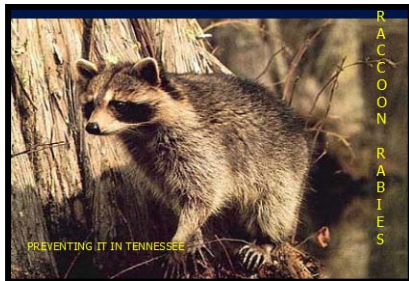


# *Rabies*

## *Virus, Epidemiology, Transmission*

### *and Free-roaming Cats*



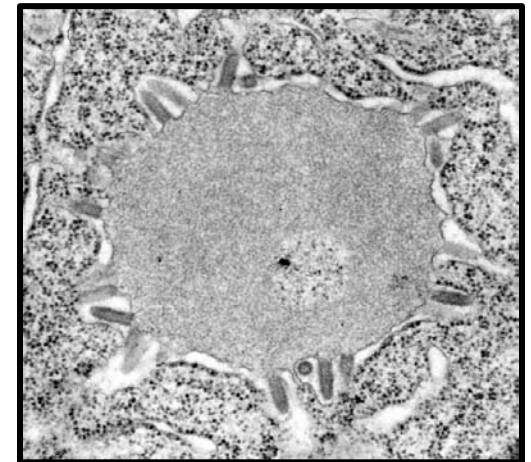
# How did Rabies Get its Name?

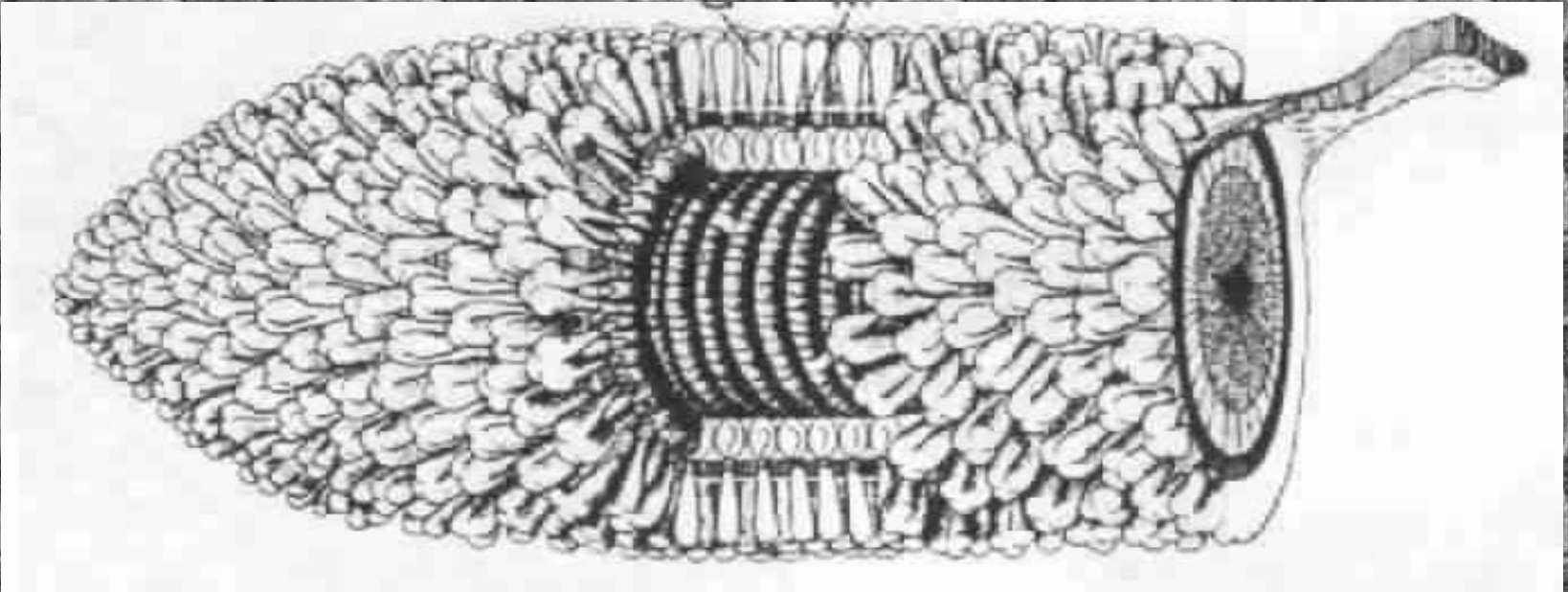
- The Greeks called rabies *lyssa* or *lytta*, which means frenzy or madness. They named human rabies *hydrophobia*, which means fear of water, a symptom shown by rabies victims.

# Rabies Virus

- *Rhabdovirus, Lyssavirus* genus
- The family *Rhabdoviridae* consists of more than 185 different viruses isolated from both plants and animals.
- Susceptible to disinfectants
- Inactivated by drying

Electron micrograph of rabies. The bullets surrounding the smooth gray circle are rabies. The circle itself is the Negri body. <http://www.ictvdb.org/Images/Murphy/rabies.htm>





- ▶ TYPICAL CHARACTERISTIC BULLET SHAPE
- ▶ VIRUS ENVELOPE WITH SPIKE-LIKE PROJECTIONS
- ▶ HELICAL SINGLE STRAND RNA VIRUS
- ▶ GENETIC VARIANTS ARE **HOST ADAPTED**

# *Lyssavirus* genus and Geographic Distribution

- Rabies virus – Worldwide  
(except Australia, Antarctica, and some islands)
- Lagos bat virus – Africa
- Mokola virus - Africa
- Duvenhage virus - Africa
- European bat lyssavirus 1 – Europe
- European bat lyssavirus 2 – Europe
- Australian bat lyssavirus – Australia

# *Lyssavirus* genus

- The genus *Lyssavirus* has only one major serogroup.
- Various serotypes have been defined.
- Placement within the genus determined by serologic cross-reactivity of viral antigens.
- Antigenically, the virus is very stable
- **Consequently, all approved vaccines are cross-reactive against all variants.**

