

Grand Rounds on West Nile Virus Infections



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by

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Case Presentation

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WEST NILE FEVER:

CLASSIC CLINICAL DESCRIPTION

- Mild dengue-like illness of sudden onset
- Duration 3 - 6 days
- Fever, lymphadenopathy, headache, abdominal pain, vomiting, rash, conjunctivitis, eye pain, anorexia
- Symptoms of West Nile fever in contemporary outbreaks not fully studied

CRITERIA FOR WNV DIAGNOSIS

- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid,

OR

- Four-fold or greater changes in virus-specific quantitative antibody titers in paired sera,

OR

- Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen,

OR

- Virus-specific IgM antibodies in serum and a negative result for other IgM antibodies in CSF for arboviruses endemic to the region where an exposure occurred,

OR

- Virus-specific IgM antibodies in CSF or serum.





Neurologic Aspects of West Nile Virus Infection

Daniel Kantor, MD



WNV NEUROINVASIVE DISEASES

- Fever (≥ 100.4 ° F or 38 ° C) as reported by the patient or a health-care provider

AND

- Meningitis, encephalitis, acute flaccid paralysis, or other acute signs of central or peripheral neurological dysfunction, as documents by a physician

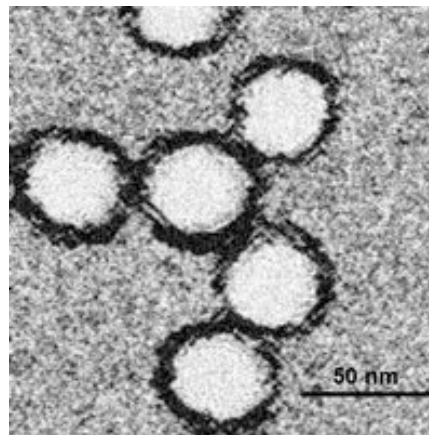
AND

- Absence of a more likely clinical explanation.



NON-NEUROINVASIVE DISEASE

- Fever (≥ 100.4 ° F OR 38 ° C) as reported by the patient or a health-care provider,
AND
- Absence of neuroinvasive disease
AND
- Absence of a more likely clinical explanation.



