Don’t touch that bat! A rabies educational case study.

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Brief Abstract

• Recently, 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 (2010-2014), 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

• 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 DSHS/CDC role!
But look how cute it is…

The scenario

• I immediately inquired about student personal information in relation to finding the student. BIO Chair and others did not know the student nor if she was a major or student at this time.

• 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 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). 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
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.
Irony at it’s finest – Recent publication for World Rabies Day


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

- RNA virus
- deadly infection of CNS of mammals
- Causes an acute encephalitis
- About 55K 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 mins 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
Presence/ absence of rabies in 2007

Disclaimer: © World Health Organization. The boundaries and names shown and the designations used on this map do not imply the expression of an 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.
1978-2013
RABIES POSITIVE ANIMALS IN MICHIGAN

LEGEND

- Bats (1320)
- Skunks (128)
- Raccoons (4)*
  "STAR IDENTIFIED TRANSLOCATION"
- Cows (10)
- Cats (27)
- Dogs (14)
- Horses (16)
- Goats (1)
- Ferret (1)
- Human (2)
- Fox (22)
- Elk (1)
- Sheep (1)
- Woodchuck (1)

http://www.michigan.gov/emergingdiseases/0,4579,7-186-25807-321094--,00.html
Laboratory-confirmed rabies in bats, 2015

Bat rabies variant
- E. fuscus
- L. borealis/L. seminculus
- L. cinereus
- L. intermedius
- L. xanthinus/L. intermedius
- N. humeralis
- T. brasiensis
- Unknown

https://www.dshs.state.tx.us/idcu/disease/rabies/maps/2015/
U.S. Epidemiology - Humans

- Human rabies cases in the U.S. are rare, with only 1 to 3 cases reported annually.
- 34 cases of human rabies since 2003
  - High male to female ratio (4.5 to 1)
  - Including 4 cases acquired via transplant from organ donor with bat rabies
- Age range from 10 to 72 (Avg. = 35)
- Many states represented (location of death)
  - Michigan (2009), Texas (2009)
- Exposures
  - 80 – 100 dogs and >300 cats with rabies each year, usually infected by wildlife when these domesticated pets are not vaccinated against rabies.

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** was documented in only 5 cases
  - 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, 5 non-indigenous cases of rabies in the US occurred in the US since 2000 (Mexico, Philippines [2], El Salvador, Haiti)
  - Recent cases of rabies in humans have implicated BATS as important wildlife reservoirs for RV, especially in US!
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.**
Approximately 12% of the bats submitted for testing at the DSHS rabies lab are positive for rabies.
Mom! Timmy's making a rabid dog face at me again!
How is rabies transmitted?

1. Virus enters via animal bite
2. Virus replicates in muscle at site of bite
3. Virus infects nerve in peripheral nervous system
   Moves by retrograde transport
4. Virus replicates in dorsal root ganglion
   and travels up spinal cord to brain
5. Brain infected
6. Virus travels from brain via nerves to other tissues such as eye, kidneys, salivary glands
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 \( (\text{normal from birth-24m}) \)
  • 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

http://www.youtube.com/watch?v=EAUBGRpyq2c

**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
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
Many different types of bat rabies!
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)
Rabies Prevention
Postexposure treatment

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

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

*A 5th dose is given to immunocompromised persons*

Tetanus booster if needed!
Things needed for working with rabies virus:
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

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

Negative

Positive for rabies!
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
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

**PCR /**Dde I** Digest of Texas Terrestrial Rabies Variants**

<table>
<thead>
<tr>
<th>Species</th>
<th>bp</th>
</tr>
</thead>
<tbody>
<tr>
<td>San Saba skunk</td>
<td>1353</td>
</tr>
<tr>
<td>S. Central skunk</td>
<td>1078</td>
</tr>
<tr>
<td>Hog-nosed skunk</td>
<td>872</td>
</tr>
<tr>
<td>Fox (TF)</td>
<td>603</td>
</tr>
<tr>
<td>Coyote (DDC)</td>
<td>310</td>
</tr>
<tr>
<td>Sonora dog (SD)</td>
<td>271, 281</td>
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<tr>
<td>Raccoon</td>
<td>234</td>
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<tr>
<td><em>Raccoon</em></td>
<td>194</td>
</tr>
<tr>
<td>Kb Standard</td>
<td>118</td>
</tr>
<tr>
<td>*</td>
<td>72</td>
</tr>
</tbody>
</table>

* Specimen provided by CDC from Eastern U.S.

Data from sequencing put in phylogenetic tree

Viruses closely related will “cluster” together in tree
References

• Bonny Mayes, MA; Pamela J. Wilson, MEd; Ernest H. Oertli, DVM, PhD, DACVPM; Patrick R. Hunt, BS; Rodney E. Rohde, PhD, MS. Epidemiology of rabies in bats in Texas, 2001-2010. J Am Vet Med Assoc 2013;243:1129–1137.


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Questions?

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www.txstate.edu/~rr33

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

Maybe your job isn’t as “pressure-filled” as you thought???

http://www.worldrabiesday.org/