

Animal Bites and Rabies



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2018

Objectives

- ✦ To inform participants about the treatment of common animal bites
- ✦ To discuss the indications for and administration of pre- and post-exposure prophylaxis for rabies
- ✦ To familiarize participants with the presentation and potential treatment options for active rabies infection

Case / Questions

- ✦ Would you rather be bitten by...
 - ◆ A. your wild two year old nephew you attempt to hug on your family vacation or
 - ◆ B. the tame monkey you attempt pet on your tropical vacation

- ✦ Would you rather be bitten by...
 - ◆ A. your sister's house cat or
 - ◆ B. your parent's lap dog?



Animal Bites

- ✦ Typically polymicrobial, including anaerobes
- ✦ Up to 75% of clenched-fist injuries have injury to underlying tendon, bone, or joint
- ✦ Cats: 80% become infected
- ✦ Dogs: Only 5% become infected
 - ◆ Treat only if severe bite or co-morbidities
 - ◆ Splenectomy patients at high risk for fatal *Capnocytophaga* sepsis following dog bites – Admit and consult ID and/or ICU!

Human, Cat, & Severe Dog Bites

- ✦ Thoroughly clean wound
- ✦ Consider x-ray to assess for deeper injury
- ✦ Tetanus booster if none in last 5 years
- ✦ Consider rabies PEP (*Stay tuned!*)
- ✦ Outpatient treatment/prophylaxis:
 - ◆ Amoxicillin-clavulanate po
 - ◆ If PCN allergic: clindamycin + quinolone (ciprofloxacin) or clindamycin + trim-sulfa

Human, Cat, & Severe Dog Bites

- ✦ Consider admission if: DM, PVD, immunocompromised, tendon/joint/bone injury, fever, cellulitis, or suspected non-adherence
- ✦ CBC with diff, CMP, CRP, and ESR
- ✦ Consider I&D with bacterial cultures
- ✦ Inpatient iv antibiotics:
 - ◆ ampicillin-sulbactam or
 - ◆ piperacillin-tazobactam or
 - ◆ cefoxitin (which may be used in PCN allergic pts if no h/o hives or anaphylaxis)

Macaque Monkey Bites

- ✦ Multiple varieties including Rhesus, Long-tailed, Japanese (Snow Monkey)
- ✦ Found throughout Asia and North Africa
- ✦ Common in zoos, research labs, primate facilities, and as pets



Macaque Monkey Bites

- ✦ Macaque monkeys often carry B virus (a.k.a. herpes B, herpesvirus simiae, herpesvirus B)
- ✦ B virus causes fatal encephalitis in humans (70% mortality)
- ✦ Clean wound within 5 minutes for at least 15 minutes to decrease risk
- ✦ Prophylaxis with valacyclovir 1 gm po Q8hrs x 14 days
- ✦ Other treatment as per human bite

Rabies



Epidemiology

- ✦ A business executive is asked to donate money to aid rabies prevention efforts. She was unaware that rabies was still “around.”
- ✦ Does rabies continue to be a problem?
- ✦ What is its cycle in nature?