PATHOGENESIS OF WEST NILE NEUROINVASIVE DISEASE



Subcutaneous virus replication in dendritic cells

Dendritic cells travel to local lymph nodes where virus replicates

Viremia

Initiation of host humoral & cellular immune response

Virus crosses blood-brain barrier

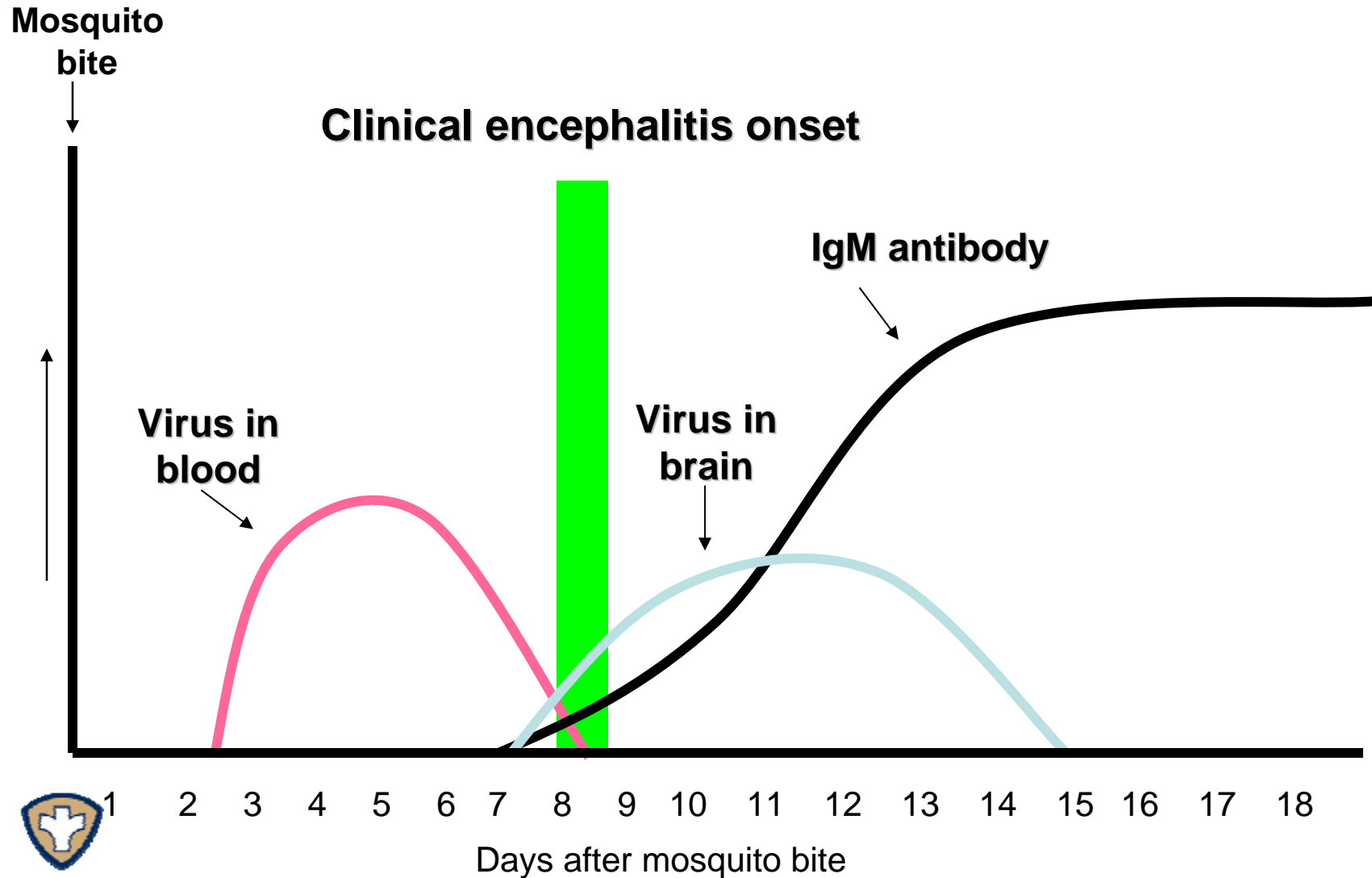
Encephalitis

IgM terminates viremia

Asymptomatic infection



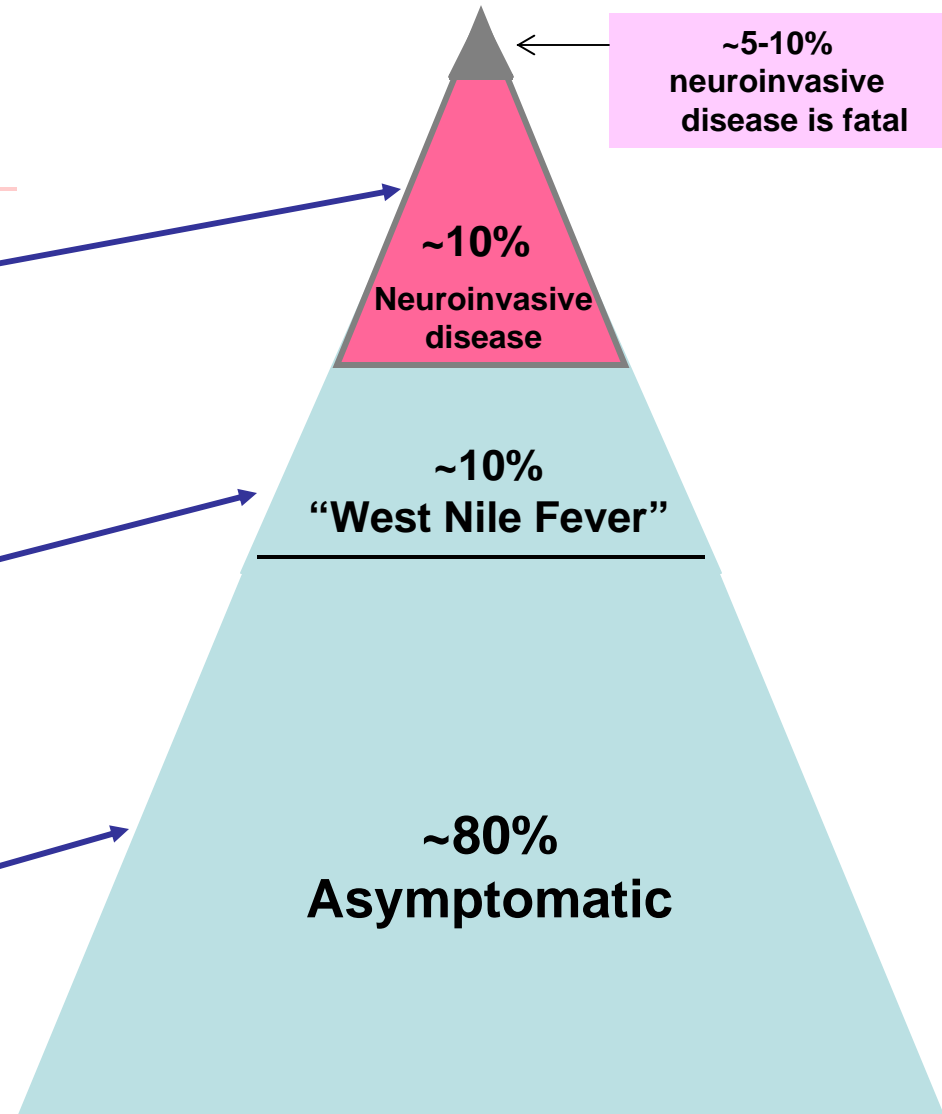
WEST NILE VIRUS AND ANTIBODY TITERS



WEST NILE INFECTION CATEGORIES

Serologic or virologic evidence of recent WNV infection

- **WN neuroinvasive disease**
 - Febrile illness with clinical and/or laboratory evidence of CNS infection
 - Encephalitis • Myelitis
- **West Nile fever**
 - Mild febrile illness without clinical or laboratory evidence of CNS infection
- **Asymptomatic**
 - Serologic but not clinical signs of infection



Most to Least Common

- Asymptomatic (80%)
- West Nile Fever (10%)
- Neuroinvasive (10%)
 - Central Nervous System (CNS)
 - Encephalitis + Meningoencephalitis (60 - 75% of Neuroinvasive)
 - Meningitis (25 – 35% of Neuroinvasive)
 - Poliomyelitis (flaccid paralysis)
 - Guillain-Barré – like syndrome



WEST NILE FEVER



- Fever
- Headache
- Fatigue
- Skin rash on the trunk of the body (occasionally)
- Swollen lymph glands (occasionally)
- Eye pain (occasionally)



BRAIN

- Headaches
- High fever
- Neck stiffness
- Stupor
- Disorientation
- Coma
- Tremors
- Seizures
- Focal muscle weakness

SPINAL CORD

- Flaccid paralysis (poliomyelitis)

PERIPHERAL

- Guillain-Barré-like syndrome

CRANIAL NERVES

- Cranial neuropathies

AUTONOMIC

- Bowel/Bladder dysfunction



- Maintain a high level of suspicion
- New neurological symptoms warrant a neuro consult
 - Cerebrovascular disorders
 - Malignancy
- Other sources of systemic infection
- Guillain-Barré syndrome
- Other arboviruses
 - Eastern and western equine encephalitis
 - St. Louis encephalitis
 - California encephalitis
 - Serum plaque reduction neutralization test (PRNT) to confirm WNV infection



