Acknowledgments

Data on equine cases of West Nile virus (WNV) infection were acquired through the efforts of private veterinary practitioners, clinicians, field investigators, laboratory diagnosticians, animal health and public health officials in all the States where suspect equine cases have been investigated to date.

First it is essential to acknowledge all those whom have investigated, confirmed, and reported cases of WNV infection in equids. Without them we would have no data to report.

Although we have learned much over past 4 years, we don’t have as much information as people would like us to have.

Special thanks to Dr. Randall Crom, USDA VS and Dr. Maureen Long, U of FL, Dr. John Shiltz, IA each of whom contributed portions of this presentation.
Describe 2002 equine epizootic
   temporally, geographically, clinically
   incidence rates, mortality (compare to 1941?)
Update equine vaccine issues
   coverage, “breakthrough”, impact on serology
WNV diagnosis – “state of the art” –equine
WNV lab tests performed by USDA in 2002 -- equine and other
USDA (& CDC?) policy changes / impact on surveillance
Equine WNV Cases, 1999

- 25 cases eventually detected, all on Long Island (22 in Suffolk Co., 3 in Nassau Co.)
  - 19 premises affected
  - dates of onset:
    - first - 26 August (Riverhead, NY)
    - last - 18 October (Mattituck, NY)
  - all horses, no other equids
  - 9 horses (36%) died or were euthanatized

- 38 non-ill horses on Long Island were also found WNV-positive
1999 WNV Outbreak Summary

- 4 states had WNV activity: CT, MD, NJ, NY
- 62 human cases, including 7 deaths
  - *all infected in the New York City area*
  - *onsets from early August to late September*
- Hundreds (thousands?) of bird deaths
  - *mostly corvids (crows, blue jays)*
  - *at least 8 different orders of birds affected*

NVSL = National Veterinary Services Laboratories of USDA-APHIS in Ames, Iowa

This is what happened in 1999 – parts of 4 states (only one county in MD) had WNV activity.
Significant WNV Events in 1999

- Virus isolated at NVSL, Ames, IA
  - Crow – September 14, 1999
  - Zoo birds – September 14, 1999
  - Horse – October 12, 1999
- NVSL isolates identified by CDC as West Nile virus – human “St. Louis” encephalitis cases reclassified
- WNV serology (neutralization test) performed at CDC and developed at NVSL
The next 4 maps show the geographic progression of WNV in any species, by State, from 1999 through 2002.

In 1999, the only equine cases (25) were in Long Island, NY.
2000 WNV Outbreak Summary

- 12 states & DC had WNV activity
- 21 human cases, with 2 deaths
  - all infected in the greater New York City area
- 60 equine cases, 23 deaths
- Thousands of bird deaths
  - mostly corvids (crows, blue jays)
Significant WNV Findings in 2000

- WNV infected mosquitoes overwintering
- Winter isolate of WNV from hawk
- Geographic spread
  - New Hampshire to North Carolina
  - Western PA (adjacent to OH)
- Fewer human cases, increased equine clinical cases
  - Positive horses in 7 states
There were 7 States with a total of 60 equine cases in 2000…. 
2001 WNV Outbreak Summary

- 27 states & DC had WNV activity
- 66 human cases, with 9 deaths
  - *infections in 10 states*
- 738 equine cases, at least 156 deaths
- >7,300 bird deaths
Significant WNV Findings in 2001

- Continued geographic spread
  - activity from Maine to Florida; as far west as Arkansas
  - positive birds detected in Canada
  - positive human in Cayman Islands
- Tripling of human cases, equine cases increased more than 10-fold
  - equine cases in 20 states
...20 States in 2001 with over 700 cases...
2002 WNV Outbreak Summary

- 44 states & DC had WNV activity
- 4,161 human cases, with 277 deaths
  - infections in 39 states & DC
- 15,252 equine cases, over 4,500 deaths estimated
- >15,000 bird deaths
Significant WNV Findings in 2002

✓ Continued geographic spread
  • “Crosses” the Continental Divide – as far west as Puget Sound in Washington state

✓ Human cases increased more than 60-fold

✓ Intense equine epizootic, especially in north-central U.S.
  • cases increased more than 20-fold
  • equine cases in 41 states
…and reports so far for 2002 show almost 15,000 equine cases from 40 states.
June 19 – WNV positive birds in TX

July 11 – WNV positive horse in ND

July 18 – WNV positive bird in OK

July 24 – WNV positive birds in WV, MN, NE

August 2 – WNV positive horses and bird in SD

August 8 – WNV positive horse in KS

August 16 – WNV positive horses in CO

August 19 – WNV positive horse in WY

August 21 – WNV identified in South Carolina

August 26 – WNV Positive Horses in Montana
June 19 – WNV positive birds in TX

July 11 – WNV positive horse in ND (flyways Eastern, Mississippi, Central (Plains), Pacific)

July 18 – WNV positive bird in OK

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West Nile Virus Emergency Management Warnings 2002

