Guide to introducing human rabies vaccine into national immunization programmes

World Health Organization

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ABBREVIATIONS and ACRONYMS

AEFI	adverse event following immunization
CCEEV	cell culture and embryonated egg-based rabies vaccine
EPI	Expanded Programme on Immunization
ERIG	equine rabies immunoglobulin
FAO	Food and Agriculture Organization of the United Nations
HRIG	human rabies immunoglobulin
IBCM	integrated bite case management
NITAG	national immunization technical advisory group
OIE	World Organisation for Animal Health
PEP	post-exposure prophylaxis
PrEP	pre-exposure prophylaxis
RABV	rabies virus
RIG	rabies immunoglobulin
WHO	World Health Organization
WOAH	World Organisation for Animal Health (formerly OIE)

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ABOUT this GUIDE

The aim of this guide is to support national immunization programme managers and others responsible for implementing human rabies vaccine programmes to:

- inform policy discussions and operational planning for introducing or expanding rabies post-exposure prophylaxis (PEP) into a national immunization programme (e.g. through the national immunization programme, or other programmes); and
- highlight considerations specific to rabies PEP for integration into existing systems, including for implementation, and monitoring and evaluation.

While the guide is mainly intended for programme managers and focuses on human vaccination, complementary animal health measures are highlighted where relevant given the zoonotic nature of rabies.

The guide was developed collaboratively with input from technical experts in rabies and immunization, vaccines and biologicals.

Management of conflicts of interests

All external contributors completed WHO declarations of interests in accordance with WHO's policy. The review demonstrated that no interests were identified.

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EXECUTIVE SUMMARY

GUIDE TO INTRODUCING HUMAN RABIES VACCINE INTO NATIONAL IMMUNIZATION PROGRAMMES

RABIES is fatal, vaccine-preventable disease responsible for an estimated 59,000 human deaths each year. Most cases are **transmitted by dogs**, and most deaths occur in **underserved populations** in Africa and Asia. Approximately 40% of deaths occur in children.

RABIES CAN BE PREVENTED through **vaccinating dogs** to reduce transmission, and by **providing post-exposure prophylaxis (PEP) to people**. PEP consists of thorough wound washing after a suspected exposure, a series of rabies vaccinations, and in some cases rabies immunoglobulin. Robust surveillance is also key to effectively target interventions.

EXPANDING ACCESS TO RABIES PEP is **critical to save lives** and end the burden of rabies – and in 2019, rabies was added to GAVI's vaccine investment strategy. However, this brings unique considerations beyond those of routine vaccinations, such as being administered in response to exposure; requiring multiple doses; and requiring collaboration with the animal health sector to address disease transmission at its source. It is also an opportunity to strengthen health systems and operationalise a **One Health approach**.

THIS GUIDE AIMS TO

support national immunization programme managers and others responsible for **implementing human rabies vaccine programmes** to:

- inform policy discussions and operational planning for **introducing or expanding** rabies post-exposure prophylaxis (PEP) into a national immunization programme; and

- highlight considerations specific to rabies PEP for **integration into existing systems**, including for implementation, and monitoring and evaluation.

THE GUIDE OUTLINES SIX STEPS FOR COUNTRIES TO FOLLOW:

1. **Decision making at the country level** to introduce the vaccine into the national immunization programme, incorporating considerations such as disease burden, delivery strategies, cost-effectiveness, health system capacity, and demand.

2. **National planning** on how to introduce the vaccine, including the delivery strategy, vaccination schedule, logistics and intersectoral collaboration required; as well as any updates to national plans.

3. **Microplanning at selected health facilities** to forecast demand, and plan and coordinate logistics, data management, intersectoral coordination and training required.

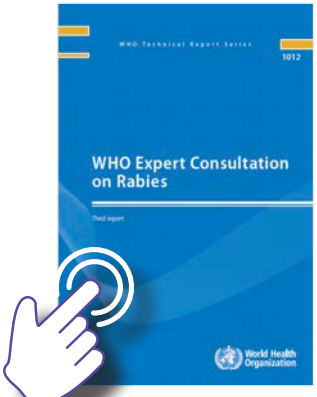
4. **Training and service delivery**, including guidance for health care workers and / or other stakeholders in how to administer the new vaccine or provide supportive supervision.

5. **Communication and social mobilisation** to increase awareness of the vaccine among health care workers and the community, including developing and implementing a communication plan.

6. **Monitoring and evaluation** to assess effectiveness of vaccine delivery and adapt plans accordingly. This can involve monitoring coverage and including the new vaccine in routine programme reviews.

For each step, it provides technical information and guidance specific to rabies, and where relevant, examples and links to **FURTHER RESOURCES**.

Technical Report Series on Rabies



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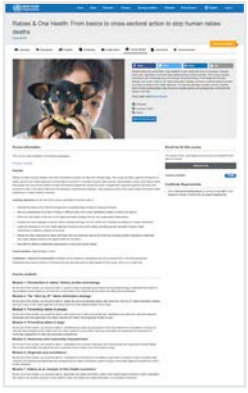
WHO Position Paper on Rabies

Global Market Study: Human Rabies Vaccines

Open WHO course on rabies



INTRODUCTION

Rabies

Rabies is a viral zoonotic disease responsible for an estimated 59 000 human deaths and more than 3.7 million disability-adjusted life years lost every year *(1)*. The disease is almost always fatal due to acute progressive encephalitis that occurs soon after clinical signs appear. Most rabies deaths occur in underserved populations in Africa and Asia of which approximately 40% are in children aged <15 years.

Rabies virus (RABV) and other lyssaviruses are transmitted through bites and scratches from infected mammals. In regions where rabies is endemic, dogs transmit up to 99% of human cases. A small proportion of cases are transmitted via wildlife (typically bats and carnivores, including ferret badgers, foxes, jackals, mongoose, raccoons, skunks and wolves). Human-to-human transmission has been confirmed only in exceptional circumstances, such as transplantation of infected tissue or organs *(2)*.

In 2018, WHO, the Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (WOAH) and the Global Alliance for Rabies Control endorsed a global target of zero deaths from dog-transmitted rabies by 2030 to achieve "Zero by 30" *(3)*. This target aligns with Goal 3 of the United Nations Sustainable Development Goals to "end the epidemics of … neglected tropical diseases and combat other communicable diseases" by 2030.

Rabies prevention

There are two main strategies to prevent rabies, both ideally supported by robust national surveillance.

1. Prevent disease in dogs. Mass dog vaccination aims to interrupt RABV transmission among dogs and therefore reduce transmission to people. Campaigns targeting 70% dog vaccination coverage have proven effective in stopping dog-mediated transmission in Africa, Asia, Europe and the Americas. Dog rabies vaccination can be complemented through owner education on rabies and responsible dog ownership *(4)*.

2. Prevent disease in people, through:

- post-exposure prophylaxis (PEP), consisting of: (i) thorough wound washing after a suspected exposure; (ii) a series of intradermal or intramuscular rabies vaccinations; and, if indicated, (iii) rabies immunoglobulin (RIG). PEP relies heavily on awareness of rabies and on how to identify and manage a potential exposure; and

- pre-exposure prophylaxis (PrEP), consisting of rabies vaccination before potential exposure. PrEP is recommended for people at occupational risk of rabies and for subpopulations in remote, highly endemic areas where prompt access to PEP is limited.

Rabies mainly kills those who cannot access timely and effective PEP. Delay in seeking PEP, inadequate wound care, unrecognized wounds, exposures to the head and neck, and noncompliance of patients with vaccination schedules, among other factors, can also contribute to PEP failure and subsequent death.

Annex A provides further details on rabies vaccines and PEP delivery.

INTRODUCING RABIES PEP into NATIONAL IMMUNIZATION PROGRAMMES

Process

Introducing a new vaccine into a national immunization programme typically involves six steps.

1. Decision-making at the country level to introduce the vaccine into the national immunization programme. This should involve rigorous evidence review and an independent recommendation to the national government to consider the impact of the new vaccine on the programme and the overall health system.

If the decision is positive, proceed to Step 2.

2. National planning on how to introduce the vaccine, including the delivery strategy, vaccination schedule, logistics and intersectoral collaboration required. National plans should also be updated.

3. Microplanning at selected health facilities to forecast demand, and plan and coordinate logistics, data management, intersectoral coordination and training required.

4. Training and service delivery including specific training for health care workers and/or other stakeholders as necessary on how to administer the new vaccine or provide supportive supervision.

5. Communication and social mobilization to increase awareness of the vaccine among health care workers and the community. This may involve developing and implementing a communication plan.

6. Monitoring and evaluation to assess effectiveness of vaccine delivery and adapt plans accordingly. This can involve monitoring coverage and including the new vaccine in routine programme reviews.

The next sections describe these steps for rabies PEP.

Considerations

Introducing rabies PEP into national immunization programmes brings unique challenges and opportunities beyond those of routine childhood vaccination. Examples are given below.

Challenges

- Rabies PEP is administered in response to possible exposure, meaning:
  - it is administered at health facilities where patients seek wound care, as opposed to use in routine immunization clinics, sites or campaigns;
  - it targets a specific population, namely bite victims of all ages who require PEP; and
  - it requires assessment of exposure risk by a medical professional before PEP is administered.
- Frequency of exposures, and the resultant need for PEP, may also vary over time; therefore accurate vaccine forecasting is needed.
- Rabies PEP involves multiple doses which require follow-up visits to ensure completion.
- Rabies PEP can involve two biological products (vaccine and RIG) that may not be equally available, which can impact stockpiling and distribution.
- Rabies is a zoonotic disease whose prevention and control requires:
  - robust human and animal surveillance data to understand disease burden, identify high-risk populations, inform vaccine forecasting and enable more efficient use of rabies PEP; and
  - collaboration with the animal health sector to register bites; confirm rabies animal cases; remove biting dogs from communities; and pursue prevention (e.g. dog vaccination).

Opportunities

- Strengthen health systems coverage and surveillance by integrating access to rabies PEP with delivery of immunization and other primary health care services to children and underserved populations.
- Accelerate the switch from intramuscular vaccination to shortened, cost- and dose-saving intradermal vaccination schedules recommended by WHO *(5)*.
- Support a comprehensive rabies prevention and control programme, of which robust disease surveillance and access to prompt, appropriate PEP for people exposed to rabies are core components.
- Demonstrate country progress on global action plans – such as the *Global strategic plan to end human deaths from dog-mediated human rabies by 2030 (3)* and Sustainable Development Goal 3.
- Operationalize One Health by strengthening animal and public health systems, workforce and surveillance capacity to prevent and control rabies and other zoonotic diseases.

- Bring new energy and focused advocacy from collaborators to create synergies, innovative ways of working, broader access, and additional resource mobilization and support for immunization.

A 2019 analysis by the WHO Rabies Modelling Consortium estimated that extended access to PEP free of charge in 67 rabies-endemic Gavi-eligible countries would prevent an additional 489 000 deaths during 2020–2035 *(6)*.

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DECISION-MAKING at the COUNTRY LEVEL

Decision-making process

Systematic and transparent decision-making about introducing rabies PEP into the national immunization programme is key. Ideally, the national immunization technical advisory group (NITAG[1]) or an equivalent independent advisory body should be requested to undertake a rigorous review of the evidence and make an independent recommendation to the national government on introducing or expanding use of rabies PEP.

Members of the NITAG should have a broad health perspective to ensure that the impact of rabies vaccine on the immunization programme and the overall human and animal health system is considered.