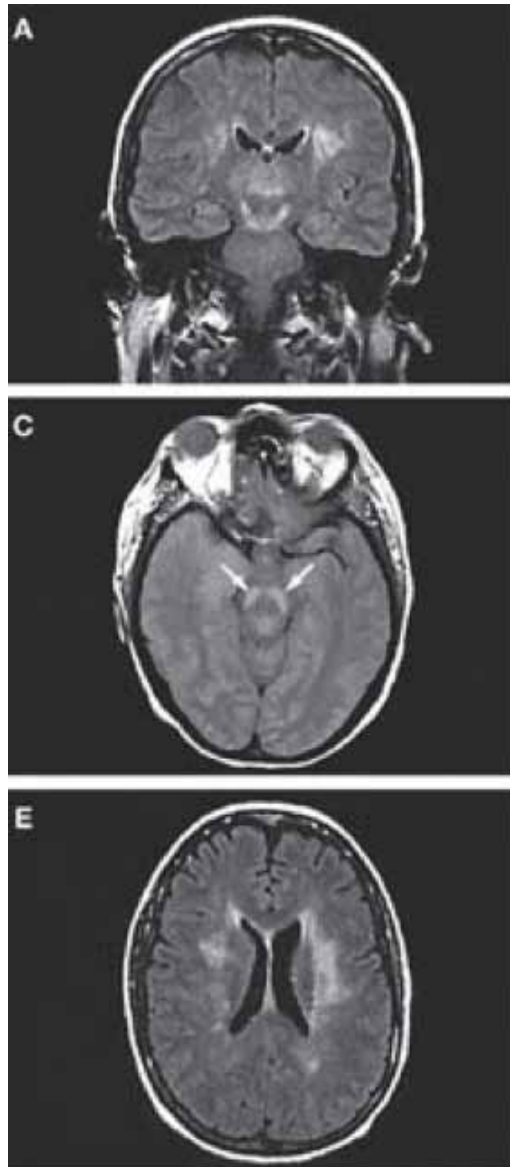
WORKUP



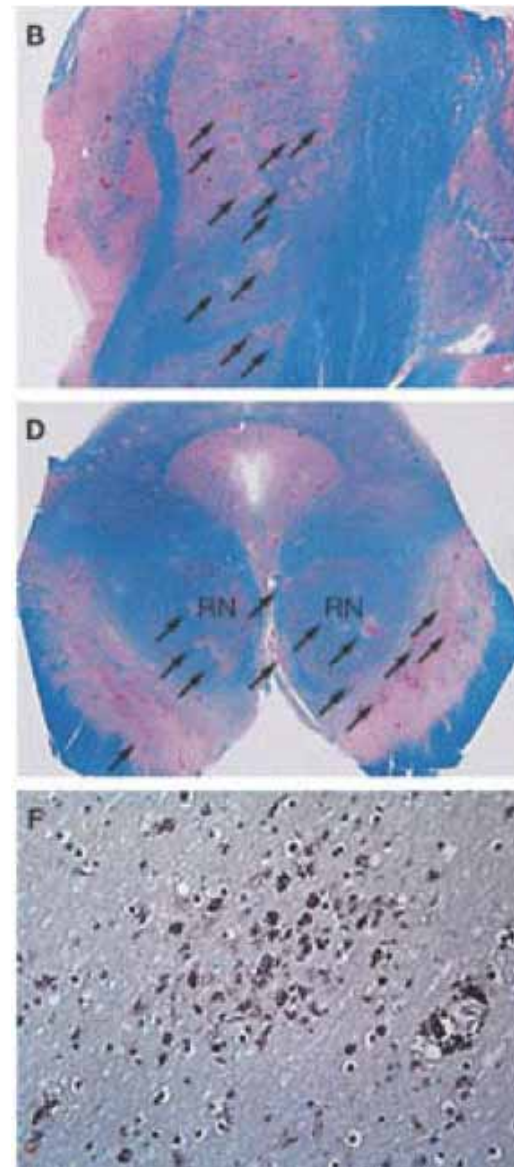
- Maintain a high level of suspicion
- New neurological symptoms warrant a neuro consult
- Routine laboratory testing
- Rule out other systemic infections
- Serum testing → DOH laboratory (IgM Antibody)
- Fundoscopic examination to rule out papilledema
- CT head with and without IV contrast
 - Can consider brain MRI with and without Gadolinium
- LP



FLAIR MRI



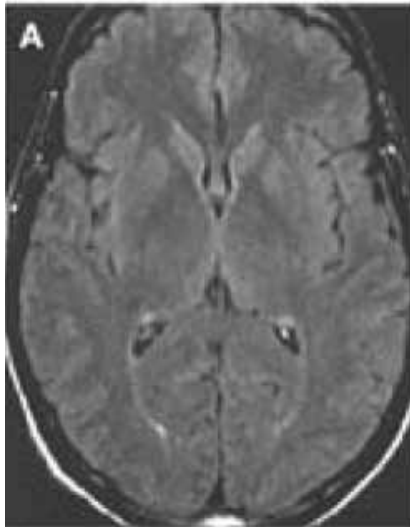
Luxol fast blue-periodic acid Schiff for myelin



