



Pre-exposure rabies vaccination (PreP) in children of endemic countries

Global Vaccine and Immunization Research Forum
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Current situation



- **Fatal viral disease > 95% caused by dog bites - 100% preventable by vaccination**
- **Rabies vaccines can be administered after exposure (PEP) or as preventative vaccination (PreP)**
- **Every dog bite in canine rabies endemic countries must be considered a risk of exposure**
- **22 million people exposed annually – mostly children**
- **One child dies of rabies every ~ 10 minutes**
- **No or limited access to PEP in remote rural regions where rabies is endemic – Vampire bat and canine**



Rabies is under-reported, misdiagnosed

DISPATCHES

Rabies Encephalitis in Malaria-Endemic Area, Malawi, Africa

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In a malaria-endemic area of Africa, rabies was an important cause of fatal central nervous system infection, responsible for 14 (10.5%) of 133 cases. Four patients had unusual clinical manifestations, and rabies was only diagnosed postmortem. Three (11.5%) of 26 fatal cases originally attributed to cerebral malaria were due to rabies.

10.5 % of children originally diagnosed with cerebral malaria in Malawi died of rabies



Where does PreP fit in?

- We have the tools: WHO pre-qualified rabies vaccines are among the most efficacious
 - IM and ID,
 - PEP and PreP
 - RV used as ‘control’ in vaccine development (i.e. malaria)
- Rabies deaths caused by lack of access, lack of knowledge about risk
- ***PreP in specific circumstances can IMPROVE ACCESS:***
 - ***“the goal of the vaccine collaboration it is to extend the full benefits of immunization to all people regardless of where they live”***

- Bill Gates

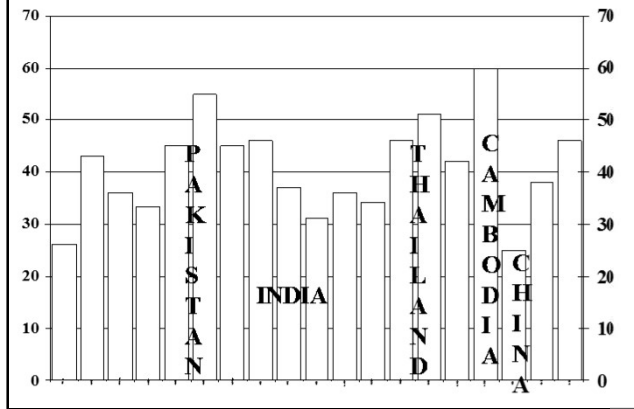
Large variety of reservoir species



Globally - rabies is unlikely to be eradicated

Dog Bite Facts

•Children aged less than 15 years are involved in 40% of the cases



Every dog bite in a rabies-endemic country must be considered a potential exposure



Dog Bite Facts



Photos: KIMS, Bangalore



Photos: Dr Steven Scholand

More than half of all children will be victims of a dog bite by the time they reach age 12



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Evidence of Rabies Virus Exposure among Humans in the Peruvian Amazon

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Abstract. In May of 2010, two communities (Truenococha and Santa Marta) reported to be at risk of vampire bat depredation were surveyed in the Province Datem del Marañón in the Loreto Department of Perú. Risk factors for bat exposure included age less than or equal to 25 years and owning animals that had been bitten by bats. Rabies virus neutralizing antibodies (rVNAs) were detected in 11% (7 of 63) of human sera tested. Rabies virus ribonucleoprotein (RNP) immunoglobulin G (IgG) antibodies were detected in the sera of three individuals, two of whom were also seropositive for rVNA. Rabies virus RNP IgM antibodies were detected in one respondent with no evidence of rVNA or RNP IgG antibodies. Because one respondent with positive rVNA results reported prior vaccination and 86% (six of seven) of rVNA-positive respondents reported being bitten by bats, these data suggest nonfatal exposure of persons to rabies virus, which is likely associated with vampire bat depredation.

