Rabies

Becky Reik

Emerging and Zoonotic Infectious Disease Section, MDHHS

MDHHS

Michigan Department of Health & Human Services

DISCLOSURE

I have no actual or potential conflict of interest in relation to this program/presentation.

MDHHS
Michigan Department of Health & Human Services

Origin of rabies

- Rabies is among the earliest recognized infectious diseases of man
- There are references to the consequences of bites from “mad” dogs in Mesopotamian writings from thousands of years ago
- A 15th century Italian scientist contributed to the evolving “germ theory” of the time, referring to the “incurable wound” associated with likely rabies exposure
- In Greek mythology, “LYSSA” was a spirit associated with rage, fury, madness and frenzy
- In Latin, “rabere” means to be mad or rave

Furious Rabies: Late Stage.

Who can get rabies?

Photo: CDC

- All mammals are susceptible to rabies.
- Bats and carnivores are the major natural reservoirs.
- Humans can get rabies *IF* rabies post-exposure prophylaxis (PEP) isn't given after an exposure.

How does it spread?

- Rabies virus is contained in the saliva and brain tissue of an infected animal
- Transmission of rabies virus usually begins when infected saliva of a host is passed to an uninfected animal

Photo: CDC

Modes of transmission

- BITES (most common way rabies is transmitted)
- Non-bite
  - Saliva or brain tissue on a mucous membrane, fresh broken skin
  - Aerosols-documented, in laboratory setting
  - Very rare: human to human-through organ and tissue transplantation; corneas (8 cases), other organs (3 cases)
- Casual contact, such as touching an animal or person with rabies or contact with non-infectious fluid or tissue (urine, blood, feces) does not constitute an exposure

Photo: CDC

Path of the virus

- Virus travels from the site of the bite (limited replication at the bite site, then penetrate peripheral nerves, both sensory and motor), then travels towards the brain*
- Virus reaches the brain and begins to multiply there and cause inflammation. This is the point where symptoms may begin. Incubation period is generally 3-12 weeks, but can vary due to many factors
- Once replication in the brain starts, the virus spreads to the salivary glands (best way to infect a new host)
- Death typically occurs within 7 days of symptom onset.

Photo: CDC

*Gluska S, et al. (2014) Rabies Virus Hijacks and Accelerates the p75NTR Retrograde Axonal Transport Machinery. PLoS Pathog10(8): e1004348. https://doi.org/10.1371/journal.ppat.1004348

Incubation vs infectious period

- The **incubation period** is the time between infection (a bite) and when symptoms begin.
  - This is the window when rabies PEP can prevent illness
- When the virus reaches the brain, it causes inflammation and the onset of clinical signs.
  - After this point, it is too late for rabies PEP
- Then the virus reaches the salivary glands and can be spread to others.
- The **infectious period** is the time between the virus reaching the salivary glands and death.

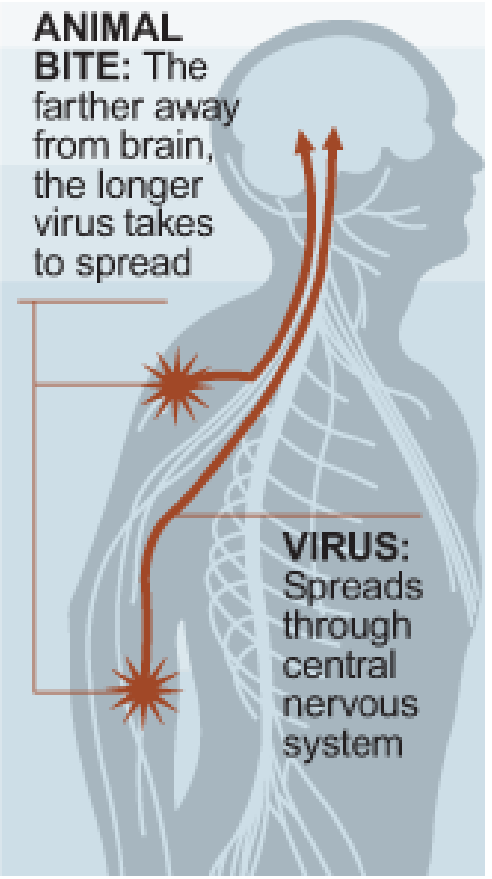


Image: The World Book Medical Encyclopedia

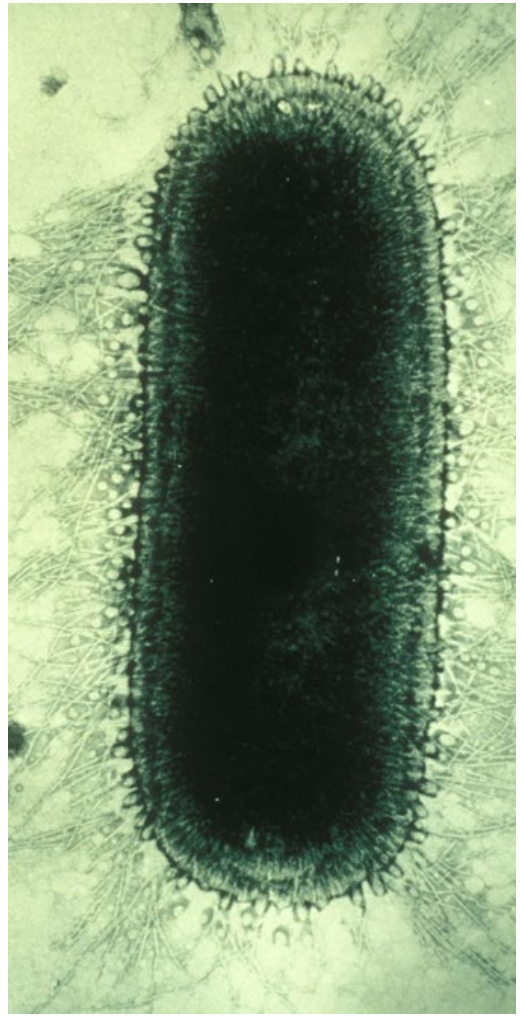
Rabies in humans

- The first symptoms of rabies may be flu-like, including general weakness or discomfort, fever, or headache.
- Patients often describe discomfort or a prickling or itching sensation at the site of bite. Within days, symptoms may progress to include anxiety, confusion, or agitation. As the disease progresses, the person may experience delirium, abnormal behavior, hallucinations, and insomnia.
- Hydrophobia, aerophobia, photophobia, and phonophobia occur in less than 50% of patients
- The acute period of disease typically ends after 2 to 10 days. Once clinical signs of rabies appear, the disease is nearly always fatal, and treatment is typically supportive.
- Documented cases of human survival from clinical rabies remain rare.
- Death is usually due to respiratory failure or cardiac arrest

