HANDBOOK ON ADULT VACCINATION IN SINGAPORE 2023

Society of Infectious Diseases Singapore
College of Family Physicians, Singapore
Chapter of Infectious Disease Physicians

Under the auspices of

SOCIETY OF INFECTIOUS DISEASE (SINGAPORE)

COLLEGE OF FAMILY PHYSICIANS SINGAPORE

ISBN 978-981-09-9326-9

4th Edition Published August, 2023

Published by:

Society of Infectious Disease (Singapore)
16 Jalan Tan Tock Seng,
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ABBREVIATIONS

ACIP	Advisory Committee on Immunization Practices
BCG	Bacillus-Calmette-Guérin vaccine
BMI	Body mass index
bOPV	Bivalent oral polio virus
CCID50	50% cell culture infectious dose
CD4	Cluster of differentiation 4
CDC	Centers for Disease Control and Prevention
COVID-19	Coronavirus disease 2019
CYD	Chimeric yellow fever–dengue
DENV	Dengue virus
FHbp	Factor H binding protein
GVHD	Graft-versus-host disease
HBsAg	Hepatitis B surface antigen
Hib	Haemophilus influenzae type B
HIV	Human immunodeficiency virus
HPV	Human papillomavirus
HSA	Health Sciences Authority
HSCT	Haematopoietic stem cell transplant
ID	Intradermal
IgA	Immunoglobulin A
IM	Intramuscular
IDU	Injection drug user
IPD	Invasive pneumococcal disease
IPV	Inactivated polio vaccine
IVIG	Intravenous immunoglobulin
JE	Japanese encephalitis
JEV	Japanese encephalitis vaccine
LD50	Lethal dose to 50% of population
MMR	Measles–mumps–rubella vaccine
MOH	Ministry of Health
MSM	Men who have sex with other men
OPV	Oral polio vaccine

PCEC	Purified chick embryo cell
PCV13	13-valent pneumococcal conjugate vaccine
PCV20	20-valent pneumococcal conjugate vaccine
PEP	Post-exposure prophylaxis
PPSV23	23-valent pneumococcal polysaccharide vaccine
PSAR	Pandemic Special Access Route
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SQ	Subcutaneous
STI	Sexually transmitted infection
TIG	Tetanus immunoglobulin
Tdap	Tetanus–reduced diphtheria–acellular pertussis vaccine
TB	Tuberculosis
VAPP	Vaccine-associated paralytic poliomyelitis
VLP	Virus-like particle
VZV	Varicella-zoster virus
WHO	World Health Organization
YFV	Yellow fever vaccine
YEL-AND	Yellow fever vaccine-associated neurotropic disease
YEL-AVD	Yellow fever vaccine-associated viscerotropic disease

INTRODUCTION

The epidemiology of infectious disease globally and in Singapore has changed dramatically since the turn of the century. The mortality and impact of infectious diseases have significantly decreased. Infectious diseases now rank below cardiovascular diseases and cancers in terms of disability-adjusted life-years (a combination of years lost due to premature mortality and years of healthy life lost due to disability) yet pneumonia (a partially vaccine-preventable disease) is consistently ranked within the top three causes of death in Singapore.[1,2] This profound improvement is multifactorial, and could be attributed to better environmental sanitation, improved access and utilisation of healthcare services, advances in medical treatment, vigilant surveillance of infectious diseases, and public health interventions including childhood vaccination.

Despite these improvements, infectious diseases can spread rapidly, leading to outbreaks. Air travel has allowed rapid global transmission of infectious diseases and Singapore is consistently ranked in the world's top 20 busiest aiports.[3,4] Furthermore, emerging infectious diseases and bioterrorism, threaten public health. Therefore, the need to be vigilant in controlling infectious diseases remains a major public health priority in Singapore.

Vaccination is a cornerstone of public health interventions in the control of infectious diseases. Vaccines can significantly lower morbidity and mortality due to vaccine-preventable diseases. They also protect the general public by reducing reservoirs of infection in the community.

In a compact city–state like Singapore, vaccines can be easily administered to a large population quickly, systematically and safely with good monitoring for adverse effects. The National Childhood Immunisation Programme implements mandatory childhood vaccination against diphtheria and measles.5 In addition, routine vaccination using internationally standardised vaccination schedules is standard of care in the ambulatory care of children.

The standards of vaccination among adults are less clear-cut due to the lack of a widely publicized and universally practiced comprehensive vaccination schedule. Adulthood encompasses all age groups from 18 years and beyond, which can span six decades or more.1 In this wide age range, individuals have a wide variety of past and present medical histories, behavioural and occupational risks, and psychosocial and cultural backgrounds. This results in a wide range of risk levels for various infectious diseases in the general adult population, which makes routine vaccination of all vaccine-preventable diseases for all adults inappropriate and inefficient.

This handbook on adult vaccination in Singapore aims to guide medical practitioners in screening adults for their vaccination requirements, as well as recommending the safe and effective administration of appropriate vaccines to adults.

This handbook is meant only to guide clinical practice, and are not intended to replace medical judgement when managing adult individuals.

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CHAPTER 1: METHODOLOGY OF DEVELOPMENT AND LEVEL OF EVIDENCE

This handbook on adult vaccinations in Singapore was developed through a collaboration between the Society of Infectious Disease (Singapore), the College of Family Physicians Singapore, and the Chapter of Infectious Diseases Physicians. The collaboration convened a committee of eight experts tasked to review the current literature on adult vaccinations and update the recommendations for Singapore. The process was aided by a medical writer.

The committee performed a comprehensive review of the literature on vaccine-preventable diseases in adults and best practices in adult vaccination. The committee then convened as a working group to update recommendations on improving adult vaccine coverage, vaccine administration, storage and handling, vaccine safety, specific vaccines and vaccine-preventable diseases, and vaccination for special adult groups. The recommendations considered the methodological quality of the evidence, benefit and risk to the target population, associated treatment burden and costs. The committee employed the GRADE Working Group method of grading quality of evidence and strength of recommendations **(Table 1)**.[1,2]

Table 1. GRADE Working Group grading of quality of evidence and strength of recommendations[1,2]

Grade of Recommendation	Benefit vs Risk and Burdens	Methodological Quality of Supporting Evidence	Implications
Strong recommendation; high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
Strong recommendation; moderate-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation

(Cont'd.) Table 1. GRADE Working Group grading of quality of evidence and strength of recommendations[1,2]

Grade of Recommendation	Benefit vs Risk and Burdens	Methodological Quality of Supporting Evidence	Implications
Strong recommendation; low-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Observational studies, case series, or expert opinion	Strong recommendation but may change when higher quality evidence becomes available
Weak recommendation; high-quality evidence	Benefits closely balanced with risks and burden	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
Weak recommendation; moderate-quality evidence	Benefits closely balanced with risks and burden	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
Weak recommendation; low-quality quality evidence	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Observational studies, case series, or expert opinion	Very weak recommendations; other alternatives may be equally reasonable

RCT, randomised controlled trial.

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CHAPTER 2: GENERAL PRINCIPLES OF ADULT VACCINATIONS

The general principles of adult vaccinations remain essentially unchanged.

Recommendations to improve vaccine coverage and administration

Adult immunisation is a cost-effective way of preventing morbidity and mortality in at-risk individuals. Literature from Singapore and other developed countries have identified several barriers to adult vaccination. These include:[1-3]

- Inadequate levels of knowledge among individuals and healthcare professionals about vaccinations in healthy and high-risk adults,
- Prioritisation of medical management over preventive care,
- Healthcare providers that do not provide vaccination,
- Limited health insurance coverage for adult vaccinations,
- Vaccination-providing facilities that are not recognised as providers by third-party payers,
- Out-of-pocket payments for some individuals or vaccines.

To improve adult vaccination coverage in the light of these barriers, the following are strongly recommended:[1]

- All healthcare providers should receive appropriate adult vaccinations.
- All healthcare providers managing adult patients, regardless of practice or specialization, should be up-to-date in their knowledge about adult vaccinations. Knowledge should include indications for each vaccine, characteristics of high-risk groups, indications for vaccine deferral, vaccine risks, benefits and adverse effects to enable informed counselling.
- All healthcare providers managing adult patients should assess the vaccination status of their patients, and should recommend the appropriate vaccinations during patient contact at the earliest time possible without compromising medical care, preferably at the first patient contact. Vaccination requirement should thereafter be assessed annually.
- Vaccines should be deferred only in the presence of temporary contraindications, lack of consent, or situations where vaccination may delay emergent care. In the case of vaccine deferral, the deferred vaccination should be given in the earliest time that the vaccine could be delivered.
- If the healthcare provider cannot provide the appropriate vaccination to an adult patient, it is their duty to refer to a healthcare provider that can provide the vaccination and to confirm that the individual received the referred vaccination during the patient's next follow-up visit.
- All vaccine providers should ensure that the receipt of vaccination is documented and also that written documentation is provided to the patient.

- As part of routine care, all healthcare providers should set some time to advise patients on all necessary vaccinations for future visits, as well as their appropriate schedules.
- All vaccine providers should ensure appropriate vaccine availability at all times.
- Healthcare institutions, insurers, payers and professional groups should implement systems that integrate vaccination assessment in routine care, be prepared in case of outbreaks of vaccine- preventable diseases, and actively promote and educate healthcare providers and individuals about adult vaccination.
- Healthcare institutions, insurers, payers should support efforts to improve adult vaccination coverage rates.

Strong recommendation; low quality of evidence.

After thorough communication, a few patients may still reject certain or all kinds of vaccines for various personal or religious reasons, and these should be acknowledged and respected. Strong recommendation; low quality of evidence.

Vaccine safety reporting

The Ministry of Health of Singapore encourages active surveillance of AEFIs, regardless of the certainty that the AEFI is related to or caused by the adult vaccination or not.7 Table 2 lists the suggested reportable AEFIs and the corresponding timing of the AEFI in relation to the vaccine administration. However, this list is only meant to be a guide and is not exhaustive. Healthcare professionals may report any unfavourable event following vaccination that has no clear cause, even those where a causal link to a vaccine has not been established.

Table 2. List of suggested reportable AEFIs

Reportable AEFI	Onset after vaccine administration
• Anaphylactoid reaction (acute hypersensitivity reaction) • Anaphylaxis • Toxic shock syndrome	Within 24 to 48 hours of vaccination
• Severe local reaction • Sepsis • Injection site abscess (bacterial/sterile)	Within 7 days of vaccination
• Seizures • Encephalopathy	Within 14 days of vaccination
• Acute flaccid paralysis • Brachial neuritis • Intussusception • Thrombocytopenia	Within 3 months of vaccination

(Cont'd.) Table 2. List of suggested reportable AEFIs

Reportable AEFI	Onset after vaccine administration
• Lymphadenitis • Disseminated BCG infection • Osteitis or osteomyelitis	Between 1 and 12 months after BCG vaccination
• Death • Hospitalisation • Disability • Any other severe and unusual events suspected to be associated to the vaccine	No time limit

**In children, persistent (>3 hours) inconsolable screaming, hypotonic-hyporesponsive episode and febrile seizures are also reportable.*

AEFI, adverse events following immunisation; BCG, Bacillus-Calmette-Guerin

Recommendation on vaccine safety and safety reporting

Adverse events, whether related to vaccination or not, can occur after the administration of adult vaccines. These events could be local reactions such as pain, swelling or redness at the administration site, systemic such as fever or rash, or other allergic reactions.[4] Local reactions are the most common, occurring in up to 80% of vaccine doses, while allergic reactions are the least frequent but could be the most severe and life- threatening in the case of anaphylaxis.

Healthcare providers, whether vaccine providers or not, play a major role in the overall surveillance, management and prevention of vaccine-related adverse reactions. These roles include benefit-risk communication, safe vaccine storage and administration, management of adverse reactions, including reporting to the Health Sciences Authority (HSA).

Injection safety

All injection safety principles used in the injection of other medicinal products should also be applied to the injection of vaccines. A sterile needle and syringe should be used for each administration of injected adult vaccines.[5] The used needle and syringe should be disposed according to hospital protocols. Single-use, auto- disable syringes or disposable monodose preparations should be used whenever possible. Syringes should not be recapped to avoid needle-stick injuries.

Strong recommendation; low quality of evidence.

Management of adverse reactions

The presentation of vaccine-related adverse reactions varies widely. Healthcare providers should use their best clinical judgement in managing any specific adverse reaction that may arise.

Anaphylaxis occurs once in every 1.5 million doses in children and adolescents; less is known about the prevalence among adults.[4,5] A retrospective study on 67 adult anaphylaxis patients in Singapore found that none were due to vaccinations.[6] Despite the rarity of anaphylaxis related to vaccinations, vaccine providers should be able to institute emergency care, including epinephrine and airway maintenance, to a person who experiences an anaphylactic reaction. All vaccine providers should be certified in cardiopulmonary resuscitation.

In the case of adverse events following immunisation (AEFI), vaccine recipients should be advised to report any unexplained symptoms to the Health Sciences Authority using the appropriate form (https://eservice. hsa.gov.sg/adr/adr/vaeOnline.do?action=load).[7]

Strong recommendation; low quality of evidence.

Benefit-risk

Each candidate for adult vaccination should be educated about the benefits of adult vaccination against its risks.[1,8] Communication of benefits should include the diseases that vaccines can prevent, the indications of the vaccine specific to the patient, the vaccine options and their efficacy, and recommended vaccination schedules. Clear communication of its benefits and risks alleviates patient anxiety, facilitates the acquisition of informed consent from the individual or legal representatives, and may improve compliance to subsequent doses. Simple and understandable terms should be used at all times. Questions should be anticipated, and opportunities for questions should be given. Patients should be provided with accurate and credible sources of additional information.

As mentioned, vaccine recipients should be advised to report any unexplained symptoms to the Health Sciences Authority using the appropriate form (https://eservice.hsa.gov.sg/adr/adr/vaeOnline. do?action=load).[7]

Strong recommendation; low quality of evidence.

Vaccines Storage and Handling

Vaccines are biological materials that can denaturate and deteriorate, which lead to loss of efficacy. This loss can be avoided through proper transport, storage and handling.

- Vaccines should be stored in their original packaging, which also protects against light and physical damage.[4,8] They should be stored according to the specified cold chain requirements by the manufacturer.
- Do not use vaccines with compromised packaging. Vaccines and diluents that remain unused beyond the expiration dates should not be used.[4,8] If an expired vaccine is administered, the incident should be reported, and the dose should be repeated (after the appropriate interval between parenteral vaccines) using a fresh vaccine.
- Vaccines that have been inappropriately exposed to excessive heat, cold, or light can have reduced potency even before the expiration date. Thus, such exposures should be minimised.

The vaccine cold chain is the process of maintaining optimal temperature during transport, storage and handling to prevent temperature-related deterioration. Temperatures should be monitored throughout the cold chain.[8] Vaccine providers should have systems and equipment in place to ensure cold chain maintenance and minimise breaks in the cold chain. Vaccines that are exposed to conditions that deviate from the recommended cold chain specified for each particular vaccine should not be used. Refer to the cold chain requirements of each specific vaccine specified by the manufacturer.

- Single-dose vaccines should be reconstituted just prior to administration, and used immediately.[8]
- Avoid the use of multi-dose vials whenever possible. However, if multi-dose vial use is unavoidable, the date of first puncture, the date of reconstitution, and the date of use should all be indicated on the vial. Strict aseptic techniques should be practised at all times including no re-use of needles or syringes to access the multi-dose vials.
- Diluents should be stored according to manufacturers' recommendations, and properly labelled to avoid using the incorrect diluent during reconstitution.
- Preloaded syringes should also be subject to proper storage and cold chain conditions.
- Unused expired vaccines or those significantly exposed to adverse conditions should be disposed in accordance with hospital standards for the disposal of biological products.

Strong recommendation; low quality of evidence.

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TYPES OF VACCINATIONS

This handbook categorises adult vaccines according to the following classification: live attenuated vaccines, inactivated vaccines, subunit vaccines, toxoid vaccines, and conjugate vaccines.[1] There are other vaccine types under clinical development, such as the DNA vaccines and the recombinant vector vaccines, which are beyond the scope of this handbook.

Live attenuated vaccines

These are infectious agents that have undergone attenuation, usually by passage through a foreign host, which renders the agent less virulent.[1] In very rare occasions, the infectious agent can regain virulence, leading to full-blown disease.[2] Additionally, immunocompromised individuals may also develop disease after the administration of live attenuated vaccines. Furthermore, these vaccines require more stringent environmental conditions to ensure that their potency is maintained. With the exception of attenuated oral typhoid vaccine, live attenuated vaccines are viral in nature, because of the simplicity of viral physiology that lends better to attenuation.

Inactivated vaccines

These vaccines are composed of infectious agents that have been killed by exposure to chemicals, heat, or radiation.[1] The agents have been rendered non-infectious and therefore eliminate the risk of disease from vaccination. These vaccines also tend to be more stable and require less stringent environmental conditions during transport and storage. However, the lack of infectivity may result in a lower immune response, thus often necessitating booster doses to achieve lifetime immunity.

Subunit vaccines

These vaccines contain only antigen/s (or subunits) of the infecting agent that elicit the highest immune response.[1] Like inactivated vaccines, subunit vaccines carry no risk of causing disease.

Toxoid vaccines

In some bacterial infections, pathology is through toxin production (e.g., tetanus or diphtheria).[1] Toxoid vaccines contain inactivated toxins (toxoid) that do not cause pathology but elicit an immune response that affords immunity to the individual.

Conjugate vaccines

These vaccines are appropriate for infectious agents that have a polysaccharide coat that diminishes the host immune response.[1] Furthermore, polysaccharides typically elicit a B cell response that is independent of T cell response. Conjugate vaccines circumvent these problems by covalently attaching a carrier protein to the polysaccharide component of the vaccine.[2] The carrier protein elicits a more profound immune response and protective serological memory by activating T cell response in addition to the humoral response.

CHAPTER 3: GENERAL RULES OF ADULT VACCINATIONS

GENERAL RULES

Temporal considerations

The main consideration in the timing and spacing of vaccine administration, whether in adults or in children, is the potential for interaction between the vaccine and circulating antibodies—wherein antibodies produced from previous vaccinations may interfere with the antigenicity of the newly administered vaccine dose.[3] Live attenuated vaccines may be prone to interference, as these vaccines require replication in the host to elicit an adequate response.[3] Inactivated vaccines are not likely to have antibody interaction.

Interference is avoided by ensuring that subsequent doses of the same vaccine should be spaced according to guideline recommendations as well as the manufacturer recommendations. Due to presence of immunologic memory, intervals longer than routinely recommended between the doses do not impair the immunologic response.[3] However, reducing the interval may expose the vaccine to reduced efficacy, and should be avoided.

In addition, for patients receiving antibody-containing products, it is recommended that the live vaccine be administered first, followed by a 2-week interval before administering antibody-containing product.[3] If the antibody-containing product is administered less than 2 weeks after vaccination, a second vaccine dose should be administered after the time interval shown in **Table 3**, unless serologic testing indicates the presence of protective antibody levels. Antibody testing should be done after the time interval indicated in the same Table.

If the antibody-containing product is administered first, refer to **Table 3** to determine the time interval after which it is safe to administer live vaccines, particularly measles- or varicella-containing vaccine; or refer to the product label.[4]

If administration of immunoglobulin is necessary, MMR or varicella vaccines can be administered simultaneously but note that vaccine-induced immunity can be compromised. The vaccine should be administered at a body site different from the immunoglobulin injection site.[3] Vaccination should be repeated after the interval noted in **Table 3**, unless serologic testing indicates antibodies have been produced. When immunoglobulin is given with the first hepatitis A vaccine dose, a non-clinically relevant reduction in antibody formation is expected.

Zoster vaccine and oral typhoid vaccine are not affected by antibodies and may be administered at any time in relation to antibody-containing products.

Strong recommendation; moderate-quality evidence.

Simultaneous administration

Most vaccines can be administered simultaneously or within the same day without reducing efficacy or increasing AEFIs.[3-6] Furthermore, giving adults all the indicated vaccines on the same day reduces the risk of missed vaccinations. Thus, it is recommended that all indicated vaccines be given to adult vaccine recipients within the same visit.

When performing simultaneous vaccine administration, each vaccine should use a separate syringe. It is helpful to use a standardized site map to facilitate same sites for different vaccines, or indicate if vaccination was given either in "upper" or "lower" portion of the injection area selected.

The only exceptions to the rule of simultaneous administration are pneumococcal conjugate vaccine (PCV) and the Menactra brand of quadrivalent meningococcal conjugate vaccine in patients with functional or anatomical asplenia. In these patients, there should be a 4-week interval between the administration of the two vaccines (PCV and Menactra) to avoid interference of the meningococcal conjugate vaccine with PCV.[3]

If for any reason, live parenteral or intranasal vaccines are not administered simultaneously, these should be administered sequentially with a 4-week interval between administrations.[3] This reduces the risk that the antibodies elicited from the first vaccination would interfere with the following live vaccine. If the interval between live vaccine administrations was less than 4 weeks, the following vaccine should be repeated after 4 weeks, or the patient should undergo serological testing to evaluate the response to the initial dose.

Table 3. US CDC-recommended intervals between administration of antibody-containing products and subsequent measles-containing vaccine or varicella-containing vaccine[4]

Indication	Dose	Recommended interval before measles or varicella vaccination
Blood Transfusion		
Packed RBCs (hematocrit 65%)	10 mL/kg (60 mg IgG/kg) IV	6 months
Whole blood (hematocrit 35-50%)	10 mL/kg (80–100 mg IgG/kg) IV	6 months
Plasma/platelet products	10 mL/kg (160 mg IgG/kg) IV	7 months
Hepatitis A Ig, duration of international travel		
Contact prophylaxis	0.1 mL/kg (3.3 mg IgG/kg) IM	6 months
<1-month stay	0.1 mL/kg (3.3 mg IgG/kg) IM	6 months
≥1-month stay	0.2 mL/kg (10 mg IgG/kg) IM	6 months
Hepatitis B Ig (prophylaxis)	0.06 mL/kg (10 mg IgG/kg) IM	3 months
Intravenous immune globulin		
Replacement therapy	300-400 mg/kg IV	8 months

(Cont'd.) Table 3. US CDC-recommended intervals between administration of antibody-containing products and subsequent measles-containing vaccine or varicella-containing vaccine[4]

Indication	Dose	Recommended interval before measles or varicella vaccination
Post-exposure measles prophylaxis (includes immunocompromised people)	400 g/kg IV	8 months
Post-exposure varicella prophylaxis	400 g/kg IV	8 months
Kawasaki disease	2 g/kg IV	11 months
Rabies Ig prophylaxis	20 IU/kg (22 mg IgG/kg) IM	4 months
Tetanus Ig	250 units (10 mg IgG/kg) IM	3 months
Varicella zoster Ig	125 units/10 kg (60–200 mg IgG/kg) IM (maximum 625 units)	5 months

CDC, US Centers for Disease Control and Prevention; RBC, red blood cells; Ig, immunoglobulin; IgG, immunoglobulin G; IV, intravenous; IM, intramuscular; IU, international units.

Live oral vaccines (polio, typhoid or rotavirus) may be given at any time before or after each other, or at any time before or after live parenteral or intranasal vaccines.[3,6] Two inactivated vaccines, or the combination of live and inactivated vaccines, may be given at any time before or after each other.

Strong recommendation; moderate-quality evidence.

Missed doses

When the vaccine recipient has missed a dose, the dose should be given on the next visit. In most cases, additional doses are not required.[3]

Strong recommendation; moderate-quality evidence.

Contraindications and precautions

This section discusses the general contraindications and precautions for adult vaccination. See also the discussions on each vaccine for vaccine-specific contraindications and precautions.

In rare occasions, a potential vaccine recipient may have contraindications and precautions to vaccination. It is important to know which conditions are true contraindications and precautions, and whether these conditions are permanent or temporary, to ensure that all eligible individuals would receive the appropriate vaccination.

Among adults, vaccines are contraindicated in the event of anaphylaxis due to a vaccine component (e.g., animal protein, antibiotic, preservative or stabilizer) or a previous vaccine dose.[3] In patients with history of anaphylaxis to latex, vaccines in latex-containing vials or syringes should not be administered, unless the benefit of vaccination clearly outweighs the risks.

Pregnancy and immunosuppression are temporary contraindications to the administration of live attenuated vaccines.[3,6] There is no evidence that any live vaccine causes birth defects. However, since the theoretical possibility of foetal infection exists, live vaccines should generally be delayed until after delivery. In patients on immunosuppression, there is a risk of developing full-blown disease following live attenuated vaccination. When indicated, these vaccines should be administered once the temporary contraindication is no longer applicable.[3]

These contraindications generally do not apply to inactivated vaccines because of the absence of potential for foetal or host infection. Furthermore, immunocompromised patients may benefit from the protective effects of vaccines due to their susceptibility to infections, and these should be given whenever benefit clearly outweighs risks.[7]

However, there are no efficacy and safety data for inactivated human papilloma virus vaccine in pregnant women; this vaccine should be withheld until pregnancy has been completed.

Vaccination for pregnant women and immunocompromised patients is further discussed in the chapter on Vaccination in Special Populations on page 86.

All the permanent precautions in vaccination are related to pertussis-containing paediatric vaccines. These are temperature of 40.5°C or higher within 48 hours of a dose, collapse or shock-like state (hypotonic hyporesponsive episode) within 48 hours of a dose, persistent inconsolable crying lasting 3 or more hours occurring within 48 hours of a dose, or a seizure, with or without fever, occurring within 3 days of a dose.

The occurrence of one of these events in a child following DTaP vaccine is not a precaution to later vaccination with the adolescent/adult formulation of pertussis vaccine (Tdap).

Strong recommendation; moderate quality of evidence.

There will be occasions when vaccinations may need to be deferred: 1) moderate to severe acute illness for all vaccines; and 2) antibody-containing products for measles-mumps-rubella (MMR) vaccine and non-zoster varicella-containing vaccines.[3] There is no evidence to suggest that concurrent acute illness affects vaccine efficacy or safety. However, if the person is unwell, the vaccination can be deferred until the person has recovered so as to avoid attributing any new symptoms to the vaccine. Another reason for caution is the possibility of vaccination complicating the course of concurrent acute illness. Hence, delay of both live and inactivated vaccines may be recommended until the resolution of acute illness.

