Nepal Paediatric Society (NEPAS)

Immunization Guidebook and Recommendations 2025

Third Edition

NEPAL PAEDIATRIC SOCIETY (NEPAS)

IMMUNISATION GUIDEBOOK AND RECOMMENDATIONS 2025

(3RD EDITION)

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DISCLAIMER

The Nepal Paediatric Society (NEPAS) has developed these guidelines to optimize the utilisation of available licensed vaccines within the nation, aiming to provide the highest possible protection for individual children in an office-based practice setting. While these recommendations offer a framework for best practice, it is acknowledged that member physicians may exercise professional discretion in their application to specific clinical scenarios, provided such decisions remain within the suggested parameters. It is crucial to understand that these guidelines, formulated for individual patient care, should not be construed as the Society's endorsement for the generalised or mass administration of particular vaccine products in national or sub-national public health programs. Decisions regarding vaccine use in large-scale immunisation initiatives require separate and specific evaluations based on epidemiological data, programmatic feasibility, cost-effectiveness analyses, and national health policy directives. Furthermore, these guidelines are subject to periodic review and updates to reflect evolving scientific evidence and the availability of new vaccines or changes in the national immunisation schedule.

ACKNOWLEDGEMENT

We extend our deepest gratitude to the many individuals who have contributed to the creation of this Immunization Guidebook 2025. This project would not have been possible without the invaluable time, expertise, and dedication of our esteemed reviewers. Their insightful feedback, meticulous attention to detail, and constructive criticism have been instrumental in shaping the accuracy, clarity, and comprehensiveness of this guide. We sincerely appreciate their commitment to ensuring that this resource serves as a reliable and up-to-date tool for healthcare professionals and the wider community.

Our heartfelt thanks also go to the contributing authors. Their profound knowledge and passion for immunization have enriched the content of this book immeasurably. Their willingness to share their expertise and contribute their unique perspectives has been vital in creating a guide that is both informative and practical. We deeply value their collaboration and commitment to this important endeavor.

A special acknowledgment is due to Dr. Arun Neopane, the esteemed President of NEPAS. Dr. Neopane's unwavering support, insightful guidance, and profound understanding of public health have been pivotal throughout this project. His vision and encouragement have inspired us, and his expertise has been invaluable in navigating the complexities of immunization guidelines and best practices. We are immensely grateful for his leadership and dedication to advancing immunization efforts.

The collective efforts of our reviewers, authors, and Dr. Neopane have been the cornerstone of this Immunization Guidebook 2025. Their collaborative spirit and shared commitment to promoting health through immunization have made this publication a reality. We are profoundly thankful for their contributions and believe that this guide will serve as a valuable resource in the ongoing efforts to protect communities through effective immunization practices.

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Message from the President
Nepal Paediatric Society (NEPAS)

It is a pleasure to write this message for the *Immunisation Update* publication by the Vaccinology and Immunology Chapter of Nepal Paediatric Society. I extend my heartfelt appreciation to the editorial team and contributors for their dedication in creating this valuable resource, which strengthens knowledge and awareness on immunisation among healthcare professionals and the wider community.

Nepal's National Immunisation Program (NIP) has made remarkable progress in improving child health, introducing new vaccines and maintaining high coverage to reduce vaccine-preventable diseases. Despite this success, challenges remain, such as addressing inequities, countering misinformation, and ensuring no child is left behind.

Vaccination is not just a public health measure—it is a fundamental right. As paediatricians and healthcare professionals, we must advocate universal immunisation, working alongside government and communities to safeguard every child's health.

While the national schedule forms a strong base, educating providers and caregivers about additional vaccines, such as those against influenza, hepatitis A, meningococcal infections, varicella and MMR which are increasingly important based on risk, epidemiology, special needs, and for those who can afford.

The Vaccinology and Immunology Chapter of the Nepal Paediatric Society has been instrumental in promoting evidence-based practices, training, and research, and shaping policy. I am confident this publication will further empower healthcare providers and strengthen their commitment to immunisation advocacy and service delivery.

Let us continue working together to ensure that every child in Nepal benefits fully, especially from vaccine preventable diseases.

Warm regards,

Maj. Gen. Dr. Arun Kumar Neopane (Retd.)
President (2023-25)
Nepal Paediatric Society

Message from the Advisor

Nepal Pediatric Society
Immunisation & Vaccinology Chapter
NEPAS

It is with great pride and a deep sense of responsibility that I extend my heartfelt congratulations to the Nepal Pediatric Society's Immunisation Chapter for the updated publication of this essential book on immunisation guidelines. This comprehensive resource reflects the collective expertise and dedication of pediatricians, public health professionals, and immunisation advocates who are committed to protecting the health and well-being of Nepal's children.

In an era where evidence-based practice is the cornerstone of effective healthcare delivery, these guidelines serve as a timely and authoritative reference for clinicians, policymakers, and health workers across the country. They not only provide clarity on immunisation protocols but also reinforce the importance of equity, access, and innovation in our national immunisation strategies.

As we navigate the evolving landscape of vaccine science and public health, let us continue to build on the foundation laid by this publication—working together to ensure that every child in Nepal receives the protection they deserve.

I commend the entire team behind this initiative for their unwavering commitment to child health and encourage all stakeholders to make full use of this vital resource in their practice.

With warm regards,
Dr Jyoti Ratna Dhakhwa
Advisor, Immunisation Chapter
Nepal Pediatric Society

Message from the Advisor

Nepal Pediatric Society – Immunisation & Vaccinology Chapter NEPAS, Past Chief Editor, Immunisation Guidebook and Recommendation 2018 (Previous Edition)

Dear Fellow Paediatricians and Healthcare Workers,

Our nation has made significant strides in child immunisation, drastically reducing the prevalence of many life-threatening diseases. The Nepal Pediatric Society has always been at the forefront of the fight against vaccine-preventable diseases. This progress is a testament to the dedication of healthcare professionals like yourselves, who work tirelessly to ensure that every child receives the vaccines they need.

However, our work is far from over. Challenges such as vaccine hesitancy, misinformation and gaps in access to healthcare services continue to threaten the healthcare of our children every day. We must remain vigilant and proactive in our efforts to combat misinformation regarding vaccination. We must continue to advocate for policies and funding, educate and empower communities, support to strengthen healthcare systems.

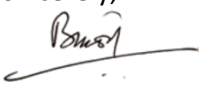
Globally, we are witnessing the development and availability of groundbreaking new vaccines that offer protection against an expanded range of diseases. It is crucial that we stay informed and consider the potential benefits of these advancements for the children of Nepal.

As we move forward for the third edition of immunisation guidebook and recommendation 2025, let us embrace a spirit of innovation and collaboration by staying informed about the latest vaccine developments and working together to overcome the challenges.

We can ensure that the children of Nepal benefit from the full potential of modern vaccinology.

Thank you for your unwavering commitment to the health of our children.

Sincerely,



Dr. Binod Lal Bajracharya

Past President Nepal Pediatric Society (2016 – 2018)

Advisor, Nepal Pediatric Society Immunisation Committee and

Past chief editor of previous edition of Immunisation Guidebook and recommendation 2018.

Message from the Chief Editor

Chairperson: Immunisation & Vaccinology Chapter NEPAS

It is with great pride and a deep sense of responsibility that I present this edition of our immunisation book. In an era where public health challenges continue to evolve, the importance of accurate, evidence-based information on immunisation cannot be overstated. Vaccination remains one of the most effective public health interventions, saving millions of lives and protecting communities from preventable diseases. Especially in a country like Nepal where the barriers are not only cultural and social but geographical too and the geography of our country poses many unseen challenges in running the immunisation program successfully.

This book is the result of a dedicated collaboration among leading experts in immunology, epidemiology, clinical practice, public health and the members of different chapters of the NEPAL PEDIATRIC SOCIETY. Our goal has been to provide a comprehensive, accessible, and up-to-date resource for healthcare professionals, policymakers, educators, and students alike. Whether you are on the front lines of patient care, involved in planning immunisation programs, or simply seeking to deepen your understanding of vaccines, we hope this book serves as a valuable tool.

We have strived to present the latest scientific findings, policy updates, and real-world applications in a clear and practical format. Each chapter has been carefully reviewed to ensure that it reflects current global and regional guidelines, while also addressing the complexities and controversies that can arise in immunisation practices. In this book we have tried to answer umpteen queries which arise in our day-to-day practice regarding immunising children in different situations. Although it might not answer all our queries, we have tried to answer as many as possible. I hope this book will help all our colleagues to practice Paediatrics with evidence and a mind full of confidence. I extend my sincere gratitude to all the contributors, reviewers, and editorial team members who have brought their expertise and passion and many sleepless nights to this project. Your commitment to promoting health through knowledge is both inspiring and essential.

May this book contribute meaningfully to the ongoing efforts to ensure safe, equitable, and effective immunisation for all.

Dr. Sangita Shakya
Editor-in-Chief

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- Principles of Immunology &Vaccination
- The role of Paediatricians in the Advocacy of Immunisation in Nepal
- Adverse Events Following Immunisation

Dr. Henish Shakya

BASIS OF IMMUNE RESPONSE

Immunity is generally divided into two types: innate (natural) and adaptive (acquired) immunity. Innate immunity includes physical barriers like the skin and mucous membranes, as well as immune cells such as neutrophils, monocytes, macrophages, and natural killer (NK) cells. This type of immunity responds immediately when a pathogen enters the body and is nonspecific. Adaptive immunity, on the other hand, involves B lymphocytes (which mediate humoral/antibody-based immunity) and T lymphocytes (which mediate cellular/cell-based immunity). The innate immune system helps activate adaptive immunity by presenting antigens to both B and T lymphocytes.

Active immunity is the protection gained through natural infection or vaccination and tends to be long-lasting, as it usually results in the formation of memory cells. When the antigen re-enters the body, a robust immune response is triggered. Passive immunity, on the other hand, is provided through maternal antibodies or immunoglobulin, and it is short-lived.

Humoral immunity is mediated by B lymphocytes, which serve as the primary defense against extracellular microbes and their toxins. When activated, B cells transform into plasma cells that secrete antibodies. For efficient antibody production, B cells require assistance from T helper cells. The antibodies secreted by B lymphocytes function through neutralization, complement activation, or enhancing opsonophagocytosis, leading to a rapid elimination of pathogens.

Cell-mediated immunity is driven by T cells, which are the primary defense against intracellular microbes. There are two main types of T cells involved in this process. Helper T cells release cytokines that promote the growth and differentiation of T cells, as well as stimulate other cells like B lymphocytes, macrophages, and NK cells. Cytotoxic T cells work by destroying infected cells. T-cell responses tend to be stronger, longer-lasting, and more cross-protective compared to humoral immune responses.

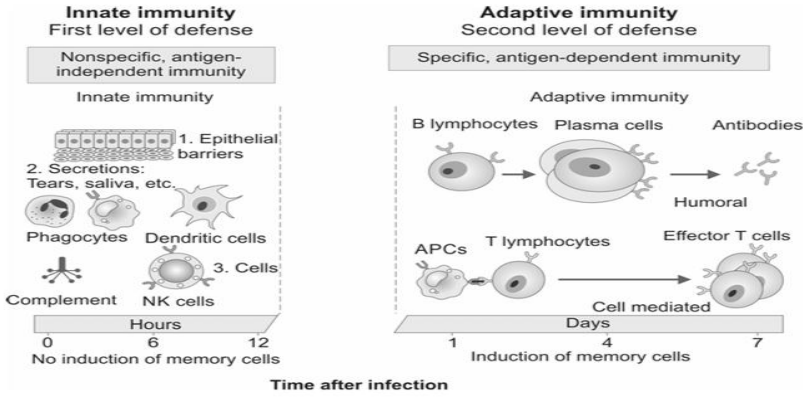

Fig1. Innate and Adaptive Immunity

Primary and Secondary Immune response:

When an antigen is introduced for the first time, the immune response starts after a lag of 7-10 days. This is called primary response. In primary immune response, the antigen exposure results in the rapid appearance of low antibody titers (IgM followed by IgG), which eventually return to baseline levels.

Secondary immune responses start on subsequent exposure (booster) to the same antigen. There is no lag phase, response starts in <7 days, persists for a long time, mainly IgG type with high Ab titers. In secondary immune responses, booster exposure to antigen reactivates immune memory (memory B cells) and results in a rapid (<7 days) increase of IgG Ab titer by a rapid proliferation of memory B cells and their evolution into abundant Ab-secreting plasma cells.

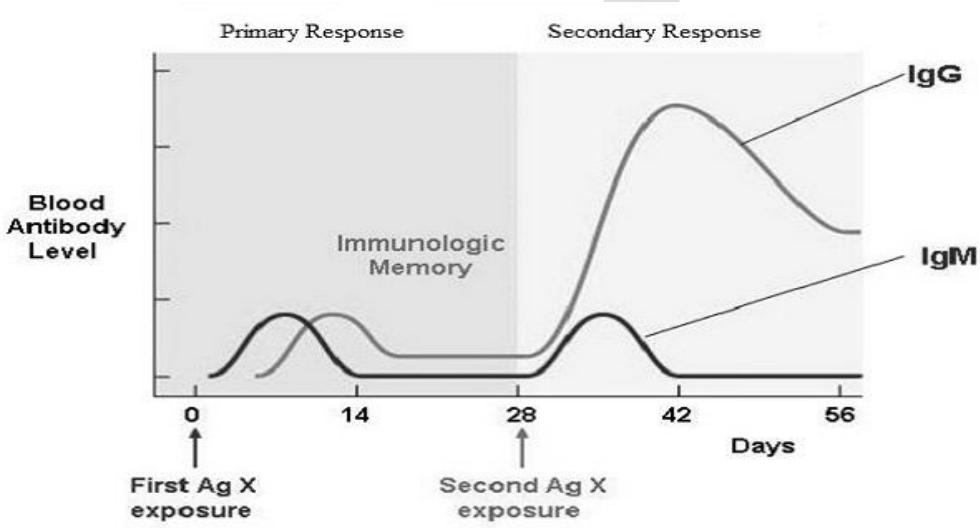

Fig 2: Immune Response and Secretion of antibodies

BASIC CONCEPTS OF VACCINATION

Vaccination: vaccination is the process of administrating the vaccine which may or may not evoke a protective immune response.

Immunisation: It is the purposeful induction of specific immune response by administering specific antigens to stimulate antibody production (active immunisation) or by protecting the individual by giving pre-formed antibodies for temporary immunity (passive immunisation).

Seroconversion: It is the four-fold increase in antibody titers after vaccination or detectable postvaccination titer who had no detectable antibody before vaccination.

Sero-protection: It implies the state of protection from disease due to the presence of certain level of antibodies in the serum.

Vaccine efficacy: This is the ability of the vaccine to protect an individual. It can be assessed through clinical trials, cohort studies, or case control studies. It is calculated as:

(Disease incidence in unvaccinated – disease incidence in vaccinated)/disease incidence in unvaccinated

Vaccine Types:

Vaccines may be broadly classified as follows:

1. Live-attenuated vaccines: BCG, OPV, MR, MMR, varicella, rotavirus, yellow fever, live Influenza vaccine
2. Inactivated vaccines:
    a. Whole-cell inactivated: Whole-cell pertussis vaccines, rabies, inactivated poliovirus (IPV), and hepatitis A
    b. Toxoids: Tetanus and diphtheria
    c. Sub-unit vaccines: They differ from inactivated whole-cell vaccines, by containing only the antigenic parts which are necessary to elicit a protective immune response.
    d. Protein Subunit vaccines—acellular pertussis, HBV, and some influenza
        i. Pure polysaccharide vaccines: Typhoid, pneumococcal polysaccharide vaccine (PPSV), and meningococcal polysaccharide vaccine
        ii. Conjugated polysaccharide vaccines: Hib-CV, typhoid-CV, PCV, and meningococcal-CV
        iii. Virus-like particle (VLP): HPV
        iv. DNA and RNA vaccines: COVID-19 vaccines

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THE ROLE OF PAEDIATRICIANS IN THE ADVOCACY OF IMMUNISATION IN NEPAL

Dr. Jyoti Ratna Dhakhwa

Immunisation is one of the most effective public health interventions, crucial for preventing life-threatening diseases among children. In Nepal, where infectious diseases continue to pose significant health challenges, Paediatricians have been playing a pivotal role in advocating for immunisation. Their efforts are essential in ensuring high vaccine coverage, reducing child morbidity and mortality, and fostering a healthier future generation. This article explores the multifaceted roles Paediatricians are playing and can play in promoting immunisation in Nepal, including education, policy influence, community engagement, professional training, leadership, research, and addressing vaccine hesitancy.

Education and Awareness

One of the primary responsibilities of Paediatricians is to educate parents and caregivers about the importance of vaccines. In Nepal, where cultural beliefs and misinformation can influence health decisions, Paediatricians serve as trusted sources of accurate information. They can explain the benefits of immunisation, dispel myths, and alleviate fears regarding vaccine safety and side effects. By doing so, they build public confidence in vaccines, empowering parents to make informed decisions that protect their children from vaccine preventable diseases. Paediatricians must inquire about a child's immunisation status and, when possible, advise on proper immunisation, including optional or additional vaccines.

Paediatricians can also engage in public awareness campaigns through local health programs, schools, and community centers. Paediatricians can promote vaccination routinely and also through special efforts such as promoting catch-up, periodic intensification of routine immunisation (PIRI), supplementary immunisation activities (SIAs) including vaccination campaigns, and during national immunisation month in Baisakh, in which Full Immunisation Declaration and Sustainability is celebrated, in World Immunisation Week, and in World Immunisation Day every year. Collaboration with media outlets can further amplify their educational messages, reaching a broader audience. This proactive approach helps increase vaccine acceptance and demand, contributing to higher immunisation rates. The current role of the Paediatricians as playing in promoting the use of HPV Vaccines in female child is a good example.

Influencing Policy and Advocacy

Paediatricians in Nepal actively participate in shaping immunisation policies by working closely with governmental bodies, such as the Ministry of Health and Population (MoHP). They contribute their expertise to national advisory committees, influencing vaccine schedules, the introduction of new vaccines, and strategies to enhance immunisation coverage. Currently, the Chairs of National Immunisation Advisory Committee (NIAC) and National AEFI Investigation Committee are Paediatricians.

Their advocacy can extend to securing government support for vaccine procurement and distribution, ensuring consistent supply chains, maintenance of cold chains, and reaching all targeted population for vaccination, even in remote areas. By voicing the needs of children and advocating for equitable access to vaccines, Paediatricians help bridge gaps in healthcare services, especially in underserved communities.

Community Engagement and Outreach

In Nepal's diverse cultural landscape, community trust plays a crucial role in healthcare acceptance. Paediatricians should actively engage with local leaders, religious figures, and community organizations to promote immunisation. They should continue to organize outreach programs, health camps, and vaccination drives, particularly targeting remote and marginalized populations.

Private health institutions offer a wider variety of **additional** vaccines, and paediatricians are crucial in promoting their appropriate use. By offering these expanded options, paediatricians not only administer vaccines but also play a vital role in educating communities about disease prevention.

Their involvement at the grassroots level enhances community participation and reduces resistance to immunisation programs.

Professional Training and Capacity Building

Paediatricians also should be instrumental in training healthcare workers, including nurses and community health volunteers, on safe vaccination practices. They ensure that immunisation guidelines are properly understood and followed, minimising the risks of adverse events.

Additionally, Paediatricians promote continuous medical education to keep healthcare providers updated on the latest vaccine developments, efficacy, and safety protocols. Nepal Pediatric Society (NEPAS) does come with guideline on immunisation and it is regularly updated. These professional meaures like training, orientation etc are crucial for maintaining public trust and the overall success of immunisation programs.

Leadership and Collaboration

As leaders in child health, Paediatricians collaborate with national and international organizations such as their organization Nepal Paediatric Society (NEPAS), World Health Organization (WHO), and UNICEF and also international organizations like IAP, APPA, SAPA and IAP. These partnerships enhance immunisation strategies through resource sharing, joint research, and coordinated advocacy campaigns.
These leadership roles enable us to influence public health priorities, ensuring that immunisation remains at the forefront of Nepal's healthcare agenda. Paediatricians also advocate for improved health infrastructure and policies that support sustainable immunisation programs.

Research and Surveillance

Paediatricians should contribute to research on vaccine coverage and equity, effectiveness, and safety, which is vital for evidence-based decision-making. Their involvement in disease surveillance helps monitor immunisation program outcomes, identifying areas needing improvement or additional interventions.

By publishing research findings and participating in medical conferences, Paediatricians contribute to the global knowledge pool on immunisation, influencing practices beyond national borders.

Vaccine-preventable diseases surveillance

Paediatricians should support the surveillance of priority vaccine-preventable diseases (VPDs) of the National Immunisation Program conducted nation-wide with technical support of WHO, by timely reporting the suspected cases as per case definitions, supporting in investigation of the cases, and facilitating sample collection as required. These VPDs includes acute flaccid paralysis (AFP) for polio surveillance, suspected measles-rubella, neonatal tetanus, and acute encephalitis surveillance for Japanese encephalitis.

Addressing Vaccine Hesitancy

Vaccine hesitancy is a growing concern worldwide, and Nepal is no exception. Paediatricians play a critical role in addressing this issue by engaging in effective communication with parents, public and communities. We must use evidence-based approaches to counter rumours, misinformation, and disinformation, emphasizing the safety and necessity of vaccines.

In the digital age, Paediatricians also participate in social media campaigns and public forums, actively combating misinformation and building public confidence in immunisation. Our authoritative voice helps counteract fear and skepticism, leading to increased vaccine uptake.

CONCLUSION

Paediatricians in Nepal are at the forefront of immunisation advocacy, performing a wide range of roles that contribute to the success of vaccination programs. Our efforts in education, policy influence, community engagement, professional training, leadership, research, VPD surveillance and addressing vaccine hesitancy are vital for safeguarding children's health and proper use of immunisation.

As Nepal continues to combat infectious diseases and strives to achieve universal immunisation coverage, the role of Paediatricians remains indispensable. Our commitment to child health not only saves live but also paves the way for a healthier, more prosperous nation.

In conclusion, the impact of Paediatricians on immunisation advocacy in Nepal is profound and far-reaching. By continuing to champion vaccines and collaborating with policymakers, communities, and international partners, we ensure that every child in Nepal has the opportunity to grow up healthy and protected from preventable diseases.

ADVERSE EVENTS FOLLOWING IMMUNISATION

INTRODUCTION

Immunisation is the cornerstone of public health saving millions of lives each year protecting the individual and the public from vaccine-preventable diseases (VPDs).[1] Vaccines are administered prophylactically to healthy people, frequently young children, as opposed to medications, which are administered therapeutically to those who are ill. The safety of vaccines is therefore expected to be significantly higher than that of medications.[2] Vaccines used in National Immunisation Program (NIP) are extremely safe and effective, nevertheless adverse events may occur. Vaccines are subject to the same risk of side effects as other pharmacological medications.

An Adverse Event Following Immunisation (AEFI) is any untoward medical occurrence which follows immunisation and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease. Reported adverse events can either be true adverse events – i.e. resulting from the vaccine or immunisation process – or coincidental events that are not due to the vaccine or immunisation process but are temporally associated with immunisation.[3]

The vaccine reactions are based specifically as cause-specific (vaccine quality defect or vaccine product related reaction) or based on seriousness/frequency (common/minor, rare/serious).[1]

AEFI includes events that are:[4]

1. Vaccine induced: where an unfavorable reaction to the vaccine is caused by one of its components.
2. Vaccine related: where the incident is connected to a defect in the production process, such as when a batch of vaccines is contaminated or a manufacturer puts it into subpar syringes.
3. Immunisation–error related: when the reaction is due to improper handling, prescribing, or administering the vaccine, such as when it is accidentally transported with a frozen vaccine or is injected into the wrong body part.
4. Immunisation stress related: when the adverse effects is related to a dread of getting an injection. Physical reactions including dizziness, fainting, tingling in the hands or around the mouth, vomiting, or even convulsions are possible as a result of this.
5. Coincidental: the event is associated temporally with vaccination by chance or caused due to underlying disease.

According to WHO, frequency of occurrence of reported adverse reaction[1] :

Very common	≥ 10%
Common (frequent)	≥ 1% and < 10%
Uncommon (infrequent)	≥ 0.1% and < 1%
Rare	≥ 0.01% and < 0.1%
Very rare	< 0.01%

TYPES OF ADVERSE EVENTS FOLLOWING IMMUNISATIONS BASED ON SEVERITY

- **Serious AEFI**

Serious AEFI is an event that results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect. Any medical event that requires intervention to prevent one of the outcomes above may also be considered as serious.

- **Severe AEFI**

Severe AEFIs are minor AEFIs with increased intensity/severity, e.g., high-grade fever following pentavalent vaccination or post-DPT swelling extending beyond nearest joint. They are caused when recipient's immune system reacts to antigens, adjuvants, stabilizers, preservatives contained in the vaccine. They are very rarely life-threatening nor do they cause any disability although there is some risk of morbidity. The patient may not be hospitalized and will not have sequelae.

- **Minor AEFI**

Minor AEFIs usually occur within a few hours of injection, resolve after short period of time, and pose little danger. Minor AEFIs can be local reactions (pain, swelling, and redness) or systemic reactions (fever > 38°C, irritability, malaise, etc.), which can be managed with antipyretics and anti-inflammatory and resolve within 2–3 days.

When such events are associated with the national immunisation programme, the confidence level in the public towards the programme might get affected. It is therefore important to monitor vaccination programme effectively for its safety and occurrence of adverse events and respond promptly and appropriately to public concern.[5] In order to increase immunisation acceptance and improve quality, the surveillance of adverse events must become an integral part of immunisation program.

CAUSE-SPECIFIC TYPES OF ADVERSE EVENT FOLLOWING IMMUNISATION[6]

- **Vaccine product-related reaction**

An AEFI that is caused by a vaccine due to one or more of the inherent properties of the vaccine product (or ingredients), e.g., extensive limb swelling following Diphtheria, Pertussis, and Tetanus (DPT) vaccination. In this scenario, vaccine might have been used correctly without compromising with manufacturing process, transport, or storage. Thus, absolutely correct use of vaccine may also cause this type of AEFI. In most cases, such events are usually not serious in nature.

- **Vaccine quality defect-related reaction**

An AEFI that is 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, e.g., failure by the manufacturer to completely inactivate a lot of Inactivated Poliovirus Vaccine (IPV) leads to cases of paralytic polio.

- **Immunisation error-related reaction**

An AEFI that is caused by inappropriate vaccine handling, prescribing, or administration and thus by its nature is preventable. These include:

Transmission of infection by contaminated multidose vial or reuse of disposable syringes and needles.

Reconstitution error: Vaccine reconstituted with the incorrect diluent.

Injection administered at incorrect site: Bacillus Calmette–Guérin (BCG) given subcutaneously (SC), rabies, or hepatitis B vaccine given SC or DPT administered SC.

Improper storage and transport of vaccine: Vaccines frozen during storage and administered, can give rise to sterile abscess. These vaccines are also ineffective.

Contraindication is ignored: Live vaccine administered to an immunosuppressed subject.

- **Immunisation anxiety-related***:* An AEFI arising from anxiety about the immunisation, e.g., vasovagal syncope in an adolescent immediately before or following vaccination. The anxiety may spread to others, especially in school settings.

- **Coincidental event***:* An AEFI that is caused by something other than the vaccine product, immunisation error, or immunisation anxiety, e.g., fever after vaccination (temporal association) and malarial parasite isolated from blood.

AEFI reporting in Nepal

Most vaccinations in Nepal are given through the government system through outreach sessions and sessions in health facilities. All serious AEFI cases should be reported and investigated as per the national AEFI surveillance system. Further, signals and events associated with a newly introduced vaccine, AEFI that may have been caused by an immunization error, significant events of unexplained cause, events causing significant parental or community concern, should also be reported. To make reporting simple and to get as many cases reported, health workers and medical personnel are asked to notify all serious AEFIs, AEFIs that may have been caused by program errors, events causing concern of the parents or community, signals after a new vaccine are investigated. Report is sent to Health Office of the district, Provincial Health Directorate, and Family Welfare Division at national level regional health directorate and investigaton is carried out. The flow of reporting is as follows:

a. Reported in AEFI Reporting form

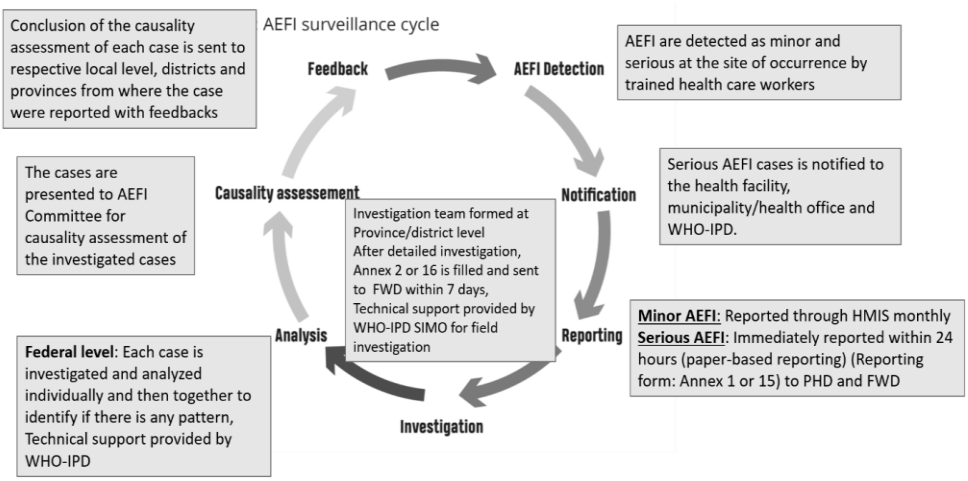
b. AEFI investigater reports details of the case along with the investigations done in chronological order of the events

c. AEFI Investigation form is filled

d. Causality assessment as per protocol is prepared and the causality is ascertained by the National AEFI Investigation Committee

e. Feedback is then sent to the reporting and treating health workers, including field investigators.

In the context of AEFI surveillance, causality assessment is a systematic review of data about AEFI case(s) in order to determine the likelihood of a causal association between the event and the vaccine(s) received.[7] Causality assessment is the systematic evaluation of the information obtained about an AEFI to determine the likelihood that the event might have been caused by the vaccine/s received. It should be noted that causality assessment should not be conducted by the field investigators nor the reporting paediatrician. The causality assessment is only conducted by the National AEFI Investigation Committee, which is the committee mandated by the Immunization Act 2072 of Nepal.



National AEFI Investigation Committee

In Nepal, National AEFI Investigation Committee is mandated by the Immunization Act 2072. The committee conducts causality assessment of serious AEFI cases and monitors vaccine safety.

The members of AEFI Investigation Committee, Nepal is formed as follows:

a. A person nominated by the Ministry from among senior paediatricians - **Chairperson**
b. Representative, Department of Drug Administration – **Member**

c. Representative, Nepal Paediatric Society – **Member**
d. One person among senior paediatricians – **Member**
e. One person among senior public health experts – **Member**
f. One person among senior pathologists – **Member**
g. Chief, Immunisation Section, Department – **Member Secretary**

Paediatricians can help by:

- Making sure that the following AEFI are reported
- All serious AEFI
- Signals and events associated with a newly introduced vaccine
- AEFI that may have been caused by an immunisation error
- Significant events of unexplained cause occurring within 30 days after vaccination
- Events causing significant parental or community concern
- Making reporting forms available in their respective institutions
- Co-operating in AEFI investigations. Supporting in field investigations of AEFI as per need.
- Reporting all severe and serious AEFIs, as soon as possible within 24-hours
- Helping in management of serious AEFIs

In conclusion, vaccines used in our NIPs are safe and effective. However, like other pharmaceutical products, vaccines are not completely risk-free and adverse events will occasionally result from vaccination. In addition to the vaccine themselves, the process of immunisation is a potential source of an adverse reaction. With an active National AEFI Investigation Committee in place, and that the National Immunization Program conducts AEFI surveillance for vaccine safety, all serious AEFI cases should be reported so that it can be reviewed by the National AEFI Investigation Committee.

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VACCINE

- Bacille Calmette-Guerin (BCG) Vaccine
- Diphteria-Pertusis-Tetanus Vaccine (DPT, DTaP, dTap, DT, dT, TT)
- Haemophillus Influenzae Type B Vaccine (Hib)
- Poliomyelitis Vaccine
- Hepatitis B Vaccine (HBV)
- Rotavirus Vaccine
- Pneumococcal Vaccine (PCV)
- Measles Rubella/Measles Mumps Rubella Vaccine (MR/MMR)
- Japanese Encephalitis Vaccine (JE)
- Typhoid Vaccine (TCV)
- Human Papilloma Virus Vaccine (HPV)
- Influenza Vaccine
- Varicella Vaccine
- Hepatitis A Vaccine
- Meningococcal Vaccine (MCV)
- Rabies Vaccine
- Cholera Vaccine
- Yellow Fever Vaccine
- Covid Vaccine
- Dengue Vaccine
- Malaria Vaccine

BCG VACCINE

BACKGROUND

Tuberculosis (TB) is one of the major public health problems in Nepal and immunisation for preventing tuberculosis is a high priority public health intervention.[1]

Despite being a preventable and usually curable disease, tuberculosis (TB) has reclaimed its position as the World's leading cause of death from a single infectious agent, after being surpassed by COVID-19 for three consecutive years [2], and caused almost twice as many deaths as HIV/AIDS. More than 10.8 million people continue to fall ill with TB every year and the numbers has been rising since 2023.[3] In view of the rising cases and deaths, urgent action is required for which a goal of ending TB epidemic by 2030 has been adopted by all Member States of the United Nations (UN) and the World Health Organization. [2, 4]

EPIDEMIOLOGY AND DISEASE BURDEN IN NEPAL

Tuberculosis (TB) is an infectious disease caused by the bacteria of *Mycobacterium tuberculosis complex,* which includes *Mycobacterium tuberculosis, M. bovis*, *M. africanum*, *M. canettii*, *M. caprae*, *M. microti*, and *M. pinnipedii,* causing infections in humans and animals. Most infected individuals show no disease symptoms; however, it can be fatal if not treated. In children, tuberculosis occurs most commonly in the age group of below 5yrs.[4]

Pulmonary tuberculosis (PTB) is the most common form of TB in children with extra-pulmonary TB accounting for around 30–40% of cases. Children who develop the disease, usually do so within the first year following infection and therefore, childhood TB is an indicator of ongoing transmission of *M. tuberculosis* in the community.[5]

Globally, 1.7 billion people are estimated to be infected with *M. tuberculosis* and 5–15% of them are likely to develop tubercular disease during their lifetime. [6]

Majority of cases remain undiagnosed in children as cough and sputum production is less common and the disease is paucibacillary. In the first year of primary infection, risk of developing a progressive disease in children such as meningitis and miliary TB accounts for 40–60%. [7, 8]

In 2023, an estimated 10.8 million people fell ill with TB worldwide, of which 55% were men, 33% were women and 12% were children and young adolescents (WHO global TB report). People living with HIV accounted for 6.1% of the total cases. The TB incidence rate is estimated to have increased by 4.6% between 2020 and 2023, reversing declines of about 2% per year between 2010 and 2020.[3]

Globally TB caused an estimated 1.25 million deaths, including 161 000 people with HIV in 2023, down from 1.32 million deaths estimated in 2022. Eight countries accounted for more than two thirds of the global deaths: India, Indonesia, China, Philippines, Pakistan, Nigeria, Bangladesh, and the Democratic Republic of Congo. The top five countries accounted for 56% of the global deaths. [3]

TB remains a significant public health challenge in Nepal as well. It is among the top ten causes of deaths. As per the global TB report, Nepal accounts for an estimated 68000 cases of TB and 16000 deaths in 2023. In 2080/81 (2023/24), the national notifications were 40776 with 23% of them being elderly people aged 65 years and over. Three provinces (Madhesh, Bagmati and Lumbini) contributed to 68% of the annual TB notifications. The treatment success rate for Drug Susceptible TB (DS-TB) was 92% and the death rate was 3.3%.[9]

ABOUT THE VACCINE

Bacillus Calmette–Guérin vaccine is one of the oldest vaccines, first used in humans in 1921.[10] A large scale use of BCG vaccine started when WHO initiated the program of expanded program on Immunisation (EPI) in 1974. With the Alma Ata declaration of 'Health for All', expanded program on immunisation spread across the globe with immunisation as a key focus area of Primary Health Care. Nepal started implementation of the EPI program with inclusion of BCG from 1979.[11] It is the first vaccine to be introduced in NIP of Nepal. BCG vaccine is derived from the bovine TB strain.[10] It continues to be the only effective vaccine against TB. The two common strains in use are Copenhagen (Danish 1331) and Pasteur, of which the former was produced in India at the BCG Vaccine Laboratory, Guindy, Tamil Nadu till recently.

BCG vaccine currently in use in Nepal's immunisation program is supplied as a lyophilised (freeze-dried) preparation in vacuum sealed, multi-dose vials with normal saline as diluent. The reconstituted vaccine contains some dead and 0.1–0.4 million live viable bacilli per dose. The vaccine is light sensitive and deteriorates on exposure to ultraviolet rays. The vaccine does not contain any preservative and bacterial contamination and consequent toxic shock syndrome may occur if kept for long after reconstitution.[12, 13]

VACCINE INDICATION

For a healthy child: from birth till one month of age, preferably within 1 week after birth.

VACCINATION IN SPECIAL CIRCUMSTANCES / POPULATIONS

HIV-infected Infants

Evidence indicates that children born with HIV and vaccinated with BCG at birth face a higher risk of developing disseminated BCG disease if they later develop AIDS. BCG is a safe vaccine in immunocompetent infants, but severe AEFI can occur in HIV-infected infants. However, early initiation of antiretroviral therapy (ART), before immunological and/or clinical HIV progression, has been shown to substantially reduce the risk of Bacillus Calmette-Guerin Immune Reconstitution Inflammatory Syndrome (BCG-IRIS) regional adenitis.[14] Observational data from a cohort study in South Africa confirmed a low risk: 0.6% of the 12748 children receiving ART and vaccinated with BCG developed lymphadenitis.[10, 14] In some

countries, delays in diagnosis of HIV infection in HIV-exposed infants result in further delay in BCG vaccination. The impact of such delays on HIV-positive children and on the incidence of TB is yet to be determined.

Preterm Infants and Low-birth Weight Infants

Limited evidence from small observational studies in high TB endemic areas suggests that BCG vaccination at birth is safe and effective for healthy preterm infants born at 32–36 weeks of gestation.[14,15-20] However; data on BCG vaccination for very preterm and extremely preterm infants are scarce.[21] Three randomised controlled trials (RCTs) in West Africa, a high TB endemic region, indicated that early BCG vaccination of low-birth-weight infants (down to approximately 1500 g) positively impacts overall infant mortality, though safety and efficacy were not specifically studied.[14,21-24] For very low birth weight and extremely low birth weight infants, there is insufficient data to evaluate the safety, immunogenicity, and efficacy of BCG vaccination.[25]

CONTRAINDICATIONS FOR BCG VACCINE

- BCG vaccine is contraindicated in patients with a hypersensitivity to any component of the vaccine.
- Children with known or suspected HIV infection, who are symptomatic or have laboratory evidence of immunosuppression
- Children under immunosuppressive therapy such as corticosteroids including monoclonal antibodies against tumor necrosis factor (TNF), radiation, alkylating agent
- Children with impaired immunity, known or suspected congenital immunodeficiency, leukemia or generalised malignant disease
- Pregnant women- As BCG vaccine is a live vaccine, it is not recommended in pregnancy though it has not been shown to harm the fetus. [10]

PRECAUTIONS

The multidose presentation of BCG vaccine necessitates careful handling. Because reconstituted BCG lacks preservatives, opened vials pose a contamination risk and must be discarded promptly – either at the session's end or within 6 hours, whichever comes first. Non-compliance with national storage and safety protocols can lead to bacterial contamination and severe adverse events like toxic shock syndrome. Recognizing that BCG contains live mycobacteria, strict aseptic procedures are essential throughout its preparation and administration to ensure patient safety.[10]

CO- ADMINISTRATION WITH OTHER VACCINES

Evidence have shown that BCG vaccine can be safely co-administered with diphtheria-pertussis-tetanus (DTP), polio, hepatitis B, Haemophilus influenzae type

b (Hib) and Measles Rubella (MR) vaccines.[10, 26] There is no evidence to suggest reduced immunogenicity, and no safety concerns have been reported. [26]

ADVERSE EVENTS FOLLOWING IMMUNISATION

BCG Lymphadenitis

Local BCG vaccine side effects include abscesses, injection site reactions, lymph node swelling (lymphadenopathy), and slow healing at the injection site. BCG lymphadenitis, significant swelling of armpit, collarbone, or lower neck lymph nodes after vaccination, needs medical attention. Suppurative lymphadenitis (pus-forming) is less common (100-1,000 per million doses) than the non-suppurative form (periodic monitoring needed). Suppurative lymphadenitis involves increasing swelling, softening, fluid collection, and skin changes (redness, hardness). Untreated, it can rupture, drain pus, form sinuses, and take months to heal.[27, 28]

Disseminated BCG Infection

It is diagnosed definitively based on the presence of all three of the following features:

1. BCG cultured and identified by culture, biochemical methods
2. Dissemination evidenced by either A or B:
    A. Positive blood or bone marrow culture
    B. Evidence of infection at two or more anatomic sites beyond the region of vaccination
3. A systemic syndrome compatible with mycobacterial disease, e.g., fever, weight loss, anemia, and death.

The occurrence of disseminated BCG infection necessitates investigations for immunodeficiency conditions such as severe combined immunodeficiencies (SCIDs), chronic granulomatous disease (CGD), complete DiGeorge syndrome, and Mendelian susceptibility to mycobacterial disease (MSMD). These conditions may involve underlying genetic defects, including NF-kappa B essential modulator (NEMO), tyrosine kinase 2 (TYK2), and HIV.[27, 28]

BCG-induced osteitis or osteomyelitis

Rare but serious BCG side effect: bone infection (osteitis), 0.01-30 per million doses, usually resolves well. Osteitis in infants suggests immune issues. Treatment is often surgery and 3-4 anti-TB drugs (e.g., isoniazid, rifampicin, ethambutol, streptomycin, clarithromycin; avoid pyrazinamide). No standard treatment guidelines exist.[27]

SCHEDULE AND DOSES AND ROUTE OF ADMINISTRATION

Nepal's national BCG policy: Single dose immediately after birth for healthy newborns. Any child missing BCG vaccine at birth should be vaccinated at the

earliest opportunity. Nepal's missed vaccination schedule allows BCG vaccination in routine immunisation upto <5 years of age if missed.[29]

According to WHO guidance, a single catch-up BCG vaccination (following a negative TB test) is advised for individuals in the following situations:

- Residing in high TB risk areas,
- Moving to high TB risk areas, and
- For at-risk workers in all areas who have not been vaccinated before.

Administer by trained staff intradermally (tuberculin syringe, 26G/27G needle) on the right shoulder (deltoid), cleaned with sterile saline.

Dosage: 0.05 mL (<1 year), 0.1 mL (>1 year), not weight-based.

Correct injection forms a 5 mm wheal. Expect a papule (2-3 weeks), growing (4-8 mm, 5-6 weeks), often ulcerating and scarring (6-12 weeks). Ulcer may persist. No scar in 10% doesn't mean failure.[30]

VACCINE EFFICACY

BCG Vaccine Efficacy and Effectiveness against Pulmonary Tuberculosis

The efficacy and effectiveness of BCG vaccination against TB vary significantly across different studies and populations. Several observational studies support the findings from randomised controlled trials (RCTs) that BCG vaccination provides high protection against pulmonary tuberculosis (PTB) in neonates and moderate protection in school-age children who are TST-negative. A systematic review concluded that protection from primary infant BCG vaccination could last up to 15 years in some populations. [31]

Efficacy and Effectiveness against Meningeal and Miliary Tuberculosis:

Evidence from a meta-analysis of six randomised controlled trials (RCTs) demonstrated a high degree of vaccine efficacy, reducing severe TB in vaccinated individuals by 85%. The highest protection was observed in those immunised during the neonatal period, with a 90% reduction in severe TB, and in school-age children who were TST-negative, with a 92% reduction in severe disease. [31]

BCG Vaccine Protection against Primary Infection with M. Tuberculosis:

BCG-vaccinated children exposed to persons with open PTB had 19% less infection than unvaccinated children. [32]

Efficacy and Effectiveness against Other Mycobacterial Diseases

BCG vaccination has been effective in preventing leprosy, with an overall pooled relative risk (RR) of 0.45 (95% CI: 0.34–0.56). In African settings, BCG has approximately 50% efficacy (RR: 0.5, 95% CI: 0.37–0.69) against Buruli ulcer. Additionally, BCG provides protection against nontuberculous mycobacteria (NTM) lymphadenitis in children.[33-37]

Nonspecific Effects of BCG including COVID-19

Observational studies have noted that countries with long-term national BCG vaccination policies experienced lower severity and mortality rates from COVID-19.[38-40]

BCG REVACCINATION IN ADOLESCENTS AND ADULTS

Various studies have shown little to no evidence that BCG revaccination in adolescents and adults, following primary BCG vaccination in infancy, provides protection against M. tuberculosis infection or TB disease.[41-43] However, a study in Malawi found that BCG revaccination in both children and adults offered an additional 49% protection (95% CI: 0–75%). These differences between studies and populations may be due to varying patterns of natural exposure to different mycobacterial species and other confounding factors.[40]

VACCINE STORAGE & PREPARATION

The vaccine is sensitive to light and deteriorates when exposed to ultraviolet rays. In its lyophilised (freeze-dried) form, it can be stored at 2–8°C for up to 12 months without losing potency. The supplied diluent should be used for reconstitution, but sterile normal saline can be used if the diluent is unavailable. The vaccine vial includes a vaccine vial monitor (VVM) to check its potency.

The reconstituted vaccine should be stored at 2–8°C, protected from light, and discarded within 4–6 hours of reconstitution. WHO recommends that all BCG vaccines used in immunisation programs adhere to WHO standards.

VACCINE SAFETY

BCG vaccination is generally safe. Approximately 95% of recipients develop a reaction at the injection site, which starts as a papule and may progress to ulceration. Healing typically occurs within 2–4 months, leaving a superficial scar. This reaction is considered normal. [32, 44, 45]

Mild reactions to BCG vaccination are mostly local, sometimes accompanied by regional manifestations. Local adverse effects include abscess formation, injection site reactions, lymphadenopathy, and delayed healing of the ulcer at the vaccination site. Severe complications can include osteitis/osteomyelitis and disseminated BCG infection.[35, 44]

ABSENCE OF SCAR FOLLOWING NEONATAL BCG VACCINATION

Studies from India have reported scar failure rates of 8.6% and 10% following neonatal BCG vaccination.[45] In a study of 655 children, 591 (90.2%) developed a scar. Among the 64 children who did not develop a scar, positive in vitro responses to PPD were observed in 88.2%, 94.7%, and 80% of infants vaccinated at 0–1 day, 2–30 days, and 31–90 days, respectively. Therefore, the absence of a BCG scar at the vaccination site does not necessarily indicate immunisation failure, as most of these children show positive in vitro lymphocyte migration inhibition (LMI) responses.[46]

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DIPHTHERIA - PERTUSSIS - TETANUS

Dr. Neema Shrestha

BACKGROUND

Vaccine against Diphtheria – Pertussis – Tetanus (DPT) was introduced in the National Immunisation Schedule of Nepal in 1977/78. Since the introduction of the vaccine, mortality and morbidity due to diphtheria, pertussis and tetanus has drastically reduced in Nepal. Completion of three primary doses and booster doses are required to confer protection against these illnesses.

DIPHTHERIA

Pathogenesis

Diphtheria is an acute infectious disease caused by a gram – positive bacilli *Corynebacterium diphtheriae.* The word diphtheria come from the Greek work for leather, referring to the tough pharyngeal membrane which is a hallmark of the disease.

The disease is caused by a toxin produced by the bacterium which inhibits cellular protein synthesis and is responsible for local tissue destruction and formation of the pseudo-membrane. They mostly affect the throat and the tonsils. Toxin produced at the membrane site is absorbed into the bloodstream and subsequently distributed to body tissues. It is responsible for major complications such as myocarditis, polyneuropathies, and nephritis, and can also cause thrombocytopenia.[1] Incubation period for diphtheria is 2 – 5 days (1 – 10 days). Transmission of *C. diphtheria* occurs from person to person via respiratory droplets or close contact. Typical symptoms of the infection include a sore throat, fever, swollen neck glands and weakness. Within 2–3 days of infection, the dead tissue in the respiratory tract forms a thick, grey coating that can cover tissues in the nose, tonsils and throat, making it hard to breathe and swallow.[2]

Epidemiology

Although commonly perceived as a childhood illness affecting individuals under 12, susceptibility to diphtheria extends to adults, particularly around the age of 40 and those with underlying health issues. The natural decline of immunity over time means that individuals who are not up-to-date on their vaccinations and boosters face an elevated risk of contracting the infection.[3]

PERTUSSIS

Pertussis, or whooping cough, is an acute infectious disease caused by the bacterium *Bordetella pertussis.*

Pathogenesis

B. pertussis is a small, aerobic gram-negative rod. *B. pertussis* produces multiple antigenic and biologically active products, including pertussis toxin (PT), filamentous hemagglutinin (FHA), agglutinogens, adenylate cyclase, pertactin, and tracheal cytotoxin. These products are responsible for the clinical features of pertussis disease. An immune response to one or more of these products produces immunity following infection. Immunity following B. pertussis infection is not permanent. Pertussis is primarily a toxin-mediated disease. The bacteria attach to the cilia of the respiratory epithelial cells, produce toxins that paralyse the cilia, and cause inflammation of the respiratory tract, which interferes with the clearing of pulmonary secretions. The incubation period of pertussis is commonly 7 to 10 days (4 - 21 days). The clinical course of the illness is divided into three stages: catarrhal, paroxysmal, and convalescent. Transmission most commonly occurs person-to-person through contact with respiratory droplets, or by contact with airborne droplets of respiratory secretions.[4]

Epidemiology

Pertussis remains a major health problem among children worldwide. Data from a modeling study suggest that more than 24 million new pertussis cases occurred globally among children younger than age 5 years in 2014 and caused an estimated 160,700 deaths.[4] The World Health Organization estimates that there are 20–40 million cases of pertussis around the world annually, of which 90% occur in developing countries.

TETANUS

Tetanus is an acute, often fatal, disease caused by an exotoxin produced by the bacterium *Clostridium tetani*. It is characterised by generalised rigidity and convulsive spasms of skeletal muscles. The muscle stiffness usually begins in the jaw (lockjaw) and neck and then becomes generalised. The *C. tetani* bacterium is a spore-forming, gram-positive, slender, anaerobic rod. The organism is sensitive to heat and cannot survive in the presence of oxygen. The spores, in contrast, are extremely resistant to heat and the usual antiseptics.[5]

Pathogenesis

C. tetani usually enters the body through a wound. In the presence of anaerobic conditions, the spores germinate. *C. tetani* produces two exotoxins, tetanolysin and tetanospasmin. Tetanospasmin is a neurotoxin and causes the clinical manifestations of tetanus. Toxins are produced and disseminated via blood and lymphatics. Tetanospasmin, also referred to as tetanus toxin, acts at several sites within the central nervous system, including peripheral motor end plates, the spinal cord, and the brain, and in the sympathetic nervous system. The typical clinical manifestations of tetanus are caused when tetanus toxin interferes with the release of neurotransmitters, blocking inhibitor impulses. This leads to unopposed muscle contraction and spasm. Seizures may occur, and the autonomic nervous system may also be affected.[5]

Epidemiology

Although tetanus affects people of all ages, the highest prevalence is seen in newborns and young people. The incidence of neonatal tetanus is decreasing due to routine vaccination worldwide, which is combined with other vaccines, pertussis, and diphtheria (DPT). In 2023, 84% of infants worldwide were vaccinated with 3 doses of diphtheria-tetanus-pertussis (DTP) containing vaccine.[5] The World Health Organization (WHO) estimated that there were 34,000 neonatal tetanus (NT) deaths worldwide in 2015. This 96% reduction from an estimated 787000 NT deaths since 1988 represents significant progress towards the maternal and neonatal tetanus elimination (MNTE) goal.[6]

DISEASE BURDEN IN NEPAL

Historically, Diphtheria, Pertussis, and Tetanus were significant causes of morbidity and mortality in Nepal. However, with the introduction and expansion of the national immunisation program (EPI) since 1989, there has been a substantial decline in the incidence of these vaccine-preventable diseases. Despite progress, these diseases have not been entirely eliminated, and sporadic cases and outbreaks can still occur.

Vaccine preventable diseases reported in Nepal 2020- 2022 [7]

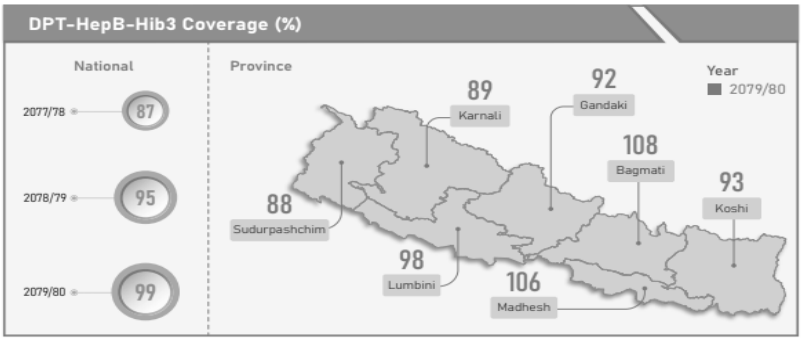
Year	Diphtheria	Pertussis	Total Tetanus (Neonatal Tetanus)
2020	38	4224	333 (3)
2021	29	4588	927 (2)
2022	95	4828	768 (3)

Immunisation coverage for Nepal 2019-2023 [8]

Year	BCG coverage (%)	DPT 3 coverage (%)
2019	96	93
2021	92	84
2022	95	91
2023	96	90

Overall, 80% of children age 12–23 months are fully vaccinated with basic antigens. Ninety-five percent (95%) of children age 12–23 months received BCG vaccine, 89% received the third dose of DTP-HepB-Hib, 86% received the third dose of OPV, and 89% received a dose of MR in the year 2022.[8]

DPT-HepB-Hib3 Coverage [9]



VACCINES

DTwP is composed of tetanus and diphtheria toxoids as well as killed whole-cell pertussis (wP) bacilli adsorbed on insoluble aluminum salts. In Nepal, the DPT (whole-cell) vaccine is administered as part of National Immunisation Schedule and acellular DTaP (aP) vaccine is licensed for use.

Acellular pertussis (aP) vaccines demonstrate efficacy in clinical trials; however, observational data suggest that incorporating at least one dose of whole-cell pertussis (wP) vaccine in routine immunisation schedules correlates with enhanced and more durable disease protection. Conversely, wP vaccines exhibit greater reactogenicity and a higher incidence of adverse events. Mechanistically, wP vaccines more closely mimic natural *Bordetella pertussis* infection compared to aP vaccines. In contrast to natural infection and wP vaccination, aP vaccines elicit limited cellular immunity and Th1 responses, which are critical for bacterial clearance and sustained protection. Aluminum-adjuvanted aP vaccines preferentially stimulate Th2 responses, resulting in elevated antibody titers that may not accurately reflect protective immunity. Furthermore, aP vaccination induces a significant decline in antibody levels between doses despite an initial strong response. wP vaccines are licensed for children younger than 7 years of age. Due to their safety profile, aP vaccines have offered the possibility of vaccinating older children, adolescents, and adults.[10] A study found reduced-dose aP vaccine efficacy to be around 85% for laboratory-confirmed diseases when the vaccine was given to adolescents and adults. [11]

DwPT Vaccine

The vaccine includes diphtheria and tetanus toxoids (inactivated toxins) and whole-cell pertussis components. This combination stimulates the immune system to develop protection against all three diseases. The content of diphtheria toxoid varies from 20 to 30 Lf and that of tetanus toxoid varies from 5 to 25 Lf per dose. Each dose of 0.5 ml contains: Diphtheria Toxoid ≤ 25 Lf (≥ 30 IU), Tetanus Toxoid ≥ 2.5 Lf (≥ 40 IU), B. pertussis (whole cell) ≤ 16 OU (≥ 4.0 IU), HBsAg (rDNA) ≥ 10 mcg, purified capsular Hib Polysaccharide (PRP), Conjugated to Tetanus Toxoid (carrier protein) 10 mcg, Adsorbed on Aluminium Phosphate, Al^{+++} ≤ 1.25 mg, and Preservative: Thiomersal 0.005%.

DwPT vaccines have been shown to be effective in preventing diphtheria, tetanus, and pertussis. The whole-cell pertussis component provides robust immunity against whooping cough. While effective, the whole-cell pertussis component is associated with higher rates of local reactions, such as pain, redness, and swelling at the injection site, compared to acellular pertussis vaccines (DTaP). Systemic reactions like fever may also be more common. However, serious adverse events are rare. DwPT vaccines are widely used in many countries, especially in national immunisation programs. Other countries also use it as their recommended vaccine schedule similar to our national schedule.[12]

DTaP Vaccines

The introduction of the whole cell vaccines paid rich dividends in terms of decline in disease morbidity and mortality. Once disease rates declined, concerns about frequent local side-effects, as well as public anxiety about the safety of wP vaccines, led to the development of aP vaccines in Japan in 1981. These were licensed in the US in 1996 and have now replaced the whole cell vaccines in many developed countries.

All aP vaccines are associated with significantly lesser side-effects, and other advantage of the aP vaccines is the reproducible production process with its use of purified antigens and the removal of LPS and other parts of the bacterial cell wall during the purification of soluble antigenic material. These vaccines contain ≥ 1 of the separately purified antigens pertussis toxin (PT), filamentous hemagglutinin (FHA), pertactin (PRN), and fimbrial hemagglutinins 1, 2 & 3 (FIM type 2 and type 3).

DwPT vs DaPT

Comparison with DTaP Vaccines: Acellular pertussis vaccines (DTaP) contain purified components of the pertussis bacterium and are associated with fewer side effects. However, some studies suggest that immunity from DTaP vaccines may wane more quickly than that from whole-cell vaccines, potentially leading to increased susceptibility to pertussis over time.

EFFICACY

The pooled efficacy of wP vaccine against pertussis in children was 78% according to a systematic review in 2003.[3] The efficacy of wP alone ranged from 61% to 89%, and the efficacy of combination DTwP vaccines ranged from 46% to 92%.[3] Immunity against all three components wanes over the next 6–12 years and thus regular boosting is needed.

The efficacy and duration of protection with DTaP vaccines against diphtheria/ tetanus and pertussis is similar to that afforded by the whole cell vaccines. There is considerable controversy on the relative efficacy of different aP vaccines with varying number of components.

A Cochrane review by Zhang et al after studying 6 aP vaccine efficacy trials and 52 safety trials concluded that the efficacy of multicomponent (≥ 3) aP vaccines varied from 84% to 85% in preventing 'typical whooping cough' and from 71% to 78% in

preventing mild disease. In contrast, the efficacy of one- and two-component vaccines varied from 59% to 75% against 'typical whooping cough' and from 13% to 54% against mild disease. [4] Though a few countries have demonstrated high levels of effectiveness of mono- and bi- component aP products in preventing pertussis by employing them in their immunisation programs,[5] the available evidence overwhelmingly favours multi-component (≥ 3) aP vaccines over mono- or bi- component aP vaccines.[6]

ADVERSE EVENTS FOLLOWING IMMUNISATION

Pertussis vaccination, particularly with whole-cell (wP) formulations, is associated with common minor adverse effects like local reactions, fever, fussiness, anorexia, and vomiting in approximately half of recipients after primary doses. These effects are largely attributed to the pertussis component. While serious adverse events, including fever >40.5°C (0.2–4.4 per 1000 doses), persistent crying (4–8.8 per 1000 doses), hypotonic hyporesponsive episodes (HHE) (0.06–0.8 per 1000 doses), seizures (0.16–0.39 per 1000 doses), and encephalopathy (0.007 per 1000 doses), have been reported with DTwP vaccines, they are rare. Historical concerns linking wP vaccines to catastrophic outcomes like SIDS and autism have been definitively disproven. **Absolute contraindications to pertussis vaccination include anaphylaxis or encephalopathy within 7 days of a prior DTwP dose**. Precautions for subsequent DTwP doses include prolonged crying, high fever (>40.5°C), HHE within 48 hours, and seizures within 72 hours, as these events typically do not recur and lack evidence of permanent sequelae. Progressive neurological illnesses are a relative contraindication to the initial DTwP dose, but stable neurological disorders are not. Acellular pertussis (DTaP) vaccines demonstrate a significantly reduced incidence of both minor and major adverse effects compared to wP vaccines. The absolute contraindications for DTaP are the same as for wP vaccines. Serious adverse events following prior pertussis vaccination, though less frequent with DTaP, are managed as precautions.

SCHEDULE

National schedule: Three primary doses at 6, 10 and 14 weeks.

NEPAS recommends two boosters of DPT at 18-24 months and at 4-6 years.

CDC schedule: 3 primary doses given at 2, 4 and 6 months of age along with 2 boosters at 15–18 months and at 4-6 years.

DOSE & ROUTE OF ADMINISTRATION

0.5 ml intramuscularly and the preferred site is the anterolateral aspect of the thigh. The immunogenicity (protective titer for diphtheria > 0.1 IU/ml and for tetanus > 0.01 IU/ml) and effectiveness against diphtheria/ tetanus of three doses of the vaccine exceeds 95%.

STORAGE

The vaccine is stored at 2 to 8°C and never be frozen, and if frozen accidentally, should be discarded.

TETANUS TOXOID (TT)

Antibodies to tetanus decline over time and hence regular boosting is needed to ensure adequate levels of antibodies during any apparent/inapparent exposure to tetanus bacilli/toxin. TT containing 5 Lf of toxoid is one of the most heat stable and commonly used vaccines. The vaccine should be stored between 2 and 8°C and the dose is 0.5 ml intramuscularly. [7] Administration of boosters more frequently than indicated leads to increased frequency and severity of local and systemic reactions as the preformed antitoxin binds with the toxoid and leads to immune complex-mediated reactions (Swollen limbs & Arthus type 2 reactions).

Recommendations for use

The role of standalone TT vaccines is diminishing and replacement with Td/Tdap is recommended for more comprehensive protection. In individuals who have completed primary and booster vaccination with DTwP/DTaP, TT boosters every 10 years provide sufficient protection.[13]

TT/Td IN PREGNANCY

WHO has evolved exhaustive guidelines for administration of TT in pregnant women and recommends replacement of TT with Td in a phased manner.[7]

In national immunisation schedule we give Td in Nepal.

- For **the first pregnancy:** 2 doses are recommended.

- **Td 1:** As early as possible during pregnancy, preferably after the first trimester (around 20 weeks of gestation) for better stability of the pregnancy.
- **Td 2:** At least 4 weeks after the first dose (Td 1) and ideally at least one month before the expected delivery date to ensure the development of antibodies that can be transferred to the baby.

- For **the second pregnancy onwards:** 1 booster dose is recommended if the previous pregnancy was within the last 3 years and the woman received the complete 2-dose series in the prior pregnancy. This booster dose should also be given preferably after the first trimester.

Unimmunised: For pregnant women who have not been previously immunised, two doses of TT at least one month apart should be given during pregnancy so that protective antibodies in adequate titers are transferred to the newborn for prevention of neonatal tetanus. The first dose should be administered at the time of first contact/ as early as possible and the second dose of TT should be administered 1 month later and at least 2 weeks before delivery. A single dose of TT would suffice for subsequent pregnancies that occur in the next 5 years; thereafter, 2 doses of TT would again be necessary.

Fully immunised: Five childhood doses (3 primary doses plus two boosters) and one adolescent booster Tdap: No further doses are necessary in pregnancy.

Partially immunised: Three primary doses: For women who have received 3 primary doses in infancy, two doses during the 1st pregnancy are indicated. The 2nd pregnancy requires 1 more dose and gives lasting protection for the reproductive years.

Three primary and one childhood booster: 1 dose each in the first and second pregnancy provide lasting protection.

Three primary and two childhood boosters: Only 1 dose in the first pregnancy provides lasting protection.

TT IN WOUND MANAGEMENT

All patients with skin wounds or infections require tetanus prophylaxis evaluation. Proper wound care, including cleaning, removal of dead tissue, irrigation, and drainage is vital to prevent an environment conducive to tetanus toxin production. The indications for tetanus toxoid (TT) and tetanus immunoglobulin (TIG) are outlined in Table 1. It is recommended to use Td or Tdap instead of TT for boosters and catch-up vaccinations. Evidence indicates that tetanus is highly unlikely in individuals who have received three or more vaccine doses and a booster during wound management, generally making passive protection with TIG unnecessary unless the patient is immunocompromised. For completely unimmunised children, a catch-up schedule of three TT doses at 0, 1, and 6 months should be provided.

Partially immunised children need enough doses to complete a three-dose series. Children with unknown or undocumented vaccination histories should be treated as unimmunised. For more comprehensive protection, it is recommended to replace TT booster doses given during wound management and for catch-up vaccination with DTwP, DTaP, Td, or Tdap, depending on the child's age and prior vaccinations.

Table 1: Tetanus prophylaxis in wound management

	Dose of TT	Clean, minor wounds	All other wounds	Given in past
	TT	TIG*	TT	TIG*
Unknown, < 3 doses, immunodeficient	Yes	Yes	Yes	Yes
≥ 3 doses	No**	No	No***	No

Including, but not limited to, wounds contaminated with dirt, feces, soil, saliva; puncture wounds; avulsions; and wounds resulting from missiles, crushing, burns, and frostbite.

* TIG: Tetanus immunoglobulin (250–500 IU IM)

** Yes, if more than 10 years since last dose

*** Yes, if more than 5 years since last dose

DT VACCINE

This vaccine comprises diphtheria and tetanus toxoid in similar amounts as in DTwP/DTaP, should be stored at 2 to 8^0C and the dose is 0.5 ml intramuscularly. It is recommended in children below 7 years of age where pertussis vaccination is contraindicated.

Td/Tdap VACCINE

Studies show that diphtheria antibody levels decline over time resulting in increasing susceptibility of adolescents and adults to diphtheria. For diphtheria, the average duration of protection is about 10 years following a primary series of 3 doses of diphtheria toxoid.[9] Good childhood vaccination coverage (at least 70%) provides herd effect by reducing circulation of toxigenic strains and prevents outbreaks in adults despite susceptibility. When childhood vaccination programs break down as happened in the former Soviet Union in the early 1990s, massive outbreaks of diphtheria involving primarily adults have occurred. Thus, it is desirable to regularly boost adult immunity against diphtheria in addition to tetanus every 10 years. Td contains the usual dose of tetanus toxoid and only 2 units of

diphtheria toxoid, is stored at 2 to 8°C and is administered intramuscularly in a dose of 0.5 ml.

The DTwP, DTaP and DT vaccines cannot be used in children aged 7 years and above due to increased reactogenicity due to the higher diphtheria toxoid and pertussis components. So, Td or Tdap vaccine is indicated as replacement for DTwP/ DTaP/DT for catch-up vaccination in those aged above 7 years and Td as replacement for TT in all situations where TT is given.

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HAEMOPHILUS INFLUENZAE TYPE b VACCINE

Dr. Poonam Sharma

BACKGROUND

Haemophilus influenzae type b (Hib) is a bacterium causing life-threatening infections, and was the leading cause of bacterial meningitis and severe pneumonia primarily in children under 5 years. Other diseases caused by the organism include sepsis, epiglottitis, septic arthritis and cellulitis. [1]

PATHOGENESIS

Hib bacteria is transmitted via respiratory droplets and can colonise the throat and later invade the bloodstream, leading to severe infections. Hib is an encapsulated bacterium which protects it from the host's immune system and allows it to enter the bloodstream, reaching the brain, lungs, joints, and other organs, causing serious infections.[1]

EPIDEMIOLOGY

There were more than 20000 cases of Hib-related meningitis and pneumonia in children under five years in Nepal before the introduction of Hib vaccine in Nepal with a high fatality rate of 50%. The sequel of brain damage and hearing loss was also high in survivors. [2]

With the introduction of vaccine against the bacteria, there has been more than 90% reduction in Hib related infections leading to significant decrease in childhood mortality from meningitis and pneumonia. Herd immunity has also helped in reduction of overall bacterial transmission. [3]

DISEASE BURDEN IN NEPAL

Hib vaccine was introduced in Nepal in 2009, before which it was the major cause of under-five mortality with lack of proper surveillance making many cases undiagnosed or untreated. Once there was introduction of Hib vaccine in Nepal's National Immunisation Program, Hib-related meningitis cases dropped by over 80%. There was also significant reduction in pneumonia deaths among vaccinated children and improved overall childhood survival rates. Hib vaccine has drastically reduced childhood deaths in Nepal. Early vaccination is essential to prevent severe infections like meningitis and pneumonia. Ensuring full immunisation coverage will further eliminate Hib disease burden. [2]

HIB VACCINE

All Hib vaccines are conjugated vaccines where the Hib capsular polysaccharide (polyribosylribitol phosphate or PRP) is conjugated with a protein carrier so as to provide protection in the early years of life when it is most needed. It is available as a monovalent vaccine (only Hib) or as a pentavalent vaccine (DTP-HepB-Hib). It is highly safe and has been used for over two decades globally.

INDICATION

All infants should receive the Hib vaccine as part of routine immunisation including premature babies, children with immunodeficiency (HIV/AIDS, cancer) and asplenic children (those without a spleen due to disease/surgery).[1, 3]

CONTRAINDICATION

Although there are few contraindications, it is avoided in rare cases of severe allergic reaction (anaphylaxis) to a previous dose of Hib vaccine or known hypersensitivity to any vaccine component.[1, 3]

PRECAUTIONS

The vaccine can be given safely in mild illness (cold, fever <38.5°C). However, it is avoided until the child recovers in cases of moderate to severe illness (high fever, respiratory distress).[1,3]

ADVERSE EVENTS FOLLOWING IMMUNISATION

Common side effects of the Hib vaccination include pain, redness, and swelling at the injection site (observed in 20-25% of cases), and mild fever in some instances. Rarely, a child may experience a high fever exceeding 39°C, and allergic reactions (anaphylaxis) are extremely rare. Oral paracetamol and cold compression are common approaches for managing minor Adverse Events Following Immunisation (AEFI), while medical attention is necessary for severe reactions.

SCHEDULE AND DOSES

National Immunisation Schedule:

Hib vaccine is given as part of the pentavalent vaccine (DTP-HepB-Hib) at: 6, 10 and 14 weeks. No booster dose is given for healthy children in NIP.

CDC schedule:

For routine Hib vaccination, the CDC recommends a 3 dose primary series of Hib vaccines starting at 2, 4 and 6 months of age, with a booster dose at 12-15 months.[3]

Booster Dose:

NEPAS recommends a booster dose at 18-24months of age to complete the Hib vaccination series. An extra dose (5th) can be allowed if combination vaccine is given at 4-6Y.

Timing: The booster dose should be administered at least 8 weeks after the most recent Hib vaccination.

Catch up vaccination [4]

Catch-up is recommended till 5 years of age

6–12 months: Two primary doses 4 weeks apart and one booster

12–15 months: One primary dose and one booster

Above 15 months: Single dose

If the first dose was administered at age 7 through 11 months, administer the second dose at least 4 weeks later and a final dose at age 12–18 months at least 8 weeks after the second dose. [4]

Catch-up vaccination is not recommended for healthy children >5 years. However, the vaccine should be administered to all individuals with functional or anatomic hyposplenia irrespective of age. [4]

ROUTE OF ADMINISTRATION

Hib vaccine is given as an Intramuscular (IM) injection. The preferred injection site in infants is anterolateral thigh and deltoid muscle in older children.