Photo: CDC

Rabies virus outside of a host

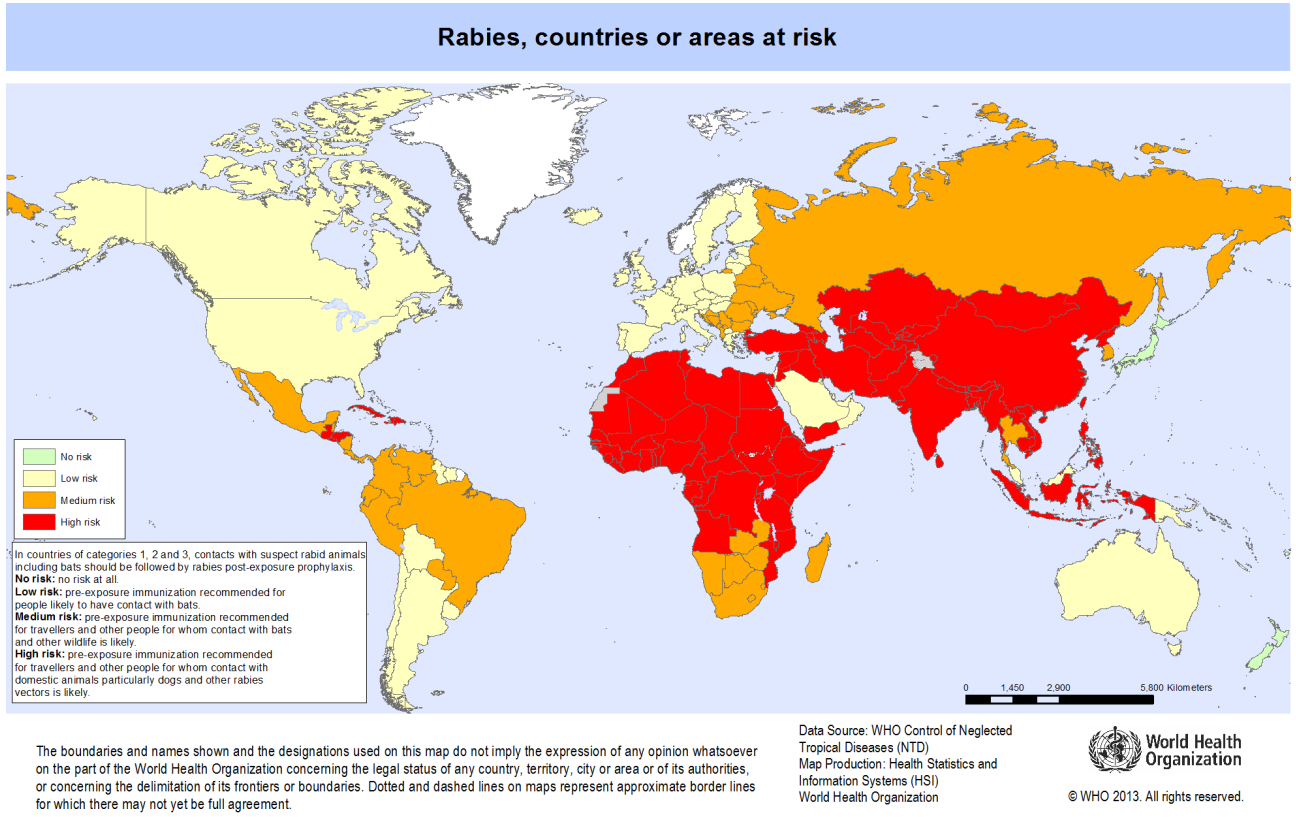
- Rabies is not a hardy virus outside of a host.
- Common disinfectants will kill the rabies virus.
- Rabies virus becomes noninfectious when it **dries out** and when it is **exposed to sunlight**.
- Different environmental conditions affect the rate at which the virus becomes inactive, but in general, if the material containing the virus is dry, the virus can be considered noninfectious[1].



[1] CDC “How is rabies transmitted?” https://www.cdc.gov/rabies/transmission/index.html

Photo: Norden, a Smith-Kline Company

Global distribution and risk



Source: WHO

- Found on every continent except Antarctica
- Around the world, rabies kills more than 59,000 people every year—that is nearly one death every nine minutes
- **Globally, 98% of rabies deaths are a result of dog bites**
- Most affected are countries in Africa and Asia
- Almost half of the victims are children under the age of 15 years

Global vs. US risk

Worldwide

Dogs are responsible for >90% of global rabies human deaths.

