Update on Rabies

Daniel J. Dire, MD, FAAP, FACEP, FAAEM
Departments of Pediatrics and Emergency Medicine
University of Texas Health Sciences Center-San Antonio
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Disclosure

Daniel J. Dire, MD has no relationships with commercial companies to disclose.

Lecture Outline
- History of Rabies
- Epidemiology
- Pathophysiology
- Clinical Findings
- Diagnosis of Rabies
- Post-Exposure Management
- Other Considerations

The Natural History of Rabies

1975 1991

Scope of the Problem

Rabies facts
- Rabies occurs in more than 150 countries and territories.
- 40% of those bitten are children aged under 15.
- Dogs are the source of 99% of human rabies deaths.
- Wound cleaning and immunisation within a few hours after contact with a suspect rabid animal can prevent the onset of rabies and death.
- Each year, more than 15,000 people worldwide are treated after exposure – this is estimated to prevent 327,000 rabies deaths annually.
History of Rabies

- Plutarch: reported that rabies could be spread by dog bites
- Homer: in the Iliad, wrote about Sirius, the Dog Star of Orion
- Democritus: first described rabies in 500 B.C.
- Aristotle: wrote Natural History of Animals in the 4th Century B.C.

History of Rabies continued

- Hippocrates
- Zenophon
- Epimarchus
- Virgil
- Horace
- Ovid
- Lukian: felt that rabid humans could spread the disease by biting another person
- Cardanus (1501-1576 AD): first to describe the infectivity of saliva

History of Rabies continued

- 1st Century A.D: Celsus recommended caustics, burning, cupping and sucking the wounds of bite victims
- 1026: Howel the Good of Wales
- 1271: Rabid wolf in Franconia
- 1500: Spain ravaged by dog rabies
- 1586: Dog epizootics in Flanders, Austria, Hungary, & Turkey

History of Rabies continued

- 1684: Canine Rabies in Paris
- 1734: Many rabid dogs in Europe
- 1750: First rabid dogs in South America
- 1753: Rabid dogs in Virginia
- 1768: First major epizootic in U.S.
- 1771: Foxes and dogs carried the disease to swine and other domestic animal in U.S.

History of Rabies continued

- 1785-1789: “Canine madness” was raging all over the colonial states
- 1810: Epizootic in foxes, dogs, and wolves in Ohio
- 1830s: Skunk rabies on the Great Plains
- 1850s: Skunk rabies in California
- 1860s: Rabies spread by roaming dogs throughout the U.S.

History of Rabies continued

- 1881: Louis Pasteur published first report on a vaccine
History of Rabies continued

- 1903- Negri described the Negri Body
- 1906- Babes studied the Negri Body
- 1940- Rabies virus grown in chick embryos
- 1962- Constantine demonstrates non-bite transmission of rabies in animals in a cave
- 1968- Rabies virus isolated from the air in same cave

Epidemiology of Rabies

- N=1598 in 2013
- 17 different species
Epidemiology of Rabies - USA

Rabies in Domestic Animals, 1958-2008

Epidemiology of Rabies

Other Rabid Animals Reported in 2013 in CONUS
- Groundhogs
- Bobcats
- Coyotes
- Deer
- Opossums
- Wolves
- Otters
- Rabbit (1)
- Marmot (1)

Epidemiology of Rabies - Texas

Laboratory-confirmed rabies in all species, 2014

Epidemiology of Rabies

Reservoir species of terrestrial Rabies

Estimated Risk of Human Rabies
- Skunk bite: 0.05
- Bat bite: 0.001
- Cat bite: 0.001
- Dog bite: 0.00001
- Non bite exposure: 0.000001*

* PEP not indicated
Human Rabies Worldwide

- Estimated Annual Human Rabies Cases
  - Europe 10-20
  - Latin America 200-400
  - Africa 500-1000
  - Asia 30,000-50,000

Epidemiology of Rabies

- Rabies Update - Daniel J. Dire, MD, FACEP, FAAP

Rabies in Europe

- Bats and the trivial bite story
  - Most human rabies cases acquired in the USA are due to rabies virus variants associated with insectivorous bats and, in particular, a specific variant associated with Eastern pipistrelle and silver-haired bats. Insectivorous bats are small – less than 20 grams with tiny needle-like teeth.
  - Trauma alone, from a bat bite, is unlikely to send anyone to an emergency room.
  - For example, an adult male dismissed a bite from a bat and decided that the risk of rabies in bats was small enough to not seek post-exposure prophylaxis. He died of rabies several weeks later.
Bat bite on finger

