Rabies Post-Exposure Prophylaxis (RPEP) and Pre-Exposure Prophylaxis (PrEP)

The State of Rabies Prevention and Control in New York — 2015

Andie Newman, DVM, MPH, DACVPM
State Public Health Veterinarian, New York State Department of Health
alexandra.newman@health.ny.gov, 518-473-4439

Rabies Basics
What is Rabies?

- RNA virus in the *Rhabdoviridae*
  - Genus *Lyssavirus*
  - Other lyssaviruses include: Lagos bat virus, Duvenhage virus, Mokola virus, Australian bat lyssavirus, and European bat lyssavirus types 1 and 2; several newly discovered
- Infectious disease affecting the central nervous system (nerves, spinal cord, brain)
- Virus maintained in nature by mammals
  - Not a disease of birds, reptiles, amphibians
- Human infections result from contact with rabid animals
  - Domestic animals: bridge between rabid wildlife and humans

Rabies Virus Host Species

- Principal hosts: mesocarnivores and bats
  - All mammals *theoretically* susceptible
- Genetically distinct virus variants maintained by different reservoir (host) species
  - Transmission typically occurs between members of same species (e.g., bat-to-bat)
  - “Spill-over” transmission to non-reservoir species (e.g., bat-to-human, raccoon-to-dog)
  - Reservoir hosts often located in distinct geographic regions
Terrestrial Rabies Virus Variants, 2009–2013

Rabid Bats – 2013

Rabid bats documented in all states except Hawaii.
Domestic Animal Rabies – 2013

Dogs

Cats

Rabies in New York State

• Current reservoir species
  – Bats (multiple species)
  – Raccoons
• “Spillover” infections diagnosed in many other domestic and wild animal species
  – Skunks, red fox, grey fox, cats
  – Woodchucks, cattle, fishers, goats, otters, dogs, horses, deer, guinea pig, bobcats, bears, beavers, swine, camel, ferrets, domestic rabbits
• “Rabies vector species” – most likely to be rabid
  – Bats, raccoons, skunks, red and grey foxes
Confirmed Rabid Wild Animals – NYS, 2005–2014*

- Raccoons: 54%
- Bats: 22%
- Skunks: 16%
- Foxes: 6%
- Other species: 2%

*Outside of NYC. Data courtesy of Wadsworth Center

Rabid “Other” Wildlife — NYS, 2005–2014*

- Woodchucks: 46
- Deer: 16
- Otters: 5
- Coyotes: 5
- Bobcats: 4
- Fishers: 4
- Mink: 1

*Outside of NYC. Data courtesy of Wadsworth Center
Rabies Pathogenesis

- No transmission or diagnosis during incubation
- *Always* in brain before salivary glands
  - Transmission only during clinical signs or up to several days prior (domestic animals)
- No virus in the blood

*Outside of NYC. Data courtesy of Wadsworth Center*
Clinical Signs of Rabies in Animals

- Can’t tell just by looking
- Change in behavior
  - unusual aggression, lack of fear
- Change in voice
- Paralysis, paresis (weakness)
- Dysphagia, drooling
- Incoordination
- Lethargy, convulsions, death
- Signs may vary within and among species

Clinical Course of Human Rabies

- Incubation Period – typically 1–3 months
  - Range <1 week to >1 year (rarely several years)
- Prodrome – non-specific symptoms (2–10 days)
  - Fever, chills, irritability, malaise, nausea
  - Paresthesia (30–70% of cases)
- Acute neurologic phase (2–7 days)
  - Maniacal behavior (furious) vs. more complacent/paralytic (ascending)
  - Hydrophobia, aerophobia
- Coma (5–14 days)
- Death, usually within 2 weeks
Treatment

- None proven effective after the onset of clinical illness
- Experimental treatments
  - “Milwaukee Protocol”

