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Rabies vaccine administered to soldiers of the Polish Army leaving for foreign missions

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Summary:

This work presents WHO guidelines on the treatment of rabies after exposure, taking into account the types of wounds and methods of treatment depending on the state of the animal – the rabies carrier. Situations and the method of administration of VERORAB vaccine within rabies-risk areas were described. Contraindications for its administration were also included.

Key words: rabies, exposure, serology testing, vaccination.

Rabies is a disease of viral etiology, an acute zoonotic disease of the central nervous system of mammals, always fatal for humans. The source of infection are usually wild animals such as bats, squirrels, foxes, deer and domesticated animals such as dogs, cats, cows.

Infection with rabies is possible almost anywhere in the world, although some places in the world are regarded as free of rabies. Antarctica, Japan, Scandinavia and Oceania are considered to be such places. Until recently, United Kingdom and Australia have been free of rabies infection, but the disease has been brought there by bats. A very large number of infections occur in China and India, where rabies risk is comparable to the risk of AIDS. About 100 000 people in the world die every year because of rabies, mostly in tropical countries. In Europe and Poland, fox is the main source of infection. Each species of animals has a biotype of the virus, so fox virus can be distinguished in this case.

Man does not have a separate biotype. Animals bitten by a fox with rabies may be a source of infection for humans. This refers mainly to cats and dogs, more often to other domestic animals. Small rodents such as mice or rats usually do not pose a threat of rabies to humans. Man does not become infected by small rodents, as their biotype cannot cause the disease. Poikilothermous animals do not transmit the virus.

One can get infected with rabies only directly through a bite or getting licked, but not by objects licked by such an animal, unless the contact occurred within a few minutes after this fact. So far, there have been no cases of infection caused by a patient with rabies, although the patients' saliva includes rabies virus. A man sick with rabies is not dangerous, because the passaged virus loses its virulence.

The most dangerous is a bite in the face above the nose, then the neck and bare limbs. Rabies virus is sensitive to X-rays and UV, to chemicals such as phenol and formaldehyde, as well as drying. At low temperatures, it can survive for up to several years, as it withstands cooling to -70 ° C.

Areas at risk of rabies

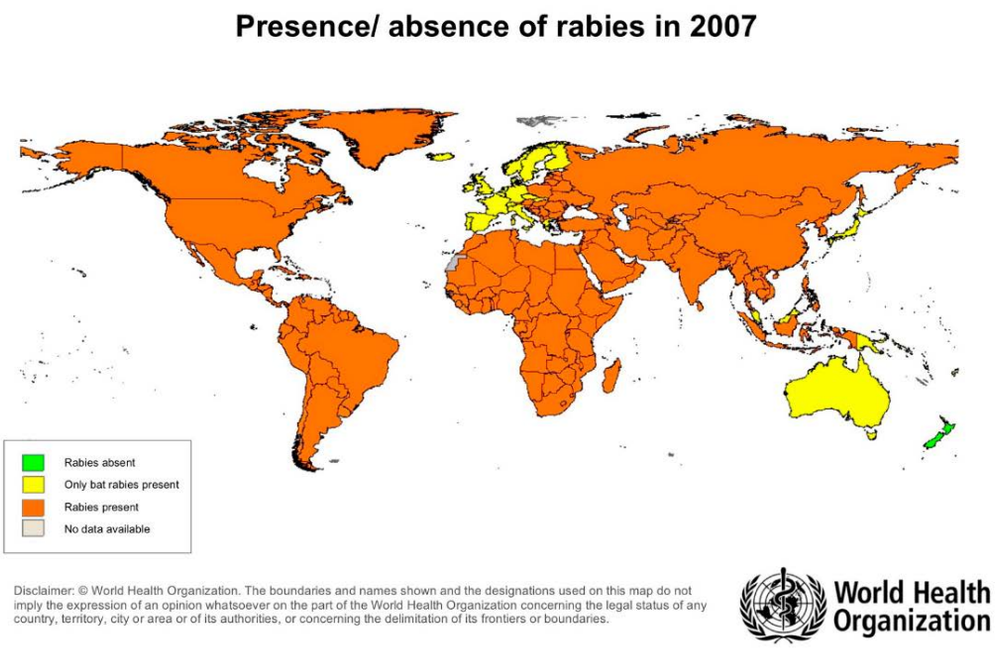

Figure 1: Presence/absence of rabies, at: http://www.who.int/rabies/rabies_maps/en/index.htm

