HANDBOOK ON ADULT VACCINATION IN SINGAPORE 2020

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

Under the auspices of

SOCIETY OF INFECTIOUS DISEASE (SINGAPORE)

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Abbreviations

ACIP	Advisory Committee on Immunization Practices
BCG	Bacillus-Calmette-Guerin vaccine
BMI	Body mass index
CCID50	50% Cell culture infectious dose
CDC	Centers for Disease Prevention and Control
HSCT	haematopoietic stem cell transplant
Hib	Haemophilus influenzae type B
HbsAg	Hepatitis B surface antigen
HIV	Human immunodeficiency virus
HPV	Human papillomavirus
ID	Intradermal
IM	Intramuscular
IPV	Inactivated polio vaccine
IDU	Injecting drug use
IPD	Invasive pneumococcal disease
IVIG	Intravenous immunoglobulin
JE	Japanese Encephalitis
JEV	Japanese encephalitis vaccine
LD50	Lethal dose to 50% of population
MMR	Measles-mumps-rubella vaccine
MSM	Men who have sex with other men
OPV	Oral polio vaccine
PCV13	13-valent pneumococcal conjugate vaccine
PEP	Post-exposure prophylaxis
PPSV23	23-valent pneumococcal polysaccharide vaccine
SQ	Subcutaneous
STI	Sexually transmitted infection
TIG	Tetanus immunoglobulin
Tdap	Tetanus-reduced diphtheria-acellular pertussis vaccine
TB	Tuberculosis
VAPP	Vaccine-associated paralytic poliomyelitis
VZV	Varicella zoster vaccine
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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1. World Health Organization. Singapore: WHO statistical profile. Available at: www.who.int/gho/countries/sgp/en/. Accessed 08 June 2019.

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3. Ong A, Goh KT, eds. A Guide on Infectious Diseases of Public Health Importance In Singapore (7th Edition). Singapore: Ministry of Health; 2011.

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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
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

Grade of Recommendation	Benefit vs Risk and Burdens	Methodological Quality of Supporting Evidence	Implications
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

References:

1. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924-926.

RCT, randomised controlled trial.

2. Guyatt G, Gutterman D, Baumann MH, et al. Grading strength of recommendations and quality of evidence in clinical guidelines: report from an American College of Chest Physicians Task Force. Chest 2006;129:174-181.

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.

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.

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
• 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

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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1. National Vaccine Advisory Committee. Recommendations from the National Vaccine Advisory committee: standards for adult immunization practice. Public Health Rep 2014;129:115-123.

2. Hwang SW, Lim HB. Barriers and Motivators of Influenza Vaccination Uptake Among Primary Healthcare Workers in Singapore Proceedings Singapore Healthcare 2014;23.

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Chapter 3:
General Rules of Adult Vaccinations

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.

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	3 months
< 1-month stay	0.1 mL/kg (3.3 mg IgG/kg) IM	3 months
≥ 1-month stay	0.2 mL/kg (10 mg IgG/kg) IM	3 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
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]

Strong recommendation; low quality of evidence

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Chapter 4:
Specific Vaccines For Adults

CHOLERA VACCINE

Cholera is an acute diarrhoeal illness characterised by profuse watery diarrhoea causing severe dehydration. It is caused by some strains of *Vibrio cholera*. The most common serogroup is 01 and 0139. In Singapore, cases of *Vibrio cholera* 01, biotypes 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 three notified cases in 2018.[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, oral cholera vaccines are available and the parenteral vaccine is no longer recommended **(Table 4)**.

Table 4. Cholera Vaccine for Adults

	Oral inactivated	Oral attenuated
Description	Each 3-mL dose contains approximately $1x10^{11}$ inactivated *V. cholerae* 01 serotypes Inaba and Ogawa, biotypes classic and El Tor strains, and 1 mg of recombinant cholera toxin B subunit[3]	Each reconstituted sachet contains 4 x 10^8 to 2 x 10^9 CFU of live attenuated *V. cholera* CVD 103-HgR.
Summary of evidence	According to a meta-analysis of 23 randomised and quasi-randomised trials, the efficacy of cholera vaccines in general was found to be 51% (95% CI 41%, 59%), with the oral vaccine protecting adults against cholera for up to 3 years.[4] Field trials show that efficacy can go as high as 85%.[4] Oral vaccines were not associated with increased systemic and local adverse effects.	Vaccine efficacy against the occurrence of moderate to severe diarrhoea at 10 days postvaccination was 90.3% (95% CI 62.7%, 100.0%) and at 3 months post-vaccination was 79.5% (95% CI 49.9%, 100.0%).[5]
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 vising areas where the risk of diarrhoeal disease (i.e., "travellers' diarrhoea") is high.	Protection against disease caused by *V. cholerae* serogroup O1 in adults 18 through 64 years of age traveling to cholera-affected areas.
	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.	Administer a single oral dose a minimum of 10 days before potential exposure to cholera.

