

Review Article

# Dengue Fever—Diagnosis, Risk Stratification, and Treatment

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## Summary

**Background:** Dengue fever is a common infectious disease in the tropical and subtropical zones, with more than 100 million symptomatic cases per year. Mosquitoes of the genus *Aedes* (*Aedes aegypti*, *Aedes albopictus*) are vectors of the disease, and their spread has led to rising case numbers around the world. Physicians in Europe, too, are increasingly being confronted by this challenge.

**Methods:** This review is based on the findings of a selective search in international publication databases, as well as on the WHO guideline of 2009 and the current recommendations of the Robert Koch Institute.

**Results:** Dengue fever takes a mild course in more than 90% of cases. Severe dengue fever, up to and including shock and/or mucosal hemorrhages, is rare and carries a mortality of 1–5%. The disease characteristically takes a triphasic course (febrile phase, critical phase, recovery phase). It is diagnosed by the direct demonstration of the pathogen (e.g., with the reverse transcriptase polymerase chain reaction [RT-PCR] up to day 5 of the illness) or by serology. Patients are classified into one of three risk groups depending on their findings and comorbidities and are then treated

either as outpatients or in the hospital. The treatment is symptomatic, as no treatment directed against the cause of the disease is available. The key measures are adequate volume replacement and, in patients with hemorrhage, the transfusion of blood products. Preventive steps include vaccination after a documented initial infection and the meticulous avoidance of mosquito bites.

**Conclusion:** Climate change and global mobility have led to a worldwide increase in dengue fever. The disease only rarely takes a severe course. In such cases, rapid symptomatic treatment as needed is the key to the avoidance of severe complications.

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Dengue—formerly known as dengue fever—is an infectious disease occurring in the (sub-)tropics which is responsible for more than 100 million symptomatic infections each year (1). The disease takes a mild course in more than 90% of cases, while severe presentations associated with even shock and/or hemorrhages are rare (1). Case numbers are rising worldwide and in Central Europe usually include individuals returning from trips abroad to Central and South America, South and Southeast Asia, and also to a lesser extent Africa (1). The precise endemic areas can be obtained from the information sources of the Robert Koch Institute (RKI) (2). According to these sources, case figures have increased in Germany

during the first third of 2024 to 737 registered cases (the highest total number of cases reported to date was 1176 in 2019 [2]). Because of global warming due to climate change, the vectors of the dengue virus (DENV), i.e. mosquitoes of the genus *Aedes* (*Aedes aegypti*, *Aedes albopictus*), are also increasingly spreading in milder climatic zones such as Europe (1, 3, 4). Thus, the first reported indigenous dengue outbreak was on Madeira, Portugal, in 2012, and the first northernmost outbreak was near Paris, France, in 2023 (5, 6). Medical staff in Europe are therefore now finding themselves confronted with the management of patients affected by dengue. This article summarizes and discusses the important aspects of prevention, diagnostics, and treatment of dengue fever.