VACCINE EFFECACY

Developed countries where the vaccine was introduced for universal immunisation have witnessed virtual elimination of Hib disease with no serotype replacement. The vaccine has also been shown to impart herd protection by reducing nasopharyngeal carriage. Hib vaccine has a 95-100% protection after 3 doses. It also has herd immunity effect; thus, un-vaccinated children also benefit due to reduced bacterial transmission. Primary immunisation with pentavalent vaccine is reported to induce an excellent immunity lasting till the 2nd year of life. [4]

It is also recognized now that immunological memory is insufficient for continuous protection against Hib disease. Hence, a booster dose is mandatory for sustained protection. A booster dose with diphtheria, tetanus, and whole-cell pertussis (DTwP)-Hib vaccine effectuated a good anamnestic response to all vaccine components, being especially strong for Hib in children previously vaccinated with pentavalent vaccine. [4]

VACCINE STORAGE AND SAFETY

Hib vaccine is stored in refrigerator at 2°C to 8°C. Freezing destroys vaccine efficacy; thus, it is advised not to freeze the vaccine. The middle shelf of the refrigerator is preferred for storage to avoid temperature fluctuations.[4]

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POLIO VACCINE

Dr. Luna Amatya

BACKGROUND

Poliomyelitis (Polio) is a highly infectious viral illness that largely affects children under 5 years of age leading to permanent disability. Global vaccination efforts have drastically reduced the incidence of polio, bringing the disease to the brink of eradication. [1, 2]

In 1988, the World Health Assembly adopted a resolution for the worldwide eradication of polio, marking the launch of the Global Polio Eradication Initiative. Wild poliovirus cases have decreased by over 99% since 1988, from an estimated 350000 cases in more than 125 endemic countries to 6 reported cases in 2021. Of the 3 strains of wild poliovirus (type1, type 2 and type 3), wild poliovirus type 2 was eradicated in 1999, and wild poliovirus type 3 was eradicated in 2020.[2] As of 2022, endemic wild poliovirus type 1 remains in two countries: Pakistan and Afghanistan (WHO).[2] Polio Eradication Nepal (PEN), surveillance and support team was established in June 1998 by the Ministry of Health and Population in collaboration with World Health Organization (WHO). PEN was later renamed Programme for Immunisation Preventable Disease (IPD). [2, 3]

PATHOGENESIS

Polioviruses are single-stranded ribonucleic acid (RNA) enteroviruses of the Picornaviridae family. Infection occurs via the fecal- oral route, meaning that one ingests the virus and viral replication occurs in the alimentary tract. [4] Virus is shed in the feces of infected individuals. In 95% of cases only a primary, transient presence of viremia occurs, and the poliovirus infection is asymptomatic. In about 5% of cases, the virus spreads and replicates in other sites such as brown fat, reticuloendothelial tissue, and muscle. The sustained viral replication causes secondary viremia and leads to the development of minor symptoms such as fever, headache and sore throat.[5] Paralytic poliomyelitis occurs in less than 1% of poliovirus infections. Paralytic disease occurs when the virus enters the central nervous system and replicates in motor neurons within the spinal cord, brainstem, or motor cortex, resulting in the selective destruction of motor neurons leading to temporary or permanent paralysis. In rare cases, paralytic poliomyelitis leads to respiratory arrest and death. In case of paralytic disease, muscle pain and spasms are frequently observed prior to onset of weakness and paralysis. Paralysis typically persists from days to weeks prior to recovery. [6]

EPIDEMIOLOGY

Poliomyelitis is an acute infection caused by three polioviruses serotypes- types 1,2, or 3 and was the leading cause of permanent disability in children in the past. Almost all the children used to be infected feco-orally or oro-orally, 0.5% of the infected, developed disability. Most epidemic and endemic cases of poliomyelitis are caused by type 1, followed by type 3.[7]

At one time, poliovirus infection occurred throughout the world. Vaccination resulted in reduced circulation of wild polio virus (WPW) and its elimination from United States in 1979.[8] A polio eradication program conducted by the Pan American Health Organization led to elimination of polio in Western Hemisphere in 1991. The Global Polio Eradication Initiative has dramatically reduced wild poliovirus transmission throughout the world. Type 2 and 3 wild polioviruses have been eradicated worldwide, and endemic circulation of type 1 wild poliovirus persists only in two countries. By 2019, only 125 cases caused by wild poliovirus were reported globally, a reduction of more than 99% from 1988, and polio remained endemic in only two countries. However, on 25 September 2015, WHO announced that Nigeria was no longer a polio endemic country as there were no reported cases of polio caused by the wild poliovirus over the past 12 months. [7]

DISEASE BURDEN IN NEPAL

Nepal reported 32 confirmed cases of polio since 1998. The last indigenous case in the country was reported in 2000 (4 cases), and Nepal remained polio free for the ensuing four years from 2001 to 2004. However, 4-6 cases of polio imported from neighbouring countries were detected yearly in 2005-2010 with the exception of 2009. In 2024, the presence of type 3 poliovirus was detected in sewage samples which was confirmed by the National Institute of Health of Thailand, the WHO's collaborating center. However, after 2010, no cases of polio had been reported in Nepal. [9]

POLIO VACCINES

Two highly effective vaccines are available for the prevention of poliomyelitis: inactivated polio vaccine (IPV) and live attenuated trivalent oral poliovirus vaccine (OPV). IPV first became available in 1955 and was followed by OPV in 1963. [3]

ORAL POLIO VACCINE (OPV)

Oral polio vaccine (OPV) is composed of live-attenuated polioviruses derived of their parent WPV strains by passage in nonhuman cells to obtain the three vaccine strains (Sabin 1,2, and 3). Attenuation reduces its neurovirulence and transmissibility. There are several licensed formulations of OPV:

1.mOPV1, mOPV2, or mOPV3
2.bOPV containing types 1 and 3.

The tOPV containing types 1,2, and 3 has been discontinued globally. Nepal is polio free since 2010 and has switched to bOPV from tOPV since April 17, 2016 (Baisakh 5, 2073). [10]

OPV is administered as two drops (0.1 ml) directly into mouth. It is a very heat sensitive vaccine and must be kept frozen for long-term storage or after thawing, at temperatures between 2 - 8 °C for maximum of 6 months. Vaccine vial monitor 2 (VVM2) gives a visual indication of whether the vaccine has been kept at the correct temperature conditions. [7]

VACCINE SCHEDULE

Dose: 2 drops
Route of administration: Oral
Schedule: 6, 10 and 14 weeks

CONTRAINDICATION AND PRECAUTIONS TO VACCINATION

Contraindications: Immunodeficient patients (especially humoral immunodeficiencies) and their household contacts.

Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component.

Precautions: Moderate to severe acute illness with or without fever

CO-ADMINISTRATION WITH OTHER VACCINES

Oral polio vaccine is usually administered concurrently with other vaccines including Bacillus Calmette–Guérin (BCG), diphtheria, pertussis, and tetanus (DPT), hepatitis B, measles, Hib, pneumococcal conjugate vaccine (PCV) and/or rotavirus vaccines. There is no interference with regard to effectiveness or increased incidence with rota virus vaccine even though there is a less immunological interference with first dose. [7]

ADVERSE EVENTS FOLLOWING VACCINATION

Vaccine Associated Paralytic Poliomyelitis (VAPP)

Vaccine-associated paralytic poliomyelitis is paralytic polio occurring in a vaccine or a close, which is caused by a strain of poliovirus that has genetically changed in the intestine, from the original attenuated vaccine strain contained in OPV. [7] VAPP is defined as:

- A case of AFP with residual paralysis (compatible with paralytic poliomyelitis) lasting at least 60 days
- Occurring in an OPV recipient between 4 and 40 days after the dose of OPV was administered
- In a person who has had known contact with a vaccine recipient between 7 and 60-75 days after the dose of OPV was administered

- Isolation of vaccine-related polio virus from any stool samples and no isolation of WPV was frequently used as criteria.

The incidence of VAPP is around 2-4 per million births per year and epidemiologically different in different countries. [7]

VACCINE-DERIVED POLIOVIRUS (VDP)

The attenuated viruses in live OPV vaccines may reacquire neurovirulence and transmission capacity through replication and genetic divergence effect by >1% genetic divergence [or >10 nucleotide (nt) changes] for PV1 and PV3 and 0.6% (or >6 nt changes) for PV2. Such mutated viruses can circulate in a community for an extended period of time and cause paralysis, which is known as cVDPV. 90% of reported cVDPV are due to type 2 polio virus.[7] These viruses are further subdivided into three categories:

1. Circulating VDPVs (cVDVP) when evidence of person-to-person transmission in the community exists
2. Immunodeficiency-associated VDPVs (iVDPVs), which are isolated from people with primary B-cell or combined immunodeficiency disorders
3. Ambiguous VDPVs (aVDPVs), which are either clinical isolates from persons with no known immunodeficiency, or sewage isolates of unknown origin.

If the circulation of cVDPV continues to circulate for >6months following detection, which represents programmatic failures to contain the cVDPV, then they are known persistent cVDPVs. [7]

INACTIVATED POLIO VACCINE (IPV)

Inactivated polio vaccine (IPV) is made from selected WPV strains, Mahoney or Brunhilde (type 1), MEF-1 (type 2), and Saukett (type 3), or from Sabin strains and is now grown in Vero cell culture or in human diploid cells. [7]

IPV manufacturing relies on inactivation of cell culture-derived polioviruses with formaldehyde, in a final formulation containing sufficient antigen units for each serotype. IPV may contain formaldehyde, as well as traces of streptomycin, neomycin, or polymyxin B. Some formulations of IPV contain 2-phenoxyethanol (0.5%) as a preservative for multi-dose vials. The vaccine should be refrigerated to preserve potency but not frozen as this could diminish potency. IPV is available as 10-dose, 5-dose, and single dose vials; IPV vials can be used upto 28 days after opening the vials. [7]

IPV is very safe, whether given alone or in combination with other vaccines. There might be transient minor local erythema (0.5-1%), induration (3-11%), and tenderness (14-29%).

Inactivated polio vaccine has been shown to be highly effective in eliciting humoral antibody response to poliovirus in both high-income and low-income settings. The immunogenicity of IPV schedules depends on the age of administration and number of doses antigenic properties, interval age at last dose between the doses,

and due to interference by maternal antibodies. At completion of the two-dose immunisation series, seroprotection rates ranged from 89% to 100% for poliovirus type 1, from 92 to 100% for poliovirus type 2, and from 70 to 100% for poliovirus type 3. Seroprotection rates after three doses are clearly higher than after two, particularly when the schedule is 2-4-6 months. [7]

VACCINE SCHEDULE

Dose: 0.5 ml

Route of administration: intramuscular/ subcutaneous

CDC: IPV is given at 2 months, 4 months, 6-18 months and fourth dose at 4 years.

IAP: 6, 10 and 14 weeks; IPV booster dose at 15-18 months and a second booster of IPV at 4-6 years alone or as combination with DPT (DTwP/DTaP) vaccines.

NEPAS recommends 2 booster doses of IPV at 18-24 months and 4-6 years of age.

INTRADERMAL INACTIVATED POILO VACCINE (Fractional dose IPV)

Fractional dose of IPV, one fifth of a full dose, reduce the cost and allow immunisation of larger number of persons with a given vaccine supply. Studies have generally demonstrated that a single fractional dose of IPV gives lower sero-conversion rates than a full dose but after two doses, the rates are similar to those after two full doses. [7]

In national immunisation scheduleof Nepal, two doses of fIPV are given at 14 weeks and 9 months.

CO-ADMINISTRATION OF OPV AND IPV OR SEQUENTIAL USE OF IPV AND OPV

IPV followed by OPV

Sequential administration of IPV followed by OPV reduces or prevents VAPP while maintaining the high levels of intestinal mucosal immunity conferred by OPV.[7]

Concurrent IPV and OPV

In developing country settings, the concurrent administration of OPV and IPV has induced uniformly high antibody responses to all three poliovirus types, as evidenced from the studies from Thailand and Pakistan.A single dose of IPV will effectively close immunity gaps to poliovirus type 2 (and types 1 and 3) in previously tOPV-vaccinated children. [7]

For all countries using OPV in the National Immunisation Program, WHO continues to recommend the inclusion of at least one dose of IPV in the vaccination schedule. The primary purpose of this IPV dose is to induce an immunity base that could be

rapidly boosted if there is an outbreak of polio due to poliovirus type 2 after the introduction of bOPV2. The inclusion of IPV may reduce risks of VAPP and also boost both humoral and mucosal immunity against poliovirus types 1 and 3 in vaccine recipients. [7]

CONTRAINDICATION AND PRECAUTIONS TO VACCINATION

Contraindication: *Severe* allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component.

Precautions: *Moderate* to severe acute illness with or without fever

Pregnancy

ADVERSE EVENTS FOLLOWING VACCINATION

Signs of an allergic reaction- hives, difficulty in breathing, swelling of face, lips, tongue or throat

Irritability, tiredness

Fever > 39 degree C

Injection site tenderness, pain or swelling

Erythema at injection site, induration

Drowsiness, mild fussiness or crying

Vomiting

VACCINE STORAGE AND SAFETY

The vaccine should be stored at 2 – 8 degree C. The vaccine is very safe. As IPV contains trace amounts of streptomycin, neomycin and polymyxin B, allergic reactions may be seen in individuals with hypersensitivity to these antimicrobials.

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HEPATITIS B VACCINE

Prof. Dr. Ramchandra Bastola

BACKGROUND

Hepatitis B is a viral infection that primarily affects the liver and can cause acute and chronic diseases. The hepatitis B virus (HBV) is transmitted through blood, bodily fluids, and from mother to child during childbirth. Chronic HBV infection can lead to severe complications, including cirrhosis, liver failure, and hepatocellular carcinoma. To combat the global burden of hepatitis B, the World Health Organization (WHO) recommends universal vaccination as a cornerstone of prevention.[1]

PATHOGENESIS

Hepatitis B infection is caused by the hepatitis B virus (HBV), a DNA virus of the Hepadnaviridae family. The pathogenesis of HBV in neonates and children differs from that in adults, primarily due to the immune system's immaturity at birth and differences in infection transmission modes.[2,3]

Neonates typically acquire HBV through vertical transmission (mother-to-child) during childbirth, especially if the mother is HBsAg and HBeAg positive.[2]

Horizontal transmission can occur in early childhood via exposure to infected bodily fluids or household contacts.[4] HBV enters hepatocytes (liver cells) via specific receptors (e.g., NTCP—sodium taurocholate co-transporting polypeptide).[3] The viral DNA enters the nucleus, where it forms covalently closed circular DNA (cccDNA), serving as a template for viral replication. HBV replicates without directly damaging hepatocytes.

Viral proteins, including HBsAg (surface antigen) and HBeAg (envelope antigen), are produced and secreted into the bloodstream.

Neonates have immature immune systems, leading to poor recognition and response to HBV.[1] High levels of HBeAg suppress neonatal T-cell responses, facilitating immune tolerance. This results in persistent infection with minimal liver damage initially.

In older children or as immune function matures, HBV-specific cytotoxic T lymphocytes (CTLs) target infected hepatocytes. CTL activity leads to liver inflammation and damage (hepatitis).

In neonates and children, HBV pathogenesis is characterized by immune tolerance, high chronicity rates, and long-term risks of liver complications. Early intervention through vaccination and immunoglobulin administration is crucial to interrupt the infection cycle.

EPIDEMIOLOGY

WHO estimates that 254 million people were living with chronic hepatitis B infection in 2022, with 1.2 million new infections each year. In 2022, hepatitis B resulted in an estimated 1.1 million deaths, mostly from cirrhosis and hepatocellular carcinoma (primary liver cancer). [1]

Hepatitis B is a major global health problem. The burden of infection is highest in the WHO Western Pacific Region and the WHO African Region, where 97 million and 65 million people, respectively, are chronically infected. Sixty-one million people are infected in the WHO South-East Asia Region, 15 million in the WHO Eastern Mediterranean Region, 11 million in the WHO in the WHO European Region and 5 million in the WHO Region of the Americas. [1]

DISEASE BURDEN IN NEPAL

Nepal is considered to have a low prevalence of HBV infection compared to other Asian countries.

A nationally representative serosurvey conducted in 2012 assessed HBsAg prevalence among children born before and after the introduction of the hepatitis B vaccination program. The survey found low HBsAg prevalence in both cohorts, indicating a low burden of chronic HBV infection among Nepalese children.[5] To combat HBV infection, Nepal introduced a national three-dose hepatitis B vaccination program between 2002 and 2004, targeting infants to reduce infection rates among children. The program does not currently include a birth dose to prevent perinatal HBV transmission.

The World Health Organization (WHO) reported that Nepal achieved over 90% coverage with hepatitis B vaccine doses provided during infancy for several years.[6] This high vaccination coverage has been instrumental in controlling HBV transmission among children. Studies estimate the hepatitis B surface antigen (HBsAg) carrier rate to be approximately 0.9% in the general population.[7]

ABOUT THE VACCINE

Safe and effective vaccines against hepatitis B have been available since 1982. The active substance in the hepatitis B vaccine is the viral surface protein HBsAg (hepatitis B surface antigen). The currently available vaccine containing the surface antigen of hepatitis B is produced by recombinant technology in yeast and adjuvanted with aluminum salts. Hepatitis B vaccines are available as monovalent formulations for birth doses or for vaccination of older persons at risk, and in combination with other vaccines for infant vaccination, including diphtheria-tetanus-pertussis (DTP), Haemophilus influenzae type b (Hib), and inactivated polio vaccine (IPV).[8]

The Hepatitis B vaccine is available in Nepal as part of the national immunisation program for children under 5 years as combination vaccine with DPT and Hib and also as single antigen for high-risk population as well as post exposure prophylaxis.

VACCINE INDICATION

For healthy children: The vaccine given in three doses at 6, 10, and 14 weeks of age as a pentavalent vaccine along with DPT and Hib and given as part of the national immunisation schedule.

If the mother is HBs Ag positive, monovalent Hepatitis B vaccine along with hepatitis B immunoglobulin (HBIG) shall be given to newborn in two different sites, within 12 hours of life to provide immediate protection and prevention of mother to child transmission (PMTCT) risk.[9]

For high-risk child: Booster doses may be considered for high-risk groups (e.g., immunocompromised children).[10]

CONTRAINDICATION

Hepatitis b vaccine is contraindicated in the event of allergic reactions to a previous dose of hepatitis B vaccine. Vaccination should be postponed in the event of severe acute febrile illness; minor infections are not contra-indications.

PRECAUTIONS

People who are moderately or severely ill should wait until they recover before getting a Hepatitis B vaccine. However, administering the vaccine to people with minor illnesses, such as a cold, is fine.

ADVERSE EVENTS FOLLOWING IMMUNISATION

The hepatitis B vaccine has an excellent safety profile, with minor side effects such as mild fever or soreness at the injection site but if AEFI like anaphylaxis occur injection adrenaline @ 0.01 mg/kg per dose, repeated every 5-15 minutes, should be given for up to 3 doses.[11]

SCHEDULE AND DOSES

The primary three-dose hepatitis B vaccination series for monovalent vaccines, consists of one monovalent birth dose followed by either two doses of monovalent or hepatitis B-containing combination vaccine administered during the same visits as the first and third doses of DPT-containing vaccines. Alternatively, four doses of hepatitis B vaccine may be given for programmatic reasons (e.g., one monovalent birth dose followed by three monovalent or hepatitis B-containing combination vaccine doses) administered during the same visits as the three doses of DPT-containing vaccines. [12]

The classical schedule is 0, 1 and 6 months. This has the seroconversion rates of >90% after 3 dose schedule.

For healthy child (according to NIP)

At 6 weeks: Pentavalent 0.5ml IM @Left thigh

At 10 weeks: Pentavalent 0.5ml IM @Left thigh

At 14 weeks: Pentavalent 0.5ml IM @Left thigh

NEPAS recommends 4th dose at 18-24 months of age. An extra dose (5th) can be allowed if combination vaccine is given at 4-6Y.

For healthy children (according to CDC)

First dose at birth

Second dose at 1 -2 months

Third dose between 6 and 18 months

Administration of 4 doses is permitted when a combination vaccine containing Hep B is used after the birth dose.

Infants born to HBs Ag-positive mothers: [9]

Administer hepatitis B immunoglobulin (HBIG) along with the birth dose within 12 hours of birth for maximum protection.

Hep B vaccine 0.5ml IM + Hepatitis B immunoglobulin (HBIG) 0.5 ml IM in two different site within 12 hours of birth regardless of birth weight.

Birth weight <2000 grams: Administer 3 additional doses of Hep B vaccine beginning at age 1 month (total 4 doses)

Final (3rd or 4th dose): Administer at age 6 months.

Test for HBsAg and anti-HBs at age 9-12 months. If Hep B series is delayed, test 1-2 months after the final dose. Do not test before 9 months.[9]

Preterm infants

Greater than 2000 g: As for full-term infants.

Less than 2000 g: Administer the birth dose as per schedule, but it may not count toward the primary series. Re-vaccination is often recommended after 1 month of age.[8]

The dose in children and adolescents (aged less than 18 years) is 0.5 mL/10 µg and in those 18 years and older is 1 mL/20 µg. It should be injected intramuscularly in the deltoid/anterolateral thigh.

Vaccination for healthcare workers

Hepatitis B vaccination is crucial for individuals in high-risk settings, including healthcare and public safety workers, as well as trainees handling blood or body fluids in medical, dental, nursing, laboratory, and allied health fields. Vaccinating high-risk groups is a key public health strategy to reduce HBV transmission and protect both the individuals and the wider community. For adults with HBV risk factors, the standard vaccination schedule involves doses at 0, 1, and 6 months.

An alternative, accelerated schedule can be used, administering the first dose at any visit, the second at least four weeks later, and the third at least eight weeks after the second and sixteen weeks after the first.[8]

Vaccination for special circumstances

HIV-positive children should receive a 3-dose hepatitis B vaccination series using an adult formulation (double the standard paediatric dose). Patients with chronic renal failure, who are at high risk of HBV infection due to potential hemodialysis, may require hepatitis B vaccination schedules involving more than three standard doses, higher antigen content (e.g., double the usual adult dose), or a combination of both.[8]
Patients suffering from chronic renal failure are at particular risk of infection with HBV, since they may need hemodialysis. These patients have been offered schedules that include more than three doses of the standard vaccine, or vaccine containing a higher dose of HBsAg (e.g., double the usual adult dose) on each occasion, or both.

Interrupted schedules and minimum dosing intervals

For all ages, when Hepatitis B vaccine schedule is interrupted, the vaccine series dose not need to be restarted. If the series is interrupted after the first dose, the second dose should be administered as soon as possible, and the second and third dose should be separated by an interval of at least 8 weeks. If only the third dose has been delayed, it should be administered as soon as possible.

Booster doses

Routine booster doses of hepatitis B vaccine are not indicated following the completion of the primary immunisation series in immunocompetent children. However, in immunocompromised individuals and those with comorbidities, such as chronic renal disease, annual serological monitoring of hepatitis B surface antibody (anti-HBs) titers is recommended. Booster vaccination should be administered when anti-HBs levels decline below the established protective threshold.[8]

POST EXPOSURE PROPHYLAXIS FOR HEALTHCARE PERSONNEL

Following a percutaneous or mucosal exposure to blood, three factors need to be considered when deciding the nature of postexposure prophylaxis (PEP). These include: [13]

- HBsAg status of the source
- Vaccination status of the exposed HCP
- Vaccination response status of the HCP.

Post Exposure management of Health care professional (HCP)

	Post exposure testing	**Post exposure prophylaxis**	

HCP status	Source Patient	HCP testing	HBIG	Vaccination	Post vaccination Serology Testing
Documented responder after complete series	No action needed				
Documented Non-responder after two complete series	Positive/ Unknown	--	HBIG × 2 separated by 1 month	--	Not applicable
	Negative	No action needed			
Response unknown after complete series	Positive/ unknown	<10 mIU/ml	HBIG x 1	Initiate revaccination	Yes
	Negative	<10mIU/ml	--	Initiate revaccination	Yes
	Any result	≥10mIU/ml	--	No vaccination	-
Unvaccinated/ Incompletely vaccinated or vaccine refusers	Positive/ Unknown	--	HBIG ×1	Complete vaccination	Yes
	Negative	--	None	Complete vaccination	Yes

VACCINE EFFICACY

The vaccine is over 95% effective in preventing HBV infection and its complications.[1]

CO-ADMINISTRATION WITH OTHER VACCINES

Hepatitis B vaccines do not interfere with the immune response to any other vaccine and vice versa. The immune responses and safety of hepatitis B-containing combination vaccines are comparable to those observed when the vaccines are administered separately. [8]

STORAGE

Pentavalent vaccines should be stored at a temperature between 2–8°C in refrigerator or vaccine carrier with conditioned ice packs. The vaccine should never be frozen and should be discarded if it is frozen or the VVM reaches the discard point.[14]

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ROTA VIRUS VACCINE

Dr. Anwesh Bhatta

BACKGROUND

Rotavirus is the most common cause of severe diarrhoeal disease in infants and young children worldwide. The term “rotavirus” is derived from Latin meaning “wheel” It is an RNA virus, which gives an appearance of wheel when seen under electron microscope. Based on ‘G’and ‘P’ outer proteins on the virus, 5 strains (G1, G2, G3, G4 and G9) are known which comprises 90% of the serotypes found worldwide.[1]

The virus is transmitted via feco-oral route and can lead to the symptoms such as vomiting, fever, acute watery diarrhoea with a potential of leading to severe dehydration and death. The diagnosis can be established by stool testing.[2]

Rotavirus is a leading cause of acute watery diarrhoea in children <5 years of age. Recognizing the substantial burden of rotavirus disease, global health organizations like the World Health Organization (WHO) recommended the inclusion of rotavirus vaccines in national immunisation programs**.** Nepal introduced the rotavirus vaccine into its national immunisation schedule in July 2020. As of end of 2023, 123 countries around the world have incorporated rotavirus vaccine into their national immunisation programs.[3]

PATHOGENESIS

Rotavirus primarily infects the mature enterocytes lining the villi of the small intestine. The virus disrupts the absorptive and secretory functions of these cells, leading to malabsorption of water and electrolytes, resulting in watery diarrhoea. The virus also induces intestinal inflammation and may stimulate the enteric nervous system, further contributing to diarrhoea. The loss of villous structure and function is a hallmark of rotavirus infection.

EPIDEMIOLOGY

Rotavirus is highly contagious and spreads through the fecal-oral route. Transmission can occur through contaminated hands, surfaces, and objects. Outbreaks are common in settings with close contact, such as daycare centers and hospitals. In temperate climates, rotavirus infections tend to peak during the cooler months. In Nepal, while seasonality may exist, rotavirus infections occur throughout the year with a significantly higher cases seen in March.[4]

DISEASE BURDEN IN NEPAL

Diarrhoeal diseases, including those caused by rotavirus, have historically been a major cause of morbidity and mortality among children under five in Nepal. Before the introduction of the vaccine, rotavirus was responsible for a significant proportion of hospitalisations and deaths due to diarrhoea in this age group. Studies conducted in Nepal have shown high rates of rotavirus infection among children with diarrhoea. Although studies on the Rota viral diarrhoea prevalence in Nepal is scarce, one study has shown Rota virus to be causative of acute diarrhoea in 28% of cases of diarrhoea.[4] In one study, the overall burden of rotavirus infection was 24% among hospitalised children which was much higher

than among non-hospitalised children (12%).[5] The introduction of the rotavirus vaccine has led to a demonstrable reduction in rotavirus-related hospitalisations and deaths.[1]However, the specific data for rotavirus diarrhoea in Nepal is not available in NDHS.

ABOUT THE VACCINE

The three oral rotavirus vaccines available are:

1. **Rotarix**: Rotarix is a monovalent, human, live attenuated rotavirus vaccine containing one rotavirus strain of G1P.

2. **RotaTeq**: Rotateq is a live, oral pentavalent vaccine that contains five rotavirus strains produce human–bovine reassortant vaccine containing five vaccine viruses (types G1, G2, G3, G4 and P1A)

3. **RotaSiil:** Rotasiil is a lyophilized pentavalent vaccine licensed for use in India in 2018. It contains human bovine reassortant strains of rotavirus serotypes G1, G2, G3, G4, and G9. This is the world's first thermostable vaccine which can be stored without refrigeration at or below 25 °C. This characteristic allows for easier storage and distribution, potentially improving vaccine coverage.[6-8]

Nepal government has introduced Rotarix vaccine into the immunisation schedule, 2 doses at 6 and 10 weeks of age.

Rotavirus vaccines are only recommended for use in young infants during 2 and 4 months of age (Rotarix, 2-dose schedule) or at 2, 4, and 6 months of age (RotaTeq and Rotasiil, 3-dose schedule).[6-9] It is important to note that Rotarix vaccine cannot be initiated beyond 15 weeks of age and 2nd dose should not be given beyond 24 weeks of age.[6-9] Similarly, first dose of Rotateq cannot be given beyond 12 weeks of age and 3rd dose should be given by 32 weeks of age.

VACCINE INDICATION

For healthy children: Rotavirus vaccination is recommended for all healthy infants as part of the routine childhood immunisation schedule.

For high-risk children: Rotavirus vaccination is also recommended for premature infants and children with certain underlying medical conditions, such as chronic gastrointestinal diseases or immunodeficiencies (with careful consideration and consultation with a specialist).[7-9]

CONTRAINDICATIONS

Rotavirus vaccines are contraindicated in infants with a history of:

- Severe allergic reaction (anaphylaxis) to a previous dose of rotavirus vaccine or any component of the vaccine.
- Intussusception (a serious bowel obstruction).
- Severe Combined Immunodeficiency (SCID).[7, 8]

PRECAUTIONS

Infants with a history of chronic gastrointestinal disease should be vaccinated with caution and after careful consideration of the risks and benefits.

Vaccination should be postponed in infants with moderate to severe acute illness (e.g., diarrhoea or vomiting) until they have recovered.

ADVERSE EVENTS FOLLOWING IMMUNISATION

Rotavirus vaccines are generally safe and well-tolerated. Common mild side effects include: Irritability, mild diarrhoea or vomiting and fever.

A very rare but serious adverse event associated with rotavirus vaccines is intussusception. Parents should be advised to seek immediate medical attention if their infant develops symptoms such as severe abdominal pain, vomiting, bloody stools, or lethargy after vaccination.[7, 8]

SCHEDULE AND DOSES

In Nepal, according the the national immunisation program, 2 doses of Rotarix are given orally at 6 weeks and 10 weeks respectively.[10]

Rotasiil OR Rotateq *should be administered orally as a 3-dose regimen at 2, 4 and 6 months of age*.

VACCINE EFFICACY

Rotavirus vaccines have demonstrated high efficacy in preventing severe rotavirus gastroenteritis. Studies have shown that the vaccines can significantly reduce hospitalisations and emergency room visits due to rotavirus infection. In clinical trials and real-world studies, the rotavirus vaccines have been shown to reduce the risk of severe rotavirus gastroenteritis by around 85-98%. The vaccines are somewhat less effective at preventing all rotavirus infections, with efficacy rates ranging from 60-85%, but they still provide significant protection.[7-9]

STORAGE

Rotavirus vaccines should be stored according to the manufacturer's recommendations, typically at temperatures between 2°C and 8°C. Proper cold chain management is essential to maintain vaccine potency.[7-9]

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PNEUMOCOCCAL VACCINE

Dr. Shama Shakya

BACKGROUND

Streptococcus pneumoniae (pneumococcus) is an important pathogen that results in more than 1 million children's deaths each year. Childhood invasive pneumococcal disease is prevalent and typically severe, and a major cause of life-threatening pneumonia, bacteremia, endocarditis, and meningitis, may also cause sinusitis, otitis media and bone and joint infections.

The bacteria were first isolated by Louis Pasteur in 1881 from the saliva of a patient with rabies. Efforts to develop effective pneumococcal vaccines began as early as 1911. However, with the advent of penicillin in the 1940's, interest in pneumococcal vaccination declined until many patients still died despite antibiotic treatment. By the late 1960s, efforts were made to develop polyvalent pneumococcal vaccine. The first pneumococcal vaccine was licensed for use in US in1977. The first conjugate pneumococcal vaccine was licensed in United States in 2000.[1]

PATHOGENESIS

The pathogenesis of pneumococcal infection is a complex interplay between pneumococcal virulence determinants and the host immune response. Molecular studies have considerably advanced our knowledge and understanding of the precise structures and functions of the different determinants and their pathogenic roles, the mechanisms, by which pneumococci attach, invade, evade lung defense and cause severe disease.

All wild strains of *S. pneumoniae* are provided with a polysaccharide capsule. To date, 93 distinct capsular types have been described. Types that are anti-genetically related to each other are included in groups (labeled, e.g., 9A, 9L, 9N, and 9V), whereas types without close antigenic relationship to other types are given numbers only (e.g., types 1, 2, 3, 4, 5). The capsular polysaccharides are composed of repeating units of oligosaccharides and for most of them the chemical structure is known. Molecular analysis of the genes responsible for the synthesis of some of the capsular substances has shown that they are arranged in cassettes comprising all the genetic material necessary for capsule synthesis. Being naturally transformable, pneumococci may exchange genetic material between different strains. By such processes capsule specificity, in a cassette type-recombination event, can be exchanged in vitro as well as in vivo. Capsule transformation was described as early as 1928 and is, according to recent evidence, a rather common event in nature.[2]

EPIDEMIOLOGY

Pathogen: Streptococcus pneumoniae (pneumococcus) is a Gram-positive, lancet-shaped, polysaccharide encapsulated diplococcus, occurring occasionally as individual cocci or in chains. More than 90 pneumococcal serotypes have been identified by type specific capsular polysaccharides.[1]

Host: The causative organism, Streptococcus pneumoniae, colonized in the upper respiratory tract of healthy individual. More than 90% of children between 6 months

and 5 years of age harbor S. pneumoniae in the nasopharynx. Rate of pneumococcal carriage peak during the first and second year of life and decline gradually thereafter. Pneumococcal infections are most prevalent during winter months. The period of communicability is unknown and may be as long as the organism is present in respiratory tract secretions but probably is less than 24 hours after effective antimicrobial therapy is begun.[1]

Incubation Period: It varies by type of infection; may be as short as 1 day.[3]

Transmission: S. pneumoniae is transmitted mainly through respiratory droplets. Infants and young children are thought to be the main reservoir of this agent with cross-sectional point prevalence of nasopharyngeal carriage ranging from 27% in developed to 85% in developing countries.[3]

Disease Spectrum: Pneumococcal infections range from severe invasive diseases (like meningitis and bacteremia) to milder non-invasive forms (like otitis media). The serotypes causing these infections vary globally, by disease type and by age. While over 90 serotypes exist, only about 10 serogroups commonly cause childhood infections. Vaccination (e.g., PCV-7) has reduced disease from targeted serotypes but led to an increase in non-vaccine serotype infections ("replacement phenomenon"). Some serotypes are also more likely to be antibiotic-resistant.[4]

Table 1: Characteristics of different Serotypes [5]

Serotypes	Characteristics
1,5, and 14	• 28-34%0f IPD • 30% of IPD in 20 of the world's poorest countries • Serotype 14 is antibiotic resistant
3	• OM, pneumonia, especially complicated necrotizing pneumonia • Usually causes non-invasive disease
6A	• NP carriage, an important cause of IPD • Antibiotic resistant
6B	• Antibiotic resistant
7F	• Important in India, increased case fatality rates
19A	• Most prevalent in the US, in India (8-13%) • IPD, AOM, mastoiditis • Antibiotic resistant
19F and 23F	• Responsible for 9-18% cases globally • Antibiotic resistant
AOM: Acute otitis media; IPD: Invasive pneumococcal disease; NP: nasopharyngeal carriage	

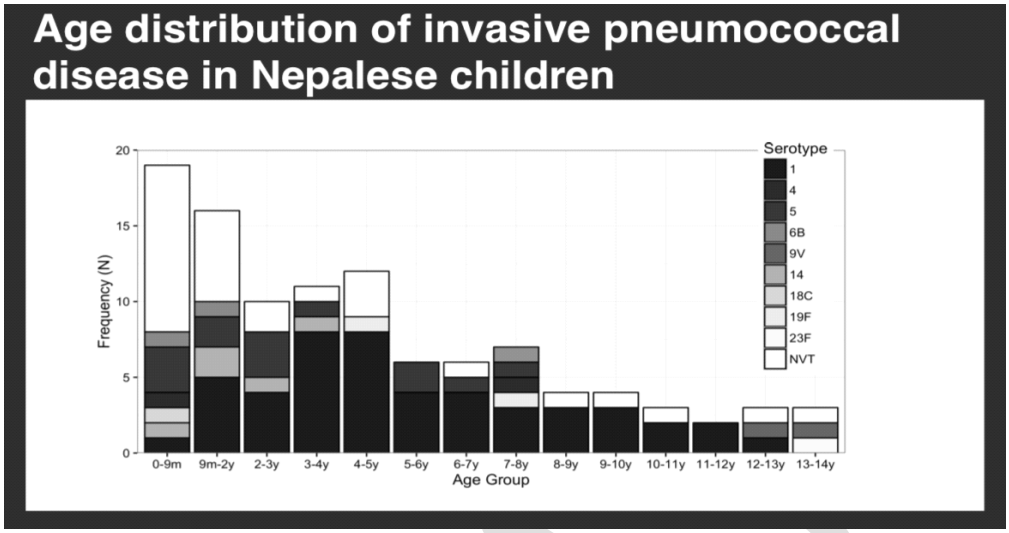

Fig1: Serotype distribution according to age [6]

GLOBAL BURDEN

The World Health Organization (WHO) estimates that around 1.6 million people die from pneumococcal disease annually, with 0.7-1 millon of those deaths occurring in children under 5.[7] In 2015, more than 294,000 children under the age of 5 died each year from pneumococcal disease in the form of pneumonia, meningitis, and other serious infections. Pneumococcal pneumonia accounts for 25% to 30% of invasive PD in children age 2 years or younger[2]. Pneumococcal bacteremia accounts for 40% of invasive disease in age 2 years or younger.[2] Pneumonia accounts for 14% of all deaths of children under 5years old, killing 740,180 children in 2019.[7] Pneumococcus is the leading cause of bacterial meningitis among children younger than 5 years. It is also a common cause of acute otitis media.[2,6,8]

DISEASE BURDEN IN NEPAL

Nepal, one of the world's poorest nations, with a per capita income of <$250 and a total population of approximately 26 million, has a population of children aged <1 year of 742,164 and a population of children aged <5 years of 3,633,687. The mortality rate among children aged <5 years is very high, at 27.3 per 1000 live births with pneumonia as the leading cause of death. Nepal's low rate of treatment of suspected pneumonia cases is to blame for the high fatality rates: only 15%-18% of all patients with pneumonia who reside in rural or hilly areas are brought by caretakers to health care facilities, according to Ministry of Health estimates.[3]

PNEUMOCOCCAL VACCINES

Currently two types of vaccines are licensed for use:

(I) Pneumococcal Polysaccharide Vaccine (PPSV)

(II) Pneumococcal Conjugate Vaccines (PCVs).

1. PNEUMOCOCCAL POLYSACCHARIDE VACCINE (PPSV)

The unconjugated pneumococcal polysaccharide vaccine is a 23valent vaccine (PPSV 23) containing 25µg per dose of the purified polysaccharide of the following 23 serotypes of pneumococcus— 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14,15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, 33F. These serotypes account for over 80% of serotypes associated with serious diseases in adults. It is a T cell independent vaccine that is poorly immunogenic below the age of 2 years, has low immune memory, does not reduce nasopharyngeal carriage and does not provide herd immunity. The vaccine is administered as a 0.5 ml dose either intramuscularly in the deltoid muscle or subcutaneously. It is stored at 2 to 8°C. It is a safe vaccine with occasional local side effects. Not more than two lifetime doses are recommended, as repeated doses may cause immunologic hypo responsiveness to subsequent doses.[5,9]

Immunogenecity

A single dose of PPSV 23 results in the induction of serotype-specific immunoglobulin G (IgG), IgA and IgM antibodies; the IgG antibodies predominantly belong to the IgG2 subclass. Though the total antibodies, as measured using the ELISA, are similar between age groups, however, functional antibody responses, are lower in the elderly compared to young adults.[5,9, 10]

Efficacy and effectiveness

Data on the efficacy and effectiveness of PPV 23 is conflicting. A systematic review commissioned by WHO concluded that the evidence was consistent with a protective effect against invasive pneumococcal disease and pneumonia in healthy adults and against invasive pneumococcal disease in the elderly. There was no evidence of efficacy against invasive disease or pneumonia in other high-risk populations with underlying diseases or highly immuno- suppressed individuals in both adults and children. One study in Uganda in HIV-infected adults showed an increased risk of pneumonia among those vaccinated with PPSV23.[5,9,10]

2. PNEUMOCOCCAL CONJUGATE VACCINES (PCVS)

In order to overcome the immunological limitations of PPSV, the individual polysaccharides of a set of pneumococcal serotypes were conjugated to carrier proteins in order to make them immunogenic in infants, confer more long-lasting protection and induce immunological memory. Pharmaceutical companies developing conjugated vaccines are using same protein carriers—cross-reactive material (CRM), a nontoxic mutant diphtheria toxin, diphtheria toxoid, tetanus toxoid, or a meningococcal outer membrane protein complex, which were used successfully to make conjugate Haemophilus influenzae type B (Hib) vaccines.[5,10]

Vaccine's Serotypes Composition

The serotypes and conjugating proteins in PCVs available in Nepal (Table 2)

Table 2: Serotype composition and conjugating proteins of PCVs [11]

Formulation	Carrier Protein	Serotypes													
PCV-10	Protein D, TT, DT	1	X	4	5	XX	6B	7F	9V	14	18C	X	19F	XX	23F
PCV-10v	CRM^{197}	1	X	X	5	6A	6B	7F	9V	14	X	19A	19F	X	23F
PCV-13	CRM^{197}	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	X	23F
(CRM: cross reactive material, PCV: Pneumococcal conjugate vaccine)															

Serological correlates of protection: Any new PCV has to meet the following criteria laid down by the WHO

- Immunoglobulin G (IgG) (for all common serotypes collectively and not individually) of ≥0.35 µg/mL measured by the WHO reference assay (or an alternative)
- The serotype-specific IgG geometric concentration ratios.

Immunogenicity

Comparisons of opsonophagocytic activity (OPA) antibody titers should focus on serotype-specific geometric mean titer (GMT) ratios, not a ≥1:8 thresholds. Both vaccines demonstrate comparable immunogenicity based on the proportion of subjects achieving serotype-specific IgG antibody levels ≥0.35 µg/mL per manufacturer schedules. Immunogenicity has also been assessed across various schedules.[11]

Duration of protection

In South Africa, results of surveillance showed that 6.3 years after vaccination with PCV9, vaccine efficacy remained significant against IPD (78%; 95% CI, 34–92%). This was consistent with immunogenicity data showing that specific antibody concentrations among HIV-uninfected children remained above the assumed protective levels compared to unvaccinated HIV-uninfected controls during this period.[12]

Effectiveness of incomplete series

In pivotal clinical trials, the effectiveness of 1 dose of PCV13 was estimated as 48%, 2 doses 87% and 2+1 doses 100%. One dose catch-up for toddlers showed 83% effectiveness.[5]

Safety

The safety of PCV has been well studied, and all formulations are considered to have an excellent safety profile in numerous studies. The main adverse events observed are injection-site reactions, fever, irritability, decreased appetite, and increased and/or decreased sleep that were reported about 10% of the vaccines.[10]

Serotype Replacement
Early observations, which showed that though PCV reduced nasopharyngeal carriage with vaccine serotypes, a carriage with nonvaccine serotypes increased, led to concerns about replacement disease due to serotypes not contained in the vaccines. WHO recommends that surveillance for replacement disease should continue, especially in developing countries where the potential for replacement may be different from that in industrialized countries.[10]

VACCINE INDICATION

I. Pneumococcal Polysaccharide Vaccine (PPSV)

■ Minimum age: 2 years

■ Recommended only for the vaccination of persons with certain high-risk conditions as mentioned below in Table 4.

■ Administer PPSV at least 8 weeks after the last dose of PCV to children aged 2 years or older with certain underlying high-risk medical conditions.

■ An additional dose of PPSV should be administered after 5 years to children with anatomic/functional asplenia or an immune compromising condition.

■ PPSV should never be used alone for the prevention of pneumococcal diseases (PD) amongst high-risk individuals.

II. Pneumococcal Conjugate vaccines (PCV)

- **Healthy Children Indication**

Both PCV10 and PCV13 are licensed for active immunisation for the prevention of PDs caused by the respective vaccine serotypes in children from 6 weeks to 5 years of age. In addition, PCV13 is also licensed for the prevention of PD in adults > 50 years of age. New PCV-10v is licensed for active immunisation for the prevention of PDs caused by the respective vaccine serotypes in children from 6 weeks to 2 years of age only and not beyond.

- **High-risk group of children**

Administration of PPSV23 after PCV13/PCV10 among children aged 2–18 years who are at increased risk for pneumococcal disease should be undertaken as per following instructions:

- Children aged ≥ 2 years with underlying medical conditions (Table 4) should receive PPSV23 after completing all recommended doses of PCV13/PCV10. These children should be administered 1 dose of PPSV23 at age ≥2 years and at least 8 weeks after the most recent dose of PCV.

Table 3: Schedule for PCV

Age at first dose	Primary series PCV-13	Primary series PCV-10	Primary series 10vPCV-10	Booster dose All PCVs
6 weeks to 6 months	3 doses	3 doses	3 doses	1 dose* 12-15 months
7-11 months	2 doses[+]	2 doses[+]	2 doses[+]	1 dose during 2nd year
12-23 months	2 doses[+]	2 doses[+]	2 doses[+]	Not applicable
24-59 months	1 dose	2 doses		Not applicable

*At least 6 months after the third dose
[+]At least 8 weeks apart

Notes:

• Routine use of PCV-10/13 is not recommended for healthy children aged >5 years.
• Minimum age for administering the first dose is 6 weeks.
• Minimum interval between two doses is 4 weeks for children vaccinated at age 12 months, whereas, for those vaccinated at age>12 months, the minimum interval between doses is 2 months (8 weeks). [13]

Table 4: Children at high risk for pneumococcal disease[1]

Risk Group	Condition
Immunocompetent children (High risk)	Chronic heart disease (particularly cyanotic congenital heart disease and cardiac failure)
	Chronic lung disease (including asthma if treated with prolonged high dose oral corticosteroids)
	Diabetes mellitus
	Cerebrospinal fluid leak
	Cochlear implant
Children with functional or anatomic asplenia (Very high risk)	Sickle cell disease and other hemoglobinopathies
	Congenital or acquired asplenia, splenic dysfunction
Children with immunocompromising conditions	HIV infection
	Chronic renal failure and nephrotic syndrome

(Very high risk)	
	Diseases associated with treatment with immunosuppressive drugs or radiation therapy (e.g., Malignant neoplasms, leukemias, lymphomas, and Hodgkin disease, or solid organ transplantation)
	Congenital immunodeficiency includes B-(humoral) or T-lymphocyte deficiency; complement deficiencies, particularly C1, C2, C3 and C4 deficiency; and phagocytic disorders (excluding chronic granulomatous disease)
	Prematurity (PT) and very low birth weight (VLBW). These infants have up to ninefold higher incidence of IPD as compared to full size babies.

Note: When elective splenectomy, immunocompromising therapy, or cochlear implant placement is being planned, PCV-13/PCV10 and/or PPSV23 vaccination should be completed at least 2 weeks before surgery or initiation of therapy.

TABLE 5: Recommendations for pneumococcal immunisation with PCV13 and/or PPSV23 vaccine for children at high risk or presumed high risk of pneumococcal disease.[1,4,9]

Age	Previous dose of any pneumococcal vaccine	Recommendations
<23 months	Nil	Age-appropriate recommendations
24–71 months	4 doses of PCV-13	•Dose 1 of PPSV23 at least 8 weeks after last dose of PCV13 • Dose 2 of PPSV23, 5 years after dose 1
24–71 months	3 previous doses of PCV13 before 24 months of age	• Dose 1 of PPSV23 at least 8 weeks after last dose of PCV13 • Dose 2 of PPSV23, 5 years after dose 1
24–71 months	<3 doses of PCV 13	• 2 doses of PCV13 at least 8 weeks apart • Dose 1 of PPSV23 at least 8 weeks after last dose of PCV13 • Dose 2 of PPSV23, 5 years after dose 1
24–71 months	1 dose of PPSV23	• 2 doses of PCV13 at least 8 weeks apart and 8 weeks after last dose of PPSV23 • 1 dose PPSV23, 5 years after dose 1 and 8 weeks after

		PCV13
6–18 years with medical conditions	Nil	• 1 dose of PCV13 • Dose 1 of PPSV23, 8 weeks later • Dose 2 of PPSV23, 5 years after dose 1
	1 dose of PCV13	• 1 dose PPSV23 • 2nd dose PPSV23, 5 years later
	>1 dose of PPSV23	• 1 dose PCV13, >8 weeks later • 1 dose PPSV23, 5 years later
• A second dose of PPSV23, 5 years after the first dose is recommended. or other immunocompromising conditions. • All other children with underlying medical conditions should receive one dose of PPSV23. • No more than two doses of PPSV23 are recommended. •PCV-13 and Menactra cannot be administered at the same visit in children with functional or anatomic asplenia. They should be administered separately, PCV first followed by Menactra 4 weeks later.		
(HIV: human immunodeficiency virus; PCV: pneumococcal conjugate vaccine; PPSV: pneumococcal polysaccharide vaccine		

As of 2022, 155 out of 194 WHO member states have introduced PCV into their national immunisation programs, which includes 64 Gavi supported countries. Majority (103) of the countries were using PCV-13, whereas 31 countries use PCV-10 and 8 countries were using both (PCV-10 and -13).
In 2015, Nepal became one of the first countries in Southeast Asia to introduce PCV-10 nationwide to infants as part of the routine infant immunisation schedule and is given in two doses at 6 and 10 weeks, followed by a booster at 9 months.[6]

CHOICE OF SCHEDULE

The WHO recommends a minimum of three doses of vaccine, given in either a 3p + 0 or a 2p + 1 schedule. If a three-dose primary series is used, the first dose may be given as early as 6 weeks of age with a minimum of 4 weeks between doses. If 2p + 1 schedule is chosen, the first dose may be given as early as 6 weeks of age, preferably with an 8-week interval between the two primary doses, and the booster dose administered between 9 months and 15 months.[10]

The national immunisation schedule in Nepal includes the 10-valent Pneumococcal Conjugate Vaccine (PCV-10) to protect against pneumococcal diseases like pneumonia, meningitis, and ear infections. The recommended dose schedule for PCV-10 in Nepal is **3 doses**:

- **Dose 1:** At 6 weeks of age.
- **Dose 2:** At 10 weeks of age.

- **Dose 3 (Booster):** At 9 months of age.

NEPAS recommends Dose 4 at 18-24 months of age.

Interchangeability

When primary immunisation is initiated with one of these vaccines, the remaining doses should be administered with the same product. However, if it is not possible to complete the series with the same type of vaccine, the other PCV product should be used.[13]

CONTRAINDICATIONS

- Children should not get PCV if they had a severe (life threatening) allergic reaction to a previous dose of this vaccine or to any component of the vaccine, including diphtheria toxoid.
- Infants with a moderate or severe illness (temperature >=39^{o}C) should not be vaccinated until they improve. Mild illness such as an upper respiratory tract infection is not a contraindication and children should be vaccinated.[13]

WARNINGS AND PRECAUTIONS

PCV 13 will only protect against pneumococcal serotypes included in the vaccine and may not protect all individuals receiving the vaccine. Safety and immunogenicity data on PCV13 are not available for immune-compromised individuals (e.g., individuals with splenic dysfunction, HIV infection, malignancy, nephrotic syndrome) and vaccination should be considered on an individual basis. Premature infants may suffer from apnea after primary immunisation series. Very premature infants (born <30 weeks of gestation) may require monitoring for at least 48 hours after vaccination. Different injectable vaccines should always be given at different injection sites. The safety and immunogenicity for other routes (e.g., subcutaneous) have not been evaluated.[13]

ADVERSE EVENTS FOLLOWING IMMUNISATION

Common AEFI with both PCV10 and PCV13:

- **Local Reactions:** Pain, swelling, redness, or tenderness at the injection site.
- **Systemic Reactions:** Fever, fussiness, irritability, loss of appetite, and drowsiness.
- **Other:** Some studies have reported more frequent occurrences of rash, diarrhoea, and generalized allergic reactions with PCV13 compared to PCV10, but the differences are generally not considered clinically significant.[13]

ROUTE OF ADMINISTRATION

The vaccines are given intramuscularly into the antero-lateral aspect of the thigh in infants and into the deltoid muscle in older age groups a 0.5ml dose. It can be administered at the same time as other routine childhood vaccinations if administered in a separate syringe at a separate injection site. Concurrent administration of PCV-13 and PPV-23 is not recommended.[13]

VACCINE STORAGE AND SAFETY

PCV should be stored and transported between 2^{o}C and 8^{o}C. Liquid vaccines, including the pneumococcal vaccine, must not be frozen. PCV is relatively safe and well tolerated; severe adverse reactions attributable to the vaccine are extremely rare.

RECENT UPDATES IN PNEUMOCOCCAL VACCINES (TABLE 6)

1. 10v PCV:

A new 10vPCV has been marketed in India as Pneumosil. Pneumosil is indicated for active immunisation against invasive disease and pneumonia caused by S. pneumoniae serotypes 1, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F, and 23F; in infants from 6 weeks of the age group for three-dose regimen (dosing schedule: 6, 10, and 14 weeks), till the age of 2 years. The WHO has approved it for active immunisation against invasive disease, pneumonia, and acute otitis media. It is available in Nepal.[14]

2.14v-PCV:

In 2022, a 14-valent PCV vaccine was permitted for use in India. PCV14 contains 14 serotypes, 12 of them the same as in Prevnar. In addition, it contains serotypes 22F and 33F. It is not marketed in Nepal.[15]

3. PCV-15:

PCV-15 is indicated for active immunisation for the prevention of invasive disease caused by S. pneumoniae serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F in individuals 6 weeks of age and older. It is not marketed in Nepal.[14]

4. PCV-20:

Prevnar 20 is indicated for active immunisation for the prevention of pneumonia and invasive disease caused by S. pneumoniae serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, and 33F in adults 18 years of age and older. For >19 years, it is indicated for those with certain chronic conditions. It is preferred as a single 0.5 mL dose for those >65 years of age.
It is not marketed in Nepal yet.[14]

5. PCV-21*:*

PCV-21 is the most recent PCV which was approved by the FDA in 2024. It protects against 21 serotypes 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, and 35B; and is designed to help protect individuals 18 years of age and older from the serotypes that cause the majority of invasive pneumococcal disease. It is not marketed in Nepal.[14]

Table 6: Comparison of PCV serotypes available in Nepal with newer PCV

Formulation	Carrier Protein	Serotypes														
PCV-10	Protein D, TT, DT	1	X	4	5	X X	6 B	7F	9V	14	18 C	X	19 F	X X	23 F	
PCV-10v	CRM 197	1	X	X	5	6A	6 B	7F	9V	14	X	19 A	19 F	X	23 F	
PCV-13	CRM 197	1	3	4	5	6A	6 B	7F	9V	14	18 C	19 A	19 F	X	23 F	
PCV-14	CRM 197	1	3	4	5	X	6 B	7F	9V	14	18 C	19 A	19 F	22 F	23 F	33 F
PCV-15	CRM 197	1	3	4	5	6A	6 B	7F	9V	14	18 C	19 A	19 F	22 F	23 F	33 F
PCV-20	CRM 197	1	3	4	5	6A	6 B	7F	9V	14	18 C	19 A	19 F	22 F	23 F	33 F
											8	10 A	11 A	12 F	15 B	15 C
PCV-21	CRM 197	X	3	X	X	6A	X	7F	X	X	X	19 A	X	22 F	X	33 F
		31	24 F	23 B	23 A	20 A	17 F	16 F	15 B	9 N	8	10 A	11 A	12 F	15 B	35 B
(CRM: cross reactive material, PCV: Pneumococcal conjugate vaccine)																

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MEASLES-MUMPS-RUBELLA VACCINE

(MR, MMR)

Dr. Grishma Uprety

BACKGROUND

Measles, mumps, and rubella are viral infections that can all be associated with serious diseases in non-immune people. Measles virus causes an estimated 21 million infections and 345,000 deaths a year worldwide.[1]

The most concerning of these is rubella as it can cause congenital rubella syndrome (CRS) with devastating effects. The incidence of all three infections has decreased significantly in countries with routine immunisation programmes targeted at these diseases.

PATHOGENESIS

Measles

Measles has a high predilection for respiratory tract and is also the portal of entry along with conjunctivae. Patients are infectious from 3 days before to up to 4-6 days after the onset of rash.

The incubation period, prodromal disease, exanthematous phase, and recovery are the four stages of the infectious period. The virus spreads to the reticuloendothelial system during incubation after migrating to the local lymph nodes and causing primary viremia. The virus spreads to the bodily surfaces when secondary viremia occurs. Cell-to-cell plasma membrane fusion linked to viral replication kills cells in a variety of bodily tissues, including central nervous system cells. Fever, conjunctivitis with photophobia, coryza, cough, fever, and Koplik spots are the symptoms of the infection.[2]

An infection with measles virus provides a lifelong immunity. Most of the infection subsides in a two-week period however it is associated with some grave complications like Sub Acute Sclerosing Panencephalitis, Acute Demyelinating Encephalomyelitis, and Measles Inclusion Body Encephalitis.

Mumps

Mumps virus targets the salivary glands, central nervous system (CNS), pancreas, testes, thyroid, ovaries, heart, kidneys, liver, and joint synovia. Initial viral replication occurs in the epithelium of the upper respiratory tract. Infection spreads to the adjacent lymph nodes by the lymphatic drainage, and viremia ensues, spreading the virus to targeted tissues. Mumps virus causes necrosis of infected cells and is associated with a lymphocytic inflammatory infiltrate. Salivary gland ducts are lined with necrotic epithelium, and the interstitium is infiltrated with lymphocytes. Swelling of tissue within the testes may result in focal ischemic

infarcts. The cerebrospinal fluid (CSF) frequently contains a mononuclear pleocytosis.[2]

Rubella

Virus replicates in the respiratory epithelium then spreads to the regional lymph nodes ensuing an intense form of infection after 10 to 17 days. Viral shedding from the nasopharynx begins approximately 10 days after infection and may be detected up to 2 week following onset of the rash.[2]

Maternal viremia results in congenital infection. The virus can infect any fetal organ after infecting the placenta and then moving through the growing fetus's vascular system. The most severe and pervasive abnormalities are caused by maternal infection during the first eight weeks of pregnancy. According to estimates, the probability of congenital abnormalities is 90% if the mother contracts an infection before week 11, 33% between weeks 11 and 12, 11% between weeks 13 and 14, and 24% between weeks 15 and 16.

EPIDEMIOLOGY

Globally, after years of declining measles, measles cases in 2022 increased by 18% and deaths increased by 43% worldwide (as compared to 2021). According to a new report by the WHO and the United States Centers for Disease Control and Prevention, the estimated number of measles cases is 9 million and the number of deaths stands at 136,000.[3] Even though a safe and cost-effective vaccine is available, in 2023, there were an estimated 107 500 measles deaths globally, mostly among unvaccinated or under vaccinated children under the age of 5 years. The proportion of children receiving a first dose of measles vaccine was 83% in 2023, well below the 2019 level of 86%.[4]

After the mumps vaccination program started in 1967, there has been a more than 99% decrease in mumps cases in the United States. However, mumps outbreaks still occur, particularly in settings where people have close, prolonged contact, such as universities, schools, and correctional facilities.

Developed countries have remarkably reduced the burden of CRS by universal immunisation against rubella.

BURDEN OF THE DISEASE IN NEPAL

Between 24 November 2022 and 10 March 2023, 690 measles cases, including one associated death (case fatality ratio: 0.14 %), have been reported from seven districts in western Nepal, and three districts in eastern Nepal (mainly in the Terai ecological region). The majority of the cases (n=591; 86%) have been reported in children aged less than 15 years. While measles is endemic in Nepal and is reported every year, the magnitude and extent of the current outbreak are

unusually high compared to the previous years.[5] A total of 1,022 measles positive cases (including laboratory con rmed, epi-linked and clinical cases) in FY 2079/80.[6]

Based on an in-depth review of the data and reports provided by independent country national verification committees, the Commission certified on 3 August 2018 that Nepal achieved a 97% reduction in rubella cases in 2017 (22 cases) as compared to 2008 (786 cases) surpassing the target of 95% or more reduction. Nepal was certified in Bhadra 2075 (August 2018) for the achievement and control of Congenital Rubella Syndrome. Nepal has achieved this goal two year ahead of the regional target year of 2020 and one year ahead of the national target of 2019.[6]

Mumps outbreak peak was observed from May-October 2023, with the incidence of 160 cases. Affected children were mostly belonging to Morang district (108,68%) followed by Sunsari (43,27%). Incidence of disease occurred mostly in school (129;81%). Most commonly affected children were of age group of 5-9 years.[7]

MR & MMR VACCINE

Most of the developed countries use MMR vaccines. The burden of measles has been markedly reduced after the introduction of vaccine. Trisevac contains live attenuated strains of Edmonston-Zagreb measles virus propagated on human diploid cell culture, L-Zagreb mumps virus propagated on chick embryo fibroblast cells and Wistar RA 27/3 rubella virus propagated on human diploid cell culture.[8] Each dose of the vaccine contains not less than 1000 cell culture infective (CCID) doses of Measles, 5000 CCID of Mumps virus and 1000 CCID of Rubella virus.

MR vaccine is a live attenuated vaccine for immunisation against measles and rubella. In Nepal, according to the National Immunisation Protocol, patient receives a first dose of MR at 9 months and a second dose at 15 months of age. A booster dose of MMR at 5 years of age is also recommended. MMR is currently being used in Nepal in private clinics. This vaccine is a live and weakened or attenuated virus which works by stimulating the immune system to produce antibodies, thereby developing immunity.[9]

INDICATIONS

In Nepal, according to the National Immunisation Program, child receives a first dose of MR at 9 months and a second dose at 15 months of age.

For catch up vaccination, 2 doses of MR vaccines are given with the minimum interval of at least 4 weeks.

Measles containing vaccine can be administered to infants 6 months through 11 months of age during outbreaks. These children should be re-vaccinated with two doses of measles containing vaccine; the first at ages 12 through 15 months and at least 4 weeks after the previous dose, and a second dose at ages 4 through 6 years.

Measles vaccines appear to be safe in HIV-infected children, but the evidence is limited. When the burden of measles is high, measles vaccination at 6 months of age is likely to benefit children of HIV-infected women, regardless of the child's HIV infection status.

VACCINE DOSAGE AND ADMINISTRATION

0.5ml of the reconstituted vaccine is given subcutaneously.

Site of administration: Left upper arm

MR at 9 and 15 months of age as per National Immunisation schedule of Nepal.

NEPAS recommends 2 doses of MMR at 18 months and 4-6 years of age.

CDC schedule: 1st dose at 12-15months and 2nd dose at 4-6 years.

Interaction with medicinal products

Due to high risk of inactivation, MMR should not be given within 6 to 11 months after injection of IVIG and 6 weeks after the injection of blood products.[10]

Tuberculin positive individuals may transitionally become tuberculin negative after vaccination.

CONTRAINDICATIONS

1. Individuals receiving corticosteroids, immunosuppressive agents, undergoing radiotherapy.
2. Should not be taken in febrile state, pregnancy, severe anemia, following administration of gamma globulin or blood transfusions
3. Known allergy to vaccine compound.

PRECAUTIONS

- Moderate or severe illness
- Receipt of antibody-containing blood products in the past 3-11 months
- History of Thrombocytopenic Purpura or ITP

ADVERSE EVENTS FOLLOWING IMMUNISATION

AEFI following the use of combined vaccines (MR and MMR) are similar to those with single antigens. Use of MR vaccine can result in mild lymphadenopathy, urticaria, rash, malaise, sore throat, fever, headache, arthralgia, and arthritis. The type and rate of serious adverse events does not differ significantly for MMR or MR combinations compared with the individual antigens.[8]

EFFICACY

Measles: One dose of vaccine is 95% effective in preventing measles. Based on the data analyzed in the review, the number of cases decreased from 7% in unvaccinated children to under 0.5% in children who receive one dose of the vaccine. After two doses, effectiveness was similar at around 96%.[2]

Mumps: One dose of vaccine is 72% effective in preventing mumps. This rose to 86% after two doses. From data analyzed in the review, the number of cases decreased from 7.4% in unvaccinated children to 1% in children who were vaccinated with two doses.

Rubella: One dose of vaccine is 89% effective in preventing rubella.

POST-EXPOSURE PROPHYLAXIS

It is not harmful to get MMR vaccine after being exposed to measles, mumps, or rubella, and doing so may possibly prevent later disease.

Getting MMR vaccine within 72 hours or immunoglobulin (IG) within six days of being exposed to measles, may give some protection against the disease, or have milder illness. Unlike with measles, MMR has not been shown to be effective at preventing mumps or rubella in people already infected with the virus (i.e., post-exposure vaccination is not recommended).

During outbreaks of measles or mumps, everyone without presumptive evidence of immunity should be brought up to date on their MMR vaccination. And some people who are already up to date on their MMR vaccination may be recommended to get an additional dose of MMR for added protection against disease.[11]

STORAGE

It can be stored in the refrigerator at temperatures between 2°C and 8°C. The diluent (the liquid used to reconstitute the vaccine) can also be stored in the refrigerator or at room temperature but should never be frozen. If the vaccine is reconstituted (mixed with the diluent), it's recommended to administer it immediately. If not used immediately, it can be stored in the refrigerator for up to 8 hours, protected from light. All MMR vaccines must be protected from light, which can inactivate the vaccine viruses.

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JAPANESE ENCEPHALITIS

Dr. Nikhil Agrawal

BACKGROUND

Japanese encephalitis virus (JEV), is a mosquito-borne flavivirus which is the most important cause of viral encephalitis in Asia based on its frequency and severity.[1] The JEV has shown a tendency to extend to other geographic regions. Case fatality rates (CFR) averages 30% and a high percentage (30-50%) of the survivors are left with permanent neuropsychiatric sequelae. The majority of cases occur in children below 15 years of age.[2] Currently, an estimated 3 billion people live in the 24 countries, mainly in the South-East Asia and Western Pacific Regions, considered at risk of JE.[2] JE is endemic throughout most of Asia and parts of the western Pacific. For travelers to Asia, the risk of JE is extremely low but varies based on season, destination, duration, and activities. Risk is likely to be higher for expatriates or travelers with longer duration of travel or whose plans include extensive outdoor activities in rural areas.[3]

PATHOGENESIS

Following the bite of an infected Culex mosquito, Japanese encephalitis virus (JEV) replicates locally and spreads via the bloodstream, potentially causing a secondary viremia. Neuroinvasion across the blood-brain barrier allows JEV to enter the central nervous system, where it preferentially infects neurons in key brain regions. While direct viral damage occurs, a significant part of the pathogenesis involves the host's immune response. Activated microglia and astrocytes release inflammatory mediators, contributing to neuroinflammation and neuronal death. This combination of direct viral damage and immunopathology leads to the severe neurological signs and potential long-term consequences of Japanese encephalitis.

EPIDEMIOLOGY

Japanese encephalitis (JE) is a significant mosquito-borne viral encephalitis prevalent in Asia and parts of the Western Pacific. The disease is caused by the Japanese encephalitis virus (JEV), a flavivirus transmitted primarily by Culex species mosquitoes, particularly Culex tritaeniorhynchus. The virus is maintained in an enzootic cycle between these mosquitoes and amplifying vertebrate hosts, mainly pigs and wading birds, which develop sufficient viremia to infect more mosquitoes. Humans are typically dead-end hosts as they do not develop high enough or prolonged enough levels of the virus in their bloodstream to infect feeding mosquitoes. Transmission is closely linked to rural agricultural areas, especially rice cultivation and flood irrigation, which provide breeding grounds for vector mosquitoes. In temperate climates, JE transmission is seasonal, peaking

during the warmer and wetter months from May to October, while in tropical and subtropical regions, transmission can be year-round, often intensified during monsoon seasons. While most JEV infections in humans are asymptomatic, a small proportion can lead to severe encephalitis characterized by high fever, headache, altered mental status, seizures, and potentially long-term neurological sequelae or death. The epidemiology of JE is influenced by factors such as mosquito vector density, the presence of amplifying hosts, human behavior, agricultural practices, climate, and the implementation of vaccination programs.

Two epidemiological patterns of JE are recognised: epidemic and endemic. Epidemic patterns are observed mainly in northern areas (Bangladesh, Bhutan, People's Republic of China, Taiwan, Japan, South Korea, North Korea, Nepal, northern Vietnam, northern India, northern Thailand, Pakistan, and Russia) which demonstrate typical seasonal characteristics with occasional outbreaks. Endemic patterns found in southern areas (Australia, Burma, Brunei Darussalam, Cambodia, Indonesia, Laos, Malaysia, Papua New Guinea (PNG), Philippines, Singapore, southern Vietnam, southern Thailand, southern India, Sri Lanka, and Timor-Leste) occur sporadically throughout the year.[4]

TRANSMISSION

JE virus is transmitted to humans from animals and birds through the bite of an infected Culex species mosquito. These mosquitoes feed mostly at night, between dusk and dawn; pigs and wading birds are the principal hosts. Culex species mosquitoes become infected when they bite animals (particularly pigs) or birds already infected with JE. JE is mostly found in rural and peri-urban settings. Flooded rice fields and marshes provide ideal breeding grounds for Culex species mosquitoes. In temperate regions of Asia, most cases occur in the warm season, when large outbreaks can occur.[2]

Cases of JE can also occur outside the normal high transmission season. In the tropics and subtropics, JE can occur year-round, but transmission often intensifies during the rainy season and pre-harvest period in rice-cultivating regions. [2]

ACUTE ENCEPHALITIS SYNDROME

Clinically, a case of acute encephalitis syndrome (AES) is defined as a person of any age, at any time of year with the acute onset of fever and a change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) and/or new onset of seizures (excluding simple febrile seizures). [5]

GLOBAL BURDEN

Japanese encephalitis is one of the most important causes of viral encephalitis in Asia. According to WHO, nearly 50,000 cases of JE occur worldwide per year and 15,000 of them die.[6] In endemic areas, the annual incidence of disease ranges from 10 to 100 per 100,000 populations. It is postulated that the actual incidence of JE is nearly 10 times higher than reflected in recent reports to WHO.[7,8]

Vaccination is the cornerstone of JE control and prevention measures. A 2011 systematic review of JE disease burden estimated that approximately 68,000 cases occur globally each year; only about 10% of these cases are reported to WHO.

DISEASE BURDEN IN NEPAL

Japanese encephalitis was confirmed in western part of Nepal in 1978. From 2007 to 2015, 1,823 JE cases were reported with a cumulative mean incidence of 0.735/100,000 population and a case fatality rate of 6.6%. In FY 2079/80, 758 Acute encephalitis syndrome (AES) cases were reported of which 76 (10.0%) were laboratory confirmed for JE.[9] The death rate in the up-to-24 years of age group was 74%. The JE cases were most commonly reported in the age group of 1–14 years. There is a strong seasonal pattern of JE occurrence in Nepal which peaked in August and declined by October each year, which corresponds to the monsoon season. The JE cases were reported in 63 of 75 districts (84%), expanding in the mountain and hill regions. There was a strong clustering of JE incidence in the south-western and south-eastern Terai region, which is endemic for JE. **[10]**

An epidemic of JEV occurred for the first time in Nepal in 1978 in the lowland (Terai) region, a rice-growing area bordering Uttar Pradesh and where about half of the population of Nepal live, including 12.5 million children <15 years old. A total of 422 cases were reported with 119 deaths. **[11-14]**

Sporadic cases of JE had been reported even earlier than 1978, however, from all hospitals in the Terai areas.[13] During the next few years, the disease fluctuated between 50 and 800 cases annually, with a case- fatality rate between 30% and 50%. [15] Most cases occurred between July and November, peaking in August to October after the monsoon season.[15,16] Outbreaks in 1985 and 1986 in the Terai region resulted in 595 and 1299 cases, respectively, in all age groups, with mortality rates of 26.5% and 27.5%, respectively.[17] Interestingly, outbreaks in two districts, Kailali and Kanchanpur, occurred despite the absence of pigs or ducks as reservoir hosts. Analysis of epidemiological data collected during the 1986 epidemic in the Koshi Zone in the Terai region in southeastern Nepal suggested that the virus had only been recently introduced. Children accounted for most of the hospital admissions but had a markedly lower fatality rate than adults, the overall fatality rate being 15% .[18]

From 1993 to 1997, the total number of cases of JE within the 25 districts of the Terai increased from 446 cases in 1993 to 2953 cases in 1997.[19] JEV spread from the Terai to the Kathmandu Valley in September and October 1995 to cause an outbreak with a mortality of 53%.[20] Annual epidemics continue to occur in the Terai region, often associated with epidemic activity across the border in Uttar Pradesh. JE vaccination has been undertaken in high-risk districts of the Terai using inactivated vaccine, although a highly successful trial using a single dose of the Chinese SA-14-14-2 live vaccine in 1999 has made this a more plausible tool for use in the future.[21-23]

VACCINES

The Japanese encephalitis (JE) vaccines currently available are:

1. Live attenuated, cell culture-derived SA 14-14-2 (Chengdu).
2. Newer JE vaccines:
    a. Inactivated SA 14-14-2 vaccine (IC51; IXIARO by Intercell and)
    b. Inactivated Vero cell culture-derived Kolar strain, 821564XY, JE vaccine (JENVAC).
    c. Live attenuated recombinant SA 14-14-2 chimeric vaccine (JE-CV, IMOJEV).
    d. Inactivated Vero cell-derived JE vaccine (Beijing-1 JE strain)

LIVE-ATTENUATED CELL CULTURE-DERIVED SA 14-14-2 VACCINE

This vaccine is based on the genetically stable, neuro-attenuated SA 14-14-2 strain of the JEV, which elicits broad immunity against heterologous JEVs. Reversion to neurovirulence is considered highly unlikely. WHO technical specifications have been established for the vaccine production.[24] Chengdu Institute of Biological Products is the only manufacturer authorized to export this vaccine from China. The live-attenuated vaccine was licensed in China in 1989. Since then, more than 200 million children have been vaccinated.[25] Extensive use of this and other vaccines has significantly contributed to reducing the burden of JE in China from 2.5/100,000 in 1990 to <0.5/100,000 in 2004. This vaccine is also licensed for use in Nepal (since 1999); South Korea (since 2001); India (since 2006); Thailand (since 2007); and Sri Lanka.[25]

India and Nepal were among the first to introduce the SA 14-14-2 vaccine through mass campaigns and routine immunisation services.[26]

DOSAGE AND ADMINISTRATION

In Nepal, the live vaccine SA 14-14-2 (Chengdu) is given as 0.5 ml dose

administered subcutaneously to children at 12 months of age. As per the missed vaccination schedule, the vaccine (one dose) is given upto <5 years of age if the child missed vaccination as per national immunization schedule.

