

Rabies: To PEP, or not to PEP?

That is the question.



Roadmap

- Epidemiology & pathobiology of rabies
- Pre-exposure series
- Exposure risk assessment
- Post-exposure prophylaxis
- Reporting Requirements
- Resources

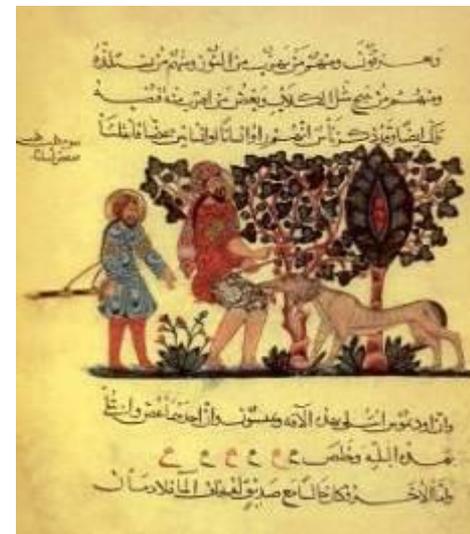


EPIDEMIOLOGY



Rabies – The Disease

- Rabies has been around for centuries; described as early as 2300 B.C.
- Transmission is direct, primarily via inoculation by bite, with infectious virus present in saliva.
- The reservoir for rabies is the animal pool that circulates rabies virus (diverse species of mammals each with a specific strain).
- Rabies is >99% fatal once symptoms occur.



Still Considerable Concern About Rabies In...

The U.S.

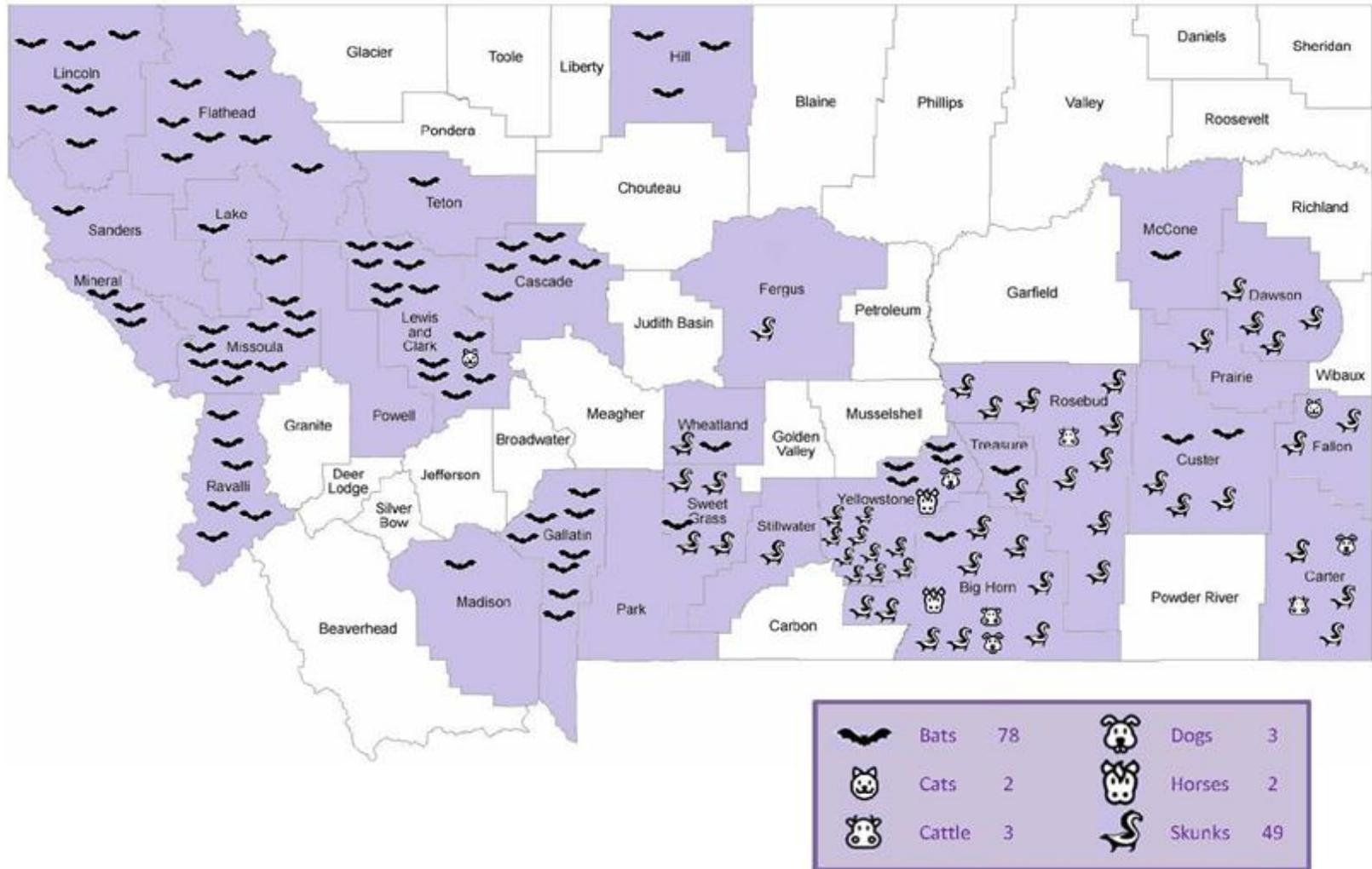
- CDC estimates that more than 1 million people per year worldwide require medical attention for animal bites (far fewer than occur)
- Over 7,000 cases of rabies in animals are reported to the CDC annually
- Although the number of post exposure treatments given in the United States each year is unknown, it is estimated to be about 40,000

