



Dengue Vaccine

Pink Book Web-on-Demand Series November 01, 2022

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Learning Objectives

- Describe the Advisory Committee on Immunization Practices General Best Practice Guidelines on Immunization.
- Describe an emerging immunization issue.
- For each vaccine-preventable disease, identify those for whom routine immunization is recommended.
- For each vaccine-preventable disease, describe characteristics of the vaccine used to prevent the disease.
- Locate current immunization resources to increase knowledge of team's role in program implementation for improved team performance.
- Implement disease detection and prevention health care services (e.g., smoking cessation, weight reduction, diabetes screening, blood pressure screening, immunization services) to prevent health problems and maintain health.

Continuing Education Information

- CE credit, go to: <https://tceols.cdc.gov/>
- Search course number: **WD4564-110122**
- CE credit expires: **July 1, 2024**
- CE instructions are available on the **Pink Book Web-on-Demand Series** web page
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Disclosure Statements

The findings and conclusions in this presentation are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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Dengue

Dengue

- **Vector-borne infectious disease**
- **Caused by one of any four closely related viruses**
 - DENV-1
 - DENV-2
 - DENV-3
 - DENV-4
- **People can be infected with a dengue virus as many as four times in a lifetime**



Dengue Pathogenesis

- Immune response after infection with a dengue virus provides long-term immunity to the same serotype but only short-lived protection against other serotypes
- Risk for severe dengue variable based on many factors
 - Second infection most likely to cause severe dengue

Dengue Pathogenesis

- **Multiple mechanisms likely contribute to increased disease severity during a second DENV infection.**
 - Antibody-dependent enhancement occurs, exacerbating immune response
 - Accompanying enhanced immune response occurs that contributes to intravascular leakage and clinical fluid accumulation (e.g., ascites, pericardial effusion, and pleural effusion)

Dengue Clinical Features

- Asymptomatic infection or mild illness to severe disease

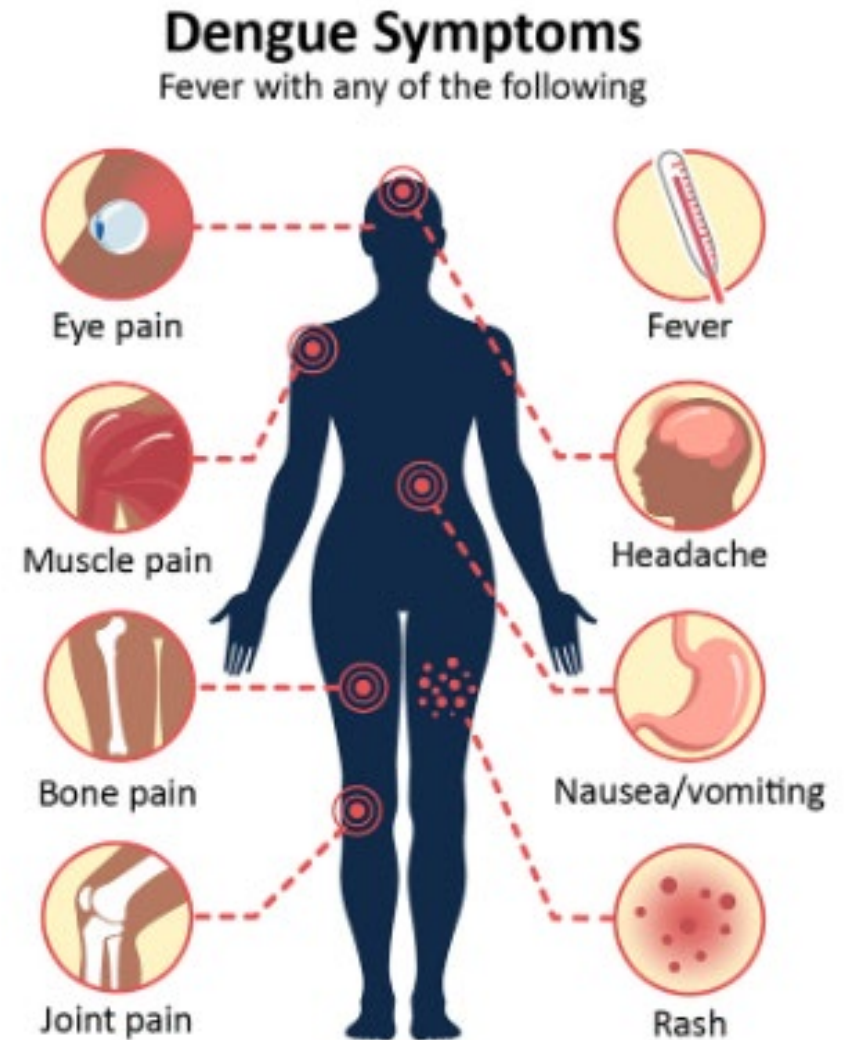


- Early clinical findings require a high index of suspicion because early recognition and supportive therapy can reduce risk of death

