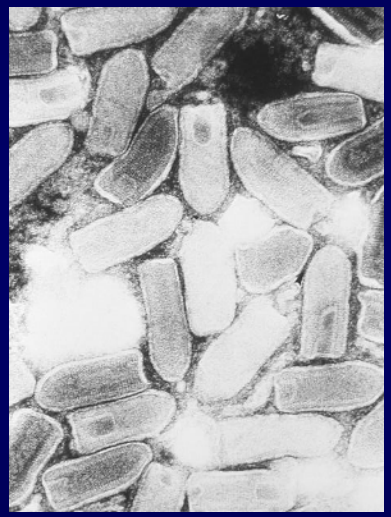
HUMAN RABIES BIOLOGICALS: SUPPLY ISSUES & PROPHYLAXIS MANAGEMENT



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INTRODUCTION

- Rabies is an acute, progressive, viral encephalomyelitis, due to animal bite
- The case to fatality rate is the highest of any infectious disease
- Agents reside in the Genus *Lyssavirus*
- The disease remains a leading viral zoonosis as regards global public health significance, primarily related to affected dogs in developing countries, and mammalian wildlife hosts in the developed world

RABIES IN THE USA

- Human rabies is uncommon (1-8 cases per year), but the risk is not with ~ 20,000 – 40,000 human exposures per year
- Approximately 7,000 – 10,000 animal rabies cases are diagnosed per year
- Wildlife reservoirs include raccoons, skunks, foxes, mongoose, and bats
- Distributed in every state except Hawaii

RABIES PREVENTION

- Pre-exposure Vaccination
- Postexposure Prophylaxis (PEP)

RABIES BIOLOGICALS

- Rabies Vaccines (for pre- and PEP)
- Rabies immune globulin (only in PEP)

PRE-EXPOSURE VACCINATION

- Provided to subjects at risk before occupational or vocational exposure to rabies
- Subjects include diagnosticians, laboratory & vaccine workers, veterinarians, cavers, travelers, etc.
- Simplifies postexposure management

POSTEXPOSURE PROPHYLAXIS

- Provided to subjects after rabies exposure
- Consists of wound care, rabies immune globulin infiltration, and vaccine IM
- If prompt and proper, survival virtually assured after viral exposure

HUMAN RABIES VACCINES

- Two Human Rabies Vaccines in USA:
  Human Diploid Cell Vaccine Imovax® (HDCV)
  Purified Chick Embryo Cell RabAvert® (PCEC)

- RVA no longer available

- Intradermal application no longer available in USA

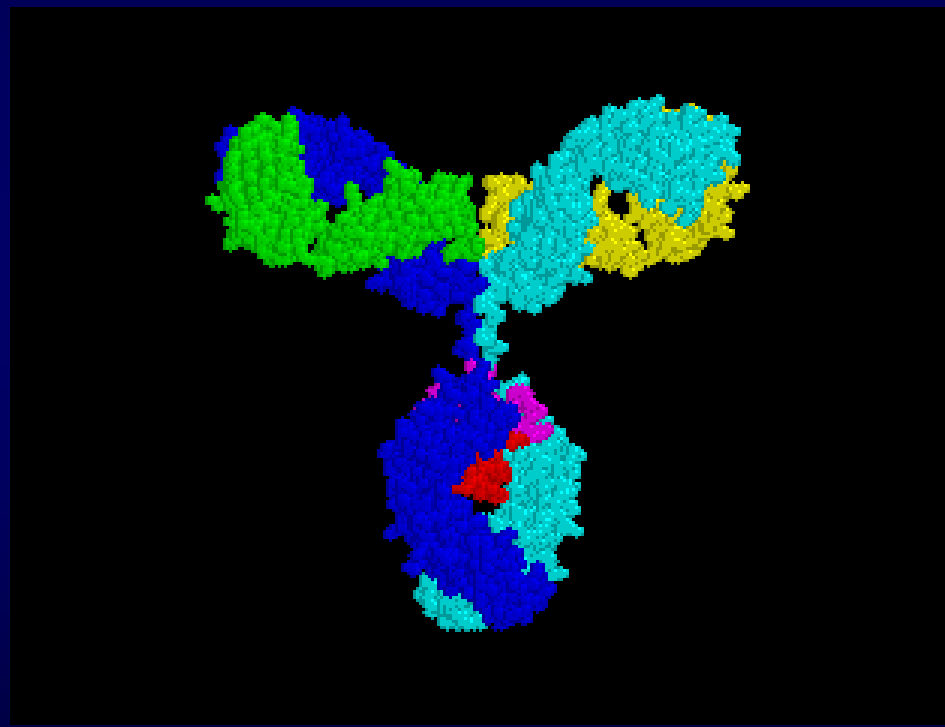
RABIES IMMUNE GLOBULINS

- Two Human Rabies Immune Globulins (HRIG) in the USA:

