

Assessment & Prevention of Rabies in the Emergency Department



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CASE PRESENTATION
SEPTEMBER 4TH 2014

Patient Case



- EG, a 57 y/o CF, presents to ED with c/o “bat bite”
- **S:** EG was bitten by bat while draining the pool. EG stated the bat drew blood. The bat then drowned in the pool.
 - Onset: “few hours”
 - Duration: 1 bite
 - Severity: mild; no associated symptoms
- **O:** BP 137/65, HR 66, temp 97.7 F, **wt 96 kg**
 - ROS: bite puncture on left thumb

What is Rabies?



- Viral infection of CNS in mammals
- Primarily transmitted via saliva or CNS tissues of rabid animals
 - Site of entry → peripheral nerves → CNS → salivary glands
 - Rapid viral replication in brain
 - Cerebral infection = behavioral changes
- Incubation period: variable, 1-3 months in humans

Rabies Terminology



Exposure

- Potential introduction of virus

Infected

- Virus was transmitted during exposure
- Virus has not penetrated CNS; non-contagious
- Virtually 100% potential success rate with PEP

Rabies

- Expression of clinical symptoms
- Incurable phase; comfort/experimental care only
- Virtually 100% fatality rate

Clinical Signs & Symptoms

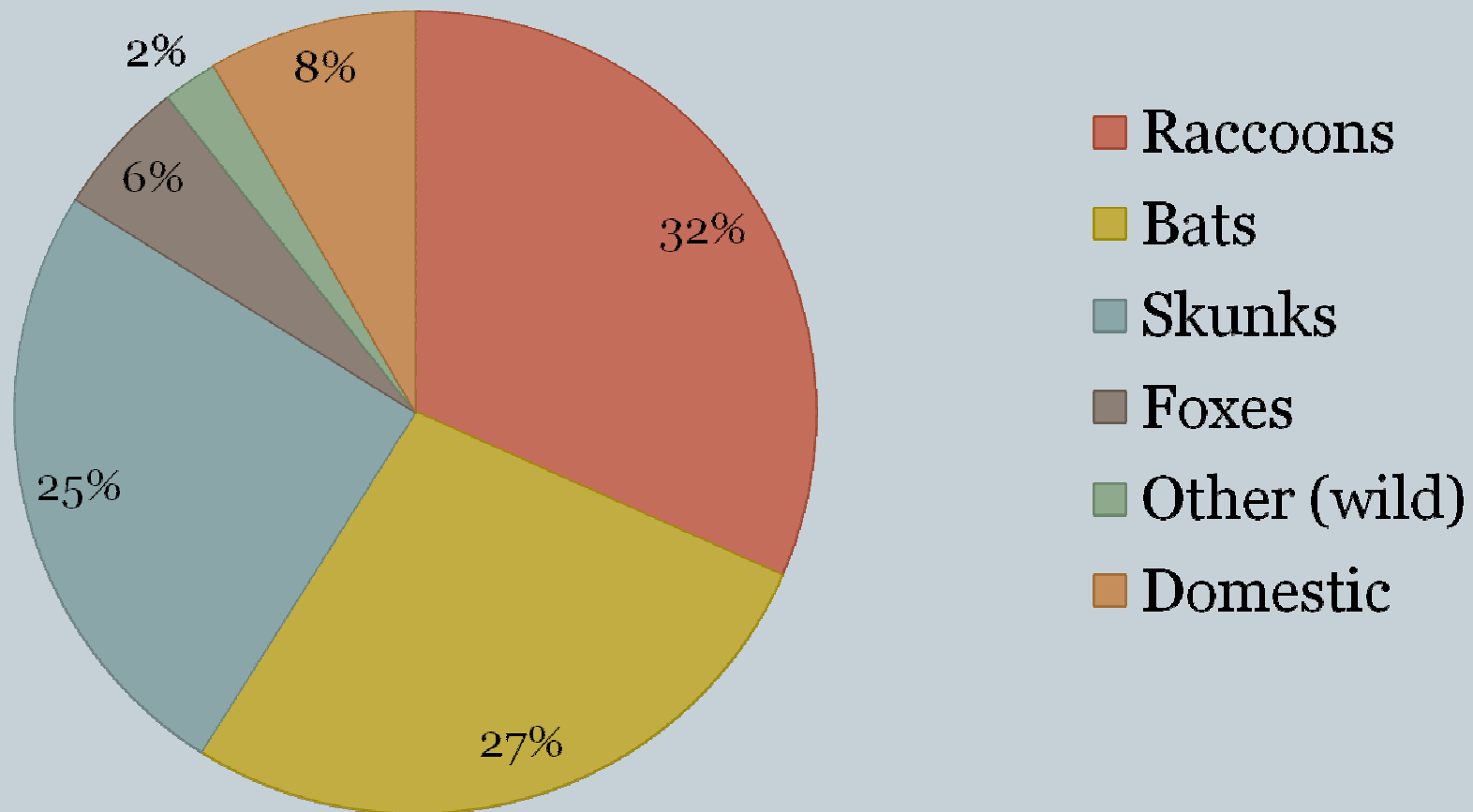


- Prodomal: neuropathic pain/paresthesia at wound site (virus entry site)
 - Flu-like symptoms, weakness, discomfort, fever
- Encephalitis, myelitis
- Furious vs. paralytic types
 - Spasms in response to stimuli (**hydrophobia**), dysphagia
 - Agitation, confusion, hallucinations
 - Autonomic instability, excessive salivation
- Progressive worsening of neurologic symptoms
 - Mortality within ~2-10 days after onset

