Rabies Epidemiology and Vectors

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FDA workshop: Developing Rabies Monoclonal Antibody Products as a Component of Rabies Post-Exposure Prophylaxis

FDA White Oak Campus, July 17, 2017

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www.rabiesalliance.org

Global Epidemiology of Rabies

- Global perspective on:
  - rabies prevalence in animals
  - rabies exposures in humans
  - rabies infections in humans
- Different vectors in different countries
- Distribution of different rabies virus strains

Rabies virus and human disease

Lyssavirus Genus (ICTV website): Currently listed with 14 species (+ more?)

Human infections documented:

<- ABLV: occasional

<- Duv: occasional

<- ELBV1 and 2: occassional

<- Mokola: occasional

<- Rabies: Estimated at around 59,000

All human cases symptomatically "rabies-like"
Main route of transmission is by bite / scratch

Distribution suggests that Lyssaviruses co-evolved in bats, over millenia.

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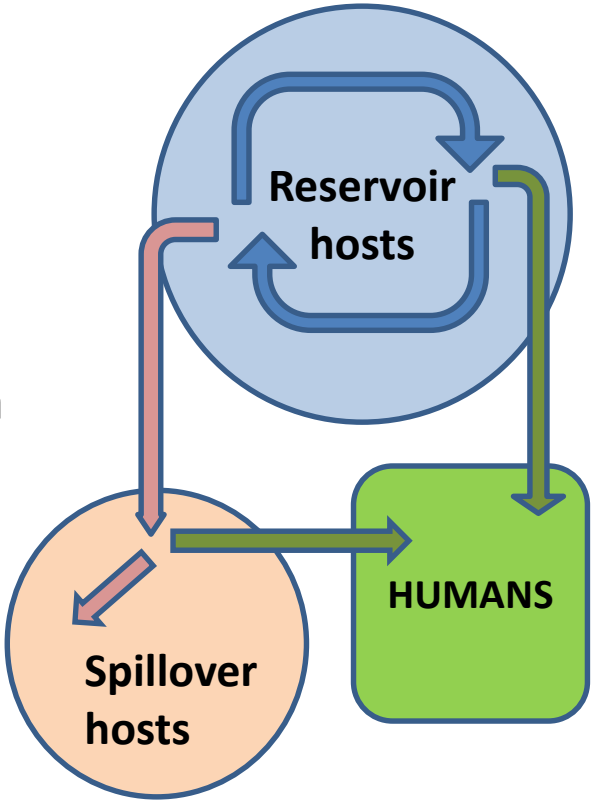
Rabies transmission patterns

- Rabies virus can theoretically infect any mammal
- Most likely origin is bats and bats worldwide known to be infected with lyssaviruses
- Not all mammals maintain the disease indefinitely (ie. act as **reservoirs**)
- Most common reservoirs are carnivores and bats
- From these reservoirs a broad range of animals can be infected (**spillover hosts**)
- Humans can be infected by any infected host (**vectors**)
- Contact patterns of different animals with humans create different public health risks



- By far the most common public health threat globally is from the domestic dog (>99% human cases result from dog bites)