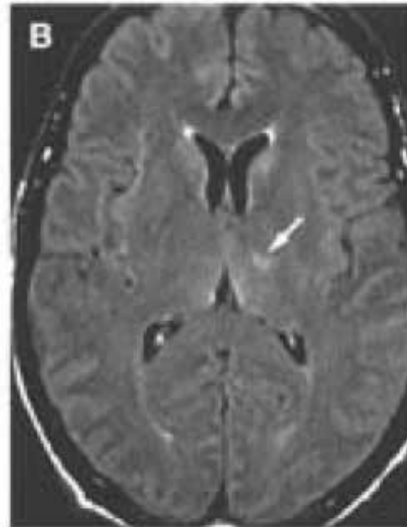
HAM56 antibody --
macrophages

FLAIR MRI

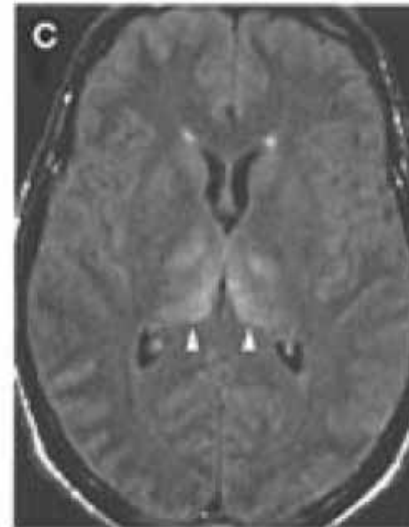
Day 5



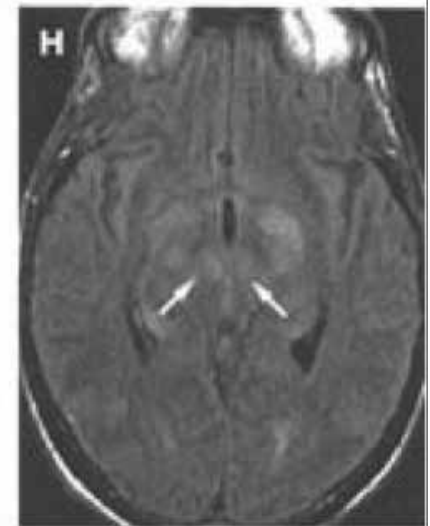
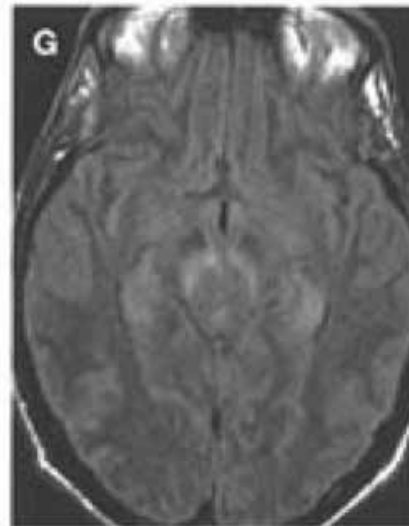
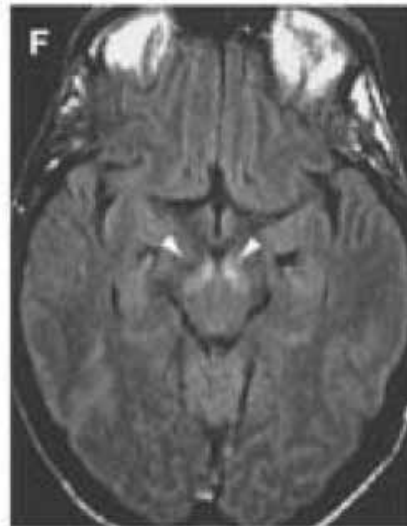
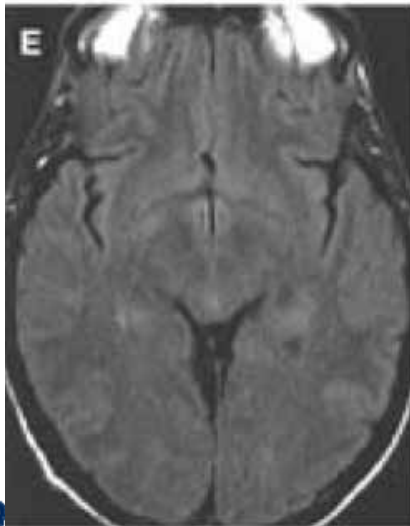
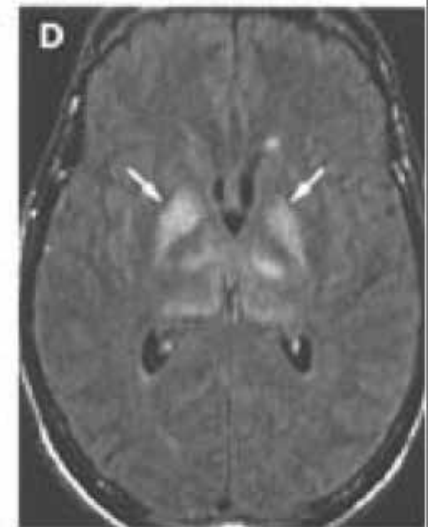
Day 10



Day 14



Day 36





CEREBROSPINAL FLUID (CSF)



- CSF cell count -- Neutrophilic pleiocytosis
 - Usually 5 – 500 cells/m³
- CSF protein – Elevated
 - Usually > 44 mg/dL
- CSF glucose – Normal
- IgM antibody-capture, enzyme-linked immunosorbent assay (MAC-ELISA)
- CSF WNV PCR – 50% false negative





MANAGEMENT



- Primary prevention (cover and drain)

- No antiviral drugs available

- Supportive care
 - Airway management
 - Seizure management
 - Non-sedating analgesia
 - Rehydration



NEGATIVE PROGNOSTIC INDICATORS

- **Age**

- **Immunosuppression**
 - Disease states
 - Diabetes mellitus
 - Transplant recipients
 - Immunosuppressant medications
 - Pregnancy
 - Intrauterine infection of fetus
 - WNV is passed through breast milk

- **Abnormal MRI**

LONG TERM SEQUALE

- None
- Fatigue
- Headaches
- Myalgia
- Residual tremor
- Parkinsonism
- Weakness and cranial neuropathies
- Seizures
- Cognitive deficits
- Complications of ICU stay



Public Health Aspects of West Nile Virus Infections

Robert Harmon, MD, MPH





SPECIAL THANKS TO:



- Dr. Saad Zaheer and his Epidemiology unit
- Local hospitals, infection control teams, attending physicians, residents, etc
- Duval County Medical Society
- Florida Dept. of Health experts
- City of Jacksonville/Mosquito control
- Many others, including the news media





WNV: BACKGROUND AND ECOLOGY



- First isolated in West Nile district of Uganda in 1937
- Commonly found in humans and birds and other vertebrates in Africa, Eastern Europe, West Asia, and the Middle East, but was not reported in the Western Hemisphere until the late 1990s
- Basic transmission cycle involves mosquitoes feeding on birds infected with the West Nile virus
- Infected mosquitoes then transmit West Nile virus to humans and animals when taking a blood meal



EPIDEMIOLOGY

- Agent is Flavivirus
- Member of Japanese encephalitis virus antigenic complex
- Culex and >30 other mosquito species are vectors
- Birds, such as crows, jays and >160 other species, are reservoirs
- WNV infection has been reported in >20 mammals, including horses
- Virus is carried in mosquito salivary glands
- Incubation period in humans is 3 to 14 days after bite



Modes of WNV Transmission in Humans

- Mosquito bites
- Blood transfusion
- Organ transplantation
- Trans-placental
- Breast feeding
- Lab accident
- No evidence of other human-to-human spread

