

A Medical Perspective on Rabies

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National Center for Emerging and Zoonotic Infectious Diseases

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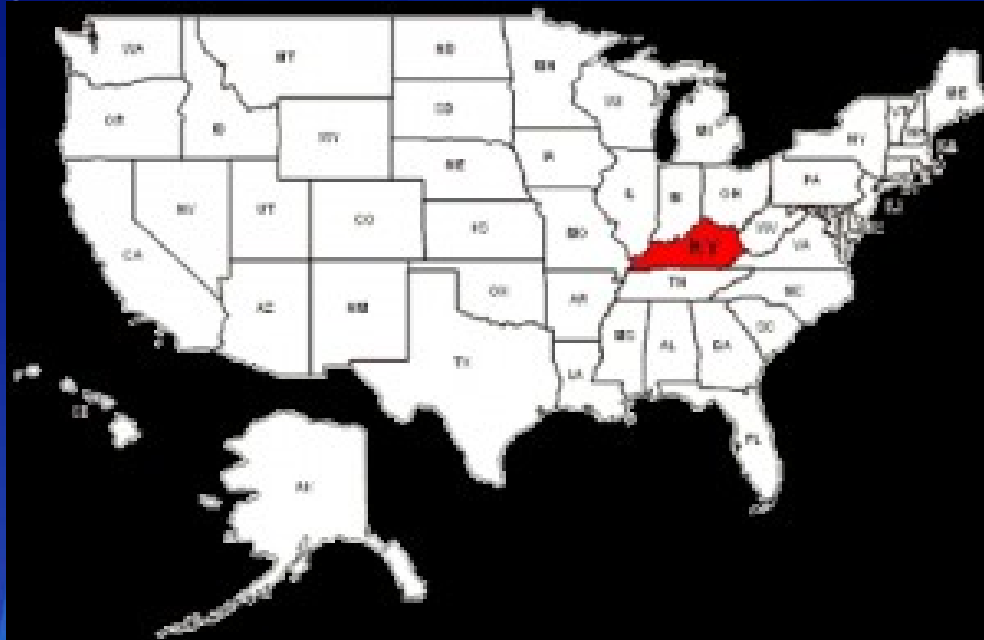
Epidemic Intelligence Service



Outline

- ❑ **Human rabies case series**
 - Kentucky, 2009
 - Louisiana, 2010
 - California, 2011
- ❑ **Teaching points/ Unique features**

Kentucky, 2009



Kentucky, 2009 Clinical Presentation

- ❑ 43-year-old previously healthy man
- ❑ 10/5 Presents to employee health with fever and cough
- ❑ 10/6 Returns with worsening fever/chills, left arm numbness, and chest pain
- ❑ 10/6 Presents to ED for evaluation of chest and back pain “spasms”
- ❑ 10/7 Returns to ED unable to sit still, writhing
- ❑ 10/8 Presents to primary care physician with fever, low blood pressure, and elevated heart rate

Kentucky, 2009 Hospital Course

- ❑ Rapid mental status deterioration requiring intubation for airway protection
- ❑ Transferred to a referral hospital in Kentucky
- ❑ Workup for encephalitis, no etiology was identified
- ❑ Hospital course complicated by slow heart rate, low blood pressure, and kidney failure requiring hemodialysis
- ❑ 10/29 Brain death was diagnosed, ventilatory support withdrawn and the patient died

