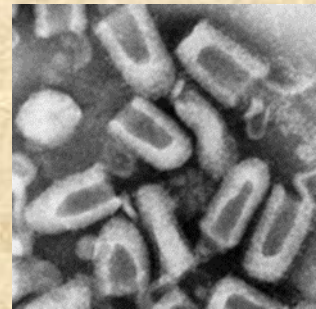
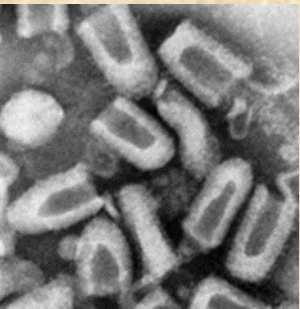




# Rabies Update: Epidemiology, Diagnostics, Treatment and More!

**Rodney E. Rohde**, PhD, MS, SM(ASCP)<sup>CM</sup>SV<sup>CM</sup>, MB<sup>CM</sup>, FACSc  
TEDx Speaker & Global Fellow – Global Citizenship Alliance  
Texas State Honorary Professor of International Studies  
*Regents' Professor*  
*University Distinguished Chair & Professor, Clinical Laboratory Science (CLS)*  
*Associate Director, Translational Health Research Initiative*  
*Past President, Texas Association for CLS*

**Texas State University**  
CLS, Encino Hall 363 (Dean, 201H)  
601 University Drive  
San Marcos, TX 78666-4616  
512-245-3300 (Dean); 512-245-2562 (CLS); 512-245-7860 (fax)  
Email: [rrohde@txstate.edu](mailto:rrohde@txstate.edu)

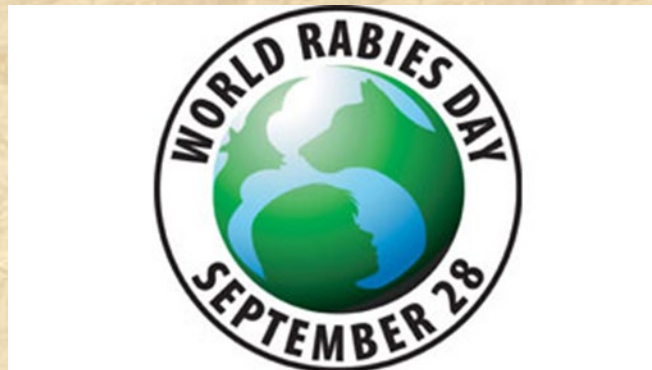


<https://www.elsevier.com/connect/8-things-you-may-not-know-about-rabies-but-should>



Raccoons are the most commonly reported rabid animal in the United States. (Photo © istock.com/Betty4240)

**Tell me what you know about rabies.....**



From Zoo to You

JUNE 12, 2019

# CDC: Bats Now Leading Cause of U.S. Fatal Rabies Cases

*By Tom Rosenthal*

Bites and scratches from bats infected with rabies are now the leading cause of rabies deaths among people in the United States, while rabid dogs that American travelers encounter overseas are the second-leading cause of rabies fatalities, the CDC announced in a Vital Signs report released today ([MMWR Morb Mortal Wkly Rep](#) 2019 Jun 12. [Epub ahead of print]).

Although the overall bat population in the United States is declining, bats are responsible for approximately seven in 10 rabies deaths among people infected with the rabies virus in the United States, according to the CDC.



More later...

# Rabies in the US 2021: 'This recent spate of cases is a sobering reminder that contact with bats poses a real health risk'

by NEWS DESK

January 7, 2022

Headlines, US News

1 Comment

Easy Print  
Print Manual (PDF)

OPEN

NewsDesk @infectiousdiseasenews

In 2021, the US Centers for Disease Control and Prevention (CDC) reported a total of five human rabies cases/deaths, including three cases from September to November linked to bat bites/exposure.



*Myotis lucifugus, or Little Brown Bat/CDC*

In today's **Morbidity and Mortality Weekly Report (MMWR)**, health officials discuss the three latter cases.

During September 28–November 10, 2021, CDC confirmed three human rabies deaths in the United States, **all in persons who did not seek postexposure prophylaxis (PEP)** after bat exposures that occurred during August 2021.

**CDC** Centers for Disease Control and Prevention  
CDC 24/7: Saving Lives. Protecting People™

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Morbidity and Mortality Weekly Report (MMWR)

CDC



## Notes from the Field: Three Human Rabies Deaths Attributed to Bat Exposures — United States, August 2021

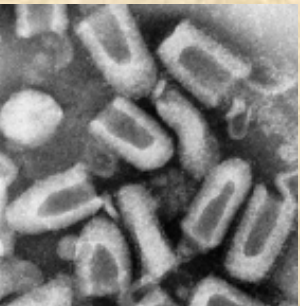
Weekly / January 7, 2022 / 71(1);31–32

Amber Kunkel, ScD<sup>1,2</sup>; Faisal S. Minhaj, PharmD<sup>1,2</sup>; Florence Whitehill, DVM<sup>1,2</sup>; Connie Austin, DVM, PhD<sup>3</sup>; Christine Hahn, MD<sup>4</sup>; Amanda J. Kieffer, DVM<sup>5</sup>; Leila Mendez<sup>6</sup>; Jael Miller<sup>7</sup>; Leslie A. Tengelsen, DVM, PhD<sup>4</sup>; Crystal M. Gigante, PhD<sup>1</sup>; Lillian A. Orciari, MS<sup>1</sup>; Agam K. Rao, MD<sup>1</sup>; Ryan M. Wallace, DVM<sup>1</sup> ([View author affiliations](#))

# Brief Abstract



- In October of 2015, a student at Texas State handled a “downed/sick” bat and was not aware of the risk surrounding contact with a bat. The case will be discussed in terms of (1) the scenario that took place with the student; (2) rabies public health education; and (3) laboratory diagnostics of specimens submitted for rabies testing.





# Learning Objectives

1. Describe a step-by-step plan on what to do in the scenario of someone coming into contact with bats (or other wildlife).
2. Recognize the critical importance of obtaining an animal exposure history from any person/patient presenting with an unknown cause of a progressive encephalopathy.
3. Describe the epidemiology associated with U.S. cases of rabies in the past five years, especially the importance that wildlife reservoirs (e.g. insectivorous bats) have played in the transmission of rabies to humans.
4. Review the type of samples to be collected, the guidelines for collection of these samples, the different laboratory methods (human and animal tests) used to diagnose rabies infections, including the standard test, for a suspected rabies case in a human.





# But look how cute it is...

## The scenario



Bats in sleeping bags??

- Early October 2015, the Texas State BIO Dept. contacted me about a “student finding a bat on campus and bringing it in to help save it.”
- Only after the BIO Chair accepted the bat (and took it to a wildlife faculty member for speciation and care) did he think to be concerned about the risk to the student per handling.
  - *Of course....the student was long gone at that time.*
- I received an email regarding the situation due to my background in public health zoonosis and diagnostics.
- YES, it was a Friday around 3:30PM...ahhh, it felt just like the old days of being back in my Texas DSHS & CDC role!



# But look how cute it is...

## The scenario



- I immediately inquired about student personal information in relation to contacting the student. BIO Chair and others did not know the student, nor if she was a major or even if she was a student.
- Next step was to contact our Risk Management team in connection with our student health center physician.
  - This started a chain of events of public announcements and emails to the entire university population and local press to help with locating student.
- I worked with the university via DSHS contacts to get the bat tested for rabies ASAP.
  - Bat was sent with a rush status for testing. *YES...of course*, it was positive for rabies (as most downed bats tend to be). And....it's the weekend.....







# But look how cute it is...

## The scenario



- Fortunately, and prior to knowing the bat was positive for rabies, our efforts at locating her worked....

From: Carranco, Emilio

Sent: Friday, October 02, 2015 6:22 PM

To: rrohde, others

Subject: Student Exposed to Rabid Bat Located

Dr. Rohde,

I spoke with her. She did handle the bat with bare hands. Doesn't think that she was bitten or scratched, but not completely sure. I referred her to a local ER for evaluation. It is a judgment call about the rabies vaccine. So, we will see if the ER physician thinks there was enough risk to warrant a series of rabies shots. The student was scared. So, if there is any risk, she will probably want the shots. I asked her to follow up with me after the ER evaluation. Thanks for your expertise in this matter and the immediate contacts with the DSHS rabies lab testing.

Emilio Carranco, M.D., M.S.

Director, Student Health Center

TX State Student Health Center



# But look how cute it is...

## The scenario



- Since the bat was positive for rabies, and because she couldn't completely rule out a scratch or bite puncture....game on!

From: Carranco, Emilio

Sent: Thursday, October 08, 2015 9:07 AM

To: Rohde, Rodney E; Romano, Elsie R

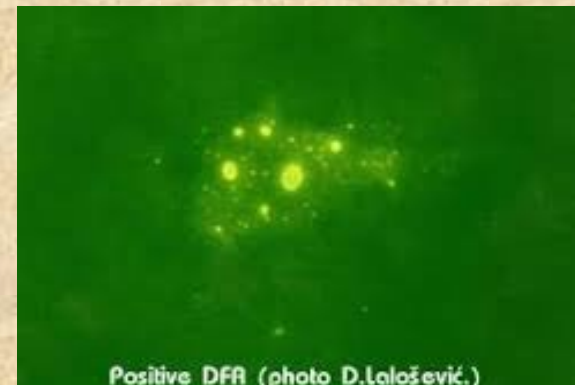
Subject: RE: Student Exposed to Rabid Bat Located

I sent a message to Elsie, Jake (UPD), University New Service, VP of Student Affairs and San Marcos Animal Control on Friday evening letting them know that student had been located. She got her rabies series started. She was very appreciative that the university followed up as we did. ***The Emergency Alert/Warning system really worked well for us in this case.***

Emilio Carranco, M.D., M.S.

Director, Student Health Center

TX State Student Health Center



Positive DFA (photo D.Lalošević.)





# But look how cute it is..

## The scenario



- Fortunately, a good outcome. That is not always the case, especially with bat rabies cases!

From: Carranco, Emilio

Sent: Thursday, October 08, 2015 12:02 PM

To: Romano, Elsie R; Rohde, Rodney E

Subject: RE: Student Exposed to Rabid Bat Located



*Seems like most people still don't understand that "downed bats" should raise concerns about the bat being sick or rabid. They also don't seem to understand that bat bites or scratches may go unnoticed. Many people use dog scenarios when considering the risk of exposure (obvious bite).*

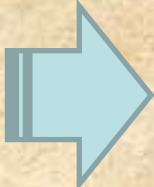
I think your idea about an educational case scenario for the TACLS Conference makes sense. I think for Texas State, we should consider an annual notice to our campus community reminding them about the benefits and risks of bats. We get 6,000-7,000 new students to Texas State every year who are not familiar with our bat issues. So, we really need an ongoing bat and rabies education program. A mass e-mail annually might be the easiest way to get the word out. The e-mail should probably come from Environmental Health Safety & Risk Management or the Student Health Center, but Health Professions might be another option. The subject line and amount of text in the message are key elements in getting students and others to read these public health notices (subject can't seem like spam mail and text has to be short and to the point). Many students get their e-mail via smartphones. So, the messages have to be mobile friendly.

Emilio Carranco, M.D., M.S.

Private Information

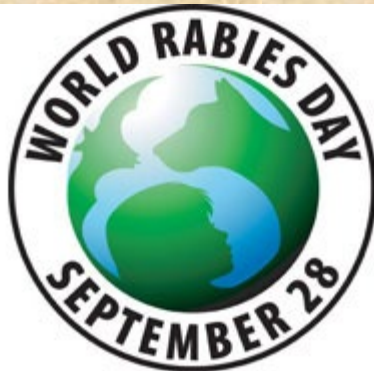


# Irony at it's finest – Recent publication for World Rabies Day



Wilson, P.J. & Rohde, R.E. 8 things you may not know about rabies but should. Elsevier Connect, September 28, 2015.

<http://www.elsevier.com/connect/8-things-you-may-not-know-about-rabies-but-should>



Wilson, P.J. & Rohde, R.E. The many faces of rabies: High- and low-risk animals, different ways to get rabies – and tips to prevent it. September 22, 2016.

