

Mini-Review

Mad dogs and Englishmen

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Although many advances have been made, rabies remains a neglected, preventable, under-reported, and untreatable disease with the highest case fatality rate of any infectious disease. To help counter this, the Alliance for Rabies Control (ARC) and the US Centers for Disease Control and Prevention (CDC) jointly inaugurated the first World Rabies Day (WRD) on September 8, 2007. A number of veterinary organizations and schools, volunteers, and the World Health Organization (WHO) joined in supporting this effort designed to increase awareness and education of both the lay public and health professionals. This report summarizes volunteer experience in this effort in a Midwestern US community. Approximately 280 adult, middle-, high school, lay and health professional individuals attended these programs between August 26 and November 4, 2007. The questions and comments from participants at all levels reinforce the need for continuing and expanded efforts in rabies education. Sample teaching-discussion materials will also be described.

Keywords: Rabies, rabies education, World Rabies Day.

“Mad dogs and Englishmen go out in the midday sun.
In Bangkok at twelve o’clock they foam at the mouth and run,
But mad dogs and Englishmen nevertheless go out in the midday sun.”
(Noel Coward-1932)

Of the 55,000 estimated deaths annually from rabies, Asia accounts for over half [1]. And about half of these deaths occur in children under 15 years of age. India accounts for a large share of these, and China reported over 3000 rabies deaths in 2006, followed by Thailand, which reported deaths during the same period [2]. 2007 has been a watershed year in attacking this horrible, yet completely preventable disease.

September 8, 2007 was World Rabies Day (WRD) and an estimated 51.4 million people were contacted globally through the joint sponsorship of the US-CDC and World Rabies Day (WRD) organization, with support from several others worldwide (**Table 1**). Several events in various countries supported this effort and these are summarized on the WRD web site [3]. In addition, several other meetings dealing with the prospects for more effective rabies control and eventual elimination

took place during 2007, and these have been summarized by Dodet [1]. The Paris meeting (OIE-World Organization for Animal Health, EU-European Union) in May was especially important, as it underscored the need for international cooperation and the joining of veterinary and medical forces in combating this dreadful, universally fatal, yet preventable disease [3].

One of the priorities listed as part of the effort to reduce the human death toll and the reservoir in animals is educating the public about the risk of rabies from animal bites, what constitutes an exposure, how to handle a dead bat or other potentially rabid animal, the critical importance of prompt and thorough wound cleansing, the need for prompt medical attention, and complying with the recommended vaccine/immunoglobulin schedule. Unfortunately, not only public awareness but also health professional performance often falls short of recommended criteria.

This report summarizes educational efforts in a Midwestern community in support of WRD efforts between September 6 and November 4, 2007. About

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Table 1. World Rabies Day activities and outreach as of December 10, 2007.

Activity	Number of participants/activities/people contacted
WRD events	86,000
Public outreach*	51.4 million individuals
Animal vaccinations	275,000
Countries participating	74
Veterinary School	
USA and Caribbean	24/31
India	15
Others-Indonesia, Mexico, Philippines	
**TV, radio, newspaper, public forums	

Source: *Dr. Cathleen Hanlon (E-mail: make.rabies.history@gmail.com),

**Peter Costa (E-mail: peter.costa@worldrabiesday.org).

280 people of various ages and backgrounds attended these programs (**Table 2**). The results indicate the need for continuing these efforts. Much to my surprise, a local physician asked me if one still had to get multiple shots in the abdomen if bitten by a potentially rabid animal!

Materials and methods

Materials

All presentations were developed by the author or downloaded from available public domain materials using PowerPoint presentation software. In addition, focused, single page handouts prepared by the author were distributed to participants, as well as selected materials from the CDC rabies web site (e.g. bats and rabies [5]). Existing slide presentations were utilized, with some modifications [6]. (For sample materials, see **Appendix**.)

Methods

The presentations were in seminar style with slides, discussion, and adequate time for questions. Typical one-hour sessions allowed 45 minutes for the presentation and 15 minutes for questions. Attendees were also encouraged to ask pressing questions during the presentations. The technical level of the presentations varied, depending on the background of the audience. Detailed discussions of PrEP and PEP were given for all levels of participation. Evaluation forms were also distributed. One of the hospitals videotaped the presentation and kept handouts for their library, so that other providers unable to attend could review the material.

Results

Topics covered included history, epidemiology, clinical features, and prevention. The challenges to rabies control in developing countries and special concerns for travelers were also covered.

Table 2. Community presentations.

