



West Nile Virus in the United States

History • Epidemiology • Clinical Presentation • Morbidity & Mortality

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What we will cover



History

From a 1937 discovery in Uganda to the 1999 New York outbreak and nationwide spread



Epidemiology

Burden of disease in the US — who gets infected, where, and when



Disease presentation

The clinical spectrum: silent infection, West Nile fever, and neuroinvasive disease



Morbidity & mortality

Hospitalization, long-term sequelae, and case-fatality by age and risk group



Implications

Recognition, supportive care, and prevention counseling

What is West Nile virus?

- A single-stranded RNA flavivirus (family *Flaviviridae*)
- Related to St. Louis encephalitis, Japanese encephalitis, dengue, and Zika viruses
- First isolated in 1937 from a woman in the West Nile district of Uganda
- Caused sporadic outbreaks in Africa, the Middle East, and Europe through the 20th century — severe epidemics in Romania (1996) and Russia (1999) foreshadowed its US arrival
- Now found on every continent except Antarctica

The transmission cycle



Birds

Reservoir — amplify the virus; corvids (crows, jays) are highly susceptible



Culex mosquitoes

Vector — infected by feeding on birds, then bite humans



Humans & horses

Dead-end hosts — viremia too low to infect new mosquitoes

No spread by casual person-to-person contact.

HISTORY

Summer 1999: arrival in New York City

- **August 1999** — a cluster of unusual encephalitis cases in Queens, NY
- Simultaneously, crows were dying in unusual numbers and exotic birds died at the Bronx Zoo
- Initially misdiagnosed as St. Louis encephalitis; a zoo veterinary pathologist's persistence linked the bird deaths to the human outbreak
- The virus was genetically nearly identical to a strain circulating in Israel — the first time WNV had ever been found in the Western Hemisphere
- How it crossed the Atlantic is still unknown — an infected bird, mosquito, or traveler

