

# Protocol

## Neonatal management of dengue: clinical and preventive approach

**Manejo neonatal del dengue: abordaje clínico y preventivo**

**Manejo neonatal da dengue: abordagem clínica e preventiva**

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### Summary

Dengue is a viral disease transmitted by the *Aedes aegypti* mosquito. This infection has shown a global increase in cases, particularly affecting the Americas region. In Uruguay, the most recent outbreak (2024) recorded 702 autochthonous and 410 imported cases, underscoring the need to strengthen surveillance and management strategies.

Dengue can complicate pregnancy with risks of preterm birth and low birth weight, although a statistically significant association has not been confirmed. The risk of vertical transmission ranges from 1.6-10.5%, increasing if the infection occurs close to delivery.

Newborns can acquire the infection vertically (trans-placentally) or horizontally (mosquito bite). A wide variability in clinical presentation can be observed, ranging from asymptomatic patients, mild symptoms, or severe cases with potential mortality, requiring differential diagnosis with sepsis. Recommended tests include PCR in cord blood, NS1 antigen detection, and IgM, adapted to the clinical timing.

Breastfeeding is safe and recommended in all cases, even for infected mothers, given its protective role.

These recommendations aim to optimize the identification and management of at-risk neonates, ensuring a comprehensive and preventive approach to dengue.

**Key words:** Dengue  
Infant, Newborn

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Unpublished work.

We declare that we have no conflicts of interest.

Neonatology Academic Unit. CHPR. Dr. Mario Moraes endorses publication.

This work has been unanimously approved by the Editorial Committee.

Date received: December 23, 2024.

Date approved: May 22, 2025.

## Resumen

El dengue es una enfermedad viral transmitida por el mosquito *Aedes aegypti*. Esta infección ha mostrado un aumento global de casos, afectando especialmente a la región de las Américas. En Uruguay, el brote más reciente (2024) registró 702 casos autóctonos y 410 importados, lo que subraya la necesidad de fortalecer estrategias de vigilancia y manejo.

El dengue puede complicar el embarazo con riesgos de parto pretérmino y bajo peso al nacer, aunque no se ha confirmado una asociación estadísticamente significativa. El riesgo de transmisión vertical oscila entre 1,6%-10,5%, aumentando si la infección ocurre cerca del parto.

Los recién nacidos pueden adquirir la infección de forma vertical (transplacentaria) u horizontal (picadura de mosquito). Se puede observar una amplia variabilidad del cuadro clínico, oscilando desde pacientes asintomáticos, síntomas leves o casos graves con potencial mortalidad, requiriendo un diagnóstico diferencial con sepsis. Las pruebas recomendadas incluyen la reacción en cadena de polimerasa (PCR) en sangre de cordón, detección de antígeno NS1 e IgM, adaptada al momento clínico.

La lactancia materna es segura y recomendada en todos los casos, incluso con madres infectadas dado su papel protector.

Estas recomendaciones buscan optimizar la identificación y manejo de neonatos en riesgo, asegurando un enfoque integral y preventivo frente al dengue.

**Palabras clave:** Dengue  
Recién Nacido

## Resumo

A dengue é uma doença viral transmitida pelo mosquito *Aedes aegypti*. Esta infecção tem mostrado um aumento global de casos, afetando especialmente a região das Américas. No Uruguai, o surto mais recente

(2024) registrou 702 casos autóctones e 410 importados, o que salienta a necessidade de fortalecer as estratégias de vigilância e manejo. A dengue pode complicar a gravidez com riscos de parto prematuro e baixo peso ao nascer, embora uma associação estatisticamente significativa não tenha sido confirmada. O risco de transmissão vertical oscila entre 1.6-10.5%, aumentando se a infecção ocorrer próximo ao parto.

