



## Dengue Fever: An Updated Review article for Physicians, Nursing, and Clinical Laboratory Professionals.

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### Abstract

**Background:** Dengue is a high-impact arboviral disease transmitted by *Aedes aegypti* and *Aedes albopictus*, with clinical severity ranging from self-limited fever to plasma leakage, hemorrhage, and shock. Global expansion reflects urbanization, climate variability, and mobility.

**Aim:** To provide an updated, practice-focused synthesis for physicians, nursing, and clinical laboratory professionals spanning pathophysiology, phased recognition, diagnostics, management, and prevention.

**Methods:** Narrative integration of current clinical frameworks: febrile–critical–recovery staging; early laboratory patterns (leukopenia, thrombocytopenia, transaminitis); confirmatory testing (NS1, PCR, serology); risk stratification; supportive care algorithms; vector control and vaccination.

**Results:** Early identification of warning signs around defervescence and judicious fluid stewardship reduce severe outcomes; transfusion decisions are driven by clinical bleeding rather than platelet thresholds. NS1/PCR confirm early infection; serology assists later but may cross-react with other flaviviruses. Multidisciplinary coordination (clinical, nursing, laboratory) improves triage, monitoring, and prevention. Vector control (source reduction, biological and chemical methods) plus context-sensitive vaccination (CYD-TDV) complement clinical care.

**Conclusion:** Outcomes hinge on timely diagnosis, phase-appropriate fluids, vigilant monitoring, and integrated public-health measures. Team-based pathways and laboratory–clinic alignment are pivotal to lowering mortality (~1% with optimal support) and epidemic burden.

**Keywords:** dengue; *Aedes*; NS1; PCR; antibody-dependent enhancement; warning signs; fluid therapy; transfusion; vector control; CYD-TDV..

### 1. Introduction

Dengue is an arthropod-borne viral infection transmitted predominantly by *Aedes* mosquitoes—especially the highly anthropophilic *Aedes aegypti* and the adaptable *Aedes albopictus*—that thrive in tropical and subtropical climates. Clinically, dengue has earned colloquial names such as “breakbone fever” and “7-day fever,” reflecting hallmark manifestations of abrupt high-grade pyrexia, severe myalgia, arthralgia, retro-orbital pain, and profound

fatigue. While a large proportion of infections are asymptomatic or paucisymptomatic, the clinical spectrum spans from a self-limited febrile illness to life-threatening complications marked by plasma leakage, bleeding, and organ impairment. The global footprint of dengue has expanded substantially over recent decades, driven by rapid urbanization, expanding vector habitats, climate variability, and unprecedented human mobility. As a result, dengue has become endemic in many regions, with recurrent

outbreaks that strain public health infrastructure and clinical services, and with annual case counts surpassing one hundred million and tens of thousands of deaths worldwide [1][2][3].

Dengue virus (DENV) comprises four antigenically distinct serotypes (DENV-1 through DENV-4). Primary infection typically confers long-lasting, serotype-specific immunity but only transient, partial cross-protection against the others. Secondary infection with a heterologous serotype can precipitate more severe disease through immunopathologic mechanisms, notably antibody-dependent enhancement (ADE). In ADE, non-neutralizing or sub-neutralizing antibodies from a prior infection facilitate viral entry into Fc-receptor-bearing cells, amplifying viremia and the downstream inflammatory cascade. The most feared clinical entities—dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS)—are characterized by a triad of increased vascular permeability, thrombocytopenia, and coagulopathy, culminating in hemoconcentration, serosal effusions, mucosal bleeding, and shock if not promptly recognized and managed [1][2][3]. The natural history of dengue often proceeds through three phases. The febrile phase presents with sudden fever, headache, myalgia, arthralgia, rash, nausea, and mild bleeding (e.g., epistaxis or gingival oozing). The critical phase typically coincides with defervescence (often days 3–7), during which capillary leakage may rapidly evolve, heralded by rising hematocrit, decreasing platelet counts, abdominal pain, persistent vomiting, lethargy, hepatomegaly, or clinical fluid accumulation. Without careful fluid management, patients may progress to shock. The recovery phase is marked by reabsorption of extravasated fluids, stabilization of hemodynamics, and gradual improvement in laboratory indices; however, excessive fluid administration during the critical phase can manifest as pulmonary edema or heart failure during recovery, emphasizing the need for vigilant, phase-appropriate care [1][2][3].

Diagnosis rests on a combination of clinical suspicion (based on epidemiology and symptomatology) and laboratory confirmation. Early in illness, NS1 antigen detection and nucleic acid amplification tests can confirm infection; serology (IgM/IgG) aids diagnosis later but is confounded by cross-reactivity with related flaviviruses and by prior exposures. Routine hematology often demonstrates leukopenia and thrombocytopenia, with hemoconcentration signaling plasma leakage. Point-of-care ultrasound can detect third-spacing (pleural effusions, ascites) in those with evolving severity. Management is primarily supportive and centers on meticulous fluid therapy tailored to dynamic vascular permeability. For uncomplicated cases, oral rehydration, antipyretics (avoiding NSAIDs that heighten bleeding risk), and close follow-up suffice. In suspected progression to DHF/DSS, judicious

intravenous crystalloid resuscitation guided by frequent clinical and laboratory reassessment is the cornerstone; colloids are reserved for refractory shock. Transfusion decisions hinge on clinical bleeding rather than platelet counts alone. Early recognition of warning signs and timely escalation to higher-acuity settings improve outcomes [2][3].