In China, the vaccine is given as 0.5 mL dose to be administered subcutaneously to children at 8 months of age and a second opportunity again at 2 years. In some areas, a booster dose is given at 7 years.[25]

JEEV and JENVAC can be given to immunocompromised patients. It is administered in a 2-dose schedule, intramuscular to children 1 year of age onwards. The second dose is given at least 4 weeks after the first dose.

STABILITY

The infectious titer of the vaccine is not appreciably changed after storage at 37°C for 7–10 days, at room temperature for 4 months, or at 2–8°C for at least 1.5 years.[25]

IMMUNOGENECITY

After a single dose, antibody responses are produced in 85–100% of nonimmune 1–12 years old children. A neutralization antibody titer of more than 1:10 is generally accepted as evidence of protection and post vaccination seroconversion.[26] 3

EFFICACY AND EFFECTIVENESS

Five major efficacy trials of SA 14-14-2 vaccine, completed in China from 1988 to 1999 in 1–10 years old, consistently yielded high protection rates, above 98%.[26-28] Case control studies and numerous large-scale field trials in China have consistently shown an efficacy of at least 95% following two doses administered at an interval of 1 year.[7]

EFFICACY IN NEPAL

A field trial in Nepal in 1999 reported efficacy of a single dose of 99.3% in the same year and 98.5% 1 year later.[21,22] At 5 years, the protective efficacy of vaccine was 96.2% in this study.[29] The study provides evidence that SA 14-14-2 will be useful to combat epidemics.[26]

CONTRAINDICATIONS AND PRECAUTIONS

Persons with a proven or suspected history of hypersensitivity/anaphylactic reaction to any component of CD. JEVAX, including gelatin. Persons with fever, acute infectious disease, or active untreated tuberculosis, malnutrition, general allergy and convulsion, undergoing any type of immunosuppressive therapy, weak functioning immune system should not receive this vaccine. Pregnancy and lactation are other contraindications.

ADVERSE EVENTS FOLLOWING IMMUNISATION

As in the case for all medications, administration of JE vaccine can also cause adverse reactions. Some minor reactions include fever, rash, nausea, local redness, pain or sensitivity in the injection site. These usually do not last longer than 48 hours. Rarely anaphylactic reactions like severe rashes, wheezing, low blood pressure and difficulty in breathing may occur.

VACCINE STORAGE AND SAFETY

The vaccine should be stored at 2 -8˚C and protected from light. The diluents should be stored between 2 -30˚C.

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TYPHOID VACCINE

Dr. Nikhil Agrawal

BACKGROUND

Enteric (typhoid) fever remains a major public health challenge in low- and middle-income countries, particularly in the Indian subcontinent, where disease activity is highest. Caused by *Salmonella enterica* serovar Typhi (S. Typhi), typhoid fever is an acute systemic infection affecting the mononuclear phagocyte system, intestinal lymphoid tissue, and gallbladder. Both *S. Typhi* and *S. Paratyphi* spread via the "4 Fs"—flies, fingers, feces, and fomites—especially in areas lacking clean water, sanitation, and hygiene (WASH). Improved WASH infrastructure is key to reducing transmission. Though historically neglected compared to HIV/AIDS, tuberculosis, and malaria, recent focus on typhoid has increased due to rising antimicrobial resistance. New typhoid conjugate vaccines, better surveillance, and WASH improvements have contributed to a reduced disease burden.

PATHOGENESIS

Ingested S. typhi, following a silent primary bacteremia, reaches the reticuloendothelial system and multiplies intracellularly within macrophages. After an incubation period of 7–14 days on average (ranging from 3 to 60 days), patients experience an illness with a wide range of clinical severity, more severe forms being characterized by persistent high fever, abdominal discomfort, malaise, and headache. Constipation or diarrhoea may occur in older children and adults, and younger children suffer more often from diarrhoea. Complications are estimated to occur in 10–15% of hospitalised patients and are more frequent among untreated patients whose illness has persisted for 2 weeks or more. The most common life-threatening complications are intestinal hemorrhage, intestinal perforation, and encephalopathy with hemodynamic shock. Intestinal perforation has been reported in some outbreaks at unexpectedly high rates (>40%) and associated with high mortality (18–43%).

EPIDEMIOLOGY

In 2021, there were 9.3 million global cases of enteric fever and 107.5 thousand deaths (56.1−180.8). The age-standardized incidence rate decreased from 152/100,000 person-years in 2017 to 128/100,000 person-years in 2021, and the mortality rate decreased from 1.87/100,000 person-years to 1.50/100,000 person-years. There were wide geographical differences, with South Asia contributing the most cases and deaths. Age-standardized incidence exceeded the threshold for “high burden” of enteric fever (100/100,000 person-years) in 23 countries in 2021.[1]

Children under five accounted for 40% of deaths with incidence and mortality peaking during the second year. Case-fatality was highest in low SDI countries and showed a global trend toward reduction, except among children aged 1–4 years.

The use of typhoid conjugate vaccines, which are effective in infants and young children and offer extended protection, along with improved data collection and surveillance to guide vaccine distribution efforts across high-incidence areas. [1]

DISEASE BURDEN IN NEPAL

Nepal is a relatively small country with a population of 29 million having significant geographic, social, and religious diversity. Enteric fever is endemic all over the country and proves to be a huge burden on government and private healthcare facilities. The prevalence of typhoid fever is high throughout the country which includes mountains, Kathmandu valley (capital city of Nepal, also known as the capital of enteric disease) and southern belts, most of the cases are reported from May to October.[2]

Additionally, in most healthcare facilities, it is one of the leading diagnoses for fever. World Health Organization conservatively estimates the annual prevalence of typhoid fever is 0.3% in the country.[3]

The first typhoid case in Nepal was reported from an adult British Nepalese soldier from Dharan in 1984 followed by an infant in 1989.[4] Enteric fever episodes were reported sporadically at healthcare facilities in a densely populated area of Kathmandu valley[5] which were followed by a different outbreak of S. typhi and paratyphi A in the valley.[6] In a decade (1993–2003), a total of 82, 467 blood cultures were carried out in Kathmandu valley of which 12,252 bacteria were isolated. Out of the isolated bacterium, Salmonella was found positive in 9124 (74.5%) blood cultures: 6,447 (70.7%) for Salmonella enterica serotype typhi (S. typhi) and 2,677 (29.3%) for Paratyphi A (S. paratyphi A).[7] In 2004, Salmonella enterica serotype typhi was detected from 368 patients in Kathmandu[8] which included 30 typhoid patients from Kathmandu Medical College and Teaching Hospital;[9] at the same year, 112 cases from Dhulikhel hospital;[10] while 189 cases were reported from Bir Hospital in 2006.[11] Salmonella enterica serotype Paratyphi A appeared as a significant source of enteric fever in Kathmandu in 2006.[11] S. typhi and S. paratyphi A were also isolated from gallbladders of 24 cholecystectomy patients[12] and immunoreactivity was found in chronic biliary carriers of S. typhi in Kathmandu.[13] A fatal myocarditis complicating typhoid fever was reported in an Israeli traveler returning from Nepal.[14]

Typhoid disease burden is not confined to Kathmandu; many cases have been reported from outside Kathmandu valley as well. A large number of (n = 5963) typhoid fever was recorded from Bharatpur during 2002 (population, 92,214);[15] 132 strains of S. enterica typhi, isolated from 2,568 blood samples from the eastern part of Nepal with one case of acute febrile encephalopathy[16] and 82 cases of enteric fever in the western part of Nepal between 2000 and 2005.[17,18]

Typhoid fever incidence varies substantially in Asia. Very high typhoid fever incidence has been found in India and Pakistan. In comparison, typhoid fever frequency was moderate in Vietnam and China and intermediate in Indonesia.[19] However, it is the Indian subcontinent which has the highest incidence of the disease worldwide.[20]

VACCINES

Historically, different vaccine preparations have been developed against typhoid fever, many preparations are obsolete and not available now. Typhoid fever vaccines have been used for more than a century. Clinical trials, some conducted decades ago, have demonstrated efficacy of a range of typhoid vaccines which include:

- Whole cell inactivated vaccines
- Virulence capsular polysaccharide vaccines
- Live-attenuated vaccines; and more recently
- Virulence conjugate vaccines (TCVs)

The World Health Organization (WHO) has recommended that countries consider the use of typhoid vaccines for high-risk groups and populations, and for outbreak control. Despite this, typhoid vaccines have not been widely applied in typhoid endemic areas or are often used in outbreaks.[21]

VI CAPSULAR POLYSACCHARIDE CONJUGATE VACCINES

To overcome the limitations of polysaccharide vaccine, VI capsular PS [derived either from Salmonella enterica subspecies enterica serovar Typhi (S. typhi), or from Citrobacter freundii sensu lato (C. freundii s. l.)] is conjugated to carrier proteins, TT or CRM197, converting T-independent PS to T-dependent antigen.[22]
The TCVs demonstrate (i) superior efficacy and effectiveness than unconjugated Vi-PS vaccines; (ii) longer duration of protection; (iii) immunogenicity among younger children, including infants; (iv) reasonably good herd immunity; and (v) induction of immune memory.[22]

The WHO-SAGE Working Group on Typhoid Vaccines has recommended only a single dose of the TCV at any time between 6 and 23 months of age in the endemic countries.[21,23]

VACCINES AVAILABLE IN NEPAL

Two vaccines are available in NEPAL which includes Typbar-TCV and TYPHIBEV.

The WHO has prequalified 2 typhoid conjugate vaccines (TCVs): Typbar-TCV and TYPHIBEV. By conjugating the Vi capsule to a protein carrier (eg, tetanus toxoid), these vaccines induce a more robust and enduring T-cell-mediated immune response than previous vaccines; these can be used in children under 5 and infants as young as 6 months.[24]

INDICATION

IAP/ACVIP Recommendation Typhoid Vaccines.[25, 26]

- A single dose of TCV 25 µg is recommended from the age of 6 months onward routinely.
- TCV can be administered simultaneously with measles-containing vaccine when it is offered at age of 9 months or beyond.
- For a child who has received only typhoid polysaccharide vaccine, a single dose of TCV is recommended at least 4 weeks following the receipt of polysaccharide vaccine. Routine booster for TCV at 2 years is not recommended as of now. The WHO position paper in 2018 has remarked that the body of evidence for the 5 µg vaccine is very limited.

CONTRAINDICATION AND PRECAUTIONS

The primary contraindication to a typhoid conjugate vaccine is a known severe allergic reaction to a previous dose or any of the vaccine's components.

ADVERSE EVENTS FOLLOWING IMMUNISATION

Local reactions: Injection site pain, inflammation, induration, erythema and lymphadenopathy. Fever, asthenia, malaise, flu-like episode, abdominal pain.

Gastrointestinal disorders: Nausea, vomiting, diarrhoea.

Immune system disorders: allergic-type reactions such as pruritus, rash, urticarial, difficulty breathing, hypotension, serum sickness.

Musculoskeletal and connective disorders: Myalgia, arthralgia, cervical pain.

Nervous system disorders: headache, loss of consciousness, tremor.

SCHEDULE AND DOSES

Typhoid Conjugate Vaccine is a one-dose typhoid vaccine, requiring a single 0.5 mL intramuscular injection, and is expected to provide long-lasting protection in adults, children, and infants over 6 months of age. Till now booster dose is not recommended. Example: TypbarTCV, TyphiBEV.

In routine immunisation schedule of Nepal, one dose of typhoid conjugate vaccine (TCV) is given at 15 months of age. For children who miss TCV, it should be provided at the earliest opportunity. One dose is given upto <5 years of age as per the vaccination schedule of Nepal for missed children (delayed schedule).

Injectable Polysaccharide Typhoid Vaccine given as intramuscular injection, 0.5ml for children 2 years and older. One dose is recommended at least 2 weeks before

travel, with repeated doses recommended every 2 years for those remaining at risk. Example: Typhim Vi.

Oral typhoid vaccine is a live attenuated vaccine in capsule formulation. Recommended for children aged 6 years and older. A course of 3 or 4 doses taken on alternate days, with the 4th dose being an option. 1 capsule on days 1, 3, and 5 (and day 7 if following a 4-dose schedule), taken 1 hour before food. Example: Vivotif.

EFFICACY

Given as a single-dose intramuscular dose, TCVs were found to be 79% to 95% effective in the first 2 years after vaccination in studies covering more than 100,000 children in diverse locations. The antibody response can persist for up to 7 years.[27] The injectable polysaccharide vaccine provides protection for about 2 years. The oral vaccine provides protection for up to 5 years.

STORAGE

Storage recommended in a refrigerator at 2˚-8˚C. Do not freeze.

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HUMAN PAPILLOMA VIRUS VACCINE

Dr. Sangita Shakya

BACKGROUND

Cervical cancer, caused by Human Papillomavirus (HPV), is the fourth most common cancer globally and the most common in Nepal. It's also the 4th leading cause of cancer deaths in Nepal, with an incidence rate of 14.2 per 100,000 women, nearly four times the WHO's target of 4 per 100,000 for elimination.[1]

It is projected that the new cases will be 26 million and 17 million deaths per year by 2030. Low income and low to middle income countries accounted for half of all cancers worldwide in 1975, it has become 55% in 2007 and postulated to be 61% by 2030.[2]

HPV infections are transmitted through sexual contact. Most of the time the HPV infection shows no symptoms but persistent genital infection leading to cervical cancer. HPV can also cause other diseases like ano-genital cancer and genital warts in both men and women.

Nepal launched a nationwide HPV vaccination campaign on February 4, 2025, targeting adolescent girls aged 10-14 to protect them from cervical cancer. The campaign, coinciding with World Cancer Day, aims to administer a single dose of the HPV vaccine to over 1.6 million girls, including those in schools and out-of-school girls. This initiative marks the introduction of HPV vaccination into Nepal's National Immunisation Program.[3]

Nepal has a cervical cancer incidence of 14.2 per 100,000 women, in contrast to the WHO's desired target of 4 per 100,000 women, nearly four times the target to eliminate the public health issue of cervical cancer [1]. In 2020, about 90% of new cervical cancer cases and deaths occurred in low- and middle-income countries. In 2022, there were an estimated 662,044 cases of cervical cancer worldwide.[4]

In Nepal, an estimated 1,493 women die from cervical cancer annually, with 2,244 new cases diagnosed each year.[1] Cervical cancer is the most common cancer and leading cause of cancer-related deaths among Nepalese women. The age-standardized incidence rate is 14.2 per 100,000 women, and the age-standardized mortality rate is 11.1 per 100,000 women.[1] In 37 countries, cervical cancer is the leading cause of cancer deaths in women. In 2022, there were an estimated 348,709 deaths from cervical cancer worldwide. This makes it the fourth most common cause of cancer deaths in women globally.[5]

PATHOGENESIS

Cervical cancer (CC) remains a public health problem and ranks fourth in cancer mortality in women worldwide. The main etiologic factor for CC development is a persistent infection with high-risk (HR) human papillomavirus (HPV), responsible for almost 100% of all CC cases. However, some studies report that between 5 and 8% of CC cases are HPV-negative; significantly, the majority are adenocarcinomas. [6, 7]

More than 200 HPV types have so far been identified. Around 15 types are classified as high-risk types, including HPV 16, 18, 31, 33, 45, 52, and 58, associated with cervical, anogenital, and oropharyngeal cancers, and HPV16 is found in approximately 60% of the CC cases. [7] Low-risk HPV types, mainly types 6 and 11, commonly cause benign anogenital warts.

HPVs are small, non-enveloped viruses with an 8-kb circular double-stranded DNA contained in a 55 nm icosahedral capsid. The viral genome holds the long control region (LCR) that regulates genome replication and transcription of the early (E1-E7) and the late-expressed genes L1 and L2. [8]

HPV targets the cervix transformation zone, leading to premalignant lesions and potentially cancer. Initial classification used CIN grades I-III and carcinoma in situ. The Bethesda system revised this, renaming CIN I as low-grade squamous intraepithelial lesion (LSIL) and CIN II-III as high-grade SIL (HSIL), reflecting a better understanding of lesion progression.[9]

HPV infects basal cervical epithelial cells via micro-wounds, likely binding to host membranes through heparan sulfate proteoglycans (HSPGs),[10] integrins, tetraspanins, and growth factor receptors (KGFR/EGFR), with EGFR signaling crucial for endocytosis.[11] Following uptake, the capsid interacts with retromer components for nuclear transport of the L2-DNA complex via microtubules. Viral proteins E1/E2 initiate replication, with E2 partially repressing E6/E7. Limited E6/E7 expression delays differentiation, supporting low-level replication. Differentiation upregulates early genes (E4, E5) for genome amplification, with E5 modulating EGFR/KGFR. Late genes L1/L2 are expressed in differentiated cells for virion assembly and release facilitated by E4.

The immune system clears most HPV infections, with 60% resolving within one year and 90% within two years. Persistent infections beyond two years increase the risk of cervical intraepithelial neoplasia (CIN).[12]

EPIDEMIOLOGY

In 2022, there were approximately 662,044 cervical cancer cases (ASIR: 14.12/100,000) and 348,709 deaths (ASMR: 7.08/100,000) globally, ranking it as the fourth leading cause of cancer morbidity and mortality in women. China and India accounted for 42% of cases and 39% of deaths. Higher Human Development Index (HDI) levels correlate with lower cervical cancer rates across all age groups. [3] Between 2003 and 2012, overall ASIR and ASMR declined slightly, while early-onset cases increased. Projections indicate a substantial rise in cases (56.8%) and deaths (80.7%) by 2050 if current trends continue, especially in transitioning

countries. The WHO launched a global initiative in 2020 with 2030 targets: 90% HPV vaccination for girls by 15, 70% screening for women at 35 and 45, and 90% treatment for precancerous lesions or cancer. Despite progress in some transitioning countries, cervical cancer remains a significant global public health issue. [13]

DISEASE BURDEN IN NEPAL

Cervical cancer is the most common cancer in women in Nepal, and is a leading cause of cancer-related deaths in women. Most cervical cancers in Nepal are caused by HPV-16 or HPV-18. About 2% of women in Nepal are estimated to have HPV-16/18 at any given time.[14] Nepal's national guidelines recommend visual inspection with acetic acid (VIA) every five years for women aged 30–60. However, screening utilization is low, and most patients are diagnosed at an advanced stage. The WHO recommends HPV testing as a preferred screening strategy.

Nepal has a population of 11.5 million women aged 15 years and older who are at risk of developing cervical cancer. Current estimates indicate that every year 2244 women are diagnosed with cervical cancer and 1493 die from the disease. Cervical cancer ranks as the 1st most frequent cancer among women in Nepal and the 2nd most frequent cancer among women between 15 and 44 years of age. About 2.0% of women in the general population are estimated to harbor cervical HPV-16/18 infection at a given time, and 80.3% of invasive cervical cancers are attributed to HPVs 16 or 18.[1]

HPV VACCINE

Human papillomavirus (HPV) vaccines are vaccines intended to provide acquired immunity against infection by certain types of human papillomavirus (HPV).[13]
The first HPV vaccine became available in 2006.[15]
Currently there are six licensed HPV vaccines:

1. Three bivalent (protect against two types of HPV)- which protects against HPV types 16 & 18
2. Two quadrivalent (against four)- which protects against additional 2 strains 6 & 11
3. One nonavalent vaccine (against nine) – which protects against 16,18,6,11,31,33,45,52 &58

All have excellent safety profiles and are highly efficacious or have met immunobridging standards. All of them protect against HPV types 16 and 18, which are together responsible for approximately 70% of cervical cancer cases globally. [16] The quadrivalent vaccines provide additional protection against HPV types 6 and 11. The nonavalent provides additional protection against HPV types 31, 33, 45, 52 and 58. It is estimated that HPV vaccines may prevent 70% of cervical cancer, 80% of anal cancer, 60% of vaginal cancer, 40% of vulvar cancer, and show more than 90% effectiveness in preventing HPV-positive oropharyngeal cancers. They also protect against penile cancer. They additionally prevent genital warts (also known as anogenital warts), with the quadrivalent and nonavalent vaccines providing virtually complete protection. The WHO recommends a one or two-dose schedule for girls aged 9–14 years, the same for girls and women aged 15–20 years, and two doses with a 6-month interval for women older than 21 years. The vaccines provide protection for at least five to ten years.

VACCINE INDICATION

It is indicated in all children from age 9 to 14 years- 2 doses 6 months apart is ideal.
3 doses for girls and women aged 15-25 years.[17, 18]

The primary target for HPV vaccination in most recommending countries is girls aged 9–14.[18] Vaccination schedules vary by age. In 2023, 27% of girls aged 9–14 globally received at least one dose (45% in 37 countries using a single-dose schedule). By September 2024, 57 countries implemented single-dose schedules. As of November 2024, at least 144 countries (74% of WHO member states) included HPV vaccine for girls in national schedules; 47 countries (24%) also did so for boys in 2022. High vaccination coverage can also provide herd immunity to unvaccinated individuals.

The HPV vaccine is on the WHO's List of Essential Medicines, and the WHO recommends it as part of routine vaccinations globally, prioritizing cervical cancer prevention (82% of HPV-related cancers, >95% HPV-caused). In 2020, 88% of cervical cancers and 90% of deaths occurred in low- and middle-income countries, compared to 2% in high-income countries. The WHO's primary target is girls aged 9–14, aiming for 90% vaccination coverage by age 15. Secondary targets include females ≥15, boys, and MSM. HPV vaccination is a cost-effective measure against cervical cancer, especially in resource-limited settings, but cervical cancer screening remains necessary post-vaccination.[19]

As of September 2024, 57 countries are implementing the single-dose schedule.[19] A growing number of vaccine products initially prequalified for use in a 2-dose schedule can now be used in a single-dose schedule. Before, it was unsure whether two doses of the vaccine may work as well as three doses.[20] The US Centers for Disease Control and Prevention (CDC) recommends two doses in those less than 15 years and three doses in those over 15 years.[21]

As of 2022, 47 countries (24% of WHO member states) have introduced HPV vaccine in their national immunisation programme for boys. For instance, it is the case in Switzerland, Portugal, Canada, Australia, Ireland, South Korea, Hong Kong, the United Kingdom, New Zealand, the Netherlands, and the United States.[22]

In males, Gardasil and Gardasil 9 offer near-complete protection against HPV types 6 and 11, which cause genital warts. These vaccines also reduce the risk of precancerous lesions linked to penile and anal cancers and are effective against high-risk HPV types 16 and 18. Cervarix, unlike Gardasil-based vaccines, does not protect against genital warts and is not approved for males. Due to the lower incidence of penile and anal cancers compared to cervical cancer, HPV vaccination in young men is likely less cost-effective than in young women. Gardasil is also beneficial for men who have sex with men (MSM), who have a higher risk of genital warts and these cancers.

CONTRAINDICATION

- A severe allergic reaction (e.g., anaphylaxis) may occur to any of the components of vaccine

- HPV vaccine is not recommended for use during pregnancy.
- The vaccine has not been causally associated with adverse outcomes of pregnancy or with adverse effects on the developing fetus. But data are limited on vaccination during pregnancy. Pregnancy testing before vaccination is not needed. However, if a woman is found to be pregnant after initiation of the vaccination series, the following dose should be delayed until after the completion of the pregnancy

PRECAUTION

A moderate or severe acute illness is a precaution to vaccination, and vaccination should be deferred until symptoms of the acute illness improve. A minor acute illness (e.g., diarrhoea or mild upper respiratory tract infection, with or without fever) is not a reason to defer vaccination.

ADVERSE EVENTS FOLLOWING IMMUNISATION

The most common adverse reactions reported during clinical trials of HPV vaccines were local reactions at the site of injection. Pain, redness or swelling were reported by 20% to 90% of recipients with rise in temperature of 100°F.

No serious adverse events have been associated with either HPV vaccine based on monitoring by CDC and the Food and Drug Administration.

Other reported systemic adverse reactions include nausea, dizziness, myalgia and malaise.

SCHEDULE AND DOSES

HPV vaccination is administered as: A two-dose series (0, 6-12 months) for most persons who initiate vaccination at ages 9 through 14 years. A three-dose series (0, 1-2, 6 months) for persons who initiate vaccination at ages 15 through 45 years, and for immunocompromised persons.

An alternative single-dose schedule can be used for ages 9 to 20 years, for HPV vaccines for which evidence is available for single-dose use. Current evidence shows single dose schedule has comparable efficacy and duration of protection as a two-dose schedule and may offer programmatic advantages, be more efficient and affordable, and contribute to improved coverage.[23]

The National Immunisation Program of Nepal conducted nation-wide HPV vaccination campaign in February 2025 for grade 6-10 schoolgirls and out-of-school girls 10 – 14 years of age, with one-dose HPV vaccination schedule using bivalent HPV vaccine. Following this, HPV vaccine has been integrated in routine immunisation and every year one dose HPV vaccination will be provided to schoolgirls in grade 6 and out-of-school girls aged 10 years.[24]

NEPAS recommends one dose for boys aged 9-14 years. 3 doses at 0, 2, and 6 months if age older than 15years for girls or in immunocompromised.

ROUTE OF ADMINISTRATION

HPV vaccine is injected intramuscularly in the deltoid muscle in the upper arm or the anterior aspect of thigh.

The vaccine should be well shaken before use.
This vaccine should not be mixed with any other vaccine.

VACCINE EFFICACY

The vaccine is nearly 100% effective at preventing external genital warts.
It's over 99% effective at preventing pre-cancer caused by HPV types 16 or 18.

The 9-valent HPV vaccine protects against more than 99% of HPV disease related to genotypes 6, 11, 16, and 18.

The vaccine is most effective when given before exposure to HPV.

STORAGE

The HPV vaccine should be stored in a refrigerator at 2° to 8° C. It should be protected from light and not frozen.

Nepal launched a nationwide HPV vaccination campaign on February 4, 2025, to protect girls from cervical cancer. The campaign is part of Nepal's National Immunisation Program.

The Family Welfare Division came up with this initiative and this campaign was mainly based in schools and the target population was between class 6 through class 10 assuming that our target population is between 9 to 14 years.

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INFLUENZA VACCINE

Dr. KM Roma

BACKGROUND

Influenza is an infectious respiratory illness caused by the single-stranded RNA orthomyxovirus, affecting the nose, throat, and lungs. It ranges from mild to severe, with complications potentially leading to hospitalization or death. Young children, especially those with bronchial asthma, are at higher risk for severe outcomes.[1]

Seasonal influenza

Seasonal influenza is the annual circulation of influenza viruses, peaking in winter in temperate zones. Transmission is via respiratory droplets and contaminated surfaces, with outbreaks lasting 6-8 weeks or longer. Seasonality is affected by humidity, temperature, and crowding. Outbreak timing and severity vary with viral traits and population immunity. Illness severity ranges from mild to fatal, especially in high-risk groups. Due to ongoing viral evolution, seasonal flu vaccines are updated biannually.

Three main influenza types cause seasonal illness: A, B, and C. Type A viruses are subtyped by hemagglutinin (H) and neuraminidase (N). Current circulating subtypes are A(H1N1) (also the 2009 pandemic strain) and A(H3N2). Two type B lineages, Victoria and Yamagata, also circulate seasonally. Type C typically causes milder infections with sporadic cases. Seasonal flu vaccines include only types A and B due to their greater public health impact.[2]

Pandemic influenza

An influenza pandemic occurs when a novel virus—previously not circulating in humans and to which most people lack immunity—emerges and spreads widely, often outside the typical flu season. Because immunity is low, infection rates can be very high. Pandemic severity varies, with some causing severe illness and others milder cases, though reasons for this variation remain unclear. The 1918–1919 “Spanish Flu” pandemic caused an estimated 20–50 million deaths globally, while later pandemics in 1957 and 1968 were less deadly. In 2009, a new influenza A (H1N1) strain emerged, causing a global pandemic. This strain has since become part of the seasonal influenza virus pool. At present, there is no pandemic virus actively circulating around the world.[3]

Zoonotic or variant influenza

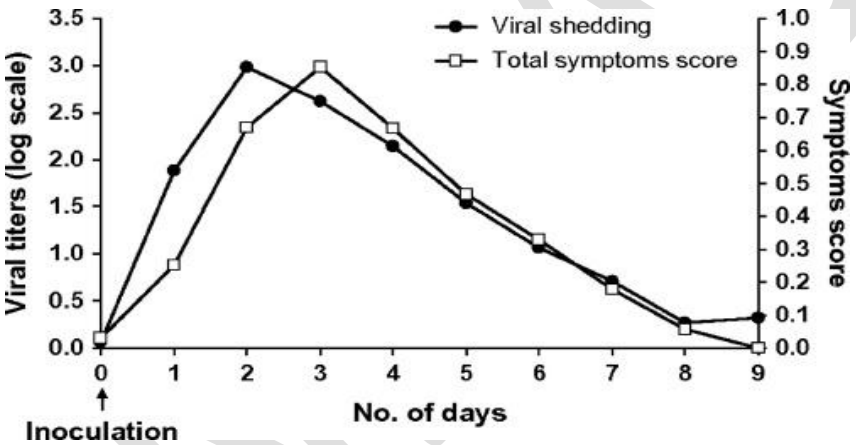
Humans can occasionally contract animal influenza viruses like avian A(H5N1) and A(H9N2) or swine A(H1N1) and A(H3N2). These are distinct from human strains and typically don't spread easily between people. Rare human infections occur through direct animal contact or contaminated environments, causing illness from mild to severe. If these viruses gain efficient human-to-human transmission, epidemics or pandemics could arise. Sporadic human cases are reported, such as

the 2011 variant A(H3N2) from pigs. "Variant" also describes non-seasonal H1 and H3 swine viruses found in humans. Other animal viruses infecting humans, like avian A(H5N1), A(H7N7), A(H7N9), and A(H9N2), are termed "avian influenza" or "zoonotic influenza".[4]

PATHOGENESIS

When the influenza virus enters the respiratory tract through aerosol or contact with infected saliva or respiratory secretions, it binds to and replicates within epithelial cells. The virus reproduces within cells of the upper and lower respiratory system. Viral replication along with the immune response to the infection results in the damage and loss of cells that line the respiratory tract. As the infection subsides, the epithelium regenerates and this regeneration may last up to a month. Coughing and fatigue can persist for as long as 2 weeks following the infection.[5-7]

A recent study aggregated data from several studies where human volunteers were exposed to the influenza virus, and the viral replication along with flu-like symptoms was documented. This graph summarizes the results:



Influenza can lead to complications in both the upper (e.g., sinusitis, otitis media) and lower (e.g., bronchitis, croup) respiratory tracts. A serious complication is pneumonia, which can be:

- Primary viral pneumonia, caused by direct viral damage to the lungs, especially severe in high-risk groups but can also affect healthy individuals (e.g., pregnant women).
- Secondary bacterial pneumonia, where symptoms return after initial recovery and is caused by bacteria like S. pneumoniae, S. aureus, and H. influenzae.

While antibiotics can treat bacterial pneumonia, early fatality rates were high due to limited treatment options. The exact reason influenza leads to pneumonia remains unclear despite various theories.

EPIDEMIOLOGY

Influenza is a global health concern, with an estimated annual attack rate of 5–10% among adults and 20–30% among children.[1] The burden of influenza is higher in children under the age of two. In 2017, influenza-related deaths represented 0.26% of total mortality. Additionally, influenza was responsible for 5.6% of deaths due to lower respiratory tract infections (LRTI), equating to approximately 145,000 fatalities across all age groups globally.[8] The incidence of influenza and its associated acute lower respiratory infections (ALRI) is markedly higher in developing nations compared to their developed counterparts.[9] A recent systemic review has revealed that influenza was responsible for 10% of hospital admissions due to respiratory illnesses in children under 18 with admission rates of 5% in infants under six months and 16% in children between the ages of 5 and 17.[10]

On June 11, 2009, the WHO officially announced that the ongoing Influenza A/H1N1 outbreak was the first pandemic of the 21st century; following the identification of a new strain of the Influenza A virus subtype H1N1 in April 2009. As of May 30, 2010, a global update from the World Health Organization (WHO) indicated that over 214 countries have reported lab-confirmed instances of the H1N1 2009 pandemic influenza, resulting in more than 181,114 fatalities.[3]

DISEASE BURDEN IN NEPAL

Influenza represents a significant public health challenge In Nepal, yet its epidemiological characteristics remain largely unexplored. The Early Warning and Response System (EWARS), collects weekly data on cases and fatalities associated with six priority diseases, including Severe Acute Respiratory Infection (SARI). Currently, 118 reporting sites contribute to EWARS. In 2019, these sites documented a total of 10,542 cases of SARI. During the study period, the predominant strain of influenza identified was A/Pdm09, accounting for 53.1% of cases in Nepal.[11] A study by Adhikari et al. corroborated these findings, indicating that the pandemic influenza AH1N1 was the leading strain in 2009.[12] In contrast, earlier research by Upadhayay et al.[11] and Jha et al.[13] indicated that influenza A/H3 was responsible for 60.1% and 51.0% of infections in 2014 and 2016, respectively. Additionally, Jha et al. previously noted that Nepal experiences two peaks of influenza annually, occurring in January and July/ August –August/ September. Identification of H5N1 in humans was the first recorded case of such an infection in Nepal.

Nepal experiences year-round circulation of influenza B, A/H3N2, and A/H1N1pdm09, with increases from July to November. Peak transmission occurs post-monsoon and in winter. Screening for Pandemic influenza A (H1N1) began on April 27, 2009; the first case was identified on June 21, and community spread was announced on October 15, 2009.

INFLUENZA VACCINE

Flu vaccinations induce antibody production within about two weeks, providing protection against the vaccine's included viruses. Annual vaccination with the latest

strain-specific vaccine is crucial due to yearly viral changes. Seasonal flu vaccines target the most prevalent upcoming strains. Trivalent vaccines protect against two influenza A subtypes (H1N1 and H3N2) and one influenza B lineage (Victoria). Quadrivalent vaccines offer broader protection by including an additional influenza B lineage (Yamagata). These vaccines are authorised for individuals aged 6 months and older.

INDICATIONS

1. Children aged 6 months to 5 years
2. The “high-risk” children over 5 years which includes
    a. Chronic conditions like heart, lung (excluding asthma), blood, and kidney problems (including nephritic syndrome), chronic liver disease, and diabetes.
    b. Weakened immune systems due to congenital or acquired immunodeficiency, including HIV.
    c. Those on long-term salicylate therapy.
    d. Laboratory personnel and healthcare professionals (this category seems out of place as it refers to adults, not children).

CONTRAINDICATIONS

Contraindications include a history of serious reaction to influenza vaccine and age under 6 months. Vaccination should be deferred in individuals with moderate or severe illness, with or without fever, until recovery.

SITE OF INJECTION

Deltoid muscle in the upper arm is the preferred site, although the vastus lateralis muscle in the anterolateral thigh may be used if the deltoid site cannot be used due to lesser muscle mass in younger children.

PRECAUTIONS

Moderate to severe acute illness.

History of Guillain-Barré Syndrome (GBS) within six weeks following the administration of the influenza vaccine.

History of egg allergy.

History of reported reactions to egg that include symptoms beyond urticaria e.g., angioedema, swelling, respiratory distress, light-headedness, palpitations, or recurrent vomiting. Patients, who have required anaphylaxis treatment or other emergency medical interventions, should receive the vaccine in an inpatient or outpatient medical setting. The vaccination must be conducted by a healthcare professional equipped to identify and manage severe allergic reactions.

ADVERSE EVENTS FOLLOWING IMMUNISATION

Adverse effects are usually mild and brief, particularly when compared with symptoms of severe flu. Some minor side effects that might happen include:

• Pain, inflammation, or swelling at the injection site

• Mild fever

• Pain

However, infrequently, influenza vaccination may lead to serious issues, including severe allergic reactions.[3]

VACCINE SCHEDULE AND DOSE

Inactivated influenza vaccine (IIV) is administered intramuscularly in a 0.5 mL dose for all age groups starting from 6 months.[3]

- **Children 6 months to under 9 years:** For those with no prior influenza vaccination history, a primary series of two doses, separated by at least 4 weeks, is required, followed by annual vaccination.
- **Individuals 9 years and older:** Annual single-dose vaccination is recommended.

The Nepal Paediatric Society (NEPAS) recommends annual influenza vaccination for all individuals aged 6 months and older, utilizing either inactivated influenza vaccine (IIV) or recombinant influenza vaccine (RIV).

EFFICACY

The efficacy of influenza vaccines exhibits considerable variation, influenced by several factors including the definition of cases (for instance, laboratory-confirmed influenza versus the less specific influenza-like illness), the match between the vaccine strains and the circulating influenza strains, vaccine preparation, dose, previous exposure to antigens, age and underlying health conditions of the individual. Inactivated vaccines demonstrate an efficacy of 59%. Currently, there is a lack of published data regarding the efficacy and effectiveness of influenza vaccines. Quadrivalent vaccines showed an efficacy of 63.2% against moderate to severe influenza in children aged 6 months to 35 months.

VACCINE STORAGE

Store the influenza vaccine in the refrigerator at 2 to 8°C. Never subject the influenza vaccine to freezing temperatures.

UPCOMING VACCINES

Improved vaccinations through universal influenza vaccine that will provide strong, broad, and long-lasting protection and significantly reduce global influenza mortality and hospitalisations is under research. A universal vaccination to protect against symptomatic influenza over multiple years is unlikely to be available within the next decade.[14] Current research suggests that adding adjuvants to cell-based vaccinations and utilizing new platforms, such as mRNA technology, will offer additional benefits over current vaccines.

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VARICELLA ZOSTER VACCINE

Dr. Saurav Khetan

BACKGROUND

Varicella-zoster virus (VZV) is one of the eight herpesviruses known to cause human infection and is distributed worldwide. VZV infection causes two clinically distinct forms of disease: varicella (chickenpox) and herpes zoster (shingles). VZV is a worldwide pathogen known by many names: chickenpox virus, varicella virus, zoster virus, and human herpesvirus type 3 (HHV-3). Primary VZV infection results in the diffuse vesicular rash known as chickenpox and it mostly infects children and teens. After the primary infection virus goes dormant in the nerves, including the cranial nerve ganglia, dorsal root ganglia and autonomic ganglia. Many years after the patient has recovered endogenous reactivation of latent VZV typically results in a localised skin infection known as herpes zoster or shingles commonly seen in late teens and adults.

Primary varicella infection in children is generally a mild disease compared to more severe presentations in adults or immunocompromised patients. The rates of infection, hospitalisations and mortality have all declined since the introduction of the varicella vaccine in 1995.[1]

PATHOGENESIS

Varicella-zoster virus (VZV) typically enters the host through the respiratory tract, initiating replication in the nasopharynx and regional lymph nodes. Chickenpox infection is transmitted from person to person primarily by inhalation of aerosols generated from vesicular fluid from varicella or herpes zoster lesions. Transmission may occur if infected respiratory tract secretions are aerosolised. Although historically, the infectious period for chickenpox was generally considered as being from 48 hours before, to 4 to 7 days after, onset of rash, a recent review suggested that transmission rarely occurs before the onset of rash, and may continue until all the lesions have crusted over.[2] A primary viremia then disseminates the virus to various organs, including the liver, spleen, and sensory ganglia. Subsequent replication in these organs leads to a secondary viremia, during which the virus infects the skin, causing the characteristic vesicular rash. VZV establishes latency in the dorsal root ganglia, which can later reactivate to cause herpes zoster (shingles).[3]

EPIDEMIOLOGY

Cases of varicella are seen throughout the year but, they are seen more commonly in the winter and early spring. Varicella is spread mainly by the respiratory route. The highest prevalence occurring in the 4 - 10 years old age group. Chickenpox is a very contagious disease caused by the varicella-zoster virus (VZV). It causes a blister-like rash, itching, tiredness, and fever. Each year, chickenpox causes about 4 million cases, about 10,600 hospitalisations and 100 to 150 deaths.[4] Factors affecting risk of exposure include area of residence i.e., overcrowding, childcare or day-care centres, school and other.

DISEASE BURDEN

The incidence and death cases due to varicella zoster viral infection (VZVI) were 8,39,63,744 and 14,553 respectively in 2019 globally.[5] The age-standardized incidence rate (ASIR) increased slightly all over the world, while the age-standardized DALY rate (ASDR) decreased from 1990 to 2019.[5] The ASIR and ASDR drastically decreased in children (aged <20 years old), while it significantly increased in old-aged adults (aged >50 years old), with highest ASIR and ASDR in the High-income Asia Pacific and Western Sub-Saharan Africa, respectively.[6] The age-standardized death and DALYs rate of VZVI decreased with the increase of sociodemographic index (SDI).[4]

VARICELLA VACCINES

Two live attenuated varicella virus vaccines are available: Single-antigen varicella vaccine and MMRV vaccine. Both vaccines are derived from the Oka strain of live, attenuated VZV. The Oka strain was isolated in Japan in the early 1970s from vesicular fluid in a healthy child who had natural varicella and was attenuated through sequential propagation in cultures of human embryonic lung cells, embryonic guinea-pig cells and human diploid cells (WI-38).[4] The virus had undergone further passage through human diploid-cell cultures (MRC-5) for a total of 31 passages.

Varicella zoster vaccine is a single-antigen varicella vaccine that can be used among healthy persons aged >12 months.[7] This is a lyophilized vaccine which contains a minimum of 1350 plaque forming unit (PFUs) of Oka/Merck VZV in each 0.5 mL dose3. Each dose also contains 12.5 mg of hydrolysed gelatin, trace amounts of neomycin and fetal bovine serum, 25 mg of sucrose, and trace residual components of MRC-5 cells. When reconstituted this vaccine can be stored at room temperature for a maximum of 30 minutes.

MMRV vaccine can be safely used among healthy children aged from 12 months to 13 years.[7] The attenuated measles, mumps and rubella vaccine viruses in MMRV are identical and of equal titre to those in the measles, mumps, and rubella (MMR) vaccine.[4] The titre of Oka/Merck VZV is higher in MMRV than in single-antigen varicella vaccine, a minimum of 3.99 log10 PFUs compared with 1,350 PFUs (approximately 3.13 log10) in each 0.5 mL dose. Even this vaccine can be stored for a maximum of 30 minutes after reconstitution.

IMPACT OF VACCINE ON CLINICAL MANIFESTATIONS

Approximately 20 percent of children who receive one dose of vaccine may develop varicella infection, known as "breakthrough disease".[7] The breakthrough infection is often mild and has atypical rash. Vaccinated children have decreased duration of fever, maculopapular rashes and a smaller number of rashes compared to an unvaccinated child. Even the rates of complication were shown to be less in vaccinated child than unvaccinated child.

VACCINE SCHEDULE [8, 9]

CDC and ACVIP recommends offering the vaccine to all healthy children with no prior history of varicella with special emphasis in all children belonging to certain high-risk groups as enumerated below:

- Children with humoral immune deficiencies.
- Children with HIV infection but with CD4 counts 15% and above the age related cut off.
- Leukaemia but in remission and off chemotherapy for at least 3–6 months.
- Children on long-term salicylates. Salicylates should be avoided for at least 6 weeks after vaccination.
- Children likely to be on long-term steroid therapy. The vaccine may be given at any time if the children are on low dose steroids/ alternate day steroids but only 4 weeks after stopping steroids if the patients have received high dose steroids (> 2 mg/kg) for 14 days or more.
- In household contacts of immunocompromised children.
- Adolescents who have not had varicella in past and are known to be varicella IgG negative, especially if they are leaving home for studies in a residential school/college.
- Children with chronic lung/heart disease.
- Seronegative adolescents and adults if they are inmates of or working in the institutional set up, e.g., school teachers, day care centre workers, military personnel and health care professionals.

For post-exposure prophylaxis in susceptible healthy nonpregnant contacts preferably within 3 days of exposure (efficacy 90%) and potentially up to 5 days of exposure (efficacy 70%, against severe disease 100%).

CONTRAINDICATION

During pregnancy
Individuals with a history of anaphylactic reactions to any component of the vaccine (including neomycin)
Individuals with clinically manifested HIV infection and in immunocompromised

PRECAUTIONS

When used in adult females, pregnancy should be avoided for 3 months after vaccination.
Due to the theoretical risk of Reye syndrome, the use of salicylates is discouraged for 6 weeks following varicella vaccination.

ADVERSE EVENTS FOLLOWING IMMUNISATION

Adverse reactions, documented carefully in prelicensure/ post licensure studies, include local reactions such as pain, redness and swelling at vaccination site, injection site rash, fever and a systemic varicella like rash in around 5%. Transmission of the vaccine virus from vaccines to contacts is rare especially in the absence of a vaccine related rash in the vaccines. However, vaccine recipients who develop a rash should avoid contact with persons without 'evidence of immunity' who are at high risk for severe complications. The side effect profile is similar with the 2-dose schedule.

DOSAGE, ROUTE OF ADMINISTRATION AND SCHEDULE [9]

Recommended dose is 0.5 ml to be administered subcutaneously. Minimum infectious virus content should be 1000 Plaque Forming Units. ACVIP recommends two doses of vaccine for all age group. The vaccines are licensed for age 12 months and above. After a single dose of varicella vaccine, approximately 15% of vaccines remain at risk of developing a breakthrough varicella disease. Two doses of varicella vaccine offer superior individual protection as compared to a single dose.

Single antigen Varicella vaccine

Primary immunisation
First dose: age of 12 months
Second dose at 4–6 years.
NEPAS recommends first dose at 13 months and second at 16 to 19 months of age as in our country first dose uptake is not 90%.

Catch-up vaccination
Children below the age of 13 years should receive 2 doses 3 months apart and those aged 13 years or more should receive 2 doses at an interval of 4–8 weeks. All high-risk children should, receive two doses 4–8 weeks apart irrespective of age.

MMRV vaccine
Routine 2-dose vaccination
First dose at 12 through 15 months' old
Second dose at 4 through 6 years' old
Second dose catch-up vaccination
If the 2nd dose is administered after the 7th birthday, the minimum interval between doses is:
3 months for children younger than 13 years
4 weeks for people 13 years and older
People 13 years or older
MMRV vaccine is not approved for people in this age group, so use the single-antigen varicella vaccine.

VACCINE STORAGE

Varicella vaccine must be kept at 2-8°C temperatures

RECOMBINANT ZOSTER VACCINE (SHINGLES)

This vaccine contains the glycoprotein E (gE) antigen of the Varicella Zoster Virus (VZV), which is obtained by culturing genetically engineered Chinese Hamster Ovary cells, in media containing amino acids, with no albumin, antibiotics, or animal-derived proteins. The gE protein is purified by several chromatographic steps, formulated and lyphophilised.
Composition: Each 0.5-mL dose contains: 50 µg of the r gE antigen, 50 µg of MPL and 50 µg of QS-21. The vaccine does not contain any preservative.

Schedule: The schedule consists of 2 doses; the first dose is followed by the 2nd dose, 2-6 month later, by IM route. This can be administered simultaneously with unadjuvanted inactivated seasonal influenza vaccine, 23 valent pneumococcal polysaccharide vaccine (PPV23) or Tdap.
Contraindications: Hypersensitivity to the active substances or to any of the excipients
Schedule:
ACVIP recommends the recombinant Zoster vaccine, to all immunocompetent adults aged ≥ 50 y, irrespective of prior receipt of varicella vaccine or zoster vaccine live (ZVL).
It should be administered intramuscularly in a 2-dose schedule, with the 2nd dose administered 2-6 months after the first dose.
If the 2nd dose is administered at an interval of < 4 weeks, it is an invalid dose and should be repeated at least 4 weeks after the early dose.
In USA in 2021, this vaccine is recommended for those > 18 y, who are at increased risk of Herpes Zoster due to immunodeficiency or immunosuppression caused by known disease or therapy.

POST-EXPOSURE PROPHYLAXIS (PEP)

PEP should be issued only for those in contact with chickenpox or those in contact with:

- Disseminated shingles
- Immunocompetent individuals with exposed shingles lesions (for example, ophthalmic shingles)
- Immunosuppressed individuals with localised shingles on any part of the body in whom viral shedding may be greater

VZ PEP usually isn't needed if someone already has varicella antibodies (VZV IgG). For healthy individuals (including pregnant people), a history of chickenpox, shingles, or two vaccine doses usually means they're immune. If there's no such history, antibody testing can help decide if PEP is useful. If VZV IgG is less than 100 mIU/ml, antiviral PEP is recommended. For those with weakened immune systems, past infection or vaccination isn't a reliable sign of immunity, so their antibody levels should be checked quickly. Immunosuppressed individuals with VZV IgG levels of 150 mIU/ml or higher likely won't benefit from PEP. Therefore, if their VZV IgG is below 150 mIU/ml (quantitative test) or negative/equivocal (qualitative test), they should be offered treatment.[10]

Types of PEP

Antiviral post-exposure prophylaxis is recommended for all at-risk individuals who are susceptible to varicella-zoster virus, including newborns. For neonates exposed to their mothers within one week before or after birth, antiviral treatment should be supplemented with intravenous varicella immunoglobulin (either a hyperimmune product like Varitect CP or standard IVIG).[10]

Antivirals

Oral aciclovir (or valaciclovir) is now the first choice of PEP for susceptible immunosuppressed individuals, all susceptible pregnant women at any stage of

pregnancy and infants at high risk. Antivirals (oral aciclovir or valaciclovir) should be given from day 7 to day 14 after the first day of exposure.[10]

Recommended doses of oral antivirals[10]

	Oral aciclovir	**Oral valaciclovir**
Neonates	20 mg/kg 4 times daily	
Children and infants under 2 years of age	10 mg/kg 4 times daily, days 7 to 14 after exposure	Not licensed but can be used
Children 2 to 17 years of age	10 mg/kg (up to a maximum of 800mg), 4 times daily, from days 7 to 14 after exposure	20 mg/kg (up to a maximum 1,000mg) 3 times daily, from days 7 to 14 after exposure
Adults	800mg 4 times daily, from days 7 to 14 after exposure	1,000mg 3 times daily, from days 7 to 14 after exposure

Varicella-Zoster Immunoglobulin (VZIG)

It is recommended that a treatment dose of 25 IU/kg to 50 IU/kg (1 to 2 ml/kg) (up to a maximum of 5mls (one vial)) is administered as a single dose as post-exposure prophylaxis for neonates, exposed to intrauterine VZ infection within the last 7 days of pregnancy, with rash onset in the mother presenting within 1 week of delivery. The product should be given by slow i.v. infusion (0.1 ml/kg/ hr for the first 10 minutes and then slowly increased to a maximum for 1ml/kg/hr for the rest of the infusion).[10]

Normal intravenous immunoglobulin (IVIG)

Contacts who cannot receive antivirals should be given IVIG at a dose of 0.2g per kg body weight (4 ml/kg for a 5% solution) instead. This will produce serum VZV antibody levels equivalent to those that were achieved with VZIG.[10]

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HEPATITIS A VACCINE

Dr. Anna Sharma

BACKGROUND

Hepatitis A (HAV) is now classified as the sole member of the *Hepatovirus* genus within Picornaviridae. HAV is one of the most common causes of acute hepatitis infection worldwide. This non-enveloped, icosahedral virus, measuring 27 to 32 nm, is transmitted feco-orally and displays notable differences in its physical form when excreted versus circulating in the blood.

PATHOGENESIS

HAV is typically acquired through ingestion (through fecal-oral transmission) and replicates in the liver. After 10 to 12 days, virus is present in blood and is excreted via the biliary system into the feces.[1] Following an incubation period of 15–50 days (mean, 30 days) after HAV infection, patients develop symptoms of acute hepatitis with elevated levels of serum aspartate/alanine aminotransferases (AST/ALTs). Before symptoms, there are waves of viremia and copious amounts of fecal viral shedding. Feces are the primary source of HAV transmission because of their high viral load. In comparison, serum HAV concentrations are two or three $\log_{10}$ units lower than in the feces. Therefore, risk of transmission is highest during the prodromal phase before symptoms or biochemical manifestations.[2]

The virus is also shed in the saliva at even lower concentrations.[3] Concordant with clinical hepatitis, anti-HAV immunoglobulin M (Ig)M and subsequently anti-HAV IgG appear in the serum and saliva, accompanied by a marked reduction of fecal virus shedding and viremia. Although anti-HAV IgM is detectable for up to 6 months, anti-HAV IgG persists, conferring lifelong immunity.[4]

CLINICAL FEATURES

The clinical manifestations and outcomes of HAV infection exhibit significant age-dependent variations. Symptoms include: Abrupt onset of fever, malaise, anorexia, nausea, abdominal discomfort, dark urine, jaundice. In children younger than age 6 years, most (70%) infections are asymptomatic. In older children and adults, infection is usually symptomatic, with jaundice occurring in more than 70% of patients.[1] In adults, symptomatic acute hepatitis A occurs in more than 70% of cases, with 3% to 20% experiencing relapsing or prolonged hepatitis.

Acute liver failure is rare, with less than 1% of adult cases, but when it does occur, approximately 30% may require liver transplantation. In contrast, children demonstrate a markedly different clinical profile, with fewer than 30% exhibiting symptomatic acute hepatitis A. Severe clinical manifestation are rare in Hepatitis A infection however atypical manifestations may occur, like immunologic, neurologic, hematologic, pancreatic, and renal manifestations.

The incubation period of hepatitis A is approximately 28 days (range 15 to 50 days). The clinical course of hepatitis A is indistinguishable from that of other types of acute viral hepatitis. Clinical illness usually does not last longer than 2 months, although 10% to 15% of persons have prolonged or relapsing signs and symptoms for up to 6 months. Virus may be excreted during a relapse or prolonged Illness.[1]

EPIDEMIOLOGY

Hepatitis A occurs sporadically and in epidemics worldwide, with a tendency for cyclic recurrences. Epidemics related to contaminated food or water can erupt explosively, such as the epidemic in Shanghai in 1988 that affected about 300 000 people.[5] Geographical distribution areas can be characterized as having high, intermediate or low levels of hepatitis A virus infection. However, infection does not always mean disease because infected young children do not experience any noticeable symptoms.[5]

DISEASE BURDEN IN NEPAL

Hepatitis A virus accounted for only 4% of adults with acute hepatitis in reports from 1986 to 2002 from Kathmandu. However, in 2013, it was noted that HAV was the major cause (40%) of acute hepatitis in adults and HEV accounted for only 13.3%. While hepatitis A virus infection was only common during childhood till recent years, it is re-emerging as an important etiology of acute hepatitis in young adults. [6]

Major causative agent for acute viral hepatitis (AVH) among hepatitis positive patients were hepatitis E virus (HEV) in 36 (69.2%), followed by hepatitis A virus (HAV) 8 (15.3%), hepatitis B virus (HBV) 7 (13.4%) and hepatitis C virus (HCV) 1 (1.9%).[7] In a study of children with Hepatitis in Nepal, among 287 children studied, 266 had Hepatitis A. There were 11.5% toddlers, 42.2% preschool children, 35.5 % school children and 10.8 % adolescents. The incidence of Hepatitis A was 92.7% in this study. This high prevalence of Hepatitis A among these children is highly suggestive that if Hepatitis A is taken care of, then overall hepatitis burden among pediatric population would be significantly reduced.[8]

HEPATITIS A VACCINES

TYPE OF VACCINES

Inactivated Hepatitis A vaccine:

Most of the currently available vaccines are derived from HM 175/ GBM strains and grown on MRC-5 human diploid cell lines. The virus is formalin inactivated and adjuvanted with aluminum hydroxide. The vaccine is stored at 2–8°C. The serologic correlate of protection is 20 mIU/mL. All hepatitis A vaccines are licensed for use in children aged 1 year or older.

Live Attenuated Vaccine:

This vaccine is derived from the H2 strain of the virus attenuated after serial passage in Human Diploid Cell (KMB 17 cell line). It has been in use in China since the 1990's in mass vaccination programs. The vaccine meets WHO requirements and is now licensed and available in India. Controlled trials conducted among large numbers of children 1–15 years of age have shown up to 100% efficacy for pre-exposure prophylaxis and 95% efficacy for post exposure prophylaxis. The result of 5-year follow-up study showed that the single dose of live- attenuated vaccine is well tolerated and provides long-term immunogenicity in healthy Indian children. [1]

As per WHO position paper, both inactivated and live-attenuated hepatitis A vaccines are highly immunogenic and immunisation will generate long-lasting, possibly life-long, protection against hepatitis A in children as well as in adults.[9]

Note: HepA-HepB (Twinrix) is licensed in USA for person age 18 years or older and administered as a 3-dose series at 0, 1, and 6 months.

MECHANISM OF ACTION OF VACCINE

The administration of the hepatitis A vaccine leads to immune activation of lymphocytes, which proceed to engulf the hepatitis A antigen, leading to the release of inflammatory mediators that stimulate B and T cells to attack the viral antigen. Following this stimulation, the B cells and T cells then differentiate into memory cells, antibody-producing B cells, cytotoxic T cells, and helper T cells to provide immunity against infection with Hepatitis A.

INDICATIONS

Although WHO has recommended universal mass immunisation of children with Hepatitis A vaccine, due to various reasons, this policy has not been implemented in most of the resource limited countries in the world.[9]

Recommendation in children

All children 12–23 months old as part of routine childhood vaccination as a 2-dose series 6 to 12 months apart.

1. All children and adolescents 2–18 years old who have not previously received hepatitis A vaccine. [10]

   The hepatitis A vaccine may be offered to all healthy children with special emphasis in risk groups as enumerated below: [11]
2. Patients with chronic liver disease and clotting factor disorder.
3. Carriers of hepatitis B and hepatitis C.
4. Congenital or acquired immunodeficiency.
5. Transplant recipients.
6. Adolescents seronegative for HAV who are leaving home for residential schools.

7. Travelers to countries with high endemicity for hepatitis A.
8. Household contacts of patients with acute HAV infection within 10 days of onset of illness in the index case. It may not always be effective under such circumstances when the contact has had the same source of infection as the index patient.

Recommendation in Adults

People with any liver disease of any etiology. This includes:

A. People with chronic liver disease

B. People who have received a liver solid organ transplant

c. People with chronic hepatitis B or chronic hepatitis C

1. People aged ≥1 year if they travel to areas with moderate to high endemicity for hepatitis A. This includes expatriates, and people who are visiting friends and relatives.[10]
2. People whose lifestyle risks them to get hepatitis A infection like:
   A. People who have anal intercourse (including men who have sex with men, and sex industry workers)
   B. People who inject drugs
3. Any person who wishes to obtain immunity.

CONTRAINDICATION

Hepatitis A vaccine should be deferred in persons with history of hypersensitivity to previous dose or hypersensitivity to vaccine components.

ADVERSE EVENTS FOLLOWING IMMUNISATION

Mild reactions like pain, swelling and redness at the injected site is seen in less than 20% cases. Systemic reactions like low grade fever and malaise are reported in less than 10%.

SAFETY

Adverse reactions are minor and usually include local pain and swelling. Cumulative global experience from the use of several hundred million doses of inactivated hepatitis A vaccines testify to their excellent overall safety profile. The vaccine may be safely given with other childhood vaccines and interchange of brands is permitted though not routinely recommended.[11]

SCHEDULE AND DOSES:

Inactivated hepatitis A vaccine can be given after 1 year of age. Two dose series of 0.5 ml are given intramuscularly. The second dose is given 6-12 months after the first dose.[9, 10]

NEPAS recommends 2 doses of Inactivated Hepatitis A vaccine at 13 months and 19 months of age. If using Hepatitis A live vaccine one dose is enough given after 18 months of age. As per marketed brand dose needs to be doubled after certain age.

In infants 6 to 11 months of age, it is recommended before travelling to endemic areas. Although hepatitis A vaccine is considered safe and immunogenic in infants, hepatitis A vaccine doses administered before 12 months of age could result in a sub-optimal immune response, particularly in infants with passively acquired maternal antibody. Therefore, hepatitis A vaccine doses administered at <12 months of age are not considered to provide long-term protection, and the 2-dose hepatitis A vaccine series should be initiated at age 12 months according to the routine immunisation schedule.[10]

Live attenuated vaccines are licensed to use in some parts of the world like China, India and other South Asian countries. Single subcutaneous dose of live attenuated vaccine is given after 1 year of age. It is contraindicated in severely immunocompromised patients and in pregnancy.

EFFICACY AND EFFECTIVENESS

In general, two doses of inactivated hepatitis A vaccine induce protective efficacy of 90–95%, or more. The median predicted duration of protection has been estimated at 45.0 years.[7] The vaccine efficacy is lower in the elderly, immunocompromised, those with chronic liver disease, in transplant recipients and those with preexisting maternal antibodies. Immunity is life-long due to anamnestic response and no boosters are recommended at present in the immunocompetent.

For live attenuated vaccine, controlled trials conducted among large numbers of children 1–15 years of age have shown up to 100% efficacy for pre-exposure prophylaxis and 95% efficacy for post exposure prophylaxis.[11]

STORAGE

Inactivated hepatitis A vaccine should be stored in a refrigerator at 2˚C to 8˚C and protected from light. It should not be freezed.

POST EXPOSURE PROPHYLAXIS

Travelers exposed to HAV who are asymptomatic and who have not received hepatitis A vaccine should receive 1 dose of single-antigen hepatitis A vaccine and/or immunoglobulin (0.1 mL/kg) as soon as possible, ideally ≤2 weeks following exposure. The efficacy of immunoglobulin or vaccine when administered >2 weeks after exposure has not been established.[10]

Hepatitis A vaccines should be administered as post exposure prophylaxis (PEP) for all people aged ≥12 months who have been exposed to HAV ≤2 weeks and have not previously completed the hepatitis A vaccine series. In addition to

hepatitis A vaccine, administer immunoglobulin (0.1 mL/kg) to people who are immunocompromised or who have chronic liver disease, and to people aged >40 years, depending on the risk assessment, which should include consideration of the exposed person's age, immune status, underlying conditions, exposure type (risk of transmission), and availability of immunoglobulin.[10]

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MENININGOCOCCAL VACCINES

Dr. Shobha Sapkota

BACKGROUND

Neisseria meningitidis belongs to the family Neisseriaceae. It is a Gram-negative, non-spore forming, non-motile, encapsulated, and nonacid-fast diplococci and appears in kidney bean shape under the microscope. There are at least 12 serotypes based on unique capsular polysaccharides of N meningitidis, with serotypes A, B, C, W, X, and Y responsible for the majority of meningococcal infections. Further classification into serosubtype, serotype and immunotype is based on class 1 outer membrane proteins (PorA), class 2 or 3 (PorB) outer membrane proteins and lipopoly-oligosaccharide structure, respectively. [1]

Although meningococcal strains usually reside harmlessly in the nasopharynx, transition from asymptomatic carriage to invasive disease may occur owing to a number of factors, including differences in the genetic composition and capsule structure of pathogenic and non-pathogenic strains. Isolates from carriers may be capsulated or non-capsulated, whereas blood and CSF isolates are invariably capsulated. [2]

PATHOGENESIS

In humans, N. meningitidis colonizes the nasopharynx and is often non-pathogenic and commensal. To cause serious disease and meningitis, the bacteria must survive in the bloodstream, pass through the blood-brain-barrier (BBB) to enter and infect the central nervous system (CNS). A number of virulent factors are involved such as the polysaccharide capsule, pili and adhesins that play a role in its survival in the bloodstream and travels through the BBB. Factor H-binding protein aids in evading the host immune system through its interaction with factor H. The polysaccharide capsule is the most important virulence factor as it also is involved in adhesion to and invasion of CNS tissues. Adherence is further aided by Opa and Opc proteins. These proteins, along with Neisseria adhesin A and focal adhesion kinase, also play a role in the invasion.

Development of invasive meningococcal disease depends on the virulence of the organism, innate susceptibility of the host and presence or absence of serum antibodies capable of activating complement mediated bacteriolysis and/or opsonophagocytosis of host CNS. [3]

Host factors that result in the absence of protective bactericidal activity (due to a deficiency in complement or antibody production) are also risk factors for invasive meningococcal disease. These include functional or anatomic asplenia as well as persistent complement deficiencies (i.e., C3, C5–9, properdin, factor D and factor H).

Conditions associated with poor antibody responses (e.g., congenital or acquired antibody deficiencies such as seen in hypogammaglobulinemia and glomerulonephritis) also pose a risk for invasive disease. Environmental factors that increase exposure to the organism include crowding and close contact with a person carrying the organism.[4]

EPIDEMIOLOGY

In most countries, Neisseria meningitidis is recognized as a leading cause of meningitis and fulminant septicemia and a significant public health problem. Endemic disease mostly afflicts young children. Older children, adolescents, and young adults mainly suffer during epidemics. In developing countries, the background incidence of meningococcal disease is 15–20 cases per 100,000 peoples per year. When three or more cases of meningococcal disease occur in a 3-month period in the same locality, amounting to at least 10 cases per 100,000 persons suffering from the disease, the situation is referred as outbreak. However, in sub-Saharan Africa disease is hyperendemic due to unknown reasons and is considered to have the highest annual incidence (10–25/100,000 population) of meningococcal disease in the world.

Meningococcal disease patterns vary globally by serogroup [5]

- African meningitis belt: Highest incidence globally; primarily caused by serogroup A, with outbreaks from C, W135, and recently X.
- Americas: Mainly caused by serogroups C and B; Y and W135 are also significant in some areas.
- Europe: Predominantly serogroup B, with incidence ranging from 0.2 to 14 per 100,000.
- Australia and New Zealand: Serogroup B is dominant—due to vaccination success against serogroup C in Australia and a B epidemic in New Zealand.
- Asia: Limited data, but serogroups A and C appear to be most common.

In the African meningitis belt, the World Health Organization (WHO) definition of a meningococcal epidemic is >100 cases/100,000 population/year. In endemic regions, an incidence of >10 cases, 2–10 cases, and <2 cases per 100,000 population in a year characterizes high, moderate, and low endemicity, respectively.3 However, the situation has changed after the introduction of monovalent MenA vaccine in the year 2010, and meningococcal group A disease has reduced sharply. The epidemic period coincides with dry season of November–March and the cases reduce with onset of monsoon and again increase November onward. The outbreaks occur when season is dry and the temperature is low. [6]

BURDEN OF DISEASE IN NEPAL

In the Kathmandu Valley of Nepal, an epidemic of serogroup A meningococcal meningitis resulted in 875 cases and 95 deaths during the first six months of 1983.

The overall annual attack rate was 103 cases/100,000 population; the case fatality ratio was 11%. The highest age-specific attack rate (223/100,000) occurred among children under age 1 year. Three times as many cases occurred in Kathmandu during December 1983 and January 1984 as in the same period a year previously. A mass vaccination campaign was initiated on February 8, 1984, and 330,000 doses of bivalent A/C meningococcal vaccine were administered, achieving approximately 65% coverage of the target population. A marked decline in the number of meningitis cases occurred coincident with the initiation of the mass campaign. In 1985 meningococcal meningitis occurred at a much lower rate than in 1984. [7]

To date, three studies explained the meningococcal epidemic (1982-1984) that occurred in the Kathmandu valley of Nepal. The first recorded meningitis epidemic caused by N. meningitidis serogroup A took place in April-May,1982 in Kathmandu valley of Nepal, resulting in 875 cases and 95 deaths. The epidemic continued until Feb 1984 and then declined after mass vaccination. In 1989, an intercontinental spread of meningitis epidemic occurred in Nepal along with Saudi Arabia and Chad and it was thought to be introduced through pilgrims on their return from the hajj. Since then, some hospital-based studies and case reports have reported meningococcal meningitis in Nepal. [7]

The circulating N. meningitidis isolates in Kathmandu, Nepal is serogroup A which has not changed over the past 35 years. All isolates are susceptible to the commonly used antibiotics. The prevalence of meningococcal meningitis in Kathmandu, Nepal is low, but might have been underestimated due to the sole use of culture-based diagnostic methods. Therefore, detection of meningococci in CSF samples by alternative sensitive methods like PCR may be useful in the precise estimation of the actual disease burden. [7, 8]

MENINGOCOCCAL VACCINE

Two types of meningococcal vaccines have been developed but all are not available everywhere in the world. They include

- Meningococcal polysaccharide vaccines (MPSV)
- Meningococcal polysaccharide-protein conjugate vaccines (MCV)

Meningococcal Polysaccharide Vaccines

These are either bivalent (A + C) or quadrivalent (A, C, Y, and W-135) and contain 50 µg of each of the individual polysaccharides, available in lyophilized form, reconstituted with sterile water and stored at 2–8°C.

These “T cell independent” vaccines do not induce immunological memory and the response in children younger than 2 years is poor. Hence, these are indicated for adults and children older than 2 years (only under special circumstances in children 3 months to 2 years of age)

2) Conjugated Meningococcal Polysaccharide Vaccine (MCV)

A) Conjugate Meningococcal serogroup C vaccine

B) Monovalent Serogroup A (10mcg of group A polysaccharide conjugated to tetanus toxoid)

C) Quadrivalent A, C, Y and W-135 conjugate vaccine

D) Monovalent Serogroup B

E) Pentavalent Meningococcal Vaccine: A single pentavalent vaccine against meningococcal A, B, C, Y, and W is being tested in different phases.[6]

On October 25, 2023, the Advisory Committee on Immunisation Practices recommended that MenACWY-TT/MenB-FHbp may be administered to persons aged ≥10 years when both a quadrivalent meningococcal conjugate vaccine (MenACWY) and meningococcal B vaccine (MenB) are indicated at the same visit.[9]

VACCINE SCHEDULE AND DOSE

1. Polysaccharide (MPSV: Meningococcal polysaccharide vaccine)

   0.5ml SC or IM, recommended in children > 2 years.

Revaccination after 3–5 years in high-risk children and adolescents.

2. Conjugated Meningococcal Vaccine (MCV) 0.5ml deep IM, for use among persons aged 2 through 55 years.

NEPAS recommends MCV 2 doses 3months apart for age group 9 to 23 months in high-risk group or in epidemics. Single dose after age of 2 years. In adolescent age we recommend 1 dose at 16-18 years i.e., before going to college. Booster 5 yearly in high-risk group for conjugate vaccine. If Polysaccharide vaccine used booster is needed every 2-3 yearly.

WHO recommends a single deep intramuscular dose of meningococcal A conjugate vaccine (MenAfriVac) at 9-18 months, based on herd immunity from campaigns, disease epidemiology, and programmatic/economic factors. Catch-up vaccination should occur ASAP for those who miss the recommended age. In specific contexts requiring vaccination before 9 months, a 2-dose priming schedule (MenAfriVac 5mcg) starting at 3 months with an 8-week interval is advised for children aged 3-24 months. MenAfriVac 10mcg is for catch-up and periodic campaigns in individuals 12 months and older.

3. Monovalent (Serogroup A)

0.5 ml intramuscular single administration for individuals 1–29 years of age

4. If the serogroup B vaccine is available and utilized, the preferred strategy per ACIP guidelines is to administer it later in adolescence (i.e., aged 16–18 years) to maximize protection during the highest age risk period.

Recommendation on Dosage in different categories

During disease outbreaks: Due to the limited efficacy of polysaccharide vaccines in children <2 years of age, conjugate vaccines should be used for protection of those aged 12– 24 months, particularly for MenA disease. [10]

Note: **Menactra (MenACWY vaccine) should not be co-administered with 13vPCV (Prevenar 13)**. This is because Menactra may interfere with the immune response against some pneumococcal serotypes. If a person needs both vaccines, they should receive 13vPCV first, followed by Menactra at least 4 weeks later.

VACCINATION OF PERSON WITH HIGH-RISK CONDITIONS/SITUATIONS [7]

Children with terminal complement component deficiencies: A two-dose primary series of MCV administered 8–12 weeks apart is recommended for persons aged 24 months through 55 years with persistent deficiencies of the late complement component pathway. A booster dose should be administered every 5 years.

Children with functional/anatomic asplenia/hyposplenia (including sickle-cell disease): Administer two primary doses of either MCV with at least 8 weeks between doses for individuals aged 24 months through 55 years. Vaccination should ideally be started 2 weeks prior to splenectomy.

Persons with human immunodeficiency virus: Administer two doses at least 8 weeks interval.

Laboratory personnel and healthcare workers: Who are exposed routinely to N. meningitidis in solutions that may be aerosolized should be considered for vaccination. A single dose of MCV is recommended. A booster dose should be administered every 5 years if exposure is ongoing.

Adjunct to chemoprophylaxis: In close contacts of patients with meningococcal disease (healthcare workers in contact with secretions, household contacts, and daycare contacts) single dose of appropriate group MCV is recommended.

International travelers: Students going for study abroad: Some institutions have policies requiring vaccination against meningococcal disease as a condition of enrolment (mandatory in most universities in the USA). Persons aged ≤21 years should have documentation of receipt of a MCV not >5 years before enrolment. In the US, ACIP recommends routine vaccination of all adolescents with single dose of MCV4 at age 11–12 years with a booster dose at age 16 years.