WNV HUMAN INFECTION CASES – DUVAL COUNTY, 2011

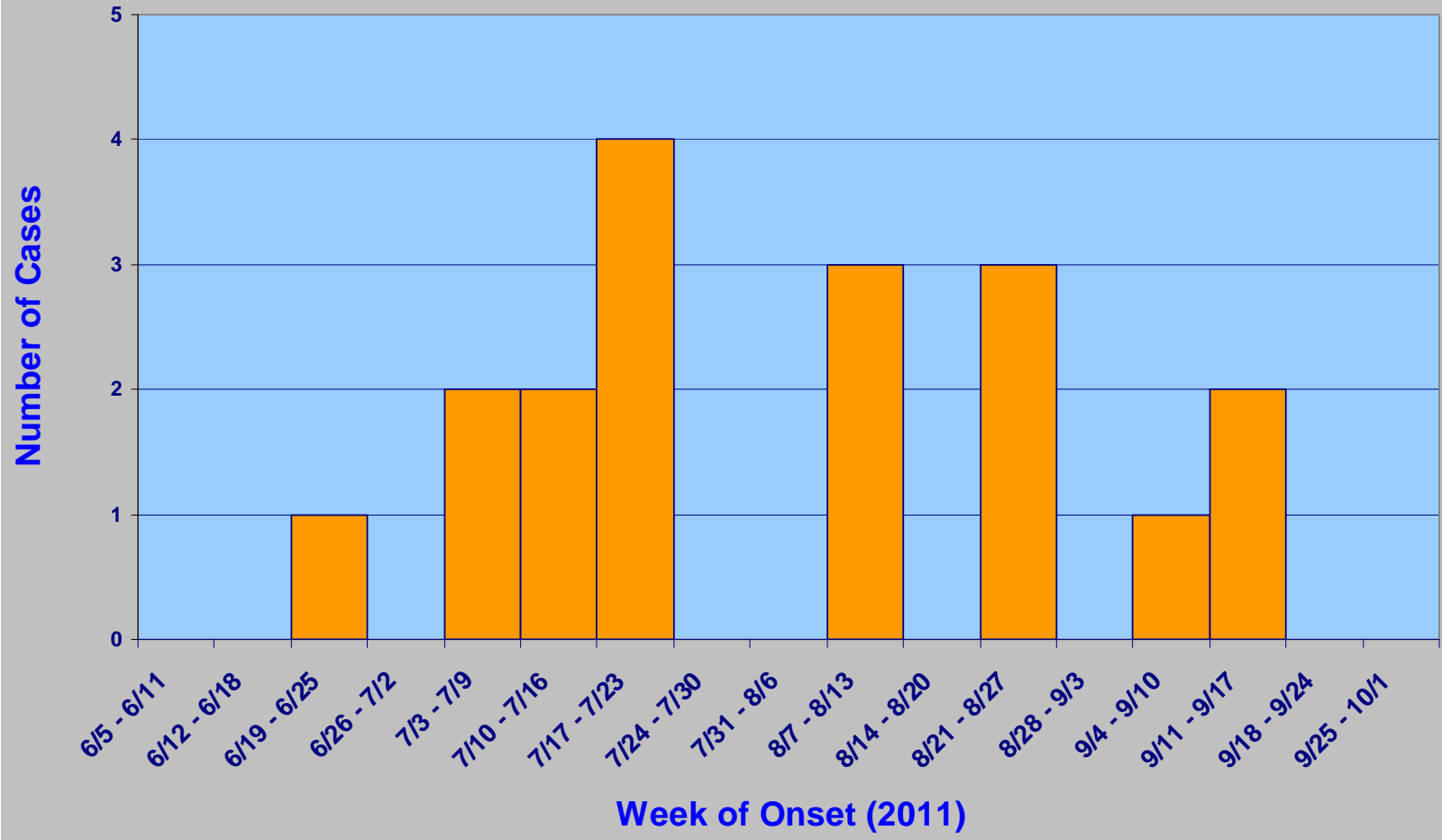
- Total: 18
- Onset dates: June 23 – Sept. 15
- Age range: 38-85
- Males: 10, Females: 8
- Known pre-existing conditions: 9
- Hospitalized: 16
- Meningitis or encephalitis: 11
- Deaths: 2 (ages 57 & 64)

WEST NILE VIRUS IN DUVAL COUNTY

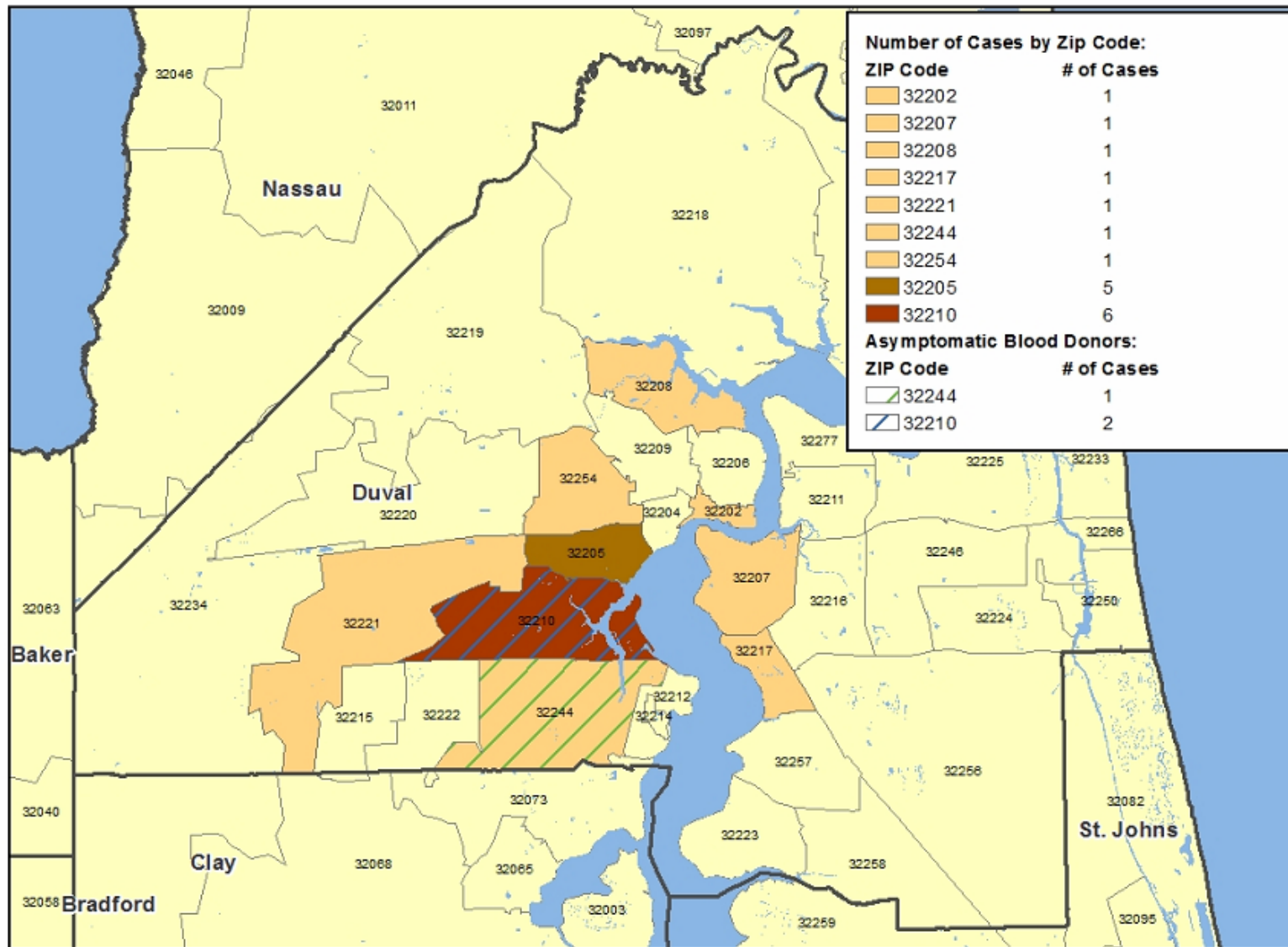
- 3 asymptomatic viremic (+) blood donors
- Interesting factors among cases
 - 53% - smokers
 - 76% - hx outside exposure
 - 18% - homeless
 - 59% - underlying immune issues