	Oral inactivated	Oral attenuated
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.	For oral administration only. Prepare and administer in a healthcare setting equipped to dispose of medical waste. Reconstituting the buffer component in 100 mL of purified bottled water; then add the active component (lyophilized V. cholerae CVD 103-HgR). Instruct recipients to avoid eating or drinking for 60 minutes before or after oral ingestion of vaccine.
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze.	Store both buffer and active components at −25°C to −15°C. Protect from light and moisture. Packets do not require thawing prior to reconstitution. Packets should not be out of frozen storage for more than 15 minutes prior to reconstitution; when out of frozen storage, packets should not be exposed to temperatures above 27°C.
Common adverse events	Gastrointestinal symptoms including stomach pain and discomfort, diarrhoea, bloating, gas, nausea and vomiting. Headache.	Tiredness, headache, abdominal pain, nausea/vomiting, lack of appetite.
Contraindications	Anaphylaxis to any vaccine component or a previous dose	
Precautions	Vaccination should be postponed during acute illness. During travel, exercise caution and hygienic practices with food and water intake.	The safety and effectiveness of the live attenuated vaccine has not been established in immunocompromised persons. Shedding in the stool of recipients for at least 7 days may occur. There is a potential for transmission of the vaccine strain to non-vaccinated close contacts (e.g., household contacts). Use caution when considering whether to administer to individuals with immunocompromised close contacts.
Pregnancy and breastfeeding	No contraindication	No contraindications; however, the vaccine strain may be shed in the stool of the vaccinated mother for at least 7 days after administration, with a potential for transmission of the vaccine strain from mother to infant during vaginal delivery.
Medisave	No	

Strong recommendation; moderate quality of evidence.

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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 may require hospitalization. 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 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. In 2018, 3,285 cases of dengue were reported in the country.[2] Serotype DENV-2 accounted for the majority of the dengue infections in 2018.

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. Though this vaccine is beneficial in preventing dengue, especially in countries with high endemicity, an increased risk of hospitalization 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 dengue virus serotype 1* (4.5 - 6.0 log10 CCID50/dose)**; CYD dengue virus serotype 2* (4.5 - 6.0 log10 CCID50/dose)**; CYD dengue virus serotype 3* (4.5 - 6.0 log10 CCID50/dose)**; and CYD dengue virus serotype 4* (4.5 - 6.0 log10 CCID50/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.[4,5] • 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%).
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 among individuals aged 12 to 45 years living in endemic areas.[6] 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 (but 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 ≥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 (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.[7] • 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.
Pregnancy and breastfeeding	Contraindicated Category X
Medisave	No

* Produced in serum-free Vero cells by recombinant DNA technology
**CCID50: 50% Cell Culture Infectious Dose.

Strong recommendation; moderate quality of evidence.

References:

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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 hematopoietic 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 due to invasive Hib infection.[1] In 2018, there were only five reports of Hib infection.[3] Data on adults is lacking.

Vaccine description

The vaccine against Hib infection is a polysaccharide-protein conjugate vaccine, which is also available in 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 95%.[2,4] Clinical trials on people living with HIV, HSCT recipients, or patients on immunosuppressant therapy reported an efficacy of at least 80%.[5-8]
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, or immunosuppression from cancer chemotherapy or HIV infection, and HSCT.[2,9]
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 apart.
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.
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.

References:

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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 2018, there were 75 reported cases of hepatitis A.[2] Outbreaks may occur, which are usually due to contaminated food. Nonetheless, contact tracing is recommended during potential outbreaks.

Vaccine description

The available 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 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]
Indication/Target population	Prevention of hepatitis A infection, especially among individuals at high risk of infection or severe outcomes. These include:[5] • Travellers to countries with high endemicity, • Those with clotting factor disorders, • 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 liver disease, • Those awaiting or have received liver transplantation, • Men who have sex with other men (MSM), and, • Those using illegal drugs.