1999, NEW YORK CITY

62

reported cases in the first US outbreak

7

deaths — mostly older adults with encephalitis

First WNV detection in the Western Hemisphere



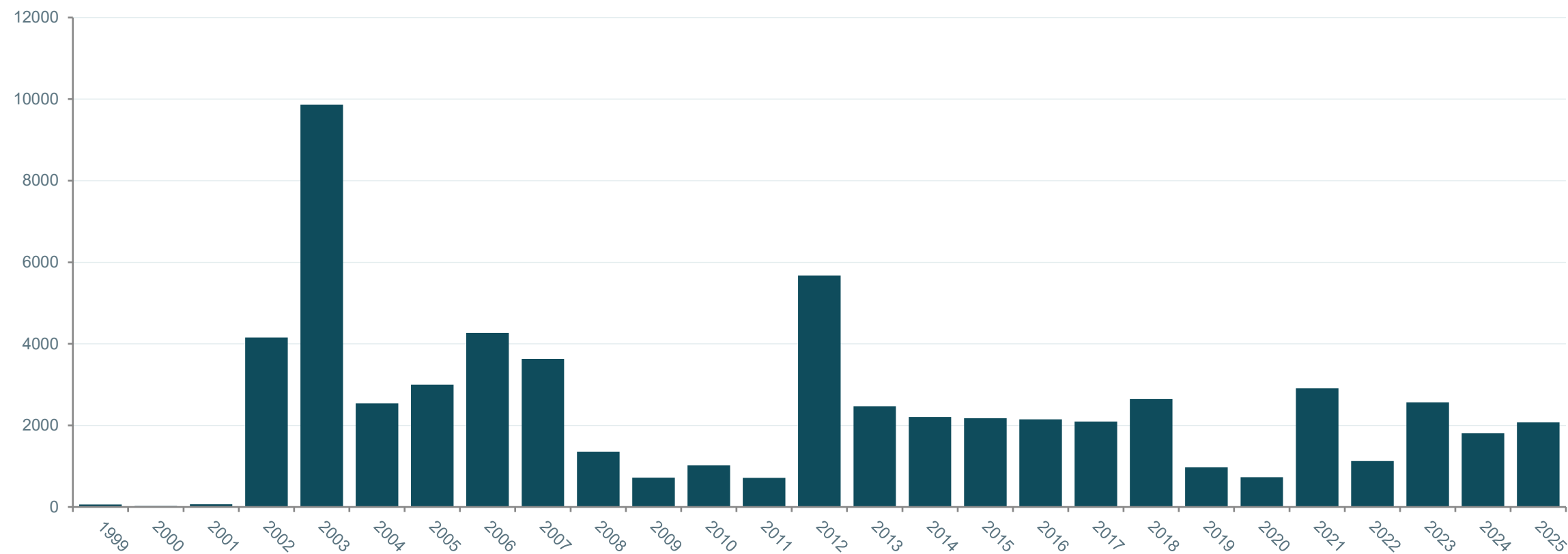
HISTORY

Coast to coast in five years



Why so fast? Abundant susceptible birds, competent *Culex* mosquitoes nationwide, and no pre-existing human or avian immunity in the Americas.

Reported WNV disease cases by year, 1999–2025



Peak years: 2003 (9,862 cases) and 2012 (5,674 cases — deadliest year, 286 deaths). Since 2004, WNV has been endemic, with a 10-year median of ~2,200 cases per year. 2025 count is preliminary.

The US burden at a glance

#1

Most common mosquito-borne disease in the continental United States

≈60,000

Reported cases since 1999 — including ~30,000 neuroinvasive cases

≈3,000

Deaths reported since 1999

Millions

Estimated total infections — CDC estimates ~7 million+, since ~80% are never recognized

No licensed human vaccine and no specific antiviral treatment exist — **surveillance, mosquito control, and personal protection remain the only defenses.**

Who, where, and when



When

- **Peak season July–September**
- 84% of cases have onset in these three months
- Transmission possible May–November; longer in warm climates



Where

- **All 48 continental states report cases**
- Highest incidence: Great Plains & Mountain West (e.g., ND, NE) and parts of the South (MS)
- Largest case counts recently: TX, CA, CO, IL — Texas alone had 40% of neuroinvasive cases in 2024



Who

- **Median age of cases: 64 years**
- About two-thirds of reported cases are men (outdoor exposure)
- Incidence rises steeply with age — highest in adults ≥ 70 , lowest in children

How people get infected



The bite of an infected mosquito

Nearly all human infections. Culex species feed from dusk to dawn and breed in standing water — birdbaths, gutters, buckets, storm drains.

Rare, non-mosquito routes



Blood transfusion

US blood supply screened since 2003 — risk now extremely low



Organ transplantation

Recognized since 2002; recipients can develop severe disease



Mother to child

Transplacental, perinatal, and possibly via breast milk — all very rare



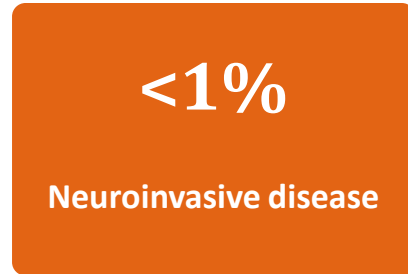
Occupational

Percutaneous exposure in laboratory workers

Not spread by touching, kissing, coughing, or caring for an infected patient — standard precautions suffice.

The clinical spectrum of infection

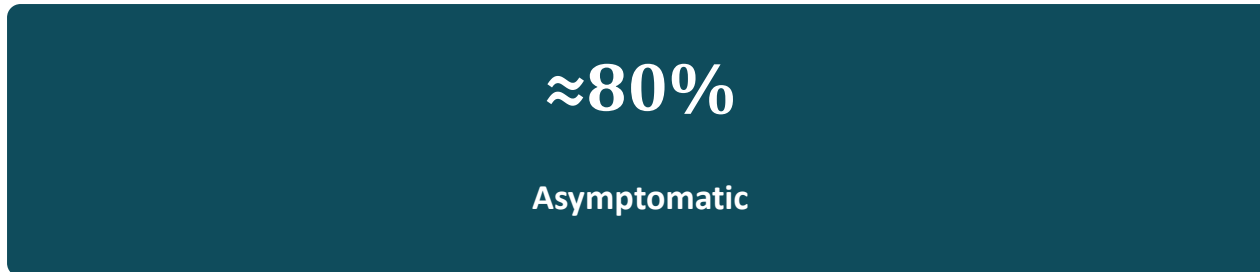
Severity ▲



About 1 in 150 infections — meningitis, encephalitis, or acute flaccid myelitis



About 1 in 5 infections — febrile illness, usually self-limited



Most people never know they were infected

West Nile fever: the typical illness



Incubation

2–6 days

typical (range 2–14 days; longer if immunocompromised)

Abrupt onset; illness usually lasts under a week, but fatigue and weakness can linger for weeks to months.