WNV Epi Curve for Duval County - 2011



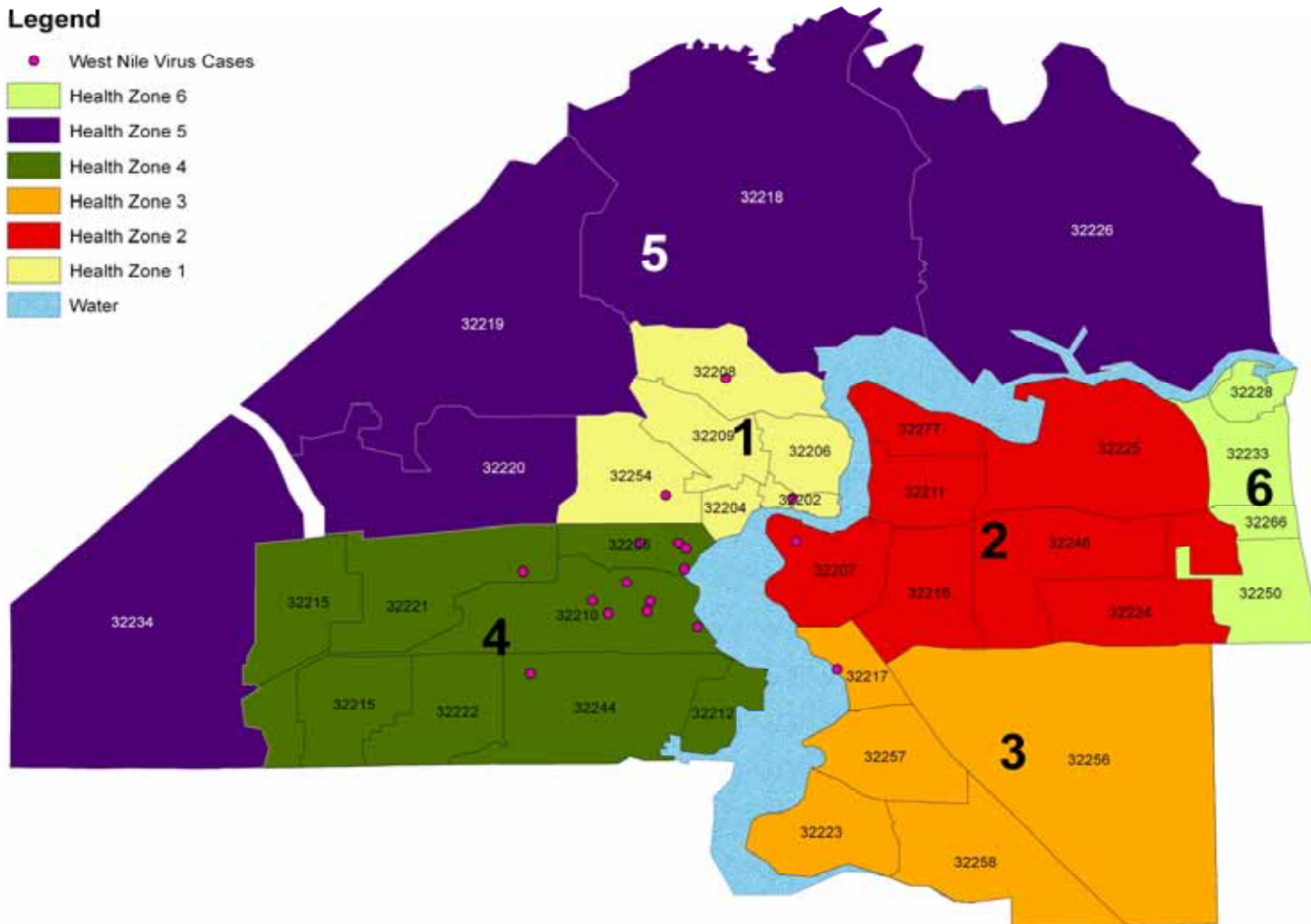
Human and Asymptomatic Donor Cases in Duval County (2011)



West Nile Virus Cases for Duval County by Zip Codes (Jan. - Sept. 2011)

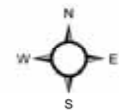
Legend

- West Nile Virus Cases
- Health Zone 6
- Health Zone 5
- Health Zone 4
- Health Zone 3
- Health Zone 2
- Health Zone 1
- Water



Source: Duval County Health Dept, IPHIR Division, October 2011

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HUMAN WNV INFECTIONS

DUVAL COUNTY, 2001 – 2011 (AS OF OCT. 4TH, 2011)

Year	Reported Human Disease Cases				Presumptive Viremic Donors
	Neuroinvasive Disease Cases	Non-Neuroinvasive Disease Cases	Total Cases	Deaths	
2001	1	0	1	0	
2002	1	0	1	0	
2003	4	4*	8*	0	
2004	7	0	7	0	
2005	1	0	1	1	
2006	0	0	0	0	
2007	0	0	0	0	
2008	0	0	0	0	
2009	0	0	0	0	
2010	1	0	1	0	
2011	15	3**	18**	2	3
Total	30	7	37	3	3