Dengue Clinical Features

■ Clinical findings:

- Fever
- Nausea, vomiting
- Rash
- Aches and pains
- Positive tourniquet test
- Leukopenia
- Any warning signs



Dengue Warning Signs

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleeding
- Lethargy or restlessness
- Postural hypotension
- Liver enlargement
- Increased hematocrit level concurrent with a rapid decrease in platelet count



Severe Dengue Clinical Features

- **Defined by**
 - Severe plasma leakage leading to shock or fluid accumulation with respiratory distress
 - Severe bleeding
 - Severe organ impairment
- **Requires monitoring and treatment in hospital likely in the intensive care setting**
- **Organ impairment carry a high risk for death**
- **Age, comorbidities, genetics, and virus strain are risk factors**

Dengue Epidemiology

Epidemiology

Transmission

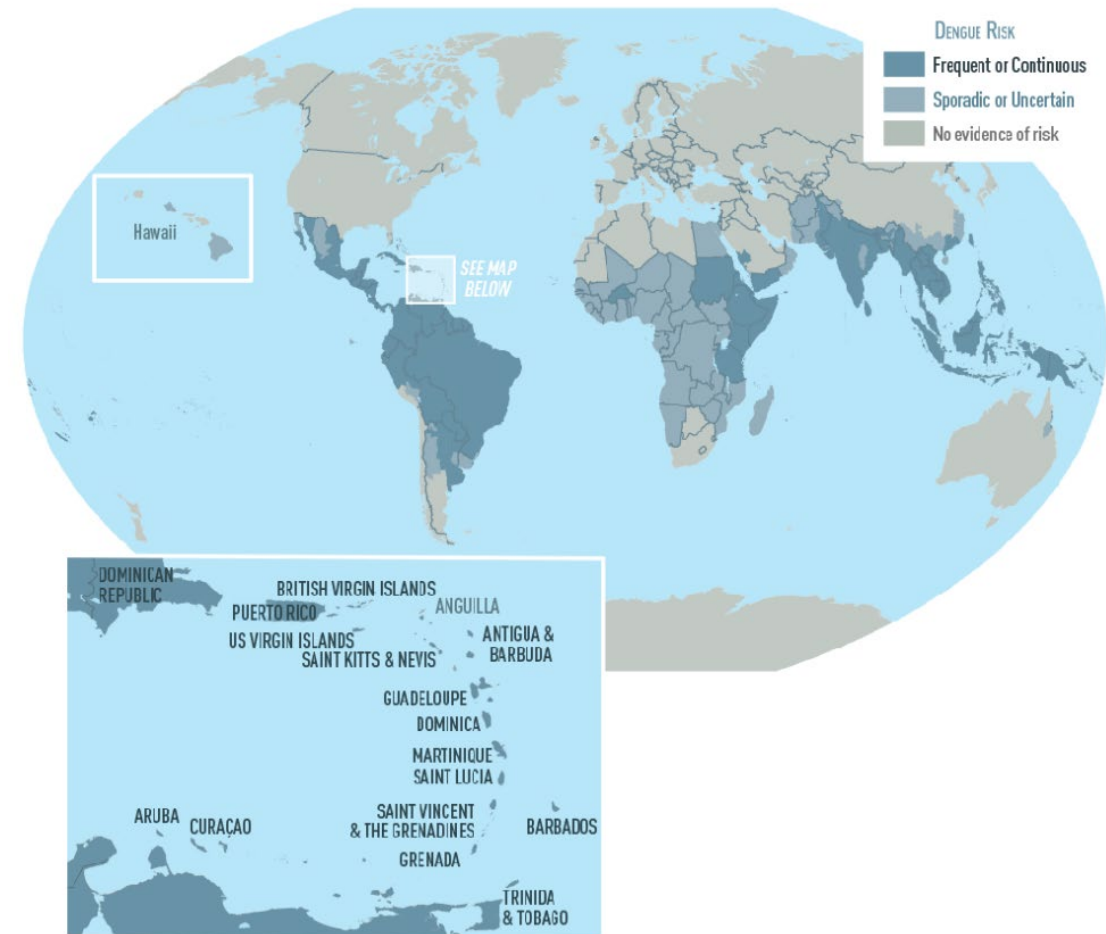
Bite of infected *Aedes* spp mosquitoes; rarely mother to child or through blood, laboratory, or healthcare setting exposures