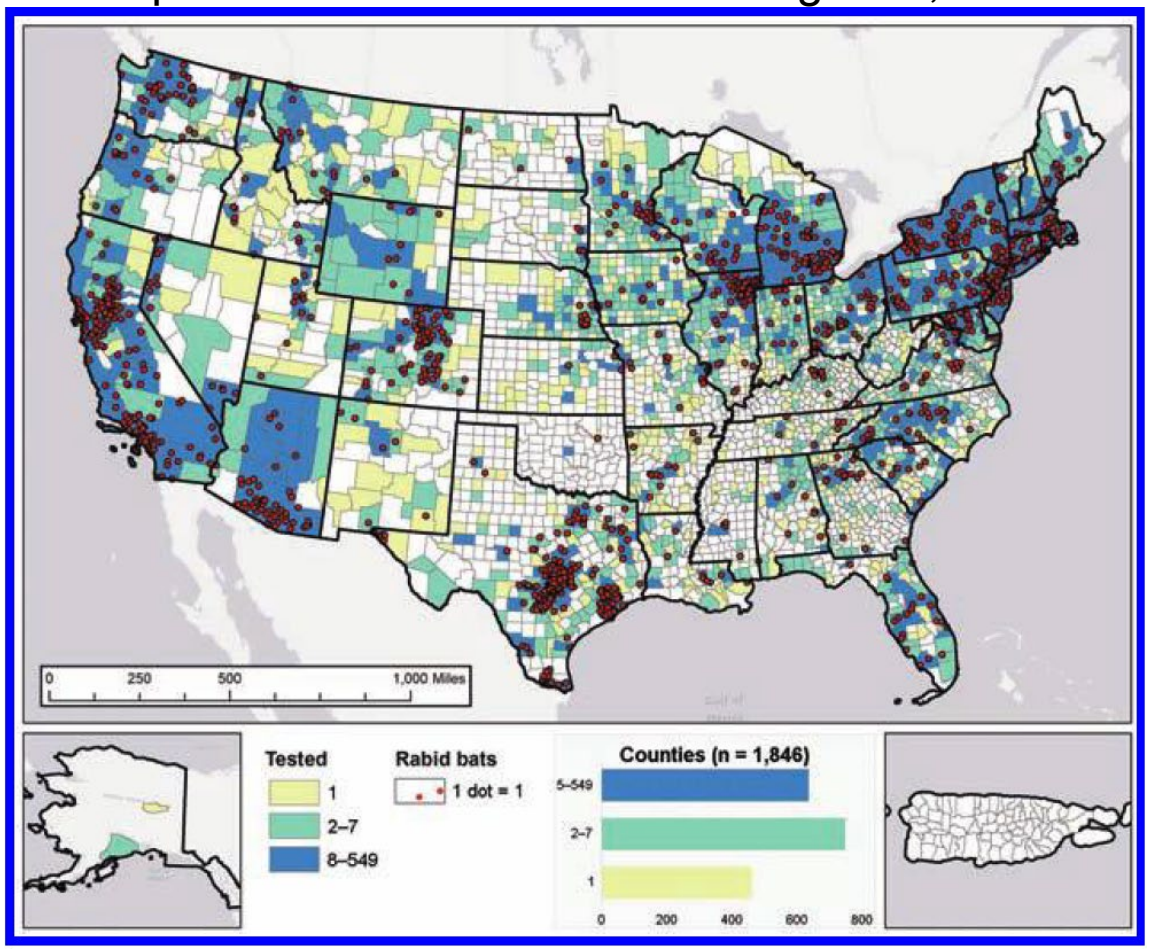
United States

Bats are responsible for >70% of U.S. rabies human deaths

Bats and rabies

- In 2015, for the first time, bats were the most frequently reported rabid animal in the U.S. (31%), surpassing raccoons
- At least 20 rabies virus variants associated with bats
- Surveys of bat populations have found a low prevalence of rabies (0-0.5%)[1]
- Bats likely die from rabies, but surveys also show evidence of survival, although low level (antibodies to rabies)[2]
- Don't know how long a bat might shed virus and be infectious
- In the U.S., human cases of rabies are most often associated with bat variants

Reported cases of rabies involving bats, 2018



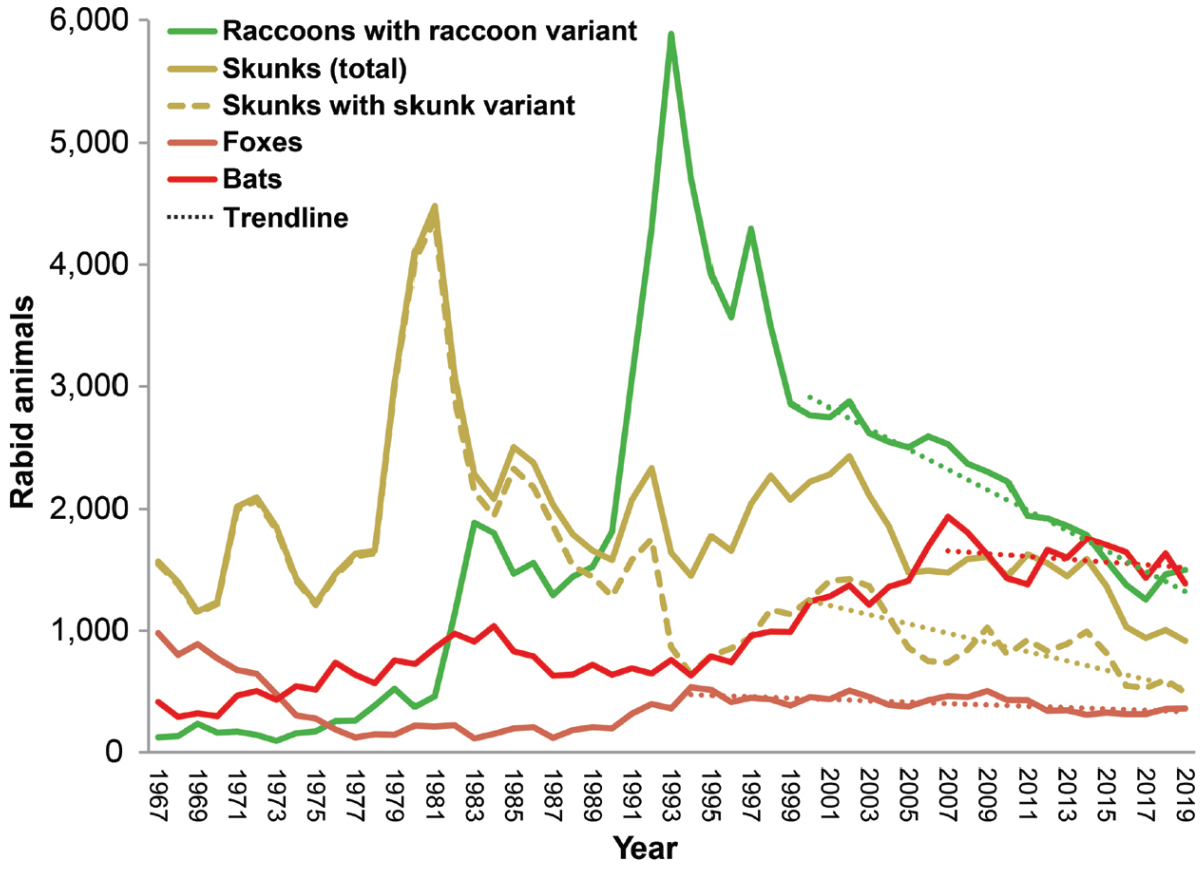
[1] Kuzman and Rupprecht, 2007, "Bat Rabies", In: Rabies, pp259-307, Academic Press.

