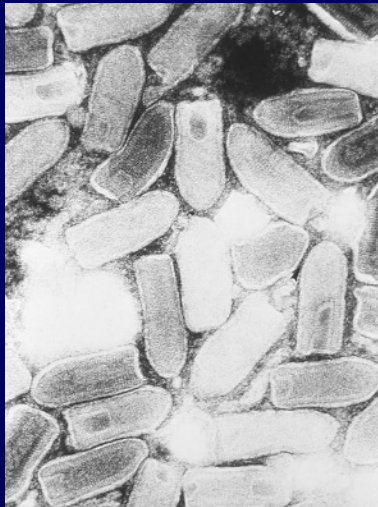


# HUMAN RABIES BIOLOGICALS: UPDATE ON MANAGEMENT OF SUPPLY



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The views expressed in this presentation are those of the author and not necessarily the institution

# INTRODUCTION

- As a major zoonosis in the USA, rabies occurrence is difficult to predict with accuracy.
- While the disease is controlled in domestic animals, wildlife serve as enzootic reservoirs.
- National surveillance provides basic information on animal rabies trends, but human rabies exposures are not reportable.
- Concomitant with the above points, emerging production and regulatory issues, commercial market shifts, etc., complicate the ability to plan accurately for the supply of human rabies biologicals or to forecast shortage situations.

# EVENTS SINCE FEBRUARY ACIP

- 3/5: Formation of ad hoc rabies working group
- 3/27: First 2008 human case diagnosed, CA
- 4/18: 2008 NASPHV animal rabies compendium
- 4/24: Draft interim plans in event of shortage
- 5/7: 2008 ACIP rabies prevention document
- 5/19: Sanofi announcement on restrictions of vaccine for postexposure (PEP) use only
- 6/4: Zoonoses conference call and state update
- 6/8: Ongoing discussions at NASPHV/CSTE
- 6/17: Further restrictions to Novartis supply

## OBJECTIVE OF THE AD HOC WORKING GROUP

- To draft interim recommendations for human rabies prevention in the event of a forecast shortage of biologicals used in prophylaxis

## TIPPING POINTS FOR USE OF INTERIM ACTIONS

- Based upon a combination of historical animal rabies surveillance data, prior mass human rabies exposure situations, and conventional aggregate commercial seasonal distributions of product over time, a national shortage in biologicals would be forecast when expected PEP needs are projected to out strip estimated rate of use of available supplies of human rabies vaccines or immune globulins.

# FOCUS OF THE AD HOC WORKING GROUP

- Coordination and communications
- Diagnostic and animal control focus
- Risk assessments under various scenarios
- Alternative schedules and routes
- Travel medicine
- Economic implications
- Investigational products

# AD HOC WORKING GROUP MEMBERS

- D. Briggs, Kansas State University, *Alliance for Rabies Control***
- B. Cherry, NY State Department of Health, *CDC Zoonoses Working Group Liaison***
- R. Chipman, USDA/APHIS/WS, *Wildlife Society Infectious Diseases Work Group***
- P. Cieslak, OR Public Health Division, *ACIP***
- L. Conti, FL Department of Health, *Am. College of Veterinary Preventive Medicine***
- V. Dato, PA Department of Health, *Am. Association of Public Health Physicians***
- J. Duchin, Public Health, Seattle & King County, & University of Washington, *National Association of County and City Health Officials***
- B. Grogg, OK International Travel Medicine Clinic, *International Society of Travel Medicine***
- G. Hansen, KS Department of Health & Environment, *Council of State & Territorial Epidemiologists***
- S. Jenkins, VA Department of Health, *American Veterinary Epidemiology Society***
- S. Katz, Duke Children's Health Center, *Infectious Diseases Society of America***
- J. Kazmierczak, WI Division of Public Health, *National Association of State Public Health Veterinarians, Inc.***
- L. Robinson, TX Department of State Health Services, *Binational Rabies Committee***
- W. Schaffner, Vanderbilt University School of Medicine, *National Foundation for Infectious Diseases***
- D. Shlim, Jackson Hole Wyoming Travel and Tropical Medicine Clinic, *International Society of Travel Medicine***
- B. Sun, CA Department of Public Health, *Compendium of Animal Rabies Prevention & Control Committee***
- C. Trimarchi, NY State Department of Health, *American Public Health Laboratory Association***
- J. Turner, University of Virginia, *American College Health Association***

# HHS WORKING GROUP MEMBERS

## CDC

**National Center for Immunization and Respiratory Diseases:**

W. Atkinson, G. Wallace

**National Center for Preparedness, Detection and Control of Infectious Diseases:**

N. Marano, M. Meltzer

**National Center for Zoonotic, Vector-borne & Enteric Diseases:**

P. Arguin, J. Blanton, K. Christian, R. Franka, H. Henderson, I. Kuzmin, S. Recuenco, C. Rupprecht, A. Tumpey

## FDA

**Center for Biologics Evaluation & Research**

R. Levis, D. Scott



# CONTINGENCY PLANS DURING A SHORTAGE SITUATION

- Revised health communications/assessments.
- Renewed basic prevention and control activities.
- Alterations in rabies exposure criteria/triage.
- Pre-exposure vaccination changes.
- PEP management modifications.

# ACTIONS IN A SHORTAGE FORECAST

- Centralized national-state health communications, to maximize use of supply.
- Mandatory consultations with knowledgeable public health officials, related to disease risk and need for PEP.
- Renewed education and outreach for key medical providers.

# BASIC RABIES PREVENTION PRINCIPLES

- Postpone PEP administration until animal control can locate and capture any suspects.
- Forestall any PEP during observation period of domestic dogs, cats, and ferrets.
- Withhold PEP until timely diagnostic results are obtained for all rabies suspects.

