

Emerging Clinical Syndromes of West Nile Virus Infection

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West Nile Virus—Clinical Disease

- **Historically infrequent outbreaks of mild febrile illness**
- **Since 1996:**
 - **More frequent outbreaks**
 - **More reports of severe CNS disease, fatalities**
- **Understanding of clinical picture based mainly on recent outbreaks**

WNV Human Infection “Iceberg”

1 CNS disease case
=
~150 total infections

<1%
CNS
disease

~10% fatal
(<0.1% of total infections)

~20%
“West Nile Fever”

Very crude
estimates

~80%
Asymptomatic

West Nile Virus—“Classical” Clinical Description

- Incubation period of 2-15 days
- Most illness: “West Nile fever”
 - Self-limited dengue-like illness
 - Fever, headache
 - Rash, lymphadenopathy
 - Nausea, vomiting
- Rarely pancreatitis, hepatitis, myocarditis

West Nile Virus—“Classical” Clinical Description

- Severe neurologic illness categories
 - **Meningitis**
 - Fever, nuchal rigidity, CSF pleocytosis
 - **Encephalitis**
 - Altered mental status
 - **“Meningoencephalitis”**
 - **Acute flaccid paralysis**

WNV—Clinical Questions

- **Limitations of previous analyses**
 - **Retrospective chart reviews**
 - **Multiple observers**
 - **Incomplete and inconsistent studies**
 - **Long-term outcome data virtually nonexistent**
- **True spectrum of disease unclear**

WNV Clinical Investigations--2002

- **Prospective clinical case series**
 - Detailed serial neurologic exams
 - 16 patients identified
- **WNV Fever Study**
- **Detailed neurodiagnostic studies on large numbers of patients**
- **House-to-house serosurvey**



Clinical Syndromes—Understanding the Scope of Illness

- West Nile fever
- Emerging clinical syndromes
 - Movement disorders
 - Parkinsonism
 - Flaccid paralysis
 - Rhabdomyolysis
- Outcomes / prognosis
- Future directions



West Nile Fever

- Felt to represent the majority of symptomatic infections
- Determination of proportion with WNF in WNV outbreak setting
- Subacute progression to severe CNS disease unlikely
- Increased detection—fewer cases truly asymptomatic??

WNV and Movement Disorders

- Tremor
 - Sometimes associated with other viruses
 - Documented in 15 (94%) of prospective series patients
 - Static / kinetic; sometimes with movement
 - Occasionally disabling



WNV and Movement Disorders

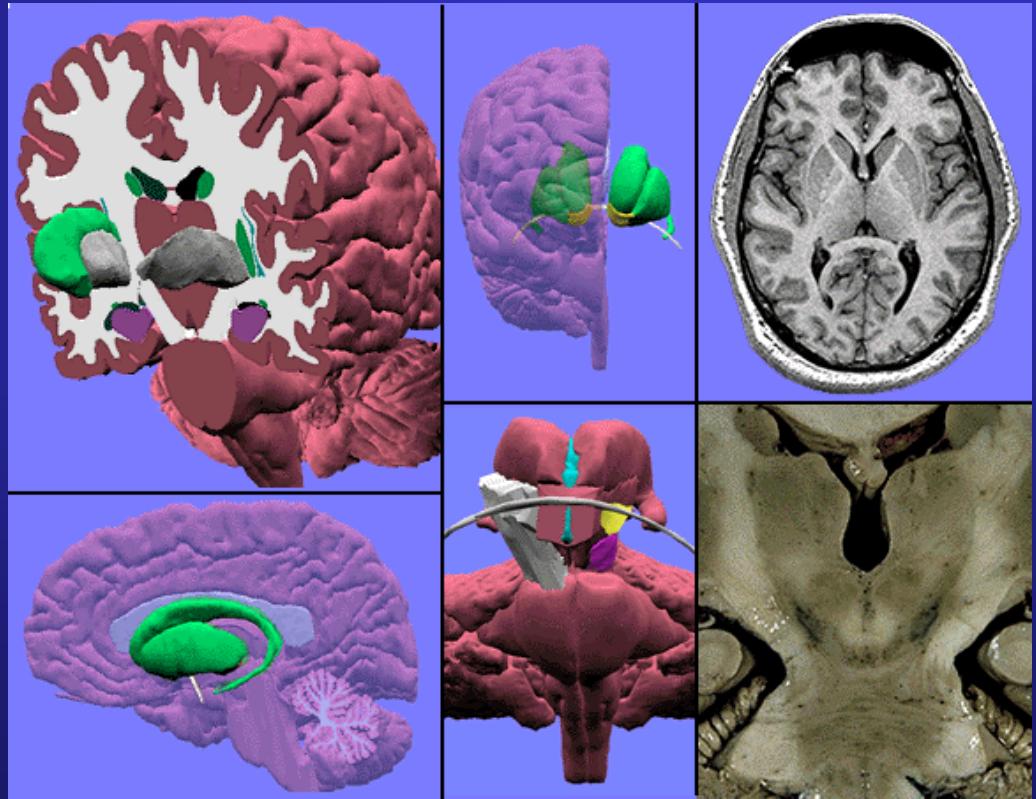
- **Myoclonus**
 - Observed in 10 (63%); described in 12 overall
 - Upper extremity, facial involvement most frequent
 - Nocturnal myoclonus
- Both tremor and myoclonus—onset generally > 5 days following initial symptoms

