

# Emerging Vector-borne Diseases: Focus on Arboviral Disease Threats to Arizona

## 2011 Arizona Infectious Disease Training & Exercise

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# Background on Arboviruses

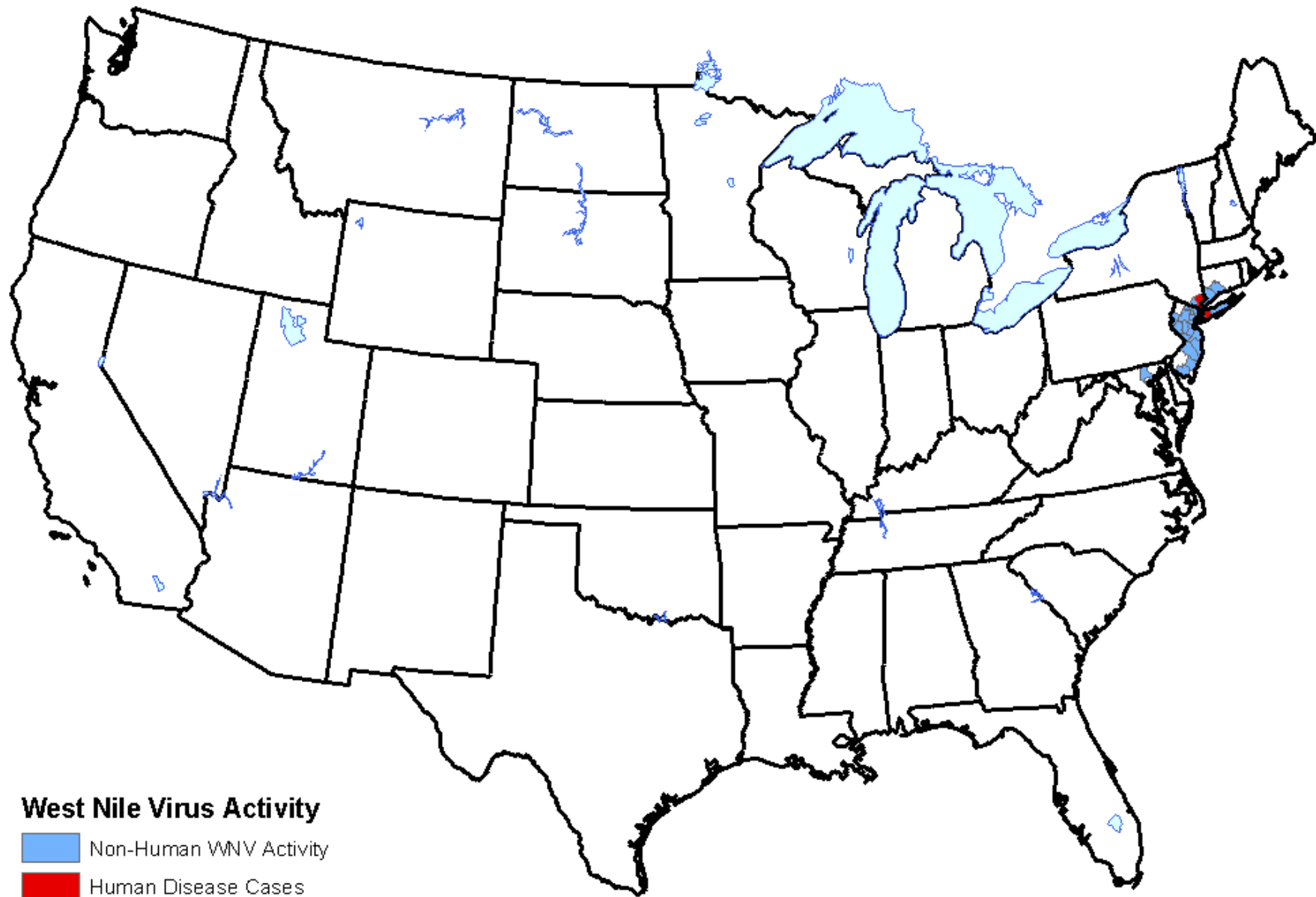
# Arboviruses

- Roughly 450 arthropod-borne viruses
  - Approximately one-third are human pathogens
- Primarily single-stranded, enveloped RNA viruses
- Transmitted through the bite of infected arthropods
  - Mosquitoes
  - Ticks
  - Sand flies
  - Biting midges
- Maintained in nature through transmission cycles between birds or mammals and arthropod vectors



# Human Arboviral Diseases in the U.S.

Virus	Genus	Vector	Geographic Location in US
California serogroup	<i>Bunyavirus</i>	Mosquitoes	Widespread mostly upper Midwest
Colorado tick fever	<i>Coltivirus</i>	Ticks	Western US
Dengue	<i>Flavivirus</i>	Mosquitoes	Puerto Rico, Florida, Texas, and Hawaii
Eastern equine encephalitis	<i>Alphavirus</i>	Mosquitoes	Eastern seaboard and Gulf States
Powassan	<i>Flavivirus</i>	Ticks	NE and north central
St. Louis encephalitis	<i>Flavivirus</i>	Mosquitoes	Most states in continental US
Western equine encephalitis	<i>Alphavirus</i>	Mosquitoes	Central and Western
West Nile	<i>Flavivirus</i>	Mosquitoes	Most state in continental US