Common signs & symptoms

- Fever, chills
- Headache (often frontal)
- Marked fatigue, malaise
- Myalgias and arthralgias
- Nausea, vomiting, diarrhea
- Transient maculopapular rash (trunk/limbs)
- Eye pain, photophobia
- Lymphadenopathy (occasional)

Nursing pearl: WNV fever mimics 'summer flu.' In July–September, ask about mosquito exposure and time outdoors — especially in older adults with fever and profound fatigue.

Neuroinvasive disease: three syndromes



WNV meningitis

- Fever, severe headache
- Nuchal rigidity, photophobia
- Similar to other viral meningitides
- Best prognosis of the three



WNV encephalitis

- Altered mental status, confusion
- Tremor, myoclonus, parkinsonism
- Seizures possible
- More common in older adults; drives most deaths



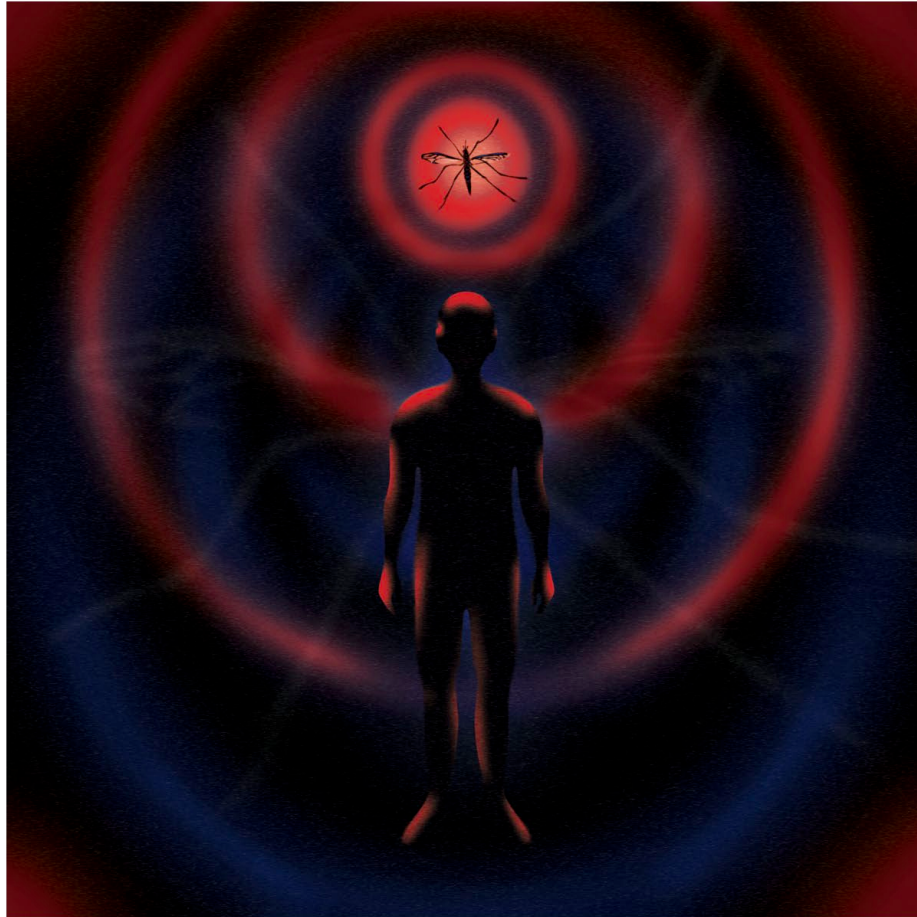
Acute flaccid myelitis

- Sudden asymmetric limb weakness or paralysis
- Polio-like anterior horn cell injury
- Absent reflexes; sensation often preserved
- Can cause respiratory failure requiring ventilation

Syndromes overlap — many patients have features of more than one. Suspect neuroinvasive WNV in any acute febrile neurologic illness in summer or fall.