Weak recommendation; low quality of evidence.

INVALID CONTRAINDICATIONS FOR VACCINATION

The following are considered invalid contraindications to vaccination:[3]

- Mild illness. Mild acute illnesses or low-grade fever do not affect vaccine safety and efficacy, and the impact on the course of illness is far exceeded by the benefits of vaccination.
- Antibiotic or antiviral use, with some exceptions. Oral typhoid vaccine should be administered 72 hours after antimicrobial use. Live attenuated influenza vaccines should be given 48 hours after the use of antivirals active against the influenza virus.
- Exposure to infectious disease.
- Recovery from illness (convalescence).
- Non-severe allergic reactions.
- Family history of AEFI.
- Multiple vaccines.
- Pregnant or immunosuppressed household member. It is critical that healthy household contacts of pregnant women and immunosuppressed persons be vaccinated. Vaccination of healthy contacts reduces the chance of exposure of pregnant women and immunosuppressed persons to infectious diseases.[3]

Most vaccines, including live vaccines (MMR, varicella, zoster, rotavirus, live attenuated influenza vaccine, and yellow fever) can be administered to infants or children who are household contacts of pregnant or immunosuppressed persons, as well as to breastfeeding infants (where applicable). The vaccines that should not be administered in this situation are oral polio vaccine (OPV) and live attenuated oral cholera vaccine, as there may be faecal transmission from the vaccine recipient to an immunocompromised contact in whom unrestricted viral replication could potentially cause neurological deficit. The inactivated polio vaccine is recommended instead.

Transmission of varicella vaccine virus has been reported rarely. Vaccine recipients may develop local vesicles around vaccine injection site and can potentially lead to transmission. In these cases, physical contact with immunosuppressed individuals should be avoided until resolution of lesions. Transmission of zoster vaccine virus to household or other close contacts has not been reported.

- Breastfeeding. This is not a contraindication to most vaccines except yellow fever vaccine, unless there is unavoidable travel to an area endemic for yellow fever. There may be lack of evidence for the use of some vaccines in breastfeeding such as dengue vaccine, Japanese encephalitis vaccine, MMR and BCG.
- Administration of tuberculin skin test (TST). A TST may be falsely negative when performed within 4 weeks of MMR vaccination.

Strong recommendation; moderate quality of evidence.

IMPORTANT QUESTIONS TO ASK

The following questions may aid in screening for contraindications, precautions or possible interactions or interference to vaccines:

1. Is the potential vaccine recipient moderately or severely ill?
2. Does he/she have an allergy to medications, food or any vaccine?
3. Has a previous vaccination resulted in a serious AEFI?
4. Does he/she have a history of neurological problems?
5. Does the potential recipient have concurrent cardiovascular, pulmonary, renal, metabolic, or haematological disorder?
6. Does the potential recipient have malignancy or immunodeficiency?
7. Did the potential recipient receive immunosuppressive medications?
8. Did the potential recipient receive blood, blood products, or immunoglobulin therapy in the past year?
9. Is the potential recipient currently pregnant, or likely to become pregnant in the next month?
10. Did the potential recipient receive vaccination in the past 4 weeks?

If there is one "yes" response to any of these questions, the individual should be more thoroughly evaluated to confirm the presence of any valid reason to withhold vaccination.[3]

Transmission of varicella vaccine virus has been reported rarely. Vaccine recipients may develop local vesicles around vaccine injection site and can potentially lead to transmission. In these cases, physical contact with immunosuppressed individuals should be avoided until resolution of lesions. Transmission of zoster vaccine virus to household or other close contacts has not been reported.

- Breastfeeding. This is not a contraindication to most vaccines except yellow fever vaccine, unless there is unavoidable travel to an area endemic for yellow fever. There may be lack of evidence for the use of some vaccines in breastfeeding such as dengue vaccine, Japanese encephalitis vaccine, MMR and BCG.
- Administration of tuberculin skin test (TST). A TST may be falsely negative when performed within 4 weeks of MMR vaccination.

Strong recommendation; moderate quality of evidence.

References:

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CHOLERA VACCINE

Cholera is an acute gastrointestinal illness characterised by profuse watery diarrhoea causing severe dehydration. It is caused by specific strains of *Vibrio cholerae*. The most common serogroup is O1 and O139. In Singapore, cases of *V. cholerae* O1, biotype El Tor and serotype Ogawa have been reported.[1] It is a legally notifiable disease in Singapore, and official reporting has identified that it occurs sporadically in Singapore, with only two notified cases in 2021.[2] It is a water-borne disease and person-to-person spread may occur via the faecal–oral route. Primary prevention is mainly through proper disposal of human waste, adequate supply of clean drinking water, and good food-handling practices. Currently, the oral cholera vaccine, Dukoral, is available and the parenteral vaccine is no longer recommended **(Table 4)**.

Table 4. Cholera Vaccine for Adults

	Oral inactivated
Description	Each 3-mL dose contains approximately $1x10^{11}$ inactivated *V. cholerae* O1 serotypes Inaba and Ogawa, biotypes classic and El Tor strains, and 1 mg of recombinant cholera toxin B subunit.[3]
Summary of evidence	According to a Cochrane analysis of 40 randomised and quasi-randomised efficacy and safety trials in healthy adults and children (>5 years), protective vaccine efficacy over 2-years follow-up was 66% (95% CI, 57%–73%).[4] Field trials show that efficacy can go as high as 85%.[3] Oral vaccines were not associated with increased systemic and local adverse effects.
Indication/ Target population	Prevention of severe diarrhoea due to cholera or enterotoxigenic *Escherichia coli* infection. In adults, it is advised for those who will be visiting areas where there is risk of cholera. Useful during humanitarian crisis relief missions, especially in water-affecting crises such as tsunamis, typhoons or floods.
Schedule	Two doses should be taken 1 week apart. If interval exceeds 6 weeks, restart with two doses. The second dose should be given 7 days before travel. A booster dose may be given after 2 years.
Administration	Taken orally on an empty stomach. Avoid food or drinks 1 hour before and 1 hour after vaccine administration. Dissolve granules in 150 mL of cool water. Mix the solution with the contents of the vial. Drink within 2 hours.
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze.
Common adverse events	Gastrointestinal symptoms including stomach pain and discomfort, diarrhoea, bloating, gas, nausea and vomiting. Headache.
Contraindications	Anaphylaxis to any vaccine component or a previous dose.

(Cont'd.) Table 4. Cholera Vaccine for Adults

	Oral inactivated
Precautions	Vaccination should be postponed during acute illness. During travel, exercise caution and hygienic practices with food and water intake.
Pregnancy and breastfeeding	No contraindication
Medisave	No

Strong recommendation; moderate quality of evidence.

References:

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DENGUE VACCINE

Dengue is a febrile illness caused by a mosquito-borne virus (single positive-stranded RNA virus of the genus *Flavivirus*).[1] There is no specific anti-viral treatment for dengue. The disease may be caused by any one of four dengue viruses (serotypes DENV 1–4). In most cases, dengue is a self-limiting illness, but it may require hospitalisation. Recovery from one serotype provides lifelong immunity against that particular serotype but not the other three subtypes. Hence a person can be infected by up to four serotypes during his or her lifetime. There is a small risk of severe disease after any dengue infection, but the second infection by a serotype different from the first has been found to be associated with the highest risk of severe dengue (the third and fourth infections are usually associated with a milder clinical course).

Dengue is endemic and a legally reportable disease in Singapore. As of June 2022, there were 18,218 cases of dengue reported in the country with circulation of the previously uncommon DENV-3 serotype.[2]

At present, a parenteral live-recombinant tetravalent vaccine against dengue is available **(Table 5)** and licensed for use in more than 20 countries including Mexico, the Philippines, Brazil and Thailand.[3] Singapore HSA approved the vaccine for use in October 2016. Although this vaccine is beneficial in preventing dengue, especially in countries with high endemicity, an increased risk of hospitalisation for dengue and clinically severe dengue has been observed among individuals who have not been previously infected by the dengue virus. Hence, the vaccine is currently not recommended for persons without prior dengue infection.

Table 5. Dengue Vaccine (CYD Tetravalent Dengue Vaccine) for Adults

Description	Live, attenuated virus vaccine. Each dose (0.5 mL) contains CYD virus serotype 1* (4.5–6.0 $\log^{10}$ $CCID_{50}$/dose)**; CYD virus serotype 2* (4.5–6.0 $\log^{10}$ $CCID_{50}$/dose)**; CYD virus serotype 3* (4.5–6.0 $\log^{10}$ $CCID_{50}$/dose)**; and CYD virus serotype 4* (4.5–6.0 $\log^{10}$ $CCID_{50}$/dose).**
Summary of evidence	• The efficacy of the vaccine against laboratory-confirmed dengue, measured for 12 months after the last dose was 59.2% in the year following the primary series, and 79.1% against severe dengue.[4] • Efficacy varied by infecting serotype, age and serostatus. • Vaccine efficacy was significantly higher for DENV-3 (71.6%) and DENV-4 (76.9%) than DENV-1 (54.7%) and DENV-2 (43.0%).[4]

(Cont'd.) Table 5. Dengue Vaccine (CYD Tetravalent Dengue Vaccine) for Adults

Indication/Target population	In adults, dengue vaccine was approved by the HSA in October 2016 for the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4 in individuals aged 12 to 45 years living in endemic areas.[5] Vaccination is not recommended for individuals who have not been previously infected by dengue virus.
Schedule	• 3 injections of one reconstituted dose (0.5 mL) to be administered at 6-month intervals. • If flexibility in the vaccination schedule is necessary, a time window of +/– 20 days is acceptable.
Administration	Subcutaneous injection
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze. Protect from light.
Common adverse events	• Swelling and pain at the injection site • Fever, loss of appetite, restlessness, vomiting and diarrhoea (mostly encountered in children)
Contraindications	• Anaphylaxis to any vaccine component or a previous dose • Congenital or acquired immune deficiency that impairs cell-mediated immunity, including immunosuppressive therapies (e.g., chemotherapy or high-dose systemic corticosteroids for ≥2 weeks) • Symptomatic HIV infection • Asymptomatic HIV infection with evidence of impaired immune function (i.e., depressed CD4 counts) • Pregnant or breastfeeding women
Precautions	• Administration should be postponed during acute severe febrile illness. • Continue personal protection measures against mosquito bites after vaccination. • Vaccination should only be recommended when the potential benefits outweigh the potential risks (e.g., for those living in areas with a high dengue seroprevalence or where epidemiological data indicate a high burden of dengue disease). • Previous infection by dengue virus can be substantiated through serotesting.[6] • Vaccination is not recommended for individuals with no evidence of prior dengue infection. • Vaccination is not recommended for individuals living in non-endemic areas, with no evidence of prior dengue infection and planning to travel to endemic areas.

(Cont'd.) Table 5. Dengue Vaccine (CYD Tetravalent Dengue Vaccine) for Adults

Pregnancy and breastfeeding	Contraindicated Category X
Medisave	No

**Produced in serum-free Vero cells by recombinant DNA technology.*

***$CCID_{50}$: 50% cell culture infectious dose.*

Strong recommendation; moderate quality of evidence.

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1. Centers for Disease Control and Prevention. Clinical guidance: Dengue virus. Available at: https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-related-infectious-diseases/dengue. Accessed 08 June 2022.
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HAEMOPHILUS INFLUENZAE TYPE B VACCINE

Haemophilus influenzae type B (Hib) is a Gram-negative coccobacillus that is transmitted mainly via droplet or direct contact with respiratory secretions. Hib infection mainly affects children, presenting as pneumonia, meningitis, epiglottitis, septic arthritis, cellulitis, otitis media or pericarditis.[1] Rarely, invasive Hib infection may occur in adults with functional or anatomic asplenia, IgG2 subclass immunodeficiency, or immunosuppression from cancer chemotherapy or human immunodeficiency virus (HIV) infection, as well as recipients of haematopoietic stem cell transplant (HSCT).[2]

Incidence

In Singapore, Hib infection is rare, with only 0.1% of pneumonia cases and 4.9% of meningitis cases in children being due to invasive Hib infection.[1] In 2022, there were only two reports of Hib infection (median number of cases from 2017–2021 = 4).[3]

Vaccine description

The vaccine against Hib infection is a polysaccharide-protein conjugate vaccine, which is also available as fixed combination with other vaccines **(Table 6)**. Immunity is not lifelong, and boosters may be required for long-term protection.

Table 6. Hib Vaccine for Adults

Description	Each dose contains 10 mcg of purified capsular polyribosyl-ribitol-phosphate polysaccharide of Hib covalently bound to tetanus toxoid 30 mcg.
Summary of evidence	Studies on Hib conjugate vaccines were conducted mostly among infants, which reported an efficacy of over 90% after 3 doses.[2,4] Clinical trials in people living with HIV, HSCT recipients, or patients on immunosuppressant therapy reported an efficacy of at least 80%.[5,6]
Indication/Target population	Prevention of invasive Hib infection in adults at risk, such as those with functional or anatomic asplenia, sickle cell disease, IgG2 subclass immunodeficiency, immunosuppression from cancer chemotherapy or HIV infection, and HSCT.[2,7]
Schedule	At-risk adults require one dose. HSCT patients are recommended to be vaccinated 6–12 months after transplantation with 3 doses, and the interval between each dose should be at least 4 weeks.
Administration	Intramuscular injection. Subcutaneous injection for patients with thrombocytopenia or bleeding disorders.
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze. Protect from light.

(Cont'd.) Table 6. Hib Vaccine for Adults

Common adverse events	• Swelling and pain at the injection site • Fever, loss of appetite, restlessness, vomiting and diarrhoea (but mostly encountered in children)
Contraindications	Anaphylaxis to any vaccine component or a previous dose. HIV infection is NOT a contraindication.
Precautions	Administration should be postponed during acute severe febrile illness.
Pregnancy and breastfeeding	No data available Category C
Medisave	No

Strong recommendation; moderate quality of evidence.

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HEPATITIS A VACCINE

Viral hepatitis A is usually a self-limiting viral hepatitis caused by the hepatovirus, which is transmitted via the faecal–oral route.[1] In children, the course is commonly subclinical, but severity increases with age. Furthermore, it has low potential for chronicity and long-term complications. Infection affords lifelong immunity to the virus.

Incidence

While hepatitis A is endemic in many countries, it occurs sporadically in Singapore. In 2021, there were 15 reported cases of hepatitis A.[2] The numbers have likely been impacted by the closure of borders in many countries as a result of the COVID-19 pandemic. Outbreaks may occur, which are usually due to contaminated food. Nonetheless, contact tracing is recommended during potential outbreaks.

Vaccine description

The available monovalent adult hepatitis A vaccine contains formalin-inactivated hepatitis A whole-virus **(Table 7)**. It is available in paediatric and adult formulations.[3] The live attenuated vaccine is not available in Singapore.

In addition, a combined hepatitis A and B vaccine is available, given intramuscularly on months 0, 1 and 6. Aside from the dosing schedule, all other features of this vaccine are similar to those of the hepatitis A vaccine **(Table 7)**.

Natural infection with hepatitis A affords lifelong immunity, and vaccination in seropositive individuals affords no additional benefit. However, the prevalence of hepatitis A in Singapore is believed to be low. Thus, routine pre-vaccination serological testing is not recommended.[3]

Strong recommendation; low quality of evidence.

Table 7. Hepatitis A Vaccine for Adults

Description	Injection containing inactivated hepatitis A virus
Summary of evidence	A systematic review of eight clinical trials among adults and children reported an efficacy of 86%. There are reports of efficacy reaching almost 100% after the second dose among healthy adults.[3,4]

(Cont'd.) Table 7. Hepatitis A vaccine for Adults

Indication/Target population	Prevention of hepatitis A infection, especially among individuals at high risk of infection or severe outcomes. These include[5]: • All susceptible travellers to countries with moderate-to-high endemicity • Those at occupational risk (i.e., working with hepatitis A–infected primates or hepatitis A virus in the laboratory setting; healthcare workers are generally not considered high risk) • Those with underlying chronic liver disease • Those awaiting or have received liver transplantation • Men who have sex with other men (MSM) • Those using illegal drugs Can be recommended for Immunocompromised, seronegative patients, if[6]: • HIV–infected adults • Those with solid or haematologic cancer • HSCT and solid-organ transplant patients • Those with asplenia or sickle cell disease • Those with chronic inflammatory diseases on immunosuppressive medications May be administered for post-exposure prophylaxis, if indicated, within 2 weeks of exposure. Additional hepatitis A immunoglobulin (0.1 mL/kg) may be administered to persons aged >40 years, depending on the provider's assessed risk of exposure.
Schedule	Two doses spaced 6 to 12 months apart
Administration	Intramuscular injection
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze.
Common adverse events	• Pain, swelling, redness or induration at the injection site, fatigue, malaise, fever • Appetite loss, irritability, headache, drowsiness • Gastrointestinal symptoms (e.g., diarrhoea, nausea or vomiting)
Contraindications	Anaphylaxis or allergic to any vaccine component or known to be allergic to previous dose Seropositivity to hepatitis A is not a contraindication
Precautions	Administration should be postponed in individuals with acute severe illness. Use with caution in individuals with known hypersensitivity to neomycin.
Pregnancy and breastfeeding	No data available Category C
Medisave	No

References:

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CHAPTER 4: SPECIFIC VACCINES FOR ADULTS

HEPATITIS B VACCINE

Hepatitis B is the major cause of chronic viral hepatitis. It is caused by an orthohepadnavirus, which is transmitted vertically from mother-to-child, sexually and through transfer of contaminated blood or serous fluids.[1,2] Acute infection may occasionally lead to fulminant hepatic necrosis. The risk of developing chronic hepatitis B infection depends on the age at which infection is acquired. Chronic infection occurs in 90% of those infected perinatally but about 5% or less of those infected as adults.[3] Chronic hepatitis B is the identified cause of up to 80% of all hepatocellular carcinoma cases worldwide.

Incidence

A seroprevalence study in Singapore showed that in 2010, the prevalence of HBsAg among adults aged 18 to 79 years was 3.6%, and the prevalence of immunity (anti-HBs of at least 10 mIU/mL) was 43.9%.[4] In 2021, only 16 new cases of acute hepatitis B were reported.[5] Despite the low incidence and high immunity in Singapore (since 2006, the childhood coverage of hepatitis B vaccine has ranged from 95% to 97% under the National Childhood Immunisation Programme[6]), hepatitis B vaccination is recommended in certain populations due to their increased risk and the serious potential sequelae of chronic infection.

Strong recommendation; high quality of evidence.

Vaccine description

There are two types of parenteral hepatitis B (purified recombinant HBsAg subunit) vaccines available in Singapore, which have variation in their dosing regimens **(Table 8)**.

In addition, a combined hepatitis A and B vaccine is available. Features of this vaccine are similar to those of the hepatitis B vaccine.

Table 8. Hepatitis B Vaccine for Adults

	Recombinant vaccine
Description	The adult preparations contain the following dose of purified recombinant HBsAg: • 10 mcg (HBvaxPRO®) • 20 mcg (Engerix B®) • 40 mcg (HBvaxPRO® Dialysis formulation)
Summary of evidence	More than 90% of healthy adults younger than age 40 years develop a protective antibody response following a complete Hep B vaccine series. However, there is an age-specific decline in immunogenicity. By 60 years, only 75% develop protective antibody titers.[2]

(Cont'd.) Table 8. Hepatitis B Vaccine for Adults

	Recombinant vaccine
Indication/Target population	It is highly recommended to have given it as part of the childhood immunisation programme, but opportunistic vaccination should be given to those who are not vaccinated and especially those who are at risk.[7] Prevention of hepatitis B infection in previously unvaccinated adults, particularly those at high risk of infection or severe outcomes. These include[2,8]: • Sex partners and household contacts of HBsAg-positive patients • Persons with more than one sex partner during the previous 6 months • Patients being evaluated or treated for sexually transmitted diseases, MSM • Current or recent injection-drug users (IDU) • Residents and staff of facilities for developmentally disabled individuals • Healthcare and public safety workers with risk for exposure to blood or blood-contaminated body fluids • End-stage renal disease patients • Diabetes mellitus patients • International travellers to regions with high or intermediate hepatitis B prevalence • People living with HIV Immunocompromised, seronegative adults with[9]: • Chronic liver disease, including hepatitis C virus infection, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, and ALT/AST levels greater than twice the upper limit of normal • Solid or haematologic cancer • HSCT or solid-organ transplant recipient • Asplenia or sickle cell disease • Chronic inflammatory disease on immunosuppressive medications

(Cont'd.) Table 8. Hepatitis B Vaccine for Adults

	Recombinant vaccine
Schedule	**There are a few different immunisation schedules for hepatitis B vaccine, depending on the vaccine product used and the speed in which protection is needed.**[7] **Engerix B®[3,10]:** • Three doses, with the second and third dose given 1 and 6 months after the first dose. No booster is required after three doses. If rapid seroconversion is required, the third dose may be given 8 weeks after the second dose, with a follow-up at 12 months. • For patients on dialysis: 40 mcg at elected date followed by 1 month, 2 months and 6 months from the date of the first dose. **HBvaxPRO[11]:** • For healthy adults, 3 doses of 10 mcg of the vaccine can be given, with the second dose given at 1 month and the third dose given at 6 months after the first dose. When accelerated vaccination is required, third dose can be given at 2 months after first dose but has to be followed up by a booster dose at 12 months after first dose. • For patients on dialysis: 40 mcg of the vaccine can be given at elected date followed by 1 month, and 6 months from the date of the first dose.
Administration	Intramuscular injection (deltoid). Subcutaneous in patients with bleeding disorders or thrombocytopaenia.[10] Do not administer intradermally or in the gluteus maximus.[10]
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze.
Common adverse events	• Local pain, soreness, tenderness, pruritus, erythema, ecchymosis, swelling, warmth and nodule formation in the injection site • Fatigue, asthenia, malaise and/or fever • Nausea and diarrhoea • Headache • Pharyngitis or upper respiratory tract infections
Contraindications	Anaphylaxis to any vaccine component or a previous dose

(Cont'd.) Table 8. Hepatitis B Vaccine for Adults

	Recombinant vaccine
Precautions	• Administration should be postponed in individuals with acute severe illness. • Seroconversion should be assessed among the elderly, or additional doses may be recommended.[2] • Booster doses of hepatitis B vaccine is recommended in certain circumstances such as haemodialysis patients and other immunocompromised persons such as post-HSCT transplantation or with HIV infection. The need for booster doses is considered for those with ongoing risk for exposure.
Pregnancy and breastfeeding	Data on pregnant or breastfeeding women is lacking – administer only when benefit clearly outweighs risks.[10] Category C
Medisave	Up to S$500 per year per account

Pre-vaccination testing may be recommended in individuals at high risk of infection, as described above.[2]

Weak recommendation; low quality of evidence.

Post-vaccination testing is not routinely recommended but may be done in patients whose management will depend on their immune response – for example, people undergoing haemodialysis, people living with HIV or other immunocompromised patients, healthcare workers, and sex partners of HBsAg-positive individuals.[2] Post-vaccination testing should be performed 1 to 2 months after the last vaccine dose.

Weak recommendation; low quality of evidence.

Persons who do not respond to the first series of hepatitis B vaccination (i.e., anti-HBs <10 mIU/mL) should be given a second 3-dose series, unless documented as HBsAg-positive.[2] Retesting at the end of the second series is recommended.

Weak recommendation; low quality of evidence.

References:

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HUMAN PAPILLOMAVIRUS VACCINE

Human papillomavirus (HPV) is a double-stranded DNA virus that is transmitted by direct contact (mostly sexual) which infects the epithelium, leading to the development of skin or genital warts, and cancerous or precancerous mucosal lesions.[1,2]

Of the more than 100 HPV subtypes, 40 subtypes infect the mucosal epithelium.[1] Of these, 16 subtypes are considered high risk or oncogenic, acting as carcinogens that lead to cervical cancer and other anogenital cancers. These include subtypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 69, 73 and 82. The most common ones are subtypes 16 and 18, which account for 50% and 20% of cervical cancer cases worldwide respectively. Initial HPV infection is considered a necessary step in the oncogenesis of cervical cancer.

Incidence

A 2014 cross-sectional survey of 891 Singaporean women aged older than 12 years found that the prevalence of HPV infection detected by linear array polymerase chain reaction was 9.3% overall, and 5.1% for high-risk subtypes.[3] The most common high-risk subtypes were (in descending order) types 51, 16, 52, 58 and 66. Risk factors for infection included multiple sexual partners (adjusted OR 1.4) and lower educational level (less than 6 years of formal schooling) (adjusted OR 4.1).

Vaccine description

There are three types of HPV vaccine. The bivalent vaccine is protective against subtypes 16 and 18; the tetravalent vaccine against subtypes 6, 11, 16 and 18; and more recently, the 9-valent against subtypes 6, 11, 16, 18, 31, 33, 45, 52, and 58 **(Table 9)**.[1,2] The vaccines are recombinant vaccines and were intended to prevent HPV infection as well as premalignant cervical lesions and cervical cancer. Men should receive the tetravalent or 9-valent vaccine. The labelled indication for adults for the HPV vaccine in Singapore is for individuals up to age 26 years as the goal is primary prevention of HPV infection. HPV vaccination may be considered in adults aged 27-45 years. However, appropriate counselling by physician needs to include potentially reduced efficacy if adult has already been exposed to HPV infection, and routine administration of HPV vaccination in this age group is not recommended.

Table 9. Human Papillomavirus (HPV) Vaccine for Adults

	Bivalent vaccine (Cervarix)	Tetravalent vaccine (Gardasil 4)	9-valent vaccine (Gardasil 9)
Description	Each dose contains HPV 16 L1 protein (20 mcg) and HPV18 L1 (20 mcg).	Each dose contains HPV 6 L1 protein (20 mcg), HPV 11 L1 (40 mcg), HPV 16 L1 (40 mcg) and HPV 18 L1 (20 mcg).	Each dose contains HPV 6 L1 (30 mcg), HPV 11 L1 (40 mcg), HPV 16 L1 (60 mcg), HPV 18 L1 (40 mcg), HPV 31 L1 (20 mcg), HPV 33 L1 (20 mcg), HPV 45 L1 (20 mcg), HPV 52 L1 (20 mcg), and HPV 58 L1 (20 mcg).