And Montana

- ~1500 persons presented to ER due to bites or injuries received by animals
- On average 20 cases of rabies in animals are reported in Montana annually (>90% are bats, skunks)
- Number of post exposure treatments given in the Montana each year is newly reportable, and is estimated to be about >100

*Hospital discharge data is provided through the Montana Hospital Discharge Data System courtesy of the Montana Hospital Association. Data from 2010-2013. Codes 906, excluding arthropods.

Animal Rabies Distribution 2009-2014



PATHOBIOLOGY

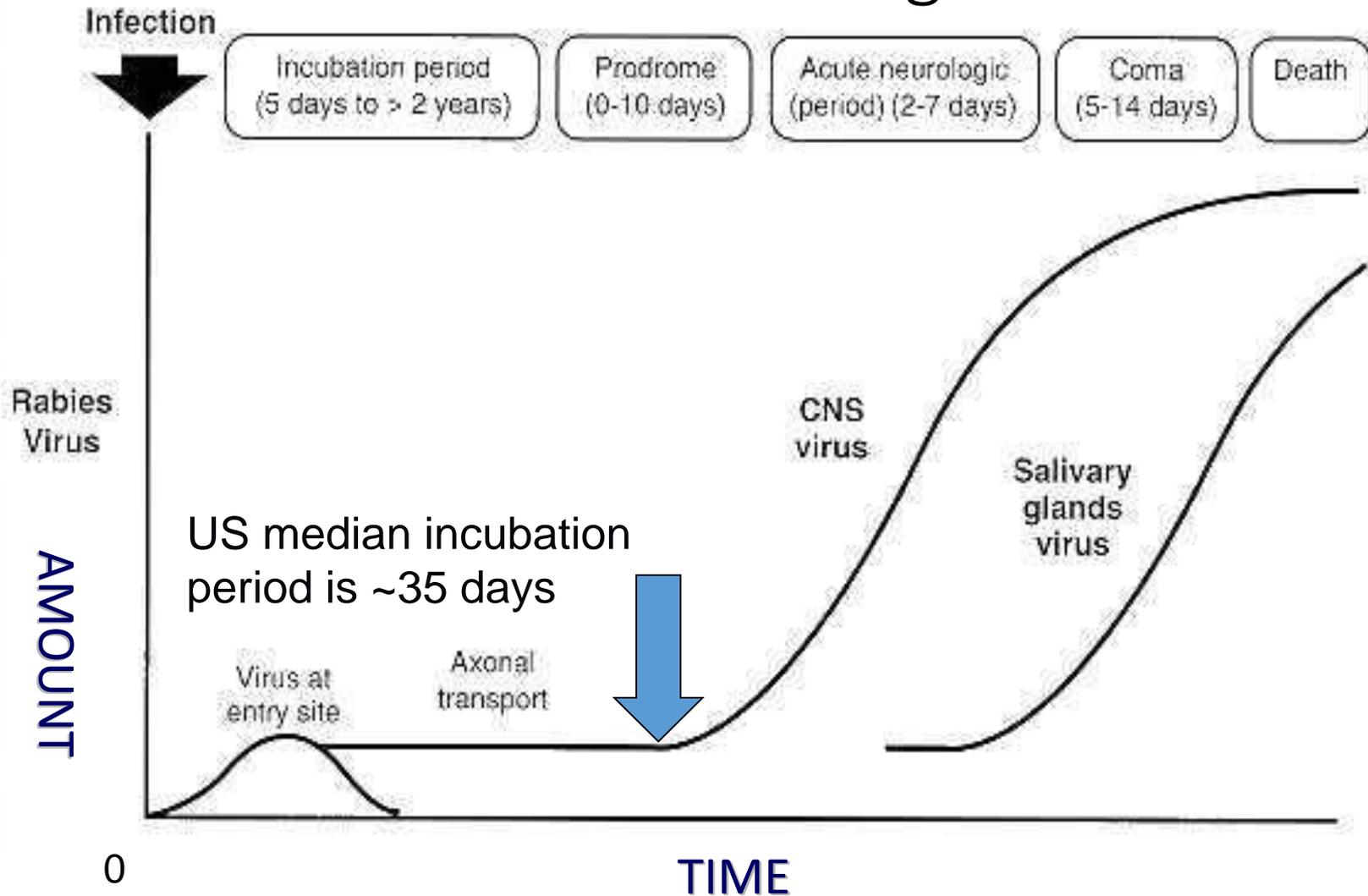


Transmission/Pathogenesis

- Most commonly spread by **bite contact** between the rabid animal and the recipient
- Viral particles travel out from brain (centrifugal spread) → nerve cells → salivary glands → excretion = infectious
- Virus in salivary glands means end stage of the disease: death usually occurs within several days
- Incubation period: Usually 4 weeks; can range from 10 days to a year or more (??)



Scheme of Rabies Virus Pathogenesis



Neuronal retrograde viral transport is estimated at ~50 - 100 mm/day (Tsiang et al., 1991)

Signs and Symptoms



- Animals (domestic)

- Fearfulness
- Aggression
- Excessive drooling
- Difficulty swallowing
- Staggering
- Seizures
- Depression
- Self-mutilation
- Light sensitivity



- Animals (wildlife)

- Any of above
- Unusual behavior
 - Nocturnal animal active during day
 - Lose fear of humans

- Humans

- Early symptoms are non-specific
 - Fever
 - Headache
 - General malaise
- Progresses to encephalitis or myelitis
 - Autonomic instability
