Stanford MEDICINE
School of Medicine

West Coast TID Meeting

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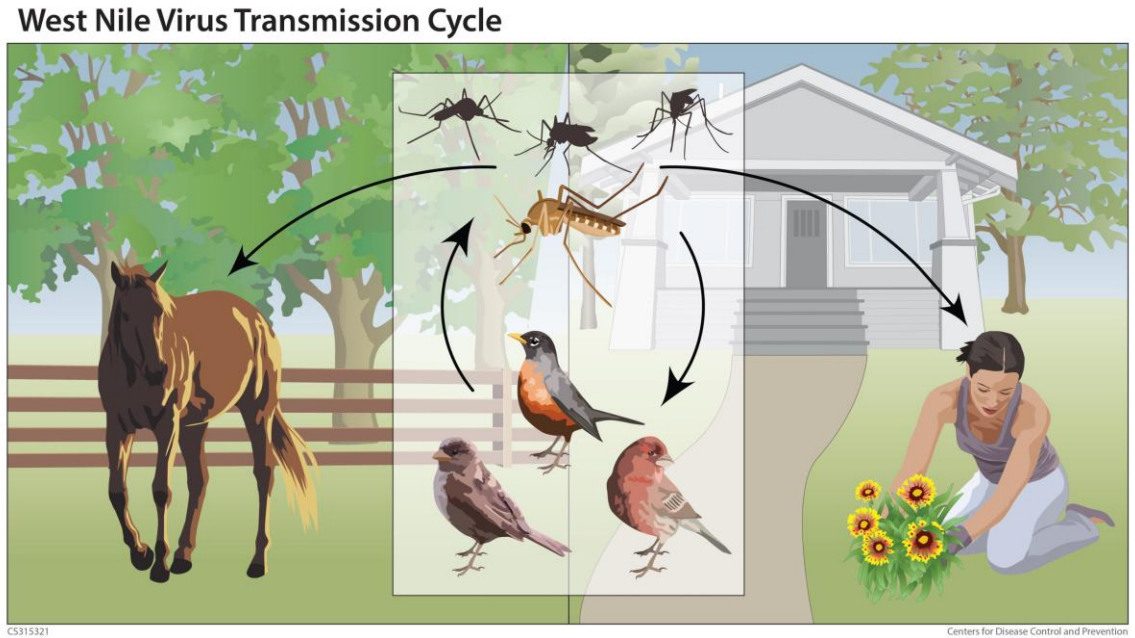
West Nile Virus (WNV)

Single-stranded RNA virus, genus *Flavivirus*



1999 – first case in Northern Hemisphere in NYC
Now endemic in US

Majority of cases July – October

Transmission
1. Mosquito vector
2. Blood products
3. Transplant

cdc.gov

WNV Clinical Presentation

Immunocompetent patients

- Incubation period **3 - 14 days**
- 80% asymptomatic
- 20% symptomatic
  - Febrile illness, myalgias, nausea/vomiting, rash
  - **<1% develop neuroinvasive disease**
    - meningitis
    - encephalitis
    - meningo-encephalitis
    - poliomyelitis-like flaccid paralysis
  - 10% Mortality