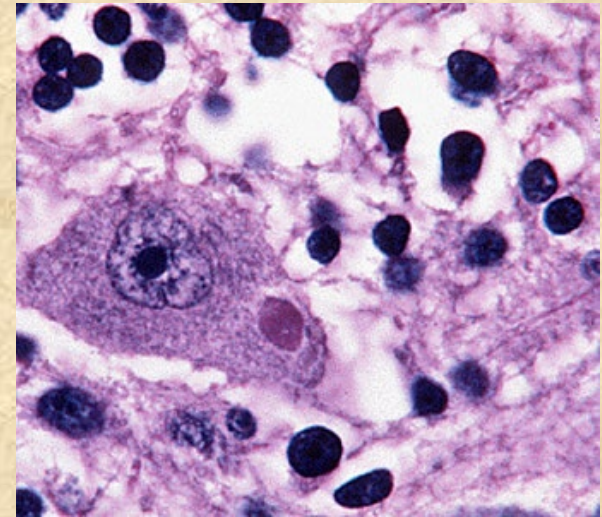
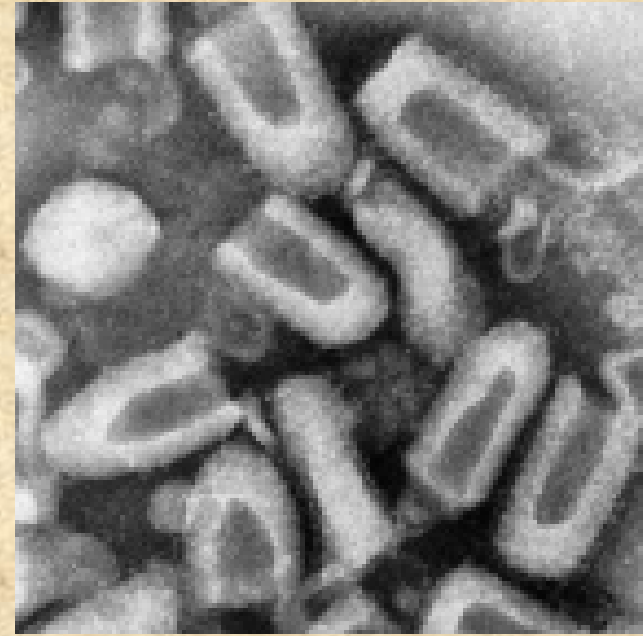
<https://www.elsevier.com/connect/the-many-faces-of-rabies>



New and MORE signage placed on campus – after this event!

# RABIES

- RNA virus
- deadly infection of CNS of mammals
- Causes an acute encephalitis
- About 59K people die every year from rabies
- ~ 1-2 deaths a year in US
- “Ancient disease” - described in writings by Egyptians dating back to 2300 B.C.





# Human Rabies in the World

Every 10 to 15 mns somebody  
dies of rabies in the world



In most instances a  
dog is at the origin of  
exposure

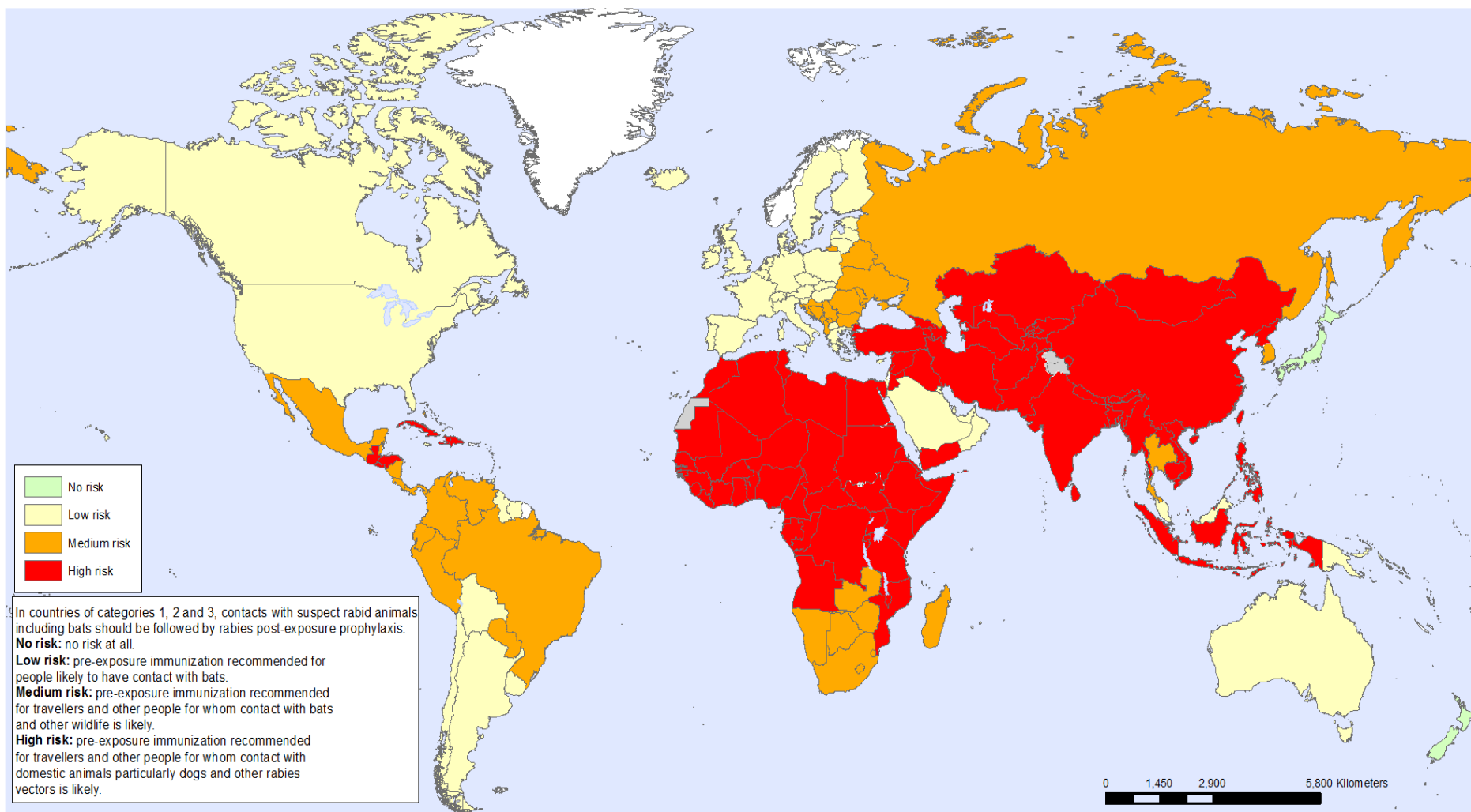
A thousand people receive  
rabies post-exposure treatment  
every hour in the world



Thanks to D. Warrell for the pictures



## Rabies, countries or areas at risk

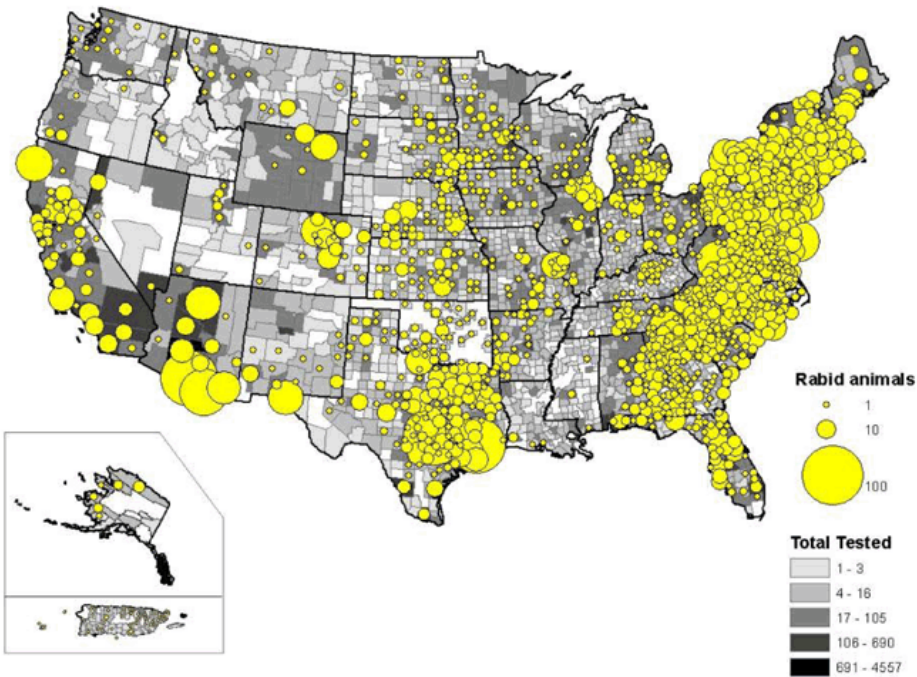


The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: WHO Control of Neglected  
Tropical Diseases (NTD)  
Map Production: Health Statistics and  
Information Systems (HSI)  
World Health Organization



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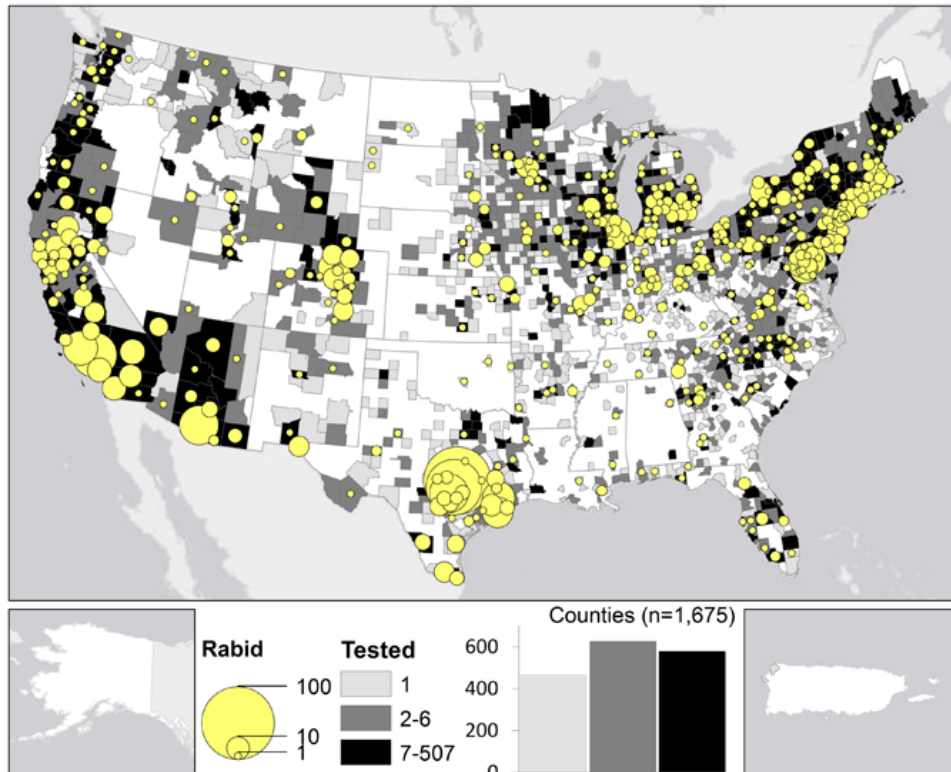


2022

<<<<<<Rabid animals [ **land based**, terrestrial ]