(Cont'd.) Table 9. Human Papillomavirus (HPV) Vaccine for Adults

	Bivalent vaccine (Cervarix)	Tetravalent vaccine (Gardasil 4)	9-valent vaccine (Gardasil 9)
Summary of evidence	Vaccines were found to be highly immunogenic in 99% of recipients.		
Indication/Target population	Prevention of HPV infection, precancerous lesion, and cervical cancer in adult women aged 26 and below.	• Prevention of HPV infection, precancerous lesion, and cervical cancer in adult women aged 26 and below. • Prevention of HPV infection and genital warts in adult men aged 26 and below.	• Prevention of cervical, vulvar, vaginal, and anal cancer; premalignant genital lesions (cervical, vulvar and vaginal); premalignant anal lesions; HPV infections; cervical adenocarcinoma in situ; and external condyloma acuminata causally related to HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, in adult women aged 26 and below. • Prevention of premalignant lesions and HPV infections caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58; anal cancer caused by HPV types 16, 18, 31, 33, 45, 52, and 58 and condyloma acuminata caused by HPV types 6 and 11, in adult men aged 26 and below.
	May be considered for adults aged 27 to 45 years.		

(Cont'd.) Table 9. Human Papillomavirus (HPV) Vaccine for Adults

	Bivalent vaccine (Cervarix)	Tetravalent vaccine (Gardasil 4)	9-valent vaccine (Gardasil 9)
Schedule	• Three doses (0, 1–2 months, and 6 months) is recommended for persons aged 15 years to 45 years and immunocompromised persons above the age of 9 years. Delay in administration does not warrant restarting the dosing series.[1] • Two dose schedule (0 and 6 months) is recommended for all other persons between 9 years and 14 years of age. • If vaccination providers do not know or do not have available the HPV vaccine product previously administered, or are in settings transitioning to the 9-valent vaccine, any available HPV vaccine product may be used to continue or complete the series for females for protection against HPV 16 and 18; the 9-valent or quadrivalent vaccine may be used to continue or complete the series for males. There are no data on efficacy of fewer than 3 doses of the 9-valent vaccine.[4]		
Administration	Intramuscular injection		
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze. Protect from light.		
Common adverse events	• Injection site reactions such as pain, redness, swelling, pruritus or haematoma • Headache, dizziness, fever, myalgia, arthralgia, rash and/or fatigue • Nausea, vomiting, diarrhoea and/or abdominal pain		
Contraindications	Anaphylaxis to any vaccine component or a previous dose		
Precautions	• Administration should be postponed in individuals with acute severe illness. • HPV vaccine is not a treatment for external genital lesions; cervical, vulvar or vaginal cancers; or cervical intraepithelial neoplasia, vulvar intraepithelial neoplasia or vaginal intraepithelial neoplasia. • HPV vaccine is not a substitute for routine cervical cancer screening.		
Pregnancy and breastfeeding	In pregnant women, vaccination should be delayed until after the completion of pregnancy. No specific intervention is recommended when the vaccine is administered to a pregnant woman.[1] Breastfeeding women may receive vaccination.[1] Category C		
Medisave	S$500 per year per account up to age 26 years		No

Strong recommendation; moderate quality of evidence.

A Pap smear or screening for HPV DNA or HPV antibody is not recommended prior to vaccination.

Weak recommendation; low quality of evidence.

Women who have received HPV vaccination are still recommended to receive routine Pap smear screening as per cervical-cancer screening guidelines.

Women with equivocal or abnormal Pap smear results may still receive the vaccine, because such results may not necessarily mean HPV infection or infection of all included HPV subtypes, and hence may still benefit from vaccination.[1]

Strong recommendation; low quality of evidence.

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INFLUENZA VACCINE

Human influenza is a highly infectious respiratory viral illness with three types: influenza A, B and C.[1] Influenza A and B are known to cause moderate to severe disease and epidemics, while influenza C causes a mild upper respiratory disease that does not lead to epidemics. Avian influenza is caused by a strain of type A influenza and is not currently vaccine-preventable, although there are vaccines in development.

Clinical symptoms of influenza include fever, chills, headache, malaise, myalgia, anorexia, and respiratory symptoms such as sore throat, cough and nasal discharge.[1] Elderly patients may present with non-specific symptoms such as confusion.

Epidemiology

In April 2009, the World Health Organization declared an influenza pandemic caused by a novel H1N1 strain. By September 2009, around 270,000 people in Singapore were infected, leading to 18 deaths. The pandemic ended in August 2010. Influenza circulates year-round in Singapore with peaks coinciding with southern hemisphere (April to June) and northern hemisphere winters (December to March). More recent data showed that between 2,500 to 3,900 people in Singapore experience influenza-like illness every week.[2] In 2018, the monthly proportion of confirmed influenza, amongst those with influenza-like illness, ranged from 17% (August 2018) to 56% (November 2018).[3] Influenza (and other respiratory virus) circulation in Singapore dramatically reduced during the COVID-19 pandemic attributed to the non-pharmaceutical measures implemented for COVID-19 control, e.g., mask-wearing, social distancing, travel restrictions.[4] However, we can expect the circulation of influenza and other respiratory viruses to increase again following progressive relaxation of restrictions and increased travel globally. Due to the potential of influenza to cause mortality and epidemics or pandemics, control and surveillance of the disease is a major health priority.

It is transmitted mainly through respiratory droplets and direct contact with respiratory secretions.[1] Control measures include hygiene (e.g., frequent hand washing) and vaccination.

Vaccine description

Currently the influenza vaccines available in Singapore include the inactivated parenteral trivalent and quadrivalent vaccines **(Table 10)**. Influenza viruses undergo substantial antigenic drift that leads to the emergence of different strains from year to year. This antigenic drift, confounded by waning antibody levels, leads to a possible reduced vaccine efficacy to certain circulating strains. Thus, the vaccine is updated prior to each hemisphere's winter season according to the prevalent influenza strains at the time. At least yearly vaccination is recommended. If there is a significant strain change in northern hemisphere vaccine composition compared to southern hemisphere vaccine, repeat vaccination may be recommended. Despite the variable efficacy for particular seasons, vaccination is the single-best currently available prevention for influenza and its complications.

The live attenuated influenza vaccine is not yet available in Singapore. There are other vaccines for older adults such as high-dose vaccine, adjuvanted influenza vaccines and vaccines manufactured by cell-based and recombinant technology that are not available in Singapore.[5]

Strong recommendation; moderate quality of evidence.

Table 10. Influenza Vaccine for Adults

Vaccine type	Parenteral trivalent vaccine	Parenteral quadrivalent vaccine
Description	Each dose contains 15 mcg each of three influenza surface antigens selected according to the prevailing WHO recommendations released biannually. Covers against an influenza A H1N1 virus, an influenza A H3N2 virus, and one of two B viral lineages currently in circulation (either Victoria or Yamagata).	Each dose contains 15 mcg each of four influenza surface antigens selected according to the prevailing WHO recommendations released biannually. Covers against an influenza A H1N1 virus, an influenza A H3N2 virus, and both B viral lineages currently in circulation (Victoria and Yamagata).
Summary of evidence	A meta-analysis of 31 studies reported that trivalent inactivated vaccines had a 59% efficacy among adults aged 18 to 65 years.[6]	The immunogenicity and safety of the quadrivalent vaccine is similar to that of the trivalent vaccines.[7]
Indication/Target population	Prevention of influenza A and B infection. Healthy adults are recommended influenza vaccination both for individual protection and for the overall reduction of disease burden and virus circulation, evident when there is a good match between the vaccine and circulating strains.[8] Among adults, vaccination is strongly recommended in the following high-risk populations[8,9]: • Those aged 65 years and older • Those with chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, neurological, haematological or metabolic (including diabetes mellitus) disorders • Immunocompromised individuals (including those receiving immunosuppression or people living with HIV) • Pregnant women (all trimesters) or those who could become pregnant • Residents of chronic (intermediate or long-term) care facilities • Healthcare personnel • Morbidly obese patients (BMI of 40 or greater)[10] • Household contacts and caregivers of children younger than 5 years of age and adults 50 years of age and older[10] • Household contacts and caregivers of people with medical conditions that put them at higher risk for severe complications from influenza, as described previously	

(Cont'd.) Table 10. Influenza Vaccine for Adults

Vaccine type	Parenteral trivalent vaccine	Parenteral quadrivalent vaccine
Schedule	Single dose repeated yearly with the most updated vaccine*	
Administration	Intramuscular or subcutaneous injection (check product insert as this differs across brands)	Intramuscular injection
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze. Protect from light. Discard after a year.	
Common adverse events	• Headache, sweating, myalgia, arthralgia, fever, malaise, shivering and/or fatigue • Redness, swelling, pain, ecchymosis or induration at the injection site	• Irritability, myalgia, fatigue, appetite loss, drowsiness, headaches, shivering, fever, sweating • Nausea, vomiting, diarrhoea, abdominal pain, arthralgia • Injection site redness, swelling, induration
Contraindications	Anaphylaxis to any vaccine component or a previous dose. The flu vaccine may contain egg/chicken protein and certain antibiotics (e.g., gentamycin, kanamycin or neomycin). Patients with a previous anaphylaxis to these components should not receive vaccination.	Hypersensitivity to influenza vaccine or to any of the excipients or components. The vaccine contains egg/chicken proteins, formaldehyde, gentamicin sulphate and sodium deoxycholate.
Precautions	• Administration should be postponed in individuals with acute severe illness. • Visually inspect the vaccine for any foreign particulate matter and/or variation of appearance (the vaccine should be colourless to slightly opalescent after shaking). • Patients with a history of Guillain–Barré syndrome (GBS) with an onset related in time to influenza vaccination may be at increased risk of again developing GBS if given influenza vaccine. • Administration should be postponed in individuals with acute severe illness.	

**In the event of a major change in vaccine composition, revaccination with the most updated vaccine should be considered even though the person has been vaccinated within the year with the previous vaccine, particularly for individuals at high risk of influenza-related complications.*

(Cont'd.) Table 10. Influenza Vaccine for Adults

Vaccine type	Parenteral trivalent vaccine	Parenteral quadrivalent vaccine
Pregnancy and breastfeeding	No contraindication Category B	
Medisave	Claimable (S$500 per year per account) for persons with higher risk of developing influenza-related complications and severe pneumococcal disease, respectively.	

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JAPANESE ENCEPHALITIS VACCINE

Japanese encephalitis (JE) is caused by the JE virus (JEV) of the *Flaviviridae* family.[1-3] It is transmitted through bites from the *Culex* mosquito from animal reservoirs such as pigs and wild birds, and as such has a geographic preference for rural areas.[2] In tropical countries, the disease has no definite seasonality. Infection is usually asymptomatic but can develop into encephalitis in 1 out of every 300 cases. The encephalitis is characterised by a prodrome of fever, headache, abdominal pain, nausea and vomiting, which progresses to altered sensorium and coma with a fatality rate of 20% to 50%. Among adult survivors, long-term complications such as parkinsonism, paralysis or psychiatric disorders may occur.[4]

Incidence

JEV is the most common vaccine-preventable cause of encephalitis in Asia and is present in most parts of Asia and certain areas in the western Pacific. The mosquito-borne transmission of the virus occurs primarily in rural agricultural areas, often associated with rice cultivation and flood irrigation.[5] In contrast, local transmission of JEV has not been detected in Africa, Europe, or North and South Americas.

Since the phase-out of pig farming in Singapore, JE has become rare.[2] It is endemic in agricultural areas of some neighbouring countries.[1]

Vaccine description

A live attenuated vaccine and an inactivated vaccine against JEV are available in Singapore **(Table 11)**. Routine vaccination against JEV is not recommended due to the very low incidence of JE and the absence of the swine host. The JEV vaccination is recommended for persons travelling to regions with a JEV infection risk.

Table 11. JEV for Adults

Strong recommendation; moderate quality of evidence.

Vaccine type	Live attenuated (Imojev)	Inactivated (Ixiaro)
Description	Each dose contains 4 to 5.8 log plaque-forming units of live, attenuated, recombinant JEV.	Each dose contains 6 AU (antigen units) of inactivated JEV strain SA 14-14-2.
Summary of evidence	Field studies in endemic areas found that the seroprotection rate of the live attenuated vaccine ranged from 84% to 99.6%.[6-8]	A meta-analysis of randomised controlled trials of the inactivated vaccine found a seroprotection rate of 95% after the 2-dose series.[9]

Strong recommendation; moderate quality of evidence.

(Cont'd.) Table 11. JEV for Adults

Vaccine type	Live attenuated (Imojev)	Inactivated (Ixiaro)
Indication/Target population	• Prevention of JE infection. Vaccination is strongly recommended for people travelling to and staying for ≥1 month or with extensive outdoor rural exposure in areas where JE is endemic, such as China, India, Bangladesh, Nepal, Sri Lanka and Southeast Asia (Cambodia, Indonesia, Laos, Myanmar, the Philippines, Thailand and Vietnam).[1,3,10] • Travellers to an area with an ongoing JE outbreak. • The live attenuated vaccine is indicated for ages 9 months and above, while the inactivated vaccine is suitable from 2 months of age.	
Schedule	Single dose	• Regular schedule: 2 doses, first dose injection on Day 0 and the second dose injected on Day 28. • Accelerated schedule (suitable for adults aged 18 to 65 years): First dose injected on Day 0 and the second dose injected on Day 7.
Administration	• Subcutaneous injection. • Do not administer intravenously.	• Intramuscular injection. • Do not administer intravenously.
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze. Protect from light.	
Common adverse events	• Headache, myalgia, fatigue, fever or influenza-like illness • Redness, induration, tenderness, swelling or itching at the injection site • Nausea	
Contraindications	Anaphylaxis to any vaccine component or a previous dose. The live attenuated vaccine should not be given to immunocompromised patients who are either immunodeficient or are undergoing immunosuppressive therapies such as chemotherapy or high-dose systemic corticosteroids for 14 days or more. Further, a gap of at least 1 month is recommended between cessation of immunosuppressive therapies and vaccination.	

(Cont'd.) Table 11. JEV for Adults

Vaccine type	Live attenuated (Imojev)	Inactivated (Ixiaro)
Precautions	Vaccination is not a substitute for avoidance measures against mosquito bites. Such measures should be exercised when travelling to areas with a high prevalence of mosquito-borne infections.	
Pregnancy and breastfeeding	The live attenuated vaccine is contraindicated in pregnancy. Both vaccines are contraindicated in breastfeeding.	
Medisave	No	

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MEASLES–MUMPS–RUBELLA VACCINE

The measles–mumps–rubella (MMR) vaccine **(Table 12)** is a live-attenuated combination vaccine for the prevention of measles (measles virus, genus *Morbillivirus,* family *Paramyxoviridae*), mumps (mumps virus, genus *Rubulavirus*, family *Paramyxoviridae*) and rubella (rubella virus, a togavirus of the genus *Rubivirus*).[1] These infections are transmitted via respiratory droplets or by the airborne route (measles).

Measles presents with fever, cough, nasal congestion, conjunctivitis, and rash, and may lead to complications such as pneumonia and encephalitis, otitis media and, more rarely, subacute sclerosing panencephalitis.[2] Mumps primarily causes parotitis but may lead to meningitis, encephalitis and orchitis, especially among adults. Rubella presents with low-grade fever, rash, conjunctivitis, coryza and lymphadenopathy but may lead to haemorrhagic complications, Guillain–Barré syndrome and encephalitis on rare occasions. Additionally, maternal rubella during the first 8 to 10 weeks of gestation may lead to congenital rubella syndrome, miscarriage or stillbirth in 90% of cases.

Epidemiology

Due to the high infectivity and grave potential sequelae of these infections, prevention through vaccination is a public health priority. Since 2008, the vaccination coverage for MMR among children ranged from 94.7% to 95.2% under the National Childhood Immunisation Programme.[3] However, 152 and 12 cases of measles have been reported in Singapore in 2019 and 2020, respectively.[4,5] The corresponding rates for mumps were 422 and 285 cases; and for rubella, 2 and 1 cases.[4,5] It is unclear as to whether these individuals were vaccinated in childhood.

Table 12. MMR Vaccine for Adults

Description	Each dose contains at least 1,000 $CCID_{50}$ (50% cell culture infectious dose) of measles virus; 12,500 $CCID_{50}$ of mumps virus; and 1,000 $CCID_{50}$ of rubella virus.
Summary of evidence	A 12-year study in Singapore reported that the efficacy of the MMR vaccine was consistently above 92% seroprotective.[6]

(Cont'd.) Table 12. MMR Vaccine for Adults

Indication/Target population	Prevention of measles, mumps and rubella[7] • Among adults, vaccination is recommended for those who have not received complete vaccine series for measles, mumps, or rubella during childhood; or do not have any evidence of immunity such as previous infection or protection in serological testing, unless there is a medical contraindication. • Persons at higher risk of infection include those in educational institutions, healthcare personnel and international travellers to areas with possible suboptimal vaccination coverage, including some industrialised countries where refusal to vaccinate is advocated by some groups. • COVID-19 has adversely impacted a number of countries' routine immunisation programmes, which may increase the probability of measles outbreaks; hence review of MMR vaccination/immunity should be considered for travellers. • Immunocompromised patients, specifically for the following only: 3 months after chemotherapy and cancer is in remission and at least 6–12 months after anti-B-cell antibody therapy; HSCT; seronegative individuals 2 years after transplant if they have no GVHD and do not receive any immunosuppressive drug; HIV-infected patients with CD4 T-lymphocyte counts ≥200 cells/mm.[8] Individuals receiving high-dose steroids (prednisone ≥20 mg/day) for a prolonged period (≥14 days) should either receive MMR vaccine 1 month prior to starting steroid or at least 1 month after steroid course is completed.[9] • Unvaccinated women planning to become pregnant should be vaccinated at least 28 days before conceiving. Pregnancy status should be confirmed prior to vaccine administration. They should be advised not to get pregnant until 28 days after vaccination.[10]
Schedule	Two doses given at least 28 days apart.[11,12] In children, only doses given at age above 12 months count towards the full 2-dose series.
Administration	Subcutaneous injection
Storage and handling	During shipment, the vaccine may be frozen without affecting efficacy. During storage, keep refrigerated (between 2°C and 8°C). Protect from light.
Common adverse events	• Pain at injection site • Fever, rash

(Cont'd.) Table 12. MMR Vaccine for Adults

Contraindications	• Anaphylaxis to any vaccine component, a previous dose, or neomycin • Pregnancy • Active untreated tuberculosis (TB) • Immunodeficiency due to a medical condition or immunosuppressive therapy
Precautions	• Administration should be postponed in individuals with acute severe illness. • Caution should be exercised in vaccine recipients with individual or family histories of convulsions; history of cerebral injury or any other condition in which stress due to fever should be avoided; hypersensitivity (anaphylactic, anaphylactoid or immediate-hypersensitivity) to eggs, or current thrombocytopenia. • If a tuberculin skin test needs to be performed, it should be administered either before or simultaneously with the vaccine. • Antibody-containing blood products may interfere with seroconversion after MMR vaccination. Vaccination may be delayed by 3 to 11 months following administration of these products.[6] **(Table 3, page 17)**
Pregnancy and breastfeeding	Pregnant women should not receive the vaccine. Category C Vaccination should be avoided in breastfeeding women as some studies indicate that live attenuated rubella vaccine virus may be secreted in breast milk.
Medisave	Up to S$500 per year per account

$CCID_{50}$: 50% cell culture infectious dose.

Strong recommendation; strong quality of evidence.

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MENINGOCOCCAL VACCINE

Meningococcal disease is a potentially severe illness caused by *Neisseria meningitidis*.[1-3] It has three presentations: (1) meningeal syndrome, presenting as acute meningitis (headache, fever, nausea, vomiting, photophobia, neck stiffness and neurological deficits) and a case fatality rate of 5% to 10%; (2) septic form or meningococcal septicaemia, characterised by haemorrhagic rash and shock that is highly fatal; and (3) pneumonia.[2,3] The disease is transmitted through direct person-to-person contact or respiratory droplets from ill patients or asymptomatic carriers.

Incidence

Virulent *Neisseria meningitidis* is predominantly encapsulated, and of the 12 identified capsular serogroups, A, B, C, W, X, and Y cause the vast majority of cases. The dynamic epidemiology of these serogroups is unpredictable and varies with time and geographical region.[4]

The incidence of meningococcal disease is high in sub-Saharan Africa, although rare in Singapore, with only 9 cases reported in 2018.[3,5] Thus, the risk of meningococcal disease in Singapore or during travel to most countries is low. However, risk during travel to Mecca for the Hajj or Umrah[3] and residence in college dormitories in certain countries[5] is increased.

Vaccine description

The meningococcal vaccines available in Singapore against meningococcal serogroups A, C, Y and W-135 are the quadrivalent polysaccharide and quadrivalent conjugate vaccines **(Table 13)**.

A recombinant lipidated protein vaccine against serogroup B is also available, given as 2–3 doses.

Persons with reduced immune response (asplenia, complement deficiencies) and persons with increased risk for exposure (travellers and microbiologists) should receive 2 doses of the vaccine (1 dose insufficient in risk exposure group), specifically the quadrivalent meningococcal conjugate vaccine, with 2 months interval between doses (an exemption is those who were first vaccinated at or before age 11 years, who may be boosted at age 16 years).

In Singapore, the vaccine should be given to adults travelling to endemic or hyperendemic areas, particularly those travelling to Mecca for pilgrimage. The Saudi authority requires a valid certificate of the vaccination 10 days prior to arrival. Other high-risk groups may also be vaccinated. Otherwise, routine vaccination is not recommended.[1,3]

Strong recommendation; moderate quality of evidence.

Table 13. Meningococcal Vaccine for Adults

Vaccine type	Polysaccharide vaccine	Conjugate vaccine	Recombinant lipidated protein vaccines (serogroup B)
Description	Each dose contains 50 mcg each of *N. meningitidis* polysaccharide serotypes A, C, Y and W-135.	Each dose contains around 16 mcg of *N. meningitidis* polysaccharide serotypes A, C, Y and W-135 conjugated to diphtheria toxoid.	**Trumenba:** Each dose contains 60 mcg each of *N. meningitidis* serogroup B rLP2086 subfamilies A and B **Bexsero:** Each dose contains 50 mcg each of fusion proteins from of *N. meningitidis* serogroup B and 25 mcg of *N. meningitidis* serogroup B outer membrane vesicle.

(Cont'd.) Table 13. Meningococcal Vaccine for Adults

Vaccine type	Polysaccharide vaccine	Conjugate vaccine	Recombinant lipidated protein vaccines (serogroup B)
Summary of evidence	Vaccines are seroprotective in 90% of healthy recipients.[3]	Vaccines are seroprotective in 98% of healthy recipients.[3]	There are currently two recombinant lipidated protein vaccines, the MenB-FHbp (Trumenba) and MenB-4C (Bexsero). The two vaccines are not interchangeable and the same vaccine must be used for all doses in a series. Trumenba: A four-fold rise in titre of serum bactericidal assay using human complement was detected in 66.9% to 85.9% of patients (depending on the FHbp variant) after two doses. Limited immunogenicity data is available for individuals aged 40 years and above. Bexsero: An antibody titre of 5 in serum bactericidal assay using human complement was detected in 100% of infants after 1 month of receiving Bexsero, while a titre of ≥4 was detected in 9–84% of adolescents and adults when checked 4–7.5 years after the 2-dose primary series. Robust immune response (titres ≥4) was observed in 93–100% of subjects post booster. No data is available in individuals aged 50 years and above.

(Cont'd.) Table 13. Meningococcal Vaccine for Adults

Vaccine type	Polysaccharide vaccine	Conjugate vaccine	Recombinant lipidated protein vaccines (serogroup B)
Indication/Target population	Prevention of invasive meningococcal disease among high-risk groups[1-3,6]: • Those travelling to Benin, Burkina Faso, Burundi, Cameroon, Chad, Côte d'Ivoire, Central African Republic, Democratic Republic of Congo, Eritrea, Ethiopia, Gambia, Ghana, Guinea, Guinea Bissau, Kenya, Mali, Mauritania, Niger, Nigeria, Rwanda, Senegal, South Sudan, Sudan, Tanzania, Togo and Uganda • Those travelling to Mecca during Hajj or Umrah (mandatory, requires a certificate)* • Patients with anatomic or functional asplenia • Patients with sickle cell disease • Immunocompromised patients, including those with complement component deficiencies or those taking specific medications such as complement inhibitors (eculizumab or ravulizumab) • People living with HIV • Personnel handling *N. meningitidis* isolates • Close contacts of meningococcal disease patients • People at risk due to an outbreak in the community *Strong recommendation; moderate quality of evidence.* Vaccine may also be considered for the following subgroups[3,6]: • Students living in dormitories • Unvaccinated students • Military personnel *Weak recommendation; low quality of evidence.*		Prevention of invasive meningococcal disease caused by *N. meningitidis* serogroup B in high-risk groups, as mentioned on the left column.[7]

**Visit the Kingdom of Saudi Arabia Ministry of Health website for the most updated requirements for meningococcal vaccination prior to pilgrimage to Mecca.*

Available at: https://www.saudiembassy.net/hajj-and-umrah-health-requirements?