# Introduction and Spread of Novel Arboviral Diseases



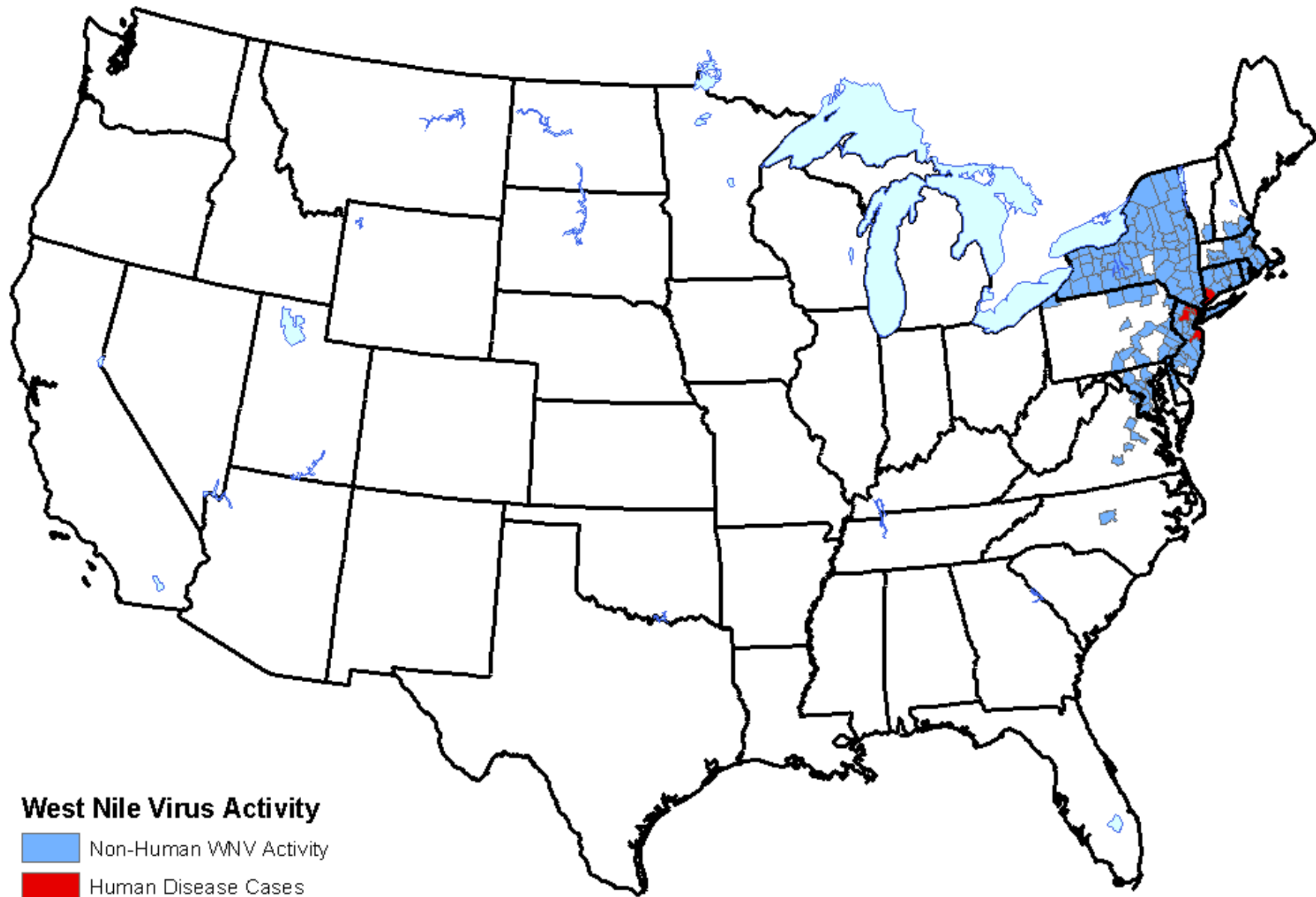
**West Nile Virus Activity**

-  Non-Human WNV Activity
-  Human Disease Cases



**1999**

National Center for Infectious Diseases  
**West Nile Virus Activity**  
Cumulative results for 1999 calendar year

**CDC**



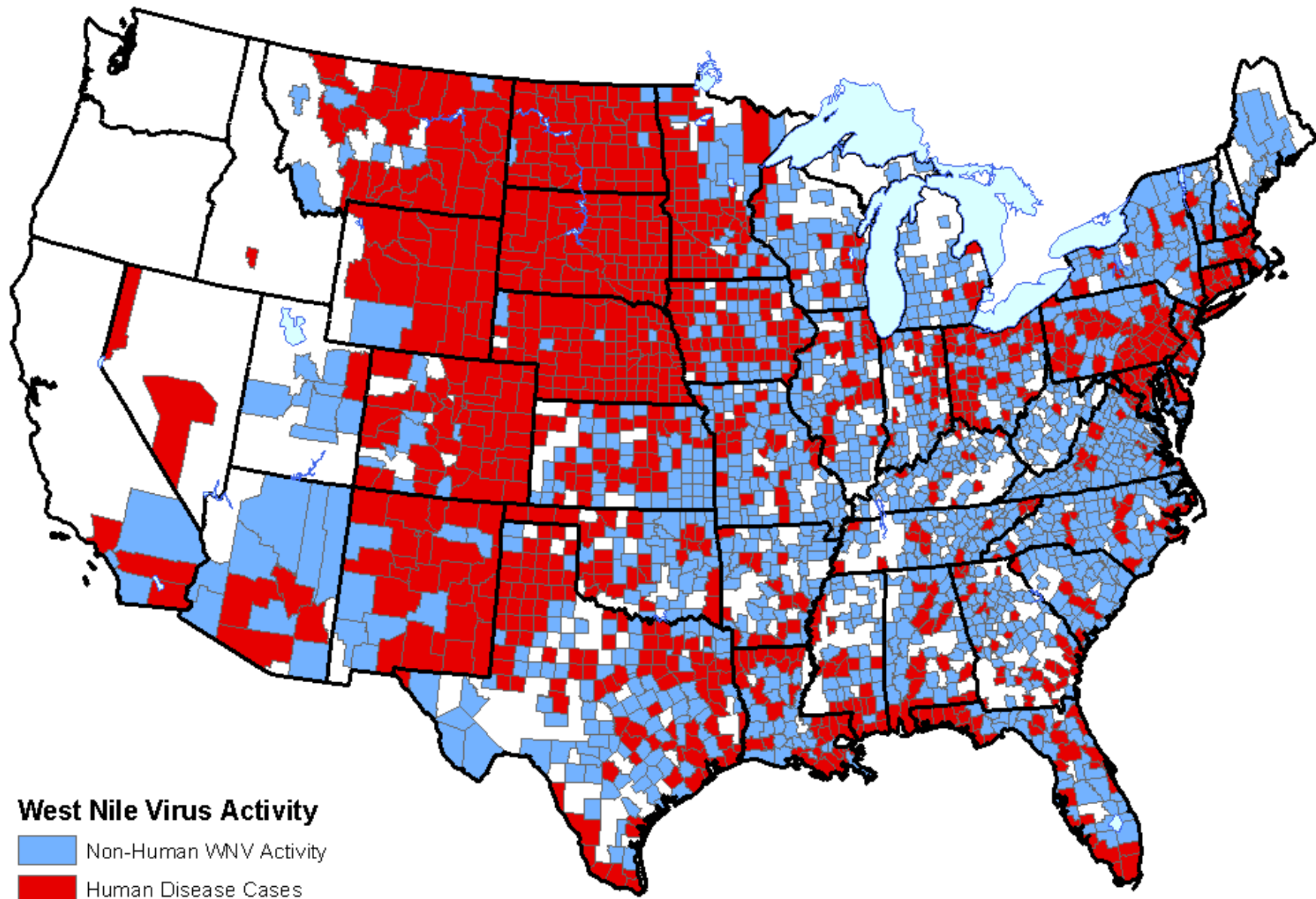
**West Nile Virus Activity**

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National Center for Infectious Diseases  
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Cumulative results for 2000 calendar year