Prevention integrates vector control, personal protection, and—where appropriate—vaccination. Vector reduction hinges on eliminating breeding sites (stagnant water in containers), improving water storage practices, deploying larvicides, and implementing community-based strategies. Personal measures include repellents, protective clothing, and screened living spaces. Vaccination strategies are nuanced, reflecting the interplay between serostatus, age, and local epidemiology; consequently, programs prioritize settings where benefits outweigh risks and align with contemporary guidance. Nevertheless, vaccines complement rather than replace vector control, surveillance, and clinical preparedness. From a public health perspective, the growing geographic reach of competent vectors, coupled with urban density and global travel, ensures that dengue will remain a prominent threat. Strengthened surveillance systems, rapid diagnostic access, and scalable clinical pathways for triage and fluid management are essential to mitigate morbidity and mortality. Education of clinicians and communities about the timing of the critical phase, recognition of warning signs, and avoidance of antiplatelet/NSAID agents can avert preventable complications. In summary, dengue is a high-impact arboviral disease whose burden reflects a convergence of virology, vector ecology, climate, and human behavior. Most infections are mild, but a subset progresses to severe disease with capillary leak and hemorrhage—patterns especially associated with secondary heterologous infections and ADE [1][2][3]. Sustained gains in outcomes will depend on integrated strategies: early, accurate diagnosis; phase-appropriate fluid therapy; vigilant monitoring; effective vector control; context-sensitive vaccination; and robust health systems capable of surging during epidemics [1][2][3].

#### **Etiology:**

Dengue fever is caused by four antigenically distinct serotypes of dengue virus—DENV-1, DENV-2, DENV-3, and DENV-4—each a positive-sense, single-stranded RNA virus in the genus *Flavivirus*. Primary infection with any one serotype induces durable, likely lifelong immunity to that specific serotype, yet provides only transient and incomplete cross-protection against the others; thus, individuals remain susceptible to subsequent infections with heterologous serotypes [4][5][6]. This serotype specificity underpins dengue's epidemiology: in regions where multiple serotypes cocirculate, persons may experience sequential infections across their lifetime. The virus is maintained and amplified within

a human–mosquito–human transmission cycle, with *Aedes aegypti* serving as the principal vector and *Aedes albopictus* as an important secondary vector in many geographies. After ingesting viremic blood, the mosquito undergoes an extrinsic incubation period during which the virus disseminates to salivary glands; subsequent bites can then transmit virus to a new human host. Vertical (transovarial) transmission in mosquitoes has been documented and may facilitate viral persistence during inter-epidemic periods. In parts of Asia and Africa, sylvatic cycles involving nonhuman primates and forest *Aedes* species also exist, posing occasional spillover risks to humans [4][5][6].

Several determinants modulate transmission intensity. Vector competence varies by mosquito species and even by local populations, while environmental conditions—temperature, rainfall, and urban microhabitats—shape vector density and biting behavior. Rapid urbanization, water storage practices that create container breeding sites, and global mobility further expand the ecological niche of *Aedes* and promote serotype introductions into naïve populations. From the viral side, genetic diversity within each serotype (genotypes and lineages) influences fitness, transmissibility, and epidemic potential, contributing to periodic shifts in dominant circulating strains. On the host side, viremia typically coincides with the first several days of illness and is sufficient to infect mosquitoes even before clinical recognition. Preexisting, serotype-specific immunity directs neutralizing antibody responses; however, because protection is not cross-serotype, community-level risk accumulates as people with different infection histories interact within multi-serotype settings [4][5][6]. Together, these agents, vector, environment, and host factors explain why dengue has entrenched across the tropics and subtropics and why endemic regions experience cyclical, often explosive outbreaks when ecological conditions and population immunity align.

#### **Epidemiology:**

Dengue fever represents the most rapidly expanding mosquito-borne viral illness worldwide and poses an immense public health burden. Current estimates indicate that more than 100 million cases occur annually, with 20,000 to 25,000 deaths, many of which disproportionately affect children. The disease is now endemic in more than 100 countries, spanning Asia, the Americas, Africa, and parts of Oceania, with epidemics occurring annually. The growing geographic distribution of both the virus and its vectors has transformed dengue into a global health concern rather than one confined to specific tropical zones [7][8]. The transmission of dengue virus (DENV) is sustained through two principal cycles: a sylvatic cycle and a human–mosquito–human cycle. In the sylvatic cycle, mosquitoes transmit the virus among nonhuman primates, maintaining viral reservoirs in forested ecosystems. In contrast, the

human–mosquito cycle is primarily urban and accounts for the majority of disease burden globally. In this cycle, *Aedes aegypti* and *Aedes albopictus* mosquitoes acquire the virus when feeding on a viremic human host and then transmit it to others during subsequent bites. The likelihood of mosquito infection depends heavily on the viral load in the human host's blood meal, which explains why individuals with high viremia contribute disproportionately to community spread [7][8].

Among the two primary vectors, *Aedes aegypti* is historically linked to the majority of global transmission. It thrives in densely populated areas, breeds in artificial water containers, and prefers to bite indoors during daylight hours, making it an exceptionally efficient vector. However, *Aedes albopictus* has gained attention due to its expanding geographic range. Unlike *A. aegypti*, it tolerates colder climates and exhibits aggressive feeding behavior outdoors, though it feeds less frequently. These traits have allowed *A. albopictus* to colonize parts of North America, Europe, and temperate regions, raising concerns about future outbreaks in previously unaffected areas. In addition to vector-mediated spread, dengue can be transmitted through less common routes, including perinatal transmission from mother to child, breast milk, blood transfusion, and organ transplantation. Although rare compared to mosquito-borne transmission, these routes highlight the virus's adaptability and its potential to affect vulnerable populations, particularly infants and immunocompromised individuals. Epidemiologic patterns of dengue have also evolved over time. Between 1990 and 2010, the mean age of affected patients was 27.2 years, but since 2010 this has risen to 34 years, suggesting shifting demographics of infection [7]. This increase may be linked to changing patterns of immunity in populations, urbanization, and evolving serotype circulation. Importantly, dengue outbreaks have historically been associated with different viral serotypes at different times. The introduction of new serotypes or genotypes into a community often precipitates large-scale epidemics, while co-circulation of multiple serotypes contributes to hyperendemicity and increased risk of severe disease [8].

