Understanding Rabies in NC; Prevention, Control and Epidemiology

Carl Williams DVM, DACVPM
Public Health Veterinarian
NC Division of Public Health
Wildlife Medicine Symposium
January 20, 2024
Overview

Structure of Public Health in North Carolina

Public Health Law

Rabies virus and disease

Rabies surveillance

Prevention of rabies
Public Health Infrastructure

CDC and State DOHs must cooperate and have limited powers (although rarely tested)

Tremendous responsibility falls on MDs/Primary Health Care Providers

Susceptible -> Exposed -> Infectious -> Recovered
Public Health Mission in NC

• 130A-1.1. Mission and essential services.
  • The General Assembly recognizes that unified purpose and direction of the public health system is necessary to ensure that all citizens in the State have equal access to essential public health services.
  • The General Assembly declares that the mission of the public health system is to promote and contribute to the highest level of health possible for the people of North Carolina by:
  • Preventing health risks and disease;
  • Identifying and reducing health risks in the community;
  • Detecting, investigating, and preventing the spread of disease;
  • Promoting healthy lifestyles;
  • Promoting a safe and healthful environment;
  • Promoting the availability and accessibility of quality health care services through the private sector; and
  • Providing quality health care services when not otherwise available
Reportable Diseases

• ~ 80 Reportable Conditions in NC:
  • High consequence or fatal:
    • Rabies, Anthrax, Elevated blood lead levels
  • Spread quickly:
    • Measles, Pertussis
  • May become established without intervention
    • Malaria, Zika
  • May be spread through common food supply
    • E. coli O157:H7, Salmonellosis

• Health Care Providers and Laboratories responsible
Public Health Authority in NC

• NCGS 130A-41 Powers and duties of local health director:
  • To investigate the causes of infectious, communicable and other diseases;
  • To exercise quarantine authority and isolation authority pursuant to G.S. 130A-145;
  • To examine, investigate and control rabies pursuant to Part 6 of Article 6 of this Chapter;

• The LHD may delegate (some) responsibility to Animal Control (AC) agencies
  • There must be written agreements (MOA) between agencies specifically delineating responsibility
  • AC officers must defer human rabies risk assessments to local CD nurses
Local Board of Health, or County Commissioners, or Consolidated Human Services Agency

**Local Health Director**

**Communicable Disease Staff**
- Advise Clinicians, Veterinarians, Exposed Persons, Pet owners

**Animal Services Officers**
- Advise Veterinarians, Pet owners, Instruct Exposed Persons to call CD staff or Health Care Provider

**Typical Organizational Structure for Rabies Control**

- County Sheriff
- County Manager
Rabies: What’s in a Name?

- Rabies is an acute encephalitis or meningoencephalitis due to a lyssavirus infection.
- The etiological agents of rabies encephalitis belong to the
  - Mononegavirales order,
  - Rhabdoviridae family
  - Lyssavirus genus
  - Multiple species (17 on image)
- Only one species, classic rabies virus, is present in North America

Rabies Virus Genome

• The rabies virus genome is single-stranded, antisense, nonsegmented, RNA of approximately 12 kb.

• There is a leader-sequence (LDR) of approximately 50 nucleotides, followed by N, P, M, G, and L genes.
Rabies Pathogenesis

• Bite
  • Any penetration of the skin by teeth constitutes exposure
  • It is assumed that all bite exposures result in contamination of the wound with saliva
Rabies in Animals in the United States

- In North America many unique, host adapted, strains of Rabies Lyssavirus exist
  - Eastern raccoon,
  - Texas grey fox,
  - North central skunk,
  - Arctic fox,
  - etc.
  - Bats (all states except HI)

Ma, et. al. Rabies surveillance in the United States during 2018. JAVMA | JAN 15, 2020 | VOL 256 | NO. 2
In 2020, rabid animals in the U.S. totaled 4,479, a decrease from 4,690 in 2019 by 4.5%.

