West Nile Virus: Information and Guidance for Clinicians

Clinician Outreach and Communication Activity (COCA) Conference Call

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Office of Public Health Preparedness and Response
Division of Emergency Operations

TODAY'S PRESENTER

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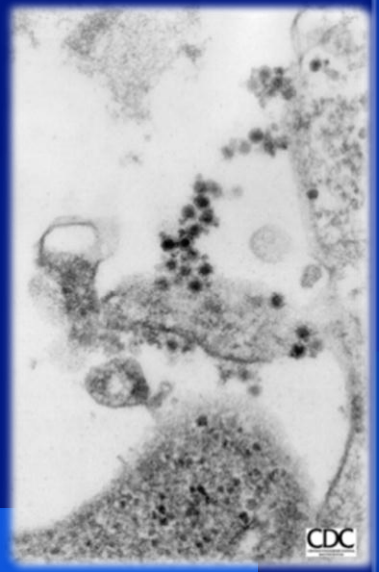
Overview

- Virology and transmission
- Clinical presentation
- Laboratory diagnosis
- Management and prevention
- Public health surveillance

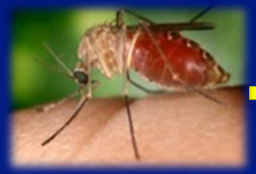
West Nile virus (WNV)



Virus genus:	Flavivirus
Transmission:	Mosquito-borne
Amplifying host:	Birds
Global distribution:	Worldwide
U.S. geographic foci:	New York in 1999 → spread nationwide