Hajj pilgrims: Vaccination in the 3 years before the date of travel is required for all travelers to Mecca during the annual Hajj. The quadrivalent vaccine is preferred for Hajj pilgrims and international travelers as it provides added protection against emerging W-135 and Y disease in these areas. A single dose 0.5 mL IM is recommended in age group 2–55 years. Single dose of polysaccharide vaccine also useful.

Travelers to countries in the African meningitis belt: A single dose of monovalent or quadrivalent vaccine is recommended. Conjugate vaccine is

preferred to polysaccharide vaccine. A booster dose of MCV is needed if the last dose was administered 5 or more years previously. [6]

CONTRAINDICATIONS

i) H/O severe allergic reaction following a previous dose.
ii) Allergic to any active substance or ingredient in the vaccine

PRECAUTIONS

Severe acute febrile illness. In this case, vaccination should be postponed.

ADVERSE REACTIONS FOLLOWING VACCINATION

Irritable, crying, unsettled and generally unhappy

Loss of appetite

Headache (usually in adolescents and adults)

Pain, redness and swelling at injection site

Occasionally an injection-site lump (may last many weeks - no treatment needed)

Mild fever

VACCINE EFFICACY

1) Polysaccharide vaccines

These vaccines are 65% to 83.7% effective, depending on age group.

2) Conjugate vaccines

These vaccines are 66% to 100% effective, and can reduce the incidence of laboratory-confirmed meningococcal disease by 77% to 100%

- Quadrivalent (ACW-135 and Y): Within 3-4 years of vaccination, effectiveness is 80-85%.
- Complete vaccination with 4CMenB is 71% effective against meningococcal serogroup B disease, and 82% effective against non-serogroup B disease

VACCINE STORAGE AND SAFETY

Refrigerated between 2°C and 8°C (36°F and 46°F). Do not freeze vaccine or diluents or expose to freezing temperatures. Protect from the light. The reconstituted vaccine should be used immediately.[9]

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RABIES VACCINE

Dr. Sangita Puree Dhungana

BACKGROUND

Rabies is a vaccine-preventable, zoonotic, viral disease affecting the central nervous system in human and animals. In up to 99% of the human rabies cases, dogs are responsible for virus transmission. Children between the age of 5 and 14 years are frequent victims. Rabies infects mammals, including dogs, cats, livestock and wildlife. Hence, the world, including Nepal, has aimed to eliminate dog-mediated human rabies deaths by 2030. [1]

Rabies spreads to people and animals via saliva, usually through bites, scratches, or direct contact with mucosa (e.g., eyes, mouth, or open wounds). Once clinical symptoms appear, rabies is virtually 100% fatal. Bat-mediated rabies is also an emerging public health threat.[2] Human deaths following exposure to foxes, raccoons, skunks, and other wild mammals are very rare. Human cases associated with rabid cats have occurred in Africa, Asia, Europe, and throughout the Americas. Education about the occurrence of rabies in cats needs to be improved, as well as the routine vaccination of cats to reduce the associated risks to public health.[3]

PATHOGENESIS

The incubation period for rabies is typically 2–3 months but may vary from one week to one year, depending on factors such as the location of virus entry and the viral load. Initial symptoms of rabies include generic signs like fever, pain and unusual or unexplained tingling, pricking, or burning sensations at the wound site. As the virus moves to the central nervous system, progressive and fatal inflammation of the brain and spinal cord develops. Clinical rabies in people can be managed but very rarely cured, and not without severe neurological deficits.[4]

There are two forms of rabies:

Furious rabies results in hyperactivity, excitable behavior, hallucinations, lack of coordination, hydrophobia (fear of water) and aerophobia (fear of drafts or of fresh air). Death occurs after a few days due to cardio-respiratory arrest.[4]

Paralytic rabies accounts for about 20% of the total number of human cases. This form of rabies runs a less dramatic and usually longer course than the furious form. Muscles gradually become paralyzed, starting from the wound site. It may be confused with Guillain Barre Syndrome. A coma slowly develops and eventually death occurs. Hydrophobia does not occur in this form. The paralytic form of rabies is often misdiagnosed, contributing to the under-reporting of the disease.[4]

Dog bite to rabies development is influenced by several factors like severity of the wound, location of the bite on the body, quantity of virus inoculated into the wound(s), and timeliness of post-exposure prophylaxis (PEP).[4]

EPIDEMIOLOGY

Rabies is estimated to cause 59 000 human deaths annually in over 150 countries, with 95% of cases occurring in Africa and Asia. 99% of rabies cases are dog-mediated and the burden of disease is disproportionally borne by rural poor populations, with approximately half of cases attributable to children under 15.[5]

All mammals are susceptible to infection by the rabies virus (RABV). Transmission of RABV by dogs is responsible for up to 99% of human rabies cases in rabies-endemic regions, with a small proportion due to transmission via wildlife (such as foxes, wolves, jackals, bats, racoons, skunks or mongoose.[4]

DISEASE BURDEN IN NEPAL

In Nepal most common transmitting animal is dog. Almost all the patients who died of rabies in the past in Nepal were bitten by dogs (stray). According to available data, children in the 5–15year age-group represent about 40% of people exposed to dog bites in rabies endemic areas.[5]

In Nepal estimated number of dog bites is 100, 000 and estimated human rabies cases <100 per year. The disease kills between 100 and 200 animals and 10–100 people in Nepal every year.[6] In Nepal, there exist two epidemiological cycles of rabies: named the urban cycle involving infection in dog populations and a sylvatic cycle involving wild animals. Dog bite accounts for approximately 92–94% of human rabies cases followed by 4% due to Jackal, Mongoose, Cat, and other domestic animals.[7] The districts in Nepal are classified as high risk (20 districts), moderate risk (39 districts) and low risk (16 districts) with regard to rabies.[8]
In the fi scal year 2073/74 (2016-17),39744 animal bite cases were reported in the national annual report, out of which 37226 (94%) were dog bite cases. In the fiscal year 2074/75(2017/18), 28514 animal bite cases, including 26312 dog bite cases (92%), were reported.[1]
Data on Rabies in humans in Nepal may be underreported. With the exception of hydrophobia, clinical signs of rabies can be unreliable, and contribute to under or misdiagnosis of rabies in humans. Additionally, rabies patients often die at home, or leave hospital when no treatment can be offered, and are therefore not included in clinical databases and mortality statistics.

PREVENTION

Vaccinating dogs/cats

Vaccinating dogs, including puppies, through mass dog vaccination programs is the most cost-effective strategy for preventing rabies in people because it stops the transmission at its source. Rabies in cats is also emerging, so it is necessary to vaccinate them.[5]

Awareness

Making people aware of dog behavior and bite prevention on how to avoid the bites of rabid dogs/cats, to seek treatment when bitten and to vaccinate animals can successfully disrupt the rabies transmission cycle.

Vaccinating People

Effective vaccines are available to immunise people both before and after potential exposures.

Pre-exposure prophylaxis (PrEP)

It is recommended for people in high-risk occupations (laboratory workers handling live rabies and related viruses) and people whose professional or personal activities might lead to direct contact with infected animals (animal disease control staff and wildlife rangers). PrEP might be indicated before recreation or travel in some areas, and for people living in remote, highly rabies-endemic areas with limited local access to rabies biologicals.

WHO recommends PrEP for individuals at high risk of Rabies Virus Exposure

1. Sub-populations in highly endemic settings with limited access to timely and adequate PEP. PrEP should be considered in sub-populations living in remote, rabies-endemic areas, where the dog bite incidence is >5% per year or vampire bat rabies is known to be present.
2. Individuals at occupational risk
3. Travelers who may be at risk of exposure

The WHO also recommends vaccinating those who are at high risk of the disease, such as children who live in areas where it is common.[9]
Recommended regime is ID 2 dose each site or IM 1 dose on deltoid or lateral thigh on day 0 and 7. 3rd dose or booster dose recommended after 3 weeks to 3years if Virus Neutralizing Antibodies (VNA) levels fall to <0.5 IU/mL. If antibodies level cannot be obtained, then 3rd dose can be given.[9]

Pre-exposure vaccine is needed for children in Nepal. The majority of bites that occur in children go unrecognized and unreported and, consequently, exposed children do not receive the benefit of timely and complete courses of post-exposure prophylactic treatment. Additionally, paralytic rabies is often misdiagnosed as acute neurological syndrome. Thus, there is the possibility of a disproportionately high number of young children contracting and dying of undiagnosed rabies.
NEPAS strongly recommends our children to have pre-exposure prophylaxis for rabies.

Post-exposure prophylaxis (PEP)[4] is the emergency response to rabies exposure. This prevents the virus from entering the central nervous system. A well performed wound risk assessment and PEP protocol consists of:

- Extensive wound washing with water and soap for at least 15 minutes soon after an exposure;
- A course of rabies vaccine; and
- Administration of rabies immunoglobulin or monoclonal antibodies into the wound, if indicated.[2]

Whenever necessary, Tetanus prophylaxis should be instituted. Tetanus Toxoid (0.5ml IM) can be given. Antibiotics may be recommended, if needed.

Wound washing [10]

Thorough washing and flushing of the wounds for approximately 15 minutes with soap or detergent and plenty of water is required.
If soap and detergent are not immediately available, wash with running water for 15 minutes. It should be noted that the immediate washing of the wound is a priority. The maximum benefit of wound washing is obtained when fresh wound is cleaned immediately.
After wounds have been washed, local antiseptics (viricidal topical preparation) like Povidone Iodine should be applied on the wounds.

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

*In Nepal bat transmitted rabies has not been reported[1]

RABIES VACCINE

The first rabies vaccine was introduced in 1885 and was followed by an improved version in 1908. Cell culture and embryonated egg-based rabies vaccines (CCEEVs) have been shown to be safe, highly immunogenic and well tolerated and have proved to be effective in preventing rabies. WHO recommends replacement of nerve tissue vaccines with the more efficacious, safer vaccines developed through cell culture as soon as possible.
Cell culture vaccines are: Purified chick embryo cell vaccine (PCECV), Purified vero cell vaccine (PVRV), Human diploid cell vaccine (HDCV) and Purified duck

embryo vaccine (PDEV). All cell culture vaccines have equal efficacy. These vaccines induce protective antibodies in more than 99% of Vaccinees following pre-/post-exposure prophylaxis.

As listed under the WHO - Prequalification of Medical Products, as of 2024, there are only 3 WHO pre-qualified human rabies vaccines available globally: RABIVAX-S by Serum Institute of India Pvt. Ltd., VaxiRab N by Zydus Lifesciences Limited, and VERORAB by Sanofi Pasteur.[8]

INDICATIONS

All animal bite victims of Category II and III exposures, irrespective of age and body weight, require the same number of injections and dose per injection.
It can be given IM or ID on deltoid region or anterolateral thigh. It is not given in the gluteal region.[1]

Post exposure Rabies Prophylaxis:[2]

In unimmunised healthy child: 4 dose series on 0, 3, 7 and between 14 and 28th day

For IM route, 0.5ml or 1ml dosing (full vial of >2.5 IU). For ID 0.1ml on 2 sites (for ID dosing it is given 0.1ml on each deltoid region per visit).

In unimmunised immunocompromised child 5th dose is given on day 28.

If the patient has already been immunised against rabies, vaccination is not recommended if re-exposure is less than 3 months' post vaccination. If it is more than 3 months, the dosing schedule can be reduced to 2 doses of IM injection on days 0 and 3 or a 1-site ID injection of 0.1mL .[9] No RIG is needed.

The higher concentration of antigen-presenting cells in the dermis is responsible for the strong immunologic response to vaccine administered ID, despite the lower amount of antigen injected. ID administration of rabies vaccines provides a cost-saving and dose-sparing alternative to IM vaccination. Intradermal administration reduces the amount of necessary vaccine and number of doses, therefore reducing costs by 60–80%, without compromising safety or efficacy.[5]

WHO in the recently published WHO position paper on rabies vaccines recommends a one week, 2 site intradermal PEP schedule with 0.1mL of vaccine injected on days 0, 3 and 7 for post-exposure prophylaxis.[5]

Many commercially available rabies vaccines are labeled for IM use and off label use by ID route can be given in Nepal.

CONTRAINDICATIONS AND PRECAUTIONS

After exposure to rabies, there is no contraindication to its use, because the untreated virus is virtually 100% fatal. When used in pregnant and lactating mothers no harm attributable to rabies vaccine has been observed.
Individuals receiving antimalarial prophylaxis with chloroquine or related compounds should be vaccinated via the intramuscular route, since their antibody responses to intradermal vaccination may be lower than normal.[8]

ADVERSE EVENTS FOLLOWING IMMUNISATION

The main adverse effects are local pain, swelling and redness. Less commonly fever, headache, dizziness and gastrointestinal side effects are observed. About 35 to 45 percent of people develop a brief period of redness and pain at the injection site, and 5 to 15 percent of people may experience fever, headache or nausea. Systemic hypersensitivity reactions also occur after Human diploid cell vaccine particularly following booster injections but not with other vaccines.[11] Intradermal vaccinations may cause more local irritation than intramuscular route.[5]

STORAGE

The vaccines are available in lyophilized form with sterile water. It can be stored at 2 to 8˚C. It should be used within 6 hours of reconstitution.

RABIES IMMUNOGLOBULINS

The role of RIG in passive immunisation is to provide neutralizing antibodies at the site of exposure before patients start producing their own antibodies as a result of vaccination.[1]
RIG is administered only once, preferably at or as soon as possible after initiation of post-exposure vaccination. Rabies immunoglobulin should be given with the first dose of vaccine into and around the wound site. It is not indicated beyond the seventh day after the first dose of rabies vaccine, (regardless of whether the doses were received on days 3 or 7) because an active antibody response to the rabies vaccine would have already started, and administration of RIG at this stage can suppress the immune response of the patient to the Rabies Vaccine received.[9]

Two types of RIGs are available (both are considered to have similar clinical effectiveness)

- Equine Rabies Immunoglobulin (ERIG) and
- Human Rabies Immunoglobulin (HRIG).

The dose of Human RIG is 20 IU/kg of body weight and Equine RIG is 40 IU/kg of body weight. Full dose is to be injected on the wound site.[1]

If Rabies monoclonal antibody is available dose is 3.3IU/KG.

Recommended interval between Rabies Immunoglobulin and Measles or Varicella vaccine is 4 months.[12]

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CHOLERA VACCINES

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BACKGROUND

Cholera is an important public health problem in developing countries, with poor sanitation and hygiene, as well as in displaced populations. The predominant strain is Vibrio cholerae (V. cholerae) O1 (classical and El Tor biotype).[1] V. cholerae O139 is an emerging strain.[1] Cholera is an extremely virulent disease that can cause severe acute watery diarrhoea. The Incubation period after ingestion of cholera organisms by contaminated food or water is 12 hours to 5 days. Cholera affects both children and adults and can kill within hours if untreated.

PATHOGENESIS

After penetrating the mucus layer, V. cholerae colonizes the epithelial lining of the gut. Cholera toxin, which is secreted by toxigenic V. cholerae O1 or O139, affects the small intestine. The toxin depends on a specific receptor: the monosialosyl ganglioside GM-1. The binding (B) subunit of the toxin attaches to GM-1 and releases the active (A) subunit, which enters the host cell. This activation results in massive loss of intravascular and extracellular fluids and electrolytes.[1]

DISEASE BURDEN IN NEPAL

Globally, it is estimated that there are 1.4 to 4.3 million cases, and 28,000 to 142,000 deaths due to cholera every year. The threat of a cholera outbreak is a major public health concern for governments and the international health community, and a key indicator of lack of social development.[2]

Nepal is endemic for cholera with the potential for large outbreaks. While 93 percent of households in Nepal use an improved source of drinking water and 72 percent of Nepali's live-in households with improved sanitation facilities, open defecation is still practiced in many areas. The country is also at high-risk for outbreaks due to a steady increase in urban population density accompanied by an inadequate supply of safe drinking water and improved sanitation.[3]

The Ministry of Health and Population (MoHP), with support from WHO, and UNICEF had launched a mass cholera vaccination campaign in response to the outbreak on 21 November 2021 and was carried out in the five affected municipalities in the district: Yashodhara, Maharajgunj, Shivraj, Bijaynagar, and Krishnanagar.[4]

VACCINE

Vaxchora

Vaxchora is the only cholera vaccine approved for use by CDC. The FDA approved Vaxchora for people aged 2-to-64 years traveling to an area where cholera is present. The live attenuated vaccine is taken as a single dose by mouth, should be given at least 10 days before traveling. The vaccine reduces the chance of moderate and severe diarrhoea in people ages 18-45 years by 90% at 10 days after vaccination, and by 80% at 3 months. The efficacy of the vaccine after 3 months is not known.[5]

Dukoral, Shancol and Euvichol-Plus

These three oral cholera vaccines have been approved by the World Health Organization (WHO). These are inactivated/killed vaccines.

INDICATION

Minimum age: One year

- It is recommended only for the vaccination of persons residing in highly endemic areas and travelling to areas where risk of transmission is very high.

CONTRAINDICATIONS

A history of severe systemic illness or allergic response following a prior dose of cholera vaccine is a contraindication of further use.

It should also be deferred in presence of any acute illness.

ADVERSE EVENTS FOLLOWING IMMUNISATION

The most common side effects include fever, vomiting, abdominal pain, itching, rashes, nausea, weakness, cough, vertigo, and dryness in the mouth.

SCHEDULE, ROUTE OF ADMINISTRATION AND DOSES

Oral route. Two doses are given at an interval of at least two weeks. The protective effect begins within 7-10 days of completion of the vaccination schedule. Dukoral is administered with a buffer solution that requires 150ml of clean water for adults. For continued risk of exposure, a booster may be administered after 3 years.[5,6]

NEPAS recommends cholera vaccine only during epidemics. 2 doses given to children aged 1 year and above with gap of 2weeks to 1 month.

VACCINE EFFICACY

As per a Vietnamese trial among those who received two full doses, the effectiveness was 66%, and results were similar for children ages one to five years 68%, and older volunteers 66%.[7]

STORAGE

The vaccine has a shelf-life of 2 years at 2–8°C.

The ideal method for cholera control is improvement in water supply and sanitation. As recommended by the WHO, cholera vaccines should be used preemptively in endemic areas and in crises situations and not as outbreak control measure. Vaccination should not disrupt the provision of other high priority health interventions to control or prevent cholera outbreaks.[8]

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YELLOW FEVER VACCINE

Dr. Kabita Keyal

BACKGROUND

Yellow fever is an epidemic-prone mosquito-borne vaccine preventable disease that is transmitted to humans by the bites of infected mosquitoes that bite mostly during the day.

Yellow fever is caused by an arbovirus transmitted to humans by the bites of infected *Aedes* and *Haemagogus* mosquitoes. Yellow fever is a high-impact high-threat disease, with risk of international spread, which represents a potential threat to global health security.

EPIDEMIOLOGY/ GLOBAL BURDEN

Yellow fever, one of the most feared lethal zoonotic disease re-emerging as a public health threat to tropical and sub-tropical countries of South America and Africa. A modeling study based on African data sources estimated the burden of yellow fever during 2013 was 84 000–170 000 severe cases and 29 000–60 000 deaths. As of 2023, 34 countries in Africa and 13 countries in Central and South America are either endemic for, or have regions that are endemic for, yellow fever.[1] The risk for travelers to endemic areas of Africa has been estimated as 23.8/100,000/week, in epidemic areas 357/100,000/week.[2]
Data from the US travelers produced an estimate of 0.4–4.3 cases/million travelers to Yellow Fever endemic areas.[3]

A traveler's risk for acquiring Yellow Fever is determined by various factors, including immunisation status, location of travel, season, and duration of exposure, occupational and recreational activities while traveling, and local rate of virus transmission at the time of travel. Occasionally travellers who visit yellow fever endemic countries may bring the disease to countries free from yellow fever. In order to prevent such importation of the disease, many countries require proof of vaccination against yellow fever before they will issue a visa, particularly if travellers come from, or have visited yellow fever endemic areas.[4,5]

PATHOGENESIS

Yellow fever virus is a single-stranded RNA virus that belongs to the genus *Flavivirus*. Yellow fever virus is transmitted to people primarily through the bite of infected Aedes and Haemagogus species mosquitoes. The incubation periods for arboviral diseases typically range between 2 and 15 days. Longer incubation periods can occur in immunocompromised people. It can be spread from person-to-arthropod-to-person (anthroponotic transmission). The direct person-to-person spread of arboviruses can occur through blood transfusion, organ transplantation, intrauterine transmission, and possibly human milk.

People infected with yellow fever virus are infectious to mosquitoes (referred to as being “viremic”) shortly before the onset of fever and up to 5 days after onset.[6]

CLINICAL FEATURES

Many people do not experience symptoms. Common symptoms include fever, muscle pain, headache, loss of appetite, nausea or vomiting. In most cases, symptoms disappear after 3 to 4 days. A small percentage of patients enter a second, more toxic phase within 24 hours of recovering from initial symptoms with features of high fever, jaundice, renal failure and hemorrhage. The case-fatality rate for severe cases is 30%–60%.[6]

VACCINE

Yellow fever vaccine is a live, attenuated virus preparation made from the 17D yellow fever virus strain grown in chick embryo cells. The vaccine is available as a freeze-dried preparation in a single or multiple dose vial.

INDICATION

a. Vaccine is recommended for all people aged 9 months or older living in or traveling to endemic areas i.e., certain regions of Africa and South America and is required by the International Health Regulations (IHR) for travel to and from certain Countries. Vaccination against YF at least 10 days prior to the travel.

b. Infants less than 9 months of age and pregnant women should be considered for vaccination if traveling to areas experiencing ongoing epidemic yellow fever when travel cannot be postponed and a high level of prevention against mosquito exposure is not feasible. However, in no instance should infants less than 4 months of age receive yellow fever vaccine because of the risk of encephalitis

c. Laboratory personnel who might be exposed to virulent yellow fever virus by direct or indirect contact or by aerosols should also be vaccinated.

d. Preventive mass vaccination campaigns are recommended for inhabitants of areas at risk of YF where there is low vaccination coverage.

e. A booster dose of yellow fever vaccine is not needed. The vaccine provides effective immunity within 10 days for 80–100% of people vaccinated, and within 30 days for more than 99% of people vaccinated.[7,8]

CONTRAINDICATION

a. Infants aged less than 6 months
b. Pregnant women – except during a yellow fever outbreak when the risk of infection is high;
c. People with severe allergies to egg protein and other vaccine component
d. People with severe immunodeficiency due to symptomatic HIV/AIDS
e. Thymus disorder associated with abnormal immune cell function
f. Primary immunodeficiency
g. Malignant neoplasms
h. Transplantation
i. Immunosuppressive and immunomodulatory therapies [7]

PRECAUTION

- Age 6–8 months: should only be vaccinated in case of a yellow fever epidemic or if travelling to a yellow fever–endemic zone, where there is a lesser possibility of protection against mosquito bites. A consultation with your **doctor or healthcare provider** is a must before vaccination.
- **Other groups that require proper doctor consultation before receiving the yellow fever vaccine, due to higher risks of adverse reactions include:**
- Age ≥60 years
- Breastfeeding
- HIV infection (asymptomatic) and CD4 T lymphocyte counts 200–499/mL (or 15%–24% of total lymphocytes in children aged <6 years)
- Pregnancy [7]

ADVERSE EVENTS FOLLOWING IMMUNISATION

About 10–30% of vaccines report mild systemic adverse events like low-grade fever, headache, and myalgia that begin within days after vaccination and last 5–10 days. There have been reports of rare but serious events following yellow fever vaccination: [8,9]

1. **Severe anaphylaxis:** Severe adverse reactions are rare and include immediate hypersensitivity reactions, characterized by rash, urticaria, bronchospasm, or a combination of these. Anaphylaxis after YF vaccine is reported to occur at a rate of 0.8 cases per 100,000 doses administered.

2. **Yellow fever vaccine-associated neurologic disease (YEL-AND):** It can present as a conglomerate of different clinical syndromes, including

meningoencephalitis, Guillain-Barré syndrome, acute disseminated encephalomyelitis, bulbar palsy, and Bell's palsy. The onset of illness for documented cases is 3–28 days after vaccination. The incidence of YEL-AND is 0.8 per 100,000 doses administered. The rate is higher in people aged ≥60 years.

3. **Yellow fever vaccine-associated viscerotropic disease (YEL-AVD):** YEL-AVD is a severe illness similar to wild-type disease, often leading to multisystem organ failure and death. The incidence is 0.4 per 100,000 doses administered.

SCHEDULE, DOSAGE AND ROUTE OF ADMINISTRATION

Yellow fever vaccines are given as a single dose (0.5 mL of reconstituted vaccine) and the vaccine can be injected either subcutaneously or intramuscularly. The vaccination site is usually the lateral aspect of the upper part of the arm or the anterolateral aspect of the thigh in babies and very young children.

It can be safely given along with all other childhood vaccines. Immunogenicity and efficacy are >90%. Immunogenicity is lower in pregnancy and immuno-compromised persons.[7]

VACCINE STORAGE AND SAFETY

The vaccine is available as a freeze-dried preparation in single/ multidose vials that should be stored at 2–8°C (must not be frozen) along with sterile saline as diluent. The reconstituted vaccine is heat labile, must be stored at 2–8°C, and discarded within 1 hour of reconstitution.
Unused vaccine should be discarded within 1 hour after reconstitute.[7]

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COVID-19 VACCINES

Dr. Amrit Ghimire

BACKGROUND

On a chilling New Year's Eve in 2019, the Wuhan Municipal Health Commission broke news of a perplexing pneumonia outbreak gripping the city. What began as a localized cluster soon surged outwards, crossing provincial lines within China with alarming speed. By late January 2020, the novel virus had breached international borders, appearing in countries like Thailand, Japan, and South Korea, leaving families and communities grappling with an unknown and frightening illness. Recognizing the escalating crisis, the World Health Organization issued a global alarm on January 30th, declaring the outbreak a Public Health Emergency of International Concern, urging immediate and coordinated action. As the virus relentlessly leapt across continents over the next two months, sowing fear and uncertainty, the scientific community raced against time to understand its nature. On February 11th, 2020, the WHO officially named the culprit SARS-CoV-2 and the disease it wrought COVID-19. The mounting global toll and the undeniable widespread transmission culminated on March 11th, 2020, when the WHO declared COVID-19 a pandemic, a stark acknowledgment of its pervasive reach and the urgent need for worldwide mitigation strategies.

PATHOGENESIS

COVID-19 (coronavirus disease 2019) is caused by the virus severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). It is very contagious and has quickly spread around the world. The SARS-CoV-2 is 100nm in diameter and contains single stranded RNA of 29.9 kb length. It contains 4 structural proteins (S, E, M and N) and 16 nonstructural proteins (called nsp1-16). The entry of the virus into the host cells is mediated by the surface spike (S) glycoprotein which contains homo-trimers that protrude on viral surface. The SI subunit of Spike(S) protein contains the N-terminal domain (NTD) and the receptor binding domain (RBD) that bind to the angiotensin-converting enzyme-2 (ACE-2) receptor. The ACE-2 receptor is present on respiratory epithelium which makes the respiratory tract the main portal of entry for SARS-CoV-2 in humans. SARS-CoV-2 spreads by droplets aerosolized by infected individuals when they breathe, cough, sneeze, or speak. The incubation period can range from 2 to 14 days (average of 6 days). The risk of transmission varies by viral load, distance from infectious source and loss of viral viability over time due to environmental variables such as temperature and humidity. Continued exhalation from an infectious source within enclosed spaces with inadequate ventilation or prolonged exposure (>15 minutes) or during activities (such as exercise, singing or shouting) can increase the risk of transmission.

Signs and symptoms include fever, cough, fatigue, headache, myalgia, nasal congestion, loss of taste or smell, sore throat, breathing difficulty, abdominal pain, diarrhoea, vomiting, neurological symptoms, etc. Croup, febrile seizures, and exacerbation of wheeze have also been reported following COVID-19 infection in children. Individuals with underlying medical conditions are at greater risk of

developing severe COVID-19 illness and dying from it. Children can also develop a unique phenomenon called multi-inflammatory syndrome in children (MIS-C) that is associated with elevated inflammatory markers and cardiac involvement.

EPIDEMIOLOGY

The COVID-19 pandemic has had an overwhelmingly greater impact on people's lives than the previous swine flu pandemic in 2009. No country has remained untouched by this pandemic, with multiple waves causing additional burden. By the end of 2022, over 630 million confirmed cases and nearly 7 million deaths were recorded globally.[1] Individuals with the elevated expression of angiotensin-converting enzyme (ACE2), transmembrane protease serine 2 (TMPRSS2), and pro-inflammatory cytokines have been reported to be at a higher risk of the progression of the disease.[2] Living in overcrowded houses and having lower literacy are also associated with a higher incidence of COVID-19. Symptomatic infections due to severe acute respiratory syndrome coronavirus 2 (SARSCoV-2)-related coronavirus disease 2019 (COVID-19) is less frequent in children compared to adults. But infection rate and viral loads in the nasopharynx of both children and adults appear to be similar. The hospitalisation rates and severity of illness are significantly lower in children compared to adults. Infants < 1 year and children with underlying medical conditions have an increased risk of having a severe illness.

DISEASE BURDEN IN NEPAL

Nepal, a lower middle-income nation home to 30.4 million people with a 2.3% annual population growth and a life expectancy of 69 years, faced a significant health crisis with the advent of COVID-19.[3] The country's first case, identified in a returning traveler from China in January 2020, marked the beginning of a challenging period.[2] Nepal subsequently endured two major waves of the pandemic, resulting in over 9 million reported infections and a staggering nearly 12,000 deaths by March 1, 2023.[3] These figures represent a substantial increase in the country's mortality. Recognizing the fragility of its healthcare infrastructure, which already struggled with limited resources, the Government of Nepal implemented stringent nationwide lockdowns during both waves to prevent its collapse under the surge of patients. Even prior to the pandemic, Nepal grappled with a considerable burden of infectious diseases and emerging non-communicable diseases, highlighting the compounded strain that COVID-19 placed on the nation's health. The long-term consequences of this pandemic for Nepal's healthcare system and overall disease burden will likely require sustained attention and resources.

ABOUT THE VACCINE

The normal vaccine development paradigm involves multiple steps, each following the other in a sequential pattern, a process that may take 5-10 years. To accelerate COVID-19 vaccine development, steps are done in parallel, with production of a vaccine commencing even before the outcome of a clinical trial is known, to ensure readiness for distribution once approval is given. This pattern of accelerated

development is conducted at financial risk to developers and manufacturers, with uncertainty about the success of the vaccine candidate. However, even in this accelerated development paradigm, all the usual safety and efficacy monitoring mechanisms remain in place.

Nepal began administration of COVID-19 vaccines on 27 January 2021. 1 million Oxford-Astrazeneca vaccines were provided by India as a grant while Nepal brought 2 million doses from Serum Institute of India (SII) and was one of the first to receive COVID-19 vaccines. Nepal approved China's Sinopharm BIBP vaccine (BBIBP-CorV) on 15 February 2021. About 1.52 million doses of single dose Janssen vaccine (Johnson & Johnson) arrived on July as aid from the United States. Nepal on 25 October 2021 received 100,620 doses of Pfizer-BioNtech COVID-19 vaccine provided by the United States through COVAX.[4]

As of 9 May 2022, 12.5 million Covishield ChAdOx1 nCoV-19, 19.7 million Sinovac-Coronavac, 3.5 million Janssen Ad26.COV2.S, 0.6 million Pfizer BNT162b2, COVID-19 mRNA and 5.9 million Moderna mRNA-1273 vaccines have been administered in people aged >12 years of age.[5]

COVID-19 vaccine types: [6]

- **Genetic vaccines/mRNA vaccines**: An mRNA vaccine gives cells instructions for how to make the S protein found on the surface of the COVID-19 virus. Eg: Pfizer–BioNTech and Moderna, available for people age 6 months and older.
- **Vector vaccines:** In this type of vaccine, material from the virus that causes COVID-19 is placed in a modified version of a different virus. This different virus is called a viral vector. The viral vector gives cells instructions to make copies of the COVID-19 virus S protein. Eg: Oxford–AstraZeneca, Janssen, Sputnik V, CanSino, Convidecia (inhalational), iNCOVACC (intra-nasal).
- **Protein subunit vaccine:** Subunit vaccines include only the parts of a virus that best stimulate the immune system. This type of COVID-19 vaccine has harmless S proteins in it. Once the immune system recognizes the S proteins, it creates antibodies and defensive white blood cells. Eg: Novavax COVID-19 vaccine, available for people age 12 years and older.
- **Inactivated whole-virus vaccines:** This type of vaccine contains the killed SARS-CoV-2 virus, which is recognized by the immune system to trigger a response without causing COVID-19 illness. This response builds immune memory, so that body can fight off SARS-CoV-2 in future. Eg: Sinovac, Sinopharm, Covaxin.
- **Upcoming is intra-nasal live-attenuated COVID-19 vaccine:** In trial now. Eg: Codagenix.
- **Bivalent Vaccines:** The US FDA has granted EUA for the bivalent mRNA COVID-19 vaccines. The BNT162b2 (Pfizer) vaccine contains 30 µg of mRNA (15 µg original strain, 15 µg Omicron BA.4/BA.5). The Moderna mRNA bivalent vaccine contains 50 µg of mRNA (25 µg original strain and 25 µg Omicron BA.4/BA.5). Both formulations are recommended only for the booster dose and not for the primary series.

VACCINE INDICATION

The recommended vaccine and number of 2024–2025 COVID-19 vaccine doses are based on age and vaccination history.

Routine COVID-19 vaccination schedule, October 31, 2024 [7]

Ages 6 months to 4 years

All COVID-19 vaccine doses in this age group should be from the same manufacturer.

COVID-19 vaccination history before 2024-2025 vaccine[A]	**Number of 2024-2025 doses indicated**	**Recommended 2024-2025 vaccine**[B] **and interval between doses**
Unvaccinated: • Receive an initial series with 2024–2025 vaccine		
Unvaccinated	2	**2024–2025 Dose 1** (Moderna): Day 0 **2024–2025 Dose 2** (Moderna): 4–8 weeks after Dose 1[C]
		OR
Unvaccinated	3	**2024–2025 Dose 1** (Pfizer-BioNTech): Day 0 **2024–2025 Dose 2** (Pfizer-BioNTech): 3–8 weeks after Dose 1[C] **2024–2025 Dose 3** (Pfizer-BioNTech): At least 8 weeks after Dose 2
Initiated but did not complete the initial series before 2024–2025 vaccine: • Complete the initial series with 2024–2025 vaccine		
1 dose Moderna	1	**2024–2025 Dose 1** (Moderna): 4–8 weeks after last dose[C]
1 dose Pfizer-BioNTech	2	**2024–2025 Dose 1** (Pfizer-BioNTech): 3–8 weeks after last dose[C] **2024–2025 Dose 2** (Pfizer-BioNTech): At least 8 weeks after 2024–2025 Dose 1
2 doses Pfizer-BioNTech	1	**2024–2025 Dose 1** (Pfizer-BioNTech): At least 8 weeks after last dose
Completed the initial series before 2024–2025 vaccine: • Receive 1 dose of 2024–2025 vaccine		
2 or more doses Moderna	1	**2024–2025 Dose 1** (Moderna): At least 8 weeks after last dose
3 or more doses Pfizer-BioNTech	1	**2024–2025 Dose 1** (Pfizer-BioNTech): At least 8 weeks after last dose

A. COVID-19 vaccination history refers to all doses of COVID-19 vaccine from any manufacturer received before the availability of the 2024–2025 COVID-19 vaccines and includes original, bivalent, and 2023–2024 COVID-19 vaccines.

B. Dosage for Moderna: 0.25 mL/25 ug; Dosage for Pfizer-BioNTech: 0.3 mL/3 ug.

C. An 8-week interval between the first and second COVID-19 vaccine (Moderna and Pfizer-BioNTech) doses might be optimal for some people

as it might reduce the rare risk of myocarditis and pericarditis associated with these vaccines.

Ages 5–11 years

COVID-19 vaccination history before 2024-2025 vaccine	Number of 2024-2025 doses indicated	Recommended 2024-2025 vaccine and interval between doses
Unvaccinated: • Receive 1 dose of 2024–2025 vaccine		
Unvaccinated	1	**2024–2025 Dose 1** (Moderna or Pfizer-BioNTech): Day 0
Previously vaccinated before 2024–2025 vaccine: • Receive 1 dose of 2024–2025 vaccine		
1 or more doses mRNA (Moderna or Pfizer-BioNTech) vaccine	1	**2024–2025 Dose 1** (Moderna or Pfizer-BioNTech): At least 8 weeks after last dose

Children who transition from age 4 years to age 5 years during the initial vaccination series should receive 1 dose of vaccine from the same manufacturer at the dosage for children ages 5–11 years on or after turning age 5 years:

- **Moderna**: 1 dose of 2024–2025 Moderna (0.25 mL/25 ug) 4–8 weeks after the first dose. There is no dosage change.
- **Pfizer-BioNTech**: 1 dose of 2024–2025 Pfizer-BioNTech (0.3 mL/10 ug). If the 10 ug dose is the second dose, administer 3–8 weeks after the first dose; if it is the third dose, administer at least 8 weeks after the second dose.
- **Note**: If more than 8 weeks have elapsed since receipt of the last dose of mRNA COVID-19 vaccine at the dosage for children ages 6 months–4 years, any 2024–2025 mRNA COVID-19 vaccine (i.e. Moderna or Pfizer-BioNTech) may be administered at the dosage for children ages 5–11 years.

Age >12 years

COVID-19 vaccination history before 2024-2025 vaccine	Number of 2024-2025 doses indicated	Recommended 2024-2025 vaccine and interval between doses
Unvaccinated: • Initiate vaccination with 2024–2025 vaccine		
Unvaccinated	1	**2024–2025 Dose 1** (Moderna or

		Pfizer-BioNTech): Day 0
		OR
Unvaccinated	2	**2024–2025 Dose 1** (Novavax): Day 0 **2024–2025 Dose 2** (Novavax): 3–8 weeks after Dose 1
Previously vaccinated before 2024–2025 vaccine: • Receive 1 dose of 2024–2025 vaccine		
1 or more doses mRNA (Moderna or Pfizer-BioNTech) vaccine	1	**2024–2025 Dose 1** (Moderna, Novavax or Pfizer-BioNTech): At least 8 weeks after last dose
1 dose Novavax	1	**2024–2025 Dose 1** (Novavax): 3–8 weeks after last dose
2 or more doses Novavax	1	**2024–2025 Dose 1** (Moderna, Novavax or Pfizer-BioNTech): At least 8 weeks after last dose

Dosage for Moderna: 0.5 mL/50 ug; dosage for Novavax: 0.5 mL/5 ug rS protein and 50 ug Matrix-M adjuvant; dosage for Pfizer-BioNTech: 0.3 mL/30 ug.

If more than 8 weeks have elapsed since receipt of the first dose of Novavax, any 2024–2025 COVID-19 vaccine (i.e., Moderna, Novavax, or Pfizer-BioNTech) may be administered.

COVID-19 VACCINATION GUIDANCE FOR PEOPLE WHO ARE MODERATELY OR SEVERELY IMMUNOCOMPROMISED [8]

Ages 6 months–4 years

COVID-19 vaccination history before 2024-2025 vaccine	**Number of 2024-2025 doses indicated**	**Recommended 2024-2025 vaccine and interval between doses**
Unvaccinated: • Receive an initial 3-dose series with 2024–2025 vaccine • Receive 1 dose of 2024–2025 vaccine 6 months (minimum interval 2 months) after completing initial series • May receive additional doses of 2024–2025 vaccine under shared clinical-decision making		
Unvaccinated	4	**2024–2025 Dose 1** (Moderna): Day 0 **2024–2025 Dose 2** (Moderna): 4 weeks after Dose 1 **2024–2025 Dose 3** (Moderna): At least 4 weeks after Dose 2 **2024–2025 Dose 4** (Moderna): 6 months (minimum interval 2 months) after Dose 3 **Additional doses** (Moderna): May be administered under shared clinical decision-making at least 2 months

		after last 2024–2025 Moderna dose
OR		
Unvaccinated	4	**2024–2025 Dose 1** (Pfizer-BioNTech): Day 0 **2024–2025 Dose 2** (Pfizer-BioNTech): 3 weeks after Dose 1 **2024–2025 Dose 3** (Pfizer-BioNTech): At least 8 weeks after Dose 2 **2024–2025 Dose 4** (Pfizer-BioNTech): 6 months (minimum interval 2 months) after Dose 3 **Additional doses** (Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last 2024–2025 Pfizer-BioNTech dose
Initiated but did not complete the 3-dose initial series before 2024–2025 vaccine: • Complete the 3-dose series with 2024–2025 vaccine • Receive 1 dose of 2024-2025 vaccine 6 months (minimum interval 2 months) after completing initial series • May receive additional doses of 2024–2025 vaccine under shared clinical-decision making		
1 dose Moderna	3	**2024–2025 Dose 1** (Moderna): 4 weeks after last dose **2024–2025 Dose 2** (Moderna): At least 4 weeks after 2024–2025 Dose 1 **2024–2025 Dose 3** (Moderna): 6 months (minimum interval 2 months) after 2024–2025 Dose 2 **Additional doses** (Moderna): May be administered under shared clinical-decision making at least 2 months after last 2024–2025 Moderna dose
2 doses Moderna	2	**2024–2025 Dose 1** (Moderna): At least 4 weeks after last dose **2024–2025 Dose 2** (Moderna): 6 months (minimum interval 2 months) after 2024–2025 Dose 1 **Additional doses** (Moderna): May be administered under shared clinical decision-making at least 2 months after last 2024–2025 Moderna dose
1 doses Pfizer-BioNTech	3	**2024–2025 Dose 1** (Pfizer-BioNTech): 3 weeks after last dose **2024–2025 Dose 2** (Pfizer-BioNTech): At least 8 weeks after 2024–2025 Dose 1 **2024–2025 Dose 3** (Pfizer-BioNTech): 6 months (minimum interval 2 months) after 2024–2025 Dose 2

		Additional doses (Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last 2024–2025 Pfizer-BioNTech dose
2 doses Pfizer-BioNTech	2	**2024–2025 Dose 1** (Pfizer-BioNTech): At least 8 weeks after last **2024–2025 Dose 2** (Pfizer-BioNTech): 6 months (minimum interval 2 months) after 2024–2025 Dose 1 **Additional doses** (Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last 2024–2025 Pfizer-BioNTech dose
Completed the 3-dose initial series before 2024–2025 vaccine: • Receive 2 doses of 2024–2025 vaccine spaced 6 months (minimum interval 2 months) apart • May receive additional doses of 2024–2025 vaccine under shared clinical-decision making		
3 or more doses Moderna	2	**2024–2025 Dose 1** (Moderna): At least 8 weeks after last dose **2024–2025 Dose 2** (Moderna): 6 months (minimum interval 2 months) after 2024–2025 Dose 1 **Additional doses** (Moderna): May be administered under shared clinical decision-making at least 2 months after last 2024–2025 Moderna dose
3 or more doses Pfizer-BioNTech	2	**2024–2025 Dose 1** (Pfizer-BioNTech): At least 8 weeks after last dose **2024–2025 Dose 2** (Pfizer-BioNTech): 6 months (minimum interval 2 months) after 2024–2025 Dose 1 **Additional doses** (Pfizer-BioNTech): May be administered under shared clinical-decision making at least 2 months after last 2024–2025 Pfizer-BioNTech dose

Ages 5–11 years

COVID-19 vaccination history before 2024-2025 vaccine	**Number of 2024-2025 doses indicated**	**Recommended 2024-2025 vaccine and interval between doses**
Unvaccinated: • Receive an initial 3-dose series with 2024–2025 vaccine • Receive 1 dose of 2024–2025 vaccine 6 months (minimum interval 2 months) after completing initial series • May receive additional doses of 2024–2025 vaccine under shared clinical-decision making		

Unvaccinated	4	**2024–2025 Dose 1** (Moderna): Day 0 **2024–2025 Dose 2** (Moderna): 4 weeks after Dose 1 **2024–2025 Dose 3** (Moderna): At least 4 weeks after Dose 2 **2024–2025 Dose 4** (Moderna or Pfizer-BioNTech): 6 months (minimum interval 2 months) after Dose 3 **Additional doses** (Moderna or Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last 2024–2025 mRNA dose
OR		
Unvaccinated	4	**2024–2025 Dose 1** (Pfizer-BioNTech): Day 0 **2024–2025 Dose 2** (Pfizer-BioNTech): 3 weeks after Dose 1 **2024–2025 Dose 3** (Pfizer-BioNTech): At least 4 weeks after Dose 2 **2024–2025 Dose 4** (Moderna or Pfizer-BioNTech): 6 months (minimum interval 2 months) after Dose 3 **Additional doses** (Moderna or Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last 2024–2025 mRNA dose
Initiated but did not complete the 3-dose initial series before 2024–2025 vaccine: • Complete the 3-dose series with 2024–2025 vaccine • Receive 1 dose of 2024–2025 vaccine 6 months (minimum interval 2 months) after completing initial series • May receive additional doses of 2024–2025 vaccine under shared clinical decision-making		
1 dose Moderna	3	**2024–2025 Dose 1** (Moderna): 4 weeks after last dose **2024–2025 Dose 2** (Moderna): At least 4 weeks after 2024–2025 Dose 1 **2024–2025 Dose 3** (Moderna): 6 months (minimum interval 2 months) after 2024–2025 Dose 2 **Additional doses** (Moderna): May be administered under shared clinical-decision making at least 2 months after last 2024–2025 Moderna dose
2 doses Moderna	2	**2024–2025 Dose 1** (Moderna): At least 4 weeks after last dose **2024–2025 Dose 2** (Moderna): 6 months (minimum interval 2 months) after 2024–2025 Dose 1 **Additional doses** (Moderna): May be administered under shared clinical

		decision-making at least 2 months after last 2024–2025 Moderna dose
1 doses Pfizer-BioNTech	3	**2024–2025 Dose 1** (Pfizer-BioNTech): 3 weeks after last dose **2024–2025 Dose 2** (Pfizer-BioNTech): At least 4 weeks after 2024–2025 Dose 1 **2024–2025 Dose 3** (Moderna or Pfizer-BioNTech): 6 months (minimum interval 2 months) after 2024–2025 Dose 2 **Additional doses** (Moderna or Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last 2024–2025 mRNA dose
2 doses Pfizer-BioNTech	2	**2024–2025 Dose 1** (Pfizer-BioNTech): At least 4 weeks after last dose **2024–2025 Dose 2** (Moderna or Pfizer-BioNTech): 6 months (minimum interval 2 months) after 2024–2025 Dose 2 **Additional doses** (Moderna or Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last 2024–2025 mRNA dose
Completed the 3-dose initial series before 2024–2025 vaccine: • Receive 2 doses of 2024–2025 vaccine spaced 6 months (minimum interval 2 months) apart • May receive additional doses of 2024–2025 vaccine under shared clinical-decision making		
3 or more doses Moderna or 3 or more doses Pfizer-BioNTech	2	**2024–2025 Dose 1** (Moderna or Pfizer-BioNTech): At least 8 weeks after last dose **2024–2025 Dose 2** (Moderna or Pfizer-BioNTech): 6 months (minimum interval 2 months) after 2024–2025 Dose 1 **Additional doses** (Moderna or Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last 2024–2025 mRNA dose

Children who transition from age 4 years to age 5 years during the initial vaccination series should complete the 3-dose series using the dosage for children ages 5–11 years for all doses received on or after turning age 5 years:

- Moderna series: 2024–2025 Moderna, 0.25 mL/25 ug; there is no dosage change
- Pfizer-BioNTech series: 2024–2025 Pfizer-BioNTech, 0.3 mL/10 ug

Ages 12 years and older

COVID-19 vaccination history before 2024-2025 vaccine	**Number of 2024-2025 doses indicated**	**Recommended 2024-2025 vaccine and interval between doses**

Unvaccinated: • Receive an initial series with 2024–2025 vaccine • Receive 1 dose of 2024–2025 vaccine 6 months (minimum interval 2 months) after completing initial series • May receive additional doses of 2024–2025 vaccine under shared clinical decision-making		
Unvaccinated	4	**2024–2025 Dose 1** (Moderna): Day 0 **2024–2025 Dose 2** (Moderna): 4 weeks after Dose 1 **2024–2025 Dose 3** (Moderna): At least 4 weeks after Dose 2 **2024–2025 Dose 4** (Moderna, Novavax, or Pfizer-BioNTech): 6 months (minimum interval 2 months) after Dose 3 **Additional doses** (Moderna, Novavax, or Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last dose any 2024–2025 vaccine
OR		
Unvaccinated	3	**2024–2025 Dose 1** (Novavax): Day 0 **2024–2025 Dose 2** (Novavax): 3 weeks after Dose 1 **2024–2025 Dose 3** (Moderna, Novavax, or Pfizer-BioNTech): 6 months (minimum interval 2 months) after Dose 2 **Additional doses**: (Moderna, Novavax, or Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last dose any 2024–2025 vaccine
OR		
	4	**2024–2025 Dose 1** (Pfizer-BioNTech): Day 0 **2024–2025 Dose 2** (Pfizer-BioNTech): 3 weeks after Dose 1 **2024–2025 Dose 3** (Pfizer-BioNTech): At least 4 weeks after Dose 2 **2024–2025 Dose 4** (Moderna, Novavax, or Pfizer-BioNTech): 6 months (minimum interval 2 months) after Dose 3 **Additional doses** (Moderna,

		Novavax, or Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last dose any 2024–2025 vaccine
Initiated but did not complete the initial series before 2024–2025 vaccine: • Complete the initial series with 2024–2025 vaccine • Receive 1 dose of 2024–2025 vaccine 6 months (minimum interval 2 months) after completing initial series • May receive additional doses of 2024–2025 vaccine under shared clinical decision-making		
1 dose Moderna	3	**2024–2025 Dose 1** (Moderna): 4 weeks after last dose **2024–2025 Dose 2** (Moderna): At least 4 weeks after 2024–2025 Dose 1 **2024–2025 Dose 3** (Moderna, Novavax, or Pfizer-BioNTech): 6 months (minimum interval 2 months) after 2024–2025 Dose 2 **Additional doses** (Moderna, Novavax, or Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last dose any 2024–2025 vaccine
2 doses Moderna	2	**2024–2025 Dose 1** (Moderna): At least 4 weeks after last dose **2024–2025 Dose 2** (Moderna, Novavax or Pfizer-BioNTech): 6 months (minimum interval 2 months) after 2024–2025 Dose 1 **Additional doses** (Moderna, Novavax or Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last dose any 2024–2025 vaccine
1 doses Pfizer-BioNTech	3	**2024–2025 Dose 1** (Pfizer-BioNTech): 3 weeks after last dose **2024–2025 Dose 2** (Pfizer-BioNTech): At least 4 weeks after 2024–2025 Dose 1 **2024–2025 Dose 3** (Moderna, Novavax or Pfizer-BioNTech): 6 months (minimum interval 2 months) after 2024–2025 Dose 2

		Additional doses (Moderna, Novavax or Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last dose any 2024–2025 vaccine
2 doses Pfizer-BioNTech	2	**2024–2025 Dose 1** (Pfizer-BioNTech): At least 4 weeks after last dose **2024–2025 Dose 2** (Moderna, Novavax or Pfizer-BioNTech): 6 months (minimum interval 2 months) after 2024–2025 Dose 1 **Additional doses** (Moderna, Novavax or Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last dose any 2024–2025 vaccine
1 dose Novavax	2	**2024–2025 Dose 1** (Novavax): At least 3 weeks after last dose **2024–2025 Dose 2** (Moderna, Novavax or Pfizer-BioNTech): 6 months (minimum interval 2 months) after 2024–2025 Dose 1 **Additional doses** (Moderna, Novavax or Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last dose any 2024–2025 vaccine
Completed the initial series before 2024–2025 vaccine: • Receive 2 doses of 2024–2025 vaccine spaced 6 months (minimum interval 2 months) apart • May receive additional doses of 2024–2025 vaccine under shared clinical decision-making		
3 or more doses Moderna or 3 or more doses Pfizer-BioNTech	2	**2024–2025 Dose 1** (Moderna, Novavax or Pfizer-BioNTech): At least 8 weeks after last dose **2024–2025 Dose 2** (Moderna, Novavax or Pfizer-BioNTech): 6 months (minimum interval 2 months) after 2024–2025 Dose 1 **Additional doses** (Moderna, Novavax or Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last

		dose any 2024–2025 vaccine
2 or more doses Novavax	2	**2024–2025 Dose 1** (Moderna, Novavax or Pfizer-BioNTech): At least 8 weeks after last dose **2024–2025 Dose 2** (Moderna, Novavax or Pfizer-BioNTech): 6 months (minimum interval 2 months) after 2024–2025 Dose 1 **Additional doses** (Moderna, Novavax or Pfizer-BioNTech): May be administered under shared clinical decision-making at least 2 months after last dose any 2024–2025 vaccine

CONTRAINDICATIONS AND PRECAUTIONS TO COVID-19 VACCINATION

Medical condition or history	Guidance	Recommended action
History of a severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a component of the COVID-19 vaccine	Contraindication	Do not vaccinate with the same COVID-19 vaccine type. May administer the alternate COVID-19 vaccine type.
History of a diagnosed non-severe allergy to a component of the COVID-19 vaccine	Precaution	May administer the alternate COVID-19 vaccine type.
History of a non-severe, immediate (onset less than 4 hours) allergic reaction after administration of a previous dose of one COVID-19 vaccine type	Precaution	
Moderate or severe acute illness, with or without fever	Precaution	Defer vaccination until the illness has improved
History of MIS-C or MIS-A	Precaution	Clinical recovery has been achieved, including return to baseline cardiac function; and it has been at least 90 days after the diagnosis of MIS-C or MIS-A

History of myocarditis or pericarditis within 3 weeks after a dose of any COVID-19 vaccine	Precaution	A subsequent dose of any COVID-19 vaccine should generally be avoided.

ADVERSE EVENTS FOLLOWING IMMUNISATION

Local reactions include pain, tenderness, and, less commonly, swelling and redness at the injection site.

Systemic reactions include fever, fatigue, malaise, headache, chills, myalgia, arthralgia, and diarrhoea; among younger children, particularly those younger than age 3 years, systemic reactions also can include irritability/crying, sleepiness, and loss of appetite.

Localized axillary lymphadenopathy on the same side as the vaccinated arm or groin, if vaccination was in the thigh, has been observed following vaccination with Moderna, Novavax, and Pfizer-BioNTech COVID-19 vaccines. Infrequently, people who have received dermal fillers might experience temporary swelling at or near the site of filler injection (usually face or lips) following a dose of an mRNA COVID-19 vaccine.

Myocarditis and pericarditis: People receiving any COVID-19 vaccine, especially males ages 12–39 years, should be made aware of the rare risk of myocarditis and pericarditis following COVID-19 vaccination and the option for an extended interval between doses.

Anaphylactic reactions: Anaphylactic reactions have been rarely reported following receipt of COVID-19 vaccines.

SCHEDULE AND DOSES/ ROUTE OF ADMINISTRATION

Generally, most are administered in two-dose schedule 21-28 days apart
Astra-Zeneca/Covishield 2 doses IM at 0-28 days
Pfizer: 2 doses IM at 0-21 days
Moderna: 2 doses IM at 0-28 days
Covaxin: 2 doses IM at 0-28 days
Janssen Pharmaceuticals: 2 doses IM at 0-56 days

EFFICACY

Vaccine efficacy can vary depending on the variant, the time since vaccination, and the outcome being measured (e.g., infection vs. severe disease). While protection against infection may wane, the vaccine continues to provide significant protection against severe illness, hospitalisation, and death, especially after a booster dose. Updated vaccines are formulated to address newer circulating variants and maintain protection.[9]

Pfizer vaccine was effective against the Alpha and Delta variants after two doses, although there was a slight reduction in efficacy compared to the original strain. For example, one study showed the efficacy against symptomatic disease with the Delta variant was around 88% after two doses, compared to 93.7% against the Alpha variant. CDC data from September 2023 to January 2024 showed that updated vaccines were 54% effective against getting COVID-19, including against JN.1 and XBB variants.[10]

Moderna COVID-19 vaccine has shown high efficacy in clinical trials and real-world settings. Initial Efficacy is around 94% efficacy against symptomatic COVID-19 after two doses in the initial clinical trial. High effectiveness against severe disease, hospitalisation, and death. Generally effective against earlier variants like Alpha and Beta.[11]

The AstraZeneca COVID-19 vaccine and Covishield vaccine showed an efficacy of 66.7% to 76% against symptomatic COVID-19 after two doses. Efficacy tended to be higher with a longer interval (12 weeks or more) between the first and second doses, reaching up to 81.3%. One study indicated 100% efficacy against severe disease, hospitalisation, and death starting 22 days after the first dose. Against the Delta variant, two doses showed around 60% efficacy against symptomatic disease in one study. However, it remained highly effective (around 92%) against hospitalisation due to the Delta variant.[12]

Covaxin, also known as BBV152 has overall efficacy of 77.8% against symptomatic COVID-19. This was based on the evaluation of 130 confirmed cases, with 24 observed in the vaccine group versus 106 in the placebo group Efficacy against Severe Disease: Covaxin showed 93.4% efficacy against severe symptomatic COVID-19.[13]

STORAGE

mRNA vaccines have strict cold chain needs. Pfizer requires -60°C to -80°C. Moderna needs -50°C to -15°C for long-term storage and can be kept at +2°C to +8°C for up to one month short-term. Sputnik (Gamaleya) liquid form needs -18°C, while freeze-dried can be stored at 2°C to 8°C. AstraZeneca/Oxford and Bharat Biotech's inactivated vaccines require 2°C to 8°C storage.

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DENGUE VACCINE

Dr. Henish Shakya

BACKGROUND

Dengue, a mosquito-borne disease of increasing global health significance, has demonstrated a rapid expansion in its geographic distribution across numerous nations in recent years. In Nepal, dengue represents a rapidly emerging infectious disease. Exhibiting endemicity across the majority of its provincial territories, Nepal has experienced a notable augmentation in dengue incidence. This epidemiological trend is largely attributed to the amplified distribution and establishment of the competent mosquito vectors, *Aedes aegypti* and *Aedes albopictus*. Furthermore, human mobility patterns and the introduction of viremic individuals through travel contribute significantly to viral dissemination. Epidemiological surveillance indicates the co-circulation of all four distinct dengue virus serotypes (DENV-1, DENV-2, DENV-3, and DENV-4) within the Nepalese population, with DENV-1 historically representing the predominant serotype contributing to the overall disease burden.[1]

TRANSMISSION/CLINICAL FEATURES

Dengue (break-bone fever) is a viral infection that spreads from mosquitoes to people. It is more common in tropical and subtropical climates.

Dengue virus (DENV) is a small single stranded RNA virus comprising four distinct serotypes (DEN-1 to DEN-4). These closely related serotypes of the dengue virus belong to the genus Flavivirus, family Flaviviridae. Dengue is transmitted primarily by the female mosquito Aedes aegypti, which thrives in and around urbanized areas. It is diurnal and highly anthropophilic, with domestic forms showing increased propensity towards exclusive human feeding.

Most people who get dengue will not have symptoms. But for those who do, the most common symptoms are biphasic high fever, headache, myalgia, arthralgia, retro-orbital pain, nausea, and rash. Most will get better in 1–2 weeks. Some people develop severe dengue and need care in a hospital. In severe cases, dengue can be fatal. Individuals who are infected for the second time are at greater risk of severe dengue. Severe dengue symptoms often come after the fever has gone away. It can present with severe abdominal pain, persistent vomiting, hemorrhagic manifestations (Dengue Hemorrhagic fever) and features of shock with marked plasma leakage (Dengue shock syndrome).[1]

PATHOGENESIS

The pathogenesis of dengue fever is complex and involves the virus, host genes, and the host's immune response. Dengue pathogenesis is generally due to a high viral load and activation of high numbers of non-protective T cells result in a “storm” of inflammatory cytokines and other mediators, leading to the increased plasma leakage characteristic of DHF/DSS.[2] The mosquito injects the virus into the skin

when it bites a person. The virus infects immature Langerhans cells and keratinocytes. Infected cells move to the lymph nodes, where they infect monocytes and macrophages. The body's immune response is critical to the pathogenesis of dengue fever. The body produces antibodies to fight the virus. However, antibodies from a previous infection may not neutralize a secondary infection. This can lead to antibody-dependent enhancement (ADE), which increases the numberof viruses in the body. The severity of dengue fever can range from mild to severe dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Severe dengue fever is often associated with infection by a second dengue virus serotype.

EPIDEMIOLOGY

The incidence of dengue has grown dramatically around the world in recent decades, with cases reported to WHO increasing from 505 430 cases in 2000 to 5.2 million in 2019. As of 30 April 2024, over 7.6 million dengue cases have been reported to WHO in 2024, including 3.4 million confirmed cases, over 16 000 severe cases, and over 3000 deaths.[3]

DISEASE BURDEN IN NEPAL

In 2022, Nepal faced its worst ever outbreak of dengue, with over 50 000 cases and >50 deaths reported across all 77 districts, with the highest number of cases in the capital city, Kathmandu.[4] As of 31st December 2022, altogether 54 784 dengue cases have been identified, with Bagmati province reporting the highest. The country's capital, Kathmandu, reported the highest burden of dengue cases (26%). Dengue is becoming increasingly prevalent at higher altitudes such as Kathmandu (altitude 1400 m) and has been attributed to rising temperatures (climatic changes) creating a conducive environment for Aedes mosquito breeding.[5] The high degree of pre-monsoon rainfall because of climate change and mismanaged waste disposal system were the main cause of the 2022 dengue outbreak in Nepal. The Situation Report on Dengue in Nepal – 2024 published by Epidemiology and Disease Control Division, Department of Health Services shows that a total of 34,385 dengue cases have been reported across the country, with 76 out of 77 districts affected. The outbreak has resulted in 13 verified deaths. Among the provinces, Gandaki recorded the highest number of cases with 15,806, followed closely by Bagmati with 12,253 cases.[6]

VACCINES:

Vaccination against dengue should be viewed as part of an integrated strategy to control the disease, including vector control, proper case management, community education and community engagement. Comprehensive vector control must remain a critical component of dengue control programs. Furthermore, the mosquito vectors of dengue transmit other important viruses, including yellow fever, chikungunya and Zika viruses.[7]

QDenga (TAK-003)

Currently, QDenga (TAK-003) is the only vaccine for dengue recommended by WHO. It is a live-attenuated vaccine containing weakened versions of dengue virus serotypes 1, 2, 3 and 4. It uses the DENV2 strain as the genomic backbone.

INDICATION

WHO recommends the use of TAK-003 in children aged 6–16 years in settings with high dengue transmission intensity.

Until the efficacy–risk profile for DENV3 and DENV4 in seronegative persons has been more thoroughly assessed, WHO does not recommend the programmatic use of TAK-003 vaccine in low to moderate dengue transmission settings.[7]

CONTRAINDICATION

1. Breastfeeding women: The vaccine is contraindicated for mothers during breastfeeding.
2. Pregnant women or those planning for pregnancy at least 1 month following vaccination.
3. A person with severe allergic reaction after previous vaccine dose or allergy to any vaccine component.
4. A person with severe immunodeficiency due to any disease or therapy. The vaccine is also contraindicated in individuals with symptomatic HIV infection or with asymptomatic HIV infection associated with evidence of impaired immune function. TAK-003 is contraindicated in persons with congenital or acquired immune deficiency, including those receiving immunosuppressive therapies such as chemotherapy or high doses of systemic corticosteroids within 4 weeks prior to vaccination, as with other live attenuated vaccines.[7]

PRECAUTION

1. Pregnant women: TAK-003 is not recommended during pregnancy and pregnancy should be avoided for at least 1 month following vaccination. Inadvertent vaccination of a pregnant person is not a reason to terminate the pregnancy.[7]

2. Person with HIV infection with moderate immune suppression
3. Person with moderate or severe acute illness

ADVERSE EVENTS FOLLOWING IMMUNISATION

Soreness, itchiness, or pain in the injection site. Headache, myalgia, asthenia, fever, local reaction.

SCHEDULE AND DOSING

It is given as a 2-dose schedule (0.5ml) with a minimum interval of 3 months between doses. If the second dose is delayed for any reason, it is not necessary to restart the series, and the second dose should be administered at the first available opportunity. Upper age limit for vaccination is 60 years.[7]

ROUTE OF ADMINISTRATION:

Subcutaneous over the upper arm

VACCINE EFFICACY

The effectiveness of QDenga was evaluated in the TIDES (Tetravalent Immunisation against Dengue Efficacy Study) trial, which included 20,000 participants aged between childhood and adolescence from eight countries across Asia and Latin America. During the first year following vaccination, the vaccine demonstrated 80% efficacy against virologically confirmed dengue (VCD) and was 95% effective in preventing hospitalisations due to VCD. Among the four dengue virus serotypes, efficacy was highest against DENV-2 at 98% and lowest against DENV-3 at 63%. After 4 to 5 years, the overall efficacy in preventing VCD declined to 59%, while its effectiveness in preventing related hospitalisations remained relatively high at 84%. Efficacy against VCD varied from 43% to 82% depending on the serotype. The vaccine was more effective in individuals previously exposed to dengue (seropositive), with a 63% efficacy rate, compared to 50% in those without prior exposure (dengue-naïve).[8, 9]

STORAGE

It should be stored at 2°C to 8°C. Do not freeze.

After reconstitution, it should be administered immediately or stored at 2°C to 8°C and used within 30 minutes.

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MALARIA VACCINE

Dr. Sangita Puree Dhungana

BACKGROUND

Malaria is a vector-borne disease transmitted through the bite of infected anopheline mosquitoes. In many endemic areas, malaria transmission occurs throughout the year, often with seasonal increases. In areas of highly seasonal malaria, transmission may be primarily limited to several months each year, influenced largely by rainfall patterns. The intensity of transmission generally varies as a function of parasite prevalence in the human population and the feeding habits, efficiency, density and survival rates of the mosquito vector. These in turn are strongly influenced by temperature and humidity, vector species composition and vector control measures. Because variations in ecological, climatic and vector control factors influence the abundance of vector breeding sites and the survival of mosquitoes, malaria transmission is usually heterogeneous within a country. Important contributing factors to the burden of malaria include the efficiency of the vector in transmitting malaria from one person to another, poor housing conditions resulting in increased exposure to mosquito bites, and weak health systems with limited access to quality prevention and treatment services.[1]

PATHOGENESIS

Five species of the Plasmodium protozoan parasite can infect humans – P. falciparum, P. vivax, P. ovale, P. malariae and P. knowlesi. Humans are the only known reservoirs of these parasite species – with the exception of P. knowlesi for which the natural hosts are long-tailed and pig-tailed macaques. During the following 5–8 days – or more, depending on the parasite species – the parasites develop and multiply in liver cells, after which tens of thousands of parasites are released into the blood stream where they invade erythrocytes. Further replication and rupture cycles in erythrocytes lead to the infection and subsequent destruction of additional erythrocytes and clinical manifestations of malaria.

The incubation period in non-immune persons, from the time of P. falciparum infection to initial symptoms, usually ranges from 8 to 14 days. In persons with some degree of immunity, the incubation period may be longer. In areas of high transmission, young children often experience 4–6 episodes of clinical malaria each year, even when the most effective currently available malaria control tools are used, such as insecticide-treated nets (ITNs) and diagnosis and treatment.[1]

Morbidity due to infection with P. falciparum can range from mild febrile illness, which is difficult to distinguish clinically from other undifferentiated febrile illnesses, to life-threatening disease with coma, respiratory distress, severe anaemia or circulatory shock. Case fatality rates in severe malaria have been estimated at 13–20% for hospitalised children or > 90% if the child remains at home.[2] Severe malaria may present as life-threatening anaemia. In older children, severe malaria may present as cerebral malaria, with altered consciousness and coma due to sequestration of infected erythrocytes in the cerebral microvasculature, with

respiratory distress and/or as dysfunction of multiple vital organs often associated with metabolic acidosis. Other manifestations may include hypoglycaemia, shock, renal failure and pulmonary oedema. Those who survive severe malaria may have long-term sequelae. In up to 25% of paediatric survivors of cerebral malaria, persistent neurological sequelae including impaired cognition, motor skills and visual coordination as well as seizures and attention deficit hyper activity disorder have been reported.[3] Mild to-moderate anaemia among children is common in communities with moderate-to-high P. falciparum malaria transmission.[4] Malaria infection strongly predisposes children to bacteraemia and can account for more than half of all cases of bacteraemia in malaria endemic areas.[5]

EPIDEMIOLOGY

Malaria continues to cause high levels of disease and death; an estimated 249 million cases and 608 000 deaths occurred globally in 2022. According to WHO's latest *World malaria report,* there were an estimated 263 million cases and 597 000 malaria deaths worldwide in 2023. This represents about 11 million more cases in 2023 compared to 2022, and nearly the same number of deaths. Approximately 95% of the deaths occurred in the WHO African Region, where many at risk still lack access to the services they need to prevent, detect and treat the disease.[6] Malaria is preventable and treatable. The global priority is to reduce the burden of disease and death while pursuing the long-term vision of national elimination and, ultimately, global malaria eradication. Approximately 95% of malaria cases and deaths occur in sub-Saharan Africa, with the remainder occurring largely in South-East Asia and South America.[7]

Almost all malaria deaths are caused by Plasmodium falciparum and most occur in African children under 5 years of age, with the highest burden concentrated in those under 3 years of age.[8] Plasmodium vivax is an important cause of malaria morbidity outside sub-Saharan Africa. Plasmodium vivax is an important cause of malaria morbidity outside sub-Saharan Africa.[7]

BURDEN OF DISEASE IN NEPAL

Malaria is endemic in the southern plain of Nepal which shares a porous border with India. More than 80% cases of malaria in Nepal are caused by *Plasmodium vivax*. In 1985, a malaria epidemic occurred with 42,321 cases (82% *P. vivax* and 17% *Plasmodium falciparum*). Nepal had experienced further outbreaks of malaria in 1991 and 2002. *Plasmodium falciparum* cases increased from 2005 to 2010 but since then declined. Nepal has seen a dramatic decrease in malaria cases in recent decades, with indigenous cases dropping significantly from 3,894 in 2010 to just 36 in 2022. Between 2005 and 2018, total annual malaria incidence decreased from 5393 cases in 2005 to 1064 cases in 2018.[9] Nepal aims to eliminate malaria by 2026. In 2022, there were only 36 indigenous malaria cases reported. While indigenous cases are low, imported malaria cases remain a concern, with 476 imported cases reported in 2022. According to Department of Health services, there were 533 confirmed cases of malaria, of which 24 cases were indigenous in Fiscyal year 2022/23. [10]At a provincial level, a significant

portion of high-risk wards are in Sudurpashchim Province, with other provinces also having identified risk areas in Karnali and Lumbini Province.[11]

MALARIA VACCINES

Two malaria vaccines, RTS,S/AS01 and R21/Matrix-M, are WHO-prequalified and recommended for use. Both are pre-erythrocytic vaccines that prevent P. falciparum infection in children and subsequent illness and death; they are not designed to interrupt malaria transmission. The recommended malaria vaccines prevent P. falciparum malaria, and there is no known cross protection with other Plasmodium species. However, in areas where P. falciparum and other Plasmodium species, including P. vivax, are endemic, the vaccine can provide important protection against P. falciparum malaria.[12,13]

RTS,S/AS01 and R21/Matrix-M are pre-erythrocytic vaccines targeting the central repeat amino acid sequence Asn-Ala-Asn-Pro (NANP) region of the P. falci parum circumsporozoite protein (CSP). Both vaccines are recombinant protein virus-like particles formed from a fusion protein comprising the CSP region and hepatitis B virus surface antigen (hBsAg) nanoparticles. This recombinant fusion protein is produced through expression in yeast (Saccharomyces cerevisiae for RTS,S and Hansenula polymorpha for R21).

CONTRAINDICATION

The only contraindication to the use of RTS,S/AS01 or R21/Matrix M vaccines is hypersensitivity to a previous dose of malaria vaccine or hepatitis B vaccines or to any of the vaccine components.

SCHEDULE AND DOSES

First dose of the vaccine RTS,S/AS01 is given to children aged from 5 months to 17 months. The first 3 doses should be administered at one-month intervals, with a fourth dose given 18 months after the third dose.[14] First dose of the vaccine R21/Matrix-M is given to children aged from 5 months to 36 months of age. The first 3 doses should be administered at one-month intervals, with a fourth dose given 12 months after the third dose.[15] Each dose for both is 0.5ml.

A fifth dose, given one year after the fourth dose, may be provided in areas of highly seasonal transmission and may be considered in other areas – depending on a local assessment of feasibility and cost-effectiveness – where a significant malaria risk remains for children.