Temporal pattern

Epidemics often seasonal during wetter, warmer months

Dengue Epidemiology

- Worldwide problem since 1960s
- Endemic throughout the tropics and subtropic
- Leading cause of febrile illness among travelers returning from Latin America, the Caribbean, and Southeast Asia



Dengue Disease Burden

- **Estimated 4 billion people worldwide living in areas with dengue risk**
- **Worldwide annually**
 - 400 million infections
 - 100 million people get sick from infection
 - 40,000 deaths

Dengue Epidemiology in the US

■ Dengue-endemic areas:

- American Samoa
- Puerto Rico
- U.S. Virgin Islands
- Federated States of Micronesia
- Republic of the Marshall Islands
- Republic of Palau



Dengue in the US

- Dengue is most common in dengue-endemic areas; however, outbreaks occasionally occur in the continental US
- ~90% of the population at risk for dengue in the US live in Puerto Rico. During 2010-2020:
 - ~95% of locally acquired dengue cases in the US occurred in Puerto Rico (29,779 cases)
 - Most cases and hospitalizations among persons ages 10-19 years (11,000 cases and 4,000 hospitalizations)
 - Most deaths among persons ages 20-89 years

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**Dengue
Vaccine**

Dengue Vaccine

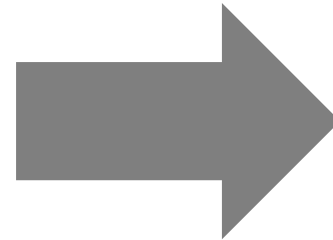
- **Dengvaxia, is the only dengue vaccine approved by the U.S. Food and Drug Administration and recommended for routine use by ACIP**
 - Not approved for US travelers visiting but not living in a dengue-endemic area
- **Dengvaxia is a tetravalent, live-attenuated vaccine**
- **Contains four genetic constructs, one for each serotype**
- **Multiple dengue vaccine candidates are in clinical development.**