Os recém-nascidos podem adquirir a infecção de forma vertical (transplacentária) ou horizontal (picada de mosquito). Pode-se observar uma ampla variabilidade do quadro clínico, que vai desde pacientes assintomáticos, sintomas leves ou casos graves com potencial mortalidade, requerendo um diagnóstico diferencial com sepsis. Os testes recomendados incluem PCR em sangue de cordão, detecção de antígeno NS1 e IgM, adaptados ao momento clínico.

A amamentação é segura e recomendada em todos os casos, mesmo com mães infectadas, dado o seu papel protetor.

Estas recomendações buscam otimizar a identificação e o manejo de neonatos em risco, assegurando uma abordagem integral e preventiva frente à dengue.

**Palavras chave:** Dengue  
Recém-Nascido

## Introduction

Dengue virus infection is a global concern due to the current increase in cases. The World Health Organization recommends maintaining surveillance, early diagnosis, and timely treatment of dengue cases.

In the Americas, Brazil and Argentina reported the highest number of cases during the 2023-2024 outbreak<sup>(1,2)</sup>.

In Uruguay, imported cases have been reported since 1997, mostly from countries in the Americas, with an increase since 2013. In 2016, the first local dengue outbreak in Uruguay in 100 years was recorded.

In early 2024, a new dengue outbreak was identified with both imported and local cases. In the latest

surveillance report from the Ministry of Public Health (MSP) dated May 31, 2024, 702 local and 410 imported dengue cases were identified. Five deaths have been reported, two attributed to dengue, two with comorbidities that may have contributed to the fatal outcomes, and one under investigation<sup>(3,4)</sup>.

In neighboring countries, Argentina and Brazil, there have been significant outbreaks, resulting in a true epidemic and overwhelming healthcare systems.

Dengue is a febrile illness caused by the dengue virus (DENV), an arbovirus belonging to the genus *Flavivirus*, within the family *Flaviviridae*, and is currently an increasing global health concern. Recently, the Pan American Health Organization and the World Health Organization (PAHO/WHO) reported that around 500 million people in the Americas are at risk of contracting dengue<sup>(5)</sup>.

Arboviruses pose an additional risk to pregnant women, not only due to their increased susceptibility to complications but also because of their potential teratogenicity and the risk of vertical transmission<sup>(6)</sup>.

In particular, the dengue virus is the most important human arthropod-borne viral disease, with four major serotypes (DENV-1, DENV-2, DENV-3, and DENV-4) that have phylogenetic and antigenic differences<sup>(7)</sup>. Primary infection with one serotype provides immunity against reinfection by a homologous virus, but if infection occurs with another serotype, the risk of severe disease increases<sup>(8-10)</sup>.

The disease is systemic and dynamic, with a variable clinical presentation and unpredictable course, ranging from asymptomatic forms to severe manifestations. Commonly, it presents with fever, joint pain, hemorrhage, and neurological symptoms. The incubation period lasts four to ten days, after which the illness can begin abruptly and go through three phases: febrile, critical, and recovery.

## Dengue and pregnancy

The disease affects all age groups, mainly adolescents and adults<sup>(13)</sup>. Pregnant women can also contract the infection, either as mild-asymptomatic or severe forms with high morbidity and mortality; however, they do not present a different risk or disease course compared to the general population<sup>(6,14)</sup>.

Complications can occur at any time during pregnancy, either during the infection or up to one month afterward. Certain complications during pregnancy, such as preterm delivery and low birth weight, have been reported; however, a 2017 meta-analysis of 14 studies found no statistically significant association between DENV infection and these complications<sup>(2,6,14-16)</sup>.

## Dengue in newborns

### Transmission

Newborns can contract the disease either horizontally through the bite of an infected mosquito or vertically through transplacental transmission, regardless of the severity of the maternal disease<sup>(16)</sup>.

In the latter case, the risk of transplacental DENV transmission to the fetus is low, with a prevalence ranging from 1.6% to 10.5%<sup>(4,17-19)</sup>. The incidence increases when maternal infection occurs up to 15 days before delivery and up to two days postpartum, due to higher viremia in the context of labor<sup>(7)</sup>.