WNV transmission cycle

Enzootic cycle
Amplification



Infection of
"Dead End"
hosts

Person-to-person transmission of WNV

- Blood transfusion
- Organ transplantation

- Intrauterine
- Breastfeeding

Pathogenesis of human WNV infection

Replication in dendritic cells at inoculation site

↓

Spread to regional lymph nodes

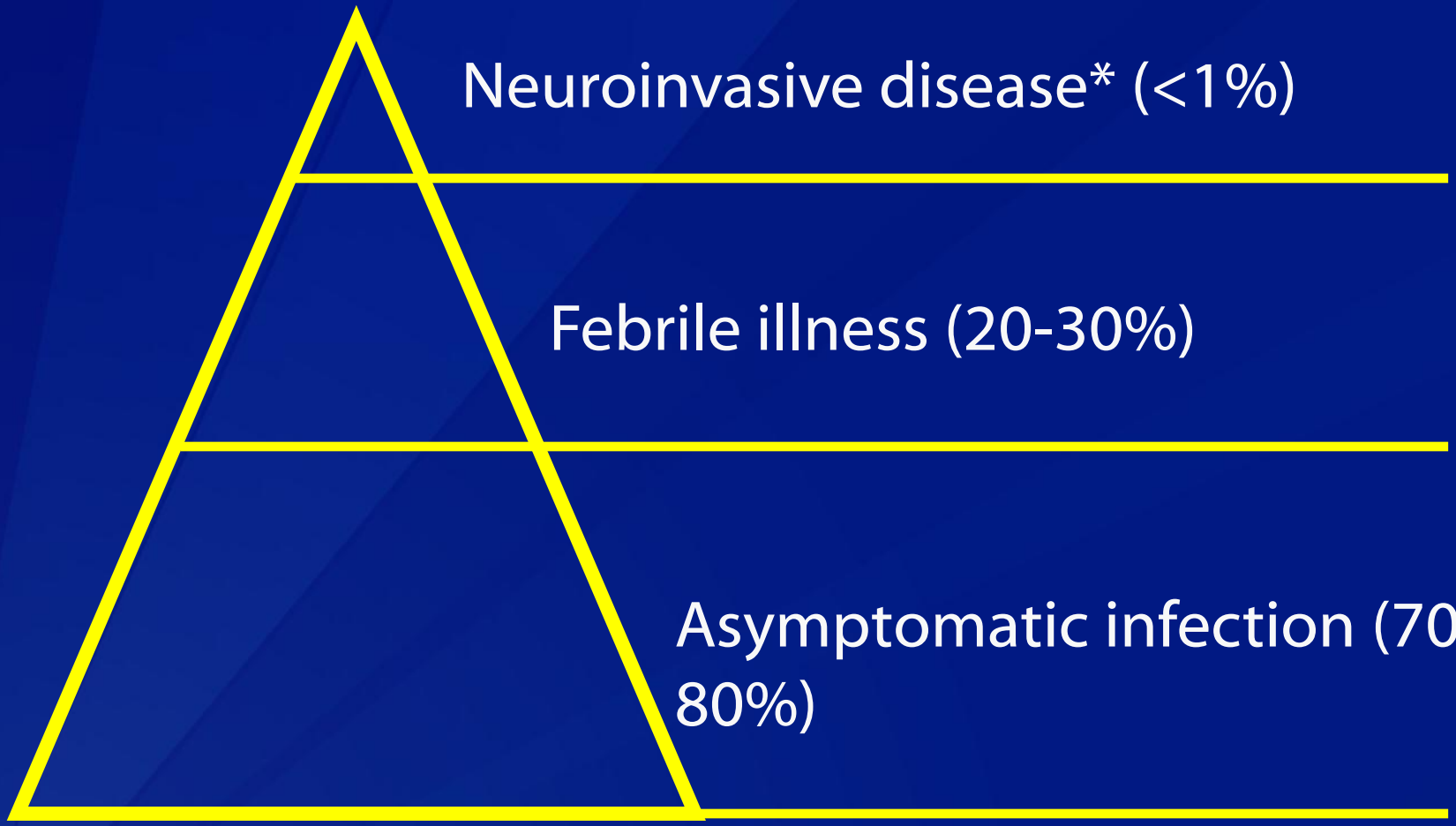
↓

Viremia

↓

Invasion of central nervous system

Clinical spectrum of human WNV infections



*Infections of central nervous system such as meningitis, encephalitis, or myelitis

WNV non-neuroinvasive disease

- Incubation period 2-14 days
- Non-specific febrile illness
- Usually resolves within a week
- Some symptoms may persist for weeks or months
- Overall case fatality <1%

WNV neuroinvasive disease

- Meningitis, encephalitis, and acute flaccid paralysis (AFP)
- Most cases require hospitalization
- Many patients with encephalitis or AFP have sequelae
- 50-75% need assisted living or rehabilitation
- Morbidity and mortality higher in elderly
- Overall case fatality 10%

Risk factors for severe disease

- Age>60 years
- Diabetes
- Hypertension
- Cancer history
- Chronic renal disease
- Chronic alcohol abuse

Lindsey, N.P., Am J Trop Med Hyg. 2012; 87(1): 179–184

WNV RNA in urine

- **In 2010, one study found WNV RNA in urine of 5 (20%) of 25 patients who had acute WNV disease 1-7 years earlier**
- **Two subsequent studies of 103 persons infected with WNV several weeks to 7 years prior; only one (<1%) with RNA in urine**
- **Possible reasons for discrepancy:**
  - Differences in test performance
  - Different study cohorts with different incidence WNV in urine
  - Shedding of WNV RNA may be intermittent

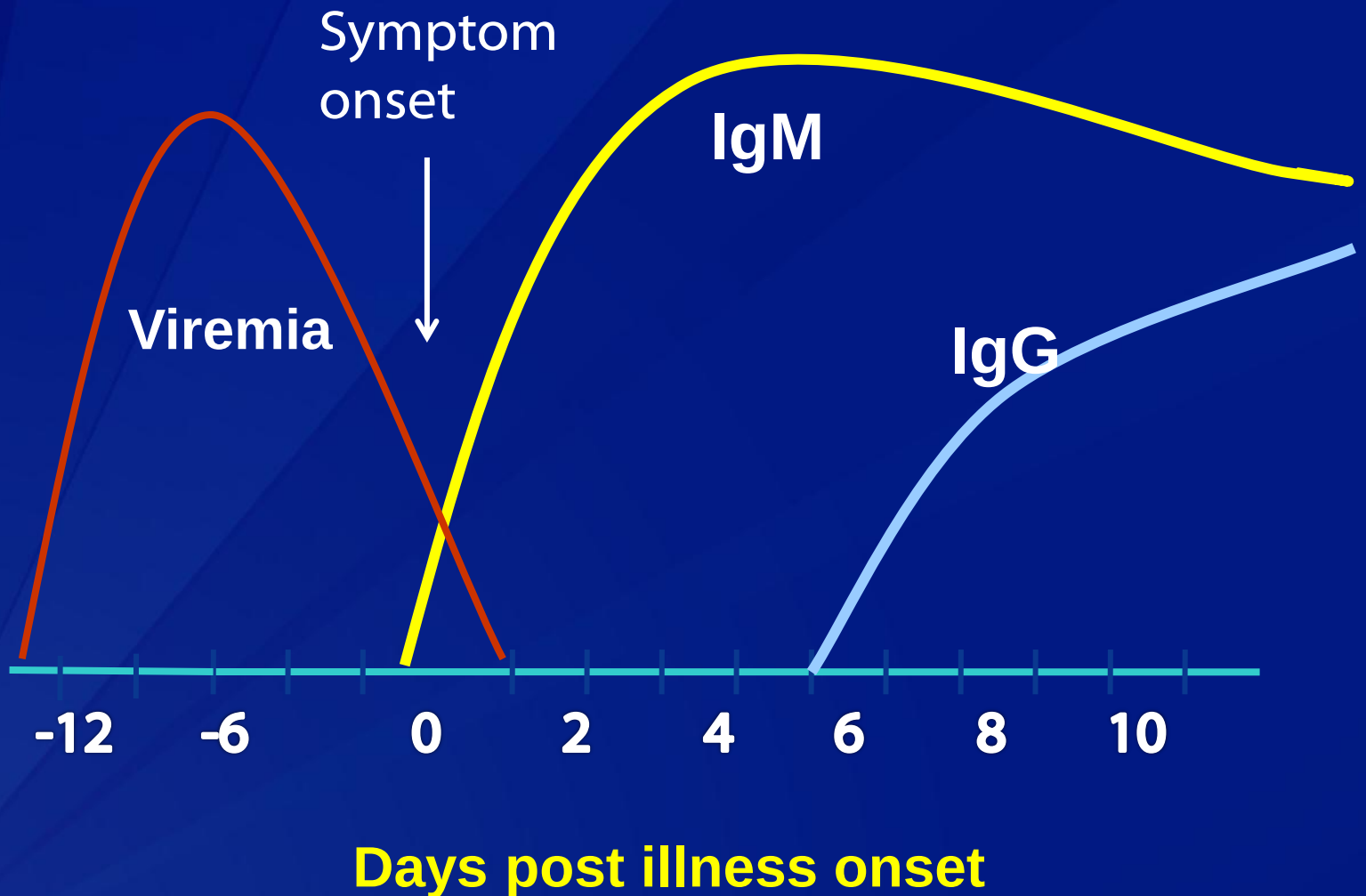
Murray K et al. J Infect Dis. 2010; 201:2–4. Gibney KB et al. J Infect Dis. 2011; 203:344–7. Baty SA et al. J Infect Dis. 2012;