## Methods

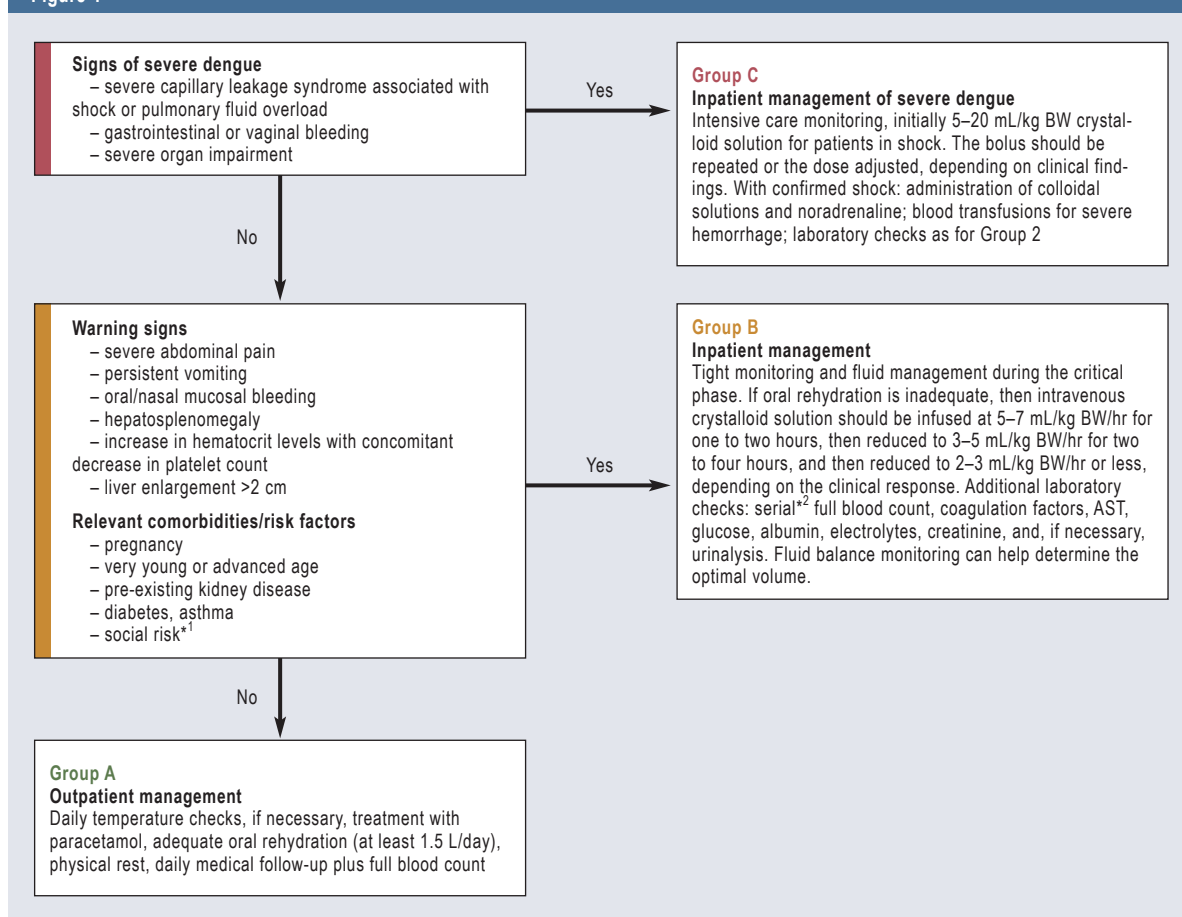
A selective search in international publication databases (PubMed, Google Scholar,

## CME plus<sup>+</sup>

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Figure 1



**Clinical management** of dengue, including risk classification and treatment recommendations, modified according to the WHO guideline and to Paz-Bailey et al. (7, 28). \*<sup>1</sup> extreme poverty, homelessness, need for nursing care, poor access to medical care. \*<sup>2</sup> every 6–12 hrs during the critical phase, then according to clinical findings  
AST, aspartate aminotransferase; BW, body weight

UpToDate) was conducted, taking into account the WHO guideline of 2009 (Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control [7]) and the recommendations of the RKI (Dengue fever fact sheet, last updated 04/2024 [8]).

## Vector and pathogenesis

*Aedes aegypti* (Egyptian tiger mosquito) and *Aedes albopictus* (Asian tiger mosquito) are diurnal mosquitoes. They breed in water reservoirs of any kind and prefer urbanized areas with high population density (1). In this habitat, female mosquitoes are capable of biting several people within a short time and transmitting the DENV virus (9).

DENV is an RNA virus from the flavivirus family whose genome consists of single-strand RNA. There are four different serotypes in all (I–IV) which differ in their genetic structure but share structural antigens (9, 10). If an infection develops with one of these serotypes, it results in the production of a specific antibody with the generation of long-lasting immunity against this serotype. There exists short-term cross-reactive immunity to heterotypic dengue viruses (11, 12).

Secondary infection with a different serotype may result in antibody-dependent enhancement (ADE) of the disease. Cross-reactive antibodies in sub-neutralizing concentration bind to other DENV serotypes and facilitate entry into antibody-binding cells such as macrophages and dendritic cells. This results in a more rapid entry of the virus into the cell, after which immune cells then aggregate into larger cell groups. This can lead to fluid escaping from capillaries (capillary leak syndrome, CLS) (10, 12–14). Although higher antibody concentrations are associated with greater viremia and a greater risk of severe disease, no direct causal association has so far been proven (15).