Group	Date (dd/mo/yr)	Number Attending
County Medical Society	06/09/2007	60
Local Medical Center 1*	07/09/2007	85
Adult Church Group	09/09/2007	15
Local Medical Center 2	10/10/2007	40
Local Hunting Club	18/10/2007	36
Church Youth Group**	04/11/2007	43
Total		279

*Medical Center attendees included physicians, nurses, nurse practitioners, physician's assistants, pharmacists, laboratory staff, administrative staff, and librarians. **Middle- and high school students plus 5 adult leaders.

Bats

First, in spite of publicity about bats, rabies, and the teenager in our part of Wisconsin who is the only known unvaccinated survivor, there were many questions about bats and rabies. Many participants said 'gee, I didn't know about that' or asked 'who do we call if we find a bat in our house?' One frequent question was 'how do I get rid of the bats in my house or cottage?' There was also great interest in how to proceed if parents found a bat in the bedroom with an infant. Regardless of the locale, it is advisable to contact local veterinary and public health authorities whenever a question arises about the presence of rabies in a given species or animal (e.g. dog, cat or other felines, jackal, wolf, fox, bat, mongoose, or rodent). As an unlikely example, a rat bite in rural Thailand carries a much higher risk than a rat bite in Chicago! Or, more likely, a bite from a pet dog in Asia with unknown vaccination status is a much greater exposure risk than one in Wisconsin, where dog vaccination is required.

Rabies vaccine

Several members of the lay groups asked questions about the safety of rabies vaccine, and were obviously concerned about this due to previous stories about use of the Semple nerve tissue vaccine.

In addition, most participants wanted to know what constituted an exposure as well as how much pre-exposure (PrEP) and post-exposure vaccination (PEP) cost. There were also a number of questions about the need and indications for PrEP prior to foreign travel and where to get PEP if needed.

Children and pets

Many people had questions about their children and grandchildren and the risk of rabies. I explained the risk of exposure in different parts of the world, and emphasized the need to educate children about avoiding stray, sick, or wild animals. I also emphasized the importance of regular pet vaccinations as recommended [7]. I also gave them handouts with key web sites and references about rabies.

Health professionals

Several health professionals were just as confused about PrEP and PEP as the lay audience. Several didn't understand the details of injection in different sites for vaccine and immunoglobulin (RIG), the procedures for transporting and storing RIG, and the

importance of timing of RIG and vaccine doses.

Client inquiry-improper storage of HRIG

One situation occurred on the day I was giving the first talk. A nurse anesthetist called me and stated that he and his wife had been exposed to a bat in their bedroom about 10 days prior. He went to a local health facility and was given 6 ml of RIG from a partially-used vial which had been stored in the refrigerator for 7 weeks after first being opened. He was given his first dose of vaccine at this visit, told to return the next day to get 4 more ml of RIG (he needed 10 ml based on body weight, and had been instructed to get more vaccine on days 3, 7, 14, and 28. So when he had consulted me he had received RIG and 2 doses of vaccine. I told him what the proper procedures for RIG/vaccine handling were, that opened vials of RIG should be discarded if not used promptly, and that he should complete the vaccine series. I also suggested that his wife should consider PEP, since the bat may have bitten her as well. Neither one could find a bite mark or remember being bitten, but wanted PEP regardless. He asked if he should repeat the RIG, and I told him not to since he had already received two doses of vaccine. Fortunately, he has not developed any local infection relating to the improperly handled RIG.

Rabies treatment

The thorny issue of rabies treatment was raised at every program. This was due to the highly publicized case of the teenager from our area who was treated with the 'Milwaukee Protocol' [8-10] and survived. She is currently a freshman in college, and can drive a car, but she has some neurologic sequelae with speech and coordination difficulty. She spoke at a public forum at the Milwaukee County Zoo in August, where I was able to visit with her.

I stated that no one really knows the answer to her survival but suggested three possibilities to the audiences:

- She survived because of her intensive, ketamine-based deep anesthesia treatment.
- She survived in spite of the treatment.
- She survived due to factors not related to her treatment.

Based on the available evidence, I believed that her remarkable recovery was in large part due to her rapid and high neutralizing antibody response plus the outstanding nursing care she received. I also cited

other case reports from the literature supporting this notion [11, 12]. In ten other cases, where attempted, the “Wisconsin” protocol has failed.

Rabies and organ transplantation

One final question raised by a health care provider was the risk of rabies from organ transplantation. I discussed this briefly and referred her to recent reports [13, 14]. Rabies was not diagnosed ante-mortem in the donor described in the original report, indicating need for a greater awareness of rabies risk in transplantation programs.