WNV infection and renal disease

- Recent publication found relationship between WNV neuroinvasive disease and risk of developing of kidney disease
- People with chronic kidney disease, diabetes, and hypertension are at increased risk of developing WNV neuroinvasive disease
- Unclear cause and effect relationship between severe WNV and chronic kidney disease
- Further study is need to determine what role WNV infections may have in subsequent kidney disease

Nolan MS et al. PLoS One, published online July 6, 2012

WNV infection and antibody dynamics



WNV antibody testing

- **IgM antibodies in serum or CSF**
  - Performed by commercial and public health laboratories
  - Provides presumptive diagnosis of recent WNV infection
- **IgG antibodies in serum or CSF**
  - Performed by commercial and public health laboratories
  - Suggest past flavivirus infection
- **Plaque reduction neutralization test (PRNT)**
  - Performed predominantly in public health laboratories
  - Confirms specificity of IgM and IgG antibodies

Limitations of WNV antibody testing

- Serum collected <7 days of onset may lack detectable IgM
- IgM can persist >1 year, positive result may = past infection
- IgG only indicates past infection
- Both IgM or IgG tests may be false-positive due to cross-reactive antibodies to closely related flavivirus
- Blood products can contain WNV Ab; complicate interpretation

WNV molecular testing

- WNV RNA in serum or CSF
- Performed by commercial and public health laboratories
- Indicates recent WNV infection
- Low sensitivity as viral RNA is usually absent by time of symptom onset
- May be useful in immunocompromised patients

WNV disease treatment

- Supportive care and management of complications
- No proven antiviral or adjunctive therapy
- Case reports or trials with several therapies
- No ongoing trials or products for compassionate use

WNV disease treatment evaluations

Product	West Nile virus studies			Trials with other flaviviruses
	In vitro data	Case reports	Clinical trials	
Ribavirin	X	X		X
Corticosteroids		X		X
Immunoglobulins				
Polyclonal		X	X	
Hyperimmune		X	X	
Monoclonal			X	
Interferon	X	X	X	

Prevention of human WNV infections

- **No WNV vaccine licensed for use in humans**
- **Community mosquito control programs**
  - Use of larvicides, adulticides, and larvae-eating fish
- **Household and personal protective measures**
  - Use air conditioning and install window/door screens
  - Reduce mosquito breeding sites
  - Wear long-sleeved shirts and long pants
  - Apply insect repellents
  - Limit outdoor exposure during peak biting times
- **Screen and remove infected blood products**

Transfusion-associated WNV infections

- **First documented in 2002**
- **Routine screen of blood supply for WNV started in 2003**
  - >2,500 infected products removed from blood supply
- **Rare transfusion-associated events still occur**
  - Testing of pooled sample can fail to detect low viremic units
  - Some products are not screened (e.g. granulocytes)