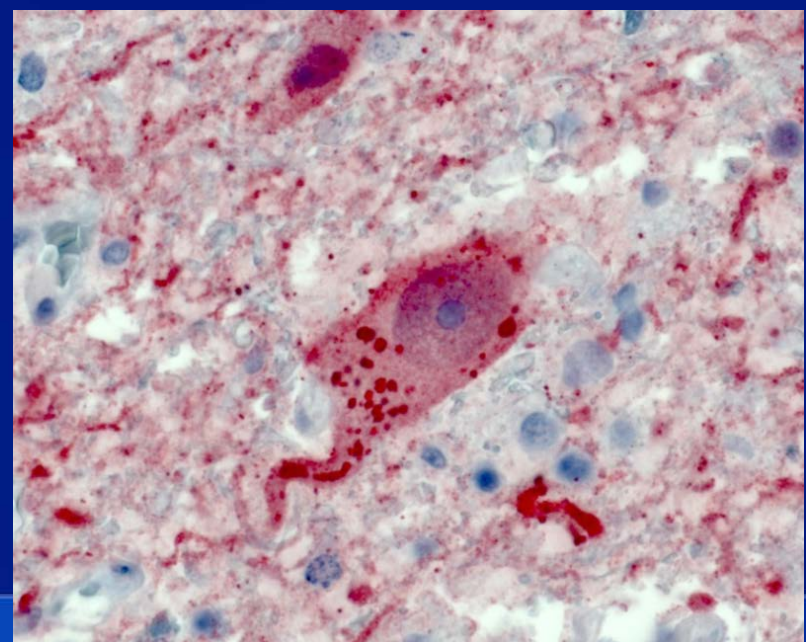
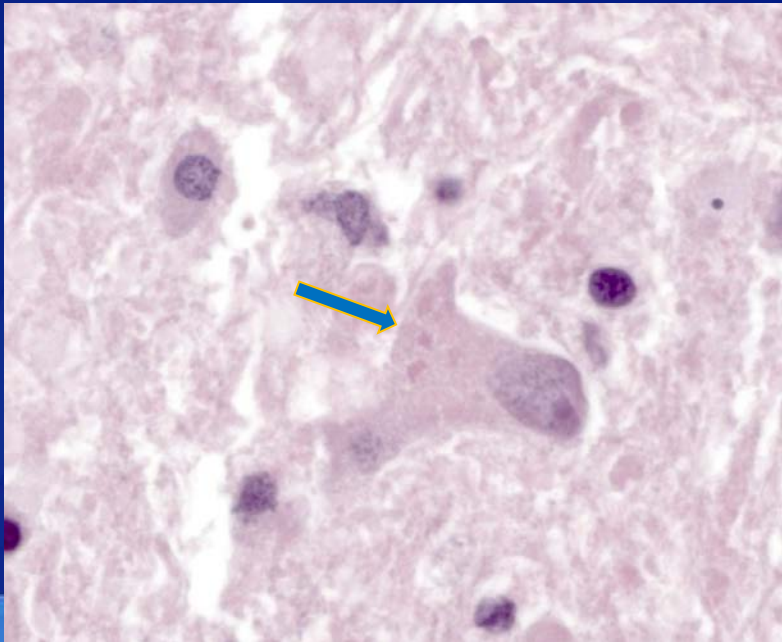
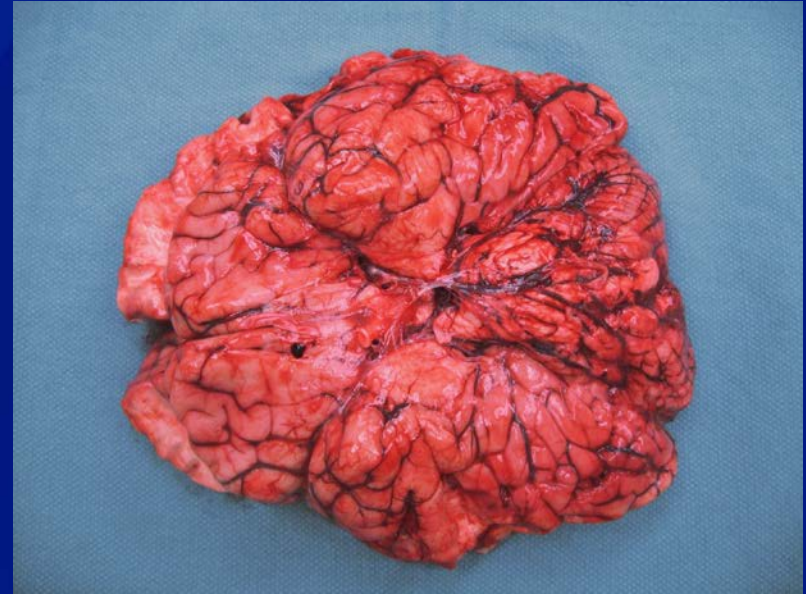
Differential Diagnosis

- ❑ Rabies thought unlikely given the absence of animal exposure
- ❑ One day prior to the patient's death
 - CDC contacted for consultation
 - Antemortem samples submitted for diagnostic testing

Preliminary Results

- ❑ Rabies specific antibodies in serum
- ❑ Diagnosis expected to be confirmed at autopsy
- ❑ Pathologists concerned about the biosafety risks of performing an autopsy on a patient with suspected rabies
 - Infectious aerosols

Postmortem Findings



Postmortem Findings

- ❑ Rabies viral RNA detected by RT-PCR
- ❑ Typed as a variant common to the tricolored bat (*Perimyotis subflavus*)



Public Health Investigation

- ❑ No specific source of rabies virus exposure
- ❑ Mechanic in a rural farming community in southern Indiana
- ❑ Mentioned seeing a bat after removing a tarpaulin from a tractor
- ❑ Never reported any bite or nonbite exposures to any animal

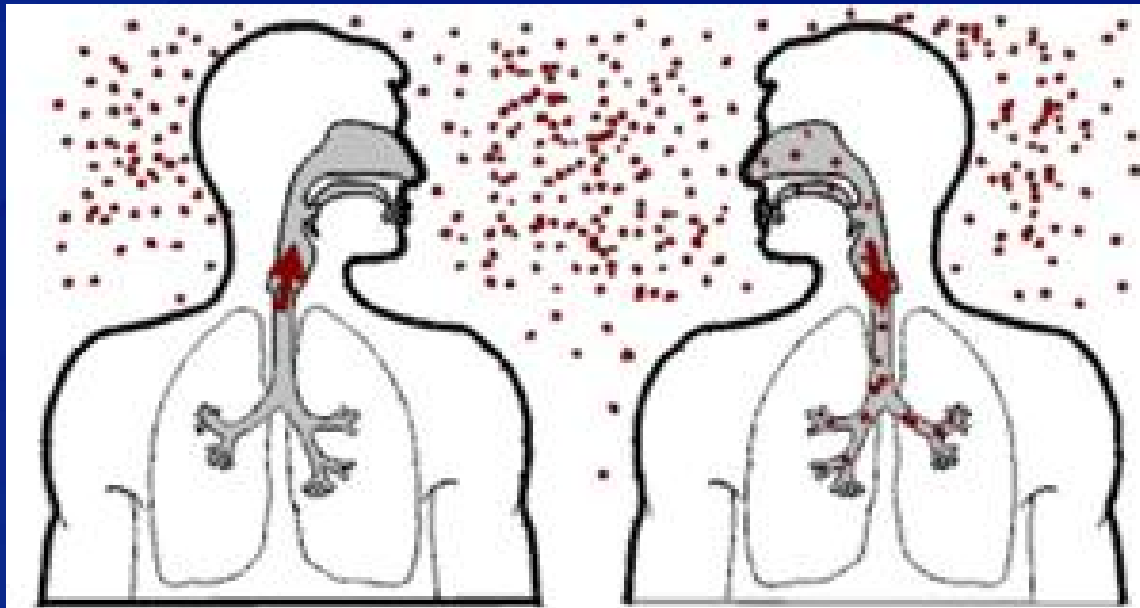
What is the risk to healthcare workers and other contacts of patients with rabies?