Rabies Surveillance in Animals: US



2012 Reported Rabies Cases in Animals (US)



Rabies in Humans



- **Worldwide:** 55,000+ deaths/year
 - Dog bites are responsible for vast majority of human rabies
- **US:** 34 cases from 2003 – 2013
 - Bat bites are responsible for majority of human rabies
- Highest fatality rate (CFR) of any infectious disease
- Mortality due to a failure to seek medical treatment
 - Often unaware of exposure
 - Mortality may also be associated with deviation from protocols
- Preventable with pre- or post-exposure prophylaxis (PEP)

Cases of Rabies in Humans in the US (2003 – 2013)

Year	Cases (Deaths)	State	Exposure	Rabies Variant
2003	3 (3)	VA PR CA	Unknown Bite Bite	Raccoon Dog/mongoose (PR) Bat, Ln
2004	8 (7*)	FL AR OK, TX WI* CA	Bite Bite (donor) Transplant x 4 Bite Unknown	Dog (Haiti) Bat, Tb Bat, Tb Bat, unknown Dog (El Salvador)
2005	1 (1)	MS	Contact	Bat, unknown
2006	3 (3)	TX IN CA	Contact Bite Bite	Bat, Tb Bat, Ln Dog (Philippines)
2007	1 (1)	MN	Bite	Bat, unknown
2008	2 (2)	CA MO	Bite Bite	Fox (Mexico) Bat, Ln
2009	4 (3*)	TX* IN MI VA	Contact Unknown Contact Contact	Bat, unknown Bat, Ps Bat, Ln Dog (India)
2010	2 (2)	LA WI	Bite Unknown	Bat (Mexico) Bat, Ps
2011	7 (6*)	CA* NJ NY MA SC NC	Unknown Bite Contact Contact x 2 Unknown Contact	Unknown Dog (Haiti) Dog (Afghanistan) Dog (Brazil), Bat Bat Raccoon
2012	1 (1)	CA	Bite	Bat, Tb
2013	2 (2)	MD TX	Transplant Unknown	Raccoon Dog (Guatemala)

Risk of Exposure/Transmission



Possible/Probable Risk

- Saliva **or** CNS tissue from rabid animal introduced into wound **or** mucous membrane
- Bite from reservoir species
 - Special considerations for bats (US) & dogs (abroad)
 - Vampire bats
- Organ transplant from rabid donor

No Risk

- Petting or handling rabid animals
- Contact with blood, urine, or feces from rabid animals
- Bite while in Hawaii
- Bite from non-reservoir species
 - Vampires

Patient Case



- **Type of exposure:** bite (higher risk of transmission than non-bite exposure) ✓
- **Epidemiology/species:** bat (most common cause of human rabies cases in US) ✓
- **Circumstances of exposure:** likely somewhat provoked based on subjective information (unprovoked attacks more likely to indicate the animal is rabid) ✗

PEP Overview



- Cleanse wound thoroughly with soap & water
 - Address trauma/injuries
- Assess risk of rabies
 - Contact health department
- Administer PEP accordingly (vaccine +/- HRIG)
- Initiate PEP regardless of time interval since exposure
 - Exception: DO NOT administer vaccine after onset of clinical symptoms in patients with confirmed rabies

PEP Principles

Vaccine

- Pre- or post-exposure
- Administer regardless of vaccination history
- Antibody response in 7-10 days
- 4 dose series (previously unvaccinated)
- Initiate on day 0
- Dose: 1 ml IM (deltoid or thigh)