Anthony Fauci: A Mosquito in My Backyard Made Me the Sickest I've Ever Been

Oct. 7, 2024



- Severe fatigue
- Fever 103°F
- Delirium
- Spent 5 days in hospital
 - Initially diagnosed as sepsis
 - Discharged on antibiotics
- Extreme weakness and affected cognition
- Recovery over weeks

Morbidity: the long shadow of WNV

77%

of reported cases were
hospitalized (2024)

91%

of neuroinvasive cases were
hospitalized (2024)

>50%

of neuroinvasive patients report
symptoms beyond 1 year

30–40%

of hospitalized patients need
ongoing/facility care at discharge

Common long-term sequelae

- Persistent fatigue, weakness, and myalgias
- Cognitive impairment — memory, concentration, processing speed
- Depression and other mood changes
- Tremor, movement disorders, and residual limb paralysis after myelitis



Recovery from neuroinvasive disease is often measured in months to years — many patients need rehabilitation, home services, or long-term care.

Mortality: who dies of West Nile virus?

≈10%

case-fatality in neuroinvasive disease overall

≈2%

in neuroinvasive patients under age 50

≈20%

in neuroinvasive patients aged 70 and older

30–40%

with hematologic cancer or transplant-related immunosuppression

- ≈3,000 deaths reported in the US since 1999
- 2024: 173 deaths (9.6% of reported cases); nearly all deaths occur in neuroinvasive disease
- Deadliest years: 2012 (286 deaths), 2002 (284), 2003 (264)
- Death after uncomplicated West Nile fever is rare

Risk factors for severe disease



Age over 60

The single strongest risk factor — risk climbs each decade



Immunosuppression

Transplant recipients, chemotherapy, biologics, advanced HIV



Cancer

Especially hematologic malignancies



Chronic conditions

Diabetes, hypertension, chronic kidney disease



Transplant-transmitted infection

Severe disease in a majority of infected recipients



Outdoor exposure

Work or recreation outside at dusk/dawn in season increases infection risk

Diagnosis



Think WNV when...

Unexplained fever, meningitis, encephalitis, or acute flaccid paralysis in summer–fall, especially with mosquito exposure.

- **WNV IgM antibody in serum or CSF is the mainstay of diagnosis**
- IgM appears 3–8 days after symptom onset — an early negative doesn't rule it out; repeat testing may be needed
- IgM persists 30–90 days (sometimes longer) — a positive can reflect earlier infection
- **CSF in neuroinvasive disease: lymphocytic pleocytosis with elevated protein, normal glucose**
- Cross-reactivity with other flaviviruses (dengue, Zika, SLE, vaccines) — confirmatory neutralization testing (PRNT) via public health labs
- RT-PCR has low sensitivity in immunocompetent patients (brief viremia) but is useful in the immunocompromised
- MRI may show thalamic/basal ganglia or spinal cord changes, but is often normal early

Treatment and management



Supportive care only

- **No specific antiviral therapy and no licensed human vaccine**
- Antipyretics and analgesia; IV fluids for poor intake
- Airway protection and ventilatory support for encephalitis or flaccid paralysis
- Seizure management; prevention of secondary infections and pressure injuries
- Early PT/OT and rehabilitation planning

Priorities

- **Serial neuro checks — trend mental status, new weakness, swallow function**
- Respiratory monitoring in myelitis: vital capacity, work of breathing
- Fall and aspiration precautions; safe mobility with weakness and tremor
- Standard precautions only — no isolation needed
- Arboviral disease is nationally notifiable — ensure cases are reported to public health
- Support and educate families: recovery is slow; connect them with rehab resources

Prevention: what we teach patients



Use EPA-registered repellents

DEET, picaridin, IR3535, or oil of lemon eucalyptus — safe for pregnant and breastfeeding women when used as directed



Cover up

Long sleeves and pants outdoors; treat clothing/gear with permethrin



Time it right

Culex mosquitoes bite dusk to dawn — extra caution during evening hours



Dump standing water weekly

Buckets, planters, birdbaths, gutters, tires — mosquitoes breed in a bottle cap of water



Mosquito-proof the home

Intact window/door screens; air conditioning when available



Community measures

Report dead birds; support local mosquito surveillance and control programs

With no vaccine and no antiviral, prevention counseling is the highest-impact intervention we have — and nurses deliver it best.