Rabies Virus Transmission

- ❑ **Bite exposure = Any bite from a rabid mammal**
 - Most common and most dangerous route of exposure
- ❑ **Nonbite exposure = The introduction of rabies virus (from saliva or other potentially infectious material, e.g., neural tissue) into fresh, open cuts in skin or onto mucous membranes**
 - Lower risk
- ❑ **Postexposure prophylaxis should be administered for either type of exposure**

Aerosol Transmission of Rabies Virus

- ❑ Two hypothesized human rabies cases associated with bat caves
- ❑ Two hypothesized human rabies cases occurring in research laboratory settings



Aerosol Transmission of Rabies Virus

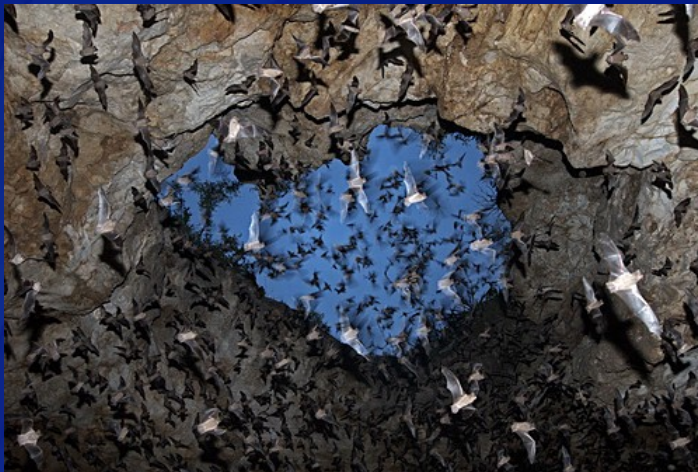
Bat Caves

- ❑ 1956: Entomologist studying the ecology of bats died of rabies after visiting several caves in central Texas
 - No reported bites or contact with any bats or other animals
 - Chronic skin eruption on his neck that he scratched or rubbed while wearing the same gloves he used to handle the bats
 - Introduction of virus into the wound?



Aerosol Transmission of Rabies Virus Bat Caves

- ❑ **1959: Mining engineer who frequented caves in Texas to evaluate them for guano mining**
 - One history states he was bitten by a bat but then later denied it
 - Another states that he denied any bat bites but had an unexplained bleeding lesion on his face when leaving the cave
 - Introduction of virus into the wound?



Aerosol Transmission of Rabies Virus

Laboratory Exposure

- ❑ 1972: 56y/o veterinarian died of rabies 2 weeks after homogenizing rabid goat brain using a blender known to produce a lingering aerosol
 - Likely removed his mask to do mouth pipetting of aliquots of the homogenate
 - Mucous membrane exposure?

Aerosol Transmission of Rabies Virus Laboratory Exposure

- ❑ 1977: 32y/o lab technician became ill after spraying suspensions of a modified live rabies virus in a pharmaceutical manufacturing machine
 - Survived but was left with severe neurologic sequelae
 - It is hypothesized that the virus involved had developed higher infectivity after passing through animal and tissue culture systems

Aerosol Transmission?

- ❑ Risk is extremely low but possible in extraordinary circumstances
 - Reasonable to take appropriate precautions to avoid contact with bats and to avoid producing aerosols when working with high concentration live rabies virus in the laboratory
- ❑ Minimize aerosol generation by using a handsaw rather than an oscillating saw and avoiding contact of the saw blade with brain tissue while removing the calvarium during autopsy

Risk to Healthcare Providers and Contacts of Human Rabies

- ❑ Human to human rabies virus transmission has occurred via organ and tissue transplantation
- ❑ Theoretically, virus transmission could also occur in the same way as animal to human transmission
 - Rabies virus present in human saliva

Human to Human Rabies Virus Transmission Reported Cases

- ❑ Very few anecdotal reports of human to human transmission via human bites, lactation, kissing, intercourse
- ❑ Difficult to exclude possible animal exposure
- ❑ No laboratory-diagnosed cases of human to human rabies virus transmission other than the transplant cases
- ❑ Thousands of human rabies patients cared for over the past century without well-documented cases of transmission of rabies from patient to provider

Risk to Healthcare Providers and Contacts of Human Rabies

- ❑ Risk is very low but present
- ❑ Important to do educational outreach and risk assessments of contacts of human rabies patients

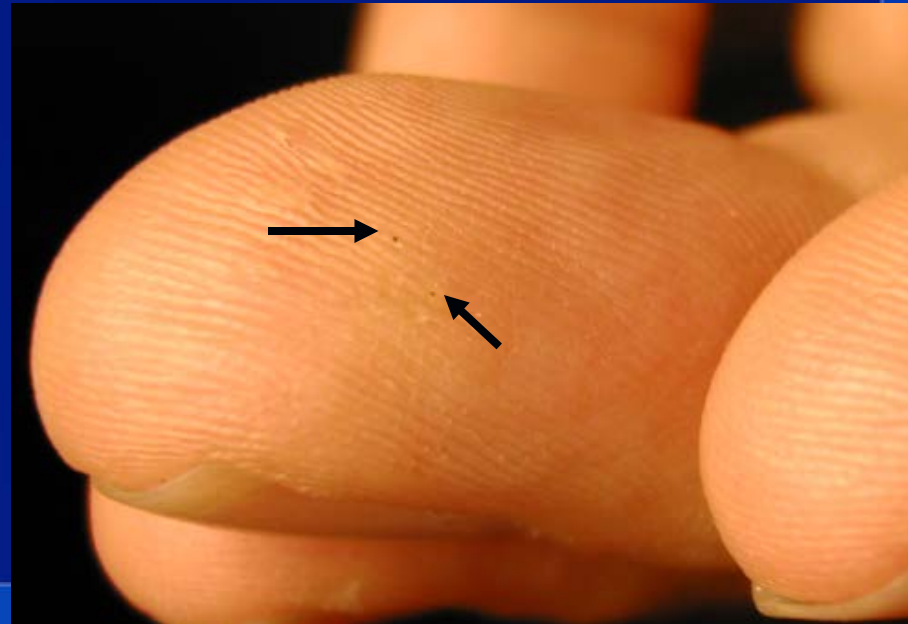
Why was no animal exposure
identified?