# Mechanisms of Attachment

- The initial events of attachment, penetration, and uncoating result in release of the viral nucleocapsid **into the cytoplasm of the host animal cell.**
- The virus G protein binds most effectively to cells of neuronal origin, reflecting the **neurotropism of rabies virus.**

# Mechanism of Transmission

- Consequently, transmission of the virus to a new host is **highly dependent on the proximity of neurons at the site of introduction.**
- **Rabies virus is not spread by urine, feces or blood.**



# Strains of virus

- Species susceptibility
  - Varies by strain (variant)
  - All domestic animals and people
- Geographic distribution
  - Characteristics of reservoir host
  - Ecology (e.g. natural barriers)



# Strains of virus

- Identity of species of origin can be done by monoclonal antibody (mAb) testing.
- Reservoir (adapted) host to other species- spillover



# Rabies Epidemiology

- Biased epidemiologic information
  - clinical reports
  - examination of specimens submitted to public health or veterinary diagnostic laboratories
- Reporting of both human and animal rabies cases grossly underestimate the magnitude of the problem.

# HOW RABIES CASES ARE LOST TO THE REPORTING SYSTEM

ALL TRUE CASES OF RABIES

CASES OBSERVED BY MAN

SUSPECTED OF BEING RABID

CAPTURED

SENT TO DIAGNOSTIC LAB

SPECIMEN SUITABLE FOR TESTING

DIAGNOSIS POSITIVE = TRUE POSITIVE

NOT OBSERVED

NOT SUSPECTED OF BEING RABID

NOT CAPTURED

NOT SENT TO DIAGNOSTIC LAB

SPECIMEN NOT SUITABLE FOR TESTING

DIAGNOSIS NEGATIVE = FALSE NEGATIVE



# Exposure does not always result in disease

- No virus in saliva
- Virus may not multiply and progress to CNS
- If clinical signs occur then course of disease is invariably fatal.
- Data gap – What proportion of exposures results in disease and does it vary by species (e.g., raccoons, bats, skunks)

# Rabies prevalence in U.S.

- True prevalence is unknown.
- Reports of cases in animals and humans are reported to local and state health departments, then to the CDC.
- Reporting methodology varies.
- Minimal information on species (e.g., cat without any indication of owned, community cat, feral, etc.)

# Rabies Epidemiology

Host range in the U.S.

–Reservoir (adapted) hosts

- Order *Carnivora*

- Skunks

- Raccoons

- Foxes

- Order *Chiroptera* (primarily insectivorous bats)

# Virus and Host Adaptations

- **Spillover** infections of distinct rabies virus variants to non-maintenance (non-adapted, non-reservoir) hosts occurs but does not typically result in sustained transmission (e.g. infection in domestic animals and humans are spillover).



# Virus and Host Adaptations

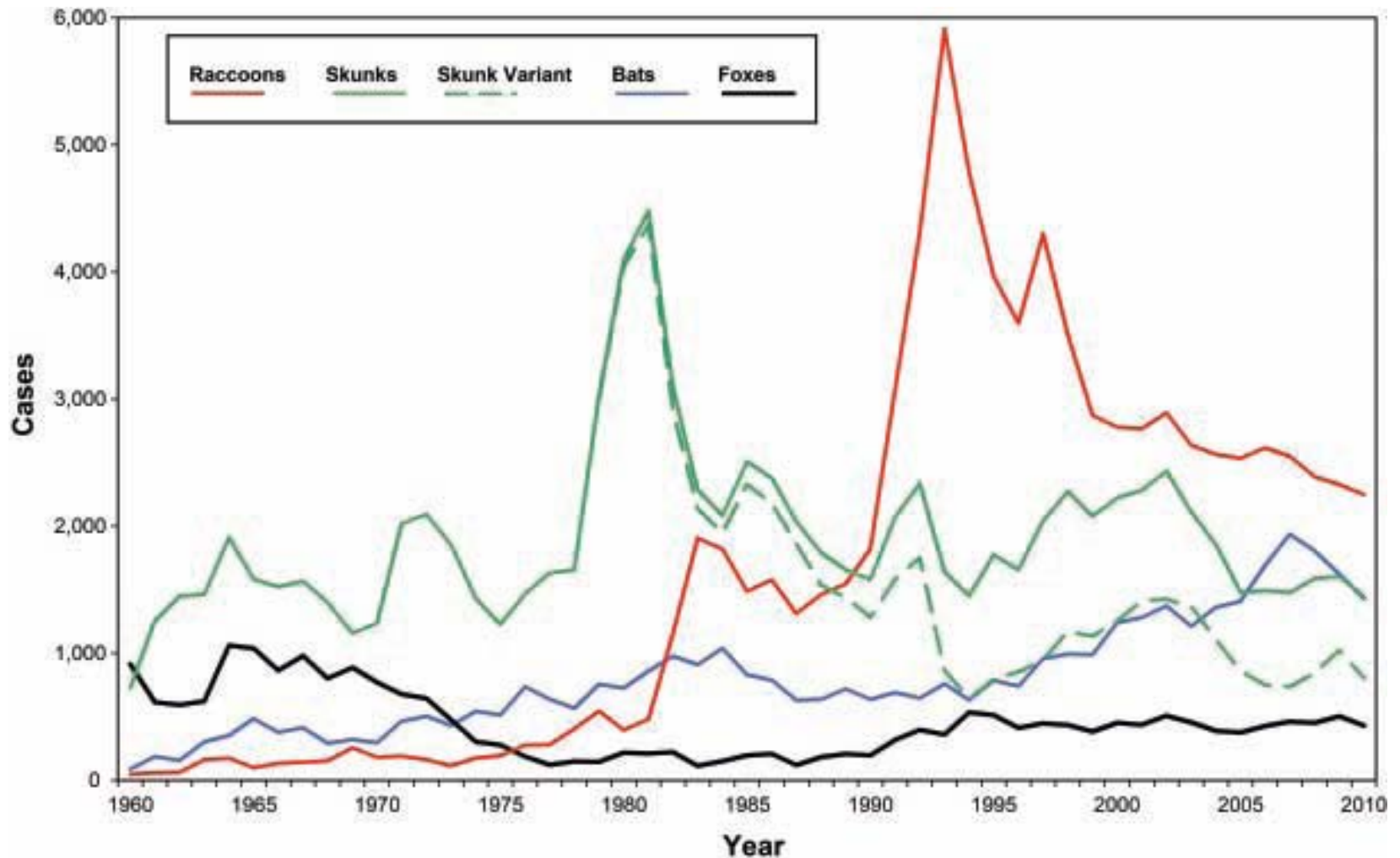
- Occasionally, switching of rabies virus variants to new host species occurs.
  - Canine virus variants were probably the source of some fox and skunk variants.
  - More recently, skunk variants have apparently adapted to other hosts (e.g., New Mexico).

