

Aseptic Meningitis Epidemic in an Area of Intense West Nile Virus Epizootic Activity

Baltimore, Summer 2001



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PRELIMINARY

Background:

Aseptic meningitis syndrome

- Acute onset fever, headache, neck pain/stiffness, vomiting, meningeal signs
- No confusion/stupor
- CSF:
 - ↑ WBC
 - ↑ protein
 - normal glucose
- Negative bacterial culture of CSF

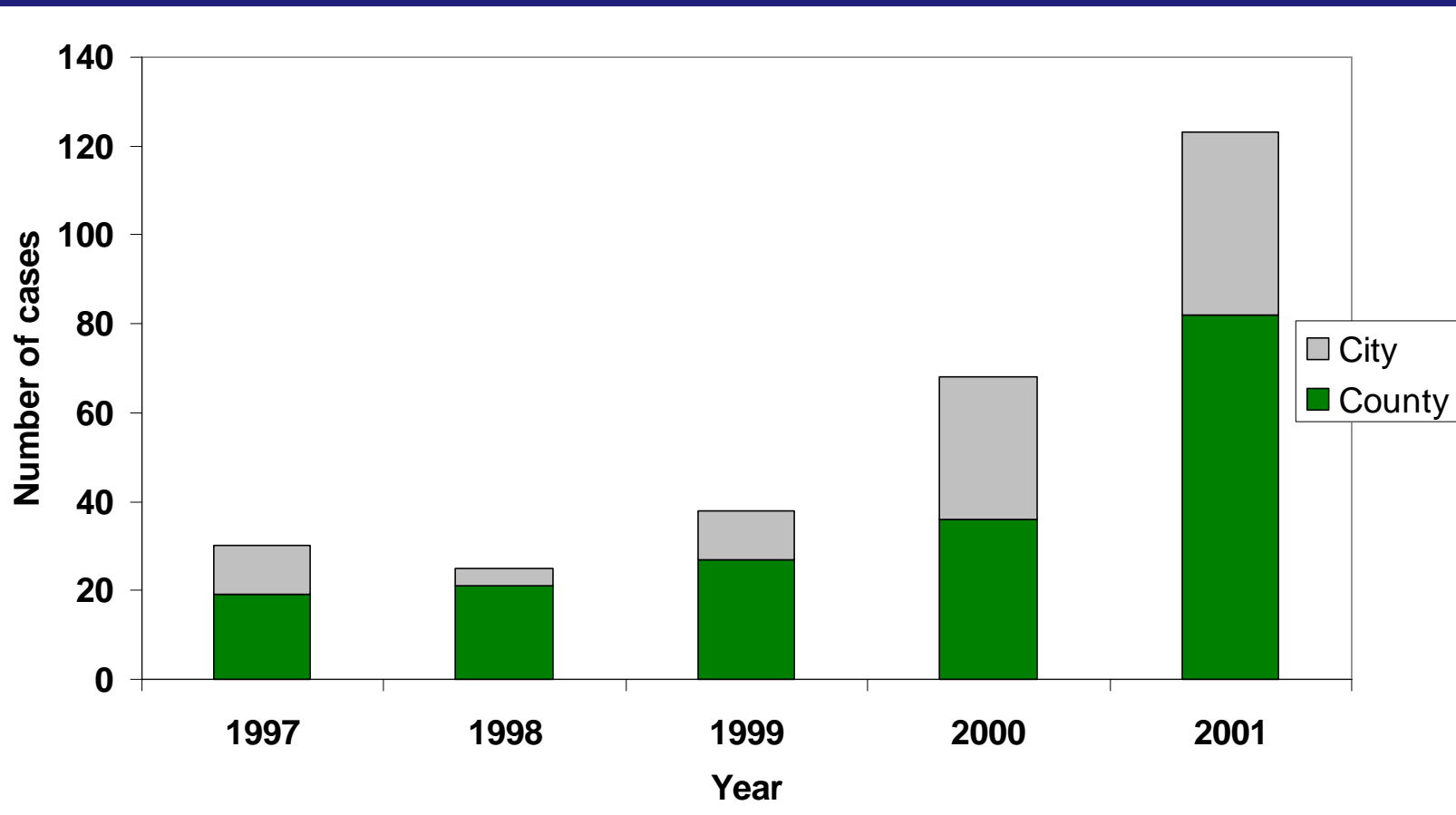
Background: Aseptic meningitis in U.S.