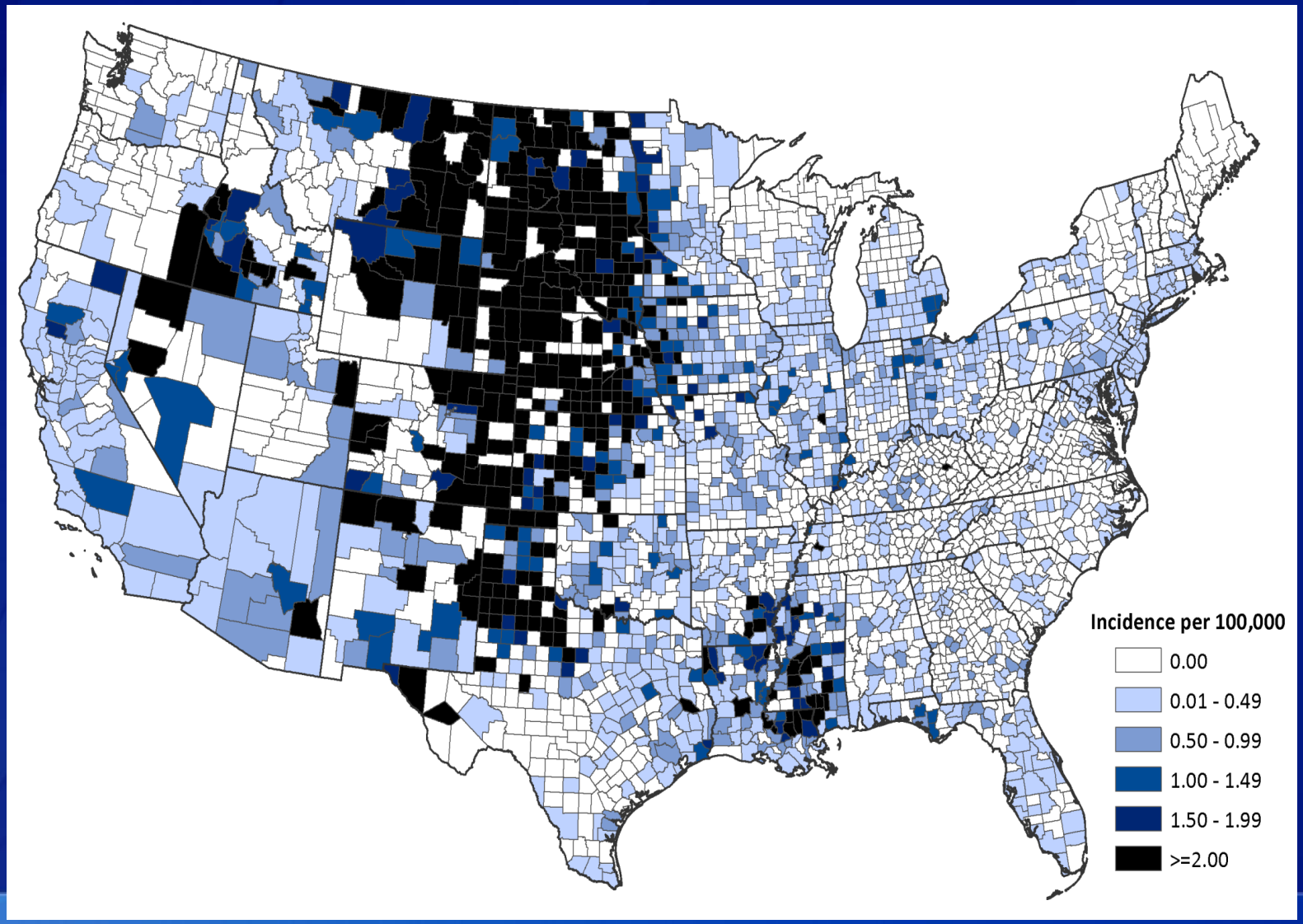
Transplant-associated WNV infections

- **Since 2002, roughly one transplant-associated WNV cluster recognized each year**
- **Recipients at increased risk of severe disease**
- **Organ donor screening practices for WNV vary**
  - Screening is not mandatory
  - Concern for false-positive tests leading to organ wasting
  - Current screening techniques may fail to detect positive donors