# Hosts

- Host range –Since 1975, over 80% of the reported rabid animals in the U.S. have been wildlife.
- In 2010, 92% of rabid animals were wildlife species.



# Cases of rabies among wildlife in the United States, by year and species, 1960 to 2010.



# Virus and Host Adaptations

- Rabies involving distinct rabies virus variants is associated with specific hosts (excluding bats) in geographically definable regions.
- Transmission is primarily between members of the same species (host adaptation).

# Virus and Host Adaptations

- Raccoon rabies virus variant transmitted to a raccoon is more likely to be maintained long enough to be transmitted to another host.
- Raccoon rabies virus variant transmitted to a cat is less likely (but not impossible) to be maintained long enough to be transmitted to another host.

# Distribution of Major Terrestrial Reservoirs of Rabies in the U.S. and Puerto Rico, 2010



# Hosts

- Resistance to **exposure** or **infection** can vary by:
  - Species (reservoir versus spillover)
  - Ecology – species that might not be exposed because of their ecological niche or may not survive exposure.
  - Location of the bite
  - Amount of virus in the saliva

# Rabies prevalence in U.S.

- Rabies in domestic animals has declined 80% since 1953 due to
  - Vaccines for companion animals (introduced in the late 1940's)
  - Leash laws
  - Removal of stray animals (e.g., animal control facilities and staffing)
- Since 1981 cat cases of rabies have exceeded dog cases.



# Rabies prevalence in U.S.

- Wild animals account for >90% of reported cases
- Increase of reports in wild animals since 1960
  - A true increase (raccoons) - from Mid-Atlantic to Northeast and Southeast
  - Increased surveillance.

# Surveillance continues....



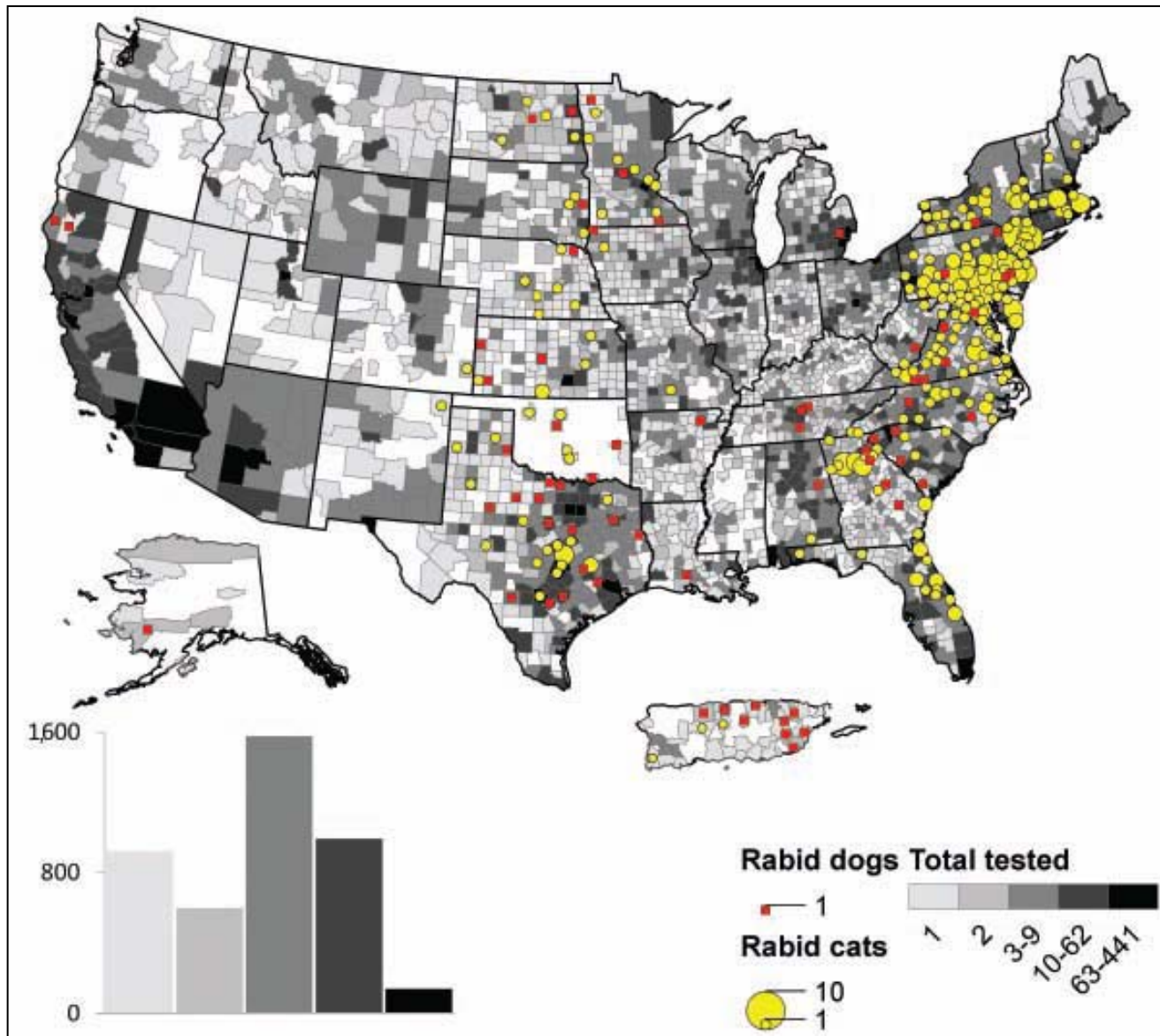
# Rabies surveillance in the United States during 2010