Epidemiology: United States

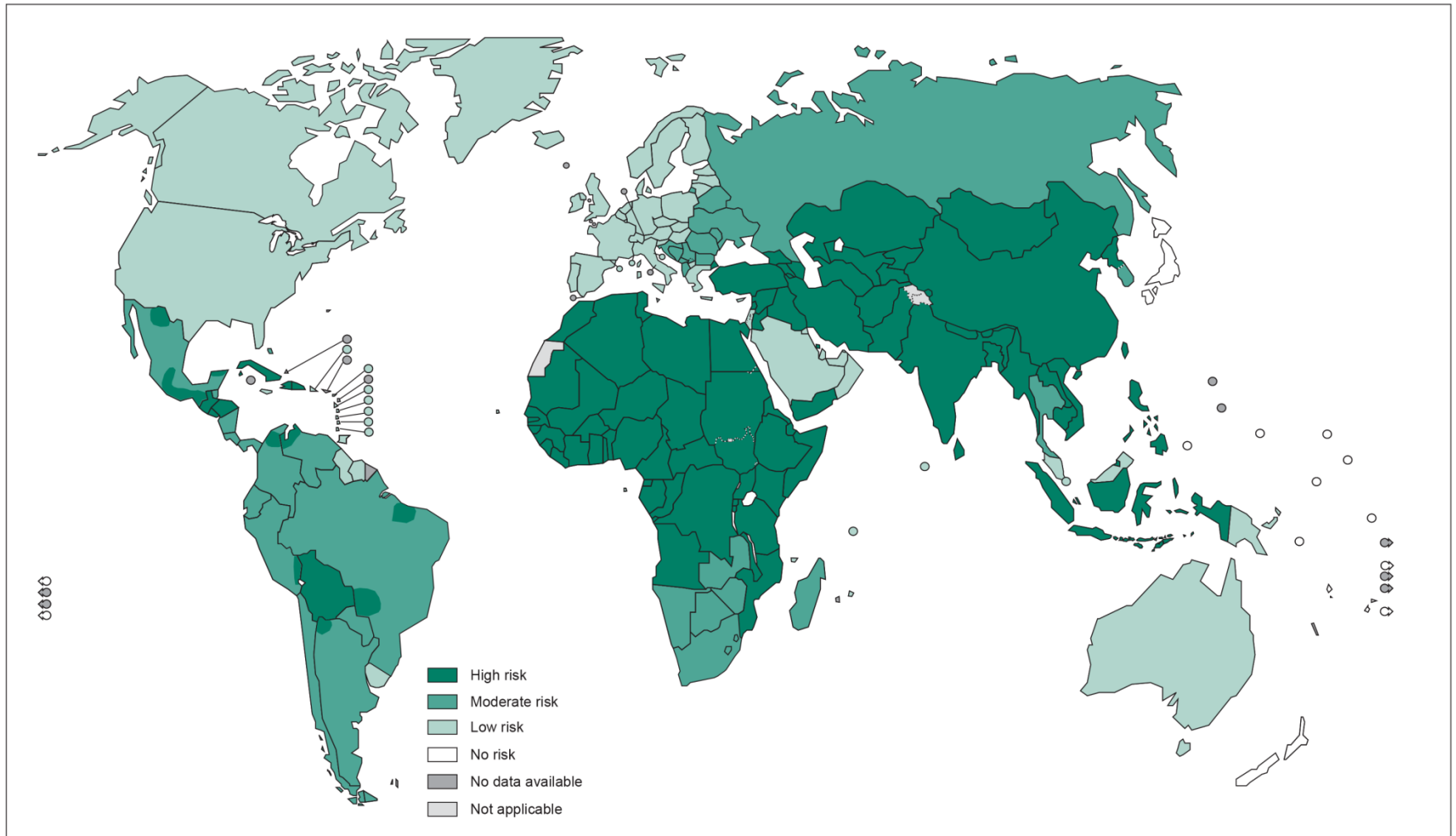
- ✦ 2008-2017: 23 cases human rabies
 - ✦ 8 contracted outside the US
- ✦ 20,000-40,000 persons receive PEP yearly
- ✦ >\$300 million per year spent on rabies prevention (includes animal vaccination)
- ✦ Still common in wild animals with 1000's of cases each year
- ✦ Hawaii is the only rabies-free state

Epidemiology: Worldwide

- ✦ 30,000 to 50,000 deaths each year
- ✦ Children < 15 years at greatest risk
- ✦ 95% of human deaths occur in Asia & Africa
 - ✦ India has particularly high rates of human rabies
- ✦ Dogs primary reservoir (99%)
- ✦ WHO Zero by 30 strategy



Distribution of risk levels for humans contacting rabies, worldwide, 2013

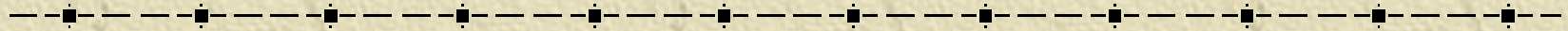


The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2014. All rights reserved

Data Source: World Health Organization
Map Production: Control of Neglected
Tropical Diseases (NTD)
World Health Organization



The infectious path of rabies virus



4. The virus incubates in raccoon's body for approximately 3-12 weeks. The raccoon has no signs of illness during this time

3. Rabies virus spreads through the nerves to the spinal cord and brain

2. Rabies virus enters the raccoon through infected saliva.



1. Raccoon is bitten by a rabid animal

5. When it reaches the brain, the virus multiplies rapidly passes to the salivary glands, and the raccoon begins to show signs of disease.

6. The infected animal usually dies within 7 days of becoming sick

Postexposure Prophylaxis (PEP)

- ✦ A patient presents to the walk-in clinic following an unprovoked bite from a stray cat that was not captured. The clinician has not seen a similar patient in several years.
- ✦ Have the guidelines for PEP changed recently?

PEP- 2017

- ✦ Soap and water x 15 minutes + iodine or other viricidal agent
- ✦ RIG (Human)
 - ◆ 20 IU/kg
 - ◆ ALL in wound, if possible
 - Any leftover, give im in large muscle
 - ◆ Do not give in same location as the vaccine
 - ◆ Do not use same syringe to give RIG and vaccine

PEP- 2017 (cont)

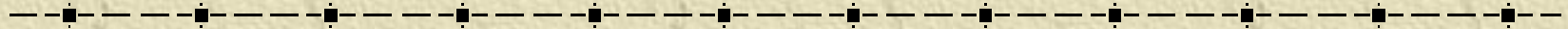
✦ Vaccine (Cell culture)

- ✦ Human Diploid Cell Vaccine (HDCV) or Purified Chick Embryo Cell Vaccine (PCECV)
- ✦ 1 cc IM in deltoid for adults and older kids
 - Lateral thigh okay for small children < 2yo
 - NEVER give gluteal
- ✦ Day 0, 3, 7, 14
 - Day 28 vaccine and post-vaccination titers 2-4 wks later for immunocompromised pts
 - WHO recommends day 0, 3, 7 and intradermal for low-income settings

Rabies & Animal Bites

- ✦ An emergency room doctor is about to evaluate a patient who has been bitten by a [insert animal name here].
- ✦ How do the recommendations for PEP vary depending on the type of animal that inflicted the bite?