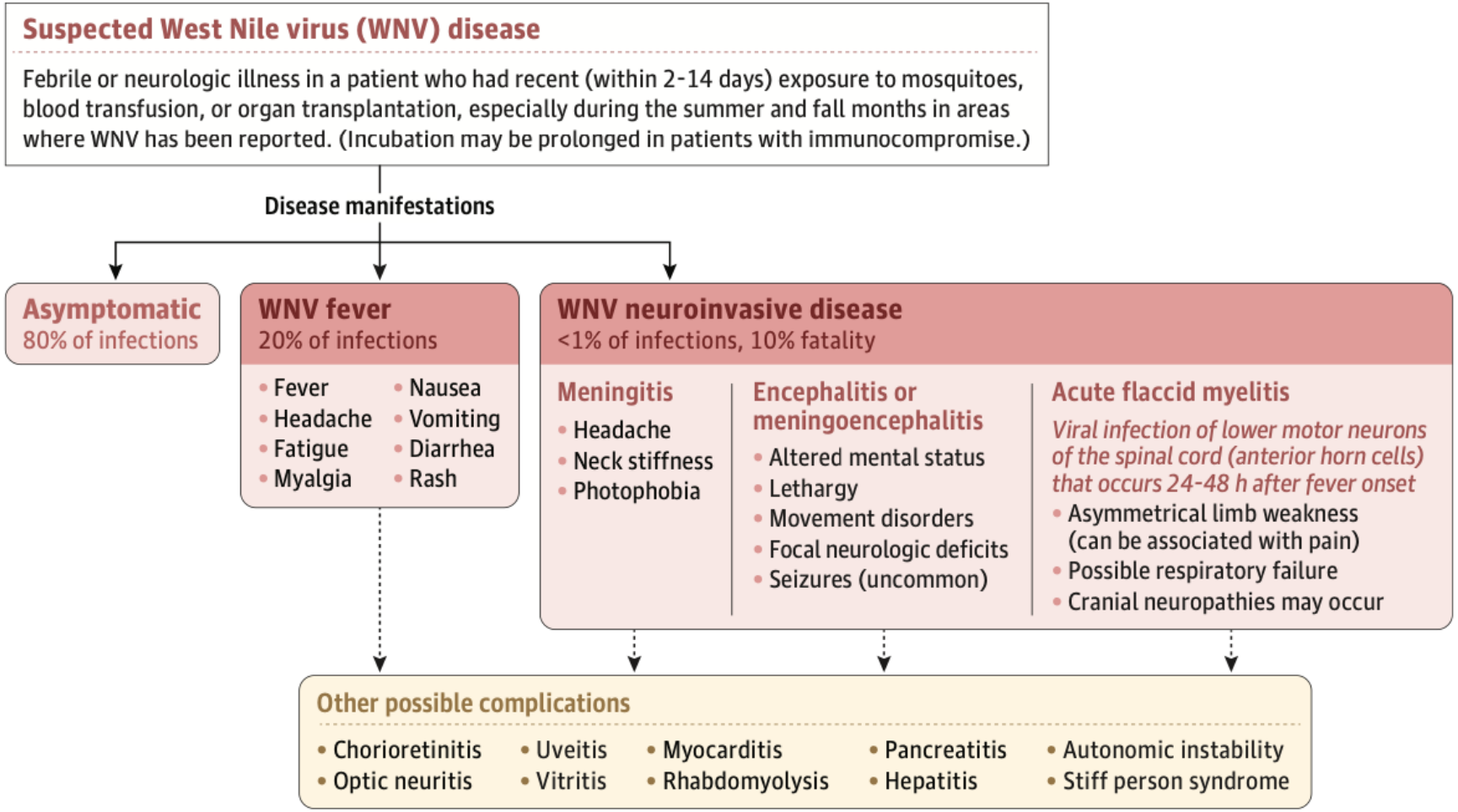
Immunocompromised patients

- Incubation period **median 13.5 – 15 days**
- Greater risk of neuroinvasive disease
  - Blood or transplant-related transmission associated **with 50-75% neuroinvasive disease**
  - 38% Mortality

Gould CV, Staples JE, Guagliardo SAJ, et al. West Nile Virus: A Review. *JAMA*. 2025