Discussion

Without formal survey instruments it is difficult to gauge the impact of these efforts. Nevertheless, I believe these efforts are worthwhile. One of the problems in the US is that rabies is relatively infrequent in humans [15] due to concerted efforts with dog and other pet vaccinations. Another perplexing issue is the increasing importation of dogs with uncertain vaccination status into the country [16]. Since most of the animal rabies in North America occurs in bats, raccoons, skunks, and foxes [15], international travelers need to be reminded to avoid picking up stray dogs and cats, especially puppies and kittens [17]. Understanding of the importance of capturing sick or dead bats is still inadequate, as evidenced by another report about possible exposure in a pregnant woman in Michigan [18].

Another issue on the horizon is that of PrEP and PEP for travelers to China for the Beijing 2008 Olympic games. While the risk may be low in Beijing, it is not zero, and the incidence in China is second only to India, with over 3000 human rabies cases reported in 2006. Imported human rabies immunoglobulin is not currently readily available in China, except in Hong Kong. The locally manufactured equine product is also scarce. So if bitten, a traveler may have to fly to Hong Kong, Bangkok, Singapore, or home for PEP. This was recently reviewed by Shaw et al [19]. Readers may also find the recent WHO position paper on rabies vaccines helpful when advising travelers and others about the risks of Nerve tissue-based vaccines [20].

The message that seemed to register most at all these programs was the one that about 50 per cent of rabies deaths are in children under 15 years of age, and the need to ‘save the children’. Finally, Development of standardized presentations for lay

and professional groups may be helpful to ensure accuracy and reduce time-consuming duplication of effort [1, 2].

A recent report from Germany [21], also underscores the need for strengthening training for health care providers in assessment and management of unique situations related to rabies exposure. Questions frequently arise on the International Society of Travel Medicine (ISTM) listserv (*travelmed@yorku.ca*) regarding PrEP and PEP in travelers [22].

Conclusions

1. Rabies remains an enigmatic, yet preventable, disease with the highest case fatality rate of any infectious disease.
2. Ongoing public and professional health education continue to be critical for future efforts to control and decrease the human death toll from rabies.
3. This requires commitment from both the public and private sectors, especially in those parts of the world where rabies is highly endemic and where adequate modern vaccine supplies and RIG are in short supply or lacking altogether.
4. There are many challenges to success, including the need of competing programs for financial support, such as the new emphasis on chronic disease in low-income and middle-income countries [23, 24].

Appendix

What did Noel Coward, Edgar Allen Poe, and Louis Pasteur have in common?

Noel Coward, the noted British composer, director, and actor wrote this little ditty as a satirical take-off on the pomposity of his day. The ‘mad dogs’ undoubtedly refers to rabies, which was rampant in the UK in the early 20th century. The entire lyrics can be found by Googling ‘Mad Dogs and Englishmen’.

There is also a new book titled *Mad Dogs and Englishmen*, just published [25], covering the history of rabies in Britain from 1830-2000.

Edgar Allen Poe, the American author may have died of rabies rather than alcoholism, according to one author. This was written up in the *New York Times*, September 15, 1996. Professor Henry Wilde was consulted and is quoted: Poe ‘had all the features of encephalitic rabies’. Of course, we will never know for sure.

Louis Pasteur, who is regarded as the father of modern microbiology, reported the first successful PEP using nerve tissue vaccine in a young boy, Joseph Meister, in 1885 [26].

Sample teaching-discussion materials

- The WRD web site has a wealth of material (www.worldrabiesday.org). From the home page, click on Teaching Materials on the left. The 'Learning to Make Rabies History Curriculum' is available in PowerPoint or PDF format, and the teacher's notes in PDF. These materials are presented in English, French and Swahili. Fact Sheets are also available in English, Portuguese, and Spanish. The veterinary toolkit includes: a) Talking points for veterinarians to use with their clients (PDF), b) How veterinarians can partner with the World Rabies Day Initiative (PDF), and c) What you should know about rabies (Brochure from AVMA). (This was accessed on 13DEC2007.)
- The Alliance for Rabies Control (ARC), the UK-based charity (Professor Debra Briggs, executive director) publishes a free newsletter (Rabid Bytes-5 issues to date) on their web site. www.rabiescontrol.org Accessed 14DEC2007. The latest issue has an article about African Wild Dogs and a historical rabies case from Edinburgh. This is another useful site for informing people about important global rabies developments. The issue also includes several pictures of WRD activities in various locales.
- The CDC web site (www.cdc.gov/rabies) has a recently updated home page with icons to link to specific areas. There is also a spotlight: New World Rabies Day e-card that can be used for continuing educational emphasis and awareness about rabies. Under general information for general use there are two links: Rabies exposure, and Bats and Rabies. The bats link includes an excellent two-page brochure (PDF) which is a useful handout for programs, and which also includes information about bat-proofing your home or cottage. Under Information for specific groups, the links are: a) Just for Kids, b) State Health, c) veterinarians, and d) Healthcare Professionals. The kids section has a number of interesting activities for kids in addition to rabies facts. (Accessed 12DEC2007.)
- Professor Henry Wilde and his associates from Chulalongkorn University in Bangkok have conducted a survey of rabies experts to address difficult case issues and found a lack of uniformity and some

