# Rabies Surveillance and Prevention

## Recommendations for Providers

Alicia Lepp
Epidemiologist
Division of Disease Control
North Dakota Department of Health

Michelle Feist
Epidemiology and Surveillance Program Manager
Division of Disease Control
North Dakota Department of Health

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DEPARTMENT of HEALTH

# Rabies - Background

- Lyssavirus belonging to the Rhabdoviridae family
  - "bullet-shaped virus"
  - RNA virus
- Rabies is a virus that affects the central nervous system in mammals
  - Virus travels within the nerves
  - Within the brain, virus multiplies rapidly
    - Signs of disease begin to develop

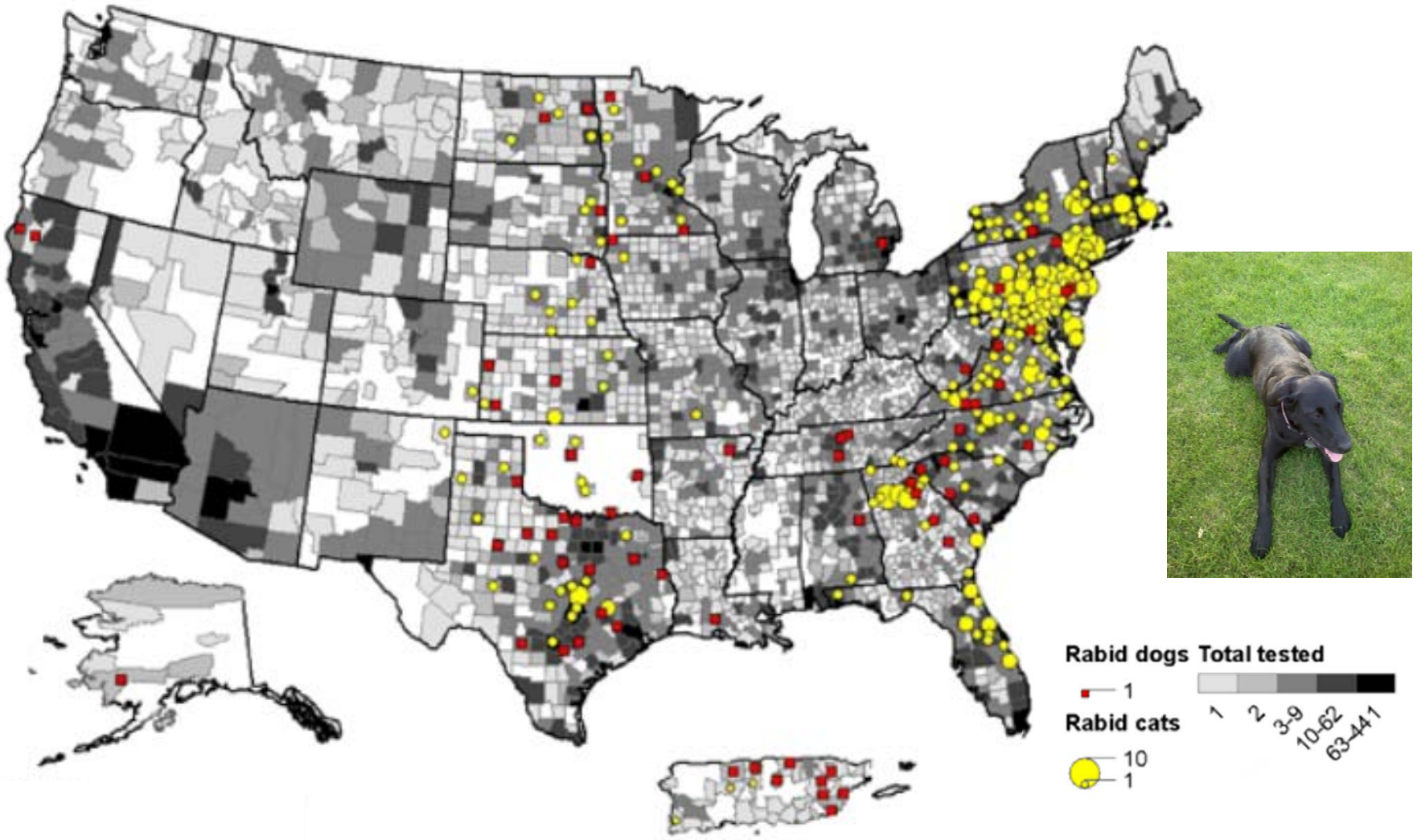
# Rabies - Background

- More than 90 percent of rabies cases reported each year in the United States occur in wildlife
  - 36.5% raccoons
  - 23.5% skunks
  - 23.2% bats
  - 7% foxes
  - 1.8% other species
- Raccoons and skunks are responsible for most reported animal cases in the United States
  - In ND – skunks
- Different variants (bat, skunk, raccoon, etc.)

# Terrestrial Rabies Reservoirs(2010)


http://www.cdc.gov/rabies/location/usa/surveillance/wild_animals.html

# Rabid Cats and Dogs Reported in the U.S. (2010)

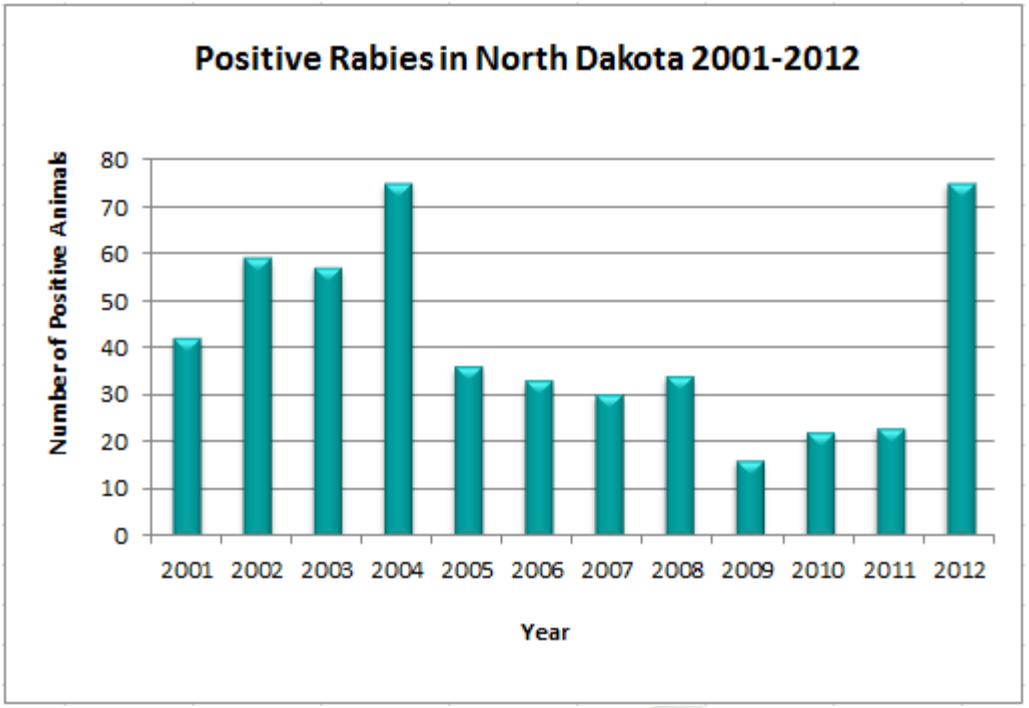





http://www.cdc.gov/rabies/resources/publications/2010-surveillance/cats-and-dogs.html