ROUTE OF ADMINISTRATION

0.5ml IM

VACCINE EFFICACY

In areas with highly seasonal malaria transmission (where malaria transmission is largely limited to 4 or 5 months per year), the R21 vaccine was shown to reduce symptomatic cases of malaria by 75% during the 12 months following a 3-dose series. A fourth dose given a year after the third maintained efficacy. This high efficacy is similar to the efficacy demonstrated when RTS,S is given seasonally.[16]

STORAGE

Neither of the vaccines includes preservative, and vials should therefore be discarded at the end of the vaccination session or within 6 hours after opening, whichever comes first. The vaccines should be stored at 2–8 °C. The shelf-life is 3 years for RTS,S/AS01 and 2 years for R21/Matrix-M.[14,15]

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IMMUNISATION IN SPECIAL CIRCUMSTANCES

- Hemato-oncological conditions
- GI and Hepatobiliary conditions
- Nephrological conditions
- Paediatric Allergy Immunology and Rheumatological conditions (PAIR)
- Cardiological conditions

IMMUNISATION IN SPECIAL CIRCUMSTANCES

PEDIATRIC HEMATOLOGY ONCOLOGY

Dr. Ritu Lamichhane

OVERVIEW OF CHILDHOOD CANCER AND SURVIVAL

Globally an estimated 400,000 cases of childhood cancer were reported annually in individuals aged 0–19 years. Approximately 1500 new childhood cancer are diagnosed in Nepal. While survival rates in high-income countries approach 80%, they remain significantly lower (nearly 30%) in low-income countries, including Nepal. In Nepal, childhood cancer presents a significant public health challenge due to delayed diagnoses, limited access to specialized care, and a lack of comprehensive population-based cancer registries. These factors contribute to poor survival outcomes, underscoring the urgent need for improved awareness, early diagnosis, and equitable healthcare services.

CHALLENGES OF CANCER TREATMENTS AND ADDRESSING IMMUNITY GAPS

The primary treatments for childhood cancer include chemotherapy, radiotherapy, and surgery, often used alone or in combination. In addition, hematopoietic stem cell transplantation (HSCT) and cellular therapies are critical modalities for managing certain high-risk malignancies. These treatments aim to cure the disease or improve survival rates. However, they are not without risks, as they also affect healthy cells, including those of the immune system, leading to immunosuppression, lymphopenia, and neutropenia, which heighten the risk of infections. Many of these infections, including vaccine-preventable diseases (VPDs), can further compromise a child's health. In addition, many patients may have incomplete primary vaccinations at diagnosis, increasing their risk of preventable infections. This makes them more vulnerable to infections preventable by primary vaccination. Reimmunisation remains a critical tool to mitigate these risks.

Studies show that children treated for cancer often lose immunity to vaccine-preventable diseases. Zignol et al. found that, six months post-chemotherapy, 52% lost hepatitis B immunity, 25% measles, 21% mumps, 18% rubella, 13% tetanus, and 8% polio. Similarly, Mustafa et al. reported reduced antibodies against pertussis, diphtheria, and tetanus after 12 months. Younger age at diagnosis increased this risk, regardless of cancer type. These findings highlight the need to restore immunity in pediatric oncology patients' post-chemotherapy.

IMMUNE RECONSTITUTION TIMELINE

Immune recovery following cancer treatment varies based on the therapy:

- After chemotherapy, immune reconstitution typically begins within weeks to months but may be delayed if the treatment regimen includes antilymphocyte antibodies.
- For patients undergoing HSCT or cellular therapies, initial immune recovery also occurs within weeks to months, but complete adaptive immunity reconstitution may take longer (up to a year or more).
- Neutrophil counts are often the first to recover, followed by T-cell and B-cell functions, which may take additional time to fully normalize.

Understanding these timelines is essential for planning vaccinations and other preventive measures.

Sources of Infectious Threats

Infections can arise from:

- Endogenous flora (e.g.,pneumococcus, meningococcus, *Haemophilus influenzae* type b).
- Environmental exposures (e.g., tetanus).
- Vector-borne diseases (e.g., dengue, malaria).
- Direct transmission (e.g., influenza, SARS-CoV-2, measles, pertussis).

Children with cancer face heightened vulnerability due to a lack of preexisting immunity and frequent exposure to group settings like schools or daycare. Their limited ability to follow nonpharmaceutical preventive measures further elevates their risk of infection.

Factors like mucosal barrier integrity, skin health, and immune system function influence infection risk. Vaccination reduces this risk, preventing both primary and secondary bacterial infections.

Immune Recovery and Vaccination Considerations

Immune recovery after chemotherapy, HSCT, or cellular therapies varies by treatment and patient age. Neutropenia, loss of memory B and T cells, and reduced NK-cell function heighten the risk of infection and viral reactivation. Chemotherapy and transplantation often decrease protective antibody levels, even in previously vaccinated children.

Despite weakened responses, vaccination during cancer treatment can still reduce infection severity and mortality. Reimmunisation after treatment is essential to restore immunity, even for children with residual immunosuppression. Approaches to post-chemotherapy reimmunisation include repeating primary vaccination schedules, testing antibody levels to assess immunity, administering booster doses without considering residual immunity, or following the regular age-appropriate schedule. Most guidelines recommend waiting at least six months post-chemotherapy for sufficient immune recovery

OPTIMAL VACCINATION TIMING

The timing of vaccination remains critical:

- Most vaccines are administered 3–6 months post-chemotherapy, HSCT, or cellular therapies, after the absolute lymphocyte count (ALC) recovers to ≥1.0 × 10^9/L.
- Inactivated influenza, pneumococcal, and COVID-19 vaccines are recommended during treatment.
- Other inactivated vaccines, if given during treatment, should ideally be administered during maintenance therapy and at least two weeks before the next cycle. These doses may require revaccination unless serologic protection is confirmed.
- The CDC's Advisory Committee on Immunisation Practices, AAP, and IDSA recommend administering inactivated vaccines at least three months after chemotherapy to optimize immune response. Live-attenuated varicella and MMR vaccines are also safe and effective after this period, except for children treated with anti-B cell therapies (e.g., rituximab, blinatumomab). For these patients, vaccination should be considered 6–9 months post-therapy upon evidence of B cell recovery.
- During Ongoing chemotherapy:

  Live Vaccines: Not recommended

  Non-Live vaccines: Can be given-> DPT, Hib, IPV, HBV, HAV, Influenza

  May be given-> Pneumococcal, Meningococcal,

  Insufficient data-> Typhoid, HPV, JEV

VACCINATION RECOMMENDATION IN CHILDREN POST CHEMOTHERAPY

Inactivated Vaccine	Patients Who Have Not Started or Completed Vaccination at Cancer Diagnosis	Patients Who Have Completed Vaccination Schedule at Cancer Diagnosis
DTaP	Continue primary series during lower-intensity phases (e.g., ALL in maintenance)	Continue primary series; booster 3-6 months after therapy completion
Haemophilus influenzae type b (Hib)	Continue primary series during lower-intensity phases (e.g., ALL in maintenance)	Continue primary series; booster 3-6 months after therapy completion
Hepatitis A	Start immunisation series in high-risk settings in seronegative children	Continue primary series or booster 3-6 months after therapy completion
Hepatitis B	Start immunisation series in high-risk settings in seronegative children	Continue primary series or booster 3-6 months after therapy completion
Human Papillomavirus (HPV)	Not recommended	Continue primary series or booster 3-6 months after therapy completion
Influenza	2 doses if not previously	2 doses if not previously

(Inactivated IIV)	vaccinated and ≤8 years of age. Otherwise, 1 dose yearly ideally given at mid-point between chemotherapy cycles	vaccinated and ≤8 years of age. Otherwise, 1 dose yearly ideally given at mid-point between chemotherapy cycles
Meningococcal, conjugate (MenACWY)	Not recommended	Booster dose for those previously vaccinated, otherwise per routine schedule
Pneumococcal, conjugate (PCV13)	Consider continuation of primary series during lower-intensity phases (e.g., ALL in maintenance)	Continuation of primary series or booster 3–6 months after therapy completion
Pneumococcal, polysaccharide (PPSV23)	Not recommended	Administer at least 8 weeks from last PCV20 for those aged ≥2 years of age
Poliovirus, inactivated (IPV)	Consider continuation of primary series during lower-intensity phases (e.g., ALL in maintenance)	Continuation of primary series or booster 3–6 months after therapy completion

Live Vaccines	Patients Who Have Not Started or Completed Vaccination at Cancer Diagnosis	Patients Who Have Completed Vaccination Schedule at Cancer Diagnosis
Varicella	Not recommended	Continuation of primary series or booster 3–6 months after therapy completion
MMR	Not recommended	Continuation of primary series or booster 3–6 months after therapy completion
Rotavirus	Not Recommended	Not Recommended
Oral Typhoid	Not recommended	Not recommended
BCG	Single dose only if negative tuberculin test (max age 5 years)	Single dose (Max age 5 years)

VACCINATION RECOMMENDATION IN CHILDREN RECEIVING HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) AND CHIMERIC ANTIGEN T CELL (CAR-T) THERAPY

Inactivated	Autologous/Allogeneic	CAR-T Recipients

Vaccine	HSCT Recipients	
DTaP	2 or 3 doses, starting 3-6 months post-HSCT and immune recovery	>6 months after CAR-T and >2 months after immunoglobulin replacement, if not seropositive
Haemophilus influenzae type b (Hib)	3 doses, starting 3-6 months post-HSCT and immune recovery	>6 months after CAR-T and >2 months after immunoglobulin replacement, if not seropositive
Hepatitis A	2 doses (0, 6 months) starting >3-6 months post-HSCT and immune recovery	>6 months after CAR-T and >2 months after immunoglobulin replacement, if anti-HAV titer <10 IU/L
Hepatitis B	3 doses (0, 1-2 months, 6 months) starting > 3-6 months post-HSCT	>6 months after CAR-T and >2 months after immunoglobulin replacement, if anti-HBs titer <10 IU/L
Human Papillomavirus (HPV)	2 or 3 doses (per age-specific guidelines), starting 6-12 months post-HSCT and immune recovery	>6 months after CAR-T and >2 months after immunoglobulin replacement, and age eligible
Influenza (Inactivated IIV)	2 doses if not previously vaccinated and ≤8 years of age, starting at 4-6 months post-HSCT (community outbreaks) with second dose 1 month later, otherwise ≥ 6 months post-HSCT	>6 months after CAR-T and >2 months after immunoglobulin replacement, and age eligible
Meningococcal, conjugate (MenACWY)	2 doses (serogroups A, C, W, Y and serogroup B vaccine) starting > 6 months post-HSCT	>6 months after CAR-T and >2 months after immunoglobulin replacement per routine schedule
Pneumococcal, conjugate (PCV13)	3 doses starting > 3–6 months post-HSCT, consider 4th dose in patients with chronic GvHD	>6 months after CAR-T and >2 months after immunoglobulin replacement, if not seropositive
Pneumococcal, polysaccharide (PPSV23)	After 3 doses of PCV20, administer PPSV23 at 12 months post-HSCT (and at least 8 weeks from last PCV20) if no chronic GvHD	Administer at least 8 weeks from last PCV20 for those aged ≥2 years of age
Poliovirus, inactivated (IPV)	3 doses starting 6–12 months post-HSCT	>6 months after CAR-T and >2 months after immunoglobulin replacement, if not seropositive
Live Vaccines	**Autologous/Allogeneic HSCT Recipients**	**CAR-T Recipients**

Varicella	2 doses (4 weeks apart) given at least ≥24 months post-HSCT with no evidence of chronic GVHD, not receiving immunosuppression, and > 8 months since last dose of supplemental immunoglobulins, if not seropositive	2 doses (4 weeks apart) given at least > 1-year post-CAR-T-cell therapy, > 2 years posttransplant, > 1 year off all systemic immunosuppressive therapy, and > 8 months since last dose of supplemental immunoglobulins, if not seropositive
MMR	2 doses (4 weeks apart) given at least ≥24 months post-HSCT with no evidence of chronic GVHD, not receiving immunosuppression, and > 8 months since last dose of supplemental immunoglobulins, if not seropositive	2 doses (4 weeks apart) given at least > 1-year post-CAR-T-cell therapy, > 2 years posttransplant, > 1 year off all systemic immunosuppressive therapy, and > 8 months since last dose of supplemental immunoglobulins, if not seropositive
Rotavirus	Not Recommended	Not Recommended
Oral Typhoid	Not Recommended	Not Recommended

CONSENSUS STATEMENT:

Timing of Vaccination Post-Chemotherapy: Vaccinations should be initiated at least 3–6 months after the completion of chemotherapy, allowing sufficient immune recovery. For live vaccines, a longer delay of 6–12 months is recommended depending on the patient's immune status, age, and the specific therapy received. **(Level of Evidence: 2B, Grade: B - Strong)**

1. **Immune Monitoring and Reimmunisation:** It is essential to assess the patient's immune status, including serological tests, prior to reimmunisation. Repeating primary vaccination schedules or administering booster doses should be guided by antibody levels to ensure restored immunity while minimizing unnecessary vaccinations. **(Level of Evidence: 2C, Grade C- weak)**

2. **Special Considerations for High-Risk Patients:** For patients undergoing hematopoietic stem cell transplantation (HSCT) or CAR-T cell therapy, vaccinations should be delayed until immune recovery milestones are achieved. Inactivated vaccines may begin 3–6 months post-HSCT, while live vaccines require at least 1–2 years and evidence of immune competency, including the absence of graft-versus-host disease or immunosuppressive therapy. **(Level of Evidence: 1B, Grade: A- Strong)**

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RECOMMENDED VACCINATION FOR ASPLENIC AND HYPOSPLENIC PATIENTS

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BACKGROUND

Patients with asplenia or hyposplenia are at high risk of serious infections with encapsulated organisms. Vaccination with pneumococcal (both conjugate and polysaccharide), Hib conjugate vaccine, meningococcal conjugate vaccine and typhoid conjugate vaccines is indicated in addition to all routine vaccines. In patients with planned splenectomy, vaccination schedules should be completed at least 2 weeks prior to splenectomy for achieving a superior immunologic response. In those who have undergone emergency splenectomy, studies have indicated that vaccination done 2 weeks after splenectomy is associated with a superior functional antibody response as compared to vaccination immediately after surgery. All live vaccines may be safely given. [1]

RECOMMENDATION FOR INDIVIDUAL VACCINE: [2,3]

1. PNEUMOCOCCAL VACCINE

Types: PCV 13 (PNEUMOCOCCAL CONJUGATE VACCINE), PPSV23 (PURIFIED CAPSULAR POLYSACCHARIDE VACCINE)

PCV 13 – for all ages

PPSV23 – for ages >2years

Pneumococcal vaccine	**Dose**	**Timing**	**Booster**
Naïve subjects those who have not received pneumococcal vaccine	PCV13 (1 dose) followed by PPSV23(1 Dose) at least 8 weeks later	If splenectomy: At least 2 weeks before elective surgery, preferably 4-6 weeks	PPSV23: 1 dose after 5 years
In patient who have previously received PPSV23, administer	1 dose of PCV13 >1 year later.	After 2 weeks post-operatively in emergency cases	
In patient who have received PCV 13,	Repeat 1 dose of PCV13 followed by PPSV >8 weeks later		

Children should receive an age-appropriate series of PCV13. Unvaccinated children 2-5 years should receive 2 doses of PCV13. Children ≥6 years should receive a dose of PCV13 if they have not previously received a dose of PCV13. Persons aged ≥2 years should receive 2 doses of PPSV23 separated by 5 years, beginning 8 or more weeks after completing all recommended doses of PCV13.In circumstances where both PCV13 and PPSV23 are indicated, doses of PCV13

should be administered first followed by PPSV23 8 weeks after the last dose of PCV13. [4]

2. MENINIGOCOCCAL VACCINE

Types: Conjugated vaccine and inactivated, i.m. (conjugate formulate provides immunological memory and protection longer than polysaccharide vaccine)

Formulations:

A. Monovalent conjugate vaccine against serotype C(MenC): age > 2 months.
B. Tetravalent conjugate vaccine (Men ACWY)

Meningococcal	Dose	Timing	Booster
	Naïve subjects: 2 dose of MEN ACWY 8-12 weeks apart	As soon as possible in functional asplenia	Men ACWY: 1 dose every 5 years
	In patient previously vaccinated with single dose of Men ACWY or Men C, repeat entire cycle (2 dose 8-12 weeks apart)		

3. HEMOPHILUS INFLUENZAE TYPE b

Naïve subjects: 1 dose of conjugate Hib vaccine.

In subjects previously vaccinated, repeat 1 dose of Hib vaccine.

No booster dose required.

4. INFLUENZA VACCINE

Annual influenza vaccine

5. MMR:

2 doses of MMR administered 4-8 weeks (preferably 3 months apart) from each other in subjects without immunity

No booster doses

6. ARICELLA VACCINE

2 dose of varicella vaccine 4-8 weeks (preferably 3 months) apart from each other in subjects without immunity

7. DPT : Splenectomy:

a. If elective: dTaP at least 2 weeks before elective surgery, preferably 4-6weeks, or

b. In emergency cases: dTaP after 2 weeks post-operatively

Naïve or incompletely immunised: repeat entire cycle

In subjects previously vaccinated with primary cycle: 1 booster dose

Booster dose: 1 dose every 10 yearly

ANTIBIOTIC PROPHYLAXIS

Prophylaxis with oral penicillin V 125mg/bd for children < 5 years, 250mg/bd for children > 5 years of age for at least 2 years after splenectomy.

Lifelong prophylaxis in patient who have had an invasive pneumococcal infection or disease.

For sickle cells anemia: prophylaxis as soon as the diagnosis is made.

VACCINATION IN PATIENTS WITH CHRONIC LIVER DISEASE

Patients with chronic liver disease (CLD) with or without cirrhosis remain at risk of developing hepatic decompensation when infected with viral or bacterial pathogens. The Advisory Committee on Immunisation Practices (ACIP) currently recommends vaccination in CLD against: [5]

1. HAV
2. HBV
    a. Seroconversion ranges between 16-79%, vaccine efficacy may be sub-optimal however booster dose when given, showed significant improvement in high dose group (79%).
3. Influenza
4. Pneumococcus
5. Herpes zoster
6. DPT
7. SARS-CoV-2

As the severity of the liver disease progresses, vaccine efficacy declines, and therefore, vaccines should be ideally administered early in the disease course for optimal immune response. [5]

The immunogenicity, efficacy and duration of protection of vaccines are lower than healthy children and hence if indicated higher antigen content or more doses (hepatitis B) may be required. Assessment of antibody response and frequent boosters (hepatitis A and Hepatitis B) are recommended. [1]

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VACCINATION IN CHILDREN WITH KIDNEY DISEASES

Nephrology Team

A: CHILDREN WITH NEPHROTIC SYNDROME

Table 1: Principles of Immunisation with Live Vaccines in Patients with Nephrotic Syndrome[1]

Immunosuppression	**Advice**
Receiving high dose prednisolone (≥2 mg/kg/d; ≥20 mg/day if>10 kg) for <14 d	Vaccinate immediately after discontinuing treatment
Receiving high dose prednisolone (≥2 mg/kg/d; ≥20 mg/day if>10 kg) for ≥14 d	Vaccinate 1-month after discontinuing corticosteroids
Receiving low-moderate dose prednisolone (<2 mg/kg/d or equivalent: <20 mg/d)	No live vaccines, until discontinuation of steroid therapy
Low-dose alternate day prednisolone and pressing need for vaccine	Live vaccine may be administered
Patients receiving cyclophosphamide	Avoid live vaccines until off therapy for 3 months
Patients receiving calcineurin inhibitors, levamisole or mycophenolate mofetil	Avoid live vaccines until off therapy for 1 month
Therapy with rituximab	Avoid live vaccines until after B-cell recovery (~6-9 months)
Immunocompetent siblings and household contacts	Do not administer oral polio vaccine; may receive measles-mumps-rubella, rotavirus and varicella vaccines
Household contacts older than one year	Administer influenza vaccine annually

Table 2: Specific Vaccines for Patients with Nephrotic Syndrome[1]

Vaccine	Age	Previously received	Vaccine	Schedule
Pneumococcal: Conjugate (PCV, 13-valent preferred to 10-valent) Polysaccharide, (23-valent, PPSV23)	6-72 month	*Completely immunised	PCV13/10 PPSV23	One dose ≥2-yr-old One dose when ≥2-year- old & ≥8 wk after last PCV13/10 dose[b]
		No or incompletely immunised	PCV10/13 PPSV23	Two doses, ≥8 wk apart[c] One dose when ≥2-yr-old & ≥8 wk after last PCV13/10 dose[b]
	>72 month	*Completely immunised	PPSV23	1 dose[b]
		No or incompletely immunised	PCV10/13 PPSV23	1 dose 1 dose, ≥8 wk after last PCV13/10 dose[b]
Varicella[d]	>15 month	No evidence of immunity[e]	Live attenuated	Two doses 4-8 wk apart
Influenzae	>6 month		Inactivated	Annually
Hepatitis B	Any	No, or anti-HBs <10 mIU/mL	Subunit (10 mcg/0.5mL)[f]	3 doses at 0, I & 6 months OR in an accelerated schedule with ≥4wk gap between doses 1 & 2, ≥8 wk between doses 2 & 3 And ≥ 16 wk between doses 1 and 3[f]

* Completely Immunised – children who received PCV13 at 6 weeks, 10 weeks and 9 months

a Efficacy of vaccines might be attenuated while on high dose corticosteroids or other immunosuppression;

b Repeat after 5-yr if still experiencing disease relapses;

c If the two doses are administered at <1-yr-old, give one additional dose during second year of life;

d Avoid in patients <15 months;

e immunity refers to past diagnosis of varicella or herpes zoster, verified by a physician; documented receipt of 2-doses of vaccine 4-8 weeks apart; or serological evidence of immunity;

f Consider post-vaccination testing for adequacy (anti-HBs antibody ≥10 mIU/mL) and administering higher (20 µg) or additional doses

B. Pediatric Kidney Transplant Candidates (CKD) and Transplant recipients[2,3]

Table 3: Recommended Vaccines for Pediatric Kidney Transplant Candidates and Recipients who have completed the Routine Immunisation Schedule of Nepal**.**

Vaccine	Inactivated/ Live attenuated	Dose /Route of administration	Dosage schedule	Candidates (CKD)	Recipients	Comments
Influenza	Inactivated	0.5ml/IM	1 dose (Annually)	Yes	Yes	Annual vaccine recommended
Hepatitis B	Inactivated	1ml/IM	4 doses (0,1,2,6 month)	Yes	Yes	Monitor antibody titre every 6-12months; give booster if titer≤10mIU/ml
PCV 13	Inactivated	0.5 ml/IM	1 dose	Yes	Yes	Booster recommended every 5 years
MenACWY	Inactivated	0.5 ml/IM	2 doses (11 & 16 years)	Yes	Yes	_
Hep A	Inactivated	0.5 ml/IM or SC	2 doses (0,6 month)	Yes	Yes	_
MMR	Live attenuated	0.5ml SC	2 doses (0,2 month)	Yes	No	Not recommended in transplant recipients
Varicella	Live attenuated	0.5 ml SC	2 doses (0,2 month)	Yes	No	Not recommended in transplant recipients
DPT	Inactivated	0.5 ml IM	2 doses (15-18 mths & 4-6 yrs)	Yes	Yes	Booster required every 10 years; use Tdap or Td

Important Note: All vaccines should be completed at least 1 month (preferably 6 weeks) before transplantation.

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IMMUNISATION IN IMMUNODEICIENCY AND RHEUMATIC CONDITIONS

Dr. Dharmagat Bhattarai

BACKROUND

Immunisation is the single most precious scientific technology to save from disease of interest in clinical use today. Immunisation plays a critical role in preventing infectious diseases, particularly in children who are at higher risk due to underlying immune system dysfunctions. Children with primary immunodeficiencies (PIDs) [now better known as inborn errors of immunity (IEIs)] and pediatric rheumatic diseases (PRDs) receiving immunosuppressive therapy present unique challenges in vaccination planning.[1] This population is at an increased risk of infections due to both the underlying condition and the immunosuppressive treatments received for disease management.[2-4] Balancing the benefits of vaccination while ensuring safety is essential. This review examines immunisation strategies for these vulnerable groups, considering current guidelines and evidence-based recommendations.

BURDEN IN NEPAL

Most of the immunodeficiencies are both underdiagnosed and underreported. Prevalence grossly ranges from 0.06% - 5% of population. However, the lesser figure in statistics actually reflects the low rate of exploration. In Nepal, an internet survey shows the diagnosis of more than 525 confirmed cases of PIDs and more than 2000 cases of proven PRDs amid a severe lack of subspecialists, awareness, and diagnostic facilities.[5, 6] Worldwide prevalence of rheumatological diseases is reported only up to 4%-13.4%.

IMMUNISATION IN CHILDREN WITH PRIMARY IMMUNODEFICIENCIES (PIDS)

PIDs/IEIs represents a heterogeneous group of over 580 genetic disorders affecting various components of the immune system.[7] They are characterized by defective immune responses, increasing susceptibility to infections, and aberrant immune-regulation.[8] The degree of immunosuppression varies, and immunisation strategies must be tailored accordingly. The immunisation strategy for these children depends on the severity of the immunodeficiency and the specific immune components affected. Disorders/conditions associated with a high increment in susceptibility include combined immunodeficiencies (CID), severe antibody deficiencies, severe innate immune defects, cancer chemotherapy, intensive phase of solid organ transplantation, low CD4 count (<200 cells/mm^3), and patients on high dose glucocorticoids or biologics. Mild antibody deficiencies, complement defects, systemic autoinflammatory disorders (SAIDs), milder immune dysregulation, asymptomatic Human immunodeficiency virus (HIV) infection, a low dose steroid or any immunosuppression are kept under disorders or conditions associated with a modest increase in susceptibility.[8]

ADVERSE EFFECTS OF VACCINES IN PATIENTS WITH IMMUNODEFICIENCIES

Some vaccines of concern may have mild to fatal consequences in patients with PIDs. Measles-Mumps-Rubella (MMR) or MMR with Varicella (MMRV) vaccines (especially the varicella component), may cause serious consequences including death in children with severe T-cell defects e.g., severe combined immunodeficiency (SCID), and CD40L deficiency. Rubella vaccine can also bring a nuisance of persistent infections in patients with T-cell defects or CID. Patients with cell-mediated, humoral, or combined immune defects may have severe poliomyelitis following oral polio vaccine.
Bacillus Calmette-Guerin (BCG) vaccine may cause severe disease in vaccinated children who have immunogenetic defects e.g., SCID, defects of the interleukin (IL)-12/interferon (IFN)-gamma axis.[9]

VACCINATİON PROSPECTS IN DISTINCT PIDS

Patients with different PIDs behave differently with vaccines according to their basic defects. Depending upon the basic immunopathology, their immunogenicity, seroconversion, and protection differ. Thus, we should have a differential approach for patients with different kinds of PIDs/IEIs. The basic approach to all major groups of PIDs/IEIs is described in Table 1. Contraindicated vaccines and vaccine efficiency in major PID subgroups are summarized in Table 2.

INACTIVATED VACCINES

Efficacy of inactivated vaccines may be reduced in patients with severe antibody deficiencies, CID, or those receiving immunosuppressive therapy or intravenous immunoglobulin (IVIg) replacement therapy (IGRT). IGRT can interfere with vaccine-induced antibody responses.[2,10] It is possible to understand the seroconversion in any patient who is not on IGRT**.** Annual inactivated influenza vaccine administration is advised for all patients with PIDs.[11]
HPV vaccine is of special importance in cases with WHIM syndrome and *GATA2* mutation.[8] Non-viable polysaccharide vaccine should be preferred in immunocompromised patients.

LIVE-ATTENUATED VACCINES

Live vaccines are contraindicated in children with IEIs due to the risk of vaccine-induced disease. Children with severe immunodeficiencies should avoid live vaccines.[2, 8] MMR/MMRV vaccines are contraindicated in children with profound T-cell defects.[12]

Table 1. Immunisation in different categories of PIDs[1-3,8,11,13]

Patients with Primary Immunodeficiencies (PIDs) or Phenocopies of PIDs

Category	Inactivated vaccines	Live vaccines	OPV	Polysaccharide vaccines	Conjugate vaccines
Severe CID	No value	Contraindicated	Contraindicated	No possibility of harm, benefit unlikely, administration NOT recommended	
Mild CID	May benefit if not receiving IVIg	Milder/hypomorphic/partial syndromes (e.g., Partial DiGeorge) may tolerate if CD4> 500 cells/mm^3	Inactivated forms preferred	Administration recommended, use according to routine schedule	
Severe antibody deficiencies	On IGRT- Not necessary/Not effective (Inactivated influenza is exception®) Not on IGRT- Can receive inactivated one	MMRV- contraindicated	Not preferred	No possibility of harm, benefit unlikely, administration NOT recommended	
Mild antibody deficiencies	May be vaccinated (some protective antibody response remains)	May be vaccinated (some protective antibody response remains)	Avoided (for concern of VAPP)	Response is poor if vaccinated	Immunogenic (so, vaccination is preferred)
Immune-dysregulation, PRDs or SAIDs	Depending upon the group	Contraindicated if on immunosuppressive		Safe but lower immunogenicity response	

Phagocytic defects	Should receive#	Live bacterial vaccines (BCG and oral salmonella vaccine)- avoided Live viral- should be given to CGD and Neutropenia but not to LAD of CHS	Not preferred	No possibility of harm, benefit possible, administration recommended
Innate Immune defects	Safe and effective	Live bacterial- contraindicated; Live viral- mostly contraindicated if involves interferon pathways and NFKB pathway	Possibility of harm, action- not recommended	Asplenia, IRAK4- and MyD88-deficient patients are susceptible to invasive disease, so pneumococcal, Hemophilus, meningococcal vaccination is of great importance
Complement defects	All vaccines are safe and effective in these patients because they have intact specific cellular and humoral pathways. They can get additional immunisation against vulnerable organisms like *Streptococcus pneumoniae*, *Hemophilus influenzae*, and *Neisseria meningitidis*			
Phenocopies of PIDs	As recommended for general population, unless they are receiving immunosuppressive therapy or having neutropenia (same for *NLRP3* defects)			
Syndrome of autoantibodies to INF-γ, IL-17/IL-22	Safe	Live bacterial and viral vaccine- contraindicated		Safe
Household contacts of PIDs	recommended	Most live vaccines are considered safe	Contraindicated	Should be given
Patients on Immunosuppression/Immunomodulators				

Corticosteroids	As scheduled in general (if high doses- deferred until stopping high doses)	For topical/local/skin applications/aerosols/or dose<20mg or 2 mg/kg Pred)- safely given; For higher doses (<14 days)- no vaccines during therapy For higher doses (>14 days)- delayed for 4 weeks after termination		Individualized as per dose, duration, and route
Low level* immunosuppression DMARDs (+biologics)	Safe	Safe	Inactivated Polio preferred	Safe
High level* immunosuppression DMARDs (+biologics)	Response impaired- so better to be administered 2 weeks before initiation	Contraindicated; given at least 4 weeks before initiation of therapy		Individualized as per type of drugs, dose, duration, and route
Patients on IVIg/IGRT	IVIg- individualized; IGRT- Most vaccines represented on IGRT	MMRV- avoid in first 3-11 months after IVIg (hinders immune response) Other viral- may be given except contraindicated	may be given except contraindicated	Conjugate polysaccharide vaccines may also be considered (except, in patients with any sort of hypogammaglobulinemia)

CGD- Chronic Granulomatous Disease; CHS- Chediak Higashi syndrome; CID- Combined Immunodeficiencies; DMARD- Disease-modifying anti-rheumatic drugs; IVIg- Intravenous Immunoglobulin; IGRT- IVIG replacement therapy; LAD- Leukocyte adhesion defect; MMRV- Measles, Mumps, Rubella Varicella vaccine; OPV- Oral Polio Vaccine; PIDs- Primary Immunodeficiencies; Pred- Prednisolone; PRD- Pediatric Rheumatic diseases; SAID- Systemic autoinflammatory diseases; SCID- Severe Combined Immunodeficiencies; VAPP- vaccine-associated paralytic polio

®This is because IVIg may not contain antibodies to prevailing strains and the vaccine itself may induce beneficial cellular immunity.
#Inactivated influenza is very important in chronic granulomatous disease because influenza mortality is increased with staphylococcal coinfection.
*Low-level immunosuppression refers to methotrexate at a dosage of 0.4 mg/kg/wk or less, azathioprine at a dosage of 3 mg/kg/d or less, or 6-mercaptopurine at a dosage of 1.5 mg/kg/d or less. High-level immunosuppression means high levels of drugs listed above or TNF-agonists, anti-B lymphocyte mAbs or cancer chemotherapy

Table 2. Vaccine perspectives and risks in major groups of PIDs [8,11,14]

Immunodeficiency	Diseases	Major contraindicated vaccines	Efficiency	Interpretation
Major Cellular	Complete defects (e.g., SCID, complete DiGeorge syndrome, MHC defects)	All live vaccines	All vaccines are mostly inefficient	Inactivated vaccines can be administered. Inactivated influenza, PCV and/or PPSV23, conjugated Hib recommended.
	Partial defects (Partial DiGeorge syndrome, Ataxia Telangiectasia, Actinopathies)	All live vaccines	Efficiency depends upon the degree of immunosuppression	Inactivated vaccines can be administered. Inactivated influenza, PCV and/or PPSV23, conjugated Hib recommended.
	Combined immunodeficiencies	All live vaccines	Efficiency depends upon the degree of immunosuppression	
Major Humoral	Severe defects (XLA, CVID)	OPV, BCG, Typhoid, MMRV, Rotavirus, LAIV	Efficiency is unclear.	Intravenous immunoglobulin affects the response to MMRV
	Mild defects (Selective IgA deficiency; Ig-subgroup deficiency)	OPV, BCG	Immune response is weak but vaccines are efficient	All other live vaccines can be administered.
Phagocytic defects	CGD, LAD, MPO deficiency	Live bacterial vaccines (BCG, Live typhoid	All inactive vaccines and other live vaccines	-

		vaccine)	are efficient	
Complement defects	All types of complement pathway defects	None	All vaccines are efficient	Capsulated polysaccharide vaccines should be administered
Complex monogenic disorders	Defects of IL-12/IFN axis, IPEX, Systemic autoinflammatory disorders	None due to primary disease	If under immunosuppression, it should be individualized	None
Secondary Immunodeficiencies	Asplenia/ Functional asplenia	None	All vaccines are efficient	Capsulated polysaccharide vaccines should be administered
	Neoplasia, chemotherapy, solid organ transplantation, Immunosuppressant, radiotherapy	All live vaccines (especially depending upon immune status)	Efficiency depends upon immunological status	-
	HIV/AIDS	BCG, MMRV, OPV, LAIV (No live vaccines if severe immunosuppression and low CD4 counts)	All inactive vaccines are efficient	Pneumococcal, Haemophilus and meningococcal vaccines are beneficial
	Severe chronic renal diseases	LAIV	Status dependent	Pneumococcal and Hepatitis B vaccine should be given

AIDS- Acquired Immune Deficiency Syndrome; BCG- Bacillus Calmette Guerin; CGD- Chronic granulomatous disease; CVID- Common variable immunodeficiency; HIV- Human Immunodeficiency Virus; IFN- interferon; IL-12- Interleukin-12, IPEX- Immunodeficiency polyendocrinopathy enteropathy X-linked, LAD- Leukocyte adhesion defects; LAIV- Live attenuated influenza vaccine; MMRV- Measles-Mumps-Rubella-Varicella vaccine; MPO- Myeloperoxidase; OPV- Oral polio vaccine; PCV: Pneumococcal conjugate vaccine; PPSV23: 23-valent unconjugated pneumococcal polysaccharide vaccine; SCID- Severe combined Immunodeficiency; XLA- X-linked agammaglobulinemia

Immunisation in Children with Pediatric Rheumatic Diseases (PRDs) and children on Immunosuppressants

PRDs, including chronic arthritis, connective tissue disorders, autoimmune and autoinflammatory disorders, and vasculitis, often require immunosuppressive therapies that alter vaccine responses. The introduction of disease-modifying antirheumatic drugs (DMARDs) and more recently biologic DMARDs (bDMARDs) for treating PRDs has revolutionized the treatment. However, it has increased the possibility of infections to a concerning level. So, the context of vaccination has been even more relevant in modern times. There are different kinds of vaccination practices for children with PRDs across the globe. Even today, data are limited especially regarding bDMARDs. However, inactivated vaccines are generally safe and should be administered to children with PRDs, even when on immunosuppressive therapy.[3,4]

Influenza (annual), pneumococcal, hepatitis B, and human papillomavirus (HPV) vaccines are strongly recommended vaccines for them. Some immunosuppressive drugs, such as methotrexate, mycophenolate mofetil, and bDMARDs like TNF inhibitors (TNFi) (e.g., etanercept, adalimumab, infliximab), may reduce vaccine immunogenicity but do not generally warrant withholding vaccines.[14] B-cell-depleting therapies, such as rituximab, significantly impair humoral responses, necessitating careful selection and timing of vaccination. Ideally, vaccines should be administered at least 4-6 weeks before starting rituximab, and revaccination may be required after B-cell recovery. Studies suggest that the MMR/MMRV vaccines may be administered safely in children receiving low-dose methotrexate (<15 mg/m² per week) or biologics without additional immunosuppressants. Live vaccines should be avoided in children receiving high-dose corticosteroids, cyclophosphamide, or combination immunosuppressive therapy. The overarching principles of vaccination (as per international consensus recommendations) are summarized in Table 3.

IMMUNISATION WITH NON-VIABLE (INACTIVATED) VACCINES

Though immunogenicity is questionable, all non-viable vaccines, generally found safe in studies, are recommended to patients with all kinds of PRDs regardless of medications. Vaccination with anti-CD20 agents (e.g., rituximab) and tumor necrosis factor inhibitors (TNFi) are of great concern regarding immunogenicity and humoral response to vaccines. Many studies have emphasized on immunogenicity and safety of influenza vaccines in PRDs. Studies could not find a significant difference between vaccinated patients with PRDs and healthy children.[15] A couple of studies on the safety and efficacy of vaccines against hepatitic diseases (e.g., Hepatitis B, Hepatitis A, etc) done on patients with juvenile idiopathic arthritis (JIA) and childhood systemic lupus erythematosus (cSLE), found comparable seroprotection rate and antibodies concentration.[16] Mycophenolate was found to have more effect on seroconversion in comparison, especially in patients who received the hepatitis B vaccine (HBV).

In general, Pneumococcal, Influenza, and Hepatitis B Vaccines are strongly recommended, as patients with PRDs are at increased risk of infections due to both the disease itself and immunosuppressive treatment.[3] Human Papillomavirus (HPV) Vaccines are again safe and effective in adolescents on immunosuppressants.[17] As per recommendation, HPV vaccination should be administered to all unvaccinated children with SLE whereas 10 or 13-valent pneumococcal conjugate vaccine is recommended for all PRDs patients.

Table 3. Encompassing rules of vaccination in PRDs[3, 4, 18]

Category	Encompassing Principles
Basic	Pretreatment vaccination status, boosters, indications of vaccination, and disease exposure history should be annually evaluated in all children with PRDs.
	Immunisation should be administered preferably during the inactive phase of the disease.
	Treatment of PRDs (especially organ- or life-saving) should never be postponed for the sake of pretreatment vaccination gap.
	If possible or if deferring is acceptable, DMARDs or bDMARDs (especially drugs like anti-CD20 monoclonal antibodies) are preferably given 2-4 weeks after needful vaccination.
	-attenuated vaccinations should always be avoided or given with significant precautions. However, MMR and varicella vaccination can be administered in specific situations. Otherwise, we can adhere to national schedule in feasible situations, favorable safety data and immunogenicity.
	Non-viable vaccines can be given to all children on glucocorticoids and DMARDs unless specifically contraindicated, questionable immunogenicity, or unfavorable pathophysiology.
Non-live vaccines specific	Non-viable influenza vaccination is strongly recommended for all children with PRDs on immunosuppression.
	All unvaccinated children with PRDs should receive PCV10 or PCV13.
	Tetanus vaccination is recommended as per rules to general population excepting those on B-cell depleting therapy. This subgroup must receive passive immunisation if they have indication of TT vaccination.
	HPV vaccination should be considered for all unvaccinated children with SLE.
Live-attenuated vaccines specific	MMR booster can be given to children on methotrexate, low-dose glucocorticoids, TNF inhibitors, anti-IL6, and anti-IL1 therapy.
	VZV vaccination should be strongly recommended for unvaccinated or uninfected patients on methotrexate, low-dose glucocorticoids, TNF inhibitors, anti-IL6, and anti-IL1 therapy.
	Yellow fever vaccination should not be administered in any immunosuppressed individuals.

bDMARDs- Biologic disease-modifying anti-rheumatic drugs; DMARD- Disease-modifying anti-rheumatic drugs; HPV- Human papilloma virus; IL-interleukin; MMR-

Measles-Mumps-Rubella vaccine; PCV- Pneumococcal conjugate vaccine; PRDs- Pediatric Rheumatic diseases; SLE- Systemic lupus erythematosus; TNF- Tumour necrosis factor; TT- Tetanus toxoid; VZV- varicella zoster vaccine

IMMUNISATION WITH VIABLE/LIVE-ATTENUATED VACCINES

The safety of live vaccines like MMRV in patients with pediatric rheumatic diseases (PRDs) and those on biologic disease-modifying antirheumatic drugs (bDMARDs) has been a long-standing concern due to risks of disease flare, vaccine-induced illness, and poor immune response. While traditionally contraindicated in this population, emerging evidence indicates that children treated with low-dose methotrexate (MTX) or bDMARDs might be able to receive these vaccines safely.[17-19] Since most of the children receive MMR vaccination in early childhood before the onset of autoimmune disorder, there is a paucity of data on primary MMR vaccination response in the immunosuppressed cohort. A recent review emphasized that the booster vaccination of viable vaccines in immunosuppressed patients with PRDs is generally safe but not optimally immunogenic.[20] Current recommendation points that MMR boosters can be given safely to children on methotrexate, glucocorticoids, and limited bDMARDs.

TIMING AND MONITORING OF IMMUNISATION

Whenever possible, vaccines should be administered before the initiation of immunosuppressive therapy (especially before therapy like B-cell-depleting drugs) to ensure optimal immune responses. However, therapy should not be deferred in the name of vaccination only if it is a dire necessity and need of the hour. Post-vaccination monitoring is of prime importance during immunisation. Antibody titers should be checked in patients receiving bDMARDs especially those receiving B-cell depleting agents (e.g., rituximab) to assess vaccine effectiveness.[3] Some patients may require additional doses or higher antigen formulations for adequate protection.

CONCLUSION

Immunisation in children with IEIs/PIDs and PRDs on immunosuppressants requires a nuanced immunisation approach to achieve the best risk-benefit assessment tailored to the individual patient. Inactivated vaccines are largely safe and remain the cornerstone of protection, while live vaccines should be used cautiously. Collaborative care involving Paediatricians, immunologists, and rheumatologists is essential to ensure optimal immunisation outcomes for these vulnerable populations.

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IMMUNISATION IN CHILDREN WITH HEART DISEASES

Dr. Subash Chandra Shah

BACKGROUND

Cardiac disease in children can be congenital or acquired. Congenital cardiac disease includes a number of malformations of the heart, major blood vessels or heart valves. Acquired cardiac disease can include rheumatic heart disease or cardiac disease secondary to Kawasaki disease and malnutrition and cardiomyopathy as well. Children with underlying cardiac disease have increased risk for certain illnesses, such as influenza, pneumonia, and RSV (bronchiolitis) when compared to children who do not have cardiac disease. This can be exacerbated by an increased risk of exposure due to the need for frequent health care appointments and hospital stays. Those at highest risk include children with cyanotic heart disease or cardiac failure.[1]

VACCINE RECOMMENDATIONS

Children with cardiac disease can safely receive vaccines according to the national immunisation schedule of Nepal. Additional vaccines such as influenza and meningococcal vaccine are also recommended.

Family members and household contacts are recommended to be up to date with all vaccines including pertussis, annual influenza vaccines.

Close contacts of children with cardiac disease can receive live-attenuated vaccines without the need for additional precautions.[2]

VACCINE PRECAUTIONS

Recommendations should be taken into consideration while vaccinating children with cardiac disease in the following conditions:

- Live-attenuated vaccines may be contraindicated in immunocompromised children. However, all children with reduced immune competence should have their immunological status assessed with paediatric immunology to determine vaccine safety prior to all live vaccines.[3]

- The vaccination needs to delay about one year who has received blood product/ and or immunoglobulin. This does not apply to oral Rotavirus immunisation.

- Additional vaccines are recommended for asplenic or have hyposplenism.

- Children for whom cardiac surgery is indicated:

- Before surgery – inactivated vaccines can be administered up until 1 week prior to surgery, live-attenuated vaccines can be administered up until 3 weeks prior to surgery.

- vaccines indicated following surgery should be delayed for at least one week due to the potential for confusing expected vaccine side effects with post-operative complications.[3]

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OTHERS

- Missed Opportunities and Catch-up vaccination
- Immunisation during disaster
- NEPAS Recommendations 2025

MISSED OPPORTUNITIES AND CATCH-UP VACCINATION FOR 2025

Dr. Binod Lal Bajracharya

No one should miss out on the right to the protection that vaccines offer, simply because they are unable to access services in time.

What is a missed opportunity for vaccination (MOV)? [1]

Missed opportunities for vaccination (MOV) include any contact with health services by a child who is eligible for vaccination (unvaccinated, partially vaccinated) which does not result in the individual receiving all the vaccine doses for which he or she is eligible.

What is catch up vaccination?

Catch-up vaccination refers to vaccinating an individual who has missed receiving vaccines on time as specified in the national immunisation schedule.

Most common reasons of MOV are;

1. The failure or inability of health providers to screen patients for eligibility (for instance due to poor retention or limited availability of home-based records);
2. Perceived contraindications to vaccination on the part of providers and parents;
3. Vaccine shortages;
4. Rigid clinic schedules that separate curative services from vaccination areas; and
5. Parental or community resistance to immunisations.

Missed opportunities for vaccination can occur:

1. During visits to health facilities/mobile health services for immunisation services ("vaccination contact");
2. 2. During visits to health facilities/mobile health services for curative services (e.g., treatment of mild fever, cough, diarrhoea, injuries; "treatment contact");
3. 3. During visits to health facilities/mobile health services for other preventive services (e.g., growth monitoring, nutrition assessments and oral rehydration training sessions, etc.); and
4. 4. While accompanying a family member to a health facility for any type of service.

Objective Assessment of Missed Opportunities for Vaccination [2]

1. To evaluate the magnitude of missed opportunities for vaccination in a given health facility, district, province/state or country;
2. To understand the underlying causes of missed opportunities in the selected health facilities or districts;
3. To explore what can be adjusted or done differently to reduce missed opportunities and improve coverage and equity.

2024 CATCH-UP VACCINATION SCHEDULE: (4 MONTHS–18 YEARS) [3]

1. Hepatitis B vaccine. (Minimum age: birth)

- Unvaccinated child should complete a 3-dose series at 0, 1–2, 6mos.
- A 2-dose series at least 4wks apart

2. Rotavirus vaccines (Minimum age: 6wks)

- Administer a 2-dose series (Rotarix) or a 3-dose series (Rotateq). If any dose in the series is either Rotateq or unknown, default age <20 weeks give now. If ≥24 weeks do not give anymore.

3. Diphtheria, tetanus, and cellular pertussis (DTaP) vaccine. (Minimum age: 6wks.)

- The 5th dose of DTaP vaccine is not needed if 4th dose was given at age ≥4yrs and ≥6mos after 3rd dose

4. Haemophilus influenzae type b (Hib) conjugate vaccine. (Minimum age: 6wks),

- If the 1st dose was given at age 7−11mos, give the 2nd dose at least 4wks later and a 3rd (and final) dose at age 12−15mos or 8wks after 2nd dose, whichever is later.
- If 1st dose was given at ages 12−14mos, give 2nd (final) dose at least 8wks after dose 1. If 1st dose is given before 1st birthday and 2nd dose is given <15mos of age, a 3rd (and final) dose should be given at least 8wks after 2nd dose.
- If 1 dose was given at age ≥15mos, no further doses needed.
- For unvaccinated children aged 15–59mos, give only 1 dose.
- Unvaccinated children age ≥60 mos who are not considered high risk **do not require catch-up vaccination.**

5. Pneumococcal vaccines. (Minimum age: 6wks)

- Give 1 dose of PCV13 or PCV 15 or PCV20 to healthy children ages 2–4yrs with any incomplete pneumococcal vaccination.
- PCV20 is not indicated in healthy children if the child has previously received 4 doses of PCV13 or PCV15 or another complete PCV series.

6. Inactivated poliovirus vaccine (IPV). (Minimum age: 6wks)

- In the first 6mos of life, minimum age and minimum intervals are only recommended if the child is at risk for imminent exposure to circulating poliovirus (e.g., travel to or a new emerge of circulating polio virus, a polio-endemic region or during an outbreak).
- If both trivalent OPV (tOPV) and IPV were given as part of a series, a total of 4 doses should be given to complete the series. Doses should be at least 4wks apart, with the final dose given on or after the 4th birthday and at least 6months after the previous dose. If only OPV were given, and all doses given before 4yrs of age, 1 dose of IPV should be given at age ≥4yrs, at least 6mos after last OPV dose.

7. JE vaccine:

Complete 1 dose of JE vaccine at the age of 12 months, if delayed or missed complete within 23 months of age. (In Practice)

8. MR vs MMR Measles, mumps, and rubella vaccine.

(Minimum age: MR 9 mo MMR 12mos for routine vaccination)

- Unvaccinated persons should complete a 2-dose series at least 4wks apart.
- Maximum age for MMRV vaccine: 12yrs
- Minimum interval between MMRV doses: 3mos

9. Varicella vaccine. (Minimum age: 12mos)

- Ensure that all children aged 7–18yrs without evidence of immunity receive 2 doses of varicella vaccine. For children aged 7–12yrs, the recommended interval between doses is 3mos, for children aged ≥13yrs, the routine interval between doses is 4–8wks.

10. Hepatitis A vaccine (HepA). (Minimum age: 12mos)

- Unvaccinated children through 18yrs should complete 2 doses ≥6mos apart.
- Children who previously received 1 dose at age ≥12mos should receive 2nd dose ≥6mos after 1st dose, or soon after came to physician's notice,

11. Meningococcal vaccines. (Minimum age: 2months for Menactra)

Age 13-15yrs: give 1 dose and a booster at age 16-18yrs (≥8wks between doses). Children age <10yrs may receive 1 dose

12. Tetanus, diphtheria, and acellular pertussis (Tdap) vaccine. (Minimum age: 7yrs for routine vaccination)

- Persons 13−18yrs who have not received Tdap vaccine should receive 1 dose of Tdap (adolescent booster).

13. Human papillomavirus (HPV) vaccines. (Minimum age: 9yrs) for 9vHPV

- Give HPV vaccine to all adolescents age 11–12yrs (can start at 9yrs) and through age 18yrs.
- Give 2 doses at 0, 6−12months if initiating vaccination at age 9−14yrs.

Minimum interval between doses is 5mos; repeat dose if given too soon.

- Give 3 doses at 0, 1−2, 6mos if initiating vaccination at age ≥15yrs.

Minimum intervals are 4wks between 1st and 2nd dose, 12wks between 2nd and 3rd dose, and 5months between 1st and 3rd dose; repeat dose if given too soon.

14. Influenza vaccines. (Minimum age: 6mos)

For inactivated influenza vaccine [IIV], 2yrs for live attenuated influenza vaccine [LAIV4], 18yrs for recombinant influenza vaccine [RIV4])

- Use any age and health status-appropriate influenza vaccine annually.

For information on individual vaccines see product monographs, contact the manufacturer.

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नजिकैको स्वास्थ्य संस्थामा गई आ-आफ्ना बालबालिकालाई छुटेको नियमित खोप लगाउन हुन अनुरोध गरिन्छ । साथै छर-छिमेकमा कसैले खोप लगाउन छुटेका छन् कि बुझेर खोप लगाउन समन्वय गरिदिनहुन पनि अनुरोध गर्दछौं ।

याद राखौं जबसम्म सबै बालबालिकाले खोप लगाउदैनन्
तब सम्म कोही पनि सुरक्षित हुँदैनन् ।

खोप नि:शुल्क पाइन्छ | खोप सुरक्षित छ | खोपले जीवन रक्षा गर्छ

नेपाल सरकार
स्वास्थ्य तथा जनसंख्या मन्त्रालय
राष्ट्रिय स्वास्थ्य शिक्षा, सूचना तथा सञ्चार केन्द्र

नियमित खोप तालिका
र नियमित खोप छुट भएका
५ वर्ष सम्मका बालबालिकालाई खोप दिने तालिका

खाप	मात्रा, सइ लगाउन स्थान र माध्यम	नियमित खाप तालिका	नियमित खाप छुट भएका तर १२ महिनासम्मा आएमा	नियमित खाप छुट भएका बच्चा १२ महिना देखि २३ महिनासम्मा आएमा	नियमित खाप छुट भएका बच्चा २४ महिना देखि ५ वषसम्मा आएमा
बि.सि.जी.	०.०५ मि. लि. दाँया पाखुराको माथिल्लो भाग छाला भित्र (ID)	१ मात्रा: जन्मिने बित्तिकै	बच्चाको उमेर १ वर्ष भित्र भएमा ०.०५ मि. लि. र १ वर्ष वा माथिका लागि ०.१ मि. लि. एक मात्रा दिने (०.१ मि. लि. दिँदा एफ.आई.पि.भी. दिने सिरिन्जले खोप दिने)		
रोटा	१ टयुब (मुखमा, गालाको भित्री भागमा)	२ मात्रा: ६ र १० हप्तामा	एक महिनाको फरकमा २ मात्रा दिने		२ वर्ष माथिका उमेर समुहको बच्चाहरुलाई रोटा खोप दिनु हुँदैन
पोलियो	मुखमा दुई थोपा	३ मात्रा: ६, १० र १४ हप्तामा	एक महिनाको फरकमा ३ मात्रा दिने		
एफ.आई.पि.भी	०.१ मि. लि. दाँया पाखुराको माथिल्लो भाग छाला भित्र (ID)	२ मात्रा: १४ हप्ता र ९ महिनामामा	चार महिना (१६ हप्ता)को फरकमा २ मात्रा दिने		
पि.सि.भी	०.५ मि. लि. दाँया तिघ्राको विच बाहिरी भाग मासुमा (IM)	३ मात्रा: ६ हप्तामा, १० हप्तामा र ९ महिनामा	७ महिना मुनिको बच्चा भएमा पहिलो भेटमा पहिलो मात्रा, एक महिनाको फरकमा दोस्रो मात्रा र ९ महिनामा तेस्रो मात्रा दिने ७ देखि १२ महिनासम्मका बच्चालाई एक महिनाको फरकमा ३ मात्रा दिने	दुई महिनाको फरकमा २ मात्रा दिने	
डि.पि.टी.-हेप.बी-हिब (पेन्टाभ्यालेन्ट)	०.५ मि. लि. बाँया तिघ्राको विच बाहिरी भाग मासुमा (IM)	३ मात्रा: ६, १० र १४ हप्तामा	एक महिनाको फरकमा ३ मात्रा दिने		३ मात्रा दिने: पहिलो र दोस्रो मात्रा १ महिनाको फरकमा दिने र तेस्रो मात्रा दोस्रो लगाएको ६ महिनाको फरकमा दिने
बादुरा रुबेला	०.५ मि. लि. बाँया पाखुराको माथिल्लो भाग छाला र मासु विच (SC)	२ मात्रा: ९ र १५ महिनामा	९ महिना देखि १५ महिना मुनिको बच्चा भएमा पहिलो भेटमा पहिलो मात्रा र एक महिनाको फरकमा १५ महिनामा दोस्रो मात्रा दिने		१५ महिना देखि ५ वर्ष सम्म एक महिनाको फरकमा २ मात्रा दिने
जापानिज इन्सेफलाइटिस्	०.५ मि. लि. दाँया तिघ्राको माथिल्लो बाहिरी भाग छाला र मासु विच (SC)	१ मात्रा: १२ महिनामा	१ मात्रा		
टाइफाइड	०.५ मि. लि. बाँया तिघ्राको विच बाहिरी भाग मासुमा (IM)	१ मात्रा: १५ महिनामा	१ मात्रा		

ID – Intradermal, IM – Intramuscular, SC – Subcutaneous

सम्झनुहोस्: गर्भवती महिलाले पहिलो गर्भमा कम्तिमा एक महिनाको अन्तरमा २ पटक टि.डी. खोप लगाउनै पर्छ ।

पूर्ण खोप लगाऔं, बालबालिकालाई खोगहरूबाट सुरक्षित बनाऔं ।

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स्वास्थ्य सेवा विभाग
परिवार कल्याण महाशाखा

IMMUNISATION DURING DISASTER

Dr. Ram Hari Chapagain

INTRODUCTION

Immunisation is the process whereby a person is made immune or resistant to an infectious disease, typically by the administration of a vaccine. Vaccines stimulate the body's own immune system to protect the person against subsequent infection or disease. [1]

Immunisation is a tool proven for controlling and eliminating life-threatening infectious diseases and is estimated to avert between 2 and 3 million deaths each year. Its importance has been proven during COVID pandemic. It is one of the most cost-effective health investments, with proven strategies that make it accessible to even the most hard-to-reach and vulnerable populations.

BRIEF HISTORY OF IMMUNISATION IN NEPAL

In 1979, the National immunisation Program (known at the time as the Expanded Program on immunisation) was initiated in three districts with only two antigens [Bacille Calmette-Guérin (BCG) and Diphtheria, Pertusis, and Tetanus (DPT)] and was rapidly expanded to include all 75 districts with each of the six recommended antigens [BCG, DPT, oral polio vaccine (OPV), and measles] by 1988.

In 2003, the monovalent hepatitis B (HepB) vaccine was introduced. Later, in 2009, a vaccine against Hemophilus influenzae type B (Hib) was also introduced. In addition, pneumococcal conjugate vaccine (PCV-10) and inactivated polio vaccine-intramuscular (IPV-IM) were introduced in 2015 in phases.

In 2018, inactivated polio vaccine-intramuscular was replaced by fractional dose of inactivated polio vaccine (fIPV)-intradermal and rotavirus vaccine was also planned to be included in the immunisation schedule. MR second dose has been added in schedule in 2016 and typhoid conjugate was added in 2022 in national immunisation schedule.

All children in Nepal need to receive the recommended number of doses of BCG, DPT-HepB-Hib, OPV, PCV, fIPV, and measles/rubella vaccines during their first year of life and JE, typhoid and MR 2 are given during 2 year of life and the 2022 Nepal

Demographic and Health Survey (NDHS) revealed that 80% of children aged 12-23 months were fully vaccinated against all basic antigen. [2]

A regular vaccine supply is maintained in Nepal with a three months minimum stock. Vaccine safety and vaccine storage are the main issues during disasters when power cuts and damage to health institutions occur and disrupt cold chain maintenance.

IMMUNISATION DURING DISASTERS

Humanitarian crises and emergencies are ubiquitous and frequently unpredictable in time and location. However, with increasing awareness of populations and regions at risk, responses to such events are becoming more and more systematic and better organized. Apart from attending to the immediate need for emergency medical care, food, shelter and access to water and sanitation, preventive public health measures are looked upon as critical issues for consideration as response to a humanitarian emergency. One such measure is the potential use of vaccines against vaccine preventable diseases.[3,4]

Measles is most often recommended, and is widely accepted as a priority health intervention in emergencies.[5-7] Simultaneous introduction with other antigens is not generally recommended, but campaigns can include polio vaccination where outbreaks or threats to eradication programs exist and tetanus vaccination for people with open wounds or pregnant women. Vitamin A supplementation is almost universally recommended for implementation during a measles vaccination campaign. Vaccine coverage or needs assessments are also recommended to determine the targeted specific age ranges. Coverage rates of less than 90% for under 15 years old are given as qualifying criteria for recommendation of immediate mass immunisation.

Of the vaccines considered for diseases with epidemic potential, three are recommended only after the outset of an outbreak: hepatitis A, meningococcal meningitis, and yellow fever. Vaccinations for measles and polio are both recommended preventively and after the start of an outbreak, and cholera is not recommended after the start of an outbreak.[4] Vaccines for tetanus, pertusis, and diphtheria are generally not recommended for mass vaccination campaigns, and should rather be implemented through routine immunisation programs when conditions stabilize.

Routine immunisations through national expanded programme for immunisation (EPI) services should be reinstated as soon as conditions stabilize, and may indeed be one indication of a rehabilitating health system.

Tetanus toxoid

A single dose of tetanus/diphtheria (Td) toxoid should be given to anyone who will be entering the disaster area if they have not received a booster within the previous five years.

Wounds received in flood waters are not in fact tetanus prone, so individuals who are certain that they have had a booster within the last 10 years may safely choose to decline another booster. Single antigen tetanus should NOT be used unless Td is not available.

Hepatitis A

A single dose of hepatitis A vaccine should be given to anyone who meets the following conditions:

Living or working in a shelter,

Providing medical or personal care to survivors,

Working in a jail, prison, detention center, or other law enforcement capacity,

Working with the mentally handicapped

Functioning as a first responder.

Working with corpses or in a mortuary.

Working, preparing or handling food in a shelter.

Administration of the dose creates protective antibody in about two weeks. A booster dose should be offered after six months to all those immunised to assure long-term immunity.

Hepatitis A immunisation is not indicated for those engaged in clean-up or those exposed to flood waters. There is no increased risk of hepatitis A in sewer workers or those working in flood waters. If an individual has had a single dose of Hepatitis A

vaccine more than six months ago, give the booster. If the individual has had the two-dose series, no booster is required.

Hepatitis B

Three doses of hepatitis B vaccine are required to protect those at risk for exposure. This includes anyone who meets the following conditions:

Providing medical care to anyone; or functioning as a first responder,

Caring for the mentally or physically handicapped in a residential setting,

Working in a refugee shelter and possibly exposed to blood or body fluids,

Working in law enforcement; or working with corpses or in a mortuary.

The accelerated schedule should be used. The immunisations should be given on day 0, day 7 and day 21. This provides immunity in approximately one month. A booster dose should be given in one year to provide lasting immunity.

If the individual has previously completed a hepatitis B vaccine series, no further treatment is needed. If they have received only one previous hepatitis B vaccination, a single booster dose must be administered.

Rabies

A three-dose series for pre-exposure immunisation is needed for anyone who will be working directly with animals including those working in animal shelters and those capturing loose animals. These are given on day 0, day 7 and day 21. The series should be administered as soon as possible and the next two doses should be scheduled accordingly.

A single booster dose should be given if the person has had previous rabies immunisation, but has not had a booster or antibody tested within the last five years. If an individual has had pre-exposure immunisation and is exposed to rabies, an immediate booster should be given and a second dose in three days to complete the five-shot series for post-exposure treatment.

Human rabies immunoglobulin (HRIG) is not required if the person has ever received rabies immunisation, even if the series is not complete. If a partially immunised person is exposed to rabies, the series should be continued as post-exposure by counting the number of doses already given and completing the four doses by day 14. Post-exposure is given on days 0, 3, 7, and 14.

Influenza

As soon as it becomes available, influenza immunisation should be given to the entire population of the disaster affected areas. Because most of the displaced population will have been absorbed into the community without an increase in housing space, there is bound to be massive overcrowding in homes and schools. After normalization, opening the schools are in priority.

The opening of school always brings with it an increase in respiratory and infectious diseases. This can be expected to be much worse in these crowded conditions. Children, high risk adults, medical and relief workers and those in shelters or institutions should be the first to be immunised but the most effective situation would be to immunise as much of the population as possible to create herd immunity.

Measles

It is standard practice to give a booster dose of measles vaccine to all children under 15 years of age who are residing in shelters or refugee camps.

Everyone over the age of 12 months who is in a shelter or other crowded group setting should receive one dose of measles, mumps, rubella (MMR) vaccine unless they have a documented record of two doses of MMR or were born before 1957.

Varicella

Everyone over the age of 12 months who is in a shelter or other crowded group setting should receive one dose of varicella vaccine unless they have a documented record of immunisation or a reliable history of chickenpox.

Records

Permanent medical records of all immunisations given should be created using standard forms and systems. In addition, all persons given immunisations in a disaster area should be given a wallet-sized card with their name and date of birth and the date of each immunisation given. Where a series of shots are required (such as hepatitis B or rabies), there should be blanks on the card for the number of shots in the series so that the documentation remains on one card.

IMMUNISATION DECISION DURING DISASTER

WHO has considered three important decision making steps on the use of vaccines in acute humanitarian emergencies.[8] (Figure 1)

The steps are as follows:

Step 1: Determine and grade risk of the VPD (epidemiological risk assessment).

Step 2: Assess vaccines and amenability to service delivery (considerations for vaccines).

Step 3: Assess contextual constraints and facilitators, alternative interventions and competing needs (contextual considerations and competing needs).

The decision- making framework provides a clear and consistent approach to assess the:

- Local epidemiological risk of VPDs among the affected population,
- Vaccine selection and characteristics to consider, and
- Local contextual constraints that further assist in effective and timely decisions.

The ultimate aim of the decision-making framework is to assist the user to thoughtfully, deliberately, ethically, and rationally determine whether or not the delivery of one or more vaccines to specific target populations during the acute phase of an emergency would result in the overall saving of lives, a reduction in the population burden of disease, and generally more favorable outcomes than would otherwise be the case.

Figure 1: Decision making steps on vaccine use during acute humanitarian emergencies [8]

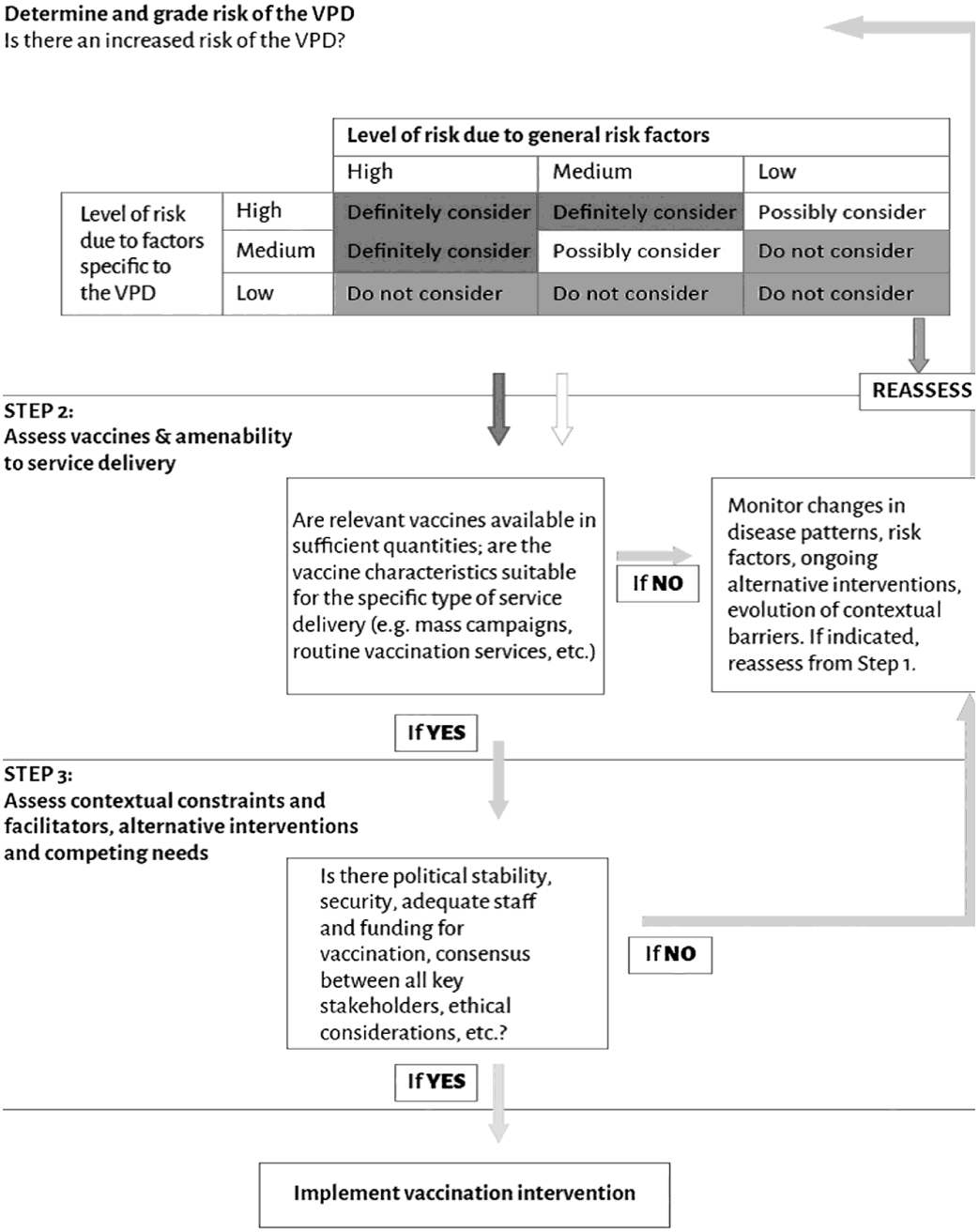

Table 1: Determining the presence of key general risk factors [8]

Risk factors	Main effects on VPDs	Key questions to ask	Possible indicators to consider
High prevalence of malnutrition	Increased risk of infection, disease progression and case fatality	Is there evidence of a nutritional crisis, either already established or unfolding? Is there an unusually high prevalence of acute and/or chronic malnutrition among children or the general population (e.g., history or reports of specific micronutrient deficiencies especially vitamin A)?	Prevalence of acute malnutrition among children aged 6–59 months, ≥15% or ≥ 2% measured within the last three months above and beyond seasonal levels Average nutritional intake or food ration <2100 kcal per person per day Deteriorating food security indicators (e.g., price of staple foods or livestock, yield of last harvest)
High burden of chronic diseases	Increased risk of infection, disease progression and case fatality	Is there unusually high burden of chronic diseases in the general population?	Prevalence of chronic diseases including diabetes, cardiovascular, cancer, immunosuppressive drugs, and renal diseasesin the general population
Young population and/or high birth rate	Greater pool of susceptible for VPDs mainly affecting children Higher herd immunity threshold	Are there a high number of children? Is there an increase in deliveries?	Proportion of children aged under 5 years ≥ 15% Crude birth rate ≥30 per 1000 people per year
High HIV/AIDS burden	Increased risk of infection, disease progression and case fatality	Do persons with HIV/AIDS make up a high proportion of the population? Is there a low access to highly- active antiretroviral therapy (HAART), or have HAART programmes been disrupted by the emergency?	sero-prevalence ≥15% and ART coverage <50% or probably ng due to the emergency
Low access to curative and supportive health services	Increased case fatality for all VPDs Increased risk of some vertically	Has the emergency resulted in reduce access to quality outpatient and inpatient curative health	<1 basic health unit per 10 000 people or <1 hospital per 250 000 people High proportion of non-

	transmitted VPDs (neonatal tetanus, hepatitis B)	services and if so, to what extent?	functional or inaccessible health facilities

Overcrowding	Increased transmissibility of airborne, droplet and faecal-oral VPDs	Does the population live in a large camp or a high-density urban community? How close together are residential structures?	Size of camp >10 000 people <3.5 m² covered floor area per person
Insufficient water, sanitation & hygiene	Increased transmissibility of faecal-oral diseases (mostly), vector-borne, airborne and droplet diseases	Does the population inadequate access to water, sanitation and hygiene (e.g., soap, health promotion)? Camp settings near unprotected water sources (swamps or vector-breeding sources)?	<15 litres water available per person per day >20 persons per Latrine <250 g of soap per person per month

Table 2: Relevance of each general risk factor to each VPD [8]

	High prevalence of malnutrition	High prevalence of chronic disease	Young population &/or high birth rate	High HIV/ AIDS burden	Low access to curative health services	Over-crowding	Insufficient water, sanitation & Hygiene
AIRBORNE-DROPLET							
Diphtheria	Moderate	Low	Low	Unknown	Moderate	High	Low
Hib disease	Moderate	Low	High	Moderate	High	Moderate	Moderate
Influenza	Unknown	Moderate	High	Moderate	Moderate	High	Unknown
Measles	High	Low	High	Moderate	High	High	Moderate
Meningococcal meningitis	Low	Low	Low	Moderate	High	High	Low
Mumps	Low	Low	High	Low	Low	Moderate	Low
Pertusis	High	Low	High	Low	Moderate	High	Low
Pneumococcal disease	High	High	High	High	High	High	Low
Rubella	Moderate	Low	High	Low	Moderate	Moderate	Low
Tuberculosis (meningitis and disseminat	High	High	Low	High	High	High	Low

ed disease)							
Varicella	Moderate	Low	Moderate	High	Low	High	Moderate
FECAL-ORAL							
Cholera	Moderate	Low	Low	Unknown	High	High	High
Hepatitis A	Unknown	Low	Low	Low	Low	Low	High
Hepatitis E	Unknown	Low	Low	Low	Low	Low	High
Polio	Low	Low	Low	Low	Low	High	High
Rotavirus	Moderate	Low	High	Low	High	Moderate	Low
Typhoid fever	High	Low	Low	Moderate	Moderate	Moderate	High
VECTOR- BORNE							
Japanese encephalitis	Unknown	Low	Moderate	Unknown	Moderate	Low	Moderate
Yellow fever	Moderate	Low	High	Unknown	Low	Low	Moderate
OTHER or MIXED							
Hepatitis B	Unknown	Low	High	High	Moderate	Moderate	Moderate
HPV	Low	Low	Low	High	Low	Low	Low
Rabies	Low	Low	Moderate	Low	High	Low	Moderate
Tetanus	Low	Low	High	Low	High	Low	High

Table 3: Immunisation during different phases of disaster can be maintained by the following:

Phase	Activity	Remarks
Preparedness	Maintain routine vaccination; ensure that adequate stocks of vaccines for typhoid, hepatitis A and rabies, as well as polyvalent anti-snake venom, are utilized by the national immunisation programs.	Services and demands of these vaccines may be more after a disaster strikes.
	Stocking of other items required for vaccination like syringes, vaccine carriers/ iceboxes etc	To be use in case of emergency.
	Proper maintenance of current cold chain and alternative plans of cold chain.	Cold chain disruption may occur during disaster
Response Phase	Vaccination and immunisation will not have priority now.	Shifts skilled manpower from lifesaving actions.
	Continue and strengthen routine vaccination	Long term benefits for better health. Routine immunisations through national immunisation programme should be reinstated as soon as conditions stabilize, and may indeed be one indication of a rehabilitating health system.