**CDC**



**2003**

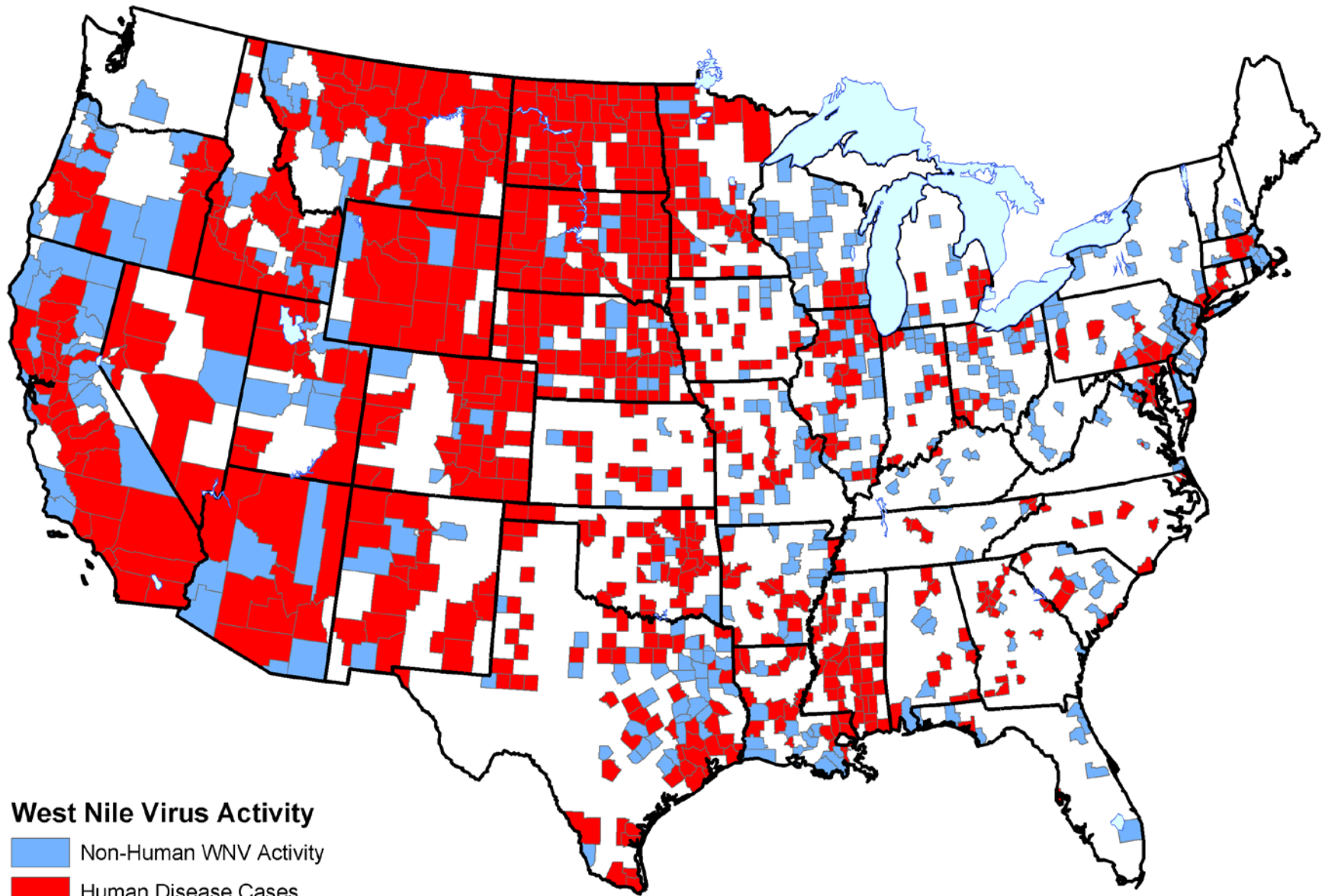
National Center for Infectious Diseases

**West Nile Virus Activity**



Cumulative results for 2003 calendar year reported as of May 20, 2004

**CDC**





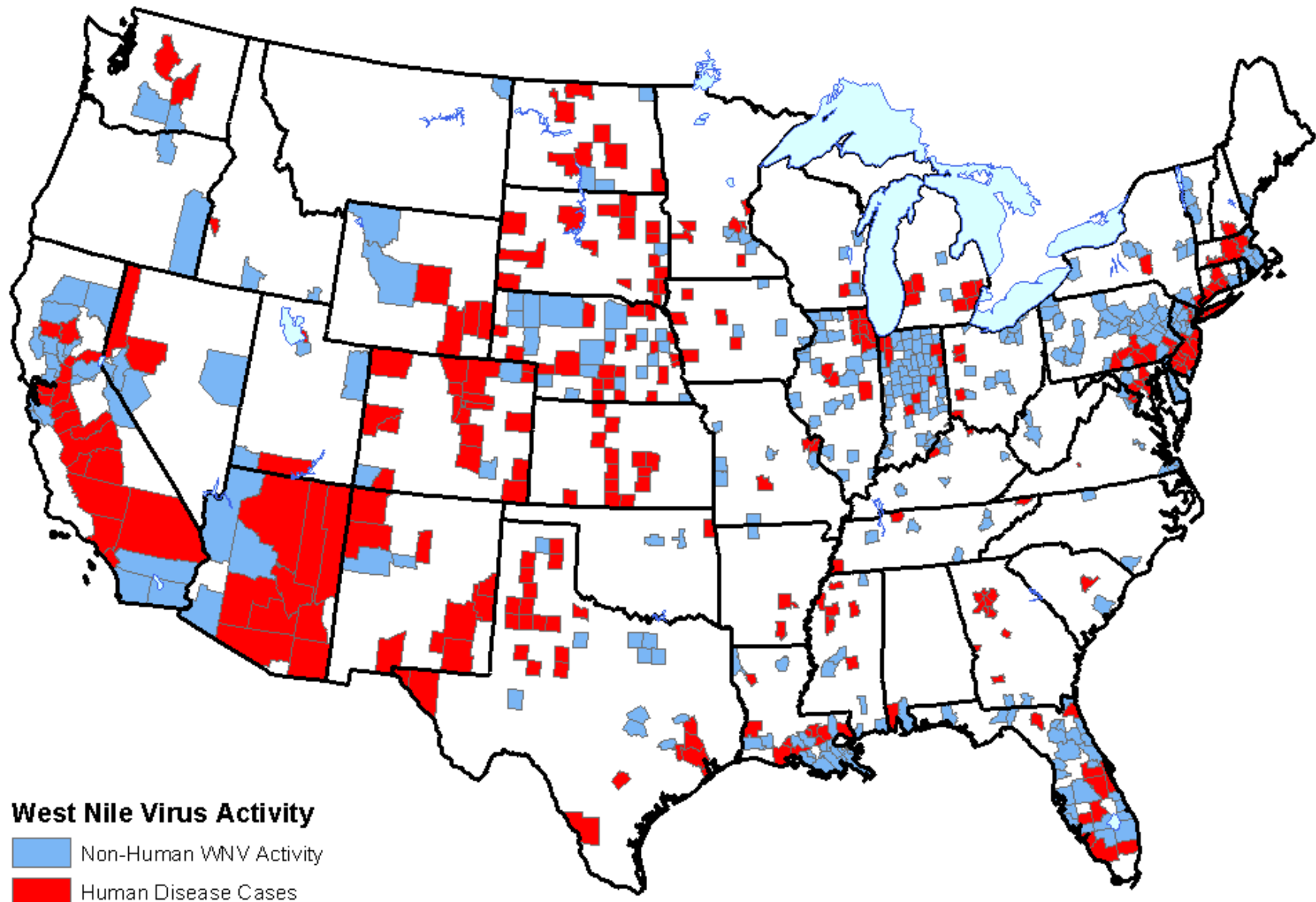
**West Nile Virus Activity**

-  Non-Human WNV Activity
-  Human Disease Cases

**2007**

National Center for Infectious Diseases  
**West Nile Virus Activity**  
Cumulative results for 2007 calendar year

**CDC**



2010

National Center for Infectious Diseases  
West Nile Virus Activity  
Cumulative results for 2010 calendar year