## Reminder – *PASSIVE* surveillance

Rabid Bats>>>>>>>>>



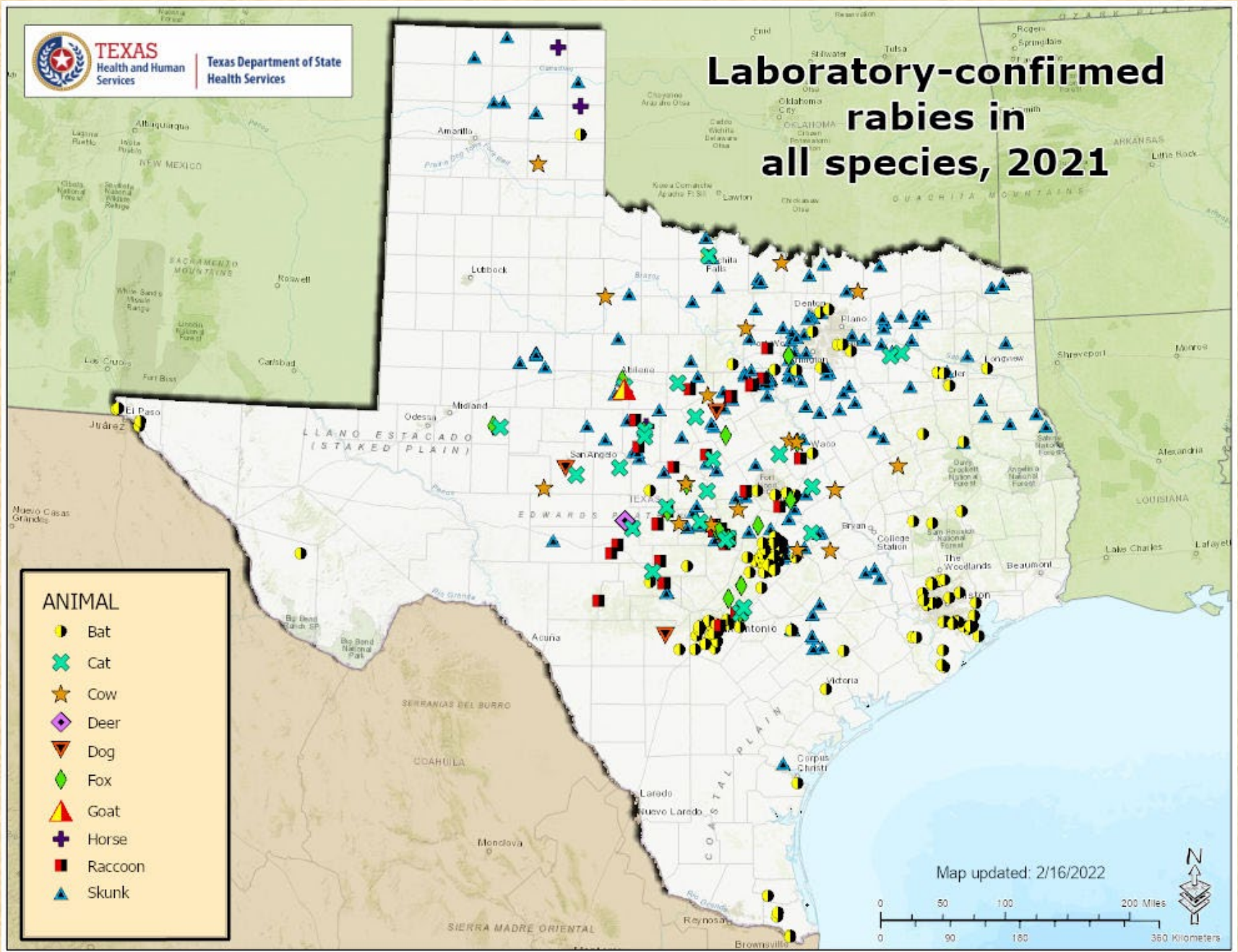




TEXAS  
Health and Human  
Services

Texas Department of State  
Health Services

# Laboratory-confirmed rabies in all species, 2021





**Table 1. Confirmed Cases of Rabies in Wild Animal Species:  
Texas 2019 and 2020**

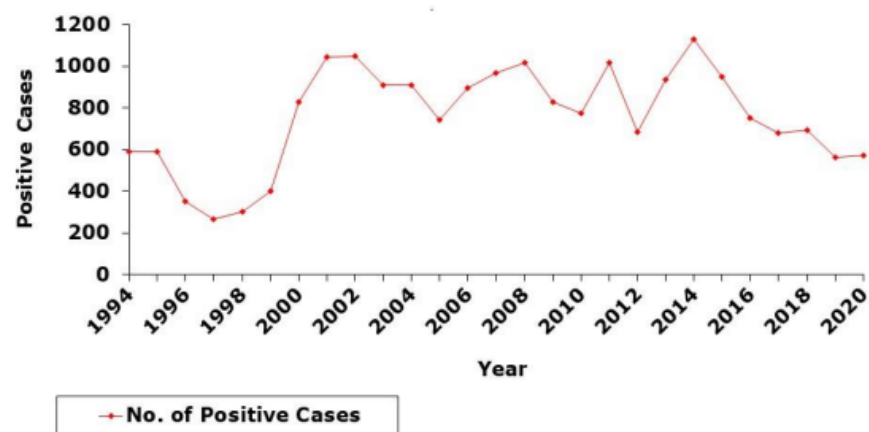
Species	2019	2020
Bat	289	268
Coyote	1	0
Fox	29	28
Raccoon	43	25
Skunk	173	208
<b>Total</b>	<b>535</b>	<b>529</b>

Data for 2021  
unavailable

**Table 2. Confirmed Cases of Rabies in Domestic Animal Species:  
Texas 2019 and 2020**

Species	2019	2020
Bovine	4	8
Caprine	0	2
Cat	16	25
Dog	6	8
Equine	4	1
Ovine	0	1
<b>Total</b>	<b>30</b>	<b>45</b>

**Figure 1. Positive Animal Rabies Cases:  
Texas 1994 - 2020**



Rabies in Animals, Texas - 2020

4/20/21





**TEXAS**  
Health and Human  
Services

Texas Department of State  
Health Services

# Laboratory-confirmed rabies by variant, 2021

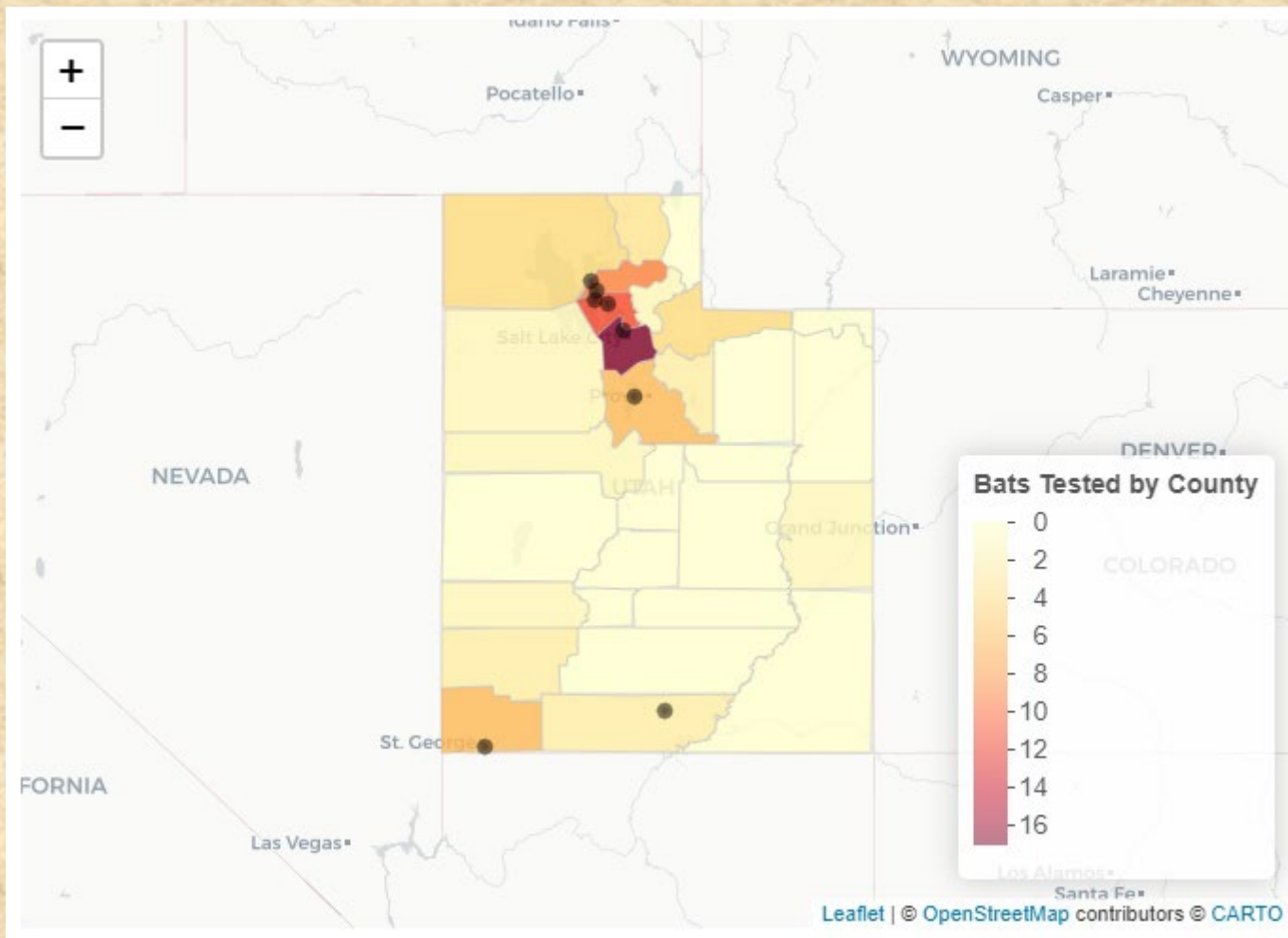
## Rabies virus variant

 Bat rabies

 Skunk rabies

Map updated: 2/16/2022





## Rabid Bat by County, Utah

As of July 31, 2022, 8 positive bats were reported in Utah. Positive bats were identified in Davis (2), Kane (1), Salt Lake (1), Utah (1), Washington (1), and Weber (2) counties. During a five-year period between January and July, an average of 5.8 bats are reported positive in Utah. The five-year average number of positive bat specimens in Utah for the month of July is 3.4.



# Rabid animals, Utah

- In 2021, 18 positive bats and 1 positive fox were reported in Utah. The five-year average in Utah is 16.6 positive bats per year.
- Positive bats were identified in Beaver (1), Cache (4), Davis (2), Morgan (1), Salt Lake (4), Sevier (1), Summit (1), Utah (3), and Washington (1) counties.
- The positive fox was identified in Washington County.
- Of the 18 positive bats, the species were as follows: Mexican Free Tailed (6), Myotis (6), Silver Haired (2), Western Pipistrelle (1), Big Brown (2), and Hoary (1). Of the 313 animals submitted to the Utah Public Health Laboratory (UPHL) in 2021 for rabies testing, there were 168 bats, 48 cats, 62 dogs, 11 raccoons, 6 skunks, and 18 other species.

## Morbidity and Mortality Weekly Report (MMWR)

CDC

# Human Rabies — Utah, 2018

Weekly / February 7, 2020 / 69(5);121–124

Although human rabies is extremely rare in Utah, rabies risk assessments and the administration of post-exposure prophylaxis (PEP) are an everyday occurrence. **Since 1944** there have only been two confirmed cases of human rabies infection in Utah; both were fatal.

On November 3, 2018, the Utah Department of Health (UDOH) was notified of a suspected human rabies case in a man aged 55 years. The patient's symptoms had begun 18 days earlier, and he was hospitalized for 15 days before rabies was suspected. As his symptoms worsened, he received supportive care, but he died on November 4. On November 7, a diagnosis of rabies was confirmed by CDC. This was the first documented rabies death in a Utah resident since 1944.

<https://www.cdc.gov/mmwr/volumes/69/wr/mm6905a1.htm>



## Human Rabies Cases since 2003

Date of onset	Date of death	Reporting state	Age (y)	Sex	Exposure*	RVV†
10 Feb 03	10 Mar 03	VA	25	M	Unknown	Raccoon, eastern United States
28 May 03	5 Jun 03	PR	64	M	Bite, Puerto Rico	Dog-mongoose, Puerto Rico
23 Aug 03	14 Sep 03	CA	66	M	Bite	Bat, Ln
9 Feb 04	15 Feb 04	FL	41	M	Bite, Haiti	Dog, Haiti
27 Apr 04	3 May 04	AR	20	M	Bite (organ donor)	Bat, Tb
25 May 04	31 May 04	OK	53	M	Liver transplant	Bat, Tb
27 May 04	21 Jun 04	TX	18	M	Kidney transplant	Bat, Tb
29 May 04	9 Jun 04	TX	50	F	Kidney transplant	Bat, Tb
2 Jun 04	10 Jun 04	TX	55	F	Arterial transplant	Bat, Tb
12 Oct 04	Survived	WI	15	F	Bite	Bat, unknown
19 Oct 04	26 Oct 04	CA	22	M	Unknown, El Salvador	Dog, El Salvador
27 Sep 05	27 Sep 05	MS	10	M	Contact	Bat, unknown
4 May 06	12 May 06	TX	16	M	Contact	Bat, Tb
30 Sep 06	2 Nov 06	IN	10	F	Bite	Bat, Ln
15 Nov 06	14 Dec 06	CA	11	M	Bite, Philippines	Dog, Philippines
19 Sep 07	20 Oct 07	MN	46	M	Bite	Bat, unknown
16 Mar 08	18 Mar 08	CA	16	M	Bite, Mexico	Fox, Tb related
19 Nov 08	30 Nov 08	MO	55	M	Bite	Bat, Ln
25 Feb 09	Survived	TX	17	F	Contact	Bat, unknown
5 Oct 09	20 Oct 09	IN	43	M	Unknown	Bat, Ps
20 Oct 09	11 Nov 09	MI	55	M	Contact	Bat, Ln
23 Oct 09	20 Nov 09	VA	42	M	Contact, India	Dog, India
2 Aug 10	21 Aug 10	LA	19	M	Bite, Mexico	Bat, Dr
24 Dec 10	10 Jan 11	WI	70	M	Unknown	Bat, Ps
30 Apr 11	Survived	CA	8	F	Unknown	Unknown
30 Jun 11	20 Jul 11	NJ	73	F	Bite, Haiti	Dog, Haiti
14 Aug 11	31 Aug 11	NY	25	M	Contact, Afghanistan	Dog, Afghanistan
21 Aug 11	1 Sep 11	NC	20	M	Unknown (organ donor)‡	Raccoon, eastern United States
1 Sep 11	14 Oct 11	MA	40	M	Contact, Brazil	Dog, Brazil
3 Dec 11	19 Dec 11	SC	46	F	Unknown	Bat, Tb
22 Dec 11	23 Jan 12	MA	63	M	Contact	Bat, My sp
6 Jul 12	31 Jul 12	CA	34	M	Bite	Bat, Tb
31 Jan 13	27 Feb 13	MD	49	M	Kidney transplant	Raccoon, eastern United States
16 May 13	11 Jun 13	TX	28	M	Unknown, Guatemala	Dog, Guatemala
12 Sep 14	26 Sep 14	MO	52	M	Unknown	Bat, Ps
30 Jul 15	24 Aug 15	MA	65	M	Bite, Philippines	Dog, Philippines
17 Sep 15	3 Oct 15	WY	77	F	Contact	Bat, Ln
25 Nov 15	1 Dec 15	PR	54	M	Bite	Dog-mongoose, Puerto Rico
5 May 17	21 May 17	VA	65	F	Bite	Dog, India
6 Oct 17	21 Oct 17	FL	56	F	Bite	Bat, Tb
28 Dec 17	14 Jan 18	FL	6	M	Bite	Bat, Tb
15 Jul 18	23 Aug 18	DE	69	F	Unknown	Raccoon, eastern United States