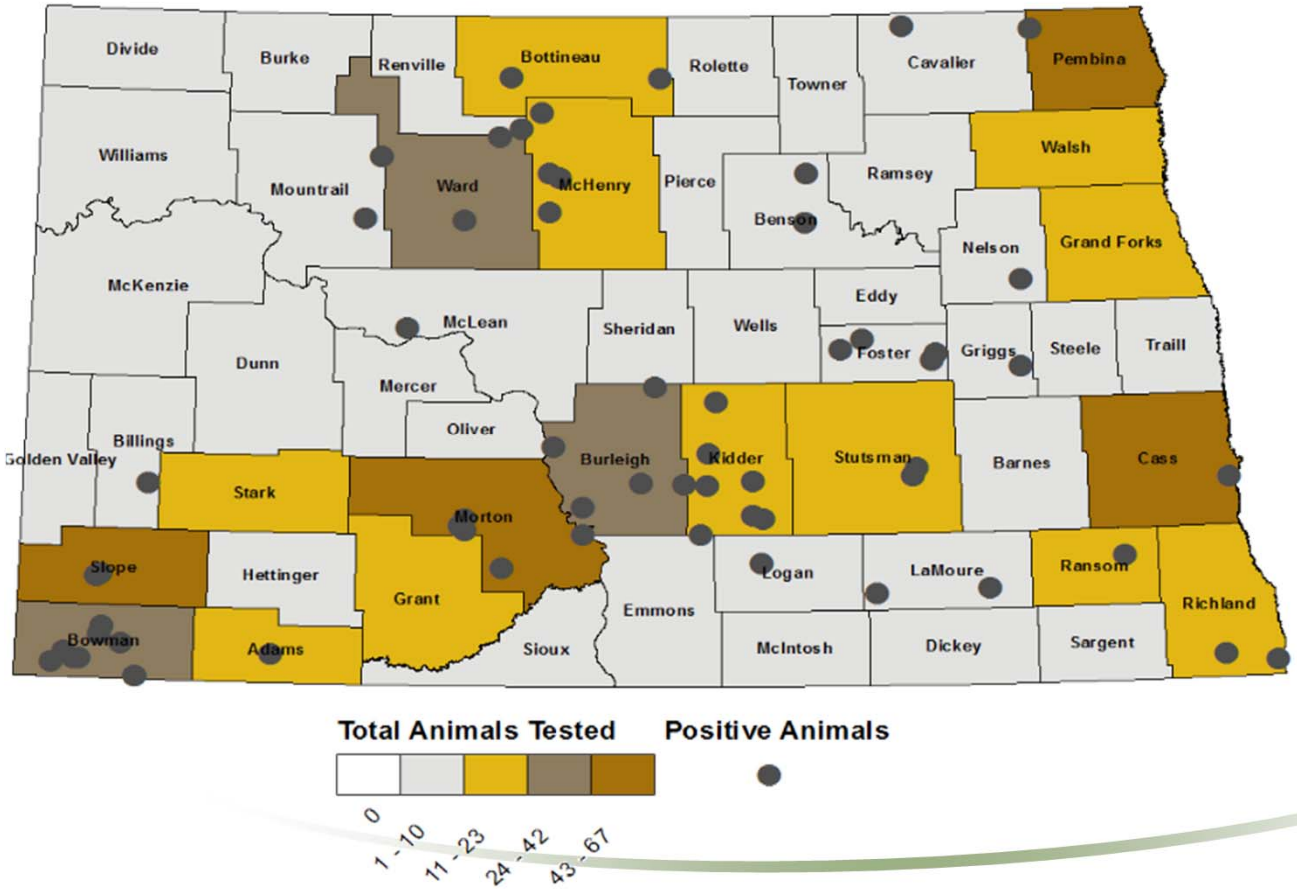
# Rabies in North Dakota

- ~ 350 to 450 animals tested per year
  - 729 animals tested in 2012
- ~ 30 positive rabies animals per year
  - 8% positive



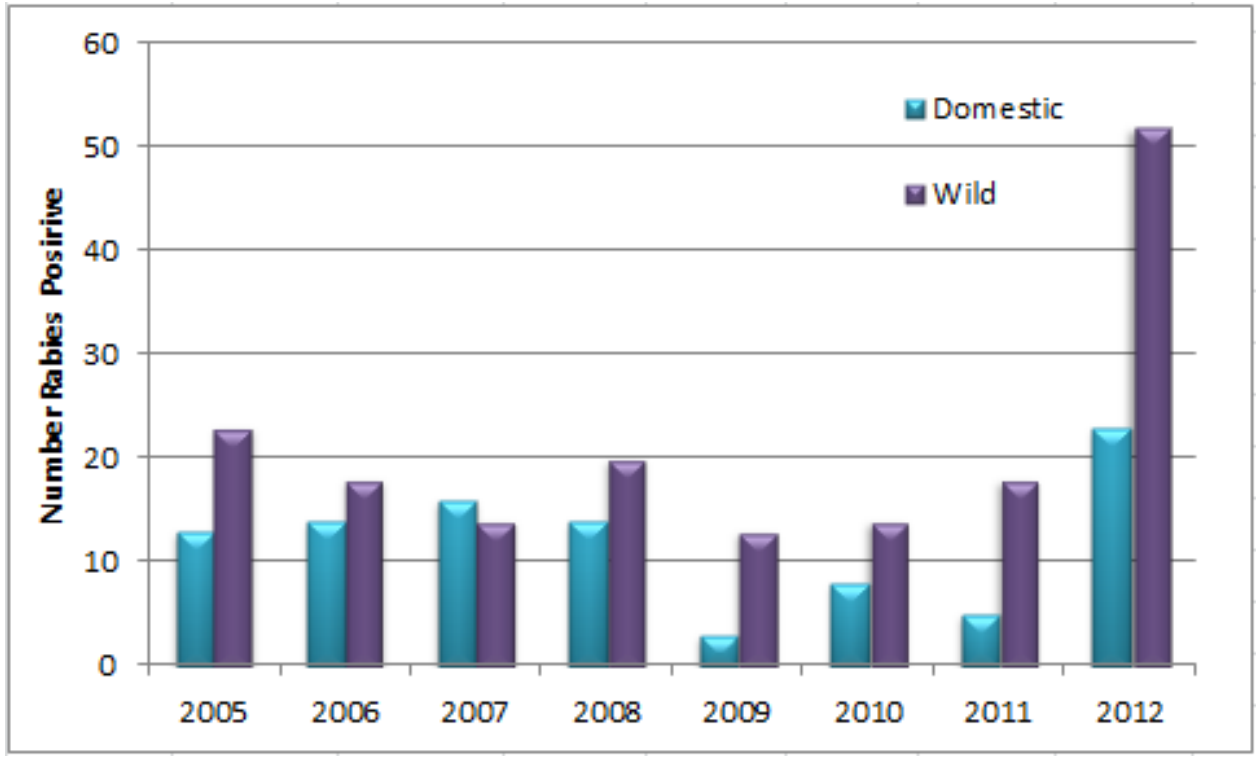
# Rabies in North Dakota

- Positive Animals Rabies Cases by County, North Dakota, 2012




| Species | Number Confirmed |
|---|---|
| Bat | 2 |
| Cat | 6 |
| Cow | 12 |
| Horse | 4 |
| Sheep | 1 |
| Skunk | 50 |
| Total | 75 |

# Positive Rabies in Domestic and Wild Animals



# Human Rabies Around the World

- Rabies is a global health issue
- Human cases are underreported
  - Most rabies cases occur in countries with inadequate diagnostic facilities and surveillance systems for rabies
- Exposure to rabid dogs is the cause of over 90% of human exposures and over 99% of human rabies deaths[1]
- Limited access to healthcare and resources

1- http://www.cdc.gov/rabies/location/world/index.html

# US soldier dies of rabies after dog bite in Afghanistan

*Published May 03, 2012 / NewsCore*

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WASHINGTON – A 24-year-old American soldier died of rabies after being bitten by a dog last year in Afghanistan, US health officials said Thursday following an investigation into the rare case.

The otherwise healthy soldier started experiencing symptoms of shoulder and neck pain and tingling sensations in his hands soon after arriving at Fort Drum, N.Y., in mid-August 2011.

His condition escalated to include nausea, vomiting, anxiety and trouble swallowing. By the time he was admitted to an emergency room, he was dehydrated and hydrophobic, meaning he developed an intense fear of drinking liquids because of the painful muscle spasms he experienced while swallowing.

**This Week in *MMWR***

Photo/CDC

This issue of *MMWR* includes a report on human rabies diagnosed in a U.S. soldier who reported being bitten by a dog in Afghanistan.

# Rabies in the U.S.

- Human cases – 1 to 3 each year
  - 49 human cases since 1995[1]
    - Variant Type
      - Bat(35), Dog(11), Fox(1), Raccoon(1), unknown (1)
    - Exposure Type
      - Bite (17), Transplant (4), unknown (28)
- Estimated 25,000 to 35,000 human exposures[1]
  - Most from domestic animal exposure
- Cases of human and animal rabies are mandatory reportable conditions to the NDDoH
  - Website - www.ndhealth.gov/disease/Rabies/