- Viruses
 - Enteroviruses
 - Arboviruses (SLE, LAC, WNV)
 - Herpesviruses (HSV 2, HSV 1, EBV, HHV 6, VZV)
 - HIV
 - Lymphocytic choriomeningitis? Mumps?
- Numerous other causes
 - e.g., Lyme disease, leptospirosis, 2^o syphilis, partially-treated bacterial meningitis, parameningeal disease, TB, cryptococcus, autoimmune disease, medications

Background: WNV meningitis in U.S.

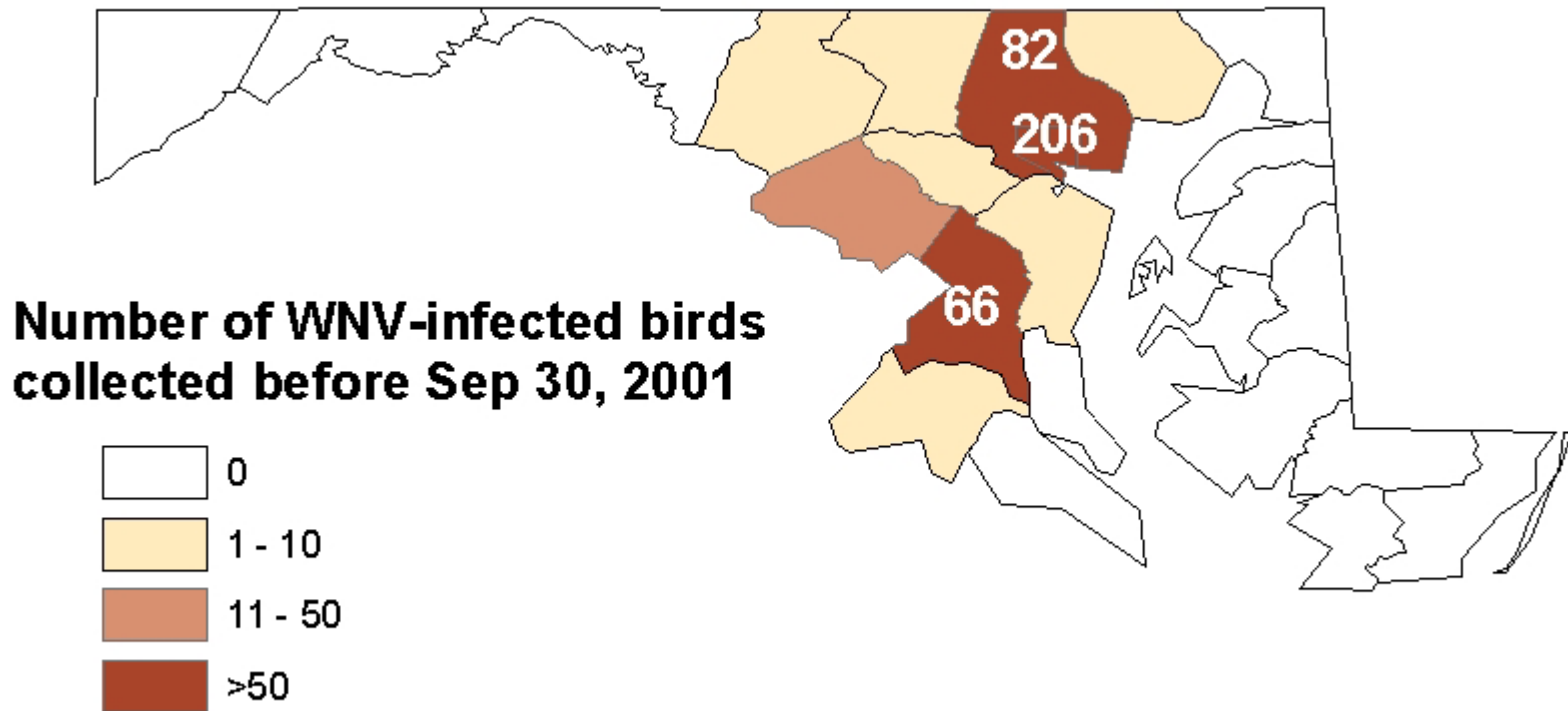
- Relative contribution of WNV to all aseptic meningitis?
- U.S. 1999-2000:
 - 21 persons hospitalized with WNV meningitis
 - 52 persons hospitalized with WNV encephalitis
- Selection bias in U.S. surveillance:
 - WNV testing prioritized for encephalitis > meningitis

Background: Aseptic meningitis cases reported from Baltimore, Jun 1-Sep 30



Data source: Maryland Dept of Health & Mental Hygiene (DHMH)

Background: WNV avian epizootic Maryland, 2001



Data source: ArboNET—WNV surveillance system

Objectives

1. Describe apparent aseptic meningitis epidemic
2. Estimate relative contribution of WNV and enteroviruses
3. Assess WNV surveillance among patients reported with aseptic meningitis

