WEST NI LE VI RUS INFECTION 2004 WESTWARD MIGRATION

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County of Los Angeles Department of Health Services

UCLA Grand Rounds
July 2, 2004


DHS
Acute Communicable Disease Control
OUTLINE

- West Nile Virus Overview
- West Nile Virus Outbreaks and entry to U.S. 1999
- Surveillance
- Epidemiology and Clinical Presentation
- Diagnosis
- New Modes of Transmission
- Prevention
ARTHROPOD-BORNE ENCEPHALITIS (1)

- **Agents:** Eastern equine, Western equine, St. Louis, La Crosse, California, West Nile viruses
- **Incubation:** 2-15 days
- **Reservoir:** Unknown, probably wild birds
- **Transmission:** Bite of infective mosquitoes
ARTHROPOD-BORNE ENCEPHALITIS (2)

- Presentation: Ranges from asymptomatic to aseptic meningitis to encephalitis
- Diagnosis: Serologic tests
- Treatment: Supportive
- Prevention: Mosquito avoidance, Mosquito abatement
WEST NI LE VI RUS

▶ Single-stranded RNA enveloped virus of the family Flaviviridae, genus Flavivirus

▶ Japanese encephalitis virus
  ✓ West Nile virus (WNV)
  ✓ Saint Louis encephalitis virus
  ✓ Japanese Equine encephalitis virus
  ✓ Murray Valley virus complex
  ✓ Kinjin virus
BACKGROUND: WNV INFECTIONS (1)

- 1937: First isolated in West Nile district of Uganda
- 1957: Israeli nursing home outbreak
  ✓ Associated with severe neurologic disease and higher mortality rate
- 1990s: Frequency and severity of WNV outbreaks increased
BACKGROUND: WNV INFECTIONS (2)

- Outbreaks in:
  - 1994 Algeria
  - 1996 Romania: associated with severe neurologic illness
  - 1997 Czech Republic
  - 1998 Italy
  - 1999 Russia: associated with severe neurologic illness
  - 1999 USA: entry into US/NY outbreak

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WEST NILE FEVER: BACKGROUND AND EPIDEMIOLOGY (1)

- Worldwide distribution
- Enzootic many parts of the world: Africa, Middle East, West Asia, Australia
- Caused primarily outbreaks of febrile illnesses: soldiers, children, and healthy adults
WEST NILE FEVER: BACKGROUND AND EPIDEMIOLOGY (2)

- Commonly found in humans and birds and other vertebrates
- 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
WEST NILE VIRUS (WNV) TRANSMISSION CYCLE

Mosquito Vector

Incidental Infections

Bird Reservoir Hosts

West Nile Virus

Incidental Infections

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ECOLOGY

- Virus maintained bird—mosquito—bird cycle
- Small birds serve as 1° amplifying host
- Temperate climate cycle starts spring when mosquitoes 1\textsuperscript{st} emerge and lasts until fall
- Like SLE, culex mosquitoes are 1° amplifying vectors. Other mosquitoes can act as bridge vectors biting both humans and birds
MYSTERY ILLNESS, NEW YORK CITY (1)

- August 1999, New York City (NYC)
- Infectious Disease physician reported 2 cases of encephalitis from northern Queens to NYC Dept of Health (NYC DOH)
  - Fever, altered mental status, abnormal CSF
  - One patient with severe muscle weakness
- NYC DOH initiated active case surveillance at nearby hospitals
At the same time...

The Bronx zoo reported large numbers of zoo birds dying with encephalitis...

Local residents reported large number of dead crows

Zoo birds and dead crow work-up:

- Molecular techniques identified WNV

SLE does not normally kill avian reservoirs!
Human case work-up:
✓ WNV identified by molecular, immunohistochemical, and serologic techniques
First documented West Nile Virus in Western hemisphere
First arboviral outbreak in NYC since the Yellow Fever epidemics of the 19th century
...THERE WAS WNV IN THE NYC AREA
WEST NI LE VI RUS STRAI N

- 1999 NY WN strain from a flamingo “nearly identical” to 1998 Israel avian strain
- RT-PCR found > 99.8% similarity
- Avian strain isolated from a dead goose brain in 1998 similar to Israel epizootic outbreak
- Virus prior originated in Middle East

Emerg Inf Dis 2001
D16:\WNV_UCLA July 2_2004.ppt  No. 16
### 1999 VERIFIED WNV SURVEILLANCE REPORTS

<table>
<thead>
<tr>
<th>Year</th>
<th>States</th>
<th>Humans/Fatilities</th>
<th>Birds</th>
<th>Mosquito Pools</th>
<th>Horses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999</td>
<td>4</td>
<td>62/6</td>
<td>?</td>
<td>16</td>
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</tbody>
</table>

- ✔ Household-based human serosurvey in Queens determines 2.6% seroprevalence
- ✔ WNV infected mosquitoes trapped in Ft. Totten, suggesting overwintering of WNV
HOW DID WNV GET HERE?