Table 7. Hepatitis A vaccine for Adults

Indication/Target population	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 (deltoid)
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 to any vaccine component or a 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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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 hepatitis B can lead to chronic infection in around 5% of patients.[2,3] 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 2018, only 51 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	In children, efficacy of three vaccine doses is 95%. However, the immunogenicity declines with age: from 90% in healthy adults less than 60 years old, to 75% in those aged 60 years and above.[2]
Indication/Target population	Prevention of hepatitis B infection in previously unvaccinated adults, particularly those at high risk of infection or severe outcomes. These include:[2,7] • 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.

Indication/Target population	Immunocompromised, seronegative adults if with:[8] • 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.
Schedule	**Engerix B:**[9] • 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: four double doses (2 x 20 mcg) at elected date followed by 1 month, 2 months and 6 months from the date of the first dose. **HBvaxPRO:**[10] • Three doses, 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.
Administration	Intramuscular injection (deltoid) Subcutaneous in patients with bleeding disorders or thrombocytopaenia[2] Do not administer intradermally or in the gluteus maximus.[2]
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze.
Common adverse events	• Local pain, soreness, tenderness, pruritus, erythema, ecchymoses, 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
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 only 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 outweigh risks.[1] 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 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 on 891 Singaporean women aged older than 12 years of age 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 4.0).

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).
Summary of evidence	Both vaccines were found to be highly immunogenic to 99% of vaccine recipients.		This vaccine is immunogenic in 99.6 to 100% of vaccine recipients.

	Bivalent vaccine (Cervarix)	Tetravalent vaccine (Gardasil 4)	9-valent vaccine (Gardasil 9)
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.		
Schedule	• Three doses (0, 1-2 months, and 6 months) is recommended for persons aged 15 years to 45 years and immunocompromised persons above 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 (deltoid or anterolateral thigh)		
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 hematoma • 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		

	Bivalent vaccine (Cervarix)	Tetravalent vaccine (Gardasil 4)	9-valent vaccine (Gardasil 9)
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.

References:

1. Human papillomavirus. 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.

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INFLUENZA VACCINE

Human influenza is a highly infectious respiratory viral illness with three types: influenza A, B and C.[1,2] 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.[1] By September 2009, around 270,000 people in Singapore were infected, leading to 18 deaths. The pandemic ended on 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 2,000 and 44,300 people in Singapore experience influenza-like illness every week.[3] In 2018, the monthly proportion of confirmed influenza, amongst those with influenza-like illness, ranged from 17% (August 2018) to 56% (November 2018).[4]

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, intra-dermal vaccine that are also not available in Singapore.

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.[5]	The immunogenicity and safety of the quadrivalent vaccine is similar to that of the trivalent vaccines.[6]
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.[7] Among adults, vaccination is strongly recommended in the following high-risk populations:[7,8] • 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), • Household contacts and caregivers of children younger than 5 years of age and adults 50 years of age and older, and, • Household contacts and caregivers of people with medical conditions that put them at higher risk for severe complications from influenza, as described previously.	
Schedule	Single dose repeated yearly with the most updated vaccine*	
Administration	Intramuscular or deep subcutaneous injection	Intramuscular injection
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze. Protect from light. Discard after a year.	

Vaccine type	Parenteral trivalent vaccine	Parenteral quadrivalent vaccine
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-Barŕe 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. • Patients with a history of GBS with an onset related in time to influenza vaccination may be at increased risk of again developing GBS if given influenza 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.	

**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.*

References:

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2. Influenza. 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.

3. Ministry of Health, Singapore. Weekly Infectious Disease Bulletin (2018). Available at: https://www.moh.gov.sg/resources-statistics/infectious-disease-statistics/2018/weekly-infectious-diseases-bulletin. Accessed 24 April 2019.

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6. Graaf HD, Faust SN. Expert Rev Vaccines 2015;14:1055-1063.

7. Esposito S, Bonanni P, Maggi S, et al. Hum Vaccin Immunother 2016 Jul 2;12(7):1777-94.

8. National Adult Immunisation Schedule-Recommendations for Adult Vaccinations. MOH Circular 23/2017, dated 19 September 2017.

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 reservoir such as pigs and wild birds, and as such has a geographic preference for rural areas. 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 that 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.