DENV also appears to be directly involved in the development of CLS: The non-structural protein 1 (NS1) produced by the virus is a component of the viral replication complex and causes direct damage to the endothelium by inflammatory disruption of the endothelial glycocalyx (9, 16). Furthermore, DENV infects and activates platelets, causing them to be more easily phagocytosed. This effect, together with a not fully understood impairment of megakaryopoiesis, results in DENV-induced thrombocytopenia (17).

# Clinical presentation

The clinical features of DENV infection vary strongly and range from asymptomatic infection in around 75% of cases to severe shock symptoms associated with hemorrhagias, organ impairment, and in one to five percent of cases subsequent death (1, 7, 10). Earlier disease terms for DENV infection such as “dengue fever”, “dengue hemorrhagic fever”, or “dengue shock syndrome” have been replaced by the current WHO definition of 2009 (7, 18). In order to improve triaging of patients and to simplify clinical management, a distinction is now made with symptomatic infection between

- dengue without warning signs (infected patients recover without major complications)
- dengue with warning signs (infected patients develop complications and progress to severe disease).

Sufferers with fluid loss and even shock and/or shortness of breath and/or significant hemorrhage and/or severe organ dysfunction are classified as having severe dengue (Figure 1) (7).

The incubation period after infection with DENV is four to seven days (with a maximum of 14 days). The disease itself characteristically takes a triphasic course (febrile phase, critical phase, and recovery phase) (Figure 2), although monophasic courses are also possible, especially in non-endemic areas. Fever develops at the start, lasting several days, and is associated with nausea, retrobulbar headache, myalgias, and arthralgias (break-bone fever). This initial phase is occasionally accompanied by hepatomegaly, swollen lymph nodes, and a transient maculopapular exanthema (7, 9, 10, 19). In around one to two percent of cases, CLS develops during the defervescence phase, associated with ascites, peripheral edema, pleural effusions, and even shock (7, 9, 10). Irrespective of this, those affected can also develop severe thrombocytopenia and internal bleeding (7, 9, 10). Other forms of organ involvement can also occur (Box 1). Increased vascular permeability typically resolves after 48 to 72 hours, the platelet count rises, and the critical symptoms disappear (Figure 2) (7, 9, 10). A prospective study from Sri Lanka reports the development of post-infection fatigue after the recovery phase in 51 of 158 dengue patients (32%) (relative risk [RR] versus non-dengue patients 4.93; 95% confidence interval: [2.3; 10.4],  $p < 0.001$ ) (20). There are also case reports of post-infectious hair loss (21).

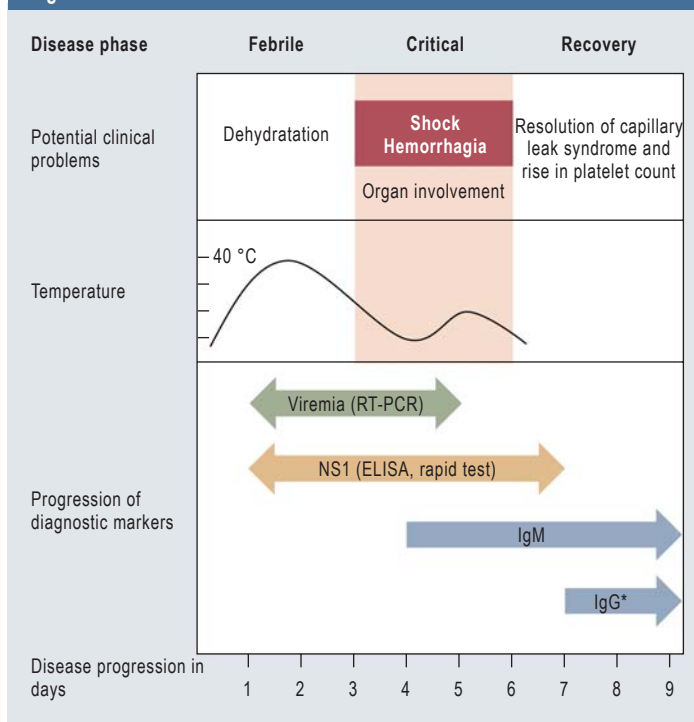
# Notifiable disease

Suspected and confirmed severe dengue is a notifiable disease in Germany according to Section 6 of the German Infection Protection Act (22). In addition, there is a laboratory reporting obligation in the event of a proven infection in accordance with Section 7 of the Infection Protection Act (23). If there is any uncertainty, advice may be sought from the National Reference Center for Tropical Infectious Pathogens at the Bernhard Nocht Institute for Tropical Medicine in Hamburg, Germany.

