

# Rabies: Human Vaccination and PEP

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Jennifer Hsu, MD FACP

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I have no disclosures.

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# Objectives

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- Review clinical features of rabies in humans
- List available rabies vaccinations in the U.S
- Discuss appropriate use of rabies pre- and post-exposure prophylaxis



# Cases

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- 62 yo physician calls in with a potential bat exposure
- No bats seen, but awakened with marks on exposed skin
- Sleeping with family in condo undergoing exterior renovation



# Cases

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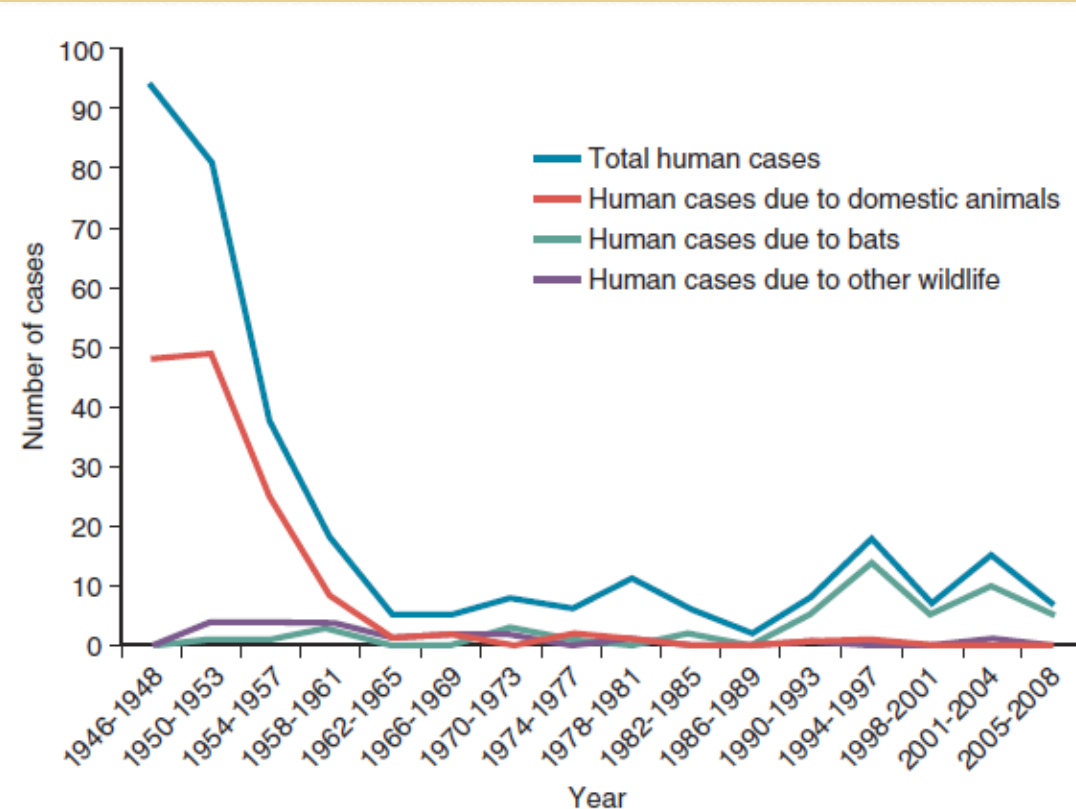
- Healthy 30 yo home health physical therapist was bitten by a patient's dog
  - Numerous unkempt dogs on the property and vaccination status unknown
  - Owner would not cooperate with quarantine
- 33 year old male awakened to find a flying bat
  - Flew into sleeping child's room
  - No bites or direct contact observed

# Cases

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- 43 year old male punctured his scalp on a nail
  - Working in attic where bat guano present
  - No live bats seen
- 58 year old woman hit by a bat
  - Riding bike at dusk
  - Bat flew into her arm and caused an abrasion

# Rabies in the U.S. by year, 1945 - 2008



# Transmission in the U.S.

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- Human epidemiology is reflects that of local animal rabies: bats (especially silver-haired bats), raccoons, skunks, and foxes
- The major canine variants of rabies were eliminated in the U.S. in 2006
  - Result of aggressive vaccination campaign
  - Fatal case of rabies in an army soldier returning from Afghanistan in 2011 who sustained a dog bite 7 months prior