Gilbert et al 2012

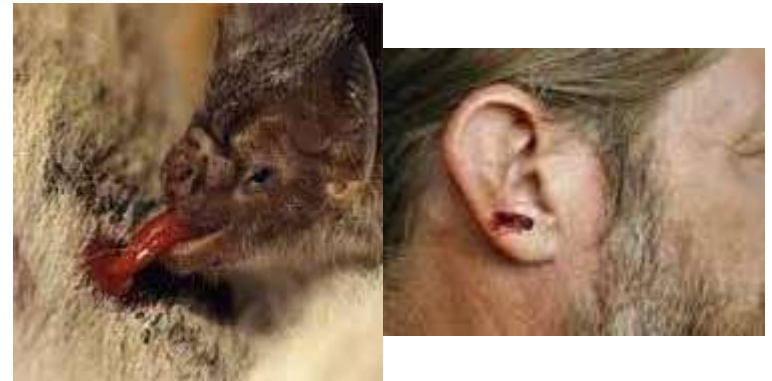


TABLE 3

Indication of bat exposure and prior pre- or post-exposure prophylaxis history among seropositive survey respondents

Gender (age in years)	Location	RFFIT (IU/mL)	IFA		Bat exposure*	Bat bite	PreEP/PEP
			IgG	IgM			
Male (48)	Truenococha	0.4	1:128	–	Yes	No	No
Male (54)	Truenococha	ct	1:128	–	Yes	Yes	No
Male (34)	Santa Marta	0.6	–	–	Yes	Yes	No
Male (40)	Santa Marta	< 0.05	–	1:8	Yes	No	nd
Female (49)	Santa Marta	0.4	–	–	Yes	Yes	nd
Male (39)	Santa Marta	2.8	–	–	Yes	Yes	No
Male (49)	Santa Marta	0.4	–	–	Yes	Yes	No
Male (47)	Santa Marta	0.6	–	–	Yes	Yes	No
Female (27)	Santa Marta	0.1	1:8	–	Yes	Yes	PEP

*Bat exposure defined as a bite, scratch, or direct contact with unprotected skin.

ct = cytotoxic; IFA = indirect fluorescent antibody; IU = international unit; Ig = immunoglobulin; nd = not determined; PEP = post-exposure prophylaxis; PreEP = pre-exposure prophylaxis; RFFIT = rapid fluorescent focus inhibition test.

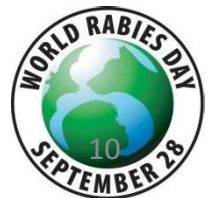
63 sera obtained from respondents (age 2 – 62) mean age 29 years;

11% (7 out of 63) showed rVNA (titer 0.1 – 2.8 IU/mL)



PreP Studies in Children

- Many published clinical trials available
- Successful long term immunity proven:
 - in association with DPT-IPV in infants – five year follow up proved successful booster response
 - in association with JE vaccine in toddlers
 - in school age children
 - Using both IM and ID administration