1- http://www.cdc.gov/rabies/location/usa/surveillance/human_rabies.html

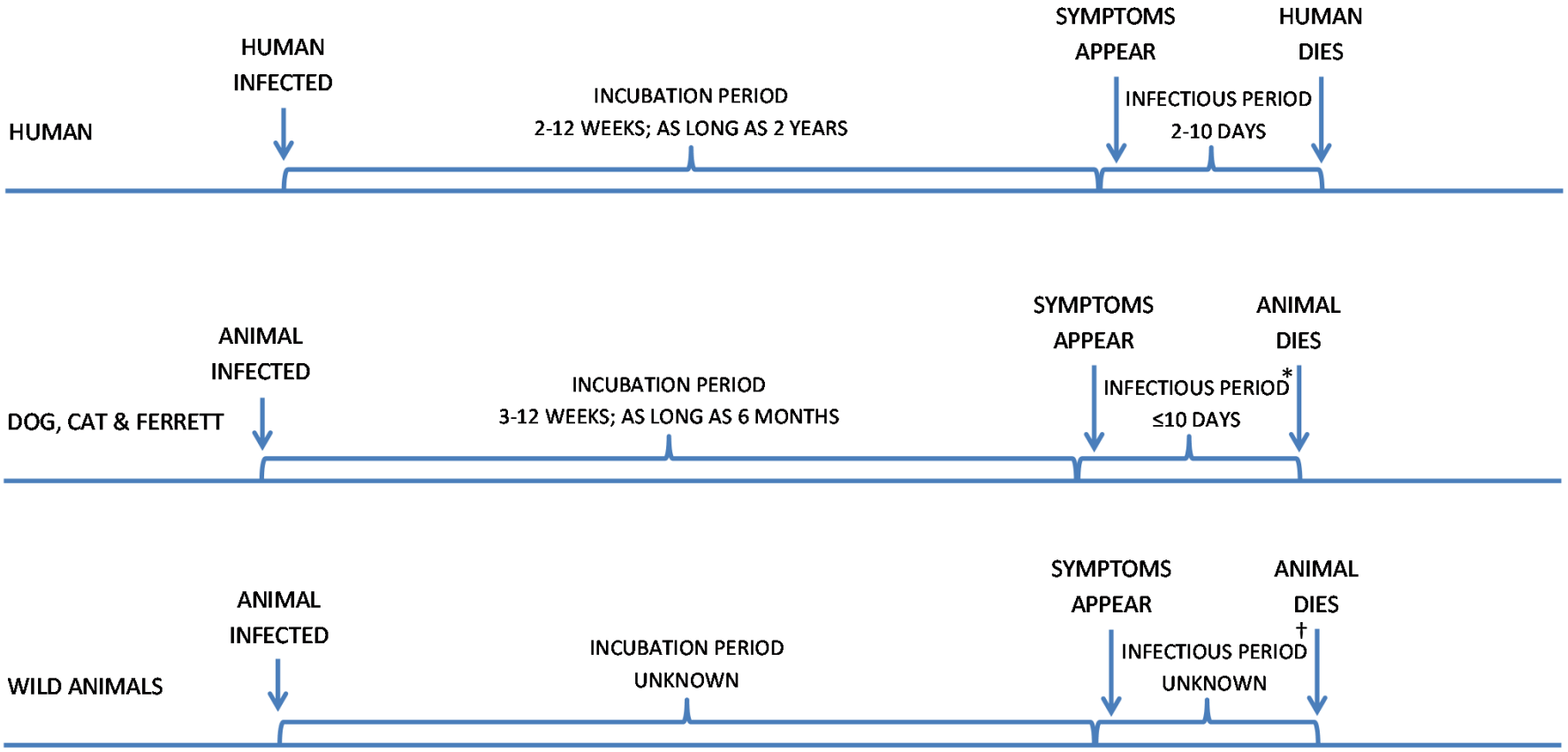
# Exposures and PEP, North Dakota, 2000

- PEP initiated by exposure species
  - Dog – 70
  - Cat – 27
  - Cow – 12
  - Horse – 8
  - Muskrat - 6
  - Skunk – 4
  - Skunk/dog – 3
  - Bat – 2
  - Raccoon, Mink, Unknown – 3

- Cost to fully vaccinate is variable, average of $2,500[1] to $5,000
  - Approx. $506,250 in vaccination costs
  - Est. $364,000 potentially avoided costs by vaccinating pets, quarantine, etc.

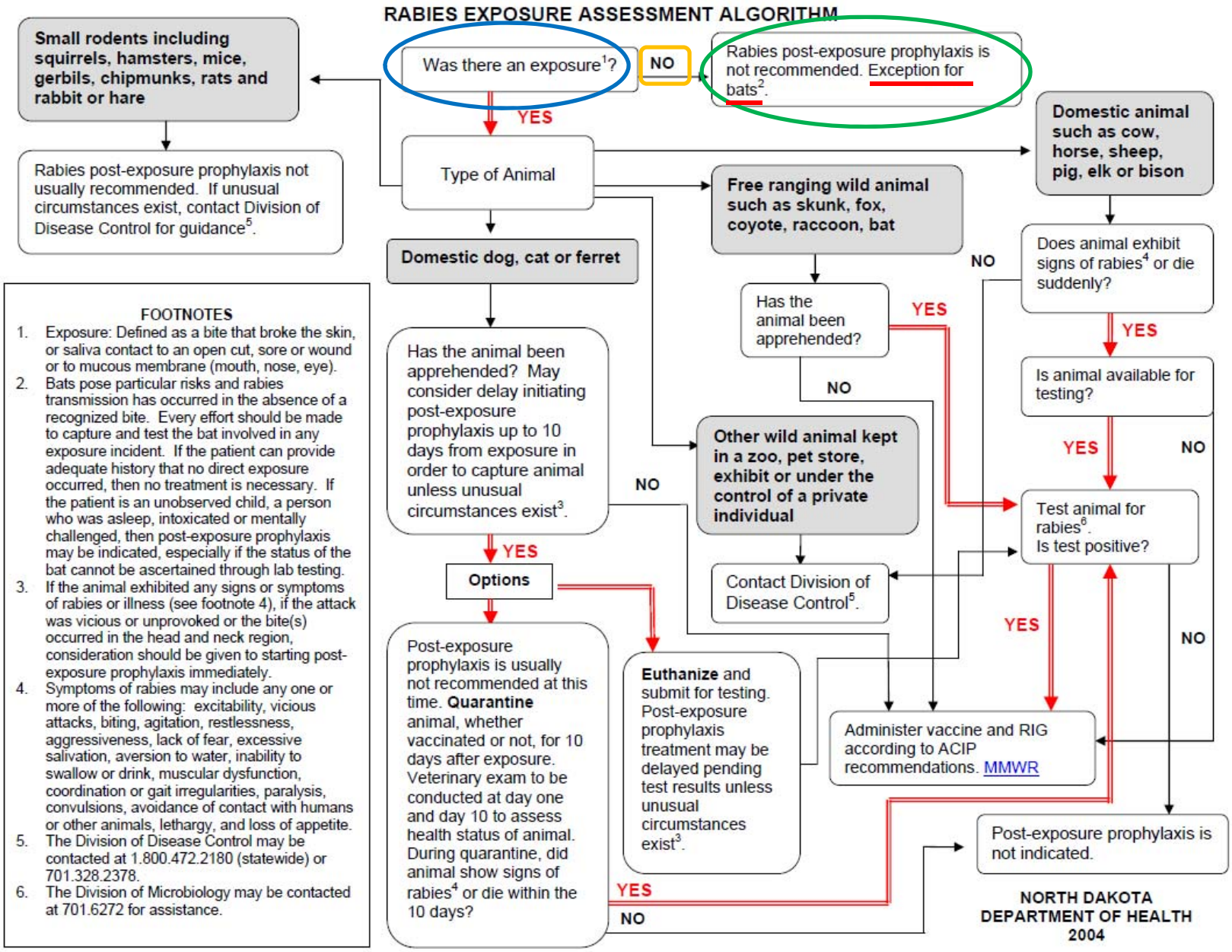
1-Vaidya, Sagar A, et al: **Estimating the risk of rabies transmission to humans in the U.S.: a delphi analysis.** *BMC Public Health* 2010, 10:278

# Rabies Exposure Timeline




* May be infectious for a number of  days before clinical signs appear. When investigating human exposures, it is recommended to consider the 10 days prior to onset of clinical signs (or date of death if no signs of illness) as part of the animal's infectious period.