Dengue Vaccine

Ages 9 through 16 years

Living in U.S. areas where dengue is endemic

Laboratory confirmation of previous dengue infection



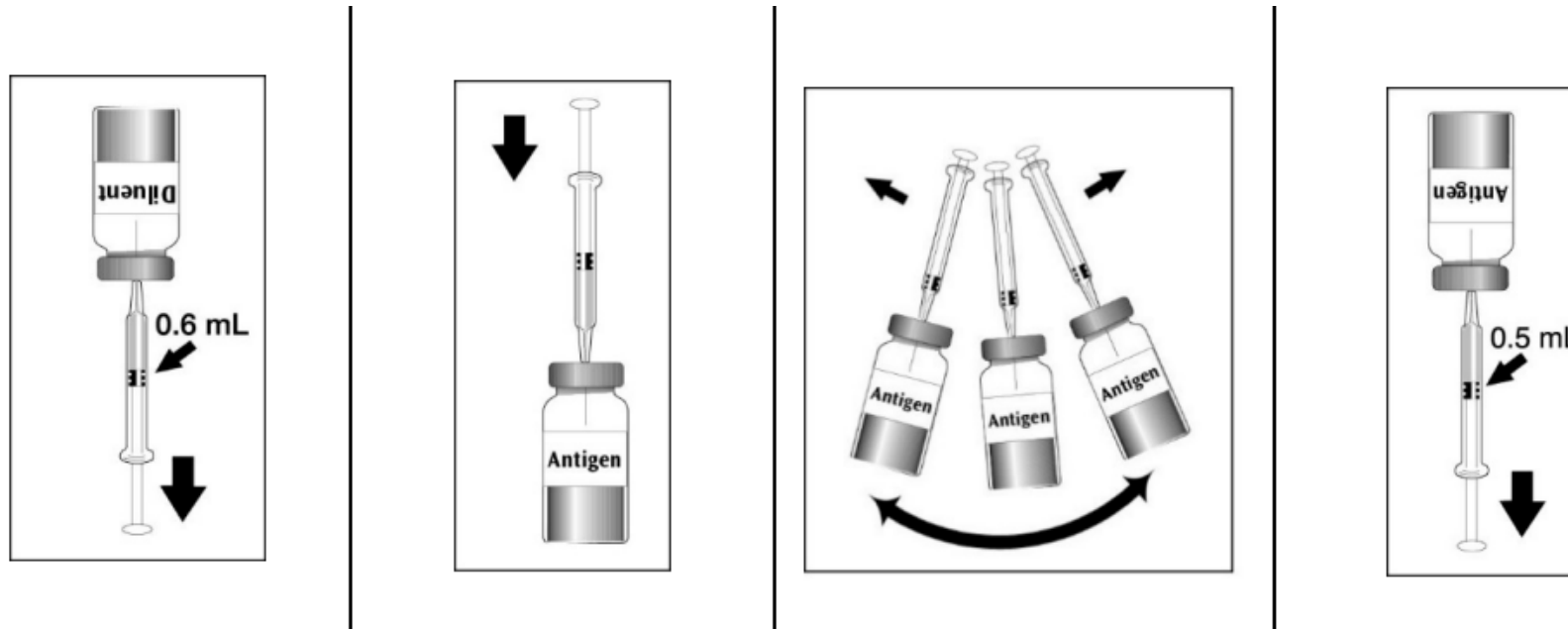
Dengue Vaccine Efficacy

- **82% vaccine efficacy against VCD in immunogenicity subset**
- **Over 5-year follow-up period**
 - 79% efficacy against hospitalization
 - 84% efficacy against severe dengue
- **Protection from hospitalization and severe disease last for at least 6 years**

Preparation and Administration for IPV-Containing Vaccines

■ Preparation:

- Supplied as a lyophilized powder to be reconstituted with the supplied saline diluent



Preparation and Administration for IPV-Containing Vaccines

- **Injection volume: 0.5 mL**
- **Administration Route: Subcutaneous injection**

Knowledge Check

- Lucas is age 10 years. He lives in Texas but frequently visits a dengue-endemic area in South America. He had dengue virus infection last year, which was laboratory confirmed. **Should you administer dengue vaccine today?**
 - Yes
 - No



Answer

- Should you administer Dengue vaccine today?
 - No



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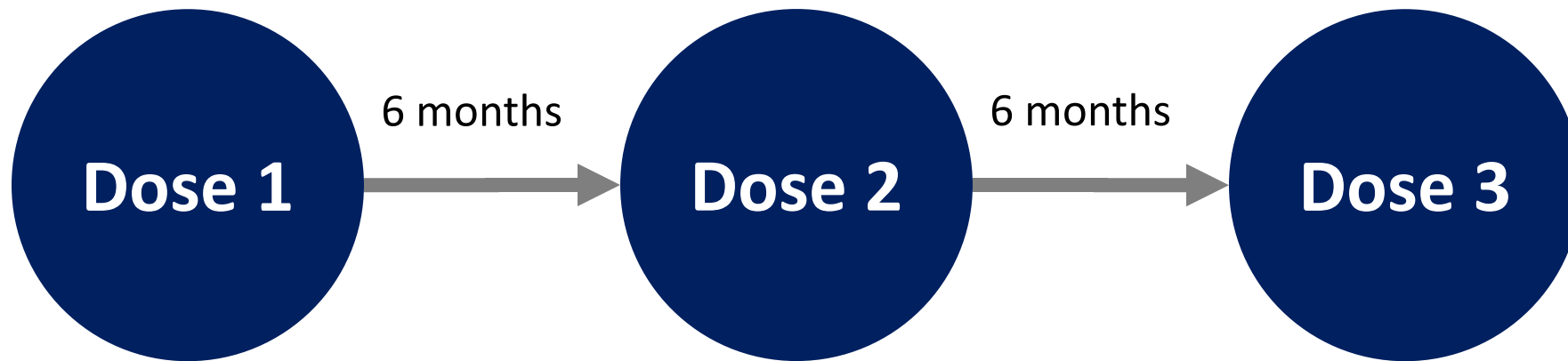
**Clinical
Considerations**