Incidence

JEV is the most common vaccine-preventable cause of encephalitis in Asia and is present in most parts of Asia and 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.[4] In contrast, the 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.[3] It is endemic in some agricultural areas in some neighbouring countries.

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 lack of the necessary swine host. It is recommended for persons traveling to regions with JEV infection risk.

Strong recommendation; moderate quality of evidence.

Table 11. JEV Vaccine for Adults

Vaccine type	Live attenuated (IMOJEV)	Inactivated (IXIARO)
Description	Each dose contains 4 to 5.8 log plague-forming units of live, attenuated, recombinant JEV.	Each dose contains 6 mcg (total protein content) 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%.[5-7]	A meta-analysis of randomised controlled trials of the inactivated vaccine found a seroprotection rate of 95% after the 2-dose series.[8]
Indication/ Target population	Prevention of JE infection. Vaccination is strongly recommended for people traveling to and staying for 1 month or more 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).[1,9] Travelers to an area with an ongoing JE outbreak.	
Schedule	Single dose 30 days before travel.	Two doses taken 1 month apart, with the second dose preferably 30 days or more before travel. If risk of exposure persists after 1 year, a booster is recommended after 1 to 2 years of the primary vaccination.

Vaccine type	Live attenuated (IMOJEV)	Inactivated (IXIARO)
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 due to immunodeficiency or immunosuppression.	
Precautions	Postpone administration in patients with acute severe illness. 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	Contraindicated	
Medisave	No	

Strong recommendation; moderate quality of evidence.

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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 and rash, and may lead to secondary bacterial infections such as otitis media and pneumonia.[1,2] 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 96 to 99% under the National Childhood Immunisation Programme.[3] However, 52 and 37 cases of measles have been reported in Singapore in 2017 and 2018, respectively.[4] The corresponding rates for mumps were 524 and 474 cases; and for rubella, 15 and 19 cases. 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.[5]
Indication/ Target population	Prevention of measles, mumps and rubella[1,2,6] • Among adults, vaccination is recommended for all adults 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 have become advocated by some groups. • Immunocompromised patients specifically for the following only: 3 months after chemotherapy and 6 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. • Unvaccinated women planning to become pregnant should be vaccinated 3 months before conceiving. Pregnancy status should be confirmed prior to vaccine administration. They should be advised not to get pregnant until 3 months after vaccination.

Schedule	Two doses given at least 28 days apart.[7,8] 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
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 7 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

CCID50: 50% Cell Culture Infectious Dose.
Strong recommendation; strong quality of evidence.

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2. Ong A, Goh KT, eds. A Guide on Infectious Diseases of Public Health Importance In Singapore (7th Edition). Singapore: Ministry of Health; 2011.

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8. Centers for Disease Control and Prevention. Recommended Adult Immunization Schedule—United States – 2015. Atlanta, GA: Centers for Disease Control and Prevention; 2015.

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

While the incidence of meningococcal disease is high in sub-Saharan Africa, it is rare in Singapore, with only 9 cases reported in 2018.[3,4] 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 may be boosted at age 16 years).

MPSV4 polysaccharide vaccine is the only licensed meningococcal vaccine for adults aged ≥56 years and requires one dose.

In Singapore, the vaccine should be given to adults traveling 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 vaccine (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.	Each dose contains 60 mcg each of *N. meningitidis* serogroup B rLP2086 subfamilies A and B

Vaccine type	Polysaccharide vaccine	Conjugate vaccine	Recombinant lipidated protein vaccine (serogroup B)
Summary of evidence	Vaccines are seroprotective in 90% of healthy recipients.[3]	Vaccines are seroprotective in 98% of healthy recipients.[3]	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.
Indication/ Target population	Prevention of invasive meningococcal disease among high-risk groups:[1-3,6] • Those traveling to Benin, Burkina Faso, Burundi, Cameroon, Chad, Cote 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 traveling 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 under eculizumab therapy; • 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:[3,5] • Students living in dormitories, • Unvaccinated students, and, • 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.[6]

Vaccine type	Polysaccharide vaccine	Conjugate vaccine	Recombinant lipidated protein vaccine (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).[6]	Conjugate vaccine is to be given to patients aged 55 and below. Data on individuals aged 56 and older is limited. Conjugate vaccine is to be given to patients aged 55 and below. Data on individuals aged 56 and older is limited.	
Schedule	Single dose, at least 10 days prior to travel[3] 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]		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.
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.		