(Cont'd.) Table 13. Meningococcal Vaccine for Adults

Vaccine type	Polysaccharide vaccine	Conjugate vaccine	Recombinant lipidated protein vaccines (serogroup B)
	Polysaccharide vaccine is preferred for adults aged 56 years or older who have not previously received conjugate vaccine and who require a single dose only (e.g., travellers).[7] The MPSV4 vaccine is no longer available in Singapore.	Conjugate vaccine is indicated for routine administration in individuals aged 11–18 years. It is also indicated in persons with increased risk of infection and those with certain medical conditions or immunodeficiencies (complement component deficiencies or use of complement inhibitors, human immunodeficiency virus). Since the discontinuation of the MPSV4 vaccination in Singapore, conjugate vaccines have been used in individuals aged over 55 years. Nimenrix can be administered to children from 6 months of age, adolescents and adults. Please refer to the package insert for the age criteria for other conjugate vaccines.	Serogroup B meningococcal vaccine is recommended for young adults aged 16–23 years. The preferred age of administration is 16–18 years, especially for college students living in shared facilities.[7] The vaccine is also recommended for adults at increased risk of serogroup B disease due to complement component deficiencies; functional or anatomical asplenia; taking complement inhibitor, personnel with occupational exposure to the bacteria and/or during the outbreak setting.[7]

(Cont'd.) Table 13. Meningococcal Vaccine for Adults

Vaccine type	Polysaccharide vaccine	Conjugate vaccine	Recombinant lipidated protein vaccines (serogroup B)
Schedule	Travel for pilgrim requires at least one dose of conjugate vaccine within 5 years (at least 10 days prior to the planned arrival to Hajj areas) or one dose of polysaccharide vaccine within the last three years.[8] Primary series: Two doses, given 2 months apart, are recommended to those with anatomical or functional asplenia, persistent complement component deficiencies, or human immunodeficiency virus infection. Revaccination is recommended every 5 years for individuals as long as the risk remains increased.[3]		Trumenba: Two doses given 6 months apart (accelerated schedule: 1 month apart for individuals at increased risk of invasive meningococcal disease, followed by a third dose at least 4 months after the second dose). A booster dose (using either regimen as above) should be considered for individuals at continued risk of invasive meningococcal disease. Bexsero: Primary immunisation contains two doses given 2 months apart for ages 5 months to 23 months. Ages 2 onwards receive two doses spaced 1 month apart. Booster dose schedule is as follows: Infants 6–11 months: one dose given after 2 months from primary series. 12 months onwards: one dose given after 12–23 months from primary series. For ages 2 and above, booster should be considered only in individuals with high risk of exposure.

(Cont'd.) Table 13. Meningococcal Vaccine for Adults

Vaccine type	Polysaccharide vaccine	Conjugate vaccine	Recombinant lipidated protein vaccines (serogroup B)
Administration	Subcutaneous injection		Intramuscular injection
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze.		
Common adverse events	• Pain, induration, redness or swelling at the injection site • Headache, fatigue, irritability or drowsiness • Diarrhoea or anorexia		
Contraindications	Anaphylaxis to any vaccine component or a previous dose.		
Precautions	• Vaccination should be postponed in individuals with acute severe illness. • Vaccination may not protect against all serotypes of *N. meningitidis*. • Response may be impaired in some immunocompromised individuals. • Administration of pneumococcal conjugate vaccine and Menactra brand meningococcal conjugate vaccine should be separated by a 4-week interval in patients with functional or anatomical asplenia.		• Vaccination should be postponed in individuals suffering from an acute severe febrile illness. • Give with caution to individuals with thrombocytopenia or any coagulation disorder or to those receiving anticoagulant therapy, unless the potential benefit clearly outweighs the risk of administration. • Response may be impaired in some immunocompromised individuals.

(Cont'd.) Table 13. Meningococcal Vaccine for Adults

Vaccine type	Polysaccharide vaccine	Conjugate vaccine	Recombinant lipidated protein vaccines (serogroup B)
Pregnancy and breastfeeding	Meningococcal conjugate vaccines may be given to pregnant women who are at increased risk for serogroup A, C, W, or Y meningococcal disease. Data on breastfeeding women is lacking – administer only when benefit clearly outweighs risks. Category C		Serogroup B meningococcal vaccines should only be given to pregnant or breastfeeding women who are at increased risk for serogroup B meningococcal disease who decide, after talking with a doctor, that the benefits of receiving the vaccine outweigh the risk.
Medisave	No		

Strong recommendation; moderate quality of evidence.

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PNEUMOCOCCAL VACCINE

Encapsulated strains of *Streptococcus pneumoniae* are the causative organisms of invasive pneumococcal disease (IPD), and capsular polysaccharides are the primary basis of its pathogenicity.[1] IPD can manifest as bacteraemia, meningitis, bacteraemic pneumonia or sinusitis.[2] Invasive disease is most common in children 4 years old or younger, but incidence starts rising from ages 35 years and above.[1] Patients aged 65 years and above are at high risk of morbidity and mortality.

Disease burden

In Singapore, the mean hospitalisation rate for IPD was 380 cases per year between 2000 and 2008.[2] About half of IPD patients were adults, and fatality rate was around 21%. In 2018, the number of reported pneumococcal disease cases was 130.[3]

Despite this low number and a declining trend of invasive disease, prevention of IPD through vaccination is still a public health priority. Data on the overall disease burden, including non-invasive pneumococcal infections, is lacking but likely to be significant. Aside from the high morbidity and mortality associated with IPD, asymptomatic pneumococcal carriage can be as high as 50% as *S. pneumoniae* is part of the normal flora of the respiratory tract.[1] The underlying mechanism behind the transition from asymptomatic carriage to invasive disease is unclear.

Vaccine description

Currently, there are two categories of pneumococcal vaccines available to prevent IPD and pneumonia: the pneumococcal conjugate vaccines and the 23-valent pneumococcal polysaccharide vaccine (PPSV23 or Pneumovax23).

The conjugate vaccines include the 10- (PCV10 or Synflorix), 13- (PCV13 or Prevenar 13) and the 20-valent (PCV20 or Apexxnar) vaccine. At the time of writing, all three conjugate vaccines are licensed in Singapore, but only the 10- and 13-valent vaccines are included in the MOH Subsidised Vaccine List (SVL). The 20-valent conjugate vaccine is currently licenced for use in adults aged 18 years and above only. The 15-valent conjugate vaccine (Vaxneuvance by Merck Sharp & Dohme) is available in the United States but is not yet licensed for use in Singapore.

Currently the two most widely used pneumococcal vaccines are PPSV23 and PCV13 **(Table 16)**. Studies on these two vaccines suggest that the PCV13 may provide broader protection than the PPSV23. The PCV13 is also given to children 6 weeks and older, compared with 2 years and older for PPSV23.

The Advisory Committee on Immunization Practice (ACIP) has published recommendations on the use of PCV20 in adults aged 19 years and above (See **Table 17 A** and **17 B**).[4,5] At the time of writing, there is no NAIS guidance on the use of PCV20.

Table 14. Comparison Between PPSV23, PCV13 and PCV20

Strong recommendation; low quality of evidence.

Vaccine type	23-valent polysaccharide vaccine (PPSV23)	13-valent conjugate vaccine (PCV13)	20-valent conjugate vaccine (PCV20)
Description	Each dose contains 25 mcg each of pneumococcal polysaccharides from 23 serotypes. See **Table 15**	Each dose contains pneumococcal polysaccharides from 13 serotypes conjugated to carrier proteins. See **Table 15**	Each dose contains pneumococcal polysaccharides from 20 serotypes conjugated to carrier protein. See **Table 15**
Summary of evidence	Around 80% of healthy recipients developed antibodies to vaccine serotypes.[1] Efficacy in preventing IPD ranged from 60% to 80% in adults aged ≥65 years.[6] Efficacy in adults with underlying illnesses may be reduced.	Vaccine efficacy among adults ≥65 years old was around 75% against vaccine-type IPD.[7]	No clinical efficacy studies were conducted for PCV20, but immunogenicity studies demonstrate that immune responses were non-inferior to those elicited by PCV13 for matched serotypes.[8]
Indication/Target population	Prevention of IPD and pneumonia See **Table 16**		
Schedule	• See **Table 16** for schedule details. • When both PCV13 and PPSV23 are indicated, PCV13 should be administered first; likewise, based on the clinical experience with PCV13, when both PCV20 and PPSV23 are indicated, PCV20 should be given first.[8] PCV13 and PPSV23 should not be administered during the same visit. • The vaccine should be administered 2 weeks prior to elective splenectomy, cochlear implantation or immunosuppressive therapy.[1] • PPSV23 or PCV13 may be co-administered with the influenza vaccine. Based on clinical experience with PCV13, PCV20 may be co-administered with the influenza vaccine.		
Administration	Subcutaneous or intramuscular	Intramuscular	Intramuscular

(Cont'd.) Table 14. Comparison Between PPSV23, PCV13 and PCV20

Strong recommendation; low quality of evidence.

Vaccine type	23-valent polysaccharide vaccine (PPSV23)	13-valent conjugate vaccine (PCV13)	20-valent conjugate vaccine (PCV20)
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze. Protect from sunlight.		
Common adverse events	• Local reactions at the injection site • Fever, lymphadenopathy, headache, rash, urticaria, myalgia, arthralgia, asthenia, fatigue, malaise • Arthus-type reaction and acute hypersensitivity reactions	• Local reactions at the injection site • Decreased appetite, fever, headache, rash, joint pains, chills, fatigue • Diarrhoea and vomiting • Limitation of arm movement	
Contraindications	Anaphylaxis to any vaccine component or a previous dose.		
Precautions	• Vaccination should be postponed in individuals with acute severe illness. • Vaccination may not protect against all serotypes of *S. pneumoniae*. • Response may be impaired in some immunocompromised individuals.		
Pregnancy and breastfeeding	Data on pregnant or breastfeeding women is lacking – administer only when benefit clearly outweighs risks.[1]		
Medisave/Subsidy	Subsidised (subject to means-testing) at polyclinics and CHAS-enabled GP clinics for Singaporean adults in whom the vaccine is recommended as per National Adult Immunisation Schedule from 1 November 2020. Prevailing MediSave rules will continue to apply to any co-payments after the application of subsidies.[9]		

CHAS, Community Health Assist Scheme; IPD, invasive pneumococcal disease; PCV13, pneumococcal conjugate vaccine 13; PCV20, 20-valent pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine.

Table 15. Serotypes of Pneumococcal Vaccines

Serotypes	Vaccine				
	PPSV23	PCV10	PCV13	PCV15	PCV20
1	x	x	x	x	x
2	x				
3	x		x	x	x
4	x	x	x	x	x
5	x	x	x	x	x
6A			x	x	x
6B	x	x	x	x	x
7F	x	x	x	x	x
8	x				x
9N	x				
9V	x	x	x	x	x
10A	x				x
11A	x				x
12F	x				x
14	x	x	x	x	x
15B	x				x
17F	x				
18C	x	x	x	x	x
19A	x		x	x	x
19F	x	x	x	x	x
20	x				
22F	x			x	x
23F	x	x	x	x	x
33F	x			x	x
Comment		Same as PCV13 but without 3, 6A and 19A	Contains the same serotypes in PPSV23, except 6A which is unique	PCV13 plus 22F and 33F	PCV13 plus 8, 10A, 11A, 12F, 15B, 22F, and 33F

PPSV23 refers to 23-valent pneumococcal polysaccharide vaccine; PCV10, PCV13, PCV15, and PCV20 refer to the 10-, 13-, 15- and 20-valent pneumococcal conjugate vaccines, respectively.

Table 16. PCV13 and PPSV23 Vaccination Schedule for Adults in Singapore

Target population	Corresponding schedule		
	PCV13 recommendation	PPSV23 recommendation	Additional doses of PPSV23
Adults aged 18–64 years who are immunocompetent, otherwise healthy with no chronic diseases	Not indicated	Not indicated	Not indicated before 65 years.[d]
Adults aged 18–64 years who are immunocompetent but with chronic diseases • Chronic pulmonary disease[a] • Chronic cardiovascular disease[b] • Chronic liver disease[c] • Diabetes mellitus	Not indicated	One dose	Not indicated before 65 years.[d]
Adults aged 18–64 years: • Cochlear implant • Cerebrospinal fluid leaks	One dose (preferably before PPSV23)[e]	One dose, 8 weeks after PCV13	Not indicated before 65 years.[d]
Adults aged 18–64 years at high risk for invasive pneumococcal disease because of: • Functional/Anatomic asplenia[f] • Immunocompromising states[g]	One dose (preferably before PPSV23)[e]	One dose, 8 weeks after PCV13	One booster after 5 years.[d] If this is administered before 65 years, a third dose of PPSV23 is indicated after 65 years.
Adult's age ≥65 years, regardless of immune status	One dose (preferably before PPSV23)[e,h]	One dose, 1 year after PCV13[h]	Not indicated
Adults aged 18–64 years with chronic renal failure[i,j]	One dose (preferably before PPSV23)[e,h]	One dose, 8 weeks after PCV13[h]	Not indicated before 65 years.[d]

(Cont'd.) Table 16. PCV13 and PPSV23 Vaccination Schedule for Adults in Singapore

Target population	Corresponding schedule		
	PCV13 recommendation	PPSV23 recommendation	Additional doses of PPSV23
Adults age ≥65 years with chronic renal failure[i,j]	One dose (preferably before PPSV23)[e,h]	One dose, 8 weeks after PCV13[h]	Not indicated

[a]Including asthma, chronic obstructive pulmonary disease (COPD) or chronic bronchitis and emphysema, bronchiectasis, cystic fibrosis, interstitial lung fibrosis, pneumoconiosis and bronchopulmonary dysplasia (BPD) and asthma. The chronic pulmonary conditions (for which PPSV23 is indicated) mentioned in the MOH Circular 23A/2017.[10] are non-exhaustive, i.e. other diseases/conditions not mentioned as examples can be included, if categorised as chronic pulmonary disease. [b]Including those requiring regular medication and/or follow-up for ischemic heart disease, congenital heart disease, hypertension with cardiac complications, and chronic heart failure. [c]Including biliary atresia, cirrhosis and chronic hepatitis. There is no routine recommendation for PPSV23 for hypertension alone (without cardiac complications) in people <65 years. [d]No further doses until the person reaches age 65 years. From age 65 years onwards, administer 1 dose of PPSV23 at least 5 years after any prior dose of PPSV23. [e]Only 1 dose of PCV13 is indicated per lifetime for adults. [f]Including conditions such as homozygous sickle cell disease and coeliac syndrome that may lead to splenic dysfunction. [g]Congenital or acquired immunodeficiencies, HIV infection, Leukemia, lymphoma, Hodgkin's disease, generalized malignancy, iatrogenic immunosuppression, solid organ transplant including renal transplant and multiple myeloma. [h]If PPSV23 previously given, delay PCV13 for at least 12 months, and PPSV23 for at least 5 years after the last dose of PPSV23. [i]Stage 4 and 5 and those on renal dialysis. [j]The National Adult Immunisation Schedule does not include PCV13 for this patient subgroup, and the vaccine cannot be claimed with Medisave. However, this expert panel strongly recommends PCV13 for these patients, in line with recommendations from the Advisory Committee on Immunization Practices.

Table 17 A. ACIP Recommendations for use of 20-valent Pneumococcal Conjugate Vaccine in Adults Aged ≥19 to 64 Years[4,5,10]

Group	Recommendations
Healthy adults aged ≥19 to 64 years with no underlying medical conditions or risk factors	No recommendations for PCV20.
Adults aged ≥19 to 64 years with underlying medical conditions or other risk factors including: • Chronic heart disease such as congestive heart failure and cardiomyopathies • Chronic liver disease • Chronic lung disease such as chronic obstructive pulmonary disease, emphysema, and asthma • Diabetes mellitus • Alcoholism	If naïve to pneumococcal vaccines, give 1 dose of PCV20. If previously received PPSV23 only, give 1 dose of PCV20 at least 1 year after their last PPSV23 dose. If previously received PCV13 only, give 1 dose of PCV20 at least 1 year after their last dose. If previously received both PCV13 and PPSV23, no additional pneumococcal vaccine is recommended. Review again at age 65 years.

(Cont'd.) Table 17 A. ACIP Recommendations for use of 20-valent Pneumococcal Conjugate Vaccine in Adults Aged ≥19 to 64 Years[4,5,10]

Group	Recommendations
Adults aged ≥19 to 64 years with underlying medical conditions or other risk factors including: • Cochlear implant • CSF leak • Congenital or acquired asplenia • Sickle cell disease or other hemoglobinopathies • Immunocompromising conditions such as: o Chronic renal failure o Congenital or acquired immunodeficiencies o Malignancy o HIV infection o Hodgkin disease o Iatrogenic immunosuppression o Leukemia o Lymphoma o Multiple myeloma o Nephrotic syndrome o Solid organ transplant	If naïve to pneumococcal vaccines, give 1 dose of PCV20. If previously received PPSV23 only, give 1 dose of PCV20 at least 1 year after their last PPSV23 dose. If previously received PCV13 only, give 1 dose of PCV20 at least 1 year after their last dose. If previously received both PCV13 and PPSV23, consider giving PCV20 at least 5 years from last pneumococcal dose.

CSF, cerebrospinal fluid; PCV20, 20-valent pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine.

Table 17 B. ACIP Recommendations for use of 20-valent Pneumococcal Conjugate Vaccine in Adults aged ≥65 Years[4,5,10]

Group	Recommendations
Healthy persons Those with underlying medical conditions or other risk factors including: • Chronic heart disease such as congestive heart failure and cardiomyopathies • Chronic liver disease • Chronic lung disease such as chronic obstructive pulmonary disease, emphysema, and asthma • Diabetes mellitus	If naïve to pneumococcal vaccines, give 1 dose of PCV20. If previously received PPSV23 only, give 1 dose of PCV20 at least 1 year after their last PPSV23 dose. If previously received PCV13 only, give 1 dose of PCV20 at least 1 year after their last dose.

(Cont'd.) Table 17 B. ACIP Recommendations for use of 20-valent Pneumococcal Conjugate Vaccine in Adults aged ≥65 Years[4,5,10]

Group	Recommendations
Adults aged ≥65 years with underlying medical conditions or other risk factors including: • Cochlear implant • CSF leak • Congenital or acquired asplenia • Sickle cell disease or other hemoglobinopathies • Immunocompromising conditions such as: o Chronic renal failure o Congenital or acquired immunodeficiencies o Malignancy o HIV infection o Hodgkin disease o Iatrogenic immunosuppression o Leukemia o Lymphoma o Multiple myeloma o Nephrotic syndrome o Solid organ transplant	If previously received both PCV13 and PPSV23, and PPSV23 was given before age of 65 years, consider giving PCV20 at least 5 years from the last pneumococcal dose. If previously received both PCV13 and PPSV23 and PPSV23 was given ≥65 years, the benefits of administering PCV20 are unclear, and any further dose should be based upon a shared clinical decision.*

PCV20, 20-valent pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine.
**The incremental public health benefits of providing PCV20 to adults who had received PCV13 only or both PCV13 and PPSV23 have so far not been evaluated.*

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POLIO VACCINE

Poliomyelitis (also known as infantile paralysis or polio) is a central nervous system disorder caused by infection with poliovirus types 1, 2 or 3.[1-3] These viruses are transmitted via the faecal-oral route. Infection is asymptomatic in most cases, but paralytic disease occurs in 1% of infected cases.[2] There is no known cure for infantile paralysis.

Incidence

As a result of Singapore's participation in the global drive to eradicate polio through vaccination, indigenous polio has been eradicated from Singapore since 1973.[1] At present, vaccination coverage for polio under the National Childhood Immunisation Programme is at least 95%.[4]

However, polio remains endemic in Afghanistan and Pakistan.[1] Since the objective of polio vaccination is global eradication, and because of the high number of travellers from these regions to Singapore, polio vaccination remains a public health priority in Singapore. Some polio-free countries with low vaccination coverage remain at risk for poliomyelitis outbreaks after importation of WPV type 1. Countries that have low oral polio vaccine (OPV) coverage in routine immunisation are also at risk of experiencing poliomyelitis cases and outbreaks caused by circulating vaccine-derived poliovirus (cVDPVs).

Vaccination

Adults who present for vaccination should have their past records reviewed. Most adults do not need polio vaccine as polio is included in Singapore's National Childhood Immunisation Schedule. However, some adults are at higher risk **(Table 18)** of exposure to the poliovirus and may need 1 to 3 doses of inactivated polio vaccine (IPV), depending on the number of doses they have had in the past.

The childhood polio immunisation schedule prior to 2013 comprised six doses of OPV. However, the World Health Organization (WHO) no longer recommends an OPV-only regimen to reduce the risk of vaccine-associated paralytic poliomyelitis (VAPP) observed with the use of OPV. Hence, the OPV only schedule was replaced with a sequential IPV-OPV schedule, consisting of four doses of IPV, and a fifth dose of OPV at the age of 10 to 11 years (called Primary 5). This regimen is recommended in countries with high immunisation coverage (i.e., >90%), such as Singapore. Trivalent OPV (containing types 1, 2 and 3) was replaced with bivalent OPV (containing types 1 and 3) in 2016 to meet the WHO requirement.[5] Type 2 OPV was withdrawn because type 2 wild polioviruses are no longer in circulation and Sabin type 2 vaccines have contributed to a disproportionate number of VAPP cases.

Up until January 2021, bivalent oral polio vaccine (bOPV) was used for the 5th dose of polio vaccine for children aged 10 to 11 years (Primary 5), given as a part of Health Promotion Board's (HPB) school-based vaccination programme. With the current supplier for Singapore having discontinued the manufacturing of bOPV and the possibility of eventual global cessation of OPV-usage in the future, the 5th dose in the primary series was replaced with an IPV-containing vaccine in January 2021.[6] The primary series now consists of 5 IPV-containing doses.

In Singapore, both IPV and OPV are available **(Table 16)**. Even though OPV is easy to administer, IPV is preferred in primary care settings due to the absence of the risk of reactivation,[1-3] and is therefore appropriate for immunocompromised patients.[1] In addition, IPV is more readily available in the primary care setting and is also available in combination with other vaccines.

Table 18. Polio Vaccine for Adults

Vaccine type	Oral vaccine	Inactivated vaccine
Description	Each dose (0.1 mL or two drops) contains at least 10^6 $CCID_{50}$ for type 1, and $10^{5.8}$ $CCID_{50}$ for type 3 of live attenuated Sabin strains of polioviruses.	Each dose contains type 1, 2 and 3 inactivated poliovirus in quantities compliant with WHO recommendations.
Summary of evidence	Immunity results in 95% of 3-dose vaccine recipients, but gastrointestinal immunity is higher than in IPV. Immunity is likely lifelong.	Immunity results in 99% of 3-dose vaccine recipients. Duration of immunity is uncertain.
Indication/Target population	Prevention of poliomyelitis Among adults, vaccination is recommended in the following at-risk groups: • Those travelling to areas where polio is endemic or where polio transmission has been known to occur. Advisories have been raised for travellers to Afghanistan, Democratic Republic of Congo, Indonesia, Mozambique, Kenya, Niger, Nigeria, Pakistan, Papua New Guinea and Somalia[7] • Those handling poliovirus isolates • Unvaccinated contacts of the vaccine recipient *Strong recommendation; low quality of evidence.* Vaccination need not be given to unvaccinated low-risk adults. Booster doses need not be given to vaccinated low-risk adults. *Weak recommendation; low quality of evidence.*	
Schedule	• Single dose for previously vaccinated adults • For unvaccinated adults, give three doses, with the second and third dose given after 1–2 and 6–12 months after the first dose.[2] If an accelerated schedule is necessary, each dose should be spaced 4 weeks apart. • In cases of unavoidable immediate travel, at least one dose should be administered prior to departure. • Recipients of IPV should receive a booster dose 10 years after the primary vaccination if risk of infection persists.	

Strong recommendation; low quality of evidence.

(Cont'd.) Table 18. Polio Vaccine for Adults

Vaccine type	Oral vaccine	Inactivated vaccine
Administration	Oral	Intramuscular (preferred) or subcutaneous injection
Storage and handling	Store between 2°C and 8°C, or at -20°C.	Keep refrigerated (between 2°C and 8°C). Do not freeze. Protect from sunlight.
Common adverse events	Rarely, allergic reactions	• Local reactions at the injection site • Transient fever
Contraindications	Anaphylaxis to any vaccine component (including neomycin, streptomycin or polymyxin B) or a previous dose.	Anaphylaxis to any vaccine component (including neomycin or polymyxin B) or to a previous dose.
Precautions	• Vaccination should be postponed in individuals with acute severe illness, persistent vomiting or diarrhoea. • Non-immune persons in close contact with a recently vaccinated subject may very rarely be at risk of vaccine-associated paralytic poliomyelitis.	Response may be diminished in immunocompromised patients. When possible, give the vaccine when the underlying condition has resolved. However, in cases of chronic immunodeficiency, vaccination is recommended.
Pregnancy and breastfeeding	Data on pregnant or breastfeeding women is lacking – administer only when benefit clearly outweighs risks.[1] Category C	
Medisave	No	

$CCID_{50}$, 50% cell culture infectious dose.

Strong recommendation; moderate quality of evidence

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RABIES VACCINE

Rabies is a zoonotic disease caused by the *Lyssavirus* (*Rhabdoviridae* family).[1,2] The virus is transmitted primarily through the bite of infected animals, as the virus is found primarily in the saliva. Minor modes of transmission include other animal contact, such as a penetrating scratch with bleeding, or through licking of broken skin or mucosa.

From the site of inoculation, the rabies virus progressively invades the peripheral nervous system and then the central nervous system, causing an acute viral encephalomyelitis, which is almost always fatal.[1] The initial symptoms include headache, fever, malaise and sensory changes at or around the site of animal bite. It progresses to excitability, hallucinations, aerophobia (abnormal fear of drafts of air), then hydrophobia (fear of water) secondary to pharyngeal spasms, delirium, convulsions and death within days.

Epidemiology

The last published reported case of rabies in Singapore was in 1953.[2] Rabies elimination in Singapore is mainly a result of intensive oral vaccination of animal reservoirs and tight implementation of quarantine. However, rabies remains endemic in many countries worldwide. High-risk areas include Southeast Asia, East Asia, Central Asia, the Indian subcontinent, and North and Central Africa.[1]

Vaccine description

The inactivated rabies vaccine registered in Singapore is propagated in a purified chick embryo cell (PCEC) culture **(Table 19)**. Other available types of rabies vaccines recommended by the WHO include:

- Purified Vero cell rabies vaccine, which contains inactivated and lyophilised Wistar strain of rabies virus grown on Vero cell cultures in fermenters allowing mass cultivation. Each dose of reconstituted vaccine contains at least 2.5 IU of inactivated rabies virus.
- Human diploid cell vaccine contains the Pitman-Moore L503 or Flury strain of rabies virus grown on MRC-5 human diploid cell culture.
- Primary Hamster kidney cell vaccine uses the Beijing strain.
- Purified duck embryo vaccine uses duck embryo cells as substrate.

Routine vaccination is not recommended.[1-3] Pre-exposure prophylaxis is recommended for high-risk groups, such as those travelling to rabies-endemic areas and those with occupational exposure to mammals or the rabies virus. Post-exposure prophylaxis using the same vaccine but with a different schedule should be given according to the risk of the bite **(Table 20)**.[1,2] In addition, post-exposure prophylaxis may include administration of rabies immunoglobulin.