HUMAN WNV, FLORIDA AND



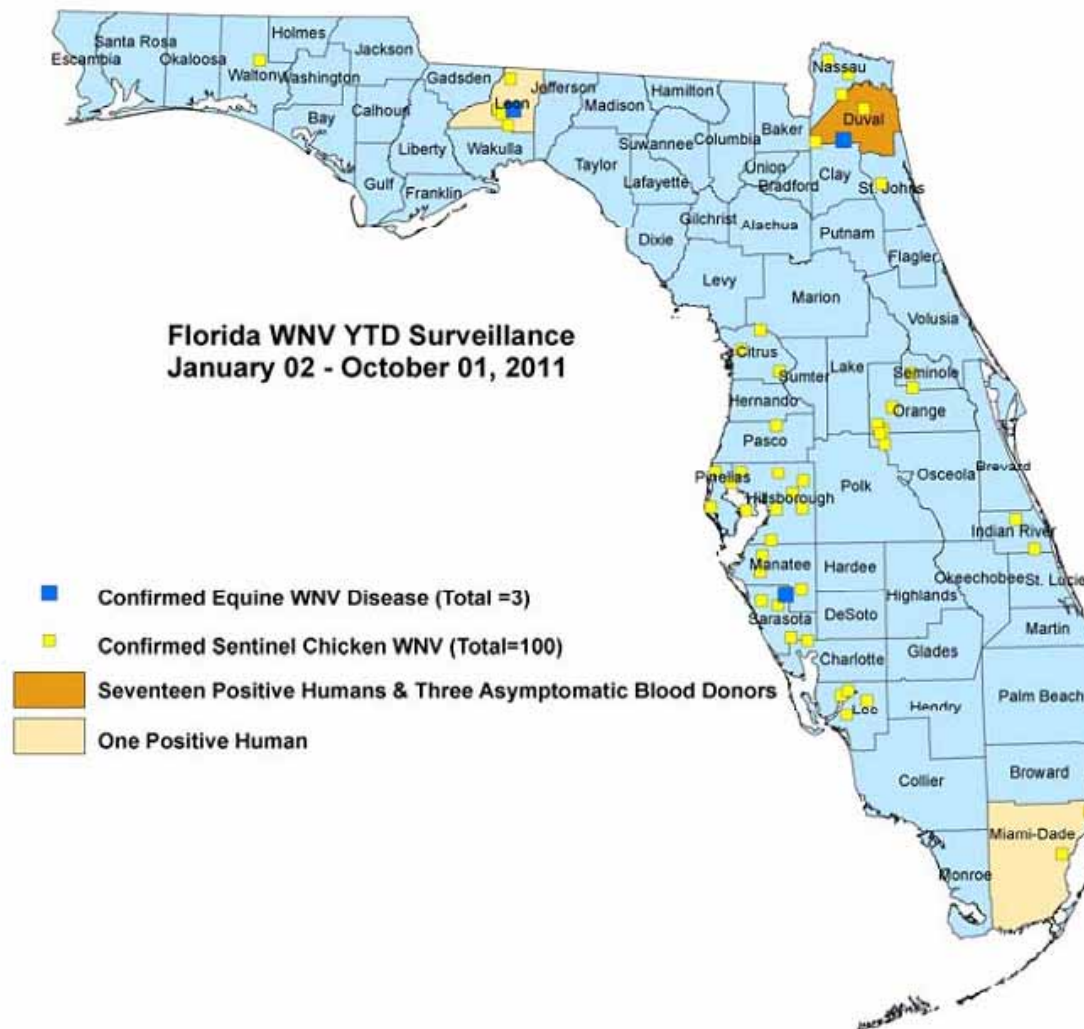
DUVAL COUNTY, 2001 – 2011 (AS OF OCT. 4TH, 2011)

Year	Florida	Duval
2001	12	1
2002	28	1
2003	94	8
2004	41	7
2005	21	1
2006	3	0
2007	3	0
2008	3	0
2009	3	0
2010	12	1
2011	20	18
Total	240	32



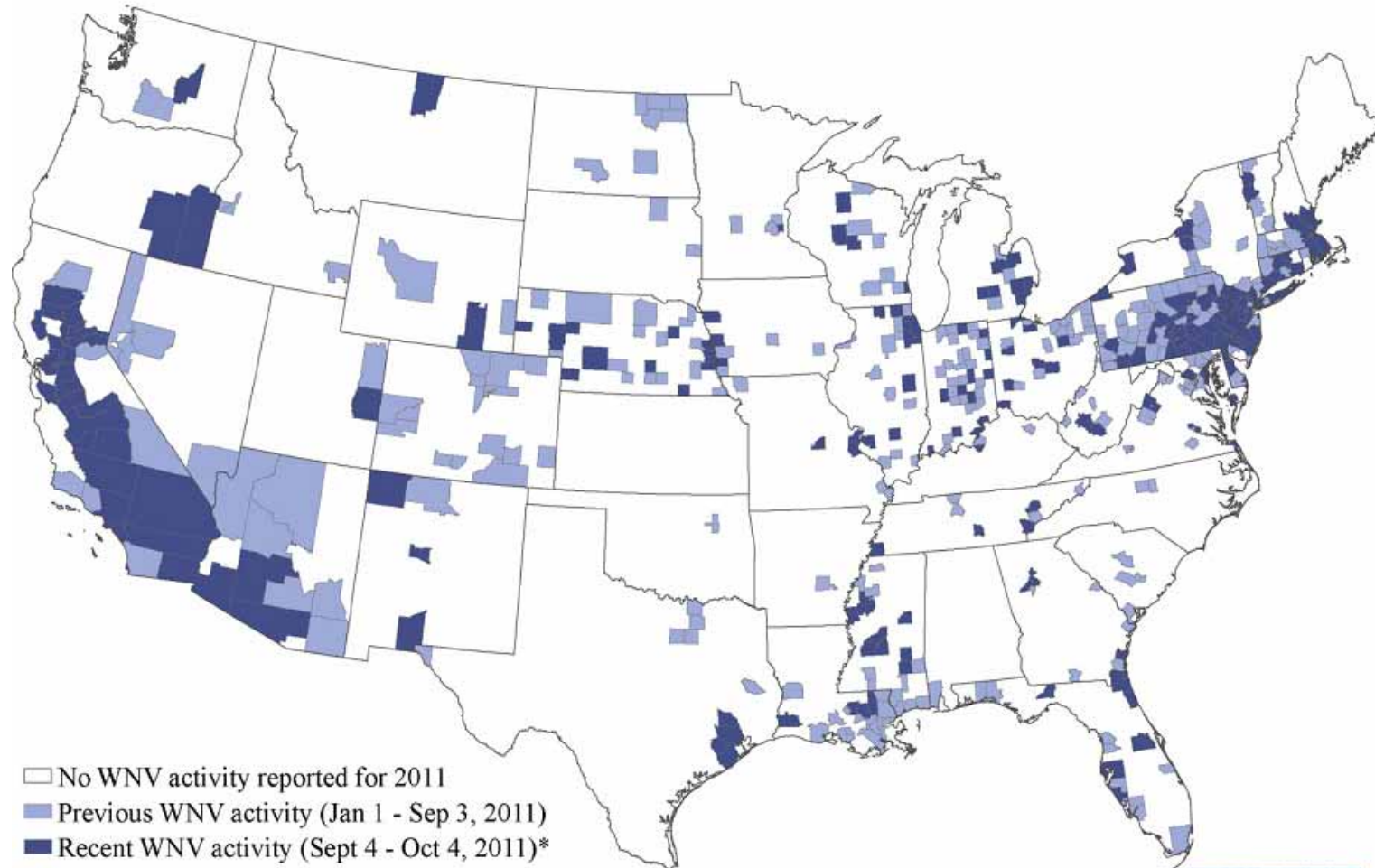
FLORIDA WNV

SURVEILLANCE: JAN. 2 - OCT. 1, 2011



WNV ACTIVITY BY TIME

PERIOD & COUNTY, U.S. (AS OF OCT. 4TH, 2011)