Almost 3/5 of all animal rabies cases in 2020 were found in 8 states:

- TX
- PA
- VA
- NY
- NC
- NJ
- MD
- CA
North Carolina Surveillance
Indications for Rabies Testing

• NC State Laboratory for Public Health is the only lab in the state that tests animals for rabies
  • Specimen – brain tissue
• High risk wildlife that have exposed a person or domestic animal
• Cats, dogs or ferrets that cannot undergo a 10-day confinement (§ 130A-199 requires testing)
  • Showing signs of rabies
  • Too ill
  • Too vicious
• Veterinarian requests testing for diagnostic purposes – domestic animal
• Submit head of animal/whole bat
## Rabies Positive Mammals and Percent Positivity by Species, North Carolina, 2022

<table>
<thead>
<tr>
<th>ANIMAL</th>
<th># pos</th>
<th># tested</th>
<th>% pos</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raccoon</td>
<td>95</td>
<td>319</td>
<td>29.6%</td>
</tr>
<tr>
<td>Skunk</td>
<td>66</td>
<td>82</td>
<td>80.5%</td>
</tr>
<tr>
<td>Fox</td>
<td>46</td>
<td>90</td>
<td>51.1%</td>
</tr>
<tr>
<td>Bat</td>
<td>25</td>
<td>1016</td>
<td>2.5%</td>
</tr>
<tr>
<td>Cat</td>
<td>15</td>
<td>779</td>
<td>1.9%</td>
</tr>
<tr>
<td>Cow</td>
<td>4</td>
<td>62</td>
<td>6.5%</td>
</tr>
<tr>
<td>Dog</td>
<td>2</td>
<td>744</td>
<td>0.3%</td>
</tr>
<tr>
<td>Sheep</td>
<td>2</td>
<td>25</td>
<td>8.0%</td>
</tr>
<tr>
<td>Coyote</td>
<td>1</td>
<td>10</td>
<td>10.0%</td>
</tr>
<tr>
<td>Bobcat</td>
<td>1</td>
<td>1</td>
<td>100.0%</td>
</tr>
<tr>
<td>Goat</td>
<td>1</td>
<td>78</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

Source: N.C. State Laboratory of Public Health

Data Accessed Jan 2023
Rabies North Carolina: Number of Positive Wild Mammals by Species by Year, North Carolina, 2001 – 2022 (n = 8,504)
Rabies Positive Dogs and Cats, North Carolina, 1991 – 2022 (n = 666)

![Graph showing the number of rabies cases in dogs and cats from 1991 to 2022.]

NC State Laboratory of Public Health
Data Accessed Jan 2023
Estimated Burden of Human Rabies in the World

• Human mortality from rabies is estimated to be 55,000 deaths per year
• Mostly in Africa and Asia
• Due to uncontrolled canine rabies
  • Weekly Epidemiological Record No. 49/50, 2007, 82, 425–436
  • http://www.who.int/wer
Burden of Rabies in the US

• Estimated 40,000 – 50,000 post-exposure prophylaxis treatments (cost > $3000 each)

• ~$245 - $510 million annually
  – Vaccination of companion animals
  – Diagnostic testing
  – Post- and pre-exposure prophylaxis

(doesn’t include associated healthcare costs, animal control, lost time from work)

Human Rabies in the US: 2008-2022

30 cases

- 17 due to bat variant
  - 6 reported bite
  - 7 reported contact
  - 4 had unknown exposures

- 9 canine variant
  - exposure outside US
  - 1 mongoose – Puerto Rico

- 3 raccoon variant
  - one exposed in NC, one transplant recipient

- 1 unknown exposure and variant

[https://avmajournals.avma.org/view/journals/javma/aop/javma.23.02.0081/javma.23.02.0081.xml](https://avmajournals.avma.org/view/journals/javma/aop/javma.23.02.0081/javma.23.02.0081.xml)
Human Rabies Reported Cases
North Carolina, 1929 - 2022 (n = 26)

NC Department of Health and Human Resources
Reported Communicable Diseases, Data Accessed Jan 2023
Rabies Prevention
Vaccination Laws