- No one knows... Some speculations
  - Infected human host
  - Bio-terrorism event
  - Importation of infected birds or mosquitoes, larva
  - Migration of infected birds
  - Storm-transported vertebrae host (bird)
OUTCOME OF WEST NILE VIRUS INFECTION AMONG HOSPITALIZED PATIENTS

- At discharge (NY and NJ, 2000)
  - More than half did not return to functional level
  - Only one-third fully ambulatory

- At one year (NYC 1999 patients)
  - Fatigue 67%, memory loss 50%, difficulty walking 49%, muscle weakness 44%, depression 38%

- Case fatality: 4–18%
2000!

Its Back or

The Year of the Corvid
## 2000 VERIFIED WNV SURVEILLANCE REPORTS

<table>
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<th>Year</th>
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<td>11 + DC</td>
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<td>4,305</td>
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<td>63</td>
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- Field-studies determine that dead crow = enzootic WNV foci
- Household-based serosurveys identify seroprevalence in Staten Island, Suffolk City, and Fairfield City, CT, to be lower than Queens in 1999
YEAR 2001

The Calm before the Storm!
### 2001 Verified WNV Surveillance Reports

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<tr>
<td>2001</td>
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<td>66/9</td>
<td>7,332</td>
<td>919</td>
<td>731</td>
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- First major outbreaks in the South, GA and FL
YEAR 2002

- Largest arborviral epidemic ever documented in North America
- New modes of transmission documented!
  - Blood
  - Organ
  - Perinatal
  - Percutaneous
- New clinical syndromes documented
  - Acute Flaccid Paralysis Syndrome
West Nile Virus Activity

- Blue: Non-Human WNV Activity
- Red: Human Disease Cases

National Center for Infectious Diseases

West Nile Virus Activity
Cumulative results for 2002 calendar year reported as of April 15, 2003
## 2002 Verified WNV Surveillance Reports

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<td>2002</td>
<td>44 + DC</td>
<td>4,156/284</td>
<td>15,941</td>
<td>6,604</td>
<td>14,571</td>
</tr>
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</table>

Horse vaccine became available
YEAR 2003

NIMBY: “Not in My Backyard”

Now playing Coast to Coast!
Welcome to Colorful Colorado!
HUMAN WNV DISEASE CASES, U.S., 2003*: REGIONAL DISTRIBUTION

* Reported as of 1/20/2004

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WNV SURVEILLANCE ACTIVITY 2003

- 9,858 human cases confirmed in Arbonet from 47 states
  - Colorado greatest number—2,477 cases
- 262 deaths nationwide
- Peak activity late July-Sept (~75%)
- WNV—fever 69% cases, 29% CSF+
- WNV activity in birds, mosquito pools, horses, and humans in 48 states
## 2003 VERIFIED WNV SURVEILLANCE REPORTS

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<td>2003</td>
<td>46 + DC</td>
<td>9122/223</td>
<td>11613</td>
<td>7856</td>
<td>4533</td>
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WEST NILE VIRUS: HUMAN ILLNESS

- Most cases asymptomatic or mild to moderate symptoms
- Fewer than 1% of WNV viral infections result in severe neurological disease
- Median age in 2003 was 47 (0-99 yrs)
  - Fatal cases: median age 77 (0-97 yrs)
- Mortality rate in 2003: 2%
  - 7% of WN neuroinvasive disease cases

Carol Ann Glaser, DVM, et al.
SUMMARY OF 2003 WNV ACTIVITY

- WNV activity has dramatically increased throughout US from 1999 to 2003
- In 2003: human cases in 45 states
  - No human cases documented in Alaska, Hawaii, Oregon, Washington State, and Maine
- Increased proportion of cases WNV Fever in 2003
  - More WNV diagnostics available at state, county, private laboratories
- States with greatest WNV activity: Colorado, S. Dakota, N. Dakota
Individual presented to LA Hospital with aseptic meningitis first week in August 2002

Denied history of travel outside of LAC, mosquito bites, blood or organ transfusion, IVDU