There is no evidence of dengue in the newborn through breast milk. Although viral fragments with infectious potential have been detected in breast milk, there are several protective factors that prevent infection, including the antiviral properties of breast milk itself and the epithelial and mucosal barriers with their respective antibodies. For this reason, breastfeeding is recommended for newborns of mothers with DENV infection<sup>(4,17,20,21)</sup>.

Fetal exposure to DENV infection, while providing the newborn with protection against the specific serotype, may increase the risk of more severe infection if contracted later in life due to the presence of heterologous anti-dengue antibodies<sup>(15,22)</sup>.

### Clinical manifestations and diagnosis

Neonatal dengue is an underdiagnosed disease, requiring a high index of suspicion, along with timely evaluation and diagnosis, given its symptoms that are similar to those of sepsis.

In newborns, the clinical presentation can be highly variable, ranging from asymptomatic cases and mild symptoms to severe cases with potential mortality<sup>(23)</sup>. Severe forms are rare; in most cases, the disease is self-limiting and progresses favorably<sup>(24)</sup>.

The onset of symptoms has been observed between the first and eleventh day of life, with a mean onset on the fourth to fifth day. Symptoms may include fever, irritability, intense crying, petechiae, skin rash, hemorrhages of varying severity, plasma extravasation effusions, and shock<sup>(16,25)</sup>.

Although the onset of clinical symptoms may be delayed, close monitoring and management of the newborn are recommended in cases of meconium-stained amniotic fluid in pregnant women with suspected dengue<sup>(16,25,26)</sup>.

For diagnosis, PCR testing of cord blood samples is recommended as a specific study to detect the viral genome in the newborn<sup>(3,19)</sup>.

Other serological tests are based on the detection of

virus-specific IgM around the fourth to fifth day after the symptom onset, when viremia is highest. After the fifth day, IgM serology becomes the preferred method. It peaks two weeks after the onset of fever. The disadvantage of serological tests is that they may produce false positives, since flaviviruses share antigenic epitopes<sup>(12,26)</sup>.

Molecular biology techniques are currently available, such as the non-structural glycoprotein 1 (NS1) test. NS1 is secreted by infected cells and is essential for viral replication, increasing in the first hours after infection and peaking three to five days after symptom onset. Several studies describe it as a potential marker of severe disease, given the correlation between its plasma levels and the degree of viremia. It can be obtained from saliva, urine, serum, dried blood samples, and cerebrospinal fluid. Its advantage lies in being a rapid, simple, and accessible method with high sensitivity (87%-95%) during the first three days, decreasing thereafter towards the tenth day of infection; urine levels (which are relatively lower) remain stable up to 14 days after infection<sup>(27)</sup>.

Dengue detection using dried blood spots on filter paper (a method used for neonatal screening in our country) has proven to be useful, especially in places without laboratory facilities or when a venous blood sample cannot be collected. Its importance is highlighted for performing retrospective infection diagnosis. It is important to note that using NS1 PCR for diagnosis does not replace other serological tests, and it could indicate infection by other arboviruses. Currently, there is no circulation of other arboviruses in Uruguay, making NS1 testing particularly valuable for the detection of neonatal DENV<sup>(26)</sup>.

As part of the newborn evaluation, a complete blood count with peripheral smear will be requested; it is very important to rule out thrombocytopenia and leukopenia (less than 5,000/mm<sup>3</sup>), the latter being the earliest and most frequent abnormality. The rest of the laboratory tests will be determined at the clinician's discretion, based on the symptoms presented.

## Neonatal management strategies

The management of neonates can be organized into two scenarios depending on the maternal diagnosis, with a third scenario in the case of horizontal infection.

Due to the presentation of symptoms similar to sepsis, it is recommended to begin antibiotic treatment according to the sepsis guidelines of each service.

*Scenario 1: newborn of a mother with suspected dengue*

Symptoms in newborns have been described from nine hours up to eleven days of life, with a mean onset of four days. Therefore, the child of a mother with suspected dengue should be closely monitored during the first two weeks of life.