Vaccine type	Polysaccharide vaccine	Conjugate vaccine	Recombinant lipidated protein vaccine (serogroup B)
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.
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		

*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.moh.gov.sa/en/Hajj/HealthGuidelines/HealthGuidelinesDuringHajj/Pages/MeningococcalMeningitis.aspx.

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 slowly rises starting from age 35 years.[1] Patients aged 65 years and above are at high risk of morbidity and mortality.

Disease burden

In Singapore, the mean hospitalization rate for IPD was 380 cases per year during the period of 2000 to 2008.[2] Around 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% because *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 three types of pneumococcal vaccines available to prevent IPD and pneumonia: the 10-valent conjugate vaccine, the 13-valent conjugate vaccine, and the 23-valent polysaccharide vaccine. Only the latter two **(Table 14)** are approved for use in adults. Studies on these two vaccines suggest that the conjugate vaccine may have a broader protection than the polysaccharide vaccine. The 10-valent conjugate vaccine is not approved for adults. In children, the conjugate vaccine is given to children 6 weeks and older, compared with 2 years and older for the polysaccharide vaccine.

Table 14. Pneumococcal Vaccine for Adults

Vaccine type	23-valent polysaccharide vaccine (PPSV23)	13-valent conjugate vaccine (PCV13)
Description	Each dose contains 25 mcg each of pneumococcal polysaccharides from 23 serotypes.	Each dose contains pneumococcal polysaccharides from 13 serotypes conjugated to carrier proteins.
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.[4] Efficacy in adults with underlying illnesses may be reduced.	Vaccine efficacy among adults ≥65 years old was around 75% against vaccine-type IPD.[5]
Indication/Target population	Prevention of IPD and pneumonia See **Table 15**	

Vaccine type	23-valent polysaccharide vaccine (PPSV23)	13-valent conjugate vaccine (PCV13)
Schedule	• See **Table 15** for schedule details. • When both PCV13 and PPSV23 are indicated, PCV13 should be administered first; 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] • A second dose may be considered 5 years after the primary vaccination among high-risk individuals.[1] • PPV23 or PCV13 may be co-administered with the influenza vaccine	
Administration	Subcutaneous or intramuscular	Intramuscular
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] Category C	
Medisave	Claimable (S$500 per year per account) for persons with higher risk of developing influenza-related complications and severe pneumococcal disease, respectively.	

Strong recommendation; low quality of evidence.

Table 15. Target Population for PCV13 and PPSV23[5-9]

Target Population	Corresponding Schedule		
	PCV13 Recommendation	PPSV23 Recommendation	Additional Doses
Adults aged 18-64 who are immunocompetent, otherwise healthy with no chronic diseases	Not indicated	Not indicated	Not indicated
Adults aged 18-64 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
Adults aged 18-64 years: • Cochlear Implant • CSF leaks	One dose first	One dose, 8 weeks after PCV13	Not indicated
Adults aged 18-64 years at high risk for invasive pneumococcal disease because of: • Functional / Anatomic asplenia [d] • Immunocompromising states [e]	One dose first	One dose, 8 weeks after PCV13	One booster after 5 years
Adults age ≥65 years, regardless of immune status	One dose first [f]	One dose, 1 year after PCV13 [f]	Not indicated
Adults aged 18-64 years with chronic renal failure [g,h]	One dose first [f]	One dose, 8 weeks after PCV13 [f]	Not indicated
Adults age ≥65 years with chronic renal failure [g,h]	One dose first [f]	One dose, 8 weeks after PCV13 [f]	Not indicated

[a] Including chronic obstructive pulmonary disease (COPD) or chronic bronchitis and emphysema , bronchiectasis, cystic fibrosis, interstitial lung fibrosis, pneumoconiosis and bronchopulmonary dysplasia (BPD).

[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.

[d] Including conditions such as homozygous sickle cell disease and coeliac syndrome that may lead to splenic dysfunction.

[e] Congenital or acquired immunodeficiencies, HIV infection, Leukemia, lymphoma, Hodgkin's disease, generalized malignancy, iatrogenic immunosuppression, solid organ transplant including renal transplant and multiple myeloma.

[f] If PPSV23 previously given, delay PCV13 for at least 12 months.

[g] Stage 4 and 5 and those on renal dialysis.