- Approximately 92% of reported rabid animals were wildlife.
  - 2,246 raccoons (36.5%)
  - 1,448 skunks (23.5%)
  - 1,430 bats (23.2%)
  - 429 foxes (6.9%)
  - **303 cats (4.9%) Most frequent domestic species**
  - 71 cattle (1.1%)
  - 69 dogs (1.1%)

# Rabies surveillance in the United States during 2010

- Compared with 2009, number of reported rabid animals decreased across all animal types **with the exception of a 1% increase in the number of reported rabid cats.**

# Reported cases of rabies in cats and dogs , 2010

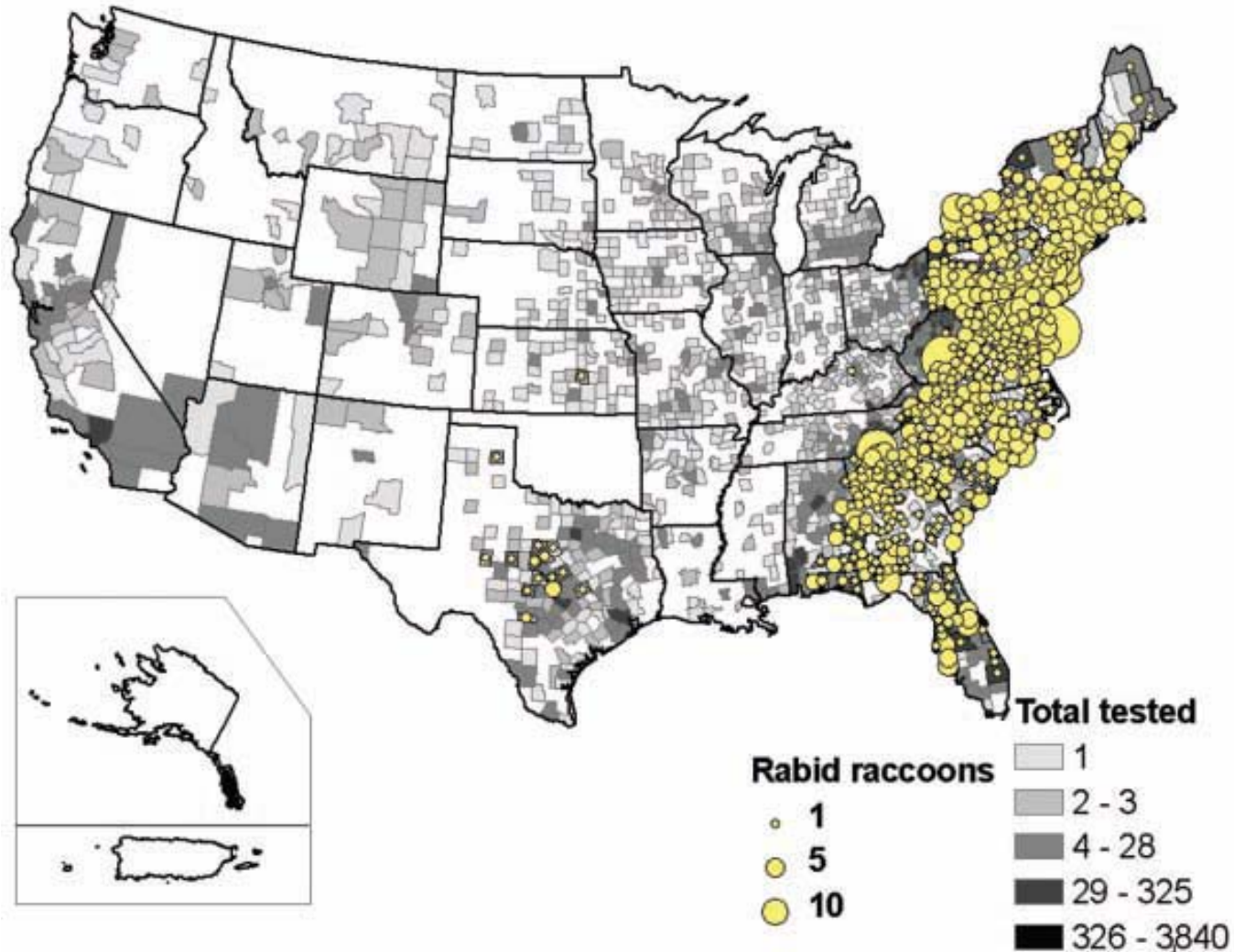


# Distribution of rabies virus in the Mid-Atlantic Region

- No prior rabies in terrestrial mammals prior to 1979.
- Raccoon virus variant had been endemic in South Florida since early 1900's.
- Illegal translocation of raccoons (some rabid) to W.V.
- Spread up and down the east coast.
- Multiple species affected in region, all with raccoon strain.