- **NCGS 130A-185. Vaccination of all dogs, cats and ferrets**
  - (a) The owner of every dog and cat over four months of age shall have the animal vaccinated against rabies. The time or times of vaccination shall be established by the Commission. Rabies vaccine shall be administered only by a licensed veterinarian or by a certified rabies vaccinator.
- We learned from Old Yeller and Atticus
Prevention – Laws and Guidance

• Animals
  • Compendium of Animal Rabies and Control, 2016
    • National Association of State Public Health Veterinarians
    • Incorporated into our statute: 130A-197 Management of dogs, cats and ferrets exposed to rabies.
    • Used as guidance for other species

• Humans
  • Advisory Committee on Immunization Practices (ACIP)
    • Human Rabies Prevention—United States, 2008
    • Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies, 2010
    • Use of a Modified Preexposure Prophylaxis Vaccination Schedule to Prevent Human Rabies: Recommendations of the Advisory Committee on Immunization Practices — United States, 2022
    https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/rabies.html
Effective Rabies Control; Prevention of Human Rabies Cases
Response to Animal Bites

• Wound care
• Antibiotic therapy
• Tetanus Booster or TIG administration\(^1\)
  • Many immigrants not adequately vaccinated against tetanus, thorough history needed
• Rabies specific risk assessment
  • Most dog/cat bites do not require rabies PEP
  • Bites from RVS often require PEP initiation

Rabies exposures

• Saliva or brain/nervous system tissue are only infectious materials
  • Blood, urine, feces ≠ infectious
  • Rabies virus becomes non-infectious when it dries out or is exposed to sunlight

• Route of transmission
  • Bite
  • Non bite: infectious material into open wound or onto mucous membranes, theoretically scratches
    • Rare but has been documented
    • Petting, contact with non-infectious materials ≠ exposure
Rabies exposures

• Exposing animal high-risk or low risk?
  • High:
    • raccoon, skunk, fox, coyote, bobcat, beaver, groundhog (other large carnivores)
  • Low:
    • small rodents (squirrel, mouse, rat, mole, hamster, guinea pig), rabbits
  • Low risk acting aggressively/neurologic → high risk
ANIMAL EXPOSURE

Terrestrial Mammal

Handling, petting, exposure to low-risk bodily fluids (e.g., blood, urine, stool)

NO TREATMENT

Domestic animal (e.g., dog, cat, ferret, livestock)

Available for observation or brain testing? (e.g., saliva, CSF, brain)

DO NOT TREAT

Small animal / rodent (e.g., rat, mouse, squirrel, rabbit)

Available for immediate brain testing?

Carnivores / larger rodents (e.g., raccoon, fox, skunk, coyote, woodchuck, beaver)

Immediate brain testing

Bat

Any bite, scratch, or mucous membrane exposure

Negative DO NOT TREAT

Positive TREAT

Not Done TREAT

High endemicity site

Low endemicity site

Circumstances

Normal DO NOT TREAT

Abnormal TREAT

Normal behavior or Attack provoked

DO NOT TREAT

Abnormal behavior or Unprovoked attack

TREAT

Low endemicity site (Most in US)

Positive TREAT

High endemicity site (Uncommon in US)

Circumstances?

Normal behavior or Attack provoked

DO NOT TREAT

Abnormal behavior or Unprovoked attack

TREAT

Basis for 10-day Confinement - Cats

- 86 cats experimentally infected with rabies virus
- 26 died from rabies
- 23 had detectable rabies virus in saliva
- Range of viral shedding extended from 1 day prior to symptom onset to 7 days after symptom onset
- Most cats died 5 – 6 days after symptom onset

Basis for 10-day Confinement - Dogs

• 117 dogs experimentally infected with rabies virus
• 54 died from rabies
• 25 had detectable rabies virus in saliva
• Range of viral shedding extended from 3 days prior to symptom onset to 7 days after symptom onset
• Most dogs died 3 – 4 days after symptom onset