 - Dysphagia
 - Hydrophobia
 - Paresis or paresthesia
- Progressive worsening neurologic signs
- Negative test for other etiologies of encephalitis

Rabies Human Deaths



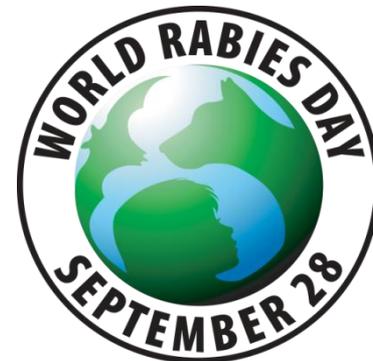
- Annual human deaths **worldwide** are approximately 55,000; every 15 minutes a patient dies of rabies.
- 40-70% rabies victims are children under 15 years of age.
- Modern cell culture vaccines and animal control measures in developed countries have reduced the incidence of rabies deaths.
- In the **United States**, an average of 3 deaths per year since 1990.
- In **Montana**, 2 cases/deaths in 1996 & 97, both bat variants, no apparent “wounds”, one reported bat in house 30 days prior, other exposure unknown but had frequent animal contact as “trapper”

PREVENTION & CONTROL



Humans Rabies Prevention: General Population

- Pre-exposure vaccination of domestic animals
- Avoid contact with wildlife reservoirs
- Prompt recognition and reporting of potential exposures to public health and medical community
- Public education
 - Avoid animal bites
- Public policy
 - Animal control



Pre-exposure Vaccination (Humans)

- Recommended for veterinarians, veterinary technicians, animal control officers, animal shelter workers, rabies lab personnel and persons working with wildlife
- Provides protection from unapparent exposures and when treatment is delayed
- Also recommended for persons spending 1 month or more in countries with endemic dog rabies and in which PEP would likely be significantly delayed to geographic distances/ lack of medical infrastructure