The mother-newborn pair should be admitted to a vector-free, enclosed area. Mosquito netting and transparent fabric should be provided for the mother.

It is recommended that the newborn remain hospitalized until the maternal infection is either confirmed or ruled out.

Exclusive breastfeeding should be maintained unless there are contraindications<sup>(25)</sup>.

At birth, if there is a high suspicion of maternal disease, a cord blood sample should be collected for PCR and serology.

If infection is ruled out, newborn care will follow standard protocols.

If any abnormalities develop during this period, or if the diagnosis is confirmed, management should follow the guidelines of scenario two, regardless of the mother's serological status<sup>(12,14)</sup>.

*Scenario 2: newborn of a mother with confirmed dengue*

Whenever possible, the mother-newborn pair should be admitted to a vector-free, enclosed area.

Mosquito netting and transparent fabric should be provided for the mother. If this is not possible, the newborn should be admitted to an isolation ward.

Close monitoring will be carried out to identify any symptoms or potential complications in the newborn. This will include strict monitoring of temperature, respiratory rate, and skin lesions.

Breastfeeding should be maintained, either directly at the breast or via expressed milk, if possible, unless there are contraindications.

Laboratory tests will be performed at birth, at 48 hours, and on the fifth day of life. Unlike Scenario 1, PCR and IgM serology should be performed within the first 48 hours of life, repeating them after the fifth day if necessary<sup>(12)</sup>.

Table 1 summarizes the recommendations for this scenario.

For a newborn with symptoms or laboratory abnormalities, supportive treatment should be initiated. Conversely, if the newborn shows good progress in the first five days, they will be discharged, ensuring adequate outpatient follow-up until 14 days<sup>(14,28)</sup>.

Figure 1 presents an algorithm outlining the management of pregnant women with suspected dengue.

*Scenario 3: newborn who acquires the disease horizontally after discharge*

This may present as a febrile newborn. In these cases, it is recommended to follow the fever-without-focus protocol of the Hospital Pediátrico del Centro Hospitalario Pereira Rossell<sup>(29,30)</sup>.

If dengue is suspected, the patient should be classified according to scheme 1. For dengue without warning signs, outpatient treatment may be possible, pro-

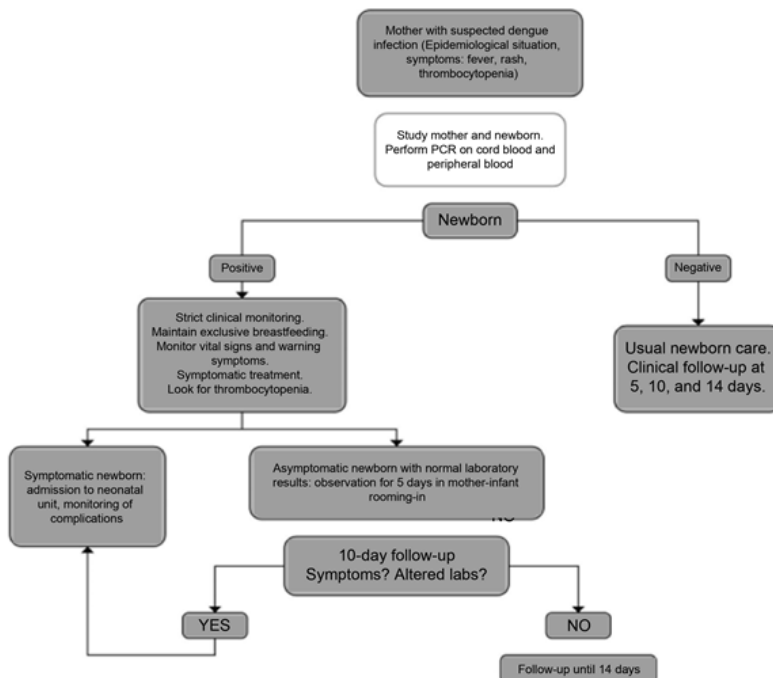
vided proper follow-up at the clinic can be ensured.