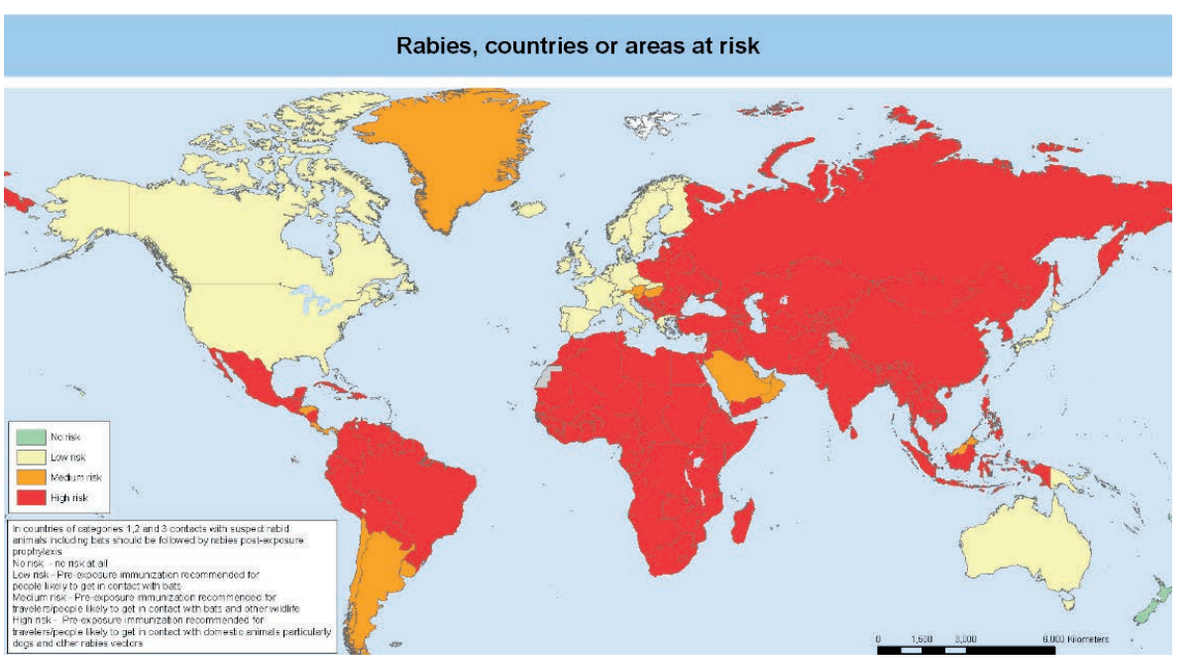

Figure 2: Rabies areas or areas at risk, at: http://www.who.int/rabies/rabies_maps/en/index.html

Composition

After reconstitution, 1 dose (0.5 ml) contains:
Active substance:
Rabies virus, Wistar Rabies PM/WI38 1503-3M strain (inactivated) not less than 2.5 IU, proliferated in VERO cells. The amount determined using the NIH test (National Institutes of Health test) in accordance with international standards.

Excipients:
Powder: maltose, human albumin.
Solvent: sodium chloride, water for injections.

Available packages:
1 vial of powder with 1 dose + 1 pre-filled syringe and needle with solvent of 0.5 ml - in a cardboard box;
5 vials of powder with 1 dose + 5 ampoules with solvent of 0.5 ml - in a cardboard box.

What is VERORAB and what is it used for?
VERORAB is a vaccine powder and solvent for suspension for injection. It is indicated for the prevention of rabies in children and adults. It can be used before and after exposure, as a primary vaccination or a booster.

Vaccination before exposure should be offered to persons at high risk of infection with rabies virus. Everyone who is constantly exposed to infection, such as employees of the diagnostic, R&D and manufacturing departments carrying out work with

Table 1: The procedure, depending on the status of the animal

Circumstances	Proceedings concerning		Remarks
	animals	patients	
The animal is not available. Suspicious or non-suspicious circumstances.		Transport to a specialist rabies treatment centre for therapy.	Treatment(b) is always full.
The animal is dead. Suspicious or non-suspicious circumstances.	Send the brain to be examined at an authorized laboratory.	Transport to a specialist rabies treatment centre for therapy.	Treatment is interrupted. if the test result is negative, otherwise it is continued.
The animal is alive. Non-suspicious circumstances.	Subject to veterinary observation(a).	The decision to postpone anti-rabies treatment.	Treatment (b) is administered depending on the result of veterinary observation of the animal.
Suspicious circumstances.	Subject to veterinary observation.	Transport to a specialist rabies treatment centre.	Treatment (b) is interrupted if veterinary observation showed no signs of rabies