Two main transmission patterns are recognized: epidemic dengue and hyperendemic dengue. Epidemic dengue typically arises when a single serotype is introduced into a susceptible population, leading to widespread transmission across all age groups. These outbreaks were more common before World War II and were associated with relatively low rates of dengue hemorrhagic fever (DHF). In contrast, hyperendemic dengue occurs when two or more serotypes co-circulate within the same region, creating repeated exposures across populations. This scenario is associated with a higher risk of DHF due to immunological phenomena such as antibody-dependent enhancement. In hyperendemic

regions, children bear the highest burden of disease, and severe manifestations are relatively more frequent compared to epidemic scenarios [9]. In conclusion, dengue fever's epidemiology reflects the complex interplay of viral serotypes, vector ecology, climate, and human demographics. The global spread of *Aedes* vectors, combined with hyperendemic circulation of multiple serotypes, has intensified the frequency and severity of outbreaks. Recognizing these patterns is crucial for tailoring prevention strategies, designing effective vector control programs, and preparing health systems for the cyclical burden of dengue epidemics worldwide [9].

#### **Pathophysiology:**

Dengue virus (DENV), a member of the *Flaviviridae* family, is a small 50-nm enveloped virion with a positive-sense, single-stranded RNA genome of approximately 10.7 kb. Its structure includes three structural proteins (capsid [C], membrane [M], and envelope [E]) and seven nonstructural proteins that facilitate replication, viral assembly, and evasion of host immune defenses. Transmission to humans occurs primarily through the bite of infected *Aedes aegypti* or *Aedes albopictus* mosquitoes. Despite the virus's pathogenic potential, up to 75% of infections remain asymptomatic, while others range from self-limiting febrile illness to severe, life-threatening disease [1]. The incubation period averages 4 to 7 days, after which symptoms typically last 3 to 10 days. Clinical presentations rarely appear after two weeks, helping distinguish dengue from other febrile illnesses. Between 0.5% and 5% of infections progress to severe dengue, characterized by plasma leakage, hemorrhage, and shock. In the absence of supportive care, mortality rates may exceed 20%, particularly among pediatric populations, though with appropriate treatment, case fatality rates drop to below 1% [1].

#### **Initial Infection and Dissemination**

The early cellular events following a mosquito bite remain incompletely understood, but skin-resident dendritic cells and macrophages appear to be the first targets. These infected antigen-presenting cells internalize DENV via receptor-mediated endocytosis and subsequently migrate to regional lymph nodes. The virus then disseminates systemically through the lymphatic and circulatory systems. Viremia, detectable in blood 24–48 hours before symptom onset, coincides with viral replication in monocytes, macrophages, hepatocytes, and endothelial cells, which are key contributors to systemic manifestations [1].

#### **Immune Response and Disease Spectrum**

Disease severity is determined by a complex interplay of host immunity and viral serotype characteristics. During primary infection, neutralizing antibodies against the infecting serotype confer long-lasting protection. However, during a secondary infection with a heterologous serotype, preexisting antibodies may paradoxically exacerbate disease via

antibody-dependent enhancement (ADE). In ADE, non-neutralizing antibodies bind to viral particles but fail to inactivate them, instead facilitating their entry into Fc receptor-bearing cells. This increases viral replication and amplifies the inflammatory response. The cascade of immune activation includes release of cytokines and vasoactive mediators—such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukins, and interferons—that disrupt endothelial integrity. This leads to the hallmark microvascular permeability, causing plasma leakage into interstitial spaces. Intriguingly, increased vascular permeability is observed as viral titers decline, suggesting that host immune mechanisms, rather than direct viral cytopathic effects, drive the critical phase [1].

#### **Clinical Progression**

Typical dengue fever manifests as high fever, myalgia, arthralgia, retro-orbital pain, rash, and mild mucosal bleeding. Severe dengue, on the other hand, is characterized by dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). These syndromes are associated with thrombocytopenia, coagulopathy, hemoconcentration, and hypovolemic shock. Endothelial dysfunction, coupled with immune-mediated platelet destruction, underlies the hemorrhagic manifestations. Hepatic involvement may present as elevated transaminases, while severe cases can progress to multi-organ dysfunction [1][2].

#### **Host and Viral Factors**

Severe disease is not solely limited to secondary infections; even primary infections with highly virulent strains can cause serious illness. Host genetic predispositions, such as variations in HLA alleles and cytokine gene polymorphisms, influence susceptibility. Age and comorbidities also modulate outcomes, with children and individuals with chronic illnesses more prone to complications. On the viral side, differences in serotype and genotype affect virulence, transmissibility, and immune evasion. In essence, the pathophysiology of dengue reflects a balance between viral replication, host immune defense, and the collateral damage induced by exaggerated immune responses. While the virus initiates infection by targeting skin immune cells, the progression to severe disease is largely mediated by immune-driven endothelial dysfunction and plasma leakage. Understanding these mechanisms clarifies why early recognition and supportive care are critical to reduce mortality, and why vaccine development is complicated by the risk of ADE and the need for balanced immunity against all four DENV serotypes [3].

#### **History and Physical**

Dengue fever presents with a wide spectrum of clinical manifestations, and careful recognition of its three distinct phases—febrile, critical, and recovery—is essential for accurate diagnosis, timely intervention, and prevention of complications. Each stage reflects underlying virologic and

immunopathologic changes and provides clinical cues for patient monitoring and management.

### Febrile Phase

The febrile phase marks the onset of illness and is characterized by a sudden rise in temperature, often peaking near 40 °C, that persists for 2 to 7 days. In approximately 6% of patients, particularly those with dengue hemorrhagic fever (DHF) or severe dengue, fever may demonstrate a saddleback or biphasic pattern, where an initial decline is followed by a second spike lasting at least another 24 hours [10]. Patients are commonly present with systemic and constitutional symptoms, including intense myalgia, arthralgia, headache, retro-orbital pain, sore throat, nausea, vomiting, and anorexia. Dermatologic manifestations often include facial flushing and generalized blanchable macular erythema, which typically appears within 1 to 2 days of fever onset and again toward the end of the febrile period. Alternatively, some patients develop a maculopapular rash within 24 hours. Conjunctival injection and pharyngeal erythema may also be noted. Because the febrile phase mimics other viral illnesses, such as influenza or measles, misdiagnosis is common without epidemiologic context or laboratory confirmation [10].