† It is unknown as to how long a wild animal can shed rabies virus in its saliva before clinical signs of illness appear. Any exposure to a wild animal that cannot be tested, even if apparently healthy, should be treated as if the animal is rabid.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NO
Rabies post-exposure prophylaxis is not recommended. Exception for bats[2].
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Small rodents including squirrels, hamsters, mice, gerbils, chipmunks, rats and rabbit or hare
Rabies post-exposure prophylaxis not usually recommended. If unusual circumstances exist, contact Division of Disease Control for guidance[5].
Type of Animal
Domestic dog, cat or ferret
Free ranging wild animal such as skunk, fox, coyote, raccoon, bat
Domestic animal such as cow, horse, sheep, pig, elk or bison
Has the animal been apprehended? May consider delay initiating post-exposure prophylaxis up to 10 days from exposure in order to capture animal unless unusual circumstances exist[3].
Has the animal been apprehended?
Does animal exhibit signs of rabies[4] or die suddenly?
Is animal available for testing?
Other wild animal kept in a zoo, pet store, exhibit or under the control of a private individual
Contact Division of Disease Control[5].
Test animal for rabies[6]. Is test positive?
Options
Post-exposure prophylaxis is usually not recommended at this time. Quarantine animal, whether vaccinated or not, for 10 days after exposure. Veterinary exam to be conducted at day one and day 10 to assess health status of animal. During quarantine, did animal show signs of rabies[4] or die within the 10 days?
Euthanize and submit for testing. Post-exposure prophylaxis treatment may be delayed pending test results unless unusual circumstances exist[3].
Administer vaccine and RIG according to ACIP recommendations. MMWR
Post-exposure prophylaxis is not indicated.
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FOOTNOTES
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3. If the animal exhibited any signs or symptoms of rabies or illness (see footnote 4), if the attack was vicious or unprovoked or the bite(s) occurred in the head and neck region, consideration should be given to starting post-exposure prophylaxis immediately.