Human Rabies in the United States

- Rare, average 1–3 cases/year
  - Estimated 55,000+ cases annually worldwide
- Vastly reduced since 1950s with comprehensive domestic animal vaccination and reduction in free-roaming dogs
- Canine variant rabies eliminated in mid-1990s
  - Dogs can still get other rabies virus variants!
- ~1/4 of U.S. cases are exposed overseas
  - Canine variant rabies responsible for >95% of ~55,000 annual worldwide rabies deaths
  - Canine rabies still present in many parts of the world, esp. Asian and African countries
### Virus Variants of U.S. Human Rabies Cases, 1995–2013 (N=54)

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<tr>
<th>Country</th>
<th>Number</th>
<th>Percentage</th>
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<tr>
<td>Canine Variant (Overseas)</td>
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<tr>
<td>Bat Variant</td>
<td>39</td>
<td>72%</td>
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<td>Raccoon Variant</td>
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<td>6%</td>
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### Rabies Transmission
Transmission – Infectious Materials

- **Infectious**
  - Saliva
  - Cerebrospinal fluid (CSF)
  - Neural tissue

- **Possibly infectious**
  - Tears
  - Vomitus

  (because contains saliva)

- **Not Infectious**
  - Blood
  - Urine
  - Feces
  - Guano
  - Skunk spray
  - Milk (pasteurization kills)
  - Dried virus (dead)

Types of Rabies Exposures

- **Bite exposure (most common)**
  - Any penetration of the skin by teeth

- **Open wound exposure**
  - Introduction of saliva or other potentially infectious material into an open wound (e.g., broken skin that has bled within past 24 hours)

- **Mucous membrane exposure**
  - Introduction of material onto any mucous membrane (eyes, nose, mouth)

- **Other exposures**
  - When a bite, open wound, or mucous membrane exposure can’t be ruled out
    - “Bat-in-the-bedroom” type situations
    - Surgical transplant recipients – corneal, solid organ, vascular tissue
    - Inhalation of aerosolized rabies virus (laboratory)

Not Exposures

- Animal scratches without wound contamination with saliva/infectious material
- Petting or other direct contact with a rabid animal
- Saliva contact with intact skin
- Indirect exposures
  - E.g., contact with dog that attacked a raccoon
- Bats in homes with awake/alert persons
- Situations where no animal was seen
- Exposures involving rabbits or small rodents
  - Unless unusual situation

Preventing and Managing Rabies Exposures
Rabies Prevention

• Prevent exposures – Avoid contact
  – Stray or unknown domestic animals
  – All wildlife, including bats
  – Educate children about animal bites

• Domestic animal vaccination
  – Rabid wildlife → pet → humans
  – Required for dogs, cats, ferrets

• Manage potential exposures
  – Animal observation or testing
  – Pre-exposure (PrEP) and post-exposure (PEP) prophylaxis

Determine the Rabies Status of the Animal by Observation or Testing

- Was the animal was shedding virus at time of the bite?
- If healthy, domestic animal* – confine and observe for signs of rabies for 10 days after the bite
  - Generally preferred over testing – accurate
  - Regardless of animal's vaccination status
- Euthanize and test animal if:
  - Any wild animal
  - Domestic animal exhibits signs of rabies during the 10-day observation period
  - Unowned (stray)/unwanted domestic animal

*Domestic animals: dogs, cats, ferrets, horses, donkeys, mules, cattle, sheep, goats, and pigs

Animal Specimen Testing at Wadsworth Center Rabies Laboratory

- Routine specimens – same day testing, M–F
- Emergency testing – available in certain situations, needs approval from BCDC
  - When result would not be available within ~3 days of exposure
  - High-risk exposures, e.g., bite from vector species or animal with neurologic illness
- Consult rabies lab regarding specifics of sample preparation, packaging, and shipping
- Unsatisfactory specimens regarded as positive
- NYC Public Health Laboratory is also approved to test animals
Rabies Post-Exposure Prophylaxis

RPEP

Rabies Postexposure Prophylaxis (RPEP)