The NITAG committee and its members must be perceived as objective, independent and unbiased. The independence of the NITAG and its reliance on evidence-based decision-making reinforces the credibility of the decision, helps to resist pressure from interest groups and enhances its ability to secure government and/or donor funding for introducing the vaccine. NITAGs function best when they are supported by a secretariat or technical sub-committee that collects and synthesizes the evidence. Further information on NITAGs is available from WHO *(7)*.

Subsequently, an inter-agency coordinating committee[2] can serve to coordinate partner activities and contribute funding for the immunization programme. As with other decisions pertaining to the national immunization schedule, the national government is responsible for deciding whether or not to introduce rabies PEP.

Often, a high-level advocate or "champion", such as the First Lady, can be a powerful driver to initiate country discussion and decision-making about rabies vaccination.

[1] NITAGs should consist of national experts in a broad range of disciplines (e.g. senior paediatricians, immunization and vaccine experts, epidemiologists, public health experts, health economists, health systems experts and social scientists), who can analyse different types of scientific evidence and issues that should be considered in making an informed decision.

[2] A committee made up of representatives of the health ministry, WHO, UNICEF, and other domestic and external partners to improve coordination among partners in support of the national immunization programme.

Key considerations

The decision to introduce or expand rabies PEP should consider:

- data on the estimated burden of human rabies cases;
- accessibility of rabies PEP and supply in the country;
- number and location of health facilities providing PEP;
- possible delivery strategies for rabies PEP, including administration route and health care worker capability;
- cost, cost–effectiveness and affordability of rabies PEP;
- awareness, perceptions and demand (i.e. health-seeking behaviour) for rabies vaccine;
- capacity and performance of the Expanded Programme on Immunization (EPI) and associated clinical programmes;
- experience of rabies PEP introduction from countries with a similar level of health system capacity;
- existence of a National Rabies Prevention and Control Plan (ideally cross-sectoral); and
- status of animal health interventions for rabies prevention.

Cost and cost–effectiveness

Financial sustainability is also key to introducing a new vaccine and should cover the ability to finance rabies vaccine and any additional expenses incurred in adapting the immunization programme or introducing new delivery strategies. Providing risk-based rabies PEP in combination with mass dog vaccination is consistently identified as the most cost–effective method of preventing human rabies deaths in endemic settings. Using intradermal vaccination and shorter, WHO-recommended vaccination schedules is also cost- and dose-saving.

Costs to consider when budgeting for rabies vaccine introduction include:

- cost of vaccine, depending on vaccine type, source and delivery route (intramuscular versus intradermal);
- cost of delivery route(s) where this is incremental to existing programmes, e.g. for expansion of cold chain, dry storage, vaccine transport systems;
- training of relevant health workers at all levels;
- development of materials for community sensitization and mobilization;
- implementing community sensitization and mobilization activities;

- advocacy activities with key stakeholders at national, subnational and district levels;
- strengthening laboratory-based human and animal disease surveillance and data reporting; and
- strengthening animal sector interventions.

The United Nations Children's Fund (UNICEF) provides data on prices of vaccines procured by UNICEF, including for rabies *(8)*.

Possible delivery strategies for rabies vaccine

The delivery strategy for rabies vaccine should be carefully considered. The advantages and disadvantages, costs and likely success of different strategies will vary according to the country-specific context.

Ideally, strategies for delivery of rabies vaccine should be:

- compatible with existing vaccine-delivery infrastructure and cold chain capacity;
- affordable, cost–effective and sustainable; and
- able to achieve the highest possible access for at-risk populations.

In practice, countries may need to balance strategies that maximize access to vaccines with those considered most feasible, affordable and sustainable.

Examples of rabies vaccination systems currently operating in endemic countries include:

- Widespread community bite clinics or rabies units located in hospitals, specializing in delivering wound care, risk assessment and PEP (e.g. the Philippines, Sri Lanka, Viet Nam)
    - advantages: readily accessible to bite victims
    - disadvantages: expensive to maintain and operate logistics to ensure vaccine is available at numerous sites
    - typical administration route: intramuscular, but intradermal possible (see Box 1)
- PEP available at a few hospitals or clinics predominantly in urban areas (e.g. Cambodia)
    - advantages: lower cost to maintain, particularly when using intradermal vaccination
    - disadvantages: only accessible in cities; less accessible for rural, at-risk communities
    - typical administration route: intradermal

- Introduction into routine vaccination programmes, operating out of a network of selected health centres (not currently in use)
    - advantages: uses existing and often robust vaccine distribution and storage networks
    - disadvantages: community members need to identify selected health centres with vaccine, which may cause additional burden to health centres with the addition of new and different vaccines
    - typical administration route: intramuscular or intradermal.

BOX 1. Route of administration for rabies PEP: intradermal versus intramuscular

Rabies vaccines can be administered intradermally or intramuscularly for prophylaxis before and after exposure. Intradermal administration uses just 0.1mL of vaccine per dose, whereas intramuscular administration uses 0.5–1.0 mL of vaccine per dose (i.e. the entire vial).

Intradermal administration can therefore be dose- and cost-saving, particularly where use of multiple doses is licensed and demand is sufficient to administer the vaccine within 6 hours after opening, for example in settings where several bite victims are anticipated, or where the remainder of the vial can be used for PrEP. Administration should be conducted only by health care workers who are trained in this method, as inadvertent intramuscular or subcutaneous routes may have reduced efficacy. Intradermal administration is the preferred route in most settings where canine rabies is endemic.

In 2018, WHO recommended shorter intradermal and intramuscular schedules for rabies PEP and PrEP. While the previous schedules remain acceptable, the new schedules save cost, doses, visits and time. In many countries, these WHO-approved schedules constitute off-label use. To facilitate uptake and realize the benefits of the latest WHO recommendations, vaccine manufacturers are strongly encouraged to work with national regulatory authorities to include intradermal administration and shorter, WHO-recommended schedules as an approved use on the vaccine label.

See Annex A for further information on rabies vaccine administration routes.

Source: Rabies vaccines: WHO position paper – April 2018. Wkly Epidem Rec. 2018; 16(93):201–220 (https://www.who.int/publications/i/item/who-wer9316, accessed 21 March 2022)

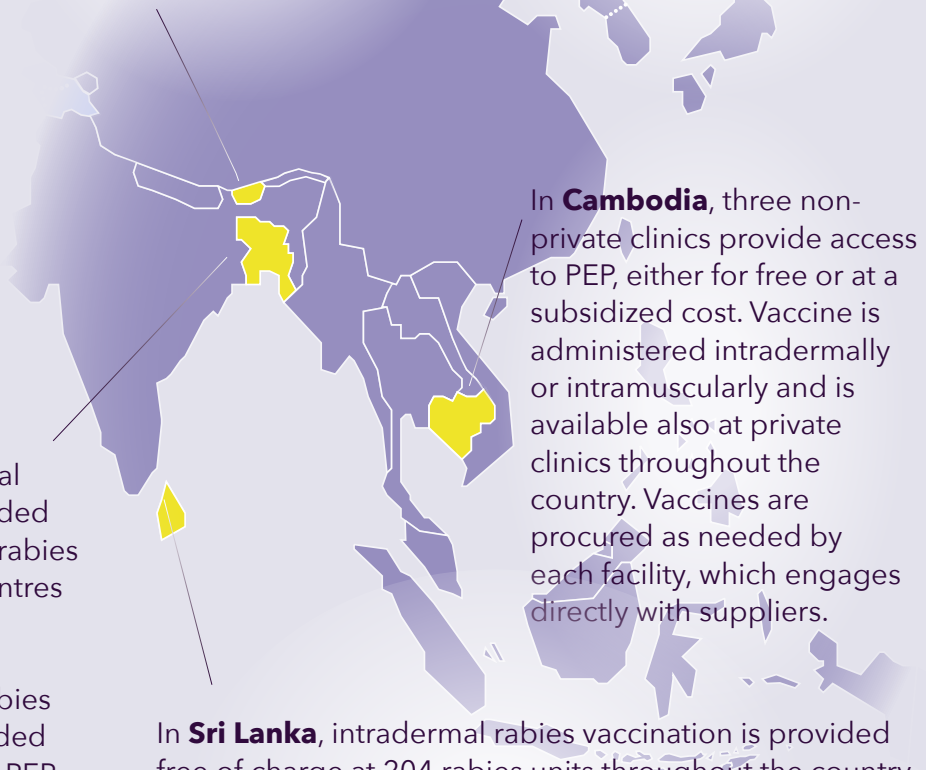
Box 2 provides examples of rabies PEP distribution strategies in Asia.

Key stakeholders

Close collaboration among the EPI programme, the health care system, involved health facilities, immunization decision-making bodies, animal health professionals, municipalities and educators, inter alia, can foster supportive partnerships for introducing or expanding rabies PEP. Ongoing communication among stakeholders before, during and after rabies PEP introduction is therefore essential for successful implementation.

BOX 2. Examples of rabies PEP delivery in four Asian countries

In **Bhutan**, intradermal rabies vaccines are provided free of charge at national, regional and district hospitals, and at basic health units throughout the country. RIG is also provided gratis, although at fewer health facilities due to its high cost. Rabies vaccines are administered by the same staff as EPI vaccines and are not available through the private sector. Vaccines are procured annually through a central process and distributed to hospitals on request. Basic health units obtain vaccine from district hospitals as needed.



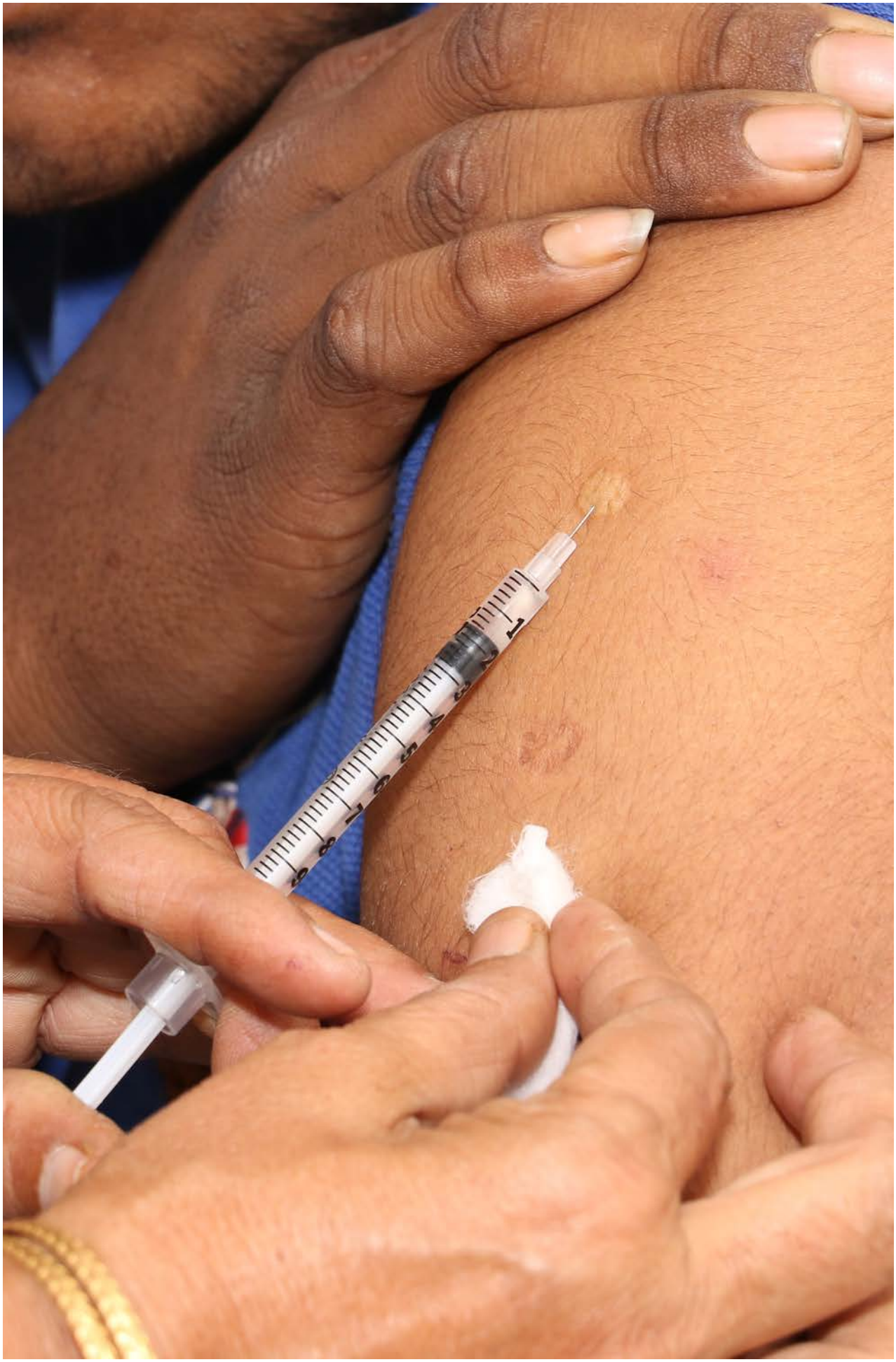
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

