RABIES SURVEILLANCE AND PREVENTION

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RABIES 101

- An acute, progressive viral encephalomyelitis
- The highest case fatality rate of any convectional etiological agent
- Leading viral zoonosis
- Distributed on all continents but Antarctica
- One of the oldest described infectious diseases, known for more than 4 thousand years

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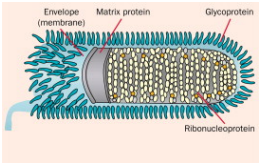
RABIES VIRUS

- ***Lyssavirus*** **of the** ***Rhabdoviridae*** **family**
- Bullet-shaped, RNA virus
- Infects only mammals
- Various strains of rabies virus exist



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RABIES PATHOGENESIS

- **Transmission occurs primarily through a bite**

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RABIES CLINICAL STAGES

- **Incubation period**
- **Prodromal stage**
  - Nonspecific signs
- **Acute neurologic phase**
- **Coma**
- **Death**
  - 3 documented cases of recovery from rabies in the US in patients not previously vaccinated for rabies

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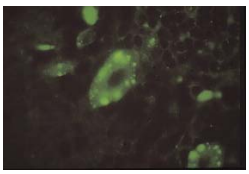
RABIES DIAGNOSIS

- **History of animal exposure and typical neurologic clinical signs**
- **Laboratory diagnosis**
  - Gold standard: postmortem demonstration of viral antigens in CNS by DFA
  - In humans, antemortem detection virus or viral antibodies, antigens or RNA in serum, cerebrospinal fluid, saliva, or skin/hair follicles obtained via nuchal biopsy can confirm a clinical diagnosis



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GLOBAL BURDEN OF RABIES

- **Over 55,000 deaths estimated each year**
- **Most occur in developing countries**
  - 95% in Africa and Asia
  - Children between the ages of 5-14 years
- **Tens of millions of human exposures per year**
- **Outside of the US, the domestic dog is the single most important animal reservoir**
- **Wildlife are important reservoirs, especially in developed countries, such as those in Europe and North America**

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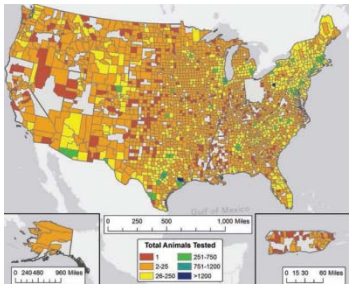
RABIES DISTRIBUTION IN THE UNITED STATES

- **Rabies diagnostic testing by county in 2013**



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TERRESTRIAL RABIES VIRUS VARIANTS IN US

- **Regional distribution of terrestrial rabies virus variants**

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BATS AND RABIES

- **The most common rabies virus variants responsible for human rabies in the United States are bat rabies**
- **Any potential exposure to a bat requires a thorough evaluation**
- **Post exposure prophylaxis should be considered when:**
  - Direct contact between human and bat occurred
  - Same room as bat who might be unware that a bite or direct contact occurred

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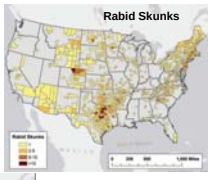
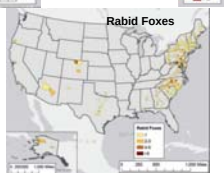
RABIES IN WILD ANIMALS, US, 2013





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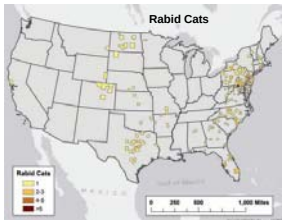
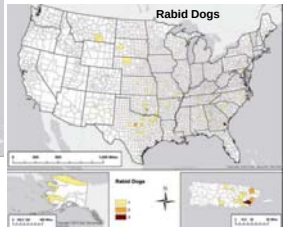
RABIES IN DOMESTIC ANIMALS, US, 2013





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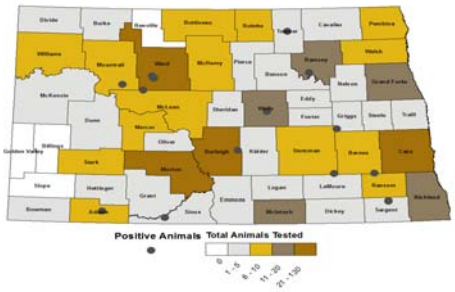
RABIES IN NORTH DAKOTA, 2014



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EVALUATING NEED FOR POSTEXPOSURE PROPHYLAXIS

- **Type of animal**
  - Domestic or wild?
  - Is the animal available for observation or testing?
- **Type of contact**
  - Bite?
  - Open skin or mucous membrane exposure to animal saliva or neural tissue?
- **Circumstances of the incident**
  - Provoked or unprovoked?
- **Epidemiology of animal rabies in the area**
- **Animal immunization history**