Table 2: The procedure, depending on the status of the animal

Category of severity	Type of contact with a wild(a) or domestic animal with suspected or confirmed rabies or with an animal that cannot be subjected to observation	Recommended treatment
I	Touching or feeding animals. Licking of intact skin by an animal	Treatment is not to be used if reliable medical documentation is available.
II	Bitten exposed skin. Minor scratches or abrasions without bleeding. Licking of intact skin by an animal.	Administer vaccine immediately.
III	Single or multiple bites or scratches through the full thickness of skin, licking of mucous membranes by an animal	Administer immunoglobulin and rabies vaccine immediately.

rabies virus, as well as soldiers leaving for stabilization missions of the Polish military contingents should be vaccinated. Control serologic testing is recommended to be carried out every 6 months.

Vaccination **before exposure** should also be considered in individuals at risk of frequent exposures to rabies virus, such as:

- veterinarians and their assistants, and caregivers of animals;
- persons who, because of their profession or in their spare time, have contact with species such as dogs, cats, skunks, raccoons, bats or other species that potentially may have rabies. Examples of such people are foresters, hunters, forestry workers, speleologists, taxidermists;
- adults and children leaving or travelling to areas at risk of rabies infection;
- soldiers and civilian employees of the army leaving for stabilization missions of the Polish military contingents, including medical personnel.

In areas at low risk of rabies, veterinarians and their assistants (including students), animal carers and foresters are considered a group at risk of occasional exposure and they should receive a primary vaccination against rabies.

Serological tests for antibodies against rabies should be carried out at regular intervals depending on the degree of exposure of individuals.
Booster doses should be administered consistently depending on the degree of exposure of individuals.

Prevention of rabies **following exposur**e (vaccination after exposure): if there is the slightest risk of infection with rabies, vaccination should be administered immediately. In some countries, vaccination must be submitted in specialized rabies treatment centres.

Treatment after exposure includes topical, nonspecific wound treatment, passive immunization with immunoglobulins (RIGs) and vaccination, depending on the type of wounds and the condition of the animal (Table 1 and 2).

Do not use VERORAB vaccine:
Before exposure in the case of:

- fever or acute illness. Vaccination should be postponed;
- hypersensitivity to the active substance, any of the excipients, polymyxin B, streptomycin or neomycin.

Following exposure: there are no contraindications to vaccination after exposure because rabies infection always causes death.

Take special care with VERORAB vaccine:

As with all injectable vaccines, appropriate treatment should be readily available in the event of an anaphylactic reaction immediately after vaccination, especially in the case of post-exposure vaccination of persons with known hypersensitivity to polymyxin B, streptomycin or neomycin.

Do not inject into the buttock, since lower levels of neutralizing antibodies were observed after administration in this part of the body.

It is necessary to perform regular serological testing. Such serological tests are carried out by confirmation of total neutralization of the test virus, using fluorescence inhibition. This examination should be performed every 6 months for people at continuous risk of exposure and every 2-3 years after each booster dose in persons from groups at risk of periodic exposure. If antibody levels are lower than the protective level, i.e. 0.5 IU/ml, a booster dose should be given.

In case of administration of the vaccine in individuals with immunodeficiency or immunosuppressive disease caused by the ongoing immunosuppressive therapy (such as corticosteroids), serological antibody levels in these individuals should be determined after 2-4 weeks following vaccination. When the determined level of antibodies is lower than that considered protective, i.e. 0.5 IU/ml, an additional dose should be given.

In pregnant women.
Because of the severity of the disease, the vaccination schedule cannot be altered due to pregnancy. If a woman becomes pregnant during the vaccination course, medical attention should be sought immediately, only a doctor may adjust the vaccination schedule to the situation.

Breastfeeding.
This vaccine may be used during breastfeeding. A doctor should be consulted before taking any medicine.

Driving and operating machinery.
Dizziness was often reported after vaccination, which may temporarily affect the ability to drive and use machines.

Use of other vaccines and drugs.
A doctor should be informed if a patient is taking medicines, even those without a prescription. Corticosteroids and other immunosuppressive drugs may adversely affect the production of antibodies and make the vaccination ineffective.

Immunoglobulin must be given at a different location than the vaccine (opposite side).

How to use VERORAB?

Before reconstitution, the powder is uniformly white. In order to reconstitute the vaccine:

- remove the cap from the vial;
- inject the solvent from the vial or pre-filled syringe into the vial with powder;
- shake gently to obtain a homogeneous suspension. The reconstituted vaccine is a clear liquid;
- immediately draw 0.5 ml of the suspension;
- inject.

