Public Health Importance of Rabies

- Rabies is the infectious disease with the highest known case fatality rate.
- Between 2000-2009:
  - 31 cases of human rabies reported in the U.S
    - 23 (74.2%) due to U.S. variants
    - 18 (78.3%) were due to bat variants
- PEP (Post-Exposure Prophylaxis) Issues
  - Treatment is costly, including biologics and professional fees
  - PEP requires a series of vaccines be administered
  - Limited number of biologics manufacturers (supply issues)

Rabies causes an acute encephalitis in all mammals, including humans, and the outcome is almost always fatal. Modern rabies prophylaxis is nearly 100% effective in preventing rabies in exposed individuals. Human rabies cases today occur in individuals who fail to seek medical assistance, usually because they were unaware of their exposure to rabies.

Rabies is caused by a lyssavirus and all mammals are susceptible to infection. However, only a few species of mammals are considered to be important reservoirs for the virus, each with a distinctive variant of the virus. In the U.S., terrestrial variants include skunk, raccoon, fox and coyote. On the next slide is a map of the distribution of the various terrestrial rabies variants in the U.S. In addition, insectivorous bats are reservoirs for the rabies virus in most states in the U.S.

In the U.S., the annual cost of preventing rabies is estimated to be over $300 million. This includes the cost of vaccinating domestic animals, animal control efforts, maintenance of rabies diagnostic laboratories and medical treatments such as post-exposure prophylaxis (PEP). An estimated 40,000 people receive rabies PEP each year in the U.S. The cost of PEP for individual patients can vary greatly, but may average between $5,000 and $10,000.
The term “terrestrial” refers to species who live on the land, as opposed to water, air, or in trees. There are several different strains of terrestrial rabies circulating in the U.S., with multiple strains associated with skunk and fox. In Michigan, the north central skunk strain occurs in SE Michigan and the “thumb” region of the state. In the U.S., terrestrial strains of rabies “spill over” into other wild and domestic animals more often than bat strains do.
Rabies occurs in bats throughout the state. There have been rare instances in Michigan of bat-strain rabies detected in other wildlife species besides bats, primarily in fox. Human rabies deaths are rare due to very conservative post-exposure assessment/treatment guidelines. The most recent human case of rabies in Michigan occurred in 2009 and was due to a bat strain (the previous case to 2009 was in 1983 and was also bat strain).

Most cases of rabies in animals are detected in mid and southeastern Michigan, associated with the more populous counties. In addition, a skunk strain of rabies is present in the “thumb” area of the state and is responsible for most cases of rabies in species other than bats.

The Michigan Department of Community Health’s Bureau of Laboratories tests three to four thousand animals a year. Bats, cats and dogs are the most commonly submitted specimens. Bats are the animal most frequently testing positive for rabies in Michigan, followed by skunks, cats, fox and horses.

Michigan law requires that dogs and ferrets be vaccinated against rabies, but vaccination is not required for cats at this time. In Michigan, cats and dogs frequently bite people. MDCH tests many dogs and cats that bite people, and few are found to be positive for rabies.

Most states require rabies vaccination for dogs. Rabies biologics for domestic animals have been extensively studied and are potent and effective. Rabies rarely occurs in consistently vaccinated domestic animals. Fewer states have laws requiring rabies vaccination for cats. As a result, cats, specifically feral or stray cats, are becoming an increasing risk for the public, particularly in areas with a terrestrial rabies virus reservoir. Skunk strain rabies is occasionally detected in stray cats in SE Michigan. Cats kept exclusively indoors can still be exposed to rabid bats inside the home.
In the southeastern and “thumb” area of the state, there is a focus of terrestrial rabies associated with skunks. As you can see from the map, this strain of rabies can “spill over” into other species of animals, including unvaccinated domestic pets and livestock. As a result, there is a greater variety of animals detected with rabies in this region.
Special Features of MDCH Rabies Specimen Testing

- MDCH Laboratory can test rabies specimens 7 days a week, including holidays and weekends (by special arrangement)
- Individual results are provided to the submitter via phone each day
- Specimens received by 8 AM are usually completed the same day

Special rabies submission kits are available free of charge to any agency submitting specimens to MDCH for testing. Animal control/shelters and local public health agencies most often submit specimens to MDCH, but veterinarians, hospitals, wildlife biologists and others also submit specimens.

