A Healthy 18-Year-Old Presents With Questions About Travel Vaccinations

consultant360.com/whats-take-home/healthy-18-year-old-presents-questions-about-travel-vaccinations

Ronald N. Rubin, MD

What's the Take Home?

Volume 65 - Issue 5 - May 2025

Introduction. An 18-year-old high school senior and her parents present to their long-time family physician's office with questions about travel vaccinations.

Patient history. The patient's school recently awarded her with a fellowship trip to Central America under the auspices of the World Health Organization. She will volunteer as an aide in a large hospital in Panama City. The patient is a top student who enjoys science subjects and hopes to pursue a career in medicine. She is healthy and has no medical issues.

She has had all required and recommended childhood vaccines (MMR, polio) and is vaccinated against human papillomavirus, COVID-19, and influenza. She feels that completing this fellowship will markedly strengthen her college admission process. However, her parents have read online about the presence of and risk for infection from a variety of "tropical fevers" in tropical climates and would like more bona fide medical input before agreeing to let their daughter travel. They are aware of the availability of vaccines against yellow fever and medication for Malaria prophylaxis but are concerned after reading about dengue fever.

Correct Answer: D. Although dengue fever is endemic and a risk in Panama, she should not receive anti-dengue vaccine at this time.

Discussion. I previously reviewed vibriosis with its ever-northward migration having reached the Chesapeake due to several factors including increased international travel and global warming.[1] The current case involves dengue fever, which is endemic in Central America and has started to increasingly appear in Puerto Rico.[2]

Dengue or dengue fever is a "tropical fever". The virus itself is an RNA flavivirus, which is carried in the salivary glands of mosquitoes, the main carrier being *Aedes aegypti.* When an infected mosquito takes its blood meal from a human, the virus in its saliva is transmitted to the human and causes disease. About 80% of cases are essentially asymptomatic.[3] Worldwide, an estimated 50 million cases occur yearly.[2] The traditional nomenclatures of “dengue”, namely “dengue hemorrhagic fever” and “dengue shock syndrome”, have been contracted into “dengue fever” and “severe dengue”. The latter term is used when complications of either one or more of (1) vascular leak, (2) hemorrhage/thrombocytopenia, or (3) vascular collapse with shock occur.

All dengue fever infections follow a similar course. About 4 days to 14 days post-mosquito borne infection, the febrile phase ensues. Patients manifest high (103º-104ºF) fevers, emesis, severe myalgias/arthralgias, and headache. This phase of illness lasts 3 days to 7 days. The next phase is termed the "critical phase" if life-threatening complications like vascular leak or hemorrhages occur. With vascular leak, an immune-mediated dysfunction of vascular endothelium results in copious loss of fluids into extravascular tissues with edema, ascites. pleural effusions, volume loss, and profound hemoconcentration with rises in hematocrit. Hypotension, vascular collapse, and shock may result. With hemorrhagic complications, there is a lowering of platelet count and clinically significant spontaneous skin and mucosal bleeding. Whether uncomplicated dengue fever or severe dengue has passed through the critical phase, the recovery phase follows, which is quite dramatic and rapid¾resolution of all symptoms and pathophysiologies occur within 2-3 days.[2]

Approximately 80% to 85% patients who contract dengue fever are asymptomatic, 10% to 15% will have significant febrile illness that could potentially devolve into severe dengue syndromes, with approximately 5% doing so. The overall mortality is 0.1%, with cases devolving into severe dengue having a 1% to 2% mortality.[3]

As dramatic as the syndrome can be, there is currently no specific anti-viral therapy for dengue. The entire clinical illness and any of its complications are treated supportively with anti-pyrectics, fluids, and active monitoring. Some questions to consider when treating a patient with dengue:

- Is the patient’s blood pressure (BP) stable?
- Can the patient take adequate PO fluids?

- Is the patient's hematocrit increasing or is their platelet count decreasing?
- Is there clinically significant bleeding?

Any bleeding will require hospital and potentially intensive care unit care. With severe dengue and vascular leak, professional monitoring of BP, fluid status, and expertise in proper titration of crystalloid versus colloid (and in what amounts) is needed to walk the fine line between intravascular volume depletion and extravascular volume overload and shock, which is where most dengue mortality occurs. Hemorrhagic dengue similarly requires appropriate monitoring of platelet counts and hemoglobin and the use of transfusions of blood products as well.

The differential diagnosis for dengue includes other "tropical fevers" including malaria, yellow fever, and Zika. In any endemic area, there will be ongoing monitoring of what mosquitoes are present and in what numbers, and clinical case monitoring for dengue incidence. For the viral tropical fevers, diagnosis is differentiated and confirmed immunologically by serologic testing. The optimal tests vary by phase and timing of the disease. For dengue in the febrile phase, patients will be viremic and test positive by polymerase chain reaction (PCR) testing specific for viral RNA and Elisa antibody testing for antibodies against specific dengue induced viral proteins. After Day 7, the above viral testing decays, but IgM anti-dengue antibodies become manifest. In this case, Elisa testing can be used to confirm the diagnosis.[3]

Virology, Viral Antigenicity, and Immune Pathophysiology

As mentioned earlier, dengue virus is an RNA virus, specifically a flavivirus. The flavivirus family has several bad actors including the extremely dangerous yellow fever virus, West Nile virus, and Zika. Dengue and the others all are caused by mosquitoes (most commonly *Aedes aegypti,* which favors humans for its blood meals such that these conditions favor warm and wet climates and are thus "tropical fevers".