Table 19. Rabies Vaccine for Adults

Vaccine type and description	• Purified chick embryo cell (PCEC) vaccine contains at least 2.5 IU of inactivated rabies virus (strain Flury LEP) cultured in PCEC.	• Vero cell vaccine contains at least 2.5 IU of inactivated rabies virus (WISTAR Rabies PM/WI38 1503-3M strain) cultured in Vero cells.
Summary of evidence	Clinical trials on PCEC rabies vaccines on a 3-dose schedule demonstrate immunogenicity in 100% of pre-exposure healthy recipients by day 28. Clinical trials on the same vaccine given to individuals exposed to rabies on a 5- or 6-dose schedule demonstrate seroprotection in 98% by day 14, and in 100% by day 30.[3] The various brands of vaccine are interchangeable.	
Indication/Target population	Pre-exposure prophylaxis for high-risk individuals[1,2,4]: • Individuals travelling to high-risk countries • Those with occupational exposure to mammals, such as veterinarians, veterinary staff, animal control and wildlife workers, hunter and trappers in areas with confirmed rabies, and spelunkers • Those with exposure to the rabies virus, such as laboratory workers handling the virus Post-exposure prophylaxis for Category II and III rabies exposure **(Table 20)**	
Schedule	**Primary pre-exposure prophylaxis[4]:** • 3 doses given on days 0, 7, and 21 or 28. • A booster injection is given 1 year later, and every 5 years for high-risk occupations. • 2 doses may be given on days 0 and 7 if a 3-dose regimen is not possible due to a short lead time. However, the patient should be counselled of the limited data regarding long-term immunity. The data are still emerging. **Post-exposure prophylaxis[4]:** • Please refer to **Table 20**.	
Administration	Intramuscular injection in the deltoid. Do not inject intravascularly, as this could result in severe adverse reactions. Intramuscular route is the preferred route for pre-exposure and post-exposure prophylaxis. There is data for the use of an intradermal route for either pre-exposure and post- exposure prophylaxis, but vaccine administration via this route requires expertise of the healthcare provider. The intradermal immunisation is reliable only if the whole of the dose is given properly into the dermis and is given only by those experienced in the intradermal technique. The vaccine used needs to be one of the WHO-approved vaccines.	

(Cont'd.) Table 19. Rabies Vaccine for Adults

Storage and handling	Keep refrigerated (between 2°C and 8°C).
Common adverse events	Pain at injection site Fever, rash, and flu-like symptoms
Contraindications	Anaphylaxis to any vaccine component (including egg, egg products, chick proteins, chlortetracycline, amphotericin B or neomycin) or a previous dose
Precautions	Administration should be postponed in individuals with acute severe illness.
Pregnancy and breastfeeding	There is limited data on the safety of rabies vaccine in pregnant and breastfeeding women. Vaccinate with caution if benefits clearly outweigh risks.[5,6] Category C
Medisave	No

Strong recommendation; moderate quality of evidence.

Pre-vaccination testing is not recommended in previously unvaccinated individuals. In previously vaccinated individuals where risk is ongoing, serological testing for neutralising antibodies, using rapid fluorescent focus inhibition test (RFFIT), may be performed every 2 years.[3] Booster may be given if antibody titres fall below 0.5 IU/mL.

Strong recommendation; moderate quality of evidence.

Post-exposure management

Post-exposure management consists of wound treatment and risk assessment for appropriate post-exposure treatment. Treatment and immunisation after a possible rabies exposure will depend on the circumstances of exposure, including the nature of exposure, the species involved, the country/area and the immune status of the exposed person.

Wound treatment

Treatment of wounds with rabies risk includes immediate cleansing with soap and thorough flushing under running water for several minutes. A suitable disinfectant should be applied and the wound covered with a simple dressing. Wounds should not be sutured.

Risk assessment

The assessment for the risk of rabies considers the endemicity of rabies in the country, the animal source, the category and site of exposure and the immune status of the individual. While Singapore is considered rabies-free, rabies is still endemic in most of its neighbours in Southeast Asia.[1] Hence, vigilance and rapid referral are still paramount in the management of animal bites.

Bite from a mammal known to be a rabies reservoir or vector species increases the risk of the bite.[7] This includes dogs, cats, bats, ferrets, raccoons, skunks, and foxes. Importantly, persons who were in the same room as a bat and who might be unaware that a bite or direct contact had occurred (e.g., during sleeping) may present as high risk. There are also increasing reports of macaque bites that could potentially be high risk. A literature review found 159 reports of rabies from non-human primate exposures in South America, Africa, and Asia, including Southeast Asia.[8]

Aside from country and animal source, the practitioner should also consider the wound category, the site of exposure and the patient's immune status. **Table 18** summarises the recommendations by bite category and immune status. Injuries to the face and neck should be assessed and treated with greater urgency.

Table 20. Treatment of Animal Bite by Category According to Rabies Vaccines and Immunoglobulins: WHO Position April 2018[4]

The WHO rabies exposure categories are:
Category I: Touching or feeding animals, animal licks on intact skin (no exposure)
Category II: Nibbling of uncovered skin, minor scratches or abrasions without bleeding (exposure)
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)

	Category I exposure	Category II exposure	Category III exposure
Immunologically naïve individuals of all age groups	Wash exposed skin surface. No PEP required.	Wound washing and immediate vaccination: • Rabies vaccine IM on days 0, 3, 7 and between days 14 and 18 • A fifth dose given on day 28 is recommended for immunocompromised individuals • RIG not indicated	Wound washing and immediate vaccination: • Rabies vaccine IM on days 0, 3, 7 and between days 14 and 18 • A fifth dose given on day 28 is recommended for immunocompromised individuals • RIG is recommended
Previously immunised individuals of all age groups	Wash exposed skin surface. No PEP required.	Wound washing and immediate vaccination: • Rabies vaccine IM on days 0 and 3 • RIG not indicated	Wound washing and immediate vaccination: • Rabies vaccine IM on days 0 and 3 • RIG not indicated

Strong recommendation; moderate quality of evidence.

Table 21. Rabies Immunoglobulin

Vaccine type and description	Sterile, 300 IU/mL solution for injection supplied in 1 mL and 5 mL single-dose vials
Summary of evidence	Clinical studies using rabies immunoglobulin in conjunction with rabies vaccine of duck-embryo origin found that a dose of 20 IU/kg resulted in amply detectable levels of passive rabies antibody 24 hours after injection in all recipients.[9,10]
Indication/Target population	Post-exposure prophylaxis, along with rabies vaccine, for all persons suspected of exposure to rabies
Schedule	20 IU/kg bodyweight as a single dose
Administration	• Administer as soon as possible after exposure, preferably at the time of the first vaccine dose. • Infiltrate the full dose thoroughly in the area around and into the wound(s), if anatomically feasible. • Inject the remainder, if any, intramuscularly at an anatomical site distant from the site of vaccine administration. • Do not exceed the recommended dose to avoid suppression of active production of rabies antibodies from vaccination.
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze.
Common adverse events	Injection site pain, headache, injection site nodule, abdominal pain, diarrhoea, flatulence, nasal congestion and oropharyngeal pain
Contraindications	None
Precautions	• Severe hypersensitivity reactions may occur. Patients with a history of prior systemic allergic reactions to human immunoglobulin preparations are at a greater risk of developing severe hypersensitivity and anaphylactic reactions. Have epinephrine available for treatment of acute allergic symptoms, should they occur. • Patients with isolated immunoglobulin A (IgA) deficiency may develop severe hypersensitivity reactions to rabies immunoglobulin, or subsequently, to the administration of blood products that contain IgA. • Rabies immunoglobulin is made from human blood, and the risk of transmitting infectious agents (e.g., viruses, the variant Creutzfeldt–Jakob Disease agent and, theoretically, the Creutzfeldt–Jakob Disease agent) cannot be completely eliminated.

(Cont'd.) Table 21. Rabies Immunoglobulin

Pregnancy and breastfeeding	• There are no data on use in pregnant women to inform a drug-associated risk. It also is not known whether rabies immunoglobulin can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity. The immunoglobulin should be given to a pregnant woman only if clearly needed. • There is no information regarding the presence of rabies immunoglobulin in human milk, the effect on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for rabies immunoglobulin and any potential adverse effects on the breastfed infant.
Medisave	No

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TETANUS, DIPHTHERIA AND PERTUSSIS VACCINES

In adults, vaccination against tetanus, diphtheria and pertussis may be done using the tetanus toxoid–reduced diphtheria toxoid–acellular pertussis (Tdap) vaccine.[1] This is a combination vaccine that protects against tetanus, diphtheria and pertussis.

Tetanus is a muscular spastic disease caused by the toxin of *Clostridium tetani*, a saprophytic obligate anaerobe. It is usually introduced to the body through contamination of wounds, where it thrives in areas of low oxygen tension.[2]

Diphtheria is caused by *Corynebacterium diphtheriae*. The bacteria produce a toxin that causes an obstructive pseudo-membrane in the upper respiratory tract, or myocardial damage.[2] Untreated diphtheria may be severe and fatal. It is transmitted through respiratory droplets or close person-to-person contact. Although diphtheria is rare in Singapore, an isolated case was reported in 2017 and believed to be locally acquired, with a fatal outcome.[3]

Pertussis, or whooping cough, is caused by *Bordetella pertussis*. It presents as progressive cough developing into severe coughing fits that terminate in a characteristic whooping cough, as well as cyanosis and vomiting.[1,2,4] Disease is most severe among infants, but adults may also develop the disease.[4]

Incidence

Surveillance indicated one reported case of tetanus in Singapore in 2018. There were no reports of diphtheria in Singapore in 2018 but two cases were reported in 2017. There were a total of 108 reported cases of pertussis in 2018, with a steep decrease in incidence over the last five years, with only two cases reported in 2022 (median number of cases from 2017 to 2021 were 62).[5]

Of note, during the majority of the COVID-19 pandemic years 2020–2022, there was widespread use of masks and some degree of travel restrictions, which likely contributed to the decline in incidence of infections transmitted via droplet route, such as pertussis. The incidence will need to continue to be tracked as the restrictions ease.

Vaccination

Vaccination against tetanus, diphtheria and pertussis, using the DTaP vaccine, is part of the National Childhood Immunisation Programme.[6] Since 2008, childhood coverage rates have been at least 95%. Among adults, a recent study in Singapore found that 92.0% of the general population, including citizens and permanent residents, had basic antibody protection against diphtheria (antibody levels of at least 0.01 IU/mL), and 71.4% had at least short-term protection against tetanus (antibody levels greater than 0.1 IU/mL).[7] However, seroprotection prevalence declined significantly with age. Those at risk for diphtheria were those aged 50 and above, and those aged 60 and above were at risk for tetanus.

Among adults, vaccination against these three diseases is recommended for multiple subgroups (see **Table 22**). Adult vaccination using Tdap boosts waning immunity to tetanus and diphtheria vaccines and reduces carriage of pertussis among adults. The National Adult Immunisation Schedule recommends a dose of Tdap for each pregnancy.[8]

A vaccine containing tetanus and diphtheria toxoid only (Td) is available and may be given as an alternative.

Table 22. Tetanus–Diphtheria–Pertussis Vaccines for Adults

	Tetanus–diphtheria–acellular pertussis (Tdap) vaccine	Tetanus–diphtheria (Td) vaccine
Description	Each dose contains at least 2 IU of diphtheria toxoid, at least 20 IU of tetanus toxoid, 8 mcg of pertussis toxoid, 8 mcg of filamentous haemagglutinin and 2.5 mcg of pertactin.	Each dose contains 2 IU of diphtheria toxoid and 20 IU of tetanus toxoid.
Summary of evidence	Randomised controlled trials showed that the vaccine was protective against tetanus and diphtheria in more than 98% of adult recipients, and immunogenic in 77% to 97% of adults, against pertussis antigens, depending on the antibody produced.[9]	
Indication/Target population	Booster vaccination to reduce morbidity of tetanus, diphtheria and pertussis. Tdap vaccination is recommended in the following groups[1,2,10]: • Adults with no previous history of immunisation or if their last vaccination was at least 10 years ago.[11] The National Adult Immunisation Schedule currently does not recommend Tdap, except in pregnant women, due to lack of local data on cost-effectiveness in adults and elderly.[8,12] There are cost-effectiveness data for the use of Tdap in elderly in other populations.[13] • Adults in close contact with an infant aged less than 12 months.[14]	Booster vaccination to reduce morbidity of tetanus and diphtheria. Td vaccination is recommended in the following groups[4]: • Adults, including the elderly, if their last vaccination was at least 10 years ago. • For pregnant women who are unvaccinated against tetanus, Tdap should be used in place of one of the 3 Td injections.

(Cont'd.) Table 22. Tetanus–Diphtheria–Pertussis Vaccines for Adults

	Tetanus–diphtheria–acellular pertussis (Tdap) vaccine	Tetanus–diphtheria (Td) vaccine
Indication/Target population	• Pregnant women during each pregnancy, administered from 16 through 32 weeks' gestation, regardless of previous receipt of Tdap. Tdap may be administered beyond 32 weeks, and at this time, maternal vaccination may afford less protection for infants but would potentially protect the mother from pertussis infection and thereby reduce the risk of exposure for her infant.[15] • If the single dose Tdap was not administered during pregnancy, it should be administered immediately post-partum. • Healthcare personnel with direct patient contact are recommended to receive Tdap if they have not previously received it.	
Schedule	Single dose, with tetanus booster every 10 years.	One dose on days 0, 7, and 21 or 28. For pregnant women who are unvaccinated against tetanus, Tdap should be used in place of one of the three Td injections.
Administration	Intramuscular injection, preferably at the deltoid area	
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze.	
Common adverse events	Pain, redness, swelling, mass or sterile abscess at the injection site Headache, malaise, dizziness, nausea and gastrointestinal disorders	

(Cont'd.) Table 22. Tetanus–Diphtheria–Pertussis Vaccines for Adults

	Tetanus–diphtheria–acellular pertussis (Tdap) vaccine	Tetanus–diphtheria (Td) vaccine
Contraindications	• Anaphylaxis to any vaccine component or a previous dose • Encephalopathy of unknown aetiology occurring within 7 days following a previous pertussis-containing vaccination • Transient thrombocytopenia or neurological complications following an earlier vaccination against diphtheria and/or tetanus	
Precautions	• Administration should be postponed in individuals with acute severe illness.	
Pregnancy and breastfeeding	Recommended as per above indication Category C Breastfeeding is not a contraindication.[10]	
Medisave	Up to S$500 per year per account for pregnant women at 16 weeks age of gestation and beyond	No

Strong recommendation; moderate quality of evidence.

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TETANUS POST-EXPOSURE PROPHYLAXIS

The risk of developing tetanus after an injury depends on the characteristics of the wound and the vaccination status of the individual. In general, wounds that are likely to be contaminated with *Clostridium tetani* (tetanus-prone wounds) include wounds contaminated with dirt, faeces, soil, and saliva, puncture wounds, avulsions, and wounds resulting from missiles, crushing, burns and frostbite.[1] **Table 23** describes the recommendations for tetanus post-exposure prophylaxis in adults. Adults who have never been vaccinated against tetanus, diphtheria, or pertussis (no dose of paediatric DTP/DTaP/DT or Td) should receive a series of three vaccinations containing tetanus and diphtheria toxoids, including the dose given at time of tetanus prophylaxis for a wound.[2] The schedule appears in **Table 24**.

Table 23. Tetanus Post-Exposure Prophylaxis Recommendations in Adults[1]

No. of doses of absorbed tetanus-toxoid-containing vaccines	Clean and minor wound		All other wounds*	
	Tdap or Td†	TIG	Tdap or Td†	TIG§
Unknown or <3	Yes	No	Yes	Yes
≥3	No¶	No	No**	No

Td, tetanus and diphtheria toxoids; Tdap, tetanus toxoid, reduced diphtheria toxoid and acellular pertussis; TIG, tetanus immune globulin.

Adapted from Table 6 in Liang et al., 2018.

**Such as, but not limited to, wounds contaminated with dirt, faeces, soil and saliva; puncture wounds; avulsions; and wounds resulting from missiles, crushing, burns and frostbite.*

†Tdap is preferred to Td for persons aged ≥11 years who have not previously received Tdap. Persons aged ≥7 years who are not fully immunised against pertussis, tetanus or diphtheria should receive one dose of Tdap for wound management and as part of the catch-up series.

§TIG may be considered for severely immunocompromised persons (e.g., HIV/AIDS not on treatment) with contaminated wounds, regardless of tetanus immunisation status.[3,4]

¶Yes if >10 years since the last tetanus toxoid–containing vaccine dose.

***Yes if ≥5 years since the last tetanus toxoid–containing vaccine dose.*

Table 24. Tetanus Post-Exposure Prophylaxis Vaccine Descriptions

Vaccine type	Tetanus toxoid-containing vaccine	Tetanus immunoglobulin
Description	Each 0.5 mL of single dose contains at least 40 IU of tetanus toxoid adsorbed on hydrated aluminium hydroxide 0.6 mg.	Each dose contains 250 IU of human tetanus immunoglobulin.

(Cont'd.) Table 24. Tetanus Post-Exposure Prophylaxis Vaccine Descriptions

Vaccine type	Tetanus toxoid-containing vaccine	Tetanus immunoglobulin
Summary of evidence	After three properly spaced doses, recipients achieve antitoxin levels considerably greater than the protective level of 0.1 IU/mL.[5] After 10 years from the last dose, most persons have antitoxin levels that only approach the minimal protective level.	
Indication/ Target population	Prophylaxis of tetanus	• Prophylaxis of tetanus • Treatment of clinically manifest tetanus (dose: 3,000–6,000 IU)
Schedule	Two doses given 1 or 2 months apart, followed by a booster dose 6 to 12 months after the second injection. Boosters may then be given every 10 years thereafter.[2]	Single dose. Double the dose for dirty deep wounds with tissue destruction, infected wounds, if the injury occurred 24 hours before administration, or for adults with above-average body weight.
Administration	Intramuscular injection, preferably at the deltoid area. Deep subcutaneous injection may also be used. Do not administer intravascularly or intradermally.	Intramuscular injection at a separate site and a different syringe
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze.	
Common adverse events	• Pain, erythema, induration and oedema at the injection site • Transient fever, pruritus, generalised urticaria or oedema, dizziness, hypotension, myalgia, arthralgia and headache	• Local pain and tenderness at the injection site • Fever, cutaneous reactions and chills

(Cont'd.) Table 24. Tetanus Post-Exposure Prophylaxis Vaccine Descriptions

Vaccine type	Tetanus toxoid-containing vaccine	Tetanus immunoglobulin
Contraindications	Anaphylaxis to any vaccine component or a previous dose	Anaphylaxis to any vaccine component or a previous dose
Precautions	Administration should be postponed in individuals with acute severe illness.	Patients with IgA deficiency due to antibodies against IgA may develop an anaphylactic reaction to tetanus immunoglobulin and should be used only when extremely necessary.
Pregnancy and breastfeeding	Tdap is recommended in pregnancy to prevent pertussis in infant.[4] Use Tdap instead of tetanus toxoid if pregnant woman needs it for tetanus wound prophylaxis (also see section on Tdap vaccine for details).	Tetanus immunoglobin has not been studied specifically in pregnant women in clinical trials.[6] Clinician to discuss risk/benefit.

Strong recommendation; strong quality of evidence.

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TYPHOID VACCINE

Typhoid fever is caused by the typhoid bacilli, *Salmonella typhi* and *Salmonella paratyphi*.[1,2] It is a systemic infection that presents initially with fever, headache, malaise, anorexia, and insomnia. Gastrointestinal symptoms are common, with constipation being more common than diarrhoea in adults. Severe disease may lead to ileitis, hepatosplenomegaly, pneumonia, and encephalitis that could be fatal in up to 20% of cases.[1]

Epidemiology

Typhoid is transmitted by consumption of contaminated water or food such as shellfish, fruits and vegetables, milk and milk products.[1,2] Faecal–oral transmission may also occur. In Singapore, 73 and 30 cases of typhoid fever were reported in 2019 and 2020, respectively.[3]

Vaccine description

Vaccination for typhoid fever may be advised for travellers where endemicity is high and standards of hygiene are low.[1,2] Vaccination confers only 72% protection in the first year and only protects against typhoid fever from *S. typhi*, but not *S. paratyphi*. Hence, adequate food and water hygiene is still required.

The available typhoid vaccines in Singapore include the injectable polysaccharide vaccine **(Table 25)**. The live oral vaccine, Vivotif (Ty21a), is no longer available in Singapore.

Table 25. Typhoid Vaccine for Adults in Singapore

Vaccine type	Polysaccharide vaccine
Description	• The typhoid-only vaccine contains 25 mcg of purified Vi capsular polysaccharides of *S. typhi* (Ty2 strain). • The combination vaccine contains 25 mcg of purified Vi capsular polysaccharides of *S. typhi* (Ty2 strain) and 160 antigen units of hepatitis A virus GBM strain (inactivated)
Summary of evidence	Vaccination confers protective efficacy of 55% (95% CI, 30%–70%) against typhoid fever.[4]
Indication/Target population	Prevention of typhoid fever, especially for: • Travellers to areas of high endemicity and poor hygiene standards • Persons with intimate exposure to a documented *Salmonella* serotype *Typhi* chronic carrier (defined as excretion of *Salmonella* serotype *Typhi* in urine or stool for >1 year).
Schedule	Single dose. Booster may be given every 3 years if risk persists.

(Cont'd.) Table 25. Typhoid Vaccine for Adults in Singapore

Vaccine type	Polysaccharide vaccine
Administration	• Intramuscular or subcutaneous injection. Do not inject intravascularly. • For the combined typhoid and hepatitis A vaccine, only slow intramuscular injection into the deltoid is recommended.
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze. Protect from light.
Common adverse events	• Redness, pain and swelling at the injection site • Fever, headache, body aches, malaise, nausea and itching
Contraindications	Anaphylaxis to any vaccine component or a previous dose
Precautions	• Administration should be postponed in individuals with acute severe illness. • Vaccination does not replace food and water hygiene practices.

**The live vaccine (Vivotif) is no longer available in Singapore.*

References:

1. Typhoid and paratyphoid fever. In: Ong A, Goh KT, eds. A Guide on Infectious Diseases of Public Health Importance In Singapore. 7th ed. Singapore: Ministry of Health; 2011.
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VARICELLA VACCINE AND POST-EXPOSURE PROPHYLAXIS

The varicella-zoster virus (VZV), a herpes virus, is the causative agent for chicken pox and zoster (a reactivation of the virus).[1,2] Varicella is highly contagious, with an attack rate of over 90% within households.[2] It is transmitted via droplets, aerosol or direct person-to-person contact, but may also be transmitted indirectly through contact with freshly contaminated items.

The presentation of varicella is fever, malaise, and an itchy, vesicular rash that starts on the scalp and face.[1] While illness may be mild in children, severity increases with age. Complications include pneumonitis, encephalitis and invasive group A streptococcal infections; complications can become fatal. Subsequent reactivation later in life leads to zoster (shingles), which is more common among immunocompromised and elderly individuals.

Infection in early pregnancy until the 20th week of gestation could lead to congenital malformations in 2% of cases.[2,3]

Incidence

Varicella is endemic worldwide.[1] In Singapore, the incidence is around 500 cases per 100,000 population.[2] Seroprevalence of varicella antibodies among adult Singaporeans is at around 88%.[4]

Vaccine description

The vaccination for VZV is a live attenuated vaccine **(Table 26)** intended for the prevention of varicella.[3] The vaccine is also found in combination preparations with MMR.

Table 26. Varicella Vaccine for Adults

Strong recommendation; moderate quality of evidence.

Description	Each dose contains at least $10^{3.3}$ plaque-forming units of the attenuated VZV
Summary of evidence	Vaccination confers protective efficacy in 99% of adult vaccine recipients after the second dose.[3]
Indication/Target population	Prevention of varicella in all adults without evidence of immunity, especially healthcare personnel with potential exposure to VZV
Schedule	Two doses spaced 4 weeks apart. No booster is recommended.
Administration	Subcutaneous injection
Storage and handling	Keep refrigerated (between 2°C and 8°C). Protect from light.
Common adverse events	• Redness, pain and swelling at the injection site • Fever, headache, body aches, malaise, nausea and itching

(Cont'd.) Table 26. Varicella Vaccine for Adults

Contraindications	• Pregnancy • Anaphylaxis to any vaccine component or a previous dose, including neomycin • Immunocompromised state, except HIV-infected patients with CD4 count >200 cells/mm^3 and primary immune deficiency disorder without defective T-cell–mediated immunity
Precautions	• Administration should be postponed in individuals with acute severe illness. • There is a small risk of transmitting the vaccine virus from vaccine recipients to susceptible individuals. • In the case of immunosuppressive therapy, the 2-dose vaccine schedule separated by a 4-week interval should be completed 4 weeks before treatment.[5]
Pregnancy and breastfeeding	• Pregnant women should not receive the vaccine. Pregnancy should be avoided until 3 months after vaccination. • Caution should be exercised when administering to breastfeeding mothers, as VZV may be secreted in breast milk.
Medisave	No

Pre-vaccination serological testing is not routinely recommended, but may be recommended when vaccinating healthcare personnel *(weak recommendation; low quality of evidence)*.

Post-exposure prophylaxis using a single dose of varicella vaccine may prevent or modify the course of illness if for some reason varicella immunoglobulin is not used. It may be recommended to unvaccinated individuals with exposure to varicella who have no contraindications to receive the vaccine, and should be given within the first 5 days (preferably within the first 3 days) from exposure. Although post-exposure prophylaxis after 5 days of exposure is not recommended,[3] exposure to chickenpox is not a contraindication to vaccination and the vaccination should be offered to anyone who has no evidence of immunity.

People without evidence of immunity who have contraindications to vaccination and who are at risk for severe varicella and complications are recommended to receive post-exposure prophylaxis with varicella zoster immunoglobulin.[6,7] People who should receive varicella zoster immunoglobulin after exposure include immunocompromised people, pregnant women without evidence of immunity, and some neonates and infants. If there is uncertainty regarding immunity in a person who has been potentially exposed, pregnant or immunocompromised (in whom the varicella vaccine is contraindicated), the rapid varicella serology testing may be employed, if applicable. Varicella zoster immunoglobulin provides maximum benefit when administered as soon as possible after exposure but may also be effective if administered as late as 10 days after exposure.