Exposure History of Human Rabies

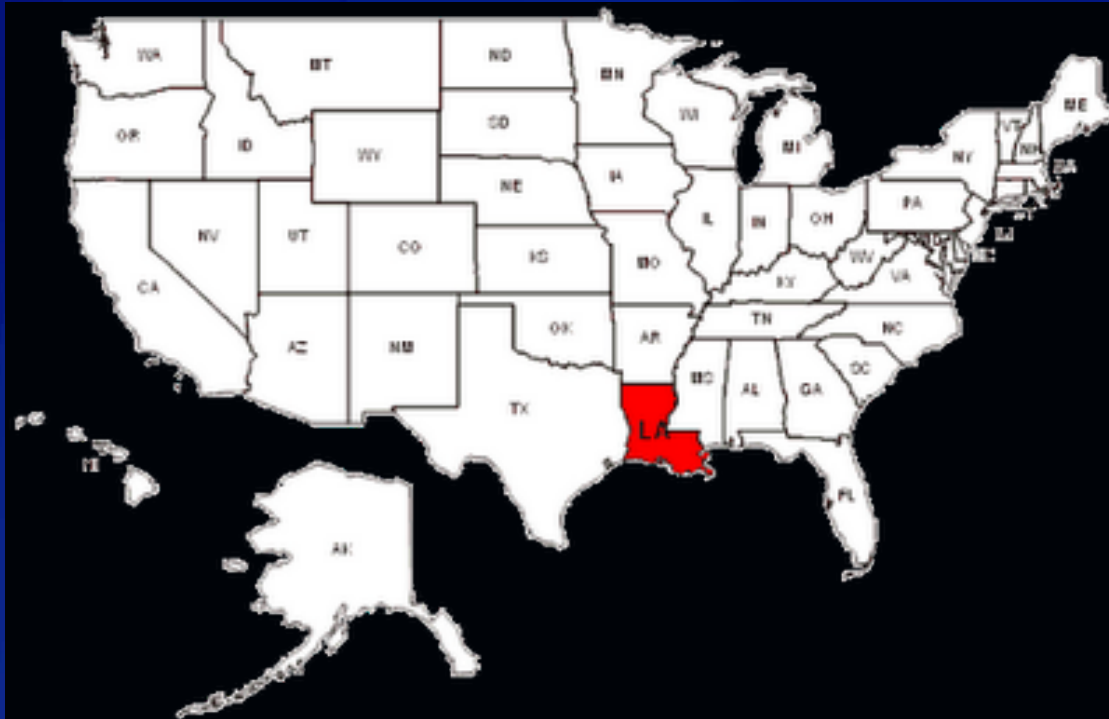
- ❑ 108 cases of human rabies reported in U.S. 1960-2010
- ❑ 54 (50%) definite exposure (animal bite, laboratory exposure, or transplanted organ or tissue)
- ❑ 26 (24%) probable exposure (physical contact with or close proximity to an animal but no known bite)
- ❑ 28 (26%) no known exposure
 - 16 bat RABV variant
 - 8 dog RABV variant
 - 1 raccoon RABV variant
 - 1 skunk RABV variant

Lack of Animal Bite History

- ❑ Lack of awareness of risk of rabies from animal bites (bats in particular)
- ❑ Short window of opportunity to evaluate patients for animal bite history
- ❑ Long incubation period
- ❑ Bat bite injuries are mild
 - No medical intervention
 - Not recognized as animal bite



Louisiana, 2010



Louisiana, 2010 Clinical Presentation

- ❑ 19-year-old previously healthy male from Mexico
- ❑ 7/29 Arrived in Louisiana to work on a sugarcane plantation
- ❑ 7/30 Sought medical attention for generalized fatigue, left shoulder pain, and left hand numbness
- ❑ 8/3 Evaluated at a local health clinic for increased sensitivity of the left shoulder, weakness of the left hand, loss of reflexes, and left-sided drooping eyelid
- ❑ Transferred to a referral hospital in New Orleans

Louisiana, 2010 Hospital Course

- ❑ Admitted to the ICU for suspected acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome)
- ❑ Developed a fever of 38.4° C
- ❑ Intubated due to respiratory distress
- ❑ Less responsive to external stimuli, developed fixed and dilated pupils
- ❑ Episodes of abnormally slow heart rate and low body temperature

Louisiana, 2010 Hospital Course

- ❑ Elevated white blood cells and protein in cerebrospinal fluid
 - Suggested encephalitis
- ❑ Laboratory testing negative:
 - HIV
 - Syphilis
 - Herpes simplex virus
 - Arboviruses
 - Lyme disease

Louisiana, 2010 Hospital Course

- ❑ 8/13 Diagnosis of rabies suspected based on clinical history and available data
- ❑ 8/20 Rabies-specific antibodies detected in cerebrospinal fluid and serum
- ❑ 8/21 Removed from mechanical ventilation in accordance with the family's wishes

Postmortem Findings

- ❑ Antigenotyping identified a vampire bat rabies virus variant
- ❑ Confirmed by genetic sequencing analysis



Public Health Investigation

- ❑ **Patient was bitten by a vampire bat**
 - Bitten on heel of his left foot while sleeping
 - Bite occurred July 15 in Michoacán, Mexico
- ❑ **Did not seek medical attention and did not receive rabies postexposure prophylaxis**

Why did it take so long to
diagnose rabies?