CDC

# Reported WNV Disease Cases U.S., 1999-2010

- 30,684 cases from 47 states and DC
- 1,219 (4%) fatal cases
- Based on serosurvey data, ~1.8 million persons infected with WNV since 1999

# Introduction and Spread of Arboviruses: Contributing Factors

- No previous immunity and minimal cross protective immunity
- Presence of the vectors
- Presence of the reservoirs
- Appropriate ecology and climate to support virus proliferation
- Environmental/behavioral factors

# Potential Emerging Arboviral Diseases in Arizona



# Presence of Risk – Mosquito Species

- During 2010, several mosquito species identified in AZ capable of transmitting non-endemic arboviruses

Genus	Species	Diseases
<i>Aedes</i>	<i>aegypti</i>  <i>vexans</i>	Chikungunya Dengue Rift Valley Fever Yellow fever Zika ?Rift Valley Fever
<i>Anopheles</i>	<i>franciscanus</i>	Mosquito malaria
<i>Culex</i>	<i>quinquefasciatus</i> <i>tarsalis</i>	Japanese encephalitis Rift Valley Fever Usutu
<i>Psorophora</i>	<i>columbiae</i>	Venezuelan equine encephalitis

Chikungunya

# Chikungunya Virus (CHIKV)

- Mosquito-borne *alphavirus*
- First identified in 1952 in Tanganyika
- Reservoirs include non-human and human primates
- Endemic in Asia and Africa
- Recent expansion of the virus caused large epidemic of disease
  - 1.5 million cases in ½ year in India during 2006
  - >300,000 cases on an Island with population 700,000



# Chikungunya Fever (CHIK)

- Majority (72-97%) of infected persons are symptomatic
- Average incubation period: 3-7 days (range 1-12 days)
  - Humans viremic 2-5 days after illness onset
- Typically presents as high fevers with severe arthralgias
  - Joint symptoms can be prolonged
- Other symptoms include: headache, rash, and myalgias
- Rare cases of encephalitis, hepatitis, death

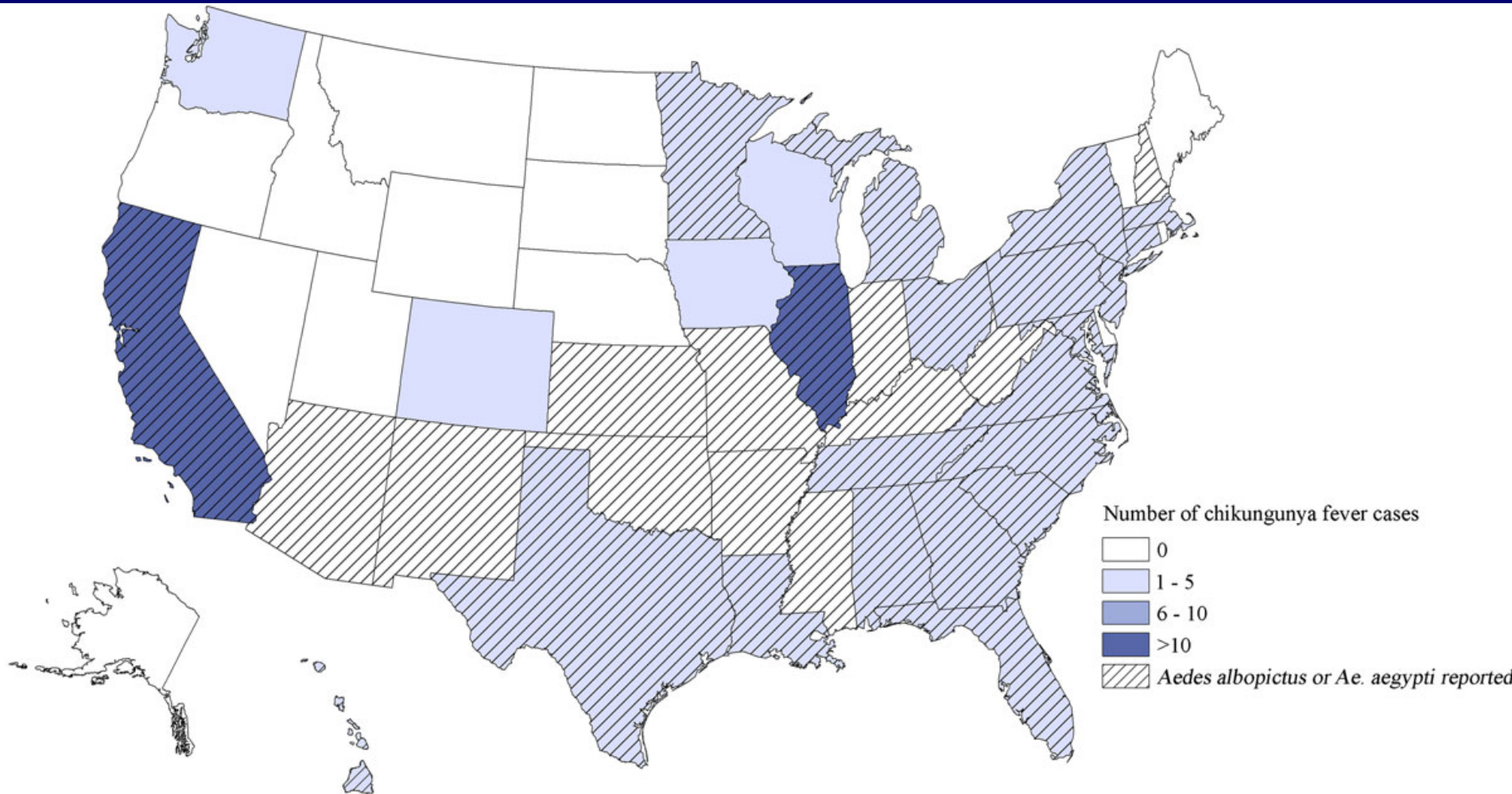
# CHIK Diagnosis and Treatment

- Diagnosis
  - Viral culture positive in first 3 days after illness onset
  - RT-PCR often positive in first week of illness
  - CHIK IgM and IgG positive ~4 days after illness onset
  - Testing available at CDC, one commercial lab and NYS lab
- Treatment
  - No specific antiviral medications
  - Supportive care

# Imported CHIK in U.S.

- 1995-2005: Only 3 cases diagnosed among travelers entering the U.S.
- 2006-2009: 106 cases among returning travelers from 25 states and D.C.
  - Median age 49 years (range 20-78)
  - 57% female
  - India most frequent (79%) travel destination

# CHIK Cases - U.S., 1995-2009



# Considerations for CHIK

- Currently not present in Western Hemisphere
- Risk of introduction and spread; there is no immunity and appropriate vectors and hosts exist
- 61% of return travelers with CHIK were potentially viremic while in U.S.
- No evidence of local transmission
  - Is it just a matter of time?