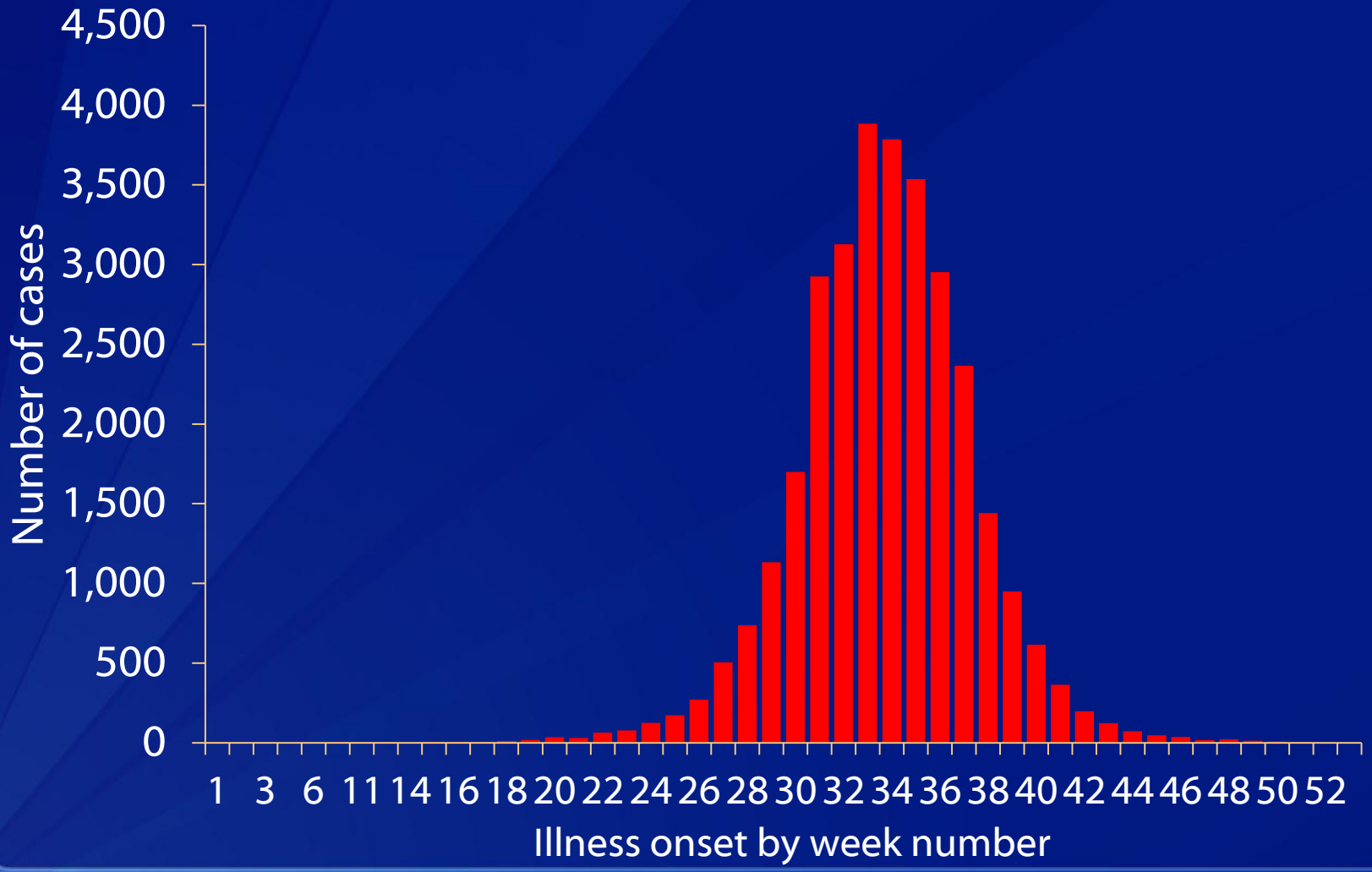
Arboviral surveillance

- **ArboNET is unique surveillance system**
  - Human disease cases, viremic blood donors, veterinary cases, dead birds, mosquitoes, and sentinel animals
- **Data are updated weekly on CDC website**
  - www.cdc.gov/ncidod/dvbid/westnile/index.htm
- **WNV is nationally notifiable disease**
  - Clinicians and laboratories required to report WNV disease cases to local health department

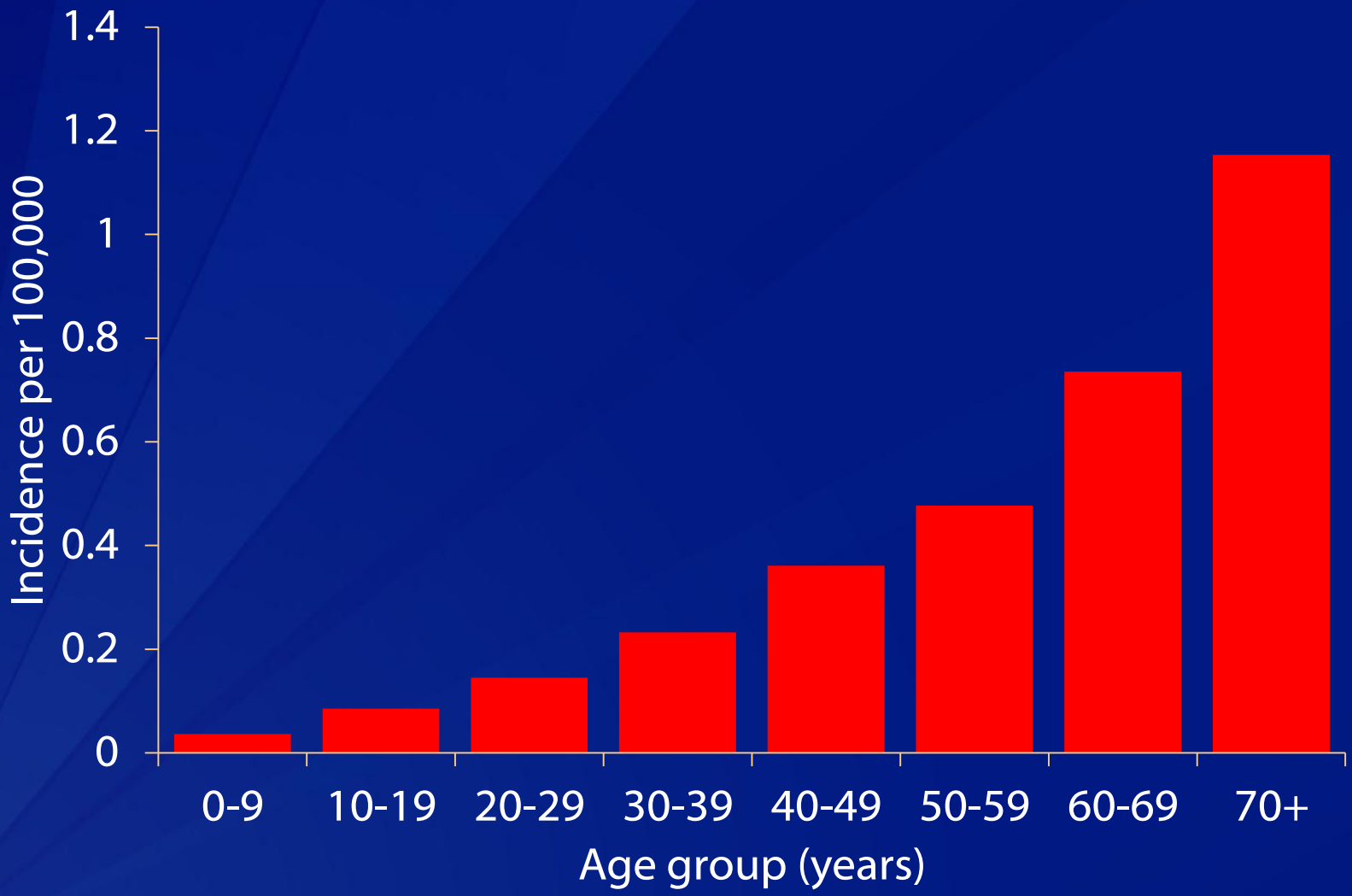
Average annual incidence of WNV neuroinvasive disease by county – United States, 1999-2011



