

Recommendations on pre-exposure rabies vaccine schedules

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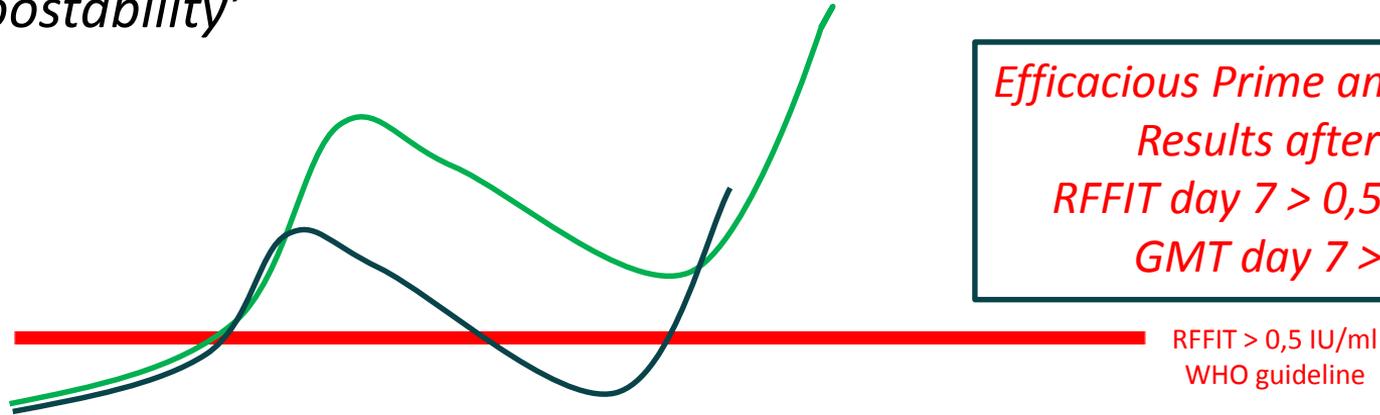
Rabies Pre-exposure guideline 2017 in Belgium

- 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)

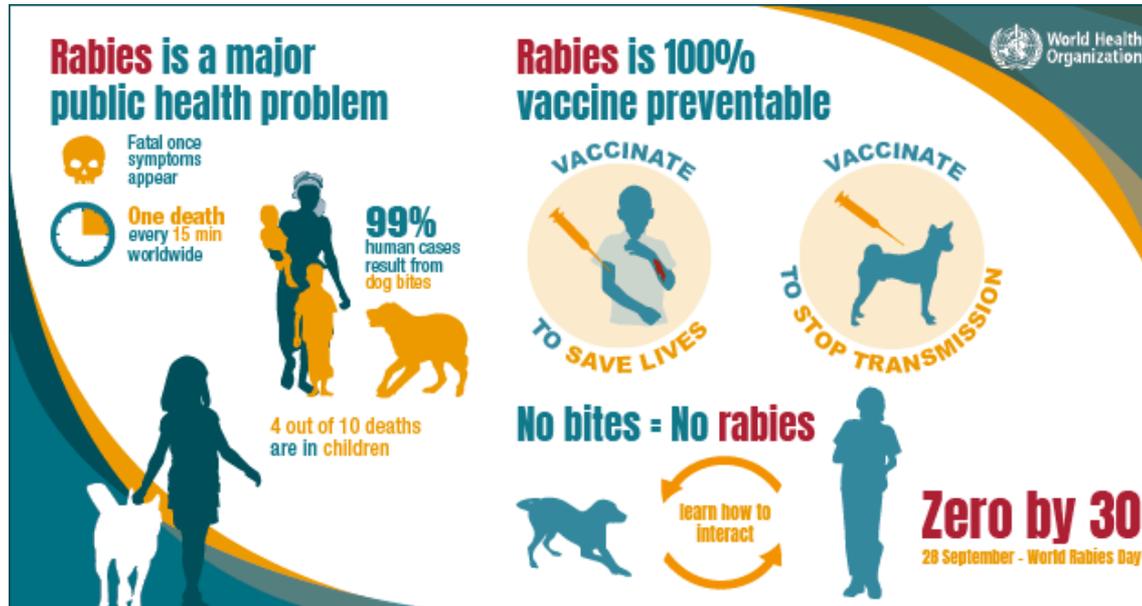
Concept of PRIME and BOOST

- 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?

WHO Background

Zero by 2030

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



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.

■ Review procedures

- Technical experts in the field: new evidence - clinical trials ongoing: preliminary - final results - urgent needs
- SAGE, Working Group on Rabies vaccines, WHO: established in July 2016: meetings Oct 2016 - Mar 2017 - Oct 2017
- Strategic Advisory Group of Experts (SAGE), WHO: Oct 2017

■ 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**

Key improvements to recommendations on rabies immunization

Post-exposure prophylaxis (PEP)	Rabies immunoglobulin (RIG)	Pre-exposure prophylaxis (PrEP)
Emphasis on intradermal applications (cost- and dose-savings) as opposed to intramuscular applications	Update of administration routes and dosing guidelines for greater feasibility and provisioning	<p>Emphasis on intradermal applications (cost- and dose-savings) as opposed to intramuscular applications</p> <p>Formulation of safe and efficacious accelerated regimens</p>
Generation of new, accelerated regimens	Practical guidance on prioritized allocation of RIG in resource-constrained settings	More practical guidance for people at varying degrees of rabies risk from their work or travel
More flexibility for intradermal applications in immunocompromised individuals	eRIG and hRIG are clinically equivalent in preventing rabies	
Monoclonal antibodies as a potential to improve access to RIG		
Updates for bat exposures		

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 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

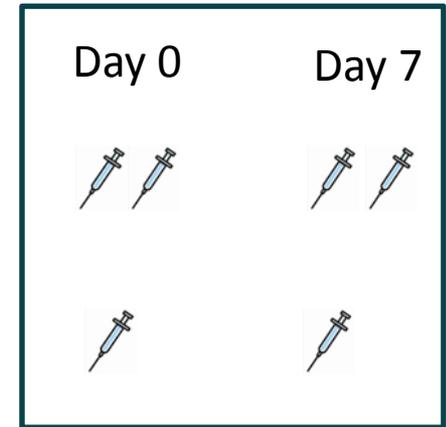
- Rabies vaccines can be administered by two different routes, intra-dermal (ID) or intra-muscular (IM), and according to different schedules; also different techniques are interchangeable.
- One ID dose is 0,1 ml of vaccine and one IM dose is an entire vial of vaccine, irrespective of the vial size (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 Background

■ 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

Rabies PrEP guideline in BE (from 5/2018)

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

- **ID**_{0.1ml} **d 0 - 7 ID (double dose)**
d 0 ID (double dose) > d X ID after travel (double dose)

- **IM**_{1.0 ml} **d 0 - 7 IM**
d 0 IM > d X after travel

(Not use anymore d 0 – 4 – 8)

Rabies PrEP completed,
additional vaccines needed
after bite

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!