# CHIK Preparedness

- Increase awareness of the threat and disease
- CDC alert state health dept of positive cases
- CDC working with WHO/PAHO to finalize CHIKV Preparedness Plan for the Americas
- CDC creating toolkit for public health officials, physicians, vector control personnel, and public

# Dengue

# Dengue Virus (DENV)

- Mosquito-borne *flavivirus*
- First identified in 1944 in Hawaii and New Guinea
- Has 4 serotypes (DENV-1, 2, 3, 4)
  - Each serotype provides specific lifetime immunity
  - All serotypes cause severe and fatal disease
  - Genetic variation within serotypes; some more virulent or have greater epidemic potential
- Reservoirs include non-human and human primates
- Several million cases/yr throughout tropical areas
  - Recent sustained transmission in Florida



# Dengue (DEN) Clinical Syndromes

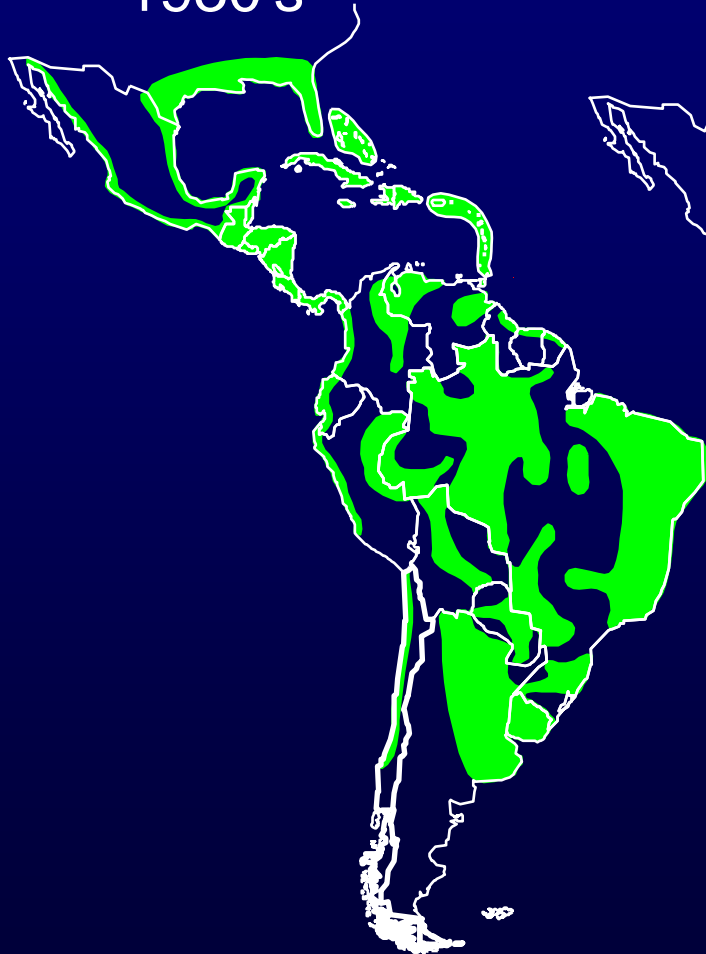
- Majority of infections are asymptomatic
- Incubation period: 3-14 days
- Classic DEN fever
  - Fever, headache, muscle and joint pain, nausea/vomiting, rash, hemorrhagic manifestations
- DEN hemorrhagic fever (DHF)
  - Severe abdominal pain, persistent vomiting, marked change in temperature, hemorrhagic manifestations, or change in mental status
- DEN shock syndrome (DSS)
  - DHF with evidence of circulatory failure

# Dengue Diagnosis and Treatment

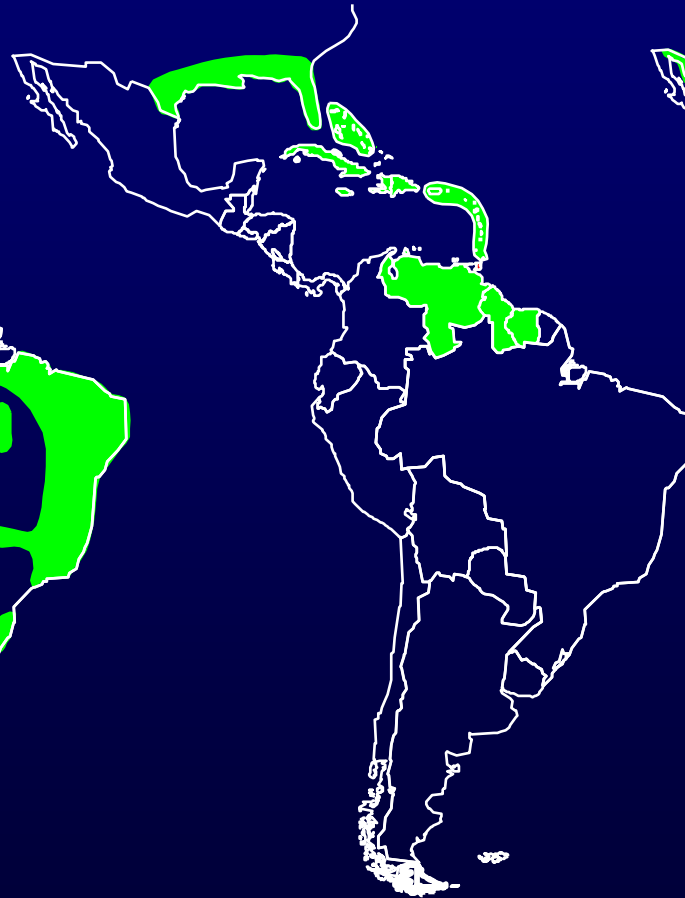
- Diagnosis
  - Viral isolation in first days after illness onset
  - RT-PCR typically positive within 5 days
  - IgM and IgG positive after 6 days
  - Need to differentiate between related flaviviruses
- Treatment
  - No specific antiviral medications
  - Symptomatic with emphasis on adequate hydration and aggressive fluid management for DHF and DSS

# *Aedes aegypti* Distribution in the Americas

1930's



1970



2007



# The Emergence of Dengue Hemorrhagic Fever in the Americas

Prior to 1981



1981-2008



# Considerations for DEN

- More severe disease with secondary DEN infections, due to immune enhancement
- If patient developed fever >2 wks after travel, DEN unlikely
- Mosquito barriers needed for infected persons until fever subsides
- Personnel projective measures are key as humans are the main amplifying reservoir
  - Use AC, having intact screens, wear insect repellent

Usutu

# Usutu Virus (USUV)

- Mosquito-borne *flavivirus*
- First identified in 1959 in South Africa
- Birds are main reservoir
- Endemic in Africa but has recently expanded into Europe
- Responsible for large bird die-offs
- Rare human cases with fever and rash have been reported

# Usutu Virus in Central Europe

- Beginning in August 2001, die-off of Eurasian blackbirds observed near Vienna, Austria
- Birds necropsied
  - Viral isolates 97% identical to Usutu virus

**Emergence of *Usutu virus*,  
an African Mosquito-Borne  
*Flavivirus* of the Japanese  
Encephalitis Virus Group,  
Central Europe**

Herbert Weissenböck,\* Jolanta Kolodziejek,† Angelika Url,\* Helga Lussy,†  
Barbara Rebel-Bauder,\* and Norbert Nowotny†‡



# Venezuelan Equine Encephalitis

# Venezuelan Equine Encephalitis Virus (VEEV)

- Mosquito-borne *alphavirus*
- First identified in 1938 in Venezuela
- Enzootic (I-E, II, III, and IV) and epizootic (IA-D) strains
- Reservoirs: rodents (enzootic) and horses (epizootic)
- Endemic in South and Central America
  - Previous outbreak in Texas during 1971
  - Less pathogenic strain in Florida
- Outbreaks with several thousands of cases

