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

<table>
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<tr>
<th></th>
<th>2010</th>
<th>2018</th>
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<tr>
<td><strong>Indication</strong></td>
<td>- Category III exposure who have not previously been vaccinated against rabies</td>
<td>- Category III exposures in immunologically naive patients</td>
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<td>- Category II exposure for immunodeficient</td>
<td>- Category II exposure for immunodeficient (even if previously immunized)</td>
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<tr>
<td><strong>Dose calculation</strong></td>
<td>- According to body weight (40 IU/kg for eRIG, and 20 IU/kg for hRIG)</td>
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Prioritization of RIG allocation if limited amount available

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<td><strong>RIG allocation</strong></td>
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- 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

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<th>Administration</th>
<th>2010</th>
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<td></td>
<td>once, ASAP &lt;7th days after the 1st dose of vaccination</td>
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<td>Skin testing before eRIG administration</td>
<td>Skin testing before RIG no longer recommended</td>
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- 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).
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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<th>Infiltration sites</th>
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<th>2018</th>
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<td>- Infiltration into and/or around wound site(s) for the degree that is anatomically feasible</td>
<td>- Only the quantity necessary for infiltration into and/or around wound site(s)</td>
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<td>- The remaining, if any, injected IM at a distant site</td>
<td>- The remainder is used for other patients (unused should be discarded by the end of the day)</td>
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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!