

Slide 1: whole picture

Slide 2: Hello, Clinical Problem Solvers! This is Rafael Medina dos Santos. I'm a fifth year medical student from Brazil at State University of Maringá. And I'm thrilled to walk you through an illness script for dengue!

Slide 3: Dengue is a flavivirus transmitted mainly by the mosquito, *Aedes aegypti*. There are 4 serotypes ranging from DENV-1 to DENV-4. But how prevalent is dengue? According to the World Health Organization (WHO), dengue fever is the most critical mosquito-borne disease in the world – it's also the most rapidly spreading! There has been a 30-fold increase in global incidence over the past 50 years. The most significant dengue epidemics in recent years have occurred in Southeast Asia, the Americas, and the Western Pacific. This issue is so serious that in 2020 the Pan American Health Organization (PAHO) reported 716,314 confirmed cases and 580 deaths in the Americas region. The countries reporting most cases are Brazil, Paraguay, and Argentina. What about the USA? Well, according to the CDC, dengue outbreaks have been reported especially in Hawaii, Texas, and Florida. It's actually common in the US territories of American Samoa, the US Virgin Islands, and Puerto Rico.

Slide 4: Dengue can be benign, but also can be very dangerous! So, it's essential to recognize it quickly because it can be life-saving!

Critical dengue usually occurs in patients who have already become infected with one serotype of the virus and, years later, become infected again with another serotype which may be due to antibody-dependent enhancement.

Antibody -dependent enhancement occurs when antibodies from the primary infection cannot neutralize the virus. Instead, they help the virus infect cells more efficiently. The outcome is an increase in the overall replication of the virus and a higher risk of severe dengue.

But, some patients may progress critically even in the first infection, probably due to genetic predisposition.

Slide 5: Dengue begins abruptly after a typical incubation period of 5–7 days. The course follows 3 phases: febrile, critical, and convalescent. Most patients present with the febrile phase of the illness and can have headache, maculopapular rash or petechiae, myalgias, minor bleeding, and retro-orbital pain. Fortunately, most patients do recover completely after a few days. However, some evolve into the critical phase with plasma leakage, shock, severe bleeding.

Following the critical phase, the convalescent phase is characterized by the reabsorption of the extravasated intravenous fluids and pleural and abdominal effusions. Within time, the patient's parameters go back to normal.

Slide 6: Dengue can be classified as dengue without warning signs, dengue with warning signs, and severe dengue.

So, what makes severe dengue life-threatening? In these cases, there is a massive release of pro-inflammatory cytokines that lead to a sudden and generalized increase in capillary permeability, leading to the transfer of intravascular fluid to the interstitium, causing relative hypovolemia and

hemoconcentration. Unfortunately, it can progress to circulatory shock and multiple organ failure! Thrombocytopenia is also common and it is caused by the peripheral destruction of platelets by the action of immune complexes and the complement system. Other laboratory abnormalities include elevated hematocrit, leukopenia, and elevated transaminases.

Severe dengue is almost always preceded by the appearance of warning signs, clinic-laboratory alterations that are easily identifiable, which suggest the onset of plasma leakage. So, if there is something you should take away from this video, it is the following warning signs! We must be able to identify them and respond quickly!

Warning signs in Dengue

- Abdominal pain;
- Persistent vomiting;
- Fluid accumulation (ascites, pleural and / or pericardial effusion);
- Mucosal bleeding;
- Lethargy and / or restlessness;
- Hepatomegaly > 2 cm below the costal margin;
- Progressive increase in hematocrit with decreasing platelets;
- Orthostatic hypotension.

Sadly, some patients evolve in an unfavorable way even without plasma leakage. Some individuals develop severe bleeding (e.g., digestive, intracranial hemorrhage) or specific organ damage (e.g., meningoencephalitis, myocarditis, hepatitis) which can occur at any time during the course of the disease.

Slide 7: Diagnosis can be made through PCR or NS1 antigen if less than 5 days of the disease onset. If more than 5 days, IgM serologic test should be used. IgG is not typically useful for diagnostic testing because it remains detectable for life after a dengue virus infection. However, a 4-fold increase in IgG can suggest an acute or recent infection.

Slide 8: Regarding differential diagnosis, it is important to consider Zika and Chikungunya since they can have similar chief concerns and are transmitted by *Aedes* mosquito.

Zika is a self-limiting disease. Despite its low morbidity, it is associated with cases of Guillain–Barré syndrome and fetal microcephaly, so pregnant women should avoid travelling to regions endemic to the disease. Chikungunya, just like dengue, is characterized by a sudden fever, skin rashes and arthralgia. However, it is followed by persistent rheumatic symptoms. For a more comprehensive differential diagnosis list, see our fever in a returning traveler on the website.

Slide 9: Dengue therapy is supportive (analgesics, antipyretic, antiemetic and antipruritic drugs), with an emphasis on hydration (oral in mild cases, intravenous in severe cases). Always remember

NEVER prescribe salicylates (AAS) or NSAIDs! Due to their effects on platelet inhibition, they can cause a substantially increased risk of bleeding.

Prevention requires mosquito avoidance: use repellents and do not allow water to accumulate to prevent mosquito breeding.

Remember: Dengue is a severe disease and being able to recognize its warning signs is crucial!

I hope you all enjoyed it! See you next time!