

Emerging and zoonotic disease risk mitigation: Rabies prevention as a template for best practices

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The idea of “low hanging fruit” - Rabies Prevention is neglected and might be - the rotten apple fallen to the ground.

Objective

- The objective of this study was to evaluate rabies serology results from an ELISA-based method in comparison to virus neutralization methods due to reports of discrepant results.

Methods

- Laboratory comparison of rabies serology
- 90 samples, blinded
 - Rabies vaccine recipients,
 - Normal non-rabies vaccinated persons, and
- Non-rabies vaccinated patients w/acute infections :
 - Arbovirus (West Nile), Measles, Mumps, Rubella, Herpes Simplex Viruses 1&2, Varicella zoster virus, Anaplasmosis and Ehrlichiosis, Rocky Mountain Spotted Fever, Babesiosis, Lyme, and Syphilis.
- Kansas State University (KSU)
 - RFFIT – virus neutralization
- ELISA - Commercial
- NYS State Dept of Health (NYSDOH)
 - TC/SNT (modified RFFIT)



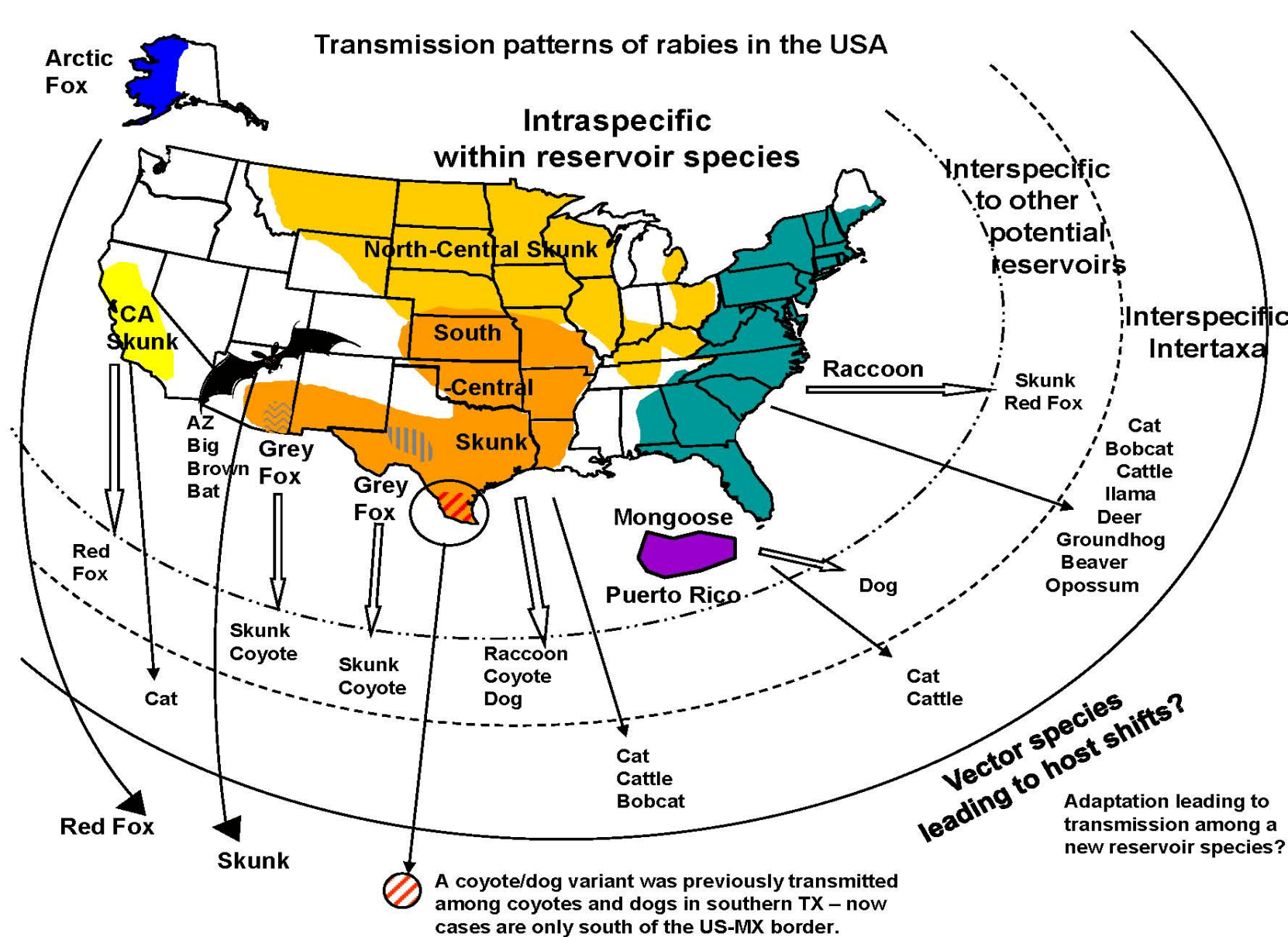
Background

Although the word alone evokes a highly charged response, rabies remains a severely neglected disease. It is estimated that more than 55,000 humans die every year. Elimination and ultimate extinction of the main global source of human rabies from dog-to-dog transmission of rabies can be achieved. This action alleviates the main threat to humans.

Current Threats –

Translocation, Emergence of new local variants, decline in diagnostic expertise and capacity,...

Like many zoonotic and emerging diseases, rabies prevention requires the cooperation of animal control, law enforcement, natural resource personnel, veterinarians, diagnosticians, public health professionals, physicians, and other professionals. Despite the forced extinction of dog-to-dog types of rabies viruses in most of Europe and the Americas, the recent translocation of dogs from Puerto Rico, Thailand, India, and Iraq, which developed rabies from their places of origin upon movement into the United States, demonstrates the risk of human travel and movement of animals, some of which can be mitigated through carefully crafted requirements. While the methods for measuring immunity to rabies and for diagnosis are powerful, they include some limitations innate to biological assays.



Results

ELISA	RFFIT		
	pos	neg	
pos	27	34	61
neg	1	15	16
	28	49	77