### Critical Phase

The critical phase occurs during defervescence, usually between days 3 and 7 of illness, when body temperature declines to 37.5–38 °C or lower. This stage is the most perilous because the reduction in fever often masks the emergence of serious pathophysiologic changes. The hallmark of this phase is increased capillary permeability, resulting in plasma leakage into the interstitial space. Clinically, this is preceded by a rapid drop in platelet count and a concomitant rise in hematocrit levels, signaling hemoconcentration. Leukopenia often precedes thrombocytopenia by up to 24 hours and serves as an early indicator of impending severity. Warning signs include persistent abdominal pain, vomiting, mucosal bleeding, hepatomegaly, lethargy, restlessness, or clinical evidence of fluid accumulation (ascites, pleural effusion). If unrecognized or untreated, patients may develop dengue shock syndrome, disseminated intravascular coagulation (DIC), or multi-organ failure. The critical phase is relatively short, usually lasting 24 to 48 hours, but it requires intensive monitoring, as progression can be abrupt and fatal [10].

### Recovery Phase

The recovery phase begins as vascular integrity is restored, and extravascular fluids are gradually reabsorbed over 2 to 3 days. Patients often demonstrate clinical improvement with increased appetite, convalescent rash (sometimes described as “islands of white in a sea of red”), and overall well-being. Interestingly, relative bradycardia is frequently observed during this period. Laboratory findings

normalize progressively, with platelet counts rising and hematocrit levels returning to baseline. However, excessive or mismanaged fluid replacement during the critical phase can predispose patients to complications in recovery, such as pulmonary edema or heart failure, underscoring the need for careful fluid management [10].

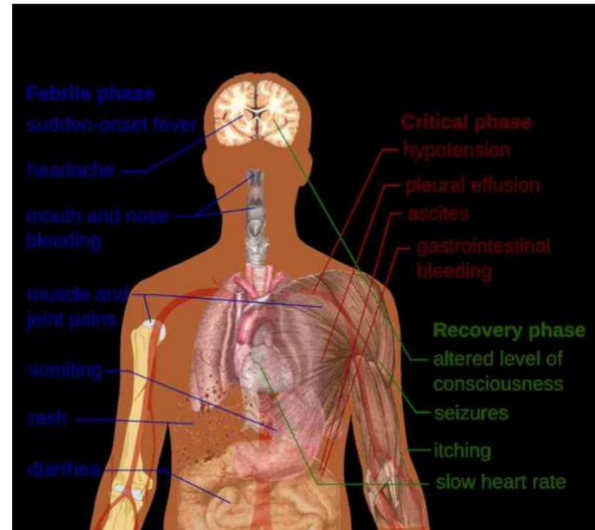


Figure 1: Dengue Fever Symptoms.

### Expanded Dengue Syndrome

Beyond the classical triphasic course, expanded dengue syndrome encompasses atypical or severe organ involvement, reflecting the virus's systemic impact. Neurological manifestations include febrile seizures in young children, encephalitis, aseptic meningitis, and intracranial hemorrhage. Hepatic involvement may range from hepatitis and elevated transaminases to fulminant liver failure. Gastrointestinal complications such as pancreatitis or acalculous cholecystitis can occur. Cardiac manifestations, including myocarditis and pericarditis, contribute to hemodynamic instability, while pulmonary complications may include acute respiratory distress syndrome (ARDS). Renal sequelae, such as acute kidney injury or hemolytic uremic syndrome, are also documented. These systemic complications are often associated with profound shock and carry significant mortality risks. The history and physical examination of dengue fever should focus on delineating the three classical phases, recognizing warning signs during the critical phase, and identifying atypical manifestations that signal expanded dengue syndrome. Awareness of these patterns equips clinicians to intervene early, monitor high-risk patients closely, and prevent progression to fatal outcomes. Ultimately, the structured recognition of febrile, critical, and recovery phases, along with vigilance for systemic complications, forms the foundation for effective clinical management of dengue [10].

## Evaluation

The evaluation of dengue fever hinges on synthesizing epidemiologic context, clinical features, and laboratory data into a coherent, time-sensitive assessment. At presentation, common laboratory abnormalities—thrombocytopenia, leukopenia, and elevated aspartate aminotransferase—serve as important signals that, when paired with exposure history, raise diagnostic suspicion for dengue rather than other acute febrile illnesses. These parameters also assist with early risk stratification because falling platelet counts and rising hematocrit often herald the transition toward clinically significant plasma leakage. Contemporary clinical practice classifies illness along a spectrum as dengue or severe dengue, and this framework guides both monitoring intensity and disposition decisions [11][12][13]. A patient meets the working threshold for probable dengue when fever is accompanied by travel to, residence in, or epidemiologic linkage with a dengue-endemic area together with two or more typical manifestations—nausea, vomiting, rash, myalgias, arthralgias, a positive tourniquet test, or leukopenia. This constellation reflects the viremic, inflammatory phase of illness and often precedes the critical defervescence window in which capillary permeability may abruptly increase. Because early symptoms are nonspecific, serial clinical examinations and repeated labs are essential to detect evolution toward severity. The emergence of warning signs marks a pivotal inflection point and includes intensifying abdominal pain, persistent emesis, clinical fluid accumulation such as ascites or pleural effusion, mucosal bleeding, lethargy or restlessness, hepatomegaly exceeding 2 cm, and the characteristic laboratory coupling of a rising hematocrit with thrombocytopenia. Recognition of this pattern should trigger escalation of monitoring, judicious fluid planning, and consideration of inpatient care to preempt hemodynamic decompensation [11][12][13].