Thorough ecological investigation revealed no evidence of WNV in birds, mosquito pools, or sentinel chicken flocks in LAC
SINGLE HUMAN CASE IN LAC, 2002 (2)

- Case remains a mystery
- Laboratory results confirmed at State DHS and CDC
- Individual recovered uneventfully
WNV SURVEILLANCE ACTIVITY IN CALIFORNIA 2003

- Sentinel chicken flocks positive from Riverside and Imperial counties July-September 2003
- 32 mosquito pools WNV positive: Imperial, LAC and Riverside
- 96 dead birds positive for WNV throughout So. CA
  - 64 positive WNV LAC: infected dead birds of 1,615 tested in 2003 (one horse)
  - The greatest number from the San Gabriel Valley
WEST NILE VIRUS
LOS ANGELES COUNTY 2003

- Only one confirmed case West Nile Fever October 2003
- 61-years-old sx: fever, headache, N&V prior hx Hepatitis B and C, IVDU
- Remembered frequent mosquito bites
- No travel history
SPREAD OF WEST NILE VIRUS IN US AS OF JUNE 29, 2004

www.cdc.gov/ncidod/dvbid/westnile/index.htm

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WNV: CALIFORNIA 2004
JUNE 30, 2004

- LAC: > 250 infected crows
- California > 593
- Mosquito pools > 21
- Chickens positive > 72
- 11 CA cases: 8 in San Bernadino, 2 in Los Angeles, 1 in Riverside
CLINICAL PRESENTATION
WEST NILE DEFINITIONS

WNND = West Nile neuro-invasive disease:
- Encephalitis
- Aseptic meningitis
- Acute Flaccid paralysis

West Nile fever – “dengue like”
Asymptomatic

2002: 4,156 cases with 2,946 WNND
2003: 9,100 cases with 2,600 WNND
WNV HUMAN INFECTION
“ICEBERG”

1 CNS disease case = ~150 total infections

<1% CNS disease

~20% “West Nile Fever”

~80% Asymptomatic

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

Very crude estimates

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“BENIGN” WEST NILE FEVER

- 2003 experience suggests it may not be so benign:
  - Duration of illness=22 days*

- Cohort study Colorado:
  - Of 40 cases**: 
    - Body aches 98%
    - Eye pain 63%
    - Skin rash 63%
    - Swollen lymph nodes 48%
    - Nausea or vomiting 48%
  - Anecdotal reports: lingering fatigue, weakness, muscle fasciculations for weeks..sometimes months

*International Conference on Emerging Infectious Disease
**Pape J, 5th National Conference on WNV in US
WNV ASEPTIC MENINGITIS (1)

- 722 cases in 2002
  - 361 (50%) male
  - Median age: 46 years (3 month-91 years)
    - Age groups:
      - 0-39 years: 253 (35%)
      - 40-69 years: 367 (51%)
      - 70 and older: 102 (14%)

- Number of deaths: 15 (2%)
  - Number of males: 11 (73%)
  - Median age: 74 years (40-91 years)

O’Leary et al. Vector-Borne and Zoonotic Disease 2004
WNV ASEPTIC MENINGITIS (2)

- Fever, HA, nuchal rigidity (100%)
- Nausea, vomiting, neck pain, myalgia (80%)
- Variable frequency:
  - Low back pain
  - Tremors
  - Parkinsonism
  - Myoclonus
  - Flaccid paralysis of limb
  - Cranial Nerve palsies
  - Cerebellar signs

- Outcome: good

Carol Ann Glaser, DVM, et al.
WNV ENCEPHALITIS (1)

- 2,220 encephalitis cases in 2002
  - 1239 (56%) male
  - Median age: 64 years (1 month-99 years)
    - Age groups
      - 0-39 years: 359 (16%)
      - 40-69 years: 974 (44%)
      - 70 and older: 887 (40%)
- Number of deaths: 261 (12%)
  - Number of males: 164 (63%)
  - Median age 78 years (19-99 years)

O’Leary et al. Vector-Borne and Zoonotic Disease 2004

O’Leary et al. Vector-Borne and Zoonotic Disease 2004

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WNV ENCEPHALITIS (2)

- Almost all: fever, headache, altered mental status
- Variable frequency of:
  - Tremors
  - Weakness
  - Cerebellar signs/symptoms (some develop after MS improved)
  - Brainstem/Cranial nerve >50% (nystagmus, dysphagia, decreased gag)
  - “locked-in” syndrome
- Outcomes variable: ~70% baseline at 8 months

Carol Ann Glaser, DVM, et al.
RISK FACTORS FOR WNV ENCEPHALITIS?