# REASSESSING EXPOSURES

- Interim guidelines would provide a new risk-stratified approach to human rabies PEP decisions.
- Such modifications conserve supplies by curtailing use in low risk situations, such as non-bite exposures.
- PEP may be withheld after bites from certain animals where adequate surveillance exists and documents no local terrestrial rabies reservoir.
- For bat scenarios, PEP should only be administered to individuals with a strong belief that they would not awaken from a bite, or be unable to report that actual physical contact occurred. Where available, all suspect bats should be captured, tested and PEP deferred until diagnostic confirmation.

# RABIES VACCINATION OPTIONS DURING A SHORTAGE

- Administer only 1 booster in prior vaccinates.
- Drop 5<sup>th</sup> (final dose) of vaccine in naïve patient.
- Use alternative schedules (e.g., 2-1-1).
- Utilize ID route for immunization.
- Consider other biologicals, based on INDs.

# RABIES PRE-EXPOSURE VACCINE ISSUES DURING A SHORTAGE

- Divert most supplies to a primary PEP focus.
- Prioritize use for true, ‘first responder’ highest groups at risk.
- Use alternate routes for administration.

# PRE-EXPOSURE NEEDS

- Required in 'first responder' subjects at risk, before occupational exposure to rabies
- Subjects include animal control workers, diagnosticians, veterinary staff, etc.
- Staff activities directly determine potential PEP management of other exposed patients

# TRAVEL MEDICINE ISSUES

- In the event of a shortage, it would be prudent to de-prioritize vaccination for any international travel indications in favor of reserving supplies for use in PEP regimens.
- Primary education of travelers about rabies occurrence abroad and primary bite avoidance (e.g., not approaching mammals, and avoiding encountering them accidentally by being more aware of their presence) is critical.
- People who take up residence overseas, longer term travelers, and frequent at risk travelers may obtain vaccination abroad where safe injection practices are used with an approved cell culture vaccine.

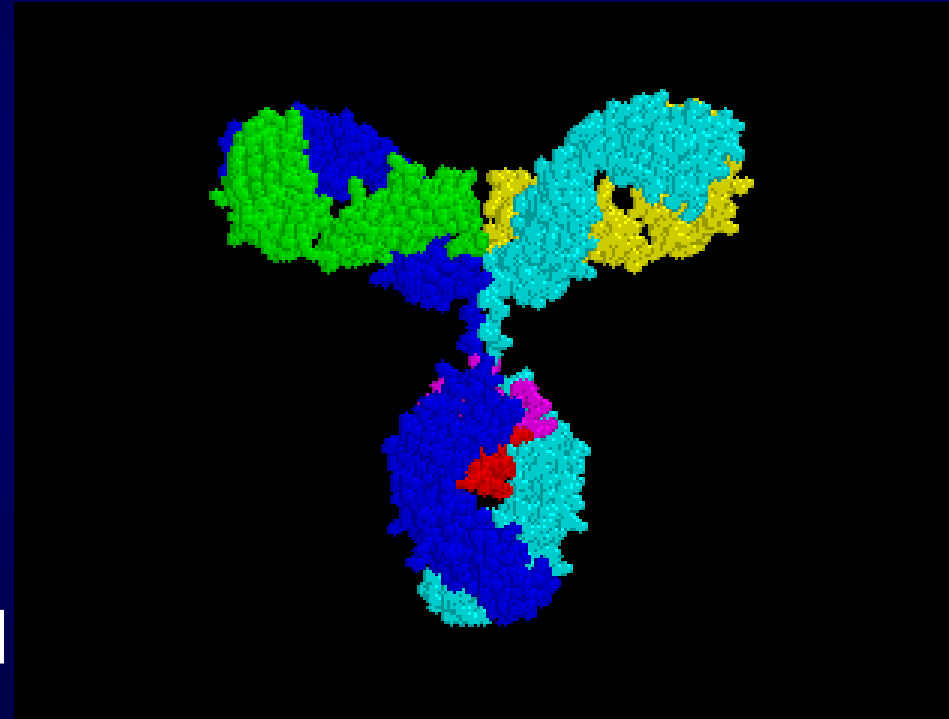


# ECONOMIC IMPLICATIONS

- Dhankhar et al. cost effectiveness study (in press)
  - always cost effective to administer PEP if a patient bitten by a known rabid animal or a major reservoir,
  - all other transmission risk situations, net cost ranges from ~ \$4million to \$4 billion per life saved.
- Could conserve supply by administering PEP up to a maximum defined risk of rabies virus transmission.
- Precise risk estimates of rabies virus transmission do not exist.
- Until more precise estimates for transmission are obtained, it is not possible to examine definitively the economics of strategies attempting to limit the use of biologicals by pre-set thresholds of risk alone.

# RABIES IMMUNE GLOBULINS

- No immediate supply limitations forecast at this time
- Vaccine supply may impact future campaigns in volunteers
- Market changes in plasma collection could create an impact beyond 2009



# SUMMARY

- Supplies of biologicals used in human rabies prophylaxis are expected to remain less than ideal over the next several years.
- CDC, FDA, HHS, industry, state health departments, and national stake holders continue to work together towards productive solutions to mitigate current human rabies vaccine supply issues.
- Deliberations of an ad hoc national rabies working group has resulted in the development of draft interim recommendations related to contingency actions that would be utilized in the event of any forecast actual shortages in the future.

# REFERENCES

- Advisory Committee on Immunization Practices, Human Rabies Prevention, 2008, MMWR 57: RR-3.
- NASPHV, Compendium of Animal Rabies Prevention & Control, 2008, MMWR 57:RR-2.
- World Health Organization, Expert Consultation on Rabies, Geneva, Switzerland, 2005, Tech Rep Ser 931:1-88.