# Diagnosis

Diagnostic investigations for DENV infection include various methods, chosen according to the particular time course of the disease: The virus RNA can be identified molecularly from blood, serum, and urine by reverse tran-

Figure 2



**Overview of the various disease phases** of dengue and potential clinical problems, fever progression, and the detectability of diagnostic markers (modified according to the WHO guideline for dengue [7])

\* corresponds to the appearance of IgG during a primary infection; day 0 corresponds to onset of symptoms; RT-PCR, reverse transcriptase polymerase chain reaction; NS1, non-structural protein 1; ELISA, enzyme-linked immunosorbent assay; IgM, immunoglobulin M; IgG, immunoglobulin G

scriptase polymerase chain reaction (RT-PCR) for up to five days from symptom onset and NS1 from serum and plasma using enzyme-linked immunosorbent assay (ELISA) for up to seven days from symptom onset (10). The immunological isolation of antibodies against DENV is achieved from serum or plasma by ELISA and is possible from the fourth day after symptom onset at the earliest (10). When interpreting the immunology test results, it should be borne in mind that cross-reactions with other flaviviruses (the initiating cause of yellow fever, Japanese encephalitis, Zika) and ESME viruses (ESME, early summer meningoencephalitis) are possible—both in the presence of infection and after active immunization—and secondary infections can produce discrepant results (7, 9, 10). This can result in false-positive findings (7, 9, 10).

Rapid tests have meanwhile been developed for the combined identification of NS1 and dengue IgM/IgG in blood but have a lower sensitivity and specificity compared with laboratory-based test procedures. Thus, a meta-analysis conducted in 2022 showed a bundled sensitivity of 90% [87; 92] and a bundled specificity of 89% [87; 92] (24). These rapid tests, however, could offer advantages for primary outpatient care, given that the combined assay of direct and serological pathogen identification presents a wider diagnostic window (9, 25).

Box 1

# Potential end-organ manifestations in dengue, broken down according to organ area (7, 9, 38)

Various end organs can be affected by dengue:

- **Heart:** myocarditis, pericarditis, cardiac arrhythmia, hypokinesia of the myocardium
- **Vessels:** thrombosis, pulmonary embolism
- **Nervous system:** encephalopathy, encephalitis, Guillain-Barré syndrome, paresthesias, transverse myelitis, optic neuropathy, dengue-related stroke/intracranial hemorrhage
- **Eyes:** conjunctivitis, subconjunctival and retinal hemorrhages, vascular retinal occlusions, chorioretinitis, maculopathy
- **Abdomen:** acute liver failure, acute pancreatitis

## Risk assessment

The first step in treating patients with dengue involves assessing the degree of severity of the disease and associated risk factors. Risk factors for a severe course or death that are unrelated to dengue are those features that also predispose to potential organ failure (for example, pregnancy, age under 12 or over 70 years, chronic hemolytic diseases, or chronic renal disease [glomerular filtration rate (GFR) <90 mL/min/1.73 m<sup>2</sup>]) (7, 10). Various prospective studies undertaken in areas endemic to dengue have also identified prognostically unfavorable disease-specific factors: previous dengue, thrombocytopenia with concurrent increase in hematocrit, and recurrent vomiting are associated with a risk up to 2.5 times higher for severe dengue (26, 27).

It should be noted that these warning signs per se are no expression or definition of a severe disease course. Whether outpatient or inpatient management is recommended depends on the presenting risk factors/warning signs and comorbidities (classified in three groups, *Figure 1*). Patients in Group A are treated on an outpatient basis. According to WHO, hospitalization is recommended for patients in Groups B and C (*Figure 1*) (7, 28).

## Treatment

There are currently no specific treatment options for the management of dengue (29). Therapeutic trials involving drugs that have an impact on the host's immune response to DENV were evaluated in experimental models of inflammatory response to DENV (for example, corticosteroids, immunoglobulins, and chloroquine) (9, 30). They were unable to show any treatment advantage over placebo in clinically relevant endpoints such as viremia or disease duration (9, 30). So far, antiviral treatment strategies have been of little success (9, 31). Most recently, however, the antiviral substance JNJ-A07 proved to be promising, as it interacts with non-structural proteins (NS proteins) and modulates the viral replication complex (28, 32). Its tolerability and clinical efficacy in dengue are currently being tested in clinical trials (32).