In **Cambodia**, three non-private clinics provide access to PEP, either for free or at a subsidized cost. Vaccine is administered intradermally or intramuscularly and is available also at private clinics throughout the country. Vaccines are procured as needed by each facility, which engages directly with suppliers.

In **Bangladesh**, intradermal rabies vaccination is provided through 66 public district rabies prevention and control centres (RPCCs) and one national RPCC. Each district has at least one centre, where rabies vaccine and RIG are provided for free. Public supplies of PEP are procured annually and distributed to RPCCs through a public bidding system and using an independent cold chain. If vaccine is out of stock in public clinics, it can be purchased by patients privately through pharmacies.

In **Sri Lanka**, intradermal rabies vaccination is provided free of charge at 204 rabies units throughout the country. Higher volume hospitals carry both vaccine and RIG, while lower volume hospitals carry only rabies vaccine. There is limited availability of PEP in the private sector, where it is more costly. Rabies vaccines are procured centrally three times a year and supplied from the central to regional and district levels throughout the year according to government delivery plans. Most stock is carried at the district and central level, with distribution to other health facilities as needed.

Source: Li AJ, Sreenivasan N, Siddiqi UR, Tahmina S, Penjor K, Sovann J, et al. Descriptive assessment of rabies post-exposure prophylaxis procurement, distribution, monitoring, and reporting in four Asian countries: Bangladesh, Bhutan, Cambodia, and Sri Lanka, 2017–2018. Vaccine. 2019; 37(Suppl 1):A14-A19.



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NATIONAL PLANNING

Once a decision has been taken to introduce rabies vaccine, detailed planning is needed. The delivery strategy, selected health facilities, vaccination schedule, logistics and intersectoral collaborations must be carefully considered and the national comprehensive multi-year plan for immunizations updated. Stepwise guidance is provided in the *WHO–UNICEF Guidelines for developing a comprehensive multi-year plan (9)*.

In addition to updating the comprehensive multi-year plan[1] to include rabies PEP, a detailed introduction plan should be developed that: (i) outlines all activities and steps required for a successful introduction by programme component; (ii) identifies government departments, institutions or external partners that are responsible for each activity; and (iii) includes a timeline and a detailed budget.

Given the unique considerations for introducing rabies PEP, it is critical that countries allow sufficient time to plan and implement all specified activities and that the introduction is not rushed. Sequencing activities in a detailed chronogram will highlight critical milestones necessary for the introduction to proceed smoothly.

Countries are encouraged to refer to the tools (Annex 3) and checklist (Annex 4) contained in the WHO guide *Principles and considerations for adding a new vaccine to a national immunization programme: from decision to implementation and monitoring (10)*.

National introduction versus scaling up introduction with selected pilot sites

Strategies for distributing rabies vaccine should be compatible with existing vaccine delivery infrastructure and cold chains and be affordable and sustainable. However, in many countries, rabies vaccine has never been available at scale, or routinely distributed to health facilities using the immunization programme supply chain.

Countries may therefore consider introducing rabies vaccine into existing immunization services at selected pilot sites before rolling them out nationwide. This allows time to identify and address issues such as:

- feasibility of integrating rabies vaccine distribution with existing vaccine supply system(s);
- logistical and programmatic issues such as accurate vaccine forecasting and workforce training;
- adapting stock monitoring and utilization tools for rabies vaccine;
- fine-tuning training and communication plans;

[1] The comprehensive multi-year plan (cMYP) is gradually being replaced with a national immunization strategy (NIS).

- rabies vaccine completion rates;
- quality of disease surveillance, for instance by health care facilities and in communities, to identify animal cases and share information between sectors;
- cost of delivery; and
- other lessons learnt to refine rabies vaccine delivery strategies.

Selection of health facilities

Facilities to administer rabies vaccine should be jointly selected by relevant partners considering the following criteria:

- high-volume public facilities (i.e. large catchment populations);
- adequate health worker staffing;
- facilities already providing immunization services;
- facilities with sufficient cold chain capacity;
- facilities ideally open with flexible hours; and
- burden of rabies in catchment area.

Previous experience with administering rabies vaccine may be used to fine-tune selection and avoid disruption of current health care-seeking behaviours.

Considerations for health facility placement and number

The quantity and placement of health facilities should aim to make PEP accessible to all at-risk populations.

Defining at-risk populations. If RABV transmission persists in a community from dogs or wildlife, PEP should be accessible for exposed persons. In many rabies-endemic countries, this means all populations are potentially at risk, unless dog vaccination programmes have resulted in rabies-free areas.

Where animal surveillance systems are deemed adequate *(11)*, surveillance data can be used to determine populations at higher risk for RABV exposures and prioritize the locations of PEP facilities. Where surveillance systems are inadequate to define risk, an absence of cases should be viewed cautiously, and more active measures of case detection or risk determination may be needed (e.g. active surveillance or surveys).

Defining accessibility. Accessibility may have different criteria depending on the socioeconomic status of the community and country. In general, persons with RABV exposures should be able to receive PEP within 24 hours of exposure, and without experiencing undue

costs or an unreasonable amount of time to receive care. Transport cost, travel time and lack of transport options to reach health facilities are frequent causes of PEP avoidance and should be considered when determining catchment areas of facilities.

Defining the catchment area. The catchment area (i.e. the region in which communities are expected to travel to the facility for PEP) can vary based on population characteristics and should prioritize accessibility, especially for at-risk and marginalized populations. Well-connected areas with easily accessed public transit (e.g. market towns) may require fewer PEP centres. Areas that are poorly connected and of low income or marginalized populations may require more PEP centres.

Health facility assessments

Before introducing rabies vaccine, facilities should also be assessed to understand:

- catchment area and population
- patient volume and flow
- access to clean water and wound washing facilities
- vaccine stock management
- cold chain capacity, including:
    - refrigerators: type (e.g. electric, solar, gas); number; status; temperature; space capacity for rabies vaccine
    - frequency of power cuts and types of back-up power sources/generators
    - availability of temperature monitoring devices and logbooks
    - review of procedures and logbooks
- availability of cold boxes, ice packs, safety boxes, and safe injection equipment.

Vaccine forecasting

Demand for rabies vaccine is based on health-seeking behaviour following animal bites, rather than targeting specific age groups as in EPI programmes. Rabies vaccine forecasting and use is therefore based on animal bite burden and health-seeking behaviour. It can also be informed by previous consumption (e.g. month, season or year). Ideally, PEP should be consistently available at relevant local, regional and national facilities to enable exposed persons to complete their vaccination course without undue disruption (e.g. in time, travel).

Forecasting demand based on animal bite burden requires available, reliable data on dog bite incidence and the prevalence of rabies in dogs to estimate community exposures. In many countries, however, these data are unavailable or unreliable, and may underestimate the true

- total human population;
- annual animal bite incidence;
- % of bites that are reported;
- % of reported bite victims that will seek care;
- % of reported bite victims that will receive rabies vaccine;
- route of administration and dosing schedule for rabies vaccine (i.e. intradermal or intramuscular; number of doses);
- adherence rates to rabies vaccination schedules; and
- annual rabies vaccine consumption in similar settings.

Higher estimates of demand should be used initially to avoid stock-outs of rabies vaccine. Forecasts should be re-evaluated regularly – even biweekly or monthly during initial implementation – as more information becomes available (e.g. from routine household surveys, health facility and national census data), and consider:

- changes in population size;
- availability of more accurate bite data;
- changes in health-seeking behaviour of bite victims (e.g. health-seeking behaviour may increase as community awareness of rabies and vaccine availability increases, thereby increasing demand);
- increase in health facility referrals e.g., due to enhanced awareness or surveillance; and
- vaccine programme data, including number of visits, vaccine series completion rates, wastage, etc.

The frequency of RABV exposures, and the resultant need for PEP, can be highly variable over time. Programmes should monitor vaccine distribution and PEP usage at health centres and use existing or establish alert systems to replenish vaccines when indicated.

Procurement

To align rabies vaccine procurement and distribution with existing systems, rabies vaccine can be procured through the national immunization programme via UNICEF. Rabies vaccine should be requested in the same manner as other routine immunizations, with request forms modified as required.

Distribution and storage

The shelf-life of rabies vaccines is ≥ 3 years. Vaccine should be stored centrally and can be distributed to subnational levels monthly. If rabies vaccine is integrated into the immunization system, cold stores at the central and subnational levels should be evaluated for space and used as appropriate. Health facilities can either collect vaccine from the subnational stores or have it delivered to them once a month, depending on the existing mechanisms. To avoid shortages, health facilities should maintain a one-week emergency stock of rabies vaccine; subnational jurisdictions should maintain a one-month emergency stockpile.

Cold chain

All formulations of rabies vaccines currently available are lyophilized. They should be refrigerated at 2–8 °C and protected from sunlight. Some products have a vaccine vial monitor (Annex A, Table A.1). If the refrigerator is a side-opening model, vaccines should not be stored in the door as the temperature may fluctuate when opening and closing the refrigerator.

The temperature of the refrigerator should be monitored and adjusted as necessary. This can be done by checking the thermometer regularly (minimum twice daily) and keeping a 30-day temperature recorder (30-DTR) in the refrigerator to continuously track the storage temperature and to detect episodes of low and high temperature alarms. The temperature records and alarm episodes should be reviewed monthly to ascertain the quality of vaccine to be used or not.

If transport of vaccine is required, ice packs should be used to maintain cold chain at 2–8 °C. Frozen icepacks should be kept at room temperature for 5–10 minutes or longer until the ice inside can be heard to move when shaken, before placing the vaccines inside them (i.e. conditioned ice packs).

At the health facilities, rabies vaccine can be stored in vaccine refrigerators to ensure availability of adequate temperature monitoring devices and appropriate storage conditions. Rabies vaccine can also be stored in pharmacy refrigerators, although these are unlikely to be routinely supervised.