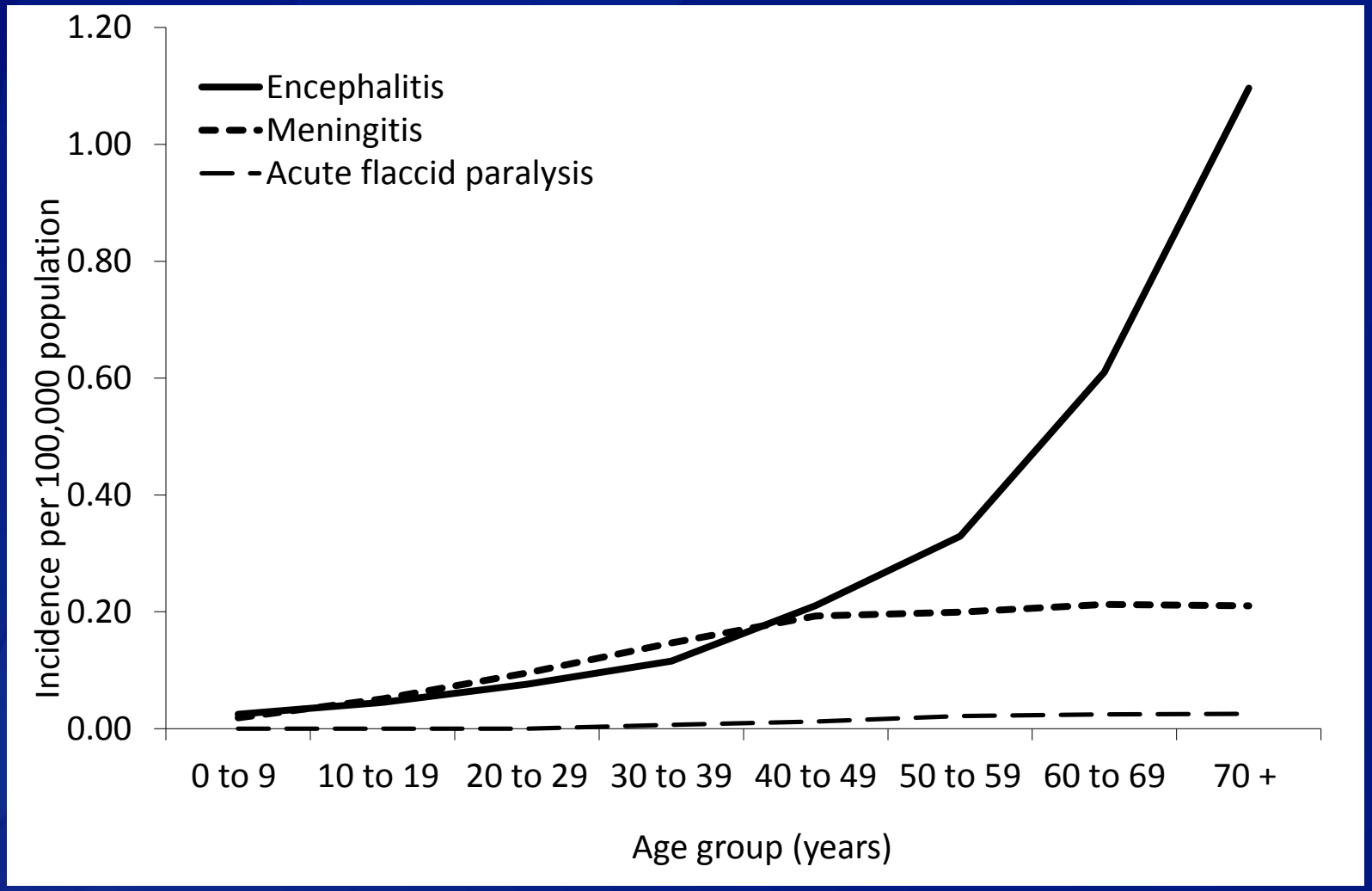
Number of WNV neuroinvasive disease cases by week of illness onset – United States, 1999-2011