4. Symptoms of rabies may include any one or more of the following: excitability, vicious attacks, biting, agitation, restlessness, aggressiveness, lack of fear, excessive salivation, aversion to water, inability to swallow or drink, muscular dysfunction, coordination or gait irregularities, paralysis, convulsions, avoidance of contact with humans or other animals, lethargy, and loss of appetite.
5. The Division of Disease Control may be contacted at 1.800.472.2180 (statewide) or 701.328.2378.
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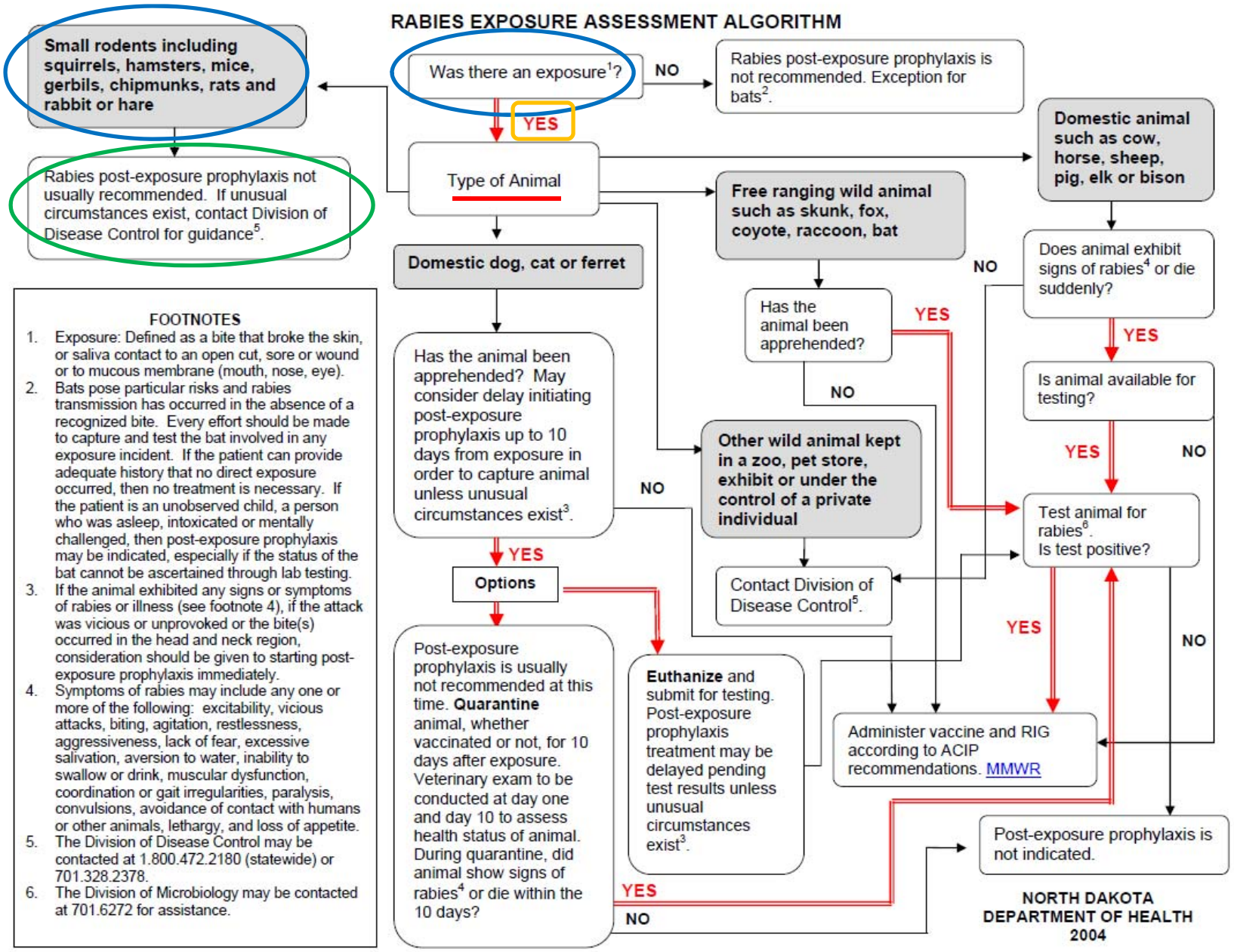
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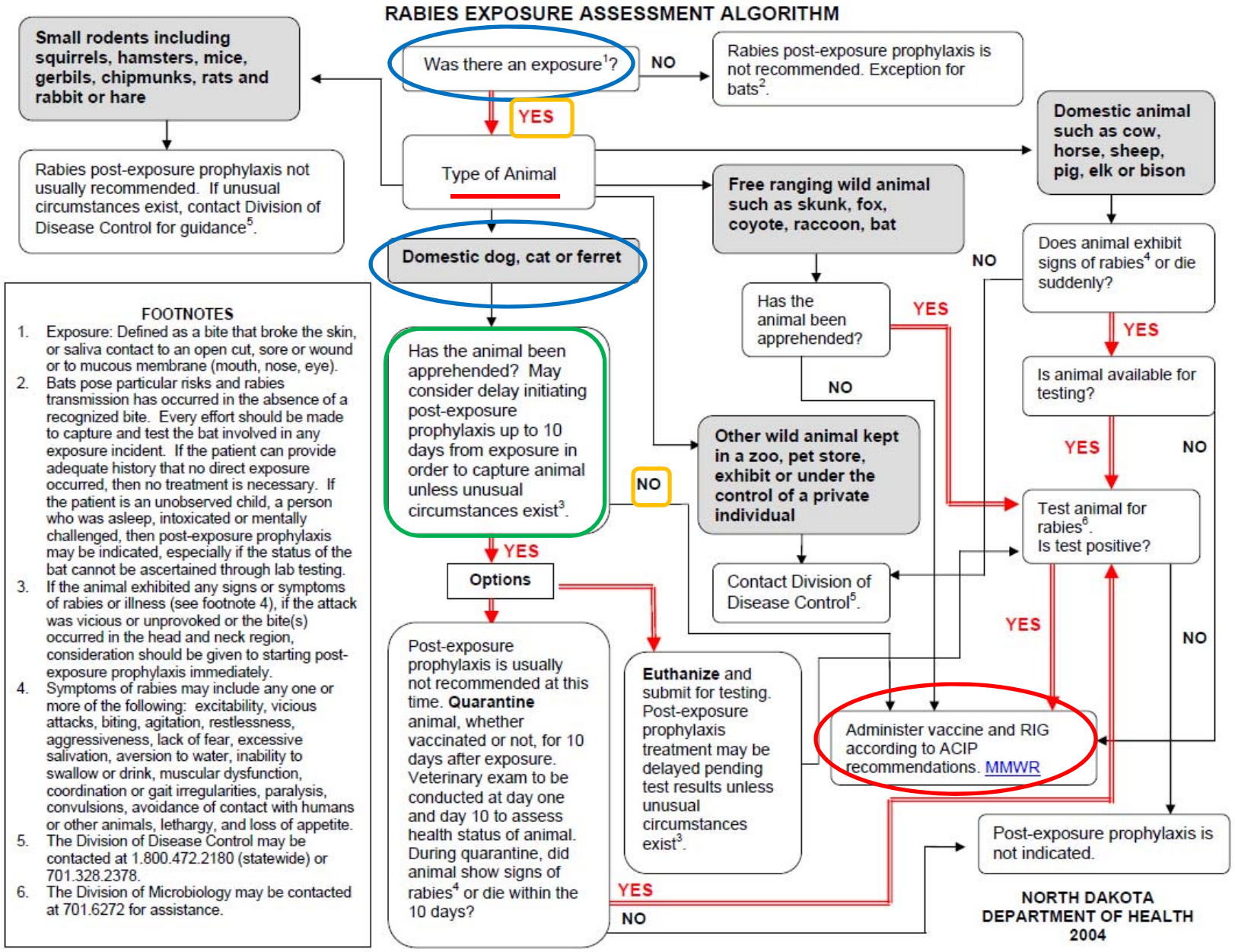
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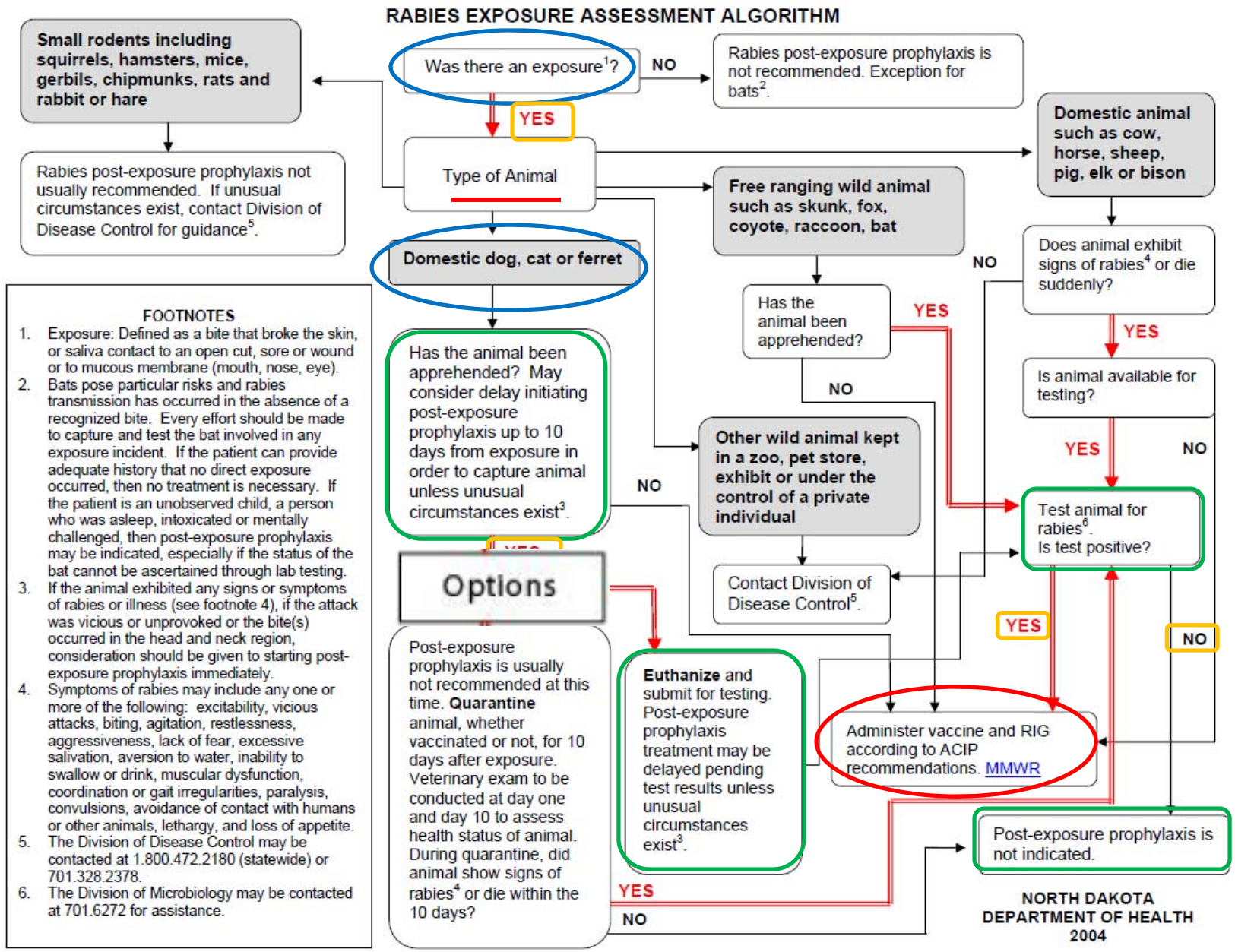
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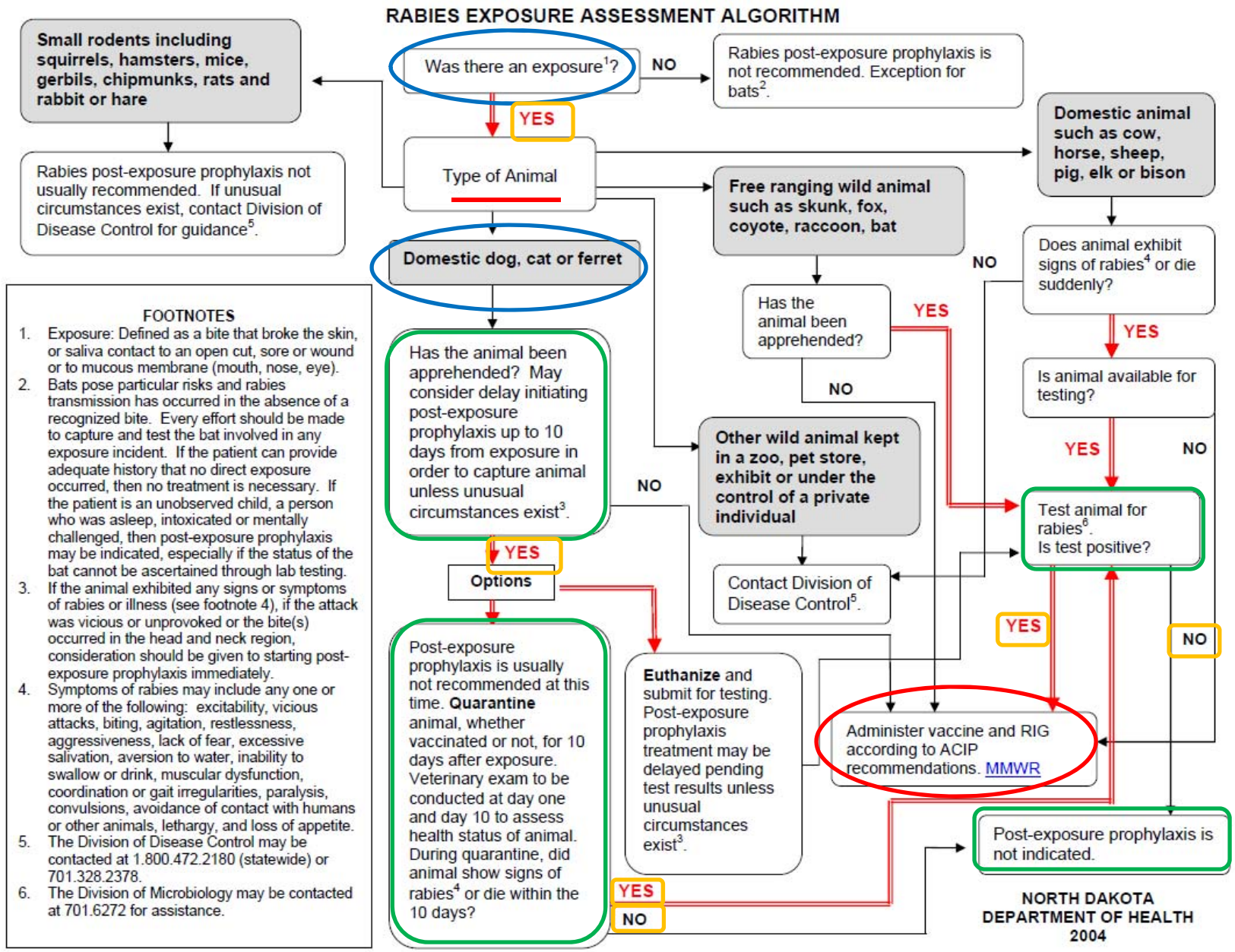
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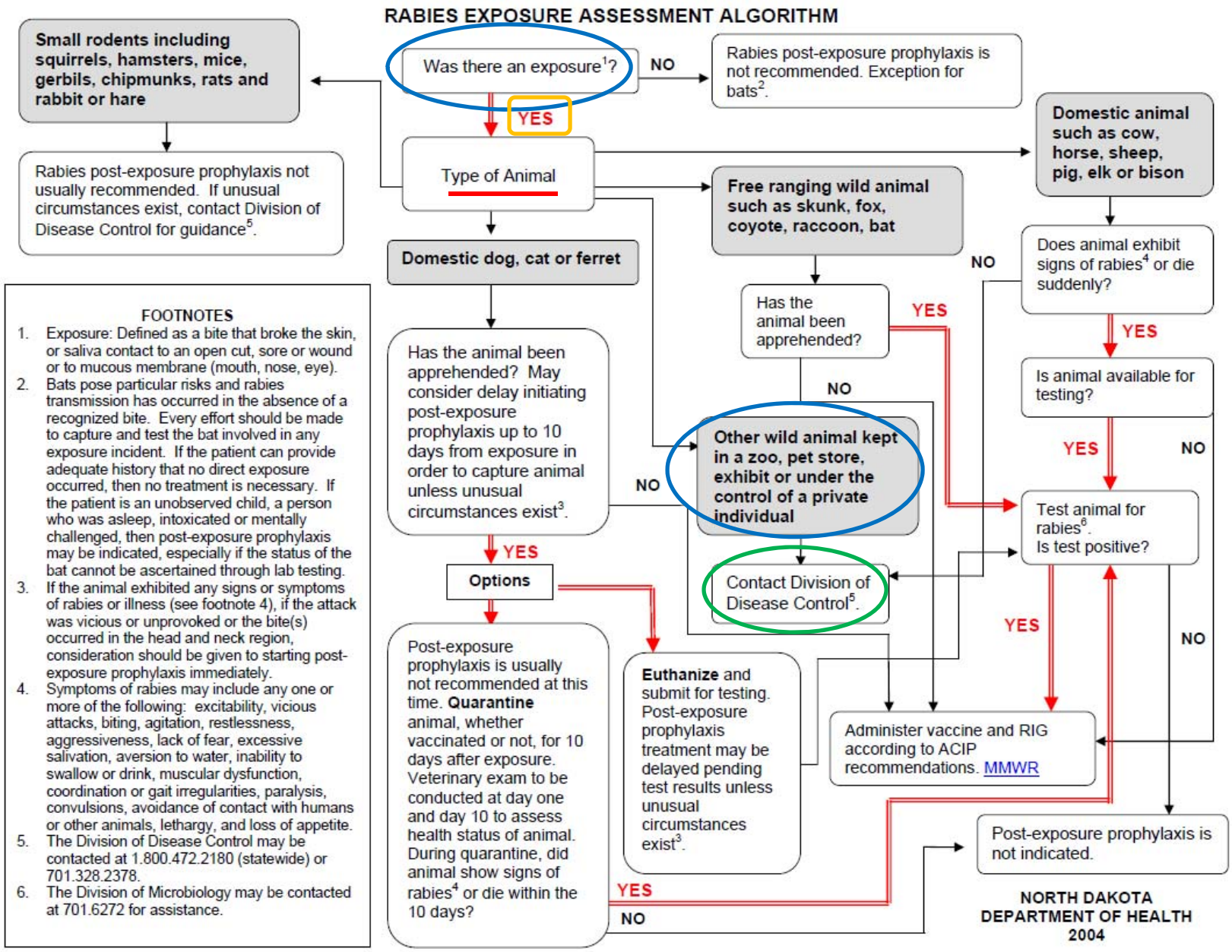
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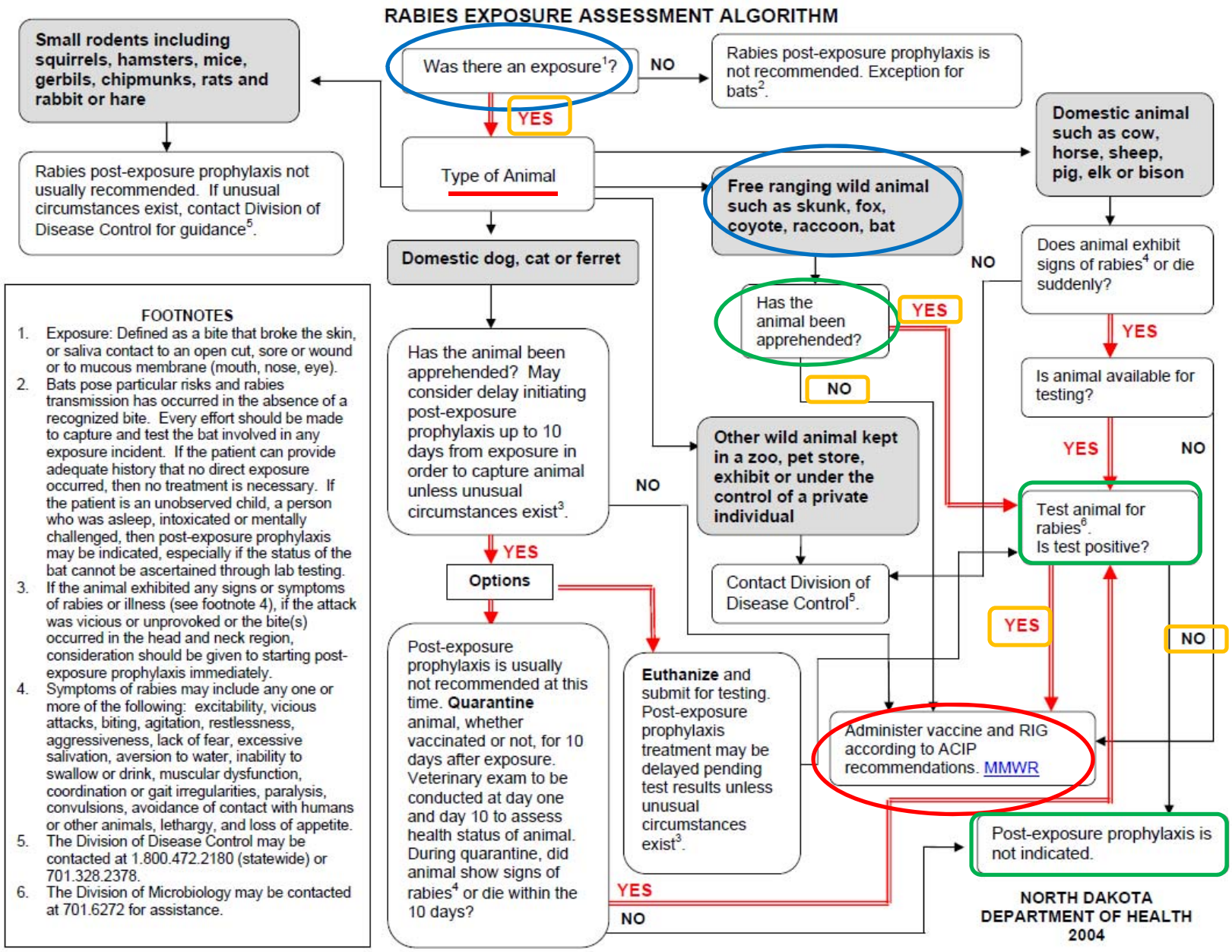
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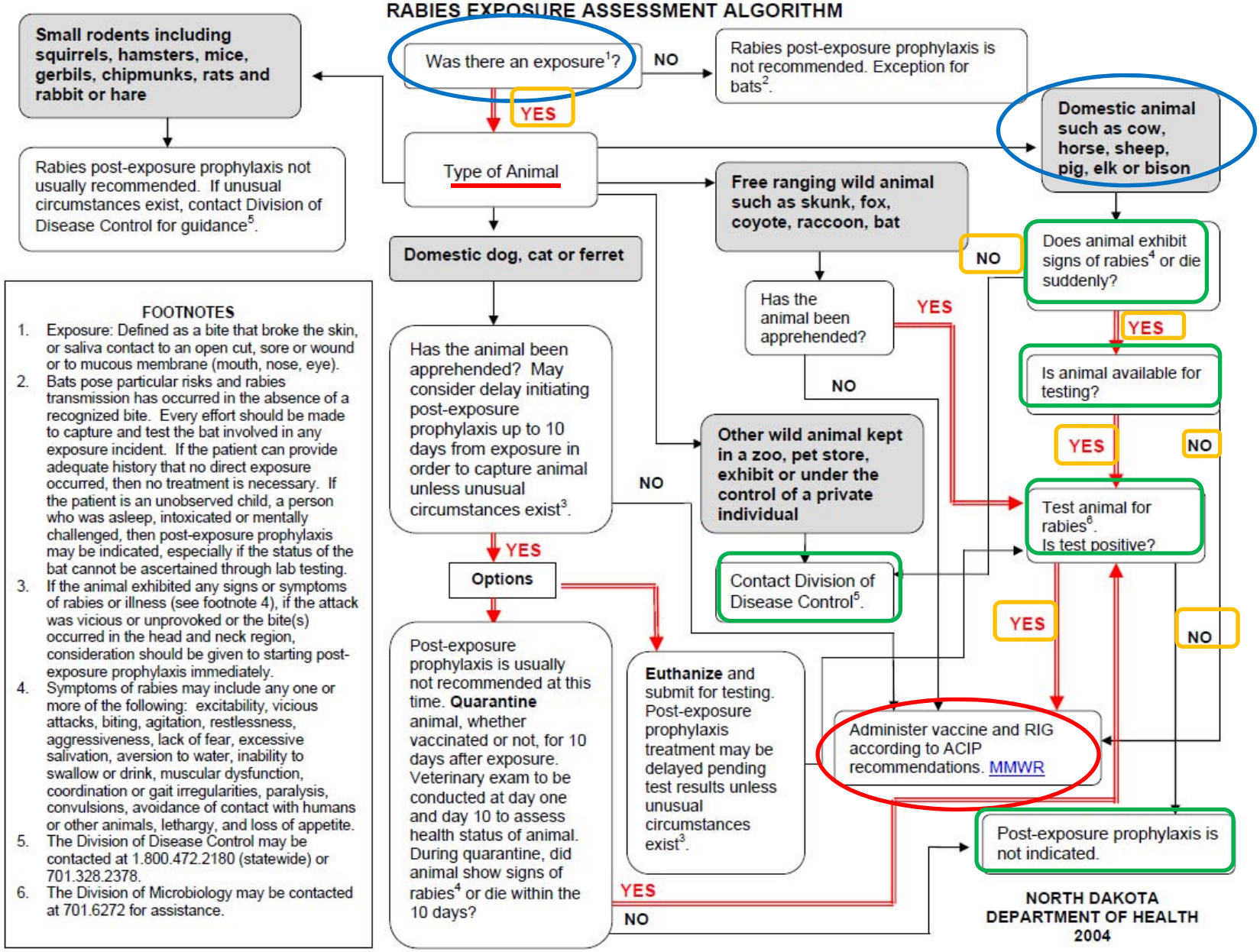
2. Bats pose particular risks and rabies transmission has occurred in the absence of a recognized bite. Every effort should be made to capture and test the bat involved in any exposure incident. If the patient can provide adequate history that no direct exposure occurred, then no treatment is necessary. If the patient is an unobserved child, a person who was asleep, intoxicated or mentally challenged, then post-exposure prophylaxis may be indicated, especially if the status of the bat cannot be ascertained through lab testing.
3. If the animal exhibited any signs or symptoms of rabies or illness (see footnote 4), if the attack was vicious or unprovoked or the bite(s) occurred in the head and neck region, consideration should be given to starting post-exposure prophylaxis immediately.
4. Symptoms of rabies may include any one or more of the following: excitability, vicious attacks, biting, agitation, restlessness, aggressiveness, lack of fear, excessive salivation, aversion to water, inability to swallow or drink, muscular dysfunction, coordination or gait irregularities, paralysis, convulsions, avoidance of contact with humans or other animals, lethargy, and loss of appetite.
5. The Division of Disease Control may be contacted at 1.800.472.2180 (statewide) or 701.328.2378.
6. The Division of Microbiology may be contacted at 701.6272 for assistance.
NORTH DAKOTA DEPARTMENT OF HEALTH
2004