* Includes WNV human disease cases, viremic blood donors, veterinary disease cases, and infections in mosquitoes, birds, and sentinel animals



REPORTED CASES OF WNV, U.S. 2011 (AS OF OCT. 4TH, 2011)

	WNV (N = 432)	
	Number of Cases	Percent
Sex		
Male	256	59%
Female	176	41%
Ages (years)		
< 20	22	5%
20 – 39	63	15%
40 – 49	72	17%
50 – 59	89	21%
60	186	43%



ONSET OF ILLNESS OF REPORTED CASES OF WNV, U.S. 2011 (AS OF OCT. 4TH, 2011)

	WNV (N = 432)	
	Number of Cases	Percent
Onset of Illness		
January	0	0
February	0	0
March	1	<1%
April	0	0
May	3	1%
June	6	1%
July	78	18%
August	234	54%
September	110	25%

CLINICAL CHARACTERISTICS OF

REPORTED CASES OF WNV, U.S. 2011 (AS OF OCT. 4TH, 2011)

	WNV (N = 432)	
	Number of Cases	Percent
Clinical Syndrome		
Non-neuroinvasive	143	33%
Neuroinvasive		
Encephalitis	172	40%
Meningitis	105	24%
Acute Flaccid Paralysis	12	3%
Outcome		
Hospitalization	322	75%
Death	23	5%



HUMAN WNV, U.S. 2011

(AS OF OCT. 4TH, 2011)

State	Reported Human Disease Cases				Presumptive Viremic Donors
	Neuroinvasive Disease Cases	Non-Neuroinvasive Disease Cases	Total Cases	Deaths	
California	59	28	87	0	16
Mississippi	24	22	46	4	8
New York	21	12	33	2	6
Arizona	21	8	29	2	8
Michigan	22	1	23	2	0
Nebraska	12	11	23	0	8
Florida	16	2	18	2	3
Illinois	13	5	18	2	2
Other	101	54	155	8	8
Totals	289	143	432	22	22

SURVEILLANCE

➤ **Sentinel Chickens**

- Flocks are placed around the county from mid-May to late Nov./Dec.
- Blood samples are routinely taken to determine if disease organisms are being spread among birds by mosquitoes

➤ **Light Traps**

- Special collection devices placed in many Jacksonville neighborhoods to monitor mosquito populations
- Mosquito samples are submitted to state lab for analysis

➤ If surveillance shows presence of EEE, SLE, or WN in an area, inspectors look for mosquito breeding source

➤ Once found, it is eliminated or treated

There are several methods to controlling mosquitoes:



Biological



Source Reduction



Chemical

- Focuses on the larval stage of the mosquito lifecycle
- **Natural Mosquito Predators** → minnows, various birds, bats, insets, and other aquatic organisms
 - Mosquito fish (*Gambusia* species) → water/ditches can be stocked with these small minnows
 - Briquettes or solutions that are composed of bacteria (*Bacillus thuringensis israeliensis*) → toxic to mosquito larvae but harmless to other wildlife



Mosquitoes do not thrive where competition is fierce!

SOURCE REDUCTION

- Involves eliminating mosquito-breeding areas
- **Drainage** → eliminates standing water needed for mosquito development
- Homeowners
 - Drain standing water (in buckets, tires, cans, toys, boats, bird baths, pet dishes, plastic bags, gutters, etc)
 - Premise sanitation is the best prevention of ‘homegrown’ mosquitoes

It only takes a teaspoon of water for a mosquito to develop!



STANDING WATER AREAS



CHEMICAL CONTROL

➤ **Insecticides**

- Larvicides → materials applied to standing water where mosquitoes breed
- Adulticides → insecticides that target adult flying mosquitoes

➤ **Fog Trucks**

- Sprays areas in Jacksonville between 7 pm and 11 pm, Monday through Thursday

➤ **Aircraft**

- Insecticide sprayed with low-flying aircraft over rural and residential areas of Duval County
- Missions are typically flown during dusk or dawn



WNV PREVENTIVE MEASURES

To prevent mosquitoes from living and multiplying around your home or business.....

DRAIN standing water.

- Drain water from garbage cans, buckets, pool covers, coolers, toys, flower pots or any other containers where sprinkler or rain water has collected.
- Discard old tires, drums, bottles, cans, pots and pans, broken appliances and other items that aren't being used.
- Empty and clean birdbaths and pet's water bowls at least once or twice a week.
- Protect boats and vehicles from rain with tarps that don't accumulate water.
- Maintain swimming pools in good condition and appropriately chlorinated. Empty plastic swimming pools when not in use.





MORE WNV



PREVENTIVE MEASURES

To protect yourself from mosquito bites and from the diseases mosquitoes carry.....

COVER your skin with:

- **CLOTHING** - If you must be outside when mosquitoes are active, cover up. Wear shoes, socks, long pants and long sleeves.
- **REPELLENT** - Apply mosquito repellent to bare skin and clothing.
Always use repellents according to the label. Use repellents with DEET, picaridin, oil of lemon eucalyptus, and IR3535 are effective.
Use mosquito netting to protect children younger than 2 months old.

COVER doors and windows with screens.

- Keep mosquitoes out of your house. Repair broken screening on windows, doors, porches, and patios.





ADDITIONAL INFORMATION



- DOH continues to conduct statewide surveillance for mosquito borne illnesses, including West Nile virus infections, Eastern equine encephalitis, St. Louis encephalitis, malaria, and dengue.
- Residents of Florida are encouraged to report dead birds via the website <http://www.MyFWC.com/bird>.
- For more information on mosquito-borne illnesses, visit DOH's Environmental Public Health website at <http://www.doh.state.fl.us/Environment/medicine/arboviral/index.html>
- For more information, visit the Duval County Health Department's website at <http://www.dchd.net> or contact the Epidemiology Department at 904-253-1850
- For CDC info, see www.cdc.gov/ncidod/dvbid/westnile/index.htm