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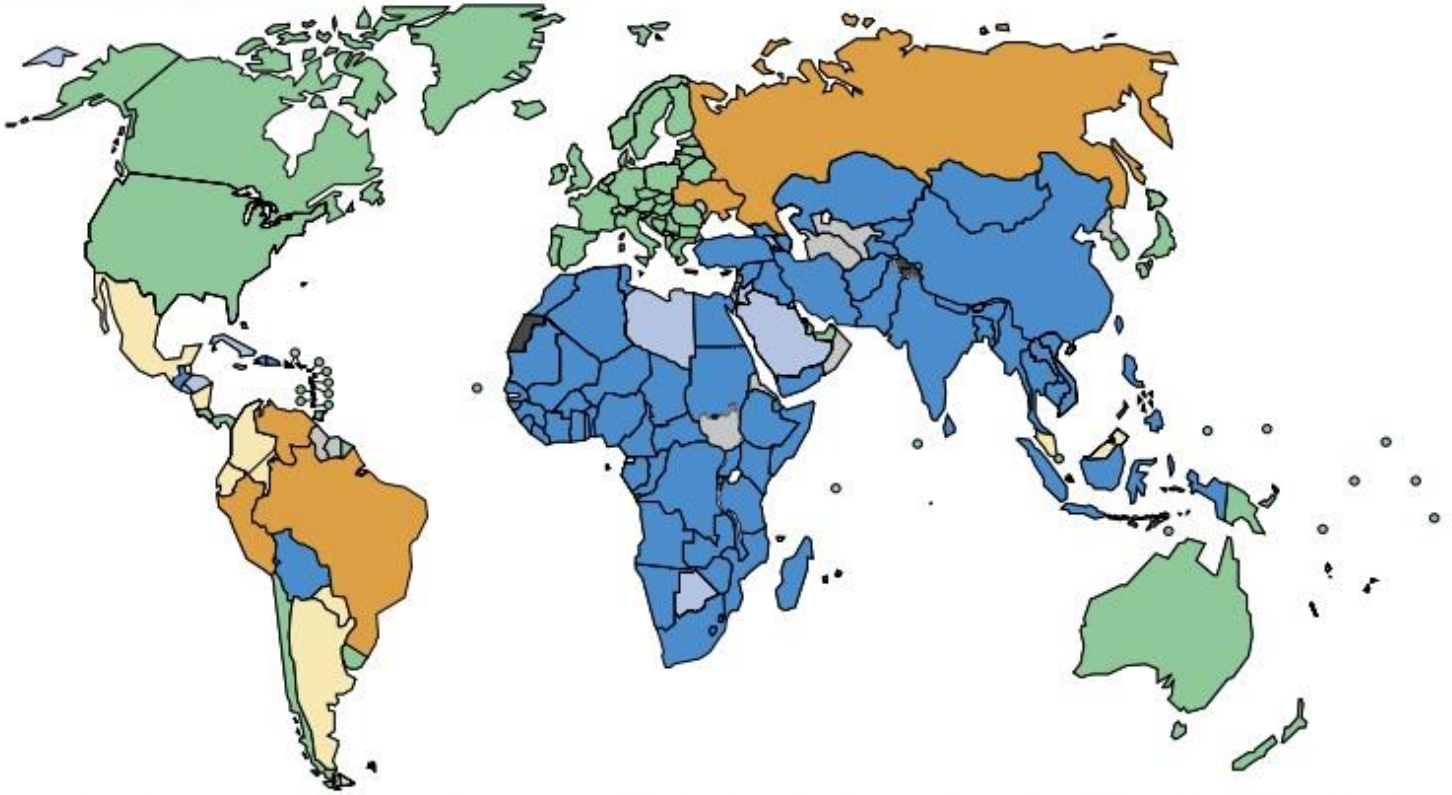
WHO Canine rabies risk map

Map 1 **Endemicity of dog rabies and dog-transmitted human rabies, 2016**
Carte 1 **Endémicité de la rage canine et de la rage humaine à transmission canine, 2016**



Endemic dog-transmitted human rabies: dog rabies and dog-transmitted human rabies present in the country – Endémie de la rage humaine transmise par les chiens: la rage canine et la rage humaine à transmission canine sont présentes dans le pays

Endemic dog rabies: dog rabies in the majority of the country, but no dog-transmitted human rabies cases – Endémie de la rage canine: rage canine présente dans la majeure partie du pays, mais aucun cas de rage humaine transmise par les chiens

Sporadic dog-transmitted rabies: dog rabies in few areas of the country with sporadic human cases – Cas sporadiques de rage transmise par les chiens: rage canine présente dans quelques zones du pays, accompagnée de cas humains sporadiques