# VEE Clinical Disease

- Most infected persons are asymptomatic
- Average incubation period: 2-5 days
- Typically presents as malaise, fever, chills, and severe retro-orbital or occipital headache
- CNS involvement less frequent with seizures, somnolence, confusion, and photophobia
- Disease resolves within 1 week, malaise can persist
- Less than 1% of cases die

# VEE Diagnosis and Treatment

- Diagnosis
  - Viral isolation possible early in illness
  - RT-PCR may be positive in first week of illness
  - IgM and IgG antibody positive towards the end of the first week of illness
  - Testing available at the CDC
- Treatment
  - No specific antiviral medications
  - Supportive care

# Considerations for VEE

- Outbreak may occur with both human and horse disease
- Potential of human-to-human spread via respiratory secretions
- Could have several different strains impact the same area

Zika

# Zika Virus (ZIKAV)

- Mosquito-borne *flavivirus*
- First identified in 1947 in Uganda
- Reservoirs include ?nonhuman primates
- Endemic in Africa and part of Asia
- 14 cases reported until an outbreak of the disease noted in Micronesia in 2007

# Zika Virus in Yap



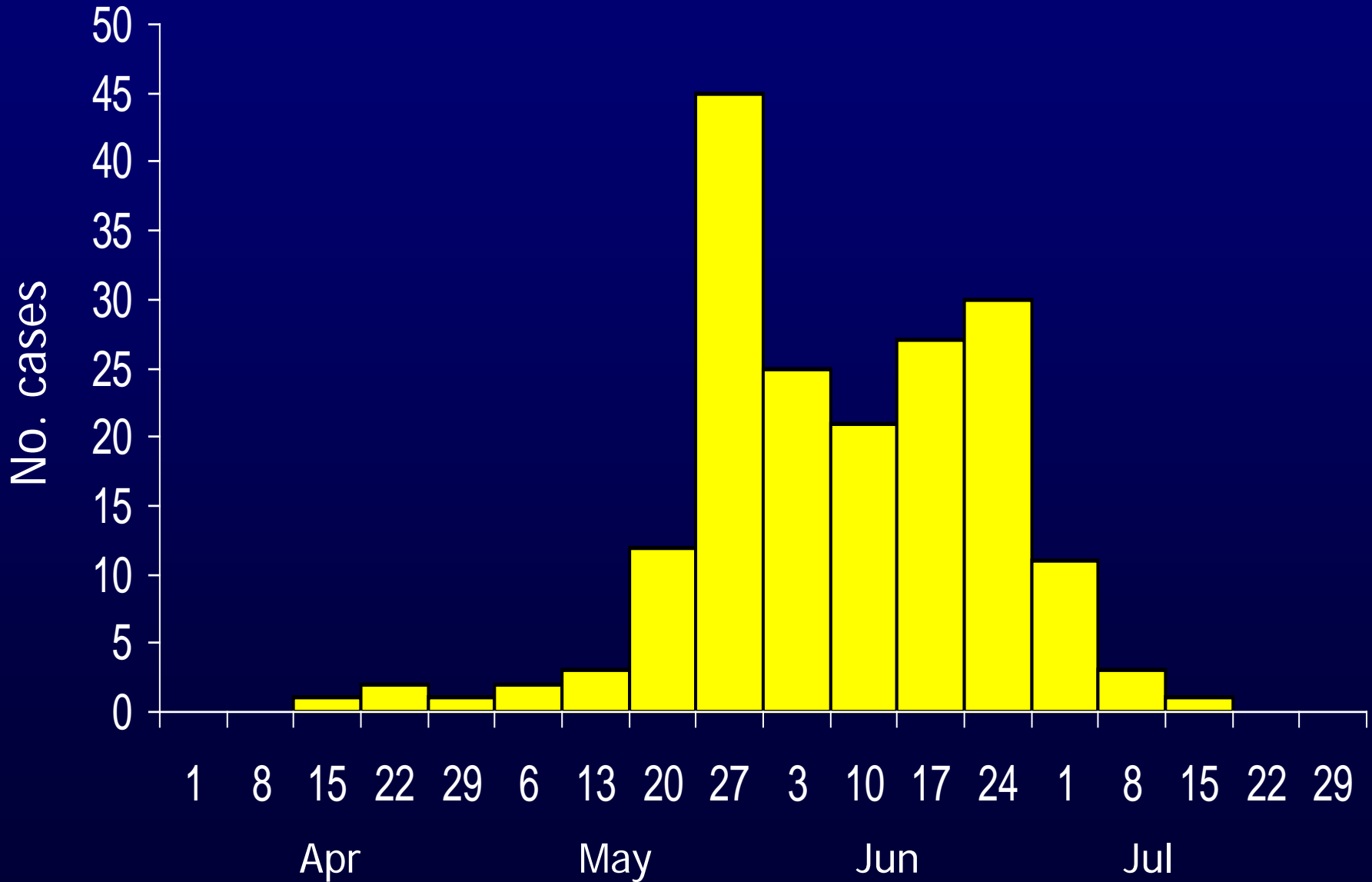


# Outbreak of Zika on Yap



- Over 2 months, 500+ cases of fever with rash, conjunctivitis, or arthralgia were reported
- Suspected dengue but subsequent testing identified Zika
- Prospective surveillance identified at least 180 cases with clinically compatible disease
  - 60% were female
  - Median age 33 years (range: 7m – 76yrs)
- Serosurvey showed that 74% of pop'n was infected

# Clinical Cases by Onset Week



# Syndrome in Confirmed ZIKV cases

N=31

	n	%
Macular or papular rash*	28	90
Arthralgia*	20	65
Subjective fever	20	64
Conjunctivitis*	17	55
Headache	13	43
Retro-orbital pain	12	39

\* Case defining criteria



# Summary of Clinical Findings

- Self-limited syndrome
- No hospitalizations
  - Patient in bed for days
- No hemorrhagic complications
- No deaths

# Zika Diagnosis and Treatment

- Diagnosis
  - CDC has recently developed Zika IgM assay and can perform neutralization testing
- Treatment
  - No specific antiviral medications
  - Supportive care

# Considerations for Zika

- Prior to 2007, had not caused large outbreak of disease
- Disease appears to be mild
  - High attack rate
  - Large outbreaks may reveal more severe manifestations
- Preventing mosquito bites is main prevention measure

# Prevention of Emerging Arboviral Diseases

- No or limited number of vaccines available for potential emerging arboviral diseases
- Prevention will rely on reducing vector exposure and early disease recognition
  - Personal protective measures (e.g., repellent)
  - Community level vector control programs
  - Increased suspicion for novel disease
  - Protecting viremic persons from mosquito bites

Japanese Encephalitis

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Venezuelan Equine Encephalitis

Chikungunya

Questions

Powassan

Dengue

Zika

????

Rift Valley Fever

????

Yellow Fever

????