Given the lack of clinically effective causal therapeutic options, treatment of dengue is based on the control of symptoms (WHO guideline of 2009) (7, 28). Apart from antipyretic therapy (for example, paracetamol), the core element of treatment in severe dengue remains unaltered in the form of fluid resuscitation with crystalloid solutions, which serves to compensate for arterial hypovolemia secondary to CLS (*Figure 1*) (7). Various prospective studies have shown that there are no advantages of colloidal solutions over substitution with crystalloids (7, 28, 33). Fluid replacement should be reevaluated at short intervals, given that third space fluid shifts with temporary reabsorption can develop. Treatment-induced systemic volume overload, on the other hand, is associated with relevant adverse effects, such as acute respiratory distress syndrome (ARDS) and abdominal compartment syndrome (7, 10). A multicenter study from Asia and Latin America showed that clinically detectable fluid accumulation was present in 447 of 1734 (26%) dengue patients. Of these 447 patients, 179 (40%) developed shock or respiratory distress. The risk for developing respiratory distress during intravenous fluid resuscitation increased, together with the increased volume of fluid given (hazard ratio [HR]: 1.18 per 10 mL/kg body weight;  $p < 0.001$ ) (33).

Apart from that, hemorrhages are also a feared complication of severe dengue. They typically develop in the form of gastrointestinal or vaginal bleeding and should necessitate prompt blood transfusion and platelet administration (7). Since CLS can cause hematocrit levels to appear high or normal, despite manifest bleeding, blood products should already be transfused from levels less than 45% in adults with dengue associated with severe hemorrhages (7). Prophylactic platelet administration in the presence of marked thrombocytopenia without apparent bleeding is a subject of controversy. A multicenter trial from Malaysia and Singapore during which patients with thrombocytopenia (platelets <20 000/ $\mu$ L) without bleeding were substituted with platelets did not show any superiority of prophylactic platelet transfusion in preventing bleeding in comparison with supportive care (34).

In summary, early detection of CLS or dengue-associated severe bleeding and subsequent, closely adjusted fluid replacement therapy are the core therapeutic elements for reducing morbidity and mortality in severe dengue (*Box 2*) (28).

## Prophylaxis

Given the pathophysiological significance of secondary infection, it is essential to avoid (recurrent) DENV infection (9, 10). With the absence of any immunization options, the focus so far has been on consistently avoiding bites from *Aedes aegypti* and *albopictus*. The fundamental measures required for this (wearing bright clothes with as little skin exposure as possible, application of repellents containing diethyltoluamide [DEET] on exposed parts of the skin, programs to reduce *Aedes* breeding sites) still form the cornerstone for successful prophylaxis today (7, 28). Mosquito nets play a minor role since the vectors are active during the day (7, 28). Meanwhile, there is now the option of immunoprophylaxis with the advent of two new commercially available vaccines, Dengvaxia and Qdenga

Box 2

## Selected special clinical challenges arising from dengue and corresponding recommended course of action according to the WHO guidelines and to Tassara et al. (7, 38)