\*Data for exposure history are reported when plausible information was reported directly by the patient (if lucid or credible) or when a reliable account of an incident consistent with rabies virus exposure (eg, dog bite) was reported by an independent witness (usually a family member). Exposure histories are categorized as bite, contact (eg, waking to find bat on exposed skin) but no known bite was acknowledged, or unknown (ie, no known contact with an animal was elicited during case investigation). †Variants of the rabies virus associated with terrestrial animals in the United States and Puerto Rico are identified with the names of the reservoir animal (eg, dog or raccoon), followed by the name of the most definitive geographic entity (usually the country) from which the variant has been identified. Variants of the rabies virus associated with bats are identified with the names of the species of bats in which they have been found to be circulating. Because information regarding the location of the exposure and the identity of the exposing animal is almost always retrospective and much information is frequently unavailable, the location of the exposure and the identity of the animal responsible for the infection are often limited to deduction. ‡Infection was not identified until 2013, when an organ recipient developed rabies.

Dr = *D rotundus*. Ln = *L noctivagans*. My sp = *Myotis* species. Ps = *P subflavus*. Tb = *T brasiliensis*.

# U.S. Epidemiology - Humans

- Human rabies cases in the United States are rare, with only 1 to 3 cases reported annually. **Forty-eight** cases of human rabies deaths have been reported in the United States (**2003-2021**). Multiple contracted outside of the U.S. and its territories but died in U.S.
- Many states represented (location of death)
  - **NO deaths in 2019 or 2020 in U.S.**
- 5 most recent cases in IL, TX, ID, MN (all bat) & NY (via a dog bite in Philippines) – **ALL IN 2021**
- High male to female ratio (4.5 to 1)
- Age range from 6 to 80 (Avg. = ~35)
- Exposures
  - 80 – 100 dogs and >300 cats with rabies each year, usually infected by wildlife when these domesticated pets are not vaccinated against rabies.





A third person died in New York after he was bitten by a dog in the Philippines. He started developing symptoms after he returned to the United States. The C.D.C. said it was not able to determine why the man did not receive a vaccine.

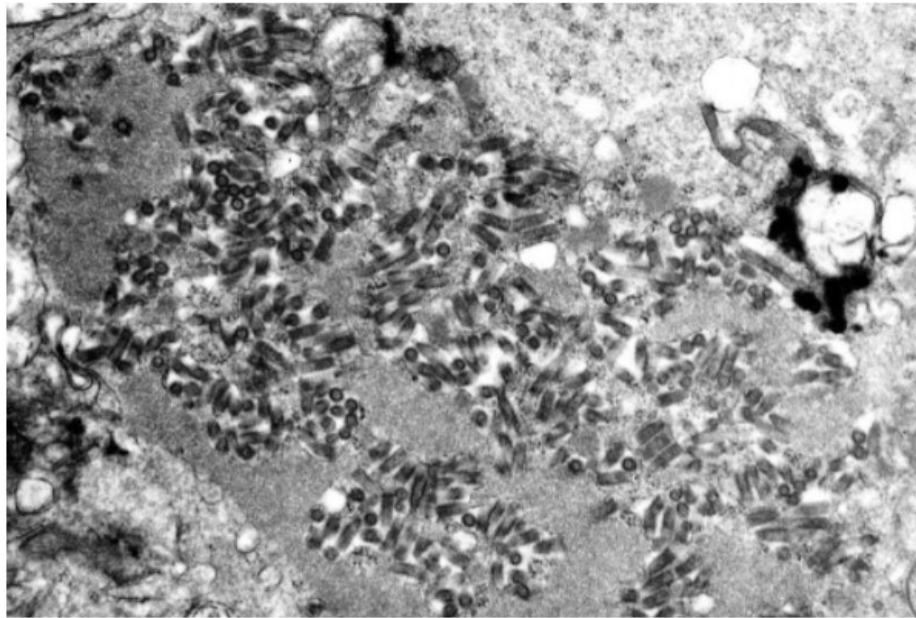
In another case, a 7y old child in Texas picked up a bat with his bare hands and then released it.

Three of those deaths, including that of a 7-year-old child, involved direct contact with bats and occurred over a five-week period starting in late September. The deaths occurred in Idaho, Illinois and Texas, and all three people experienced symptoms three to seven weeks after contact with bats. They died two to three weeks after symptoms began, according to a C.D.C. report.

Private Information

## U.S. Records 5 Rabies Deaths in 2021, Highest Number in a Decade

Three of the deaths involved direct contact with bats, the C.D.C. said.



An electron microscope image of rabies virions, dark and bullet-shaped, within an infected tissue sample. F.A. Murphy/CDC, via Associated Press



By Jenny Gross

A fourth person from Minnesota who died from rabies last year received the vaccine, but his weakened immune system did not respond to it, the C.D.C. said.

In one case, a man in Illinois who had a bat roost in his home awoke in August to find a bat on his neck, according to a statement from the Illinois Department of Public Health. The bat was captured and tested positive for rabies, but the man declined to take a vaccine because of a longstanding fear of vaccines.

About a month after contact with the rabid bat, the IL man started experiencing neck pain, headaches, difficulty controlling his arms, finger numbness and difficulty speaking, before dying.

# Notes from the Field: Three Human Rabies Deaths Attributed to Bat Exposures — United States, August 2021

Weekly / January 7, 2022 / 71(1);31–32

Amber Kunkel, ScD<sup>1,2</sup>; Faisal S. Minhaj, PharmD<sup>1,2</sup>; Florence Whitehill, DVM<sup>1,2</sup>; Connie Austin, DVM, PhD<sup>3</sup>; Christine Hahn, MD<sup>4</sup>; Amanda J. Kieffer, DVM<sup>5</sup>; Leila Mendez<sup>6</sup>; Jael Miller<sup>7</sup>; Leslie A. Tengelsen, DVM, PhD<sup>4</sup>; Crystal M. Gigante, PhD<sup>1</sup>; Lillian A. Orciari, MS<sup>1</sup>; Agam K. Rao, MD<sup>1</sup>; Ryan M. Wallace, DVM<sup>1</sup> ([View author affiliations](#))

[View suggested citation](#)

During September 28–November 10, 2021, CDC confirmed three human rabies deaths in the United States, all in persons who did not seek postexposure prophylaxis (PEP) after bat exposures that occurred during August 2021. This increase in bat-associated human rabies deaths in the United States followed only three deaths during the previous 48 months. The cases during fall 2021 occurred in two adults and one child, all male, from Idaho, Illinois, and Texas. Initial symptoms included pain and paresthesia near the site of exposure progressing to dysphagia, altered mental status, paralysis, seizure-like activity, and autonomic instability. All three patients had recognized direct contact (e.g., bite or collision) with a bat approximately 3–7 weeks before symptom onset and died approximately 2–3 weeks after symptom onset. The deaths were associated with three bat species: *Lasiurus noctivagans* (silver-haired bat), *Tadarida brasiliensis* (Mexican free-tailed bat), and *Eptesicus fuscus* (big brown bat) ([Figure](#)). All three species are common in the United States and have been implicated in previous rabies cases. One patient submitted the bat responsible for exposure for testing but refused PEP, despite the bat testing positive for rabies virus, due to a long-standing fear of vaccines. The other two patients did not realize the risk for rabies from their exposures, either because they did not notice a bite or scratch or did not recognize bats as a potential source of rabies. Case and contact investigations were led by the appropriate state and local health departments, and all human laboratory testing occurred at CDC. This activity was reviewed by CDC and conducted consistent with applicable federal law and CDC policy.\*

## Article Metrics

### Altmetric:



- News (249)
- Blogs (2)
- Twitter (50)
- Facebook (1)
- Mendeley (5)

### Citations:

### Views:

Views equals page views plus PDF downloads





# U.S. Epidemiology - Humans

Be aware if you've got bats in your home. That's the message from the Illinois Department of Health as it announced that an 80-year-old man died of rabies after waking up to find a bat on his neck. It is the first human case of rabies in the state since 1954.

The man refused rabies treatment at the time of the incident in mid-August, health officials said in a [press release](#). A month later, he started experiencing rabies symptoms such as neck pain, headache, difficulty controlling his arms, finger numbness and difficulty speaking.

Rabies infections in humans are extremely rare in the United States, since the disease is preventable and treatable. Typically one to three cases are reported each year, and [there were no cases reported in 2019](#), according to the most recent data available from the CDC.

But rabies exposure is far more common; 60,000 Americans receive the post-exposure treatment every year. Without prompt treatment, though, the [virus](#) infects the nervous system and is typically fatal.



## SHOTS - HEALTH NEWS

[Bats In The Bedroom Can Spread Rabies Without An Obvious Bite](#)



September 2021

# The numbers...continued

- In US, rabies is rare; majority due to *indigenously* acquired rabies since 2000 (\*includes recent transplant cases)
  - Most attributed to bat associated RV variants, although a **bite** is rarely documented due unawareness / lack of pain or blood.
  - Some type of encounter occurred in ~45%
  - Cases represent various bat histories: bite, direct contact with bats with multiple opportunities to be bitten, & possible direct contact with a bat; other cases are dog bites
  - In addition, multiple non-indigenous cases of rabies in the US occurred since 2000 (Mexico, Philippines, El Salvador, Haiti, etc.)
  - Recent cases of rabies in humans have implicated BATS as important wildlife reservoirs for RV, especially in US!

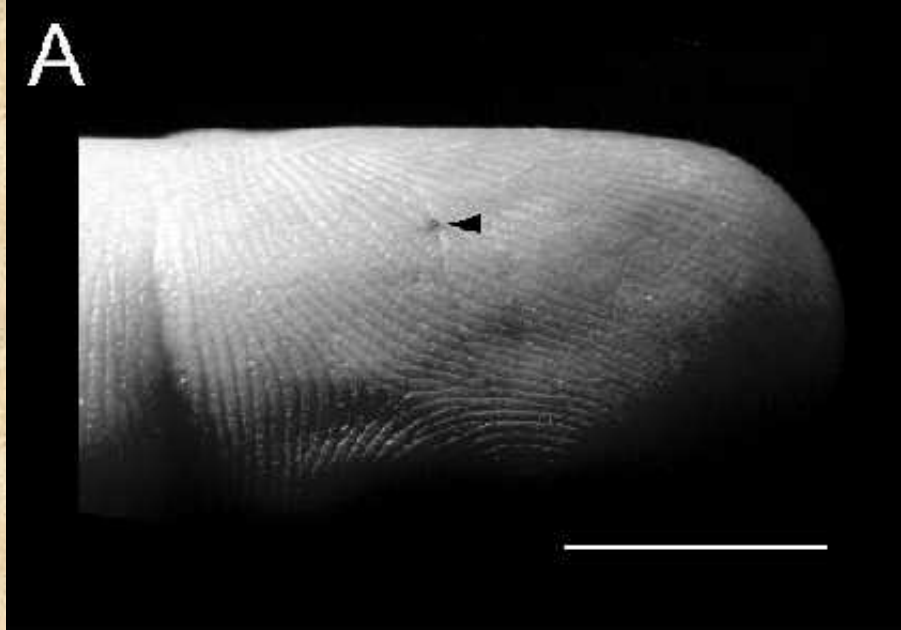




# The numbers...continued



- Even *minor bites* are “entry portals” for RV and subsequently they become a transmission route
  - These bat bites are difficult, if not impossible, to identify, which makes decision to treat difficult
  - This led to recommendations for (PEP) in these situations:
    - the possibility of rabies cannot be eliminated by testing (animal is not available)
    - Potential exposure to bats (no proof of bite after a bat is found in room of sleeping or mentally challenged person or child)
  - Although human rabies deaths are rare in the US, the estimated public health costs associated with disease detection, prevention, and control have risen, exceeding \$300 million annually.