MD Recognition of Human Rabies

- ❑ 50/108 (46%) presented for evaluation at least once prior to hospital admission (1960-2010)
- ❑ 16/33 (48%) of human rabies cases diagnosed postmortem (2000-2010)
 - 5 cases associated with transplantation
 - 2 cases initially evaluated for Creutzfeldt-Jakob disease
 - 1 case identified by the California Encephalitis Project
 - 1 case identified by CDC's Unexplained Deaths Project

Signs and Symptoms of Human Rabies

Variable	Positive, N=108 n (%)	Negative, N=144 n (%)	Odds Ratio (95% CI*)	P-value
Mean Age (Range)	34.35 (2-82)	30.72 (<1-78)		0.173
Aerophobia	10 (9.3%)	1 (0.7%)	14.59 (1.84-115.83)	0.001†
Hydrophobia	36 (33.3%)	9 (6.3%)	7.50 (3.42-16.43)	<0.001†
Paresthesia or localized pain	54 (50.0%)	21 (14.6%)	5.86 (3.22-10.64)	<0.001†
Priapism or spontaneous ejaculation	4 (3.7%)	2 (1.4%)	2.73 (0.50-15.19)	0.41
Dysphagia	53 (49.1%)	43 (29.9%)	2.26 (1.35-3.80)	0.003†
Localized weakness	44 (40.7%)	34 (23.6%)	2.22 (1.29-3.83)	0.004†
Male Gender	83 (76.9%)	87 (62.6%)	1.98 (1.13-3.49)	0.019†
Fever	90 (83.3%)	113 (78.5%)	1.37 (0.72-2.61)	0.422
Muscle spasm	45 (41.7%)	59 (41.0%)	1.03 (0.62-1.71)	1
Hypersalivation	28 (25.9%)	38 (26.4%)	0.98 (0.55-1.72)	1
Anxiety	33 (30.6%)	51 (35.4%)	0.80 (0.47-1.37)	0.50
Hallucinations	26 (24.1%)	42 (19.2%)	0.77 (0.44-1.36)	0.39
Autonomic instability	29 (26.9%)	47 (32.6%)	0.76 (0.44-1.31)	0.34
Agitation or combativeness	55 (50.9%)	86 (59.7%)	0.70 (0.42-1.16)	0.20
Nausea or vomiting	38 (35.2%)	66 (45.8%)	0.64 (0.38-1.07)	0.09
Ataxia	20 (18.5%)	38 (26.4%)	0.63 (0.34-1.17)	0.17
Anorexia	19 (17.6%)	37 (25.7%)	0.62 (0.33-1.15)	0.17
Insomnia	11 (10.2%)	27 (18.8%)	0.49 (0.23-1.04)	0.08
Confusion or delirium	67 (62.0%)	123 (85.4%)	0.28 (0.15-0.51)	<0.001†
Seizures	27 (25.0%)	79 (54.9%)	0.27 (0.16-0.47)	<0.001†
Malaise or fatigue	39 (36.1%)	101 (70.1%)	0.24 (0.14-0.41)	<0.001†
Headache	29 (26.9%)	90 (62.5%)	0.22 (0.13-0.38)	<0.001†

* CI = Confidence interval, † Statistically significant

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Ataxia	20 (18.5%)	38 (26.4%)	0.63 (0.34-1.17)	0.17
Anorexia	19 (17.6%)	37 (25.7%)	0.62 (0.33-1.15)	0.17
Insomnia	11 (10.2%)	27 (18.8%)	0.49 (0.23-1.04)	0.08
Confusion or delirium	67 (62.0%)	123 (85.4%)	0.28 (0.15-0.51)	<0.001†
Seizures	27 (25.0%)	79 (54.9%)	0.27 (0.16-0.47)	<0.001†
Malaise or fatigue	39 (36.1%)	101 (70.1%)	0.24 (0.14-0.41)	<0.001†
Headache	29 (26.9%)	90 (62.5%)	0.22 (0.13-0.38)	<0.001†

* CI = Confidence interval, † Statistically significant

Vampire bats!