- **Intravenous fluid resuscitation for severe dengue without shock:**
  - continuous administration of isotonic crystalloid solution (*Figure 1*)
  - adjust according to vital signs (stable circulation with pulse pressure >20 mm Hg), urine output (>0.5 mL/kg body weight/hr) and hematocrit levels (target: normal levels)
  - avoid excessive fluid replacement
  - transition to oral rehydration is possible in many cases after 24 to 48 hours.
- **Evaluation of hematocrit in severe dengue:**
  - assessment of hematocrit dynamics within the context of the patient's clinical condition
  - absent clinical improvement and high, or progressively rising, hematocrit levels despite intravenous volume bolus are signs of persistent capillary leak syndrome; repeat the volume bolus (*Figure 1*)
  - If there is no clinical improvement despite normalization/fall in hematocrit levels after fluid bolus, consider hemorrhage and blood transfusions
- **Course of action with oral/nasal mucosal bleeding due to dengue:**
  - These are not considered severe hemorrhages relevant to therapy
  - tight monitoring and hospitalization, do not transfuse blood products
- **Course of action for fluid overload in dengue:**
  - oxygen administration via nasal cannula (target SpO<sub>2</sub> >91%)
  - Transition to the recovery phase may be assumed in the presence of good circulatory function, no fever for 48 hours, stable urine output, and falling hematocrit levels; stop intravenous fluid resuscitation
  - Consider furosemide (0.5 mg/kg body weight) once or twice daily to support diuresis
  - If there are signs of persistence of the critical phase: reduce fluid replacement to a minimum, stop diuretics, tight monitoring
- **Neurological complications of dengue:**
  - neurologic involvement in dengue in around 5% of cases
  - The most common complications are paresthesias. These are usually self-limiting during the transition to the recovery phase.
  - In the event of severe neurological involvement such as Guillain-Barré syndrome (GBS), specific GBS therapy may be required

SpO<sub>2</sub>, oxygen saturation in blood measured by pulse oximeter

(35, 36). Only Qdenga, a tetravalent live vaccine, is available for travelers from Europe because with the administration of Dengvaxia numerous cases of severe dengue developing from infection with the wild-type virus following vaccination have been reported (35, 36). Vaccination with Qdenga is administered twice subcutaneously, with a three-month interval. Qdenga is only recommended for individuals with exposure after a confirmed initial infection because the protective effect is higher in those previously infected (efficacy in previously seronegative persons after two doses of vaccine 78.5% [65.0; 86.9] in the first year, 67.0% [53.6; 76.5] in the second year, and 54.3% [41.9; 64.1] in the third year after vaccination versus 81.9% [75.3; 86.7] in the first year, 74.8% [68.6; 79.8] in the second year, and 65.0% [58.9; 70.1] in the third year after vaccination in seropositive persons) (35, 37).

### Summary and future prospects

Climate change and global mobility have resulted in a worldwide increase in dengue. While the infection is, or was, primarily a challenge in tropical and subtropical regions, primary medical care in Europe is also becoming increasingly confronted with dengue. This review article

summarizes current recommendations for diagnostic assessment and treatment of dengue, and clinically challenging case situations are discussed in the *eMethods* section.

### Conflict of interest statement

The authors declare that they have no conflicts of interest.

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#### Supplementary material eMethods :

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Supplementary material to accompany the article

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## e METHODS

### Case examples with evidence-based discussion of their clinical management

#### Case example 1

A young male adult with no significant past medical history presented in our emergency center with fever (38.5 °C), abnormal fatigue, and severe myalgias. He had just returned from a holiday trip to Southeast Asia four days prior to the index presentation. His laboratory studies showed mildly elevated C-reactive protein (CRP) (15 mg/L, normal range <5 mg/L) with his other results within normal range. Tests for Covid and influenza were unremarkable. A dengue test was conducted in view of his positive travel history. Reverse transcriptase polymerase chain reaction (RT-PCR) was used to identify the pathogen directly, while non-structural protein 1 (NS1) was also detected using an enzyme-linked immunosorbent assay (ELISA). We recommended further outpatient care with physical rest and adequate fluid intake plus symptomatic treatment with paracetamol. We also advised daily follow-up reviews by the family doctor. The patient was also informed about warning signs indicating a severe course of dengue and was offered the opportunity to present again at any time.

#### Prerequisites for outpatient symptomatic treatment

Apart from adequate oral rehydration (at least 1.5 L/day), daily follow-up reviews by a general practitioner or other doctor are decisive for successful outpatient care, together with clinical examination and laboratory checks (full blood count) for the first five days after disease onset (*Figure 2*). If any pathological abnormalities are present (platelet fall together with a hematocrit rise, gastrointestinal or, in women, vaginal bleeding), then hospitalization is recommended. Furthermore, it is advised not to use non-steroidal anti-inflammatory drugs (NSAIDs) for analgesic and anti-inflammatory treatment due to the potential risks of bleeding. Use of paracetamol is recommended for analgesic and antipyretic therapy (7, 9, 10).