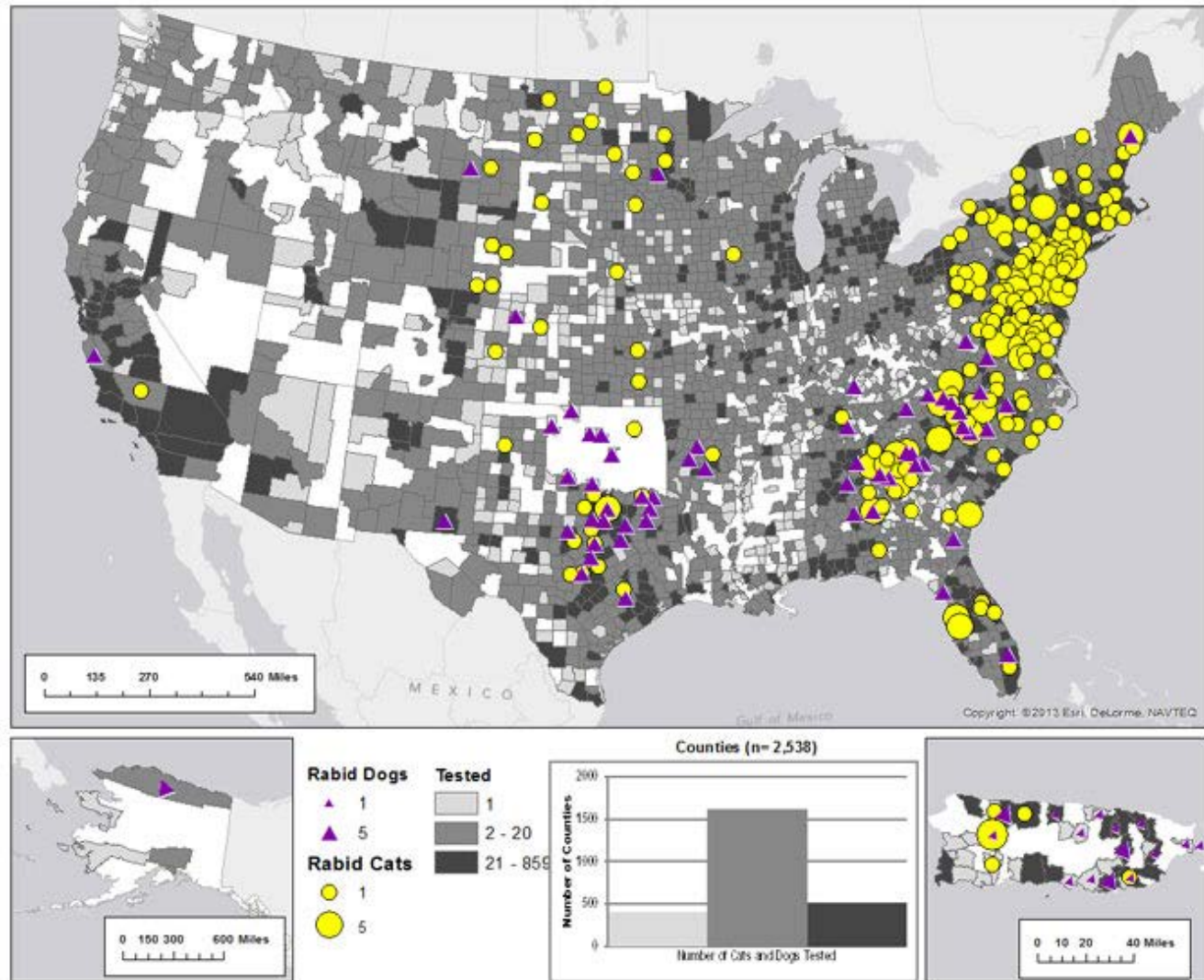
Non-mammals



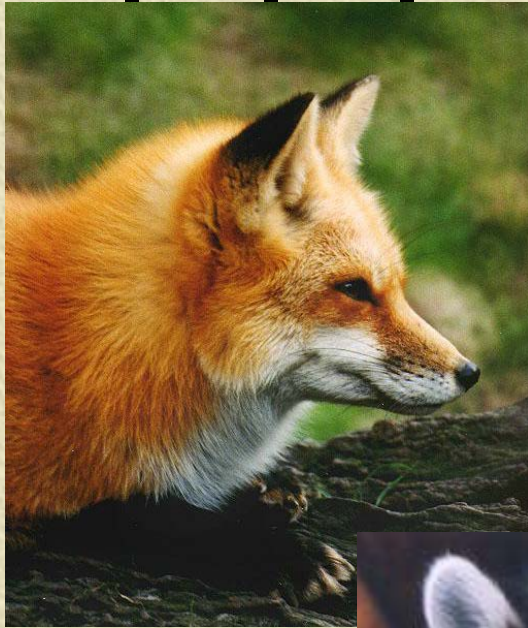