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REVIEW: WHEN SHOULD POSTEXPOSURE PROPHYLAXIS BE ADMINISTERED

Animal type	Evaluation	Prophylaxis
Dogs, cats, and ferrets	Healthy; available for observation	No[a]
	Rabid or suspected rabid	Yes
	Unknown	Consult public health
Bats, most carnivorous wild mammals	Regard as rabid	Yes
Livestock, large rodents (eg, groundhogs), small rodents, lagomorphs (eg, rabbits, hares), other mammals	Consider individually	Consult public health Bites from small rodents, rabbits, and hares almost never require PEP

[a] Unless animal develops clinical signs of rabies during observation period.

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WOUND CARE FOR RABIES EXPOSURE

- Wounds are at high risk for infection
- Thoroughly cleans the wound with soap and water
- Irrigate with water or a dilute water povidone-iodine solution

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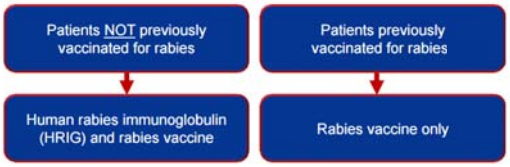
ACIP RECOMMENDATIONS FOR RABIES POSTEXPOSURE PROPHYLAXIS

- Two categories for treatment with postexposure prophylaxis



- Even in those previously vaccinated, it is important that patients receive a vaccine booster to ensure active immunity

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HUMAN RABIES IMMUNE GLOBULIN (HRIG)

- HRIG is recommended in patients who have not been previously vaccinated for rabies
- HRIG is always administered in combination with the first rabies vaccine in previously unvaccinated patients
- HRIG provides immediate passive immunity until the patient can respond to the vaccine by actively producing antibodies
- If HRIG is not administered when vaccination is begun, it can be administered up to 7 days after the first dose of vaccine
- Beyond the seventh day, HRIG is not recommended

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DOSING OF HRIG IS BASED ON ACTUAL BODY WEIGHT

- **Dosing: 20 IU/kg (0.133 mL/kg) of body weight**

Sample patient	Weight	Dosing recommendation
Adult	80 kg (176.4 lbs)	80 kg x 20 IU/kg = 1600 IU Recommend one 10-mL vial and one 2-mL vial
Adult	75 kg (165.4 lbs)	75 kg x 20 IU/kg = 1500 IU Recommend one 10-mL vial
Adult/Adolescent	60 kg (132 lbs)	60 kg x 20 IU/kg = 1200 IU Recommend four 2-mL vials
Child	40 kg (88 lbs)	40 kg x 20 IU/kg = 800 IU Recommend three 2-mL vials
Child	30 kg (66 lbs)	30 kg x 20 IU/kg = 600 IU Recommend two 2-mL vials

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ADMINISTRATION OF HRIG

- **Administer HRIG directly into and around the wound**
- **Inject as much volume into the wound area as possible**
- **For small areas (wounds on fingers, toes, ears or face) inject as much as possible into the wound then administer the remainder intramuscularly at a site distant from the vaccine administration site**

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WHEN TO ADMINISTER HRIG AND RABIES VACCINE

In patients who have NOT been previously vaccinated	In patients who HAVE been previously vaccinated
Administer HRIG on the same day as the first dose of vaccine (day 0) – Can be administered up to 7 days after the first dose of vaccine	No administration of HRIG
Administer rabies vaccine on days 0, 3, 7, and 14	Administer rabies vaccine on days 0 and 3
Immunocompromised patients receive a fifth dose of vaccine on day 28	

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RABIES PRE-EXPOSURE PROPHYLAXIS

- **Simplified management of rabies exposure**
- **Partial immunity if post exposure prophylaxis is delayed**
- **Provide protection to persons for unrecognized exposure**
- **3 1.0 mL injections on days 0, 7, and 21 or 28**
- **Pre-exposure booster doses of vaccine**

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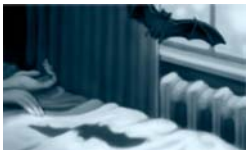
CASE 1: A BAT IN THE BEDROOM

- **Chief complaint: possible bat bite or scratch**
  - A 4 yr old girl presents to ER after live bat was found in her bedroom. Bat flew away. Child denied having contact with the bat
- **Physical findings: No apparent evidence of a bat inflicted injury**
- **Patient's rabies vaccination history: unvaccinated**



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CASE 1: A BAT IN THE BEDROOM

- **3 important factors to consider**
  - The epidemiology of bat rabies
  - The likelihood to detecting a bat bite
  - The patient's ability to accurately recount an exposure

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CASE 1: A BAT IN THE BEDROOM