All rabies vaccines are lyophilized and require reconstitution at the time of use with the accompanying sterile diluent. They should be used immediately after dilution, or within 6 hours if stored at 2–8 °C and protected from sunlight. Remaining vaccine can be used for PrEP rather than discarded, for example, for animal disease control professionals or staff at health facilities who regularly attend to clinical rabies patients. Scheduling follow-up PrEP visits for patients within similar periods may help to minimize wastage.

Monitoring vaccine stocks

As with other routine immunizations, health facilities should report data on rabies vaccine availability and utilization and request vaccines from the subnational jurisdiction monthly. Reporting of rabies vaccine availability and utilization should be compulsory to receive additional vaccine supply, and facilities trained in timely reporting to avoid stock-outs.

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MICROPLANNING at SELECTED HEALTH FACILITIES

Adequate microplanning at the health facility level is essential before introducing a new vaccine. For rabies PEP a few specific issues should be considered.

Verifying and updating the vaccine forecasts

Facilities will need to verify and update vaccine forecasts as rabies vaccine and accurate, localized data on RABV exposures, PEP need and use becomes more widely available (see vaccine forecasting, Chapter 4).

Vaccine delivery

Assessing current logistics for vaccine delivery will help inform capacity to deliver additional rabies vaccine in the future. In some countries, a regular system for rabies vaccine distribution (e.g. independently, or through manufacturer delivery) exists already and could handle additional capacity. Alternatively, sharing distribution networks with EPI or other systems could be considered to decrease overall cost of rabies vaccine distribution.

Cold chain capacity

Managing rabies vaccine in health facilities should follow the same procedures as any vaccine requiring a continuous cold chain (see cold chain, Chapter 4). A recent (i.e. conducted within the last 12–24 months), effective vaccine management assessment, combined with an updated cold chain inventory and capacity analysis can be used to inform if facilities require cold chain maintenance, strengthening or expansion prior to PEP introduction.

Recording and tracking patient care

Rabies vaccine is delivered over a series of three to five health facility visits, depending on the vaccination schedule selected. Individual, identifiable patient records are therefore needed to ensure that vaccines are administered in the correct anatomical location (i.e. away from where RIG was administered) and at the correct time.

Options for patient tracking include:

- vaccination schedule handouts for patients to bring and present to health care workers at each visit;
- facility logbooks for health care workers to look up individual patient records; and
- electronic medical records for health care providers to uniquely identify patients and manage their care.

A system for defaulter tracking (e.g. via SMS) is also critical to promote compliance. Patients and providers should also be able to quickly and reliably confirm PEP regimens needed (e.g. based on compliance to date and/or record of previous PEP or PrEP administration).

Coordination with other sectors

Where possible, the decision to provide PEP should be based on a risk-assessment that considers local rabies epidemiology, a health assessment of the offending animal, the severity of the exposure and the ability to test the animal to confirm a diagnosis of rabies (Annex B). This is easiest when health facilities have well-established, formal collaborations with other sectors (e.g. laboratories and animal health professionals).

Ideally, the health facility should have:

- access to animal health professionals who can conduct a health assessment on the offending animal;
- capability to notify public and animal health authorities of suspected rabies exposures; and
- capability to receive animal rabies diagnostic laboratory test results for patients under their care.

In many countries, animal bites, suspected animal rabies cases and PEP provision are considered reportable to relevant health authorities. These data support a robust, multisectoral approach to rabies, and can be used to monitor community risks and plan for animal and human vaccine needs. Health facilities should be aware of reporting requirements and ensure that systems are in place to collect and submit necessary information.

TRAINING and SERVICE DELIVERY

Training should be conducted as for other vaccine introductions, for example via an initial national training that is cascaded to subnational levels and to health facilities. One to two days at each level should be sufficient to cover the necessary background information, operational issues and hands-on practice. Ideally, the training on rabies PEP would be included as part of any regular annual or refresher training for health workers.

To enable close collaboration between sectors and partners, the trainings should include immunization focal points, surveillance officers, health care workers and pharmacists. At least one to two health workers should be trained at each facility who would, in turn, be expected to train other health workers.

Training materials should include information on:

- introduction to rabies;
- rabies vaccine attributes and storage conditions;
- indications for PEP (i.e. risk assessment);
- bite wound management;
- rabies vaccine administration;
- recording and monitoring doses;
- recording rabies data (i.e. minimum indicators, see Annex C);
- requesting rabies vaccine;
- communicating about rabies with key stakeholders; and
- collaborating with other sectors (e.g. laboratories, animal health professionals).

Information on palliative care for rabies patients can be included but is not essential for this training; additional information on this topic can be found in the *WHO Expert Consultation on Rabies: third report (2)*.

Training materials should be prepared (or translated) in the appropriate local language and in sufficient quantities. Summarized reference materials, job aids and training slides should be provided to participants for future reference and sharing with colleagues.

Interactive, hands-on training (e.g. field visits, videos of correct practices, small group discussions, demonstrations, skills practices) are generally more successful techniques for training adults than lectures.

Annex A provides further details on rabies PEP, including approved schedules, obtaining consent, risk assessment, safe injection practices, waste management and considerations for special groups. A general course on rabies is also available *(12)*.

COMMUNICATION and SOCIAL MOBILIZATION

Increasing health worker knowledge and community awareness through timely, complete and appropriate communication is key to introducing rabies PEP successfully and sustainably. Communities without reliable access to PEP may lack awareness of rabies and appropriate health-seeking behaviours after bites. This can lead to underuse (e.g. not seeking care) and over-use (e.g. seeking care for low- or no-risk exposures) of health services and vaccines.

Health facilities should have a community engagement plan to ensure that members are sensitized to these new services, the risks of rabies and appropriate health-seeking behaviours after bites. Health care workers should be able to communicate the rationale for when PEP is or is not recommended, to ensure that community members do not feel they received inadequate care, or to incorrectly trivialize future exposures.

Social mobilization activities should be prepared in advance of introducing the vaccine and be conducted a few days before vaccine becomes available in the community.

Materials, target audiences and channels

Materials should be developed collaboratively with experts in animal health and public health communications and include a comprehensive communications plan. Communication needs will differ by audience. Health care workers and animal health professionals will require detailed information to answer questions and deliver or refer appropriate care, whereas the public needs to be aware of rabies, the importance of seeking care at a health facility after a bite (versus relying on traditional healers) and where to access PEP.

Target audiences include:

- health care workers,
- animal health professionals,
- general public,
- bite victims,
- rabies vaccine recipients and
- other stakeholders (e.g. animal welfare organizations, community leaders).

Using multiple channels is important to disseminate and reinforce messages (e.g. brochures, posters, banners, factsheets, community announcements, TV/radio, social media, SMS

messages and WhatsApp). The WHO strategic communications framework provides further information on how to communicate effectively *(13)*.

Key messages

Messages should be clear, simple and accurate, with an appropriate level of detail for each audience. The actual wording of messages should consider culture, language and literacy, and ensure a call to action.

Key messages about rabies include:

- Rabies is present in the targeted communities.
- Rabies is transmitted through saliva from infected animals, most often through bites from infected dogs.
- Rabies is almost always fatal once clinical signs appear.
- Rabies is preventable by seeking prompt care if exposed.
- Rabies exposure is preventable through dog vaccination.
- Anyone bitten by a dog should seek immediate care.
- Children should be especially encouraged to report dog bites and facilitate timely medical care.
- Appropriate care to prevent rabies involves:
    - immediate, thorough washing of bite wounds with soap and water for at least 15 minutes; and
    - a series of rabies vaccinations and, in some cases, RIG.
- Rabies vaccines are safe and effective and save lives.
- It is critical to complete the full course of rabies vaccinations to prevent rabies.

Frequently asked questions and answers on rabies vaccines should also be developed for health workers to distribute to vaccine recipients. This should provide clear, simple answers to questions including:

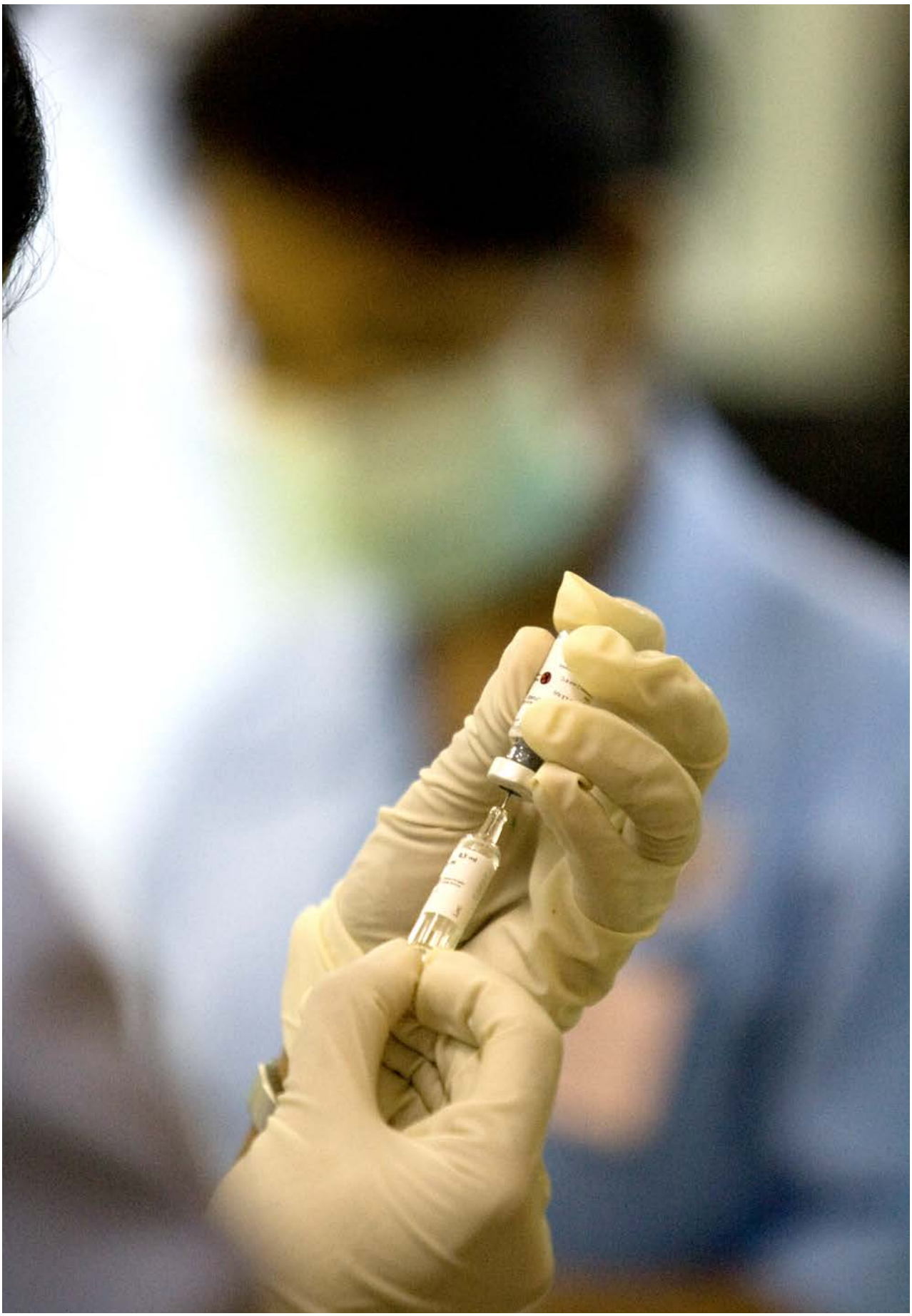
- How do you get rabies?
- What should you do after being bitten or scratched by an animal?
- Why are rabies vaccines needed?
- Are rabies vaccines safe?