Dogs, Cats, and Ferrets



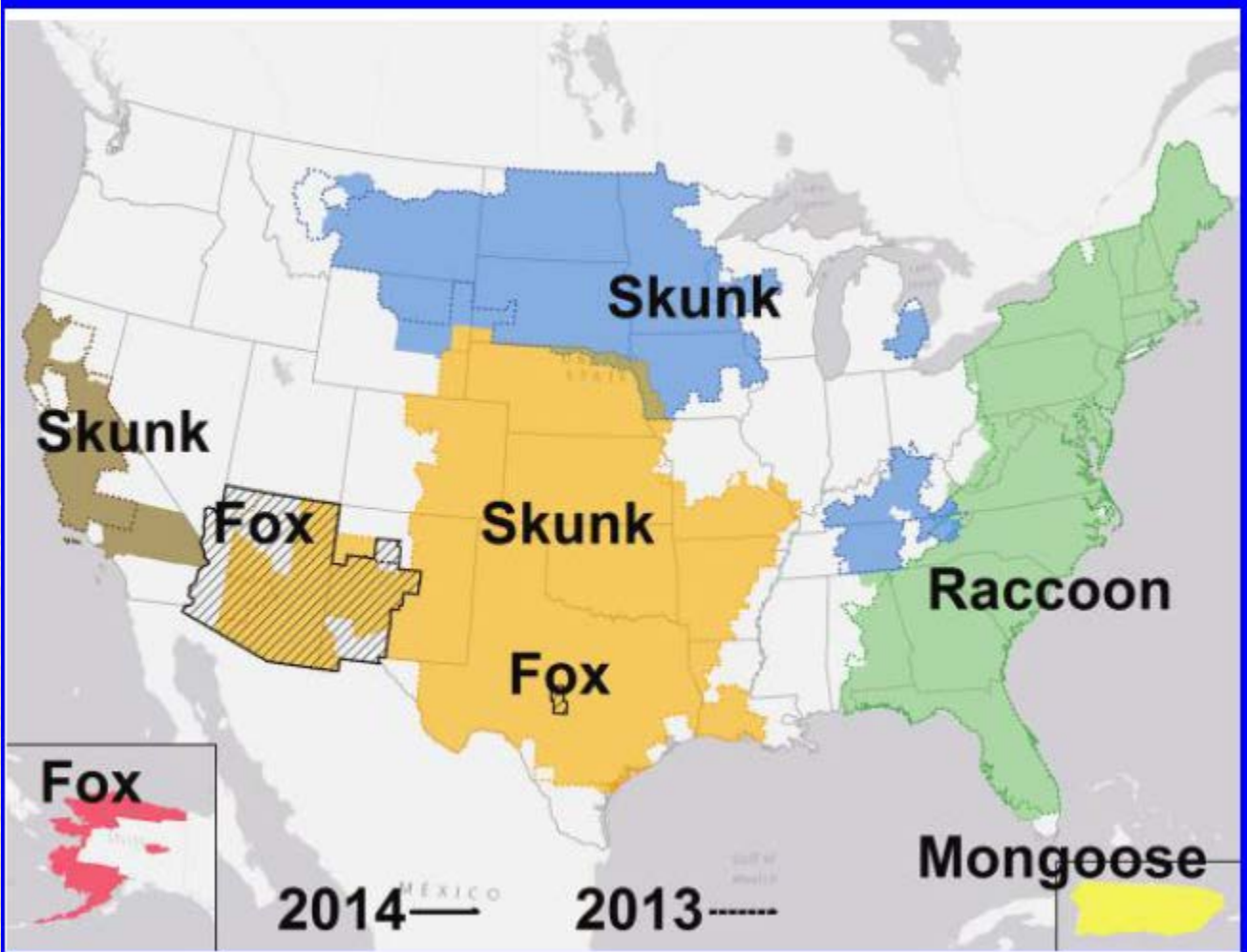
Rabid Cats and Dogs, US 2012



