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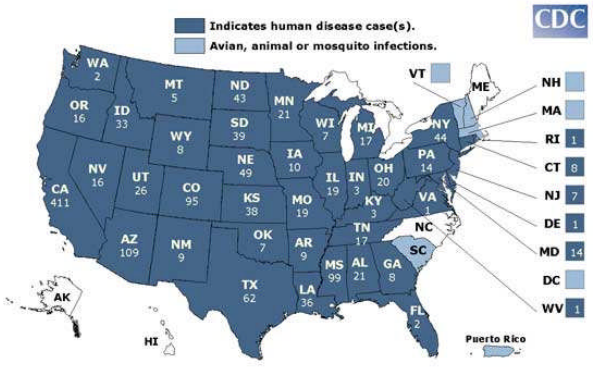
Equine West Nile Virus Encephalomyelitis

I. Definitions

A) West Nile Virus (WNV) - Flavivirus in the Japanese Encephalitis Antigenic Complex; arbovirus.
B) West Nile Fever (WNF)– viral encephalitis in people caused by the West Nile Virus

II. Backround

A) West Nile virus has emerged in regions of Europe and North America. WNV causes fatal encephalitis in humans and horses, as well as causing mortality in certain domestic and wild birds.
B) WNV was first isolated from a febrile woman in the West Nile District of Uganda in 1937. Equine disease was first noted in Egypt and France in the early 1960s.
C) WNV has been identified in Africa, Europe, the Middle East, west and central Asia, Oceania and North America. Outbreaks in humans have occurred in Algeria in 1994, Romania in 1996-1997, the Czech Republic in 1997, the Democratic Republic of the Congo in 1998, Russia in 1999, the United States in 1999-2008, and Israel in 2000. Epizootics of disease in horses occurred in Morocco in 1996, Italy in 1998, the United States in 1999-2008, and France in 2000.
D) Human cases US 2002 – 4156 cases with 284 deaths; US 2003 – 8567 cases with 199 deaths; US 2004 – 2470 cases with 88 deaths; US 2005 – 2949 cases with 116 deaths; US 2006 – 4219 cases with 161 deaths; US 2006 – 3359 cases with 98 deaths; US 2007 – 3630 cases with 124 deaths; US 2008 – 1370 cases with 37 deaths



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III. **Transmission**

A) Arbovirus transmitted primarily by *Culex spp* mosquitoes
   1) The virus has been isolated from 43 mosquito species, predominantly of the genus *Culex.*
   2) Transovarial transmission has been demonstrated though at low rates.
   3) Requires 6-10 days incubation after feeding on infected bird before mosquito is infectious
   4) Virus isolations have occasionally been reported from other hematophagous arthropods (e.g., bird-feeding argasid [soft] or amblyommine [hard] ticks), and experimental transmission has been successful.

B) Not thought to be transmitted by direct contact with birds
   1) In North America, infected birds have been found to have an abundance of virus in many tissues and to excrete virus in feces.
   2) It is possible, when handling dead birds or when carnivores eat birds infected with WNV, that exposure may occur.
   3) Preliminary reports suggest possible direct bird to bird transmission.
      (a) Raptors can acquire the virus by eating infected prey
      (b) Birds may transmit virus in feces
      (c) Transovarial transmission may occur
   4) Caution should be taken when handling live or dead birds in a WNV endemic area.

C) All mammals, with the possible exception of Lemurs, are thought to be dead end hosts.
   1) WNV has been isolated from mice and hamsters, camels, camalids, cattle, horses, dogs, humans, lemurs, and frogs.

D) Transmission does not occur by direct mammal-to-mammal contact.

IV. **Disease in birds**

A) In Europe – only subclinical infections
B) North American outbreak
   1) First indication that the virus is in an area is often the finding of dead corvids, especially crows.
   2) The birds show signs of neurologic disease
      (a) Weakness, sternal recumbency
      (b) Ataxia
      (c) Tremors
      (d) Anisocoria
      (e) Abnormal head posture
      (f) Circling
      (g) Convulsions

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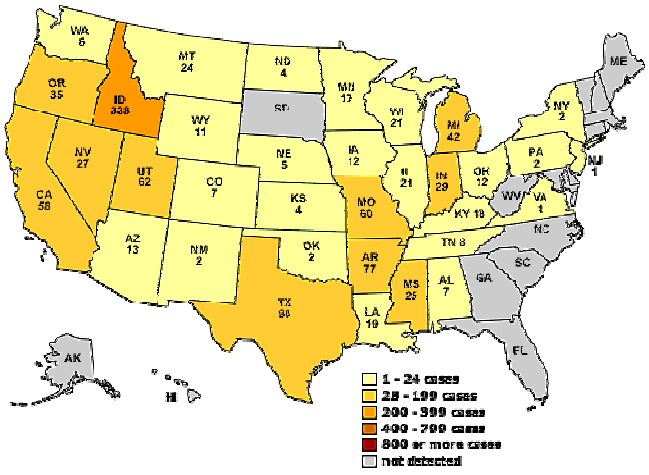
3) Disease of other organ systems - virus can be found in the heart, kidney, liver and gastrointestinal tract with abundant virus in the lumen of the GI tract.
4) Sudden death from systemic infection is common.
5) Has been identified in at least 138 species of birds in North America.