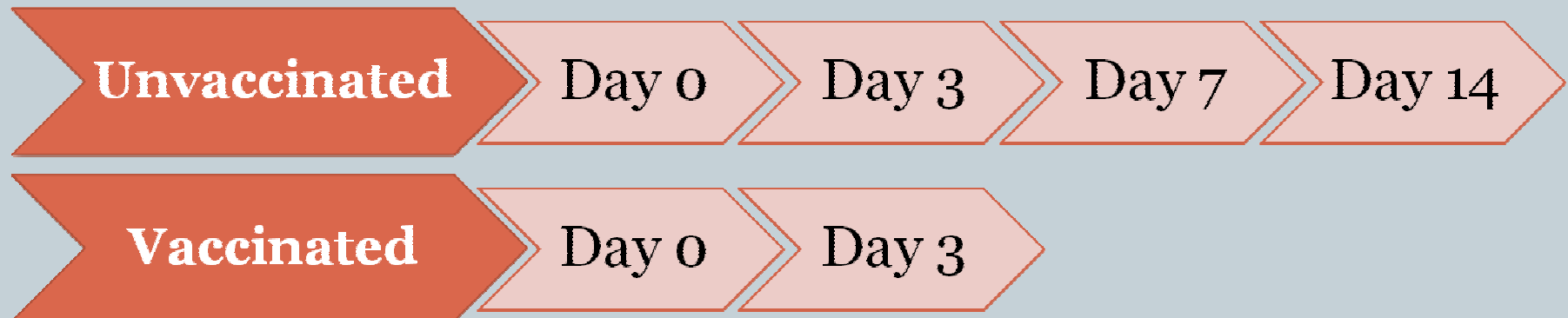
HRIG

- Post-exposure only
- Administer if no history of prior vaccination *only*
- Immediate, passive virus-neutralizing antibody coverage
- Administer with vaccine on day 0 (or up to day 7)
- Dose: 20 units/kg

PEP Principles: Vaccine



- Inactivated, cell culture vaccine (1 mL)
 - **Imovax** (human diploid cell vaccine, HDCV)
 - **RabAvert** (purified chick embryo cell vaccine, PCECV)
- **NEVER** administer in gluteal area



PEP Principles: HRIG



- Human Rabies IgG 150 units/mL (2 mL, 10 mL)
 - **HyperRab S/D**
 - **Imogam Rabies-HT**
- Administered to unvaccinated individuals only

Unvaccinated

Day 0*

Vaccinated



PEP Principles: HRIG Cont.



- Infiltrate full dose around & into any wounds
 - Remaining volume may be administered IM to deltoid
 - Use other deltoid
- Do not administer HRIG in same syringe as vaccine or to same anatomic site as vaccine
 - Subsequent vaccine doses may be administered at same site
- Do not exceed recommended dose (20 units/kg)
- Store in refrigerator

PEP: Safety & Efficacy



- **Vaccines:**
 - Local rxns: pain, redness, swelling at injection site (11-90%)
 - Systemic rxns: fever, HA, dizziness, GI symptoms (0-56%)
 - Severe rxns: anaphylaxis, hypersensitivity
 - ✦ Immune complex-like rxn (booster doses of HDCV; pre-exposure)
- **HRIG:**
 - Local rxns: pain, redness, swelling at injection site (25-50%)
 - Systemic rxns: malaise, fever, HA (50 – 75%)
 - Severe rxns: anaphylaxis, hypersensitivity
 - ✦ Warning for plasma-related infectious diseases
- **No PEP failures reported in US since routine use of vaccine + HRIG began**

More Information



- Pregnancy is ***not*** a contraindication
- Hold corticosteroids & other immunosuppressive agents during PEP
 - If unable to hold therapy, serum antibody tests recommended
- Immunocompromised individuals should receive 5 dose series of rabies vaccine
- Hold live vaccines for 3 months after HRIG

“Treatment” of Human Rabies



- No proven effective medical treatment for rabies after the development of clinical signs
- Comfort care
 - “Psychological trauma resulting from a sense of personal isolation and hopelessness from prognosis”
 - Sedation, sedation, and more sedation
- Experimental care
 - Set expectations for high probability of treatment failure
 - Rare instances of survival = neurological damage

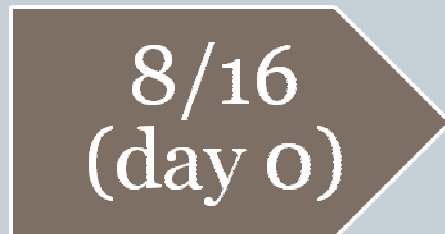
Patient Case



- Imovax 1 ml IM x 4 doses (**\$4,778.32**)



- HyperRab S/D 12.9 ml infiltrated/IM (**\$14,572.92**)



- Lidocaine 1%, Td vaccine

What to Do If You Are Bitten



- Medical urgency, not emergency!
- **Wash wound with soap & water immediately**
- Seek medication attention
 - First address any trauma or injuries related to bite
- Decision to initiate PEP based on specific situation
 - Type of exposure, species, availability of animal for rabies testing, surveillance data from geographic region
- **Consult health department**
 - Rabies is **fatal**. Avoid the guessing game; consult the experts!

References



- CDC. Human Rabies Prevention --- United States, 2008: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2008; 57(No. RR-3).
- CDC. Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2010; 59(RR-02).
- Dyer JL, Wallace R, Orciari L, et al. Rabies Surveillance in the United States during 2012. *JAVMA* 2013; 243(6):805-815 .
- HyperRAB S/D [package insert]. Research Triangle Park, NC: Talecris Biotherapeutics, Inc; 2010.
- Imogam Rabies-HT [package insert]. Swiftwater, PA: Sanofi Pasteur, Inc; 2012.
- Imovax [package insert]. Swiftwater, PA: Sanofi Pasteur, Inc; 2013.
- RabAvert [package insert]. Emeryville, CA: Novartis Vaccines and Diagnostics, Inc; 2006.

Questions?



**World Rabies
Day is
September
28th**