MDCH performs rabies testing free of charge. However, preparation and shipping costs are not covered.
Mandatory Bite Reporting

[Under Michigan's Communicable Disease Rules, promulgated under the Authority conferred on the Department of Community Health by section 5111 of Act No. 368 of the Public Acts of 1978, as amended, being 333.5111 of the Michigan Compiled Laws.]

“Animal bites...should be reported to the local health jurisdiction where the bite occurred...the local health jurisdiction where the patient lives or where the service facility is located.”

Physicians must report bites to their local health department.
Primary Rabies Reference Tools

ACIP Guidelines=Human Rabies Prevention, updated as new information becomes available

Rabies Compendium=Animal Rabies Prevention and Control, typically published yearly (not in 2009)
The 2008 ACIP Guidelines comprehensively address the issues and questions most healthcare providers have about rabies PEP.
Rabies PEP is a lifesaving treatment. Numerous studies from around the world have indicated that postexposure prophylaxis combining wound treatment, local infiltration of RIG, and vaccination, when appropriately administered is uniformly effective in preventing rabies infection. However, rabies has occasionally occurred in humans when key elements of the treatment were omitted or incorrectly administered.

Rabies vaccine should never be administered in the gluteal muscles. The preferred site is the deltoid muscle, or the anterio-lateral thigh of small children.

RIG should not be administered in the same site as vaccine.
Rabies biologics are currently readily available, although shortages can occur due to the limited number of manufacturers.

Many primary care physicians are reluctant to provide rabies vaccination to their patients. This reluctance may be partly due to unfamiliarity with ordering and administering the biologics. The current ACIP Guidelines contain detailed information on the safety of rabies biologics. Visiting a primary care physician is often less expensive and more convenient for patients. In addition, primary care clinics may be better able to assure that patients keep their follow-up appointments and complete the PEP series.
Cost of Treatment

- Rabies PEP is costly, partly due to the limited number of biologic manufacturers.
  - RIG is an expensive biologic
    - Dosed by weight
    - Single dose can result in patient charge of thousands of dollars.
  - Vaccine
    - Only two manufacturers for U. S. market (Novartis and sanofi-pasteur)
    - Average cost is $200/dose
- The PEP series for a single individual can run $5–10,000 including hospital/healthcare provider (HCP) charges.
- Most insurance (public and private) covers rabies PEP, deductible may be higher for hospital visit vs office visit.
- Biologics companies have indigent programs (www.rxhope.com)
  - Must meet eligibility requirements
  - Provides the hospital/HCP with product to replace what is used on patient
  - Do not cover hospital/HCP charges

Healthcare providers, local public health and animal control agencies need to work together to assure that patients that need treatment receive it, and patients that don’t need it don’t start it. The following slides provide more information on how to evaluate a patient for a potential exposure to rabies.
The decision to administer (or receive) rabies PEP should be based on the risk of exposure to rabies. In cases of known exposure (bat bite where animal tests positive for rabies), PEP is necessary to prevent death. Many potential rabies exposure situations are less clear cut. A good risk assessment is essential when weighing the risk of treatment (potential for rare severe adverse reactions) vs the risk of no treatment (death from rabies). In many animal bite situations, the risk of rabies is extremely low, allowing ample time to conduct a public health investigation prior to initiating treatment.
For the last decade, the Michigan Rabies Working Group has developed and updated risk assessment protocols for healthcare providers based on the ACIP Guidelines for Human Rabies Prevention. These protocols provide front-line recommendations on how to handle patients presenting with animal bites or other potential animal exposures.
The Michigan Rabies Working Group has also developed protocols on how to handle animals that have either exposed people or been exposed to rabies. These protocols are utilized by animal control and animal health professionals when making decisions about how to handle these animals (observation vs testing).
What the HCP Needs to Know Before Deciding to Initiate PEP

- **Species** of animal?
  - Wild (bat, raccoon, fox, skunk, coyote, other carnivore?)
  - Dog, cat, ferret
  - Rodent (Do not pose a risk for rabies)
- **Animal available** for testing/observation?
- **Michigan epidemiology** for that species? [www.michigan.gov/rabies](http://www.michigan.gov/rabies)
- **Observed health and behavior** of the animal?
- **Circumstances** of the bite?

