DEPARTMENT OF OPERATIONAL SUPPORT

TECHNICAL GUIDANCE FOR THE PREVENTION AND MANAGEMENT OF RABIES

JUNE 2023

INTRODUCTION

Rabies is a viral zoonotic disease responsible for an estimated 59,000 human deaths and over 3.7 million disability-adjusted life years (DALYs) lost every year[1]. In endemic areas (Africa and Asia), 99% of cases are due to dog bites and 40% of cases are children under 15 years of age. Rabies is almost invariably fatal once clinical signs appear as a result of acute progressive encephalitis. Rabies occurs mainly in underserved populations, both rural and urban, and has been documented for more than 4,000 years.

Rabies can effectively be prevented before the symptoms developed by Rabies Post-exposure Prophylaxis (PEP). Once symptoms develop, rabies is fatal. There is no curative treatment; care is palliative. **Unprovoked attacks by animals are a cause for grave concern, and medical attention should be sought immediately after washing the exposed skin.**

This guidance was developed by the Public Health Section of DHMOSH for the UN clinical staff and personnel to provide information on the prevention of rabies as well as clinical management and post-exposure prophylaxis.

For any questions on this document, contact DHMOSH Public Health Section at dos-dhmosh-public-health@un.org.

TRANSMISSION[1]

- Rabies can affect both domestic and wild animals; however, up to 99% of cases are related to domestic dogs and human bites. Bat-mediated rabies is an emerging health threat in Australia, the Americans and Western Europe.
- Transmission occurs via saliva, usually through bites, scratches, or direct contact with mucosa (e.g., eyes, mouth, or open wounds).
- Rabies infection in rodents is very uncommon, and no human rabies cases due to bites by rodents have been reported.
- Children between the age of 5 and 14 years are frequent victims of rabies.

- Rabies can be found in saliva, tears, urine and nervous tissues of human rabies cases, and exposure to these body fluids and tissues carries a theoretical risk of transmission.
- Casual contact, such as touching a person with rabies or contact with non-infectious fluid or tissue (urine, blood, faeces), is not associated with a risk for infection.
- Rabies virus becomes non-infectious when it dries out and when it is exposed to sunlight.

PREVENTION[2]

- Wash animal bites or scratches immediately with soap and water.
- Rabies is a vaccine-preventable disease.
- Vaccinating dogs, including puppies, is the most cost-effective strategy for preventing rabies in people because it stops the transmission at its source and reduced the need for Rabies PEP.
- Education on dog behaviour and bite prevention for both children and adults is an essential extension of rabies vaccination programmes and can decrease both the incidence of human rabies and the financial burden of treating dog bites.
- If you are bitten, scratched, or unsure, talk to a healthcare provider about whether you need Rabies PEP
- Vaccination of humans against rabies is also indicated in some instances (see more details below).

- Contact with someone who is receiving rabies vaccination does not constitute rabies exposure, does not pose a risk for infection, and does not require postexposure prophylaxis.

CLINICAL MANAGEMENT OF RABIES[2]

1. **Signs and symptoms:**

- The incubation period for rabies is typically 2–3 months but may vary from 1 week to 1 year, depending on factors such as the location of virus entry and the viral load. The closer the bite is to the nervous brain (e.g., bites to the face), the faster neurological symptoms will develop.
- Initial symptoms of rabies include generic signs like fever, pain and unusual or unexplained tingling, pricking, or burning sensations at the wound site.
- As the virus moves to the central nervous system, progressive and fatal inflammation of the brain and spinal cord develops.

2. **Types of rabies**
   - **Furious rabies** results in hyperactivity, excitable behaviour, hallucinations, lack of coordination, hydrophobia (fear of water) and aerophobia (fear of drafts or of fresh air). Death occurs after a few days due to cardio-respiratory arrest.
   - **Paralytic rabies** accounts for about 20% of the total number of human cases. This form of rabies runs a less dramatic and usually longer course than the furious form. Muscles gradually become paralysed, starting from the wound site. A coma slowly develops, and eventually, death occurs. The paralytic form of rabies is often misdiagnosed, contributing to under-reporting of the disease.

3. **Diagnosis**

- Current diagnostic tools are not suitable for detecting rabies infection before the onset of clinical disease.
- Unless the rabies-specific signs of hydrophobia (extreme or irrational fear of water) or aerophobia (fear of drafts or fresh air) are present, or a reliable history of contact with a suspected or confirmed rabid animal is available, clinical diagnosis is difficult.
- Diagnosis is often made post-mortem.
- WHO case definition for human rabies:
  - A subject presenting with an acute neurological syndrome (encephalitis) dominated by forms of hyperactivity (furious rabies) or paralytic signs (paralytic rabies) progressing towards coma and death, usually by cardiac or respiratory failure, typically within 7–10 days after the first sign.
  - Signs and symptoms of rabies include any of the following: hydrophobia, aerophobia, photophobia, paresthesia or localized pain, dysphagia, localized weakness, nausea or vomiting.
- The standard human case classification for rabies is:
  - **Suspected:** a case that is compatible with a clinical case definition
  - **Probable:** a suspected case plus a reliable history of contact with a suspected, probable or confirmed rabid animal
  - **Confirmed:** a suspected or probable case that is laboratory-confirmed (usually post-mortem)

RABIES PRE-EXPOSURE PROPHYLAXIS (PrEP)[2]

- Rabies vaccination as a means of pre-exposure prophylaxis (PrEP) is recommended for people in certain high-risk occupations such as:
  - Laboratory workers handling live rabies and rabies-related viruses
  - People whose professional or personal activities might lead to direct contact with bats or other mammals that may be infected with rabies (such as animal disease control staff and wildlife rangers)
- Rabies PrEP might also be indicated for outdoor travellers and people living in remote, highly rabies-endemic areas with limited local access to rabies biologics.
- WHO recommends the following Rabies PrEP schedule:

- 2-site ID vaccine administered on days 0 and 7.
- If IM administration is used, WHO recommends a 1-site IM vaccine administration on days 0 and 7.