Values for the ELISA in comparison to the RFFIT
 96% Sensitivity
 31% Specificity
 44% Positive Predictive Value
 94% Negative Predictive Value

- 27 samples were concordant as positive by both ELISA and Virus Neutralization.
- 25 samples in agreement as “below cut-off.”
- 34 false positives by ELISA
- One false negative by ELISA
- Among sera from vaccinated persons, 87% yielded concordant results by virus neutralization of ≥ 0.5 IU/ml.
- A discordant result occurred in 5 samples ~ 0.5 IU/ml.
- Among 53 samples from non-rabies-vaccinated humans, a low level of neutralizing activity was reported by NYSDOH in 21 samples and by KSU in 9 samples, most likely indicative of nonspecific antiviral activity or cross-reactive antibodies.

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Making rabies history

Conclusions

There remains a need for science-based surveillance strategies and methods, and proficiency testing and advancement of quality control practices to optimize human and animal rabies diagnostic and serological practices.

Although rabies excites the imagination, current vulnerabilities include:

- the potential for re-introduction of dog-to-dog transmitted rabies,
- a decline in diagnostic expertise and capacity,
- commercial enterprises answering a perceived need for diagnosis and serology but with limitations in test accuracy and specificity,
- and a lack of basic research, especially to understand recent advances towards treatment of clinical rabies.

Future Directions

As a global community with rapid and high volume exchange of animate beings and inanimate products, diligent attention and dedicated effort will be required to maintain, and indeed, even advance, emerging and zoonotic disease control, with rabies as a tangible “best-practices” template, beyond major advances of the last half-century.

Rabies Immunology Workshop
 April 21-22, 2010

Ever Wonder...

- How do we measure response to vaccination? What level of antibodies is “protective”?
- Does a titer of 1:5 equal 0.5 IU/mL?
- ELISA versus virus neutralization – which is “better”?
- Can we compare data over time and between laboratories?
- How do we measure the safety and potency of vaccines?
- And.....are all these the same..... for humans, domestic animals, and wildlife?

<http://www.vet.ksu.edu/rabies>

Finally Some answers.

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