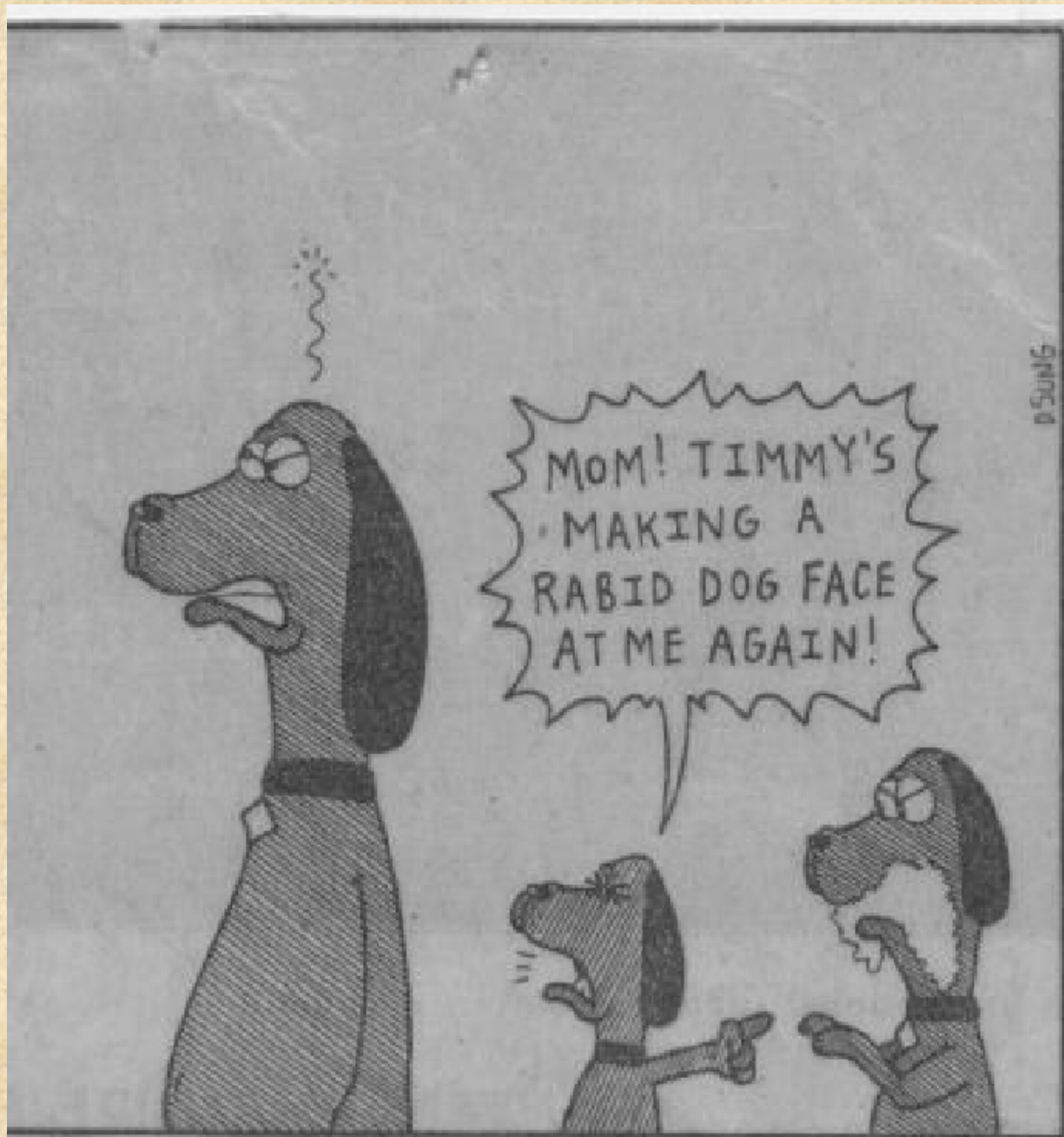
Jackson A, and Fenton. Human Rabies and Bat Bites. *Lancet*. 2001;357(9269):1714.



Approximately 12% of the bats submitted for testing at the TX DSHS rabies lab are positive for rabies.

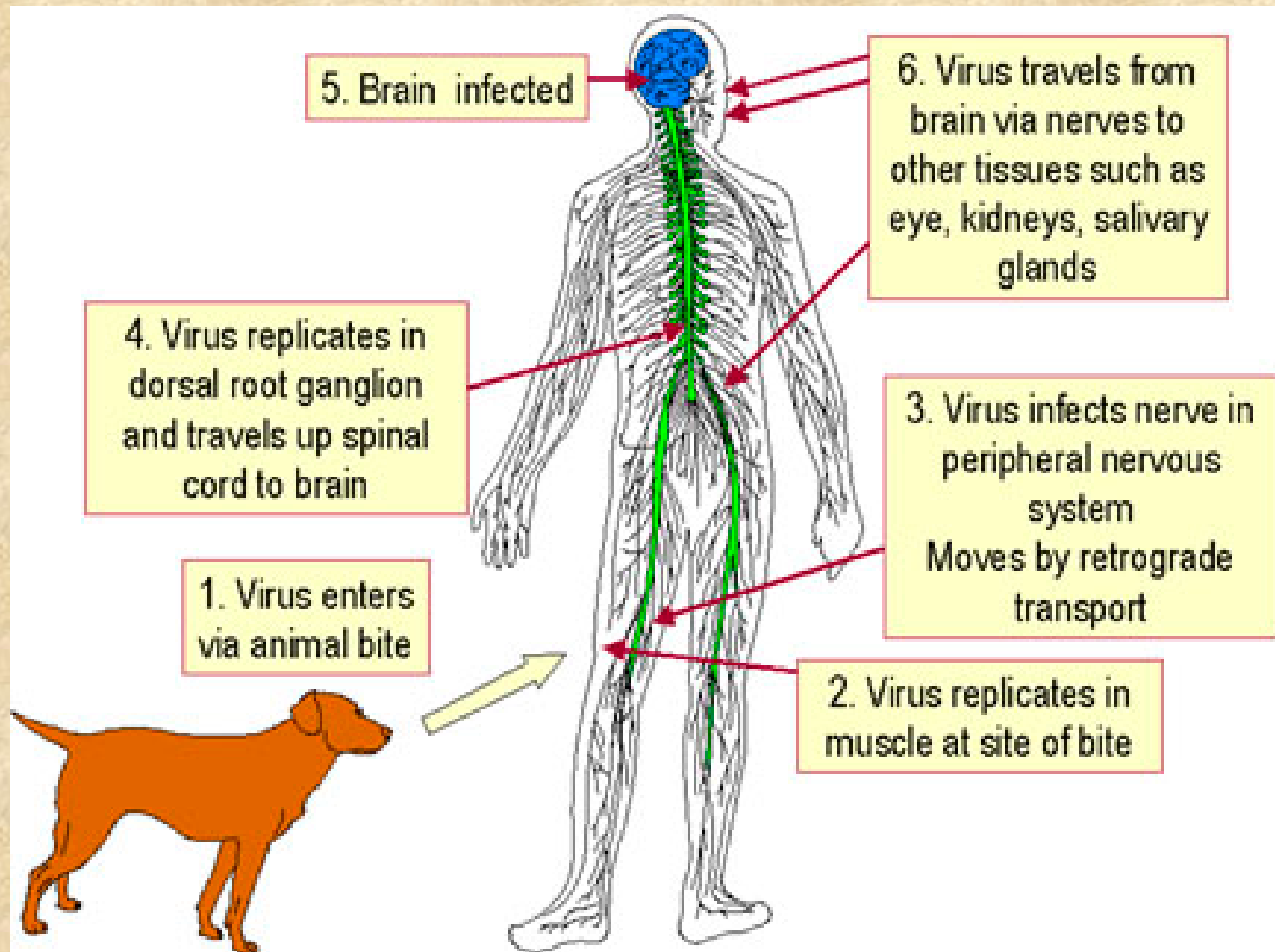


*Tadarida brasiliensis mexicana* ~ “Mexican free tail”





# How is rabies transmitted?



# Rabies in humans

\*



- **Incubation period generally 4-6 weeks**
- **Initial stage - about 2 days:**
  - healed bite wound becomes irritated and painful
  - depression and anxiety
- **Period of excitation - about 3 days:**
  - patient becomes irritable and hypersensitive
  - diaphragm and larynx undergo spasmodic contractions
  - fever of 102°F or less
  - \*positive Babinski's reflex (*normal from birth-24m*)
  - muscle spasms, convulsions, numbness and tingling, loss of muscle function
  - death from a convulsive seizure or from cardiac or respiratory failure (ANS affected)

*\*presence of a Babinski's reflex indicates damage to the nerve paths connecting the spinal cord and the brain*





“HYDROPHOBIA” — rabies results in swallowing difficulty (drinking produces spasms of the larynx) or swallowing difficulty with liquids only

\*\*Patient may also exhibit *aerophobia*

The only well-documented cases of rabies caused by human-to-human transmission occurred among eight recipients of transplanted corneas, and recently among four recipients of solid organs. Bite and non-bite exposures inflicted by infected humans could theoretically transmit rabies, but no such cases have been documented (**Centers for Disease Control**).





**Jeanna Giese** of Wisconsin is the first person known to have survived symptomatic rabies without receiving the rabies vaccine. She is only the eighth person known to have survived rabies after the onset of symptoms; the other survivors suffered from vaccine failures.



# “Milwaukee protocol”

- Supportive intensive care
- Multi-drug cocktail
  - Ketamine & amantadine – protect brain against damage (reduce excitotoxicity, brain metabolism & autonomic reactivity)
  - Benzodiazepines & barbiturates – coma induction
  - Ribavirin – used to protect heart from virus

<https://www.mcw.edu/departments/pediatrics/divisions/infectious-diseases/rabies-registry-website>



# “Milwaukee protocol (MP)”

- 17 survivors associated with our protocol, and 39 globally at some time. We quote 20%. I am trying hard to catch up (we have almost 100 known attempts) to publish.
- MP shows about a 50% good neuro outcome while those with other care (almost entirely partial PEP recipients) show at best a 20% good outcome.
- We’ve given favipiravir to 7 patients and see some clinical differences, but no change in survival.
  - Dr. Rodney Willoughby (personal communication, September 13, 2019)

# Signs of Rabies in Animals

*Foaming at the mouth & erratic behavior are well-known.*



There are actually two categories of behavior:

## **Dumb Rabies**

- \* Animals may become depressed and retreat to isolated places
- \* Wild animals may lose their fear of humans
- \* Signs of paralysis such as a drooping head, paralyzed hind limbs, abnormal facial expressions, and a sagging jaw may be exhibited by animals

## **Furious Rabies**

Animals may show extreme excitement and aggression such as:

- \* Attacking stationary objects or other animals
- \* Gnawing and biting their own limbs

Also, bouts of furious rabies often alternate with periods of depression.





A colleague's back yard....

....beware of “dumb” rabies, especially with wildlife....





# Animals commonly infected with rabies

- Raccoons
- Skunks
- Bats
- Foxes and coyotes
- **Unvaccinated** dogs, cats & livestock in endemic areas



## Animals rarely infected with rabies

- Rodents
- Rabbits
- Any cage raised or indoor pet
- **BIRDS** do not get rabies....







# Many different types of bat rabies!

More than 1,100 bat species have been discovered worldwide.

The United States is home to 47 bat species. **Texas has the**

**highest bat diversity of all the states - 31 bat species.**

<http://twrcwildlifecenter.org/living-with-wildlife/bats.php>

The predominant source of human rabies in the U.S. has changed dramatically in the last twenty years from terrestrial variants to those associated with insectivorous bats.

Never handle bats!