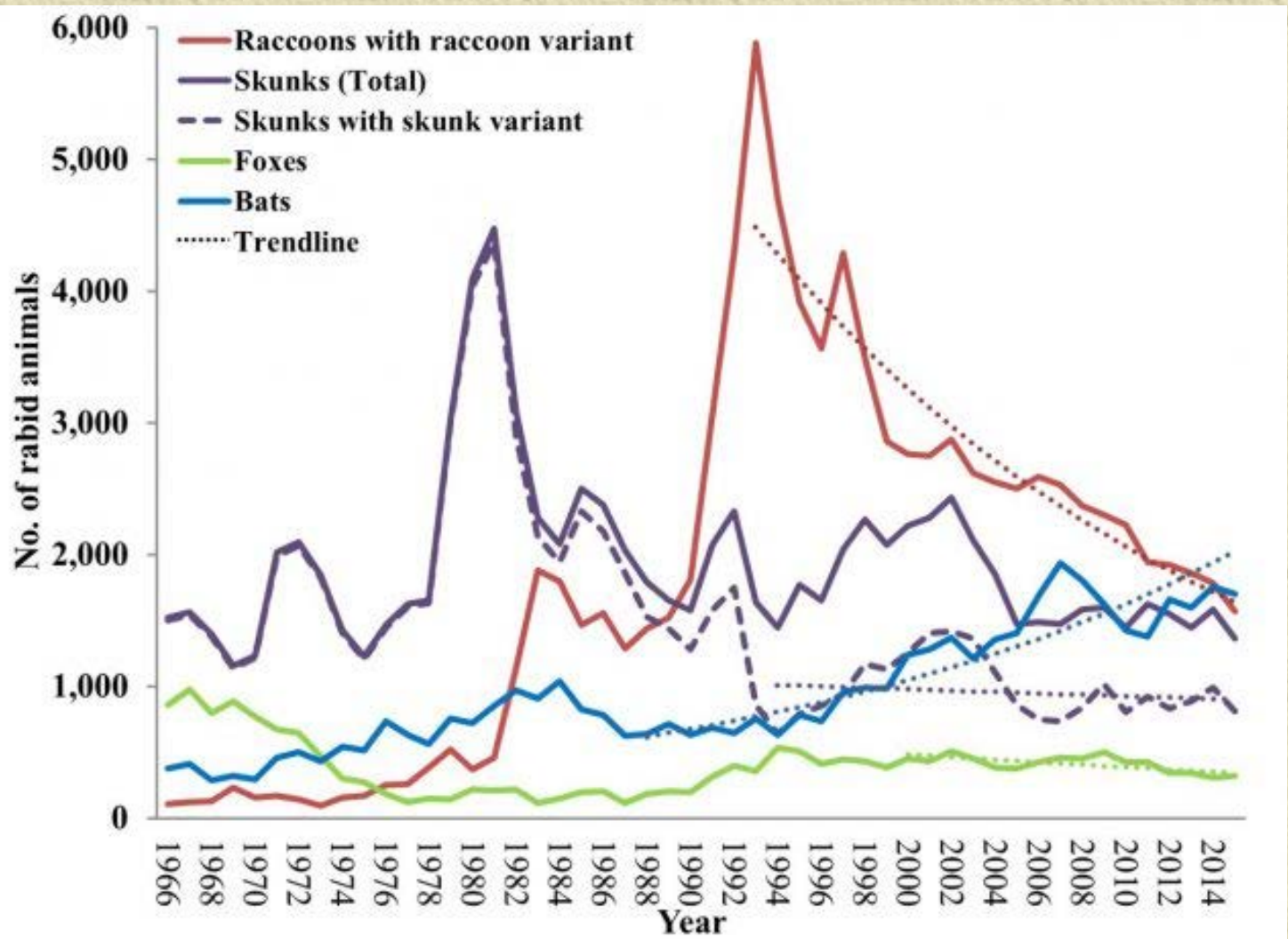
Foxes, Bats, Skunks, Raccoons, and Other Carnivores