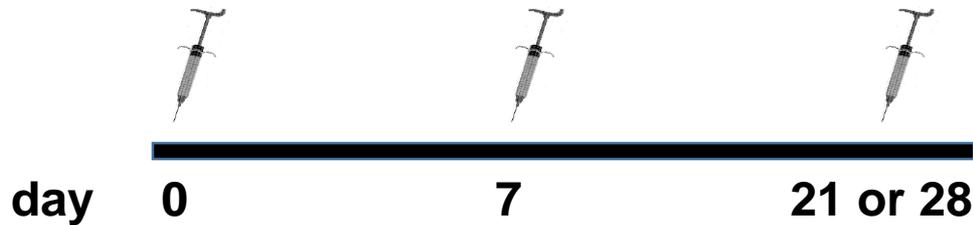
Pre-exposure Vaccination Protocol

- Three doses of vaccine administered on days 0, 7 and 21 or 28
- Dosage: 1.0 ml administered IM in the upper deltoid
- Recommendations encourage titer checks for those at high and medium risks, 6 mos. and 2 years respectively, no titer check for lower risk workers with pre-exposure series. If absent, administer booster

CDC Recommended Pre-exposure

Pre-exposure

3-dose series intramuscular or intradermal regimen



Rabies is 100% Preventable

- Avoid animal bites
- Recognize signs of rabies in animals
- Vaccinate animals and humans
- Support appropriate testing
- Seek immediate wound care and treatment
- Role of medical professional
 - Coordinate with local or state public health
 - Encourage patients to seek treatment for even minor bites



EXPOSURE RISK ASSESSMENT



Prevention steps after an animal bite or other exposure:

- Wash the wound/site well with soap and water.
- Have the animal tested for rabies or observed.
- See a Doctor, even if the bite is very small. For non-bite consult with Doctor or contact public health.
- Assess need for tetanus booster.
- **Contact, or ensure your provider contacts, your local health department for recommendations.**



Administrative Rules of Montana

– Department of Public Health



- **Report “*exposure to a human by a species susceptible to rabies infection*” to local health department (37.114.203)**
- Local health officer must investigate and inform individual whether or not treatment is recommended
 - Must report treatment options to DPHHS
 - Must also arrange for quarantine or testing of animal
- Additional requirements through Department of Livestock (ARM 32.3.1201 through 32.3.1207) describe management of animals and complement DPHHS rules.

Should Anti-Rabies Prophylaxis be Administered?

CONSIDERATIONS:

- High or lower risk animal?
- Was there an exposure?
- Likelihood & timing for animal capture for confinement or testing.
- Epidemiology of rabies in your area.



Risk categories for animals in Montana

HIGH RISK

- Bat
- Skunk
- Fox
- Cats -feral
- Groundhog



MEDIUM RISK

- Dogs
- Cats – vaccinated or not roaming
- Livestock – horses, cattle, pigs
- Other non-rodent wild animals species (opossum, bear, deer, coyote)

LOW to NO RISK

- Squirrels, chipmunks
- Rats
- Mice, voles
- Indoor small caged pet rodents
- Lagomorphs



Was There An Exposure?

- A bite (penetration of the skin by teeth) from a known or suspect rabid animal
- Scratches, abrasions, open wounds (bleeding within 24 hrs), or mucous membranes (eyes) contaminated with saliva or other potentially infectious material from a known or suspect rabid animal
- Other contact - such as petting an animal or contact with urine, feces or skunk spray - does NOT constitute an exposure

Virus inactivated by

Desiccation, Ultraviolet irradiation, Other environmental factors

Does not persist in environment



Can The Biting Animal Be Confined & Observed?

- Healthy dogs, cats, ferrets may be confined and observed for 10 days after exposure
 - Animal is monitored for signs of rabies, any illness must be evaluated by Vet which may lead to testing
 - If healthy after observation period- animal was not capable of transmitting rabies at time of exposure
- Raccoons, skunks, fox, groundhogs and other wildlife cannot be observed- clinical signs of rabies in wild animals can not be interpreted reliably.
 - Testing of the animal - or prophylaxis of bite victim - is always recommended after valid exposure unless a negative test is available
 - Small rodent exposures- almost never require PEP



Considerations for Rabies PEP

- Medical urgency, not emergency
- Consult with LHJ
- Animal species and risk of infection
- Exposure evaluation
- Likelihood and timing for animal capture for confinement or testing
- Epidemiology of rabies in your area
 - Requires advanced knowledge of rabies reservoirs
 - International travel considerations



POST-EXPOSURE PROPHYLAXIS



Recommended Post Exposure Prophylaxis

1. **Immediate flushing** and washing of the wound with soap and water, or other detergent
2. **Consult with public health**
3. **Passive immunization:** Administration of Rabies immune globulin for contacts/exposures (HRIG) – immediate protection
4. **Active immunization:** Administration of tissue culture vaccine according to the CDC regimen – patient's immune response