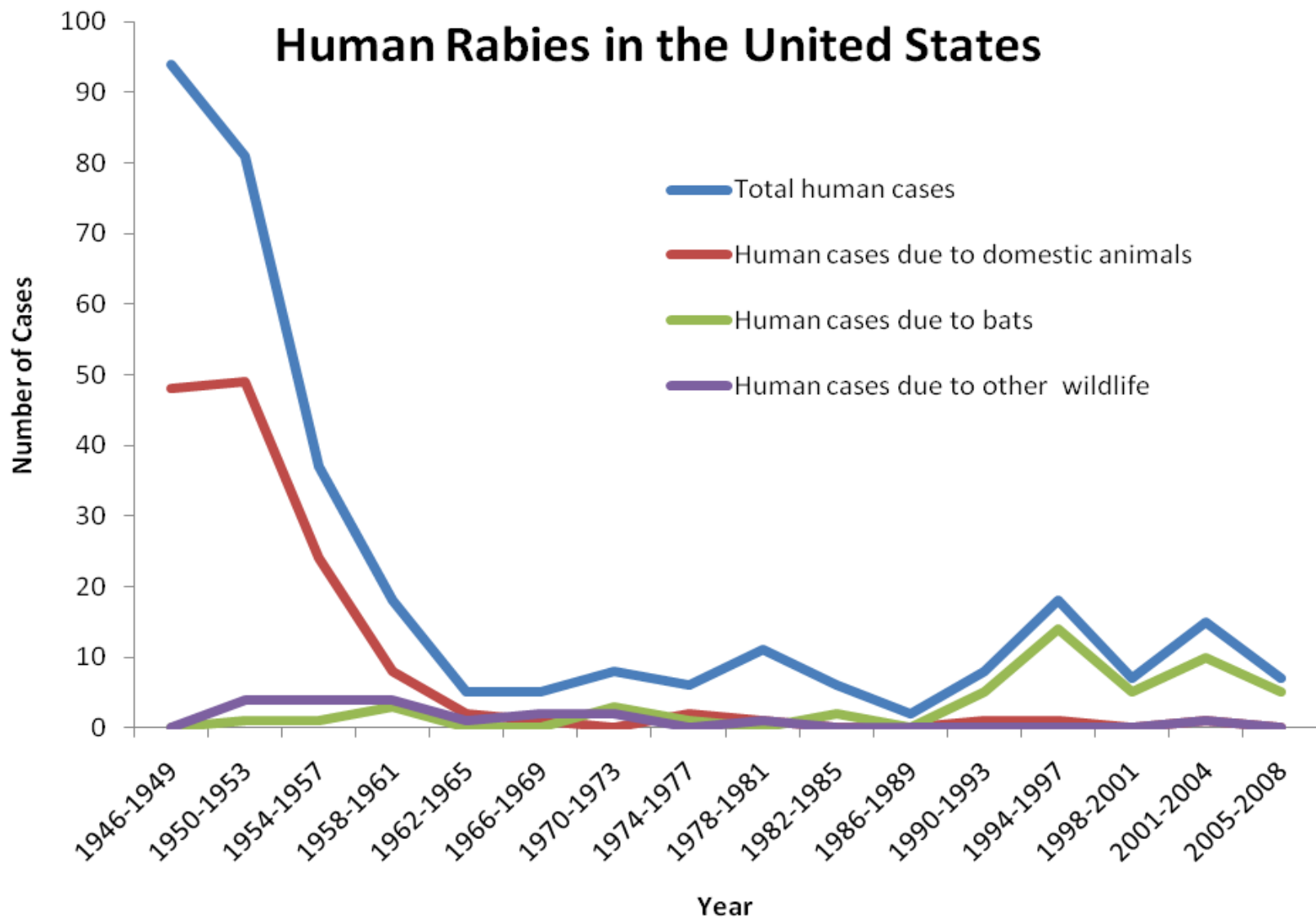


<http://animals.nationalgeographic.com/animals/mammals/common-vampire-bat/>
Photograph by Michael & Patricia Fogden/Corbis

Bats and Public Health

- ❑ First report of human rabies in the U.S. associated with a vampire bat rabies virus variant
- ❑ Bats implicated in majority of indigenously acquired human rabies in the U.S.
- ❑ Vampire bats are the leading cause of human rabies in Latin America

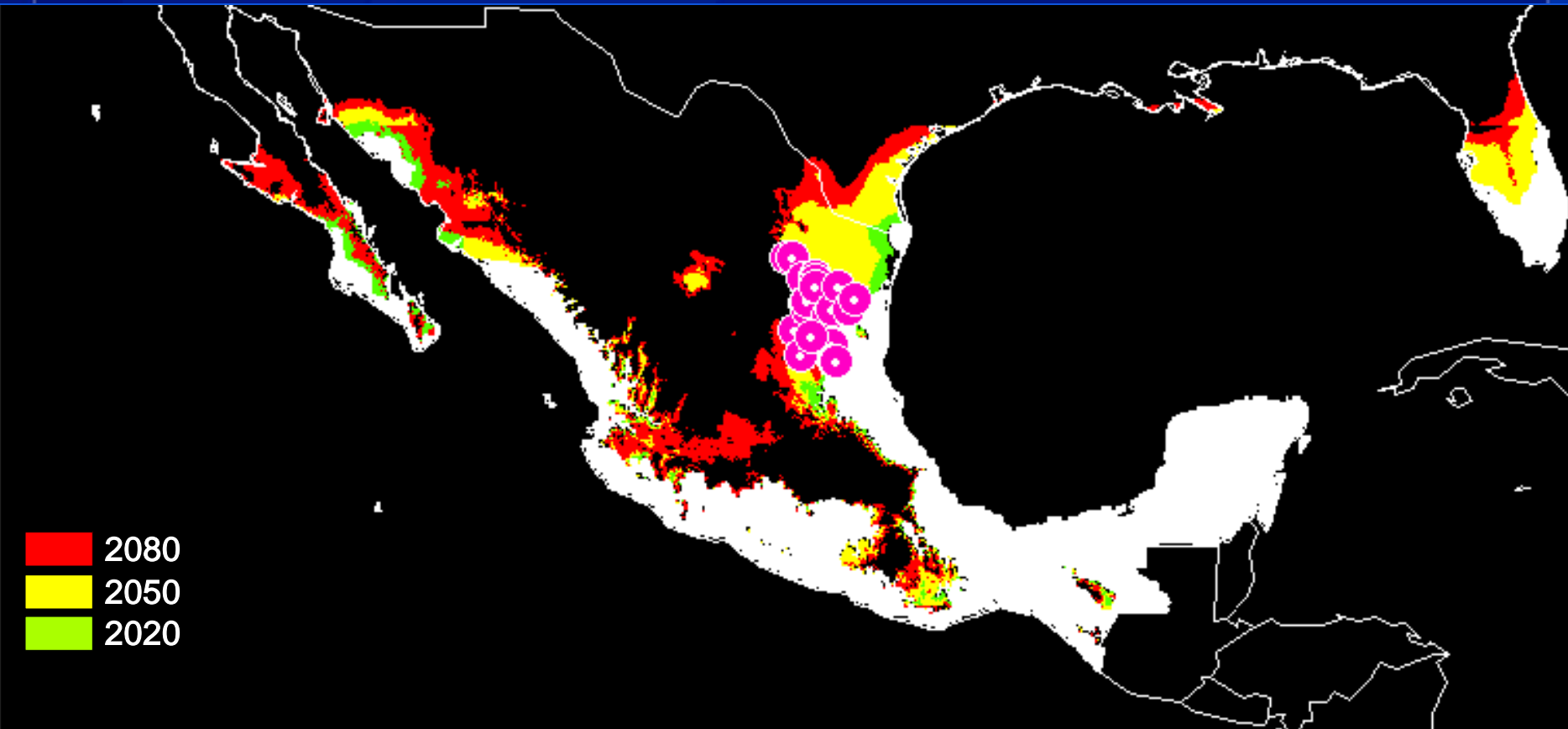
Bats and Human Rabies in the U.S.