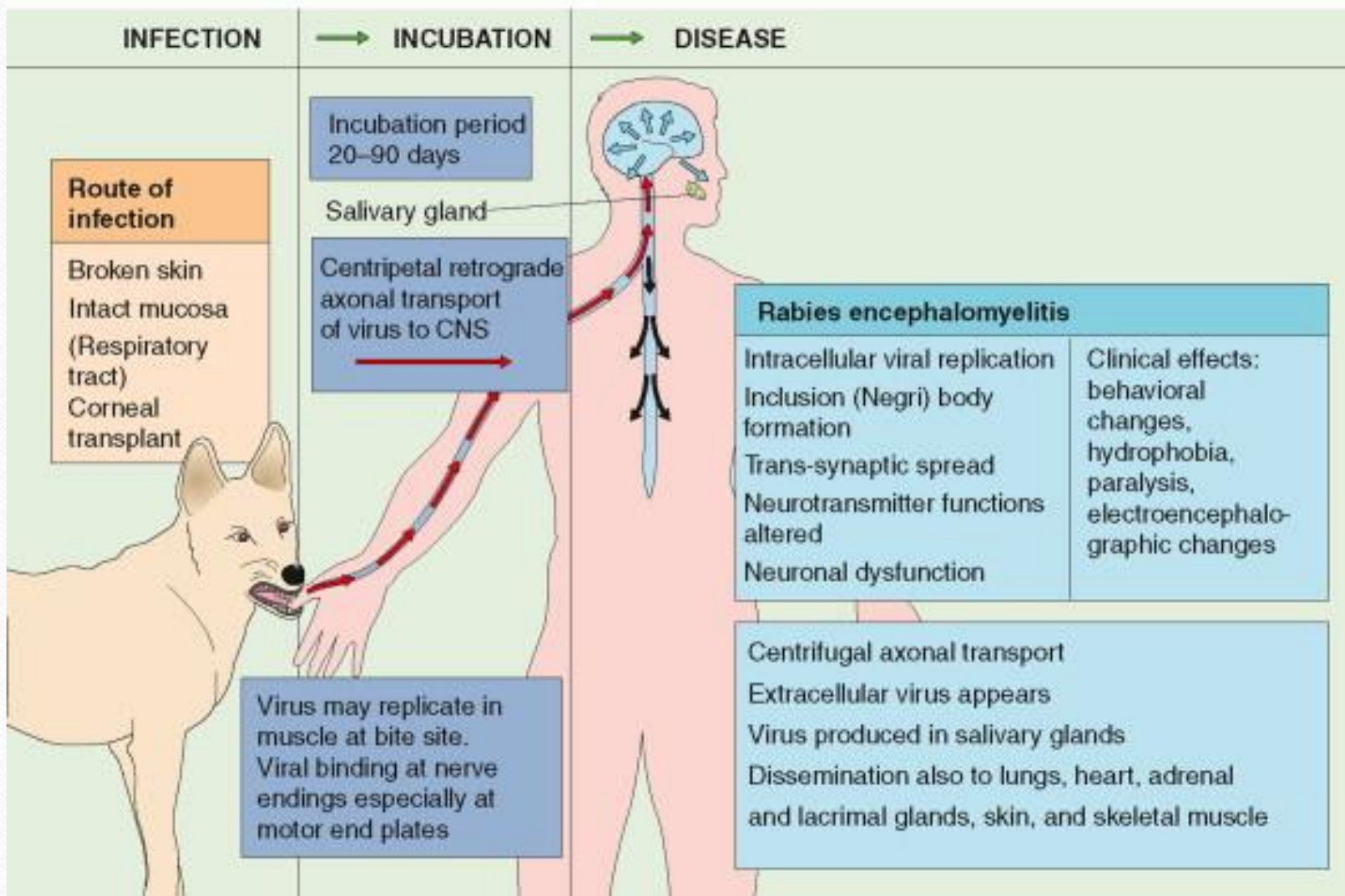


# Transplant-Based Transmission

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- 2004 (U.S.): Arkansas man died of encephalitis of unknown cause
  - 4 recipients of kidneys, liver, and an arterial segment died from rabies
  - Friends of donor subsequently reported he had been bitten by a bat
- 2005 (Germany): 26 yo woman died of encephalitis of unknown cause
  - Recipients of cornea (2 survived), liver (vaccinated; survived), lung, kidney, and K-P
  - Friend of donor subsequently reported stray dog bite in India