Rabies Postexposure (PEP)

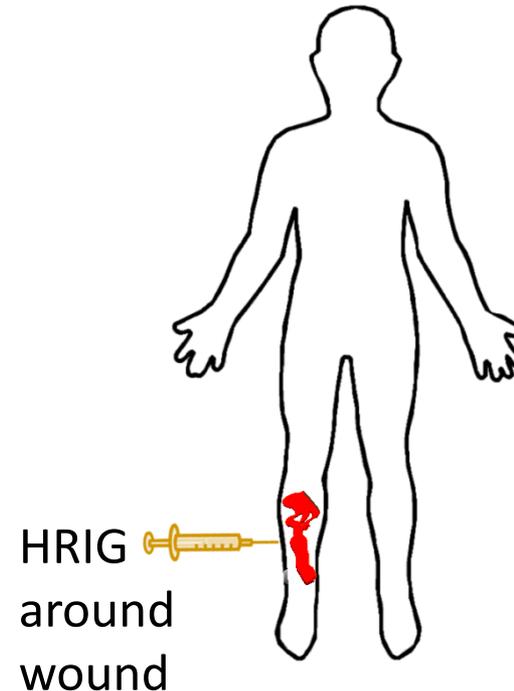
Two biologics are administered:

1. Human Rabies Immunoglobulin (HRIG) – confers immediate protection with antibodies vs. rabies
2. Rabies Vaccine - patient develops antibodies over a 2 to 4 week period



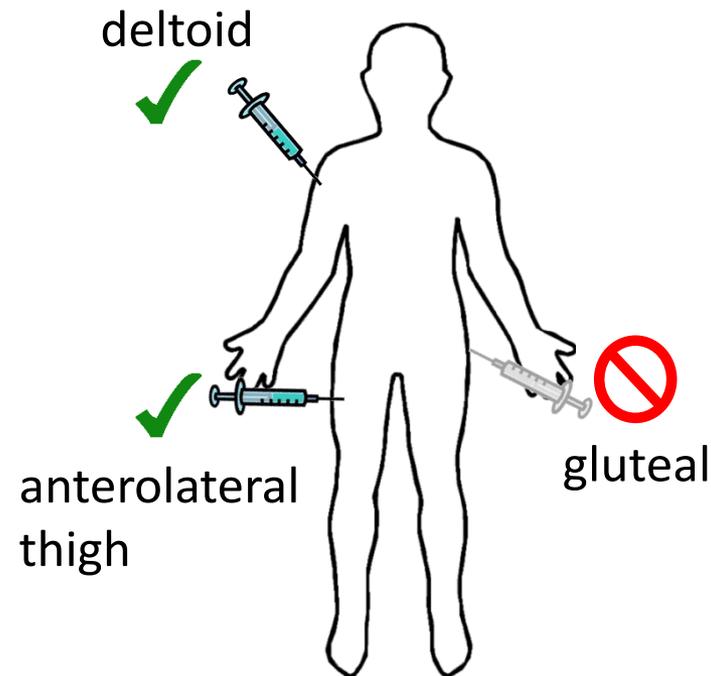
Where to administer Immunoglobulin?

- HRIG around or inside wound
- Remaining volume IM at site distant from vaccine
- 20 IU/kg body weight
- Never use same syringe as vaccine
- Do not administer more than necessary
- Do not administer after day 7 or dose 3 of vaccine



Where to administer rabies vaccine?

- Deltoid only acceptable site for adults and older children
- Younger children anterolateral thigh okay
- Opposite of HRIG site
- Never at same site of HRIG
- Never in gluteal area