WNV Clinical Presentation

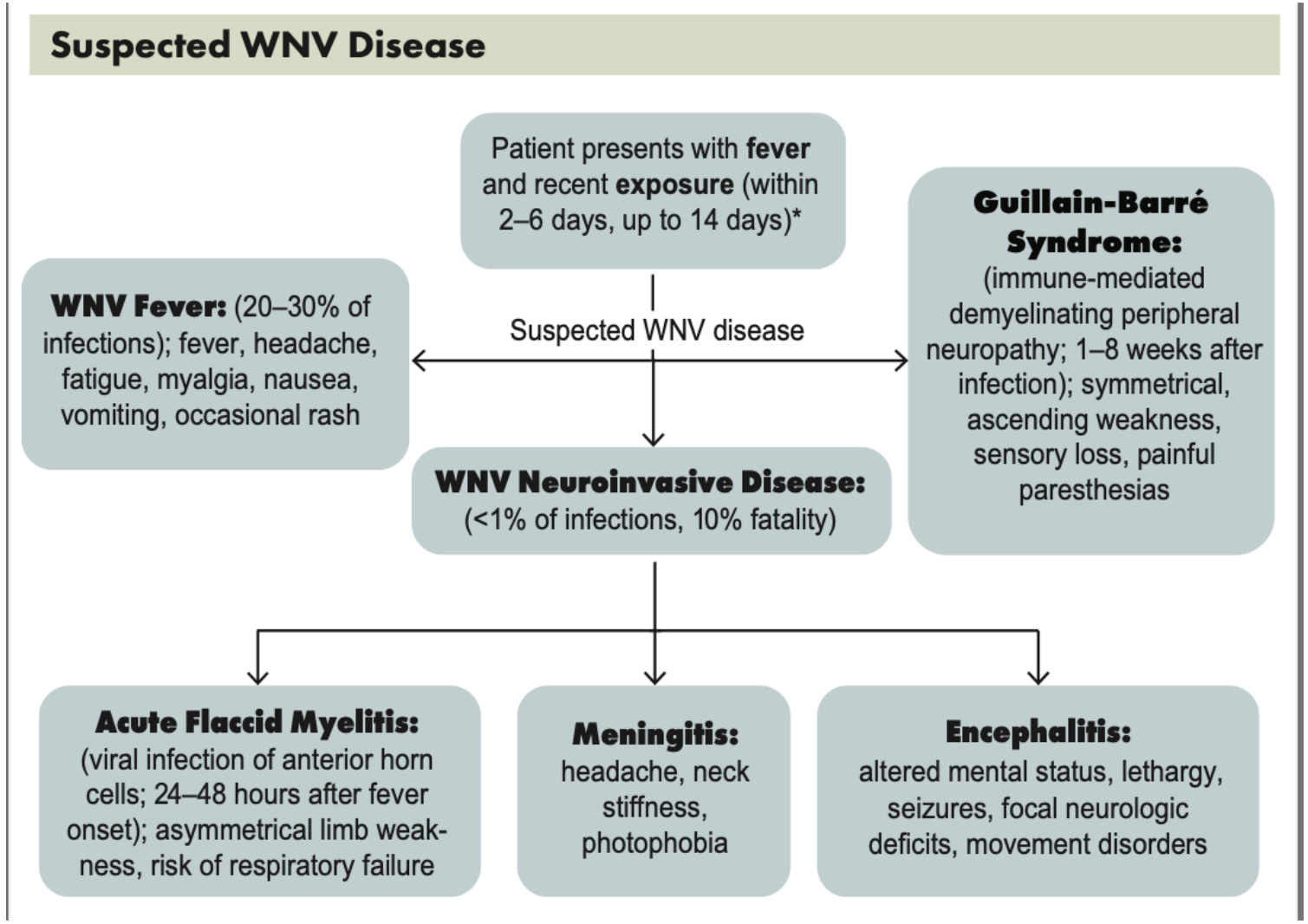
Figure 3. West Nile Virus Clinical Disease Manifestations



Source: https://www.cdc.gov/west-nile-virus/hcp/diagnosis-testing/diagnostic-testing-algorithm.html

Gould CV, Staples JE, Guagliardo SAJ, et al. West Nile Virus: A Review. *JAMA*. 2025