- Older Age -- surveillance data (>50, 10 fold; >80, 43 fold)
- HTN and cerebrovascular disease
  
  Campbell GL, Lancet Infect Dis 2002
- Age > 75 years, diabetes risk for death
  
- No association WNE and HTN
  
  Han LL, J Infect Dis 1999
- Age > 51 years, HTN, male
  
  Lillibridge KM, ICEID conference

Carol Ann Glaser, DVM, et al.
THESE RISKS

- Virus crossing blood brain barrier is enhanced by factors that disrupt above.
- Or increased duration of level of viremia due to immune disfunction.
INTERESTING FINDINGS FROM COLORADO WNV CASES 2003...

- Average duration of illness: 13.9 days
- Patients still ill at time of interview: 37%
- Known mosquito bite: 67%
- Repellant use: Never = 53.7%
  Always = 11.2%
- 60% of patients reported a rash
- 45% reported change in mental state
- 31% reported muscle tremors

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Polio myelitis Due to West Nile Virus

To the Editor: Poliomyelitis is a clinical syndrome defined by the presence of fever, meningitis, and flaccid paralysis. In the United States, this syndrome was historically associated with infection by poliovirus but is now more commonly seen with other enteroviruses. We describe a case of poliomyelitis in a patient infected with West Nile virus, a flavivirus.

A 50-year-old woman from Louisiana had a headache on the day before she traveled to Georgia for the July 4 holiday. After she arrived, her headache worsened, and she had severe myalgia. Two days after the onset of headache, weakness developed, and the patient was admitted to the hospital. She was febrile (temperature, 39.5°C) but was awake, alert, and fully cognizant. She had moderate bilateral and appendicular weakness (Medical Research Council grade 4–5), with a normal sensory examination and retained deep-tendon re-
WNV- ASSOCIATED ACUTE FLACCID PARALYSIS (AFP) (1)

- Acute Flaccid Paralysis (AFP) Syndrome
  - 6 cases reported in MMWR Sept. 20, 2002
  - Pathologic process: anterior horn cells and motor axons similar to acute poliomyelitis

- Clinical description:
  - Acute onset of asymmetrical weakness without pain or sensory loss
  - CSF: pleocytosis, elevated TP
  - EMG: motor involvement and not demyelinating process
WNV- ASSOCIATED ACUTE FLACCID PARALYSIS (AFP) (2)

- Infrequently reported with WNV infection and other flaviviruses (J EE and SLE)
- Attributed to various etiologies:
  - GBS, Radiculopathy, Transverse myelitis
- Not reported in recent outbreaks outside of US (Romania, Russia, Israel)
WNV- ASSOCIATED ACUTE FLACCID PARALYSIS (AFP) (3)

- Prominent feature in some encephalitis cases in NYC
- 2003: Colorado WNV-AFP cases from 3 counties evaluated to assess clinical outcomes, patterns of weakness, frequency of condition
WNV-AFP CASES FROM 3 CO COUNTIES
SUMMER 2003: SUMMARY FINDINGS (1)

- 32 Patients Identified with AFP:
  - 18 (56%) male
  - Median age: 56 yrs (range: 15-84)
  - 26 (81%) with no prior medical conditions

- Attack Rate: 4.4/100,000 comparable to poliovirus epidemics

- Associated neurologic illness:
  - AFP alone 3 (16%)
  - AFP+ meningitis 11 (34%)
  - AFP+encephalitis 16 (50%)

Presented at the 5th National WNV Conference February 2004

DHS
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3 distinct clinical and pathologic presentations:

- "Poliomyelitis": 27 (84%)
- GBS: 4 (13%)
- Brachial plexus dysfunction/neuritis: 1 (3%)

Clinical features of poliomyelitis

- Asymmetric weakness without sensory loss
- EMG in 14 c/w anterior horn cell disease
- MRI in 3 anterior spinal cord abnormalities
- Respiratory paralysis requiring mechanical ventilation in 11/27 cases

Presented at the 5th National WNV Conference February 2004
WNV-AFP CASES FROM 3 CO COUNTIES SUMMER 2003: SUMMARY FINDINGS (3)

- 3 Month follow-up of 27 cases of AFP
  - 3 deaths of 27 followed
  - 2 still on chronic ventilation
  - 66 days median duration of intubation in 12 persons requiring mechanical ventilation
  - 15 patients with some improvement in strength with a range of recovery
  - 7 patients with minimal or no improvement

- Conclusion: Public health burden could be substantial!