V. Equine West Nile Virus Encephalomyelitis World Wide

A) 1962-1965 - Camargue (France) – 50 cases
B) 1963 – Egypt
C) 1990 – Portugal
D) 1996 – Morocco - 42 of 94 affected horses died
E) 1998 – Italy - 14 cases in 1998, 6 died or were euthanized
F) 1998 – Israel
G) 1999 – Long Island (NY) – 13 of 25 cases fatal
H) 2000 – Northeastern USA - 23 of 65 cases fatal
   1) New Jersey (27 horses), New York (24 horses), Connecticut (7 horses), Delaware (4 horses), RI (1 horses), Massachusetts (1 horses), Pennsylvania (1 horses).
I) 2000 – France – highly fatal outbreak
J) 2001 – Eastern USA – 738 equine cases in 20 states.
   1) 33 % fatality rate (156/470).
K) 2002 – USA - 14,717 equine cases in 40 states.
L) 2003 – USA – 4,426 equine cases in 48 states.
M) USA - 2004 – 1,341 equine cases; 2005 – 1,075 equine cases; 2006 – 1061 equine cases; 2007 – 466 equine cases ; 2008 – 218 equine cases
N) Seroepidemiology (high rate subclinical infections): 31% in the Long Island outbreak, 20-70% of normal horses seropositive in endemic areas Europe. France 8% of horses in outbreak IgG titers; 4% had IgM titers.

2006 – 1061 EQUINE CASES



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VI. **Epidemiology** -- USDA case control study 2000

A) 1487 equids on 49 case farms and 101 control farms
   1) Farms located in Connecticut, Delaware, Massachusetts, New Jersey, New York, Pennsylvania and Rhode Island.

B) Findings
   1) Marginally significant association between case farms and presence of Blackbird roosts and waterfowl congregations within 1/2 mile.
   2) Insect control methods -- farm or horse level
      (a) Not associative with likelihood of infection
      (b) lack of association may be due to
         (1) Heterogeneous approach from farm to farm
         (2) Control methods targeted flies

   3) Pleasure horses at higher risk
      (a) More likely expose the vector? -- trail riding activities
   4) Increased risk when not housed in stalls at night
   5) Occurrence of cases associated with horse demographics and geographic distribution of dead birds
      (a) Endemic focus in bird roosts results in virus amplification
      (b) Proceed spillover to horses
   6) Exposure of horses is geographically clustered
      (a) But within regions of virus activity, exposure of horses appears to be a chance event
      (b) This type of pattern may respond to effective vaccination
   7) Mosquito species responsible for transmission to horses
      (a) Has not been identified
      (b) Control measures should be directed towards appropriate mosquito species

VII. **Clinical disease - North American experience**

A) Clinical signs
   1) Fever – in less than half the cases
   2) Acute onset of ataxia of all limbs
   3) Marked hypermetria
   4) Early recumbency
   5) Single foreleg lameness progressing to bilateral forelimb lameness/ataxia, monoparesis, paraparesis, tetraparesis progressing to recumbency
   6) Radial nerve paralysis
   7) Hypersensitivity to touch and sound – frequently present
   8) Somnolent – periodically falling to knees
   9) Anisocoria and a slow pupillary light response

10) Tremors and lip twitching
11) Muscle fasciculations
12) Most pronounced in the neck and triceps region
13) Difficulty swallowing
14) Facial nerve paralysis
15) Central blindness
16) Seizure activity

B) Estimated incubation period 5 – 15 days
C) Fatality rate – 40 - 33%
D) Course before death average 2 days (0 – 6 days)

VIII. Laboratory Findings

A) CBC – normal
B) Fibrinogen – normal
C) CSF – normal 3 of 4 cases
   1) Abnormal case had increase CSF protein and xanthochromia (N=1)
D) Blood chemistry normal

IX. Diagnosis

A) Serology
   1) Fluorescent antibody
   2) Virus neutralizing antibodies
   3) IgM capture ELISA
B) RT-PCR
   1) Blood – negative?
   2) CSF – negative?
   3) Brain/cord - positive
C) Virus isolation
   1) Blood – negative?
   2) Brain/cord – positive

X. Differential Diagnosis

A) Eastern, Western, Venezuelan Equine Encephalomyelitis
B) Equine herpes virus 1
C) Rabies
D) Equine Protozoal myelitis
E) Leukoencephalomacia
F) Stenotic cervical myelopathy
G) Hepatic, intestinal or renal encephalopathies

