West Nile Virus

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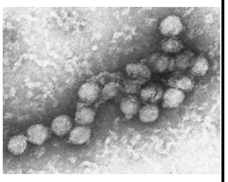
Case

- 51-year-old woman presents to clinic in August
- Recently returned from hiking with her family one week ago
- Fevers, abdominal pain, nausea/vomiting x 4d
- Myalgia, arthralgia, headache
- Recently resolved non-itchy rash
- Physical exam otherwise unremarkable
- Influenza and RSV PCR - negative, HIV PCR negative, EBV negative, etc.
- Blood and urine cultures negative

West Nile Virus (WNV)

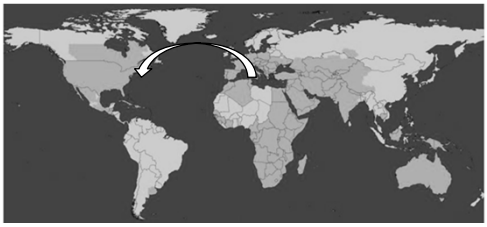
- Flavivirus
  - Japanese Encephalitis serogroup
  - Closely related to St. Louis Encephalitis Virus
- Mosquito-borne (arbovirus)
- First case:
  - Febrile woman
  - West Nile district of Uganda
  - 1937
- Sporadic outbreaks



Source: CDC/P.E. Rollin
Photo Credit: Cynthia Goldsmith

Emergence in the U.S.

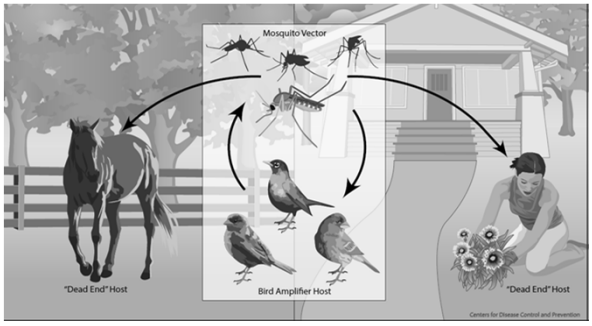
Source: CDC



- October 1999 - CDC MMWR reports outbreak of human arboviral encephalitis in NYC
- Similar to strain circulating in Israel and Tunisia
- New infectious disease emerged in the U.S.

Outbreak of West Nile-like viral encephalitis - New York, 1999.MMWR Morb Mortal Wkly Rep1999;48:845-9.

Epidemiology - Transmission



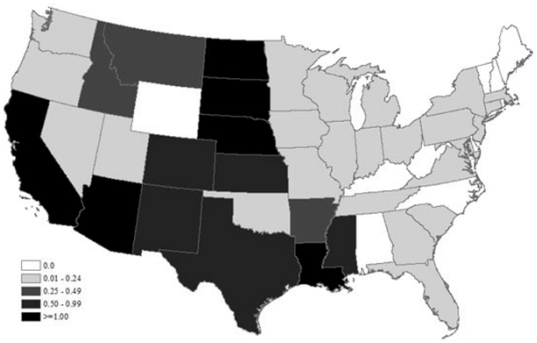
Source: CDC

- Mosquito vector: *Culex pipiens*
- Reservoir: Birds (esp. crows, ravens, jaybirds)

Epidemiology - Transmission

- Mosquito-borne
  - Seasonality: May - October
  - Weather patterns may affect outbreaks
- Blood transfusion
- Organ/Tissue transplants
- Transplacental
- Breastfeeding