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**August 26 – WNV Positive Horses in Montana**
40 states with equine cases
Attack rate = cases per number of susceptible
Overall average just under 3 per 1000 (see spreadsheet)
Total cases now more from CO, FL but Co map is virtually same
(flyways Eastern, Mississippi, Central (Plains), Pacific)
Canada cases
Comparison of Equine WNV Cases by County

- 2001 Panhandle of FL
- more in So. Fl.
- some overlap
- GA 2002 cases in different area than SE GA
Clinical presentation of Equine WN encephalitis*

- Weakness (94%)
- Ataxia (72%)
- Abnormal Mentation (67%)
- Increased Body Temperature (65%)
- Fasciculation (61%)
- Anorexia (57%)
- Cranial Nerve Deficits (44%)
- Teeth Grinding (20%)

* data compiled by Maureen Long, DVM, PhD, U of FL
Weakness or Ataxia: 100%

<table>
<thead>
<tr>
<th>Type</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Asymmetrical</td>
<td>39%</td>
</tr>
<tr>
<td>Front limbs</td>
<td>15%</td>
</tr>
<tr>
<td>Hind limbs</td>
<td>26%</td>
</tr>
<tr>
<td>Both limbs</td>
<td>40%</td>
</tr>
<tr>
<td>Dysmetria</td>
<td>39%</td>
</tr>
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Mentation/Behavior Change: 67%

Nonresponsiveness
Somnolence
Low numbers of seizures
Persistent or intermittent

Not always recumbent
Flaccid Paralysis

Can be intermittent

<table>
<thead>
<tr>
<th></th>
<th>Recumbent</th>
<th>30%</th>
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<tr>
<td>Mortality</td>
<td></td>
<td>65%</td>
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</table>
WNV Equine Case Fatality Rate 2002

- Specific data available from only 10 states; estimate from 1 additional
- Overall CFR for 10 states was 28.2 percent
  - 324 deaths/euthanasias out of 1148 cases
  - CFR by state ranged from 0 to 53 percent
- Estimated CFR for 1 state was 33.3 percent
  - About 214 deaths/euthanasias out of 644 cases
- Combining all data gives estimate of 30.0 percent CFR for 11 states (538/1792)
  - Likely that actual CFR was higher, probably about 33 percent (based on previous years’ experiences)

Estimate from Ohio
only looking at about 10% of total cases of year
no great increase or decrease in case fatality
other than Montana, Plains states not included in calculations
Can horses be a source of WNV?

- Inoculation and transmission studies
  - 3 studies, total of 16 horses (NVSL, CDC/CSU)
  - Overall, 13 horses developed viremia after being inoculated (needle or mosquito)
  - 600+ virgin mosquitoes fed on 7 viremic horses: no mosquitoes became infected (CDC/CSU)

- All results suggest the answer is no, viremias in horses are too low (one horse had 3 log 10 PFU/mL serum, others less) and are not persistent
Case-Control Study / Spatial Data Analysis
Equine Infections - Year 2000

- **Case-Control Study:** 49 “case” and 101 control premises in 7 States; 1,487 equids sampled (64 seropositive)
  - *infected horses less likely to be housed in stalls at night; more likely used for pleasure purposes*
  - *case premises more likely within ½ mile of blackbird roost or waterfowl congregation*

- **Spatial Data Analysis:**
  - *case premises clustered; within a cluster, exposure of individual equids appears to be chance event*

Case premises = one or more infected (seropositive) equids
Control premises = within 5 miles of a case premises (mean distance=2.2 miles) & no infected equids
Prevention and Control

- Mosquito control
  - source reduction
  - larviciding
  - adulticiding?
- Which mosquito species infect horses?
  - Aedes vexans/Culex salinarius vs. Culex pipiens
    - daytime/anytime vs. dusk/dawn feeding
- Vector-resistant housing
- Repellents (topical pyrethroids: permethrin)
- Fans
- Vaccine...

Source reduction is removal of water trapping containers and other man-made sites where mosquitoes may breed. Usefulness of adulticide spraying is questioned by many – may be too late by that point.

WNV-infected Aedes vexans was found on the same premises as the index equine case in 2000, so that may be a clue as to species which infect horses; other likely species for infecting horses are Culex salinarius and Culex tarsalis (western U.S.). Different species feed at different times (A. vexans anytime, C. salinarius dusk/dawn, C. tarsalis dusk/dawn).
West Nile virus
equine vaccine(s)
WNV equine vaccine

- Killed virus product given conditional license by APHIS / VS / CVB on 1 August 2001, renewed 2002
- **Full license February 2003**
- Over 6 million doses distributed
- Administration: 2 doses IM 3-6 weeks apart; one annual booster

(CVB = Center for Veterinary Biologics of USDA-APHIS-VS in Ames, Iowa.)

An equine vaccine has been approved by CVB. It is up to individual states to decide what use will be allowed under a conditional license. Used common adjuvant, demo positive PRNT @ 35 days post 2\textsuperscript{nd} vaccination.

