dengue patients. Usually, if there is no response after three boluses of crystalloids in shock setting, colloids can be administered, and when you have impending shock and you want to recover the blood pressure quickly, you can also use one or

two boluses of colloids, but their recommendation is to always establish resuscitation with crystalloids.

Thank you very much. Another question regarding dengue treatment. If a patient is unable to take acetaminophen or paracetamol, can they use ibuprofen and naproxen?

No. Their recommendation for dengue patients is to not use ibuprofen, aspirin, or any NSAID, as they can increase the risk of bleeding. In these cases, what is recommended is just physical measures to try to decrease fever and oral hydration. The specific recommendation, with evidence that they can increase bleeding, is not to give NSAIDs to dengue patients.

Thank you. That's very helpful. Our next question is about the transmission of dengue, and the question asks, are Anopheles species also capable of dengue transmission?

Yes. Anopheles species are not known to be vectors of dengue. Aedes aegypti and Aedes albopictus are the primary vectors, although there are other mosquito species globally that have been identified as being capable of transmitting dengue. Thank you.

Thank you for that clarification. Our next question refers to the information that was shared regarding dengue transmission based on changes in climate. Have you seen dengue transmission in previously uninvolved localities more recently?

Yes. Thank you for the question. I'm not exactly sure what you referred to by uninvolved localities. I can say that there have been increases in the number of dengue cases and dengue burden, overall, in the past 10 to 15 years, as shown through data reported to PAHO and the World Health Organization. So, we know that dengue cases, globally, are increasing, and the specific trends in more local areas really depends on what's happening in each local jurisdiction.

Thank you very much. A follow-up question we received was generally asking considering the lack of familiarity in providers in the continental US and that things might be going, you know, flying under the radar, do we have a good estimate of dengue cases in the continental US, perhaps Florida, etc.?

Yes. If I understand the question correctly, it's asking about dengue case ascertainment and reporting in the United States, and dengue is a nationally notifiable disease. So, all cases that are suspected to be dengue or identified by laboratories should be reported to state and local public health officials, and those should all be captured in national numbers. There is a possibility of cases being underreported if patients don't seek care or if they're asymptomatic or if dengue is not suspected among those patients. So, we know that there could be cases occurring that are not reported to public health. However, all of the cases that are suspected or identified through laboratory diagnoses should be identified in the national numbers.

Thank you. It's very helpful. We have a few questions about diagnostics, and the first question asks, Please explain the tourniquet test. Now this is something that you referred to a couple times during the presentation, and our attendee would like to know if you can explain the tourniquet test.

Of course, and I apologize I didn't explain it in the presentation. The tourniquet test, what you do is to just take the patient's blood pressure, and you record it. For example. Let's say the patient's blood pressure right now is 100/70, and then, you inflate the cuff of your pressure, blood pressure cuff, if you inflate your blood pressure cuff midway between those two numbers. So, what you do is you add 100 plus 70. You divide it by two. So, the average of your blood pressures will be 85, and you inflate your blood cuff -- blood pressure cuff during five minutes. You wait for a couple of minutes, and then you count the petechiae that present below the antecubital fossa. So, one of the images that I showed in the presentation that had a little square, that was the antecubital fossa of a patient. So, pretty much, you add the blood pressure numbers; divide it by two. Inflate your blood pressure cuff five minutes, wait two, and then you count. Usually, if you have -- usually if it's positive, you have 10 to 20 petechiae in the antecubital fossa, and it's very common that it's positive during the febrile phase in patients with dengue.

Thank you very much. Our next question asks do the recommended coagulation tests include screening for disseminated intravascular coagulation (DIC)?

Not initially, no, although these can happen in more severe dengue cases at the beginning. In most cases for most dengue patients, we only order the basic tests that I mentioned. In many places, we don't even have the availability of all these different panels that we have here, and usually, we're able to follow-up the patient and manage it with the basic CBC and liver enzymes, but not initially. If there are signs of severe dengue or anything that can suggest that the test is negative, you can order it, but in the beginning, it's not necessary.

Thank you very much. Our next question asks you mentioned hypertension as a risk factor for severe dengue. Is coronary artery disease or other cardiovascular diseases a similar risk factor?

Correct. Yes. Hypertension, diabetes, and coronary disease are all risk factors for severe dengue.

Thank you, and we have time for one last question, and the question asks, does CDC offer dengue testing, or should we consult with our health department?

Yes, thank you. We would encourage clinicians to consult first with local and state health departments, as many areas can provide testing there, and we're always -- we're in close communication with the state health departments to provide additional testing, if needed or if requested.

Great, thank you for that. I want to thank everyone for joining us today, with a special thanks to Dr. Laura Adams and Dr. Liliana Sanchez-Gonzalez for answering these questions and for sharing your time and expertise with us today. Next slide, please.

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