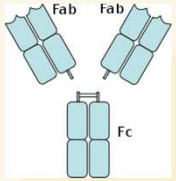
Driving progress towards rabies elimination &
2nd International meeting of the Pan-African Rabies Control Network
Birchwood Hotel, Johannesburg, South Africa
12-14 September 2018



WHO position on the use of Rabies immunoglobulins, 2018

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Rabies immunoglobulin (RIG) in the context of Post exposure prophylaxis (PEP)

- **RIG neutralizes the rabies virus at the wound site during the period before the immune system responds to the vaccine**
- **RIG is in short supply and cost-prohibitive for patients in most rabies-endemic settings**
  - ✓ **Less than 2% of at risk dog bite cases (globally) receive RIG** (Warell et al, 2012)
  - ✓ **Additionally, its use in practice is discouraged by**
    - Procedures complexity for care providers (weighing the patient and calculations, diluting the vial content in some cases, multiple injections at different sites, etc.)
    - RIG quality uncertainty and short shelf-life even with correct cold chain
- **Updated recommendations aimed to**
  - ✓ **Lower the cost per patient**
  - ✓ **Avoid wastage**
  - ✓ **Simplify practice for physicians**

WHO position on the use of RIG

2010 recommendations *vs* 2018 update

WHO POSITION ON THE USE OF RIG		
	2010	**2018**
Indication	- Category III exposure who have not previously been vaccinated against rabies - Category II exposure for immunodeficient	- Category III exposures in immunologically naive patients - Category II exposure for immunodeficient (even if previously immunized)
Dose calculation	- According to body weight (40 IU/kg for eRIG, and 20 IU/kg for hRIG)	- According to body weight (40 IU/kg for eRIG, and 20 IU/kg for hRIG)

Prioritization of RIG allocation if limited amount available

WHO POSITION ON THE USE OF RIG		
	2010	2018
RIG allocation		- Prioritization if limited amount of RIG is available

- Field data show that thorough wound washing with immediate vaccine administration and completion of PEP courses save 99% of patients
- The cases with highest priority to receive RIG are
  - ✓ Multiple bites and/or deep wounds
  - ✓ Bites to highly innervated parts of the body (head, neck, hand, genitals)
  - ✓ Patients with severe immunodeficiency
  - ✓ History of biting animal indicative of confirmed or probable rabies
  - ✓ A bite or scratch or exposure of a mucous membrane by a bat

eRIG as safe and efficacious alternative to hRIG

WHO POSITION ON THE USE OF RIG		
	2010	**2018**
Administration	- once, ASAP <7th days after the 1st dose of vaccination - Skin testing before eRIG administration	- Once, ASAP <7th days after the 1st dose of vaccination - Skin testing before RIG no longer recommended

- **Modern purified eRIG is potent although short half-life, highly purified and enzyme refined, safe and less expensive than hRIG.**
  - ✓ **It contains about 85% of antigen binding immunoglobulins fragment F(ab')2**
  - ✓ **Less than 3% of Fc and non specific protein content (reducing the risk of anaphylaxis: 1/45000 cases).**

Simplification of RIG administration

WHO POSITION ON THE USE OF RIG		
	2010	**2018**
Infiltration sites	- **Infiltration into and/or around wound site(s) for the degree that is anatomically feasible** - **The remaining, if any, injected IM at a distant site**	- **Only the quantity necessary for infiltration into and/or around wound site(s)** - **The remainder is used for other patients (unused should be discarded by the end of the day)**

- **Evidence on RIG showed that maximum infiltration of the RIG dose (calculated by body weight) into and around the wound is effective** (Madhusudana et al, 2013, and Wilde et al, 2015, Bharti et al, 2016 and 2017)
  - ✓ **The benefits from additional IM administration of any remaining RIG at a site distant to the wound are likely to be very limited**

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Monoclonal antibody (mAbs) as a viable alternative to RIG

- **A single mAb against rabies has demonstrated safety and efficacy in clinical trials when used for PEP (Gogtay NJ et al. , 2017) and was licensed in 2017 for use in India.**
- **The comparative advantages of mAbs include**
  - ✓ **Production with standardized quality and in large quantities**
  - ✓ **Elimination of the use of animals in the production process**
  - ✓ **Reduction of the risk of adverse events**
  - ✓ **Lower cost.**
- **Products containing two or more mAbs (cocktails) can work synergistically to give higher efficacy**
- **WHO recommends that a registry be maintained to monitor the clinical use and outcomes of mAb products for rabies PEP**

Merci!

World Health Organization

Global Alliance for Rabies Control

PARACON

Pan-African Rabies Control Network

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