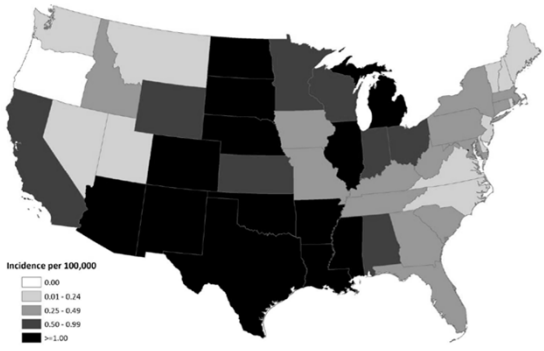
2014 Neuroinvasive Disease Cases



Reported to ArboNET

Source: CDC

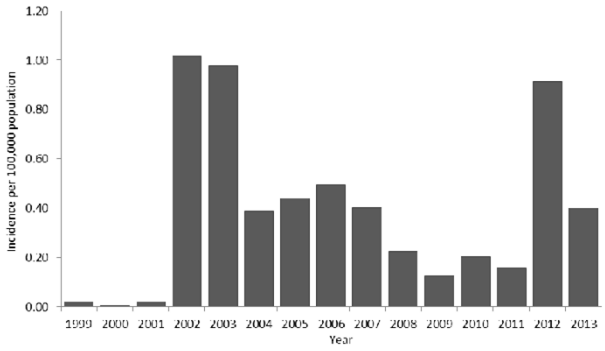
2012 Neuroinvasive Disease Cases



Reported to ArboNET

Source: CDC

West Nile virus neuroinvasive disease incidence reported to CDC by year, 1999-2013



Source: ArboNET, Arboviral Diseases Branch, Centers for Disease Control and Prevention

Incidence 2002-2013 (with 2014 cases)

Source: Ohio Department of Health
Data as of 02/02/2015

2001 - 2014 Ohio WNV

Human Case Statistics

Year	Human Cases	Deaths	Median Age	Age Range of Cases	Earliest Date of Symptom Onset	Asymptomatic Blood Donors
2001	0	0	n/a	n/a	n/a	n/a
2002	441	31	61	2 - 98 years	n/a	n/a
2003	108	8	49	11 - 90 years	n/a	6
2004	12	2	49.5	12 - 87 years	5-Jul	1
2005	61	2	53	22 - 96 years	14-Jun	14
2006	48	4	57.5	2 - 86 years	1-Aug	10
2007	23	3	52	11 - 86 years	12-Jul	9
2008	15	1	57	20 - 86 years	9-Jul	1
2009	2	0	36.5	11 - 62 years	27-Aug	0
2010	5	0	46	4 - 74 years	9-Jul	0
2011	21	1	55	14 - 83 years	1-Aug	6
2012	122	7	57.5	4 - 91 years	10-Jul	13
2013	24	4	71.5	38 - 82 years	29-Jul	4
2014	11	1	65	19 - 79 years	27-Jul	0
AVG	64	5	55	n/a	n/a	5
TOTAL	893	64	n/a	n/a	n/a	64

Source: Ohio Department of Health
Data as of 01/13/2015

WNV Infection

- **Incubation period: typically 2-6 days (range 2-14 days)**
- **70-80% subclinical or asymptomatic**
- **~20% experience flu-like illness**
- **<1% experience neuroinvasive disease**

- **Febrile and Meningitis cases**
  - **Fatigue, Headache, etc. may last weeks to months**
- **Encephalitis and poliomyelitis**
  - **Potential for long-term neurologic sequelae**

CDC. West Nile virus disease and other arboviral diseases—United States, 2012. MMWR 2013;62:513–7.

Case

- 70-year-old man w/HTN, CAD
- Presents in July with mild-mod headache and subtle personality changes
- CSF pleocytosis (419 cells/μL), lymphocyte predominance (66%), increased protein (93 mg/dL), and normal glucose (69 mg/dL)
- Fever and worsening MS requiring intubation

Adapted from: Flores EM, Hadeel Zainah A, Ouellette DR, and Johnson LE. Two Case Reports of Neuroinvasive West Nile Virus Infection in the Critical Care Unit. Case Reports in Infectious Diseases, vol. 2012, Article ID 839458, 4 pages, 2012.

Case

- MRI: chronic ischemic changes and nonspecific signals within the middle cerebellar peduncle bilaterally.
- Eleven days later, WNV IgM positive in the CSF (titers of 1:8) → WNV encephalitis.
- 40 day ICU stay with residual left-sided weakness and near-complete improvement in his mental status.