Methods: Case ascertainment

- 6 Baltimore hospitals
- Cases identified by
 - reports to DHMH
 - lab results with \uparrow WBC in CSF
 - discharge diagnoses codes
- Medical chart review



Methods: Case definition

- Baltimore City or County resident
- Onset Jun 1-Sep 30, 2001
- >5 WBC in CSF
- Negative bacterial cultures of CSF

- No evidence of fungal or parasitic CNS disease, cerebral hemorrhage, carcinomatous meningitis, cerebral vasculitis, or encephalitis

Methods:

Specimen collection and interviews

- Acute-phase
 - CSF
 - Serum
 - Rectal or nasopharyngeal swabs
- Convalescent-phase (age >12 years, unknown etiology)
 - Serum
 - Standardized interview: symptoms, duration

Methods: DHMH and CDC testing

- CSF
 - WNV IgM ELISA
 - Enteroviral culture, typing by PCR
- Serum (acute- & convalescent-phase)
 - WNV IgM ELISA
 - IFA for SLE, CE, EEE, WEE
- Nasopharyngeal and rectal swabs
 - Enteroviral culture, typing by PCR

Results: 113 aseptic meningitis cases

Age	18 years (1 wk – 74 y)
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Gender	56% male
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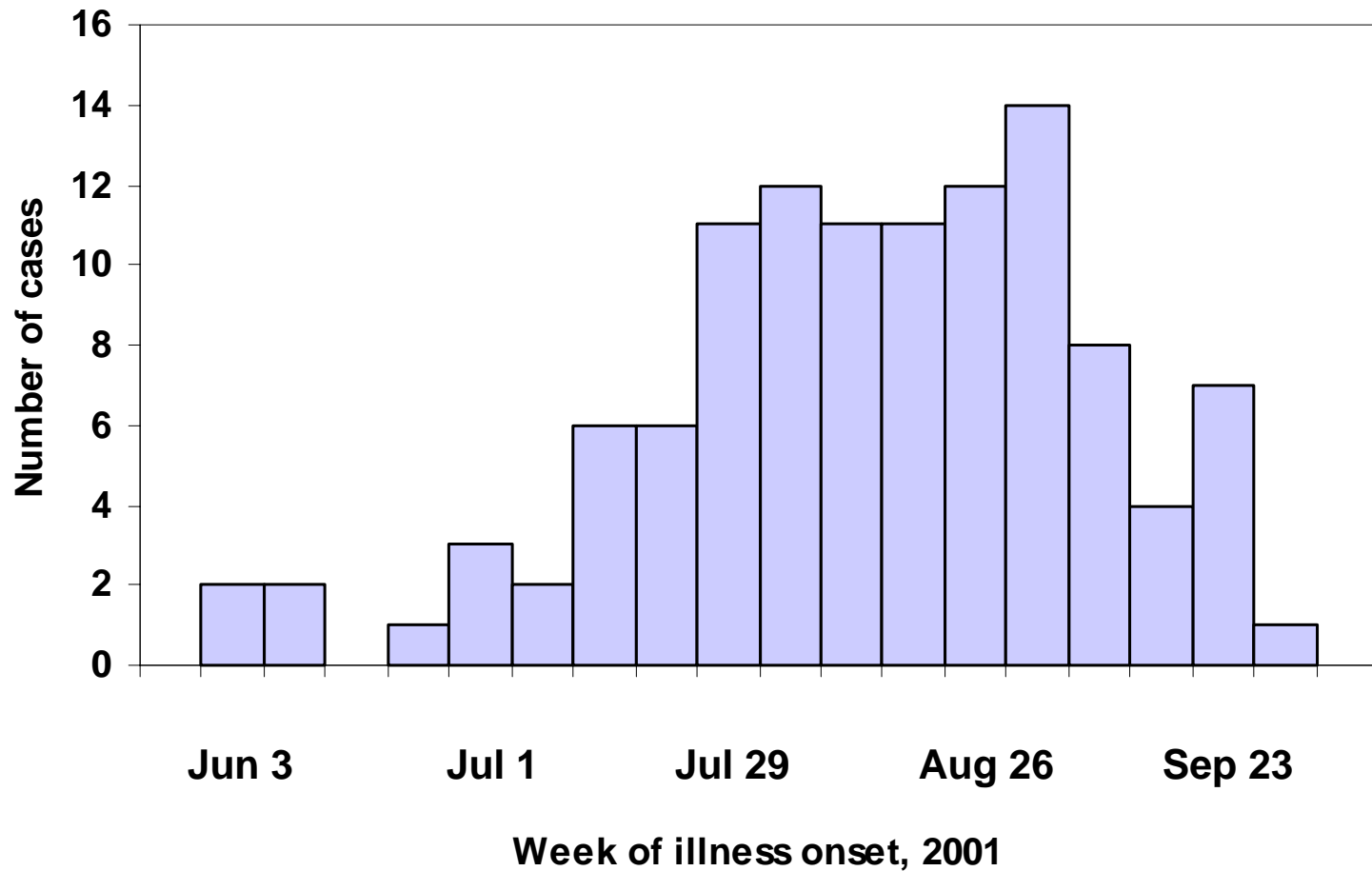
Residence	Widely distributed
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Severity