Bats and wild carnivores are the species most likely to carry rabies in the U.S.

It is important to determine if the biting animal has been or can be captured. If so, PEP can often wait for the results of testing or, in the case of healthy dogs, cats and ferrets, confinement and observation.

Knowing what strains of rabies are present in your area can help when making a decision about whether rabies PEP is indicated.

Unprovoked attacks by strangely or erratically behaving animals are of the most concern.

However, many wild and stray animals will bite if a person tries to approach or otherwise interact with them. This is normal animal behavior. It is important to find out the series of events that led to the person being bitten.
All mammals are susceptible to rabies virus. However, rodents are not reservoirs for rabies virus. Small rodents are rarely infected with rabies and have not been known to transmit rabies virus to humans.

In states with raccoon-strain rabies, woodchucks have constituted the majority of rodents diagnosed with rabies, and will be tested for rabies at the MDCH BOL if the circumstances warrant it.

Consult local and state health department officials before initiating PEP following an incident involving a rodent.
Type of Exposure

- Bite?
  - Site
  - Severity
  - Immediate cleansing
- Potentially Unrecognized Bite?
  - Bat in room with sleeping person, or witnessed in room with an unattended child, mentally disabled or intoxicated person
- Non-bite?
  - Exposure to saliva or neural tissue (blood, urine, feces do not contain rabies virus)
    - Mucous membrane exposure
    - Non-intact skin (fresh, open cuts)

All bites constitute a potential risk for rabies. Immediate and thorough cleansing of the wound has markedly reduced the likelihood of rabies in animal studies. The need for a tetanus booster and antibiotic administration should also be assessed. While severe bites may increase the risk of rabies transmission, rabies can also be transmitted by relatively minor bites inflicted by bats.

In the case of bats, it is not appropriate to look for “bite marks” to determine the need for PEP. If a person was in close proximity to a bat and is not reasonably certain that contact with the bat did not occur, then PEP may be indicated.

Non-bite exposures very rarely cause rabies. Examples of non-bite transmissions include recipients of corneas, solid organs and vascular grafts from patients who died of an unrecognized rabies infection and persons who acquired rabies from aerosol exposure in caves filled with millions of bats.

Rabies virus is inactivated by drying, exposure to ultraviolet radiation and other factors and does not persist in the environment. The virus is killed by usual methods of disinfection. If the suspect material is dry, it is considered non-infectious.
Provoked or Non-provoked Bite?

- Provoked exposures:
  - Attempting to feed animal
  - Entering animal’s territory
  - Breaking up a fight between two animals
  - Handling an injured, wild or feral animal
  - Walking, running, or riding a bike past an animal
- Unprovoked exposure:
  - Animal crossed neutral territory to initiate contact
- DETAILS of the encounter are important for a proper risk assessment

Unprovoked attacks are more typical of animals with rabies. Do not ask “Was the bite provoked?”, rather have the person tell you what they were doing when the bite occurred. A person may consider a bite from an animal they are petting unprovoked, but it is not.
When is it Appropriate to Wait to Initiate PEP?

- When the animal is likely to be found and captured for observation or testing
- When the animal is readily available for testing
- When the animal involved is a dog or cat

Day 0 is the most painful and expensive day of treatment. Costs incurred are in the thousands of dollars.

Initiating rabies PEP is a medical urgency, not an emergency. In most instances, it is appropriate to wait 48-72 hours to receive animal testing results or find and confine a dog, cat, or ferret.

RIG is typically administered on Day 0, along with the first dose of vaccine. RIG is dosed by weight (20 IU/kg). As much as is anatomically feasible should be infiltrated into the site of the bite, with the rest given in a site distant from the vaccine administration site. For this reason, multiple injections may be required to administer the full dose of RIG as directed. RIG is also the most expensive biologic, with cost varying by the weight of the patient.
What Would You Do?