If varicella zoster immunoglobulin is not available, intravenous immune globulin (IVIG) can be considered (also within 10 days of exposure).

In the absence of both varicella zoster immunoglobulin and IVIG, some experts recommend prophylaxis with acyclovir (80 mg/kg/day in 4 divided doses for 7 days; maximum dose, 800 mg, 4 times per day), beginning 7–10 days after exposure for people without evidence of immunity and with contraindications for varicella vaccination. Published data on the benefit of acyclovir as post-exposure prophylaxis among immunocompromised people are limited.

The zoster vaccine has no role in post-exposure prophylaxis.[3] *(Weak recommendation; low quality of evidence.)*

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YELLOW FEVER VACCINE

Yellow fever (YF) is caused by the yellow fever virus (genus *Flavivirus*).[1] Endemic in sub-Saharan Africa and in north to central South America, infection is usually asymptomatic but can lead to an acute biphasic illness. The first phase is characterised by fever, muscle pain, headache, chills, anorexia, nausea, vomiting and bradycardia. Approximately 15% of patients progress to the second phase (within days) characterised by re-emergence of fever and development of jaundice, abdominal pain, vomiting and haemorrhagic manifestations.[1] Fatality rate is 50% and death occurs within 10 to 14 days of the onset of illness.[1]

Epidemiology

YF is a mosquito-borne infection. In urban areas, transmission is from human to human via mosquito *(Aedes aegypti)* vector.[1] In rural areas, monkeys are reservoirs of infection.

There have been recent YF outbreaks in Brazil, Angola, the Democratic Republic of Congo and Uganda in 2016-2017.[2,3] Of significance, 11 Chinese workers infected during the 2016 yellow fever Angola outbreak imported YF into China.[4] There have been no reported cases of YF in Singapore in recent years.[5] Thus, the risk of transmission exists only for travellers to the aforementioned areas where YF is endemic. These travellers should receive YF vaccination **(Table 27)**, a live attenuated vaccine, at least 10 days prior to departure.[1]

YF vaccination requirements are regulated by the International Health Regulations.

Table 27. Yellow Fever Vaccine for Adults

Description	Each dose contains at least 1,500 LD_{50} units of live attenuated yellow fever virus.
Summary of evidence	Vaccination has an efficacy approaching 100%.
Indication/Target population	Prevention of yellow fever, particularly for travellers to endemic areas.
Schedule	Single dose. Booster doses are not routinely recommended. Boosters are recommended for certain populations who might not have had a robust or sustained durable immune response to yellow fever vaccine compared with other recipients. These include HSCT recipients and HIV-infected persons. Fractional-dose yellow fever vaccine used in recent outbreak control circumstances is not recommended for routine use.
Administration	Subcutaneous injection (deltoid). Do not inject intravascularly.

(Cont'd.) Table 27. Yellow Fever Vaccine for Adults

Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze. Protect from light.
Common adverse events	• Redness, pain and swelling at the injection site • Fever, headache, body aches, malaise, nausea and itching
Contraindications	• Anaphylaxis to any vaccine component, including eggs, or a previous dose • Thymoma or history of thymectomy or other thymus dysfunction • Immunodeficiency
Precautions	• Administration should be postponed in individuals with acute severe illness. • Vaccination does not replace protective measures against mosquito bites, which may transmit other diseases. • Very rarely, yellow fever vaccine-associated neurotropic disease (YEL-AND) may occur and can have fatal outcomes in some cases.* YEL-AND is characterised by high fever with headache that may progress to confusion, encephalitis or encephalopathy, meningitis, focal neurological deficits or Guillain–Barré syndrome. Adults older than 60 years are at higher risk. • Very rarely, yellow fever vaccine-associated viscerotropic disease (YEL-AVD) may occur.* YEL-AVD resembles fulminant infection by wild-type yellow fever virus, presenting fever, fatigue, myalgia, headache and hypotension, progressing to metabolic acidosis, muscle and liver cytolysis, lymphocytopenia and thrombocytopenia, or renal and respiratory failure. Mortality rate is at 60%. Those at higher risk include adults older than 60 years of age and those with thymus dysfunction.
Pregnancy and breastfeeding	Vaccination of pregnant or breastfeeding women should be avoided, unless travel to high-risk areas is unavoidable. Category D
Medisave	No

**For a 2-week stay, the estimated risks for illness and for death due to YF for an unvaccinated traveller visiting an endemic area can go as high as 50 and 10 per 100,000, respectively, in West Africa and 5 per 100,000 and 1 per 100,000, respectively, in South America. The incidences of YEL-AND and YEL-AVD in the USA are 0.8 and 0.3 per 100,000 doses administered, but may be higher (2.2 per 100,000 and 1.2 per 100,000 doses, respectively) in people aged ≥60 years.*

Strong recommendation; moderate quality of evidence.

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ZOSTER VACCINE

Reactivation of the varicella-zoster virus (VZV) results in zoster.[1,2] The risk of shingles and post-herpetic neuralgia increases with age. This reactivation is more common among immunocompromised and elderly individuals. Patients with zoster can transmit VZV to susceptible individuals.

There is no upper age limit for vaccination. There is no specific length of time one must wait after having shingles before receiving the shingles vaccine, but generally, one should make sure the shingles rash has disappeared before getting a vaccination.

Zoster is vaccine preventable via a recombinant, adjuvanted vaccine **(Table 28)**. Zostavax, the live attenuated vaccine, is no longer available in Singapore. Two doses of Shingrix is recommended in those who previously received Zostavax. The first dose of Shingrix may be given at least 8 weeks after Zostavax.

Table 28. Zoster Vaccine for Adults

Description	Each dose contains lyophilised VZV glycoprotein E antigen component, to be reconstituted with the accompanying vial of AS01B adjuvant suspension component.[3]
Summary of evidence	A randomised, placebo-controlled study that included older adults (≥50 years of age) found that the vaccine had an overall vaccine efficacy of 97.2% (95% CI, 93.7–99.0; p<0.001) against zoster.[4] There is evidence on efficacy in immunocompromised hosts. • A total of 80.4% (95% CI, 73.1–86.5) of patients with haematological malignancies had a persistent (until month 13) immunogenic response 2 months post vaccination versus 0.8% (0.0–4.2) with placebo.[5] • The zoster vaccine elicited sustained anti-glycoprotein-specific humoral and cell-mediated responses in renal transplant recipients (80.2% [95% CI, 71.9%–86.9%]) compared to near baseline levels with placebo.[6]
Indication/Target population	• Prevention of zoster in adults aged 50 years and older • Prevention of zoster and related complications in adults 19 years of age or older at increased risk of herpes zoster due to immunodeficiency or immunosuppression caused by known disease or therapy[7]
Schedule	Administer 2 doses (0.5 mL each) at 0 and 2–6 months. For persons who are or will be immunodeficient or immunosuppressed, the second dose can be administered 1–2 months after the first dose. There is currently no recommendation for booster. There is some evidence that clinical benefit of the recombinant zoster vaccine in adults aged ≥50 years is sustained up to 10 years after vaccination.[8,9]

(Cont'd.) Table 28. Zoster Vaccine for Adults

Administration	Intramuscular injection
Storage and handling	Keep vaccine and adjuvant refrigerated (2°C to 8°C). Do not freeze. Protect from light. Discard if the vaccine or adjuvant suspension has been frozen.
Common adverse events	• Injection site pain, redness and swelling. In a randomised, placebo-controlled study in older adults (≥50 years of age), 81.5% reported injection site reactions with the vaccine versus 11.9% with placebo.[4] • Myalgia, fatigue, headache, shivering, fever and gastrointestinal symptoms. In a randomised, placebo-controlled study in older adults (≥50 years of age), systemic reactions occurred in 66.1% of vaccine recipients versus 29.5% in the placebo group.[4] • Similar safety outcomes were noted in adults ≥70 years of age who experienced more frequent injection-site and systemic reactions with the vaccine (79.0%) versus placebo (29.5%).[10]
Contraindications	Anaphylaxis to any component of the vaccine or a previous dose
Precautions	Review the immunisation history for possible vaccine sensitivity and previous vaccination-related adverse reactions prior to administration. Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions.
Pregnancy and breastfeeding	There are no available human data to establish whether there is vaccine-associated risk in pregnant women. It is not known whether the vaccine is excreted in human milk.

Strong recommendation; moderate quality of evidence.

The zoster vaccine has no role in post-exposure prophylaxis.[11]
The zoster vaccine is not indicated for prevention of primary varicella infection.[3]

Weak recommendation; moderate quality of evidence.

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1. World Health Organization. Vaccine-preventable diseases and vaccines. In: World Health Organization. International Travel and Health. Geneva: World Health Organization; 2012.
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VACCINES IN DEVELOPMENT

Vaccines have traditionally been used to prevent infectious diseases by activating the immune system and combating disease. To date, new vaccines are being developed to help the body deter infectious diseases as well as cancer, neurological disorders, allergies and other conditions.

Table 29 includes the vaccines for infectious diseases in late-stage development, based on the World Health Organization Vaccine Pipeline Tracker.[1]

Table 29. Vaccines for Infectious Diseases in Late-Stage Development[1]

Pathogen	Candidate vaccine	Immunogen platform	Sponsor
DENV 1-4	TDV	Recombinant viral vector	Takeda
DENV 1-4	TV003/TV005	Recombinant viral vector	Butantan
Ebola virus	Ad26-ZEBOV and MVA-BN-Filo	Recombinant viral vector	Janssen Vaccines & Prevention B.V.
Mycobacterium tuberculosis	Vaccae	Other: inactivated non-tuberculous mycobacterium	AnHui Zhifei Longcom Biologic Pharmacy
Mycobacterium tuberculosis	VPM 1002 (rBCG)	Other: recombinant BCG	Serum Institute
Neisseria meningitidis	PCV13 (Prevnar 13)/ Meningococcal vaccine GSK134612	Subunit conjugate	GlaxoSmithKline
Neisseria meningitidis/ Streptococcus pneumoniae	PCV7 (Prevnar 7)/ MenC-TT	Subunit conjugate	Pfizer
Plasmodium falciparum	RTS,S/AS01	Recombinant subunit (non-VLP)	GSK
Rotavirus	BRV-TV	Live attenuated tetravalent bovine-human reassortant	Shantha Biotechnics Limited
Rotavirus	Rotasiil (liquid and lyophilised)	Bovine pentavalent	Serum Institute of India Pvt. Ltd.
Rotavirus	Trivalent Genetic Reassortment Vaccine	Live reassortant	Lanzhou Institute of Biological Products, China

(Cont'd.) Table 29. Vaccines for Infectious Diseases in Late-Stage Development[1]

Pathogen	Candidate vaccine	Immunogen platform	Sponsor
Respiratory syncytial virus	RSV F Nanoparticle	Recombinant subunit (non-VLP)	Novavax
Streptococcus pneumoniae	PCV7 (VCN7-T)	Subunit conjugate	Biomolecular Chemistry Center (CQB)
Streptococcus pneumoniae	PCV 7 (PncCRM and PncOMPC)	Subunit conjugate	National Institute for Health and Welfare, Finland
Streptococcus pneumoniae	PCV10 (Synflorix)/ Meningococcal vaccine GSK134612	Subunit conjugate	GlaxoSmithKline
Streptococcus pneumoniae	PCV11	Subunit conjugate	GlaxoSmithKline
Streptococcus pneumoniae	PCV13 (GBP411)	Subunit conjugate	SK Chemicals Co., Ltd.
Streptococcus pneumoniae	PCV13 (NBP606)	Subunit conjugate	SK Chemicals Co., Ltd.
Streptococcus pneumoniae	PCV15 (V114) + PPV-23 (Pneumovax 23)/ PCV13 (Prevnar 13)	Subunit conjugate	Merck Sharp & Dohme Corp.
Streptococcus pneumoniae	PCV7 (Prevnar7)/ DTaP-IPV-HBV/Hib combination vaccine/ Infanrix hexa	Subunit conjugate	Heinrich-Heine University, Duesseldorf
Streptococcus pneumoniae	PPV-23 (Pneumovax 23)/ ZOSTAVAX	Live attenuated tetravalent bovine-human reassortant	Merck Sharp & Dohme Corp.
Streptococcus pneumoniae	PCV13 (Prevnar 13)/ TIV	Subunit conjugate	Pfizer
Shigella spp.	*S. sonnei* O-SP-rEPA and *S. flexneri* 2a O-SP-rEPA	Subunit conjugate	NICHD

Reference:

1. World Health Organization Vaccine Pipeline Tracker. Available at: https://www.who.int/teams/regulation-prequalification/eul/eul-vaccines/tracking-the-new-vaccine-pipeline. Accessed 15 February 2022.

COVID-19 VACCINES

Coronavirus disease (COVID-19) is caused by a novel coronavirus SARS-CoV-2, which emerged in 2019 and is transmitted by the respiratory route, specifically droplet route with possibility of aerosol transmission. Infected cases may present mild to moderate respiratory illness that resolves without treatment.[1] However, certain pre-disposing factors such as advanced age, cardiovascular disease, diabetes, chronic respiratory disease, and cancer may present increased risk of severe illness and mortality.[1] Such high-risk patient groups must be prioritized for COVID-19 vaccination. The landscape of COVID-19 disease management and regulations is fast-evolving, and the epidemiological data presented in this chapter is up-to-date to September 2022.

Transmission

Viral transmission occurs through aerosols or respiratory droplets generated by infected persons during coughing, sneezing, breathing, singing, or speaking. Infection may also spread through contact with contaminated physical surfaces. Physical distancing between individuals, along with proper respiratory etiquette, hand hygiene, and protection with well-fitted masks, is recommended to slow down the viral spread.[2]

Viral variants

Mutations in SARS-CoV-2 during the pandemic have resulted in the emergence of new viral variants. So far, the Alpha, Beta, Gamma, Delta and Omicron variants have been reported in different countries, with the latest omicron variant initially detected in South Africa in 2021, now recognised as the predominant variant in multiple countries worldwide.[3] Between 13 September to 19 September 2022, Singapore has reported a total of 15,104 cases of Omicron infection in the community.[4]

All viruses change and mutate over time, with most changes having little to no impact. The SARS-CoV-2 genome is composed of several open reading frames and structural proteins, including the spike protein, which is essential for entry into host cells. Most viral mutations have a limited impact on the viruses' ability to infect, replicate, escape host immunity, and transmit; however, certain mutations can give a viral strain a competitive advantage and, through natural selection, give it the ability to become dominant. Several mutations observed in SARS-CoV-2 variants are found within the receptor-binding domain or the N-terminal domain of the S protein, which alters the three-dimensional structure of the S protein. Multiple mutations harboured in these variants, such as the Omicron (and emerging sublineages thereof), may confer an increased transmissibility, severity of disease, and escape from neutralising antibodies compared with the primary strain.

Incidence

COVID-19 was declared a pandemic by the World Health Organization (WHO) on 11 March 2020. The incidence of COVID-19 worldwide is high, with a global estimate of 611,421,786 confirmed cases and 6,512,438 deaths as of 23 September 2022.[5] In Singapore there have been 1,884,859 confirmed cases of COVID-19, and 1,609 COVID-related deaths between 3 January 2020 to 23 September 2022.[6]

COVID-19 vaccination

The COVID-19 pandemic prompted a rapid search for safe and effective vaccines against the SARS-CoV-2. In line with previous vaccine development for other coronaviruses, the S protein was a key target for COVID-19 vaccine development. Vaccination has played an important role in controlling the COVID-19 pandemic. A total of 14,311,895 vaccine doses have been administered in Singapore as of 28 August 2022.[6] Data from 11 July to 9 September 2022 released by the Ministry of Health (MOH) in Singapore shows that mortality was significantly higher in unvaccinated individuals than in vaccinated (primary with at least one booster) persons across all age groups, and especially in older people (3.70 vs 0.28 per 100,000 population in patients aged 70 and above).[7] Similarly, the proportion of critically ill and intensive care unit intubated patients was higher in the unvaccinated patients, compared to the vaccinated (4.60 vs 1.05 per 100,000 population in patients aged 70 and above).[7] Primary vaccination, together with periodic booster doses, has been shown to confer protection against symptomatic infection and severe disease, along with reduction in hospitalisation risk.[8,9] Globally, 12,640,866,343 vaccine doses have been administered as of 19 September 2022.[5]

WHO-approved COVID-19 vaccines

The use of approved COVID-19 vaccines is recommended across all viral variants, as interim scientific evidence shows that these vaccines demonstrate efficacy against severe disease cause by circulating variants, as compared to the wild-type virus.[8,10] The WHO-approved COVID-19 vaccines are administered as intramuscular injections include messenger RNA (mRNA) vaccines, nanoparticle vaccines, whole inactivated virus vaccines or vector-based DNA vaccines. The mRNA vaccines (from Pfizer/BioNTech and Moderna) represent one of the latest vaccine technologies, where mRNA is formulated in lipid particles which enables RNA delivery into host cells expressing SARS-CoV-2 spike (S) antigen. Upon delivery into cells, these vectors make several copies of the viral spike protein to sensitise the immune system. The whole inactivated coronavirus vaccines (from Sinopharm, Sinovac, and Bharat Biotech) directly introduce the inactivated SARS-CoV-2 virus (i.e., virus incapable of replication) to activate the immune system against future infections. The vector-based DNA vaccines (from AstraZeneca/Oxford, CanSinoBIO, and Janssen) use other replication-incompetent viral vectors carrying the gene (or DNA) sequence for the spike protein to produce SARS-CoV-2 spike protein copies within cells, which then lead to immune system activation. The most recently approved nanoparticle vaccines (from Novavax and Serum Institute of India) contain full-length recombinant SARS-CoV-2 spike protein organised as nanoparticles in adjuvanted forms and elicit a spike-protein-specific immune response.

The WHO recommends mRNA vaccines (including bivalent vaccines) for booster dose combinations with other COVID-19 vaccine modalities, at a 6-month interval from a previous vaccine dose. Previously infected and recovered individuals with COVID-19 are encouraged to receive COVID-19 vaccine as early as 1 month post infection. However, a 3-month interval is optimal for resuming the vaccination schedule.

Vaccines from AstraZeneca (Vaxzevria, COVISHIELD), Janssen (Ad26.COV2.S), Moderna (Spikevax), Pfizer/BioNTech (Comirnaty), Sinopharm, Sinovac (CoronaVac), Novavax (Nuvaxovid), Serum Institute of India (Covovax), CanSinoBIO (Ad5-nCoV) and Bharat

Biotech (COVAXIN) are approved by WHO's Emergency Use Listing Procedure, having met the required safety and efficacy criteria.[11] Head-to-head comparisons for these vaccines have not been made, and it is recommended that vaccination should be performed with the vaccine most readily available.

COVID-19 vaccines approved in Singapore

The Health Sciences Authority (HSA) of Singapore has authorised the use of Pfizer/BioNTech and Moderna vaccines in Singapore, under the Pandemic Special Access Route (PSAR), for their high levels of safety and efficacy in individuals aged 12 and above. These vaccines are also recommended by the Expert Committee on COVID-19 Vaccination (EC19V). On 3 February 2022, HSA granted interim authorisation to the Novavax nanoparticle vaccine (Nuvaxovid) for ages 18 and above, under PSAR. The Sinovac inactivated whole coronavirus vaccine is recommended in cases where the mRNA or nanoparticle vaccines are contraindicated due to allergic reaction to vaccine components (such as polyethylene glycol or PEG). Details on the clinical use of these vaccines are provided in **Table 30**.

In addition to COVID-19 vaccines, HSA has given interim PSAR authorisation to AstraZeneca's anti-viral monoclonal antibody (mAb) combination of tixagevimab and cilgavimab, as pre-exposure prophylaxis in adults and for COVID-19 management in infected but immunocompromised adults.[12] Monoclonal antibodies that target the SARS-CoV-2 spike protein have shown clinical benefits in treating SARS-CoV-2 infection, but antiviral activity of mAbs can vary dramatically against specific variants and subvariants. Recent data suggest that tixagevimab/cilgavimab may have limited efficacy against certain Omicron subvariants, and efficacy of this agent will vary according to local variant proportions.[13]

Table 30. COVID-19 Vaccines Approved for Clinical Use in Singapore

	mRNA vaccines	Inactivated whole coronavirus vaccines	Nanoparticle vaccines
Description	One dose of Spikevax (Moderna vaccine) carries 100 mcg of spike protein mRNA sequence embedded in SM-102 lipid nanoparticles in 0.5 mL. One dose of Comirnaty (Pfizer/BioNTech vaccine) contains 30 mcg of spike protein mRNA per 0.3 mL.	One dose contains 0.5 mL of inactivated whole coronavirus (3 to 6 mcg) adsorbed onto aluminium hydroxide adjuvant.	One dose of Nuvaxovid (Novavax vaccine) contains 5 mcg of SARS-CoV-2 recombinant spike protein adjuvanted with 50 mcg of Matrix-M adjuvant per 0.5 mL.

The COVID-19 vaccines are covered under the National Vaccination Programme and are approved for medical reimbursement under the Vaccine Injury Financial Assistance Programme for COVID-19 Vaccination (VIFAP) to cover healthcare costs arising from adverse reactions to PSAR-approved vaccines.

(Cont'd.) Table 30. COVID-19 Vaccines Approved for Clinical Use in Singapore

	mRNA vaccines	Inactivated whole coronavirus vaccines	Nanoparticle vaccines
Summary of evidence	Large-scale phase III trials show vaccine efficacy of 94-100% across all age groups, with a 90.9% efficacy in individuals with high-risk comorbidities, when wild-type SARS-CoV-2 was circulating.[14,15] A study reported 86.7% efficacy of Spikevax against the Delta variant,[16] while Comirnaty retained 88% efficacy against the same.[17] The estimated effectiveness of mRNA booster against confirmed Omicron infections ranged from 31.7% to 41.3%; against severe COVID-19 was 87.4%, with no evidence of waning up to 6 months after boosting.[8]	CoronaVac (from Sinovac): Serum neutralising antibodies (geometric mean titres) against Omicron were up to 28.7-fold lower than wild-type and significantly lower against the Delta variant.[18] Large scale real-world studies show 51% efficacy against symptomatic COVID-19, 100% efficacy against severe disease, and 100% efficacy against COVID-19 related hospitalisation.[19]	Vaccine showed 96.4% efficacy against the original SARS-CoV-2, 86.3% efficacy against the Alpha variant and 48.6% efficacy against the Beta variant in early human trials.[20]

(Cont'd.) Table 30. COVID-19 Vaccines Approved for Clinical Use in Singapore

	mRNA vaccines	Inactivated whole coronavirus vaccines	Nanoparticle vaccines
Indication/Target population	In individuals 16 years of age and older. Can be given to groups with high-risk comorbidities and immunodeficiencies. Comirnaty is recommended for children aged 5 to 17 years. The Spikevax and Comirnaty COVID-19 vaccines are now recommended for children aged 6 months to 4 years.	In individuals 18 years of age and older. Can be given to groups with high-risk comorbidities though not tested in settings of comorbidities and immunodeficiencies.	In individuals 12 years of age and older. Can be given to groups with high-risk comorbidities and immunodeficiencies.
Dosing for healthy individuals, and for those with chronic medical conditions[21]: **a) primary series**	Two doses 21-28 days apart.	Two doses 28 days apart.	Two doses 21 days apart.
b) booster doses	mRNA vaccines are recommended as boosters across vaccine categories as follows: • 1st booster to be given to all individuals aged 12 and above at least 6 months after completion of primary series. • 2nd booster is recommended for individuals aged 12 years and above, and is strongly encouraged for persons aged 50-59, around 5 months after the 1st booster dose. The bivalent vaccine boosters (Pfizer-bivalent BioNTech/ Comirnaty, for 5 years and above; Moderna/Spikevax bivalent vaccine, Novavax/Nuvaxovid and Sinovac-CoronaVac for 18 years and above) are recommended. • Persons aged 12 years and above are recommended to receive a booster with the bivalent vaccines 1 year after their last booster dose.		

(Cont'd.) Table 30. COVID-19 Vaccines Approved for Clinical Use in Singapore

	mRNA vaccines	Inactivated whole coronavirus vaccines	Nanoparticle vaccines
Dosing for immunocompromised individuals[22]: **a) primary series (3-dose schedule)**	Two doses 21-28 days apart followed by a third dose at least 2 months after the second dose.	Two doses 28 days apart followed by a third dose at least 2 months after the second dose.	Two doses 21 days apart followed by a third dose at least 2 months after the second dose.
b) booster doses	One dose of an mRNA vaccine booster, 6 to 9 months after primary series, is recommended in immunocompromised individuals aged 60 and above, and for those who are residents of aged-care facilities. A bivalent vaccine booster at 1 year after the last booster dose is recommended.		
Dosing for ages 5 to 11[21]: **a) primary series**	Two doses of Comirnaty 21-28 days apart.	Not indicated.	
b) booster doses	One booster with Comirnaty at least 5 months after completion of primary series.		
Dosing for ages 6 months to 4 years	Two doses of Spikevax, or 3 Comirnaty COVID-19 vaccine. The recommended intervals between the doses are 8 weeks.		
Administration	Intramuscular injection		

(Cont'd.) Table 30. COVID-19 Vaccines Approved for Clinical Use in Singapore

	mRNA vaccines	Inactivated whole coronavirus vaccines	Nanoparticle vaccines
Storage and handling	For Comirnaty: • Store at -90°C to -60°C for maximum 9 months. Unopened vials may be stored and transported at -25°C to -15°C up to 2 weeks and can be returned to -90°C to -60°C. For Spikevax: • Store 2°C to 8°C, protected from light, for maximum 30 days. Up to 12 hours may be used for transportation. Vaccine should not be re-frozen after thawing. • Vials may be stored, as well as transported, in thawed condition between 2°C to 8°C. Transportation is recommended at -50°C to -15°C.	Store refrigerated at 2°C to 8°C. Do not freeze.	• Store refrigerated at 2°C to 8°C protected from light. • Vials can be stored between 2°C to 25°C for up to 6 hours after first puncture.