- Why do you need several doses of vaccine?
- What can I do to prevent rabies in my community?

Misinformation and crisis management

While rabies vaccines have an excellent safety profile, misinformation in the community can generate vaccine hesitancy, refusal and scepticism. It is therefore critical to develop a crisis communication plan before introducing rabies vaccine, which can be implemented rapidly if misinformation arises. Health workers and community members should also be equipped with tools to address misinformation throughout vaccine introduction and scale-up. Basic elements of a crisis plan include:

- a committee at different levels which can immediately meet to discuss an action plan;
- identified, well-respected spokespersons at all levels;
- clear channels of communication involving various media;
- engaging with credible opinion and traditional leaders to address misconceptions and rumours;
- training of health workers on how to communicate with the public about safety concerns; and
- an action plan with specific roles and responsibilities for immunization programme partners.



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MONITORING and EVALUATION

Monitoring and evaluation of rabies vaccine introduction should include supportive supervision, adverse event monitoring, rabies vaccine monitoring, post-introduction evaluation and economic analyses as needed. Additional key indicators for measuring programme success are included in Annex D.

Supportive supervision

Supportive supervision is critical to ensure that proper procedures are followed and to troubleshoot problems that arise, particularly during the initial introduction of rabies vaccine. Supervision should be coordinated between partners and integrated into routine EPI supervision efforts. Visits can strengthen health worker capacity by providing feedback and motivation, updates on rabies and other vaccinations and identifying training needs. The *WHO training for mid-level managers module 4 – Supportive supervision (14)* contains additional information.

Monitoring adverse events following immunization

An adverse event following immunization (AEFI) is an untoward medical occurrence temporally related to vaccination that may or may not be caused by the vaccine itself or vaccine process. AEFIs can range from minor events such as a mild reaction at the injection site to life-threatening events such as anaphylaxis and death. Whereas minor AEFI can be caused by vaccines, serious AEFIs such as death, hospitalization, disability or life-threatening events can, when investigated, be found to be more commonly coincidental and unrelated to vaccination or rarely due to programmatic or human errors caused by inappropriate vaccine handling, prescribing or administration.

There are five categories of AEFIs.

1. Vaccine product-related reaction: caused or precipitated by the inherent properties of the vaccine.
2. Vaccine quality defect-related reaction: caused or precipitated by a vaccine that is due to one or more quality defects of the vaccine product including its administration device as provided by the manufacturer.
3. Immunization error-related reaction: caused by error in preparing, handling or administering vaccine.
4. Immunization stress-related reaction: caused by stress or anxiety about the immunization.
5. Coincidental: caused by something other than the vaccine product, immunization error or immunization anxiety.

Serious adverse events from currently used rabies vaccines are extremely rare and mainly constitute allergic reactions. However, a system should be in place to report adverse events in individuals who received PEP or PrEP. This would ideally involve recording of AEFI at each vaccine administration visit (e.g. in an additional column in the rabies PEP register) and integrating AEFI monitoring into existing AEFI surveillance system(s).

AEFIs should be reported and investigated using a standardized AEFI reporting form and AEFI case investigation form *(15)* respectively, per processes used for AEFI reporting for other routine immunizations. See also *WHO's reporting form for AEFIs* (Annex E) *(16)*.

Rabies vaccine monitoring

Health facilities providing rabies vaccine should maintain a vaccination register and daily tally of bite victims presenting for PEP. This should record data on bite victims (e.g. demographic data, animal case status, bite severity) and vaccine doses successfully administered.

PEP completion rates (adherence) should be evaluated approximately 6 months after vaccine introduction. Further assessment may be needed to understand potential barriers and reasons for non-completion, and delivery strategies or other logistics should be adapted in response to improve completion rates.

Adherence assessments should consider the case status of the offending animal (e.g. suspected, probable, confirmed, or not a case) and the severity of the bite (e.g. anatomical location, bite depth, number of bites) to drive more effective PEP usage. That is, the assessment should strive to reduce PEP use for bite victims where the offending animal was found not to have rabies, and increase PEP completion among persons with higher risk exposures.

Rabies PEP data can be used in combination with animal bite data to evaluate health-seeking behaviours of bite victims and inform more accurate vaccine forecasting. See Annex C for further detail on surveillance.

Human rabies monitoring

Monitoring and evaluation programmes should consider the number of human rabies cases in the vaccine catchment area. However, human rabies case detection rates in low- and middle-income countries are very low; in many such countries it is estimated that fewer than 10% of true human rabies deaths are detected *(17)*. Therefore, monitoring and evaluation of vaccine introduction could include a modelling component to estimate the likely impact of the vaccine introduction on unrecognized human rabies deaths, if feasible. Numerous modelling methods have been proposed, typically utilizing a probabilistic modelling method. Accurate data collection (see Annex C) can aid in monitoring and evaluating the effectiveness of vaccine introduction *(1, 18)*.

Post-introduction evaluation

WHO recommends that assessment of any new vaccine introduction should be combined with the next scheduled EPI programme review or other evaluation opportunity as opposed to a standalone evaluation after its introduction. Given the uniqueness of rabies PEP delivery, some countries may still wish to conduct such an evaluation or smaller scale assessments 6–12 months after introduction to evaluate impact and identify problems for corrective action.

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ANNEX A. WHO RECOMMENDATIONS for DELIVERY of RABIES POST-EXPOSURE PROPHYLAXIS

Bites from infected dogs cause most rabies cases. The consequence of an exposure to rabies virus (RABV) depends on the severity of the bite or scratch, the location on the body, the quantity and variant (genotype) of virus inoculated into the wound(s) and the timeliness of rabies post-exposure prophylaxis (PEP). The incubation period of most cases is 1–3 months; periods longer than 1 year have also occurred in rare situations. This presents an opportunity for health professionals to evaluate the risk of rabies and make informed health decisions about the need for rabies PEP.

The following categories describe risk of a RABV exposure according to the type of contact with a suspected rabid animal and the corresponding indication for rabies PEP *(1)*.

WHO rabies exposure categories and recommendations for rabies PEP

Categories of contact with suspected rabid animal*	Post-exposure prophylaxis measures
Category I: touching or feeding animals, animal licks on intact skin	Washing of exposed skin surfaces No vaccination needed
Category II: nibbling of uncovered skin, minor scratches or abrasions without bleeding	Local wound washing and treatment Immediate vaccination
Category III: single or multiple transdermal bites or scratches, contamination of mucous membrane or broken skin with saliva from licks, exposures due to direct contact with bats	Local wound washing and treatment Immediate vaccination and administration of rabies immunoglobulin

* WHO definitions of suspected, probable and confirmed rabid animals are provided in Appendix 1 and human case definitions in Appendix 2. Rabies PEP may still be appropriate when an exposure occurs to an animal that does not meet these criteria, depending on the risk assessment performed.

Wound treatment

For category II and III exposures, all bite wounds and scratches should be immediately and thoroughly washed and flushed with soap or detergent and copious amounts of water. Thorough wound washing with soap or detergent and water and/or viricidal agents reduces

the viral inoculum at the wound site. Depending on the wound characteristics, antibiotics, analgesics and a tetanus vaccination may be indicated.

Local wound washing is of utmost importance in all suspected rabies exposures or animal bites. However, it is essential for immunocompromised persons (e.g. from known immunosuppressing conditions or medications) whose adequate immune response to rabies vaccine cannot be assured.

Available rabies vaccine products

Modern rabies vaccines are highly immunogenic and effective in preventing rabies when properly administered. WHO recommends only concentrated, purified cell culture and embryonated egg-based rabies vaccines (CCEEVs) with a potency of at least 2.5 IU per vial *(2)*. WHO further recommends that production and use of nerve-tissue rabies vaccines should be discontinued and replaced with CCEEVs, due to the high rate of severe adverse events and inconsistent potency associated with nerve-tissue rabies vaccines. Rabies vaccines are intended for use in both rabies pre-exposure prophylaxis (PrEP) and PEP. Rabies vaccines are currently available only in single-dose vials, and do not contain preservative.

All four rabies vaccines currently prequalified[1] by WHO are lyophilized *(3)* (see Table).

Table. Summary of rabies vaccine characteristics

Commercial name (manufacturer)	Pharmaceutical form	Diluent	Type of vaccine vial monitor (VVM)	Shelf-life
ChiroRab® [previously Rabipur®] (Chiron Behring Vaccines)	Lyophilized	Water	VVM30	48 months at 2–8 °C
RABIVAX-S® (Serum Institute of India)	Lyophilized	Water	VVM30	36 months at 2–8 °C
VaxiRab N® (Cadila Health Care)	Lyophilized	Water	VVM30	36 months at 2–8 °C
VERORAB® (Sanofi Pasteur)	Lyophilized	0.4% sodium chloride	None	36 months at 2–8 °C

[1] WHO provides a service to UNICEF and other United Nations agencies that purchase vaccines in order to determine the acceptability, in principle, of vaccines from different sources for supply to these agencies. The detailed procedure and most recent list of prequalified vaccines are available online *(3)*.

Rabies PEP schedules

The first dose of rabies vaccine should be administered immediately after a RABV exposure and in consultation with a health professional familiar with conducting rabies risk assessments. Vaccine should always be administered when a category III exposure is recognized, even weeks or months after the contact. When vaccine supply is limited, suspected and probable RABV exposures that occurred more than 12 months previously may be considered of lower priority for vaccination, as clinical rabies rarely appears more than 12 months after exposure.

Rabies vaccine regimens require a series of vaccine injections that may be administered using any WHO-recommended schedule *(2)*. Vaccine manufacturers are strongly encouraged to submit a license variation application to national regulatory authorities for inclusion in WHO-recommended schedules using intradermal administration as an approved use on the label.

The choice of vaccination schedule should consider feasibility (e.g. cost, number of doses, time and compliance), and may also depend on clinical settings and patient preference *(4)*. National immunization programmes should choose the minimum number of vaccine schedules possible in order to avoid confusion and incorrect administration by health care practitioners.

PEP can be discontinued if the suspected rabid animal is proven to be free of rabies by appropriate laboratory examination; or, in the case of domestic dogs, cats or ferrets, the animal remains healthy throughout a 10-day observation period starting from the date of the bite. Persons who have received at least two doses of rabies vaccine before its discontinuation and as advised by the health care provider should be considered pre-exposure vaccinated and treated accordingly should a future exposure occur *(2)*.

Route of rabies PEP administration

WHO recommends administration of rabies vaccines either intradermally or intramuscularly.

Depending on the chosen schedule, rabies vaccination can require the administration of multiple injections during the same visit. If two or more doses of rabies vaccine are administered at the same visit, they should be injected in different sites/limbs, and always administered away from the site of RIG.