Jamestown Canyon

The findings and conclusions in this presentation are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention



# Additional Information on Other Potential Arboviral Disease Threats

# Japanese Encephalitis

# Japanese Encephalitis Virus (JEV)

- Mosquito-borne *flavivirus*
- First identified in 1935 in Japan
- Reservoirs include pigs and wading birds
- Endemic in most areas of Asia and western Pacific
- Up to 30,000 cases are reported per year

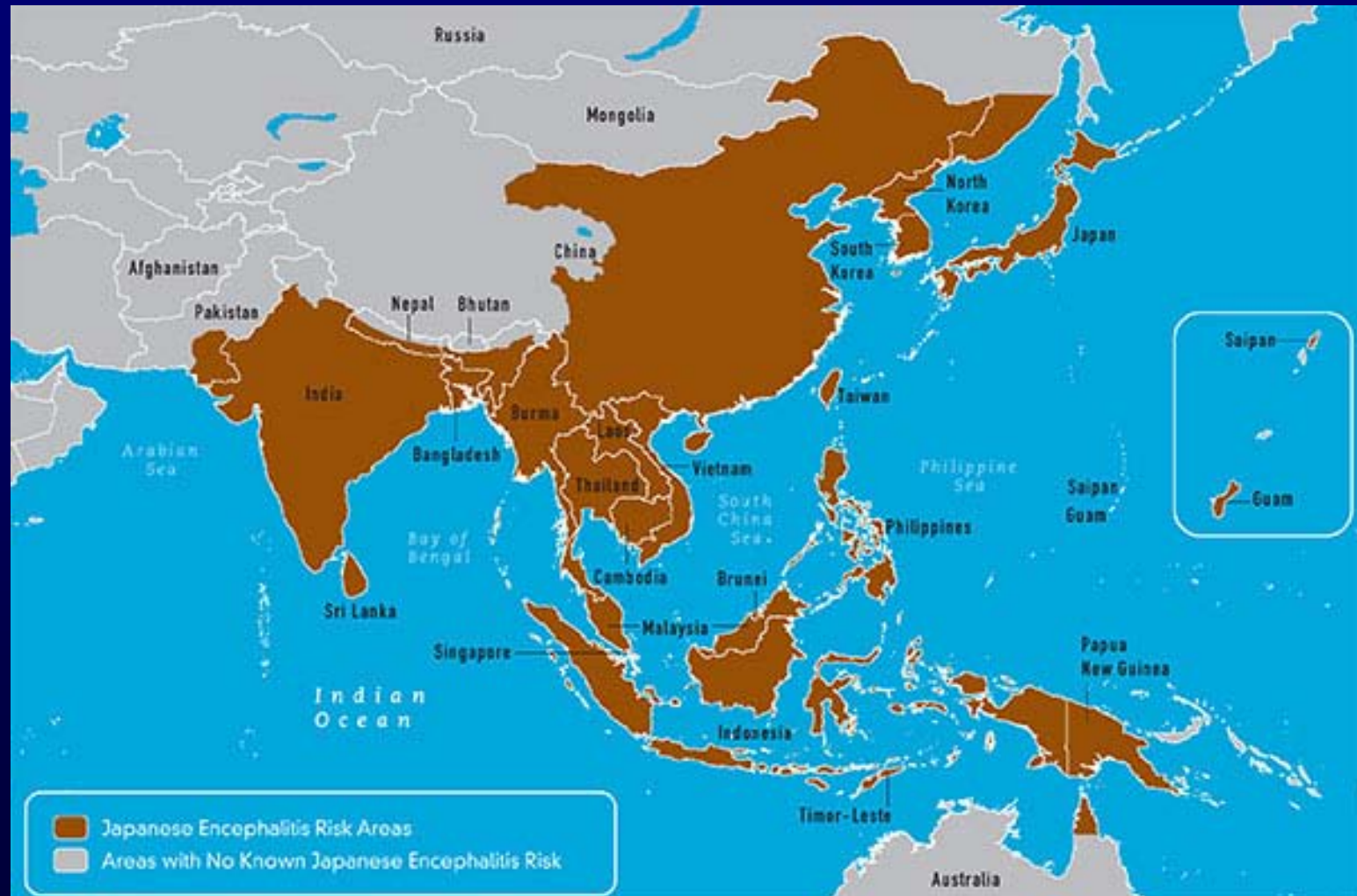
# Japanese Encephalitis (JE)

- Majority (99%) of infections are asymptomatic
- Incubation period: 5-15 days
- Acute encephalitis is most commonly identified
  - Typical onset with fever, headache, vomiting
  - Mental status changes, movement disorders, seizures, parkinsonian syndrome
- Milder disease (e.g., aseptic meningitis or undifferentiated febrile illness) also occurs
- Case-fatality ratio of severe disease 20-30%
- 30-50% with neurologic or psychiatric sequelae

# JE Diagnosis and Treatment

- Diagnosis
  - Detection of virus rare
  - Diagnosis relies on detection of IgM and IgG antibodies
  - Must rule out cross-reactivity with other flaviviruses and being positive due to vaccination
  - Testing available at CDC
- Treatment
  - No specific antiviral treatment
  - Supportive care

# Areas at risk for JE disease



# JE Disease Among Travelers

- From 1973-2008, 15 cases published among U.S. travelers
  - 11 occurred before vaccine introduced in 1992
  - Median age 29 (range: 1-68 years) and 80% males
  - 7 tourists, 6 soldiers, 1 expat, 1 unknown
  - Traveled to China, Japan, Philippines, Singapore, Thailand, Vietnam
  - Case-fatality ratio – 17%
- Since 2009, at least 3 additional cases all among unvaccinated travelers

# JE vaccine

- Only one licensed vaccine available (Ixiaro)
  - Licensed in 2009 for those 17 years and older
  - No vaccine available for children
- Two doses required 28 days apart
- Currently used by military, laboratory personnel, and at risk travelers\*

\*For more information visit current ACIP recommendations:  
<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5901a1.htm>



# Considerations for JE

- Humans not reservoirs, thus importation will rely on infected mosquitoes or livestock/birds
- Locally-acquired JE cases may be mistaken as WN or SLE disease due to cross-reactivity in antibody assays
- Vaccine aids in prevention but require >1 month to be effective and not licensed in children

# Yellow Fever

# Yellow Fever Virus (YFV)

- Mosquito-borne *flavivirus*
- First identified in 1927 in Ghana
- Reservoirs include non-human and human primates
- Endemic in tropical areas of South America and Africa
- Causes 300,000 cases and 20,000 deaths annually

# Yellow Fever (YF) Disease

- Most infections are asymptomatic
- Incubation period: 3-6 days
- Undifferentiated febrile illness most common
- Small proportion will develop severe disease with jaundice and hemorrhagic manifestations
- 20-50% of severe cases will die

# YF Diagnosis and Treatment

- Diagnosis
  - Virus often detectable during the first week of illness (initially by culture then RT-PCR)
  - IgM and IgG antibodies often present with 3-5 days after illness onset
  - Important to rule out previous vaccination as IgM has been found 3-4 years following vaccination
- Treatment
  - No specific antiviral medications
  - Supportive care

# YF Vaccine

- Live-attenuated viral vaccine available
  - Several precautions and contraindications
- Over 500 million doses given since 1936
- One dose provides at least 10 years of protection
- Rare but serious side effects can occur following vaccination