Severe dengue is defined by the development of one or more end-organ or hemodynamic complications superimposed on the clinical picture of dengue fever. The cardinal process is severe plasma leakage, which can culminate in respiratory distress from third spacing or frank shock in the absence of timely fluid resuscitation. Hemorrhagic complications range from mucosal to major bleeding and reflect a combination of thrombocytopenia, coagulopathy, and endothelial dysfunction. Organ involvement spans impaired consciousness due to encephalopathy, myocardial dysfunction with attendant hemodynamic compromise, pulmonary involvement, and marked hepatic injury characterized by transaminases exceeding 1000 IU/L. Because clinical deterioration often coincides with defervescence, structured reassessment—vital signs, fluid balance, hematocrit, platelet trend, and focused ultrasound for effusions—is indispensable during days three to seven of illness

[11][12][13]. Within the severe end of the spectrum, dengue shock syndrome carries distinct bedside signposts that should prompt immediate action. A rapidly rising hematocrit in concert with narrowing pulse pressure, severe abdominal pain, and unremitting vomiting typically precede overt hypotension. Cold clammy extremities, delayed capillary refill, and altered mentation signal failing compensation. In this setting, timely crystalloid administration titrated to perfusion endpoints and frequent re-evaluation of hematocrit and urine output are lifesaving. Over-resuscitation must be avoided because capillary integrity subsequently normalizes; thus, fluid needs fall quickly as patients enter recovery. Laboratory confirmation integrates direct and indirect assays arrayed across the illness timeline. During the early febrile days, antigen detection using enzyme-linked immunosorbent assay for NS1 and nucleic acid amplification via polymerase chain reaction provide specific diagnosis and, in the case of PCR, serotype identification. Virus isolation from body fluids is definitive but seldom required in routine care owing to resource and time constraints. As the illness advances, serology demonstrates rising dengue-specific immunoglobulins; however, interpretation requires caution due to cross-reactivity with other flaviviruses and the confounding effects of prior exposures. A confirmed diagnosis rests on culture, antigen detection, PCR, or serologic evidence and should always be contextualized with clinical evolution and epidemiology to avoid anchoring on isolated results [11][12][13].

Special populations require tailored evaluation. Pregnant patients merit particular vigilance because thrombocytopenia, hypertension, edema, and elevated liver enzymes can overlap with preeclampsia, yet the therapeutic implications diverge markedly. Close obstetric collaboration, careful trend analysis of hematologic indices, and attention to warning signs of plasma leakage help distinguish these entities and safeguard maternal–fetal outcomes. Similarly, infants, older adults, and individuals with comorbidities may display atypical trajectories and should be monitored with a lower threshold for admission. In all groups, the diagnostic objective is twofold: confirm dengue while continuously screening for impending severity. This dual focus—anchored in careful serial examination and judicious testing—remains central to reducing complications and mortality in a disease whose danger often peaks as the fever subsides [11][12][13].

## Treatment / Management

Management of dengue fever is phase-specific and centers on meticulous supportive care, judicious fluid therapy, and vigilant monitoring for early signs of deterioration. For patients without warning signs, outpatient care is appropriate. These individuals should receive antipyretic control with acetaminophen (paracetamol) and aggressive oral



rehydration using oral rehydration salts or balanced fluids. Aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), and other antiplatelet or anticoagulant agents must be avoided because they increase bleeding risk and can exacerbate gastric irritation. Clear, written education is essential: patients should be instructed to seek immediate care for warning signs such as worsening abdominal pain, persistent vomiting, mucosal bleeding, lethargy or restlessness, dizziness or syncope, clinical fluid accumulation (ascites or pleural effusion), hepatomegaly, or a rising hematocrit in the setting of falling platelets. Daily review during days three to seven—the window of defervescence and maximal risk of plasma leakage—is strongly advised, even for outpatients who initially appear well [13][14][15].

Hospital evaluation is indicated for patients with any warning signs, for those with severe dengue, and for individuals at higher risk due to age extremes, pregnancy, significant comorbidities (e.g., diabetes mellitus, cardiovascular or renal disease), immunosuppression, or social factors such as living alone without reliable access to care. Inpatient management prioritizes timely intravenous crystalloid therapy titrated to clinical response and objective markers of perfusion. Initial rates depend on hemodynamic status and degree of leakage; frequent reassessment of vital signs, capillary refill, mental status, urine output, and serial hematocrit/platelet counts guides up- or down-titration. Patients with compensated shock should receive carefully dosed crystalloid boluses with close monitoring. If hypotension or signs of poor perfusion persist despite appropriate crystalloid resuscitation, a trial of colloid may be warranted, particularly in refractory shock. Because capillary permeability improves rapidly as patients leave the critical phase, over-resuscitation can precipitate pulmonary edema or heart failure; therefore, fluid plans must anticipate and respond to the transition into recovery with timely reduction of rates. Transfusion strategies are individualized and based on clinical bleeding and hemodynamic status rather than platelet count alone. Packed red cell transfusion is appropriate when ongoing or suspected significant bleeding is accompanied by hemodynamic instability and a falling hematocrit despite adequate fluids. Platelet transfusion may be considered when counts fall below 20,000/ $\mu$ L in the presence of bleeding risk or procedures, recognizing that prophylactic transfusion at higher thresholds has not been shown to prevent hemorrhage and can expose patients to unnecessary risks. Fresh frozen plasma or cryoprecipitate is reserved for clinically significant coagulopathy with bleeding. Intramuscular injections and unnecessary invasive procedures should be avoided to reduce the risk of hematoma formation [13][14].