[h] 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.

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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 faecal-oral route. Infection is asymptomatic in most cases, but paralytic disease occurs in 1%.[2] There is no known cure for infantile paralysis.

Incidence

As a result of 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 Immunization Programme is at least 95%.[4,5]

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 to Singapore, polio vaccination remains a public health priority in Singapore.

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 16)** for exposure to poliovirus and may need 1 to 3 doses of inactivated polio vaccine (IPV), depending on how many doses they have had in the past.

The childhood polio immunisation schedule prior to 2013 comprised of six doses of oral polio vaccine (OPV). However, the World Health Organisation (WHO) no longer recommends an OPV only regimen to reduce the risk of vaccine-associated paralytic poliomyelitis (VAPP) associated with the use of OPV. Hence, the all-OPV schedule was replaced with a sequential IPV-OPV schedule, which consists of a four-dose IPV schedule and a fifth dose using OPV at age 10 to 11 years (primary five). 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 World Health Organization's (WHO) requirement.[6] 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.

In Singapore, both IPV and OPV are available **(Table 15)**. Even though OPV is easy to administer, IPV is preferred in the primary care setting due to the absence of risk for reactivation,[1-3] and hence is 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.

Strong recommendation; moderate quality of evidence

Table 16. 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 in compliance 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 traveling 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.	
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 a previous dose.

Vaccine type	Oral vaccine	Inactivated vaccine
Precautions	• Vaccination should be postponed in individuals with acute severe illness, or 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	

Strong recommendation; low 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, 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 17)**. Other available types of rabies vaccines recommended by the WHO include:

- Purified Vero cell rabies vaccine (PVRV), which contains inactivated and lyophilized 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 (HDCV) contains the Pitman-Moore L503 or Flury strain of rabies virus grown on MRC-5 human diploid cell culture
- Primary Hamster Kidney Cell vaccine (PHKCV) uses the Beijing strain
- Purified duck embryo vaccine (PDEV) uses duck embryo cells as substrate.

Routine vaccination is not routinely recommended.[1-3] Pre-exposure prophylaxis is recommended for high-risk groups, such as those traveling 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 18)**.[1,2] In addition, post-exposure prophylaxis may include administration of rabies immunoglobulin.

Table 17. 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 Fury 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 traveling 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 18)**
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 is emerging still **Post-exposure prophylaxis:[4]** • Please refer to **Table 18**.
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 need to be one of the WHO-approved vaccines.
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 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 antibodies may be performed every 2 years.[3] Booster may be given if antibody titres fall below 0.5 IU/mL.

Strong recommendation; low 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 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 is 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** summarizes the recommendations by bite category and immune status. Injuries to the face and neck should be assessed and treated with greater urgency.

Table 18. 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 14-28 • 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 14-28 • A fifth dose given on Day 28 is recommended for immunocompromised individuals • RIG is recommended
Previously immunized 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 19. 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 [vCJD] agent, and, theoretically, the Creutzfeldt-Jakob Disease [CJD] agent), cannot be completely eliminated.
Pregnancy and breastfeeding	• There are no data with use in pregnant women to inform a drug-associated risk. It 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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SMALLPOX VACCINE

Smallpox, caused by the smallpox virus (genus Orthopoxvirus) was an infection characterised by generalised vesicular rash.[1,2] Complications included osteomyelitis, arthritis and conjunctivitis. There was no available cure for smallpox.

Smallpox is the first disease to be eradicated by vaccination; eradication was declared in December 1979.[2] The vaccine used in eradication was a live attenuated preparation of vaccinia virus that induces protection against smallpox and other orthopox viruses such as monkeypox. The vaccine was administered through scarification using a bifurcate needle. Adverse reactions included mild satellite lesions or non-descript rashes. Systemic adverse events, such as disseminated vaccinia, vaccinia necrosum and encephalitis were rare.