Adapted from: Flores EM, Hadeel Zainah A, Ouellette DR, and Johnson LE. Two Case Reports of Neuroinvasive West Nile Virus Infection in the Critical Care Unit. Case Reports in Infectious Diseases, vol. 2012, Article ID 839458, 4 pages, 2012.

Non-Neuroinvasive Disease

- Acute systemic febrile illness
  - Headache
  - Weakness
  - Myalgias
  - Arthralgia
  - Lymphadenopathy
  - GI symptoms
  - Transient maculopapular rash
- Self-limiting
- Some symptoms may linger weeks-months

Neuroinvasive Disease

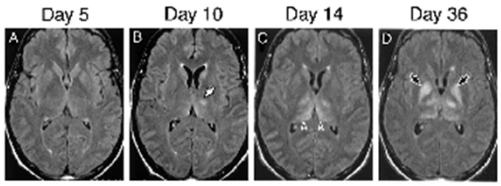
- Meningitis
  - Clinically indistinguishable from other viral meningitis etiologies
  - Fever
  - Headache
  - Nuchal Rigidity

CSF studies:

WBC	Elevated
Early	Neutrophilic
Late	Lymphocytic
Glucose	Normal
Protein	Elevated

Neuroinvasive Disease

- Encephalitis
  - Fever
  - AMS
  - Seizures
  - Focal neuro deficits
  - Tremor
  - Parkinsonism



Gea-Banacloche J, Johnson RT, Bagic A, et al. West Nile virus: pathogenesis and therapeutic options. Ann Intern Med 2004; 140:545.

Neuroinvasive Disease

- Acute Flaccid Paralysis
  - Clinically identical to poliomyelitis
    - Absent DTRs
    - Intact sensation
  - May progress to respiratory failure
  - MRI: Anterior spinal cord signal abnormalities

- Mortality:
- About 10% with neurologic disease

Case

- August 2012, man with NHL admitted for chemo & auto SCT
- Screened for subclinical infections – all negative
- 10 days after SCT: GI complaints, fever, hypotension
- 20 days after SCT: developed AMS, somnolence, resp failure
- CSF: elevated glucose (103 mg/dL) and normal protein (44 mg/dL) with two white blood cells/mm3.
- CSF culture, gram stain, AFB, HSV, Crypto, HHV6, VZV, BK virus, JC virus → all negative

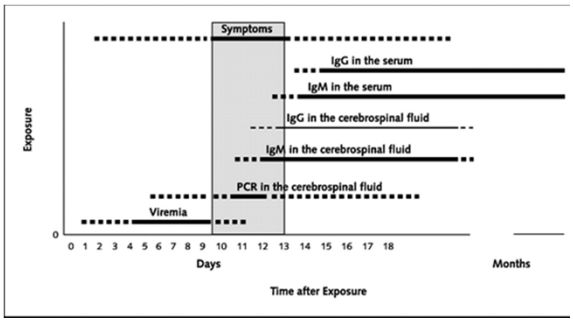
Case adapted from: CDC. Fatal West Nile virus infection after probable transfusion-associated transmission--Colorado, 2012. MMWR Morb Mortal Wkly Rep 2013; 62:622.

Case

- WNV not done
- MRI: meningeal and cortical changes consistent with inflammation
- Pt expired
- Postmortem showed diffuse encephalitis, WNV IgM positive on serum, PCR positive on brain and spinal cord tissue

Case adapted from: CDC. Fatal West Nile virus infection after probable transfusion-associated transmission--Colorado, 2012. MMWR Morb Mortal Wkly Rep 2013; 62:622.