A human vaccine candidate: rWN/DEN4Δ30

- **A live, attenuated chimeric vaccine**
- The prM and envelope (E) genes of WNV strain NY99 are inserted into a dengue-4 virus backbone (DEN4Δ30)
- **Attenuated two ways:**
 - 1) Chimerization with non-neuroinvasive dengue-4 virus
 - 2) A 30-nucleotide deletion in the 3' untranslated region
- In monkeys: highly neuro-attenuated (more so than the yellow fever 17D reference) and poorly transmissible by geese and Culex/Aedes mosquitoes

Pierce et al., J Infect Dis 2017 — Phase 1 trial

28 flavivirus-naïve adults aged 50–65 — the group at highest neuroinvasive risk — given a single 10^4 PFU subcutaneous dose

95%

seroconverted after a single dose (by day 90)

1 dose

appeared sufficient — no antibody boost from a 2nd dose

360 d

neutralizing antibody still detectable at one year

Safe

well tolerated; no neuroinvasive illness or serious vaccine-related events

Vaccines for horses — and the human gap



The horse story

- Horses, like people, are dead-end hosts but can develop severe, often fatal WNV encephalitis
- **A live yellow fever 17D–West Nile chimeric vaccine ('PreveNile')**
- Built on the yellow fever 17D vaccine backbone carrying WNV NY99 prM/E genes — the same chimeric strategy as the human candidate
- USDA-licensed in 2006 as a single-dose equine vaccine; voluntarily recalled in 2010 after serious adverse events, including some deaths in vaccinated horses

Where things stand

- **Horses today: four USDA-licensed WNV vaccines**
- Inactivated whole-virus, a recombinant canarypox-vectored vaccine, and an inactivated flavivirus (yellow fever) chimera
- **Humans: still no licensed vaccine**
- Several candidates — chimeric (rWN/DEN4Δ30, ChimeriVax-WN02), DNA, and inactivated — have looked safe and immunogenic, but none has completed licensure
- A small, unpredictable market and the large trials needed to prove efficacy are major hurdles

For now, human protection still rests on mosquito avoidance — not immunization.

KEY TAKEAWAYS

Five things to remember

1

WNV arrived in New York in 1999 and became endemic nationwide within five years — it is now the leading mosquito-borne disease in the continental US.

2

Roughly 60,000 reported cases and ~3,000 deaths since 1999 — with millions more infections never diagnosed.

3

80% of infections are silent, ~20% cause febrile illness, and <1% become neuroinvasive — meningitis, encephalitis, or polio-like paralysis.

4

Age and immunosuppression drive severity: neuroinvasive case-fatality is ~10% overall but ~20% in patients 70+, and long-term sequelae are common.

5

No licensed human vaccine or antiviral exists — though candidates like rWN/DEN4Δ30 are promising — so recognition, supportive nursing care, and prevention counseling are what matter now.



FOR FURTHER READING

Sources and resources

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- Pierce KK, et al. A Live Attenuated Chimeric West Nile Virus Vaccine, rWN/DEN4Δ30, Is Well Tolerated and Immunogenic in Flavivirus-Naive Older Adult Volunteers. J Infect Dis 2017;215:52–55.
- Amanna IJ, Slifka MK. Current trends in West Nile virus vaccine development (equine YF-WN chimera / PreveNile). Expert Rev Vaccines 2014;13:589–608.
- VDCI. 2025 Mosquito-Borne Disease Year in Review (preliminary 2025 season data).

Patient education handouts: CDC's 'Fight the Bite' materials and state health department mosquito-prevention resources are free to print and share.

<https://www.cdc.gov/vector-borne-diseases/fight-the-bite/index.html>