Rabies treatment should be authorized for the following exposures after contact with a rabid or non-testable bat:

- bites
- scratches
- saliva or nervous tissue in contact with a mucous membrane or an open break in the skin

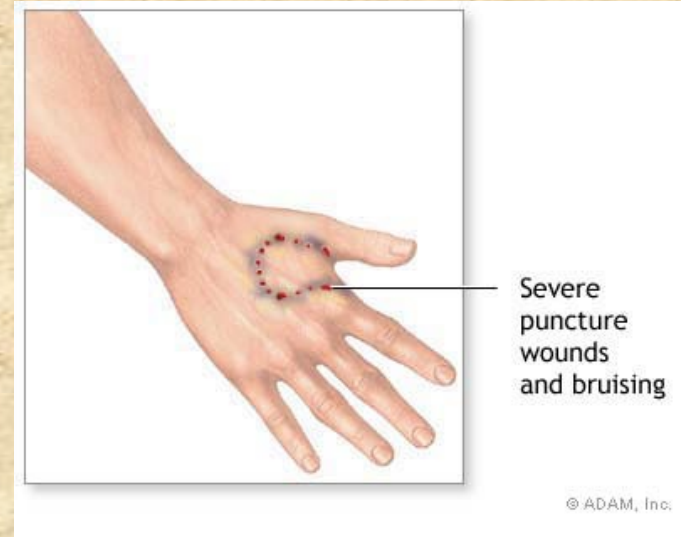


Rabies treatment recommended  
in situations in which there is a reasonable  
probability of exposure:

- direct physical contact with a bat
- bat found in room with a sleeping person
- bat found in close proximity to unattended child outdoors
- bat found in room with unattended child
- bat found in room with an impaired individual



# Rabies Postexposure Prophylaxis (PEP)



Vials of rabies vaccine  
Photo courtesy of CDC



# Rabies Prevention

## Postexposure treatment

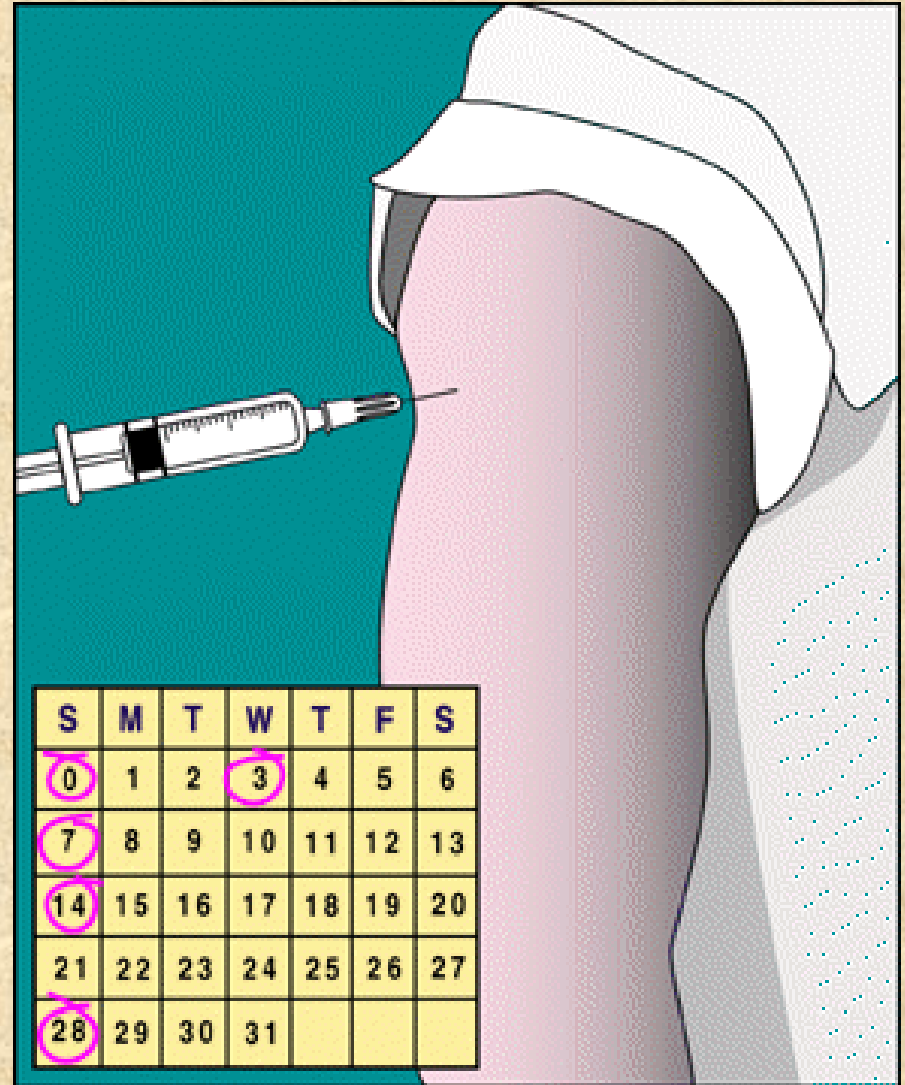
@RodneyRohde  
@txst\_CLS  
@txst\_THR

**HRIG** injected into bite wound and surrounding area

**\*VACCINE** given on days 0, 3, 7, and 14 in deltoid

*\*A 5<sup>th</sup> dose is given to immunocompromised persons*

Tetanus booster if needed!





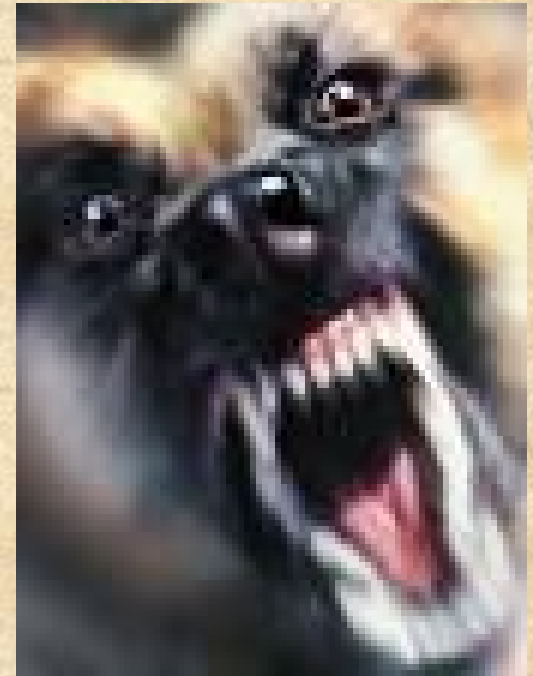
# Things needed for working with rabies virus:

*BSL 3 preferred but BSL 2 adequate with certain requirements met.*



# Rabies Testing - Animals

- **Rabies labs in Texas:**
  - Austin (DSHS)
  - City of Houston
  - SA Metro Health Lab
  - El Paso
- Specimens must be euthanized and their heads removed
- Lab personnel remove brains

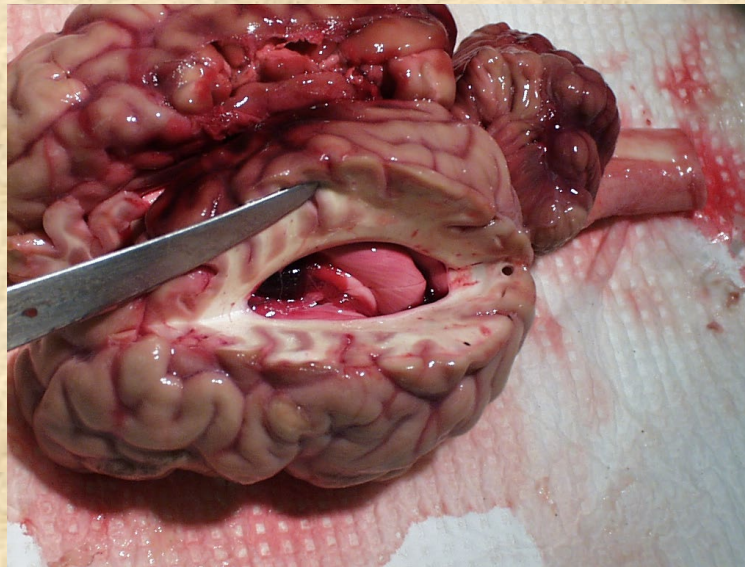
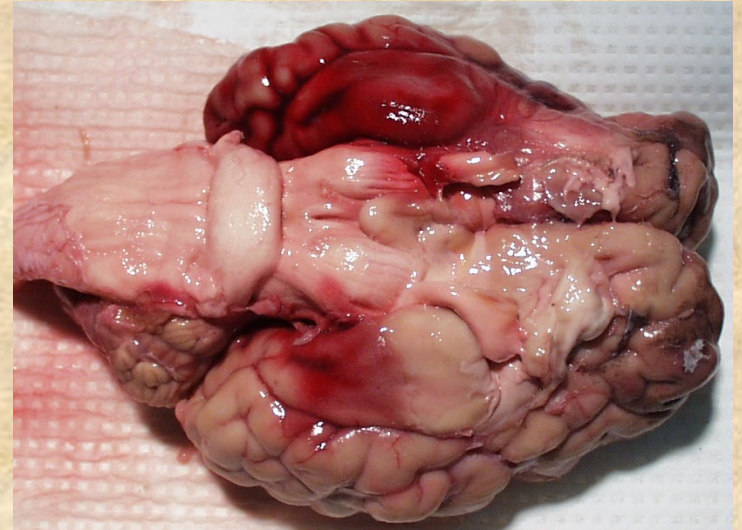
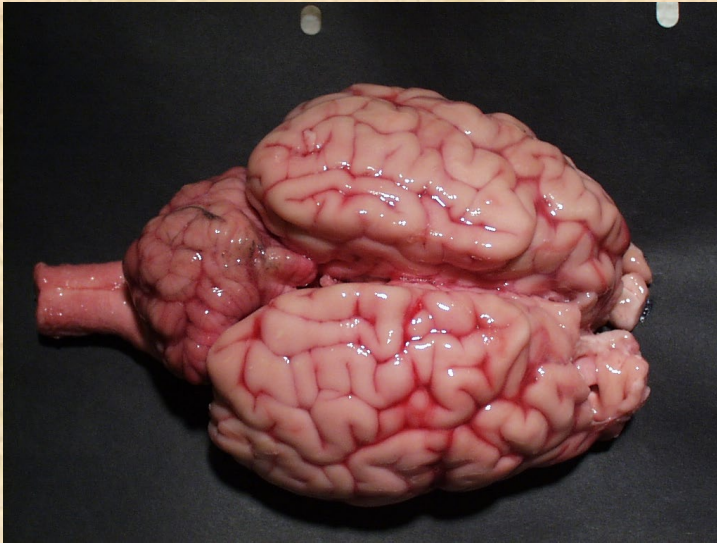








# Brain stem, Cerebellum, Hippocampus Tested for Presence of Rabies Antigen





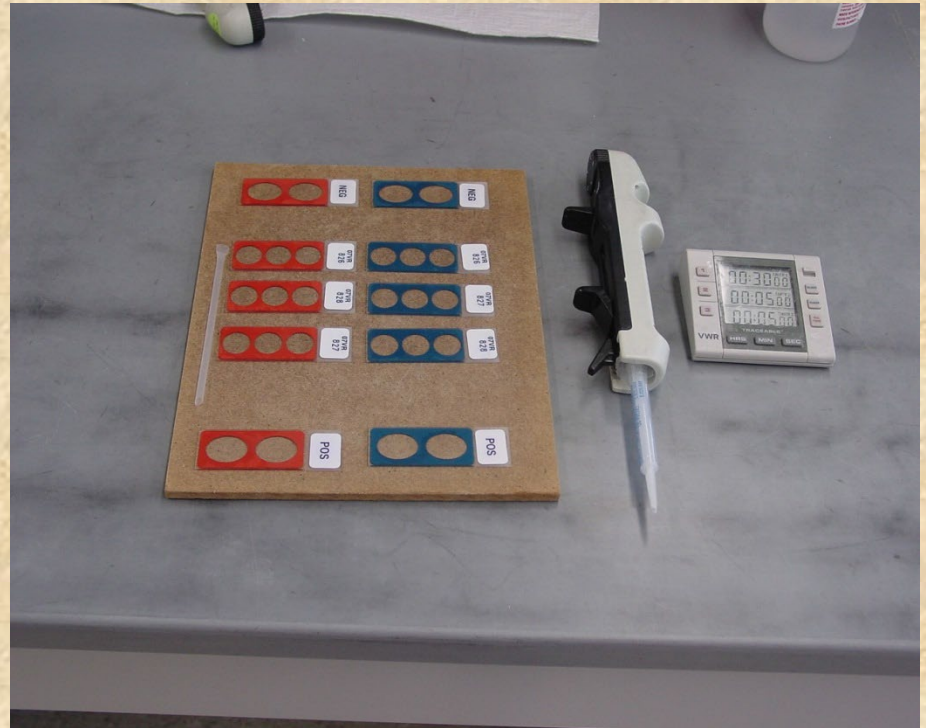
Fun days in the Necropsy lab at DSHS....



We opened more animal heads before 9AM than most people do all day....