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XI. Outcome

A) 1999 outbreak Long Island (NY) – 50% fatal
B) 2000 outbreak Northeastern USA – 40% fatal
C) 2001 outbreak Northeastern USA – 33% fatal
D) Reported mortality rates 30 – 64%

XII. Post Mortem

A) Only nervous tissue involvement
    1) Few gross lesions within the brain – occasional hemorrhages
B) Prominent rhombencephalic lesions
    1) Multifocal perivascular lymphocytic rhombencephalitis
    2) Ring hemorrhages, neutrophils and multifocal microgliosis
C) Peroxidase immunohistochemical staining
    1) West Nile virus antigen in cytoplasm
    2) Few neurons, nerve fibers, glial cells, neutrophils
D) Virus isolation
E) RT-PCR

XIII. Treatment

A) Supportive
B) Preventing self-inflicted injury
C) Fluids
D) Treat for other differential diagnoses
E) Herpes virus suspect status
F) Rabies suspect status
G) Plasma transfusion – passive antibody transfer
H) Interferon therapy

XIV. Prevention

A) Available vaccine
    1) Fort Dodge
        (a) Vaccine tested with challenge studies
            (1) No vaccinates or controls developed signs
            (2) Vaccinates did not develop viremia
    2) Millions of doses sold
    3) Few adverse reactions
        (a) Internet stories of abortion with congenital malformations
        (b) Appear to have no basis – for numbers vaccinated, few reported adverse reactions
        (c) Killed vaccine unlikely source of congenital malformations

(d) Isolation of wild virus from some aborted fetuses in Kentucky
(1) Wild virus
(2) Undefined role in abortion
(3) Isolated in small percent of aborted fetuses

4) Efficacy unknown
(a) It may take several weeks after the second dose before a measurable antibody response.
(b) Horses may develop WNV soon after receiving the first dose of vaccine
(1) Suggesting that one dose is not protective
(c) The manufacturer's recommendations
(1) 2 doses 3-6 weeks apart
(2) Yearly booster
(d) Vaccinated horses may develop disease
(1) Frequency this occurs is under investigation
(2) The percent of vaccinates which are not fully protected unknown
(e) Unvaccinated horses > 2X more likely to die

B) Recombitek ® - Merial vaccine
1) Recombinant canarypox vaccine
2) Prevents viremia up to 1 year

C) Other arbovirus encephalitis vaccines
1) EEE, WEE, VEE
2) Do not cross protect

D) Mosquito control very important
1) Stop the bird – mosquito infection cycle
(a) Mosquito control
(1) Primary infected mosquito is *Culex spp*
(2) Control tailored to this species
(3) Vector for horse could be another, less commonly infected, species
2) *Culex spp* control
(a) Range < 1000 yards
(b) Local problem – local control
3) Larval habitat destruction for *Culex spp*
(a) Any puddle that lasts more than 4 days - habitat
(b) Reduce the amount of standing water available
(1) Water troughs, water buckets
(2) Swimming pools, plastic wading pools
(3) Bird baths, wheelbarrows
(4) Clogged roof gutters
(5) Recycling containers
(6) Discarded tires
(7) Tin cans, plastic containers, ceramic pots
(8) Any water-holding container
(c) Larvicides - BTI - *Bacillus thuringiensis var. israelensis*

4) Stable horses during peak mosquito feeding times
   (a) *Culex spp* - dusk, dawn
5) Adult mosquito control – last resort
   (a) Use insect repellents
      (1) Pyrethroid-based
      (2) Containing DEET? – only equine approved products

XV. **Control**

A) What is the threat to care givers?
   1) No evidence of animal-to-person transmission
B) Can a horse infected with West Nile virus infect other horses?
   1) No documented evidence that WNV is transmitted from horse-to-horse.
C) Are horses a source of West Nile virus? Are horses terminal hosts?
   1) Historic evidence
      (a) No virus in blood when clinically ill – dead-end host
   2) 2 historic experimental induction studies
      (a) Showed low level or no viremia – dead-end host
   3) 3 experimental inoculation/transmission studies since 1999 in US
      (a) USDA & CSU/CDC
      (b) 16 horses studied - maximum viremia 10^3 /ml (most < 10^2/ml)
      (c) Below number needed to infect feeding mosquitoes – dead-end host
   4) 8 horses infected via mosquitoes (*Aedes albopictus*)
      (a) 1 hrs developed clinical signs
      (b) 600 mosquitoes fed on horses during viremia – all negative
   5) Virus
      (a) In nervous tissue – very low numbers
      (b) No virus seen in other tissues – dead-end host
D) Should a horse infected with West Nile virus be destroyed?
   1) There is no reason to destroy an infected horse
   2) Half of the horses recover from the infection