Average annual incidence of WNV neuroinvasive disease by age group – United States, 1999-2011



WNV neuroinvasive disease incidence by age group and clinical syndrome – United States, 1999-2008



Lindsey NP et al. MMWR 2010;59(No. SS-2):1-17

Demographic and outcome data for WNV disease cases by clinical syndrome – United States, 1999-2011

	Fever (N=17,344)	Meningitis (N=4,469)	Encephalitis (N=8,345)	AFP (N=429)
Male	53%	55%	60%	64%
Median Age	48 yrs	48 yrs	64 yrs	57 yrs
Hospitalized*	21%	84%	90%	86%
Died	<1%	2%	12%	11%

* Includes data from 2004-2011

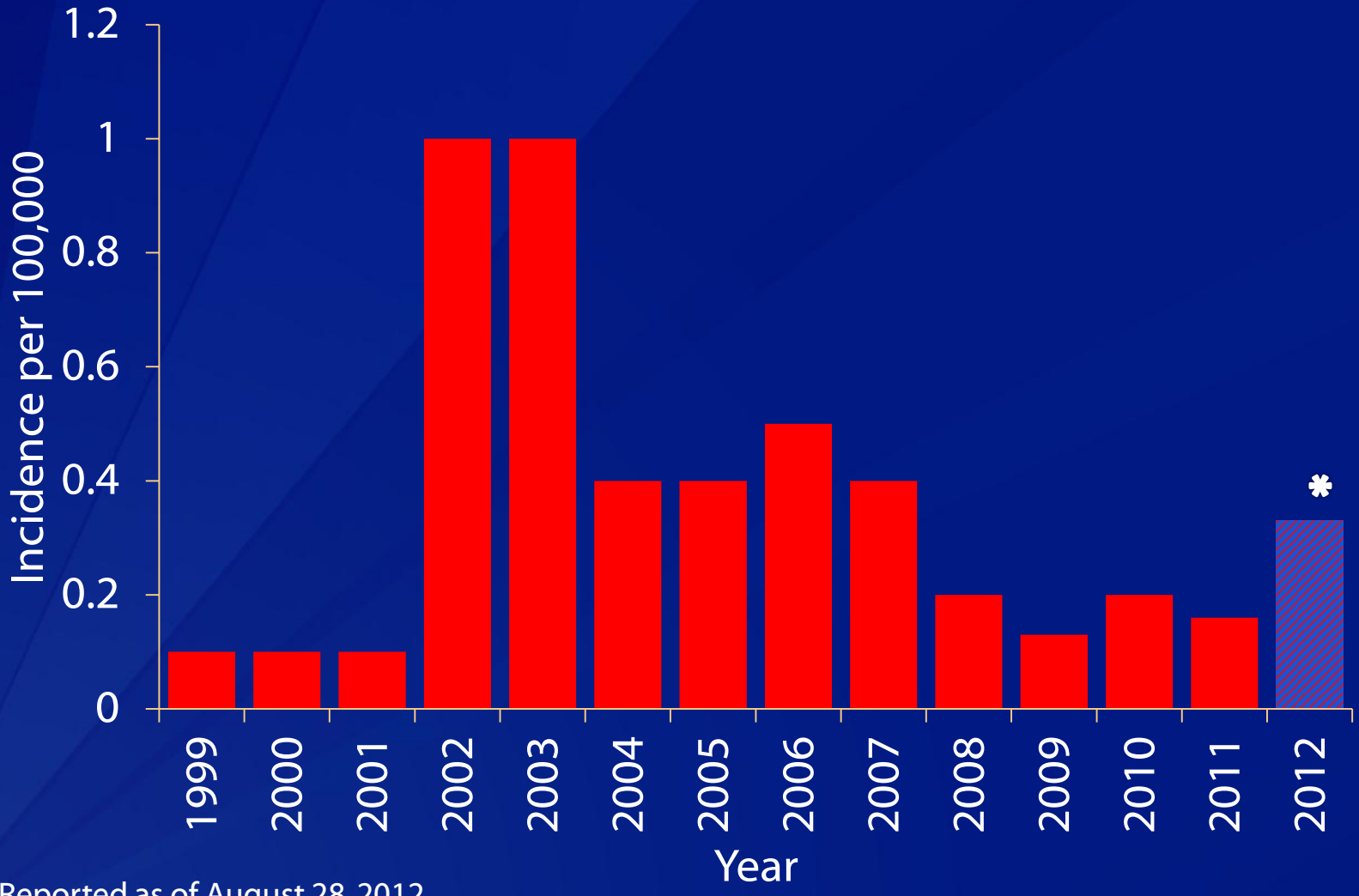
Annual number of neuroinvasive domestic arboviral diseases cases – United States, 1999-2011