Controlled dog rabies: few cases of dog rabies in limited areas of the country but no dog-transmitted human rabies cases – Maîtrise de la rage canine: quelques cas de rage canine dans des zones limitées du pays, mais aucun cas de rage humaine transmise par les chiens

No dog rabies: zero dog rabies and zero dog-transmitted human rabies cases (except from imported) – Absence de rage canine: aucun cas de rage canine et aucun cas de rage humaine transmise par les chiens (sauf cas importés)

No information – Aucune information

Not applicable – Sans objet

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. – Les limites et appellations figurant sur cette carte ou les désignations employées n'impliquent de la part de l'Organisation mondiale de la Santé aucune prise de position quant au statut juridique des pays, territoires, villes ou zones, ou de leurs autorités, ni quant au tracé de leurs frontières ou limites. Les lignes en pointillé sur les cartes représentent des frontières approximatives dont le tracé peut ne pas avoir fait l'objet d'un accord définitif.

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The burden of canine rabies

For CANINE ENDEMIC Countries (N=122)

	Deaths	Exposures to Rabid Animals *	PEPs delivered	Prevented deaths
Africa	21,502	847,326	1,387,848	139,490
Americas	182 $	122,701	835,656	23,131
Asia	37,266	14,633,844	26,589,222	2,743,164
Europe	41	91,035	362,379	17,255
Grand Total	**58,991**	**15,694,905**	**29,175,105**	**2,923,041**

From Hampson et al (2015) Reassessing the burden of Rabies

- *An estimated 19% of rabid exposures result in death if they do not receive PEP
- $ Deaths in the Americas primarily in Haiti and these may be lower now.

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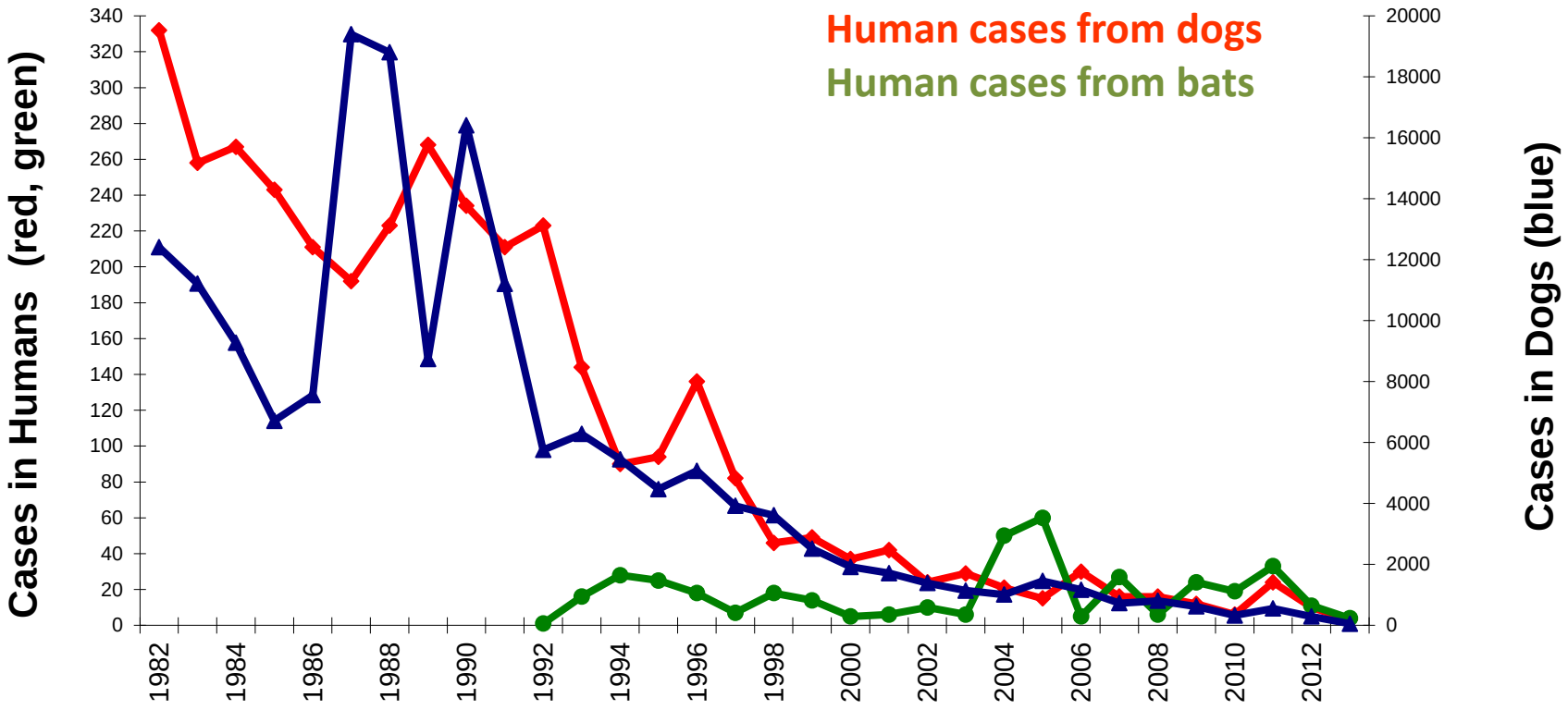
The relative importance of wildlife rabies