ACIP Dengue Vaccine Recommendations

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19-23 mos	2-3 yrs	4-6 yrs	7-10 yrs	11-12 yrs	13-15 yrs	16 yrs	17-18 yrs
Dengue (DEN4CYD; 9-16 yrs)														Seropositive in endemic areas only (See Notes)			

ACIP Dengue Immunization Recommendations

- **3-doses** of Dengvaxia administered 6 months apart at month **0, 6, and 12**, in persons 9 through 16 years of age with a laboratory confirmation of previous dengue infection and living in endemic areas

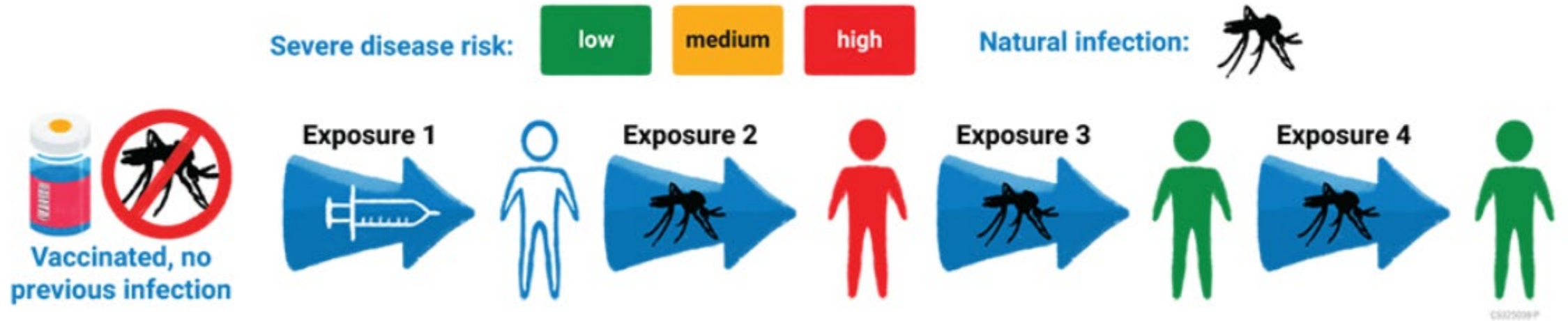


Dengue: Clinical Guidance.

- Vaccine providers must evaluate patients for **laboratory evidence of previous dengue infection** before vaccination to avoid vaccinating seronegative persons
 - Children with previous dengue infection were protected from hospitalization and severe dengue if they were vaccinated with Dengvaxia.
 - Children without previous dengue infection had a higher risk of hospitalization and severe dengue if they were vaccinated and then had a DENV infection

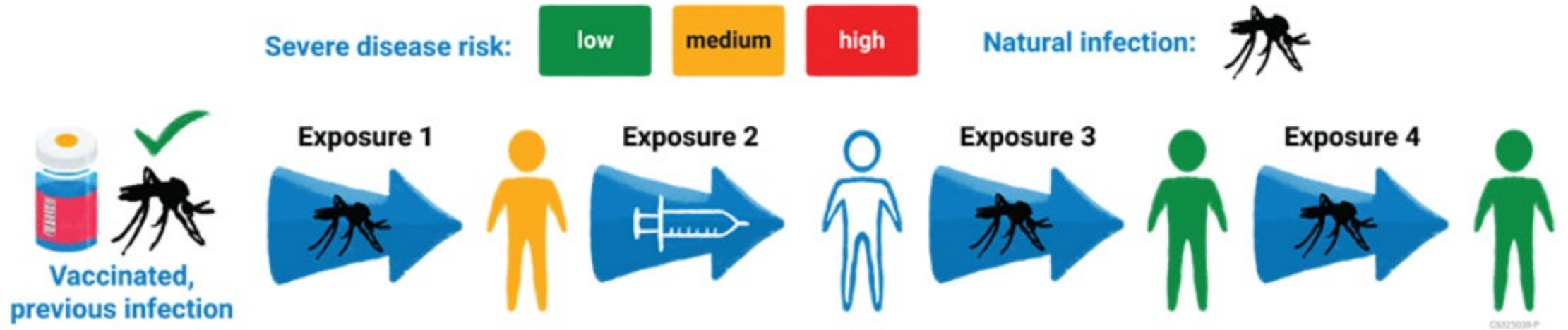
Dengue: Clinical Guidance, cont.