[2] Bowman, RA et al, Journal of Wildlife Diseases; 49(2), 2013, pp 367-374.

JAVMA • Vol 256 • No. 2 • Jan 15, 2020

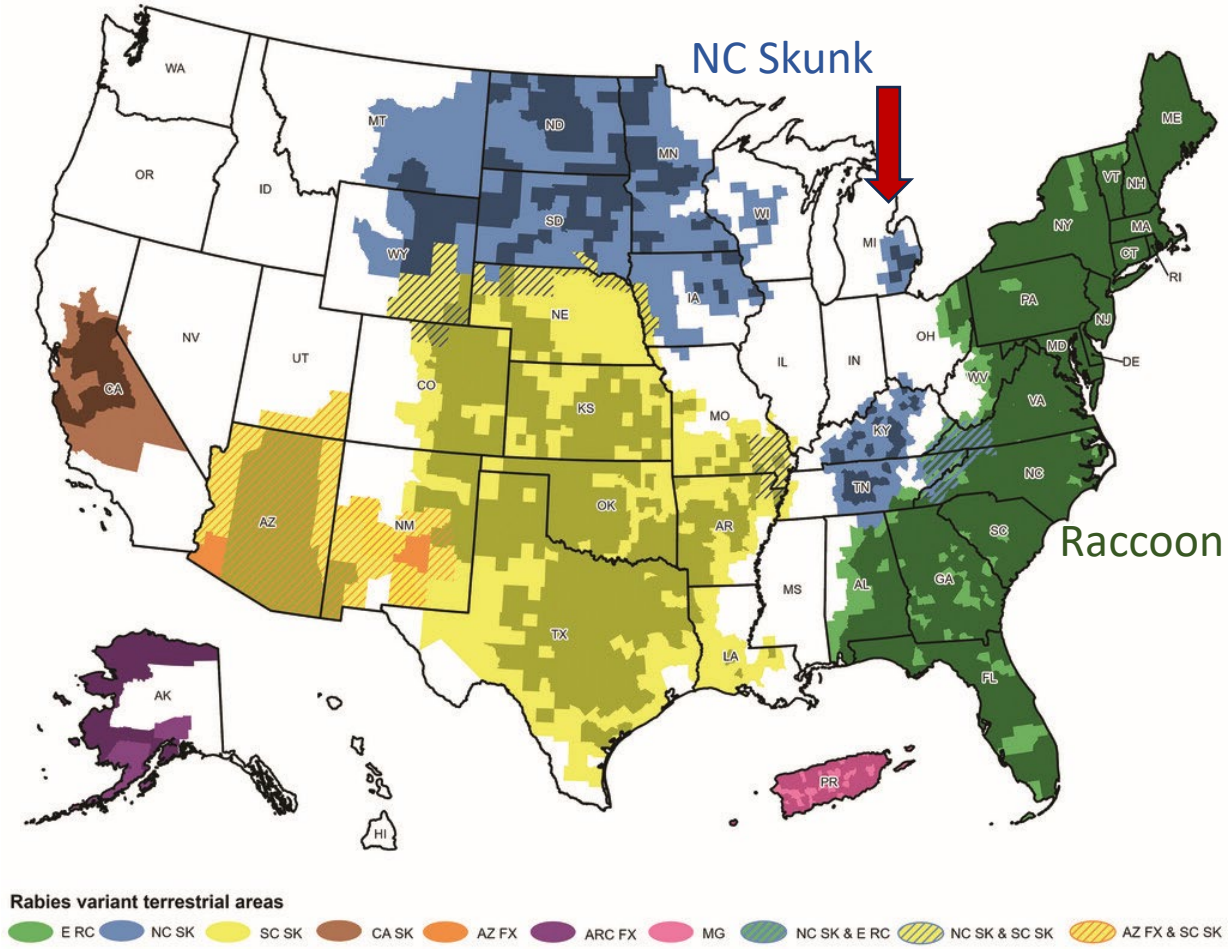
Characteristics of Rabies in the U.S.

Cases of rabies among wildlife in the United States, by year and species, 1967 through 2019