Relief Phase	Mass vaccination	Not advised until justified after evidence of progressive increase in the number of cases with the risk of an epidemic.
	Storage of vaccine in the affected areas	Ensure that proper cold chain exists in the region before dispatching vaccines.
	Supply vaccines to the affected areas	Follow the routine method if existent. Temporary use of vaccine carrier box, day carrier box etc may be used as situation demands.
	Adoption of vaccination policy	Should be decided at the national level and strictly adhered by all.
Rehabilitation Phase	Restore the best immunisation practices	Direct all actions to restore the best immunisation practices as per National immunisation Program (NIP) guidelines to achieve optimum coverage.

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NEPAL PAEDIATRIC SOCIETY RECOMMENDATIONS FOR CHILDHOOD VACCINATIONS-2025

Vaccines (Antigens)	Recommended age in Weeks (W), Months (M) & Years (Y)																			Remarks
	Birth	6W	10W	14W	6M	7M	9M	12M	13M	15M	16-18M	18-24M	2-3Y	4-6Y	9-14Y	15-16Y	17-18Y			
Government of Nepal National Immunisation Schedule-2081 (14 Antigens)																				
Bacillus Calmette Gurien (BCG)	**1st**																			
Oral Polio Vaccine (OPV)							**1st**	**2nd**	**3rd**											
Diphtheria, Pertussis, Tetanus, Hepatitis-B and Hemophilus							**1st**	**2nd**	**3rd**											

influenza-B																		
Pneumococcal Vaccine (PCV-10)		1st	2nd				3rd											
Rota Virus Vaccine (RV)		1st	2nd															
Injectable Polio (Fipv)				1st			2nd											
Measles & Rubella (MR)							1st			2nd								
Japanese Encephalitis (JE)								1st										
Typhoid Conjugate Vaccine (TCV)										1st								
Human Papilloma Virus (HPV)															1st			For Girl child

NEPAS Recommendation																		
Vaccines (Antigens)	**Recommended age in Weeks (W), Months (M) & Years (Y)**																	
	Birth	**6 W**	**10 W**	**14 W**	**6 M**	**7 M**	**9 M**	**12 M**	**13 M**	**15 M**	**16-18M**	**18-24M**	**2-3Y**	**4-6Y**	**9-14Y**	**15-16Y**	**17-18Y**	**Remarks**
Measles, Mumps & Rubella (MMR)												**1st**		**2nd**				
Inactivated Influenza (IIV)					**1st**	**2nd**						**3rd**	**4th**	**5th**				See Notes [a]
Hepatitis-A									**1st**			**2nd**						See notes [b]
Varicella									**1st**		**2nd**							2nd dose 3-6M after 1st
Human Papilloma Virus (HPV)															**1st & 2nd**	**1st, 2nd & 3rd**		See Notes [c]
Meningococcal (MCV4/ MCPSV4)													**1st**				**2nd**	See notes [d]
Pneumococcal (PCV-13)												**4th**						

Hepatitis-B												**4th**						See Notes [e]
Tetanus, Diphtheria and Pertussis ($DP_{w/a}T$)												**4th**		**5th**				
Hemoplilus influenza-B												**4th**						
Tetanus, Diphtheria and Pertussis (Tdap or Td)															**1st**			Td 10 yearly [f]
Injectable Polio (IPV/FIPV/ OPV)												**3rd**		**4th**				
Rabies Pre-Immunisation													Start					See notes [m]

NEPAS Recommendation for Catch up Immunisation																		
Vaccines (Antigens)	**Recommended age in Weeks (W), Months (M) & Years (Y)**																	
	Birth	**6 W**	**10 W**	**14 W**	**6 M**	**7 M**	**9 M**	**12 M**	**13 M**	**15 M**	**16 - 18 M**	**18 - 24 M**	**2 - 3 Y**	**4 - 6 Y**	**9 - 14 Y**	**15 - 16 Y**	**17 - 18 Y**	**Remarks**
Bacillus Calmette Guerin (BCG)																		Give till 5Y
Tetanus, Diphtheria and Pertussis (DPT, Tdap/Td)																		Till 6Y DPT. After 7y Tdap.[f]
Hepatitis-B (HBV)																		See Notes [g]
Haemophilus influenza-B (HiB)																		See Notes [h]
Pneumococcal (PCV-10/13) or PPSV-23													Start					See Notes [i]
Polio (IPV/FIPV/OPV)																		See Notes [j]
Japanese																		See Notes [k]

Encephalitis (JE)																		
Measles, Mumps & Rubella (MMR)																		2 dose 4W apart
Varicella																		See notes [l]
Hepatitis-A vaccine (Inactivated/Live)																		See notes [b]
Meningococcal (MCV4)																		See notes [d]
Human Papilloma Virus (HPV)																		

NEPAS Recommendation in Special Circumstances [A]

Vaccines (Antigens)	**Recommended age in Weeks (W), Months (M) & Years (Y)**																
	Birth	**6 W**	**10 W**	**14 W**	**6 M**	**7 M**	**9M**	**12 M**	**13 M**	**15 M**	**16 - 18 M**	**18 - 24 M**	**2 - 3 Y**	**4 - 6 Y**	**9 - 14 Y**	**15 - 16 Y**	**17-18Y**	**Remarks**
Cholera								1st	2nd									During Outbreaks
Yellow Fever							Start											See Notes [n]

Inactivated Influenza (IIV)					Start													See notes [a]
Meningococcal (MCV4)																		See notes [d]
Pneumococcal (PCV-10/13) or PPSV-23													Start					See Notes [i]
Hepatitis-B (HBV)																		See Notes [g]
Haemophilus influenza-B (HiB)																		See Notes [h]
Varicella																		2 dose 4W apart
Human Papilloma Virus vaccine(HPV)																		See notes [c]

NATIONAL IMMUNISATION PROGRAM (NIP) | **NEPAS RECOMMENDED** | **ADDITIONAL VACCINES IN SPECIAL CIRCUMSTANCES** | **NEPAS RECOMMENDED CATCH UP**

***Abbreviations**: D: Days, W: Weeks, M: Months, Y: Years, PPSV23: Pneumococcal Polysaccharide Vaccine 23 valent, MCPSV4: Meningococcal Polysaccharide vaccine ACYW-135*

a. Influenza vaccine: Age 6M to 8Yr or in immunocompromised start with 2 dose 1M apart then yearly. Age 9Y or older 1 dose yearly. Give in pre-monsoon period. In other times of year use the most recent available strain. Annual influenza vaccine to continue till 5Y of age in healthy children. If high risk of influenza related complication suspected then yearly till 18Y.

b. Hepatitis A vaccine is used after 12 months of age. 2 doses 6M apart for inactivated vaccine. If using Hepatitis A live vaccine one dose is enough given after 18m of age. As per marketed brand dose needs to be doubled after certain age. Eg. For Avaxim 80U or 0.5ml till age 15Y & 160U or 1ml for >16Y. For PrevaHAV 250U or 0.5ml for age upto15Y & 500U or 1ml for >16yr. For Havrix 720U or 0.5ml till age 18y & 1440U or 1ml for >19Y.

c. HPV: 2 doses 6-12M apart between 9-14Y & 3 doses at 0, 2, and 6M if age older than 15Y or in immunocompromised. Recommended for both girls & boys.

d. Meningococcal vaccine ACYW-135: 2 doses 3M apart for age group 9 to 23 months in high-risk group or in epidemics. Single dose after 2 years. In adolescent age we recommend 1 dose at the age of 16-18 years. Booster 5 yearly in high-risk group. If Polysaccharide vaccine used booster is needed every 2-3 yearly.

e. HBV: Infants born to HBsAg +ve mothers should receive at birth HepB 1st dose 0.5ml + HBIG (Hepatitis B Immunoglobulin) 0.5ml simultaneously IM (<12 hours) at 2 separate sites. Then HepB regular doses to continue according to Nepal Immunisation schedule. 4th dose at 18M. An extra dose can be allowed if combination vaccine is given at 4-6Y.

f. DPT- 4W gap between dose 1, 2 and 3. 6M gap between dose 3, 4 and 5. 5th dose not needed if 4th dose was after 4Y with gap of at least 6month after 3rd. Tdap can be given if age >7Y. Tdap is necessary at age of 10-14Y. If a dose of Tdap received at age 9Y or older no need of it at adolescent age. If Tdap not available/affordable give Td.

g. HBV accelerated schedule: 3 dose series at 0, 1, &4M. OR 3 dose usual series at 0, 1-2 & 6M. Double the doses at 0, 1, 2 and12M along with hepatitis immunoglobulin every 3M during chemotherapy in unimmunised and HbsAg negative children. Double dose is also needed after 18Y.

h. HiB vaccine: IF last dose in >15M old no further dose needed in healthy children. <12M of age 4W gap between dose 1, 2 & 3. >12M 8W gap between dose 1, 2 &3. 4th dose 8W after 3rd to child age 12-59M who received all 3 doses before 12M.

i. Pneumococcal Vaccine: Single dose in child >2Y. In healthy children no extra dose needed if vaccinated after 2Y of age. <12M of age: 4W gap between dose 1, 2 & 3. >12 M: 8W gap between dose 1, 2 & 3. 4th dose 8W after 3rd to children <59M who received all 3 doses before 12M without risk and in Age 60-71M with risk. 1 dose after age 6Y. If>2Y old PPSV23 can be given. Booster PCV-13 5yearly & PPSV23 2-3 yearly in high-risk children.

j. Polio vaccine: Age < 4Y-3 doses 4W apart then 4th dose after 6M of 3rd dose (If >3M age give first fIPV and bOPV on first contact). If age > 4Y- 2 doses 4W apart & 3rd dose after 6M. 4th dose needed if all dose <4Y or if 3rd dose <6M after 2nd dose. Upper age limit for OPV/IPV is 5Y.

k. Japanese encephalitis live vaccine single dose after 12 months of age. Inactivated vaccine needs 2 doses 4W apart.

l. Varicella vaccine: Before 12 Y 2 doses 3M apart. After 12Y 2 doses 1M apart is used.

m. Rabies Pre exposure is recommended for all child above 2Y in Nepal. It is given as 3 dose schedules at 0, 7 and 21 OR 28D 0.5ml IM or 0.1ml 2 site ID in deltoid region. Post exposure Rabies Prophylaxis In unimmunised healthy child is 4 dose series on 0, 3, 7 & 14 or 28D for IM 0.5ml dosing or 3 dose series on 0, 3, and 7D for 2 site ID 0.1ml (For ID dosing it is given 0.1ml on each deltoid region per visit) with immunoglobulin-20 IU/ kg for Human RIG (HRIG) or 40 IU/ kg of Equine RIG (ERIG). Full dose of HRIG or ERIG is given at wound site. In unimmunised immunocompromised child 5th dose is given on day 28. In immunised child post exposure is 2 doses at 0 and 3D either 0.5ml IM or one site ID 0.1ml. No HRIG.

n. Yellow fever vaccine: One dose for person travelling to endemic zones after 9M of age. Booster after 10Y not recommended in healthy child. Booster needed in Hematopoietic stem cell transplant recipients, and HIV-infected child.

o. Special circumstances mean High risk group like Congenital or acquired immunodeficiency (HIV, on immunosuppressive therapy, radiation), renal disease like Nephrotic syndrome, Functional asplenia/ hyposplenia, Hematological disease needing splenectomy (Thalassemia), After solid organ transplant or hematopoietic stem cell transplant, Chronic systemic disease (cardiac, pulmonary, renal, liver disease, diabetes), CSF leaks or cochlear implants.

Vaccine recommendations in children with chronic disease and/or immunosuppression (Special Circumstances)

Vaccine recommendations in children with chronic disease and/or immunosuppression					
Medical condition	**Event**	**Non-live vaccine recommendation**	**Live vaccine recommendation**	**Additional vaccine recommendation**	**Remarks**
Solid organ transplant (SOT) recipients	Pre-transplant	Accelerate schedule. Completed at least 2W prior SOT.	Completed at least 4W prior SOT.	IIV (Inactivated Influenza) PCV-13/ PPSV-23 MCV4-2 dose 2M apart HPV vaccine MMR, Varicella HiB	HiB one dose after age 5 years regardless of Hib vaccination history IIV can be given 2M post SOT
	Post-transplant	6M post SOT	1Y post SOT		
Primary Immunodeficiency	-	Routine to be given (though effectiveness doubtful)	Permitted as per diagnosis (Refer to Table 1 below)	IIV(Inactivated Influenza) PCV-13/ PPSV-23 MCV4 - 2 dose 2M apart MenB - 3 dose series at 2,4 & 12M.	MenB only if complement deficiency or taking complement inhibitors (eculizumab, ravulizumab).
HIV Infection	-	Delay vaccination until viral load < 50 copies/mL and CD4 > 15%. Use high-dose HBV vaccine (40 µg) in	Permitted > 6M age and only if CD4 count > 200 cells/µl in >6Y, >1000 cells/µl in 1-6Y,	IIV(Inactivated influenza) PCV-13/PPSV23, MCV4-2 dose 2M apart. HBV DPT to complete	

		adolescents. Give Hib vaccine regardless of age if not immune. Td booster at least 1×/10Y	>1500 cells/µl in< 1Y. OR >25%	schedule MMR & Varicella	
Hematopoietic stem cell transplant (HSTC) recipients	Pre-transplant	Accelerate schedule. Completed at least 2W prior HSTC.	Completed at least 4W prior HSTC.	IIV (Inactivated Influenza) PCV-13/ ±PPSV-23 MCV4 HPV vaccine MMR, Varicella, HiB	HiB one dose after age 5Y regardless of Hib vaccination history
	Post-transplant	Revaccination starting 3M to 6M post HSTC (including HiB, regardless of age)	1.5 to 2Y post HSCT		
Oncology Patients/ On chemotherapy/ immunosuppressives	-	Not permitted during chemotherapy except HBV in unimmunised and HbsAg negative children. [g] Revaccination starting 6M post chemo (including HiB, regardless of age)	Not permitted during and up to 6M after chemotherapy Accelerate schedule and finish before if possible. Resume 6M after completion	IIV (Inactivated Influenza) till 1Y of end of chemo. PCV-13 /± PPSV23 MCV4 MMR, Varicella HiB	After 6M chemotherapy booster dose of all vaccine given even in completely immunised children except for BCG, Rotavirus and HPV vaccines. **Live vaccines 8M to 11M after IVIG (MMR &**

					Varicella). Other live vaccine can be given after 1-2M.
Asplenia/ Hyposplenia/ Sickle cell disease/ Thalassemia	-	Routine, catch-up and Hib vaccination regardless of age HBV vaccination highly recommended if frequent transfusion. Anticipate 2W between vaccination and elective splenectomy	Permitted, as of a few days after splenectomy Anticipate 4W between vaccination and elective splenectomy	IIV (Inactivated Influenza) PCV-13 /± PPSV23 MCV4-2 dose 2M apart MenB-3 dose series at 2, 4 &12M. HBV HiB TCV	MCV4: age<7Y- Booster 3Y after 1st dose then 5 yearly. If Age>7Y- 5 yearly. MenB: 1Y after primary series then 2-3 yearly PPSV23 after 2Y of age in all splenectomy patient.
Nephrotic Syndrome	-	Accelerate schedule before immunosuppression. Permitted during and after immunosuppression.	Permitted if on alternate day therapy. Start after stopping immediately if low immunosuppression (Prednisolone <2mg/kg/day; <20mg/day if >10	Varicella and IIV (Inactivated Influenza) -to all household also PCV-13 /±PPSV23 HBV	No OPV to household contact and immunocompetent sibling.

			kg for <14D. Start after 1M of stopping therapy If on Prednisolone (≥2 mg/kg/d; ≥20 mg/day if >10 kg) for >14D, on calcineurin inhibitors, levamisole, & MMF. 3M after Cyclophosphamide. 6-9M after Rituximab.		
Rheumatological/Immunological Diseases		Accelerate schedule before immunosuppression. Permitted during and after immunosuppression.	If on Methotrexate >0.4mg/kg/week, Azathioprine >3mg/kg/day, 6-Mercaptopurine >1.5mg/kg/day, TNF-α inhibitors (Adalimumab, Infliximab, Certolizumab, Etanercept, Golimumab) wait for 3 months after	Varicella IIV MCV PCV-13 /±PPSV23 HBV DPT	If on Complement inhibitors (Eculizumab, ravulizumab) – MCV not to be missed.

			stopping. Accelerate schedule and finish at least 4wk before starting rituximab and start after 6-9M of stopping. Revaccination needed.		
Renal failure, chronic kidney disease, on dialysis	-	Accelerate schedule before dialysis. Continue during and after	All Permitted except Live attenuated influenza vaccine.	IIV (Inactivated Influenza) PCV-13 /± PPSV23 COVID HBV highly recommended, double dose in CKD and dialysis.	
Diabetes Mellitus	-	All routine	Permitted	IIV (Inactivated Influenza) PCV-13 /± PPSV23 HBV highly recommended	
Chronic liver disease	-	All routine	Permitted	IIV (Inactivated Influenza) PCV-13 /± PPSV23	

				HAV &HBV highly recommended.	
Congenital heart disease	-	All routine	Permitted	IIV (Inactivated Influenza) PCV-13 /± PPSV23	RSV if available
Chronic lung disease	-	All routine	Permitted	IIV PCV-13 /± PPSV23	RSV if available
CNS anatomic barrier defect (CSF leak, cochlear implant)	-	All routine	Permitted	PCV-13 /± PPSV23 MCV4 HiB IIV (Inactivated Influenza)	
Prematurity	-	Accelerated schedule based on chronological age	Accelerated schedule based on chronological age	IIV (Inactivated Influenza) PCV-13 /± PPSV23 MCV4-2 dose 2M apart	RSV if available Birth dose of HBV can be given if wt <2kg.

Table 1	**Primary Immunodeficiency and Live vaccines**			
	Immune Deficiency	**Disease**	**Live vaccine contraindication**	**Remarks**
1	B Lymphocyte (Humoral)	Severe antibodies deficiencies (X-linked agammaglobulinemia,	OPV, live influenza, BCG, Ty21a, RV, MMR, Varicella &	Efficacy of vaccine unclear. IVIG interferes with response to MMR &

		CVID)	Yellow fever vaccine.	Varicella
		Mild antibodies deficiencies (Selective IgA def, Ig subgroup def)	OPV & BCG. Other live vaccine can be given.	
2.	T lymphocyte (Cellular)	Complete deficiency (SCID, complete Di George syndrome)	All Live Vaccine	
		Partial deficiencies (Partial Di George syndrome, Wiskott-Aldrich syndrome, Ataxia-telangiectasia)	All Live Vaccine	May consider MMR & Varicella if CD4 is age appropriate. (>25%)
3.	Complement deficiencies	C5-C9, C3, Properdin, Factor B deficiency	None	Meningococcal and pneumococcal not to be missed.
4.	Phagocyte Dysfunction	CGD, LAD, Myeloperoxidase deficiency	BCG & Ty21a	

Abbreviations: *D: Days, W: Weeks, M: Months, Y: Years, IIV: Inactivated Influenza Vaccine, SOT: Solid Organ Transplant, CKD: Chronic Kidney Disease, PPSV23: Pneumococcal Polysaccharide Vaccine 23 valent, PCV-13: Pneumococcal Conjugate Vaccine 13 valent, MCV4: Meningococcal Conjugate Vaccine Quadrivalent ACYW-135, HPV: Human Papilloma Virus Vaccine, MMR: Mumps Measles and Rubella, HiB: Haemophilus Influenzae B Vaccine, MenB: Meningococcal B Vaccine, DPT: Diphtheria Pertussis Tetanus Vaccine, HBV: Hepatitis B Vaccine, TCV: Typhoid Conjugate Vaccine,RV: Rotaviral Vaccine, Ty21a: Typhoid Live Oral Vaccine.*

NOTE: Specifications can be different as per manufacturer of Vaccine. In special circumstances case by case basis based upon available evidence can be applied.

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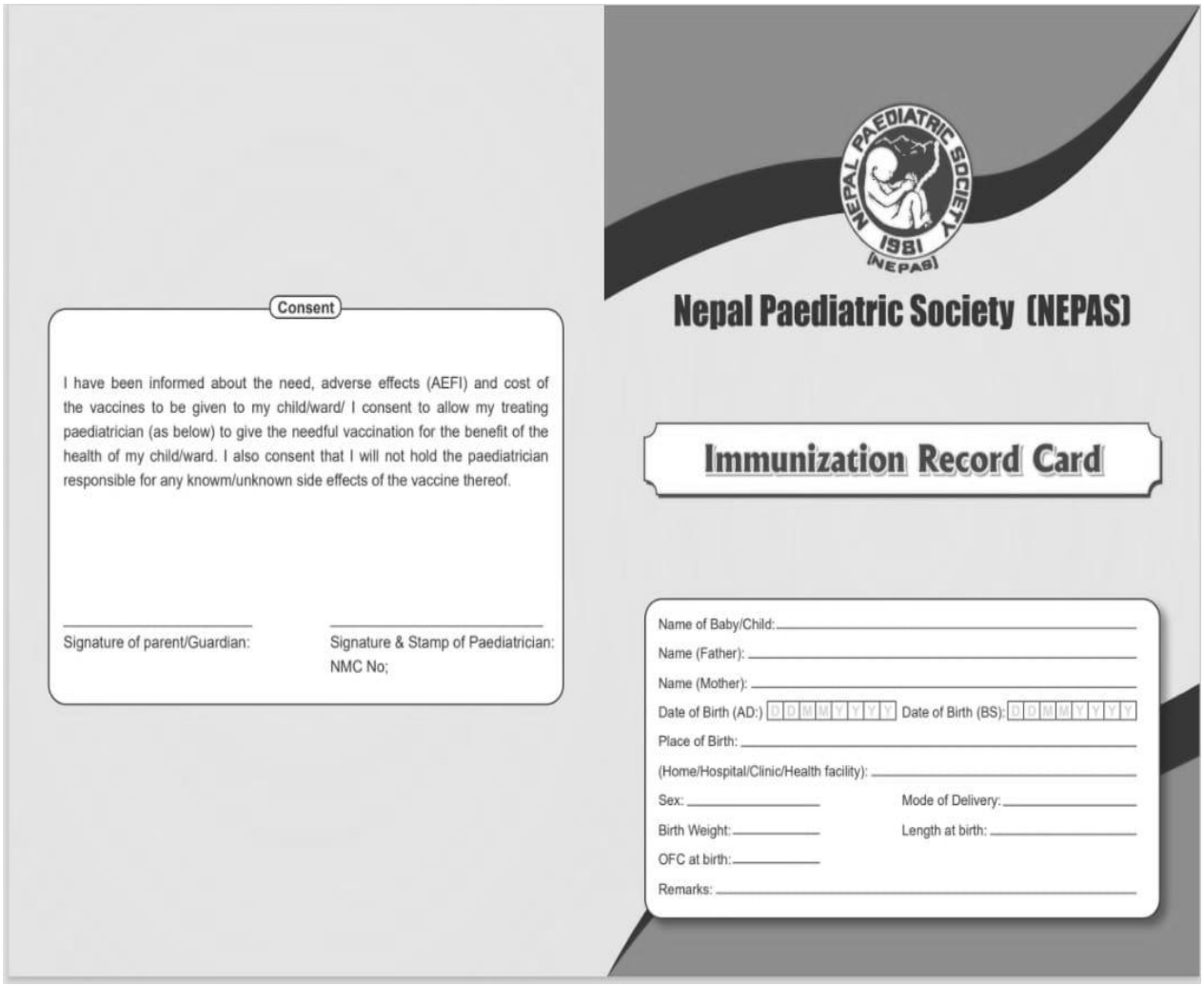
ANNEXURE



Consent

I have been informed about the need, adverse effects (AEFI) and cost of the vaccines to be given to my child/ward/ I consent to allow my treating paediatrician (as below) to give the needful vaccination for the benefit of the health of my child/ward. I also consent that I will not hold the paediatrician responsible for any knowm/unknown side effects of the vaccine thereof.

Signature of parent/Guardian:

Signature & Stamp of Paediatrician:
NMC No;

NEPAL PAEDIATRIC SOCIETY
1981
(NEPAS)

Nepal Paediatric Society (NEPAS)

Immunization Record Card

Name of Baby/Child:
Name (Father):
Name (Mother):
Date of Birth (AD:) D D M M Y Y Y Y Date of Birth (BS): D D M M Y Y Y Y
Place of Birth:
(Home/Hospital/Clinic/Health facility):
Sex: Mode of Delivery:
Birth Weight: Length at birth:
OFC at birth:
Remarks:

Vaccines as per National Immunization Schedule (13 Antigens)

Given ☐ Not Given ☐

Recommend for Missed/Catch up Vaccination:

Yes ☐ No ☐

	Government of Nepal National Immunization Schedule-2080 (14 Antigens)					
S. N.	Name & Type of Vaccine	Age	Due Date AD (DD/MM/YYYY)	Date given in AD (DD/MM/YYYY)	Remarks (Vaccine sticker/ Lot no)	Name, NMC No; & Signature of Paediatrician
1.	Bacillus Calmette Gurien (BCG)	At Birth				
2.	Oral Polio Vaccine (OPV)	6 weeks				
		10 weeks				
		14 weeks				
3.	Diphtheria, Pertussis, Tetanus, Hepatitis-B and Hemophilus Influenza-B	6 weeks				
		10 weeks				
		14 weeks				
4.	Pneumococcal Vaccine (PCV-10)	6 weeks				
		10 weeks				
		9 months				
5.	Rota Virus Vaccine (RV)	6 weeks				
		10 weeks				
6.	Injectable Polio (fIPV)	14 weeks				
		9 months				
7.	Measles & Rubella (MR)	9 months				
		15 months				
8.	Japanese Encephalitis (JE)	12 months				
9.	Typhoid	15 months				
10	HPV Vaccine	9-14 years girls				

Notes:

1. All children to follow National Immunization Schedule primarily.
2. All parents/caretakers to abide rules of the government to include their children in National Catch-up Campaigns, National Vaccination Day/week/month and mopping up operations or others as instructed.
3. All suspected AEFIs to be reported to the nearest government or private health institution/hospital/institution.
4. Vit-A, Albendazole or other campaigns of the government to be supported, advocated & followed by all paediatricians.

Nepal Paediatric Society Recommended Immunization Record

The treating paediatrician will need to counsel and discuss about the available vaccines apart from the ones given by the government of Nepal for free. They must be informed about the indication, adverse effects/AEFI and cost of the vaccines. Preferably an informed consent needs to be signed.

	Nepal Paediatric Society Recommendation (further to the Government recommendation)					
S. N.	Name & Type of Vaccine	Age	Due Date in AD (DD/MM/YYYY)	Date Given in AD (DD/MM/YYYY)	Remarks (Vaccine sticker/ Lot no)	Name, NMC No; & Signature of Paediatrician
1.	Influenza Vaccine	6 months and yearly				
2.	Hepatitis A	13 months				
		19 months				
3.	Chicken pox Vaccine	13 months				
		16-19 months				
4.	Measles, mumps & Rubella (MMR)	18 months				
		4-6 years				
5.	DPT,HBV,HiB & IPV	18 months				
	DPT & IPV	4-6 years				
6.	Pneumococcal (PCV-13 or 10)	18 months				
7.	Meningococcal (MCV4)	2 years				
		16-18 years				
8.	Rabies Pre-Immunization Post-exposure	2 years onward After birth				
9	dT or Tdap	10-14 ears then 10 yearly				
10.	Others					

Note: Please discuss with your paediatrician in case of giving vaccines to children in special circumstances or at high risk like Congenital or acquired immunodeficiency (HIV, on immunosuppressive therapy, radiation), Renal disease like Nephrotic syndrome, Functional asplenia/hypospleenia, Haematological disease needing

spleenectomy (Thalassemia), After solid organ transplant or hematopoietic stem cell transplant, chronic systemic disease (cardiac, pulmonary, renal, liver disease, diabetes), CSF leaks or cochlear implants.

Vaccines as per National Immunisation Schedule (14 Antigens)

Given ☐ Not Given ☐

Recommend for Missed/Catch up Vaccination:

Yes ☐ No ☐

	Government of Nepal National Immunisation Schedule-2080 (14 Antigens)					
S. N.	Name & Type of Vaccine	Age	Due Date AD (DD/MM/YYYY)	Date given in AD (DD/MM/YYYY)	Remarks (Vaccine sticker/ Lot no)	Name, NMC No; & Signature of Paediatrician
1.	Bacillus Calmette Gurien (BCG)	At Birth				
2.	Oral Polio Vaccine (OPV)	6 weeks				
		10 weeks				
		14 weeks				
3.	Diphtheria, Pertussis, Tetanus, Hepatitis-B and Hemophilus Influenza-B (DPwT+HBV+ Hib)	6 weeks				
		10 weeks				
		14 weeks				
4.	Pneumococcal Vaccine (PCV-10)	6 weeks				
		10 weeks				

		9 months				
5.	Rota Virus Vaccine (RV1)	6 weeks				
		10 weeks				
6.	Injectable Polio (fIPV)	14 weeks				
		9 months				
7.	Measles & Rubella (MR)	9 months				
		15 months				
8.	Japanese Encephalitis (JE)	12 months				
9.	Typhoid (TCV)	15 months				
10.	HPV Vaccine	9-14 years girls				

Notes:

All children to follow National Immunisation Schedule primarily.
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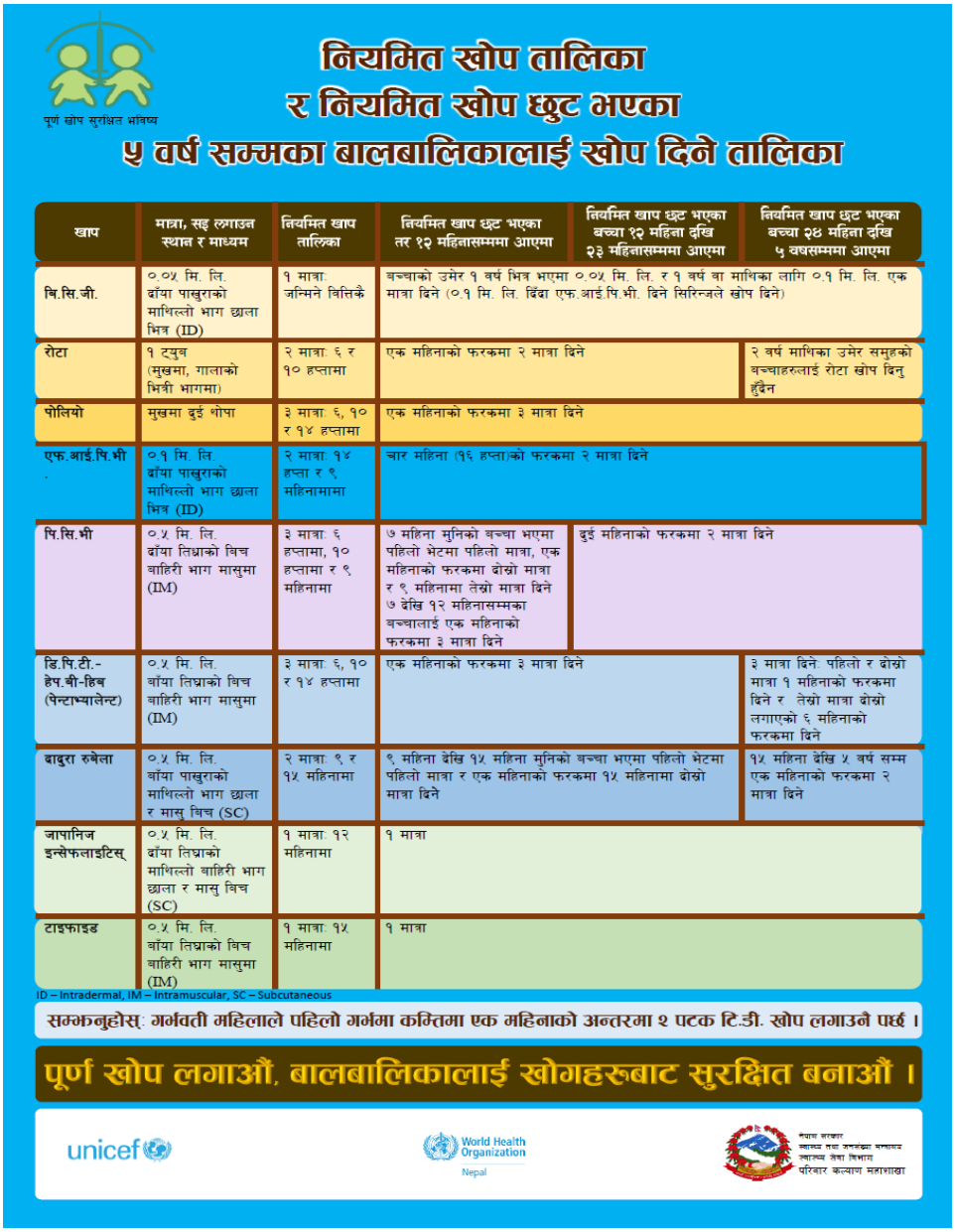
	Nepal Paediatric Society Recommendation (Additional to the Government recommendation)					
S. N.	Name & Type of Vaccine	Age	Due Date in AD (DD/MM/YYYY)	Date Given in AD (DD/MM/YYYY)	Remarks (Vaccine sticker/ Lot no)	Name, NMC No; & Signature of Paediatrician
1.	Influenza Vaccine	6 months & yearly				
2.	Hepatitis A	13 months				
		19 months				
3.	Chicken pox vaccine	13 months				
		16-19 months				
4.	Measles, Mumps & Rubella (MMR)	18 months				
		4-6 years				
5.	DPT, HBV, HiB and IPV	18 months				
	DPT and IPV	4-6 years				
6.	Pneumococcal (PCV)	18 months				
7.	Meningococcal (MCV4)	2 years				
		11-12 years				
		16-18 years				
8.	Rabies Pre-Immunisation	2 years onward (Day 0, 7 & 21)				
10	dT or Tdap	10-14 years then 10yearly				
11	Others					

Note: Please discuss with your paediatrician in case of giving vaccines to children in special circumstances or at high risk like Congenital or acquired immunodeficiency (HIV, on immunosuppressive therapy, radiation), Renal disease like Nephrotic syndrome, Functional asplenia/hyposplenia, Haematological disease needing splenectomy (Thalassemia), After solid organ transplant or hematopoietic stem cell transplant, chronic systemic disease (cardiac, pulmonary, renal, liver disease, diabetes), CSF leaks or cochlear implants.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२ वर्ष माथिका उमेर समुहको बच्चाहरुलाई रोटा खोप दिनु हुँदैन
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मुखमा दुई थोपा
३ मात्रा: ६, १० र १४ हप्तामा
एक महिनाको फरकमा ३ मात्रा दिने
एफ.आई.पि.भी .
०.१ मि. लि. बाँया पाखुराको माथिल्लो भाग छाला भित्र (ID)
२ मात्रा: १४ हप्ता र ९ महिनामामा
चार महिना (१६ हप्ता)को फरकमा २ मात्रा दिने
पि.सि.भी
०.५ मि. लि. बाँया तिघ्राको विच बाहिरी भाग मासुमा (IM)
३ मात्रा: ६ हप्तामा, १० हप्तामा र ९ महिनामा
७ महिना मुनिको बच्चा भएमा पहिलो भेटमा पहिलो मात्रा, एक महिनाको फरकमा दोस्रो मात्रा र ९ महिनामा तेस्रो मात्रा दिने ७ देखि १२ महिनासम्मका बच्चालाई एक महिनाको फरकमा ३ मात्रा दिने
दुई महिनाको फरकमा २ मात्रा दिने
डि.पि.टी.-हेप.बी-हिब (पेन्टाभ्यालेन्ट)
०.५ मि. लि. बाँया तिघ्राको विच बाहिरी भाग मासुमा (IM)
३ मात्रा: ६, १० र १४ हप्तामा
एक महिनाको फरकमा ३ मात्रा दिने
३ मात्रा दिने: पहिलो र दोस्रो मात्रा १ महिनाको फरकमा दिने र तेस्रो मात्रा दोस्रो लगाएको ६ महिनाको फरकमा दिने
दादुरा रुबेला
०.५ मि. लि. बाँया पाखुराको माथिल्लो भाग छाला र मासु विच (SC)
२ मात्रा: ९ र १५ महिनामा
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०.५ मि. लि. बाँया तिघ्राको माथिल्लो बाहिरी भाग छाला र मासु विच (SC)
१ मात्रा: १२ महिनामा
१ मात्रा
टाइफाइड
०.५ मि. लि. बाँया तिघ्राको विच बाहिरी भाग मासुमा (IM)
१ मात्रा: १५ महिनामा
१ मात्रा
ID – Intradermal, IM – Intramuscular, SC – Subcutaneous
सम्झनुहोस्: गर्भवती महिलाले पहिलो गर्भमा कम्तिमा एक महिनाको अन्तरमा २ पटक टि.डी. खोप लगाउनै पर्छ ।
पूर्ण खोप लगाऔं, बालबालिकालाई खोगहरूबाट सुरक्षित बनाऔं ।
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नेपाल सरकार
स्वास्थ्य तथा जनसंख्या मन्त्रालय
स्वास्थ्य सेवा विभाग
परिवार कल्याण महाशाखा

Table 1: Summary of WHO Position Papers - Recommendations for Routine Immunization

Antigen		Children (see Table 2 for details)		Adolescents	Adults	Considerations (see footnotes for details)
Recommendations for all immunization programmes						
BCG [1]		1 dose				Birth dose and HIV; Universal vs selective vaccination; Co-administration; Vaccination of older age groups; Pregnancy
Hepatitis B [2]		3-4-doses (see footnote for schedule options)		3 doses (for high-risk groups if not previously immunized) (see footnote)		Birth dose Premature and low birth weight Co-administration and combination vaccine Definition high-risk
Polio [3]		3-5 doses (at least 2 doses of IPV) with DTPCV				bOPV birth dose; Type of vaccine; Fractional dose IPV; Transmission and importation risk; Local epidemiology, programmatic implications and feasibility for "early" option
DTP-containing vaccine (DTPCV) [4]		3 doses	2 boosters 12-23 months (DTPCV) and 4-7 years (Td/DT containing vaccine, see footnote)	1 booster 9-15 yrs (Td)		Delayed/interrupted schedule Combination vaccine Maternal immunization
***Haemophilus influenzae* type b** [5]	**Option 1**	3 doses, with DTPCV				Single dose if > 12 months of age Not recommended for children > 5 yrs old Delayed/interrupted schedule Co-administration and combination vaccine
	Option 2	2 or 3 doses, with booster at least 6 months after last dose				
Pneumococcal (Conjugate) [6]	**Option 1**	3 primary doses (3p+0) with DTPCV				Schedule options (3p+0 vs 2p+1) Vaccine options HIV+ and preterm neonate booster Vaccination in older adults
	Option 2	2 primary doses plus booster dose at 9-18 mos of age (2p+1) with DTPCV				
Rotavirus [7]		2-3 doses depending on product with DTPCV				Not recommended if > 24 months old
Measles [8]		2 doses				Co-administration live vaccines; Combination vaccine; HIV early vaccination; Pregnancy
Rubella [9]		1 dose (see footnote)		1 dose (adolescent girls and women of reproductive age if not previously vaccinated; see footnote)		Combination vaccine and Co-administration Pregnancy
HPV [10]				1-2 doses (females)		Target 9-14 year old girls; Off-label 1 dose schedule; MACs with intro; Pregnancy; HIV and immunocompromised

Refer to https://www.who.int/teams/immunization-vaccines-and-biologicals/policies/position-papers for most recent version of this table and position papers.

This table summarizes the WHO child vaccination recommendations. It is designed to assist the development of country specific schedules and is not intended for direct use by health care workers. Country specific schedules should be based on local epidemiologic, programmatic, resource and policy considerations.

While vaccines are universally recommended, some children may have contraindications to particular vaccines.

(updated: December 2024)

Table 1: Summary of WHO Position Papers - Recommendations for Routine Immunization

Antigen		Children (see Table 2 for details)	Adolescents	Adults	Considerations (see footnotes for details)
Recommendations for certain regions					
Japanese Encephalitis [11]		*Inactivated Vero cell-derived vaccine:* generally 2 doses *Live attenuated vaccine:* 1 dose *Live recombinant vaccine:* 1 dose			Co-administration live vaccines; Vaccine options and manufacturer's recommendations; Pregnancy; Immunocompromised
Yellow Fever [12]		1 dose, with measles containing vaccine			Co-administration live vaccines
Tick-Borne Encephalitis [13]		3 doses (> 1 yr FSME-Immun and Encepur; > 3 yrs TBE-Moscow and EnceVir) with at least 1 booster dose (every 3 years for TBE-Moscow and EnceVir)			Definition of high-risk Vaccine options Timing of booster
Recommendations for some high-risk populations					
Typhoid [14]		*Typhoid conjugate vaccine (Typbar-TCV®):* 1 dose; *Vi polysaccharide(ViPS):* 1 dose; *Ty21a live oral vaccine:* 3-4 doses (see footnote); *Revaccination for ViPS & Ty21a: every 3-7 years*			Definition of high-risk Vaccine options
Cholera [15]		*Dukoral (WC-rBS):* 3 doses ≥ 2-5 yrs, booster every 6 months; 2 doses adults/children ≥ 6 yrs, booster every 2[nd] year; *Shanchol, Euvichol & mORCVAX:* 2 doses ≥1 yrs, booster dose after 2 yrs			Minimum age Definition of high-risk
Meningococcal [16]	**MenA conjugate**	1 dose 9-18 months (5µg)			2 doses if < 9 months with 8 week interval
	MenC conjugate	2 doses (2-11 months) with booster 1 year after 1 dose (≥12 months)			Definition of high-risk; Vaccine options
	Quadrivalent conjugate	2 doses (9-23 months) 1 dose (≥2 years)			
Hepatitis A [17]		Inactivated: 1 or 2 doses ≥ 12 months Live attenuated: 1 dose >18 months of age		Inactivated: 2 doses if > 40 years of age	Level of endemicity; Vaccine options; Definition of high risk groups
Rabies [18]		2 doses			PrEP vs PEP; definition of high risk; booster
Dengue (TAK-003) [19]		2 doses			High transmission areas; Pregnancy and lactation; Comorbidities
Malaria [20]		4 doses			Moderate to high transmission; Seasonal strategy
Recommendations for immunization programmes with certain characteristics					
Mumps [21]		2 doses with measles and rubella containing vaccine			High coverage with MR vaccine Combination vaccines
Seasonal influenza (inactivated tri-and quadri-valent)[22]		First vaccine use: 2 doses Revaccinate annually: 1 dose only (see footnote)	1 dose ≥ 9 years of age	Revaccinate annually	Priority risk groups
Varicella [23]		1 - 2 doses	2 doses		Achieve & sustain ≥ 80% coverage Pregnancy Co-administration with other live vaccines

Summary Table 1 - Notes

- Refer to http://www.who.int/immunization/documents/positionpapers for the most recent version of the tables and position papers.
- The attached table summarizes the recommendations for vaccine administration found in the WHO position papers which are published in the Weekly Epidemiological Review. Its purpose is to assist planners to develop an appropriate immunization schedule. Health care workers should refer to their national immunization schedules. While vaccines are universally recommended, some children may have contraindications to particular vaccines.
- Vaccines can generally be co-administered (i.e. more than one vaccine given at different sites during the same visit). Recommendations that explicitly endorse co-administration are indicated in the table, however, lack of an explicit co-administration recommendation does not imply that the vaccine cannot be co-administered; further, there are no recommendations against co-administration.
- Doses administered by campaign may or may not contribute to a child's routine immunization schedule depending on type and purpose of campaign (e.g. supplemental versus routine/pulse campaign for access reasons).
- For some antigens, recommendations for the age of initiation of primary immunization series and/or booster doses are not available. Instead, the criteria for age at first dose must be determined from local epidemiologic data.
- If a catch-up schedule for interrupted immunization is available, it is noted in the footnotes.
- Other vaccines, such as varicella and pneumococcal polysaccharide vaccines, may be of individual benefit but are not recommended for routine immunization. See the specific position papers for more details.
- For further background on immunization schedules refer to "Immunological Basis for Immunization" series which is available at http://www.who.int/immunization/documents/immunological_basis_series/en/index.html

1 BCG

- Position paper reference: Weekly Epid. Record (2018, 93:73-96) [pdf 660KB].
- Universal BCG vaccination at birth is recommended in countries or settings with a high incidence of TB and/or high leprosy burden. A single dose of BCG vaccine should be given to all healthy neonates at birth, ideally together with Hepatitis B birth dose.
- Countries with low TB incidence or leprosy burden may choose to selectively vaccinate neonates in high-risk groups.
- BCG vaccination is also recommended for unvaccinated TST- or IGRA-negative older children, adolescents and adults from settings with high incidence of TB and/or high leprosy burden, those moving from low to high TB incidence/ leprosy burden settings and persons at risk of occupational exposure in low and high TB incidence areas (e.g. health-care workers, laboratory workers, medical students, prison workers, other individuals with occupational exposure).
- BCG vaccination is not recommended during pregnancy.
- If HIV-infected individuals, including children, are receiving ART, are clinically well and immunologically stable (CD4% >25% for children aged <5 years or CD4 count ≥200 if aged >5 years) they should be vaccinated with BCG. Neonates born to women of unknown HIV status should be vaccinated as the benefits of BCG vaccination outweigh the risks. Neonates of unknown HIV status born to HIV infected women should be vaccinated if they have no clinical evidence suggestive of HIV infection, regardless of whether the mother is receiving ART. For neonates with HIV infection confirmed by early virological testing, BCG vaccination should be delayed until ART has been started and the infant confirmed to be immunologically stable (CD4 >25%).
- Moderate-to-late preterm infants (gestational age > 31 weeks) and low birth weight infants (< 2500 g) who are healthy and clinically stable can receive BCG vaccination at birth, or at the latest, upon discharge.

2 Hepatitis B

- Position paper reference: Weekly Epid. Record (2017, 92:369-392) [pdf 2.4MB].
- Hepatitis B vaccination is recommended for all children worldwide. Reaching all children with at least 3 doses of hepatitis B vaccine should be the standard for all national immunization programmes. Since perinatal or early postnatal transmission is the most important source of chronic HBV infection globally, all infants (including low birth weight and premature infants) should receive their first dose of hepatitis B vaccine as soon as possible after birth, ideally within 24 hours.
- The birth dose should be followed by 2 or 3 additional doses to complete the primary series. Both of the following options are considered appropriate: (i) a 3-dose schedule with the first dose (monovalent) being given at birth and the second and third (monovalent or as part of a combined vaccine) given at the same time as the first and third doses of DTP-containing vaccine; or (ii) 4 doses, where a monovalent birth dose is followed by 3 (monovalent or combined vaccine) doses, usually given with other routine infant vaccines; the additional dose does not cause any harm. The interval between doses should be at least 4 weeks.
- A birth dose of hepatitis B vaccine can be given to low birth weight (<2000g) and premature infants. For these infants, the birth dose should not count as part of the primary 3-dose series; the 3 doses of the standard primary series should be given according to the national vaccination schedule.
- For catch-up of unvaccinated individuals, priority should be given to younger age groups since the risk of chronic infection is highest in these cohorts. Catch-up vaccination is a time-limited opportunity for prevention and should be considered based on available resources and priority. Unvaccinated individuals should be vaccinated with a 0, 1, 6 month schedule.
- Vaccination of groups at highest risk of acquiring HBV is recommended. These include patients who frequently require blood or blood products, dialysis patients, diabetes patients, recipients of solid organ transplantation, person with chronic liver disease including those with Hepatitis C, person with HIV infection, men who have sex with men, persons with multiple sexual partners, as well as health care workers and others who may be exposed to blood, blood products or other potentially infectious body fluids during their work.

3 Polio

- Position paper reference: Weekly Epid. Record (2022, 97:277-300) [pdf 589KB].
- All children worldwide should be fully vaccinated against polio, and every country should seek to achieve and maintain high levels of coverage with polio vaccines in support of the global commitment to eradicate polio.

bOPV plus IPV

- For all countries using OPV in their national immunization programme, WHO recommends 3 doses of bOPV and 2 doses of IPV.
- The preferred schedule is to administer the 3 doses of bOPV starting from the minimum age of 6 weeks, with at least a 4 week interval between doses. The first IPV dose should be administered from a minimum of 14 weeks of age (with DTP3/Penta3), with the second IPV dose being given at least 4 months later (possibly coinciding with other vaccines administered at 9 months of age).

- The 2 doses of IPV provide immunity against paralysis from type 2 poliovirus and also boost immunity against poliovirus types 1 and 3
- This schedule provides the highest immunogenicity and may be carried out using full dose IPV (for both Salk IPV and Sabin-IPV (s-IPV)) or ID fIPV (using only Salk IPV, not sIPV) without loss of immunogenicity.
- Based on local epidemiology, programmatic implications and feasibility of delivery, countries may choose an alternative "early IPV schedule" starting with the first IPV dose at 6 weeks of age (with DTP1/Penta1), and the second IPV dose at 14 weeks (with DTP3/Penta3).
- This alternative schedule offers the advantage of providing early-in-life protection; however, a lower total immunogenicity is achieved. If this schedule is chosen, full dose IPV (for both Salk IPV and sIPV) should be used rather than fIPV due to lower immunogenicity of fIPV at early ages.
- In polio-endemic countries and in countries at high risk for importation and subsequent spread of poliovirus, WHO recommends a bOPV birth dose (zero dose) followed by the primary series of 3 bOPV doses and 2 IPV doses. The zero dose of bOPV should be administered at birth, or within the first week of life, to maximize seroconversion rates following subsequent doses and to induce mucosal protection before enteric pathogens may interfere with the immune response. Additionally, a birth dose of bOPV administered while infants are still protected by maternally-derived antibodies (up to 6 months) may prevent VAPP.
- For infants late in starting the routine immunization schedule (age >3 months) the first IPV dose should be administered at the first immunization contact along with bOPV and the other routinely recommended vaccines.
- Implementation of the infant schedule (3 bOPV doses plus 2 IPV doses) does not replace the need for SIAs. Countries with insufficient routine vaccination coverage that rely on SIAs to increase population immunity should continue using bOPV in SIAs until routine coverage improves, or until the globally coordinated withdrawal of bOPV.
- Countries that delayed the introduction of IPV or experienced stock-outs during 2016–2019 should provide catch-up vaccination as soon as possible to all children who were missed.

Sequential IPV–bOPV

- In countries with high vaccination coverage (e.g. 90–95%) and low importation risk (where neighbouring countries and/or countries that share substantial population movement have a similarly high coverage), an IPV–bOPV sequential schedule can be used when VAPP is a greater concern than the small loss of IPV immunogenicity due earlier administration.
- Where a sequential IPV–bOPV schedule is used, the initial administration of 2 doses of IPV should be followed by ≥2 doses of bOPV to ensure sufficient levels of protection in the intestinal mucosa as well as a decrease in the burden of VAPP.
- For sequential IPV– bOPV schedules, WHO recommends that the first dose of IPV be given starting from 8 weeks of age with an interval of 4–8 weeks before administration of the second IPV dose. This should be followed by at least 2 doses of bOPV separated by 4–8 weeks depending on the risk of exposure to poliovirus in early childhood.

IPV-only

- An IPV-only schedule may be considered in countries in polio-free regions with a very low risk of importation and sustained high routine immunization coverage (DTP3 >90%).
- In the current epidemiological context, WHO recommends that regions and countries be cautious about moving from a combined bOPV plusIPV schedule to an IPV-only schedule in their routine immunization programmes; a gradual approach should be taken by first ensuring high coverage with 2 doses of IPV while still using bOPV.
- A primary 3-dose series of IPV administered beginning at 6 or 8 weeks of age, with a minimum 4 week interval between doses, is recommended.
- If the primary series begins at 6 weeks, a booster dose should be given 6 months or more after the third dose.
- Alternatively, a 2-dose or fractional dose IPV schedule, starting at 14 weeks of age or older, with a second dose 4 months or more later can be considered. This schedule is currently recommended for use after OPV cessation.
- While both options provide high immunogenicity (>90%), the 3 dose primary series provides protection in early infancy.
- Two whole-cell pertussis (wP) hexavalent IPV-containing vaccines are currently licensed and awaiting WHO prequalification. After prequalification, a wP hexavalent vaccine could be administered using the schedules currently recommended for the pentavalent vaccine (i.e. at 8, 12 and 16 weeks, or 6, 10 and 14 weeks, plus a booster dose at least 6 months later).

4 DTP-containing vaccines (Diphtheria, Tetanus and Pertussis)

- Position paper reference: Diphtheria - Weekly Epid. Record (2017, 92:417-436) [pdf 526KB]; Tetanus - Weekly Epid. Record (2017, 92: 53-76) [pdf 636KB]; Pertussis - Weekly Epid. Record (2015, 90: 433-460) [pdf 667KB].
- The need for early infant vaccination with DTP-containing vaccine (DTPCV) is principally to ensure rapid protection against pertussis, because severe disease and death from pertussis is almost entirely limited to the first weeks and months of life.
- A primary series of 3 doses of DTP-containing vaccine is recommended, with the first dose administered as early as 6 weeks of age. Subsequent doses should be given with an interval of at least 4 weeks between doses. The third dose of the primary series should be completed by 6 months of age if possible.
- If either the start or the completion of the primary series has been delayed, the missing doses should be given at the earliest opportunity with an interval of at least 4 weeks between doses.
- 3 booster doses of diphtheria toxoid-containing vaccine should be provided during childhood and adolescence. The diphtheria booster doses should be given in combination with tetanus toxoid using the same schedule, i.e at 12–23 months of age, 4–7 years of age, and 9–15 years of age, using age-appropriate vaccine formulations. Ideally, there should be at least 4 years between booster doses.
- Tetanus - To ensure lifelong protection against tetanus in all people should receive 6 doses (3 primary plus 3 booster doses) of tetanus toxoid-containing vaccine (TTCV) through routine childhood immunization schedules.
- The 3 TTCV booster doses should be given at: 12–23 months of age; 4–7 years of age; and 9–15 years of age. Ideally, there should be at least 4 years between booster doses.
- National vaccination schedules can be adjusted within the age limits specified above to enable programmes to tailor their schedules based on local epidemiology, the objectives of the immunization programme, any particular programmatic issues and to better align tetanus vaccination with the immunological requirements of other vaccines (particularly for pertussis and diphtheria).
- Opportunities for tetanus vaccination may be taken at the second year of life contacts for alternative PCV schedule 2 +1, MCV second dose, and meningococcal A-containing vaccines, as well as pre-adolescence and adolescence contacts including for HPV vaccination.
- To provide and sustain both tetanus and diphtheria immunity throughout the life course and for both sexes, age-appropriate combinations of tetanus and diphtheria toxoids should be used. For children <7 years of age DTwP or DTaP combinations may be used. For children aged 4 years and older Td containing vaccine may be used and is preferred. Link
- From 7 years of age only Td combinations should be used. Age-appropriate combinations

containing pertussis vaccine with low-dose diphtheria antigen are also available.

- If tetanus vaccination is started during adolescence or adulthood, a total of only 5 appropriately spaced doses are required to obtain lifelong protection.
- Pregnant women and their newborn infants are protected from birth-associated tetanus if the mother received either 6 TTCV doses during childhood or 5 doses if first vaccinated during adolescence/adulthood (documented by card, immunization registry and/or history) before the time of reproductive age. Vaccination history should be verified in order to determine whether a dose of TTCV is needed in the current pregnancy.
- WHO confirms its earlier recommendation to shift from the use of single-antigen TT to combinations containing diphtheria toxoid, i.e. DT or Td vaccines, which has not yet been implemented in many countries despite the negligible price differential between TT and DT/Td vaccines. Countries and partners are urged to take steps to accelerate this shift.
- TTCVs can be used in immunocompromised persons including HIV-infected individuals, but the immune response may be lower than in fully immunocompetent persons. All HIV-infected children should be vaccinated against tetanus following the vaccine recommendations for the general population.
- Pertussis vaccine: Both aP-containing and wP-containing vaccines have excellent safety records.
- Available evidence indicates that licensed aP and wP vaccines have equivalent initial effectiveness in preventing disease in the first year of life, but that there is more rapid waning of immunity, and possibly a reduced impact on transmission, with aP relative to wP vaccines.
- National programmes currently administering wP vaccination should continue to use wP vaccines for primary vaccination series. Surveillance and modelling data suggest that the use of aP vaccines may result in a resurgence of pertussis after a number of years.
- National programmes currently using aP vaccine may continue using this vaccine but should consider the need for additional booster doses and strategies to prevent early childhood mortality such as maternal immunization in case of resurgence of pertussis.
- Only aP-containing vaccines should be used for vaccination of persons aged ≥7 years.
- Pertussis containing booster - A booster dose is recommended for children aged 1–6 years, preferably during the second year of life (≥6 months after last primary dose), unless otherwise indicated by local epidemiology; the contact could also be used to catch up on any missed doses of other vaccines. This schedule should provide protection for at least 6 years for countries using wP vaccine. For countries using aP vaccine, protection may decline appreciably before 6 years of age.
- Vaccinating pregnant women and household contacts - Vaccination of pregnant women is likely to be the most cost-effective additional strategy for preventing disease in infants too young to be vaccinated and appears to be more effective and favourable than cocooning.
- National programmes may consider the vaccination of pregnant women with 1 dose of Tdap (in the 2nd or 3rd trimester and preferably at least 15 days before the end of pregnancy) as a strategy additional to routine primary infant pertussis vaccination in countries or settings with high or increasing infant morbidity/ mortality from pertussis.
- Delayed or interrupted DTP-containing series - For children whose vaccination series has been interrupted, the series should be resumed without repeating previous doses. Children aged 1 to < 7 years who have not previously been vaccinated should receive 3 doses of vaccine following a 0, 1, 6 month schedule. Two subsequent booster doses using Td or Tdap combination vaccines are needed with an interval of at least 1 year between doses.
- Health-care workers should be prioritized as a group to receive pertussis vaccine.

5 *Haemophilus influenzae* type b (Hib)

- Position paper reference: Weekly Epid. Record (2013, 88: 413-428) [pdf 209KB].
- The use of Hib vaccines should be part of a comprehensive strategy to control pneumonia including exclusive breastfeeding for six months, hand washing with soap, improved water supply and sanitation, reduction of household air pollution, and improved case management at community and health facility levels.
- WHO recommends that any one of the following Hib immunization schedules may be followed: 3 primary doses without a booster (3p); 2 primary doses plus a booster (2p+1); and 3 primary doses with a booster (3p+1).
- Because serious Hib disease occurs most commonly in children aged between 4 months and 18 months, immunization should start from 6 weeks of age, or as early as possible thereafter.
- The number of primary doses should be set after consideration of the local epidemiology, vaccine presentation (Hib conjugate monovalent vaccine versus Hib conjugate vaccine in combination with other antigens) and how this fits into the overall routine immunization schedule.
- In countries where the peak burden of severe Hib disease occurs in young infants, providing 3 doses of vaccine early in life may confer a greater benefit.
- In some settings (e.g. where the greatest disease morbidity and mortality occur later, or where rate reductions of disease are not fully sustained after the routine use of Hib vaccine), it might be advantageous to give a booster dose by following either a 2p+1 or 3p+1 schedule.
- The interval between doses should be at least 4 weeks if 3 primary doses are given, and at least 8 weeks if 2 primary doses are given. Booster doses should be administered at least six months after completion of the primary series.
- If the vaccination course has been interrupted, the schedule should be resumed without repeating the previous dose. Children who start vaccination late, but are aged under 12 months, should complete the vaccination schedule (e.g. have 3 primary doses or 2 primary doses plus a booster).
- When a first dose is given to a child older than 12 months of age, only one dose is recommended.
- Hib vaccine is not required for healthy children after 5 years of age.
- The Hib conjugate vaccine is contraindicated in people with known allergies to any component of the vaccine. There are no other known contraindications or precautions.

6 Pneumococcal (Conjugate)

- Position Paper Reference: Weekly Epid. Record (2019, 94: 85-104) [pdf 444KB].
- Currently available PCVs are safe and effective and are therefore recommended for the inclusion in childhood immunization programmes worldwide.
- Use of pneumococcal vaccine should be complementary to other disease prevention and control measures, such as appropriate case management, promotion of exclusive breastfeeding for the first 6 months of life and reducing known risk factors such as indoor air pollution and tobacco smoke.
- For administration of PCV to infants, WHO recommends a 3-dose schedule administered either as 2p+1 or as 3p+0, starting as early as 6 weeks of age.
- If the 2p+1 schedule is selected, an interval of ≥8 weeks is recommended between the 2 primary doses the booster dose should be given at 9–18 months of age, according to programmatic considerations; there is no defined minimum or maximum interval between the primary series and the booster dose.

- If the 3p+0 schedule is used, a minimum interval of 4 weeks should be maintained between doses.
- Previously unvaccinated or incompletely vaccinated children who recover from invasive pneumococcal disease (IPD) should be vaccinated according to the recommended age-appropriate regimens. Interrupted schedules should be resumed without repeating the previous dose.
- Both PCV10 and PCV13 have substantial impacts against pneumonia, vaccine-type IPD and NP carriage. The choice of product to be used in a country should be based on programmatic characteristics, vaccine supply, vaccine price, the local and regional prevalence of vaccine serotypes and antimicrobial resistance patterns.
- Once a PCV vaccination programme has been initiated, product switching is not recommended unless there are substantial changes in the epidemiological or programmatic factors that determined the original choice of product, e.g. an increasing burden of serotype 19A. If a series cannot be completed with the same type of vaccine, the available PCV product should be used. Restarting a series is not recommended, even for the primary series.
- Wherever possible, catch-up vaccination at the time of introduction of PCV should be used to accelerate its impact on disease in children aged 1–5 years, particularly in settings with a high disease burden and mortality. If there is limited availability of vaccine or of financial resources for catch-up vaccination, the youngest children (e.g. <2 years of age) should be prioritized to receive catch-up doses of PCV because of their higher risk for pneumococcal disease.
- Catch-up vaccination can be done with a single dose of vaccine for children ≥24 months.
- Unvaccinated children aged 1–5 years who are at high risk for pneumococcal infection because of underlying medical conditions, such as HIV infection or sickle-cell disease, should receive at least 2 doses separated by at least 8 weeks.
- HIV-positive infants and pre-term neonates who have received their 3 primary vaccine doses before 12 months of age may benefit from a booster dose in the second year of life.
- Co-administration for programmatic reasons appears to be acceptable.
- WHO does not currently have recommendations on the use of PCV in individuals over 5 years of age.
- For considerations for pneumococcal vaccination in older adults see concept note: Weekly Epid. Record (2021, 96 (23), 217 – 228) [pdf 373KB]
- Introduction of PCV into national childhood immunization programmes and measures to sustain high coverage in children should be prioritized over initiating a pneumococcal vaccination programme for older adults.
- In countries that have a mature childhood pneumococcal immunization programme, decisions about initiating such a programme in adults, using either PPV23 or PCV13, should take into account the local disease burden and cost-effectiveness considerations.

7 Rotavirus

- Position paper reference: Weekly Epid. Record (2021, 96: 301-320) [pdf 515KB].
- Rotavirus vaccines should be included in all national immunization programmes.
- The use of rotavirus vaccines should be part of a comprehensive strategy to control diarrhoeal diseases with the scaling up of both prevention (promotion of early and exclusive breastfeeding, handwashing, improved water supply, and sanitation) and treatment packages (low osmolarity ORS and zinc).
- The first dose of rotavirus vaccine be administered as soon as possible after 6 weeks of age.
- If a child <24 months of age misses a rotavirus dose or series for any reason, WHO recommends rotavirus vaccination for that child. Because of the typical age distribution of RVGE, rotavirus vaccination of children >24 months of age is not recommended.
- The rotavirus vaccination series for each child should be completed with the same product whenever feasible. However, if the product used for a prior dose is unavailable or unknown, the series should be completed with any available licensed product.
- For a mixed series or a series with any unknown vaccine products, a total of 3 doses of rotavirus vaccine should be administered for a complete vaccination series.
- Rotavirus vaccinations may be administered simultaneously with other vaccines of the childhood immunization programme.
- WHO prequalified rotavirus vaccines are safe and well tolerated. A small potential risk of intussusception after rotavirus vaccination remains.
- Rotavirus vaccine should not be given to children with prior history of intussusception, severe allergic reaction (e.g. anaphylaxis) after a previous dose, or severe immunodeficiency, including severe combined immunodeficiency.
- Precautions include altered immunocompetence other than severe combined immunodeficiency, chronic gastrointestinal disease, and spina bifida or bladder exstrophy. Vaccination may be postponed in case of ongoing acute gastroenteritis or fever with moderate to severe illness.

8 Measles

- Position paper reference: Weekly Epid. Record (2017, 92:205-228) [pdf 600KB].
- Reaching all children with 2 doses of measles vaccine should be the standard for all national immunization programmes. In addition to the first routine dose of MCV1, all countries should add a second routine dose of MCV2 to their national immunization schedules regardless of the level of MCV1 coverage.
- In countries with ongoing transmission in which the risk of measles mortality remains high, MCV1 should be given at age 9 months. MCV2 should be given between 15-18 months, as providing MCV2 in the 2nd year of life reduces the rate of accumulation of susceptible children and the risk of an outbreak. The minimum interval between MCV1 and MCV2 is 4 weeks.
- Because many cases of measles occur in children aged >12 months who have not been vaccinated, routine delivery of MCV1 should not be limited to infants aged 9–12 months and routine delivery of MCV2 should not be limited to infants 15 to 18 months of age. Every opportunity (e.g. when children come into contact with health services) should be taken to vaccinate all children that missed one or both MCV routine doses, particularly those under 15 years of age. Policies which prohibit use of vaccine in children >1 year of age, older children and teenagers should be changed to allow these individuals to be vaccinated.
- In countries with low levels of measles transmission (i.e. those that are near elimination or verified as having eliminated endemic measles virus transmission) and therefore the risk of measles virus infection among infants is low, MCV1 may be administered at 12 months of age to take advantage of the higher seroconversion rates achieved at this age. In these countries, the optimal age for delivering MCV2 is based on programmatic considerations to achieve the highest coverage of MCV2 and, hence, the highest population immunity. Administration of MCV2 at 15-18 months of age ensures early protection of the individual, slows accumulation of susceptible young children, and may correspond to the schedule for other routine immunizations (for example, a DTP-containing booster, PCV, or meningococcal vaccines). This measure also supports the establishment of a policy on immunization and other health interventions in the second year of life. If MCV1 coverage is high (>90%) and school enrolment is high (>95%), administration of routine MCV2 at school entry may prove an effective strategy for achieving high coverage and preventing outbreaks in schools.
- For programmatic reasons (e.g. to reduce cold storage needs and vaccine wastage), it is recommended that the same vaccine formulation is used for both routine doses of MCV.

- In the following situations, a supplementary dose of MCV should be given to infants from 6 months of age: (1) during a measles outbreak as part of intensified service delivery; (2) during campaigns in settings where the risk of measles among infants < 9 months of age remains high (e.g. in endemic countries experiencing regular outbreaks); (3) for internally displaced populations and refugees, and populations in conflict zones; (4) for individual infants at high risk of contracting measles (e.g. contacts of known measles cases or in settings with increased risk of exposure during outbreaks such as day-care facilities); (5) for infants travelling to countries experiencing measles outbreaks; (6) for infants known to be HIV-infected or exposed (i.e. born to an HIV-infected woman).
- MCV administered before 9 months of age should be considered a supplementary dose and recorded on the child's vaccination record as "MCV0". Children who receive MCV0 should also receive MCV1 and MCV2 at the recommended ages according to the national schedule.
- Given the severe course of measles in patients with AIDS, measles vaccination should be routinely administered to potentially susceptible, asymptomatic HIV infected children and adults. Vaccination may even be considered for those with symptomatic HIV infection if they are not severely immunosuppressed according to conventional definitions. In areas where there is a high incidence of both HIV infection and measles, an initial dose of MCV may be offered as early as age 6 months (recorded as MCV0). The 2 routine doses of MCV (MCV1 and MCV2) should then be administered to these children according to the national immunization schedule.
- An additional dose of MCV should be administered to HIV-infected children receiving HAART following immune reconstitution If CD4+ T lymphocyte counts are monitored, an additional dose of MCV should be administered when immune reconstitution has been achieved, e.g. when the CD4+ T lymphocyte count reaches 20–25%. Where CD4+ T lymphocyte monitoring is not available, children should receive an additional dose of MCV 6–12 months after initiation of HAART.
- A supplementary dose of MCV (recorded as MCV0) should be considered for infants known to be exposed (i.e. born to an HIV-infected woman) or soon after diagnosis of HIV infection in children older than 6 months who are not receiving HAART and for whom the risk of measles is high, with the aim of providing partial protection until they are revaccinated after immune reconstitution with HAART.
- Mild concurrent infections are not a contraindication to vaccination. As a precautionary measure, measles vaccine – alone or in combination with other vaccines – should be avoided during pregnancy. MCVs should not be given to individuals with a history of anaphylactic reactions or severe allergic reactions to any component of the vaccine (e.g. neomycin or gelatin) or those with any form of severe immunosuppression.
- As a general rule, live vaccines should be given either simultaneously or at intervals of 4 weeks. An exception to this rule is OPV, which can be given at any time before or after measles vaccination without interference in the response to either vaccine.

9 Rubella

- Position paper reference: Weekly Epid. Record (2020, 95: 301-324) [pdf 772KB].
- As of September 2024, the requirement that countries attain 80% MCV coverage in routine immunization or campaigns before RCV introduction has been lifted. This component of the Rubella Position Paper will be amended in the next update; in the meantime, the new policy recommendation can be found in the Meeting of the Strategic Advisory Group of Experts on Immunization, September 2024: conclusions and recommendations
- All countries that have not yet introduced RCV should plan to do so.
- It is recommended that RCV be provided in combination with measles vaccine, and combined measles and rubella vaccine should be used for all immunization activities once RCV is introduced, including routine immunization, supplementary immunization activities (SIAs) and outbreak response.
- Since measles elimination requires ≥95% coverage, the goal for rubella vaccination coverage should also be ≥95%.
- The recommended vaccination strategy is to begin with an MR vaccination campaign targeting both sexes and a wide age range (e.g. 9 months–15 years), based on the susceptibility profile by birth cohort when possible, followed immediately by introduction of MR or MMR vaccine into the routine immunization programme. The campaign should target males as well as females in order to reduce the likelihood of creating immunity gaps.
- The first dose of RCV can be delivered at 9 or 12 months, depending on the level of measles virus transmission. RCV should be used in all subsequent follow-up campaigns.
- RCV's can be administered concurrently with inactivated vaccines.
- Live vaccines should be given either simultaneously with RCV's, or at least 4 weeks apart. An exception to this is oral polio vaccine, which can be given at any time before or after RCV's without interfering in the response to either vaccine. WHO recommends co-administration of RCV and YF vaccines.
- Rubella vaccination should be avoided in pregnancy because of a theoretical (but never demonstrated) risk of teratogenic outcomes. Women planning a pregnancy are advised to avoid pregnancy for 1 month after rubella vaccination.
- WHO recommends that people who receive blood products wait at least 3 months before vaccination with RCV, and, if possible, avoid administration of blood products for 2 weeks after vaccination.

10 Human Papillomavirus (HPV)

- Position paper reference: Weekly Epid. Record (2022, 97: 645-672) [pdf 590KB].
- HPV vaccines should be introduced as part of a coordinated and comprehensive strategy to prevent cervical cancer and other diseases caused by HPV. This strategy should include education about reducing behaviours that increase the risk of acquiring HPV infection, and information about screening, diagnosis and treatment of precancerous lesions, cancer and risk factors. Access to quality screening and treatment services should be improved.
- The priority purpose of HPV immunization is the prevention of cervical cancer, which accounts for 82% of all HPV-related cancers. The 2020 WHO Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem WHO recommends that HPV vaccines should be included in all national immunization programmes and should reach 90% of all girls by age 15 by 2030. Prevention of cervical cancer is best achieved through the immunization of girls before they become sexually active.
- The WHO-recommended primary target population for HPV vaccination is girls aged 9–14 years Prevention of cervical cancer is best achieved through the immunization of girls before they become sexually active.
- Catch-up vaccination of multi-aged cohorts (MACs) of girls aged between 9 and 18 years at the time of introducing the HPV vaccine results in faster and greater population impact, as a result of increased direct and herd protection. This approach is cost-effective, offers opportunities for economies of scale in delivery and makes programmes more resilient to any interruptions in vaccination.
- Vaccination of secondary target populations, e.g. females aged ≥15 years, boys, older males or MSM, is recommended only if this is feasible and affordable, and does not divert resources from vaccination of the primary target population or effective cervical cancer screening programmes.
- All currently licensed bivalent, quadrivalent and nonavalent HPV vaccines have excellent safety profiles and are highly efficacious or have met immunobridging standards.