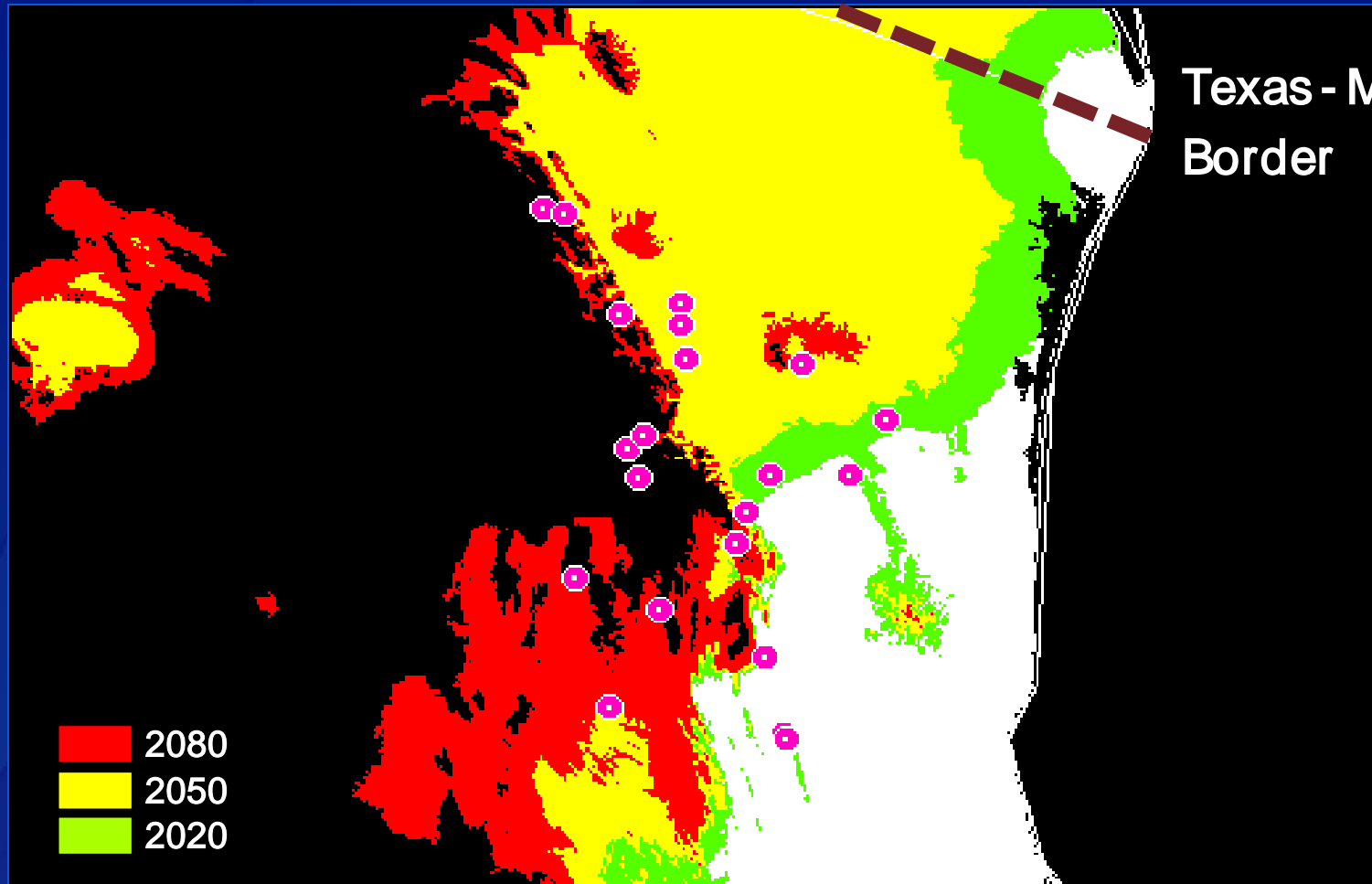
Vampire Bat Distribution



Climate Change Modeling of Vampire Bat Habitats



Texas - Mexico Border



Texas - Mexico
Border

Bats and Infectious Diseases

Bats: Important Reservoir Hosts of Emerging Viruses

Fruit bats as reservoirs of Ebola virus

Marburg Virus Infection Detected in a Common African Bat

Nipah virus infection in bats (order Chiroptera) in peninsular Malaysia.