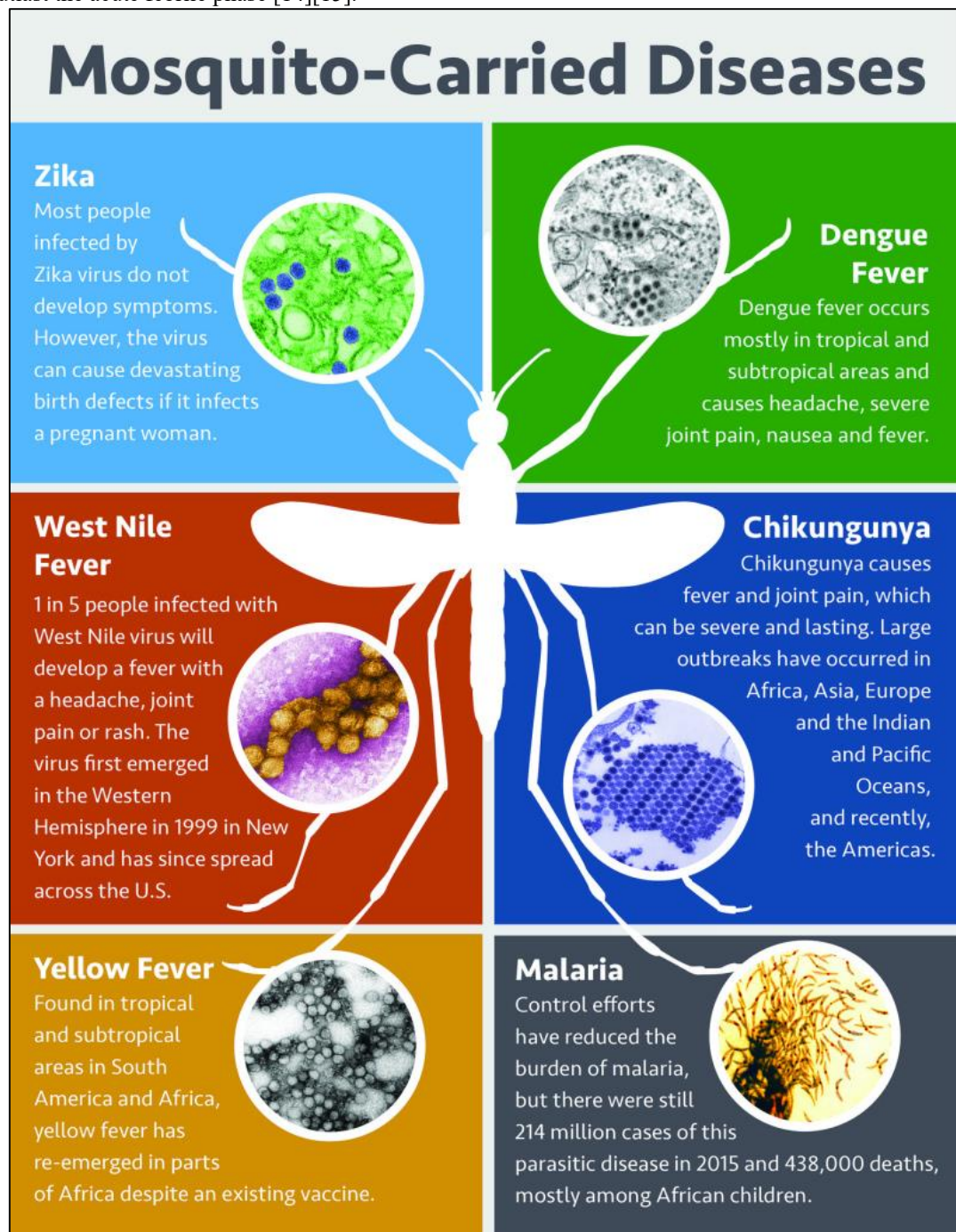
No antiviral therapy is currently recommended, and no laboratory test reliably predicts which patients will progress to severe dengue.

Consequently, structured clinical observation is the cornerstone of care. Point-of-care ultrasound can be useful for detecting early pleural effusions or ascites and for assessing intravascular volume trends, complementing serial hematocrit measurements. Electrolyte, glucose, and liver function monitoring is important, as hyponatremia, hypocalcemia, hypoglycemia, and transaminitis are common and may influence management. Antiemetics can support oral intake; proton pump inhibitors are considered for stress gastritis or high bleeding risk; and antibiotics are reserved for clear evidence of bacterial coinfection. Special populations require tailored plans. Pregnant patients need coordinated obstetric care, fetal surveillance, cautious fluid management to avoid pulmonary edema, and a high index of suspicion for obstetric mimics or complications. Children are particularly vulnerable to rapid shifts in volume status; weight-based fluid calculations and frequent reassessments are mandatory. In patients with diabetes, careful glucose control helps mitigate metabolic stress and infection-related complications. Discharge considerations include improving clinical status, stable vital signs, adequate oral intake and urine output, down-trending hematocrit with rising platelets, and resolution of warning signs. Patients should leave with explicit instructions on hydration, fever control with acetaminophen, avoidance of NSAIDs and intramuscular injections, and a clear plan for prompt reassessment if symptoms recur or worsen. Ultimately, outcomes hinge on early recognition of phase transitions, precise fluid stewardship, and patient education—interventions that collectively reduce the risk of shock, hemorrhage, and organ dysfunction [13][14].

### Differential Diagnosis

The clinical diagnosis of dengue fever presents a challenge due to its nonspecific early symptoms, which overlap significantly with many viral and parasitic infections. Patients typically present with fever, myalgia, arthralgia, rash, and constitutional complaints, but these manifestations are not unique to dengue and can lead to diagnostic uncertainty. Among the most important differential diagnoses are measles and influenza, which share features such as fever, rash, and systemic malaise in the prodromal period. A distinguishing feature of measles is the presence of Koplik spots, whereas influenza often presents with pronounced respiratory symptoms that are less common in dengue. Vector-borne illnesses are particularly critical to consider in endemic or travel-related cases. Zika virus disease can resemble dengue with fever, rash, and conjunctivitis, yet Zika tends to cause milder systemic illness but carries significant risks for congenital anomalies in pregnant women. West Nile virus infection may also mimic dengue, though neurological complications such as meningitis or encephalitis are more characteristic. Chikungunya is another arbovirus with striking clinical similarity, but it is often differentiated by the intensity and

persistence of polyarthritis and polyarthralgia, which can outlast the acute febrile phase [14][15].