Virus	Cases per year	
	Median	(Range)
West Nile	689	(19 - 2,946)
La Crosse	73	(46 - 167)
St. Louis encephalitis	8	(2 - 79)
Eastern equine encephalitis	6	(3 - 21)
Powassan	1	(0 - 12)

Estimated numbers of human WNV infections and disease cases – United States, 1999-2011

- **31,414 WNV disease cases reported to CDC**
- **Most cases are not diagnosed and reported**
- **Extrapolating from serosurvey and surveillance data**
  - 400,000 - 950,000 cases of WNV disease may have occurred in the United States from 1999 through 2011

Average annual incidence of WNV neuroinvasive disease – United States, 1999-2012



* Reported as of August 28, 2012

Preliminary WNV surveillance data for 2012 (as of 08/28/2012)

- **48 states have reported WNV activity (people, birds, mosquitoes)**
- **1,590 cases of WNV disease in people, including 66 deaths**
  - 889 (56%) neuroinvasive disease
  - 701 (44%) non-neuroinvasive disease
- **70% of cases reported from six states (TX, SD, MS, OK, LA, MI)**
  - 45% of all cases reported from Texas
- **Currently highest number of WNV disease cases reported through last week in August since 1999**

Summary

- **WNV remains an important cause of neurologic infections in the United States**
- **Seasonal outbreaks occur annually but are often quite focal and unpredictable in size and location**
- **No proven effective treatments or vaccines**
- **Diagnosis still important to:**
  - Stop unnecessary therapies (e.g., antibiotics)
  - Limit further diagnostic evaluation
  - Help predict patient outcomes
  - Direct public health prevention measures

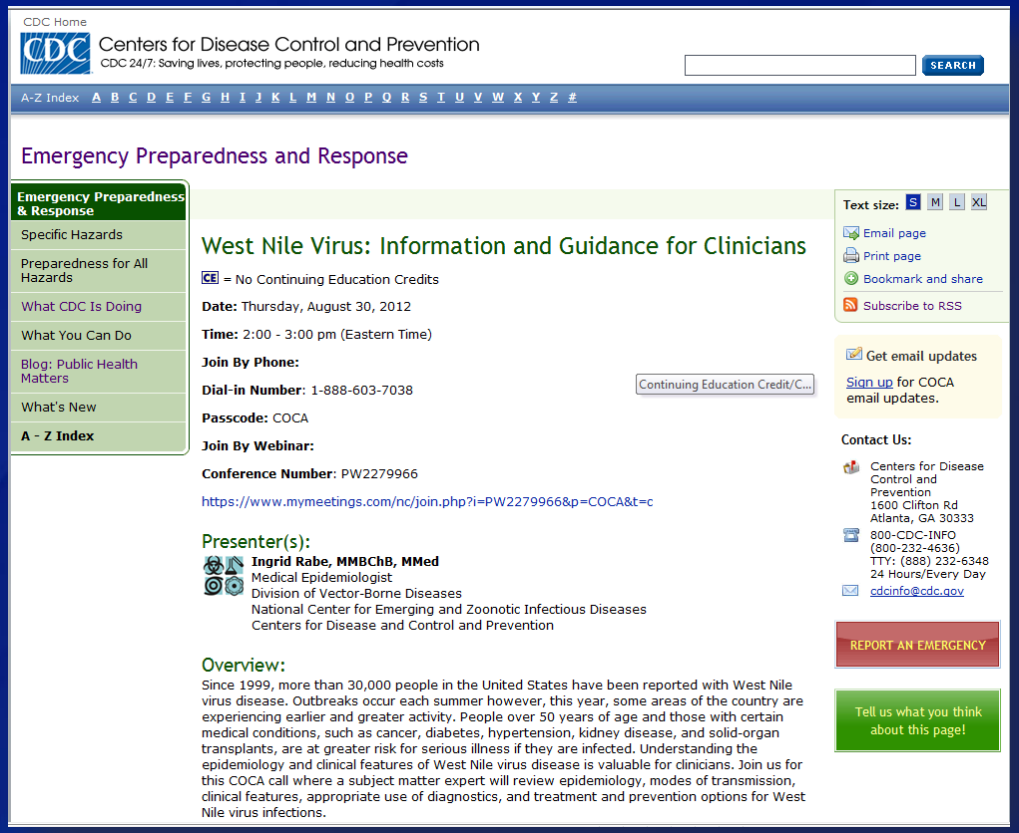
Recommendations for healthcare providers

- Consider WNV and other arboviral infections in the differential diagnosis of patients with aseptic meningitis or encephalitis
- Obtain appropriate specimens for laboratory testing
- Promptly report cases to state or local health departments to allow for appropriate control measures

Thank you

Centers for Disease Control and Prevention
Atlanta, Georgia

Thank you for joining!
Please email us questions at coca@cdc.gov



http://emergency.cdc.gov/coca

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