- More information on dosing and administration of rabies vaccine can be found here (pages 207-211, 215): https://www.who.int/publications/i/item/who-wer9316
- More information regarding for travellers and serological monitoring for professionals who are at continual or frequent risk of exposure through their activities can be found here (page 218): https://www.who.int/publications/i/item/who-wer9316

RABIES POST-EXPOSURE PROPHYLAXIS (PEP)[2]

- Post-exposure prophylaxis (PEP) is the emergency response to rabies exposure. This prevents the virus from entering the central nervous system, which would invariably result in death.
- PEP consists of:
  - Extensive washing with water and soap for at least 15 minutes and local treatment of the wound as soon as possible after a suspected exposure.
  - A series of potent and effective rabies vaccine that meets WHO standards (note that the number of vaccines depends on if the individual was previously vaccinated or not); and
  - The administration of rabies immunoglobulin or monoclonal antibodies into the wound, if indicated.

Table: Categories of contact and recommended post-exposure prophylaxis (PEP)

Categories of contact with suspect rabid animal	Post-exposure prophylaxis measures	Requires PEP
Category I - touching or feeding animals, animal licks on intact skin (no exposure)	Washing of exposed skin surfaces, no PEP	**NO**
Category II - nibbling of uncovered skin, minor scratches or abrasions without bleeding (exposure)	Wound washing and immediate vaccination	**YES**
Category III - single or multiple transdermal bites or scratches, contamination of mucous membrane or broken skin with saliva from animal licks, exposures due to direct contact with bats (severe exposure)	Wound washing, immediate vaccination and administration of rabies immunoglobulin/monoclonal antibodies	**YES**

ADMINISTRATION OF HUMAN RABIES VACCINE FOR PrEP AND PEP[2]

- WHO recommends two main immunization strategies for the prevention of human rabies:
  - **PrEP** which is the administration of several doses of rabies vaccine before exposure to the rabies virus
  - **PEP** which includes extensive and thorough wound washing at the RABV-exposure site, together with rabies immunoglobulin (RIG) administration if indicated, and the administration of a course of several doses of rabies vaccine
- For both PEP and PrEP, vaccines can be administered by either the intradermal (ID) or intramuscular (IM) route. One ID dose is 0.1 mL of vaccine; one IM dose is 0.5 mL or 1.0 mL depending on the product, i.e., the entire content of the vial.
- WHO recommends administering rabies vaccines intradermally, as this reduces the amount of necessary vaccines and therefore the cost by 60–80% without compromising any safety or efficacy.

- For all age groups, ID injection sites are the deltoid region and either the anterolateral thigh or suprascapular regions. The recommended site for IM administration is the deltoid area of the arm for adults and children aged ≥2 years and the anterolateral area of the thigh for children aged.
- Considerations for special populations:
    - **Pregnant and lactating women:** Rabies vaccines and rabies immunoglobulins (RIG) are safe and effective in pregnant and lactating women.
    - **HIV-infected and other potentially immunocompromised persons:** HIV-infected individuals receiving ART who are clinically well and immunologically stable (normal CD4 per cent>25% for children aged ≥5 years) can receive rabies vaccination.
- Post-exposure prophylaxis (PEP) consists of a dose of human rabies immune globulin (HRIG) and rabies vaccine given on the day of the rabies exposure and then a dose of vaccine given again on days 3, 7, and 14.
- More information on dosing and administration of rabies vaccine can be found here (pages 207-211, 215): https://www.who.int/publications/i/item/who-wer9316

RABIES IMMUNOGLOBULINS (RIG)[2]

- After exposure to rabies, rabies immunoglobulins (RIG) provide passive immunization by neutralizing the rabies virus. It is infiltrated into the wound site before the immune system can respond to the vaccine by producing vaccine-induced neutralizing antibodies.
- RIG should be administered only once, preferably at or as soon as possible after the initiation of PEP.
- RIG should not be given after day 7 following the first rabies vaccine dose because circulating VNAs will have begun to appear.
- For people who have never been vaccinated against rabies previously, postexposure prophylaxis (PEP) should always include the administration of both HRIG and rabies vaccine.
- More information on dosing and administration of RIG can be found here (page 215-217): https://www.who.int/publications/i/item/who-wer9316
- Note that RIG is not always present globally and is a blood product and therefore MEDEVAC may be required if RIG is not required at your location.

REFERENCES

1. **Rabies vaccines: WHO position paper – April 2018 (19 April 2018):** https://www.who.int/publications/i/item/who-wer9316
2. **WHO Rabies – Key Facts (19 January 2023):** https://www.who.int/news-room/fact-sheets/detail/rabies#:~:text=extensive%20washing%20with%20water%20and,into%20the%20wound%2C%20if%20indicated