- **Epidemiology of bat rabies**
  - Rabid bats are distributed throughout the continental US
  - As rabies reservoirs, bats are infected with host-adapted variants of the rabies virus
  - Most human cases acquired in the US originate from bats
- **Likelihood of detecting a bite**
  - Bats generally have fine, sharp teeth. Skin trauma can be minimal
- **Patient's reliability as a historian**
  - Patient was sleeping unattended and is a young child. Possible not have registered a bite
  - Other situations in which someone may not recount an accurate bite history: being heavily intoxicated, sleeping in the same room with a bat, people with developmental disabilities and other impairments

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CASE 1: A BAT IN THE BEDROOM

- **Determination**
  - Bat is unavailable for testing and should be regarded as rabies suspect
  - Patient may have been bitten by this animal and therefore possibly exposed to the rabies virus
- **PEP decision**
  - Initiate rabies PEP

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CASE 2: DOG BITES MAN

- **Chief complaint: Dog bite**
  - A post office worker presents with dog bites to the right arm. Patient claims owners were not forthcoming about the dog's rabies vaccination status. The police have been notified
- **Physical findings: superficial lacerations and puncture wounds on the right forearm**
- **Patients rabies vaccination history: unvaccinated**

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CASE 2: DOG BITES MAN

- **3 important factors to consider**
  - The epidemiology of canine rabies
  - The applicability and feasibility of animal observation
  - The medical urgency of exposure

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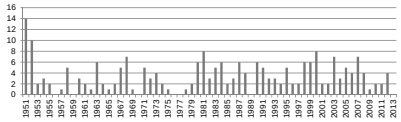
CASE 2: DOG BITES MAN

- **Epidemiology of canine rabies**
  - In the US, the occurrence of rabies among dogs is rare and sporadic, largely as a result of widespread canine vaccination
  - Since 2004, dog-to-dog rabies transmission has officially been considered eliminated in the US

Rabid Dogs Reported in ND, 1951-2013



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CASE 2: DOG BITES MAN

- **Applicability / feasibility of animal observation**
  - Rabies virus exposure from dogs, cats and ferrets can be ruled out in two ways:
    - Testing of the animal's brain tissue for rabies virus antigens
    - Observations
  - A healthy dog involved in a bite incident should be quarantined and observed for 10 days. If the dog remains alive and well after this period, the bitten person should not be considered exposed to the rabies virus
- **Medical urgency**
  - Potential rabies exposures are medical urgencies, not emergencies
    - Exceptions: bite wounds to head, face or neck or severe bite wounds

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CASE 2: DOG BITES MAN

- **Determination**
  - The epidemiology of canine rabies in ND and the US suggests a low likelihood that the dog that attached the post office worker is rabid. Patient did not sustain particularly severe wounds or wounds to the head, neck or face
- **PEP decision**
  - Administer appropriate wound care
  - Rabies PEP can be delayed until the dog has been observed for 10 days or tested
  - If rabies exposure is ruled out using either strategy, do not administer PEP

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CASE 3: SKUNK FIGHT

- **Chief complaint: Skunk bite**
- **A 60 yr old man presents to the ER with a bite wound on his left leg inflicted by a skunk that morning. The patient tried to break up a fight between the skunk and the family dog. When he kicked the skunk to knock it away, its jaws briefly locked down on his leg. Then the skunk ran away**
- **Physical findings: laceration to the calf**
- **Patient's rabies vaccination history: unvaccinated**

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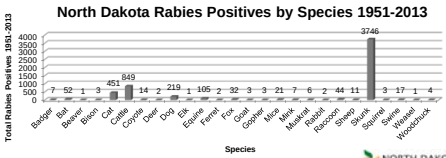
CASE 3: SKUNK FIGHT

- **Epidemiology of skunk rabies**
  - Out of all animals, skunk most frequently test positive for rabies in North Dakota
  - In the absence of being able to test the skunk for rabies, all skunks
  - should be suspected of having rabies



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CASE 3: SKUNK FIGHT

- **Determination**
  - The epidemiology of skunk rabies in ND suggests a relatively high likelihood that the skunk is rabid
  - The skunk is unavailable for testing and should be regarded as suspect
- **PEP decision: initiate rabies PEP**

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CASE 3: SKUNK FIGHT

- **There are 3 components for rabies PEP**
  - Wound cleansing
  - Rabies immune globulin (RIG)
  - Rabies vaccine

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CASE 3: SKUNK FIGHT

- **RIG**
  - Comprises IgG derived from plasma of hyperimmunized donors
  - Serves 2 purposes
    - Provides passive immunity during the lag period before active immunity
    - Neutralizes the rabies virus directly at the exposure site, before the virus has time to penetrate peripheral nerves and migrate to the central nervous system
  - Indicated in patients who have not previously received a full course of rabies PEP or pre-exposure immunization