WNV Neuroinvasive Disease

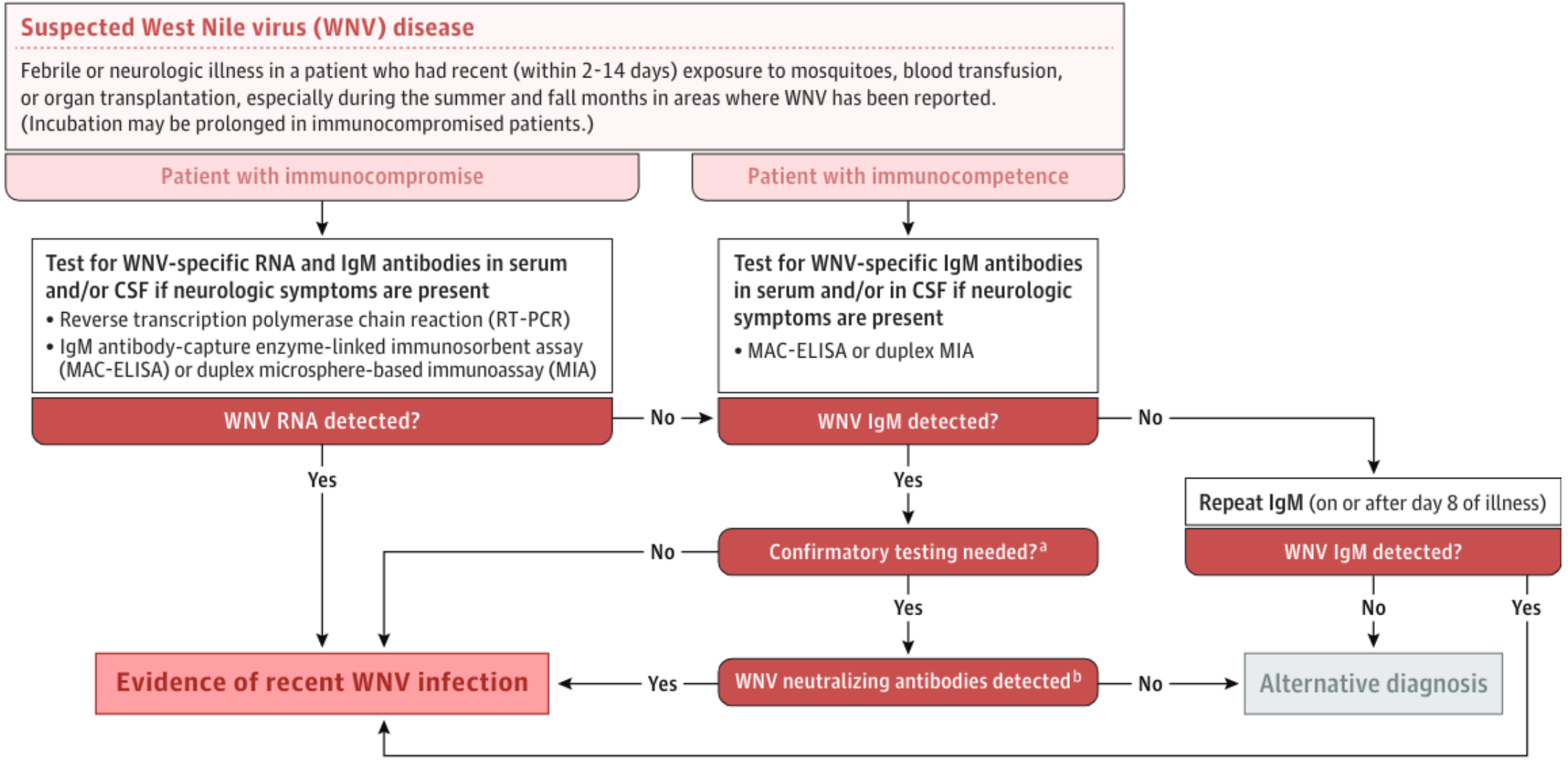


Neuromuscular involvement – poliomyelitis-like syndrome

Encephalitis, meningitis, encephalomeningitis

cdc.gov

WNV Diagnosis



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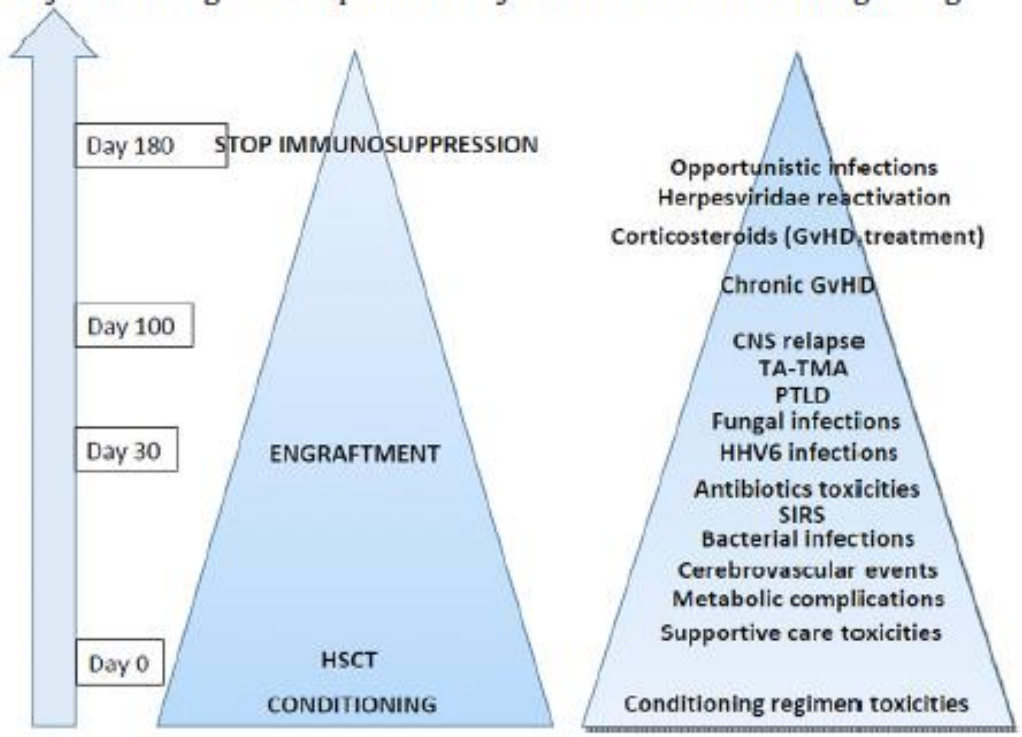
CNS complications in HSCT