https://doi.org/10.2460/javma.258.11.1205

U.S. terrestrial rabies virus variants



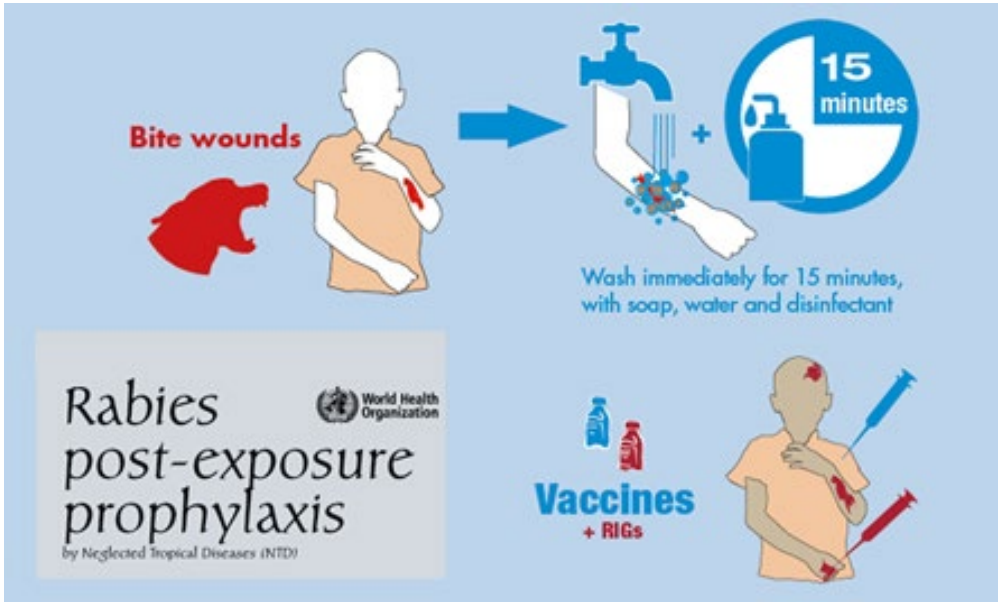
- Transmission can occur across species (e.g. from raccoon to cat), but rabies variants have adapted to specific host species.
- Rabies virus variants associated with terrestrial species occur in distinct geographic regions.
- In Michigan, the North Central skunk variant is found in southeast Michigan.

JAVMA • Vol 260 • No. 10 • July 2022

Raccoon Variant Rabies

- USDA expends a large amount of time, money, and effort to prevent westward spread of raccoon variant rabies.
- Raccoon variant rabies (or raccoon-strain rabies-RSR) in the U.S. is an example of how translocation of wildlife can lead to an epizootic outbreak
- In 2023, a 5-week-old stray kitten in Omaha, NE tested positive for raccoon variant rabies.
  - Probably a result of translocation of mother cat
  - 335 raccoons were trapped and tested
  - 18,000 vaccine baits were distributed

Human cases are now rare in the U.S.



- One to three cases reported annually in the U.S.
- Animal control and vaccination programs begun in the 1940s have eliminated domestic dogs as a reservoir of rabies in the U.S.
- Rabies PEP is expensive, but effective.
- Fatalities occur in people who fail to seek medical attention, usually because they are unaware of the risk for rabies.

U.S. Annual Public Health Burden of Rabies

- On average, 1-2 cases of human rabies are diagnosed each year
- An estimated 40,000-60,000 human rabies post-exposure treatments administered
- 4500-5000 pre-exposure vaccines administered
- 200,000-220,000 doses of human rabies vaccine administered
- Estimated $245-510 million to prevent rabies (vaccinate dogs, animal testing, biologics)
- Human mediated translocation is threat to wildlife control programs

Rabies testing for diagnosis and surveillance

Human Testing -Variety of assays, including DFA, PCR, IFA, exclusively performed at the Centers for Disease Control and Prevention (must get prior approval for testing from CDC staff)

- Can only identify disease AFTER encephalitis occurs (does not work for healthy people)
- Required specimens: CSF, serum, saliva and skin biopsy (antemortem); brain tissue (postmortem)

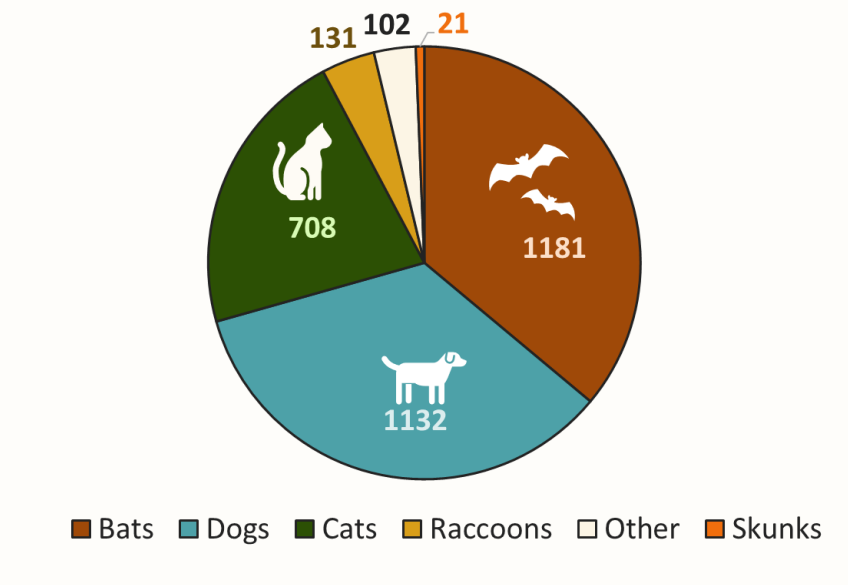
Animal Testing (exposure)-DFA performed at MDHHS Bureau of Laboratories