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CASE 3: SKUNK FIGHT

- **Volume of RIG based on patient's weight**
  - 20 IU/kg or 0.13 mL/kg
- **Infiltrated in and around all bite wounds**
  - Introduces neutralizing antibodies directly into exposure site, where they can bind to rabies virus that may be present in the tissue
- **Remaining volume should be introduced intramuscularly**
- **The muscle used should neo be the same site where the vaccine is administered**

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CASE 3: SKUNK FIGHT

- **To get maximum benefit from RIG**
  - Infiltrate all wounds
  - Administer early (i.e., on day 0)
  - Use different syringes for RIG and vaccine
  - Delay wound closure (if indicated) until wounds have been infiltrated with RIG
- **DON'T give RIG to a patient who has been previously vaccinated**
- **DON'T give more than the recommended dose**
- **DON'T administer at the same site as the vaccine**
- **DON'T give later than 7 days after the series has been initiated**

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CASE 4: RABID CAT ATTACK

- **Chief complaint: possible rabies exposure**
  - 2 days ago a 22 yr old woman was bitten by a cat on the right hand. On the same day of the incident, she received primary wound care at the ER, a tetanus booster and antibiotics. Today, she returned to the ER after learning that the cat tested positive for rabies by NDDoH Division of Laboratory Services
- **Physical findings: deep puncture wounds in the right hand**
- **Patient's rabies vaccination history: unvaccinated**

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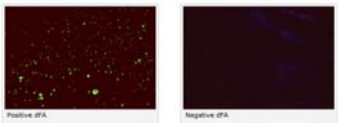
CASE 4: RABID CAT ATTACK

- **Direct fluorescent antibody (DFA) testing on animal brain tissue is performed to rule out human rabies exposure**
  - NDDoH Division of Laboratory Services
  - NDSU Veterinary Diagnostic Lab
- **Determination**
  - Rabies diagnosis in the cat suggests high probability that infectious saliva contaminated the bite wound
- **PEP decision: initiate rabies PEP**



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CASE 4: RABID CAT ATTACK

- **2 types of human rabies vaccine approved for use in US**
  - Purified chick embryo cells (PCECV)
  - Human diploid cells (HDCV)
- **Vaccination induces an active immune response against the rabies virus**
  - Previously unvaccinated
    - 1 mL vaccine administered intramuscularly on days 0, 3, 7 and 14. RIG also given on day 0
  - Previous recipient of PEP or pre-exposure vaccination
    - 1 mL vaccine administered intramuscularly on days 0 and 3. RIG should not be given
- **Should be injected in deltoid muscle. In children, outer thigh (vastus lateralis) is acceptable**
- **Administered at site most distant from where RIG was administered.**
- **Vaccine should not be infected in the gluteus**
  - Studies show lower antibody titers

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CASE 5: RABID COW SALIVA EXPOSURE

- **Chief complaint: possible rabies exposure**
- **3 days ago, a 36 yr old man's 4 yr old cow was euthanized by his veterinarian after displaying muscle twitching, coordination problems, foaming at the mouth and drooling and acting aggressively. The cow tested positive for rabies at the NDDoH Division of Laboratory Services. The Division of Disease Control followed up with the 36 yr old to determine human exposures. The individual had saliva exposure. Disease Control recommended the individual begin PEP**
- **Patient's rabies vaccination history: previously vaccinated when bitten by a dog at the age of 6**

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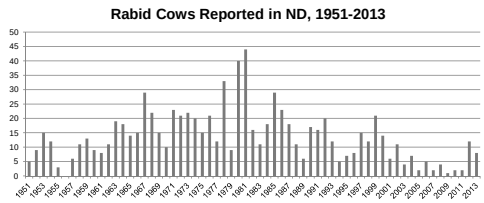
CASE 5: RABID COW SALIVA EXPOSURE

- Epidemiology of rabies in cattle



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CASE 5: RABID COW SALIVA EXPOSURE

- Vaccination for individual who has been previously vaccinated or received pre-exposure prophylaxis
- Receive 2 vaccine doses, 1.0 mL each in the deltoid
- Day 0 and 3
- RIG should not be administered

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RESOURCES

Disease Control – 800.472.2180 or 701.328.2378

CDC MMWR Human Rabies Prevention -- http://www.cdc.gov/mmwr/PDF/rr/rr5703.pdf

CDC MMWR Reduced 4-Dose Schedule -- http://www.cdc.gov/mmwr/pdf/rr/rr5902.pdf

CDC Rabies website -- http://www.cdc.gov/rabies/

NDDoH Rabies website -- http://www.ndhealth.gov/disease/Rabies/

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