Table 1
Categories of CNS Complications

Category	Causative Agents
Drug-related	Calcineurin inhibitors
	Metothrexate
	Cytotoxic agents
	Monoclonal antibodies
	Antibiotics
Metabolic	Hepatic encephalopathy
	Uremic encephalopathy
Infectious	Bacteria
	Viruses
	Fungi
	Protozoa
Cerebrovascular	Hemorrhage
	Ischemic stroke
Immune-mediated	Myositis
	Myasthenia gravis
	Demyelinating diseases
	CNS cGVHD
	CRS

CNS indicates central nervous system; cGVHD, chronic graft versus-host disease; CRS: cytokine release syndrome.

Table 2
Major Neurological Complications by Time of Onset from Allografting



Maffini et al. Neurologic Complications after Alloogeneic Hematopoietic Stem Cell Transplantation 2017.

Treatment

Product	Data	Outcome
Corticosteroids	1) 65 patients (50% received steroids) Multicenter, retrospective, observational 2) Retrospective study, 150 patients	No difference intrahospital mortality, neurologic sequelae at discharge Increased hospital mortality aHR 3.93
Interferon alfa-2b	23 patients Unblinded, randomized	Greater neurologic improvement
Ribavirin	37/233 case series WNV patients received ribavirin	Higher rates of death (41% vs 9%)
High titer WNV neutralizing antibodies (Omr-IgG-am) [Israel] **Or IVIG**	62 patients 3:1:1 (Omr-IgG-am: IVIG: saline) Phase 1/2, randomized, double-blinded, multicenter, placebo-controlled *Not available in US*	No difference in function score or mortality
WNV recombinant humanized monoclonal Ab (MGAWN1)	13 patients Phase 1/2, randomized, double-blinded, placebo--controlled *Not available in US*	2/6 deaths treatment group; 1/7 deaths placebo group Terminated early due to enrollment

Gould CV, Staples JE, Guagliardo SAJ, et al. West Nile Virus: A Review. *JAMA*. 2025.
Gnann et al. Emerging Infectious Diseases. 2019
Poran et al. Journal of Infectious Diseases 2025.

WNV in HSCT from the literature

- 2003 Michigan - 50 yo male ALL s/p MRD HSCT
  - Onset fever and R-sided weakness day +16
  - Donor stem cells WNV RNA negative
  - Progressive encephalitis and death after several weeks
  - CNS tissue on autopsy +WNV

- 2018 Texas – 8 yo male
  - Onset fever day +11
  - Neurologic symptoms day +21, comatose state
  - Repeat CSF on day +30, result WNV PCR positive on day +42
  - Received donor convalescent plasma
  - Died

Reddy et al. Bone Marrow Transplantation, 2004.
Kitagawa et al. Journ of Ped Infect Dis Society, 2018.

Donor versus recipient derived WNV

Risk Factors:

Donor – out of state, unrelated

- WNV PCR performed 10 days prior to stem cell collection
- WNV outbreak in donor area

Recipient

- Symptoms began day +18 from HSCT / hospital day +26
- No known mosquito exposures or travel
- 1 case of WNV in Santa Clara County 2025

Testing:

Donor post-donation data

- WNV IgM and IgG positive
- WNV RNA plasma negative

Stem cell aliquot

- WNV RNA negative (same in DMSO may inhibit PCR)

Blood products

- Pooled samples tested for WNV - negative

Recipient

- Pre-transplant plasma – WNV IgM/ IgG negative
- Post-transplant plasma – WNV IgM

Challenges

- Incubation time of WNV in immunocompromised hosts >14 days
- 10-day window from donor screening WNV PCR to cell collection during peak season
  - protocol within 30 days
- Donor donation anonymous and can not disclose information with the family
- Stem cell aliquot WNV PCR negative, limiting true confirmation
- Rare and devastating outcome for patient and family

Summary

- WNV transmission can occur from solid and bone marrow transplant
- High risk of neuroinvasive disease with WNV in immunocompromised hosts
- Heightened suspicion for WNV in peak season (July through October)
- Window for transmission remains despite appropriate donor screening

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