#### Case example 2

A young adult female with no significant past medical history was referred to the emergency center by her general practitioner. After returning from a trip abroad to Latin America she had presented to her GP surgery with a febrile infection for the previous five days associated with

maculopapular exanthema affecting mainly the trunk. Her fever had fallen slightly in the meantime, but petechiae on her lower legs were evident together with thrombocytopenia (22 G/μL, normal range 150–400 G/μL) and a rise in hematocrit (0.5; normal range 0.37–0.46). Aspartate aminotransferase (AST) and albumin results were normal. NS1 was detected at the emergency center, with viremia no longer detectable using RT-PCR, so a diagnosis of dengue was made. Given her marked thrombocytopenia and simultaneously high hematocrit, the patient was admitted to hospital for monitoring of her clinical and laboratory parameters and for oral rehydration. Her platelets had already risen two days later (67 G/μL). After two days, the patient was discharged into further outpatient care after no further complications.

#### Thrombocytopenia without bleeding complications in dengue

Thrombocytopenia associated with elevated hematocrit is a risk factor for severe disease, so inpatient monitoring is recommended (7, 34). No bleeding complications were apparent at the time of admission, and prophylactic administration of platelet concentrates in the absence of severe bleeding (gastrointestinal tract, vaginal bleeding) was not recommended (16, 33). The patient's fever had already fallen slightly on presentation. It may be postulated that she was already at the start of the critical phase at the time of admission. In the absence of any bleeding complications, a rise in her platelet count was expected during the recovery phase after two to three days (*Figure 2*) (7). Volume state and vital parameters (especially pulse pressure) should be regularly re-assessed during the inpatient stay to detect any potential capillary leak syndrome (CLS) in good time (7).

#### Case example 3

A young adult male was presented as an emergency with central vision loss on the left side associated with tingling of his hands and feet. He reported a three-week holiday stay in Southeast Asia. Five days prior to the index presentation, he had sought medical care in Singapore for fever and arthralgia where dengue was diagnosed. In our emergency center, we diagnosed macular edema with minor retinal hemorrhage in the left eye associated with normal sensory and motor function of the extremities and otherwise afebrile and unremarkable findings. Laboratory

results revealed no further abnormalities other than moderate thrombocytopenia (83 G/ $\mu$ L, normal range 150–400 G/ $\mu$ L). Suspected small fiber neuropathy of the extremities and macular edema with vision loss were diagnosed as complications of dengue. The patient was admitted to hospital for daily monitoring. Within two days, the neurological symptoms regressed completely, and the platelet count returned to normal. The patient was discharged after three days.

### Approach to organ-specific complications

Due to lack of data and the wide variability of organ involvement in dengue (*Box 1*), the WHO does not recommend any specific therapy for ophthalmologic, neurological, cardiac, or gastrointestinal involvement (7). With specific organ involvement, as in this case example, tight monitoring and physical rest together with a specialist consult should be initiated. Symptoms usually resolve completely within one to two weeks under this management (9).

#### Case example 4

An adolescent female patient in a reduced general condition was presented to the emergency department. Her history revealed fever of up to 39.8 °C for the previous three days associated with myalgias and recurrent vomiting. She had returned from a holiday trip to Latin America six days previously. In the emergency center, clinical examination revealed an alert female patient, oriented to all spheres, with a blood pressure of 100/85 mm Hg, a heart rate of 92/min; she complained of diffuse abdominal pain. A bedside ultrasound examination demonstrated a collapsed vena cava and discrete bilateral pleural effusions. Her laboratory results revealed thrombocytopenia (70 G/ $\mu$ L, normal range 150–400 G/ $\mu$ L), elevated AST (320 U/L, normal range 10–35 U/L), and a high hematocrit level

(0.53; normal range 0.37–0.46). RT-PCR provided direct evidence of dengue virus. On taking all the findings into account, a diagnosis of severe dengue was made and intravenous fluid resuscitation with crystalloid solutions was commenced under continuous monitoring on the intermediate care unit. Her circulatory status was stabilized over the further course, allowing the intravenous volume replacement to be reduced on confirming sufficient urine output. Her signs and symptoms returned to normal after three days, and her general condition improved, allowing the patient to be transferred to a regular ward and after another two days to be discharged to further outpatient care.