A person was bitten by a stray cat that ran away.
Next Steps to Take

- Get details of the encounter-
  - Is the animal familiar to the bite victim?
    - Can the animal be captured for testing or observation?
  - Provoked/unprovoked?
  - Did animal appear healthy?
  - Did the bite occur in a county with terrestrial rabies cases or a history of cases?
- Assess bite, tetanus booster status, need for antibiotics
- Report bite to Local Health Department/Animal Control ASAP

Is this an animal that the bite victim knows, routinely feeds, or sees regularly around? Did the person attempt to approach or handle the cat? Is the cat otherwise eating and behaving normally? Did the cat have any wounds or injuries that might indicate it fought with another animal?

Animal bites are required to be reported to local health authorities. The local health department will investigate the bite and in many cases will engage local animal control authorities to find the cat if necessary. If their investigation determines that a risk for rabies exists, the LHD will recommend that the bite victim begin rabies PEP.

Feral cats can be difficult to trap. If this is an animal that routinely hangs around the bite victim’s home, simply observing the health and behavior of the cat from a distance for 10 days can provide a reasonable assurance that the animal is not developing signs of rabies.
What Would You Do?

A neighbor’s unvaccinated dog bit a child on the face
Questions are similar to the previous example. In the case of an owned animal, it is important to assess the animal’s opportunity to be exposed to rabies vectors. For example, a small poodle who hardly ever leaves the house except on a leash is much less likely to be exposed to rabies than a dog that is tied out in the yard day and night.

A dog, cat or ferret with a history of continuously current rabies vaccinations is unlikely to become infected with rabies. Small lapses in rabies vaccination status are usually not important, but a completely unvaccinated animal is vulnerable to rabies infection should an exposure occur.

Face bites can present an increased urgency when rabies is suspected. Rabies virus travels up the nerves to reach the brain. The time it takes for that to happen contribute to the length of the incubation period for the virus. In the case of a face bite, the distance the virus has to travel is relatively short. Therefore, in a high-risk situation (ex: bat bite on the ear), it may be appropriate to begin treatment while testing is underway. If the animal tests negative for rabies, treatment can be stopped.

In most cases, bites by owned animals represent a low risk for rabies. It is often appropriate to simply observe the animal’s health for 10 days. The bite victim need not receive rabies PEP if the animal remains healthy during this observation period.
What Would You Do?

A bat is found in the room with a sleeping, pregnant woman. The bat was gently collected and released outdoors.

CDC Image Library
Next Steps to Take

- Initiate PEP
- Pregnancy is not a contraindication for PEP
What Would You Do?

A cute orphan baby skunk was being bottle fed by a family. It became ill and died about 4 days after it was found. This happened 2 weeks ago. The family became worried after talking to neighbors.
Next Steps to Take

- Assess exposure status of the family (bites, scratches, saliva in fresh cuts or on mucous membranes?)
- The north central skunk-strain of rabies is present in the southeastern and thumb area of Michigan.
- In general, PEP is recommended for individuals who are bitten by wildlife, particularly carnivores, and the animal is not available for rabies testing.
- There is no time restriction on beginning PEP. It should be started as soon as the need is recognized, provided clinically compatible signs of rabies are not present in the exposed person.
An adult is bitten when trying to pick up a squirrel that “looked sick”.

What Would You Do?
Next Steps to Take

- Rodents, including squirrels are not considered to be rabies vector species in Michigan.
- Except in very unusual circumstances (unprovoked attack by erratic behaving animal), rodents are not tested for rabies.
- Treat bite (tetanus, antibiotics).
- Rodents can carry other serious pathogens; Streptobacillus, Lymphocytic choriomeningitis virus, tularemia, plague, etc. Patients need to monitor their health for 1-2 weeks.

Wild animals frequently bite when people try to approach or handle them. This is normal wild animal behavior.

Rodent bites have not been documented to be responsible for any human cases of rabies in the U.S.
What Would You Do?

A family just purchased a gerbil from a local pet store. It bit their child when he picked it up, then was found dead in the cage the next day.
Pet rodents bites are not considered to be risk for rabies, due to the lack of opportunity for exposure to rabies.

In unusual circumstances, animals may be tested.