- The current evidence supports the recommendation that a 2-dose schedule be used in the primary target group from 9 years of age and for all older age groups for which HPV vaccines are licensed.
- The minimum interval between first and second dose is 6 months. A 12-month schedule results in higher GMTs and is suggested for programmatic and efficiency reasons.
- There is no maximum recommended interval between doses and longer intervals – up to 3 or 5 years – can be considered if useful from a programme perspective.
- Alternative single-dose schedule: As an off-label option, a single-dose schedule can be used in girls and boys aged 9–20 years. Current evidence suggests that a single dose has comparable efficacy and duration of protection as a 2-dose schedule and may offer programme advantages, be more efficient and affordable, and contribute to improved coverage. From a public health perspective, the use of a single dose schedule can offer substantial benefits that outweigh the potential risk of a lower level of protection if efficacy wanes over time, although there is no current evidence of this.
- Individuals known to be immunocompromised or HIV-infected (regardless of age or antiretroviral therapy status) should receive at least two HPV vaccine doses (minimum 6 months interval) and, where possible, three doses.
- HPV vaccines can be co-administered with other non-live and live vaccines using separate syringes and different injection sites. Co-administration of a booster dose of tetanus-diphtheria (Td) vaccination should be considered to improve programme efficiency and avoid missed opportunities to receive needed vaccinations.
- As a precaution HPV vaccine is not recommended in pregnancy. If pregnancy occurs following the first dose of vaccination, the subsequent dose should be delayed until after the pregnancy. Termination of pregnancy is not indicated if vaccination was carried out inadvertently during pregnancy. Breastfeeding is not a contraindication for HPV vaccination.

11 Japanese Encephalitis (JE)

- Position paper reference : Weekly Epid. Record (2015, 90: 69-88) [pdf 950 KB].
- JE vaccination should be integrated into national immunization schedules in all areas where JE is recognized as a public health priority.
- The most effective immunization strategy in JE endemic settings is a one-time campaign in the primary target population, as defined by local epidemiology (typically children aged <15 years), followed by incorporation of JE vaccine into the routine childhood immunization programme.
- The following vaccine dosing schedules and age of administration are recommended. The need for a booster dose in endemic settings has not been clearly established for any of the vaccines listed below:
    - *Inactivated Vero cell-derived vaccine*: Primary series according to manufacturer's recommendations (these vary by product), generally 2 doses at 4-week intervals starting the primary series at ≥6 months of age in endemic settings
    - *Live attenuated vaccine*: Single dose administered at ≥8 months of age
    - *Live recombinant vaccine*: Single dose administered at ≥9 months of age
- Preferably, inactivated mouse brain-derived vaccines should be replaced by the newer generation JE vaccines discussed in this position paper. Inactivated mouse brain-derived vaccines may continue to play a role in combatting JE in some countries, but overall these products have a less favourable safety profile due to their increased reactogenicity compared to newer JE vaccines. Other disadvantages include the variability of manufacturing, the cost, the higher number of doses required and the need for boosters.
- Despite a lack of comprehensive immunogenicity/effectiveness and safety data for all possible combinations of JE and other routine vaccines, co-administration for programmatic reasons seems acceptable, even in the context of mass campaigns. As a general rule, any live vaccine may be given either simultaneously or at an interval of 4 weeks.
- Inactivated JE vaccine can be used in immunocompromised persons including HIV-infected individuals, but the immune response may be lower than in fully immunocompetent persons. Inactivated Vero cell-derived vaccines should be used preferentially over live attenuated or live recombinant vaccines in immunocompromised persons. HIV testing is not a prerequisite for vaccination.
- If the JE risk is sufficient to warrant vaccination of pregnant women, inactivated Vero cell-derived vaccines should be used preferentially over live attenuated or live recombinant vaccines based on the general precautionary principle against using live vaccines in pregnant women especially if alternative types of vaccines are available. Pregnancy testing is not a prerequisite for JE vaccination. Inadvertent administration of live attenuated or live recombinant JE vaccine to a pregnant woman is not an indication for termination of the pregnancy.

12 Yellow Fever

- Position paper reference: Weekly Epid. Record (2013, 88: 269-284) [pdf 1.24MB].
- WHO recommends that all endemic countries should introduce YF vaccine into their routine immunization programmes.
- A single dose of YF vaccine is sufficient to confer sustained life-long protective immunity against YF disease; a booster dose is not necessary.
- It is recommended that YF vaccine be given to children at age 9-12 months at the same time as the measles vaccine.
- The vaccine is contraindicated in children aged <6 months and is not recommended for those aged 6-8 months, except during epidemics when the risk of infection with the YF virus is very high. Other contraindications for YF vaccination are severe hyper-sensitivity to egg antigens and severe immunodeficiency.
- Preventive mass vaccination campaigns are recommended for inhabitants of areas at risk of YF where there is low vaccination coverage. Vaccination should be provided to everyone aged ≥ 9 months, in any area with reported cases. Noting that YF is a live vaccine, a risk-benefit assessment should be undertaken for all pregnant and lactating women.
- Vaccine should be offered to all unvaccinated travelers aged ≥ 9 months, travelling to and from at-risk areas, unless they belong to the group of individuals for whom YF vaccination is contraindicated.
- YF vaccine may be administered simultaneously with other vaccines. As a general rule, any live vaccine may be given either simultaneously or at an interval of 4 weeks. Oral polio vaccine may be given at any time in relation to YF vaccination.

13 Tick-Borne Encephalitis (TBE)

- Position paper reference: Weekly Epid. Record (2011, 86: 241-256) [pdf 318KB].
- Since the incidence of tick-borne encephalitis may vary considerably between and even within geographical regions, public immunization strategies should be based on risk assessments conducted at country, regional or district level, and they should be appropriate to the local endemic situation. Therefore, establishing case reporting of the disease is essential before deciding on the most appropriate preventive measures to be taken.
- In areas where the disease is highly endemic (that is, where the average prevaccination incidence of clinical disease is ≥5 cases/100 000 population per year), implying that there is a

high individual risk of infection, WHO recommends that vaccination be offered to all age groups, including children.

- Because the disease tends to be more serious in individuals aged >50–60 years this age group constitutes an important target for immunization.
- Where the prevaccination incidence of the disease is moderate or low (that is, the annual average during a 5-year period is <5/100 000) or is limited to particular geographical locations or certain outdoor activities, immunization should target individuals in the most severely affected cohorts.
- People travelling from non-endemic areas to endemic areas should be offered vaccination if their visits will include extensive outdoor activities.
- Vaccination against the disease requires a primary series of 3 doses; those who will continue to be at risk should probably have ≥1 booster doses.
- Within the considerable range of acceptable dose intervals, the relevant national authorities should select the most rational primary schedule for their national, regional or district immunization programmes.
- Although there is a strong indication that the spacing of boosters could be expanded considerably from the intervals currently recommended by the manufacturers (every 3-5 years), the evidence is still insufficient for a definitive recommendation on the optimal frequency and number of booster doses. Countries should therefore continue to recommend the use of vaccines in accordance with local disease epidemiology and current schedules until more definitive information becomes available.
- For the vaccines manufactured in Austria and Germany (FSME-Immun and Encepur) that can be given starting from > 1year of age an interval of 1–3 months is recommended between the first 2 doses, and 5–12 months between the second and third doses. When rapid protection is required, for example for people who will be travelling to endemic areas, the interval between the first 2 doses may be reduced to 1–2 weeks.
- With the vaccines manufactured in the Russian Federation (TBE-Moscow and EnceVir) the recommended intervals are 1–7 months between the first 2 doses, and 12 months between the second and third doses. Booster doses are recommended every 3 years for those at continued risk of exposure.
- The currently recommended booster interval should be maintained until more data have been obtained on the duration of protection induced by the Russian vaccines.
- Regardless of the duration of the delay, interrupted schedules should be resumed without repeating previous doses.

14 Typhoid

- Position paper reference: Weekly Epid. Record (2018, 93: 153-172) [pdf 297KB].
- Typhoid vaccination programmes should be implemented in the context of other efforts to control the disease, including health education, water quality and sanitation improvements, and training of health professionals in diagnosis and treatment.
- Among the available typhoid vaccines, TCV is preferred at all ages in view of its improved immunological properties, use in younger children and expected duration of protection. Countries may consider the routine use of VIPS vaccine in individuals 2 years and older, and Ty21a vaccine for individuals more than 6 years of age.
- TCV - for infants and children from 6 months of age and in adults up to 45 years. Administration of TCV at the same time as other vaccine visits at 9 month of age or in the second year of life is encouraged. ViPS – single dose from 2 years of age. Ty21a – 3-doses to be administered orally every second day from 6 years of age.
- Catch-up vaccination with TCV up to 15 years of age is recommended when feasible and supported by epidemiological data.
- Typhoid vaccination is recommended in response to confirmed outbreaks of typhoid fever and may be considered in humanitarian emergency settings depending on the risk assessment in the local setting.
- The potential need for revaccination with TCV is currently unclear. Revaccination is recommended every 3 years for VIPS, and every 3-7 years for Ty21a.
- Use of the live attenuated Ty21a vaccine during pregnancy should be avoided because of theoretical safety concerns about potential adverse effects.

15 Cholera

- Position paper reference: Weekly Epid. Record (2017, 92:477-500) [pdf 676KB].
- Appropriate case management, WaSH interventions, surveillance and community mobilization remain the cornerstones of cholera control. Vaccination should be implemented in relevant settings as part of comprehensive cholera control strategies or while other activities are being developed.
- WC vaccines (Shanchol, Euvchol, and mORCVAX) 2 doses should be given 14 days apart to individuals ≥1 year of age. For WC-rBS vaccine (Dukoral) 3 doses should be given to children 2-5 years of age, and 2 doses to children aged ≥6 years and adults, with an interval of 1-6 weeks between doses in both groups.
- Revaccination is recommended where there is continued risk of *V. cholerae* infection. For WC vaccines revaccination is recommended after 3 years. For WC-rBS vaccine: children age 2-5 years revaccination is recommended within 6 months. If less than 6 months have passed, 1 dose for revaccination. If more than 6 months have passed, the primary series of 3 doses should be repeated. For those aged ≥6 years of age, if less than 2 years have passed, 1 dose for revaccination. If more than 2 years have passed, the primary series of 2 doses should be repeated.
- In cholera-endemic countries, vaccination of the entire population (throughout a country regardless of risk) is usually not warranted. Vaccination policies and strategies should be guided by an assessment of the risk of cholera and targeted to cholera hotspots. Strategies targeting specific age groups at higher risk of disease may be considered.
- For control of cholera outbreaks vaccination should be considered to help prevent the spread to new areas. For vaccination campaigns, a single-dose strategy using WC vaccines (Shanchol, Euvchol or mORCVAX) could be considered in areas experiencing cholera outbreaks.
- During humanitarian emergencies with a risk of cholera, but without a current cholera outbreak, vaccination with OCV should be considered as an additional preparedness measure for outbreak prevention, depending on the local infrastructure (capacity to organize a vaccination campaign).
- Pregnant and lactating women and HIV infected individuals should be included in OCV campaigns since there is a high potential benefit and minimal risks.

16 Meningococcal

- Position paper reference: Weekly Epid. Record (2011, 86: 521-540) [pdf 1.1MB] and Update for MenA conjugate Weekly Epid Record (2015, 90: 57-68) [pdf 852KB].
- Conjugate vaccines are preferred over polysaccharide vaccines due to their potential for herd protection and their increased immunogenicity, particularly in children <2 years of age.
- Both conjugate and polysaccharide vaccines are efficacious and safe when used in pregnant women.

- MenA conjugate vaccine (5µg) a 1-dose schedule is recommended at 9-18 months of age based on local programmatic and epidemiologic considerations. The vaccine should be administered by deep intramuscular injection, preferably in the anterolateral aspect of the thigh. There is no reason to expect interference when co-administered with other vaccines. The need for a booster dose has not been established.
- If in a specific context there is a compelling reason to vaccinate infants younger than 9 months, a 2-dose schedule should be used starting at 3 months of age, with an interval of at least 8 weeks between doses.
- For monovalent MenC conjugate vaccine one single intramuscular dose is recommended for children aged ≥12 months, teenagers and adults. Children 2-11 months require 2 doses administered at an interval of a least 2 months and a booster about 1 year after. If the primary series is interrupted, vaccination should be resumed without repeating the previous dose.
- Quadrivalent conjugate vaccines (A,C,W135,Y-D and A,C,W135,Y-CRM) should be administered as one single intramuscular dose to individuals ≥ 2 years. A,C,W135,Y-D is also licensed for children 9-23 months of age, and given as a 2-dose series, 3 months apart beginning at age 9 months. If the primary series is interrupted, vaccination should be resumed without repeating the previous dose.
- Meningococcal polysaccharide vaccines are less, or not, immunogenic in children under 2 years of age.
- Meningococcal polysaccharide vaccines can be used for those ≥ 2 years of age to control outbreaks in countries where limited economic resources or insufficient supply restrict the use of meningococcal conjugate vaccines. Polysaccharide vaccines should be administered to individuals ≥ 2 years old as one single dose. One booster 3-5 years after the primary dose may be given to persons considered to be a continued high risk of exposure, including some health workers. See position paper for details.

17 Hepatitis A

- Position paper reference: Weekly Epid. Record (2022, 97: 493-512) [pdf 518.2 KB].
- Vaccination against hepatitis A should be part of a comprehensive plan for the prevention and control of viral hepatitis, including measures to improve safe drinking-water, sanitation and hygiene (such as hand washing) and measures for outbreak control.
- WHO recommends that vaccination against hepatitis A virus be introduced into national immunization schedules for individuals aged ≥12 months, if indicated on the basis of: i) an increasing trend over time of acute hepatitis A disease, including severe disease, among older children, adolescents or adults; ii) changes in the endemicity from high to intermediate; and iii) considerations of cost- effectiveness.
- In highly endemic countries, most individuals are asymptomatically infected with HAV in childhood, which prevents clinical hepatitis A in adolescence and adulthood. In these countries, large-scale hepatitis A vaccination programmes are not routinely recommended, because they carry a risk of a paradoxical increase in disease incidence in unvaccinated people. If a highly endemic country nevertheless wishes to consider largescale vaccination, it is essential to undertake a thorough prior analysis of risks vs benefits and ensure a high vaccination coverage to avoid this risk.
- Groups at higher risk of hepatitis A should be vaccinated. Such groups include travellers from low-endemic countries to areas of intermediate or high endemicity, men who have sex with men, at-risk occupational groups (such as sewage workers or laboratory personnel handling hepatitis A virus specimens), people who inject drugs, people who experience homelessness, migrants, refugees, incarcerated persons; and patients with chronic liver disease or people living with HIV, particularly in countries with low and very low endemicity.
- Countries with improving socioeconomic status may rapidly move from high to intermediate hepatitis A endemicity, rendering a larger proportion of the adolescent and/or young adult population susceptible to HAV infection. In such countries, large-scale hepatitis A vaccination in early childhood is likely to be cost-effective and is therefore recommended. When introducing the vaccine, these countries should consider the need for catch-up immunization based on age-specific seroprevalence rates or other markers of susceptibility.

Inactivated vaccine:

- For children, inactivated hepatitis A vaccines can be given as a single- or 2-dose schedule,and administered intramuscularly. With a 2-dose schedule, the first dose should be given starting from age ≥12 months. The interval between doses is flexible, from 6 months up to 4–5 years or more, but is usually 6–18 months. Data on vaccine effectiveness, antibody persistence, and modelling on long-term seroprotection indicate that an off-label, single dose schedule is equivalent to the two-dose schedule in children, in addition to being less costly and easier to implement.
- For adults aged >40 years, vaccination with inactivated vaccines using the 2-dose schedule is preferred since there is insufficient evidence on the immunogenicity and long-term protection from a single dose in this age group.
- Inactivated hepatitis A vaccines produced by different manufacturers, including combined hepatitis A vaccines, are interchangeable.
- For immunocompromised individuals, until further experience has been obtained with a single-dose schedule, a 2-dose schedule of inactivated vaccine is recommended. Inactivated hepatitis A vaccines should also be considered for use in pregnant women at risk of HAV infection.

Live attenuated vaccine:

- Live attenuated vaccines are licensed for individuals aged ≥18 months and are administered as a single subcutaneous dose.
- Hepatitis A vaccines can be administered simultaneously with any of the vaccines routinely used in childhood immunization programmes.

18 Rabies

- Position paper reference: Weekly Epid. Record (2018, 93: 201-220) [pdf 370 KB].
- Production and use of nerve-tissue vaccines should be discontinued and replaced by vaccines based on RABV grown in cell culture or embryonated eggs (CCEEVs).
- There are two main immunization strategies for the prevention of human rabies: (i) PEP which includes extensive and thorough wound washing at the RABV-exposure site, together with RIG administration if indicated, and the administration of a course of several doses of rabies vaccine; (ii) PrEP which is the administration of several doses of rabies vaccine before exposure to RABV. PrEP is recommended for individuals at high risk of RABV exposure. These include sub-populations in highly endemic settings with limited access to timely and adequate PEP, individuals at occupational risk, and travellers who may be at risk of exposure.
- For both PEP and PrEP, vaccines can be administered by either the ID or IM route. One ID dose is 0.1 mL of vaccine; one IM dose is 0.5 mL or 1.0 mL depending on the product.
- The indication and procedure for PEP depend on the type of contact with the suspected rabid animal and immunization status of the patient. For category I exposures, no PEP is required; for category II, immediate vaccination is recommended; for category III, immediate vaccination is recommended, and administration of RIG, if indicated.
- PrEP schedule: 2-site ID vaccine administered on days 0 and 7. If IM administration is used, WHO recommends a 1-site IM vaccine administration on days 0 and 7.
- If any doses are delayed, vaccination should be resumed, not restarted. A change in the route of administration or in vaccine product during a PEP or PrEP course is acceptable if such a change

is unavoidable.

- No further PrEP booster doses following a primary series of PrEP or PEP are required for individuals living in, or travelling to, high-risk areas.
- Professionals who are at continual or frequent risk of exposure through their activities should have regular serological monitoring. If VNA levels fall to <0.5 IU/mL, a 1-site ID or a 1-site IM PrEP booster vaccination is recommended. If serological testing is not available for those at continual or frequent occupational risk, a periodic 1-dose (ID or IM) PrEP booster vaccination can be considered based on the assessment of relative risk.

19 Dengue (TAK-003)

- Position paper reference: Weekly Epid. Record (2024, 99: 203-224) [pdf 403KB].
- Vaccination against dengue should be viewed as part of an integrated strategy to control the disease, including vector control, proper case management, community education, and community engagement. TAK-003 does not prevent all cases of dengue.
- WHO recommends that countries consider introducing TAK-003 into their routine immunization programmes in geographical locations where high transmission intensity of dengue poses a significant public health problem. Many countries may have a heterogeneous geographical distribution of dengue transmission intensity and could consider targeted subnational introduction.
- The use of a pre-vaccination screening strategy to limit vaccination to seropositive persons is not recommended in settings with high dengue transmission as this would substantially reduce the public health impact of vaccination and increase programmatic costs.
- WHO recommends the use of TAK-003 in children aged 6–16 years in settings with high dengue transmission intensity. Within this age range, the vaccine should optimally be initiated about 1–2 years prior to the age specific peak incidence of dengue-related hospital admissions, although programmatic alignment with the administration of other school-based vaccination and health interventions is also an important consideration.
- Catch-up vaccination can also be considered for other age groups within the 6–16 year age range at the time of vaccine introduction.
- WHO does not currently recommend use of TAK-003 in children aged <6 years because of the low efficacy in this age group. Furthermore, the dengue seropositivity rate in this age group is generally low, even in high dengue transmission settings.
- The vaccine is recommended as a 2-dose schedule with a minimum interval of 3 months between doses. It is not advised to reduce the interval between doses.
- If the second dose is delayed for any reason, it is not necessary to restart the series and the second dose should be administered at the first available opportunity.
- A booster dose is not recommended.
- TAK-003 may be co-administered with other inactivated, subunit, or mRNA vaccines, except for live vaccines, for which more data are required.
- TAK-003 is not recommended during pregnancy and pregnancy should be avoided for at least 1 month following vaccination. Inadvertent vaccination of a pregnant person is not a reason to terminate the pregnancy.
- The vaccine is contraindicated for mothers during breastfeeding. TAK-003 is contraindicated in persons with congenital or acquired immune deficiency, including those receiving immunosuppressive therapies such as chemotherapy or high doses of systemic corticosteroids within 4 weeks prior to vaccination, as with other live attenuated vaccines. The vaccine is also contraindicated in individuals with symptomatic HIV infection or with asymptomatic HIV infection associated with evidence of impaired immune function.
- Persons with comorbidities, such as sickle cell anaemia, diabetes, hypertension, or underlying comorbidities that may result in bleeding tendencies (e.g. ulcerative colitis), are at higher risk of more severe disease outcomes when infected with dengue virus. Persons with such comorbidities are generally older. Persons with comorbidities who live in dengue-endemic countries could be offered vaccination, even if they fall outside the recommended age range for programmatic use (i.e. 6–16 years), provided that a substantial country-specific burden of severe dengue outcomes in these subpopulations has been documented. Until more data on efficacy-safety profiles become available, WHO recommends the lower age limit of 6 years, and the upper limit of 60 years for vaccination.

20 Malaria

- Position paper reference: Weekly Epid. Record (2024, 99: 225-248) [pdf 461KB].
- Malaria vaccines should be provided as part of a comprehensive malaria control strategy.
- WHO recommends the use of malaria vaccines for the prevention of P. falciparum malaria in children living in malaria endemic areas, prioritizing areas of moderate and high transmission. However, countries may also consider providing the vaccine in low transmission settings.
- Malaria vaccines should be provided in a 4-dose schedule in children from 5 months of age.
- The minimum interval between any doses is 4 weeks; however, to achieve prolonged protection, the fourth dose should be given 6–18 months after the third dose.
- To improve coverage, there can be flexibility in the timing of the fourth dose, including by aligning it with vaccines given in the second year of life. Alternatively, because vaccine efficacy is highest in the first months after vaccination, the fourth dose can be given just prior to seasonal peaks in malaria transmission to optimize vaccine efficacy.
- A fifth dose, given one year after the fourth dose, may be provided in areas of highly seasonal transmission and may be considered in other areas – depending on a local assessment of feasibility and cost-effectiveness – where a significant malaria risk remains for children.
- At the time of vaccine introduction, catch-up vaccination can be considered in children up to 5 years of age, subject to local epidemiology and age of high risk, feasibility, affordability and vaccine availability.
- In areas with highly seasonal malaria transmission or perennial malaria transmission with seasonal peaks, countries may consider providing the vaccine using an age-based or seasonal approach. Alternatively, countries could consider a hybrid of these approaches, giving the first 3 doses through age-based administration and subsequent annual doses seasonally.
- The vaccination series should be completed with the same product whenever feasible. If the product used for a prior dose is unavailable or unknown, the series should be completed with either of the available WHO-recommended malaria vaccines.
- Malaria vaccines may be administered simultaneously with other childhood vaccines.
- Malaria vaccines should not be given to anyone who has experienced a severe allergic reaction after a previous hepatitis B vaccination or malaria vaccine dose or vaccine component.
- Malaria vaccines are not recommended for use in adults (including health workers and pregnant persons). The vaccine is not indicated for travelers, who should use chemoprophylaxis and vector control methods to prevent malaria when travelling to endemic settings.

21 Mumps

- Position paper reference: Weekly Epid. Record (2024, 82: 49-68) [pdf 311KB].
- Recommended for use in countries who are able to achieve sustained high coverage of MR vaccination, and attain measles and rubella control and/or elimination levels.
- If implemented, mumps vaccine should be administered with measles and rubella as MMR or MMRV combination vaccine and follow the same schedule.

22 Seasonal Influenza (Inactivated Vaccine)

- Position paper reference: Weekly Epid. Record (2022, 97: 185-208) [pdf 600.KB].
- WHO recommends that all countries should consider implementing seasonal influenza immunization programmes. Having a strong influenza programme in place has been shown to be beneficial for the response to an influenza pandemic.
- For countries considering the initiation or expansion of programmes for seasonal influenza vaccination, WHO recommends that the following target groups should be considered for vaccination (not in order of priority): health workers, individuals with comorbidities and underlying conditions, older adults and pregnant women.
- Depending on national disease goals, capacity and resources, epidemiology, national policies and priorities, and disease burden, countries may consider additional (sub)populations for vaccination, such as children. Other groups to be considered for vaccination include people at high risk of severe influenza living in congregate-living settings, such as prisons, refugee camps and group homes. Programmes should pay particular attention to vaccine equity by considering disadvantaged populations and indigenous populations with a high burden of disease.
- A single dose is appropriate for those ≥ 9 years of age and healthy adults.
- Children aged 6 months -8 years should receive 2 doses at least 4 weeks apart.
- Those who have previously been vaccinated at least once should subsequently receive 1 annual dose, as should children and adolescents aged 9 years or over and healthy adults.
- Live attenuated influenza vaccines (LAIVs) are currently not recommended for children under 2 years of age and adults, including older adults and those with comorbidities, because VE has not been consistently demonstrated in these age groups. Because LAIV is a live-virus vaccine and data on its administration to pregnant women and the associated maternal and fetal risks are limited, LAIV is also not recommended during pregnancy.
- Inactivated influenza vaccine is safe to give throughout pregnancy.
- Co-administration of influenza vaccine, including with COVID-19 or live vaccines is acceptable. When 2 vaccines are administered at the same visit, the contralateral limb should be used.

23 Varicella

- Position paper reference: Weekly Epic. Record (2014, 89: 265-288) [pdf 889KB].
- Countries where varicella is an important public health burden could consider introducing varicella vaccination in the routine childhood immunization programme. However, resources should be sufficient to ensure reaching and sustaining vaccine coverage ≥ 80%. Decision-making on childhood varicella vaccination should also include consideration of the possible impact on herpes zoster.
- Depending on the goal of the vaccination programme, 1-2 doses should be given with the first dose administered at 12-18 months of age. The minimum interval between doses should be as recommended by the manufacturer, ranging from 4 weeks to 3 months.
- Countries with a high average age (≥15 years) of acquisition of infection could consider alternative vaccination strategies such as vaccination of adolescents and adults without evidence of varicella immunity. This strategy requires a 2-dose schedule.
- Varicella vaccination is contraindicated during pregnancy and pregnancy should be delayed for 4 weeks after vaccination. Termination of pregnancy is not indicated if vaccination was carried out inadvertently during pregnancy.
- Varicella vaccine can be administered concomitantly with other vaccines. Unless given together with other live viral vaccines (measles, MR, MMR), it should be administered at a minimum interval of 28 days.
- Countries should consider vaccination of potentially susceptible health-care workers (i.e. unvaccinated and with no history of varicella) with 2 doses of varicella vaccine.

(updated: January 2025)

Table 2: Summary of WHO Position Papers - Recommended Routine Immunizations for Children

Antigen		Age of 1st Dose	Doses in Primary Series	Interval Between Doses			Booster Dose	Considerations (see footnotes for details)
				1st to 2nd	2nd to 3rd	3rd to 4th		
Recommendations for all children								
BCG [1]		As soon as possible after birth	1					Birth dose and HIV; Universal vs selective vaccination; Co-administration; Vaccination of older age groups; Pregnancy
Hepatitis B [2]	**Option 1**	As soon as possible after birth (<24h)	3	4 weeks (min) with DTPCV1	4 weeks (min) with DTPCV2			Premature and low birth weight; Co-administration and combination vaccine; High risk groups
	Option 2	As soon as possible after birth High risk groups	4	4 weeks (min) with DTPCV1	4 weeks (min) with DTPCV2			
Polio [3]	**bOPV + IPV** "Preferred schedule" (fractional Salk-IPV permitted)	bOPV 6 weeks IPV 14 weeks	5 (3 bOPV and 2 IPV)	bOPV 4 weeks (min) (e.g. with DTPCV2) IPV ≥ 4 months (min) (e.g. with MCV)	bOPV 4 weeks (min) (e.g. with DTPCV3)			bOPV birth dose; Type of vaccine; Fractional dose IPV; Transmission and importation risk; Local epidemiology, programmatic implications and feasibility for "early" option
	bOPV+IPV "Early Option" (full dose IPV only)	bOPV 6 weeks IPV 6 weeks	5 (3 bOPV and 2 IPV)	bOPV 4 weeks (min) (e.g. with DTPCV2) IPV 14 weeks (min) (e.g. with DTPCV3)	bOPV 4 weeks (min) (e.g. with DTPCV3)			
	IPV / bOPV Sequential	8 weeks (IPV 1st) bOPV (4-8 weeks after 2nd IPV)	4 (2 IPV followed by ≥ 2 bOPV)	IPV (4-8 weeks)	bOPV (4-8 weeks)	bOPV (4-8 weeks)		
	IPV-only	6-8 weeks	3	4-8 weeks	4-8 weeks		IPV booster (6 months after 3rd dose) is needed when 1st dose given at < 8 weeks	Only for countries in polio-free regions with a very low risk of importation and sustained high routine immunisation coverage (DTP3 > 90%)
	Alternative IPV-only (fractional permitted)	≥14 weeks	2	≥ 4 months (e.g. with MCV)				
DTP-containing vaccine [4]		6 weeks (min)	3	4 weeks (min) - 8 weeks	4 weeks (min) - 8 weeks		3 Boosters 12-23 months (DTP-containing vaccine); 4-7 years (Td/ DT containing vaccine), see footnotes; and 9-15 yrs (Td)	Delayed/ interrupted schedule Combination vaccine; Maternal immunization

Refer to **https://www.who.int/teams/immunization-vaccines-and-biologicals/policies/position-papers** for table & position paper updates.

This table summarizes the WHO vaccination recommendations for children.The ages/intervals cited are for the development of country specific schedules and are not for health workers.

National schedules should be based on local epidemiologic, programmatic, resource & policy considerations. While vaccines are universally recommended, some children may have contraindications to particular vaccines.

(updated: January 2025)

Table 2: Summary of WHO Position Papers - Recommended Routine Immunizations for Children

Antigen		Age of 1st Dose	Doses in Primary Series	Interval Between Doses			Booster Dose	Considerations (see footnotes for details)
				1st to 2nd	2nd to 3rd	3rd to 4th		
Recommendations for all children								
Haemophilus influenzae type b [5]	Option 1	6 weeks (min) 59 months (max)	3	4 weeks (min) with DTPCV2	4 weeks (min) with DTPCV3		(see footnote)	Single dose if >12 months of age Not recommended for children > 5 yrs Delayed/ interrupted schedule Co-administration and combination vaccine
	Option 2		2-3	8 weeks (min) if only 2 doses 4 weeks (min) if 3 doses	4 weeks (min) if 3 doses		At least 6 months (min) after last dose	
Pneumococcal (Conjugate) [6]	Option 1 3p+0	6 weeks (min)	3	4 weeks (min)	4 weeks		9-18 months	Schedule options (3p+0 vs 2p+1); Vaccine options; HIV+ and preterm neonate booster; Vaccination in older adults
	Option 2 2p+1	6 weeks (min)	2	8 weeks (min)				
Rotavirus [7]		6 weeks (min) with DTP1	2 or 3 depending on product	4 weeks (min) with DTPCV2	For three dose series - 4 week (min) with DTPCV3			Not recommended if >24 months old
Measles [8]		9 or 12 months (6 months min, see footnote)	2	4 weeks (min) (see footnote)				Co-administration live vaccines; Combination vaccine; HIV early vaccination; Pregnancy
Rubella [9]		9 or 12 months with measles containing vaccine	1					Co-administration and combination vaccine; Pregnancy
HPV [10]		As soon as possible from 9 years of age (females only)	1-2	6-12 months				Target 9-14 year old girls; Off-label 1 dose schedule; MACs with intro; Pregnancy; HIV and immunocompromised

(updated: January 2025)

Table 2: Summary of WHO Position Papers - Recommended Routine Immunizations for Children

Antigen		Age of 1st Dose	Doses in Primary Series	Interval Between Doses			Booster Dose	Considerations (see footnotes for details)
				1st to 2nd	2nd to 3rd	3rd to 4th		
Recommendations for children residing in certain regions								
Japanese Encephalitis [11]	**Inactivated Vero cell-derived**	6 month	2 generally	4 weeks (generally)				Co-administration live vaccines; Vaccine options and manufacturer's recommendations; Pregnancy; Immunocompromised
	Live attentuated	8 months	1					
	Live recombinant	9 months	1					
Yellow Fever [12]		9-12 months with measles containing vaccine	1					Co-administration live vaccines
Tick-Borne Encephalitis [13]		≥ 1 yr FSME-Immun and Encepur ≥ 3 yrs TBE_Moscow and EnceVir	3	1-3 months FSME-Immun and Encepur 1-7 months TBE-Moscow and EnceVir	5-12 months FSME-Immun and Encepur 12 months TBE-Moscow and EnceVir		At least 1 every 3 years (see notes)	Definition of high-risk; Vaccine options; Timing of booster
Recommendations for children in some high-risk populations								
Typhoid [14]	**TCV (Typbar)**	>6 months	1					Definition High Risk; Vaccine options
	Vi PS	2 years (min)	1				Every 3 years	Definition of high risk
	Ty21a	Capsules 6 years (min) (see footnote)	3 or 4 (see footnote)	1 day	1 day	1 day	Every 3-7 years	Definition of high risk
Cholera [15]	**Dukoral (WC-rBS)**	2 years (min)	3 (2-5 years) 2 (≥6 years)	≥ 7 days (min) < 6 weeks (max)	≥ 7 days (min) < 6 weeks (max)		Every 6 months Every 2 years	Minimum age Definition of high risk
	Shanchol, Euvchol and mORCVAX	1 year (min)	2	14 days			After 2 years	
Meningococcal [16]	**MenA conjugate**	9-18 months (5µg)	1					Definition of high risk; Vaccine options; 2 doses if < 9 months with 8 week interval
	MenC conjugate	2-11 months	2	8 weeks			After 1 year	Definition of high risk; Vaccine options
		≥12 months	1					
	Quadrivalent conjugate	9-23 months	2	12 weeks				Definition of high risk; Vaccine options
		≥2 years	1					

(updated: January 2025)

Table 2: Summary of WHO Position Papers - Recommended Routine Immunizations for Children

Antigen		Age of 1st Dose	Doses in Primary Series	Interval Between Doses			Booster Dose	Considerations (see footnotes for details)
				1st to 2nd	2nd to 3rd	3rd to 4th		
Hepatitis A [17]	Inactivated	> 12 months	1 or 2	6-18 months (max > 4-5 years)				Level of endemicity; Vaccine options; Definition of high risk groups
	Live attenuated	18 months	1					
Rabies [18]		As required	2	7 days			(see footnote)	PrEP vs PEP; Definition of high risk
Dengue (TAK-003) [19]		6 years (min)	2	3 months (min)				High transmission areas; Pregnancy and lactation; Comorbidities
Malaria [20]		5 months	4	4 weeks (min)	4 weeks (min)	6-18 months (min 4 weeks)		Moderate to high transmission; Seasonal strategy
Recommendations for children receiving vaccinations from immunization programmes with certain characteristics								
Mumps [21]		12-18 months with measles and rubella containing vaccine	2	1 month (min) to school entry				High coverage with MR vaccine; Combination vaccines
Seasonal influenza (inactivated tri- and quadri-valent) [22]		6 months (min)	2 (6 mos to 8 years) 1 (≥ 9 years)	4 weeks			Revaccinate annually: 1 dose only (see footnotes)	Priority risk groups
Varicella [23]		12-18 months	1-2	4 weeks to 3 months per manufacturer recommendations				Achieve & sustain ≥ 80% coverage Pregnancy Co-admin with other live vaccines

Summary Table 2 - Notes

- Refer to http://www.who.int/immunization/documents/positionpapers for the most recent version of the tables and position papers.
- The attached table summarizes the recommendations for vaccine administration found in the WHO position papers which are published in the Weekly Epidemiological Review. Its purpose is to assist planners to develop an appropriate immunization schedule. Health care workers should refer to their national immunization schedules. While vaccines are universally recommended, some children may have contraindications to particular vaccines.
- Vaccines can generally be co-administered (i.e. more than one vaccine given at different sites during the same visit). Recommendations that explicitly endorse co-administration are indicated in the table, however, lack of an explicit co-administration recommendation does not imply that the vaccine cannot be co-administered; further, there are no recommendations against co-administration.
- Doses administered by campaign may or may not contribute to a child's routine immunization schedule depending on type and purpose of campaign (e.g. supplemental versus routine/pulse campaign for access reasons).
- For some antigens, recommendations for the age of initiation of primary immunization series and/or booster doses are not available. Instead, the criteria for age at first dose must be determined from local epidemiologic data.
- If a catch-up schedule for interrupted immunization is available, it is noted in the footnotes.
- Other vaccines, such as varicella and pneumococcal polysaccharide vaccines, may be of individual benefit but have not been generally recommended for routine immunization. See the specific position papers for more details.
- For further background on immunization schedules refer to "Immunological Basis for Immunization" series which is available at http://www.who.int/immunization/documents/immunological_basis_series/en/index.html

[1] BCG

- Position paper reference: Weekly Epid. Record (2018, 93:73-96) [pdf 660KB].
- Universal BCG vaccination at birth is recommended in countries or settings with a high incidence of TB and/or high leprosy burden. A single dose of BCG vaccine should be given to all healthy neonates at birth, ideally together with Hepatitis B birth dose.
- Countries with low TB incidence or leprosy burden may choose to selectively vaccinate neonates in high-risk groups.
- BCG vaccination is also recommended for unvaccinated TST- or IGRA-negative older children, adolescents and adults from settings with high incidence of TB and/or high leprosy burden, those moving from low to high TB incidence/ leprosy burden settings and persons at risk of occupational exposure in low and high TB incidence areas (e.g. health-care workers, laboratory workers, medical students, prison workers, other individuals with occupational exposure).
- BCG vaccination is not recommended during pregnancy.
- If HIV-infected individuals, including children, are receiving ART, are clinically well and immunologically stable (CD4% >25% for children aged <5 years or CD4 count ≥200 if aged >5 years) they should be vaccinated with BCG. Neonates born to women of unknown HIV status should be vaccinated as the benefits of BCG vaccination outweigh the risks. Neonates of unknown HIV status born to HIV infected women should be vaccinated if they have no clinical evidence suggestive of HIV infection, regardless of whether the mother is receiving ART. For neonates with HIV infection confirmed by early virological testing, BCG vaccination should be delayed until ART has been started and the infant confirmed to be immunologically stable (CD4 >25%).
- Moderate-to-late preterm infants (gestational age > 31 weeks) and low birth weight infants (< 2500 g) who are healthy and clinically stable can receive BCG vaccination at birth, or at the latest, upon discharge.

[2] Hepatitis B

- Position paper reference: Weekly Epid. Record (2017, 92:369-392) [pdf 2.4MB].
- Hepatitis B vaccination is recommended for all children worldwide. Reaching all children with at least 3 doses of hepatitis B vaccine should be the standard for all national immunization programmes. Since perinatal or early postnatal transmission is the most important source of chronic HBV infection globally, all infants (including low birth weight and premature infants) should receive their first dose of hepatitis B vaccine as soon as possible after birth, ideally within 24 hours.
- The birth dose should be followed by 2 or 3 additional doses to complete the primary series. Both of the following options are considered appropriate: (i) a 3-dose schedule with the first dose (monovalent) being given at birth and the second and third (monovalent or as part of a combined vaccine) given at the same time as the first and third doses of DTP-containing vaccine; or (ii) 4 doses, where a monovalent birth dose is followed by 3 (monovalent or combined vaccine) doses, usually given with other routine infant vaccines; the additional dose does not cause any harm. The interval between doses should be at least 4 weeks.
- A birth dose of hepatitis B vaccine can be given to low birth weight (<2000g) and premature infants. For these infants, the birth dose should not count as part of the primary 3-dose series; the 3 doses of the standard primary series should be given according to the national vaccination schedule.
- For catch-up of unvaccinated individuals, priority should be given to younger age groups since the risk of chronic infection is highest in these cohorts. Catch-up vaccination is a time-limited opportunity for prevention and should be considered based on available resources and priority. Unvaccinated individuals should be vaccinated with a 0, 1, 6 month schedule.
- Vaccination of groups at highest risk of acquiring HBV is recommended. These include patients who frequently require blood or blood products, dialysis patients, diabetes patients, recipients of solid organ transplantation, person with chronic liver disease including those with Hepatitis C, person with HIV infection, men who have sex with men, persons with multiple sexual partners, as well as health care workers and others who may be exposed to blood, blood products or other potentially infectious body fluids during their work.

[3] Polio

- Position paper reference: Weekly Epid. Record (2022, 97:277-300) [pdf 589KB.].
- All children worldwide should be fully vaccinated against polio, and every country should seek to achieve and maintain high levels of coverage with polio vaccines in support of the global commitment to eradicate polio.

bOPV plus IPV

- For all countries using OPV in their national immunization programme, WHO recommends 3 doses of bOPV and 2 doses of IPV.
- The preferred schedule is to administer the 3 doses of bOPV starting from the minimum age of 6 weeks, with at least a 4 week interval between doses. The first IPV dose should be administered from a minimum of 14 weeks of age (with DTP3/Penta3), with the second IPV dose being given at least 4 months later (possibly coinciding with other vaccines administered at 9 months of age).
- The 2 doses of IPV provide immunity against paralysis from type 2 poliovirus and also boost

immunity against poliovirus types 1 and 3

- This schedule provides the highest immunogenicity and may be carried out using full dose IPV (for both Salk IPV and Sabin-IPV (s-IPV)) or ID fIPV (using only Salk IPV, not sIPV) without loss of immunogenicity.
- Based on local epidemiology, programmatic implications and feasibility of delivery, countries may choose an alternative "early IPV schedule" starting with the first IPV dose at 6 weeks of age (with DTP1/Penta1), and the second IPV dose at 14 weeks (with DTP3/Penta3).
- This alternative schedule offers the advantage of providing early-in-life protection; however, a lower total immunogenicity is achieved. If this schedule is chosen, full dose IPV (for both Salk IPV and sIPV) should be used rather than fIPV due to lower immunogenicity of fIPV at early ages.
- In polio-endemic countries and in countries at high risk for importation and subsequent spread of poliovirus, WHO recommends a bOPV birth dose (zero dose) followed by the primary series of 3 bOPV doses and 2 IPV doses. The zero dose of bOPV should be administered at birth, or within the first week of life, to maximize seroconversion rates following subsequent doses and to induce mucosal protection before enteric pathogens may interfere with the immune response. Additionally, a birth dose of bOPV administered while infants are still protected by maternally-derived antibodies (up to 6 months) may prevent VAPP.
- For infants late in starting the routine immunization schedule (age >3 months) the first IPV dose should be administered at the first immunization contact along with bOPV and the other routinely recommended vaccines.
- Implementation of the infant schedule (3 bOPV doses plus 2 IPV doses) does not replace the need for SIAs. Countries with insufficient routine vaccination coverage that rely on SIAs to increase population immunity should continue using bOPV in SIAs until routine coverage improves, or until the globally coordinated withdrawal of bOPV.
- Countries that delayed the introduction of IPV or experienced stock-outs during 2016–2019 should provide catch-up vaccination as soon as possible to all children who were missed.

Sequential IPV–bOPV

- In countries with high vaccination coverage (e.g. 90–95%) and low importation risk (where neighbouring countries and/or countries that share substantial population movement have a similarly high coverage), an IPV–bOPV sequential schedule can be used when VAPP is a greater concern than the small loss of IPV immunogenicity due earlier administration.
- Where a sequential IPV–bOPV schedule is used, the initial administration of 2 doses of IPV should be followed by ≥2 doses of bOPV to ensure sufficient levels of protection in the intestinal mucosa as well as a decrease in the burden of VAPP.
- For sequential IPV– bOPV schedules, WHO recommends that the first dose of IPV be given starting from 8 weeks of age with an interval of 4–8 weeks before administration of the second IPV dose. This should be followed by at least 2 doses of bOPV separated by 4–8 weeks depending on the risk of exposure to poliovirus in early childhood.

IPV-only

- An IPV-only schedule may be considered in countries in polio-free regions with a very low risk of importation and sustained high routine immunization coverage (DTP3 >90%).
- In the current epidemiological context, WHO recommends that regions and countries be cautious about moving from a combined bOPV plusIPV schedule to an IPV-only schedule in their routine immunization programmes; a gradual approach should be taken by first ensuring high coverage with 2 doses of IPV while still using bOPV.
- A primary 3-dose series of IPV administered beginning at 6 or 8 weeks of age, with a minimum 4 week interval between doses, is recommended.
- If the primary series begins at 6 weeks, a booster dose should be given 6 months or more after the third dose.
- Alternatively, a 2-dose or fractional dose IPV schedule, starting at 14 weeks of age or older, with a second dose 4 months or more later can be considered. This schedule is currently recommended for use after OPV cessation.
- While both options provide high immunogenicity (>90%), the 3 dose primary series provides protection in early infancy.
- Two whole-cell pertussis (wP) hexavalent IPV-containing vaccines are currently licensed and awaiting WHO prequalification. After prequalification, a wP hexavalent vaccine could be administered using the schedules currently recommended for the pentavalent vaccine (i.e. at 8, 12 and 16 weeks, or 6, 10 and 14 weeks, plus a booster dose at least 6 months later).

[4] DTP-containing vaccine (Diphtheria, Tetanus and Pertussis)

- Position paper reference: Diphtheria - Weekly Epid. Record (2017, 92:417-436) [pdf 526KB]; Tetanus - Weekly Epid. Record (2017, 92: 53-76) [pdf 636KB]; Pertussis - Weekly Epid. Record (2015, 90: 433-460) [pdf 667KB].
- The need for early infant vaccination with DTP-containing vaccine (DTPCV) is principally to ensure rapid protection against pertussis, because severe disease and death from pertussis is almost entirely limited to the first weeks and months of life.
- A primary series of 3 doses of DTP-containing vaccine is recommended, with the first dose administered as early as 6 weeks of age. Subsequent doses should be given with an interval of at least 4 weeks between doses. The third dose of the primary series should be completed by 6 months of age if possible.
- If either the start or the completion of the primary series has been delayed, the missing doses should be given at the earliest opportunity with an interval of at least 4 weeks between doses.
- 3 booster doses of diphtheria toxoid-containing vaccine should be provided during childhood and adolescence. The diphtheria booster doses should be given in combination with tetanus toxoid using the same schedule, i.e at 12–23 months of age, 4–7 years of age, and 9–15 years of age, using age-appropriate vaccine formulations. Ideally, there should be at least 4 years between booster doses.
- Tetanus - To ensure lifelong protection against tetanus in all people should receive 6 doses (3 primary plus 3 booster doses) of tetanus toxoid-containing vaccine (TTCV) through routine childhood immunization schedules.
- The 3 TTCV booster doses should be given at: 12–23 months of age; 4–7 years of age; and 9–15 years of age. Ideally, there should be at least 4 years between booster doses.
- National vaccination schedules can be adjusted within the age limits specified above to enable programmes to tailor their schedules based on local epidemiology, the objectives of the immunization programme, any particular programmatic issues and to better align tetanus vaccination with the immunological requirements of other vaccines (particularly for pertussis and diphtheria).
- Opportunities for tetanus vaccination may be taken at the second year of life contacts for alternative PCV schedule 2 +1, MCV second dose, and meningococcal A-containing vaccines, as well as pre-adolescence and adolescence contacts including for HPV vaccination.
- To provide and sustain both tetanus and diphtheria immunity throughout the life course and for both sexes, age-appropriate combinations of tetanus and diphtheria toxoids should be used. For children <7 years of age DTwP or DTaP combinations may be used. For children aged 4 years and older Td containing vaccine may be used and is preferred. Link
- From 7 years of age only Td combinations should be used. Age-appropriate combinations containing pertussis vaccine with low-dose diphtheria antigen are also available.

- If tetanus vaccination is started during adolescence or adulthood, a total of only 5 appropriately spaced doses are required to obtain lifelong protection.
- Pregnant women and their newborn infants are protected from birth-associated tetanus if the mother received either 6 TTCV doses during childhood or 5 doses if first vaccinated during adolescence/adulthood (documented by card, immunization registry and/or history) before the time of reproductive age. Vaccination history should be verified in order to determine whether a dose of TTCV is needed in the current pregnancy.
- WHO confirms its earlier recommendation to shift from the use of single-antigen TT to combinations containing diphtheria toxoid, i.e. DT or Td vaccines, which has not yet been implemented in many countries despite the negligible price differential between TT and DT/Td vaccines. Countries and partners are urged to take steps to accelerate this shift.
- TTCVs can be used in immunocompromised persons including HIV-infected individuals, but the immune response may be lower than in fully immunocompetent persons. All HIV-infected children should be vaccinated against tetanus following the vaccine recommendations for the general population.
- Pertussis vaccine: Both aP-containing and wP-containing vaccines have excellent safety records.
- Available evidence indicates that licensed aP and wP vaccines have equivalent initial effectiveness in preventing disease in the first year of life, but that there is more rapid waning of immunity, and possibly a reduced impact on transmission, with aP relative to wP vaccines.
- National programmes currently administering wP vaccination should continue to use wP vaccines for primary vaccination series. Surveillance and modelling data suggest that the use of aP vaccines may result in a resurgence of pertussis after a number of years.
- National programmes currently using aP vaccine may continue using this vaccine but should consider the need for additional booster doses and strategies to prevent early childhood mortality such as maternal immunization in case of resurgence of pertussis.
- Only aP-containing vaccines should be used for vaccination of persons aged ≥7 years.
- Pertussis containing booster - A booster dose is recommended for children aged 1–6 years, preferably during the second year of life (≥6 months after last primary dose), unless otherwise indicated by local epidemiology; the contact could also be used to catch up on any missed doses of other vaccines. This schedule should provide protection for at least 6 years for countries using wP vaccine. For countries using aP vaccine, protection may decline appreciably before 6 years of age.
- Vaccinating pregnant women and household contacts - Vaccination of pregnant women is likely to be the most cost-effective additional strategy for preventing disease in infants too young to be vaccinated and appears to be more effective and favourable than cocooning.
- National programmes may consider the vaccination of pregnant women with 1 dose of Tdap (in the 2nd or 3rd trimester and preferably at least 15 days before the end of pregnancy) as a strategy additional to routine primary infant pertussis vaccination in countries or settings with high or increasing infant morbidity/ mortality from pertussis.
- Delayed or interrupted DTP-containing series - For children whose vaccination series has been interrupted, the series should be resumed without repeating previous doses. Children aged 1 to < 7 years who have not previously been vaccinated should receive 3 doses of vaccine following a 0, 1, 6 month schedule. Two subsequent booster doses using Td or Tdap combination vaccines are needed with an interval of at least 1 year between doses.
- Health-care workers should be prioritized as a group to receive pertussis vaccine.

[5] *Haemophilus influenzae* type b (Hib)

- Position paper reference: Weekly Epid. Record (2013, 88: 413-428) [pdf 209KB].
- The use of Hib vaccines should be part of a comprehensive strategy to control pneumonia including exclusive breastfeeding for six months, hand washing with soap, improved water supply and sanitation, reduction of household air pollution, and improved case management at community and health facility levels.
- WHO recommends that any one of the following Hib immunization schedules may be followed: 3 primary doses without a booster (3p); 2 primary doses plus a booster (2p+1); and 3 primary doses with a booster (3p+1).
- Because serious Hib disease occurs most commonly in children aged between 4 months and 18 months, immunization should start from 6 weeks of age, or as early as possible thereafter.
- The number of primary doses should be set after consideration of the local epidemiology, vaccine presentation (Hib conjugate monovalent vaccine versus Hib conjugate vaccine in combination with other antigens) and how this fits into the overall routine immunization schedule.
- In countries where the peak burden of severe Hib disease occurs in young infants, providing 3 doses of vaccine early in life may confer a greater benefit.
- In some settings (e.g. where the greatest disease morbidity and mortality occur later, or where rate reductions of disease are not fully sustained after the routine use of Hib vaccine), it might be advantageous to give a booster dose by following either a 2p+1 or 3p+1 schedule.
- The interval between doses should be at least 4 weeks if 3 primary doses are given, and at least 8 weeks if 2 primary doses are given. Booster doses should be administered at least six months after completion of the primary series.
- If the vaccination course has been interrupted, the schedule should be resumed without repeating the previous dose. Children who start vaccination late, but are aged under 12 months, should complete the vaccination schedule (e.g. have 3 primary doses or 2 primary doses plus a booster).
- When a first dose is given to a child older than 12 months of age, only one dose is recommended.
- Hib vaccine is not required for healthy children after 5 years of age.
- The Hib conjugate vaccine is contraindicated in people with known allergies to any component of the vaccine. There are no other known contraindications or precautions.

[6] Pneumococcal (Conjugate)

- Position Paper Reference: Weekly Epid. Record (2019, 94: 85-104) [pdf 444KB].
- Currently available PCVs are safe and effective and are therefore recommended for the inclusion in childhood immunization programmes worldwide.
- Use of pneumococcal vaccine should be complementary to other disease prevention and control measures, such as appropriate case management, promotion of exclusive breastfeeding for the first 6 months of life and reducing known risk factors such as indoor air pollution and tobacco smoke.
- For administration of PCV to infants, WHO recommends a 3-dose schedule administered either as 2p+1 or as 3p+0, starting as early as 6 weeks of age.
- If the 2p+1 schedule is selected, an interval of ≥8 weeks is recommended between the 2 primary doses the booster dose should be given at 9–18 months of age, according to programmatic considerations; there is no defined minimum or maximum interval between the primary series and the booster dose.
- If the 3p+0 schedule is used, a minimum interval of 4 weeks should be maintained between

doses.

- Previously unvaccinated or incompletely vaccinated children who recover from invasive pneumococcal disease (IPD) should be vaccinated according to the recommended age-appropriate regimens. Interrupted schedules should be resumed without repeating the previous dose.
- Both PCV10 and PCV13 have substantial impacts against pneumonia, vaccine-type IPD and NP carriage. The choice of product to be used in a country should be based on programmatic characteristics, vaccine supply, vaccine price, the local and regional prevalence of vaccine serotypes and antimicrobial resistance patterns.
- Once a PCV vaccination programme has been initiated, product switching is not recommended unless there are substantial changes in the epidemiological or programmatic factors that determined the original choice of product, e.g. an increasing burden of serotype 19A. If a series cannot be completed with the same type of vaccine, the available PCV product should be used. Restarting a series is not recommended, even for the primary series.
- Wherever possible, catch-up vaccination at the time of introduction of PCV should be used to accelerate its impact on disease in children aged 1–5 years, particularly in settings with a high disease burden and mortality. If there is limited availability of vaccine or of financial resources for catch-up vaccination, the youngest children (e.g. <2 years of age) should be prioritized to receive catch-up doses of PCV because of their higher risk for pneumococcal disease.
- Catch-up vaccination can be done with a single dose of vaccine for children ≥24 months.
- Unvaccinated children aged 1–5 years who are at high risk for pneumococcal infection because of underlying medical conditions, such as HIV infection or sickle-cell disease, should receive at least 2 doses separated by at least 8 weeks.
- HIV-positive infants and pre-term neonates who have received their 3 primary vaccine doses before 12 months of age may benefit from a booster dose in the second year of life.
- Co-administration for programmatic reasons appears to be acceptable.
- WHO does not currently have recommendations on the use of PCV in individuals over 5 years of age. [pdf 373KB]
- For considerations for pneumococcal vaccination in older adults see concept note: Weekly Epid. Record (2021, 96 (23), 217 – 228) [pdf 373KB]
- Introduction of PCV into national childhood immunization programmes and measures to sustain high coverage in children should be prioritized over initiating a pneumococcal vaccination programme for older adults.
- In countries that have a mature childhood pneumococcal immunization programme, decisions about initiating such a programme in adults, using either PPV23 or PCV13, should take into account the local disease burden and cost-effectiveness considerations.

[7] Rotavirus

- Position paper reference: Weekly Epid. Record (2021, 96: 301-320) [pdf 515KB].
- Rotavirus vaccines should be included in all national immunization programmes.
- The use of rotavirus vaccines should be part of a comprehensive strategy to control diarrhoeal diseases with the scaling up of both prevention (promotion of early and exclusive breastfeeding, handwashing, improved water supply, and sanitation) and treatment packages (low osmolarity ORS and zinc).
- The first dose of rotavirus vaccine be administered as soon as possible after 6 weeks of age.
- If a child <24 months of age misses a rotavirus dose or series for any reason, WHO recommends rotavirus vaccination for that child. Because of the typical age distribution of RVGE, rotavirus vaccination of children >24 months of age is not recommended.
- The rotavirus vaccination series for each child should be completed with the same product whenever feasible. However, if the product used for a prior dose is unavailable or unknown, the series should be completed with any available licensed product.
- For a mixed series or a series with any unknown vaccine products, a total of 3 doses of rotavirus vaccine should be administered for a complete vaccination series.
- Rotavirus vaccinations may be administered simultaneously with other vaccines of the childhood immunization programme.
- WHO prequalified rotavirus vaccines are safe and well tolerated. A small potential risk of intussusception after rotavirus vaccination remains.
- Rotavirus vaccine should not be given to children with prior history of intussusception, severe allergic reaction (e.g. anaphylaxis) after a previous dose, or severe immunodeficiency, including severe combined immunodeficiency.
- Precautions include altered immunocompetence other than severe combined immunodeficiency, chronic gastrointestinal disease, and spina bifida or bladder exstrophy. Vaccination may be postponed in case of ongoing acute gastroenteritis or fever with moderate to severe illness.

[8] Measles

- Position paper reference: Weekly Epid. Record (2017, 92:205-228) [pdf 600KB].
- Reaching all children with 2 doses of measles vaccine should be the standard for all national immunization programmes. In addition to the first routine dose of MCV1, all countries should add a second routine dose of MCV2 to their national immunization schedules regardless of the level of MCV1 coverage.
- In countries with ongoing transmission in which the risk of measles mortality remains high, MCV1 should be given at age 9 months. MCV2 should be given between 15-18 months, as providing MCV2 in the 2nd year of life reduces the rate of accumulation of susceptible children and the risk of an outbreak. The minimum interval between MCV1 and MCV2 is 4 weeks.
- Because many cases of measles occur in children aged >12 months who have not been vaccinated, routine delivery of MCV1 should not be limited to infants aged 9–12 months and routine delivery of MCV2 should not be limited to infants 15 to 18 months of age. Every opportunity (e.g. when children come into contact with health services) should be taken to vaccinate all children that missed one or both MCV routine doses, particularly those under 15 years of age. Policies which prohibit use of vaccine in children >1 year of age, older children and teenagers should be changed to allow these individuals to be vaccinated.
- In countries with low levels of measles transmission (i.e. those that are near elimination or verified as having eliminated endemic measles virus transmission) and therefore the risk of measles virus infection among infants is low, MCV1 may be administered at 12 months of age to take advantage of the higher seroconversion rates achieved at this age. In these countries, the optimal age for delivering MCV2 is based on programmatic considerations to achieve the highest coverage of MCV2 and, hence, the highest population immunity. Administration of MCV2 at 15-18 months of age ensures early protection of the individual, slows accumulation of susceptible young children, and may correspond to the schedule for other routine immunizations (for example, a DTP-containing booster, PCV, or meningococcal vaccines). This measure also supports the establishment of a policy on immunization and other health interventions in the second year of life. If MCV1 coverage is high (>90%) and school enrolment is high (>95%), administration of routine MCV2 at school entry may prove an effective strategy for achieving high coverage and preventing outbreaks in schools.
- For programmatic reasons (e.g. to reduce cold storage needs and vaccine wastage), it is recommended that the same vaccine formulation is used for both routine doses of MCV.

- In the following situations, a supplementary dose of MCV should be given to infants from 6 months of age: (1) during a measles outbreak as part of intensified service delivery; (2) during campaigns in settings where the risk of measles among infants < 9 months of age remains high (e.g. in endemic countries experiencing regular outbreaks); (3) for internally displaced populations and refugees, and populations in conflict zones; (4) for individual infants at high risk of contracting measles (e.g. contacts of known measles cases or in settings with increased risk of exposure during outbreaks such as day-care facilities); (5) for infants travelling to countries experiencing measles outbreaks; (6) for infants known to be HIV-infected or exposed (i.e. born to an HIV-infected woman).
- MCV administered before 9 months of age should be considered a supplementary dose and recorded on the child's vaccination record as "MCV0". Children who receive MCV0 should also receive MCV1 and MCV2 at the recommended ages according to the national schedule.
- Given the severe course of measles in patients with AIDS, measles vaccination should be routinely administered to potentially susceptible, asymptomatic HIV infected children and adults. Vaccination may even be considered for those with symptomatic HIV infection if they are not severely immunosuppressed according to conventional definitions. In areas where there is a high incidence of both HIV infection and measles, an initial dose of MCV may be offered as early as age 6 months (recorded as MCV0). The 2 routine doses of MCV (MCV1 and MCV2) should then be administered to these children according to the national immunization schedule.
- An additional dose of MCV should be administered to HIV-infected children receiving HAART following immune reconstitution If CD4+ T lymphocyte counts are monitored, an additional dose of MCV should be administered when immune reconstitution has been achieved, e.g.
- when the CD4+ T lymphocyte count reaches 20–25%. Where CD4+ T lymphocyte monitoring is not available, children should receive an additional dose of MCV 6–12 months after initiation of HAART.
- A supplementary dose of MCV (recorded as MCV0) should be considered for infants known to be exposed (i.e. born to an HIV-infected woman) or soon after diagnosis of HIV infection in children older than 6 months who are not receiving HAART and for whom the risk of measles is high, with the aim of providing partial protection until they are revaccinated after immune reconstitution with HAART.
- Mild concurrent infections are not a contraindication to vaccination. As a precautionary measure, measles vaccine – alone or in combination with other vaccines – should be avoided during pregnancy. MCVs should not be given to individuals with a history of anaphylactic reactions or severe allergic reactions to any component of the vaccine (e.g. neomycin or gelatin) or those with any form of severe immunosuppression.
- As a general rule, live vaccines should be given either simultaneously or at intervals of 4 weeks. An exception to this rule is OPV, which can be given at any time before or after measles vaccination without interference in the response to either vaccine.

[9] Rubella

- Position paper reference: Weekly Epid. Record (2020, 95: 301-324) [pdf 772KB].
- As of September 2024, the requirement that countries attain 80% MCV coverage in routine immunization or campaigns before RCV introduction has been lifted. This component of the Rubella Position Paper will be amended in the next update; in the meantime, the new policy recommendation can be found in the Meeting of the Strategic Advisory Group of Experts on Immunization, September 2024: conclusions and recommendations
- All countries that have not yet introduced RCV should plan to do so.
- It is recommended that RCV be provided in combination with measles vaccine, and combined measles and rubella vaccine should be used for all immunization activities once RCV is introduced, including routine immunization, supplementary immunization activities (SIAs) and outbreak response.
- Since measles elimination requires ≥95% coverage, the goal for rubella vaccination coverage should also be ≥95%.
- The recommended vaccination strategy is to begin with an MR vaccination campaign targeting both sexes and a wide age range (e.g. 9 months–15 years), based on the susceptibility profile by birth cohort when possible, followed immediately by introduction of MR or MMR vaccine into the routine immunization programme. The campaign should target males as well as females in order to reduce the likelihood of creating immunity gaps.
- The first dose of RCV can be delivered at 9 or 12 months, depending on the level of measles virus transmission. RCV should be used in all subsequent follow-up campaigns.
- RCV's can be administered concurrently with inactivated vaccines.
- Live vaccines should be given either simultaneously with RCV's, or at least 4 weeks apart. An exception to this is oral polio vaccine, which can be given at any time before or after RCV's without interfering in the response to either vaccine. WHO recommends co-administration of RCV and YF vaccines.
- Rubella vaccination should be avoided in pregnancy because of a theoretical (but never demonstrated) risk of teratogenic outcomes. Women planning a pregnancy are advised to avoid pregnancy for 1 month after rubella vaccination.
- WHO recommends that people who receive blood products wait at least 3 months before vaccination with RCV, and, if possible, avoid administration of blood products for 2 weeks after vaccination.

[10] Human Papillomavirus (HPV)

- Position paper reference: Weekly Epid. Record (2022, 97: 645-672) [pdf 590KB].
- HPV vaccines should be introduced as part of a coordinated and comprehensive strategy to prevent cervical cancer and other diseases caused by HPV. This strategy should include education about reducing behaviours that increase the risk of acquiring HPV infection, and information about screening, diagnosis and treatment of precancerous lesions, cancer and risk factors. Access to quality screening and treatment services should be improved.
- The priority purpose of HPV immunization is the prevention of cervical cancer, which accounts for 82% of all HPV-related cancers. The 2020 WHO Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem WHO recommends that HPV vaccines should be included in all national immunization programmes and should reach 90% of all girls by age 15 by 2030. Prevention of cervical cancer is best achieved through the immunization of girls before they become sexually active.
- The WHO-recommended primary target population for HPV vaccination is girls aged 9–14 years Prevention of cervical cancer is best achieved through the immunization of girls before they become sexually active.
- Catch-up vaccination of multi-aged cohorts (MACs) of girls aged between 9 and 18 years at the time of introducing the HPV vaccine results in faster and greater population impact, as a result of increased direct and herd protection. This approach is cost-effective, offers opportunities for economies of scale in delivery and makes programmes more resilient to any interruptions in vaccination.
- Vaccination of secondary target populations, e.g. females aged ≥15 years, boys, older males or MSM, is recommended only if this is feasible and affordable, and does not divert resources from vaccination of the primary target population or effective cervical cancer screening programmes.
- All currently licensed bivalent, quadrivalent and nonavalent HPV vaccines have excellent safety profiles and are highly efficacious or have met immunobridging standards.

- The current evidence supports the recommendation that a 2-dose schedule be used in the primary target group from 9 years of age and for all older age groups for which HPV vaccines are licensed.
- The minimum interval between first and second dose is 6 months. A 12-month schedule results in higher GMTs and is suggested for programmatic and efficiency reasons.
- There is no maximum recommended interval between doses and longer intervals – up to 3 or 5 years – can be considered if useful from a programme perspective.
- Alternative single-dose schedule: As an off-label option, a single-dose schedule can be used in girls and boys aged 9–20 years. Current evidence suggests that a single dose has comparable efficacy and duration of protection as a 2-dose schedule and may offer programme advantages, be more efficient and affordable, and contribute to improved coverage. From a public health perspective, the use of a single dose schedule can offer substantial benefits that outweigh the potential risk of a lower level of protection if efficacy wanes over time, although there is no current evidence of this.
- Individuals known to be immunocompromised or HIV-infected (regardless of age or antiretroviral therapy status) should receive at least two HPV vaccine doses (minimum 6 months interval) and, where possible, three doses.
- HPV vaccines can be co-administered with other non-live and live vaccines using separate syringes and different injection sites. Co-administration of a booster dose of tetanus-diphtheria (Td) vaccination should be considered to improve programme efficiency and avoid missed opportunities to receive needed vaccinations.
- As a precaution HPV vaccine is not recommended in pregnancy. If pregnancy occurs following the first dose of vaccination, the subsequent dose should be delayed until after the pregnancy. Termination of pregnancy is not indicated if vaccination was carried out inadvertently during pregnancy. Breastfeeding is not a contraindication for HPV vaccination.

[11] Japanese Encephalitis (JE)

- Position paper reference: Weekly Epid. Record (2015, 90: 69-88) [pdf 950 KB].
- JE vaccination should be integrated into national immunization schedules in all areas where JE is recognized as a public health priority.
- The most effective immunization strategy in JE endemic settings is a one-time campaign in the primary target population, as defined by local epidemiology (typically children aged <15 years), followed by incorporation of JE vaccine into the routine childhood immunization programme.
- The following vaccine dosing schedules and age of administration are recommended. The need for a booster dose in endemic settings has not been clearly established for any of the vaccines listed below:
    - *Inactivated Vero cell-derived vaccine*: Primary series according to manufacturer's recommendations (these vary by product), generally 2 doses at 4-week intervals starting the primary series at ≥6 months of age in endemic settings
    - *Live attenuated vaccine*: Single dose administered at ≥8 months of age
    - *Live recombinant vaccine*: Single dose administered at ≥9 months of age
- Preferably, inactivated mouse brain-derived vaccines should be replaced by the newer generation JE vaccines discussed in this position paper. Inactivated mouse brain-derived vaccines may continue to play a role in combatting JE in some countries, but overall these products have a less favourable safety profile due to their increased reactogenicity compared to newer JE vaccines. Other disadvantages include the variability of manufacturing, the cost, the higher number of doses required and the need for boosters.
- Despite a lack of comprehensive immunogenicity/effectiveness and safety data for all possible combinations of JE and other routine vaccines, co-administration for programmatic reasons seems acceptable, even in the context of mass campaigns. As a general rule, any live vaccine may be given either simultaneously or at an interval of 4 weeks.
- Inactivated JE vaccine can be used in immunocompromised persons including HIV-infected individuals, but the immune response may be lower than in fully immunocompetent persons. Inactivated Vero cell-derived vaccines should be used preferentially over live attenuated or live recombinant vaccines in immunocompromised persons. HIV testing is not a prerequisite for vaccination.
- If the JE risk is sufficient to warrant vaccination of pregnant women, inactivated Vero cell-derived vaccines should be used preferentially over live attenuated or live recombinant vaccines based on the general precautionary principle against using live vaccines in pregnant women especially if alternative types of vaccines are available. Pregnancy testing is not a prerequisite for JE vaccination. Inadvertent administration of live attenuated or live recombinant JE vaccine to a pregnant woman is not an indication for termination of the pregnancy.

[12] Yellow Fever

- Position paper reference: Weekly Epid. Record (2013, 88: 269-284) [pdf 1.24MB].
- WHO recommends that all endemic countries should introduce YF vaccine into their routine immunization programmes.
- A single dose of YF vaccine is sufficient to confer sustained life-long protective immunity against YF disease; a booster dose is not necessary.
- It is recommended that YF vaccine be given to children at age 9-12 months at the same time as the measles vaccine.
- The vaccine is contraindicated in children aged <6 months and is not recommended for those aged 6-8 months, except during epidemics when the risk of infection with the YF virus is very high. Other contraindications for YF vaccination are severe hyper-sensitivity to egg antigens and severe immunodeficiency.
- Preventive mass vaccination campaigns are recommended for inhabitants of areas at risk of YF where there is low vaccination coverage. Vaccination should be provided to everyone aged ≥ 9 months, in any area with reported cases. Noting that YF is a live vaccine, a risk-benefit assessment should be undertaken for all pregnant and lactating women.
- Vaccine should be offered to all unvaccinated travelers aged ≥ 9 months, travelling to and from at-risk areas, unless they belong to the group of individuals for whom YF vaccination is contraindicated.
- YF vaccine may be administered simultaneously with other vaccines. As a general rule, any live vaccine may be given either simultaneously or at an interval of 4 weeks. Oral polio vaccine may be given at any time in relation to YF vaccination.

[13] Tick-Borne Encephalitis (TBE)

- Position paper reference: Weekly Epid. Record (2011, 86: 241-256) [pdf 318KB].
- Since the incidence of tick-borne encephalitis may vary considerably between and even within geographical regions, public immunization strategies should be based on risk assessments conducted at country, regional or district level, and they should be appropriate to the local endemic situation. Therefore, establishing case reporting of the disease is essential before deciding on the most appropriate preventive measures to be taken.
- In areas where the disease is highly endemic (that is, where the average prevaccination

incidence of clinical disease is ≥5 cases/100 000 population per year), implying that there is a high individual risk of infection, WHO recommends that vaccination be offered to all age groups, including children.

- Because the disease tends to be more serious in individuals aged >50–60 years this age group constitutes an important target for immunization.
- Where the prevaccination incidence of the disease is moderate or low (that is, the annual average during a 5-year period is <5/100 000) or is limited to particular geographical locations or certain outdoor activities, immunization should target individuals in the most severely affected cohorts.
- People travelling from non-endemic areas to endemic areas should be offered vaccination if their visits will include extensive outdoor activities.
- Vaccination against the disease requires a primary series of 3 doses; those who will continue to be at risk should probably have ≥1 booster doses.
- Within the considerable range of acceptable dose intervals, the relevant national authorities should select the most rational primary schedule for their national, regional or district immunization programmes.
- Although there is a strong indication that the spacing of boosters could be expanded considerably from the intervals currently recommended by the manufacturers (every 3-5 years), the evidence is still insufficient for a definitive recommendation on the optimal frequency and number of booster doses. Countries should therefore continue to recommend the use of vaccines in accordance with local disease epidemiology and current schedules until more definitive information becomes available.
- For the vaccines manufactured in Austria and Germany (FSME-Immun and Encepur;) that can be given starting from > 1year of age an interval of 1–3 months is recommended between the first 2 doses, and 5–12 months between the second and third doses. When rapid protection is required, for example for people who will be travelling to endemic areas, the interval between the first 2 doses may be reduced to 1–2 weeks.
- With the vaccines manufactured in the Russian Federation (TBE-Moscow and EnceVir) the recommended intervals are 1–7 months between the first 2 doses, and 12 months between the second and third doses. Booster doses are recommended every 3 years for those at continued risk of exposure.
- The currently recommended booster interval should be maintained until more data have been obtained on the duration of protection induced by the Russian vaccines.
- Regardless of the duration of the delay, interrupted schedules should be resumed without repeating previous doses.