Pathophysiology

Rabies Virus

Routes of Human Exposure
- Bite is the most natural and successful way to transmit rabies.
- Exposing fresh, open bleeding wounds to live virus (i.e., fresh saliva or tissue)
- Oral exposure (consuming large amounts of live virus) may result in rabies but the risk is orders of magnitude lower.
- Inhalation of droplets or an aerosol (bat caves)
- Ocular – not documented except with corneal transplant
- Transplanted organs
- Other contact by itself, such as petting a rabid animal and contact with blood, urine, or feces (e.g., guano) of a rabid animal, does not constitute an exposure

Clinical Findings

Furious type – 80-85%
Dumb type – 15-20%
- STAGE 1 – Incubation Period
- STAGE 2 – Prodrome
- STAGE 3 – Acute Neurologic Phase
- STAGE 4 – Coma
- STAGE 5 – Death

Clinical Finding
- Hydrophobia
- Aerophobia

Diagnosis
- Negri Bodies – No longer considered pathognomonic, may be absent in 15-20%
- Rabies Antibodies – may be from shots
- Rabies Antigen – by Direct Fluorescent antibody staining
Diagnosis

- Reverse Transcriptase-Polymerase Chain Reaction test can detect virus in Saliva

Post-Exposure Management

- Immediate and thorough washing of the bite with soap and water is the most effective measure for preventing rabies

Post-Exposure Prophylaxis (PEP)

- Dogs, cats, ferrets
  - if available, observe for signs of rabies for 10 days
  - if remains healthy, cannot have transmitted rabies
  - PEP needed if animal tests positive, or not available for observation

- Wild carnivores (skunks, raccoons, fox), bats
  - high risk, test animal or PEP needed

- Livestock, small rodents, rabbits
  - low risk, treat on a case-by-case basis, consult with local and state health officials

Human Exposure

Yes → Rabies known or suspected in Area or Species?

No

Animal Captured?

Yes

Wild Animal?

No

TX

**

No

Test Brain-DFA

Neg

See Next Page

Wild Animal?

Yes

TX

Post-Exposure Immunoprophylaxis

- Should always include both:
  - Passive immunoprophylactic agent
    - Rabies Immune globulin
  - Active immunoprophylactic agent
    - Rabies Vaccine
Human Rabies Vaccine

- Purified Chick Embryo Cell Vaccine (PCEC) RabAvert®
  - Novartis Vaccines
  - 800-244-7668
- Imovax® Rabies-HT
  - sanofi-pasteur
  - 800-822-2463

Human Rabies Vaccine

- Post-Exposure Dosage of PCEC (or HDCV and RVA, if available):
  - 1.0 ml IM per dose in 
    Deltoid area (outer thigh in small children)
  - Administer one dose on
    DAYS 0, 3, 7, 14, and 28

Human Rabies Immune Globulin (HRIG)

- HyperRab™ S/D
  - Grifols Therapeutics
  - 1-800-243-4153
- Imogam® Rabies-HT
  - sanofi-pasteur
  - 800-822-2463

Human Rabies Immune Globulin (HRIG)

- Post-Exposure Dosage or HRIG
  - 20 IU/Kg body weight IM.
  - If possible, the FULL DOSE should be infiltrated around the wound
  - Any remaining HRIG should be given IM at a site distant from the vaccine

Rabies Prevention

- Oral vaccination of wild rabies vectors utilizes a Recombinant Vaccinia Virus which expresses the Immunizing Glycoprotein of Rabies (V-RG)
  - 8.5 million doses in western Europe from 1989-1995 has eliminated sylvatic rabies from large areas
  - Raccoons-projects underway in Florida, Massachusetts, New Jersey, New York, Vermont, & Ohio
  - Foxes & Coyotes-ORVP in Texas
Oral Rabies Vaccination Projects - TEXAS

- The bait matrix is composed of either Fish Meal or Dog Food with a polymer additive that acts as a binding agent.
- A low temperature sealing is used to hold a vaccine sachet inside the bait.
- The sachet contains 2 ml of V-RG.

ORVP TEXAS

- Each bait unit has a warning label printed on the outside.

WARNING: RABIES VACCINE DO NOT DISTURB
TEXAS DEPARTMENT OF HEALTH
1-512-458-7255

ORVP TEXAS

1995 – 2002 ORVP Vaccination Zones

1995 - 2002 ORVP Vaccination Zones

Coyote/Fox Success Story

ORVP Vaccination - Europe
Rabies Survival

- Rare; should be considered a fatal disease
- 6 y/o boy recovered in U.S. in 1970
- 15 y/o girl in Wisconsin in 2004. Treated with supportive care and neuroprotective measures, including a drug-induced coma and ventilator support. Intravenous Ribavirin was used under an investigational protocol. The patient was kept comatose for 7 days.
- “Wisconsin Protocol” a.k.a. “Milwaukee Protocol” not successful in most subsequent cases where it was used (1 survivor in 2011).