For the intradermal route, one dose is 0.1 mL of vaccine (irrespective of the vaccine brand). The vaccine in one vial can therefore be fractionated to maximally provide 5–10 doses for administration, depending on the vial size (0.5 mL or 1.0 mL) and type of syringe needle used. In these situations, health care providers should take steps to avoid contamination of the vial and iatrogenic infections among persons receiving vaccines from the same vial. Pre-filling syringes at the time the vial is first opened can help reduce these risks; pre-filled syringes should be stored appropriately and discarded if they are not used within the recommended 6 hours. For all age groups, the recommended injection sites are the deltoid region and either the anterolateral thigh or suprascapular regions. Health care providers must be trained in intradermal administration, as inadvertent intramuscular or subcutaneous administration can lead to a lack of efficacy and vaccination failures. Intradermal administration of rabies vaccines provides a cost-saving and dose-sparing alternative to intramuscular vaccination in most rabies-endemic settings.

For the intramuscular route, one dose is one vial of vaccine per patient. The recommended site for vaccine administration is the deltoid area of the arm for adults and for children aged ≥ 2 years, and the anterolateral area of the thigh for children aged < 2 years. Rabies vaccine should not be administered intramuscularly in the gluteal area.

If any doses are delayed, vaccination should be resumed, not restarted. A change in the route of administration during a rabies vaccine series is acceptable if such a change is unavoidable (e.g. an urban resident is bitten in a rural area where intramuscular PEP is given, and subsequently returns to an urban home setting where intradermal PEP is routinely given). Restarting the series of injections is not necessary; vaccination should continue according to the schedule for the new route of administration.

Table of rabies PEP by category of exposure

	Category I exposure	**Category II exposure**	**Category III exposure**
Immunologically naive individuals of all age groups	Washing of exposed skin surfaces No PEP required	Wound washing and immediate vaccination: • 2-sites ID on days 0, 3 and 7 ***or*** • 1-site IM on days 0, 3, 7 and between day 14–28 ***or*** • 2-sites IM on day 0 and 1-site IM on days 7, 21 RIG is **not** indicated	Wound washing and immediate vaccination: • 2-sites ID on days 0, 3 and 7 ***or*** • 1-site IM on days 0, 3, 7 and between day 14–28 ***or*** • 2-sites IM on day 0 and 1-site IM on days 7, 21 RIG administration is recommended
Previously immunized individuals of all age groups	Washing of exposed skin surfaces No PEP required	Wound washing and immediate vaccination:* • 1-site ID on days 0 and 3 ***or*** • 4-sites ID on day 0 ***or*** • 1-site IM on days 0 and 3 RIG is not indicated	Wound washing and immediate vaccination:* • 1-site ID on days 0 and 3 ***or*** • 4-sites ID on day 0 ***or*** • 1-site IM on days 0 and 3 RIG is not indicated

ID: intradermal; IM; intramuscular; PEP: post-exposure prophylaxis; RIG: rabies immunoglobulin.

* Immediate vaccination is not recommended if complete PEP already received within <3 months previously.

Source: Rabies vaccines: WHO position paper – April 2018 *(2)*.

Rabies immunoglobulin

RIG, a preparation containing antibodies against the rabies virus, comprises human RIG (hRIG) or equine RIG (eRIG). They are considered to have similar clinical effectiveness *(5)*. RIG provides passive immunization against RABV until the bite victim's immune system can develop active antibodies to the virus following administration of rabies vaccine. RIG is administered directly in and around the bite wound to neutralize RABV locally.

RIG administration is recommended after category III exposures of individuals who have not previously been vaccinated against rabies. Even without RIG, thorough wound washing accompanied by immediate vaccine administration and completion of the vaccine series is highly effective in preventing rabies. Rabies vaccines should never be withheld, regardless of whether RIG is available. RIG is not indicated for individuals of all ages who have documented evidence of previous PrEP or at least two administrations of vaccine for PEP. RIG is also not recommended more than 7 days after starting the rabies vaccine series as it is not needed and may blunt the immune response to rabies vaccine. The same syringe should not be used for both rabies vaccine and RIG.

For individuals with a category III exposure, all wounds should be infiltrated with RIG. For severe and multiple wounds, it may be necessary to dilute the product with sterile diluent as recommended by the manufacturer to a volume sufficient for effective, safe infiltration of all wounds without exceeding the maximum dose. Immediate local wound treatment with soap or detergent and water is also important, and in areas where ERIG and HRIG or anti-rabies monoclonal antibody (mAb) products are unavailable, proper wound care is critical and can make a difference between a person dying from the disease or surviving.

The treating health care worker should be prepared to manage anaphylaxis which, although rare, could occur during any stage of RIG administration. Suturing of wounds should be delayed until after RIG infiltration, or, if unavoidable, sutures should be loose to allow optimal RIG diffusion.

If RIG availability is limited, its allocation should be prioritized *(6)*. The cases with the highest priority to receive RIG are: category III exposed patients with multiple bites; those with deep wounds, or bites to highly innervated parts of the body, such as the head, neck and hands; patients with severe immunodeficiency; cases where the biting animal is a confirmed or probable rabies case; or where bites, scratches or exposure of a mucous membrane are caused by a bat.

Several mAb products against rabies have been demonstrated to be safe and effective in clinical trials. Such mAbs neutralize a broad panel of globally prevalent RABV isolates. Advantages of mAb products include large-scale production with standardized quality, high effectiveness, elimination of the use of animals in the production process and reduced risk of adverse events. If available, mAb products can be used as an alternative to RIG.

Repeat exposures

If an individual has a repeat exposure < 3 months after a previous exposure, and has already received a complete rabies vaccination series, only wound treatment is required; neither vaccine nor RIG is needed. For repeat exposures occurring > 3 months after the last

vaccination, the vaccination schedule for previously immunized individuals should be followed and RIG is not indicated.

Co-administration

Evidence supports safe co-administration of rabies vaccines with other inactivated vaccines, such as diphtheria–tetanus–pertussis, inactivated Japanese encephalitis and poliomyelitis vaccines, and live vaccines such as measles–mumps–rubella vaccine. Separate syringes and different injection sites should be used. If RIG is used, live vaccines should be postponed for 3–4 months. Rabies vaccine can also be given concomitantly with COVID-19 vaccines in adults. Currently, there is insufficient evidence for a recommendation on concomitant administration of COVID-19 vaccines in children and adolescents, however as rabies is fatal it should be administered first if co-administration is not recommended (7).[1]

Contraindications and precautions

Given the almost inevitable fatal outcome of clinical rabies, there are no contraindications to rabies vaccination. Any suspected RABV exposure should be treated immediately with rabies vaccine following the recommended schedule. Pregnancy and breastfeeding are not contraindications to PEP. There is no contraindication for individuals receiving treatment with chloroquine or hydroxychloroquine; intradermal or intramuscular routes of vaccine administration can be used. Individuals with a history of severe hypersensitivity to any of the components or excipients listed by the vaccine manufacturer should receive an alternative rabies vaccine product.

Consent for vaccination

Health workers should appropriately and fully inform the patient of the risks and benefits of the vaccination and should obtain informed consent in accordance with local laws and regulations.

Safety and adverse events following rabies PEP

Like other vaccines, local reactions such as redness, pain at the injection site, swelling, and induration are the most reported adverse events following rabies vaccine administration and occur in 35–45% of vaccinees. Mild systemic adverse events following immunization such as transient fever, headache, dizziness and gastrointestinal symptoms have been observed in 5–15% of vaccinees. Serious adverse events following immunization seldom occur and no causality has been established in cases of neurological symptoms.

For detailed information on adverse events following rabies vaccine administration, refer to the package insert provided with the vaccine by the manufacturer. Like other vaccines, health facilities administering rabies PEP should be equipped to manage and treat severe allergic

[1] WHO guidance on COVID-19 vaccine co-administration is based on pandemic conditions, and may be updated if / when COVID-19 vaccines become part of routine vaccination programmes.

reactions and keep vaccine recipients under medical supervision for 15–20 minutes following vaccination.

Physicians administering RIG should be prepared to treat anaphylaxis which, though rare, may occur at any stage of its administration.

Safe injection practices and waste management

WHO defines a safe injection as one that does not harm the recipient, does not expose the health care worker to any avoidable risks, and does not result in waste that is dangerous to the community. The correct technique for preparing and administering a vaccine must be followed to ensure that it is effective and does not result in an adverse event following immunization caused by vaccine administration errors.

Rabies vaccine is comparable to other vaccines with regards to safe injection practices and waste management. Managers should plan the ordering and distribution of injection and waste-disposal equipment, ideally integrated with the management of other vaccines used in the country. Health care worker training should include safe injection practices to prevent reuse and needle-stick injuries. Expanded Programme on Immunization (EPI) clinics and health facilities should have safety boxes and gloves, as are used for other injections.

Interchangeability of rabies vaccines

A change in the rabies vaccine product during a rabies vaccine course should not occur but is acceptable if such a change is unavoidable. Restarting the series of injections is not necessary; vaccination should continue according to the schedule. There are no available data to support interchangeability of nerve tissue rabies vaccines and cell culture and embryonated egg-based rabies vaccine (CCEEV). All nerve tissue rabies vaccine use should be discontinued in favour of CCEEVs.

Rabies vaccination documentation

Bite victims requiring rabies PEP should be provided with a PEP-specific vaccination card with dates for follow-up visits for additional vaccine dose administration. Patients should be required to produce the card at the follow-up visits. Appendix 3 provides an example rabies vaccination certificate.

Vaccination of special groups

Pregnant and lactating women

Rabies vaccines and RIG are safe and effective in pregnant and lactating women; any of the WHO-recommended PEP regimens can be used.

HIV-infected and other potentially immunocompromised individuals

The concern for immunocompromised persons is immunogenicity rather than safety. HIV-infected individuals receiving antiretroviral therapy, who are clinically well and immunologically stable (i.e. normal CD4 percentage > 25% for children aged < 5 years or CD4 cell-count ≥ 200 cells/mm³ if aged ≥5 years) can receive rabies vaccination as needed. For immunocompromised individuals (such as HIV-infected persons who are not receiving antiretroviral therapy or who are receiving antiretroviral therapy but do not meet minimum CD4 cell-count criteria) with WHO category II and III RABV exposure, the following is recommended: thorough washing of the wound should be emphasized; a full course of rabies vaccine should be administered, plus RIG in all cases, even if previously immunized.

For PrEP for immunocompromised persons, a 3-visit vaccination schedule should be followed, with either intradermal or intramuscular administration, on days 0 and 7 and between days 21 and 28; or a 2-visit schedule, with either intradermal or intramuscular vaccine administration, on days 0 and 7, with serological testing at 2–4 weeks after the first rabies vaccine administration to assess whether an additional vaccine administration is needed. Consultation with an infectious disease specialist or immunologist is advised.

References

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6. Evidence to recommendation Table 3: prioritization of RIG. Geneva: World Health Organization; 2018 (http://www.who.int/immunization/policy/position_papers/rabies_prioritization_rig.pdf, accessed 21 March 2022).

7. COVID-19 vaccines: technical documents. In: WHO Strategic Advisory Group of Experts on Immunization (SAGE) [website]. Geneva: World Health Organization (https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/covid-19-materials, accessed 22 April 2022).

ANNEX B. RISK ASSESMENT and INTEGRATED BITE CASE MANAGEMENT

Risk assessment

In countries with reliable community- and laboratory-based animal rabies surveillance, health care workers who manage animal bite victims or suspected rabies exposures should be trained to conduct a risk assessment before administering rabies vaccine. This can prevent unnecessary use of rabies vaccines. The risk assessment involves:

- clinical evaluation of the offending animal by a trained, skilled veterinarian or public health officer; and
- assessing the category and location of the exposure.