(Cont'd.) Table 30. COVID-19 Vaccines Approved for Clinical Use in Singapore

	mRNA vaccines	Inactivated whole coronavirus vaccines	Nanoparticle vaccines
Common adverse events	Pain or swelling at injection site, tiredness, headache, muscle pain, chills, joint pain, diarrhoea, fever, nausea and vomiting, and facial swelling (in case of Spikevax).	Nausea, diarrhoea, abdominal pain, headache, tremor, dizziness, drowsiness, cough, nasal congestion, muscle pain, chills pain, redness or swelling at injection site.	Pain, redness or swelling at injection site, tiredness, headache, muscle pain, chills, joint pain, and fever.
Contraindications	Not recommended for children below 12 years.	Not recommended in children and pregnant women. Not recommended if severe allergic reaction is observed.	Not recommended for children below 12 years. Not recommended if severe allergic reaction is observed.
Precautions	• In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended. • Medical supervision is required in case of anaphylaxis to the vaccine. • Vaccination should be postponed in cases of acute infection or severe febrile illness.	• Vaccination should be postponed in cases of acute infection or severe febrile illness. • As bleeding may follow intramuscular injection, vaccine should be given with caution in people with bleeding disorders or in those undergoing anticoagulation therapy.	• Medical supervision is required in case of anaphylaxis to the vaccine. • As bleeding may follow intramuscular injection, vaccine should be given with caution in people with bleeding disorders or in those undergoing anticoagulation therapy or pericarditis.

(Cont'd.) Table 30. COVID-19 Vaccines Approved for Clinical Use in Singapore

	mRNA vaccines	Inactivated whole coronavirus vaccines	Nanoparticle vaccines
Precautions	• As bleeding may follow intramuscular injection, vaccine should be given with caution in people with bleeding disorders or in those undergoing anticoagulation therapy. • Monitor for myocarditis or pericarditis in case of Spikevax.		• Monitor for myocarditis or pericarditis, paraesthesia, and hypoesthesia.
Pregnancy and breast feeding	Not contraindicated. Recommended when benefit outweighs potential vaccine risks (e.g., comorbidity).	Contraindicated.	Not contraindicated. Recommended when benefit outweighs potential vaccine risks (e.g., comorbidity).
Safety	• Ingestion of non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided for 1-2 days after vaccination. • Strenuous physical activity or exercise should be avoided for 2 weeks after each vaccine dose. • Persons with non-severe or non-specific skin reactions to a previous dose of mRNA vaccines are still suited to receive subsequent doses of the same mRNA vaccine.		

COVID-19 vaccines in development

Several countries are developing COVID-19 vaccines, with different approaches, to meet the preventive needs of the pandemic and to control emerging virus variants. These vaccines are currently being studied in phase II to phase III clinical trials **(Table 31)**.[23]

Table 31. COVID-19 Vaccines in Development, as of September 2022[23]

Candidate	Technology	Sponsor	Testing stage	Preliminary results	Country of development
ZyCoV-D	DNA vaccine (plasmid) to target membrane-bound entry proteins of SARS-CoV-2	Zydus Cadila	Phase III	Animal studies with both candidates revealed strong neutralising antibody response and T-cell response after vaccine administration	India
INO-4800		Inovio Pharmaceuticals; Advaccine	Phase II/III		
CVnCoV	mRNA-based vaccine coding the full-length spike protein	CureVac	Phase IIb/III	Phase IIb trials showed 53% efficacy against COVID-19 of any severity across age groups 18 to 60, 77% against moderate to severe disease, and 100% against COVID-19 related hospitalisation and death for this age group	Germany in partnership with the United Kingdom

(Cont'd.) Table 31. COVID-19 Vaccines in Development, as of September 2022[23]

Candidate	Technology	Sponsor	Testing stage	Preliminary results	Country of development
hAd5	Adenovirus-based vaccine targeting the spike protein and nucleocapsid of SARS-CoV-2	Immunity Bio; NantKwest	Phase I	Animal studies showed strong T-cell and B-cell based immunity in mice and airway protection in non-human primates after vaccine administration	United States of America
UB-612	Synthetic peptide-based vaccine	Vaxxinity	Phase II/III	Animal studies showed strong T-cell and B-cell based immunity in mice, rats and guinea pigs. Phase II trials showed robust antibody response in humans against Alpha, Beta, Delta, Gamma, and the Omicron variants with >3 times higher titres of neutralising antibodies against Omicron, compared to mRNA vaccines	United States of America in partnership with Brazil

(Cont'd.) Table 31. COVID-19 Vaccines in Development, as of September 2022[23]

Candidate	Technology	Sponsor	Testing stage	Preliminary results	Country of development
GRAd-COV2	Adenovirus-based vaccine encoding full length spike protein	ReiThera, LEUKOCARE & Univercells	Phase II/III	Animal studies showed strong immune response in mice and macaques. Preliminary phase I trial results demonstrate good safety and tolerance to the vaccine	Partnership between Italy, Germany and Belgium
Bacillus–Calmette–Guérin	Live-attenuated vaccine of the tuberculosis BCG strain to trigger overall immune response in the body (not SARS-CoV-2 specific)	Murdoch Children's Research Institute	Phase II/III	Previous studies indicate that BCG vaccination may protect against a range of viral infections. Since the safety and tolerability to BCG is well documented, Phase II/II trials are underway	Australia in partnership with the Netherlands, Spain and the United Kingdom
SCB-2019	Protein subunit vaccine	GlaxoSmith-Kline, Sanofi, Clover Biopharma-ceuticals, Dynavax and Xiamen Innovax; CEPI	Phase III	Phase II/III data has shown 67.2% vaccine efficacy against COVID-19 in a 100% variant environment and efficacy in preventing severe disease	Australia

(Cont'd.) Table 31. COVID-19 Vaccines in Development, as of September 2022[23]

Candidate	Technology	Sponsor	Testing stage	Preliminary results	Country of development
BBV154	Intranasal vaccine	Bharat Biotech	Phase II/III	Data from animal studies have shown one dose of vaccine confers protection against COVID-19 with subsequent viral clearance	India
GBP 510	Nanoparticle vaccine	SK bioscience Co., Ltd.; GSK; University of Washington; CEPI	Phase III	Phase I/II data showed encouraging immunogenic response and safety outcomes, with neutralising antibody titre up to 8 times higher than human sera from recovered COVID-19 patients	Korea

Next-generation strategies in COVID vaccine research

Pharmaceutical companies are now developing vaccines that are fine-tuned to fighting the widely prevalent Omicron variants and other such variants of concern. The FDA have now approved bivalent vaccines developed by Moderna and Pfizer-BioNTech, to be given as a single booster to individuals aged 12 and above.[24] These bivalent vaccines contain the mRNA of the original SARS-CoV-2 strain, as well as an mRNA sequence common to the BA.4 and BA.5 lineages of the Omicron variant. This results in effective protection against recent COVID-19 infections while also ensuring broad spectrum protection against COVID-19. Eligible individuals in Singapore aged 12 years and above can now receive the bivalent Pfizer-BioNTech/Comirnaty COVID-19 vaccine. The bivalent Moderna/Spikevax vaccine is available to eligible individuals aged 18 years and above. Adenovirus-based trivalent vaccines that can be administered by inhalation are now being researched.[25] The trivalent vaccine will target three SARS-CoV-2 proteins (spike protein, nucleocapsid and

RNA-dependent RNA polymerase), rather than just the spike protein, to provide a three-pronged defence against new viral variants.

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VACCINATION FOR ADULT TRAVELLERS

Travel may pose risks to travellers because of infectious diseases endemic to the destination. Aside from the destination, other considerations when advising travellers and deciding to vaccinate them include[1]:

1) season of travel, as some diseases may have seasonality patterns, such as Japanese encephalitis;
2) area of stay or lodging (e.g., urban or rural);
3) planned activities (e.g., outdoor camping or private indoor accommodations);
4) length of stay;
5) age and health condition; and
6) potential for exposure to animals, healthcare settings, or aid work.

It is also important to advise travellers about the following:

- Protective measures such as food and water hygiene, or mosquito bite-avoidance measures, to minimise infections from vaccine-preventable as well as non-vaccine-preventable diseases such as malaria.
- To refer to travel advisories regularly:
  - CDC destination advisories (https://wwwnc.cdc.gov/travel/destinations/list)
  - CDC travel notices (https://wwwnc.cdc.gov/travel/notices)
- Please refer to country-specific travel requirements during a pandemic from relevant websites:
  - ICA departure advisories (https://safetravel.ica.gov.sg/departing/overview)
  - MFA destination advisories (https://www.mfa.gov.sg/Where-Are-You-Travelling-To)
  - CDC destination advisories (https://wwwnc.cdc.gov/travel/destinations/list)

Table 32 summarises the critical vaccines recommended for travel.

Table 32. Critical Vaccines for Adult Travellers[1,2]

Vaccine	Country or region of destination
Japanese encephalitis (seasonal and dependent on duration and exposure)	China, India, Bangladesh, Nepal, Sri Lanka and Southeast Asia (Cambodia, Indonesia, Laos, Myanmar, the Philippines, Thailand and Vietnam)
Meningococcal vaccine	Benin, Burkina Faso, Cameroon, Chad, Côte d'Ivoire, Central African Republic, Eritrea, Ethiopia, Gambia, Ghana, Guinea, Guinea Bissau, Kenya, Mali, Mauritania, Niger, Nigeria, Senegal, South Sudan, Sudan, Uganda, Togo **Mandatory for travel to Mecca during Hajj or Umrah (requires a certificate)**
Yellow fever	Angola, Argentina, Benin, Bolivia, Brazil, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Colombia, Congo, Côte d'Ivoire, Democratic Republic of Congo, Ecuador, Equatorial Guinea, Ethiopia, French Guiana, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Guyana, Kenya, Liberia, Mali, Mauritania, Niger, Nigeria, Panama, Paraguay, Peru, Senegal, Sierra Leone, South Sudan, Sudan, Suriname, Togo, Trinidad & Tobago, Uganda, Venezuela

Strong recommendation; low quality of evidence.

Table 33 shows other vaccines that may be given to unvaccinated travellers that have a high risk of exposure at their destination.

Table 33. Vaccine Recommendation by Destination[1,3]

Country/Region of travel or special circumstance	Cholera	Hepatitis A	Hepatitis B	Japanese encephalitis*	Meningococcal disease*	Rabies	Typhoid	Yellow fever*	COVID-19
Africa and Middle East									
East Africa	++							+	++
Saudi Arabia (Hajj/Umrah)**		++	+		++				++
Southern Africa	++	++	+			+	++	++	++
Egypt and Nile River		++	++			+	++		++
Middle East		++	+			+	+	++	++
Northern Africa	++	++	+	+		+	++		++
Central Africa	++	++	+	+	++	+	++		++
West Africa	++							++	++
The Americas & the Caribbean									
South America		++	+			+	++	++	++
Caribbean	++	++	++			+	++		++
Mexico		++	+						++
Asia/Oceania									
China		++	++	++		++			++
India	++	++	+	++		++	++		++
Nepal		++		+		++	++		++
Papua New Guinea		++	+	+		+	++		++
Southeast Asia		++	+	+		+	++		++
Pregnant traveller* **	+		+			+			++

++ Most travellers will require vaccination.

+ These vaccines are recommended to some individuals due to increased risk, such as humanitarian work, intake of unsanitary food or water, exposure to animals, sexual intercourse with unvaccinated individuals, medical procedures, travel to rural areas, prolonged travel (a month or more), or outdoor exposure. Risk factors may vary according to the type of infection.

Use in conjunction with **Table 32.*

***Please refer also to the Saudi Arabian Ministry of Hajj website (https://www.saudiembassy.net/hajj-and-umrah-health-requirements) for the latest recommended vaccinations.*

****Delay travel unless necessary.*

Routine vaccinations

All travellers should ensure their routine vaccinations (i.e., polio, MMR, Tdap, varicella, influenza) are updated before all travel. **Many countries continue to require vaccination against COVID-19 and all travellers should check on the entry requirements.**

Strong recommendation; low quality of evidence.

Last-minute travel

Vaccines typically take 2 weeks to elicit some degree of protective response. However, some people may urgently need to travel to high-risk areas without having adequate time to update their vaccination status. These people should try to reduce their risk of infection during travel through accelerated immunisation schedules, counselling on risk avoidance, drug prophylaxis if applicable, and referrals to health services at their destinations.[4]

Strong recommendation; low quality of evidence.

For these individuals, indicated single-dose vaccines may be given to initiate some protection. These vaccines include hepatitis A vaccine, parenteral cholera vaccine, inactivated polio vaccine, and meningococcal vaccine.[4] However, other risk reduction measures should also be instituted.

Weak recommendation; low quality of evidence.

If multiple-dose vaccines are required (e.g., hepatitis B vaccine), last-minute travel may not provide enough time to complete a regimen that would provide any considerable protection. This retained risk should be made clear to the traveller, regardless of whether the first dose was given or not. Other risk reduction alternatives should be advised.[4]

Strong recommendation; low quality of evidence.

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CHAPTER 5: VACCINATION OF SPECIAL POPULATIONS

VACCINATION FOR ADULT IMMIGRANTS TO SINGAPORE

A number of vaccine-preventable diseases still have community transmission in Singapore. Other diseases are under strict surveillance and control by the Ministry of Health. Thus, some countries recommend that travellers to Singapore should update their vaccination status for the vaccines indicated in **Table 34**.[1,2] Furthermore, Singapore requires a yellow fever vaccination certificate prior to entry for travellers from high-risk countries.[3]

Table 34. Vaccines for Adult Immigrants to Singapore[1,3]

Category	Vaccine
Routine	Measles-mumps-rubella vaccine Tetanus-diphtheria-pertussis vaccine Varicella vaccine Polio vaccine Annual influenza vaccine Hepatitis B
Requires a certificate	Yellow fever if arriving from the following countries[3]: Angola, Argentina, Benin, Bolivia, Brazil, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Colombia, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Ecuador, Equatorial Guinea, Ethiopia, French Guiana, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Guyana, Kenya, Liberia, Mali, Mauritania, Niger, Nigeria, Panama, Paraguay, Peru, Senegal, Sierra Leone, South Sudan, Sudan, Suriname, Togo, Trinidad and Tobago, Uganda, Venezuela

Strong recommendation; low quality of evidence.

COVID-19 vaccination may be required according to the current immigration regulations. Please check the current regulations as this is constantly changing.[3]

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VACCINATION IN PREGNANT WOMEN

For many healthy women, pregnancy may provide the opportunity for first contact with the medical system, and so general practitioners have a valuable opportunity to assess their immunisation status and vaccinate, thus protecting mother and neonate. Although pregnancy is considered an immunosuppressed state, there are no data to support an inadequate response to vaccines.

Pregnant women should be screened for immunity to rubella and varicella, as exposure to these infections in a non-immune patient during pregnancy may require protection by passive immunisation. Screening for hepatitis B virus (specifically HBsAg) should also be performed, as maternal infection will require passive and active immunisation of the neonate at birth to reduce maternally transmitted infection and the risk of chronic carriage and disease.

Whilst there are no data to indicate that currently approved vaccines are teratogenic and inactivated vaccines are considered safe, it should be noted that live vaccines may pose a risk to the foetus and should not generally be administered starting 1 month before a planned pregnancy.[1] Practitioners should make an overall assessment of the benefits and risks, taking into consideration the risk profile of the specific vaccine, the risks of adverse effects to the foetus, as well as the risk profile of the pregnant woman.[2]

Table 35 summarises the general recommendations for vaccination in pregnant women.[3,4] In addition, for non-pregnant women who intend to conceive, live vaccines should only be given more than 1 month before the planned conception. In addition, administration prior to pregnancy is preferred for certain vaccines, such as those against hepatitis A and meningococcal disease.

Table 35. Vaccinations for Pregnant Women[3-7]

Indication	Vaccines recommended
Routine	Influenza (inactivated) Tdap (preferably between 16 and 32 weeks, see Tdap section)
May be given if indicated, based on travel itinerary and assessment of benefits and risks to the woman and foetus	Hepatitis A vaccine Hepatitis B vaccine Meningococcal vaccine Tetanus immunoglobulin (if there is indication) Pneumococcal vaccine (PPV23) if there is indication Inactivated Japanese encephalitis vaccine if there is indication Rabies
Not recommended	Human papillomavirus vaccine

(Cont'd.) Table 35. Vaccinations for Pregnant Women[3-7]

Indication	Vaccines recommended
Contraindicated	Varicella Measles-mumps-rubella vaccine Yellow fever vaccine (may be given after consultation with YF vaccine/travel medicine expert during epidemics and when travel to endemic areas cannot be avoided, if benefit outweighs risk) Live attenuated Japanese encephalitis vaccine
Insufficient data to make a recommendation. Delay if possible. Discuss risk and benefit.	*Haemophilus influenzae* B vaccine Recombinant zoster vaccine

See chapter on Vaccination for Travellers for additional information about travel vaccinations for pregnant women.

Strong recommendation; moderate quality of data.

Live vaccines may be given only up to 4 weeks before getting pregnant or planned conception.

Strong recommendation; moderate quality of data.

Finally, while pregnancy is not a contraindication to travel, pregnant women who have not completed the necessary vaccinations are advised to delay travel to high-risk areas until after delivery.[8]

Strong recommendation; low quality of data.

References:

1. General recommendations for immunization. In: Centers for Disease Control and Prevention. Epidemiology and Prevention of Vaccine-Preventable Diseases. Atkinson W, Hamborsky J, Wolfe S, eds. 12th ed. Washington DC: Public Health Foundation; 2012.
2. CDC. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 2011;60:26.
3. Raffles Medical Group. National Adult Immunisation Schedule (NAIS). Available at: https://www.rafflesmedicalgroup.com/services/family-medicine/healthcare-assistance/national-immunisation-schedule/national-adult-immunisation-schedule-nais/. Accessed 18 July 2022.
4. Global Advisory Committee on Vaccine Safety. Safety of Immunization during Pregnancy: A review of the evidence. Geneva: World Health Organization; 2014.
5. Bresee J. SAGE WHO Influenza Vaccine Recommendation: opportunities and challenges. Presented at: 7th Meeting with International Partners on Prospects for Influenza Vaccine Technology Transfer to Developing Country Vaccine Manufacturers; Dubai, UAE; March 2014.
6. Guidelines for Vaccinating Pregnant Woman. Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/vaccines/pregnancy/hcp-toolkit/guidelines.html. Accessed 18 July 2022.
7. Imojev Full Prescribing Information, Dosage & Side Effects. MIMS Singapore. Available at: https://www.mims.com/singapore/drug/info/imojev?type=full. Accessed 18 July 2022.
8. CDC Health Information for International Travel: The Yellow Book. Atlanta, GA: Centers for Disease Control and Prevention; 2015.

VACCINATION FOR ADULT PATIENTS WITH CHRONIC MEDICAL CONDITIONS OR IMMUNOCOMPROMISED STATES

General practitioners are increasingly seeing patients with complex comorbidities and immunocompromised states due to increasing lifespans and the widespread usage of immunosuppressant therapies. Patients with chronic medical conditions are at high risk of developing complications from certain vaccine-preventable diseases and should therefore be protected from these infections.

Patients with immunocompromised states are similarly at a high risk of infection, but their inability to mount an adequate immune response leads to the risk of adverse reactions to vaccines; for example, uncontrolled pathogen replication with live bacterial or viral vaccines. Hence these patients need careful assessment and advice.

To guide practitioners, **Table 36** summarises the recommendations for vaccinations for these patients.

Table 36. Vaccination Recommendations for Adult Patients with Chronic Medical Conditions or Immunocompromised States.[1-3]

Strong recommendation; moderate quality of evidence.

Condition	Prioritised vaccine	Routine vaccine
Asplenia or hyposplenia	• *Haemophilus influenzae* type B vaccine • 2 doses of meningococcal vaccine spaced 2 months apart, and every 5 years • One dose of 13-valent pneumococcal vaccine, followed 2 months later by the 23-valent vaccine. Single booster dose of the 23-valent vaccine after 5 years, for a maximum of 3 doses	• Hepatitis A and B vaccines, if unvaccinated • Annual influenza vaccine

(Cont'd.) Table 36. Vaccination Recommendations for Adult Patients with Chronic Medical Conditions or Immunocompromised States.[1-3]

Strong recommendation; moderate quality of evidence.

Condition	Prioritised vaccine	Routine vaccine
Chronic kidney disease*	Hepatitis B vaccine then serologic testing within 1 to 6 months of completion of the vaccine series. A second series is recommended if anti-HBs antibody titres are less than 10 IU/L. Responders should have yearly evaluation of titres, with appropriate boosters if necessary. • One dose of 13-valent pneumococcal vaccine, followed 2 months later by the 23-valent vaccine. Single booster dose of the 23-valent vaccine after 5 years	• Annual influenza vaccine
Chronic lung disease	• Annual influenza vaccine • One dose 23-valent pneumococcal vaccine (13-valent pneumococcal vaccine only if ≥65 years)	
Chronic heart disease Chronic endocrine diseases including diabetes	• One dose 23-valent pneumococcal vaccine (13-valent pneumococcal vaccine only if ≥65 years)	• Annual influenza vaccine
Chronic liver disease	• 23-valent pneumococcal vaccine	• Annual influenza vaccine • Hepatitis A and B vaccines, if unvaccinated

*For Stage 4 and 5 patients and those on renal dialysis, the National Adult Immunisation Schedule does not include PCV13 for this patient subgroup, and the vaccine cannot be claimed with Medisave. However, this expert panel strongly recommends PCV13 for these patients, in line with recommendations from the Advisory Committee on Immunization Practices.

(Cont'd.) Table 36. Vaccination Recommendations for Adult Patients with Chronic Medical Conditions or Immunocompromised States.[1-3]

Strong recommendation; moderate quality of evidence.

Condition	Prioritised vaccine	Routine vaccine
Non-malignant haematological diseases	• One dose of 13-valent pneumococcal vaccine, followed 2 months later by the 23-valent vaccine. Single booster dose of the 23-valent vaccine after 5 years	• Annual influenza vaccine • Hib and meningococcal vaccine (for sickle cell disease and primary complement immunodeficiencies)
Chronic inflammatory diseases and cancer requiring monoclonal antibody therapy	• One dose of 13-valent pneumococcal vaccine, followed 2 months later by the 23-valent vaccine. Single booster dose of the 23-valent vaccine after 5 years • Should have immunity to varicella and hepatitis B	• Annual influenza vaccine

(Cont'd.) Table 36. Vaccination Recommendations for Adult Patients with Chronic Medical Conditions or Immunocompromised States.[1-3]

Strong recommendation; moderate quality of evidence.

Condition	Prioritised vaccine	Routine vaccine
Immunocompromised states due to immunosuppression** or medical condition, including cancer on active treatment and symptomatic human immunodeficiency virus (HIV) infection	• Live vaccines are generally contraindicated unless the benefits of vaccination outweigh the risks of infection. • Give inactivated vaccines when indicated. Consider that these patients may have decreased response to vaccines and should be carefully monitored. • One dose of 13-valent pneumococcal vaccine, followed 2 months later by the 23-valent vaccine. Single booster dose of the 23-valent vaccine after 5 years.	Hepatitis A and B vaccines, if unvaccinated (highly recommended for people with HIV)
Asymptomatic HIV infection[4]	• One dose of 13-valent pneumococcal vaccine, followed 2 months later by the 23-valent vaccine. Single booster dose of the 23-valent vaccine after 5 years • Meningococcal vaccine • Hepatitis B vaccine	MMR and varicella vaccine if CD4 count >200 mm^3

**These include, but are not limited to, the following: corticosteroids (oral prednisolone ≥2 mg/kg per day or ≥20 mg per day for more than 14 days duration), chemotherapy, radiation therapy, post-organ transplant therapy, certain anti-rheumatic drugs, and drugs used for the management of inflammatory bowel disease. After high-dose steroid use, delay live vaccines for at least 4 weeks. For cancer chemotherapy, radiation therapy, and highly immunosuppressive medications (exclusive of lymphocyte-depleting agents and organ transplant immunosuppression), the waiting period is 3 months. For lymphocyte-depleting (alemtuzumab and rituximab) agents, the waiting period is ≥6 months, although some experts believe the waiting period should be ≥1 year.

(Cont'd.) Table 36. Vaccination Recommendations for Adult Patients with Chronic Medical Conditions or Immunocompromised States.[1-3]

Strong recommendation; moderate quality of evidence.

Condition	Prioritised vaccine	Routine vaccine
Recipients of hematopoietic stem cell transplant (HSCT)†	These patients are considered "never been vaccinated" and should receive the appropriate vaccinations according to risk and age: • Inactivated vaccines may be administered 6 to 13 months after transplantation. • Live vaccines may be administered 24 months after transplantation, depending on the response to the HSCT and the degree of graft-versus-host disease.	
Recipients of solid- organ transplant	Patients should be vaccinated with all indicated vaccines with the following schedule: • Vaccination with inactivated vaccines should be completed 2 weeks before transplantation. • Vaccination with live vaccines should be completed 4 weeks before transplantation. • After transplantation, live vaccines are generally contraindicated. Inactivated vaccines may be given if indicated.	

†*Discussion with the primary care physicians on the timing of vaccination due to the changing medical conditions and net immune system of the patients*

References:

1. Best Practice Guidelines for Immunization. In: Centers for Disease Control and Prevention. 04 May 2021. Advisory Committee on Immunization Practices (ACIP). Available at: https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html Accessed 20 October 2021
2. Ong A, Goh KT, eds. A Guide on Infectious Diseases of Public Health Importance In Singapore. 7th ed. Singapore: Ministry of Health; 2011.
3. Public Health Agency of Canada. Vaccination of Specific Populations. Available at: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations.html?page=7. Accessed 20 October 2021.
4. Immunocompromised travellers. In: Centers for Disease Control and Prevention. Available at: https://wwwnc.cdc.gov/travel/yellowbook/2020/travelers-with-additional-considerations/immunocompromised-travelers. Accessed 20 October 2021.

VACCINATION OF ADULTS IN THE HEALTHCARE SETTING

There are many groups at risk of infections in the healthcare setting: hospitalised patients, residents of long-term care facilities and nursing homes, and healthcare personnel who can also act as vectors of vaccine preventable diseases. Vaccination of hospitalised adult patients should follow the general recommendations for adults and the special recommendations for patients with chronic medical illness or immunocompromised states as applicable.