**Figure 2:** Mosquito-Carried Diseases.

Malaria represents an important parasitic mimic and must always be excluded in patients with fever returning from endemic areas. Unlike dengue, malaria typically shows cyclical fever patterns, hepatosplenomegaly, and can rapidly progress to cerebral or severe anemia-related complications. Yellow fever also belongs to the Flavivirus genus and can resemble dengue during early febrile illness, but its biphasic nature, jaundice, and fulminant hemorrhagic manifestations are distinguishing. A detailed clinical history remains essential. Information

regarding recent travel, mosquito exposure, vaccination status, and previous Flavivirus infections provides critical diagnostic context. Laboratory investigations help to confirm or exclude dengue. NS1 antigen detection is particularly useful in the acute phase, while serological assays (IgM/IgG) gain utility after several days but carry limitations due to cross-reactivity with other Flaviviruses such as Zika and yellow fever. Thus, interpretation must be cautious. In summary, differentiating dengue fever from other infectious diseases requires a combination of careful



epidemiologic history, awareness of overlapping syndromes, and confirmatory laboratory testing. A structured diagnostic approach ensures timely recognition of dengue while avoiding misdiagnosis of other potentially serious vector-borne or viral illnesses [15].

### Prognosis

The prognosis of dengue fever hinges on the timeliness of recognition, disciplined fluid stewardship during the critical phase, and access to supportive care. In untreated severe dengue, mortality can reach 10% to 20%, reflecting the rapid hemodynamic collapse that follows unchecked plasma leakage and hemorrhage. By contrast, with appropriate, phase-specific supportive therapy—particularly judicious crystalloid resuscitation, close monitoring of hematocrit and urine output, and early identification of warning signs—mortality falls to ~1%. This dramatic divergence underscores that outcomes are driven less by antiviral options (none are recommended) and more by a system's ability to detect defervescence-associated vascular leak and respond in real time. Prognosis is also modified by age, pregnancy, and comorbidity: infants, older adults, and patients with chronic cardiometabolic disease experience faster decompensation and narrower therapeutic windows. Social determinants matter as well; patients living alone or far from care are at greater risk because deterioration often occurs after fever abates. Recovery is typically marked by reabsorption of extravascular fluid, improving appetite, and rising platelets; however, over-resuscitation during the leak phase can complicate this period with pulmonary edema or heart failure, reminding clinicians that good outcomes depend on avoiding both under- and over-treatment [15].

### Complications

Complications span multiple organ systems and reflect the confluence of endothelial dysfunction, coagulopathy, and immune dysregulation. Hepatic injury ranges from transaminitis to acute liver failure; cardiac involvement includes myocarditis and cardiomyopathy with associated arrhythmias and depressed ejection fraction; pulmonary complications feature pneumonia and noncardiogenic edema. In the genitourinary tract, orchitis and oophoritis have been described, likely reflecting systemic inflammatory effects.

Neurologic sequelae—seizures, encephalopathy, and encephalitis—signal severe disease and carry a poorer outlook due to cerebral edema or hemorrhage. Many of these complications cluster around the critical phase and early recovery, where miscalibrated fluid therapy or delayed recognition of leak can escalate morbidity. Timely escalation of care, targeted transfusion for clinically significant bleeding, and multidisciplinary consultation are central to mitigating permanent organ injury [15].

### Postoperative and Rehabilitation Care

Rehabilitation in dengue is principally supportive and patient-centered. Oral hydration should be emphasized throughout the febrile and recovery phases; balanced fluids and oral rehydration solutions help correct third-spacing-related deficits when oral intake is feasible. The return of appetite is a practical bedside signal that viremia has waned, and vascular stability is returning. As patients improve, activity can be advanced gradually while monitoring delayed complications, such as secondary bacterial infection or prolonged fatigue. Education on continued avoidance of NSAIDs, careful resumption of normal routines, and recognition of late bleeding or respiratory symptoms is important in the convalescent period. For those who require intensive care, structured follow-up to reassess hepatic function, cardiopulmonary status, and neurocognitive recovery can identify residual multisystem effects early and guide targeted therapy [15].

### Consultations

Early involvement of an infectious diseases specialist is recommended, particularly in severe or atypical cases, and in regions where frontline clinicians may have limited experience with dengue. Consultation facilitates phase-appropriate fluid protocols, transfusion thresholds based on clinical bleeding, and differentiation from mimics such as leptospirosis or rickettsioses. The Centers for Disease Control and Prevention (CDC) offers expert guidance and a clinician hotline for real-time treatment advice, which is especially valuable during surges or in low-incidence settings where institutional expertise may be limited. Multidisciplinary engagement—including critical care, obstetrics (for pregnant patients), pediatrics, and cardiology—improves safety during rapid hemodynamic transitions and complex organ involvement [15].

### Patient Education

Because there is no widely deployed curative therapy and no single laboratory test that reliably forecasts progression to severe disease, prevention remains the most effective strategy; practically, this means avoiding mosquito bites and avoiding endemic areas when feasible. Patients and travelers should receive clear, actionable counseling on personal protection and community-level control. Preventive measures include use of bed nets from daytime onward, recognizing that *Aedes* mosquitoes are predominantly day-biting; insecticide-treated materials such as window curtains to reduce indoor vector density; and topical repellents containing DEET, IR3535, or icaridin applied according to age-appropriate guidance. Additional tactics—such as mosquito-repellent coils and the consistent practice of wearing long-sleeved shirts and pants—add layers of defense, particularly during peak biting hours and in high-density urban environments [14]. These interventions are most effective when combined and

reinforced through traveler education before departure and upon arrival in endemic regions [14].

### Biological Control

Biological strategies complement personal protection by reducing vector populations at their source. The introduction of larvivorous fish, including viviparous species such as *Poecilia reticulata*, into confined water bodies (e.g., large storage tanks, open wells) can sustainably suppress larvae; use of native larvicidal fish helps maintain ecological balance. Predatory copepods, small freshwater crustaceans, effectively control larvae in specific container habitats that are otherwise difficult to treat. Endosymbiotic control using *Wolbachia*-infected *Aedes aegypti* has emerged as a promising tool: *Wolbachia* reduces mosquito susceptibility to DENV and can lower transmission when established in local populations, offering a community-level intervention that is self-sustaining after successful releases [15]. These methods are most impactful when embedded in integrated vector management programs with surveillance-driven deployment.

