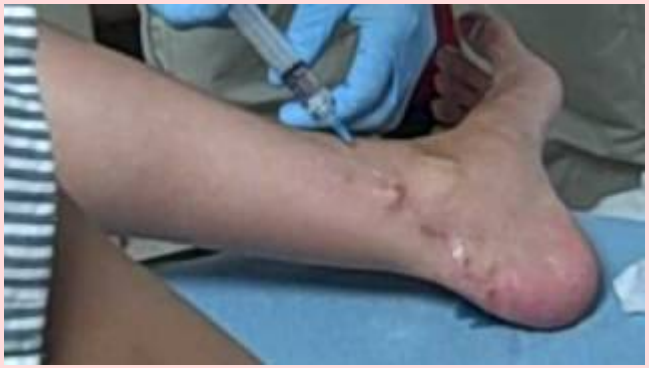
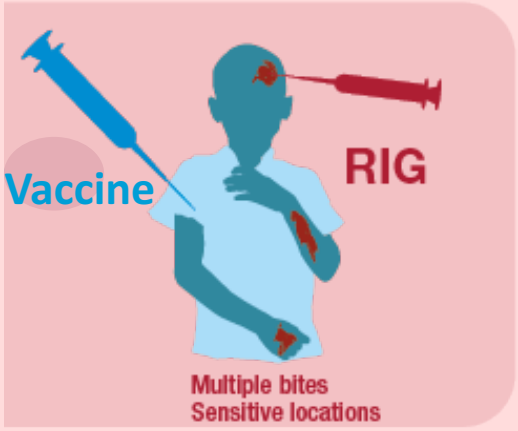
Rabies Immunoglobulins(RIG)



Recommendations

Questions 10, 11, 12, 13, 14



Question 10: Are there novel approaches to RIG (-sparing) injection vs current practice as part of PEP for category III exposed patients?

1. Evidence shows that the benefits of RIG administered **intramuscularly at a site distant to the wound are likely to be very small**, compared to infiltrating RIG in and around the wound; therefore to confer the maximum public health benefit, especially in resource constrained settings, where availability of RIG is low and is cost-prohibitive:
    - A **maximum** RIG recommended dose should be calculated (20 IU/kg of body weight of HRIG or 40 IU/kg of body weight of F(ab')2 products eRIG).
        - The dose can be **fractionated** in smaller, individual syringes.
        - Fractioning requires **aseptic retention** of the RIG to be used for other patients
    - Only the **amount necessary for infiltrating** into and around the wound is administered.
        - For small wounds administer what is anatomically feasible avoiding compartmentalization syndrome
        - For large wounds dilute with physiological buffered saline to ensure greater wound coverage
    - Remainder of calculated dose should **NOT be injected intramuscularly**

Question 11: Is there clinical equivalence in the **safe use** of eRIG compared to hRIG in category III exposed patients?

Question 12: Is there clinical equivalence in the **efficacious use** of eRIG compared to hRIG in category III exposed patients?

1. eRIG is **clinically equivalent** to hRIG
2. eRIG is considered a **safe and efficacious life- and cost-saving** biologic.
   - Both eRIG and hRIG neutralize the virus at the wound site within a few hours.
   - Based on the safety and efficacy profiles for all RIG products meeting quality standards, there is no product preference between eRIG and hRIG.
3. Given the increase in product purity and safety, **skin testing before eRIG administration is unnecessary**, no longer recommended, and should be abandoned.
4. **Post-marketing surveillance** is strongly recommended.
   - Severe adverse events or perceived lower efficacy of RIG (e.g. batches of insufficient potency or lower purification degree) should be monitored, recorded and reported, so that biological producers receive immediate feedback and can respond accordingly.
   - A classification of adverse events is available in Table 6.

Question 13: Can monoclonal antibodies be safely and efficaciously administered in category III exposed patients compared to standard RIG?

1. Monoclonal antibodies (mAbs) offer a future potential to improving access to RIG.
   - One product has demonstrated safety and bioavailability in a phase II clinical trial

2. Cocktails using two or more mAbs working synergistically show higher efficacy and increased breadth of neutralization.
   - Ideally, the production of mAbs should aim to be affordable and include two or more mAbs with non-overlapping epitopes.
   - We recommend that a registry be maintained to monitor clinical use and outcomes of mAb products.

Question 14: Are there novel approaches to RIG (-sparing) injection vs current practice as part of PEP for category III exposed patients?

1. Wash bite wounds or scratches promptly and thoroughly.
2. If RIG is not available or affordable, a complete course of rabies vaccine is indicated.
3. For patients who can reliably document previous PEP that is equivalent to a PrEP regimen, RIG is not indicated.
4. In cases of shortage or unaffordability, the following groups should be prioritized for RIG allocation:
   - Multiple bites
   - Deep wounds
   - Highly innervated parts of the body, as head, neck, hands, genitals
   - Immunocompromised patients
   - History of biting animal indicative of confirmed or probable* rabies
   - A bite or scratch or exposure of a mucous membrane by a bat can be ascertained

** Definition see p. 46*