WORLDWIDE RABIES DEATHS

Henry Wilde, MD
Professor Of Medicine
Faculty Of Medicine
Chulalongkorn University
Bangkok, Thailand
WORLDWIDE RABIES DEATHS
(Estimates same for decades)

60 - 70,000 +
Actually not known
Almost all had No PEP
WHERE ARE MOST OF THESE DEATHS FROM AND WHY NOT PREVENTED?

• LACK OF HEALTH EDUCATION

• EXTREME POVERTY

• DYSFUNCTIONAL GOVERNMENTS

• INEFFECTIVE HEALTHCARE PROVIDERS

• LACK OF ACCESSIBLE POST-EXPOSURE PROPHYLAXIS

• BIOLOGICALS NOT PROVIDED (VACCINES, RIGs)
Hand bites
PROGNOSIS OF RABID DOG BITE:

1) **Nature of wound care**
   - Timing?
   - Irrigation?
   - Antisepsis?

2) **Anatomic site of the bite**
   - Near peripheral nerve?

3) **Viral load deposited in wound?**
   - Unpredictable: zero to very high

4) **Timely post exposure prophylaxis**
   - Following of WHO guidelines
Clinical and epidemiological features of human rabies cases in the Philippines: a review from 1987 to 2006

Efren M. Dimaano a, Stephen J. Scholand b,*, Maria Theresa P. Alera a, Domingo B. Belandres a

a San Lazaro Hospital, San Lazaro Compound, Sta. Cruz, Manila, Philippines
b St. Mary’s Hospital, 56 Franklin St., Waterbury, CT 06706, USA

ARTICLE INFO

Article history:
Received 3 January 2011
Received in revised form 11 February 2011
Accepted 24 March 2011

Corresponding Editor: Jane Zuckerman, London, UK.

Keywords:
Rabies
Rabies virus
Neurological manifestations
Infectious disease incubation period
Encephalitis
Clinical medicine

SUMMARY

Background: Rabies viral infection causes a fatal encephalomyelitis. In humans, classic features include hydrophobia, aerophobia, hypersalivation, agitation, and neurological symptoms. In the Philippines, canine rabies contributes to a significant burden of human disease.

Methods: We retrospectively reviewed the medical records of 1839 patients admitted to San Lazaro Hospital, Manila, Philippines between 1987 and 2006, with a clinical diagnosis of rabies. We used the World Health Organization case definition for clinical rabies, which is defined by the presence of hydrophobia.

Results: Male patients outnumbered females by 2.2 to 1 and twice the number of adults were affected compared with children. Most patients were indigent. Dog bites occurred more than cat bites (97.1% vs. 2.9%) and most cases were caused by a single bite (86.2%), compared to multiple bites (8.7%). Bites to the face, head, and neck led to shorter incubation times, yet the incubation period varied, with most cases (42.7%) occurring in the bracket of 91–365 days post-exposure. Clinical symptoms included hydrophobia in all cases, as per our case definition, and aerophobia in 95.5%; only 9.4% had fever, 9.2% exhibited restlessness, and 6.7% exhibited hypersalivation. Localized neurological symptoms included pain (4.1%), numbness (2.6%), and itching (2.3%). None of the patients received appropriate post-exposure prophylaxis (PEP).

Conclusions: This study examines the largest cohort of rabies patients reported to-date. Better understanding of clinical disease manifestations may help in salvage efforts to save patients with rabies. Knowledge of epidemiological factors will improve preventative efforts to reduce suffering from rabies.

© 2011 International Society for Infectious Diseases. Published by Elsevier Ltd. All rights reserved.
Post-exposure rabies treatment

Nab IU/ml

RIG (passive immunization)

Vaccine (Active immunization)

Day after treatment

3 7 14 28
INJECT ANTIBODY INTO WOUNDS

WHY?

INOCULATED VIRUS HAS “WINDOW PERIOD” AT WOUND SITE

KILLING TITRE TAKES 7-10 DAYS TO APPEAR IN CIRCULATION

ENOUGH TIME FOR INVASION OF PERIPHERAL NERVE

CAN START ADVANCE TO CNS IN A PERIPHERAL NERVE
Diffusion and fate of intramuscularly injected human rabies immune globulin.

Saesow N¹, Chaiwatanarat T, Mitmoonpitak C, Wilde H.

Author information

¹Division of Nuclear Medicine, Departments of Radiology, Chulalongkorn University Hospital and the Queen Saovabha Memorial Institute, Thai Red Cross Society, 1871 Rama IV Road, 10330, Bangkok, Thailand.