- Indicated after a known or probable rabies virus exposure
  - Laboratory confirmed positive animal specimen
  - Rabies status of animal not able to be confirmed
    - Unable to locate exposing animal for testing or 10-day confinement
    - Specimen unsatisfactory for rabies testing (e.g., decomposed, inappropriate tissue sampled)
- Not indicated pending completion of 10-day confinement or testing of animal if available
RPEP in NYS – Unique Features

- **RPEP must be reported to LHD by medical provider *before* being started**
  - Opportunity to identify and confine or test biting animal
  - LHD “authorizes” RPEP if exposure meets criteria in NYSDOH guidance documents
  - Authorized RPEP = no cost to person exposed
- **County covers costs of authorized RPEP not covered by insurance/third party benefits**
  - State reimburses county for authorized RPEP
- **NYS has a financial interest in making sure RPEPs are recommended appropriately**
  *For exposures occurring in NYS outside of NYC*

RPEP – General Considerations

- **LHDs and NYSDOH provide consultation**
- **Ultimately, healthcare providers decide to administer PEP (or not) based on public health recommendations and clinical judgment**
  - They may administer without authorization by public health (patient is responsible for cost of treatment)
- **RPEP is medical urgency, not a medical emergency**
RPEP Protocol for Previously Unvaccinated Persons

- Wash wounds thoroughly
- Human Rabies Immune Globulin (HRIG)
  - Infiltrated at wound site (20 IU/kg) with remaining volume IM (day 0)
    - Even if completely healed
    - If no “site” or if MM exposure, give all IM
  - Not at same site or in same syringe as day 0 vaccine
- Vaccine
  - IM on days 0, 3, 7, and 14
  - If immunocompromised, 5th dose on day 28 and titer 1–4 weeks later
  - Do not give in gluteal muscles
    - Specific label warning for reduced titers

RPEP for Previously Vaccinated Persons

- History of complete pre- or post-exposure rabies prophylaxis (or prior titer in certain instances)
- Wash wounds thoroughly
- No HRIG
- Vaccine IM on days 0 and 3
  - Do not give in gluteal muscles
  - Serology is never used to determine whether RPEP is necessary
    - “Protective” titer has not been established
    - Would delay RPEP
    - If exposed, RPEP is given
RPEP Administration Anomalies

- Always consult public health
- Common examples:
  - Long time span between exposure and seeking care
  - Non-standard vaccination schedule/interruptions
  - Vaccine administered in gluteus
  - HRIG not given to previously unvaccinated person
  - HRIG given to previously vaccinated person
  - HRIG not infiltrated at wound site
  - Too much/not enough HRIG administered
  - RPEP started in another country

RPEP Precautions

- Immunosuppression
  - A clinical diagnosis, caused by disease or medications
  - Postpone PrEP
  - Delay immunosuppressive agents during RPEP, if possible
  - Administer 5th vaccine dose on day 28, check titer in 1–4 weeks
- Pregnancy
  - No increased incidence of abortion, premature births, or fetal abnormalities associated with rabies vaccination
  - Not a contraindication to RPEP, PrEP might be indicated if high risk
- Serious allergies to components of vaccine
  - Revaccinate with caution
Managing Adverse Reactions

- Once initiated, RPEP should not be discontinued for local or mild systemic vaccine reactions
- Management
  - Switch vaccine brands
  - Use of anti-inflammatory, antihistaminic, and antipyretic agents
  - Pretreatment with antihistamines
  - Have epinephrine readily available
  - Observe in clinic after vaccination
- Serious systemic, anaphylactic, neuroparalytic reactions are rare
  - Consult public health, weigh risks vs. benefits
- Report clinically significant events to VAERS

Rabies Pre-Exposure Prophylaxis

PrEP
Rabies Pre-exposure Prophylaxis (PrEP)

• **Recommended for**
  – Persons at risk of occupational/recreational exposure to rabies
    • E.g., diagnosticians, rabies researchers, veterinarians and staff, animal control officers, wildlife rehabilitators, trappers, cavers
  – Certain international travelers

• **Benefits**
  – Reduces cost and complexity of RPEP
  – Partial protection if RPEP is delayed
  – May protect against unrecognized exposures