## Pathogenesis of Rabies



Stage	Duration (% of cases)	Associated Findings
Incubation period	<30 days (25%) 30-90 days (50%) 90 days to 1 year (20%) >1 year (5%)	None
Prodrome / early symptoms	2-10 days	Paresthesias or pain at the wound; fever; malaise; anorexia; nausea and vomiting
Acute neurologic disease; furious rabies (80% of cases)	2-7 days	Hallucinations; bizarre behavior; anxiety; agitation; biting; hydrocephalus; autonomic dysfunction; SIADH
Paralytic rabies (20% of cases)	2-7 days	Ascending flaccid paralysis
Coma, death	0-14 days	--

# Rabies Biologics in the U.S.

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## Vaccines

- Human diploid cell vaccine (Imovax<sup>®</sup> Rabies, Sanofi Pasteur)
- Purified chick embryo cell vaccine (RabAvert<sup>®</sup>, Novartis Vaccines and Diagnostics)
- 1 mL IM for pre- & post-exposure

## Immune Globulin

- Imogam<sup>®</sup> Rabies-HT (Sanofi Pasteur)
- HyperRab<sup>™</sup> S/D (Talecris Biotherapeutics)
- 20 IU/kg locally for post-exposure

# Vaccine Safety

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- Local reactions are common – up to 90% depending on the study
- Pain is most frequent and resolves within a few days
- Systemic hypersensitivity more common with booster doses (up to 6%)
- Rare neuro effects, no deaths reported

# Vaccine Precautions

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- Immunosuppression (disease or drug) can impair Ab response
  - PrEP
    - Delay immunization if possible or consider Ab titers to ensure seroconversion
    - Focus on risk factor modification
  - PEP
    - Hold immunosuppression if possible
    - Check titers to ensure seroconversion
- Pregnancy is not considered a contraindication to PrEP or PEP if needed