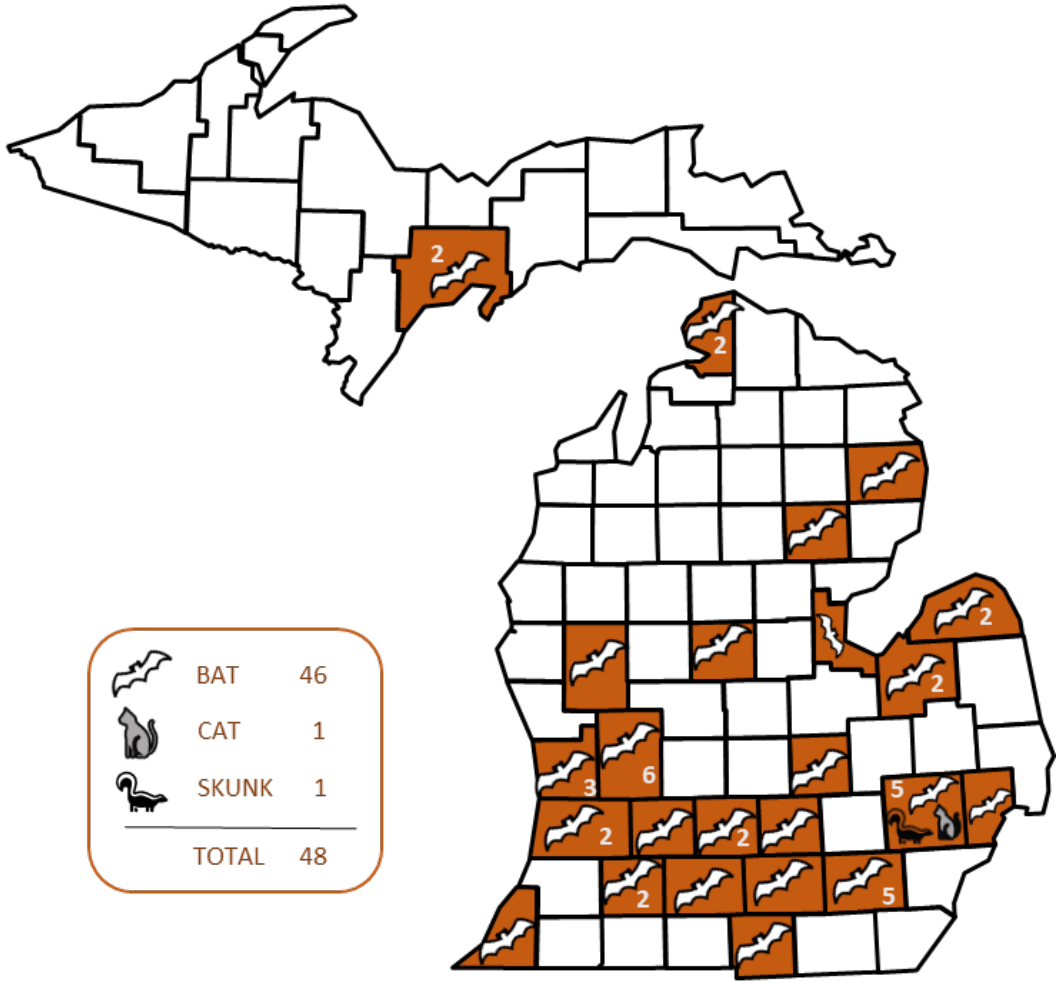
- Required specimens: brain and spinal cord (whole bats and animal heads/brains accepted)
- Testing is FREE (covered by state funding)
- Requires overnight shipping, which is not covered by state funding

Wildlife Testing (wildlife disease surveillance)-performed by USDA/WS staff

- Direct Rabies Immunohistochemistry Test (DRIT)-field test performed by trained wildlife biologists for the purpose of surveillance for rabies in wildlife species – research use only

2022 MDHHS Rabies Testing





Dogs and cats account for the majority of submissions, but bats and skunks are most likely to test positive.