Confinement for other species that bite

- Ferrets – 10 days, similar data as for dogs/cats
- Livestock – 15 days, as long as healthy and no history of being exposed to a rabies vector species
- All other species - no appropriate confinement
Exposure: bite, scratch, saliva touches eyes, nose, mouth

Incubation

1. virus enters body
2. virus dormant for variable time period
3. virus enters PNS travels toward brain
4. virus enters brain

Shedding

5. virus spreads to salivary glands
6. Animal shows signs of rabies

NCGS 130A – 197 → Four or Six Month Quarantine when Dog/Cat/Ferret exposed to Rabies

NCGS 130A – 196 → Ten day Confinement when Dog/Cat/Ferret bites a person

Exposure: bite, scratch, saliva touches eyes, nose, mouth
Animal NOT infectious, appears healthy, up to 180 day duration
Animal IS infectious, may appear healthy or ill 1-10 day duration
DEATH
# Rabies Control Measure Summary

<table>
<thead>
<tr>
<th>Control Measure</th>
<th>Use</th>
<th>Authority</th>
</tr>
</thead>
<tbody>
<tr>
<td>Countywide Rabies Program</td>
<td>Examine, investigate and control rabies</td>
<td>130A-41</td>
</tr>
<tr>
<td>10 Day Confinement</td>
<td>When a dog/cat/ferret bites a person</td>
<td>130A-196</td>
</tr>
<tr>
<td>15 Day Confinement</td>
<td>When livestock bites a person</td>
<td>State policy developed with NCDA&amp;CS in</td>
</tr>
<tr>
<td></td>
<td></td>
<td>communication with CDC</td>
</tr>
<tr>
<td>45 Day Observation</td>
<td>When a rabies vaccinated dog/cat/ferret has been exposed to rabies</td>
<td>130A-197 / NASPHV Compendium</td>
</tr>
<tr>
<td>4 Month Quarantine</td>
<td>When a dog/cat not currently vaccinated against rabies has been</td>
<td>130A-197 / NASPHV Compendium</td>
</tr>
<tr>
<td></td>
<td>exposed to rabies</td>
<td></td>
</tr>
<tr>
<td>6 Month Quarantine</td>
<td>When a ferret not currently vaccinated against rabies has been</td>
<td>130A-197 / NASPHV Compendium</td>
</tr>
<tr>
<td></td>
<td>exposed to rabies</td>
<td></td>
</tr>
<tr>
<td>Test</td>
<td>When a dog/cat/ferret in a 10 day confinement dies</td>
<td>130A-199</td>
</tr>
<tr>
<td>Test</td>
<td>Other animals tested at the discretion of the SPHV</td>
<td>130A-198</td>
</tr>
</tbody>
</table>
Humans - Pre-exposure Vaccination

Recommended for

- Veterinarians and staff
- Laboratory workers – rabies diagnostic labs or research labs
- Animal control officers
- Wildlife workers
- Travelers to rabies endemic countries; at risk
Updates to the ACIP recommendations to prevent human rabies, 2022

- A 2-dose PrEP schedule has replaced the 3-dose PrEP schedule to protect for up to 3 years. Options for maintaining protection beyond 3 years are also described.

- Risk categories have been redefined into 5 risk groups.

- The minimum acceptable laboratory value (antibody titer) used to determine whether rabies vaccine booster doses are needed was revised and standardized.

- Many people for whom serial titers were recommended every 2 years now require only a one-time titer (and booster if below a certain level) OR a one-time booster.