Rabies Cases across Latin America, 1982 – 2013

Graph drawn by PAHO, from SIRVERA data

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Terrestrial Wildlife Reservoirs in the US

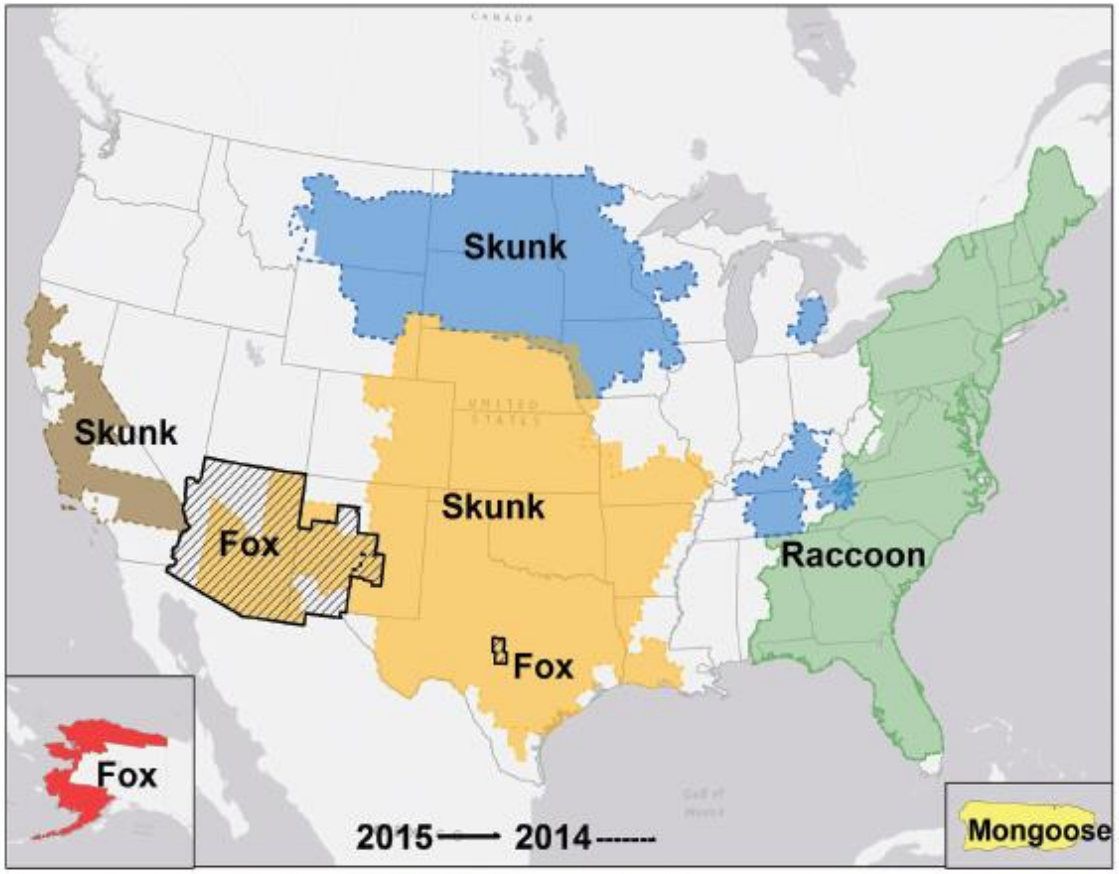

Figure 1—Distribution of major rabies virus variants among mesocarnivores in the United States and Puerto Rico for 2008 through 2014. Black diagonal lines represent fox rabies variants (Arizona gray fox and Texas gray fox). Solid borders represent 5-year rabies virus variant aggregates for 2010 through 2015; dashed borders represent the previous 5-year aggregates for 2009 through 2014.

- Where diagnostic facilities are strong we have the ability of produce very detailed maps of rabies reservoir species.
- Distinct variants of the rabies virus are adapted to different reservoir species

From: **Rabies surveillance in the United States during 2015**
Birhane et al (*J Am Vet Med Assoc* 2017;250:1117–1130)

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Rabies variants in the US

In 2015: 5,508 rabies positive animals and 26.8% of those typed

Table 3—Rabies virus variants identified in domestic and wild animals in 2015.

	Domestic animals						Wildlife						