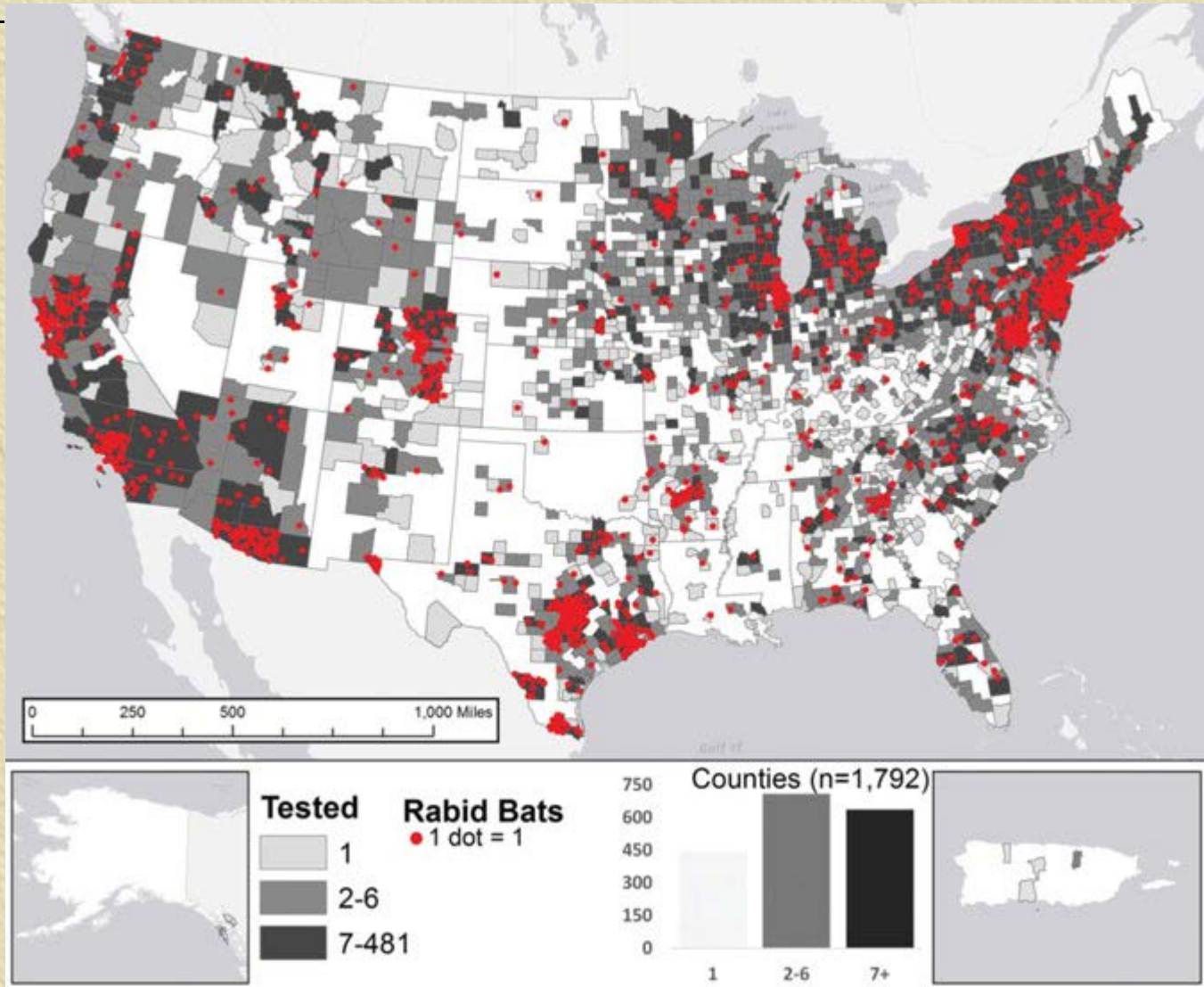
Rabies Reservoirs, US 2014



Wild Animal Rabies, US 1966-2014



Rabid Bats, US 2014



Rabies & Bats

- ✦ In recent years, majority of human rabies cases in the US have been attributed to bat variant strains
- ✦ 1980-1996: 17 of 32 human rabies cases from bat variants
- ✦ Only 1 reported bat bite!
- ✦ 8 others reported direct contact with bats
- ✦ Remaining 8 with presumed bat bite or possible transmission of bat variant via another animal

Rabies & Bats

- ✦ PEP for young children, persons sleeping, and individuals with altered mental status found in room with a bat
- ✦ PEP for any with direct contact with bat, unless certain no bite or scratch
- ✦ Begin PEP immediately
- ✦ May d/c if DFA of brain negative

Livestock



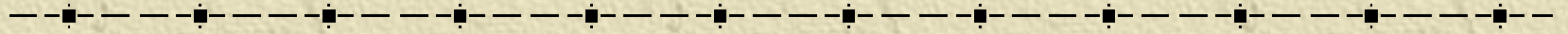
Lagomorphs & Rodents, except...



...Groundhogs/Woodchucks



Opossums



Rabies & Animal Bites

- ✦ Report all bites to health dept
- ✦ Sacrifice animal so that head preserved



PEP Adverse Effects

- ✦ A pregnant woman is seen in the ED for evaluation of a raccoon bite. PEP is recommended. She is concerned about adverse effects.
- ✦ What are the risks of PEP?
- ✦ Is it safe in pregnancy?

PEP Adverse Effects

✦ Vaccine (Cell culture)

- ◆ Local reaction: ~ 10-90%
- ◆ Systemic reaction: ~ 5-60%
- ◆ Immune-complex like reaction / hypersensitivity reaction: 6%
- ◆ ?Guillain-Barre syndrome

✦ Vaccine (Nerve tissue)

- ◆ Used in other countries
- ◆ Neuroparalytic reactions in up to 0.5%

PEP Adverse Effects

✦ RIG (Human)

- ✦ Very safe
- ✦ May have local pain and/or low grade fever

✦ RIG (Equine)

- ✦ Used in other countries
- ✦ Purified relatively safe
- ✦ Unpurified may cause anaphylaxis

✦ Vaccine & RIG safe to use in pregnancy

Vaccine Questions

- ✦ An internist is seeing a patient in clinic who was bitten by a skunk. The patient received a day 0 dose of HDCV in the ED. He presents on day 7 for his next dose of vaccine. He never received the day 3 dose. The clinic only carries PCECV vaccine.
- ✦ How should the vaccine protocol proceed after a patient has missed a dose?
- ✦ Can the vaccines be used interchangeably?