Abstract

The importance of rabies immune globulin (RIG) in postexposure rabies treatment is well known and it has been emphasized that the local injection into the animal bite sites is crucial. This preliminary study used a radioisotope tracer that allows following the fate of human rabies immune globulin (HRIG) injected intramuscularly. There was significant retention and local diffusion of the immune globulin at the injection site and significant radiotracer could still be detected at the site 24 h later.
Neutralizing antibodies to rabies following injection of rabies immune globulin into gluteal fat or deltoid muscle.

Chomchay P¹, Khawplod P, Wilde H.

Author information

Abstract

BACKGROUND: This experiment was carried out to determine whether there is any difference in circulating rabies antibody when rabies immune globulin is administered into fat or muscle tissue.

METHODS: Blood samples were taken at 24 and 48 hours after administering 40 IU/kg body weight of purified equine rabies immune globulin (ERIG) into deltoid muscle, or fatty gluteal tissue of grossly obese subjects.

RESULTS: Both groups revealed barely detectable antibody levels.

CONCLUSIONS: No conclusion was possible concerning the absorption kinetics of immune globulin from fat or muscle. However, it was evident that circulating antibody levels, using the recommended 40 IU/kg dose of ERIG, were extremely low and probably less than the required protective level at the possible bite site. This study supports current recommendations for local infiltration of virus inoculation sites with human or equine rabies immune globulin.
OVER 90% OF RABIES DEAD RECEIVED NO PEP AND NO RIG

- WORLDWIDE NUMBERS OF HUMAN RABIES DEATHS NOT KNOWN
- MANY ARE NOT REPORTED
- ALMOST ALL ARE IN POOR UNDERDEVELOPED REGIONS
- ALMOST ALL HAD NO PEP
- LESS THE 6% OF PEPS RECEIVED RIG OR WOUND INJECTION
- REASONS ARE LACK OF EDUCATION AND MOTIVATION
- PEP OR TRAVEL TO IT ARE NOT AFFORDABLE
TOTAL DOSE RIG IS GIVEN IM:
ANITBODY IS BARELY DETECTABLE IN SERUM

• DeanDJ. Bull WHO 1963; 28: 477-86


• Chomchay P. et al. Travel Med 2000; 7: 187-8

VACCINE OR RIG OFTEN NOT AVAILABLE

- KILLING VIRUS AT WOUNDS IS BEST EARLIEST ACT
  TIMELINE: VIRUS MAY ENTER PERIPHERAL NERVE
- THEN ADVANCE TOWARDS SPINAL CORD AND BRAIN
- DOSE OF RIG BASED ON BODY WEIGHT (20 OR 40 iu/Kg)
- NOT RESULTING IN VIRUS KILLING BLOOD LEVEL
- VACCINE INDUCED ANTIBODY LEVEL REQUIRES 7-14 DAYS
- OUR REASON FOR KILLING VIRUS AT INOCULUM
- FAILURES IF RIG IS NOT INJECTED INTO WOUNDS
SURVEY REPORT

Awareness about Rabies Post Exposure Prophylaxis in Pakistan Among Patients and Health Care Workers: Results from an Asian Rabies Expert Bureau Study

Naseem Salahuddin¹, Seemin Jamali², Khalid Ibraheem³ and Syed Sardar⁴

ABSTRACT

Objective: To identify the gaps in information on rabies and post exposure prophylaxis (PEP) in relation to categorization of wound severity, wound washing and appropriate use of vaccine and rabies immunoglobulin after exposure, and define actions that should be taken at dog bite management centres for prevention of rabies occurring after animal bites.

Study Design: Cross-sectional survey.

Place and Duration of Study: A multicentre study across Pakistan conducted from 1st July 2007 to 31st January 2008.

Methodology: A pre-tested questionnaire was distributed to the respective medical officers in 6 dog bite management centres across Pakistan from 1st July 2007 to 31st January 2008. Information was obtained about demographics of dog bite victims, the timing and type of PEP administered and their responses to the injury.

Results: Out of 519 completed questionnaires the mean age of dog bite victims was 24 years. Over one-third were less than 18 years of age; male/female ratio was 4.9:1; 43% lived in rural Pakistan; 67.8% were classified as lower socioeconomic class; 98% animal bites were from dogs, of which 92.5% were first time bites. 45.5% wounds were classified as Category I (no risk), 42.7%, Category II (moderate risk) and 11.9% Category III (severe risk). Tissue culture vaccine (TCV) was used 54% by intramuscular route and 45% by intradermal route. Only 118 (22.9%) patients received rabies immunoglobulin (RIG). Critical analysis of the results reveals serious gaps in understanding of wound severity classification and correct application of PEP with vaccine and RIG.