Presented at the 5th National WNV Conference February 2004

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D16\WNV_UCLA July 2_2004.ppt   No. 62
WEST NILE VIRUS
SPINAL FLUID

CSF:

- 0-1000 cells (85-95% with pleocytosis):
  - PMNs can predominate and persist up to 7 days
  - Often with reactive lymphocytes:
    - Plasma cells, “Mollaret” cells
    - Some cases have been confused with lymphoma

- Most elevated protein (90%)

- Normal glucose

Pepperell, C., JAMC 2003
Lillibridge KM., Emerg Inf Conference, 2003
OTHER DIAGNOSTICS

- MRI: more helpful than CAT SCANS
- Show leptomeningeal or periventricular enhancement
WEST NI LE VI RUS
LABORATORY AND NON-CNS

- Leukocytosis or leukopenia
- Hyponatremia
- Pancreatitis, lipase elevations
- Hepatitis, abnormal LFTs
- Myocarditis (elevated CPK, troponin, abn EKG)
- Myositis (elevated CPKs)

Carol Ann Glaser, DVM, et al.
PEDIATRIC CASES
### WNV: Pediatric Cases

<table>
<thead>
<tr>
<th>Year</th>
<th>Percentage</th>
<th>Count</th>
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<tr>
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<td>0</td>
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<td>2001</td>
<td>0%</td>
<td>0</td>
</tr>
<tr>
<td>2002</td>
<td>4%</td>
<td>150</td>
</tr>
<tr>
<td>2003</td>
<td>8%</td>
<td>763</td>
</tr>
</tbody>
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Vidwan G, Clin Inf Dis, 2004  
Dan O'Leary, CDC, personal communication, 2004
763 WNV infections in <18 years:

- West Nile Fever: 79% (n=604)
- Meningitis: 11% (n=80)
- Encephalitis: 4% (n=33)
- Unspecified neuroinvasive: 5% (n=35)
- Other/unknown 1% (n=11)
Laboratory Diagnosis of West Nile Virus Infections
THEORECTICAL DEPICTION OF WNV HUMAN VI REMIA & IMMUNE RESPONSE

- Virus Assays
- Serology Assays
- WN viremia
- IgM
- IgG
- Neutralizing Ab
- CNS illness
- DAYS POST ONSET
- ELISA P/N

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# Testing for West Nile Virus

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<tr>
<th></th>
<th>Bird Surveillance</th>
<th>Mosquito Surveillance</th>
<th>Veterinary Diagnostic</th>
<th>Human Diagnostic</th>
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<tbody>
<tr>
<td><strong>Test Target</strong></td>
<td>Virus</td>
<td>Virus</td>
<td>Antibody</td>
<td>Antibody</td>
</tr>
<tr>
<td><strong>Sample Type</strong></td>
<td>Tissues, oral swabs</td>
<td>Mosquito pools</td>
<td>serum</td>
<td>Serum, plasma, CSF tissues</td>
</tr>
<tr>
<td><strong>Available Tests</strong></td>
<td>TaqMan RT-PCR NASBA, RT-PCR, Isolation in Vero VecTest</td>
<td>TaqMan RT-PCR NASBA, RT-PCR Isolation in Vero VecTest</td>
<td>IgM ELISA Plaque Reduction Neutralization</td>
<td>IgM ELISA IgG ELISA Plaque Reduction Neutralization IgA ELISA IFA</td>
</tr>
<tr>
<td><strong>Comments</strong></td>
<td>Birds have high viremia; $10^6$-$10^9$</td>
<td>Mosquito pool titers vary; VecTest will detect approx. 65%</td>
<td>Tissues from fatal equine cases tested by RT-PCR</td>
<td>Tissues from fatal human cases tested by RT-PCR. Plasma/serum/CSF can be tested by NAT.</td>
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RECOMMENDED SEROLOGICAL TESTING ALGORITHM FOR ARBOVI RUSES

human serum/ plasma/ CSF

IgM ELISA
IgG ELISA?