Diagnosis



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Management

- Treatment is supportive
- Encephalitis: follow closely for elevated ICP and seizures
- Respiratory failure in poliomyelitis patients may develop rapidly

Prevention

- Vaccines available for prevention of equine WNV infection
- No vaccines licensed for human use.
- Mosquito control programs
- Reporting dead crows and bluejays
- Personal protection

Preparing for equine vaccination in Costa Rica, 2010.
Source: Wikimedia Commons

The 5 D's of Mosquito Control

- Drain or Dump mosquito
- Dress
- DEET
- Doors
- Dawn and Dusk

Culex pipiens mosquito
Source: Wikimedia Commons

Chikungunya

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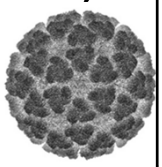
Chikungunya virus (CHIKV)

- RNA virus, *Alphavirus* genus
  - Two envelope glycoproteins (E1 and E2)
- First isolated in 1953 in Tanzania
  - Name means "that which bends up"
- Mosquito-borne
  - Enzootic
  - Mosquito-human-mosquito cycle



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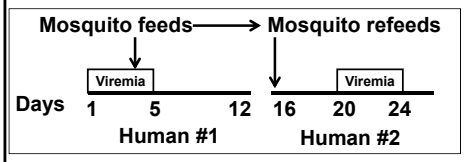
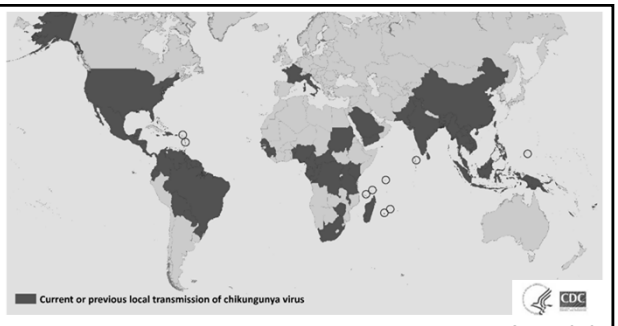


Adapted from: Preparedness and Response for Chikungunya Virus Introduction in the Americas. CDC/PAHO 2011



Source: CDC

Epidemiology

- Asian Lineage
  - Primarily transmitted by *Aedes aegypti*
- Indian Ocean Lineage
  - Adapted to *Aedes albopictus*
    - Mutation in E1 and E2 envelope glycoprotein genes

Arrival in the Americas

- Active CHIKV circulation in Saint Martin
  - October 2013
- Asian Lineage strain
  - Not efficiently transmitted by *Ae. albopictus*

Source: Wikimedia Commons

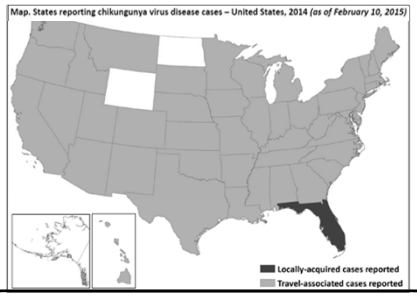
Source: Wikimedia Commons

- Local transmission in 44 countries or territories
- 1.3 million suspected cases
  - Greatest number of cases in Dominican Republic, Colombia, and El Salvador

Source: CDC
Data as of April 10, 2015

Transmission in the US

- July 2014
  - First cases of transmission within the continental US
- 2,492 cases of reported in US in 2014
  - 11 locally transmitted cases



Source: CDC
Data as of
April 10, 2015

Prospects for Spread

Aedes aegypti

Source: CDC
Photo Credit: Paul I. Howell, MPH

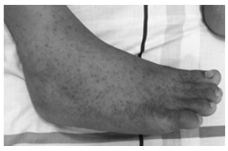
Aedes albopictus

Source: CDC
Photo Credit: Paul I. Howell, MPH

Source: CDC

Acute Infection

- Acute onset of high fever (>39° C) with severe joint pain
  - Headache and rash also common
- Incubation period about 3 – 7 days
  - Fever onset associated with viremia
- Acute phase lasts approximately 1 week



Source: Wikimedia Commons
Photo Credit: 2012-01-09 Chikungunya on the right feet at The Philippines" by Nsaa