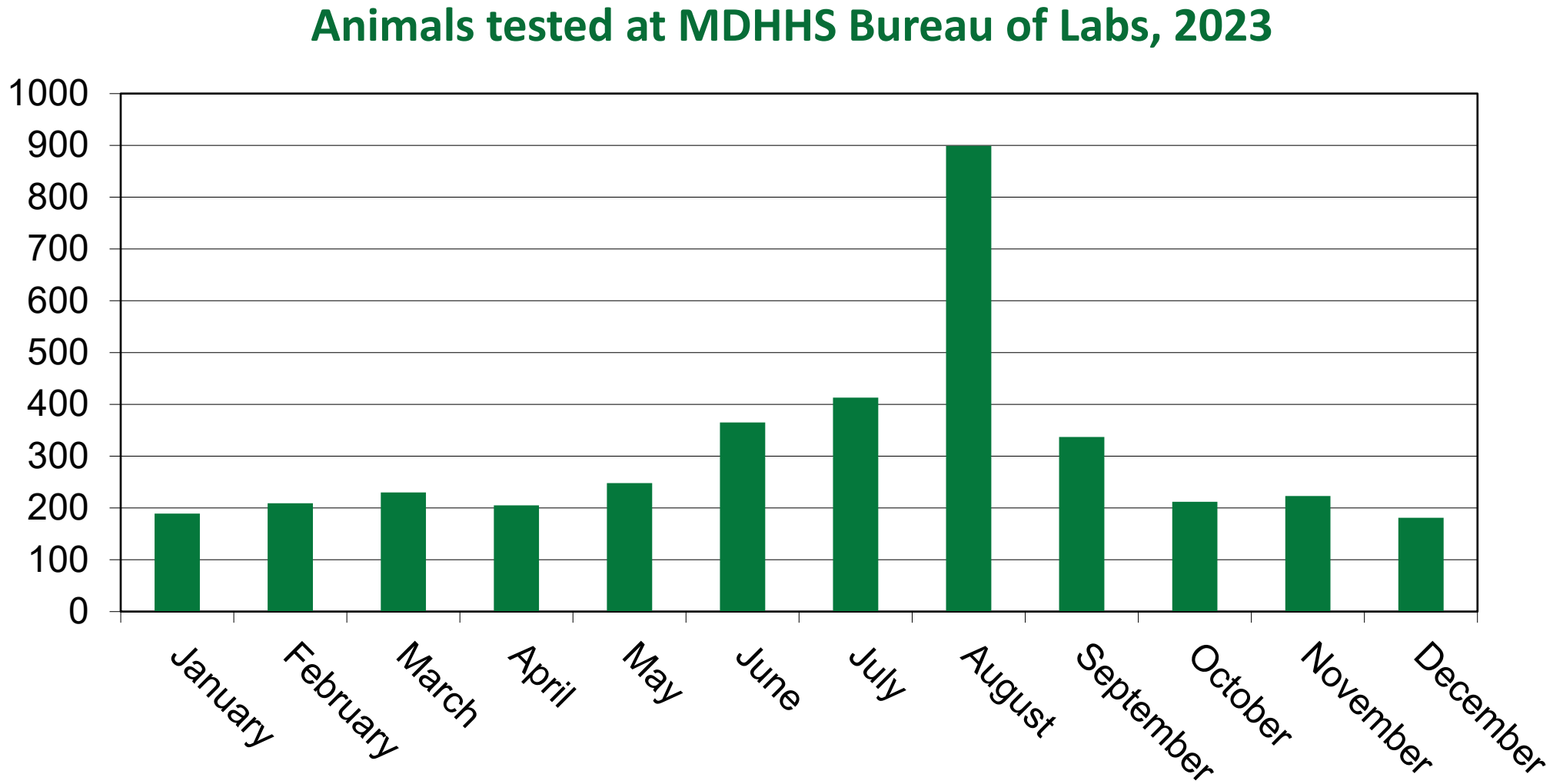
Bats and people

- Recent data suggest that transmission of rabies virus can occur from minor, seemingly unimportant, or unrecognized bites from bats.
- This is probably part of the explanation for why bats are responsible for majority of U.S. human deaths
- When bats are released and can't be tested, exposed people are recommended to receive PEP.
- We'd much rather test the bat!

Figure 10. A rabid red bat, showing the small teeth.

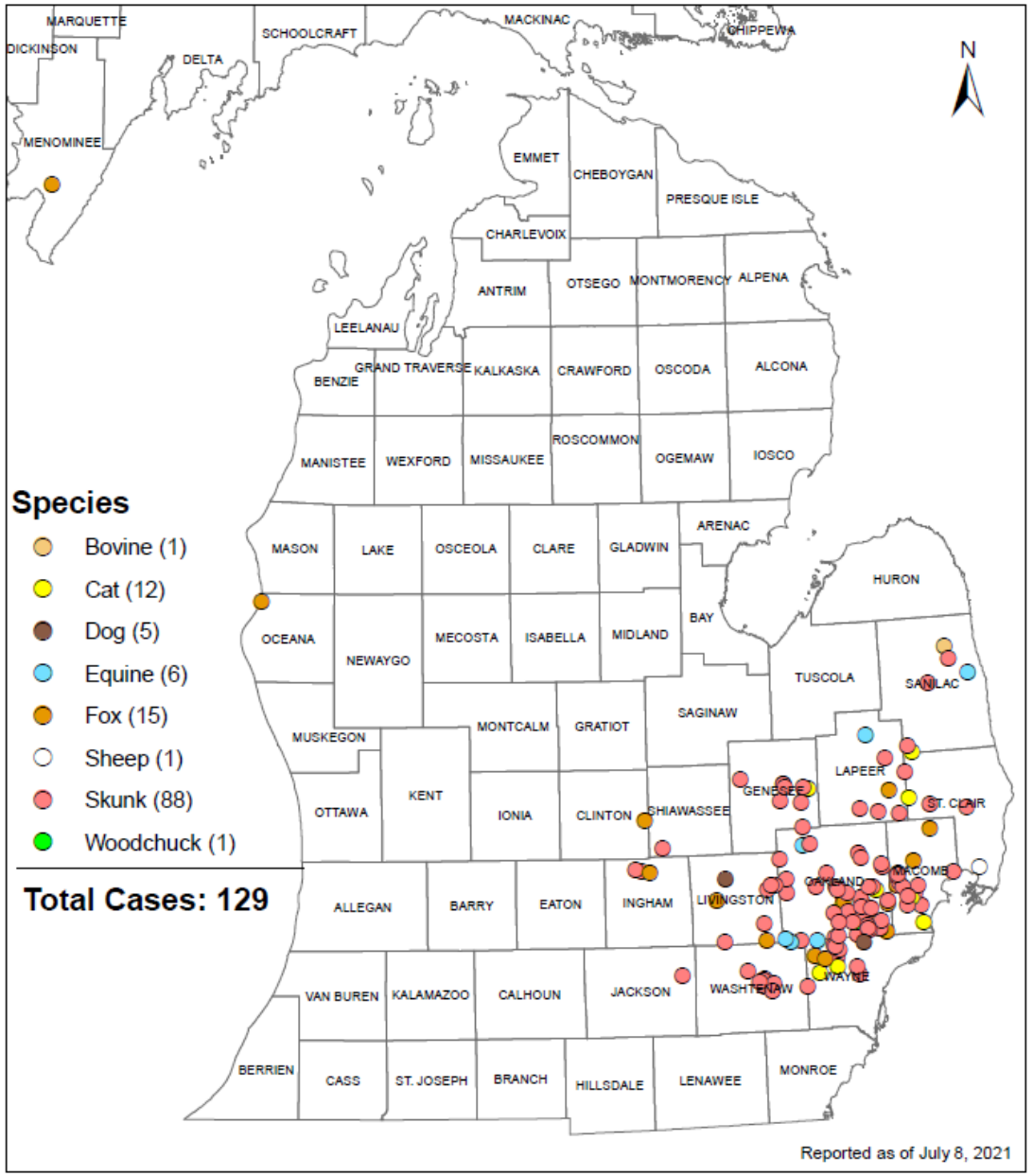
The Lancet Infectious Diseases
Volume 2 , Issue 6 , 327 - 343