Presumptive
Confirmed
POS
Plaque reduction Neutralization test (PRNT) (confirmation & specificity)
NEG
STOP

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LABORATORY DIAGNOSIS WEST NILE VIRUS (1)

- Serological Diagnosis primary method of diagnosis
- IgM and IgG Capture ELISA preferred diagnostic test: simple, sensitive and can be used for serum and CSF (MAC Elisa)
  - 80% IgM positive at clinical presentation (WNV fever)
  - 95% IgM positive within 8th Day of symptom onset
  - 500 days after infection IgM can still be positive
  - This is a troubling problem for blood bankers
- People immunized against yellow fever, JE or dengue Hx can be false positive
LABORATORY DIAGNOSIS
WEST NILE VIRUS (2)

- PCR poor sensitivity 14%-57%
- Nearly impossible to culture the virus
- Plaque reduction neutralization test (PRNT):
  - Most specific test for arthropod-borne flaviviruses
  - Can help distinguish false-positive IgM, IFA
  - Distinguish between SLE and WNV
  - Used for confirmatory testing of WNV vs. SLE
- Need 4 fold Ab titers increase
TREATMENT (1)

- Supportive treatment
  - About 25% require ICU care; 10% mechanical ventilation
- Interferon trials ongoing
- Ribavirin and interferon-alph-2b
  - In-vitro activity in high doses
  - One reported comatose patient did not improve
  - Worse outcome with ribavirin in open-label trial in Israel—unclear patient selection
Case reports stimulated interest in the use of passive immunization for treatment of WNV disease.

- IVIG might help or abort established WNV infection*
- Need to treat early—mice treated during viremic phase, before virus entered the brain
- Need earlier diagnostics

* Agrawal, Peterson JID 2003:188;1-14
WEST NILE TREATMENT TRIAL: INTRAVENOUS IMMUNOGLOBULINS

- Omrix=Israeli IVIG product
- “dramatic response” to Omr-IgG-am; 70-yrs-old, immunocompromised patient,
- “rapid improvement;” 42-yrs-old lung transplant**
- ~6 other cases: 2 improved, 2 no change, 2 death§

*Emerg Inf Dis 2001, **Transplant ID 2002
§Journal Infect Dis 2003
WEST NI LE TREATMENT TRIAL: COLLABORATIVE ANTI VIRAL STUDY GROUP (CASG) OMRI X TRIAL

- Clinical trial in US:
  - Omrix (Israeli company) partnering with NIAID;
    - Immunoglobulin that contains antibodies to WNV
    - Developed from plasma of Israeli donors with high level of antibodies to WNV
    - Goal to enroll 100 hospitalized patients >18 years with WNV-related encephalitis
  - 3 groups:
    - standard IVIG (from U.S.)
    - WNV-IVIG (Omr-Ig-am)
    - Placebo

Carol Ann Glaser, DVM, et al.
CONTACTS FOR COLLABORATIVE ANTI VIRAL STUDY GROUP (CASG) OMRI X TRIAL

- Laura Riser, CASG Clinical Administrator, University of Alabama (205) 934-2424
- Penny Jester, CASG Project Manager, University of Alabama (205) 996-7800
- Will need Human Subjects approval in place ahead of time
VACCINE DEVELOPMENT

- Media reports in 2002, 2003 suggested vaccine available by “next season”
- A number of human vaccine development efforts underway but probably at least a few years away
  - ChimeriVzx-WNV (Acambis)/Phase I trial

Carol Ann Glaser, DVM, et al.
WEIGHTED MODES OF TRANSMISSION

- Blood transfusion
  - Soft tissue transplantation
- Intrauterine infection
  - Breast feeding
  - Percutaneous exposure-occupation

- Mosquito bite
SCREENING OF THE US BLOOD SUPPLY FOR WNV IN 2003 (1)

- All blood donors are being screened for WNV infection beginning June 2003
  - All donors screened for history of headache and fever one week prior to donation
  - Screen blood donations for WNV RNA using investigational nucleic acid amplifications tests (NAT)
  - All positive specimens confirmed by ELISA method and PRNT
  - WNV Positive units removed from donor pool

DHS
Acute Communicable Disease Control Unit
SCREENING OF THE US BLOOD SUPPLY FOR WNV IN 2003 (2)

- Blood donation poses no risk to the donor for acquiring WNV.
- Screening of the national blood supply will decrease the risk of WNV associated with blood transfusions.
- Screened over 8 million units in 2003, removed 1,000 viremic donors.
SCREENING OF THE US BLOOD SUPPLY FOR WNV IN 2003 (3)

- 806 new WNV infections diagnosed by blood donor screening
- 23 cases possible transmission associated; 6 confirmed
- Viral loads in infected donations (.06-.5 pfu/mL) were lower in 2003 than 2002
TRANSPLANT-ASSOCIATED WEST NILE INFECTION
WNV INFECTION IN ORGAN DONOR AND FOUR ORGAN RECIPIENTS, AUGUST 2002

Organ Donor

WNV PCR-neg
WNV IgM-neg

36 hours

Organ Donor

WNV PCR-pos
WNV Culture-pos
WNV IgM-neg

Kidney recipient
WNME (fatal)

Kidney recipient
WNME

Liver recipient
WNF

Heart recipient
WNME

F/U: 1 seroconverting donor; Retrieved, stored plasma - WNV PCR-positive

NEJM, May 2003

Carol Ann Glaser, DVM, et al.