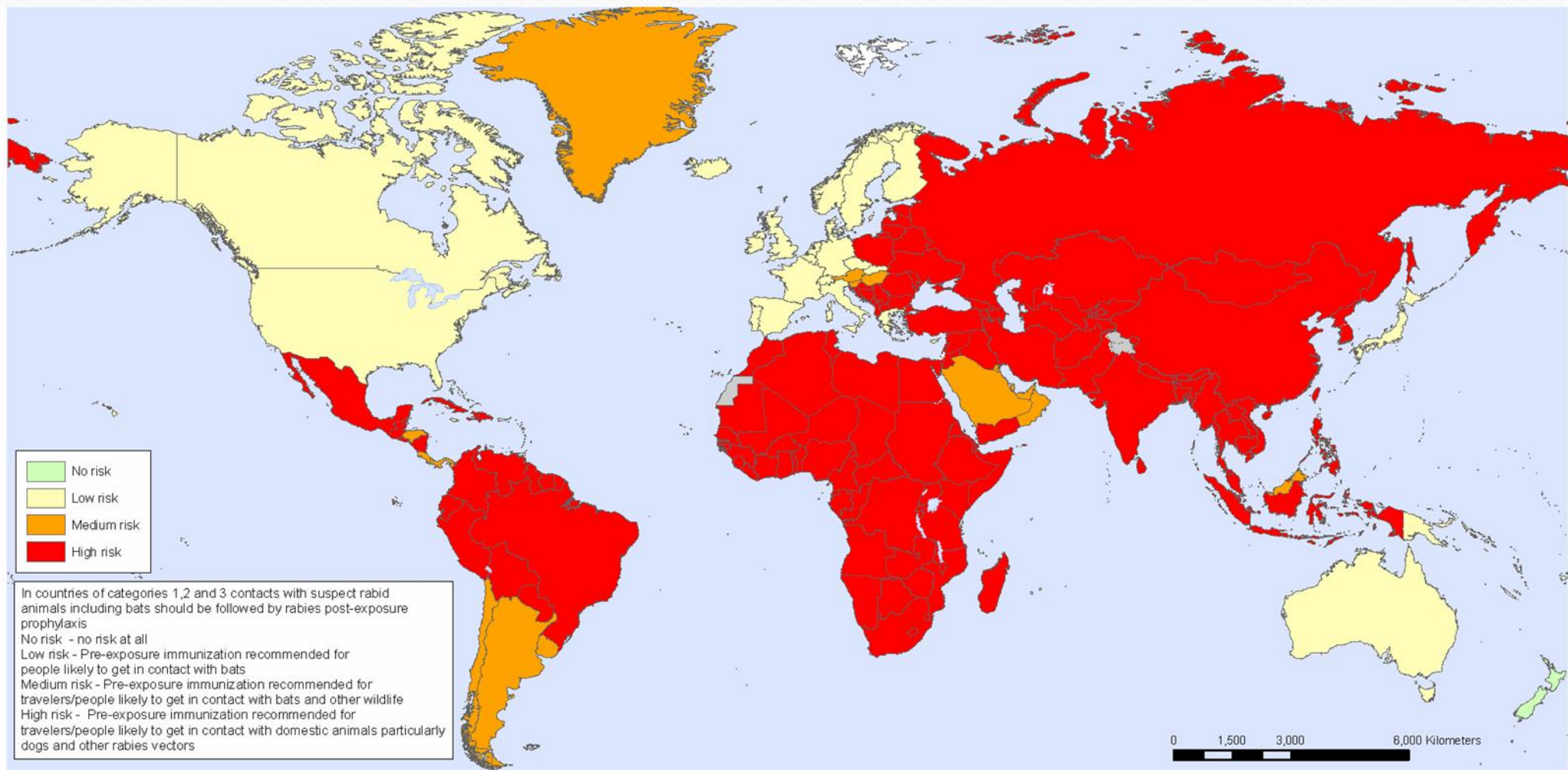
# Indications for Pre-Exposure Prophylaxis

<b>Risk Category</b>	<b>Nature of Risk</b>	<b>Typical Population</b>	<b>Pre-exposure Recommendations</b>
<b>Continuous</b>	Virus present continuously, often in high concentrations Specific exposures likely to go unrecognized Bite, nonbite, or aerosol exposure	Rabies research laboratory workers Rabies biologics production workers	Primary course Serologic testing every 6 months Booster vaccination if antibody titer is below acceptable level
<b>Frequent</b>	Exposure usually episodic, with source recognized, but exposure might be unrecognized Bite, nonbite, or aerosol exposure	Rabies diagnostic lab workers Spelunkers Veterinarians and staff Animal-control and wildlife workers in rabies-enzootic areas Frequent bat handlers	Primary course Serologic testing every 2 years Booster vaccination if antibody titer is below acceptable level

# Indications for Pre-Exposure Prophylaxis

<b>Risk Category</b>	<b>Nature of Risk</b>	<b>Typical Population</b>	<b>Pre-exposure Recommendations</b>
<b>Infrequent</b>	Exposure nearly always episodic with source recognized Bite or nonbite exposure	Veterinarians and terrestrial animal-control workers in areas where rabies is uncommon Veterinary students Travelers with specific risk	Primary course No serologic testing or booster vaccination
<b>Rare</b>	Exposure always episodic with source recognized Bite or nonbite exposure	U.S. population at large, including persons in rabies-epizootic areas	No vaccination necessary





# Pre-Exposure Prophylaxis

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- Effectiveness studies not feasible, so need surrogate markers:
  - Antibody titer of 0.5 IU/mL (WHO)
  - Complete virus neutralization at a 1:5 serum dilution by RFFIT
- Multiple studies have shown adequate Ab response by 14 days with 3 IM doses of cell culture rabies vaccine → days 0, 7, and 21 or 28
- Persisting Ab detectable at 21 months in 94% of persons tested
- Enables a rapid anamnestic response with future PrEP or PEP

# Rationale for Post-Exposure Prophylaxis

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- Timely administration of RIG and active immunization can prevent the spread of virus into the nervous system
- Once the virus has entered the peripheral nerves, current therapeutic techniques probably do not readily prevent subsequent replication and spread as the virus quickly moves centrally
- But, what about treatment...