Vaccine was available late August/September. Supply is good for this year

~200 “unfiltered” adverse event reports but approximately ½ of the horses received another vaccine at the same time, includes horses that died of lightning strike, etc.

data submitted re: challenge model

estimate 1.0-1.5 million horses fully vaccinated

DNA vaccine – field trials
WNV equine vaccine post-vaccination responses

WNV specific IgM
- No IgM response @ 1:400 detected after 1st dose
- No IgM response @ 1:400 detected after 2nd dose

Neutralizing Antibody
- Low or undetectable neutralizing Ab titers after 1st dose
- Neutralizing Ab after 2nd dose detected in many vaccinates

It is a killed virus product, so vaccinated horses may not necessarily be distinguishable from naturally infected horses. However, information collected so far suggests that vaccinated horses do not develop detectable levels of IgM antibody, so horses found to have IgM were very likely infected naturally. Horses are probably not protected from natural infection (do not have high levels of neutralizing antibody) until one or two weeks after the 2nd dose of vaccine is given.

Ft. Dodge horses 0, 14, 21 dpi after 1st dose
7, 14 dpi after 2nd dose (13 horses examined at all time points)
Also other samples from field safety trials and some samples tested after vaccine was distributed
Ft. Dodge horses – examined by PRNT
- ____horses 1:10 PRNT titer after 1st dose
- ____horses all > or = 1:100 PRNT titer after 2nd dose
WNV Cases in “Vaccinated” Horses 2002

- Given a reported vaccine efficacy of 94 percent in properly vaccinated horses:
  - On average, ~100,000 horses in a State
  - If 20 percent are vaccinated (20,000) and if clinical attack rate is about 4 per 1000, then:
    - 80 vaccinated horses should have become ill, but 94 percent (75) would be protected;
    - thus, 5 vaccinated horses would still become clinically ill (vaccine “failures”) in an “average” State in 2002.

- The more vaccinated horses, or the higher the attack rate, the more potential vaccine failures.

This is just to give some perspective on what we might expect to see in 2002 regarding clinical WNV cases in vaccinated horses.
WNV Cases in “Vaccinated” Horses 2002

- Data available from only 8 states
- 71 cases of possible vaccine failure
  - WNV illness onset 21 days or more after proper vaccination protocol
  - 5 states with at least one possible failure: FL (44), KY (17), NJ (3), PA (4), VA (3)
    - 1,201 total equine cases reported
  - 3 states reported no vaccinated equine cases: CT, ID, WA
    - only 7 total equine cases reported

1201 = total cases. Don’t know number of vaccinates
95% protected from infection
82% controls viremic

94% preventable fraction
how many vaccinated, attack rate among horses.
71 cases but no denominator data failure rate unknown

vacc. 10,000, assume attack rate of 3/1000, expected 30 but if all vacc.
expect 2 cases
expect 2 vaccine failures per 10000 vaccinated horses
WNV DNA equine vaccine

- *E. coli* plasmid containing the WNV prM and E genes
- Field trials planned – CA, KS, KY, MD, OH, OK
- Environmental assessment

DNA vaccine – field trials
West Nile virus predictions: veterinary impact in 2003

Discuss widespread, commercialization of reagents/ testing?
Impact of population of horses exposed but not clinically ill in 2000 (e.g. over 50% on NADC compound)
Impact of increased vaccination of horses
Impact of rare reports of WNV illness in other species – who will meet demand for testing of pets?
repeat cases in areas that have had previously – possibly herd/flock immunity (new non-immune)
West coast cases surprise us not to see them.
horses useful sentinel in western US
14, 901 equine WN encephalitis cases
3995 human cases with 252 deaths as of January 8
Shown on log scale

14,901 equine WN encephalitis cases
3995 human cases with 252 deaths as of January 8
Pacific flyway
What should we expect in the future?

- Areas that have had WNV in horses, will have it again (although in different horses / less numbers).
- Additional areas/states will have WNV cases in horses (i.e., the West Coast).
- Detecting equine cases of WNV will help define areas of WNV activity.
- Equine illness may be an early indicator in western areas with numerous and efficient bridge vectors (*Culex tarsalis*?).

Discuss widespread, commercialization of reagents/ testing?

Impact of population of horses exposed but not clinically ill in 2000 (e.g. over 50% on NADC compound)

Impact of increased vaccination of horses

Impact of rare reports of WNV illness in other species – who will meet demand for testing of pets?

repeat cases in areas that have had previously – possibly herd /flock immunity (new non-immune)

West coast cases surprise us not to see them.

horses useful sentinel in western US
What should we expect in the future?

- An increased number of horses will receive WNV vaccine.
- Expansion of facilities for WNV testing will influence number of horses (and other veterinary species) tested.
- Expansion of facilities for WNV testing will impact data collection.
- Additional species will be identified as susceptible to rare clinical illness from WNV infection.

Discuss widespread, commercialization of reagents/ testing?
Impact of population of horses exposed but not clinically ill in 2000 (e.g. over 50% on NADC compound)
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The next 4 maps show the geographic progression of WNV in equine and birds, by State, from 1999 through 2002.

In 1999, the only equine cases (25) were in Long Island, NY.
There were 7 States with a total of 60 equine cases in 2000….
...20 States in 2001 with 738 cases...
...and reports for 2002 show over 15,250 equine cases in 41 states.
"We’re pretty sure it’s the West Nile virus."