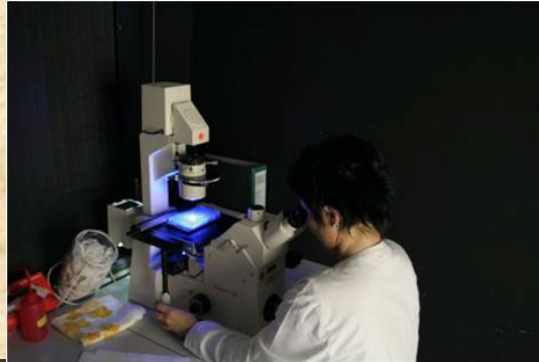
# Direct Fluorescent Antibody Test

- tissue pressed against slide
- fluid containing Anti-rabies antibodies with fluorescent tag placed on slides (incubate, rinse)
- view slides with a fluorescence microscope

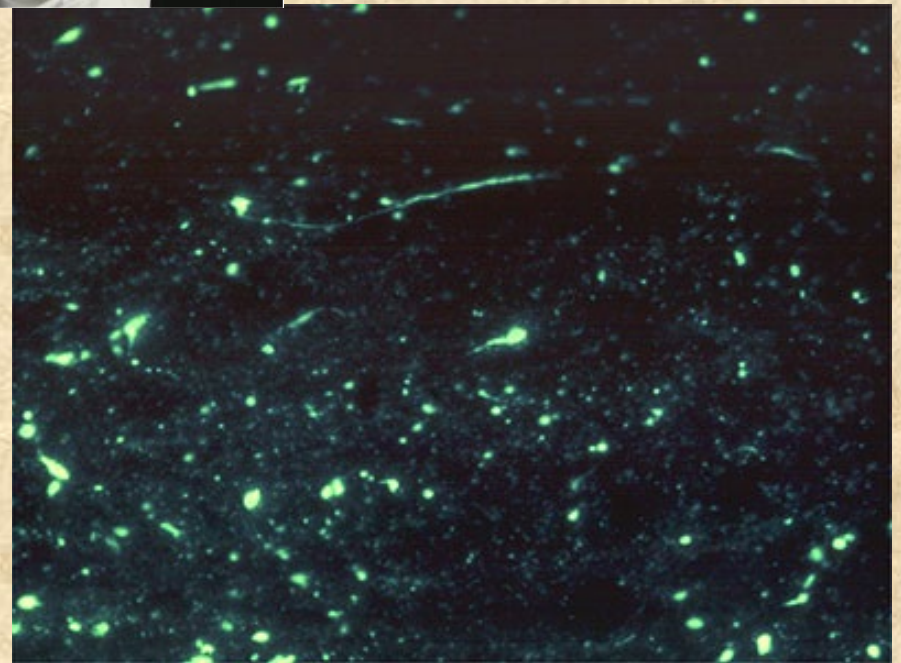




# Brain tissue after FA test staining



Negative



Positive for rabies!

Brain smears stained with anti-rabies antibodies  
tagged with fluorescent label.

# Background information: Rabies

- Diagnosis criteria
  - Rabies is FATAL in practically all cases once symptoms begin
  - Differential diagnosis should be suspected for individuals with signs or symptoms of encephalitis or myelitis
  - Absence of an exposure history does not provide evidence to terminate any suspicions (most US patients have no definitive history)
  - Indeed, several recent US cases have been diagnosed either retrospectively or after the clinical course of the disease has progressed, despite clinical observations



# Background information: Rabies

- Antemortem Testing Procedures (for humans)
  - Variety of samples should be sent for rabies suspect samples
    - Nuchal skin biopsy, saliva, serum, and CSF
  - PPE & barrier protection should be used when samples are collected
  - Follow these instructions after consultation with the state health dept., regional reference laboratory, or the CDC rabies laboratory:
  - Skin samples (5-6 mm in diameter)
    - Via biopsy from posterior region of the neck at the hairline
    - Minimum of 10 hair follicles, sampled at a depth to include the cutaneous nerves at the follicle base
    - Place specimen on piece of sterile gauze moistened with sterile water & placed in a sealed container

# Background information: Rabies

- Antemortem Testing Procedures continued
  - Preservatives or additional fluids should not be added
  - Laboratory tests to be performed include RT-PCR of extracted nucleic acid (RNA) and DFA for viral antigen in frozen sections of the biopsy sample
- Saliva
  - Collect with sterile eyedropper pipette & place in small sterile container that can be sealed
  - No preservatives or additional material
  - Laboratory tests to be performed include RT-PCR & isolation of infectious virus in cell culture
  - Tracheal aspirates & sputum are not suitable for rabies tests



# Background information: Rabies

- Antemortem Testing Procedures continued
  - Serum or CSF
    - Minimum of 0.5 ml with no preservatives added
    - Whole blood should not be submitted because it contains inhibitors against nucleic amplification techniques
    - If patient has not received vaccine or HRIG, the presence of rabies Ab in serum is diagnostic & testing of CSF is unnecessary
    - Ab to RV in CSF, regardless of immunization history, suggests a rabies infection
    - Laboratory tests for Ab include the DFA & virus neutralization
  - Brain biopsy
    - Rarity of rabies & lack of an effective treatment make brain biopsy unwarranted
    - However, biopsy samples for HSV & other types of encephalitis should be tested for RV

# Background information: Rabies

- Antemortem Testing Procedures continued
  - Biopsy sample should be placed in sterile sealed container
  - No preservatives or additional fluids should be added
  - Laboratory tests include RT-PCR & DFA in touch impressions

Integrity, type, and time of collection of antemortem specimens are critical to the correct diagnosis of a rabies infection!!!

Neurotropic nature of RV makes it important to collect a variety of samples early & intermittently during the course of a differential diagnosis

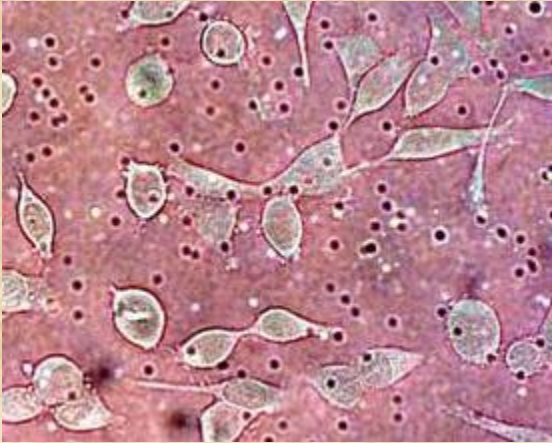
Limited success of antemortem diagnostic tests for rabies is assumed due to rabies pathogenesis



# Background information: Rabies

- Postmortem Testing Procedures
  - DFA staining of viral Ag in touch impressions of brain tissue
    - Portions of the brain stem, cerebellum, & the hippocampus should be kept refrigerated & shipped to the public health laboratory for rabies testing
    - Preservation of tissue by fixation in formalin is not recommended
    - However, if tissue has been placed in formalin, procedures have been described to analyze specimen

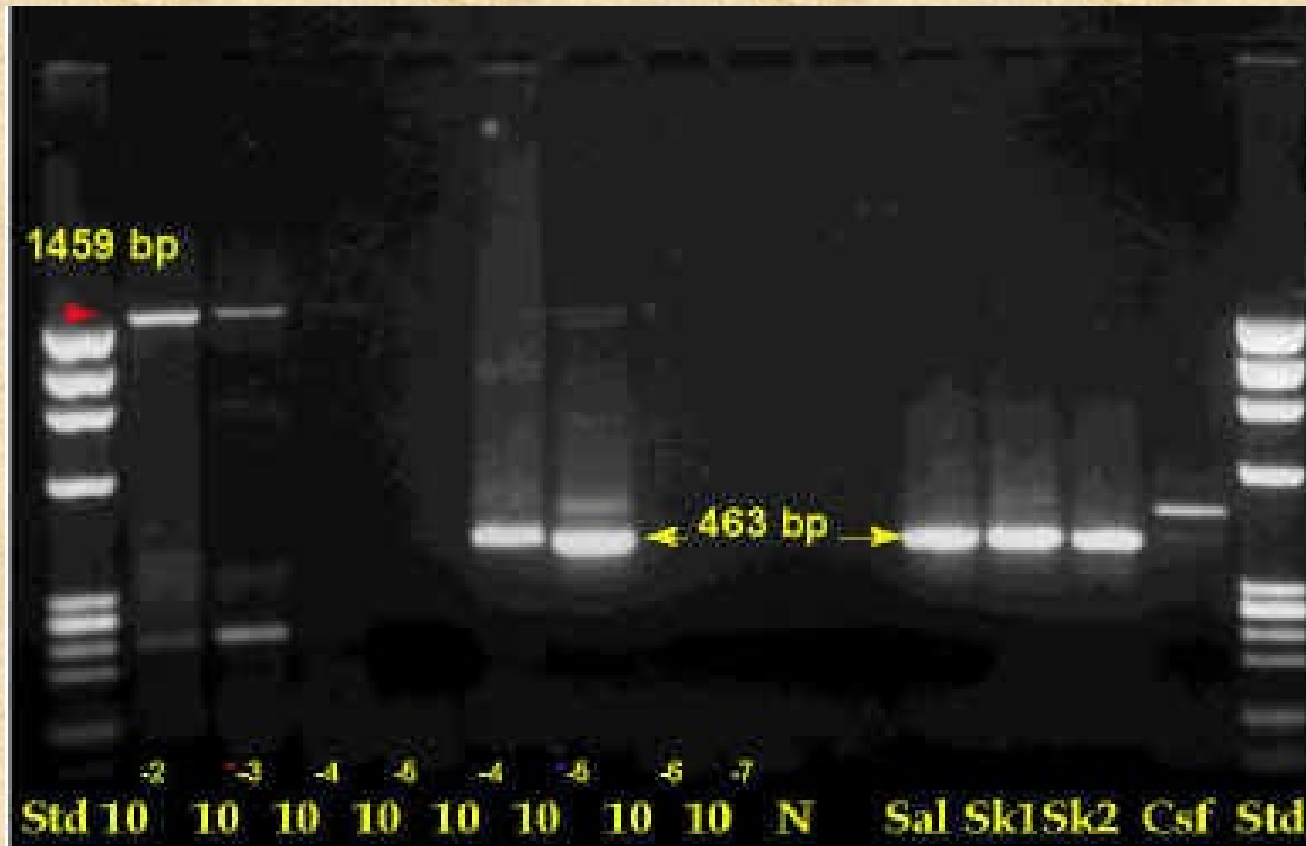
# Ways to Grow Virus



Awww, Mom...come on....humans are watching....

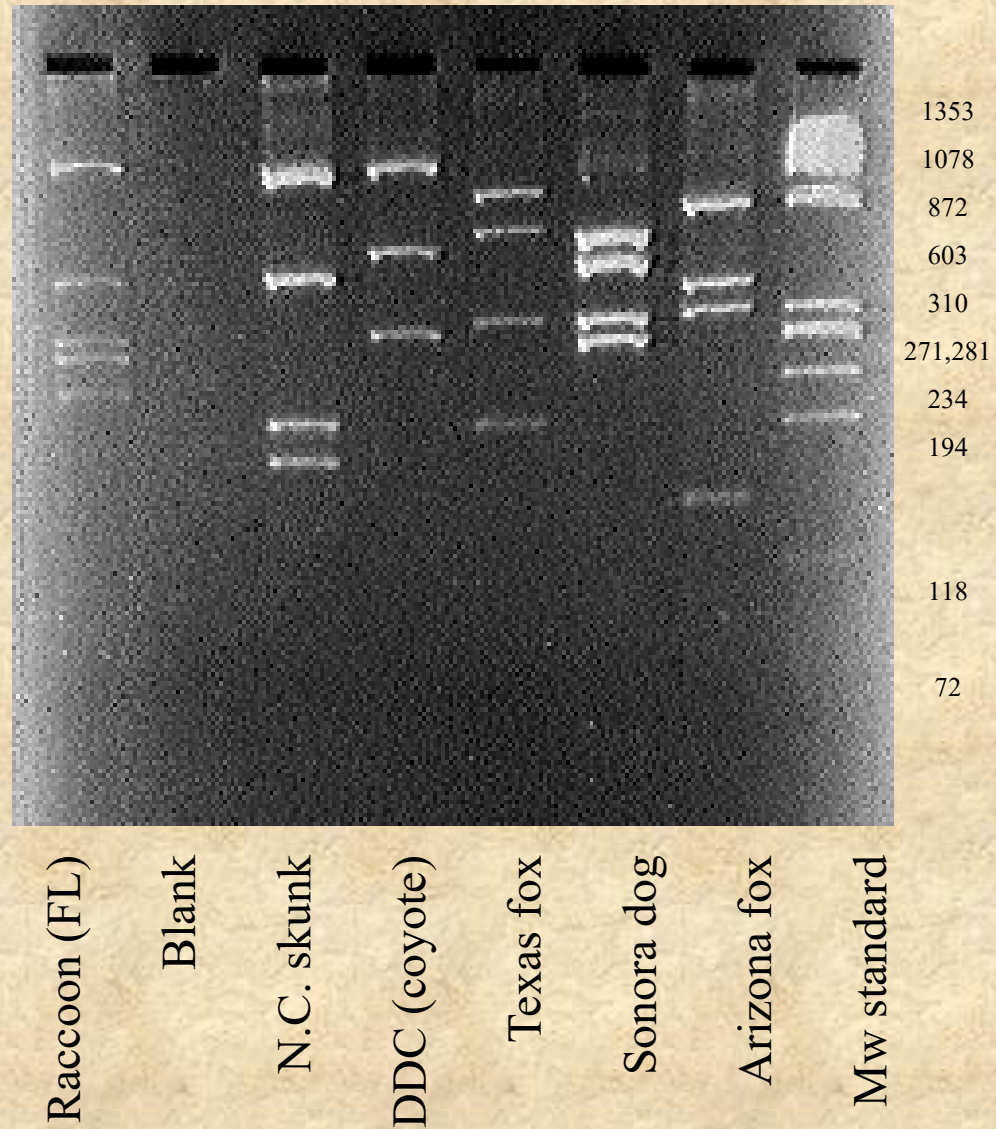
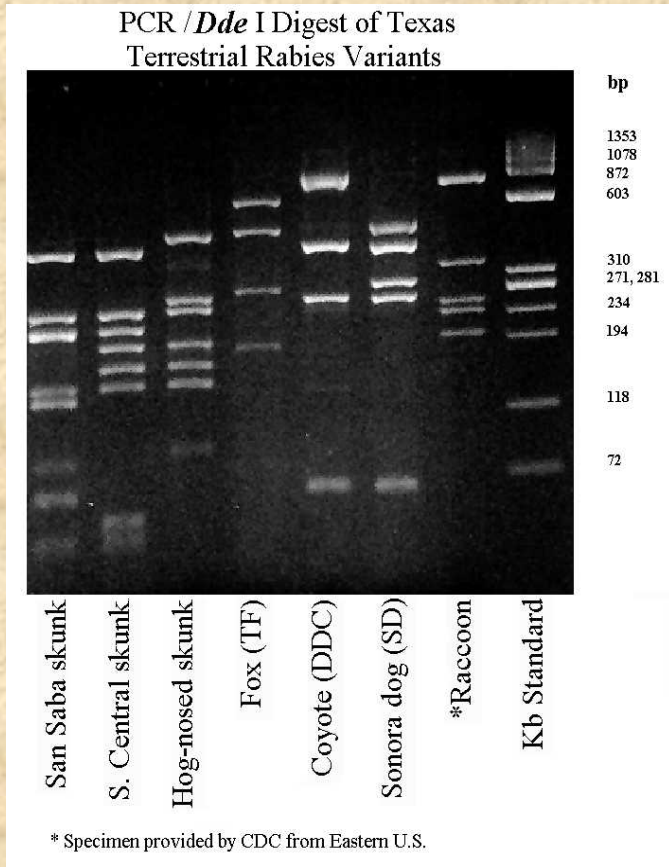