**Isolation of Hendra virus from pteropid bats:
a natural reservoir of Hendra virus**

**Bats Are Natural Reservoirs of
SARS-Like Coronaviruses**

California, 2011



California, 2011 Clinical Presentation

- ❑ 8yo female with history of supraventricular tachycardia
- ❑ 4/25 Visited pediatrician with complaints of sore throat and vomiting
- ❑ 4/28 Presented to ED with difficulty swallowing, received intravenous hydration
- ❑ 4/30 Returned to ED with neck, abdominal, and back pain
- ❑ 5/1 Returned to ED with generalized weakness and confusion

California, 2011 Hospital Course

- ❑ 5/1 Intubated after a choking event and transferred to tertiary care center
- ❑ 5/1-3 Developed ascending paralysis, enterovirus and rabies virus infection were considered
- ❑ 5/4 Rabies diagnosis made based on positive rabies serology
- ❑ 5/4 Treatment initiated with ketamine, midazolam, amantadine
- ❑ Course complicated by autonomic instability – high blood pressure, supraventricular tachycardia

California, 2011 Hospital Course

- 5/8 Spontaneous movement of head
- 5/8-15 Increasing movement of head, then upper, then lower extremities
- 5/15 Extubated



California, 2011 Hospital Course

- ❑ 5/23 Transferred to pediatric ward
- ❑ 5/31 Transferred to rehabilitation service with residual left foot drop
- ❑ 6/22 Discharged home



Public Health Investigation

- ❑ Unvaccinated feral cats living at her school
- ❑ Scratched by two different cats approximately nine weeks and one month prior to illness onset
- ❑ Public health officials implemented a program to collect and identify cats at the school
- ❑ The first cat was observed to be healthy and alive, but the second cat could not be identified



Laboratory Testing

Date	Serum				CSF		
	Rabies IFA IgG/IgM [VRDL]	Rabies IFA IgG/IgM [CDC]	Rabies VNA (RFFIT) [VRDL]	Rabies VNA (RFFIT) [CDC]	Rabies IFA IgG/IgM [VRDL]	Rabies IFA IgG/IgM [CDC]	Rabies VNA (RFFIT) [CDC]
3-May	1:16 / 1:20	1:128 / 1:128-1:512	<1:4	<1:5	<2 / <10		
5-May	1:16 / 1:40	1:128 / 1:128-1:512	<1:4	<1:5			
6-May	1:64 / 1:80	1:128 / 1:128-1:512	<1:4	<1:5	<2 / <10	1:4 / 1:4	<1:5
8-May	1:64 / 1:40-1:80	1:128-1:512 / 1:128-1:512	<1:4	<1:5	<2 / <10	1:4 / 1:8	<1:5
11-May	1:64 / 1:160	1:128-1:512 / 1:128-1:512	<1:4	<1:5	<2 / <10	Neat / 1:4	<1:5
12-May	1:64 / 1:160	1:128 / 1:128-1:512	<1:4	<1:5			
14-May	1:32 / 1:80	1:128 / 1:128-1:512	<1:4	<1:5			
19-May	1:32 / 1:80	1:128 / 1:128-1:512	<1:4	<1:5			

Laboratory Testing

Date	Saliva		Nuchal Skin Biopsy		
	Rabies PCR [CDC]	Rabies PCR [VRDL]	Rabies DFA [CDC]	Rabies DFA [VRDL]	Rabies PCR [CDC]
5-May		NEG	NEG	NEG	NEG
11-May	NEG	NEG			
12-May		NEG			
14-May		NEG			

Additional Laboratory Testing

- ❑ Extensive testing for other infectious and non-infectious etiologies was performed
- ❑ Only positive results:
 - Mycoplasma pneumoniae IgM in serum (IgG remained negative after 16 days)
 - Mycoplasma pneumoniae PCR from respiratory swab
 - Rhinovirus PCR from respiratory swab
- ❑ Felt to be less significant than the rabies virus diagnostic results

What is the case definition of
human rabies?

Human Rabies Case Definition

- ❑ ***Confirmed:*** a clinically compatible case that is laboratory confirmed by testing at a state or federal public health laboratory
- ❑ **Laboratory evidence:**
 - Detection of viral antigen by direct fluorescent antibody testing
 - Isolation of rabies virus from saliva or central nervous system tissue
 - Identification of rabies virus-specific antibody in CSF
 - Identification of rabies virus-specific antibody in the serum of an unvaccinated person
 - Detection of viral RNA in saliva, other fluids, or tissue

Human Rabies Case Definition

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Is human rabies always fatal?

Human Rabies Survivors, U.S.

- ❑ Recovery from clinical rabies without rabies vaccination prior to symptom onset
 - 15y/o female, Wisconsin, 2004
 - 17y/o female, Texas, 2009
 - 8y/o female, California, 2011
- ❑ All met case definition for human rabies based on clinical compatibility and rabies virus specific antibodies in serum and CSF
- ❑ Infectious virus, viral antigen, and viral nucleic acid was not detected from these patients

Evidence for Subclinical Human Rabies

- ❑ 2/30 (7%) raccoon hunters in Florida demonstrated rVNAs
- ❑ 9/31 (29%) Canadian Inuit hunters with animal contact demonstrated rVNAs
- ❑ 3/26 (12%) fox trappers in Alaska demonstrated rVNAs (2 of which had history of rabies vaccination)
- ❑ 7/63 (11%) individuals exposed to vampire bats in the Peruvian Amazon demonstrated rVNAs (1 of which had history of rabies vaccination)

Black, D, Wiktor, TJ. Journal of the Florida Medical Association 73, 517-520.

Orr, PH, et al. Arctic Medical Research 47 Suppl 1, 699-700.

Follmann, EH, et al. Epidemiology and Infection 113, 137-141.

CDC unpublished data.

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Questions?

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.