The virus has four distinct antigenic variants or serotypes, which differ in their antigenicity—DEN V, DENV 2, DENV 3, and DENV 4.[4] A dengue infection begets lifelong immunity, but only against the specific serotype involved. Indeed, repeated infections from the remaining three serotypes can occur. What complicates matters is the fact that a second infection by another of the serotypes results in a larger proportion of the so-called severe dengue illnesses, which is where most of the serious morbidity and mortality of dengue ensues.[4,5] This is what makes developing an effective quadrivalent vaccine so challenging. It is extremely difficult to develop a vaccine capable of protecting simultaneously against all four serotypes and prevent the dangers of a second infection in patients who acquire a different dengue serotype infection.[4-6]

Any dengue infection results in a predictable immune response. In the early acute infection period (Days 1-4), there is actual viremia and PCR for the viral RNA will detect antibody. Viral-induced proteins are developed, which are detectible by Elisa methods. After Day 4,

specific anti-dengue IgM antibody can be detected.

Vaccination Status

The above discussion clarifies the difficulties in developing an effective dengue vaccine. A proper vaccine requires the ability to induce immunity to all four serotypes including the viral antigens and virus-induced proteins as well. Two vaccines are currently availablewith approvals of multidose administration: Dengvaria and TAK-003. Both are somewhat logistically difficult and moderately effective but come with a cost of breakthrough infections, which had an increased frequency of severe dengue type clinical scenarios.[4-6] A more recent tetravalent single dose vaccine, with less breakthrough issues, has been studied and reported in a large trial.[6]

Patient Follow-Up. The patient and her family were referred to an infectious disease specialist who reviewed the CDC data on vaccinations and foreign travel, as well as the recent data appearing in the vaccine literature. She was visiting in Panama City, which is not a hyperendemic area for dengue and in addition is not a high-risk area for yellow fever. Although the Darian jungle area in Southwest Panama is a yellow fever risk, the remainder of Panama is not a yellow fever risk. Therefore, neither yellow fever nor dengue vaccination is indicated. Thus, Answer A and C are incorrect. Currently, there are no antiviral prophylactic medications available for dengue (in contradistinction to malaria oral prophylaxis) so answer C is also incorrect.

The patient proceeded with her fellowship without a vaccine and spent several months in Panama without any health issues. The patient returned home with no medical issues and will enter college in the fall.

What's the Take Home? The clinical entity dengue needs review because of two major changes seen in the last decade. First, is the ongoing geographic spread of this once "tropical fever". Considering more and more travel/transport of people and goods, the virus and its vectors, the *Aedes aegypti* mosquito, are gaining enhanced access to new locations. In addition, these "new locations" of endemic and even epidemic outbreaks are becoming more "tropical" and thus more welcoming to dengue, which I discussed in previous article on *vibrio Vulnificus* epidemiology.[1]

We must become acquainted with an illness that, for many of us, was but a small detail and footnote in our training. The good news, however, is that since the virus has significant antigenic diversity with weak (if any) cross-immunity to different antigenic strains, a person can contract dengue repetitively. Indeed, an effective tetravalent vaccine now exists that can potentially improve prevention as we learn how, when, and whom to vaccinate.

AUTHOR
Ronald N. Rubin MD[1,2]

AFFILIATIONS
[1]Lewis Katz School of Medicine at Temple University, Philadelphia, PA
[2]Department of Medicine, Temple University Hospital, Philadelphia, PA

CITATION
Rubin RN. A Healthy 18-Year-Old Presents With Questions About Travel Vaccinations*Consultant*. 2025;65(5):DOI:10.25270/con.2025.05.000009

DISCLOSURES
The author reports no relevant financial relationships.

CORRESPONDENCE:
Ronald N. Rubin, MD, Temple University Hospital, 3401 N. Broad Street, Philadelphia, PA 19140 (blooddocrnr@yahoo.com)

References

1. Rubin RN. A 70-year-old man with severe hand pain, part 2. *Consultant*. 2024;64(7):eXX. doi:10.25270/con.2024.07.000004
2. Harris E. Increased dengue infection in the US: CDC cautions. *JAMA*. 2024;332(5):447.
3. Simmons CP, Farrar JJ, Chau NVV, Wills B. Dengue. *N Engl J Med*. 2012;361(15):1423-1432.
4. Halstead SB. Three dengue vaccines—what now? *N Engl J Med*. 2024;390(5):464-465.
5. Sridhar S, Luedtke A, Langevin E, et al. Effect of dengue serostatus on dengue vaccine safety and efficacy. *N Engl J Med*. 2018;379(4):327-340.
6. Kallas EG, Cintra JA, Moreira EG, et al. Live attenuated tetravalent Butantan dengue vaccine in children and adults. *N Engl J Med*. 2024;390(5):397-408.