Dengue Antigen Exposure



Dengue: Clinical Guidance, cont.

Dengue Antigen Exposure



Laboratory Testing Requirements

- Detection of dengue virus IgG using tests meeting performance standards for prevaccination screening provides evidence of previous dengue virus infection
- CDC recommends the use of highly specific pre-vaccination screening tests for dengue IgG
- Patients with a negative test should be re-tested every 1-2 years from the ages of 9–16 or based on clinical judgement
- <https://www.cdc.gov/dengue/vaccine/hcp/testing.html>

Laboratory Testing Requirements

- **Laboratory confirmation of previous dengue virus infection is required and can be obtained by:**
 - Evidence of prior acute dengue virus infection with
 - Positive dengue RT-PCR test result, or
 - Positive dengue NS1 antigen test result
- **OR, positive results on tests meeting performance standards for prevaccination screening**
- **<https://www.cdc.gov/dengue/vaccine/hcp/testing.html>**

Laboratory Testing Requirements, Continued

- A single positive anti-dengue virus immunoglobulin M (dengue IgM) test result is not sufficient proof of dengue virus infection for vaccination with Dengvaxia due to potential cross-reactivity with other circulating flaviviruses (e.g., Zika virus) in dengue-endemic areas.

Use in Special Populations

- **Dengvaxia should be used with precaution in certain populations.**
- **Health care providers should weigh the risks of vaccination against the risk for dengue for the following populations.**
 - Pregnant persons
 - Breastfeeding persons
 - Persons with HIV infection

Pregnant Persons

- **At increased risk for dengue-related complications**
- **Not specifically studied in trial**
- **Limited number of people inadvertently vaccinated had similar frequency of adverse pregnancy outcomes**
 - Not sufficient numbers to determine a possible effect

Breastfeeding Persons

- Human data not available
- Development health benefits of breastfeeding should be weighed with risk for infection

Persons with HIV Infection

- Safety and efficacy not assessed but studies are ongoing

Coadministration

- **May be administered simultaneously with other vaccines.**
- **Doses of injectable, live-attenuated vaccines not administered simultaneously should be separated by at least 4 weeks, in accordance with best practice guidance from ACIP**

Knowledge Check

- **True/False: Verbal report is sufficient evidence of previous dengue virus infection.**
 - True
 - False



Answer

- **True/False: Verbal report is sufficient evidence of previous dengue virus infection.**
 - False



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Safety

Contraindications

Dengue

Persons who have had a severe (life-threatening) allergic reaction to a previous dose of the vaccine or ingredient

Persons with immunocompromising conditions, including those with severe immunosuppression due to HIV infection

Persons without a laboratory-confirmed previous dengue virus infection

Precautions

Dengue

Pregnancy

HIV infection without severe immunosuppression

Dengue Adverse Reactions

Dengue	
Headache	40%
Injection site pain	32%
Malaise	25%
Asthenia	25%
Myalgia	29%

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Storage and Handling

Dengue Vaccine Storage and Handling

- **Store in the refrigerator between 2°C and 8°C (36°F and 46°F)**
 - Should not be frozen
 - Refrigerate on arrival
 - Protect from light
- **After reconstitution, administer immediately or store refrigerated and use within 30 minutes**
 - If not used within 30 minutes, discard vaccine

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Resources

Additional Resources



Dengvaxia: What Healthcare Professionals Need to Know:

<https://www.cdc.gov/dengue/educationtraining/dengue-vaccine-webinar.html>

Dengue Clinical Case Management:

<https://www.cdc.gov/dengue/training/cme/ccm/index.html>

Dengvaxia: What Healthcare Professionals Need to Know



Additional Resources



Dengue Information for Healthcare Providers:

<https://www.cdc.gov/dengue/healthcare-providers/index.html>

Dengue Vaccine: Recommendations of the Advisory Committee on Immunization Practices, United States, 2021:

<https://www.cdc.gov/mmwr/volumes/70/rr/rr7006a1.htm>

Dengvaxia Package Insert:

<https://www.fda.gov/media/124379/download>

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E-mail Your Immunization Questions to Us

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Thank You From Atlanta!