WNV and Parkinsonism

- **Parkinsonism observed in 11 (68%)**
 - **Cogwheel rigidity**
 - **Bradykinesia**
 - **Postural instability**
- **Rest tremor not observed**
- **Seen both in encephalitis and meningitis cases**

WNV and Movement Disorders

- **Neuroimaging:** lesions in basal ganglia, thalamus, pons
- **Histopathology—**virus detected in basal ganglia, thalamus, brainstem



WNV-Associated Flaccid Paralysis

- Previously described; not “new” syndrome
- Relatively young; lack of premorbid conditions
- May have absence of fever, headache
- Clinical hallmarks:
 - Onset during acute infection
 - Asymmetry of weakness
 - Absence of sensory changes
 - Elevation of CSF protein and WBC

WNV-Associated Flaccid Paralysis

- Multiple alternative diagnoses (stroke, GBS, myopathy)—Rx with heparin, IVIG
- Syndrome actually localized to spinal anterior horn cells*—resultant poliomyelitis
- Recognition could limit unnecessary diagnostic procedures, treatment
- Little or no improvement short-term
 - *Dr. A. Leis, Methodist Rehab. Center, Jackson, MS

WNV and Rhabdomyolysis

- *Rhabdomyolysis*—acute destruction of skeletal muscle cells
- Infrequent manifestation of viral infection
- September 2002—rhabdomyolysis reported in Chicago WNV patients
- 14 total cases identified
- Trauma, medication effect unlikely
- Further studies to assess association

West Nile Virus--Other Clinical Syndromes (?)

- Flaccid paralysis with sensory symptoms
 - Neuropathic pain
 - Causalgia
 - Paresthesias
- Peripheral neuropathy, polyradiculopathy
- Optic neuritis
- Acute demyelinating encephalomyelitis (ADEM)
- Prenatal WNV infection with CNS developmental abnormalities
 - WNV as a teratogen?

West Nile Virus—Clinical Outcomes Data

- **Current data limited**
- **Fatality rates**
 - **10% fatality rate in CNS disease**
 - **Elderly, immunosuppressed**
 - **Independent risk factors unknown**
- **Long-term outcomes in NYC:**
 - **>50% with continued impairment at 1 year**
 - **Only 37% considered fully recovered**

West Nile Virus—Clinical Outcomes Data

- **Short-term prospective data**
 - **No deaths**
 - **Most patients (14/16; 88%) eventually went home**
- **Follow-up telephone query data**
 - **Persistent / chronic headache**
 - **Concentration, memory difficulties**
 - **Overwhelming fatigue**
 - **Persistence of tremor, parkinsonism**
- **Paralysis—no short-term improvement**

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WNV Human Infection “Iceberg” Revisited

1 CNS disease case
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~?? total infections

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~10% fatal
(<0.1% of total infections)

~?%
“West Nile Fever”

Febrile illness alone
less frequent?

~80%
Asymptomatic

WNV Clinical Syndromes—Future Directions

- **Surveillance for meningitis, encephalitis as distinct entities**
- **Enhanced surveillance for flaccid paralysis; incidence rates**
- **Population-based assessment of movement disorders, parkinsonism**
- **Long-term follow up studies**
 - **persistence of symptoms**
 - **psychosocial outcomes**
 - **development of sequelae**



WNV--Outcomes

- **Short-term prospective data**
 - Of 8 encephalitis patients, 6 went home, 1 to SNF, 1 on chronic ventilation
 - All meningitis patients discharged home
- **Follow-up call data**
 - Persistent / chronic headache
 - Concentration, memory difficulties
 - Overwhelming fatigue
 - Persistence of tremor, parkinsonism
- **AFP—no short-term improvement**

West Nile Fever (WNF)

- **Subacute progression to severe CNS disease unlikely**
 - **Development of meningitis / encephalitis /paralysis within 24-48 hours of fever onset**
 - **No subsequent hospitalization among fever outpatients**