controversy in dealing with these dilemmas. They suggested the need for more research to help provide better guidelines for rabies prevention. (Sriaroon C, et al. Common dilemmas in managing rabies-exposed subjects. *Travelmed Infect Dis.* 2005; 3:1-7.)

- The above group has also published a prospective study of 500 rabies-exposed patients dealing with issues not easily addressed using current WHO or US-CDC recommendations. Such examples can be useful in developing seminar materials for discussion. (Tepsumethanon S, et al. Problems in human rabies post-exposure prophylaxis management. *Travelmed Infect Dis.* 2007; 5:189-93.)
- For those health professionals who want a general reference on rabies as background, the Seminar by MJ and DA Warrell provides useful information. (Warrell MJ, Warrell DA. Rabies and other lyssavirus disease. *Lancet.* 2004; 363:959-69.)
- WHO's web site also provides useful information www.who.int/rabies. There are also links to Rabnet, the WHO electronic surveillance system, dog rabies control, and rabies maps. The dogs section emphasizes that dog destruction alone is not effective in rabies control. Rather, such things as multiagency mass vaccination/sterilization efforts are likely to be more productive. (Accessed 12DEC2007.)
- Thailand's rabies researchers and clinicians prepared a web site, www.soonak.com which presents technical points on rabies issues for professionals free. It is in English and Thai and contains video strips. (Accessed 18DEC2007.)
- The author also developed a single-sheet five point handout for youth groups.
- Emerging Infectious Disease journal (US-CDC) is free and available both in print and online (www.cdc.gov/eid, accessed 13DEC2007). The articles come from around the globe and also contain many interesting figures and charts which are useful for teaching (**Figs. 1, 2**).
- The US-CDC has a number of images which are useful for teaching. The image below is a schematic of the rabies virus structure (**Fig. 3**). (www.cdc.gov/rabies/virus.html. Accessed 13DEC2007.)
- Details of PrEP and PEP, WHO classification of type of contact, along with photos of correct intradermal injection technique have been updated by Briggs and Mahendra. (Briggs DJ, Mahendra BJ. Public health management of humans at risk. In: Jackson AC, Wunner WH. ed. *Rabies*, 2nd ed. New York:Academic Press Elsevier. 2007; p. 545-71.)



Fig. 1 Annual rabies cases in China from 1950-2004. (Zhang Y-Z, et al. Human rabies in China [letter] Emerg Infect Dis Dec. 2005. www.cdc.gov/incidod/EID/vol11no12/04-775.htm).

Human rabies cases per year

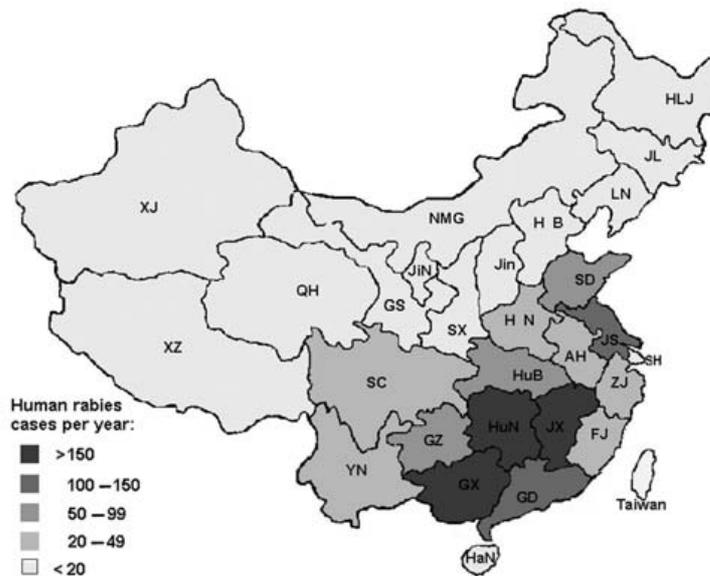


Fig. 2 Human rabies epidemic in China by location, 1996-2000. (Tang X, et al. Pivotal role of dogs in rabies transmission, China. [Dispatch] Emerg Infect Dis. 2005; 11:1970-72.)