If the newborn has a fever, they should be admitted to a vector-isolated area where proper monitoring, evaluation, and management of complications can be ensured. Table 2 summarizes the steps to follow for newborns with suspected postnatal dengue.

**Table 1.** Scenario 2. Newborn of a mother with dengue.

Admission	Patient admitted to a vector-free environment where strict symptom monitoring can be conducted, and possible complications can be treated		
	At birth	48 hours	Fifth day of life
Laboratory	Cord blood PCR NS1 Ag	Peripheral PCR IgM NS1 Ag CBC with peripheral smear	PCR and IgM are repeated if necessary. NS1 Ag may be repeated
Symptoms	Fever, irritability, intense crying, petechiae, skin rash, hemorrhages, plasma extravasation effusions, shock. (Symptoms appeared on average between the fourth and fifth day)		
Management	If on the fifth day of illness, the patient is asymptomatic with negative laboratory tests, they will be discharged with early follow-up at the clinic. If the patient presents with warning signs, they will be classified as DCSA*		

\*DCSA: dengue with warning signs.



**Figure 1.** Algorithm for managing pregnant women with suspected dengue. Extracted and modified from Quipildor M, Rapetti G, Silveti M, Moreno J, Aguilera M, Falco A. Vertically transmitted dengue: case reports. In: XXIII SADI Congress 2023. Available at: <https://infectologia.info/abstracts/dengue-de-transmission-vertical-reporte-de-casos/>.

**Table 2.** Scenario 3. Patient with suspected postnatal dengue.

Newborn with fever-without-focus lasting less than seven days	Follow the algorithm for fever-without-focus		
Sospecha de dengue	Classification of dengue (scheme 1)		
	DSSA	DCSA	DG
	Outpatient treatment, admission according to medical criteria*	Admitted for symptomatic treatment and prevention of shock	Admitted for treatment of shock and possible complications
Paraclínica a solicitar	CBC PCR (0-5 days after symptoms onset). NS1 antigen detection	CBC PCR (0-5 days after symptoms onset). NS1 Ag (can be repeated on the fifth day). IgM on the sixth day after symptoms onset	CBC PCR (0-5 days after symptoms onset). NS1 antigen (can be repeated on the fifth day). IgM on the sixth day after symptoms onset
Conducta	If all results are negative, the patient may be discharged with strict clinical follow-up at home. If the patient presents with warning signs, they will be classified as DCSA or DG.	Monitoring, evaluation, and treatment of complications	Monitoring, evaluation, and treatment of complications

\*High social risk, follow-up at outpatient clinic not guaranteed, distant health center.  
DSSA: dengue without warning signs.  
DCSA: dengue with warning signs.  
DG: severe dengue.

## Prevention and vaccines

Prevention is one of the most important factors in preventing the spread of the disease. Fumigation campaigns are recommended for vector elimination.

Adults living with the newborn should use repellent and, if possible, have mosquito nets in their homes.

In pregnant women, the topical use of repellents containing N,N-diethyl-meta-toluamide (DEET) at 30% or less is safe. The use of repellent is not recommended for newborns and infants until they are 6 months old. For those under 6 months, it is suggested to use cribs and strollers with mosquito netting, dress them in light-colored clothing, and use long-sleeved tops and pants<sup>(31-33)</sup>.

There are currently two approved vaccines. The first is TAK-003 (Qdenga), manufactured by the Japanese laboratory Takeda, and approved for use by the EMA (European Medicines Agency). The second, approved by the FDA (Food and Drug Administration), is the Dengvaxia vaccine, manufactured by Sanofi Pasteur.

Neither vaccine is an option for pregnant women or infants. In these groups, non-pharmacological preventive measures are key to reducing the risk of infection.

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**Data availability**

The dataset supporting the results of this study is NOT available in open-access repositories.

**Author contributions**

All authors of this manuscript contributed to the conception and critical review and approved the final version for publication.

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