- Clinical guidance for administering PrEP to people with weakened immune systems has been outlined and includes recommendations to confirm that the vaccine was effective.
<table>
<thead>
<tr>
<th>Risk category</th>
<th>Who this typically* affects</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk category 1</td>
<td>People who work with live or concentrated rabies virus in laboratories</td>
<td>2 doses, days 0 and 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Check titer every 6 months</td>
</tr>
<tr>
<td>Risk category 2</td>
<td>People who frequently do at least one of the following: handle bats, have contact with bats, enter high-density bat environments like caves, or perform animal necropsies</td>
<td>2 doses, days 0 and 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Check titer every 2 years</td>
</tr>
</tbody>
</table>
| Risk category 3 | People who interact with, or are at higher risk to interact, with mammals other than bats that could be rabid, for a period longer than three years after they receive PrEP  
This group includes:  
- Most veterinarians, veterinary technicians, animal control officers, wildlife biologists, rehabilitators, trappers, and spelunkers (cave explorers)  
- Certain travelers to regions outside of the United States where rabies in dogs is commonly found | 2 doses, days 0 and 7, plus:             |
|                |                                                                                                                                                                                                                         | Either a one-time titer check after 1 year and up to 3 years following the first 2-dose vaccination |
|                |                                                                                                                                                                                                                         | OR                                       |
|                |                                                                                                                                                                                                                         | 1-dose booster between 3 weeks and 3 years following the first vaccine in the 2-dose vaccination |
| Risk category 4 | Same population as risk category 3, but at a higher risk for ≤ three years after they receive PrEP                                                                                                                                 | 2 doses, days 0 and 7                    |
| Risk category 5 | General U.S. population                                                                                                                                                                                                   | None                                     |
Rationale for Rabies Pre-Exposure Immunization for People

- It may provide protection to persons with inapparent exposure to rabies
- It may protect persons whose post exposure therapy is expected to be delayed
- In the event of an exposure to rabies it simplifies therapy by
  - Eliminating need for HRIG
  - Decreasing number of vaccine doses required

Post-exposure Prophylaxis (not previously vaccinated)
ACIP Modified Essen Schedule; 4 doses, 4 visits*

D 0 x 1
D 3 x 1
D 7 x 1
D 14 x 1

D 0
HRIG 20 IU/kg

D 0
Wound Cleansing

1 ml (IM) into deltoid (adults) or into anterolateral area of thigh (children)

* Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies. March 19, 2010 / 59(RR02);1-9
Human Rabies PEP IF previously vaccinated; 2 doses, 2 visits*

Wound Cleansing

1 ml (IM) into deltoid (adults) or into anterolateral area of thigh (children)

*D 0
D 3
x 1
x 1

*RabAvert® Novartis Vaccines Rev. 10/06
*IMOVAX® Sanofi Pasteur SA (December 2005)
Why do Bats Pose Such a risk?

- The virus from bats can replicate at a lower temperature, thus small superficial wounds from bat bites can lead to infection

- And / Or

  - Bat bites are not dramatic and may not be appreciated when they occur or when the patient is examined
  - Some may recognize the bite but not comprehend its implications
  - Others, such as young persons or those with disabilities may be unable to provide and accurate history of a bite

  - Prophylaxis Against Rabies. *NEJM* 2004; 351:2626-2635
Small Rodents Present a Low Risk of Transmission
What About Opossums?

- Opossums are relatively resistant to infection with rabies and are considered a low risk for infection
- The viral dose required to infect opossums is 80,000 times that required to infect a fox
- Rabies virus binds to nAChR in skeletal muscle
- A high content of receptors in muscle of red fox makes them susceptible
- Low content of receptors in muscle of opossums makes them resistant
Rabies Resources Available to You

• NC Communicable Disease Manual
  • https://www.epi.state.nc.us/cd/lhds/manuals/rabies/toc.html
When to Call Public Health

• A bite is reported
• An exposure is suspected
• You have any questions!

919-733-3419
24/7
• UNC Animal Services Site
  • [https://www.sog.unc.edu/resources/microsites/animal-services/](https://www.sog.unc.edu/resources/microsites/animal-services/)

North Carolina law related to animal control issues is scattered far and wide throughout the state’s law books and responsibility for animal control is shared between various state agencies and local governments. The Animal Services microsite is intended to be a resource that brings many of these laws together into one place so that government officials and others who wish to understand the basics of the law can have a reasonable starting point. The FAQ, listerv and publications list found on the Animal Services site are all intended to foster knowledge and communication about these issues.
• Coates’ canon
  • [https://canons.sog.unc.edu/animal-services/]
https://www.sog.unc.edu/publications/books/north-carolina-guide-animal-services-law
Questions?