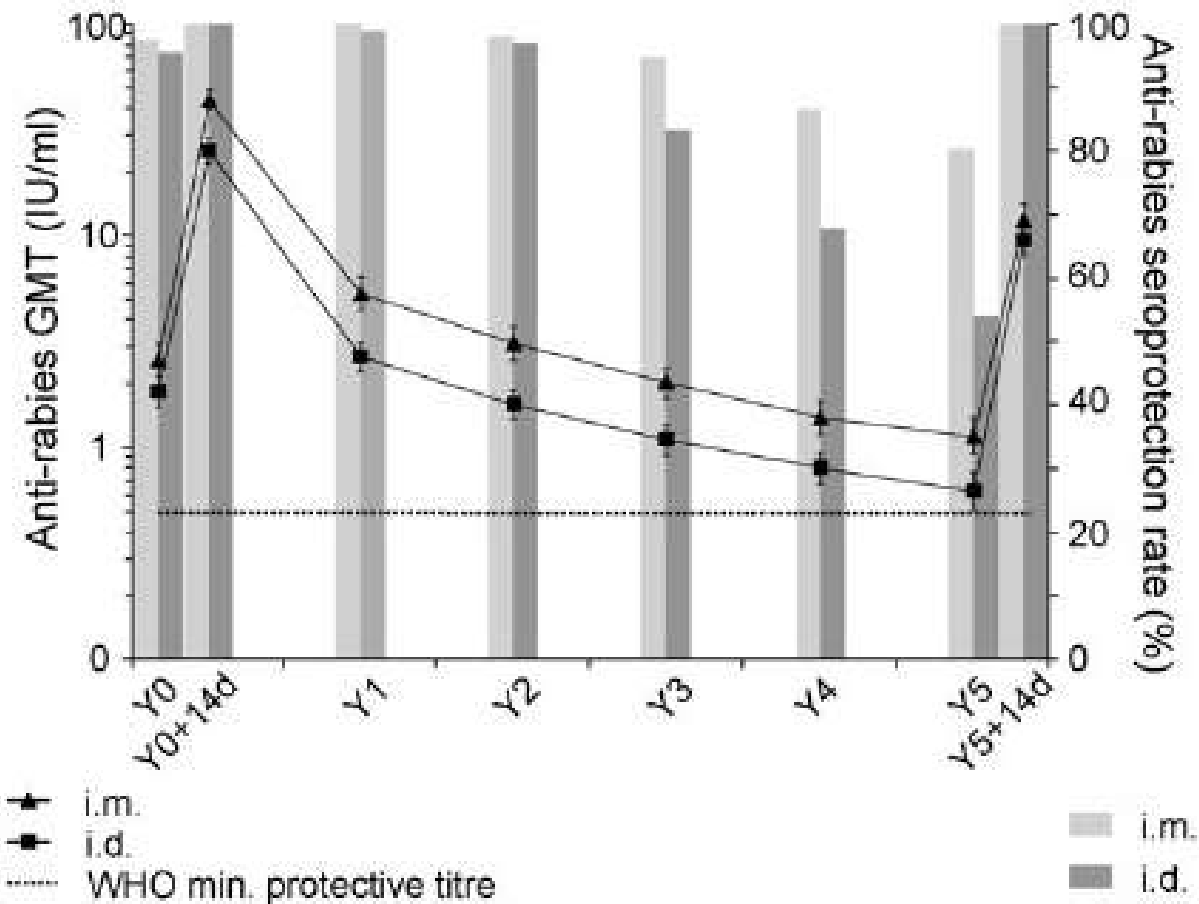


Figure 1 Anti-rabies antibody titre [geometric mean titre (GMT) and 95% CI, log-scale representation] kinetics and seroprotection (% subjects titre ≥ 0.5 IU/ml) following pre-exposure purified Vero cell rabies vaccine administered i.m. or i.d.

Interventions in One Rural Municipality

- Pre-exposure vaccination of 4600 children (84% of kids 5-14 yrs old) (3 doses within one month) – given on Jan-Feb 2012