Clinical evaluation of the offending animal. In countries with a high burden of canine rabies, post-exposure prophylaxis (PEP) should be initiated immediately, without awaiting the results of laboratory testing, when the biting animal meets the definition of being a suspected or probable case of rabies (Appendix 1). Animals that are not available for assessment or testing should be suspected rabid for the purposes of PEP. However, PEP is rarely required following exposure to small mammals, such as rodents, rabbits and hares, given the rarity of these animals developing rabies.

Vaccination may be discontinued if laboratory testing reveals the animal not to be rabid. Persons who completed at least two sessions of vaccine administration before its discontinuation should be considered pre-exposure prophylaxis (PrEP) vaccinated.

Assessing the category and location of exposure. Even if the situation is assessed to be low risk, PEP should be initiated immediately if other risk factors are present (e.g. bite to head, neck or other highly innervated site; bite in a young child; multiple or deep wounds).

Delaying PEP initiation

If community- and laboratory-based animal rabies surveillance is strong, reliable and sensitive on the basis of the results of monitoring and evaluation activities, then, and only then, can a limited delay in administering rabies vaccine while conducting testing or a veterinary assessment be considered. In this context and in the absence of other risk factors, PEP initiation may be delayed after exposure to a domestic animal (e.g. dog, cat or ferret) that is assessed as healthy by a trained professional and remains so throughout a 10-day observation period from the date of the bite. Once started, the observation of an apparently healthy domestic animal, as

defined above, may also be used to discontinue rabies vaccine if the animal remains healthy at the end of the 10-day period, according to a trained professional.

Retrospective risk assessment

Where an animal is determined to have a suspected, probable or confirmed case of rabies, a retrospective risk assessment should be conducted to identify anyone who may have had contact with that animal during its infectious period (i.e. the time period beginning 10 days before onset of clinical signs in a dog, cat or domestic ferret) until the animal's death. Such individuals can benefit from vaccination even months after exposure.

Diagnosis of rabies in humans

Diagnosis of rabies in humans relies on clinical presentation and history of exposure to a suspect rabid animal or rabies virus (RABV) (see case definitions in Appendix 1 and 2). There are no diagnostic tests that can detect RABV infection before onset of symptoms. After symptom onset occurs, there is no known effective treatment and diagnostic testing is primarily conducted to confirm cause of death, provide closure to the family and initiate community health interventions (e.g. case investigation, dog vaccination, education, surveillance).

Rabies vaccine should not be administered to persons suspected to have clinical rabies, as response to the vaccine could interfere with interpretation of antemortem diagnostic testing and may expedite the clinical process, resulting in more rapid disease progression.

Integrated bite case management

Programmes with integrated animal and human health response mechanisms after reported RABV exposures are referred to as "integrated bite case management" (IBCM). Where rabies prevention and control programmes are well established, IBCM can support targeted use of PEP based on risk assessments and diagnostics, and thereby:

- improve detection of individuals exposed to RABV;
- increase adherence to vaccination recommendations; and
- reduce unnecessary administration of vaccine or RIG.

IBCM involves using a risk assessment algorithm to inform decisions on whether to delay PEP initiation, based on both animal and human health professional assessment factors (see Appendix 4 for an example from Haiti, and Appendix 5 for recommendations for rabies PEP based on surveillance capacity).

IBCM should only be considered where the following criteria are met:

- Ability of medical professionals to accurately assess severity of the rabies exposure:
    - Medical staff are trained in the epidemiology and pathogenesis of RABV and understand risks associated with bite severity, anatomic location, age, and health status of the victim

- Ability of animal health professionals to accurately assess rabies signs and symptoms in animals[1]:
    - Animal health professionals are trained in rabies epidemiology and signs in affected animals
    - Animal health professionals have shown high accuracy in their assessment decisions
    - Healthy dogs, cats, or ferrets that can be reliably observed, either in-home or at a specialized facility, for at least 10 days after the suspected RABV exposure
    - Animals showing signs of rabies can be humanely euthanized and samples collected for testing

- Access to a animal rabies diagnostic facility that:
    - Conducts only WOAH-recognized diagnostic tests
    - Participates in routine proficiency evaluations
    - Has appropriate national or international certifications
    - Can receive, test, and report results quickly after the exposure event (otherwise test results are too delayed to inform PEP decision)

- The health facility can receive results of case investigations and laboratory results in a timely manner

- Bite victims should not be expected to travel long distances or incur undue expenses for return visits if the risk-assessment cannot be concluded at the initial visit. If there is concern about the patient's ability to return upon completion of risk-assessment, PEP should be initiated out of an abundance of caution.

[1] Programmes endorsed by WOAH's 'official control programme for dog-mediated rabies' may be better prepared to use IBCM.

ANNEX C. RABIES SURVEILLANCE

Surveillance systems are critical to rabies prevention and control and should be able to detect and monitor four events: animal bites, animal rabies, post-exposure prophylaxis (PEP) and human rabies. In an ideal system where all bites are detected and reported, all offending and suspicious animals are assessed, and all rabies PEP appropriately prescribed, human rabies deaths can be significantly reduced or eliminated.

At a minimum, rabies cases in both humans and animals should be nationally notifiable (see Appendix 6 for a full list of WHO minimum indicators for rabies).

Human rabies surveillance

Human rabies surveillance relies on identification of suspected rabies cases, laboratory investigation and assessment of case history (Appendix 2). Local health care workers should be educated to recognize suspected cases of rabies. Any confirmed cases should be notified according to national protocols. Health care facilities that provide PEP should be prepared to receive notifications of suspected human rabies deaths and have procedures to ensure that appropriate animal and public health authorities are notified. All suspected human rabies cases should be investigated, even if the victim is already deceased, as other community members and animals may have unrecognized exposures to rabies virus (RABV) that require PEP.

Animal bite surveillance

Animal bites should trigger an immediate response, including appropriate observation or postmortem testing if rabies is suspected. A timely response by medical and veterinary staff can ensure appropriate case management and follow-up and improve case detection rates. It can also motivate field and hospital staff to continue reporting cases. The response should include prompt feedback on reports and diagnostic test results, and advice on management of cases and rabies control measures to be taken.

Establishing bite incidence rates in communities is key to plan for rabies vaccine introduction and ongoing demand, and to assess impact of the rabies prevention and control programmes. In the absence of robust surveillance systems, periodic community household surveys can be used to establish rates of bite incidence and suspected RABV exposure. These rates can be extrapolated to the target population and compared to bite treatment data to monitor improvements in health-seeking behaviours and impact on human rabies deaths. The rabies vaccination coverage rate should be evaluated at least annually.

Example calculation:

*Annual community bite incidence rate * proportion of bites that are suspicious for RABV exposure * population of rabies vaccine catchment area = estimated annual human rabies exposures*

People who initiated rabies PEP / estimated annual human rabies exposures = rabies exposure vaccination coverage rate

Dog bites occur frequently in most communities and often result from interactions that are unrelated to rabies. Programmes should not be concerned if community bite rates remain relatively unchanged - dog bite rates are not a good indicator of RABV transmission in the community.

Animal rabies surveillance

Healthy animals not involved in a human exposure are unlikely to have rabies and should not be the focus of an animal rabies surveillance system. Focusing surveillance on animals with clinical signs consistent with rabies or those to which a human has been exposed will generally result in higher case detection rates, support community buy-in, minimize negative impacts on animal welfare, and result in a more cost-effective programme. Animal health professionals are most likely to encounter such animals and should be engaged in animal rabies surveillance.

Animal rabies surveillance programmes should consider the following:

- number of animals assessed for rabies;
- number of rabid animals detected (i.e. suspected, probable, confirmed);
- percentage positive rate, determined by laboratory testing;
- number of human RABV exposures referred by animal health professionals to medical facilities;
- number of human RABV exposure referred by medical facilities to animal health professionals;
- number of dogs vaccinated against rabies in the vaccine catchment area; and
- percentage rabies vaccination coverage in the dog population.

ANNEX D. KEY METRICS AND LEADING INDICATORS FOR MEASURING PROGRAMME SUCCESS

Countries should consider selecting 3–5 key metrics to measure programme success, for instance:

- number of human rabies deaths
- percentage of suspected human RABV exposures receiving PEP
- number of animal rabies cases (e.g. in dogs, other mammals).

Key metrics should be supported by leading indicators that 'predict' trends and allow investigation of root causes of success or failure. For example, number of rabies cases in animals, number of animal bites and percentage of human bite victims receiving PEP would all be leading indicators for number of human rabies deaths. The table below summarizes data points that could be used to assess different aspects of rabies programmes.

Baseline epidemiological data
• Bite victims treated
• Rabies status of biting animals
• Category of bites
• Bite victim demographics
• Adherence to vaccination schedules
• Number of reportable events submitted to animal and public health authorities
Baseline cost data
• PEP costs (patient)
• PEP costs (facility)
• Surveillance system costs
• Diagnostic costs
• Training costs
• Vaccine wastage (open vials as well as expired/incorrectly stored closed vials)
• Number of PEP facilities
Evaluation measures
• Total programme cost

- Total human rabies deaths averted
- Loss of disability-adjusted life years averted
- Cost per death averted
- Cost per disability-adjusted year life saved
- Adherence by rabies exposure status
- Days with no vaccine stock

Rabies control measures

- Number of animals assessed for rabies
- Number of rabid animals detected (suspected, probable, confirmed)
- Percentage positive rate, determined by laboratory testing
- Number of human RABV exposures referred from animal health professionals to the medical facility
- Number of human RABV exposure referred from the medical facility to animal health professionals
- Number of dogs vaccinated against rabies in the vaccine catchment area (and percentage vaccination coverage in the dog population)

Programme indicators

- Increasing number of persons initiating PEP with suspected, probable or confirmed RABV exposures
- Increasing rate of PEP adherence among persons with suspected, probable and confirmed RABV exposures
- Decreasing rate of initiation or completion among persons with non-RABV exposures
- Decreasing rate of vaccine wastage
- Decreasing frequency of vaccine stockout
- Increasing proportion of at-risk population residing in the PEP facility catchment areas
- Increasing rate of PEP facility reports of notifiable conditions to relevant health authorities, and increasing data completeness
- Increasing dog vaccination coverage in the catchment area
- Increasing number of animals assessed for rabies in the catchment area
- Programme cost effectiveness
    - Human rabies deaths prevented
    - Life-years gained
    - Total programme costs (societal costs and government costs should be identified)
    - Cost per life-year gained: WHO-CHOICE suggests a cost-effective intervention should cost less than three times the country's gross domestic product per capita per year of life gained

ANNEX E. STANDARD REPORTING FORM FOR AEFIS

Dec 2020

AEFI reporting id number:

STANDARD REPORTING FORM FOR ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

***Patient name or initials*:** ***Patient's full Address*:** Telephone: Sex: ☐ M ☐ F (Pregnant - Trimester I ☐ II ☐ III ☐ /Lactating ☐) ***Date of birth (DD/MM/YYYY)*: _ _/_ _/_ _ _ _** *OR Age at onset :* ☐☐ *Years* ☐☐ *Months* ☐☐☐ *Days* *OR Age Group:* ☐ 0 < 1 year ☐ 1- 5 years ☐ > 5 years - 18 years ☐ > 18 years – 60 years ☐ > 60 years	***Reporter's Name*:** Institution: Designation & Department: Address: Telephone & e-mail: Date patient notified event to health system (DD/MM/YYYY): _ _/_ _/_ _ _ _ Today's date (DD/MM/YYYY): _ _/_ _/_ _ _ _

Health facility (or vaccination centre) name:

Vaccine							*Diluent*		
Name of vaccine (Generic)	****Brand Name incl. Name of Manufacturer***	****Date of vaccination***	****Time of vaccination***	Dose (1st, 2nd, etc.)	****Batch/ Lot number***	Expiry date	****Batch/ Lot number***	Expiry date	Time of reconstitution

****Adverse event (s):*** ☐ Severe local reaction ☐ *>3 days* ☐ *beyond nearest joint* ☐ Seizures ☐ *febrile* ☐ *afebrile* ☐ Abscess ☐ Sepsis ☐ Encephalopathy ☐ Toxic shock syndrome ☐ Thrombocytopenia ☐ Anaphylaxis ☐ Fever≥38°C ☐ Other (specify)..... Date & Time AEFI started (DD/MM/YYYY): __ __ / __ __ / __ __ __ __ ☐☐ Hr ☐☐ Min	Describe AEFI (Signs and symptoms):

****Serious: Yes / No ;*** ➔ If Yes ☐ Death ☐ Life threatening ☐ Disability ☐ Hospitalization ☐ Congenital anomaly ☐ Other important medical event (Specify_____)

****Outcome:*** ☐ Recovering ☐ Recovered ☐ Recovered with sequelae ☐ Not Recovered ☐ Unknown

☐ Died If died, date of death (DD/MM/YYYY): __ __ / __ __ / __ __ __ __ Autopsy done: ☐ Yes ☐ No ☐ Unknown

Past medical history (including history of similar reaction or other allergies), concomitant medication and dates of administration (exclude those used to treat reaction) other relevant information (e.g. other cases). *Use additional sheet if needed :*

First Decision making level to complete:

Investigation needed: ☐ Yes ☐ No	If yes, date investigation planned (DD/MM/YYYY): __ __ / __ __ / __ __ __ __

National level to complete:

Date report received at national level (DD/MM/YYYY): __ __ / __ __ / __ __ __ __	AEFI worldwide unique ID :
Comments:	

**Compulsory field*

Source: Standard reporting form for adverse events following immunization. Geneva: World Health Organization; 2016 (https://www.who.int/publications/m/item/reporting-form-aefi, accessed 21 March 2022).

Appendix 1. Animal rabies case definitions

Case type	Definition
Suspected	A case that is compatible with a clinical case definition of animal rabies. Clinical case definition: an animal that presents with any of the following signs: - hypersalivation, - paralysis, - lethargy, - unprovoked abnormal aggression (biting two or more people or animals and/or inanimate objects), - abnormal vocalization, - diurnal activity of nocturnal species.
Probable	A suspected case plus a reliable history of contact with a suspected, probable or confirmed rabid animal and/or An animal with suspected rabies that is killed, dies or disappears within 4–5 days of observation of illness
Confirmed	A suspected or probable animal case confirmed in a laboratory
Not a case	A suspected or probable case that is ruled out by laboratory tests or epidemiological investigation (i.e. appropriate quarantine period in eligible animals).

Appendix 2. Human rabies case definitions

Case type	Definition
Suspected	A case that is compatible with the clinical case definition: a person presenting with an acute, progressive neurological syndrome (i.e. encephalitis) dominated by forms of hyperactivity (furious rabies) or a paralytic syndrome (paralytic rabies) that progresses towards coma and death, usually due to cardiac or respiratory failure, typically within 7–10 days of the first sign if no intensive care is instituted. The syndrome may include any of the following signs: aerophobia, hydrophobia, paresthesia or localized pain, dysphagia, localized weakness, nausea or vomiting.
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 confirmed in a laboratory.

Appendix 3. Example rabies vaccination certificate

TREATMENT REPORT ON A PERSON EXPOSED TO RABIES

To be completed by a MEDICAL PRACTITIONER/NURSE

PATIENT DETAILS

Name _____

Physical address _____

Ward _____

Nkosi _____ Tel _____

Age _____ Sex _____

Clinic / hospital no. _____ Mass (KG) _____

CLINICAL DETAILS

Date of exposure: _____

Anatomical bite site: _____

Category of exposure: _____

Type of animal: _____ Dog known: Yes / No

Dog vaccinated: Yes / No History Reliable: Yes / No

Animal specimen submitted: Yes / No

If Yes: Case No. _____

Rabies result: _____

TREATMENT ADMINISTERED

A. RABIES IMMUNOGLOBULIN (RIG) Batch No. _____ Dose Given: _____

Date: _____ Sign: _____

B. RABIES VACCINE

1. Previously immunised person

Batch no.: _____ Batch no.: _____

Day 0: _____ Date: _____ Day 3: _____ Date: _____

Sign: _____ Sign: _____

2. Non-immunised person

Batch no.: _____ Batch no.: _____

Day 0: _____ Date: _____ Day 3: _____ Date: _____

Sign: _____ Sign: _____

Batch no.: _____ Batch no.: _____

Day 7: _____ Date: _____ Day 14: _____ Date: _____

Sign: _____ Sign: _____

Batch no.: _____

Day 28*: _____ Date: _____ (* only for the immunocompromised patient)

Sign: _____

IF TREATMENT STOPPED: REASON FOR DISCONTINUING: _____

_____

PERSON COMPLETING THE FORM

Full Name: _____

Name and address of Health Facility: _____

Tel No.: ( ) _____ Cell No.: _____

Signature _____ Date: _____

Source: Adapted from an existing rabies vaccination certification from the Department of Health, KwaZulu-Natal, South Africa, March 2022.

Appendix 4. Risk assessment algorithm: Haiti example

The following example is based on a risk assessment algorithm applied in Haiti and shows how the decision to delay PEP depends on both animal and human health professional assessment factors. Delaying PEP should only be conducted if the programme meets certain animal health and public health criteria. The criteria apply only to category II and III exposures.

A. Initiate PEP immediately if:

PEP should be initiated immediately if ANY of the following risk factors are present:

- Animal assessment factors
  - Animal has signs of rabies
  - Animal has two or more bite victims
  - Unknown animal (unable to assess)
- Health professional assessment factors
  - Bites to head, neck, or other highly innervated site
  - Multiple and/or deep bites
  - Bites to a young child

A particularly strong effort should be made to ensure PEP initiation and follow-up if ANY of the following risk factors are present:

- The animal is found to be probable or confirmed for rabies
- The animal dies or develops signs of rabies within 10 days of observation following the bite
- The animal is lost or otherwise unavailable for assessment for the 10 days after the bite

B. Delay PEP if:

PEP may be delayed if NONE of the risk factors from (A) are present, AND either of the following is true:

- Animal is a cat or dog that is available for quarantine and observation
- Animal is available for diagnostic testing at a laboratory that performs WOAH-recognized rabies virus detection methods

PEP should be initiated immediately if ANY of the following developments occur:

- The animal is confirmed rabid by direct fluorescent antibody test, direct rapid immunohistochemical test or polymerase chain reaction
- Laboratory testing is indeterminate
- The animal dies or develops signs of rabies within 10 days of observation following the bite
- The animal is lost or otherwise unavailable for assessment for the 10 days after the bite

C. Discontinue PEP if:

PEP may be discontinued after initiation if ANY of the following developments occur:

- Bite is from a dog or cat, AND the animal remains alive and healthy throughout a 10-day observation period following exposure
- The animal tests negative by an WOAH-recognized diagnostic assay

WOAH: World Organisation for Animal Health.

Appendix 5. Recommendations for rabies PEP on the basis of surveillance capacity

Rabies surveillance programme	Programme description	When to initiate PEP	When to discontinue PEP
No routine surveillance	No trained professionals capable of assessing animals for rabies. No laboratory capacity for timely testing of samples	Initiate PEP immediately	Do not discontinue PEP, unless a trained professional has confirmed that the animal is healthy 10 days after the bite
Limited surveillance	Trained professionals capable of assessing animals for rabies available in some communities. Laboratory capacity exists, but testing and reporting may be delayed.	Initiate PEP immediately	Do not discontinue PEP, unless tests at a qualified laboratory give negative results. or A trained professional has confirmed that the animal is healthy 10 days after the bite.
Advanced surveillance (i.e. integrated bite case management)	Trained professionals capable of assessing animals for rabies are consistently and reliably available in the community in which the exposure occurred. Laboratory capacity exists and can reliably test samples and report results within several days of the bite.	Initiate PEP immediately for bites to the head, neck, other highly innervated sites, multiple or deep wounds, and for bites to children.[a] When the animal is available and determined by a trained professional to present a low risk, PEP may be delayed.	Do not discontinue PEP, unless tests at a qualified laboratory give negative results. or A trained professional has confirmed that the animal is healthy 10 days after the bite.

[a] Because of their small stature and high risk of severe exposure, children should receive PEP immediately.

Source: WHO Expert Consultation on Rabies: third report. Geneva: World Health Organization; 2018 (WHO Technical Series Report No. 1012 (https://apps.who.int/iris/handle/10665/272364, accessed 21 March 2022).

Appendix 6. WHO minimum indicators for human and animal rabies

Minimum indicators for human rabies

Human rabies cases	
Full indicator name:	Number of human rabies cases reported
Data type:	Count
Definition:	Total number, clinical or laboratory diagnosed
Disaggregation:	- Gender: male; female; unknown - Age: < 5 years; 5–14 years; ≥ 15 years; unknown - Transmission: dog, bat, other animal, unknown - Diagnosis: clinical; laboratory; unknown

Animal bites in humans	
Full indicator name:	Number of reported animal bite cases in humans
Data type:	Count
Definition:	Bites by mammals
Disaggregation:	- Gender: male; female; unknown - Age: < 5 years; 5–14 years; ≥ 15 years; unknown - Biting animal: dog, cat, bat, wildlife, livestock, unknown - WHO wound category: Category I; Category II; Category III; unknown

People receiving PEP	
Full indicator name:	Number of people receiving post-exposure prophylaxis (PEP)
Data type:	Count
Definition:	PEP is defined for this variable as wound care and at least 1 dose of rabies vaccine
Disaggregation:	- Gender: male; female; unknown - Age: < 5 years; 5–14 years; ≥ 15 years; unknown - WHO wound category: Category I; Category II; Category III; unknown

Minimum indicators for animal rabies

Dog population	
Full indicator name:	Estimated dog population
Data type:	Count
Definition:	The best evidence-based estimation of (national) dog population; a proxy is the human:dog ratio, if known
Disaggregation:	- Ownership status: owned; unowned; unknown

Dog vaccination coverage	
Full indicator name:	Number of dogs that received rabies vaccine
Data type:	Count
Definition:	The best evidence-based or estimated number of dogs vaccinated against rabies in the country
Disaggregation:	- Ownership status: owned; unowned; unknown

Dog rabies cases	
Full indicator name:	Number of dog rabies cases reported
Data type:	Count
Definition:	Total number, clinical or laboratory diagnosed
Disaggregation:	- Diagnosis: clinical; laboratory; unknown

Rabies cases in other animals	
Full indicator name:	Number of rabies cases reported in species other than dogs
Data type:	Count
Definition:	Total number, clinical or laboratory diagnosed
Disaggregation:	- Species: cat, bat, livestock, wildlife, unknown - Diagnosis: clinical; laboratory; unknown

Templates for data collection can be found in Annex 13 of WHO's Technical Report Series on Rabies *(1)*.

Reference

WHO expert consultation on rabies: third report. Geneva: World Health Organization; 2018 (WHO Technical Report Series, No. 1012; https://apps.who.int/iris/handle/10665/272364, accessed 21 March 2022).

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