Rabies: An Old Disease for a New Generation

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Louis Pasteur's ghost must still grimace at the devastation rabies inflicts on the global population. It still kills – globally and in our backyards. Rabies is the 11th highest cause of infectious disease deaths in humans worldwide (Haupt, 1999). Yet, it has been my career experience while chasing this virus, that the general citizen in the United States (US) doesn't consider the threat as "immediate" as perhaps they should. I hope to bring a renewed "face" to this old disease with respect to epidemiology, testing, and prevention/treatment.

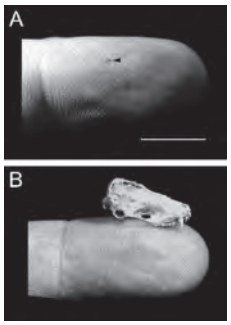

Figure 1. Puncture wound of a bite from a silver-haired bat (A, arrow) and skull of silver-haired bat (B). *"Reprinted with permission from Elsevier Science (The Lancet, 2001, Vol 357, pp 1714)"*

Epidemiology

In the US, rabies in humans is rare; just 41 deaths due to indigenously acquired rabies have occurred in the past 20 years (10 additional non-indigenous cases for a total of 51 deaths in the US since 1987). Of these, an alarming number of deaths (over 75%) are attributed to bat-associated variants of the virus, although an actual bat bite was documented in very few cases (R. Rohde et al., 2004 & Texas Department of State Health Services, 2007). Recent cases of rabies in humans have implicated bats as important wildlife reservoirs for variants of rabies virus transmitted to humans. Even minor bites by rabid bats are entry portals for the virus. Subsequently, they become a transmission route for the virus. These minor bites are often difficult, if not impossible, to identify (Figure 1), which makes the decision to implement treatment difficult (Rohde, 2004).

Terrestrial rabies (non-bat virus variants) in the US is maintained in genetically distinguishable variants of rabies virus (C. Rupprecht et al., 1987; J. Smith, 1988) and can be mapped with reasonable precision (Figure 2). Molecular characterization permits identification of primary reservoir hosts for virus variants, detailed descriptions of the geographic distribution of variants, and identification of virus spillover into animals and humans (J. Smith et al., 1995). Additionally, recent efforts in wildlife vaccination have had an enormous positive effect of reducing some terrestrial rabies virus variants (D. Johnston & R. Tinline, 2002 & T. Sidwa, et al., 2005).

Testing

The single most important standard diagnostic test for rabies in animals is the direct fluorescent antibody (Figure 3) test (D. Dean et al., 1996 & C. Hanlon et al., 1999). In cases where individuals are aware of an animal exposure with a known or suspected rabid animal, rapid and accurate laboratory testing of the animal, if the animal is available, allows hospital physicians to initiate timely Postexposure Prophylaxis (PEP). It is equally important to know that an animal is not rabid; expensive and extended rabies prophylaxis treatment can be eliminated. Even in instances where a laboratory diagnosis is delayed, once a negative rabies result is obtained, the PEP can be halted, preventing any further unnecessary medical treatment and its associated costs (Hanlon et al., 1999). The annual Compendium of Animal Rabies Prevention and Control (CDC, 2007) provides recommendations about the testing of animals suspected of rabies.

Figure 2. Geographic boundaries of currently recognized reservoirs for rabies in terrestrial mammals. *http://www.cdc.gov/ncidod/dvrd/rabies/Epidemiology/Epidemiology.htm*

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Annual Meeting *from page 10*

Shirlyn McKenzie, ASCLS President
Rick Panning, ASCLS President-elect
Susan Liddle, Host Society Liaison
Brad Adams, Dwight Bowlin, and Mary Lou Gantzer, Industry Liaisons
Kyle Riding, Student Forum Chair
Sharon Bobryk, Young Professional Committee Chair
Elissa Passiment, ASCLS Executive Vice-President
Joan Polancic, ASCLS Director of Education & Project Planning
Merle Klein, Meetings Manager, MFM Group

CEAC members included:
Nadine Fydryszewski, Chair
David Thrash, Vice-Chair
Glen McDaniel, Admin/Mgmt
Tim Randolph, Hematology/Hemostasis
Peggy Crim, Immunohematology/Immunology
Deborah Brock, Education
Lynda Britton, Microbiology
Karen Chandler, Chemistry/Urinalysis

Many thanks to each of these dedicated members and staff whose efforts provided an excellent event full of "Sun, Surf & Science!"

Rabies *from page 14*

Rabies is fatal in practically all cases once symptoms begin. Because of this, a differential diagnosis of rabies should be suspected for individuals with signs or symptoms of encephalitis or myelitis. Patients with these symptoms who respond to treatment do not require rabies testing. The absence of an exposure history does not provide evidence to terminate any suspicions of a rabies diagnosis because most patients in the US have no definitive exposure history. Indeed, several recent cases of rabies in humans in the United States have been diagnosed either retrospectively or after the clinical course of the disease has progressed, despite compatible clinical observations (Rohde, 2004). A heightened awareness is needed among the medical community of possible rabies infections in cases where clinical signs are compatible with a diagnosis of rabies. In addition, medical personnel must be aware of appropriate methods for sample collection for antemortem diagnosis and must know how to interpret the test results (Rohde, 2004).