Variant	Cats	Cattle	Dogs	Horses and mules	Sheep and goats	Other domestic*	Raccoons	Bats	Skunks	Foxes	Other wild†	Rodents and lagomorphs‡	Total
Raccoon	43	20	18	2	3	1	272	0	134	40	2	7	542
South central skunk	15	16	13	3	1	1	32	0	429	18	1	1	530
North central skunk	1	0	6	0	0	0	0	0	31	1	0	0	39
California skunk	0	0	0	0	0	0	0	0	0	0	1	0	1
Arctic fox	0	0	0	0	0	0	0	0	0	0	0	0	0
Arizona gray fox	0	0	0	0	0	0	0	0	0	0	0	0	0
Texas gray fox	0	0	0	0	0	0	0	0	0	0	0	0	0
Bat	3	2	1	0	0	0	0	358	0	3	0	0	364
Egyptian dog	0	0	1	0	0	0	0	0	0	0	0	0	1
No variant reported	182	47	28	9	3	1	1,315	1,346	771	266	37	26	4,031
Total infected	**244**	**85**	**67**	**14**	**7**	**3**	**1,619**	**1,704**	**1,365**	**325**	**41**	**34**	**5,508**
Variant typed (%)	25.4	44.7	58.2	35.7	57.1	66.7	18.8	21.0	43.5	18.2	9.8	23.5	26.8

*Other domestic includes 2 pigs with the raccoon and south central skunk rabies virus variants. †Other wild includes 1 coyote with the California skunk rabies virus variant, 1 coyote with the south central skunk rabies virus variant, and 2 otters with the raccoon rabies virus variant. ‡Rodents and lagomorphs include 7 groundhogs with the raccoon rabies virus variant and 1 rabbit with the south central skunk rabies virus variant.