# Reported cases of rabies in **raccoons**, by county, 2009



# Why is raccoon rabies problematic?

- Raccoons thrive in suburban settings
- Aggressive and swift
  - Increase in dog and cat (2X) rabies
  - Increase in other rabid species (foxes, groundhogs, livestock, etc.)
- Increase in human exposures, need for PEP risk assessment, animal control calls

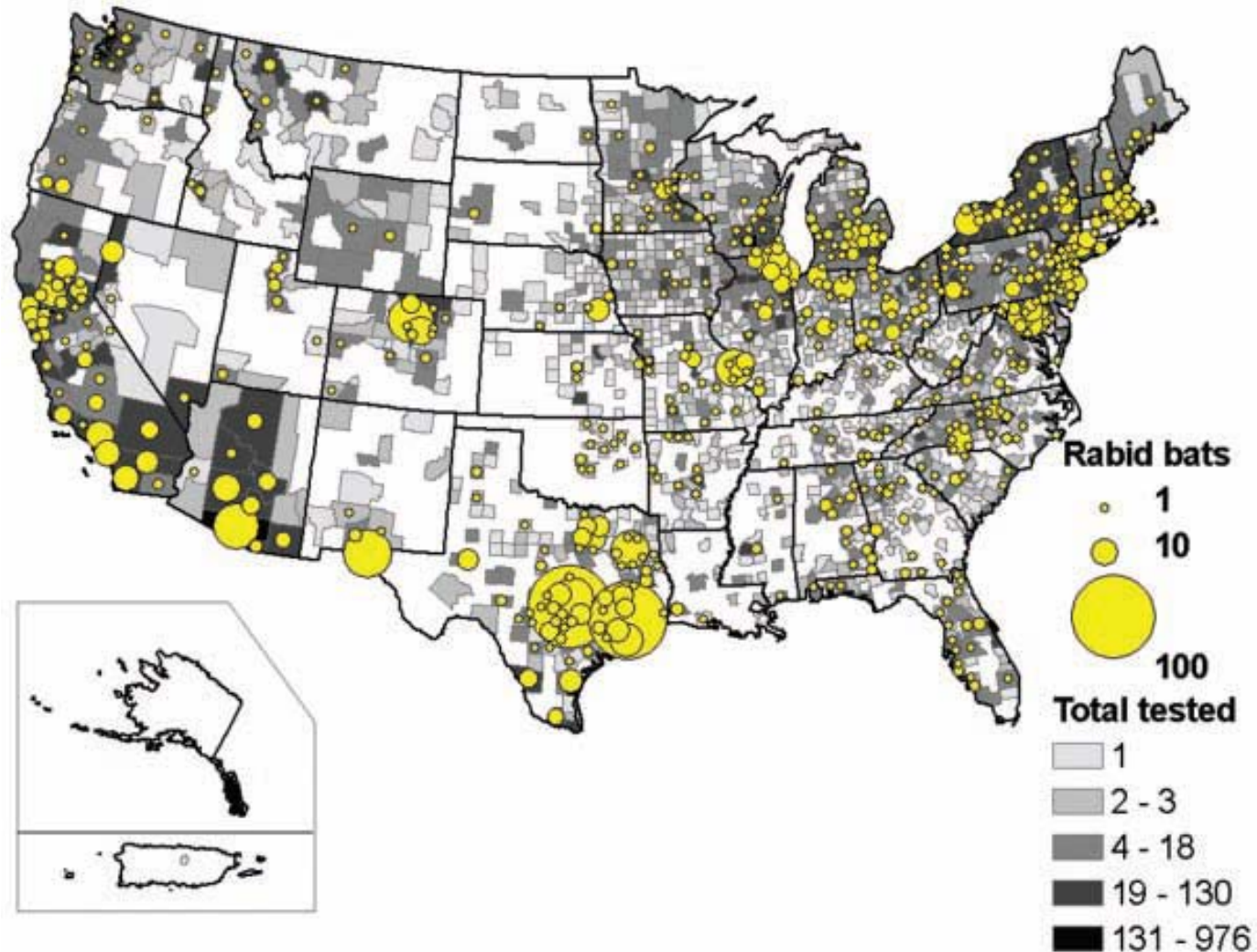


# Distribution of **bat** rabies virus

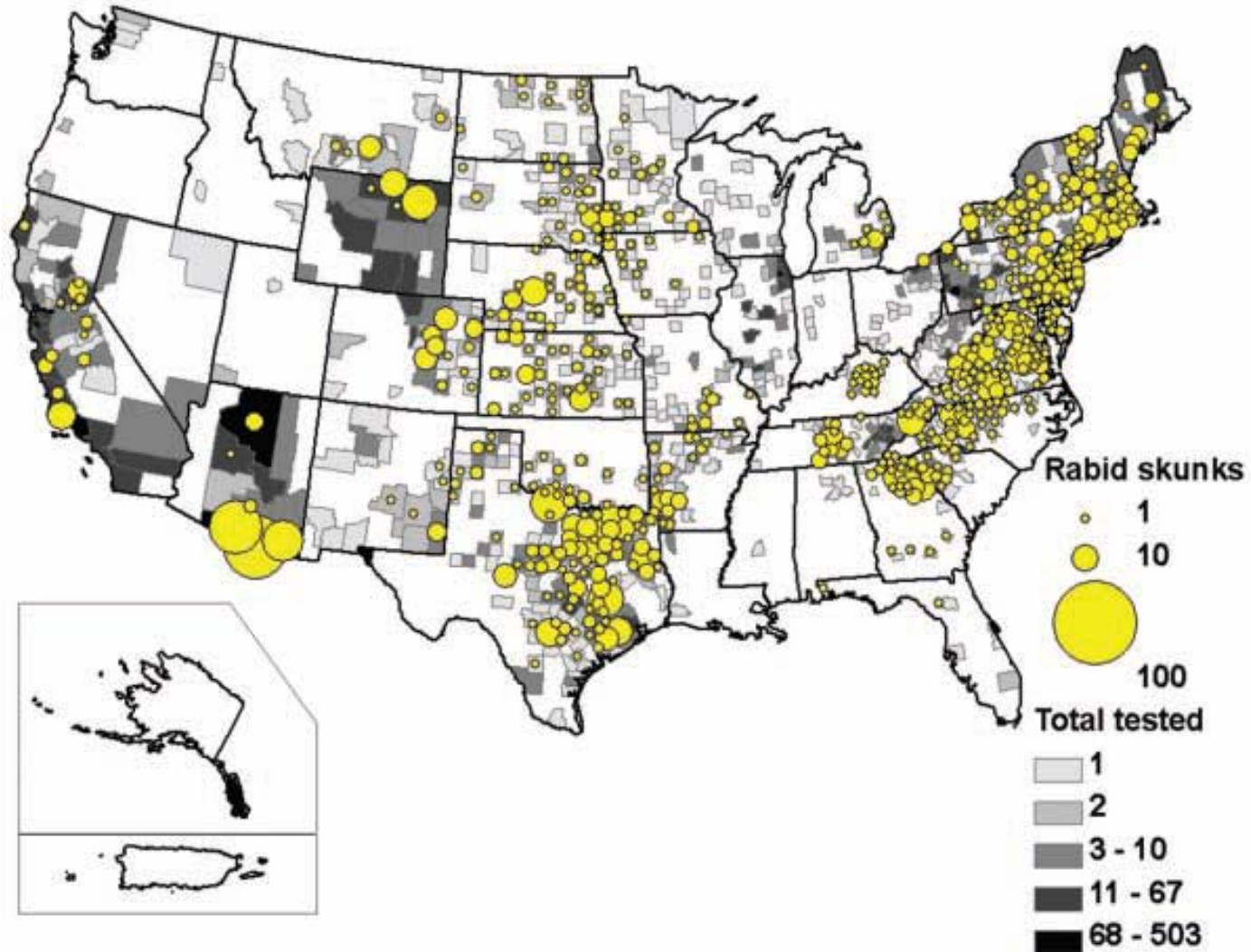
- All 49 continental United States
- Ongoing work to associate strains with species and geographic location
- Strains differ from terrestrial mammals.