Rabies Testing Seasonal Trends



Terrestrial (Non-Bat) Rabies in Michigan, 2003-2021

www.michigan.gov/rabies

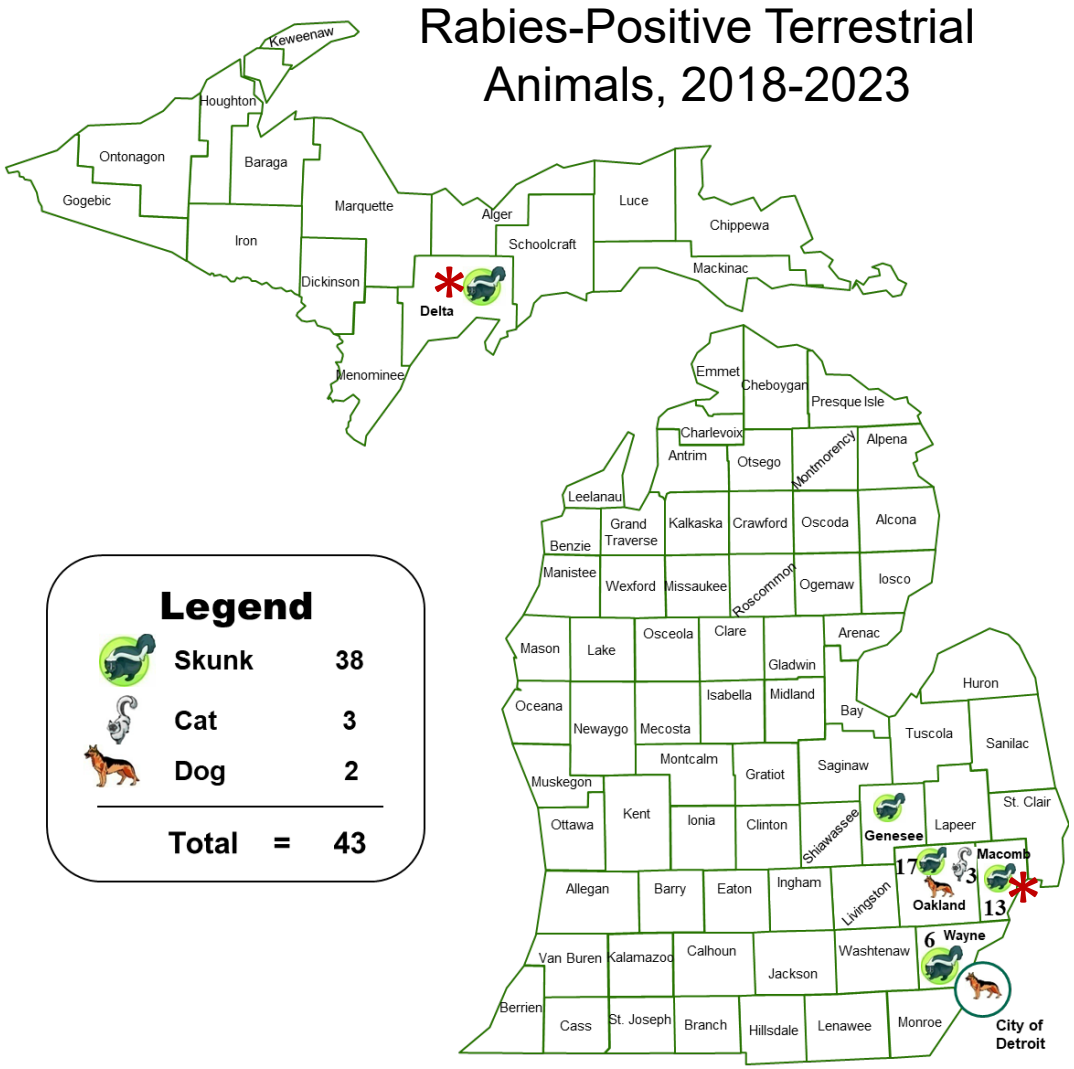


MDHHS
Michigan Department of Health & Human Services

For more information please visit:
www.michigan.gov/rabies
or
www.cdc.gov/rabies

Skunk variant rabies in Michigan

- North central skunk variant present in southeast Michigan
- Occasionally spills over into other species (3 cats, 2 dogs)
- Rabies risk assessment for domestic animal bites differs for these endemic counties in Michigan vs non-endemic counties
- Tends to have a cyclical trend that may relate to fluctuating population levels

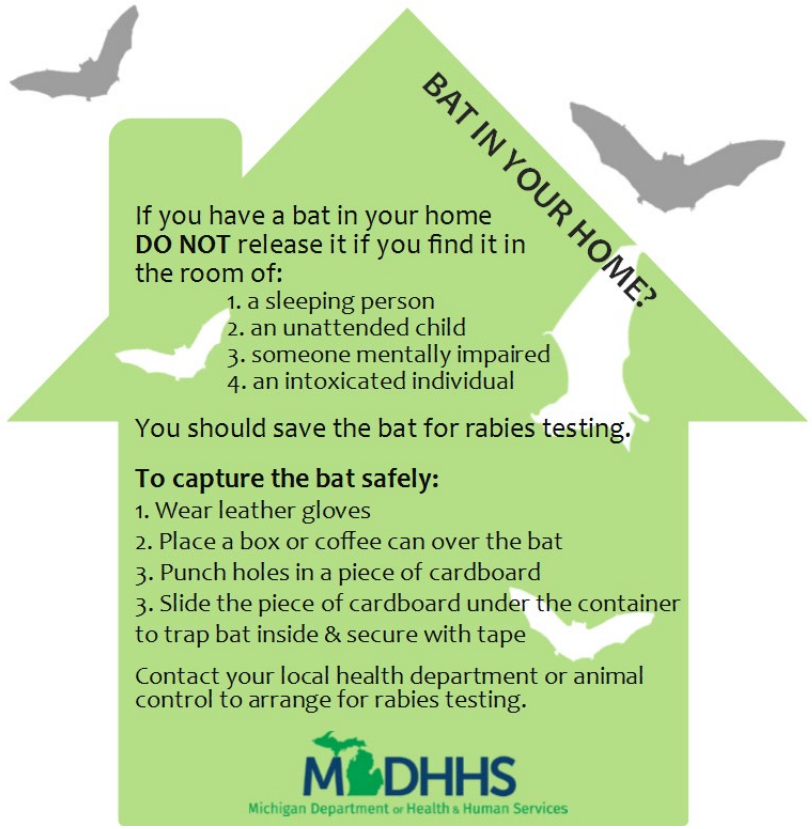


Rabies Death in Northern Michigan, 2009

A Northern Michigan man died of rabies due to a bat variant.

Woke to a bat on his arm, didn't tell his wife. Told others, but nobody mentioned to him that rabies was a concern.

Lesson: Education of the general public is needed regarding rabies risk from even minor exposures to bats.



Thank you

MDHHS
Michigan Department of Health & Human Services