[14] Typhoid

- Position paper reference: Weekly Epid. Record (2018, 93: 153-172) [pdf 297KB].
- Typhoid vaccination programmes should be implemented in the context of other efforts to control the disease, including health education, water quality and sanitation improvements, and training of health professionals in diagnosis and treatment.
- Among the available typhoid vaccines, TCV is preferred at all ages in view of its improved immunological properties, use in younger children and expected duration of protection. Countries may consider the routine use of ViPS vaccine in individuals 2 years and older, and Ty21a vaccine for individuals more than 6 years of age.
- TCV - for infants and children from 6 months of age and in adults up to 45 years. Administration of TCV at the same time as other vaccine visits at 9 month of age or in the second year of life is encouraged. ViPS – single dose from 2 years of age. Ty21a – 3-doses to be administered orally every second day from 6 years of age.
- Catch-up vaccination with TCV up to 15 years of age is recommended when feasible and supported by epidemiological data.
- Typhoid vaccination is recommended in response to confirmed outbreaks of typhoid fever and may be considered in humanitarian emergency settings depending on the risk assessment in the local setting.
- The potential need for revaccination with TCV is currently unclear. Revaccination is recommended every 3 years for ViPS, and every 3-7 years for Ty21a.
- Use of the live attenuated Ty21a vaccine during pregnancy should be avoided because of theoretical safety concerns about potential adverse effects.

[15] Cholera

- Position paper reference: Weekly Epid. Record (2017, 92:477-500) [pdf 676KB].
- Appropriate case management, WaSH interventions, surveillance and community mobilization remain the cornerstones of cholera control. Vaccination should be implemented in relevant settings as part of comprehensive cholera control strategies or while other activities are being developed.
- WC vaccines (Shanchol, Euvchol, and mORCVAX) 2 doses should be given 14 days apart to individuals ≥1 year of age. For WC-rBS vaccine (Dukoral) 3 doses should be given to children 2-5 years of age, and 2 doses to children aged ≥6 years and adults, with an interval of 1-6 weeks between doses in both groups.
- Revaccination is recommended where there is continued risk of *V. cholerae* infection. For WC vaccines revaccination is recommended after 3 years. For WC-rBS vaccine: children age 2-5 years revaccination is recommended within 6 months. If less than 6 months have passed, 1 dose for revaccination. If more than 6 months have passed, the primary series of 3 doses should be repeated. For those aged ≥6 years of age, if less than 2 years have passed, 1 dose for revaccination. If more than 2 years have passed, the primary series of 2 doses should be repeated.
- In cholera-endemic countries, vaccination of the entire population (throughout a country regardless of risk) is usually not warranted. Vaccination policies and strategies should be guided by an assessment of the risk of cholera and targeted to cholera hotspots. Strategies targeting specific age groups at higher risk of disease may be considered.
- For control of cholera outbreaks vaccination should be considered to help prevent the spread to new areas. For vaccination campaigns, a single-dose strategy using WC vaccines (Shanchol, Euvchol or mORCVAX) could be considered in areas experiencing cholera outbreaks.
- During humanitarian emergencies with a risk of cholera, but without a current cholera outbreak, vaccination with OCV should be considered as an additional preparedness measure for outbreak prevention, depending on the local infrastructure (capacity to organize a vaccination campaign).
- Pregnant and lactating women and HIV infected individuals should be included in OCV campaigns since there is a high potential benefit and minimal risks.

[16] Meningococcal

- Position paper reference: Weekly Epid. Record (2011, 86: 521-540) [pdf 1.1MB] and Update for MenA conjugate Weekly Epid Record (2015, 90: 57-68) [pdf 852KB].
- Conjugate vaccines are preferred over polysaccharide vaccines due to their potential for herd protection and their increased immunogenicity, particularly in children <2 years of age.
- Both conjugate and polysaccharide vaccines are efficacious and safe when used in pregnant women.

- MenA conjugate vaccine (5µg) a 1-dose schedule is recommended at 9-18 months of age based on local programmatic and epidemiologic considerations. The vaccine should be administered by deep intramuscular injection, preferably in the anterolateral aspect of the thigh. There is no reason to expect interference when co-administered with other vaccines. The need for a booster dose has not been established.
- If in a specific context there is a compelling reason to vaccinate infants younger than 9 months, a 2-dose schedule should be used starting at 3 months of age, with an interval of at least 8 weeks between doses.
- For monovalent MenC conjugate vaccine one single intramuscular dose is recommended for children aged ≥12 months, teenagers and adults. Children 2-11 months require 2 doses administered at an interval of a least 2 months and a booster about 1 year after. If the primary series is interrupted, vaccination should be resumed without repeating the previous dose.
- Quadrivalent conjugate vaccines (A,C,W135,Y-D and A,C,W135,Y-CRM) should be administered as one single intramuscular dose to individuals ≥ 2 years. A,C,W135,Y-D is also licensed for children 9-23 months of age, and given as a 2-dose series, 3 months apart beginning at age 9 months. If the primary series is interrupted, vaccination should be resumed without repeating the previous dose.
- Meningococcal polysaccharide vaccines are less, or not, immunogenic in children under 2 years of age.
- Meningococcal polysaccharide vaccines can be used for those ≥ 2 years of age to control outbreaks in countries where limited economic resources or insufficient supply restrict the use of meningococcal conjugate vaccines. Polysaccharide vaccines should be administered to individuals ≥ 2 years old as one single dose. One booster 3-5 years after the primary dose may be given to persons considered to be a continued high risk of exposure, including some health workers. See position paper for details.

[17] Hepatitis A

- Position paper reference: Weekly Epid. Record (2022, 97: 493-512) [pdf 518.2 KB].
- Vaccination against hepatitis A should be part of a comprehensive plan for the prevention and control of viral hepatitis, including measures to improve safe drinking-water, sanitation and hygiene (such as hand washing) and measures for outbreak control.
- WHO recommends that vaccination against hepatitis A virus be introduced into national immunization schedules for individuals aged ≥12 months, if indicated on the basis of: i) an increasing trend over time of acute hepatitis A disease, including severe disease, among older children, adolescents or adults; ii) changes in the endemicity from high to intermediate; and iii) considerations of cost- effectiveness.
- In highly endemic countries, most individuals are asymptomatically infected with HAV in childhood, which prevents clinical hepatitis A in adolescence and adulthood. In these countries, large-scale hepatitis A vaccination programmes are not routinely recommended, because they carry a risk of a paradoxical increase in disease incidence in unvaccinated people. If a highly endemic country nevertheless wishes to consider largescale vaccination, it is essential to undertake a thorough prior analysis of risks vs benefits and ensure a high vaccination coverage to avoid this risk.
- Groups at higher risk of hepatitis A should be vaccinated. Such groups include travellers from low-endemic countries to areas of intermediate or high endemicity, men who have sex with men, at-risk occupational groups (such as sewage workers or laboratory personnel handling hepatitis A virus specimens), people who inject drugs, people who experience homelessness, migrants, refugees, incarcerated persons; and patients with chronic liver disease or people living with HIV, particularly in countries with low and very low endemicity.
- Countries with improving socioeconomic status may rapidly move from high to intermediate hepatitis A endemicity, rendering a larger proportion of the adolescent and/or young adult population susceptible to HAV infection. In such countries, large-scale hepatitis A vaccination in early childhood is likely to be cost-effective and is therefore recommended. When introducing the vaccine, these countries should consider the need for catch-up immunization based on age-specific seroprevalence rates or other markers of susceptibility.

Inactivated vaccine:

- For children, inactivated hepatitis A vaccines can be given as a single- or 2-dose schedule, and administered intramuscularly. With a 2-dose schedule, the first dose should be given starting from age ≥12 months. The interval between doses is flexible, from 6 months up to 4–5 years or more, but is usually 6–18 months. Data on vaccine effectiveness, antibody persistence, and modelling on long-term seroprotection indicate that an off-label, single dose schedule is equivalent to the two-dose schedule in children, in addition to being less costly and easier to implement.
- For adults aged >40 years, vaccination with inactivated vaccines using the 2-dose schedule is preferred since there is insufficient evidence on the immunogenicity and long-term protection from a single dose in this age group.
- Inactivated hepatitis A vaccines produced by different manufacturers, including combined hepatitis A vaccines, are interchangeable.
- For immunocompromised individuals, until further experience has been obtained with a single-dose schedule, a 2-dose schedule of inactivated vaccine is recommended. Inactivated hepatitis A vaccines should also be considered for use in pregnant women at risk of HAV infection.

Live attenuated vaccine:

- Live attenuated vaccines are licensed for individuals aged ≥18 months and are administered as a single subcutaneous dose.
- Hepatitis A vaccines can be administered simultaneously with any of the vaccines routinely used in childhood immunization programmes.

[18] Rabies

- Position paper reference: Weekly Epid. Record (2018, 93: 201-220) [pdf 370 KB].
- Production and use of nerve-tissue vaccines should be discontinued and replaced by vaccines based on RABV grown in cell culture or embryonated eggs (CCEEVs).
- There are two main immunization strategies for the prevention of human rabies: (i) PEP which includes extensive and thorough wound washing at the RABV-exposure site, together with RIG administration if indicated, and the administration of a course of several doses of rabies vaccine; (ii) PrEP which is the administration of several doses of rabies vaccine before exposure to RABV. PrEP is recommended for individuals at high risk of RABV exposure. These include sub-populations in highly endemic settings with limited access to timely and adequate PEP, individuals at occupational risk, and travellers who may be at risk of exposure.
- For both PEP and PrEP, vaccines can be administered by either the ID or IM route. One ID dose is 0.1 mL of vaccine; one IM dose is 0.5 mL or 1.0 mL depending on the product.
- The indication and procedure for PEP depend on the type of contact with the suspected rabid animal and immunization status of the patient. For category I exposures, no PEP is required; for category II, immediate vaccination is recommended; for category III, immediate vaccination is recommended, and administration of RIG, if indicated.
- PrEP schedule: 2-site ID vaccine administered on days 0 and 7. If IM administration is used, WHO recommends a 1-site IM vaccine administration on days 0 and 7.
- If any doses are delayed, vaccination should be resumed, not restarted. A change in the route of administration or in vaccine product during a PEP or PrEP course is acceptable if such a change

is unavoidable.

- No further PrEP booster doses following a primary series of PrEP or PEP are required for individuals living in, or travelling to, high-risk areas.
- Professionals who are at continual or frequent risk of exposure through their activities should have regular serological monitoring. If VNA levels fall to <0.5 IU/mL, a 1-site ID or a 1-site IM PrEP booster vaccination is recommended. If serological testing is not available for those at continual or frequent occupational risk, a periodic 1-dose (ID or IM) PrEP booster vaccination can be considered based on the assessment of relative risk.

[19] Dengue (TAK-003)

- Position paper reference: Weekly Epid. Record (2024, 99: 203-224) [pdf 403KB].
- Vaccination against dengue should be viewed as part of an integrated strategy to control the disease, including vector control, proper case management, community education, and community engagement. TAK-003 does not prevent all cases of dengue.
- WHO recommends that countries consider introducing TAK-003 into their routine immunization programmes in geographical locations where high transmission intensity of dengue poses a significant public health problem. Many countries may have a heterogeneous geographical distribution of dengue transmission intensity and could consider targeted subnational introduction.
- The use of a pre-vaccination screening strategy to limit vaccination to seropositive persons is not recommended in settings with high dengue transmission as this would substantially reduce the public health impact of vaccination and increase programmatic costs.
- WHO recommends the use of TAK-003 in children aged 6–16 years in settings with high dengue transmission intensity. Within this age range, the vaccine should optimally be initiated about 1–2 years prior to the age specific peak incidence of dengue-related hospital admissions, although programmatic alignment with the administration of other school-based vaccination and health interventions is also an important consideration.
- Catch-up vaccination can also be considered for other age groups within the 6–16 year age range at the time of vaccine introduction.
- WHO does not currently recommend use of TAK-003 in children aged <6 years because of the low efficacy in this age group. Furthermore, the dengue seropositivity rate in this age group is generally low, even in high dengue transmission settings.
- The vaccine is recommended as a 2-dose schedule with a minimum interval of 3 months between doses. It is not advised to reduce the interval between doses.
- If the second dose is delayed for any reason, it is not necessary to restart the series and the second dose should be administered at the first available opportunity.
- A booster dose is not recommended.
- TAK-003 may be co-administered with other inactivated, subunit, or mRNA vaccines, except for live vaccines, for which more data are required.
- TAK-003 is not recommended during pregnancy and pregnancy should be avoided for at least 1 month following vaccination. Inadvertent vaccination of a pregnant person is not a reason to terminate the pregnancy.
- The vaccine is contraindicated for mothers during breastfeeding. TAK-003 is contraindicated in persons with congenital or acquired immune deficiency, including those receiving immunosuppressive therapies such as chemotherapy or high doses of systemic corticosteroids within 4 weeks prior to vaccination, as with other live attenuated vaccines. The vaccine is also contraindicated in individuals with symptomatic HIV infection or with asymptomatic HIV infection associated with evidence of impaired immune function.
- Persons with comorbidities, such as sickle cell anaemia, diabetes, hypertension, or underlying comorbidities that may result in bleeding tendencies (e.g. ulcerative colitis), are at higher risk of more severe disease outcomes when infected with dengue virus. Persons with such comorbidities are generally older. Persons with comorbidities who live in dengue-endemic countries could be offered vaccination, even if they fall outside the recommended age range for programmatic use (i.e. 6–16 years), provided that a substantial country-specific burden of severe dengue outcomes in these subpopulations has been documented. Until more data on efficacy-safety profiles become available, WHO recommends the lower age limit of 6 years, and the upper limit of 60 years for vaccination.

[20] Malaria

- Position paper reference: Weekly Epid. Record (2024, 99: 225-248) [pdf 461KB].
- Malaria vaccines should be provided as part of a comprehensive malaria control strategy.
- WHO recommends the use of malaria vaccines for the prevention of P. falciparum malaria in children living in malaria endemic areas, prioritizing areas of moderate and high transmission. However, countries may also consider providing the vaccine in low transmission settings.
- Malaria vaccines should be provided in a 4-dose schedule in children from 5 months of age.
- The minimum interval between any doses is 4 weeks; however, to achieve prolonged protection, the fourth dose should be given 6–18 months after the third dose.
- To improve coverage, there can be flexibility in the timing of the fourth dose, including by aligning it with vaccines given in the second year of life. Alternatively, because vaccine efficacy is highest in the first months after vaccination, the fourth dose can be given just prior to seasonal peaks in malaria transmission to optimize vaccine efficacy.
- A fifth dose, given one year after the fourth dose, may be provided in areas of highly seasonal transmission and may be considered in other areas – depending on a local assessment of feasibility and cost-effectiveness – where a significant malaria risk remains for children.
- At the time of vaccine introduction, catch-up vaccination can be considered in children up to 5 years of age, subject to local epidemiology and age of high risk, feasibility, affordability and vaccine availability.
- In areas with highly seasonal malaria transmission or perennial malaria transmission with seasonal peaks, countries may consider providing the vaccine using an age-based or seasonal approach. Alternatively, countries could consider a hybrid of these approaches, giving the first 3 doses through age-based administration and subsequent annual doses seasonally.
- The vaccination series should be completed with the same product whenever feasible. If the product used for a prior dose is unavailable or unknown, the series should be completed with either of the available WHO-recommended malaria vaccines.
- Malaria vaccines may be administered simultaneously with other childhood vaccines.
- Malaria vaccines should not be given to anyone who has experienced a severe allergic reaction after a previous hepatitis B vaccination or malaria vaccine dose or vaccine component.
- Malaria vaccines are not recommended for use in adults (including health workers and pregnant persons). The vaccine is not indicated for travelers, who should use chemoprophylaxis and vector control methods to prevent malaria when travelling to endemic settings.

[21] Mumps

- Position paper reference: Weekly Epid. Record (2024, 82: 49-60) [pdf 311KB].
- Recommended for use in countries who are able to achieve sustained high coverage of MR vaccination, and attain measles and rubella control and/or elimination levels.
- If implemented, mumps vaccine should be administered with measles and rubella as MMR or MMRV combination vaccine and follow the same schedule.

[22] Seasonal Influenza (Inactivated Vaccine)

- Position paper reference: Weekly Epid. Record (2022, 97: 185-208) [pdf 600.1kB].
- WHO recommends that all countries should consider implementing seasonal influenza immunization programmes. Having a strong influenza programme in place has been shown to be beneficial for the response to an influenza pandemic.
- For countries considering the initiation or expansion of programmes for seasonal influenza vaccination, WHO recommends that the following target groups should be considered for vaccination (not in order of priority): health workers, individuals with comorbidities and underlying conditions, older adults and pregnant women.
- Depending on national disease goals, capacity and resources, epidemiology, national policies and priorities, and disease burden, countries may consider additional (sub)populations for vaccination, such as children. Other groups to be considered for vaccination include people at high risk of severe influenza living in congregate-living settings, such as prisons, refugee camps and group homes. Programmes should pay particular attention to vaccine equity by considering disadvantaged populations and indigenous populations with a high burden of disease.
- A single dose is appropriate for those ≥ 9 years of age and healthy adults.
- Children aged 6 months -8 years should receive 2 doses at least 4 weeks apart.
- Those who have previously been vaccinated at least once should subsequently receive 1 annual dose, as should children and adolescents aged 9 years or over and healthy adults.
- Live attenuated influenza vaccines (LAIVs) are currently not recommended for children under 2 years of age and adults, including older adults and those with comorbidities, because VE has not been consistently demonstrated in these age groups. Because LAIV is a live-virus vaccine and data on its administration to pregnant women and the associated maternal and fetal risks are limited, LAIV is also not recommended during pregnancy.
- Inactivated influenza vaccine is safe to give throughout pregnancy.
- Co-administration of influenza vaccine, including with COVID-19 or live vaccines is acceptable. When 2 vaccines are administered at the same visit, the contralateral limb should be used.

[23] Varicella

- Position paper reference: Weekly Epid. Record (2014, 89: 265-288) [pdf 889KB].
- Countries where varicella is an important public health burden could consider introducing varicella vaccination in the routine childhood immunization programme. However, resources should be sufficient to ensure reaching and sustaining vaccine coverage ≥ 80%. Decision-making on childhood varicella vaccination should also include consideration of the possible impact on herpes zoster.
- Depending on the goal of the vaccination programme, 1-2 doses should be given with the first dose administered at 12-18 months of age. The minimum interval between doses should be as recommended by the manufacturer, ranging from 4 weeks to 3 months.
- Countries with a high average age (≥ 15 years) of acquisition of infection could consider alternative vaccination strategies such as vaccination of adolescents and adults without evidence of varicella immunity. This strategy requires a 2-dose schedule.
- Varicella vaccination is contraindicated during pregnancy and pregnancy should be delayed for 4 weeks after vaccination. Termination of pregnancy is not indicated if vaccination was carried out inadvertently during pregnancy.
- Varicella vaccine can be administered concomitantly with other vaccines. Unless given together with other live viral vaccines (measles, MR, MMR), it should be administered at a minimum interval of 28 days.
- Countries should consider vaccination of potentially susceptible health-care workers (i.e. unvaccinated and with no history of varicella) with 2 doses of varicella vaccine.

(updated: December 2024)

Table 3: Recommendations* for Interrupted or Delayed Routine Immunization - Summary of WHO Position Papers

Antigen		Age of 1st Dose	Doses in Primary Series (min interval between doses)**	Interrupted primary series***	Doses for those who start vaccination late		Booster
					If ≤ 12 months of age	If > 12 months of age	
Recommendations for all immunization programmes							
BCG [1]		As soon as possible after birth	1 dose	NA	1 dose	1 dose	Not recommended
Hepatitis B [2]		As soon as possible after birth (<24h)	Birth dose <24 hrs plus 2-3 doses with DTPCV (4 weeks)	Resume without repeating previous dose	3 doses	3 doses	Not recommended
Polio [3]	**bOPV + IPV**	bOPV 6 weeks IPV 14 weeks (preferred) bOPV 6 weeks IPV 6 weeks (early option)	5 (3 bOPV (min 4 weeks) & 2 IPV (min 8 weeks))	Resume without repeating previous dose	5 doses (if >3 months old IPV to be given with 1st & 3rd dose of bOPV)	5 doses (IPV to be given with 1st dose & 3rd dose of bOPV)	Not recommended
	IPV / bOPV Sequential	8 weeks (IPV 1st) bOPV (4-8 weeks after 2nd IPV)	4 (2 IPV followed by ≥ 2 bOPV) (min 4-8 weeks)		2 doses of IPV followed by 2 doses of bOPV	2 doses of IPV followed by 2 doses of bOPV	Not recommended
	IPV -only	6-8 weeks	3 (min 4-8 weeks)		3 doses	3 doses	If 1st dose given at 6 weeks of age booster to be given ≥ 6 months after the 3rd dose
	Alternative IPV-only (fractional permitted)	≥14 weeks	2 (min 4-8 weeks)		2 doses	2 doses	Not recommended
DTP-containing vaccine (DTPCV) [4]		6 weeks (min)	3 doses (4 weeks)	Resume without repeating previous dose	3 doses	3 doses with interval of at least 4 weeks between 1st & 2nd dose, and at least 6 mos between 2nd & 3rd dose (if > 7 yrs use only aP containing vaccine; if > 4 yrs Td containing vaccine is preferred and should only be used for >7 yrs)	3 boosters: 12-23 months (DTP-containing vaccine); 4-7 years (Td/DT containing vaccine), see footnotes; and 9-15 yrs (Td containing) (if > 7 yrs use only aP containing vaccine) If tetanus vaccination started during adolescence or adulthood only 5 doses required for lifelong protection
***Haemophilus influenzae* type b** [5]	Option 1	6 weeks (min)	3 doses (4 weeks)	Resume without repeating previous dose	3 doses	1 dose >5 yrs not recommended if healthy	None
	Option 2		2-3 doses (8 weeks if 2 doses; 4 weeks if 3 doses)		2-3 doses		At least 6 months (min) after last dose
Pneumococcal (Conjugate) [6]		6 weeks (min)	3 doses (3p+0) with DTPCV (4weeks) or 2 doses (2p+1) (4-8 weeks)	Resume without repeating previous dose	2-3 doses	12-24 months: 2 doses 2-5 yrs: 1 dose 1-5 yrs at high-risk: 2 doses	Booster at 9-18 months if following 2 dose schedule Another booster if HIV+ or preterm neonate Vaccination in older adults
Rotavirus [7]		6 weeks (min)	2 or 3 depending on product given with DTPCV	Resume without repeating previous dose	2 or 3 depending on product	>24 months limited benefit	Not recommended if > 24 months old
Measles [8]		9 or 12 months (6 months min, see footnote)	2 doses (4 weeks)	Resume without repeating previous dose	2 doses	2 doses	Not recommended
Rubella [9]		9 or 12 months	1 dose with measles containing vaccine	NA	1 dose	1 dose	Not recommended
HPV [10]		As soon as possible from 9 years of age (females)	1-2 doses (6-12 months)	Resume without repeating previous dose	NA	Girls: 9-14 years 1-2 doses (see footnote)	Not recommended

* For some antigens the WHO position paper does not provide a recommendation on interrupted or delayed schedules at this present time. When the position paper is next revised this will be included. In the meantime, some of the recommendations are based on expert opinion.
** See Table 2: Summary of WHO Position Papers - Recommended Routine Immunizations for Children for full details (www.who.int/immunization/documents/positionpapers/).
*** Same interval as primary series unless otherwise specified.

(updated: December 2024)

Table 3: Recommendations* for Interrupted or Delayed Routine Immunization - Summary of WHO Position Papers

Antigen		Age of 1st Dose	Doses in Primary Series (min interval between doses)**	Interrupted primary series***	Doses for those who start vaccination late		Booster Dose
					If ≤ 12 months of age	If > 12 months of age	
Recommendations for certain regions							
Japanese Encephalitis [11]	**Inactivated Vero cell-derived vaccine**	6 months	2 (4 weeks) generally	Resume without repeating previous dose	2 doses (generally)	2 doses (generally)	Not recommended
	Live attentuated	8 months	1	NA	1 dose	1 dose	
	Live recombinant vaccine	9 months	1	NA	1 dose	1 dose	
Yellow Fever [12]		9-12 months	1 dose with measles containing vaccine	NA	1 dose	1 dose	Not recommended
Tick-Borne Encephalitis [13]	**FSME-Immun & Encepur**	≥ 1 yr	3 doses (1st to 2nd 1-3 mos; 2nd to 3rd 12 mos)	Resume without repeating previous dose	3 doses	3 doses	At least 1 booster
	TBE_Moscow & EnceVir	≥ 3 yr	3 doses (1st to 2nd 1-7 mos; 2nd to 3rd 12 mos)	Resume without repeating previous dose	3 doses	3 doses	Every 3 years
Recommendations for some high-risk populations							
Typhoid [14]	**TCV-Typbar**	>6 months	1 dose	NA	1 dose	1 dose	
	Vi PS	2 years (min)	1 dose	NA	Not recommended	1 dose	Every 3 years
	Ty21a	Capsules 6 years (min) (see footnote)	3-4 doses (1 day) (see footnote)	If interruption between doses is < 21 days resume without repeating previous dose; If > 21 days restart primary series	Not recommended	> 6 yrs: 3-4 doses	Every 3-7 years
Cholera [15]	**Dukoral (WC-rBS)**	2 years (min)	2-5 yrs: 3 doses ≥ 6 yrs: 2 doses (≥ 7 days)	If interval since last dose ≥ 6 weeks restart primary series	Not recommended	2-5 yrs: 3 doses > 6 yrs: 2 doses	2-5 yrs: every 6 months. If booster is delayed > 6 months the primary series must be repeated. >6 yrs: every 2 years. If booster is delayed > 2 yrs the primary series must be repeated.
	Shanchol, Euvchol and mORCVAX	1 year (min)	2 doses (2 weeks)	Resume without repeating previous dose	Not recommended	2 doses	After 2 years
Meningococcal [16]	**MenA conjugate**	9-18 months	1	NA	2 doses if < 9 months with 8 week interval	1	Not recommended
	MenC conjugate	2-11 months	2 (8 weeks min)	Resume without repeating previous dose	2 doses	1 dose	2-11 months of age after 1 year
		>12 months	1	NA			
	Quadrivalent conjugate	9-23 months	2 (12 weeks min)	Resume without repeating previous dose	2 doses	2 doses <23 months; 1 dose ≥ 2 years	
		≥ 2 years	1	NA			

(updated: December 2024)

Table 3: Recommendations* for Interrupted or Delayed Routine Immunization - Summary of WHO Position Papers

Antigen		Age of 1st Dose	Doses in Primary Series (min interval between doses)**	Interrupted primary series***	Doses for those who start vaccination late		Booster Dose
					If ≤ 12 months of age	If > 12 months of age	
Hepatitis A [17]	**Inactivated**	> 12 months	1 or 2	Resume without repeating previous dose	Not recommended	1 or 2	Not recommended
	Live attenuated	18 months	1			1	
Rabies [18]		As required	2 (1st to 2nd 7 days)	Resume without repeating previous dose	2 doses	2 doses	Only if occupation puts a frequent or continual risk of exposure, titres should be tested if possible
Dengue (TAK-003) [19]		6 years (min)	2 doses (3 months)	Resume without repeating previous dose	Not recommended	2 doses 6-16 years	Not recommended
Malaria [20]		5 months	4 doses (4 weeks)	Resume without repeating previous dose	4 doses	4 doses	
Recommendations for immunization programmes with certain characteristics							
Mumps [21]		12-18 months	2 doses with measles and rubella containing vaccine (4 weeks)	Resume without repeating previous dose	Not recommended	2 doses	Not recommended
Seasonal influenza (inactivated tri- and quadri-valent) [22]		6 months (min)	2 (6 month to 8 years) 1(≥ 9 years)	Resume without repeating previous dose	2 doses	2 (6 month to 8 years) 1(≥ 9 years)	Revaccinate annually 1 dose only
Varicella [23]		12-18 months	1-2 (4 weeks – 3 months, depending on manufacturer)	Resume without repeating previous dose	Not recommended	1-2 doses	

Summary Table 3 - Notes

- The attached table summarizes the WHO recommendations for interrupted or delayed routine vaccination. Its purpose is to assist national decision-makers and programme managers to develop appropriate policy guidance in relation to their national immunization schedule.
- This table is designed to be used together with two other summary tables - Table 1: Summary of WHO Position Papers - Recommendations for Routine Immunization; and Table 2: Summary of WHO Position Papers - Recommended Routine Immunization for Children.
- Vaccines can generally be co-administered (i.e. more than one vaccine given at different sites during the same visit). Recommendations that explicitly endorse co-administration are indicated in the footnotes. Lack of an explicit co-administration recommendation is often due to a lack of evidence and does not necessarily imply that the vaccine cannot be co-administered. Exceptions to co-administration are stated.
- Refer to http://www.who.int/immunization/positionpapers/ for the most recent version of this table (and Tables 1 and 2) and position papers.

[1] BCG

- Position paper reference: Weekly Epid. Record (2017, 92:369-392) [pdf 660KB].
- BCG vaccination is recommended for unvaccinated TST- or IGRA-negative older children, adolescents and adults from settings with high incidence of TB and/or high leprosy burden and those moving from low to high TB incidence/ leprosy burden settings.

[2] Hepatitis B

- Position paper reference: Weekly Epid. Record (2017, 92:369-392) [pdf 2.4MB].
- In general, the dose for infants and children (aged < 15 years) is half the recommended adult dose.
- Co-administration of HepB vaccine does not interfere with the immune response to any other vaccine and vice versa.
- If delayed or interrupted scheduling of vaccination for children, adolescents and adults, 3 doses are recommended, with the second dose administered at least 1 month after the first, and the third dose 6 months after the first dose. If the vaccination schedule is interrupted it is not necessary to restart the vaccine series.

[3] Polio

- Position paper reference: Weekly Epid. Record (2022, 97:277-300) [pdf 589KB].

bOPV plus IPV

- For infants late in starting the routine immunization schedule (age >3 months) the first IPV dose should be administered at the first immunization contact along with bOPV and the other routinely recommended vaccines.

Sequential IPV–bOPV

- For sequential IPV– bOPV schedules, WHO recommends that the first dose of IPV be given starting from 8 weeks of age with an interval of 4–8 weeks before administration of the second IPV dose. This should be followed by at least 2 doses of bOPV separated by 4–8 weeks depending on the risk of exposure to poliovirus in early childhood.

IPV-only

- A primary 3-dose series of IPV administered beginning at 6 or 8 weeks of age, with a minimum 4 week interval between doses, is recommended.
- If the primary series begins at 6 weeks, a booster dose should be given 6 months or more after the third dose.
- Alternatively, a 2-dose or fractional dose IPV schedule, starting at 14 weeks of age or older, with a second dose 4 months or more later can be considered. This schedule is currently recommended for use after OPV cessation.
- While both options provide high immunogenicity (>90%), the 3 dose primary series provides protection in early infancy.

[4] DTP-containing vaccines (Diphtheria, Tetanus and Pertussis)

- Position paper reference: Diphtheria - Weekly Epid. Record (2017, 92:417-436) [pdf 526KB];
- Tetanus - Weekly Epid. Record (2017, 92: 53-76) [pdf 636KB]; Pertussis - Weekly Epid. Record (2015, 90: 433-460) [pdf 667KB].
- If either the start or the completion of the primary series has been delayed, the missing doses should be given at the earliest opportunity with an interval of at least 4 weeks between doses.
- 3 booster doses of diphtheria toxoid-containing vaccine should be provided during childhood and adolescence. The diphtheria booster doses should be given in combination with tetanus toxoid using the same schedule, i.e at 12–23 months of age, 4–7 years of age, and 9–15 years of age, using age-appropriate vaccine formulations. Ideally, there should be at least 4 years between booster doses.
- Tetanus - To ensure lifelong protection against tetanus all people should receive 6 doses (3 primary plus 3 booster doses) of tetanus toxoid-containing vaccine (TTCV) through routine childhood immunization schedules.
- If tetanus vaccination is started during adolescence or adulthood, a total of only 5 appropriately spaced doses are required to obtain lifelong protection.
- To provide and sustain both tetanus and diphtheria immunity throughout the life course and for both sexes, age-appropriate combinations of tetanus and diphtheria toxoids should be used. For children <7 years of age DTwP or DTaP combinations may be used. For children aged 4 years and older Td containing vaccine may be used and is preferred.
- From 7 years of age only Td combinations should be used. Age-appropriate combinations containing pertussis vaccine with low-dose diphtheria antigen are also available.
- Pregnant women and their newborn infants are protected from birth-associated tetanus if the mother received either 6 TTCV doses during childhood or 5 doses if first vaccinated during adolescence/adulthood (documented by card, immunization registry and/or history) before the time of reproductive age. Vaccination history should be verified in order to determine whether a dose of TTCV is needed in the current pregnancy.
- Pertussis vaccine: Only aP-containing vaccines should be used for vaccination of persons aged ≥7 years.
- Pertussis containing booster: A booster dose is recommended for children aged 1–6 years, preferably during the second year of life (≥6 months after last primary dose), unless otherwise indicated by local epidemiology; the contact could also be used to catch up on any missed doses of other vaccines. This schedule should provide protection for at least 6 years for countries using wP vaccine. For countries using aP vaccine, protection may decline appreciably before 6 years of age.
- Delayed or interrupted DTP-containing series: For children whose vaccination series has been

interrupted, the series should be resumed without repeating previous doses. Children aged 1 to < 7 years who have not previously been vaccinated should receive 3 doses of vaccine following a 0, 1, 6 month schedule. Two subsequent booster doses using Td or Tdap combination vaccines are needed with an interval of at least 1 year between doses.

[5] *Haemophilus influenzae* type b (Hib)

- Position paper reference: Weekly Epid. Record (2013, 88: 413-428) [pdf 209KB].
- The number of primary doses should be set after consideration of the local epidemiology, vaccine presentation (Hib conjugate monovalent vaccine versus Hib conjugate vaccine in combination with other antigens) and how this fits into the overall routine immunization schedule.
- If the vaccination course has been interrupted, the schedule should be resumed without repeating the previous dose. Children who start vaccination late, but are aged under 12 months, should complete the vaccination schedule (e.g. have 3 primary doses or 2 primary doses plus a booster).
- When a first dose is given to a child older than 12 months of age, only one dose is recommended.
- Hib vaccine is not required for healthy children after 5 years of age.

[6] Pneumococcal (Conjugate)

- Position Paper Reference: Weekly Epid. Record (2019, 94: 85-104) [pdf 444KB].
- For administration of PCV to infants, WHO recommends a 3-dose schedule administered either as 2p+1 or as 3p+0, starting as early as 6 weeks of age.
- If the 2p+1 schedule is selected, an interval of ≥8 weeks is recommended between the 2 primary doses the booster dose should be given at 9–18 months of age, according to programmatic considerations; there is no defined minimum or maximum interval between the primary series and the booster dose.
- If the 3p+0 schedule is used, a minimum interval of 4 weeks should be maintained between doses.
- Interrupted schedules should be resumed without repeating the previous dose.
- If a series cannot be completed with the same type of vaccine, the available PCV product should be used. Restarting a series is not recommended, even for the primary series.
- Wherever possible, catch-up vaccination at the time of introduction of PCV should be used to accelerate its impact on disease in children aged 1–5 years, particularly in settings with a high disease burden and mortality. If there is limited availability of vaccine or of financial resources for catch-up vaccination, the youngest children (e.g. < 2 years of age) should be prioritized to receive catch-up doses of PCV because of their higher risk for pneumococcal disease.
- Catch-up vaccination can be done with a single dose of vaccine for children ≥24 months
- Unvaccinated children aged 1–5 years who are at high risk for pneumococcal infection because of underlying medical conditions, such as HIV infection or sickle-cell disease, should receive at least 2 doses separated by at least 8 weeks.
- WHO does not currently have recommendations on the use of PCV in individuals over 5 years of age.

[7] Rotavirus

- Position paper reference: Weekly Epid. Record (2013, 88: 49-64) [pdf 950KB].
- Early immunization is favoured with the first dose of rotavirus vaccine to be administered from 6 weeks of age, however, in order to benefit those who may come late infants can receive doses without age restriction. Because of the typical age distribution of rotavirus gastroenteritis (RVGE), rotavirus vaccination of children >24 months of age is not recommended.
- Regardless of the duration of delay, interrupted schedules should be resumed as soon as possible without repeating previous doses.
- Rotavirus vaccinations can be administered simultaneously with other vaccines in the infant immunization programme.

[8] Measles

- Position paper reference: Weekly Epid. Record (2017, 92:205-228) [pdf 600KB].
- Reaching all children with 2 doses of measles vaccine should be the standard for all national immunization programmes. In addition to the first routine dose of MCV1, all countries should add a second routine dose of MCV2 to their national immunization schedules regardless of the level of MCV1 coverage.
- Regardless of the duration of delay, interrupted schedules should be resumed as soon as possible without repeating previous doses.
- Because many cases of measles occur in children aged >12 months who have not been vaccinated, routine delivery of MCV1 should not be limited to infants aged 9–12 months and routine delivery of MCV2 should not be limited to infants 15 to 18 months of age. Every opportunity (e.g. when children come into contact with health services) should be taken to vaccinate all children that missed one or both MCV routine doses, particularly those under 15 years of age. Policies which prohibit use of vaccine in children >1 year of age, older children and teenagers should be changed to allow these individuals to be vaccinated.
- The minimum interval between MCV1 and MCV2 is 4 weeks.

[9] Rubella

- Position paper reference: Weekly Epid. Record (2020, 86: 301-316) [pdf 413KB].
- Because rubella is not as highly infectious as measles and because the effectiveness of 1 dose of an RCV is > 95% even at 9 months of age, only 1 dose of rubella vaccine is required to achieve rubella elimination if high coverage is achieved. However, when combined with measles vaccination, it may be easier to implement a second dose of RCV's using the same combined MR vaccine or MMR vaccine for both doses.
- RCV's can be administered concurrently with inactivated vaccines. As a general rule, live vaccines should be given either simultaneously with RCV's, or at least 4 weeks apart. An exception to this is oral polio vaccine, which can be given at any time before or after RCV's without interfering in the response to either vaccine.
- Interference may occur between MMR and yellow fever vaccines if they are simultaneously administered to children < 2 years of age.
- Because of a theoretical, but never demonstrated, teratogenic risk rubella vaccination in pregnant women should be avoided in principle, and those planning a pregnancy are advised to avoid pregnancy for 1 month following vaccination.
- Administration of blood or blood products before or shortly after vaccination may interfere with

vaccine efficacy. If using only rubella vaccines persons who received blood products should wait at least 3 months before vaccination and, if possible, blood products should be avoided for up to 2 weeks post-vaccination. Vaccinated persons are not eligible to donate blood for 1 month after vaccination.

[10] Human Papillomavirus (HPV)

- Position paper reference: Weekly Epid. Record (2022, 97: 645-672) [pdf 590KB].
- The current evidence supports the recommendation that a 2-dose schedule be used in the primary target group from 9 years of age and for all older age groups for which HPV vaccines are licensed.
- The minimum interval between first and second dose is 6 months. A 12-month schedule results in higher GMTs and is suggested for programmatic and efficiency reasons.
- There is no maximum recommended interval between doses and longer intervals – up to 3 or 5 years – can be considered if useful from a programme perspective.
- Alternative single-dose schedule: As an off-label option, a single-dose schedule can be used in girls and boys aged 9–20 years. Current evidence suggests that a single dose has comparable efficacy and duration of protection as a 2-dose schedule and may offer programme advantages, be more efficient and affordable, and contribute to improved coverage. From a public health perspective, the use of a single dose schedule can offer substantial benefits that outweigh the potential risk of a lower level of protection if efficacy wanes over time, although there is no current evidence of this.
- Individuals known to be immunocompromised or HIV-infected (regardless of age or antiretroviral therapy status) should receive at least two HPV vaccine doses (minimum 6 months interval) and, where possible, three doses.
- HPV vaccines can be co-administered with other non-live and live vaccines using separate syringes and different injection sites. Co-administration of a booster dose of tetanus-diphtheria (Td) vaccination should be considered to improve programme efficiency and avoid missed opportunities to receive needed vaccinations.
- As a precaution HPV vaccine is not recommended in pregnancy. If pregnancy occurs following the first dose of vaccination, the subsequent dose should be delayed until after the pregnancy. Termination of pregnancy is not indicated if vaccination was carried out inadvertently during pregnancy. Breastfeeding is not a contraindication for HPV vaccination.

[11] Japanese Encephalitis (JE)

- Position paper reference: Weekly Epid. Record (2015, 90: 69-88) [pdf 950 KB].
- The following vaccine dosing schedules and age of administration are recommended. The need for a booster dose in endemic settings has not been clearly established for any of the vaccines listed below:
    - Inactivated Vero cell-derived vaccine: Primary series according to manufacturer's recommendations (these vary by product), generally 2 doses at 4-week intervals starting the primary series at ≥6 months of age in endemic setting
    - Live attenuated vaccine: Single dose administered at ≥8 months of age
    - Live recombinant vaccine: Single dose administered at ≥9 months of age
- Despite a lack of comprehensive immunogenicity/effectiveness and safety data for all possible combinations of JE and other routine vaccines, co-administration for programmatic reasons seems acceptable, even in the context of mass campaigns.
- Regardless of the duration of delay, interrupted schedules should be resumed as soon as possible without repeating previous doses.

[12] Yellow Fever

- Position paper reference: Weekly Epid. Record (2013, 88: 269-284) [pdf 1.24MB].
- A single dose of YF vaccine is sufficient to confer sustained life-long protective immunity against YF disease; a booster dose is not necessary.
- The vaccine is contraindicated in children aged < 6 months and is not recommended for those aged 6-8 months, except during epidemics when the risk of infection with the YF virus is very high. Other contraindications for YF vaccination are severe hyper-sensitivity to egg antigens and severe immunodeficiency.
- YF vaccine may be administered simultaneously with other vaccines

[13] Tick-Borne Encephalitis (TBE)

- Position paper reference: Weekly Epid. Record (2011, 86: 241-256) [pdf 318KB].
- Regardless of the duration of delay, interrupted schedules should be resumed as soon as possible without repeating previous doses.

[14] Typhoid

- Position paper reference: Weekly Epid. Record (2018, 93: 153-172) [pdf 297KB].
- TCV is recommended for infants and children from 6 months of age and in adults up to 45 years. Administration of TCV at the same time as other vaccine visits at 9 month of age or in the second year of life is encouraged. VIPS – single dose from 2 years of age. Ty21a is recommended as 3-doses to be administered orally every second day from 6 years of age.
- Regardless of the duration of delay, interrupted schedules should be resumed as soon as possible without repeating previous doses.
- Typhoid vaccination is recommended in response to confirmed outbreaks of typhoid fever and may be considered in humanitarian emergency settings depending on the risk assessment in the local setting.
- The potential need for revaccination with TCV is currently unclear. Revaccination is recommended every 3 years for VIPS, and every 3-7 years for Ty21a.

[15] Cholera

- Position paper reference: Weekly Epid. Record (2017, 92:477-500) [pdf 676KB].
- Regardless of the duration of delay, interrupted schedules should be resumed as soon as possible without repeating previous doses.
- Revaccination is recommended where there is continued risk of *V. cholerae* infection. For WC vaccines revaccination is recommended after 3 years. For WC-rBS vaccine: children age 2-5 years revaccination is recommended within 6 months. If less than 6 months have passed, 1 dose for revaccination. If more than 6 months have passed, the primary series of 3 doses should be repeated. For those aged ≥6 years of age, if less than 2 years have passed, 1 dose

for revaccination. If more than 2 years have passed, the primary series of 2 doses should be repeated.

- For control of cholera outbreaks vaccination should be considered to help prevent the spread to new areas. For vaccination campaigns, a single-dose strategy using WC vaccines (Shanchol, Euvchol or mORCVAX) could be considered in areas experiencing cholera outbreaks.

[16] Meningococcal

- Position paper reference: Weekly Epid. Record (2011, 86: 521-540) [pdf 1.1MB] and Update for MenA conjugate Weekly Epid Record (2015, 90: 57-68) [pdf 852KB].
- MenA conjugate vaccine (5µg) a 1-dose schedule is recommended at 9-18 months of age based on local programmatic and epidemiologic considerations.
- MenA conjugate vaccine (10 µg) should be used for catch-up and periodic campaigns from 12 months of age onwards.
- There is no reason to expect interference when co-administered with other vaccines. The need for a booster dose has not been established.
- If in a specific context there is a compelling reason to vaccinate infants younger than 9 months, a 2-dose schedule should be used starting at 3 months of age, with an interval of at least 8 weeks between doses.
- For monovalent MenC conjugate vaccine one single intramuscular dose is recommended for children aged ≥12 months, teenagers and adults. Children 2-11 months require 2 doses administered at an interval of a least 2 months and a booster about 1 year after.
- If the primary series is interrupted, vaccination should be resumed without repeating the previous dose.

[17] Hepatitis A

- Position paper reference: Weekly Epid. Record (2022, 97: 493-512) [pdf 518.2KB].
- For children, inactivated hepatitis A vaccines can be given as a single- or 2-dose schedule, and administered intramuscularly. With a 2-dose schedule, the first dose should be given starting from age ≥12 months. The interval between doses is flexible, from 6 months up to 4–5 years or more, but is usually 6–18 months. Data on vaccine effectiveness, antibody persistence, and modelling on long-term seroprotection indicate that an off-label, single dose schedule is equivalent to the two-dose schedule in children, in addition to being less costly and easier to implement.
- For adults aged >40 years, vaccination with inactivated vaccines using the 2-dose schedule is preferred since there is insufficient evidence on the immunogenicity and long-term protection from a single dose in this age group.
- For immunocompromised individuals, until further experience has been obtained with a single-dose schedule, a 2-dose schedule of inactivated vaccine is recommended. Inactivated hepatitis A vaccines should also be considered for use in pregnant women at risk of HAV infection.
- Live attenuated vaccines are licensed for individuals aged ≥18 months and are administered as a single subcutaneous dose. Live attenuated vaccines may pose a theoretical risk to the developing foetus and therefore should not be used during pregnancy, nor should they be used in severely immunocompromised patients.

[18] Rabies

- Position paper reference: Weekly Epid. Record (2018, 93: 201-220) [pdf 370 KB].
- If any doses are delayed, vaccination should be resumed, not restarted. A change in the route of administration or in vaccine product during a PEP or PrEP course is acceptable if such a change is unavoidable.

[19] Dengue (TAK-003)

- Position paper reference: Weekly Epid. Record (2024, 99: 203-224) [pdf 406KB].
- WHO recommends the use of TAK-003 in children aged 6–16 years in settings with high dengue transmission intensity.
- A 2-dose schedule with a minimum interval of 3 months between doses. It is not advised to reduce the interval between doses.
- If the second dose is delayed for any reason, it is not necessary to restart the series and the second dose should be administered at the first available opportunity.
- A booster dose is not recommended.
- TAK-003 may be co-administered with other inactivated, subunit, or mRNA vaccines, except for live vaccines, for which more data are required.
- TAK-003 is not recommended during pregnancy and pregnancy should be avoided for at least 1 month following vaccination. Inadvertent vaccination of a pregnant person is not a reason to terminate the pregnancy.
- The vaccine is contraindicated for mothers during breastfeeding. TAK-003 is contraindicated in persons with congenital or acquired immune deficiency, including those receiving immunosuppressive therapies such as chemotherapy or high doses of systemic corticosteroids within 4 weeks prior to vaccination, as with other live attenuated vaccines. The vaccine is also contraindicated in individuals with symptomatic HIV infection or with asymptomatic HIV infection associated with evidence of impaired immune function.

[20] Malaria

- Position paper reference: Weekly Epid. Record (2024, 99: 225-248) [pdf 461KB].
- Malaria vaccines should be provided in a 4-dose schedule in children from 5 months of age.
- The minimum interval between any doses is 4 weeks; however, to achieve prolonged protection, the fourth dose should be given 6–18 months after the third dose.
- Malaria vaccines may be administered simultaneously with other childhood vaccines.

[21] Mumps

- Position paper reference: Weekly Epid. Record (2024, 82: 49-60) [pdf 311KB].
- If implemented, mumps vaccine should be administered with measles and rubella as MMR or MMRV combination vaccine and follow the same schedule.
- Regardless of the duration of delay, interrupted schedules should be resumed as soon as possible without repeating previous doses.

[22] Seasonal Influenza (Inactivated Vaccine)

- Position paper reference: Weekly Epid. Record (2022, 97: 185-208) [pdf 600.1kB].
- A single dose is appropriate for those ≥ 9 years of age, and healthy adults.
- Live attenuated influenza vaccines (LAIVs) are currently not recommended for children under 2 years of age and adults, including older adults and those with comorbidities, because VE has not been consistently demonstrated in these age groups. Because LAIV is a live-virus vaccine and data on its administration to pregnant women and the associated maternal and fetal risks are limited, LAIV is also not recommended during pregnancy.
- Inactivated influenza vaccine is safe to give throughout pregnancy.
- Children aged 6 months to 8 years should receive 2 doses at least 4 weeks apart.
- Those who have previously been vaccinated at least once should subsequently receive 1 annual dose.
- Co administration of influenza vaccine, including with COVID-19 or live vaccines is acceptable. When 2 vaccines are administered at the same visit, the contralateral limb should be used.

[23] Varicella

- Position paper reference: Weekly Epid. Record (2014, 89: 265-288 [pdf 5,3MB].
- Varicella vaccine can be administered concomitantly with other vaccines. Unless given together with other live viral vaccines (measles, MR, MMR), it should be administered at a minimum interval of 28 days.
- Regardless of the duration of delay, interrupted schedules should be resumed as soon as possible without repeating previous doses.

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Immunization Act, 2072 (2016)

Date of Publication in Gazette: 2072/10/12
(26 January 2016)

An Act enacted to manage Immunization Services

Preamble: Whereas, it is expedient to necessary arrangement for providing quality immunization services with development, expansion and strengthening of immunization services in the country with a view to prevention, control, elimination or eradication of vaccine preventable disease and thereby to reduce infant, child, maternal and other individual mortality rate;

Now, therefore, the Legislature-Parliament has enacted this Act pursuant to Sub-Article (1) of Article 296 of the Constitution of Nepal.

Chapter-1

Preliminary

1. **Short Title and Commencement**:(1) This Act may be cited as "Immunization Act, 2072 (2016)".

   (2) This Act shall come into force from ninety-one days of its authentication.

2. **Definition**:Unless the subject or context otherwise requires, in this Act;

   a) "License" means a license issued to conduct immunization services pursuant to Section 11.

Dec 24, 2018

b) "Investigation Committee" means a committee formed to conduct investigation on adverse event pursuant to Section 19.

c) "Fund" means an Immunization Fund established pursuant to Section 21.

d) "Vaccine" means the vaccine administered to control, prevent, eliminate or eradicate any disease.

e) "Immunization Card" means a immunization card issued pursuant to Section 12.

f) "Immunization Program" means National Immunization Program to be conducted by the Government of Nepal as regular immunization program or campaign with a view to prevent, control, eliminate or eradicate vaccine preventable diseases and the term also includes surveillance of vaccine preventable diseases.

g) "Vaccinator" means a health worker or doctor who administers the vaccine and the term also includes any person deputed by the Ministry to administer special type of vaccine.

h) "Immunization Service" means administration of vaccine under this Act and the term also includes management, supply, storage and distribution of vaccine, materials to conduct immunization services.

i) "Doctor" means a person registered as a doctor under prevailing law.

Dec 24, 2018

j) "Prescribed" or "as Prescribed" means prescribed or as prescribed in the rules framed under this Act.

k) "Ministry" means Ministry of Health.

m) "Committee" means National Immunization Committee formed pursuant to Section 15.

n) "Advisory Committee" means National Immunization Advisory Committee formed pursuant to Section 18.

o) "Department" means Department of Health Services.

p) "Health Worker" means a person registered as a health worker under prevailing law.

Chapter-2

Provisions Relating to Immunization Service

3. **Right to Have Vaccine by Target Group:** (1) The target group shall have right to have vaccines, included into immunization program, at free of cost.

Clarification: For the purpose of this Section, "Target Group" means a person belonging to a class, community or region predetermined in immunization program as obliged to have vaccine for prevention, control, elimination or eradication of particular disease.

(2) The Ministry shall make arrangement for administration of vaccine at specific date and time mentioned in sub-section (1) in any hospital, health institution, immunization center, mobile immunization clinic or other prescribed place.

Dec 27, 2018

(3) In order to provide immunization services under this Section, the Ministry may seek support of the concerned local level, police administration and volunteers.

4. **To Have Vaccination Mandatory**: (1) The Ministry may prescribe mandatory vaccination to all for prevention, control, elimination or eradication of defined diseases.

(2) The concerned person shall be obliged to vaccinate as mentioned in sub-section (1).

5. **Obligation of Patron or Guardian**: Patron or Guardian or person shall be responsible to make arrangement for providing vaccine included in immunization program to the infant, children or other person living under his/her protection, guardianship, or custody.

6. **Not to Administer Vaccine**: Notwithstanding anything contained in this Chapter vaccinator shall not administer vaccine to such person who is not found fit to have that vaccination due to his/her health.

7. **To Inform About Vaccination**: (1) Prior to vaccine administration, the vaccinator shall give information concerning the nature of vaccine, benefits and possible risk associated with vaccine to the vaccine receiver.

(2) Information as mentioned in Sub-section (1) shall be given to the patron or guardian of the vaccine receiver if he/she is infant, disable or suffering from mental disorders.

8. **Vaccine to be as per Standard**: Vaccine to be administered under this Act shall meet the prescribed standards.

9. **Doctors and Health Workers to be responsible**: It shall be the responsibility of the concerned doctors and health workers involved in vaccination under this Act.

10. **Not to Obstruct in Operation of Immunization Program**: Nobody shall create any obstruction in operation of immunization program.

11. **To Obtain License:** (1) Private, non-governmental, community hospital or health institution willing to operate immunization services shall obtain license from the designated body as prescribed.

(2) Hospital or health institution, obtaining license pursuant to sub-section (1) to operate immunization services, shall submit a report of operation of immunization services to the designated body or health institution on regular basis.

12. **To Maintain Record of Immunization Service:** (1) Vaccinator shall maintain updated record of vaccine receivers.

(2) Vaccinator shall issue immunization card to vaccine receiver in a format as prescribed.

(3) Vaccine receiver, his/her patron or guardian shall keep the immunization card safely.

Chapter-3

Provisions Relating to Supply and Storage of Vaccine

13. **To Supply Registered Vaccine:** (1) Vaccine supplying institution shall supply only vaccines which are registered in the Department of Drug Administration.

(2) Vaccines to be supplied pursuant to Sub-section (1) shall have been manufactured in compliance with good

manufacturing practices and shall have been certified by World Health Organization(WHO) as meeting the standards of WHO prequalification.

(3) Notwithstanding anything stated in Sub-section (2) vaccine which is not yet certified by WHO may be imported in following conditions: -

(a) Manufactured in compliance with good manufacturing practices,

(b) Already used in manufacturing country or in other countries,

(c) Registered in national regulatory authority of manufacturing country, and

(d) Certification of the statement contained in clauses (a), (b) and (c) by the Department of Drug Administration.

14. **Supply, Storage and Distribution ofVaccine**: Supply, storage and distribution of vaccine, equipment required for its use and temperature to be maintained until its use shall be in such standards as prescribed by the Ministry.

Chapter-4

Provisions Relating to various Committees

15. **Committee:** (1) There shall be a National Immunization Committee to give recommendation to the Ministry on formulation of immunization policy as well

(2) The committee shall be formed as follows: -

a) Secretary of the Ministry- Chairperson

b) Director General of the Department- Member

c) Joint Secretary, Ministry of Finance - Member

d) Joint Secretary, Ministry of Federal Affairs and Local Development- Member

e) Joint Secretary, Ministry of Education-Member

f) Joint Secretary, Ministry of Women, Children and Social Welfare- Member

g) Two persons, including one woman, nominated by the Ministry among pediatricians, public health experts or health economists -Members

h) Director, Child Health Division, Department- Member-Secretary

(3) The term of office of the nominated members pursuant to Sub-section (2) shall be four years.

(4) Notwithstanding anything stated in Sub-section (3), the Ministry may remove him/her from the post at any time if the nominated member defaulted to accomplish his/her job responsibility.

(5) The Ministry shall give an opportunity to the concerned member to present his/her clarification prior to remove him/her from the membership pursuant to Sub-section (4).

(6) Child Health Division of the Department shall work as secretariat of the Committee.

Dec 24, 2018

16. **Functions, Duties and Powers of the Committee**: In addition to functions, duties and powers contained in this Act, other functions, duties and powers of the Committee shall be as follows:-

a) To formulate policy on immunization program and present it to the Ministry,

b) To give direction to the concerned body for the development, expansion and operation of immunization program,

c) To collect adequate fund to make immunization program sustainable and trustworthy,

d) To monitor and supervise or cause to be monitored or supervised the immunization program,

e) To coordinate with concerned body for the development and expansion of immunization program,

f) To form sub-committees as per necessity to conduct immunization program effectively.

g) To give direction to the Department for implementation of the recommendations made by the advisory committee or investigation committee.

17. **Meeting and Decision of the Committee:** (1) Meeting of the committee shall be convened at least four times in a year.

(2) Member secretary shall call the meeting of the Committee upon the direction of the Chairperson of the Committee.

(3) Member secretary shall, in advance of twenty four hours of convening the meeting, give notice to all members along with the agenda of the meeting.

(4) Quorum for the meeting shall be deemed to have been attained if more than fifty percent members of the Committee have been presented in the meeting.

(5) The Chairperson shall preside over the meeting and incase of his/her absence a member selected by the committee shall preside over the meeting.

(6) Decision of the majority votes shall be valid in the meeting and incase of a tie; chairperson of the meeting shall caste the decisive vote.

(7) The Committee may invite anybody else who is related to immunization program to participate in the meeting as an invitee if deems necessary.

(8) Other proceedings of the meeting shall be as determined by the Committee itself.

18. **Advisory Committee:** (1) There shall be a National Immunization Advisory Committee for the development, expansion and conduction of immunization program and to give opinion and suggestion to the Committee for immediate operation of immunization program in case of natural calamity or epidemic.

(2) The Advisory Committee shall be formed as follows: –

(a) A person nominated by the Ministry among public health specialist doctors or senior pediatricians- Chairperson

(b) Director, Child Health Division, Department- Member

(c) Chairperson, Nepal Pediatric Society or a designated representative by the chairperson of the society- Member

(d) Three persons nominated by the Ministry among epidemiologists, public health experts, health economists or senior pediatricians- Members

(e) Chief, Immunization Section, Department- Member Secretary.

(3) The term of office of the Chairperson and nominated members shall be four years.

(4) Notwithstanding anything stated in sub-section (3),the Ministry may remove him/her from the post at any time if the Chairperson and nominated members of Advisory Committee were defaulted to accomplish his/her job responsibility,.

(5) The Ministry shall give an opportunity to submit his/her clarification prior to remove Chairperson or members from his/her post pursuant to sub-section (4).

(6) Child Health Division of the Department shall work as secretariat of the Advisory Committee.

19. **Investigation Committee:** (1) An Adverse Event Investigation Committee shall be formed to conduct immediate investigation of adverse events following immunization and submit a report to the Committee.

(2) The Investigation Committee shall be formed as follows: -

(a) A person nominated by the Ministry from among senior pediatricians – Chairperson

(b) Representative, Department of Drug Administration- Member

(c) Representative, Nepal Pediatric Society- Member

(d) One person among senior pediatricians - Member

(e) One person among senior public health experts- Member

(f) One person among senior pathologists- Member

(g) Chief, Immunization Section, Department- Member Secretary

(3) The Ministry shall nominate the members mentioned in clauses (d), (e) and (f) of sub-section (2).

(4) The term of office of the Chairperson and Nominated members shall be four years.

(5) Notwithstanding anything stated in sub-section (3), the Ministry may remove him/her from the post at any time if the Chairperson and nominated members of Investigation Committee were defaulted to accomplish his/her job responsibility,.

(6) The Ministry shall give an opportunity to submit his/her clarification prior to remove Chairperson or members from his/her post pursuant to sub-section (4).

(7) Child Health Division of the Department shall work as secretariat of the Investigation Committee.

20. **May Provide Directionto Implement Recommendations:** The Chairperson of the Committee may give direction to the Department to implement recommendations if the recommendations of the Advisory Committee or the Investigation Committee require immediate implementation and the meeting of the Committee could not conclude at the same time subject to approve those recommendations in the following meeting of the Committee.

Chapter-5

Fund and Audit

21. **Fund:**(1) There shall be a Fund named as Immunization Fund for the development of immunization programs as well.

(2) The fund shall comprise following amounts: -

a) Amount received from the Government of Nepal,

b) Amount received from Nepali citizen, financial or cooperative organization or other organizations or institutions,

c) Amount received from foreign individuals, Governments or international organizations,

d) Amount received from other sources.

(3) The Committee shall get prior approval from the Ministry of Finance before receiving amount mentioned in clause(c) of sub-section 2.

(4) Amounts of the fund shall be deposited in an account operated in a commercial bank holding "A" class license in accordance with prevailing law.

22. **Use of Fund:** (1) The committee may use amount of the fund in following activities:

a) To purchase vaccine for operation of immunization program,

b) To purchase vaccine immediately for operation of immunization program in case of natural calamity or epidemic,

c) To conduct study or research for the development or extension of immunization program,

d) To make investment on manufacture of vaccine to be used in immunization program in partnership with private sector if it deems feasible from the perspective of cost effectiveness,

e) To perform administrative works as well as to conduct Committee meetings.

(2) The Committee shall get prior approval from the Ministry to spend the fund to carry out the works stated in clauses (a), (b) and (d) of sub-section (1).

23. **Not to use Fund for other work:** The committee shall not use amount of the fund in any work except as mentioned in Section22.

24. **Arrangement of Budget**: (1) The Government of Nepal shall make arrangement of adequate budget required for sustainable management of immunization program.

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(2) While disbursing amounts of the fund in other works except mentioned in clause (b) of sub-section (1) of Section 22, the Committee shall have to maintain at least ten crore rupees balance in the fund.

(3) The Government of Nepal shall, as far as possible, reimburse the amounts into the fund that has been disbursed to perform work as mentioned in clause (b) of Sub-section (1) of Section22.

25. Account of Fund and Audit: (1) Income and expenditure accounts of the fund shall be maintained in such a format as adopted by the Government of Nepal.

(2) Office of the Controller of Treasury and Account shall conduct internal audit of the fund.

(3) Final audit of the Fund shall be conducted by the Auditor General of Nepal.

Chapter-6

Punishment, Compensation and Appeal

26. Punishment: (1) If anyone operates immunization service without obtaining a license, the committee shall end such operation and impose a fine of three hundred thousand rupees to five hundred thousand rupees to the concerned.

(2) If anyone supplies unregistered vaccine, the committee shall destroy such vaccine and impose a fine of twenty-five thousand to one hundred thousand rupees to the concerned.

(3) If anyone distributes vaccine in contrary to the standard prescribed pursuant to Section 14, the committee shall destroy such vaccine and impose a fine of fifty thousand rupees.

(4) If anyone commits an act contrary to this Act or Rules framed under this Act other than what is referred to in sub-section (1), (2) or (3), the committee shall impose a fine of ten thousand to twenty-five thousand rupees to the concerned.

(5) If an act punishable under sub-section (4) is committed by an employee of the Government or public institution, the committee may request the concerned authority to take departmental action.

27. **To File a complaint:** (1) If anyone is aware of committing an act punishable under Section 26, such person may file a complaint to the committee within 35 days of such act.

(2) Notwithstanding anything mentioned in sub-section (1), even if no complaint regarding the activities contrary to this Act is filed, the committee may initiate inquiry and impose punishment pursuant to Section 26 if the committee obtains information from any source regarding the commission of such act.

28. **Provision Relating to Treatment and Compensation:**(1) If a person encounters serious health problem following vaccination and Investigation Committee has certified the same, the vaccinating body or organization shall be responsible for the treatment of the victim and provide compensation.

(2) If the Investigation Committee has certified that a person has encountered serious type of physical losses like mutilation or death following vaccination, the Committee shall make arrangement

of providing compensation from vaccinating body or organization to the victim in the event of mutilation and next of kin in case of death.

(3) Grounds to provide compensation pursuant to sub-section (1) and (2) shall he as prescribed.

29. **May Form Expert Committee:** The Committee may form an Expert Committee under the convenership of a committee member to present recommendation to impose punishment pursuant to Section 26 or to determine compensation pursuant to Section 28.

30. **Appeal:** Person not satisfied with the decision or order made by the Committee pursuant to Section 26 or 28 may file an appeal to the High court within 35 days of issuing such decision or order.

Provided that there shall not be any difficulty to file an appeal to the Appellate Court until the High Court adopts its jurisdiction.

31. **No Difficulty to File Complaint underPrevailing Law:** If an act punishable under this Act is also punishable under other prevailing laws, this Act shall not be deemed to have created any difficulty to take action or file complaint under other prevailing law.

Chapter-7

Miscellaneous

32. **May Provide Encouragement and Reward:** The Ministry may encourage or give reward to such a person or institution having excellent contribution in the area of immunization.

33. **May Require Immunization Card:** (1) Schools may ask immunization card at the time of admission of student from his/her patron or guardian.

(2) Notwithstanding anything stated in sub-section (1), a child shall not be barred from admitting in the school only on the ground of failure to submit immunization card.

(3) School shall maintain records of the students who have not received such vaccines which are included in immunization program and shall forward a report to the local government health institution.

34. **May Designate Brand Ambassador:** The Government of Nepal may designate a brand ambassador to a person who has high reputation in the country for promotion of immunization program.

35. **To Conduct Awareness Programs:** The Committee shall regularly conduct awareness programs on benefits of vaccine and possible adverse impact arising due to not receiving vaccine in time.

36. **Meeting allowance:** Chairperson, members and invited members of the Committee or sub-committees formed under this Act on account of participating in the meeting shall receive meeting allowance as prescribed by the Ministry of Finance.

37. **To Cooperate:** It shall be the duty of the concerned person or agency to provide necessary support to the immunization service.

38. **Delegation of Authority:** (1) The Ministry may delegate some of its power conferred by this Act to the Committee or body as required.

(2) The Committee may delegate some of its power conferred by this Act to Chairperson, member or any other officer as required.

39. **To Submit Annual Report:** (1) The Committee shall submit annual report to the Ministry regarding its activities performed during the year within three months of expiration of the fiscal year.

(2) The Committee may publish its annual report as mentioned in sub-section (1).

40. To Give Direction: (1)The Ministry may give necessary direction to the Committee regarding its activities.

(2)It shall be the obligation of the Committee to follow the directions given by the Ministry pursuant to sub-section (1).

41. May Frame Guidelines: The Committee may frame and implement essential guidelines subject to this Act and the Rules made under the Act.

42. Power to Frame Rules: (1) The Government of Nepal may frame required Rules to implement this Act.

(2) Without prejudice to the generality of the authority conferred by sub-section (1), the Government of Nepal may frame rules particularly on the following matters :-

(a) Standard of vaccine,

(b) License issuing process, fee for license, fee for license renewal, validity of license, revocation of license and terms and conditions to be followed by licensee,

(c) Monitoring of immunization services,

(d) Report to be submitted to the health institution,

(e) Record of immunization services,

(f) Immunization card,

(g) Other functions, duties and powers of the Committee,

(h) Meetings of Advisory Committee and Investigation Committee,

(i) Operation of fund's account,

(j) Use of fund,

(k) About Compensation given to the vaccine receiver,

(l) About Other essential matters concerning immunization.

43. <u>Repeal and Saving</u>: (1) National Immunization Fund (Operation) Regulation, 2070 (2013) has been repealed.

(2) Works carried out pursuant to National Immunization Fund (Operation) Regulation, 2013 shall be deemed to have done pursuant to this Act.

नेपाल सरकार
स्वास्थ्य तथा जनसंख्या मन्त्रालय
स्वास्थ्य सेवा विभाग
परिवार कल्याण महाशाखा

राष्ट्रिय खोप तालिका

पूर्ण खोप, सुरक्षित भविष्य

पटक/भेट	कुन उमेरमा	कुन खोप	सुई लगाउने स्थान र माध्यम	कुन रोगबाट बचाउँछ
	 गर्भवति महिला	टि.डी. पहिलो गर्भमा कम्तिमा एक महिनाको अन्तरमा २ पटक र त्यसपछिको प्रत्येक गर्भमा १ पटक	बाँया पाखुराको बिच बाहिरी भाग मासुमा (Intramuscular)	मातृ तथा नवजात शिशु धनुष्टंकार र भ्यागुते रोग
१	 जन्मने वित्तिकै सकेसम्म छिटो	बि.सि.जी. 	दाँया पाखुराको माथिल्लो भाग छालाभित्र (Intradermal)	क्षयरोग
२	 ६ हप्तामा	रोटा (पहिलो मात्रा) पोलियो (पहिलो मात्रा) पि.सि.भी (पहिलो मात्रा) डि.पि.टी. हेप-बी हिब (पहिलो मात्रा) 	•मुखमा (गालाको भित्री भागमा) •मुखमा दुई थोपा •दाँया तिघ्राको बिच बाहिरी भाग मासुमा (Intramuscular) •बाँया तिघ्राको बिच बाहिरी भाग मासुमा (Intramuscular)	•रोटा भाइरसबाट हुने झाडापखाला •पोलियो •निमोनिया (न्यूमोकोकल रोगहरु) •भ्यागुते रोग, लहरे खोकी, धनुष्टंकार, हेपाटाइटिस्-बी, हेमोफिलस इन्फ्लुएन्जा-बी,
३	 १० हप्तामा	रोटा (दोश्रो मात्रा) पोलियो (दोश्रो मात्रा) पि.सि.भी (दोश्रो मात्रा) डि.पि.टी. हेप-बी हिब (दोश्रो मात्रा) 	•मुखमा (गालाको भित्री भागमा) •मुखमा दुई थोपा •दाँया तिघ्राको बिच बाहिरी भाग मासुमा (Intramuscular) •बाँया तिघ्राको बिच बाहिरी भाग मासुमा (Intramuscular)	•रोटा भाइरसबाट हुने झाडापखाला •पोलियो •निमोनिया (न्यूमोकोकल रोगहरु) •भ्यागुते रोग, लहरे खोकी, धनुष्टंकार, हेपाटाइटिस्-बी, हेमोफिलस इन्फ्लुएन्जा-बी,
४	 १४ हप्तामा	पोलियो (तेश्रो मात्रा) एफ.आई.पि.भी. (पहिलो मात्रा) डि.पि.टी. हेप-बी हिब (तेश्रो मात्रा) 	•मुखमा दुई थोपा •दाँया पाखुराको माथिल्लो भाग छालाभित्र (Intradermal) •बाँया तिघ्राको बिच बाहिरी भाग मासुमा (Intramuscular)	•पोलियो •पोलियो •भ्यागुते रोग, लहरे खोकी, धनुष्टंकार, हेपाटाइटिस्-बी, हेमोफिलस इन्फ्लुएन्जा-बी,
५	 ९ महिनामा	एफ.आई.पि.भी. (दोश्रो मात्रा) दादुरा-रुबेला (पहिलो मात्रा) पि.सि.भी (तेश्रो मात्रा) 	•दाँया पाखुराको माथिल्लो भाग छालाभित्र (Intradermal) •बाँया पाखुराको माथिल्लो भाग छाला र मासु बीच (Subcutaneous) •दाँया तिघ्राको बिच बाहिरी भाग मासुमा (Intramuscular)	•पोलियो •दादुरा र रुबेला •निमोनिया (न्यूमोकोकल रोगहरु)
६	 १२ महिनामा	जापानिज इन्सेफलाइटिस् 	दाँया तिघ्राको माथिल्लो बाहिरी भाग छाला र मासु बीच (Subcutaneous)	•जापानिज इन्सेफलाइटिस्
७	 १५ महिनामा	दादुरा-रुबेला (दोश्रो मात्रा) टाइफाईड 	• बाँया पाखुराको माथिल्लो भाग छाला र मासु बिच (Subcutaneous) • बाँया तिघ्राको बिच बाहिरी भाग मासुमा (Intramuscular)	•दादुरा र रुबेला •टाइफाईड
८	 कक्षा ६ की छात्रा र विद्यालय नजाने १० वर्षकी किशोरी	एच.पि.भी 	बाँया पाखुराको बिच बाहिरी भाग मासुमा (Intramuscular)	पाठेघरको मुखको क्यान्सर