Conclusion: There is a dire need for improved awareness and understanding of dog bite management among health care givers in order to prevent rabies deaths.

Key words: Rabies. Post Rabies Exposure Prophylaxis. Rabies awareness.
<table>
<thead>
<tr>
<th>Reason</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Government Hospital Doctor</td>
<td>56%</td>
</tr>
<tr>
<td>Will not inject wounds</td>
<td>20%</td>
</tr>
<tr>
<td>Afraid of local reactions</td>
<td>43%</td>
</tr>
<tr>
<td>Afraid of anaphylaxis</td>
<td>56%</td>
</tr>
<tr>
<td>Afraid of infection</td>
<td>17%</td>
</tr>
<tr>
<td>Afraid causing more pain</td>
<td>20%</td>
</tr>
<tr>
<td>I only would use HRIG</td>
<td>27%</td>
</tr>
<tr>
<td>Doctor injects wounds only</td>
<td>62%</td>
</tr>
</tbody>
</table>

(Ashwath Narayana 2012)
AN “ARTIFICIAL” ANTISERUM?

AT LEAST 3 FORMS ARE IN “PIPELINE”

TO REPLACE EXPENSIVE AND SCARSE HRIG

TO REPLACE ERIG THAT STILL CONTAINS SOME HORSE PROTEIN

PRODUCT THAT CAN BE STANDARDIZED, SAFE AND AFFORDABLE
Short communication

Failures of post-exposure rabies prophylaxis

Henry Wilde

Infectious Disease Unit, Department of Medicine, Division of Research and Development, Faculty of Medicine, Chulalongkorn University, Rama IV Road, Bangkok 10330, Thailand

Received 28 July 2007; received in revised form 27 August 2007; accepted 27 August 2007
Available online 14 September 2007

Abstract

Rabies remains a public health problem in many emerging countries. Virtually all is known that should enable us to eliminate this scourge by controlling the disease in canine populations and by diligent provision of WHO recommended post-exposure prophylaxis (PEP). Nevertheless, post-exposure prophylaxis failures do occur. Most common failures are due to deviations from WHO management recommendations and lack of essential biologicals. True failures, where all was done according to WHO recommendations, are fortunately extremely rare. Presented are seven such deaths. Other examples of common management deviations that resulted in deaths are also shown.

© 2007 Elsevier Ltd. All rights reserved.

Keywords: Rabies post-exposure prophylaxis; Efficacy of post-exposure prophylaxis; Failures of post-exposure prophylaxis
COMMON PEP FAILURES

INCOMPLETE PEP
WOUND NOT CLEANSED
WOUND SUTURED BEFORE RIG INJECTED
VACCINE INJECTED INTO FAT
DELAY TO STARING PEP
NO RIG AVAILABLE OR USED
WOUNDS NOT INJECTED
NOT ALL HIDDEN WOUNDS INJECTED
PERIPHERAL NERVE DIRECTLY INJECTED
VIRUS INTRODUCED DIRECTLY INTO EYE
RIG INSUFFICIENT VOLUME FOR ALL WOUNDS
Failure of postexposure treatment of rabies in children.

Wilde H¹, Sirikawin S, Sabcharoen A, Kingnate D, Tantawichien T, Harischandra PA, Chaiyabutr N, de Silva DG, Fernando L, Liyanage JB, Sitprija V.

Author information

¹Department of Medicine, Chulalongkorn University, Bangkok, Thailand.

Abstract

Five failures of postexposure treatment of rabies in small children with multiple severe bites on the face and head are discussed. All had received rabies immune globulin and a potent tissue-culture vaccine. However, not all wounds had been infiltrated with immune globulin. Surgical closure prior to wound injection with immune globulin was performed in three cases. Another patient had wounds sutured after an intramuscular injection of immune globulin, without wound infiltration.
BARRIERS TO PEP

LACK OF HEALTH EDUCATION
PEP NOT LOCALLY AVAILABLE
HRIG, ERIG, ANTISERUM NOT AVAILABLE
REQUIRES 3-5 TRIPS TO DISTANT CLINIC
COST OF TRAVEL, LOSS OF INCOME
RIGs NOT STOCKED AT CLINIC OR HOSPITAL
PHYSICIANS UNWILLING TO INJECT RIG INTO WOUNDS

MOOVE PET CLOSER TO PATIENTS AND PROVIDE ESSENTIAL BIOLOGICALS!