### Chemical Control

Chemical approaches target both larvae and adult mosquitoes to interrupt transmission during outbreaks and high-transmission seasons. Larvicides can be applied to large breeding containers that cannot be emptied or removed, while space sprays—delivered as thermal fogs or cold aerosols—can rapidly knock down adult populations to control explosive outbreaks. Oil-based formulations are useful in certain settings because they inhibit evaporation, improving residual activity. Commonly used insecticides include organophosphorus compounds (e.g., fenitrothion, malathion) and pyrethroids (e.g., bioresmethrin, cypermethrin). Rotating active ingredients and adhering to evidence-based application intervals help mitigate resistance and preserve effectiveness [15].

### Environmental Measures

Sustainable dengue control requires environmental management to eliminate breeding sites. This begins with identifying and removing water-holding containers, repairing rooftops and sunshades to prevent pooling, and covering stored water in buckets, pots, and cisterns. Community clean-up campaigns, improved municipal water storage practices, and reliable waste management reduce the urban microhabitats that *Aedes* exploit. Routine household “source reduction” checks—weekly inspections of yards, rooftops, and indoor plants—translate public health strategy into daily action.

### Health Education

Health education underpins all prevention pillars. Clear, culturally tailored messaging about the dengue virus, its daytime-biting vectors, the critical phase timing, and warning signs enables individuals to protect themselves and to seek care early. Audiovisual tools and mass awareness campaigns can initiate population-level behavior change, while clinic-based

counseling tailors advice to individual risk (e.g., pregnancy, chronic disease). Schools, workplaces, and travel clinics are high-yield venues for disseminating practical guidance that integrates personal protection with environmental stewardship.

### Vaccination

CYD-TDV, the first licensed live recombinant tetravalent dengue vaccine, is approved in endemic areas across 20 countries and represents an important adjunct to vector control in selected contexts [16]. Programmatic use requires careful alignment with local epidemiology and serostatus-based policies to maximize benefit and minimize risk. Vaccination, however, does not replace vector control, personal protection, or clinical preparedness; rather, it adds a layer of community immunity that may attenuate outbreak magnitude when deployed strategically [16].

### Enhancing Healthcare Team Outcomes

Optimal outcomes in dengue are achieved through coordinated, multidisciplinary care. An infectious disease specialist, CDC consultant, emergency clinician, and internist typically anchor the team, aligning on supportive care algorithms, escalation triggers, and disposition. Diagnosis is confirmed through culture, antigen detection, polymerase chain reaction, or serologic testing, while recognizing that laboratory assays cannot reliably predict progression to severe disease. Within this reality, the team’s vigilance—serial examinations, bedside ultrasound for effusions, and dynamic fluid plans—becomes the decisive therapeutic asset. Primary care clinicians and nurse practitioners extend impact upstream by educating travelers and communities on bite prevention, bed nets and insecticide-treated materials, repellents, and source reduction of standing water. Downstream, they reinforce convalescent care: hydration, paracetamol-based fever control, and prompt reassessment for late bleeding or dyspnea. While untreated severe dengue confers a poor prognosis, most patients survive with supportive care, though a subset may have residual multisystem organ damage necessitating structured follow-up and rehabilitation [17][18]. In practice, enhancing team outcomes also means embedding dengue pathways into routine operations: triage tools that flag warning signs at registration; nursing protocols for weight-based fluid boluses and hourly urine output monitoring; pharmacy stewardship to avoid NSAIDs and anticoagulants; and laboratory reflex panels that pair platelets with hematocrit and liver enzymes. Public health linkages—vector control notifications triggered by clusters, and communication lines with regional laboratories—create a feedback loop between clinical care and community risk reduction. Simulation training for shock scenarios, checklists for critical-phase handovers, and real-time dashboards for serial labs can further standardize excellence across care settings. In summary, dengue prognosis improves dramatically with timely,

supportive care, while complications can be curtailed by early recognition and precise fluid management. Rehabilitation focuses on hydration and graded return of activity, with appetite as a reassuring marker of recovery. Expert consultation and CDC guidance support complex decision-making. On the prevention front, layered personal protection, biological and chemical vector control, environmental measures, health education, and targeted vaccination together reduce transmission and disease burden. Finally, team-based systems of care—from the outpatient clinic to the intensive care unit—translate evidence into consistent, lifesaving practice, ensuring that most patients not only survive dengue but also recover with minimal long-term sequelae [14][15][16][17][18].

### Conclusion:

Dengue's prognosis is determined less by antiviral options and more by the rigor of bedside recognition and system readiness. Because the critical phase coincides with defervescence, reliable pathways that pair serial examinations with hematocrit/platelet trends and point-of-care ultrasonography can preempt plasma-leak shock and hemorrhage. NS1 and PCR secure early, specific diagnoses; serology expands into confirmation later but requires cautious interpretation given flaviviral cross-reactivity. Clinical decisions should prioritize phase-specific fluid therapy, conservative use of colloids for refractory shock, and transfusion guided by bleeding—rather than platelet count alone. Nursing leadership in education, hydration support, and early escalation, together with laboratory stewardship in timely NS1/PCR reporting and reflex panels (platelets, hematocrit, AST/ALT), are central to safe care. Beyond the bedside, layered prevention—eliminating breeding sites, deploying biological and chemical controls, and applying vaccination where epidemiology and serostatus favor benefit—curbs transmission and moderates surge demand on health systems. Finally, standardized checklists (warning-sign triage, fluid titration, discharge criteria) and simulation for shock scenarios improve team performance and compress the gap between evidence and practice. With this integrated approach, mortality in severe dengue can fall from 10–20% to ~1%, and most patients recover without long-term sequelae.

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