# “Milwaukee Protocol”

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- In 2004, 15 yo girl in Milwaukee handled a bat, sustaining a bite → no PEP
- 37 days after the exposure she developed rabies encephalomyelitis
- Treated with therapeutic coma and NMDA-receptor antagonist therapy
- She recovered as did a subsequent patient without PEP
- Heavily promoted as a cure; however, 31 cases have since failed

# PEP Decisions

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- Type of exposure (bite >> non-bite)
- Epidemiology of rabies in animals in the area where the incident occurred and species of animal involved
- Circumstances of the exposure incidence (unprovoked >> provoked)
- NOTE: Rabies virus is inactivated by desiccation, UV irradiation, and does not persist in the environment. Dry = non-infectious

# PEP Decisions

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- Dogs, cats, and ferrets
  - Healthy & available: observation for 10 days; no PEP unless animal becomes ill
  - Rabid or suspicious: immediately begin PEP
  - Unknown: individualized approach
- Skunks, raccoons, foxes, and most other carnivores; bats
  - Regarded as rabid unless animal proven negative by labs
  - Consider immediate PEP



## Categories of Animal Exposure



[Return to Rabies prevention flowchart introduction](#)

### Did an actual exposure occur?

Rabies is transmitted only when the virus is introduced into bite wounds or open skin wounds or onto mucous membranes. Two general categories of exposure are recognized:

1. Bite: All bites that penetrate or abrade the epidermis, regardless of anatomic location, constitute an exposure.
2. NonBite: The contamination of open wounds, abrasions, mucous membranes, or scratches with saliva or other potentially infectious material (neural tissue, cerebrospinal fluid, salivary gland tissue) constitutes an exposure. Because the rabies virus is inactivated by desiccation and ultraviolet irradiation, in general, if the material containing the virus is dry, the virus can be considered non-infectious. It is rare for nonbite exposures to result in rabies. Clinicians are urged to consult with public health officials before initiating post-exposure prophylaxis for nonbite exposures.

BATS warrant special consideration  
when deciding whether a NonBite exposure has occurred.

Select if your situation involves a  
[NonBite exposure to a BAT](#)

When you are ready to continue with the algorithm answer the exposure question by selecting "yes" or "no".