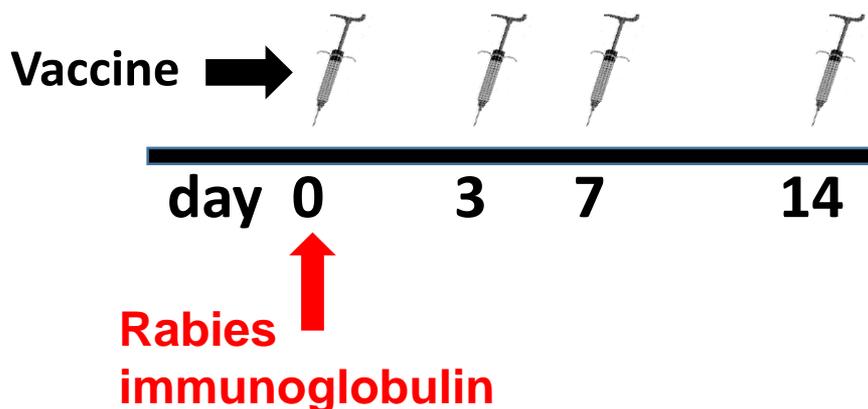


CDC Recommended PEP Schedule*

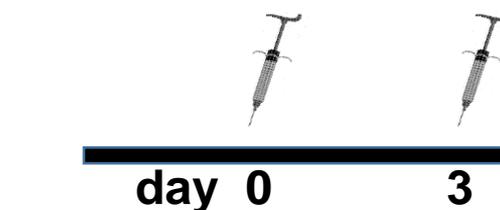
Standard intramuscular regimen.

One dose into deltoid on each of days:

Previously unvaccinated individuals



Previously vaccinated individuals



No Rabies immunoglobulin needed

*reduced dose regimen recommended in 2010

Deviations from the Schedule

- If deviation occurs, maintain original interval.
- Deviations of few days forgivable, longer needs assessment
- Example:
 - If a patient misses the dose scheduled for day 7 and presents for vaccination on day 10, the day 7 dose should be administered that day and the **schedule resumed, maintaining the same interval between doses**. In this scenario, the remaining dose would be administered on days 17.
 - When substantial deviations from the schedule occur, immune status should be assessed by performing serologic testing 7–14 days after administration of the final dose in the series.

Average Charges of PEP per person*



| Amount charged for HRIG only | Amount charged for rabies vaccine | Amount charged for complete PEP |
|---|-----------------------------------|---------------------------------|
| \$3,151 | \$485 | \$5,146 |
| 89% administered in hospital (→ +\$353 in ER visit fee) | (as high as \$1,500 per dose) | (as high as \$24,600) |

MT claims >\$100,000 annually

- paid \$30,000/year

*Data from Medicaid rabies 1/1/2010 to 2015 with a diagnosis code (071, 979.1, E949.1, V01.5, V04.5) or procedure code (90375, 90376, 90675, 90676, 90726, J2750) or ICD-9 surgical procedure code (09944)

Cost comparison

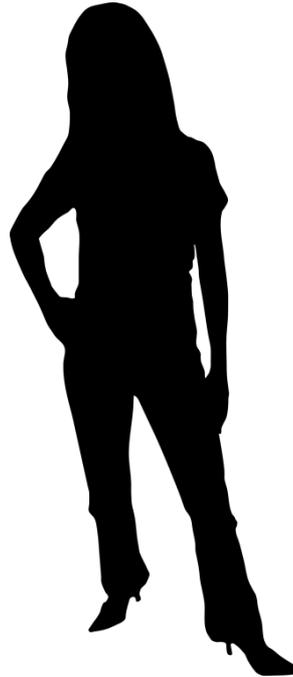
HRIG +
vaccine (x4)
(wholesale only)

\$1,800



40lbs child

\$3,400



150lbs female

\$4,400



210lbs male

HRIG + vaccine (x4) + wound cleaning + tetanus + admin = ???

Where to order?

1. **VaccineShoppe (www.vaccineshoppe.com)**
 - Sanofi Pasteur
2. Hospital pharmacy
3. Availability
4. Plan in place?
5. Standing order?

Uninsured and Underinsured

Patient assistance programs that provide medications to uninsured or underinsured patients are available for rabies vaccine and Immune globulin.

- Sanofi Pasteur's Patient Assistance Program (providing Imogam[®] Rabies-HT and Imovax[®] Rabies as well as other vaccines) is now administered through the Franklin Group. (1-800-VACCINE) or (1-866-801-5655).
- Novartis' Patient Assistance Program for RabAvert[®] is managed through RX for Hope (1-800-589-0837).



Key Rabies Information Resources

- Compendium of Animal Rabies Prevention and Control
- Human Rabies Prevention – U.S.
- Montana Code Annotated
- Administrative Rules of Montana
- Rabies Law Enforcement Guidelines
- Local public health practitioners
- Montana Department of Public Health and Human Services
 - 24/7/365 public health consultation 406.444.0273
- Montana Department of Livestock
 - Animal rabies consultation 406.444.5214

<http://dphhs.mt.gov/publichealth/cdepi/diseases/rabies.aspx>

Questions?