Figure 3. Immunofluorescence of a direct fluorescent antibody test of positive rabies antigen.

Prevention and Treatment

Rabies prevention strategies should be targeted at both humans and the main animal vectors. Appropriate education of the population and health care professionals is essential; many human deaths occur in developing countries because victims of dog bites do not seek medical treatment. In the US, this is not the case with terrestrial animal exposures; however, bat bites may result in trivial injuries and it has become all too clear that they are not identified in some cases.

The majority of animal and human exposures to rabies can be prevented by raising awareness concerning rabies transmission routes; avoiding contact with wildlife; and following appropriate veterinary care. Prompt recognition and reporting of possible exposures to medical professionals and local public health authorities are critical. The 2007 Compendium of Animal Rabies Prevention and Control can be conveniently accessed at the CDC website (http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5603a1.htm?s_cid=rr5603a1_e) and it offers a comprehensive review of education, pre- and post-exposure concerns, management of animals, rabies immune globulin, and rabies vaccines (CDC, 2007).

Conclusion

There are many critical reasons for a clinical laboratory scientist and other members of the healthcare community to stay current with rabies. For instance, recent events have illustrated the transmission of rabies to several humans via solid organ transplants and their subsequent deaths (CDC, 2004), the successful treatment and recovery from rabies of a Wisconsin teenager (R. Willoughby, 2005) and the continued implication of bats being "difficult to detect" with respect to rabies vectors (CDC, 2006).

Globally, it's estimated that 55,000 people die annually from rabies, mostly in Asian and African countries where canine rabies is endemic. Children are frequently the victims of rabies. In the US, indigenous cases of rabies in humans usually occur through transmission of rabies virus from wildlife vectors, and molecular characterization of the variants indicates that the majority of these cases originate from insect-eating bats (A. Jackson, 2005).

References

CDC (2004). Investigation of Rabies Infections in Organ Donor and Transplant Recipients —— Alabama, Arkansas, Oklahoma, and Texas, 2004. MMWR, July 1, 2004 / 53(Dispatch), 1-3.

CDC (2006). Confirmation of Human Rabies in Texas. Retrieved May 14, 2007 from http://www.cdc.gov/ncidod/dvrd/rabies/news/bat_texas.htm.

CDC (2007). Compendium of Animal Rabies and Prevention, 2007. MMWR, 56(RR03), 1-8.

Dean D.J., Abelseth M.K., Atanasui P. (1996). The fluorescent antibody test. In: Meslin FX, Kaplan MM, Koprowski H, eds. Laboratory Techniques in Rabies. 4th ed. Geneva: World Health Organization, 88-95.

Hanlon C.A., Smith J.S., Anderson G.R., et al. (1999). Special series—recommendations of a national working group on prevention and control of rabies in the United States. Article II:laboratory diagnosis of rabies. JAVMA, 215, 1444-1446.

Haupt, (1999). Rabies-risks of exposure and current trends in prevention of human cases. Vaccine 17, 1742-1749.

Jackson, A.C. (June 16, 2005). Recovery from Rabies [Editorial]. N Engl J Med 2005, 352, 24.

Johnston, D.H. & Tinline, R.R. (2002). Rabies Control in Wildlife. In A.C. Jackson & W.H. Wunner (Eds.), Rabies (pp.446-465). San Diego, CA: Elsevier.

Rohde R.E., P.J Wilson, B.C. Mayes, E. Oertli and J.S. Smith. (2004). Rabies: Methods and Guidelines for Assessing a Clinical Rarity. American Society for Clinical Pathology, 2004 Microbiology No. MB-4 Tech Sample, 21-29.

Rupprecht, C.E., Glickman, L.T., Spencer, P.A., and Wiktor, T.J. (1987). Epidemiology of rabies virus variants: Differentiation using monoclonal antibodies and discriminant analysis. American Journal of Epidemiology, 126, 298-309.

Sidwa, T., P. Wilson, G. Moore, E. Oertli, B. Hicks, R.E. Rohde and D. Johnston (2005). Evaluation of Oral Rabies Vaccination Programs for control of rabies epizootics in coyotes and gray foxes: 1995-2003. J Am Vet Med Assoc, 227(5), 785-792.

Smith, J.S. (1988). Monoclonal antibody studies of rabies in insectivorous bats of the United States. Review Infectious Disease, 10 (Suppl. 4), S637-S643.

Smith, J.S., Orciari, L.A., and Yager, P.A. (1995). Molecular epidemiology of rabies in the United States. Seminar in Virology, 6, 387-400.

Texas Department of State Health Services – Zoonosis Control Division (2007). Rabies in Humans in USA 1950 – Present (2007). Retrieved May 14, 2007 from http://www.dshs.state.tx.us/idcu/disease/rabies/cases/statistics/reports/us.pdf

Willoughby R.E., Tieves K.S., Hoffman G.M., et al. (2005). Survival after treatment of rabies with induction of coma. N Engl J Med, 352. 2508-14.