Residents of long-term care and nursing homes are at significant risk because of the potential rapid spread of infections within the institution and the several risk factors that residents may have, such as old age or underlying medical conditions. In addition, some residents may undergo medical procedures that could place them at risk of infections. Thus, they should be adequately protected through vaccination.

Similarly, healthcare personnel are constantly exposed to infectious agents and bodily fluids from patients and other contaminated objects. They are also at risk of sharps injuries and transmission of blood-borne infections. Vaccination will not only protect them from infections but also prevent transmission of these infections to patients.

Table 37 summarises the vaccination recommendations for adults in the healthcare setting.

Table 37. Vaccination for Adults in the Healthcare Setting[1,2]

At-risk group	Prioritised vaccines	Routine vaccine
All healthcare professionals, including physicians, nurses, allied medical professionals and other clinic or hospital staff	• Hepatitis B vaccine with post-vaccination serological testing 1 to 2 months **after series completion routinely.** • **Two** doses of varicella vaccine spaced 4 to 8 weeks apart or evidence of positive serology • Two doses of measles-mumps-rubella vaccine spaced 28 days apart or evidence of positive serology • Vaccines for meningococcal, meningococcal disease, typhoid and poliomyelitis should be given to laboratory staff handling infectious agents causing these diseases	• Annual influenza vaccine • Single dose of Tdap **(if last dose was >10 years ago)**

Strong recommendation; moderate quality of evidence.

References:

1. CDC. Immunization of health-care personnel: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2011;60(RR-7):1-45.
2. Schaffner W, Rehm SJ. Nurses Urged to Take a Role in Vaccinating Older Adults. Available at: https://www.nfid.org/wp-content/uploads/2019/08/nbna-geriatric-vaccination.pdf. Accessed 10 June 2022.

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Quick Guide for Adult Vaccination

At-risk group	18–25 years	26–39 years	40–49 years	50–59 years	60–64 years	65 and older
ROUTINE						
HPV for both sexes	3 doses (0-2-6 mo schedule) (until age 45 years)					
Dengue	3 doses (0-6-12 mo schedule)*					
Influenza	Annually					
MMR	2 doses at least 28 days apart for those without two documented doses as children					
Pneumococcal	See **Table 16**					
Tdap	1 dose with booster every 10 years					
Varicella	2 doses (0-1 mo schedule)					
Zoster				2 doses for the recombinant adjuvanted vaccine (0 and 2-6 mo)		
ADULTS WITH RELEVANT RISK FACTORS						
Haemophilus influenza B	1 dose					
Hepatitis A	2 doses (0-6 mo schedule)		2 doses (0-6 mo schedule) for susceptible individuals			
Hepatitis B	3 doses (0-1-6 mo schedule)					
Meningococcal	2 doses (0-2 mo schedule); 1 dose every 5 years for travel for pilgrims					
Pneumococcal	See **Table 16**					

**Until 45 years of age. Vaccination is not recommended for individuals who have not been previously infected by dengue virus.*

BCG, Bacillus-Calmette-Guerin; HPV, human papillomavirus; MMR, measles-mumps-rubella.

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Vaccine User Guide

Vaccine	Available Brands	Indication	Administration	Schedule (unvaccinated adults)
Cholera vaccine (oral inactivated)	Dukoral (Janssen)	Prevention of diarrhoea due to cholera or enterotoxigenic *Escherichia coli* infection especially during travel	Orally on empty stomach	2 doses 1 week apart, and a booster after 2 years
Dengue	Dengvaxia (Sanofi Pasteur)	Prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4 in individuals aged 12 to 45 years living in endemic areas	SQ	3 injections (0-6-12 months)
Haemophilus influenza b vaccine	Hiberix (GlaxoSmithKline) Hibtiter (Wyeth)	Prevention of invasive *H. influenza b* infection in adults at risk (asplenia, IgG2 subclass immunodeficiency, immunosuppression from chemotherapy or HIV infection, HSCT)	IM (SQ for those with thrombocytopaenia or bleeding)	Single dose
Hepatitis A vaccine	Avaxim 80 and 160 (Sanofi Pasteur) Epaxal (DKSH) Havrix 1440 Adult/ Havrix 720 Junior (GlaxoSmithKline) Vaqta (MSD)	Prevention of hepatitis A infection among high-risk individuals (travel, clotting factor disorder, occupational risk, liver disease, liver transplantation, MSM, ilicit drug use)	IM (deltoid)	2 doses 6-12 months apart
Hepatitis B vaccine*	Engerix-B (GlaxoSmithKline) HBvaxPro (MSD)	Prevention of hepatitis B infection in high-risk individuals (sexual and household contact with infected patients, multiple sex partners, STI, MSM, IDU, residents and staff of facilities for developmentally disabled individuals, healthcare and public safety workers with risk for exposure to blood or blood-contaminated body fluids, ESRD, DM, travel, HIV)	IM (SQ for those with thrombocytopaenia or bleeding)	3 doses (months 0, 1 and 6)

(Cont'd.) Vaccine User Guide

Vaccine	Available Brands	Indication	Administration	Schedule (unvaccinated adults)
Hepatitis A and B vaccine (combined)	Twinrix (GlaxoSmithKline)	Prevention of hepatitis A and B infection in high-risk individuals	IM (SQ for those with thrombocytopaenia or bleeding)	3 doses (months 0, 1 and 6)
HPV (bivalent) vaccine+	Cervarix (GlaxoSmithKline)	Prevention of HPV infection, precancerous cervical lesions and cervical cancer in women	IM (deltoid or anterolateral thigh)	3 doses (months 0, 1/2 and 6)
HPV (tetravalent) vaccine+	Gardasil (MSD)	Prevention of HPV infection, precancerous cervical lesions and cervical cancer in women; and HPV infection in men		
HPV (9-valent) vaccine	Gardasil-9 (MSD)	Prevention of HPV infection and HPV-related precancerous and cancerous lesions in women and men		
Influenza vaccine (parenteral trivalent inactivated)**	Agrippal S1 (Novartis) Fluarix (GlaxoSmithKline) Fluvax (CSL Ltd) Influvac (Abbott) Vaxigrip (Sanofi Pasteur)	Prevention of influenza A and B infection among all individuals aged 6 months and above, including adults.	IM/deep SQ	Single dose yearly
Influenza vaccine (parenteral quadrivalent inactivated)**	Fluarix Tetra (GlaxoSmithKline)	Prevention of influenza in individuals greater than 3 years of age, especially in those with an increased risk of associated complications	IM	Single dose
	FluQuadri (Sanofi Pasteur)	Prevention of influenza in individuals greater than 6 months of age, especially in those with an increased risk of associated complications		
JE live attenuated vaccine	Imojev (Sanofi Pasteur)	Prevention of JE infection, especially for travellers to endemic areas	SQ	Single dose

(Cont'd.) Vaccine User Guide

Vaccine	Available Brands	Indication	Administration	Schedule (unvaccinated adults)
JE inactivated vaccine	Ixiaro (Novartis)	Prevention of invasive meningococcal disease among high-risk groups (travel to endemic areas, travel to Mecca [mandatory], asplenia, Immunocompromised states, occupational risk and close contact to patients)	IM	2 doses 1 month apart
Measles-mumps-rubella vaccine*	M-M-R II (MSD) Priorix (GlaxoSmithKline)	Prevention of measles, mumps and rubella in all unvaccinated individuals	SQ	1 to 2 doses given 1 month apart
Meningococcal polysaccharide vaccine	Mencevax (GlaxoSmithKline) Menomune (Sanofi Pasteur)	Prevention of invasive meningococcal disease among high-risk groups (travel to endemic areas, travel to Mecca [mandatory], asplenia, Immunocompromised states, occupational risk and close contact to patients)	SQ	At least 1 dose
Meningococcal conjugate vaccine	Menactra (Sanofi Pasteur) Menveo (Novartis) Nimenrix (GlaxoSmithKline		IM	
Meningococcal recombinant lipidated protein vaccine (serogroup B)	Trumenba (Pfizer) Bexsero (GlaxoSmithKline)	Prevention of invasive meningococcal disease caused by N. meningitidis serogroup B in high-risk groups as indicated in the above column	IM	See Table 13
Pneumococcal (23-valent polysaccharide) vaccine**	Pneumo 23 (Sanofi Pasteur) Pneumovax 23 (MSD)	Prevention of IPD and pneumonia among high-risk groups (age >65 years, chronic disease, asplenia, immunocompromised states, cigarette smoking, cerebrospinal fluid leaks, candidates for elective splenectomy or cochlear implantation)	SQ/IM	See Table 14 and 15
Pneumococcal (13-valent conjugate) vaccine**	Prevenar 13 (Pfizer)		IM	

(Cont'd.) Vaccine User Guide

Vaccine	Available Brands	Indication	Administration	Schedule (unvaccinated adults)
Pneumococcal (20-valent conjugate vaccine)	Apexxnar (Pfizer)	Adults aged ≥18 years. See Table 17A and Table 17B for ACIP recommendations on use	IM	See Table 17A and Table 17B for ACIP recommendations.
Polio vaccine (oral)	Polio Sabin (oral) (GlaxoSmithKline)	Prevention of poliomyelitis, especially in high-risk groups (travel to endemic areas, occupational risk, unvaccinated contacts of a vaccine recipient)	Oral	3 doses (months 0, 1-2, and 6-12)
Polio vaccine (inactivated)	Imovax Polio (Sanofi Pasteur)		IM (preferred)/ SQ	
Rabies (purified chick embryo cell) vaccine	Rabipur (Novartis)	Pre-exposure prophylaxis for high-risk individuals (travel to endemic areas, occupational risk) and post-exposure prophylaxis for Category II and III rabies exposure	IM (deltoid or anterolateral thigh)	Pre-exposure: Days 0, 7, and 21-28 (possible to shorten; see Table 17). Post-exposure: Days 0, 3, 7 and 14 (add 1 more dose on Day 28 if immunocompromised).
Rabies (Vero cells)	Verorab (Sanofi Pasteur)	Prevention of rabies in children and adults. It can be used before or after exposure to the rabies virus, as a primary vaccination or as a booster dose.	IM (deltoid or anterolateral thigh)	
Tetanus toxoid-diphtheria toxoid (Td) vaccine	ADT (CSL Ltd)	Booster vaccination to reduce morbidity of tetanus and diphtheria, especially in high-risk groups (vaccination >10 years ago, close contact with an infant aged <12 months, women of childbearing age before pregnancy or immediately after delivery, healthcare personnel with direct patient contact)	IM (deltoid)	Single dose

(Cont'd.) Vaccine User Guide

Vaccine	Available Brands	Indication	Administration	Schedule (unvaccinated adults)
Tetanus toxoid- reduced diphtheria toxoid-acellular pertussis (Tdap) vaccine*	Adacel (Sanofi Pasteur) Boostrix (GlaxoSmithKline)	Booster vaccination to reduce morbidity of tetanus, diphtheria and pertussis, especially in high-risk groups (vaccination >10 years ago, close contact with an infant aged <12 months, women of childbearing age before pregnancy or immediately after delivery, healthcare personnel with direct patient contact), pregnant women for each pregnancy	IM (deltoid)	Single dose
Tetanus toxoid	Tetavax (Sanofi Pasteur)	Prophylaxis of tetanus	IM (deltoid)	2 doses 1 month apart
Tetanus immunoglobulin	Igantet (Grifols)	Prophylaxis of tetanus and treatment of clinically manifest tetanus	IM	Single dose
Typhoid (purified Vi capsular polysaccharide) vaccine	Typherix GlaxoSmithKline Typhim VI (Sanofi Pasteur)	Prevention of typhoid fever, especially for travellers to endemic areas and areas with poor hygiene standards and close contacts of typhoid carriers	IM/SQ	Single dose
Varicella vaccine	Okavax Live Attenuated Varicella Virus Vaccine – BIKEN (Sanofi Pasteur) Varilrix (GlaxoSmithKline)	Prevention of varicella in all adults without evidence of immunity, especially healthcare personnel with potential exposure to VZV.	SQ	2 doses 4 weeks apart
Yellow Fever	Stamaril (Sanofi Pasteur)	Prevention of yellow fever, particularly for travellers to endemic area.	IM/SQ	Single dose

(Cont'd.) Vaccine User Guide

Vaccine	Available Brands	Indication	Administration	Schedule (unvaccinated adults)
Zoster vaccine, recombinant, adjuvanted	Shingrix (GSK)	Prevention of zoster in adults aged 50 years and older	IM	2 doses at 0 and 2 to 6 months

**Claimable to Medisave (S$500 per year per account). Indicates those claimable by adults.*
+HPV claimable (S$500 per year per account) up to 26 years old.
***Influenza and pneumococcal vaccinations are claimable (S$500 per year per account) for persons with higher risk of developing influenza-related complications and severe pneumococcal disease, respectively.*

For more information on Medisave and vaccines claimable to Medisave, refer to the Ministry of Health website (Summary of Medisave Withdrawal Limits, available at: https://www.moh.gov.sg/content/moh_web/home/costs_and_financing/schemes_subsidies/medisave/Withdrawal_Limits/Summary_of_Medisave_Withdrawal_Limits.html.

IM, intramuscular; SQ, subcutaneous; ID, intradermal; HIV, human immunodeficiency virus; HSCT, hematopoietic stem cell transplant; MSM, men who have sex with men; STI, sexually transmitted infections; IDU, injecting-drug use; ESRD, end-stage renal disease; DM, diabetes mellitus; HPV, human papilloma virus; JE, Japanese encephalitis; IPD, invasive pneumococcal disease.

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VACCINATION GUIDE FOR SPECIAL POPULATIONS

Travellers

Recommended vaccination may vary according to the travel destination. Please refer to **Tables 32** and **33**.

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)*	3 (6 months after visit 2)	65 and older
Cholera (oral attenuated)	Orally on empty stomach	2 doses 1 week apart, and a booster after 2 years	✓	✓ 1 week		After 2 years
Hepatitis A	IM (deltoid)	2 doses 6-12 months apart	✓		✓	
Hepatitis B	IM (SQ for those with thrombo-cytopaenia or bleeding)	3 doses (months 0, 1 and 6)	✓	✓ 1 month	✓	
JE (attenuated)	SQ	Single dose	✓			After 1-2 years if risk persists
JE (inactivated)	IM	2 doses 1 month apart	✓	✓ 1 month		
Meningococcal (polysaccharide)	SQ		✓			
Meningococcal (conjugate)	IM		✓			
Polio (oral)	Oral	3 doses (months 0, 1-2, and 6-12)	✓	✓	✓	
Polio (inactivated)	IM (preferred)/ SQ		✓	✓	✓	Every 10 years for IPV
Typhoid (parenteral)	IM/SQ	Single dose	✓			Every 3 years if risk persists
Typhoid (oral)	Oral	One dose each taken on Days (1, 3 and 5)	✓			Every year if risk persists
Yellow fever	IM	Single dose	✓			

**Indicated where visit intervals differ*

Immigrants to Singapore

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)*	3 (6 months after visit 2)	65 and older
Hepatitis B	IM (SQ for those with thrombo-cytopaenia or bleeding)	3 doses (months 0, 1 and 6)	✓	✓ 1 month	✓	After 2 years
Influenza (quadrivalent)	IM	Single dose	✓			
MMR	SQ	1 to 2 doses given 1 month apart	✓	✓ 1 month		
Polio (oral)	Oral	3 doses (months 0, 1-2, and 6-12)	✓	✓	✓	Every 10 years for IPV
Polio (inactivated)	IM (preferred)/ SQ	2 doses 1 month apart	✓	✓	✓	
Tdap	IM (deltoid)	Single dose	✓			
Varicella	SQ	2 doses 4 weeks apart	✓	✓ 1 month		

**Indicated where visit intervals differ*

Pregnant Women

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	65 and older
Influenza (quadrivalent)	IM	Single dose	✓			
Tdap	IM	Single dose	✓			

Asplenia or Hyposplenia Patients

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	65 and older
Haemophilus influenza b	IM (SQ for those with thrombo-cytopaenia or bleeding)	Single dose	✓			
Hepatitis A	IM (deltoid)	2 doses 6-12 months apart	✓		✓	
Hepatitis B	IM (SQ for those with thrombo-cytopaenia or bleeding)	3 doses (months 0, 1 and 6)	✓	✓ 1 month	✓	
Influenza (quadrivalent)	SQ	Single dose	✓			
Meningococcal (polysaccharide)	Meningococcal (polysaccharide)	At least one dose	✓			
Meningococcal (conjugate)	SQ	Two doses (2 months apart) in patients with asplenia	✓			
Meningococcal (recombinant lipidated protein vaccine, serogroup B)	IM	Trumenba: Two doses 6 months apart Bexsero: two doses 1 month apart	✓	✓		
PCV13	IM	One PCV13 dose followed by PPSV23 after 2 months	✓			
PPSV23	SQ/IM			✓ (8 weeks after visit 1)		Single booster after 5 years

**Indicated where visit intervals differ*

Chronic Kidney Disease Patients

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	65 and older
Hepatitis B	IM (SQ for those with thrombo-cytopaenia or bleeding)	3 doses (months 0, 1 and 6)	✓			
Influenza (quadrivalent)	IM	Single dose	✓		✓	
PCV13/PPSV23	See **Table 14** and **15**					
Tdap	IM (deltoid)	Single dose	✓			

Chronic Lung Disease Patients

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	65 and older
Influenza (quadrivalent)	IM	Single dose	✓			
PCV13/PPSV23	See **Table 14** and **15**					
Tdap	IM (deltoid)	Single dose	✓			

**Indicated where visit intervals differ*

Chronic Heart Disease Patients

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	65 and older
Influenza (quadrivalent)	IM	Single dose	✓			
PCV13/PPSV23	See **Table 14** and **15**					
Tdap	IM (deltoid)	Single dose	✓			

**Indicated where visit intervals differ*

Chronic Endocrine Disease Patients Including Diabetes

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	65 and older
Influenza (quadrivalent)	IM	Single dose	✓			
PCV13/PPSV23	See **Table 14** and **15**					

**Indicated where visit intervals differ*

Chronic Liver Disease Patients

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	65 and older
Hepatitis A	IM	Two doses given 6 to 12 months apart	✓		✓	
Hepatitis B	See **Table 8**					
Influenza (quadrivalent)	IM	Single dose	✓			
PCV13/PPSV23	See **Table 14** and **15**					
Tdap	IM (deltoid)	Single dose	✓			

**Indicated where visit intervals differ*

Non-malignant Haematological Disease Patients

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	65 and older
Influenza (quadrivalent)	IM	Single dose	✓		✓	
PCV13/PPSV23	See **Table 14** and **15**					
Meningococal*	See **Table 13**					

**Conjugated meningococcal vaccine should be administered to patients with primary complement deficiencies and to those who are asplenic or who have sickle cell disease.*

Chronic Inflammatory Disease Patients Including Those with Cancer Requiring Monoclonal Antibody Therapy

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	65 and older
Influenza (quadrivalent)	IM	Single dose	✓		✓	
PCV13/PPSV23	See **Table 14** and **15**					

** Conjugated meningococcal vaccine should be administered to patients with primary complement deficiencies and to those who are asplenic or who have sickle cell disease.*

Patients with Immunocompromised States Due to Medical Conditions, Including Cancer and Human Immunodeficiency Syndrome

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	65 and older
Influenza	IM	Yearly	✓			
PCV13/PPSV23	See **Table 8**					
Meningococcal disease	SQ	Two doses given 2 months apart	✓	✓		Every 5 years if needed
Hepatitis A	IM	Two doses given 6 to 12 months apart	✓		✓	
Hepatitis B	See **Table 8**					

Adults in the Healthcare Setting

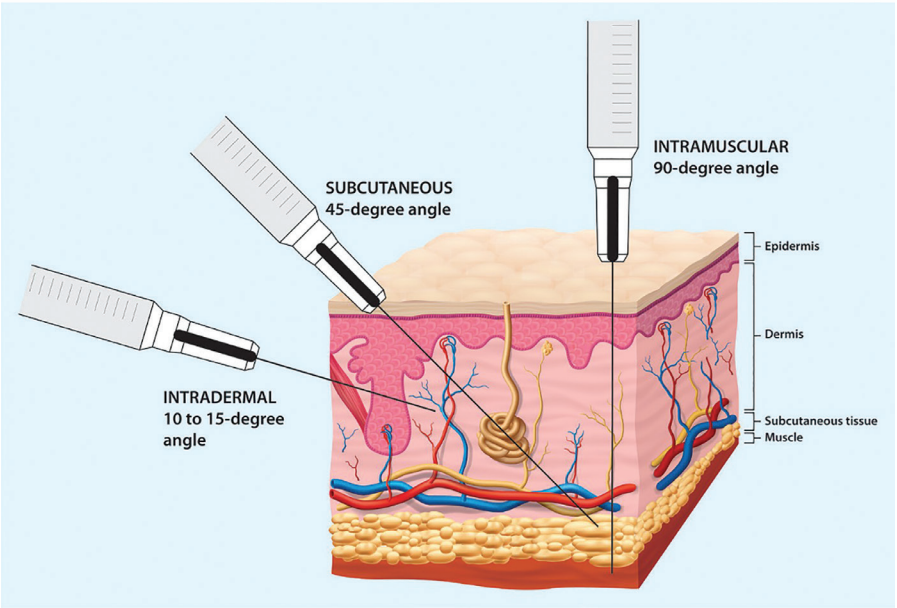
Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	65 and older
Hepatitis B	IM (SQ for those with thrombo-cytopaenia or bleeding)	3 doses (months 0, 1 and 6)	✓	✓	✓	
Influenza (quadrivalent)	IM	Single dose given annually	✓			
MMR	SQ	1 to 2 doses given 1 month apart	✓	✓		
Tdap	IM (deltoid)	Single dose	✓			Every 10 years
Varicella	SQ	2 doses 4 weeks apart	✓	✓		

Sample Vaccine Record

VACCINE ADMINISTRATION RECORD						Patient/Chart number:		
Patient name:						**Birthdate:**		**Sex:**
Vaccine	Dose	Brand	Date Given	Route	Site	Vaccine Lot Number	Vaccinator	Signature
HPV Indicate type (bivalent/tetravalent)								
	1							
	2							
	3							
Influenza Indicate type (trivalent/quadrivalent; parenteral)								
MMR								
Pneumococcal vaccine Indicate type (PCV 13, PCV 20, or PPSV23)								
	1							
	2							
Tdap								
Varicella								
	1							
	2							
Zoster								
Haemophilus influenza B								
Hepatitis A								
	1							
	2							
Hepatitis B								
Meningococcal vaccine Indicate type (polysaccharide or conjugate)								
Others (indicate vaccine type)								

VACCINE ADMINISTRATION

Intrademal, Subcutaneous & Intramuscular Injections



Subcutaneous Injection

1. Wash hands thoroughly. When pre-filled injections are not used, ensure aseptic technique when filling syringe.
2. Inspect injection site for bruising, burns, swelling, hardness, or irritation. Choose a different site if these abnormalities are noted.
3. Cleanse injection site with an alcohol swab.
4. With the non-injecting hand, pinch a skin fold between the thumb and index finger.
5. In a 45-degree angle, thrust the needle into the skin in a quick, single motion without great force.
6. Aspirate to check for blood backflow. If there is backflow, repeat the entire procedure using a different syringe.
7. Inject the vaccine.
8. Press some gauze on the injection site as the needle is pulled out.
9. Dispose the used syringe according to hospital protocol.

Intramuscular Injection

1. Wash hands thoroughly. When pre-filled injections are not used, ensure aseptic technique when filling syringe.
2. Inspect injection site for bruising, burns, swelling, hardness, or irritation. Choose a different site if these abnormalities are noted.
3. Cleanse injection site with an alcohol swab.
4. In a 90-degree angle, thrust the needle into the skin in a quick, single motion without great force.
5. Aspirate to check for blood backflow. If there is backflow, repeat the entire procedure using a different syringe.
6. Inject the vaccine.
7. Press some gauze on the injection site as the needle is pulled out.
8. Dispose the used syringe according to hospital protocol.

Intradermal Injection

1. Wash hands thoroughly. When pre-filled injections are not used, ensure aseptic technique when filling syringe.
2. Inspect injection site for bruising, burns, swelling, hardness, or irritation. Choose a different site if these abnormalities are noted.
3. Cleanse injection site with an alcohol swab.
4. With the non-injecting hand, pull the skin taut at the injection site.
5. With the needle almost flat, insert 1/8 of an inch of the length of the needle into the skin (the needle tip should be visible through the skin).
6. Inject the vaccine into the skin to form a wheal or blister.
7. Press some gauze on the injection site as the needle is pulled out.
8. Dispose the used syringe according to hospital protocol.

RELATED LINKS

Centers for Disease Prevention and Control (CDC)

www.cdc.gov

Travellers' Health Destination Website

wwwnc.cdc.gov/travel/destinations/list

CDC Vaccines and Immunization Website

www.cdc.gov/vaccines/

Health Sciences Authority, Singapore

www.hsa.gov.sg

Immunisation Chart Based on Age (Children), Health Sciences Authority of Singapore

www.hpb.gov.sg/HOPPortal/gamesandtools-article/3216

Suspected Vaccine Adverse Event Online Reporting Form

http://eservice.hsa.gov.sg/adr/adr/vaeOnline.do?action=load

Vaccine Adverse Event Report

www.hsa.gov.sg/content/dam/HSA/HPRG/Safety_Alerts_Product_Recalls_Enforcement/HSA_ VAEReportingForm.pdf

Ministry of Health, Singapore

www.moh.gov.sg

Infectious Diseases Guidelines

www.moh.gov.sg/content/moh_web/home/Publications/guidelines/infectious_diseases_guidelines. html

Infectious Diseases Statistics

https://www.moh.gov.sg/content/moh_web/home/statistics/infectiousDiseasesStatistics.html

Weekly Infectious Diseases Bulletin

https://www.moh.gov.sg/content/moh_web/home/statistics/infectiousDiseasesStatistics/weekly_ infectiousdiseasesbulletin.html

World Health Organization International Travel and Health (Vaccines) Website

www.who.int/ith/vaccines/en/

ACKNOWLEDGEMENT

This publication was made possible through the support of the following organisations (in alphabetical order):

GSK

Pfizer

sanofi

Takeda