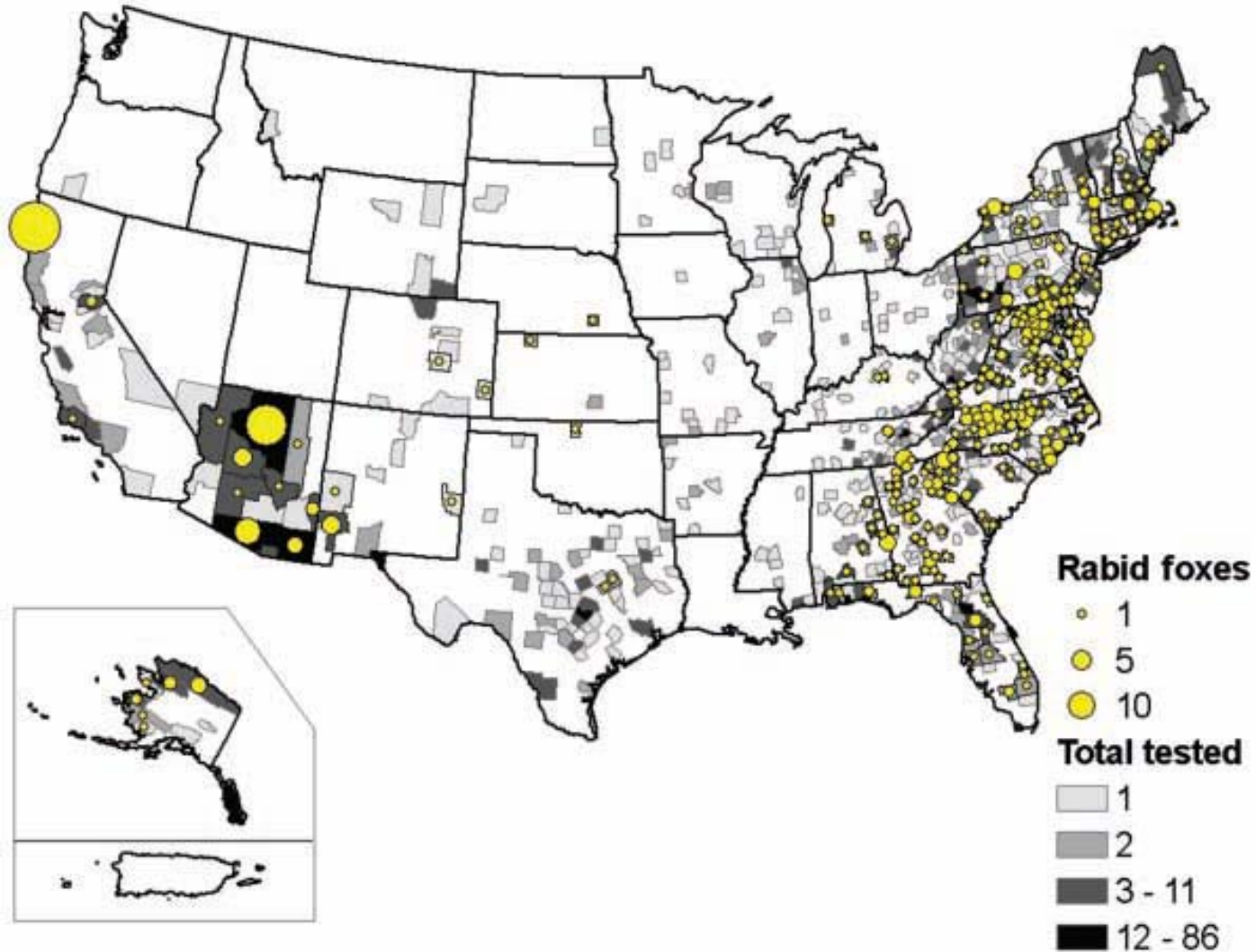
# Reported cases of rabies in **bats**, by county, 2009



# Reported cases of rabies in **skunks**, by county, 2009



# Reported cases of rabies in **foxes**, by county, 2009





Rabies in  
**other** wild  
animals  
in the U.S.,  
2009

Species	Number
Ground hogs	32
Bobcats	30
Coyotes	11
Fishers	3
Opossums	3
Beavers	2
White-tailed deer	2
River otters	2
Squirrels	2
Cougar	1
Muskrat	1
Rabbit (unspec.)	1
Ringtail cat	1
Wolf	1

# Rabies in rodents and lagomorphs

- Cases are rare but these species are susceptible.
- No role in epidemiology, dead end hosts.
- No human cases associated with exposure to rodents or lagomorphs.
- Rarely submitted for testing even with human bite exposure



# Rabies Transmission

Exposure is generally defined as **transdermal contact, typically by a bite, or mucosal contamination with potentially infectious material** (e.g., saliva or CNS tissue).