  HyperRabTM S/D

  Imogam® Rabies-HT

- Both supplied in vials at ~ 150 IU/ml

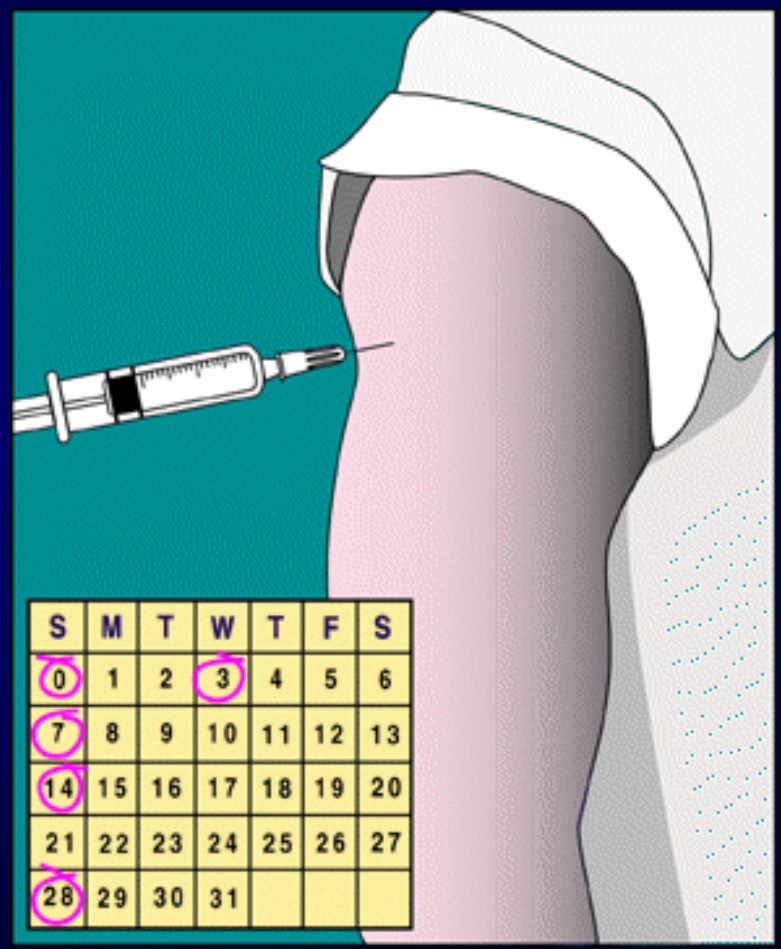


PRE-EXPOSURE VACCINATION

- Vaccine given IM on days 0, 7, and 21 or 28
- Serology occurs every 6 months to 2 years (if remaining at risk), rather than routine boosters
- If antibody titer not adequate, administer a single booster dose
- If ever exposed, a vaccine dose IM on days 0 and 3, regardless of rabies virus neutralizing antibody titer

POSTEXPOSURE PROPHYLAXIS

- Wash lesions well with soap and water (tetanus booster ad hoc)
- Infiltrate rabies immune globulin (20 IU/kg) into and around the margin of the bites (not gluteus)
- Administer vaccine on days 0,3,7,14, and 28



ISSUES AFFECTING SUPPLY:RABIES BIOLOGICALS

- Unpredictability of need based on zoonosis burden
- Episodic incidents involving multiple exposures
- Routine regulatory oversight
- Planned production changes
- Shifting market dynamics
- Untoward scenarios

POTENTIAL SOLUTIONS:SHORTAGES FORECAST?

- Novel multi-disciplinary prevention and control efforts?
- Changes in regulatory review of rabies biologicals?
- Requests for alternative products & manufacturers?
- Creation of managed strategic stockpiles?
- Incentives for applied research and development?
- Implementation of contingency recommendations to maximize proper use of critical supply to patients?

CONTIGENCY FOCUS?

- New health communications/risk assessments?
- Changes in rabies exposure criteria/triage?
- Pre-exposure vaccination alterations?
- PEP management modifications?

MITIGATION RELATED TO SUPPLY?

- Central health communications, stressed as urgency, rather than an emergency, to minimize mistakes?
- Mandatory consultations with knowledgeable public health officials, related to rabies risks?
- Engage other basic legal parameters (national/state dog/cat vaccinations, much greater rapidity of diagnostic testing, enhanced observations of biting animals, improved stray animal control in the local area, etc.)?

REASSESS EXPOSURES?

- Bite focus (common cause)
- Non-bite (rarely causes rabies – minimize?)
- Contacts with blood, urine, feces, etc. are not considered exposures
- Many scenarios, such as merely seeing a rabid animal, being in the same room, petting, etc., are not considered grounds for prophylaxis (de-emphasis on the ‘bat in the bedroom’?)

PRE-EXPOSURE VACCINE SUPPLY ISSUES?

- Divert supplies to a primary PEP focus, if needed?
- Only provide for true, highest groups at risk (occupational vs. vocational vs. travel)?
- Alternate routes besides IM, such as ID (0.1 ml)?
- After rabies exposure in the previously immunized, consider only a single vaccine dose IM on day 0?

RABIES PEP SUPPLY ISSUES?

- Drop 5th (final dose) of vaccine?
- Consider alternative schedules (e.g., 2-1-1) ?
- Utilize multi-site ID route for immunization?
- Entertain other biologicals besides HRIG?

SUMMARY

- Supplies of human rabies biologicals for pre- or PEP in the USA are manageable, but are expected to be less than ideal over the next several years
- CDC, FDA, HHS, and industry continue to work together towards productive solutions to this problem
- Formation of a national rabies working group could assist in the formation of new ad hoc recommendations related to ‘contingency plans’ in the event of any projected true shortages in the future

REFERENCES

- Advisory Committee on Immunization Practices (ACIP), 1999 MMWR 48: RR-1

- World Health Organization Expert Consultation on Rabies, Geneva, Switzerland, 2005, Tech Rep Ser 931:1-88

- NASPHV Compendium of Animal Rabies Prevention & Control, 2007, MMWR 56:RR-3