Symptom or Sign	Frequency Range (% of Symptomatic Pts)
Fever	76-100
Polyarthralgias	71-100
Headache	17-74
Rash	28-77
Myalgias	46-72
Back Pain	34-50
Nausea	50-69
Vomiting	4-59
Polyarthritis	12-32
Conjunctivitis	3-56

Table adapted from: Preparedness and Response for Chikungunya Virus Introduction in the Americas. CDC/PAHO 2011

Acute Infection

- High morbidity, low mortality
  - ~ 80% develop significant symptoms
  - Significant economic effects
- Complications
  - Mortality rate 0.3 to 1%
  - Newborns, elderly, and comorbid medical conditions
  - Encephalopathy/encephalitis, myocarditis, hepatitis, multi-organ failure
  - Vertical transmission (~50% transmission rate)

Chikungunya vs Dengue

Clinical Signs	Chikungunya	Dengue
Fever	Common	Common
Rash	Day 1–4	Day 5–7
Retroorbital Pain	Rare	**Common**
Arthralgia	**Consistent**	Rare
Arthritis	**Common**	Absent
Myalgia	Common	Common
Tenosynovitis	**Common**	Absent
Hypotension	Possible	**Common**
Minor Bleeding	Rare	**Common**
Outcome	Arthralgia for months to years	Possible fatigue for weeks
Thrombocytopenia	Early and mild	Delayed and possibly **severe**

Table adapted from: Curr Infect Dis Rep 2011;13:218-228

Chronic Disease

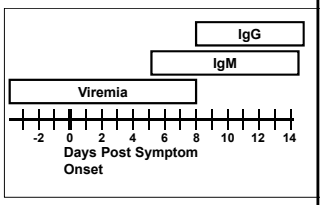
Subacute (2 to 3 months)
- **Symptom relapse after initial improvement**
- **Polyarthritis, tenosynovitis, Raynaud's**
- **Depression, fatigue, weakness**

Chronic (> 3 months)
- **15 to 50% of patients**
- **Distal polyarthritis and tenosynovitis**
  - **Previously injured joints and bones**
- **Occasionally develop a destructive arthritis**
  - **Rheumatoid arthritis-like polyarthritis**
- **Fatigue, depression, and loss of quality of life**

Diagnosis

Acute Infection
- **Frequently a clinical diagnosis**
- **Serum PCR**
- **Acute and convalescent serology**
  - **IgM positive after 5 days**
  - **4-fold increase in convalescent IgG**

Chronic Disease
- **Serology**
  - **IgM can persist for months**
- **IgG levels and persistence correlate with chronic disease activity**



Adapted from: Preparedness and Response for Chikungunya Virus Introduction in the Americas. CDC/PAHO 2011

Pathogenesis

Acute Infection
- **Virus infects musculoskeletal tissues**
  - **Skeletal muscles, myotendinous insertions, joint capsules**
  - **Triggers inflammatory cell infiltration**
- **Disseminates to the CNS in animal models**
  - **Meningeal and ependymal cells**
- **Transmitted through maternal-fetal blood exchange during delivery**

Pathogenesis

Chronic Disease

- **Persistent virus replication and/or lack of virus antigen clearance**
  - **Pro-inflammatory immune response**

Management

Treatment

- **Supportive care and pain control**
  - **NSAIDs helpful but avoid until Dengue ruled out**
- **Occasionally steroids and DMARDs in chronic disease**
  - **Rebound effect when steroids stopped**
- **Current study evaluating the use of hyperimmune immunoglobulins**

Prevention

- **Avoid mosquito bites**
- **Vector control**

Vaccine Development

- **Life-long immunity following CHIKV infection**
- **Simpler vaccine target than dengue**
- **Virus-like particle vaccine in development**
  - **Completed phase 1 dose-escalation trial**
  - **Vaccine was safe, well tolerated, and immunogenic**
- **Several other vaccine candidates also being developed**
- **Multiple financial and logistical challenges**

References

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