From: Birhane et al (2017) JAVMA

- Clearly there is spill-over from the main reservoir into other wild and domestic species.
- These are highly contact dependent and do cause exposures to humans.
- Cases in dogs are not the US dog adapted variant which was confirmed eliminated in 2007
- Only 1 human case acquired in the US (from a bat)

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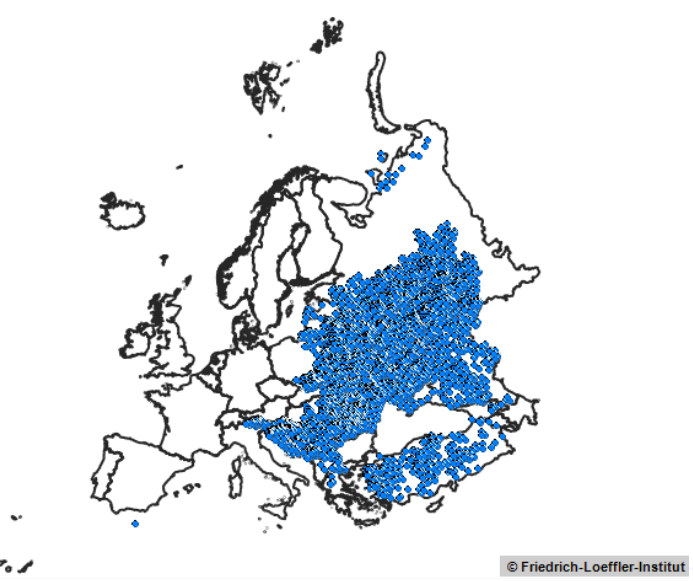
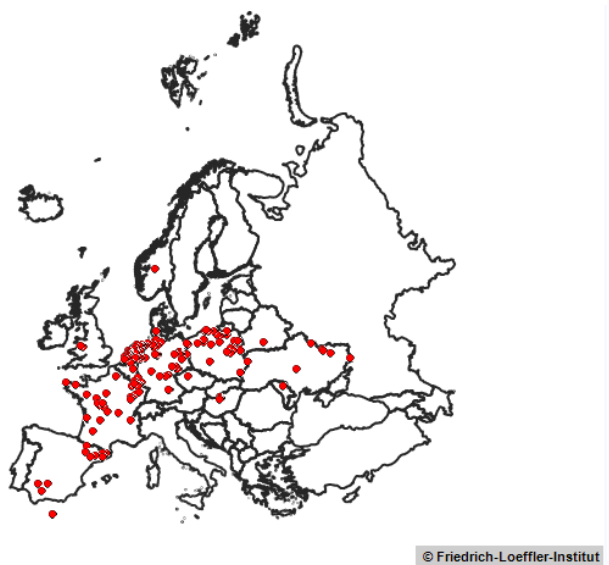
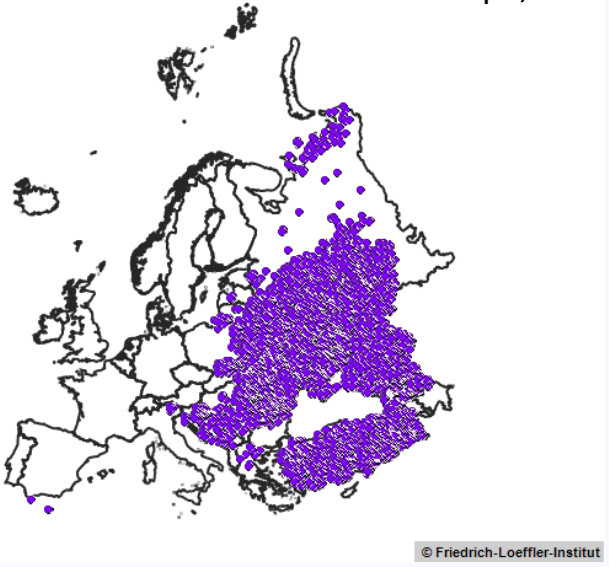
Rabies in Europe, 2010 - 2015

Data from Rabies Bulletin Europe, FLI







Terrestrial Wildlife cases
N=17, 891

Bat cases
N=193

Domestic animal cases
N=18,323

But human cases from 2010-5 = 59 (47 in Russian Fed., Georgia and Turkey)