# Rabies Transmission

- The relative risk associated with other scenarios is difficult to define.
- Experimentally
  - Saliva to mucous membrane or abraded skin
  - Oral - ingestion of rabid animal (e.g., cat eating a rabid bat)





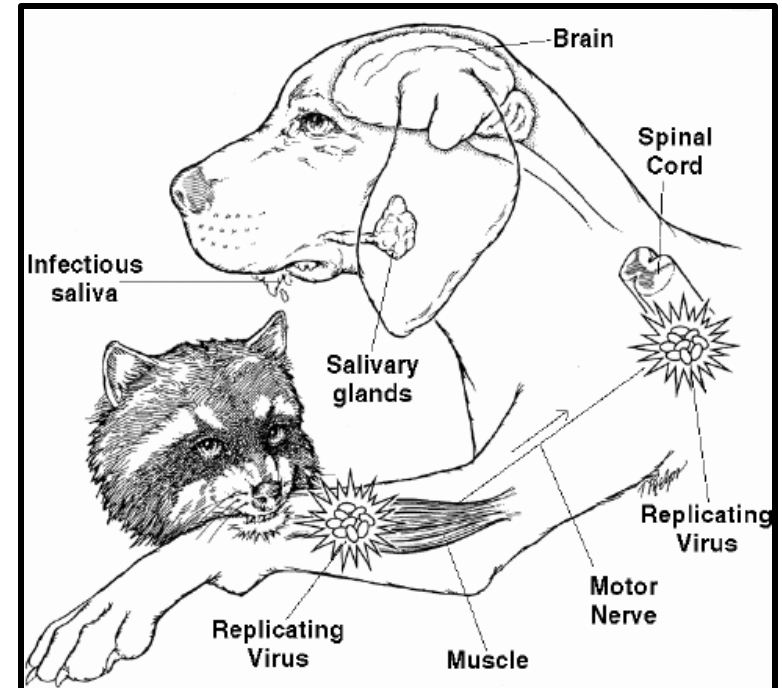
# Rabies Transmission

- Bat to cat or other species transmission may occur when no terrestrial animal reservoirs are present.
- Aerosol (rare) - laboratory, bat caves?
- Human to human – transplants only



# Pathogenesis

- Virus enters SQ or IM
- Replicates at site
- Moves to nerve root ganglia
- Replicates again
- Spreads to the CNS
- Vital nerve centers infected - irritable/aggressive
- Centrifugal spread to salivary glands, skin, etc.
- Secreted with saliva → communicable



# Period of Communicability

- Definition- the period of time during which a rabid animal is shedding virus in the saliva and therefore capable of transmitting rabies to a susceptible host.



# Period of Communicability

- Dog, cat and ferret
  - **May** shed up to 3 days prior to clinical signs until death.
  - Death usually occurs 3-5 days after clinical signs.
- Basis for 10-day quarantine if dog, cat or ferret bites a person.
- Other species - unknown



# Incubation period

- Definition - the period of time from infection (exposure) until the onset of clinical signs (disease)
- Basis for 45-day or 6-month quarantine if dog, cat or ferret is exposed to rabies



# Incubation period

- Dog - average 3-8 weeks, 10 days to 6 months
- Cat (experimental) - 9-51 days, median 18
- Ferret- preliminary data - 10-41 days
- People- average 1.5 - 4 mo  
(range, 9 days-7yrs?)
- Extremes - >1 year wild animals & humans

# Incubation period

## *May be affected by:*

- Amount of inoculum
- Nerve supply at site
- Distance to CNS
- Host resistance
- Strain of virus?



# Source of infection

- Human exposure usually from domestic animals or bats.
- Domestic animals acquire infection from wild terrestrial animals or bats.
- Rabies not self perpetuating in domestic animals except for dogs in Mexico, Latin America, Asia and Africa.





# Rabies - Clinical signs

## Dog - (canine strain)

- ◆ Prodrome (2-3 days)
- ◆ Excitative phase “furious” (1-7 days)
- ◆ Paralytic phase “dumb form”
- ◆ May not see all stages
- ◆ Entire course < 10 days
- ◆ Variability of signs
  - Not diagnostic
  - D/D = any neurologic disease.