• **Routine PrEP for general U.S. population not recommended**

• **Not a required public health function in NYS**

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Rabies Pre-exposure Prophylaxis (PrEP)

• **Primary series:** Three IM vaccine doses in the deltoid muscle
  – Days 0, 7, and 21 or 28

• **Booster vaccines as needed based on periodic serologic antibody titer results**
  – Rabies serologic antibody titer every 2 years (or following ACIP recommendations) as long as person is at risk of exposure
  – Single booster vaccine only if antibody titer <0.5 IU
Human Rabies Serology

- Available free of charge at NYSDOH Wadsworth Rabies Laboratory
  - Routine titer checks (after PrEP) for employees of
    - Government agencies
    - Non-profit agencies
    - Cornell University College of Veterinary Medicine
  - If there is an immediate concern for human health
    - Tests for seroconversion after non-standard RPEP administration or immunosuppression

- Available at Kansas State University Rabies Laboratory
  - Routine titer checks for veterinarians, rehabilitators, nuisance wildlife control, private research institutes and universities, and international travelers
  - Order “Endpoint rabies titer”, can be ordered via Quest

Resources
• Types of rabies exposures
• Indications for PrEP and RPEP
• Use of human rabies vaccine and human rabies immunoglobulin
• Adverse reactions
• Precautions and contraindications to RPEP
• Serologic testing
• www.cdc.gov/rabies

Serve as a basis for animals rabies prevention and control programs in the U.S. to facilitate standardization of procedures among jurisdictions*
• Recommendations regarding
  – Domestic animal vaccination
  – Management of animals exposed to rabies
  – Management of animals that bite humans
• Table of rabies vaccines licensed and marketed in the U.S.

*New York State Rabies Law and State Sanitary Code may differ.
Resources

- **Bureau of Communicable Disease Control, NYSDOH**
  - (518) 473-4439 – business hours, (866) 881-2809 – after hours

- **Wadsworth Center Rabies Laboratory**
  - (518) 485-6464 – business hours, (866) 881-2809 – after hours
  - [www.wadsworth.org/rabies](http://www.wadsworth.org/rabies)

- **Kansas State University Rabies Laboratory**
  - For RFFIT serology tests to monitor titers following PreP
  - (785) 532-4474

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Human Rabies Biologics in the United States

- **Human Rabies Vaccine**
  - Human diploid cell vaccine
    - Imovax® (sanofi Pasteur)
  - Purified chick embryo cell vaccine
    - RabAvert ® (Novartis)

- **Rabies Immune Globulin**
  - Imogam ® Rabies –HT (sanofi Pasteur)
  - HyperRab™ (Talecris)

For information about vaccine and immune globulin availability:
Questions?

alexandra.newman@health.ny.gov
518-473-4439

Available at:
www.health.state.ny.us/diseases/communicable/zoonoses/rabies/

How to Safely Catch a Bat
Why is Rabies a Public Health Concern?

- There is NO PROVEN TREATMENT for rabies
  - (Almost) invariably FATAL DISEASE after illness onset
- Rabies is PREVENTABLE
  - Human rabies is RARE in the U.S.
  - Rabies postexposure prophylaxis (RPEP) is COMMON
- Substantial PSYCHOLOGICAL and EMOTIONAL IMPACT of exposure
- Substantial COST of rabies prevention

Human Rabies in New York State

- 2011 – canine variant, imported from Afghanistan
  - Male, 23 years, Army soldier
- 2000 – canine variant, imported from Ghana
  - Male, 54 years, immigrant from Ghana
- 1993 – bat variant
  - Female, 11 years
  - Last domestically acquired case (1st since 1954)
RPEP Administered vs. Rabid Animals, by Species – NYS, 2008-2012

Rabid Wild Animals by Month — NYS, 2005–2014*
Trend of Rabies in Domestic and Wild Animals and Humans, U.S., 1944-2002

Confirmed Rabid Animals — NYS, 2005–2014*

*Outside of NYC. Data courtesy of Wadsworth Center