Recommendations on pre-exposure rabies vaccine schedules

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Rabies Pre-exposure guideline 2017 in Belgium

- **Pre-travel intramuscular schedule:** Rabipur® or HDCV®
  - d0 - d7 - d21 or d28 (no booster after 1y, no need for measuring antibodies)
- **Accelerated schedule off-label IM (d0 - d4 - d8)** since 2015
- **Intradermal schedule off-label ID used** in BE Defense since 2008
- **Vaccination aims “boostability” lifelong:** which simplifies future post exposure procedures
- **Rabies PEP after PrEP:** 2 x 1 IM vaccinations, 1 IM on d0 and d3, no immunoglobulins
Concept of PRIME and BOOST

Rabies pre- and postexposure prophylaxis (PEP after PrEP)

‘Boostability’

Efficacious Prime and Boost regimen?
Results after boosting:
RFFIT day 7 > 0.5 IU/ml? 100%?
GMT day 7 > 10 IU/ml?

PrEP schedule IM or ID
- d0-d7-d28
  - (d0-d7)
  - (d0)

Risk

PEP schedule IM
- d0-d3

PEP schedule ID
- (d0)
Advantages of priming before traveling to an endemic region

- Sparing immunoglobulines
- Higher antibody responses after booster vaccination
- Faster anamnestic response in the first 7 days after booster vaccination
- More affinity of antibodies
- Inapparent risk can be prevented?

Concept of PRIME and BOOST
WHO Background

Zero by 2030

- Tackling the high rabies human case fatality every year
- Review new evidence

Rabies is a major public health problem

- 99% human cases result from dog bites
- 4 out of 10 deaths are in children

Rabies is 100% vaccine preventable

- VACCINATE TO SAVE LIVES
- VACCINATE TO STOP TRANSMISSION

No bites = No rabies

Zero by 30
28 September - World Rabies Day
The WHO recommendations issued in 2010 for pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) have proven challenging to implement, and new evidence has become available.

The updated recommendations aim to be more public health-directed and to propose cost-, dose- and time-sparing regimens, while still assuring the safety and clinical effectiveness of these preventive measures.
WHO Background

Review procedures

- Technical experts in the field: new evidence - clinical trials ongoing: preliminary - final results - urgent needs


- Strategic Advisory Group of Experts (SAGE), WHO: Oct 2017
WHO Background

- Planned WHO publications
  - WHO Background paper simplifying rabies vaccination: Sep 2017
  - WHO position online 15 Jan 2018: summary of the recommendations
  - WHO guideline on rabies vaccination expected in April 2018 via the Weekly Epidemiological Record
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WHO Background

New WHO publication

WHO position: online since 15th of Jan 2018: summary of the recommendations

Rabies vaccines and immunoglobulins:
WHO position

SUMMARY OF 2017 UPDATES
WHO Background

**WHO guidelines: not so new for BE context...**

- **Boostability**
  - PrEP makes administration of RIG unnecessary after a bite.
  - Rabies vaccination likely provides lifetime protection, with vaccine booster in case of an exposure.
  - A routine PrEP booster or serology for neutralizing antibody titres in general not needed.

- **IM and ID - Vaccines - all ages**
  - Rabies vaccines can be administered by two different routes, intradermal (ID) or intramuscular (IM), and according to different schedules; also different techniques are interchangeable.
  - One ID dose is 0,1 ml of vaccine and one IM dose is an entire vial of vaccine, irrespective of the vial size (0,5 or 1,0 ml).
  - Rabies vaccines are interchangeable.
  - For adults, the vaccine should be administered in the deltoid area of the arm; for young children (aged < 2 years), the anterolateral area of the thigh is recommended.
WHO guidelines new for BE context

New Rabies PrEP regimens that are recommended in first line for individuals of all ages are:

- 2-site ID vaccine administration on days 0 and 7
  2ID: (double dose 2x 0.1 ml on day 0 and day 7

- 1-site IM vaccine administration on days 0 and 7
  2IM: single dose 1x 1ml on day 0 and day 7

The routine classical regimen d0-d7-d28 is a good and valid alternative to the proposed accelerated regimens.
Rabies PrEP guideline in BE (from May 2018)

New preferred PrEP schedule in BE from May 2018: 2ID or 2IM

After the publication in Weekly Epidemiological Record and after an email alert to BE travel clinics

Rabies vaccine (Rabipur® or HDCV®)

- **ID** 0.1ml d 0 - 7 ID (double dose)

- **IM** 1.0 ml d 0 - 7 IM

BE travel clinics who feel comfortable with ID use can use ID schedules

More guidelines will follow

- New preferred rabies PrEP schedule: two visit schedules
- Use a one visit rabies PrEP schedule in last-minute travelers!

- **ID**<sub>0.1ml</sub>  
  d 0 - 7 ID (double dose)  
  d 0 ID (double dose) > d X ID after travel (double dose)

- **IM**<sub>1.0 ml</sub>  
  d 0 - 7 IM  
  d 0 IM > d X after travel

  (Not use anymore d 0 – 4 – 8)

Changing the PrEP strategy from 3 visits > 2 visits > 1 visit possible
Final conclusion

- Pre-exposure rabies priming in travelers is important for successful rapid postbooster immune responses (‘boostability’).

- Pre-exposure rabies priming in travelers will be simplified in Belgium to two visits (from May 2018).

- Volume-sparing pre-exposure intradermal rabies vaccination schedules at ‘very low cost’ are possible to use in BE travel centers (who feel comfortable with this technique).

- Investment once in a lifetime!