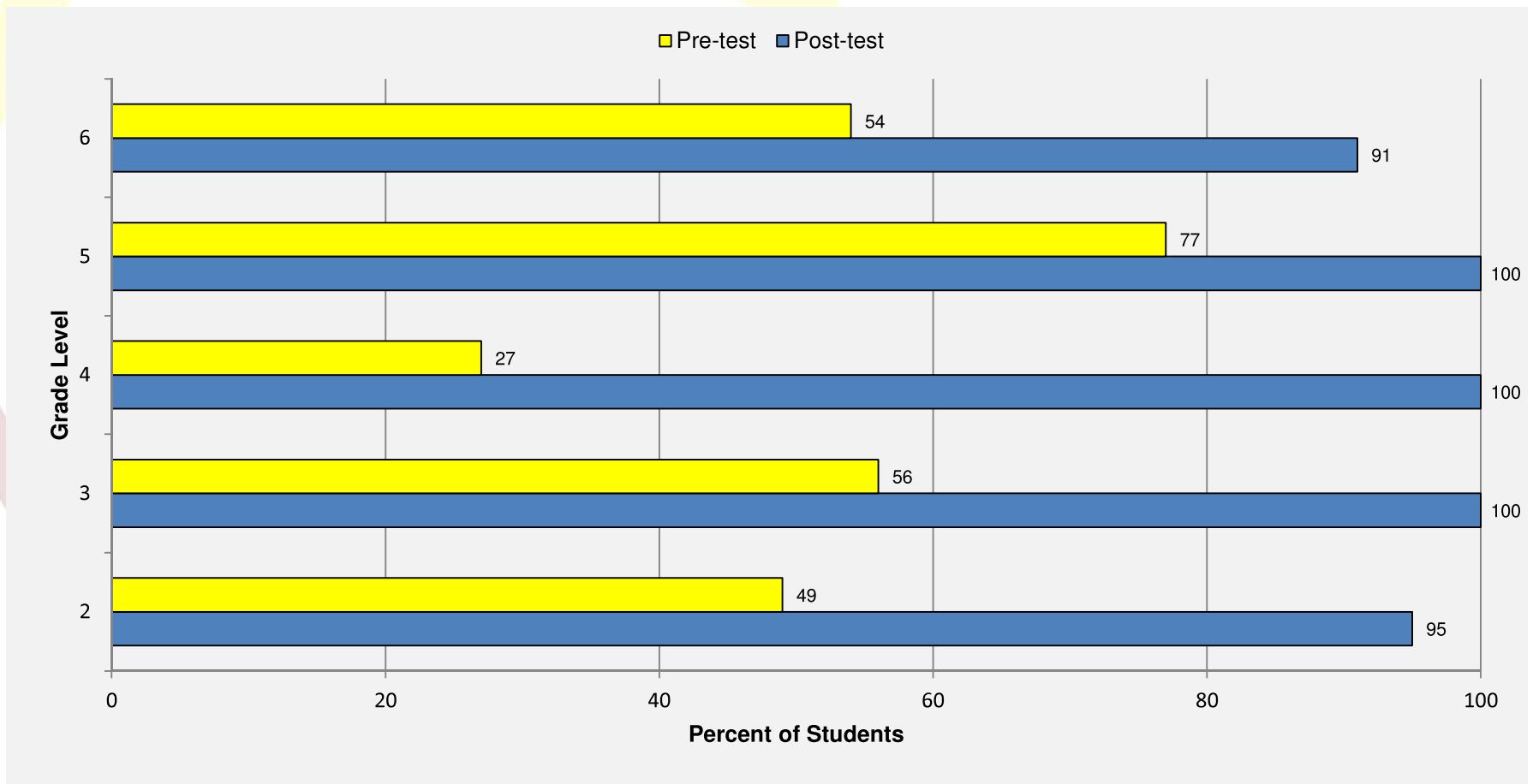


- Integration of rabies in school curriculum



Child education intervention

Percentages of students who knew about Rabies based on pre and post-tests of students in El Nido Elementary Schools, School Year 2012-13



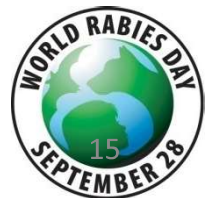
Opportunities & Challenges

- Highly efficacious vaccines are available – *requires change of strategy* to use PreP rather than PEP when more appropriate
- Can *target specific populations* rather than global coverage for PreP – reduce cost per life saved
 - Efficacy is high in all age groups: Age for roll out of PreP may vary according to risk & access
- Incorporating PreP into other vaccine regimens when appropriate – highly immunogenic with childhood vaccines – can help reduce delivery cost



Future Directions

- Increase utilization of PreP in high risk regions with limited to no access to PEP
- Move toward ID administration to reduce cost
- Improve educational awareness in association with vaccine programs
- Ultimate goal is to eliminate rabies at the major source of infection – ie canine population *but first line of defense is to save human lives*





Working with Communities for Rabies Prevention