# Considerations for YF

- Urban outbreaks in the Western Hemisphere likely to increase risk of importation
  - One unvaccinated traveler could cause an outbreak
- Vaccine can not be given to all persons and vaccine supplies are limited
- Early recognition and containment of cases important to prevent subsequent transmission

# Rift Valley Fever

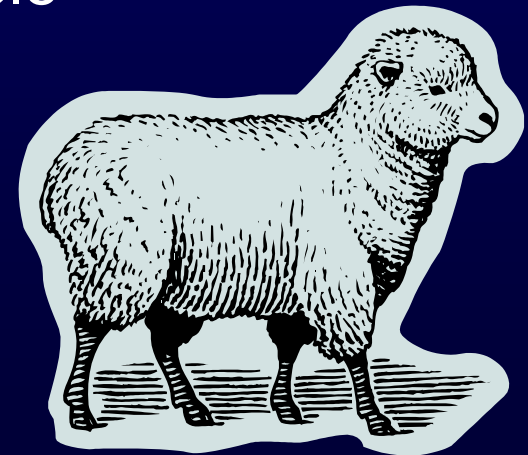


# Rift Valley Fever Virus (RVFV)

- Mosquito-borne *Phlebovirus* (Bunyaviridae)
  - *Aedes*, *Anopheles*, *Culex*
- First reported in 1931 in Rift Valley, Kenya
- Also transmitted through infected blood, body fluids (milk), or tissues
- Preferred vertebrate host are domestic ruminant livestock and humans
- Endemic in sub-Saharan and North Africa
  - Recent activity in Saudi Arabia and Yemen

# Rift Valley Fever (RVF) Disease: Animals

- RVFV infects many species of animals
  - Domestic: cattle, sheep, goats, (camels)
  - Wild: rodents, frogs, most avians, monkey, deer, moose
- Cause severe disease with high mortality particularly in domestic ruminants
  - Younger animals particularly susceptible
- Causes abortions in livestock
  - 100% in pregnant ewes
  - Often the first sign of disease



# RVF Disease: Humans

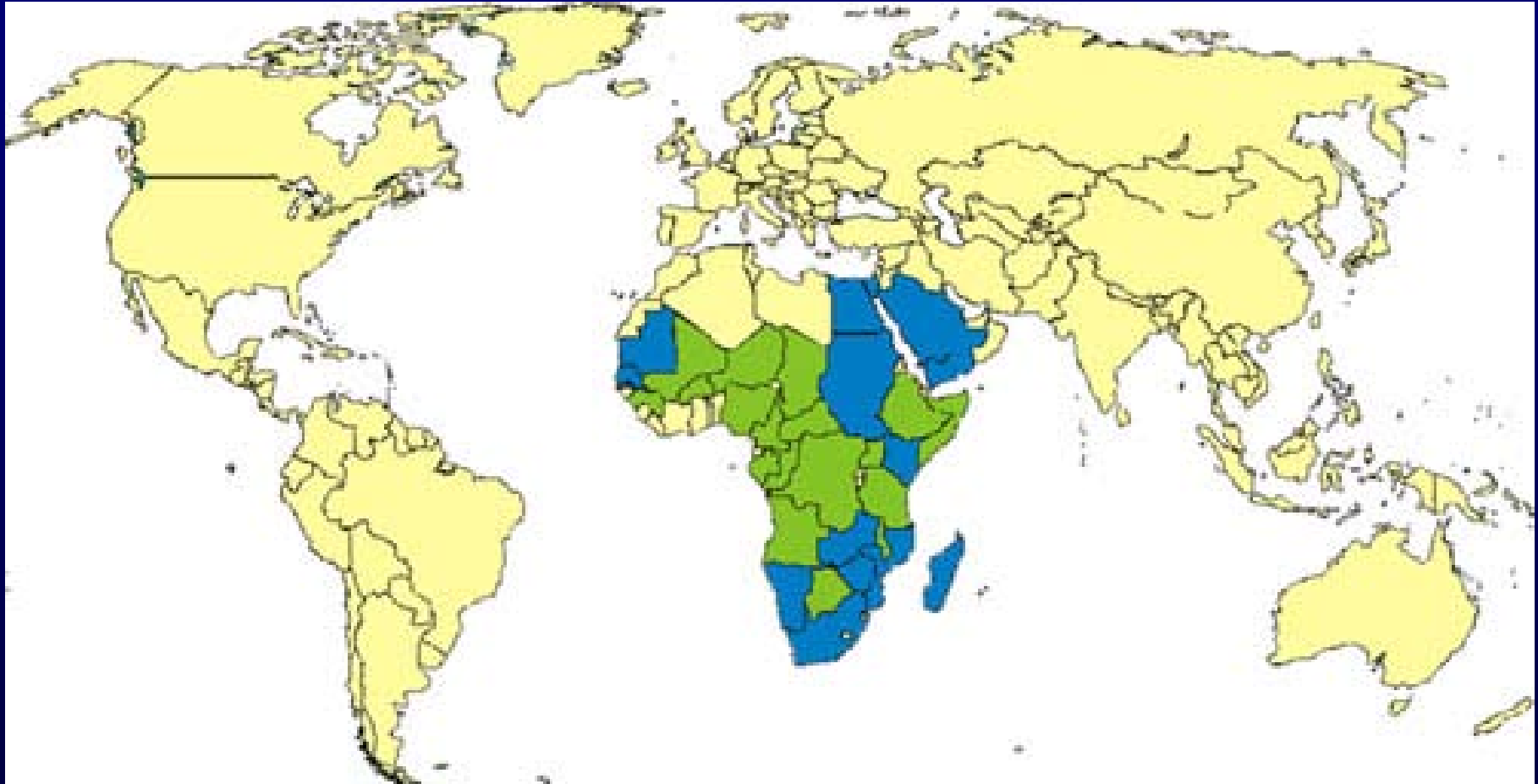
- Asymptomatic infections common
- Incubation period of 2-6 days
- Flu-like illness with fever, muscle pain, joint pain, and headache
- More severe disease can occur
  - Ocular disease (0.5-2%)
  - Meningoencephalitis (1%)
  - Hemorrhagic fever (<1%)
- Case-fatality rate varies widely, but <1% overall

# RVF Diagnosis and Treatment

- Diagnosis
  - Viral detection early in illness or in postmortem tissues
  - Serological tests
- Treatment
  - No specific antiviral medications
  - Supported care



# Rift Valley Fever Distribution Map



- Countries with endemic disease and substantial outbreaks of RVF**
- Countries known to have some cases, periodic isolation of virus, or serologic evidence of RVF**

# Considerations for RVF

- Pathways for entry into U.S.\*
  - Importation of RVF-infected animal species
  - Entry of RVF-infected persons
  - Mechanical transport of RVF-infected vectors
- USDA estimates the most vulnerable for exposure to RVF
  - Domestic ruminant livestock (sheep, goats, beef and dairy cattle)
  - Camelid species (llama, alpaca, etc)
  - 154,374,756 persons

\* Kasari TR, Carr DA, Lynn TV, Weaver JT. Evaluation of pathways for release of Rift Valley fever virus into domestic ruminant livestock, ruminant wildlife, and human populations in the continental United States. J Am Vet Med Assoc. 2008 Feb 15;232(4):514-29.