RABIES EXPOSURE ASSESSMENT ALGORITHM
Was there an exposure[1]?
NO
Rabies post-exposure prophylaxis is not recommended. Exception for bats[2].
YES
Type of Animal
Small rodents including squirrels, hamsters, mice, gerbils, chipmunks, rats and rabbit or hare
Rabies post-exposure prophylaxis not usually recommended. If unusual circumstances exist, contact Division of Disease Control for guidance[5].
Domestic dog, cat or ferret
Has the animal been apprehended? May consider delay initiating post-exposure prophylaxis up to 10 days from exposure in order to capture animal unless unusual circumstances exist[3].
YES
Options
Post-exposure prophylaxis is usually not recommended at this time. Quarantine animal, whether vaccinated or not, for 10 days after exposure. Veterinary exam to be conducted at day one and day 10 to assess health status of animal. During quarantine, did animal show signs of rabies[4] or die within the 10 days?
YES
NO
Euthanize and submit for testing. Post-exposure prophylaxis treatment may be delayed pending test results unless unusual circumstances exist[3].
Free ranging wild animal such as skunk, fox, coyote, raccoon, bat
Has the animal been apprehended?
YES
NO
Other wild animal kept in a zoo, pet store, exhibit or under the control of a private individual
Contact Division of Disease Control[5].
Domestic animal such as cow, horse, sheep, pig, elk or bison
NO
Does animal exhibit signs of rabies[4] or die suddenly?
YES
Is animal available for testing?
YES
NO
Test animal for rabies[6]. Is test positive?
YES
NO
Administer vaccine and RIG according to ACIP recommendations. MMWR
Post-exposure prophylaxis is not indicated.
FOOTNOTES
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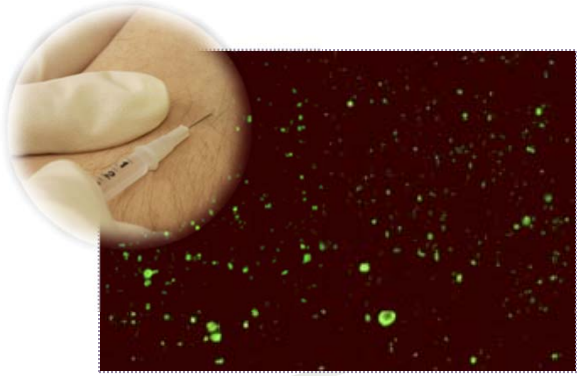
# Rabies Exposure