Vaccine Questions

✦ Missed Doses

- ✦ Must complete 4-5 doses
- ✦ Maintain same interval between doses
- ✦ Consider checking titer 7-14 days after last dose, if substantial deviation from protocol

✦ Different Vaccines

- ✦ Best to use same, but may interchange

Delayed PEP

- ✦ A graduate student was bitten by an unvaccinated puppy while in Thailand. Two months later she presents to clinic with her father, who only recently learned of the incident. The student is asymptomatic. She does not know the status of the dog.
- ✦ Is there any benefit to giving the patient delayed PEP?

Delayed PEP

- ✦ Usual incubation in humans: 3-8 weeks
- ✦ Reported incubation up to 7 years
- ✦ If PEP initially indicated and patient asymptomatic, give both vaccine & RIG...
no matter how long the delay



Delayed RIG

- ✦ A patient presents to the clinic the day after returning from Mexico. He was bitten 10 days ago by a stray dog. He was initially treated at a local clinic. RIG was not available. He was given a dose of vaccine on day 0, 3, and 7.
- ✦ What therapy should he now receive if he was given (a) cell culture vaccine or (b) nerve tissue vaccine?

Delayed RIG

✦ If cell culture vaccine-

- ✦ Resume vaccination schedule
- ✦ No RIG
 - **Never give RIG > 7 days after first dose of cell culture vaccine**

✦ If nerve tissue vaccine-

- ✦ Used in a few countries in Asia and Latin America
- ✦ Restart vaccination schedule as if day 0 using cell culture vaccine
- ✦ Give RIG

Preexposure Prophylaxis

- ✦ A biologist who studies wildlife plans to begin a field study that will involve capturing and releasing foxes.
- ✦ What precautions should he take to avoid rabies?



Preexposure Prophylaxis

✦ HDCV or PCECV

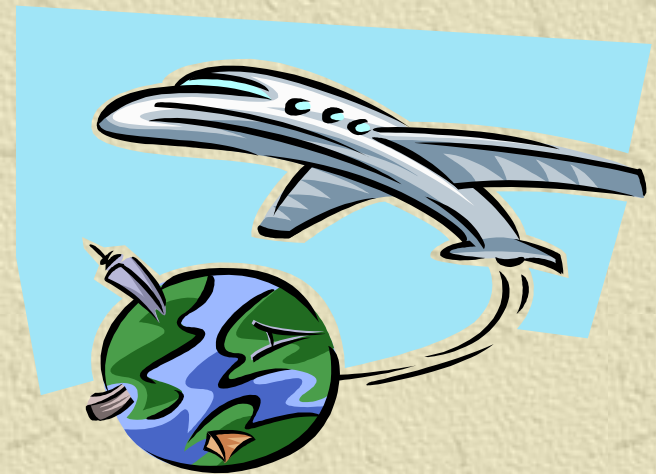
- ✦ 1 cc IM in deltoid
- ✦ Day 0, 7, 21 or 28

✦ Post-vaccination titers are recommended for high risk populations

- ✦ High frequency exposure
- ✦ Immunocompromised

Recommendations for Travelers

- ✦ A medical student plans a trip to Africa. She will be providing health care in a rural village for one month.
- ✦ What are the considerations regarding preexposure vaccination in travelers?



Recommendations for Travelers

✦ Determination of need for vaccination:

- ✦ Local incidence of rabies
- ✦ Availability of all PEP components
- ✦ Planned activities
- ✦ Duration of stay
- ✦ Patient age

✦ If recommended, give standard 3 dose preexposure vaccination

✦ Counsel to avoid animals

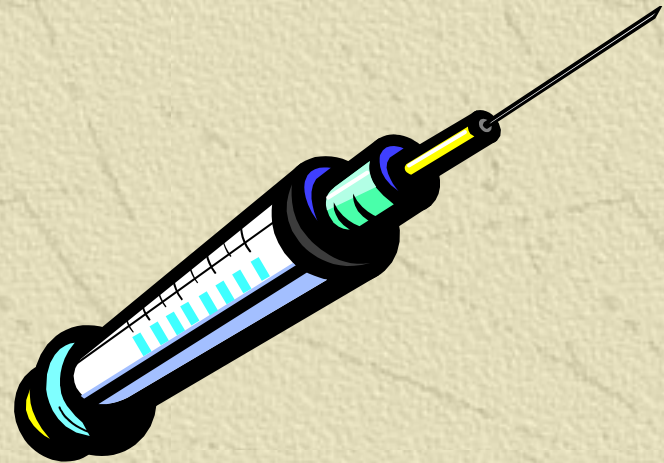
✦ If exposed, still need postexposure vaccine

PEP in Previously Immunized

- ✦ A veterinary assistant is bitten by a stray cat. The animal was sacrificed, and direct fluorescent antibody (DFA) testing of the animal's brain tissue was positive for rabies. The assistant has previously received preexposure prophylaxis.
- ✦ What type of PEP does the assistant need?