### Approach to dengue shock syndrome

The patient in the case example was alert and hemodynamically stable. This suggested a stable situation in the presence of confirmed dengue. Reduced pulse pressure (systolic minus diastolic blood pressure <20 mm Hg) is a criterion for shock in severe dengue (7, 9). Documented pleural effusions and ultrasound evidence of intravascular hypovolemia are indications of CLS. Initial generous fluid resuscitation with isotonic crystalloid solutions (bolus of 5–20 mL/kg body weight) is crucial. The bolus should be repeated if the patient's condition does not improve under these measures. After improvement, fluid resuscitation should be continued according to the regimen in *Figure 1* (7, 9, 33). Further volume replacement is guided by monitoring urine output and vital parameters, while it is essential to avoid fluid overload (7, 9). The body's own rapid volume reabsorption should be borne in mind here as this can also result in volume overload (7, 9). If crystalloid solutions are not sufficient and critically reduced organ perfusion develops, then catecholamines and colloidal solutions should be used (7).



**Questions** on the article in issue 23/2024:

# Dengue Fever—Diagnosis, Risk Stratification, and Treatment

The submission deadline is 14 November 2025. Only one answer is possible per question.  
Please select the answer that is most appropriate.

## Question 1

**Where did the northernmost indigenous dengue outbreak occur in 2023?**

- a) Near Paris, France
- b) Near Barcelona, Spain
- c) Near Rome, Italy
- d) Near London, England
- e) Near Copenhagen, Denmark

## Question 2

**Which mosquito species serve as vectors for dengue and are increasingly spreading in milder climatic zones, including Europe?**

- a) *Aedes japonicus* and *Aedes scapularis*
- b) *Aedes aegypti* and *Aedes albopictus*
- c) *Aedes vexans* and *Aedes japonicus*
- d) *Aedes polynesiensis* and *Aedes japonicus*
- e) *Aedes scapularis* and *Aedes vexans*

## Question 3

**What characteristics of the dengue virus are mentioned in the text?**

- a) DNA virus from the family of flaviviruses, spherical genome
- b) RNA virus from the family of filoviruses, double-stranded RNA genome
- c) RNA virus from the family of flaviviruses, single-stranded RNA genome
- d) DNA virus from the family of adenoviruses, double-stranded DNA genome
- e) RNA virus from the family of paramyxoviruses, spherical genome

## Question 4

**In what percentage of cases is a DENV infection asymptomatic?**

- a) approx. 10%
- b) approx. 25%
- c) approx. 35%
- d) approx. 50%
- e) approx. 75%

## Question 5

**Which possible post-infectious sequelae of DENV infection are reported in the text?**

- a) fatigue syndrome and hair loss
- b) migraine and loss of fingernails
- c) rashes and itching
- d) oral thrush and diabetes mellitus
- e) vertigo and intention tremors

## Question 6

**What measure is also recommended as part of the treatment of dengue patients under outpatient management?**

- a) daily intravenous administration of crystalloid solution
- b) daily excretion balance
- c) daily administration of noradrenaline

- d) daily follow-up examination with full blood count
- e) daily administration of anticoagulants

## Question 7

**From which day after onset of symptoms (day 0) at the earliest is it advisable to conduct a test for specific antibodies against the dengue virus in serum or plasma?**

- a) from day 1
- b) from day 2
- c) from day 4
- d) from day 6
- e) from day 9

## Question 8

**Infections with other viruses or even active immunization against these viruses can interfere with the outcome of immunological tests for dengue infection by cross-reactivity and thus produce false-positive results. Which of the following diseases do not belong to this group?**

- a) FSME
- b) Zika
- c) Yellow fever
- d) Japanese encephalitis
- e) Measles

## Question 9

**Which statement regarding immunization with the dengue vaccine Qdenga is correct?**

- a) Vaccination is only recommended for individuals who have never previously been infected with the dengue virus.
- b) Vaccination is only recommended for individuals with exposure after a confirmed initial infection.
- c) Vaccination with Qdenga is administered subcutaneously, three times at intervals of two months.
- d) Vaccination with Qdenga is not recommended for Europeans as it is not well tolerated.
- e) Vaccination with Qdenga as a travel prophylaxis should be administered once, approximately one week before starting the journey.

## Question 10

**With regard to dengue infections, which syndrome is abbreviated as “CLS”?**

- a) cardiac leak syndrome
- b) capillary lymphatic syndrome
- c) clot and leak syndrome
- d) capillary leak syndrome
- e) chronic lymphatic syndrome