TID Chat #1 - Dengue Testing in Organ Donors

ASK-THE-EXPERT | TRANSPLANT INFECTIOUS DISEASE

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The Challenge

Dengue infection in organ donors is a growing challenge in endemic regions. High rates of asymptomatic cases and potential donor-derived transmission make screening complex — yet no universally accepted recommendations exist.

Clinical Scenario

A **56-year-old woman** from Bangkok, Thailand presented with intracranial hemorrhage and was declared brain dead. Donor evaluation revealed a **positive dengue IgM** but a **negative dengue NAT**. How should this be interpreted and managed?

🔬 Interpretation

IgM+/NAT− = diagnostic grey zone

🧪 Key Diagnostics

NAT, NS1, IgM/IgG timing matters

🚩 Red Flags

Negative NAT does NOT equal no risk; 75% asymptomatic

📋 Guidelines

Risk–benefit; no global consensus

Q1 - Interpreting IgM+/NAT−

An isolated IgM-positive, NAT-negative result may represent **late convalescent infection**, cross-reactive flavivirus antibodies, recent vaccination, or a false-positive IgM — not necessarily active infection.[1] IgM can persist for months and is a poor stand-alone marker of current transmission risk.[2] In hyperendemic areas, an IgM-only result in a deceased donor may be a high-risk signal and is often considered a contraindication to donation.[3] Clinical history is essential: recent fever, thrombocytopenia, or transaminitis within 30 days increases suspicion, although **up to 75% of infections are asymptomatic**.[3]

Q2 - Key Diagnostics

NAT (PCR) and **NS1 antigen** are most sensitive in the early viremic phase (days 1–7). IgM appears after days 3–7 and may persist up to 12 weeks; IgG indicates past infection.[1,4] Combined NS1/IgM testing is preferred as it captures both early antigenemia and antibody responses.[1,4] Note: NS1 sensitivity decreases significantly in **secondary dengue infections**, limiting performance in endemic settings.[4] Current recommendations support NAT or NS1 for donor screening when dengue is suspected.[3]

Q3 - Red Flags & Practical Tips

- **Negative blood NAT does not exclude risk** — donor-derived transmission from aviremic donors has been reported; viral RNA may persist in kidney/urine after viremia resolves.[5,6]
- Asymptomatic infections are common (~75%), making clinical screening unreliable.[3]
- **Living donor strategy:** delay donation and repeat testing after 15 days; persistently negative IgG suggests false-positive IgM.[3]
- Recent fever, thrombocytopenia, or transaminitis within 30 days = warning signs regardless of NAT result.

Q4 - Guideline Comments

No universally accepted global guidelines exist. Current **Brazilian and South Asian recommendations** suggest:[3,7]

- Risk–benefit approach based on local epidemiology
- Combined NS1/IgM testing
- Rejection of IgM-positive deceased donors in high-endemic areas
- 30-day waiting period after dengue infection for living donors

⚠ Transmission risk from isolated IgM positivity remains uncertain — individualized assessment is essential.

References

1. Hunsperger EA et al. *J Infect Dis.* 2016;214(6):836–844. | 2. Chien YW et al. *BMC Infect Dis.* 2018;18:156. | 3. Santos DWCL et al. *Braz J Transplant.* 2024;27:e1124. | 4. Teoh BT et al. *Sci Rep.* 2016;6:27663. | 5. Sim JXY et al. *Am J Transplant.* 2021;21:1944–1947. | 6. Di Ascia L et al. *Kidney Int Rep.* 2024;9:186–190. | 7. Bansal SB et al. *Transplantation.* 2023;107(9):1910–1934.

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CLINICAL SCENARIO

- ✓ 56-year-old woman (Bangkok, Thailand), Brain-dead donor
- ✓ **Dengue IgM positive**
- ✓ **NAT (PCR) negative**

Key dilemma: Active infection vs past exposure?

HOW TO INTERPRET IgM+/NAT−

Possible explanations:
- ✓ Late convalescent infection
- ✓ Cross-reactive flavivirus antibodies
- ✓ Recent vaccination
- ✓ False-positive IgM

Key limitation:
IgM may persist for months → poor marker of active infection

In endemic/hyperendemic areas:
May indicate recent infection.
Often considered **high risk in deceased donors**

Diagnostic grey zone:
Limited evidence → decisions rely on **epidemiology + clinical context**

Clinical clues:
Fever, thrombocytopenia, transaminitis (<30 days) ↑ suspicion
Up to **75% asymptomatic;** **transplant urgency remains a decisive factor**

KEY DIAGNOSIS

Diagnosis relies on viral markers:

Early phase (days 1–7):
- ✓ NAT → highest sensitivity
- ✓ NS1 antigen

After day 3–7:
IgM appears (may persist up to 12 weeks)

Late phase:
IgG → past infection

Best approach:
Combine **NS1 + IgM** (better sensitivity across timeline

Limitations:
NS1 sensitivity ↓ in **secondary infections**
Performance varies in endemic settings

Current practice:
NAT or NS1 when dengue is suspected
No strong evidence for systematic screening

OUTCOMES IN RECIPIENTS

Limited data
Reported spectrum:
- ✓ Mild disease
- ✓ Severe complications

Key message:
Individualized risk–benefit assessment is essential

RED FLAGS & PRACTICAL TIPS

NAT-negative ≠ no risk
Transmission reported from **aviremic donors**
Viral RNA may persist in **kidney / urine / tissue**

Additional consideration:
Urine PCR in selected kidney donors

Clinical limitation:
~75% infections asymptomatic → screening unreliable

Living donor strategy:
Delay donation
Repeat testing after **15 days**
Persistently negative IgG → suggests false IgM

Warning signs (regardless of NAT):
- ✓ Fever
- ✓ Thrombocytopenia
- ✓ Transaminitis (<30 days)

COMMENTS ON GUIDELINES

No universally accepted global guidelines

Current recommendations:
- ✓ Risk–benefit approach
- ✓ Combined NS1 + IgM testing
- ✓ Avoid IgM+ deceased donors in high-endemic áreas

Unresolved issue:
Risk of transmission with **isolated IgM positivity remains uncertain**

CONCLUSION: A structured, context-based approach to dengue testing in organ donors improves safety, supports decision-making, and preserves access to transplantation

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Hunsperger EA, *J Infect Dis*. 2016;214(6):836–844.
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