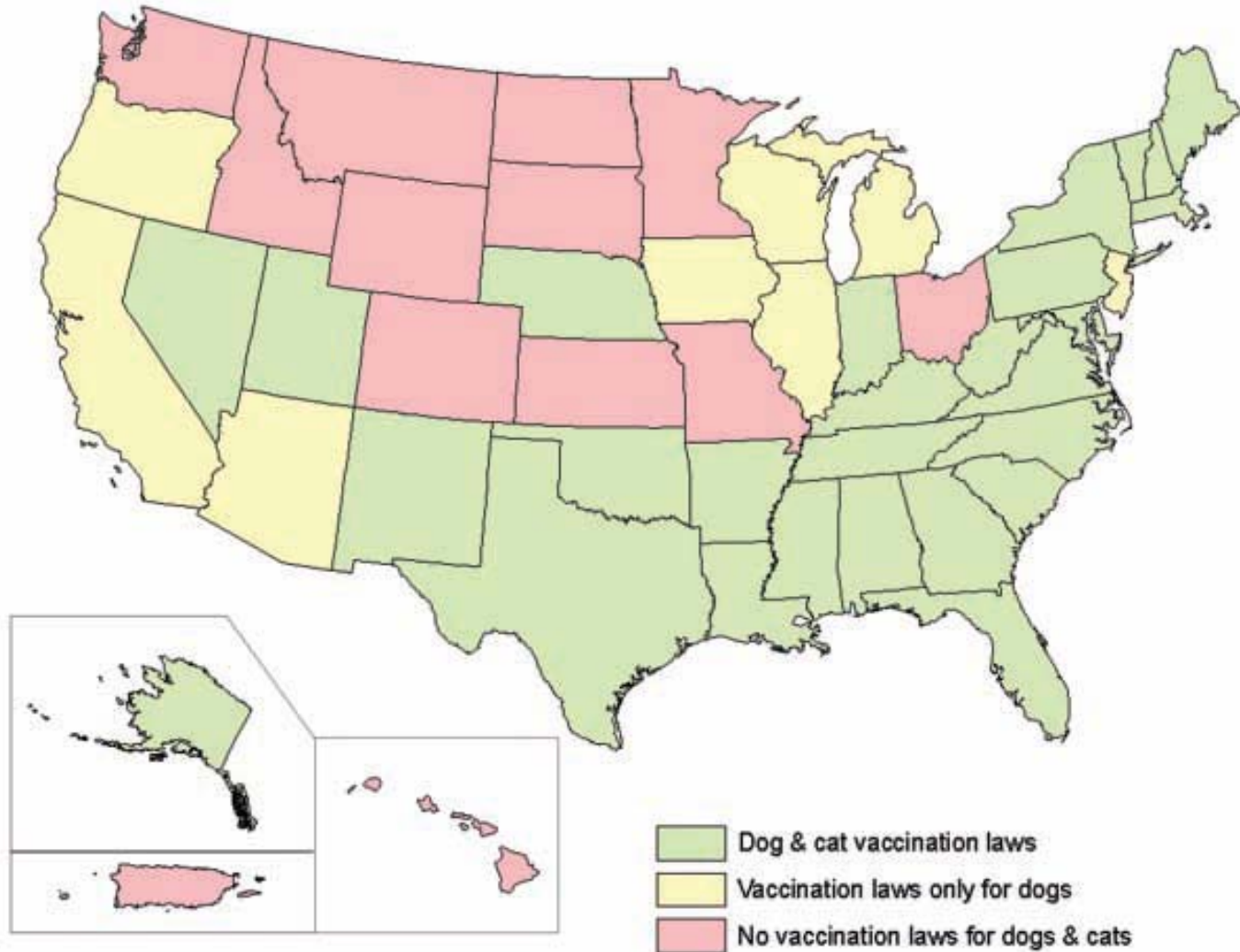


# Clinical signs - Cats

- ◆ Similar to dog
- ◆ Erratic and bizarre behavior
- ◆ Owners report early vocalization
- ◆ Can occur in very young.



# State legislation requiring rabies vaccination of cats and dogs, 2009



# Vaccination - Domestic animals

## Currently

- ◆ No MLV vaccines available in U.S.
- ◆ Inactivated (killed virus) vaccine only available for domestic animals
- ◆ Recombinant oral vaccine in wildlife
- ◆ NASPHV annual guidelines in JAVMA



# Vaccination - Domestic animals

Not considered vaccinated for 28 days after 1st inoculation.

If vaccination out of date, considered vaccinated at time booster is administered.



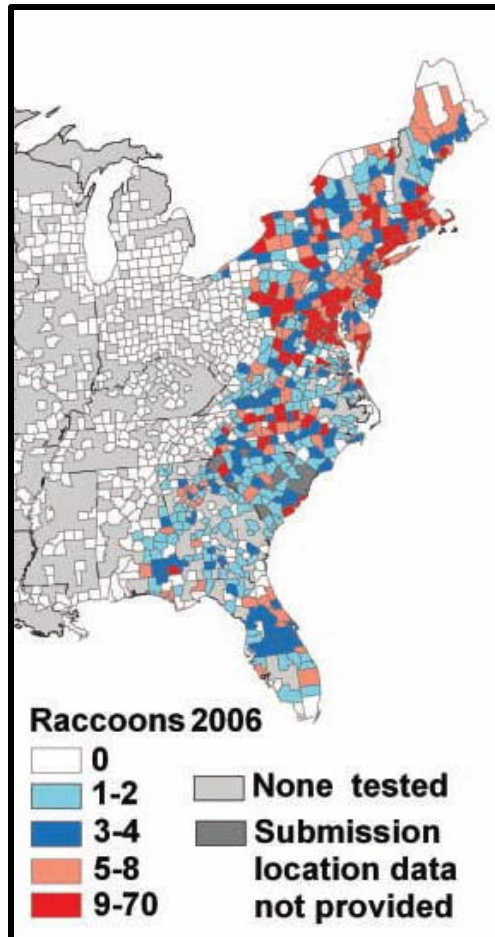
# Vaccination - Domestic animals

- Dogs, cats all given vaccine at 3 months and 1-year later; after that every 1 or 3 years.

**Second dose of vaccine after 1-year regardless of age.**



# ORV Barrier Zone for Raccoon Rabies in the United States



## Proposed ORV



# Data Gaps

- Specific sources (reservoir species of origin) and relative proportion of rabid cats infected by each variant (e.g., from raccoons, skunks, bats?)
- Behavioral components that inhibit or enhance exposure of free-roaming cats



# Data Gaps

- Probability of FR cats having a zoonotic disease agent and risk of transmission to humans or other domestic animals.
- Effect of a single dose of rabies vaccine used on individuals in a free-roaming cat colony (2 years?) and effect on population (herd immunity?)

# Data Gaps

- Immigration and emigration in various habitats (rural, semi-urban, urban), seasonal, etc.
- Data on feral or free-roaming cat survival (death rates) and birth rates by age classes and spayed status.
- What happens to cats that disappear (death or emigration)?

# Data Gaps

- Denominator data (e.g., size of colony or community cat population)
- No data on:
  - Carrying capacity
  - Long-term “natural” cat populations
  - Survival following sterilization

# Resource Material

## **Compendium of Animal Rabies Prevention and Control, 2011**

Produced by the National Association of State  
Public Health Veterinarians, Inc. (NASPHV)

<http://www.nasphv.org/Documents/RabiesCompendium.pdf>

# Resource Material

**Rabies surveillance in the United States  
during 2010?**

Published annually in the JAVMA

**Posted on Wiggin site**

# Resource Material

## **Human Rabies Prevention - United States, 2008, ACIP Guidelines**

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5703a1.htm>

# The End

Dr John New  
jnew@utk.edu