- Definition of rabies exposure
  - Introduction of virus-laden saliva into the body through a bite or contact of the virus-laden saliva or neural tissue with an open wound or the mucous membranes.
    - *Blood is not infectious*
- All animal bites or other possible exposures should be assessed by a healthcare provider!



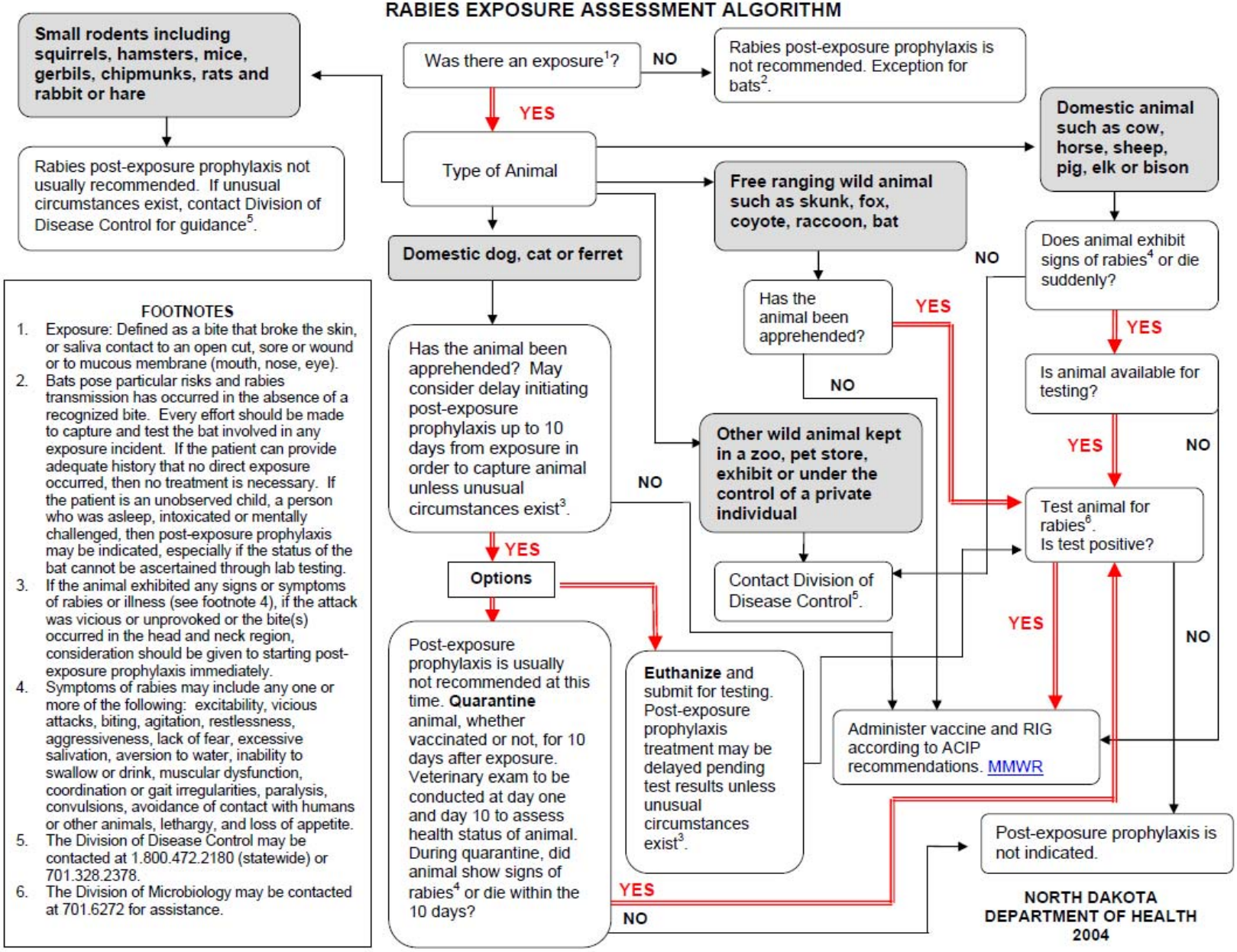
# Rabies Case Management

- Determine if exposure or possible exposure (bite or non-bite)
  - Bite from a rabid animal that breaks skin
  - Saliva from a rabid animal that comes into contact with:
    - Open sore, cut or wound in the skin
    - Mucus membrane of mouth, eyes or nose
    - Brain tissue/fluid contact with opening in skin
  - Scratches not exposures – except cats

# Rabies Case Management, cont.

- Access the exposure (high risk, wound cleansing, exposure site, etc.)
  - Domestic or wild animal
  - Vaccination status, current
  - Provoked or unprovoked attack
  - Health status/behavior of animal
  - Animal available or reasonably attainable for testing or quarantine
- Bites to the head or neck may want to consider starting rabies PEP before test results or quarantine period is over

# RABIES EXPOSURE ASSESSMENT ALGORITHM

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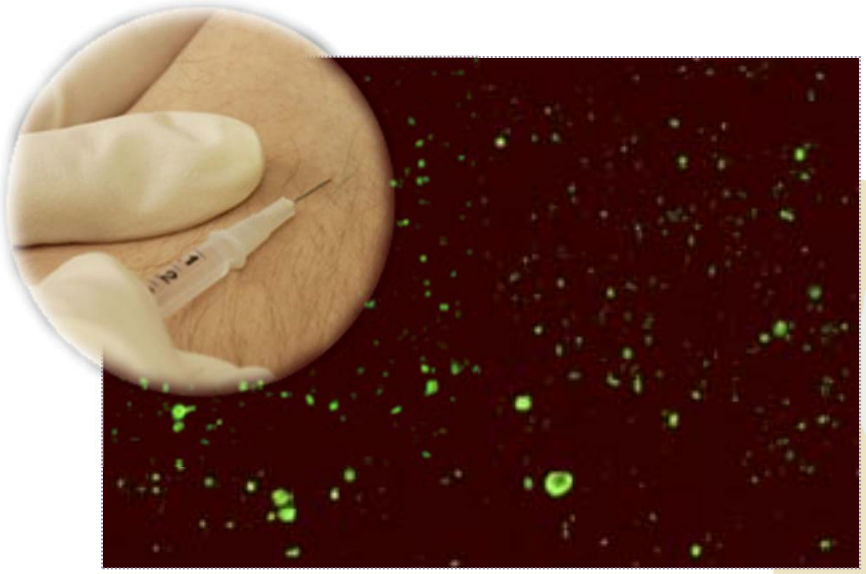
**2004**