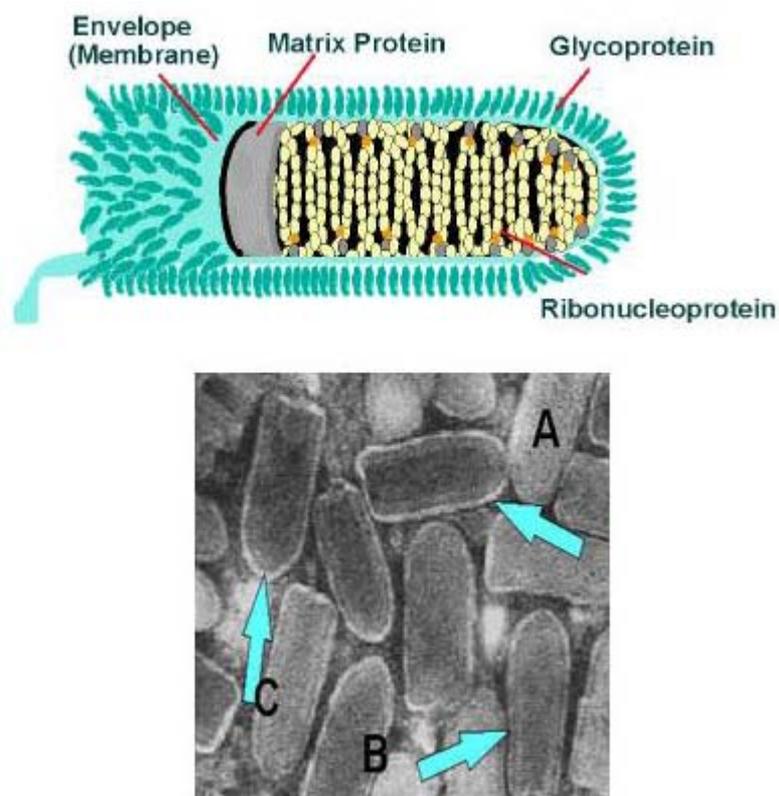


Fig. 3 Electron microscope image of bullet-shaped rhabdovirus. (www.cdc.gov/rabies/diagnosis.html. Accessed 13DEC2007.)

- This is worth reviewing before discussing with other health professionals. The 5-dose intramuscular (IM) Essen regimen is the only protocol approved for use in the USA. In Asia, the ‘Thai Red Cross’ intradermal (ID) regimen (‘2-2-2-0-2’, ID at two sites on days 0, 3, 7, and 28) is the most frequently used. Further details are available in WHO document 931, 2005. (WHO Expert Consultation on Rabies. First Report (2005). WHO Technical Report Series 931. WHO. Geneva, Switzerland.)
- Any of the above regimens require prompt administration of RIG into the wound(s) in conjunction with the first dose of vaccine with the balance IM. The dose is 20 IU/kg for HRIG and 40 IU/kg for ERIG. The weight-based dose is not to be exceeded or the RIG may interfere with response to the vaccine. If the volume required due to multiple wounds is not sufficient, dilution with sterile saline is acceptable. RIG should never be mixed in the same syringe with vaccine, and should always be given at a site distal to the vaccine (example right and left deltoid, or one deltoid and one anterior thigh for young children). Any remaining RIG not injected into wounds should be

given IM. In cases where RIG must be delayed because of unavailability, it can be administered up to 7 days after the first dose of vaccine.

- Proper and prompt wound care is essential, with thorough washing using soap and water. Unfortunately, even the most basic supplies for this are not available in many rabies clinics in the developing world (Briggs DJ, Wilde H. Personal communications, 2007).
- For international travelers, the current CDC and WHO documents provide excellent summaries. The 2008 CDC ‘yellow book’ gives specific information for US-approved PrEP and PEP regimens, and the WHO book provides information on all WHO/CDC approved regimens. It might be worthwhile to mention to travelers that the Purified Chick Embryo vaccine is marketed both under the names Rabavert and Rabipur®. Although not approved in the USA, Verorab® (purified rabies vaccine developed using VERO cells) has also been used successfully in more than 100 countries and recently reviewed by Toovey (item 16 below). (WHO. International Travel and Health. WHO, Geneva 2007; p. 120-7. The WHO

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