DHS
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D16:\WNV_UCLA July 2_2004.ppt No. 86
TRANSPLACENTAL WNV TRANSMISSION
TRANSPLACENTAL FLAVIVIRUS TRANSMISSION

- 2002: 1st Documented WNV - late 2nd trimester infection (27 week gestation)
- Full term infant
  - Chorioretinitis
  - Cystic destruction cerebral tissue
  - Laboratory evidence congenital WNV
- Other flavivirus associated with abortion/neonatal illness, no birth defects

MMWR: December 2002
TRANSPLACENTAL FLAVIVIRUS TRANSMISSION (1)

- 53+ live births evaluated to date:

  ✓ 4 with WNV infections:
    - 1 documented intrauterine infection;
      - Infant normal
    - 3 possible intrauterine transmissions
      - Transient neonatal rash → normal
      - Neuroinvasive disease (9 d)
      - Lissencephaly/fatality (WNV causative vs. coincidental?)

Personal communication, Ned Hayes/Dan O'Leary, Fort Collins

DHS
Acute Communicable Disease Control Unit
2003: Pregnancy registry for WNV/pregnancies
- Relatively reassuring
- More data needed

Personal communication, Ned Hayes/Dan O'Leary, Fort Collins
Screening for WNV NOT recommended in asymptomatic

Test individuals with (endemic area):

- Encephalitis
- Meningitis
- AFP or
- Unexplained fever

MMWR Feb 2004: 53(7): 154-157
CDC INTERIM GUIDELINES FOR PREGNANT WOMEN

- If WNV positive/evaluation of fetus:
  - Detailed ultrasound exam fetus at least 2 weeks after onset of illness
  - Amniotic fluid, chorionic villi or fetal serum can be tested
  - Sensitivity? Specificity?

MMWR Feb 2004:53(7):154-157

DHS
Acute Communicable Disease Control Unit
If WNV positive/evaluation of newborn:

- Clinical evaluation:
  - Physical exam: neurologic,
  - WNV testing, IgG and IgM;
    - Umbilical cord or from infant w/in 2 days
    - If negative and maternal illness late (≤8 days before delivery)
      - Repeat testing ≥2 weeks after 1st sample
  - Hearing exam
  - Placental exam by pathologist

MMWR Feb 2004:53(7):154-157

DHS
Acute Communicable Disease Control Unit
If Infant positive for WNV:

- CT head—if abnormal, ped neurologist
- Ophthalmologic exam
- CBC, LFTs, consider LP
- Evaluation by geneticist
- Repeat hearing at 6 months
- Follow growth/development closely
BREASTFEEDING-ASSOCIATED WNV INFECTION
WNV TRANSMISSION IN MILK

- WN viral illnesses in children aged <1 year infrequently reported
- 1999-2001, no reports
- 2002, SIX persons <1 year old with WN virus infection reported (excluded one transplacental infection)
- Ages: 0, 1, 3, 6, 9 & 11 mos.
  - 1 asymptomatic
  - 5 WNME cases
    - 1 breastfed but mother without infection
    - 4 not breast fed in month prior to illness

MMWR October 2002
DHS
Acute Communicable Disease Control Unit
ESTIMATED SENSITIVITY OF WEST NILE VIRUS SURVEILLANCE METHODS
BIRDS AND WEST NILE VIRUS

- WNV replicates well in bird - competent bird reservoirs sustain an infectious viremia for 1-4 days after exposure, subsequent life-long immunity
- Birds: house sparrow, crows, herons, pigeons, doves, chickens, and many other bird
- Drought periods and amplification of WNV spread
- Dead bird surveillance as a predictor of local WNV activity
MOSQUITO HABITAT ELIMINATION

Mosquito Control

Habitat Elimination

Adulticiding

Larviciding

DHS
Acute Communicable Disease Control Unit
10 CA common mosquito vectors that are known vectors for other arboviral species were able to be infected and transmit WNV at some level.