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Rabies Reservoir species

Terrestrial Wildlife
Airborne Wildlife
Domestic

At least 39 Genera of Insectivorous bats across many countries

But in many countries adequate surveillance has not been carried out

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Rabies prevalence in animals

- It depends on which animals you are testing:

Animals tested in the US 2015:

13% of Raccoons, 6.6% of Bats, 28% of Skunks, 18% of Foxes
0.3% of Dogs , 2% of Horses, 6.8% of Cattle

Wild-caught and apparently healthy bats in US:

0.6% of Tadarida brasiliensis, 2.5% of Eptesicus fuscus

Grounded bats underneath a large colony:

92% of T. brasiliensis

Dogs tested in Philippines:

18% in 2012, 23% in 2013, 28% in 2014, 26% in 2015, 27% in 2016

- Even sampled animals that people were bitten by may not be randomly chosen, so the interpretation of this data is often very difficult

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What else is out there?

- Rabies can jump species to establish reservoirs in new host species
- Surveillance in many canine rabies endemic countries is very poor, with few labs, small numbers of samples tested, and variant typing usually not possible locally.
- Partnerships with reference labs and support are available and are working to help countries.
- As dog rabies has been reduced in Latin America, vampire bat rabies has become a larger public health concern
- Quite possible that the dog rabies is masking more wildlife reservoirs

A tale of two worlds

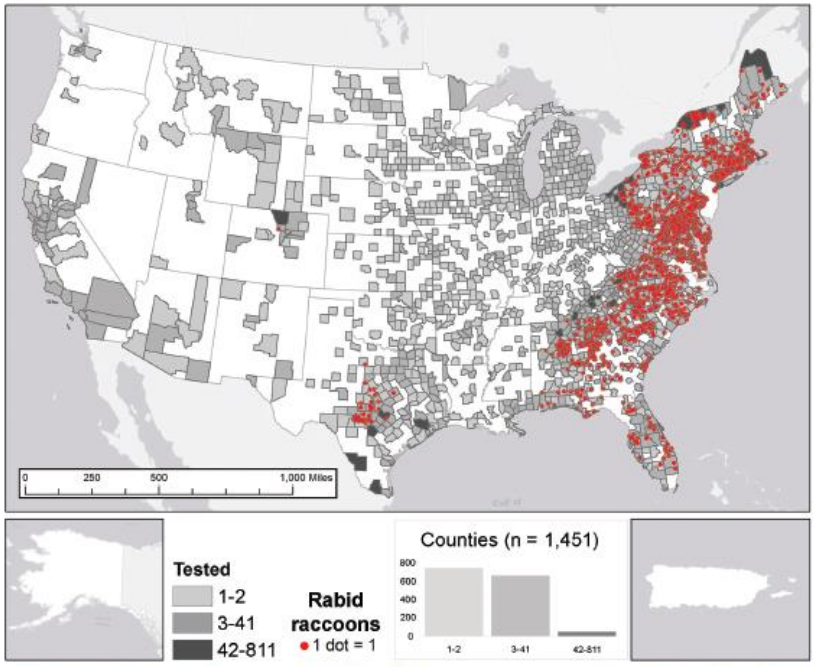

Figure 5—Reported cases of rabies involving raccoons, by county, during 2015.

- Understand the epidemiology of rabies
- Know the likelihood that a particular exposure is a rabies risk
- Good advice on and access to PEP

- **Human cases, 2015 = 3 (1 US exposure)**

- Rabies is in dogs, presumed everywhere
- Little idea of wildlife reservoir species
- All dogs (and often all animal) bites need to be treated as a rabies exposure
- Poor access to PEP

- **Human cases, 2015 = est. 21,500**

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Thank you for your attention

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www.rabiesalliance.org

End Rabies Now
www.endrabiesnow.org