Do not inject intravascularly. Before vaccination, make sure that the needle is not in a blood vessel.
Do not administer subcutaneously.
The reconstituted vaccine should be used immediately, as it contains no preservatives.

Any unused product or waste material should be disposed of in accordance with local regulations.
Vaccination schedule should be adapted to the circumstances of the indications for vaccination and immunization of persons against rabies.

Vaccination before exposure.
Three doses of VERORAB vaccine (0.5 ml) should be given on days 0, 7 and 28 or 21.

Booster doses of vaccination before exposure.
Booster dose of VERORAB (0.5 ml) should be given after one year following vaccination.

Recommendations for primary vaccination and booster doses are presented in Table 3.

Table 3: Recommendations for primary vaccination and booster doses

Primary vaccination	3 injections	On day 0, 7 and 28
Booster dose	1 year later	
Booster doses	Every 5 years	

Injection on day 28 can be done on day 21.
VERORAB vaccine can be given as a booster dose after primary vaccination against rabies with vaccine prepared in cultures of human diploid cells or VERO cells.

Vaccination after exposure.
First aid, local treatment of wounds.
All bites and scratches should be washed immediately with soap and water or detergent. This may enable effective removal of rabies virus from the site of infection. Then 70% alcohol or iodine solution or 0.1% solution of quaternary ammonium base can be used (provided soap was not left in the wound, because the products neutralize one another). Depending on the severity of injury, it may be necessary to provide antirabies immunoglobulin (RIGs) simultaneously with the vaccine.

If necessary, treatment may be supplemented by anti-tetanus prevention and (or) antibiotic therapy.

Fully immunized persons.
Two booster doses of VERORAB vaccine (0.5 ml) should be given on day 0 and 3. In this case, the administration of rabies immunoglobulin (RIGs) is not necessary and should not be done because the booster dose is always followed by an immune response associated with immune memory. Previously vaccinated persons should be able to document:

- use of the full course of vaccination before or after exposure with a vaccine produced in cell culture or
- titer of antibodies against rabies virus > 0.5 IU/ml

If in doubt or if more than 5 years have passed since the last vaccination, or if it was incomplete, the patient should not be considered as sufficiently immunized and full treatment should be started after exposure.

Recommendations for vaccination against rabies after exposure, depending on prior vaccination, are presented in Table 4.

Table 4: Recommendations.

Vaccination within the last 5 years (vaccine against rabies produced in cell culture)	2 injections on day 0 and 3
Vaccination earlier than 5 years ago or incomplete vaccination	5 injections on day 0, 3, 7, 14 and 28 with RIG immunoglobulin, if necessary

Non-immunized persons.
Five doses of VERORAB vaccine (0.5 ml) should be given on day 0, 3, 7, 14 and 28.

Rabies immunoglobulin (RIGs) should be given simultaneously with the first dose in case of severe injury. Horse or human rabies immunoglobulin can be used simultaneously with VERORAB vaccine.

Internationally recognized RIG immunoglobulin dosage is as follows:
Human rabies immunoglobulin: 20 IU/kg of body weight

Horse rabies immunoglobulin: 40 IU/kg of body weight
RIG immunoglobulins may partially suppress production of antibodies and therefore should not be used in a dose higher than recommended.
Vaccine and RIG immunoglobulin should be administered to different sites on the body, on the opposite side.

In areas at risk of rabies, it may be justified to give two doses of vaccine on day 0 in case of very serious injuries or if their location is close to the nervous system, or in case of a patient with immunodeficiency, or if a patient has not reported for a medical consultation immediately after exposure.

Method of administration:

VERORAB vaccine is given only intramuscularly, in the deltoid muscle in adults, and in the anterolateral part of the thigh in infants and young children.

Adverse reactions after vaccination with VERORAB.
Like all medicines, VERORAB vaccine can cause side effects. Mild adverse reactions at the injection site: pain, redness, swelling, itching, and induration at the injection site.

General side effects: mild fever, chills, malaise, fatigue, headache, dizziness, joint and muscle pain, gastrointestinal disorders (nausea, abdominal pain).
Very rarely: cases of anaphylactic reactions, urticaria and rash.
In infants born prematurely (at 28 weeks gestation or earlier) longer intervals between breaths may appear within 2-3 days after vaccination.

VERORAB vaccine should be stored out of the reach and sight of children, at 2°C - 8°C (refrigerator). Do not freeze. After reconstitution, the vaccine should be used immediately.
Do not use the vaccine after the expiry date stated on the packaging.

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