Hospitalization	2 (0 – 11) days
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Fatalities	None known
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Results: Week of illness onset



Results: Clinical characteristics (n = 33)

- Symptoms recalled
 - 100% headache
 - 85% fever
 - 85% eye pain or sensitivity to light
- Symptoms duration
18 (5 – 47) days
- Work/School Missed
9 (0 - 30) days

Results: CSF characteristics

n median range

Protein	111	53 mg/dL	10 - 215 mg/dL	Elevated in 52%
Glucose	110	-	-	Normal in 99%
WBC	113	135 per mL	7 - 1083 per mL	Mononuclear predominance in 59%

Results: Diagnoses

- 44 enteroviral meningitis

	<u># cases</u>
Echo 13	14
Echo 18	10
Coxsackievirus B2	5
Echo 6	1
Echo 30	1
Enterovirus 70/71	1
Not typed	12

- 2 HSV meningitis
- 1 Lyme meningitis
- 66 undetermined etiology

Results: Enterovirus meningitis, by age

Age group (in years)	N cases	# tested for enterovirus	% test-positive enterovirus
<1	12	10	80%
1-10	24	16	94%
11-20	29	23	52%
21-30	11	4	75%
31-40	26	13	38%
41-50	5	3	33%
>50	6	2	0%

Results:

66 cases undetermined etiology

Characteristics

- Age: median 26 years (2 wk – 67 y)
- 5 HIV+
- 4 prior history of meningitis

Documented negative tests for these 66 cases:

- 45 patients with ≥ 1 WNV IgM test (including 23 convalescents)
- 27 with ≥ 1 enterovirus test
- 17 with ≥ 1 *B. burgdorferi* Ab test
- 11 with ≥ 1 HSV test

Pre-investigation surveillance testing

- Reported cases—etiology reported in ~5%
- WNV testing 1st priority at state
 - Patients >17 years-old hospitalized with meningitis
 - 37% cases \geq 1 WNV IgM test
 - IgM tests of acute CSF
 - Convalescent serum requested, but rarely received—collection not feasible
- Enterovirus/other common agents testing not routinely incorporated