PEP in Previously Immunized

- ✦ Soap and water x 15 minutes + iodine or other viricidal agent
- ✦ Vaccine (Cell culture)
 - ◆ Day 0 & 3 only
 - ◆ 1 cc IM in deltoid
- ✦ No RIG



Aerosolized Rabies

- ✦ A group of college students spent their Saturday exploring a cave. They saw several bats, but did not come into contact with them. One of them has read about aerosolized rabies on the internet and is concerned.
- ✦ Is PEP appropriate in this case?

Aerosolized Rabies

-
- ✦ No PEP if no direct contact
 - ✦ Aerosolized rabies in 2 lab workers
 - ✦ Possible transmission in cave with millions of bats



Human Rabies

- ✦ 69 yo man presents to the ED with a 2 day h/o chest discomfort & left arm tingling and numbness. He rules-out for an MI and is released. He represents 2 days later with delirium, dysphagia, diaphoresis, and myoclonus. Vital signs are significant for fever and a widely variable heart rate.
- ✦ Is this syndrome consistent with human rabies?
- ✦ Is there any effective treatment?

Clinical Syndrome

✦ Initially nonspecific

- ✦ Fever, anxiety, malaise, headache
- ✦ Tingling, pruritis, & pain at site of bite

✦ “Furious rabies” = Encephalitic form

- ✦ AMS, agitation, seizures, autonomic instability with arrhythmias, abnormal vs, priapism, hypersalivation, hydrophobia & aerophobia from pharyngeal/laryngeal spasms
- ✦ Symptoms episodic- A&O between episodes

Hypersalivation



Pharyngeal Spasms



Clinical Syndrome

✦ “Dumb rabies” = Paralytic form

- ✦ Occurs in ~ 20% of cases
- ✦ Lethargy, paralysis of peripheral nerves, sensation intact, often have fever, H/A

✦ Final stage

- ✦ Coma, cardiopulmonary arrest
- ✦ Death within 2-12 days from illness onset

Treatment of Human Rabies

- ✦ Prior to 2004, only 5 patients reported to have survived clinical rabies
- ✦ All received some form of pre- or post-exposure prophylaxis, including vaccination prior to illness
- ✦ Most had significant neurologic dysfunction
- ✦ No benefit from the following:
 - ✦ Interferon alpha
 - ✦ Corticosteroids
 - ✦ IV +/- intrathecal RIG
 - ✦ Anti-herpes agents

Treatment of Human Rabies



Jeanna Giese



Precious Reynolds

Treatment of Human Rabies: “Milwaukee Protocol”, 2004

-
- ✦ 15 year old female survived clinical rabies without pre- or postexposure prophylaxis
 - ✦ Dx confirmed by appropriate rise in CSF rabies antibody titers
 - ✦ Management included drug-induced coma with antiexcitatory agents (ketamine, midazolam, phenobarbital) and antiviral agents (amantadine, ribavirin)
 - ✦ Rabies vaccine & RIG not given
 - ✦ As of Jan 2014: 5 have survived with this protocol; 27 have not

Human Rabies

✦ “Abortive Rabies”, 2009

- ✦ 17 yo female survived rabies w/o ICU care
- ✦ Received 1 dose of rabies vaccine and RIG after onset of symptoms
- ✦ 63 people in Peruvian communities with high risk for vampire bat exposure screened for rabies neutralizing antibodies; 10% positive

PEP s/p Exposure to Human Rabies

- ✦ Human-to-human transmission rare
 - ✦ 8 cases in corneal transplants prior to 2000
 - ✦ Transmission via organ transplants, 2004, 2011, 2013
- ✦ Reports of transmission following bites and kisses from infected patients
- ✦ Exposure to saliva, tears, and sputum highest risk
- ✦ Routine delivery of care NOT an indication
- ✦ Gowns, goggles, masks, and gloves, particularly during intubation and suctioning
- ✦ PEP for those w/ exposure of mucous membranes or nonintact skin to infectious body fluids

Summary

- ✦ Human and cat bites typically require antibiotic therapy
- ✦ Consider valacyclovir prophylaxis for B virus following bites from macaque monkeys
- ✦ Rabies remains a problem world-wide
- ✦ Rabies post-exposure prophylaxis should be recommended on a case-by-case basis
- ✦ Consider rabies in patients with fever and neurologic symptoms

Selected References

- ✦ CDC Rabies Hotline:1-877-554-4625
- ✦ CDC/MMWR, especially “Human Rabies Prevention- US”, 2008; 57 (No. RR-3) & 2010; 59 (No. RR-2)
- ✦ WHO Rabies Fact Sheet
- ✦ NEJM (1998) 339:105-112 & (2005) 352:2508-2514 & (2007) 357:945-946
- ✦ MMWR (2004) 53(50);1171-1173 & (2009) 59(07);185-190
- ✦ CID (2000) 30:4-12 & (2003) 36:60-63
- ✦ Infectious Diseases in Clinical Practice (2000) 9:202-207
- ✦ Annals of Internal Medicine (1998) 128:922-930
- ✦ Mandell, et al, Principles & Practice of ID

Questions