Another method for amplifying the nucleic acid portion of rabies virus uses biochemical methods. With this procedure, rabies virus RNA can be enzymatically amplified as DNA copies. Rabies RNA can be copied into a DNA molecule using reverse transcriptase (RT). The DNA copy of rabies can then be amplified using polymerase chain reaction (PCR). This technique can **confirm dFA results** and can detect rabies virus in saliva and skin biopsy samples.

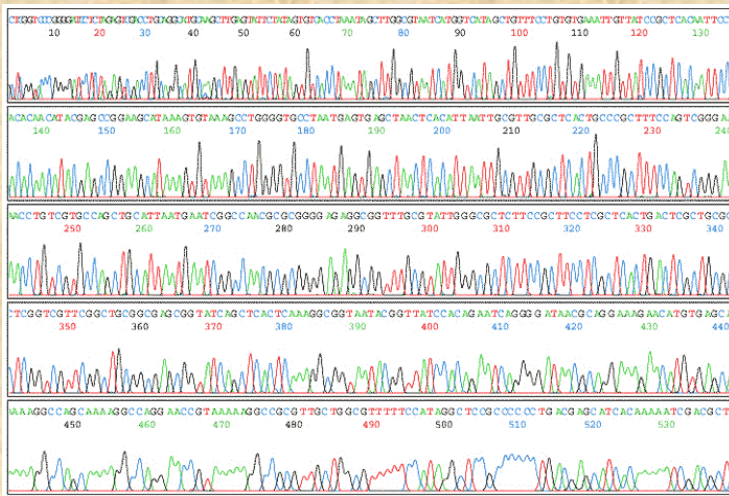


The arrows indicate positions of positive bands.

# PCR (10g:304) / *Dde* I digest of terrestrial rabies virus variants

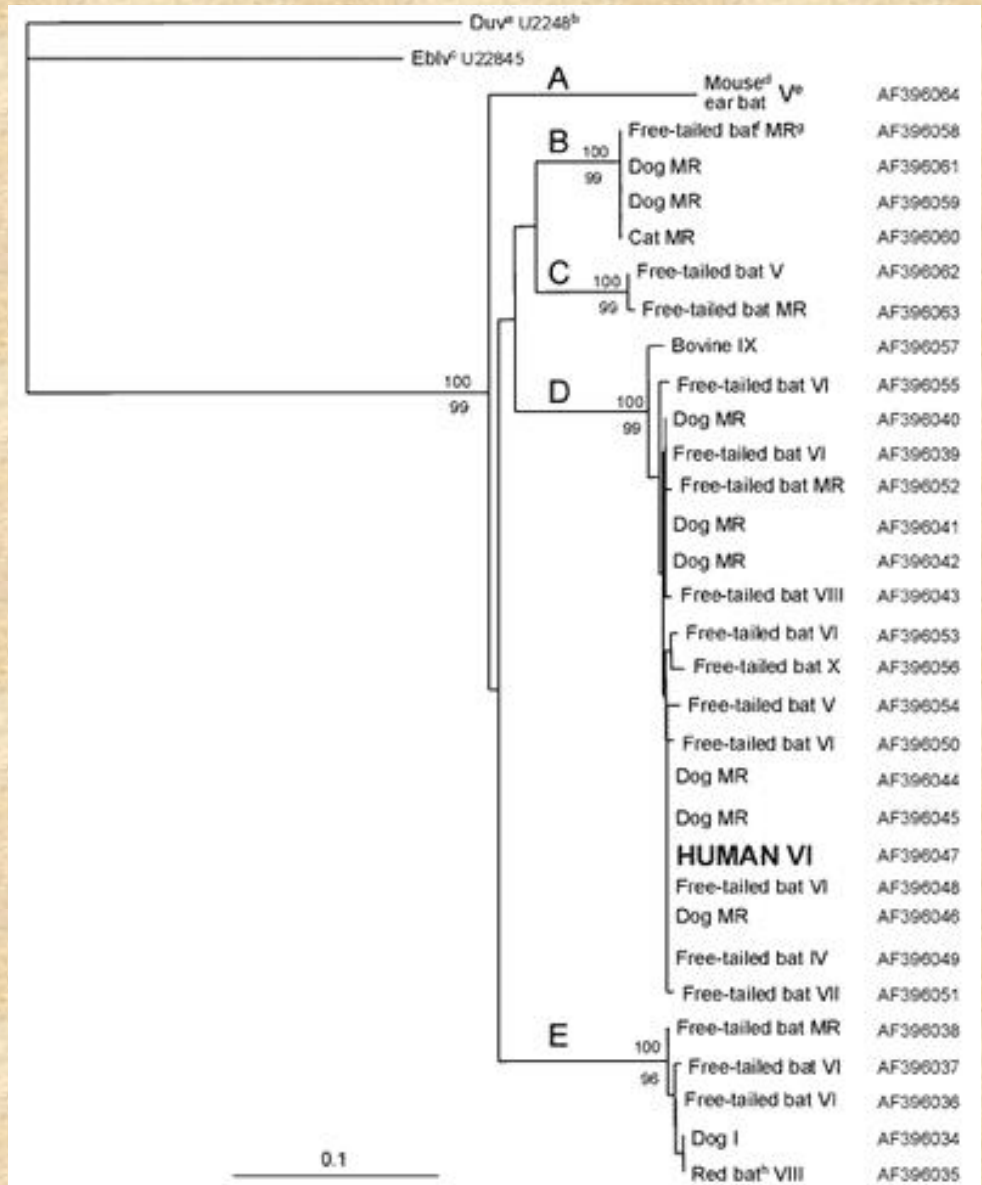






Data from  
sequencing put in  
phylogenetic tree

Viruses closely  
related will “cluster”  
together in tree



# LN34 pan-lyssavirus RT-PCR assay

One additional method, the LN34 pan-lyssavirus RT-PCR assay, represents an idealized candidate test for postmortem diagnostics, owing to its ability to detect RNA across the diversity of the viral genus, high sensitivity, potential for use with deteriorated tissues, and user-friendly design.

Providing data from a multi-site evaluation of the LN34 assay in 14 laboratories using 2,978 samples (1,049 DFA-positive) from Africa, the Americas, Eurasia, and the Middle East, high diagnostic specificity (i.e., 99.7%) and sensitivity (i.e., 99.9%) were shown when compared to the DFA test (i.e., no DFA-positive samples were negative by the LN34). The LN34 assay exhibited low variability in repeatability and reproducibility studies, suggesting a new gold standard for centralized laboratories.

Once quality control is optimized, utilization of more directed, improved point-of-care diagnostics should range from enhanced surveillance activities in the field to better assessment of exposed patients in the clinic under more real-time conditions in support of better understanding of the underlying disease epidemiology for timely responses

Rohde RE and Rupprecht CE. Update on lyssaviruses and rabies: will past progress play as prologue in the near term towards future elimination? Faculty Reviews 2020 9:(9) <https://doi.org/10.12703/b/9-9> Specific URL:

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# Acknowledgements

- Texas Department of State Health Services (formerly TDH)
- Centers for Disease Control-Rabies Unit
- ORVP participants
- Texas State University





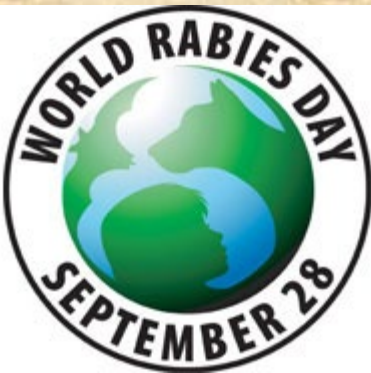


# Questions?

[rrohde@txstate.edu](mailto:rrohde@txstate.edu)

<http://rodneyerohde.wp.txstate.edu/>

<http://www.health.txstate.edu/cls/>



<http://www.worldrabiesday.org/>

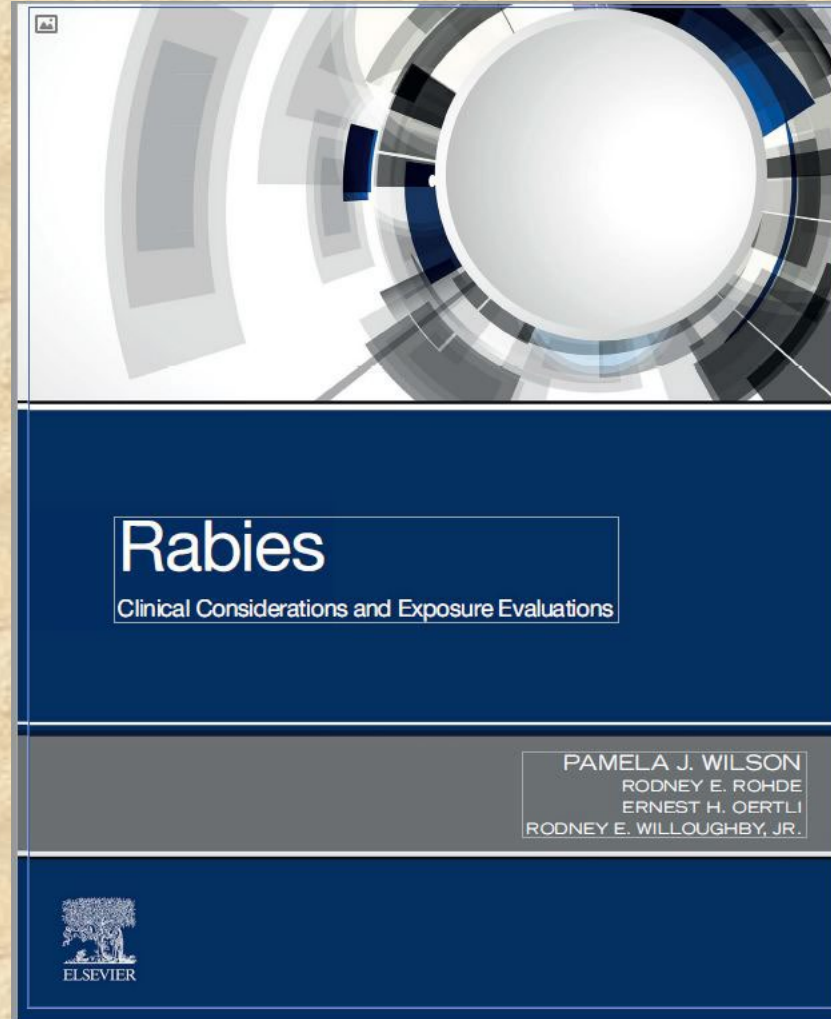
Trap, vaccinate, and release program  
In AZ



Maybe your job isn't as "pressure-filled"  
as you thought???



# “The Book” – finally....



Wilson, PJ, Rohde R.E. et al. 2019. Rabies: Clinical Considerations and Exposure Evaluations. Elsevier Press, St. Louis, Missouri 63043. (Invited book). ISBN: 978-0-323-63979-8