YES

NO

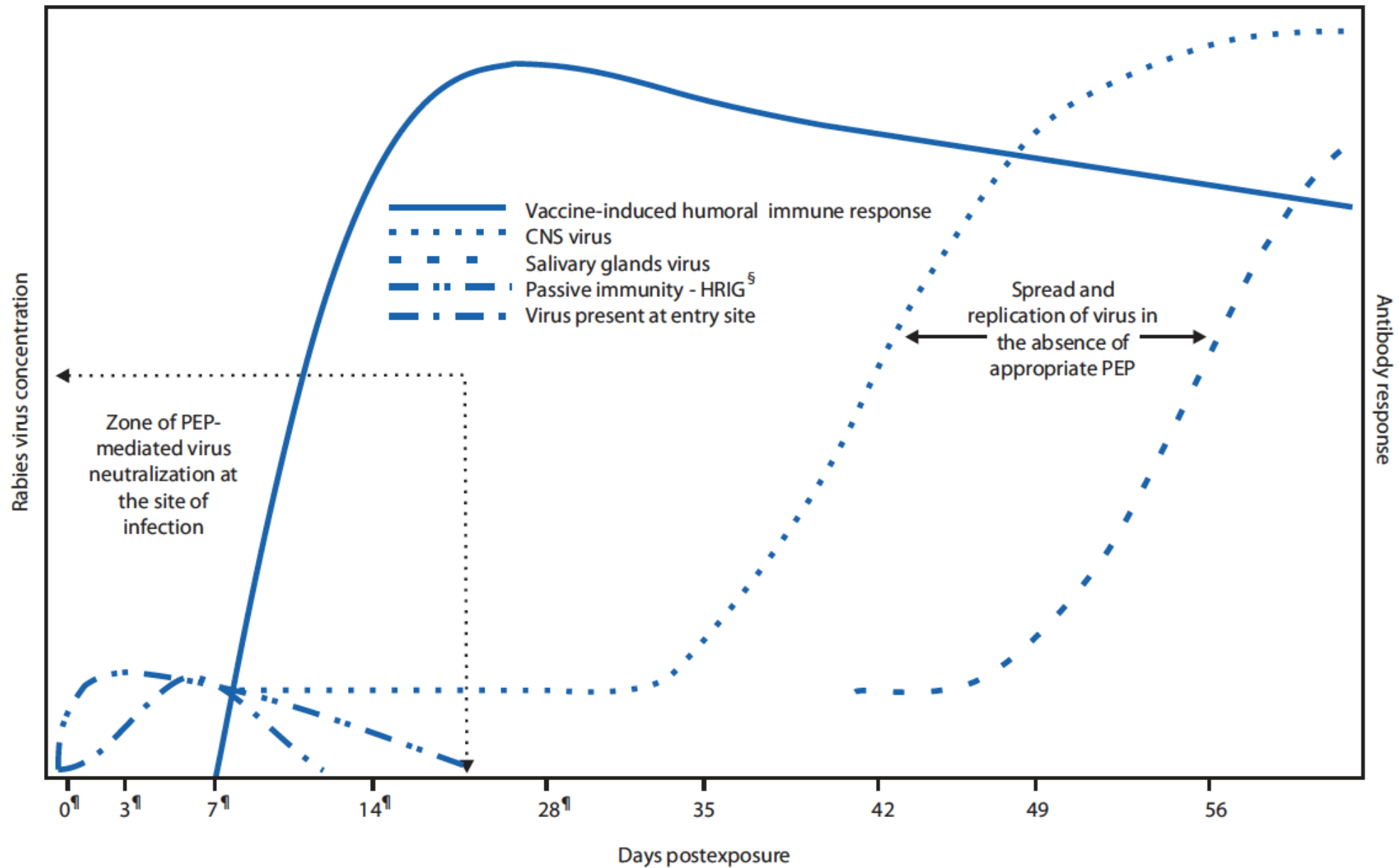
Last Revised: January 21, 2015

# PEP for Unvaccinated Persons

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- Wound cleansing with soap & water and virucidal agent such as povidone-iodine if available
- RIG 20 IU/kg infiltrated as much as possible around the wound and the remainder given IM remotely from the site of vaccination
- HDCV or PCECV 1 mL given IM on days 0, 7, 14, and 28
- No PEP failure reported in the U.S. since 1979





# PEP for Vaccinated Persons

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- Wound cleansing and RIG recommendations remain the same
- HDCV or PCECV 1 mL IM on days 0 and 3
- Antibody titers are not used in making PEP decisions due to delay in treatment and lack of a known “protective” titer

# Cases

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- 62 yo physician calls in with a potential bat exposure
- No bats seen, but awakened with new marks on exposed skin
- Sleeping with family in condo undergoing exterior renovation

**RIG and vaccination**



# Cases

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- Healthy 30 yo home health physical therapist was bitten by a patient's dog
  - Numerous unkempt dogs on the property and vaccination status unknown
  - Owner would not cooperate with quarantine

**RIG and Vaccination, unless animal can be observed.**

# Cases

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- 33 year old male awakened to find a flying bat
  - Flew into sleeping child's room
  - No bites or direct contact observed

**Bat not available; consider PEP for child.**

# Cases

---

- 43 year old male punctured his scalp on a nail
  - Working in attic where bat guano present
  - No live bats seen
- 58 year old woman hit by a bat
  - Riding bike at dusk
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# Case Discussion

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- Puncture wound from nail
  - No exposure to live bats
  - Any virus present would be inactive
  - No prophylaxis needed
- Hit by bat while riding bike
  - Direct contact with bat
  - Assume bat rabid and initiate prophylaxis

# Costs Associated with Rabies

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- Estimated public health expenditures (diagnostics, prevention, & control): \$245 to \$510 million annually
- Added cost from associated healthcare costs, animal control measures, and lost work
- Rate of PEP use in U.S. is unknown, but estimated at 20,000 – 25,000 episodes per year
- Rabies immune globulin + 4-dose vaccine series: \$3,000+