Results: Investigation testing yield

# case-patients with	N	# positive (%)
≥ 1 WNV IgM ELISA	69	0 (0%)
≥ 1 Enterovirus culture or PCR	71	44 (39%** - 62%)

** Lowest possible % if N were 113

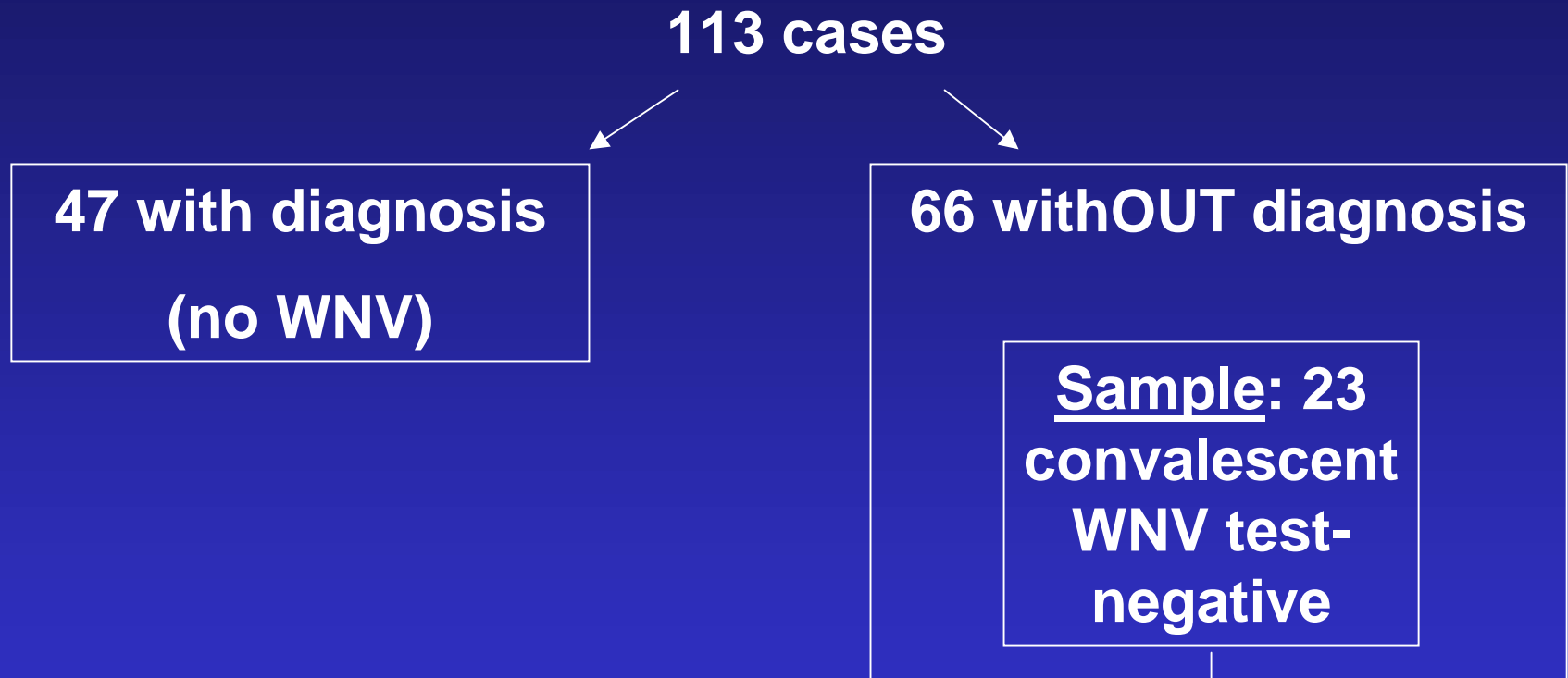
Limitations

- Limited population
 - Subset of Baltimore hospitals
 - Subset of patients within these hospitals
- Specimens not available for all patients
- Testing not comprehensive

Was WNV meningitis missed?

- Not all patients tested
- False negatives possible:
 - Tested too early?
 - 79% patients presented by day 3
 - WNV IgM takes time to develop
 - Tested too late?
 - Convalescents collected on days 12-111
 - WNV IgM eventually declines

Missed WNV meningitis?—estimates



- Best guess: **0%** of 66 WNV positive
- Upper limit of 95% confidence interval: **10%**

Conclusions: Aseptic meningitis Baltimore, summer 2001

- Despite WNV avian epizootic,
no apparent WNV meningitis epidemic
- Enteroviruses predominant identified cause of aseptic meningitis in children and adults
- Echovirus 13 most common

Conclusions: WNV surveillance among aseptic meningitis cases

- WNV testing often done before more common agents
- As first-line test in non-epidemic years, WNV IgM serology low yield

Testing common and/or treatable causes of aseptic meningitis

- Rapid (PCR) tests for enterovirus available
 - Provide specific diagnosis for most patients
 - Reduce logistically difficult WNV IgM testing
 - Reduce unnecessary anti-bacterial agent use
- Treatment (Pleconaril) for enteroviral disease may become available
- Treatable : Lyme disease, herpes simplex, varicella-zoster, HHV-6, cytomegalovirus(?)

Considerations for (WNV) meningitis surveillance: Tiered testing

- **First:** Rapidly exclude common and/or treatable agents
 - **ENTEROVIRUSES**
 - Herpesviruses
 - If immunocompromised patient, may expand panel

Considerations for (WNV) meningitis surveillance: Tiered Testing

- First: Rapidly exclude common and/or treatable agents
 - **ENTEROVIRUSES**
 - Herpesviruses
 - If immunocompromised patient, may expand panel
- **Second:** Consider WNV IgM testing
 - WNV ELISA IgM screen of acute CSF & serum
 - If early (<8 days),
WNV ELISA IgM of >day 7 serum

Acknowledgements

Infection control practitioners: Kathy Arias, Ruth Bertuzzi, Colleen Clay, Jeanne Brown, Diane Lagasse, Polly Ristiano, Donna Feldman, Phyllis Tyler, Joanne Venturelli, Matt Wallace
and laboratory, medical records & emergency dept staff
at the investigation hospitals

Maryland DHMH epidemiology & laboratories

Baltimore City and County Health Dept

REVB-CDC epidemiology & laboratories



Aseptic meningitis cases identified at 6 Baltimore hospitals by ICD-9 codes— admissions Jun 1-Sep 30