# Rabies In Domestic Animals

- Signs and symptoms of rabies develop when the rabies virus reaches and multiplies in the brain of the animal
- Signs and symptoms (changes in behavior or health)
  - Viciousness - Nervousness
  - Biting - Lack of fear
  - Restlessness - Excessive salivation
  - Loss of appetite - Sluggishness
- Incubation variable, typically 3 to 8 weeks (range 10 days to 6 months)
- Infectious period up to 5 days before symptoms appear
  - Dogs, cats and ferrets only (unknown in all other animals)

# Human Rabies Vaccine



# ACIP Rabies Workgroup

- Used evidence-based process for reduced vaccination schedule
- Reviewed six areas:
  - Rabies virus pathogenesis
  - Experimental animal models
  - Human immunogenicity studies
  - Prophylaxis effectiveness in humans
  - Documented failures of prophylaxis
  - Vaccine safety

Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies: Recommendations of the Advisory Committee on Immunization Practices. MMWR Mar. 19, 2010;59[No. RR-2]

# Rabies Virus Pathogenesis

- The key to preventing rabies is to neutralize the virus before it enters the central nervous system
- Local virus neutralization
  - Immediate and thorough wound cleansing
  - Passive immunization (RIG)
- Active immunization – vaccine series

**Appropriate PEP Ensures Patient Survival**

# Experimental Animal Models

- No statistically significant differences in survivorship were observed among animal groups receiving different number of doses of vaccine
- No differences were detected in immunogenicity and efficacy of PEP with 2, 3, or 4 dose schedules

Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies: Recommendations of the Advisory Committee on Immunization Practices. MMWR Mar. 19, 2010;59[No. RR-2]

# Human Clinical Studies

- All healthy patients developed rabies virus neutralizing antibody by day 14

Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies: Recommendations of the Advisory Committee on Immunization Practices. MMWR Mar. 19, 2010;59[No. RR-2]

# Prophylaxis Effectiveness

- Of people who have died from rabies
  - Did not receive PEP
  - Receive some PEP
    - Without RIG
    - Delays in initiation
  - Substantial PEP deviations from recommended schedule
- No case who received timely wound care, RIG and 4 doses of vaccine

Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies: Recommendations of the Advisory Committee on Immunization Practices. MMWR Mar. 19, 2010;59[No. RR-2]

# Documented PEP Failures

- 21 fatal human cases (some form of PEP)
  - 20 cases developed illness and most died before day 28
    - Virus infection of the nervous system occurred before the date of 5$^{th}$ dose
- None from failure to receive 5$^{th}$ dose

Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies: Recommendations of the Advisory Committee on Immunization Practices. MMWR Mar. 19, 2010;59[No. RR-2]

# Vaccine Safety/Economics

- No adverse events from failure to receive 5$^{th}$ dose
- Fewer adverse reactions
- Presumed cost savings of reduced schedule
  - Travel expenses
  - Time away from work
  - Health-care worker time

Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies: Recommendations of the Advisory Committee on Immunization Practices. MMWR Mar. 19, 2010;59[No. RR-2]

# Reduced 4 Dose Schedule

- Evidence reviewed and presented to ACIP during June 2009 meeting
  - Accepted the recommended 4 dose schedule for PEP for previously unvaccinated persons
    - Exception immunosuppressed individuals – 5 dose recommendation remains unchanged
- CDC released provisional recommendations few months later
- Recommendations for use published in **MMWR** on **March 19, 2010**

MMWR™
Morbidity and Mortality Weekly Report
www.cdc.gov/mmwr

Recommendations and Reports | March 19, 2010 / Vol. 59 / No. RR-2

# Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies

## Recommendations of the Advisory Committee on Immunization Practices

# Vaccination Schedule

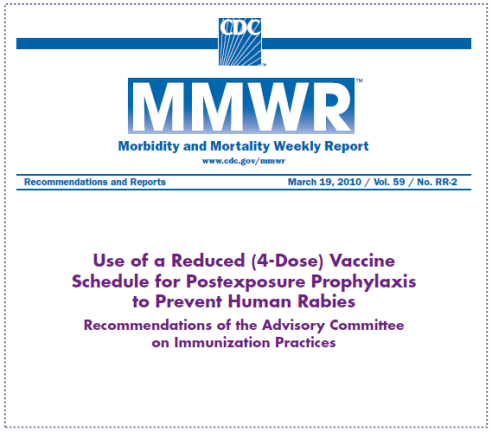
- Post-exposure prophylaxis – MMWR pg. 6

**TABLE 3. Rabies postexposure prophylaxis (PEP) schedule — United States, 2010**

| Vaccination status | Intervention | Regimen* |
|---|---|---|
| Not previously vaccinated | Wound cleansing | All PEP should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent (e.g., povidine-iodine solution) should be used to irrigate the wounds. |
| | Human rabies immune globulin (HRIG) | Administer 20 IU/kg body weight. If anatomically feasible, the full dose should be infiltrated around and into the wound(s), and any remaining volume should be administered at an anatomical site (intramuscular [IM]) distant from vaccine administration. Also, HRIG should not be administered in the same syringe as vaccine. Because RIG might partially suppress active production of rabies virus antibody, no more than the recommended dose should be administered. |
| | Vaccine | Human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) 1.0 mL, IM (deltoid area†), 1 each on days 0,§ 3, 7 and 14.¶ |
| Previously vaccinated** | Wound cleansing | All PEP should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidine-iodine solution should be used to irrigate the wounds. |
| | HRIG | HRIG should not be administered. |
| | Vaccine | HDCV or PCECV 1.0 mL, IM (deltoid area†), 1 each on days 0§ and 3. |

* These regimens are applicable for persons in all age groups, including children.
† The deltoid area is the only acceptable site of vaccination for adults and older children. For younger children, the outer aspect of the thigh may be used. Vaccine should never be administered in the gluteal area.
§ Day 0 is the day dose 1 of vaccine is administered.
¶ For persons with immunosuppression, rabies PEP should be administered using all 5 doses of vaccine on days 0, 3, 7, 14, and 28.
** Any person with a history of pre-exposure vaccination with HDCV, PCECV, or rabies vaccine adsorbed (RVA); prior PEP with HDCV, PCECV or RVA; or previous vaccination with any other type of rabies vaccine and a documented history of antibody response to the prior vaccination.

# Treatment of Wounds & Vaccination




- Not-previously vaccinated
  - Wound cleansing
    - Soap & Water, wound irrigation.
  - Rabies immune globulin (RIG)
    - 20 IU/kg body weight
    - If possible, full dose should be infiltrated around the wound site.
      - Remainder in anatomical site distant from vaccination site.
  - Vaccine *
    - 1 mL, IM (deltoid area, or outer thigh for small children).
    - 4-doses: Days 0, 3, 7 & 14.
    - Immunosuppression: 5 doses on days 0, 3, 7, 14 and 28

# Treatment of Wounds & Vaccination

- Previously vaccinated
  - Wound cleansing
    - Soap & Water, wound irrigation.
  - Rabies immune globulin (RIG)
    - Should NOT be administered!
  - Vaccine
    - 1 mL, IM (deltoid area, or outer thigh for small children).
    - 2-doses:  Days 0 & 3.

# Rabies Vaccination

- Pre-exposure vaccination
  - 3-doses of 1 mL, IM (deltoid area, or outer thigh for small children).
    - Days 0,7 & 21 or 28.
  - NO RIG
- Booster doses
  - 1-1mL, IM booster dose if does not have evidence of virus neutralizing antibodies in serum at 1:5 serum dilution by the RFFIT (rapid fluorescent focus inhibition test).

# Rabies Vaccine Review

- **Pre-exposure**
  - 3 doses
    - Days 0, 7, and 21 or 28
- **Post-exposure** (previously vaccinated)
  - 2 doses
    - Days 0 and 3
- **Post-exposure** (previously unvaccinated)
  - 4 doses*
    - Days 0, 3, 7 and 14
  - RIG administer

*Immunosuppression – PEP 5 doses on days 0, 3, 7, 14 and 28

# Rabies in Humans

- The first symptoms of rabies may be very similar to those of the flu including general weakness or discomfort, fever, or headache. These symptoms may last for days.
- There may be also discomfort or a prickling or itching sensation at the site of bite, progressing within days to symptoms of cerebral dysfunction, anxiety, confusion, agitation. As the disease progresses, the person may experience delirium, abnormal behavior, hallucinations, and insomnia.

Photo credit: CDC

# Antemortem Rabies Testing

- State health departments should be the primary contact for physicians during consultation about possible human rabies cases. After consultation with physicians, it may be deemed necessary to send human samples for rabies testing to the Rabies Laboratory at the Centers for Disease Control and Prevention (CDC).
- All four samples are required to rule out rabies:
  - Nuchal biopsy
  - Saliva
  - Serum
  - CSF

# Rabies in Humans

- There is no single effective treatment for rabies once clinical signs are evident. The following resources provide current research and thoughts regarding treatment options. These are not intended to serve as recommendations for rabies treatment.
  - Management of Rabies in Humans (CID)
    - http://cid.oxfordjournals.org/content/36/1/60.full.pdf+html
  - Milwaukee Rabies protocol
    - http://www.chw.org/display/PPF/DocID/33223/router.asp

# 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/