In 2003, monkeypox was introduced into the U.S. through the importation of exotic animals for the pet trade. Infected rodents, such as Gambian rats, imported from Africa were housed in close contact with prairie dogs destined to become pets. People in the U.S. became infected with monkeypox following contact with infected pet prairie dogs. This is just one example of a disease that can be transmitted by the bite of an infected rodent. Following this incident, the U.S. banned the importation of wild rodents for the pet trade.
What Would You Do?

A 6 yo child was walking on a sidewalk and was bitten on the hand by a monkey that jumped off its owner’s shoulder and onto the child.

Java Macaque
Next Steps to Take

- Take steps as previously described for animal bites, including assessing tetanus status and need for antibiotics.
- Report bite to Local Health Department/Animal Control ASAP.
- Rabies is generally a low risk from primate bites, but a thorough risk assessment should be conducted, including knowing the circumstances of the bite, the biting animal’s health, and its opportunity for exposure to wildlife (bats, other rabies vectors).
- Resource: MDCH “Zoo/Exotic Animal Bite Fact Sheet”

Primates are susceptible to many diseases that humans have, and can acquire these diseases from their owners or handlers. Examples include hepatitis viruses and tuberculosis. Consult the state and local health department regarding how to assess and handle primates or other exotic animals that bite people. It may be necessary to place the animal in quarantine for a period of time to observe for any changes to its health that could signal a potential public health threat.
Primate Bite – Special Concern

• Certain primate bites (macaques) are a concern for B virus, which can cause a potentially fatal encephalitis in people. It is important to determine the species of primate inflicting the bite - take pictures if possible and consult with an infectious disease physician.

If the animal is a macaque:
- Perform viral culture of the wound
- Draw blood for baseline serology for B virus exposure
- Initiate antiviral therapy

Macaque monkeys can carry B virus, a herpes virus that can produce a fatal encephalitis in humans. Macaque monkeys can remain healthy and shed this virus intermittently throughout their lives. Many veterinarians are reluctant to handle macaque monkeys because of the risk they pose to themselves and their staff. In bites involving macaques, it can be very difficult to find an animal health professional willing to evaluate these animals, further complicating these public health investigations.

Consult local and state health authorities in situations involving bites from exotic animal species.
How to Manage Mammals Which Have Bitten People
General Guidelines

- Wild Mammal (bats and carnivores)
  - Euthanize and test
- Domestic dogs, cats, ferrets; **regardless of vaccination status**
  - Healthy animal
    - Confine 10 days then release if healthy
    - If animal is unwanted or develops signs of rabies, euthanize and test
  - Animal ill with signs suggestive of rabies
    - Euthanize and test
  - Healthy stray animal
    - Hold 4 days (required by Michigan statute) then euthanize and test
    - Alternatively, hold 10 days
- Domestic Livestock: These are handled on a case by case basis. Consult MDA, MDCH.

There is no observation period recommended for wild animals. Even apparently healthy wild animals that bite people should be euthanized and tested. Not enough is known about how the rabies virus behaves in wild animals or how the virus persists in wildlife populations. It is not known how long a wild animal might have virus present in its saliva (be infectious) before it shows signs of illness.

A 10 day observation period is applied to healthy dogs, cats and ferrets ONLY. That is because rabies has been well studied in these animals and much is known about how the virus behaves in these species. In order for rabies virus to be present in the saliva, it has already infected the brain. The virus travels from the brain to the salivary glands via the nerves. Therefore, rabid dogs, cats and ferrets that bite should already be showing signs of illness/encephalitis at or around the time of the bite. Rabies is a rapidly progressive disease in these species and the animal's health and mental status will continue to decline over time.
Contact Information

• LHD Contact:
  Daytime ____________
  After-hours ____________

• Michigan Department of Community Health:
  – Daytime: 517-335-8165
  – Evening/weekend: 517-335-9030

• Michigan Department of Agriculture:
  – Daytime: 517-373-1077
  – Evening/weekend: 517-373-0440

Keep the contact information for your local health department handy.
Important Websites

- [www.michigan.gov/rabies](http://www.michigan.gov/rabies)
  MI Rabies Maps, PEP Protocols
- [www.cdc.gov/rabies](http://www.cdc.gov/rabies)
  ACIP Guidelines, physician info
- [www.nasphv.org](http://www.nasphv.org)
  Rabies Compendium