- Cx. P. quinquefasciatus from So. CA were the least efficient vectors.
- Cx. tarsalis, CX. stigmatosoma, Cx. Erythrothorax, Cx. pipiens complex were more efficient lab vectors.
MOSQUITO SURVEILLANCE AND CONTROL CARRIED OUT BY 5 VECTOR CONTROL DISTRICTS WITHIN LAC

- Chicken sero: surveillance done by Vector Control flocks throughout LAC and CA; blood collected every two weeks for serological testing for local arboviral diseases spring through November
- Mosquito pools: Vector Control place mosquito traps
- Lab testing of mosquito pools: CA DHS
- Testing results reported every 2 weeks
PUBLIC INFORMATION

GOALS

- Residential Habitat Elimination
- Personal Protection
  - Avoidance
  - Clothing
  - Repellant
PERSONAL PROTECTION: MOSQUITO REPELLANTS (1)

- DEET: based products provide long-lasting mosquito protection
- Non-DEET: based repellents cannot be relied on to provide prolonged mosquito-protection
- Fewer than 50 cases of serious toxic effects reported in the literature since 1960

PERSONAL PROTECTION: MOSQUITO REPELLANTS (2)

- DEET Safety Profile
  - 1998 EPA review: "normal use of DEET does not present a health concern to the general U.S. population"
  - 40 years history of use and over 8 billion human applications
  - Can use in children >2 mo, don’t put repellent on hands

DHS
Acute Communicable Disease Control Unit
REPORT CASES

- If child has meningitis, encephalitis, 7 days of fever with history of mosquito bite, living in endemic area (San Gabriel Valley!!)—CALL for testing
- 213-240-7941 (24/7)
- Need CSF (1-2cc.) Blood 5-10 ml. red top
CONCLUSIONS (1)

- The US WNV outbreak of 2002-03 was the Largest arboviral epidemic ever documented in North America.
- It will be here for the foreseeable future!
- WNV has a huge impact on the medical system!
  - CO 2003
    - 861 hospitalized cases = $22.4 million
    - Not calculated: missed work, outpatient costs, rehab, long term disability
  - One Medical Center
    - 10-12 admissions daily at peak season
    - 10% of all admissions July-August 2003
CONCLUSIONS (2)

- WNV infection will be a greater problem than SLE because of the large number of bird and mosquito species which can be infected and transmit WNV:
  - 162 native American bird species in 2002 producing high levels of viremia
  - Thirty-seven species of mosquitoes are competent vectors in US
CONCLUSIONS (3)

- Factors contributing to huge WNV outbreak in CO 2003:
  - Second Year Phenomenon
    - Whole season to amplify in a naïve local bird populations
  - Ideal weather for mosquito production:
    - Wet spring and hot weather!
  - Abundance of various *Culex* sp. especially *Culex tarsalis* (highly competent vector for WNV transmission)
CONCLUSIONS (4)
WNV IN CALIFORNIA 2004

- Will WNV be a problem in CA? **YES**
- Will WNV over-winter in CA? **YES**
- Will the WNV epidemic expand to other areas of CA? **YES**
- Will you be surprised by the “speed” and intensity of the outbreak? **YES**
- Will there be a lot of WNV testing in 2004? **YES**
CONCLUSIONS (5)

▶ WNV Control will require collaboration between mosquito control, public health professionals, clinicians, and the community as a whole.

▶ WNV will be public health challenge for years to come-especially in Southern California!
RESOURCES

WEBSITES:

- Los Angeles County Acute Communicable Disease Control
  http://lapublichealth.org/acd/VectorWestNile.htm

- Los Angeles County Public Health Nursing
  www.lapublichealth.org/phn/healthed.htm

- Centers for Disease Control and Prevention (CDC)
  http://www.cdc.gov/ncidod/dvbid/westnile/index.htm

- California Department of Health Services
  www.westnile.ca.gov
RESOURCES

HOTLINES:

- **Los Angeles County:**
  (800) 975-4448 or (213) 240-7786  24 hours
  Report dead birds to (877) 747-2243

- **Centers for Disease Control and Prevention:**
  English  (888) 246-2675
  Spanish (888) 246-2875
  TTY      (888) 874-2646
  Monday – Friday 5 a.m. to 8 p.m. PT
  Saturday – Sunday 7 a.m. to 5 p.m. PT
QUESTIONS AND ANSWERS
THANK YOU!