At present, the smallpox vaccine is no longer available for use among civilians.[1-3] Control of smallpox is done mainly through surveillance. Healthcare personnel should immediately notify the Ministry of Health of Singapore Communicable Disease Surveillance Team (telephone number: 98171463) for any suspicion of smallpox.[3]

Strong recommendation; low quality of evidence

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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.[1-3] 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 they thrive 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. Diphtheria may develop in both children and adults, with those aged 40 to 64 years particularly at risk.[4]

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.[1]

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 108 reports of pertussis in the 2018.[5]

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 many subgroups. Adult vaccination using Tdap **(Table 20)** boosts waning immunity to tetanus and diphtheria vaccines and reduces carriage of pertussis among adults. The National Adult Immunisation Schedule does not yet recommend Tdap in non-pregnant adults pending more local data.[8]

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

Table 20. 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 hemagglutinin and 2.5 mcg of pertactin.	Each dose contains 2 IU of diphtheria toxoid and 20 IU of tetanus toxoid.
Summary of evidence	A review of field experience with Tdap in Denmark showed that the vaccine was immunogenic in 77% of adult recipients.[9] 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, depending on the antibody produced.[10]	
Indication/Target population	Booster vaccination to reduce morbidity of tetanus, diphtheria and pertussis. Tdap vaccination is recommended in the following groups:[1,2,11] • Adults aged 19 to 64 years with no previous history of immunization or if their last vaccination was at least 10 years ago • Pregnant women during each pregnancy, administered from 16 through 32 weeks' gestation, regardless of previous receipt of Tdap. Tdap can also be considered for pregnant women after 32nd week of gestation during each pregnancy. Maternal vaccination may afford less protection for infants, but would potentially protect the mother from pertussis infection and thereby reduce the risk of exposure to her infant. • If the single dose Tdap was not administered during pregnancy, it should be administered immediately post-partum.	Booster vaccination to reduce morbidity of tetanus and diphtheria. Td vaccination is recommended in the following groups:[1,2] • Adults including the elderly if their last vaccination was at least 10 years ago, • Adults in close contact with an infant aged less than 12 months,[4] • Healthcare personnel with direct patient contact. • For pregnant women who are unvaccinated against tetanus, Tdap should be used in place of one of the 3 Td injections.
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	

	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.[3]	
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.

References:

1. Ong A, Goh KT, eds. A Guide on Infectious Diseases of Public Health Importance In Singapore (7th Edition). Singapore: Ministry of Health; 2011.

2. World Health Organization. Vaccine-preventable diseases and vaccines. In: World Health Organization. International Travel and Health. Geneva: World Health Organization; 2012.

3. Centers for Disease Prevention and Control. Tdap (Tetanus, Diphtheria, Pertussis) Vaccine Information Sheet. Available at: http://www.cdc.gov/vaccines/hcp/vis/vis-statements/tdap.pdf. Accessed 10 June 2019.

4. Centers for Disease Prevention and Control. Epidemiology and Prevention of Vaccine-Preventable Diseases. Atkinson W, Hamborsky J, Wolfe S, eds. 12th ed. Washington DC: Public Health Foundation, 2012.

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11. Liang JL, Tiwari T, Moro P, et al. Prevention of Pertussis, Tetanus, and Diphtheria with Vaccines in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2018 Apr 27;67(2):1-44.

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 21** describes the recommendations for tetanus post-exposure prophylaxis in adults.

Table 21. Tetanus post-exposure prophylaxis recommendations in adults[2]

No. of doses of absorbed tetanus-toxoid-containing vaccines in <5 years	Clean and minor wound		All other wounds*	
	Tdap or Td†§	TIG	Tdap or Td†	TIG§
Unknown or <3	Yes	Yes	Yes	Yes
≥3	No¶	No	No**	No

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

*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 immunized against pertussis, tetanus or diphtheria should receive one dose of Tdap for wound management and as part of the catch-up series.

§Persons with HIV infection or severe immunodeficiency who have contaminated wounds should also receive TIG, regardless of their history of tetanus immunization.

¶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 22. Tetanus post-exposure prophylaxis vaccine descriptions

Vaccine type	Tetanus toxoid	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.
Summary of evidence	After three properly spaced doses, recipients achieve antitoxin levels considerably greater than the protective level of 0.1 IU/mL.[3] After 10 years from the last dose, most persons have antitoxin levels that only approach the minimal protective level.	

Vaccine type	Tetanus toxoid	Tetanus immunoglobulin
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.	Single dose. Double the dose for dirty deep wounds with tissue destruction, infected wounds, if the injury occurred 24 hours before administration, or 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, generalized urticaria or oedema, dizziness, hypotension, myalgia, arthralgia and headache	• Local pain and tenderness at the injection site • Fever, cutaneous reactions and chills
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	Data on pregnant or breastfeeding women is lacking – administer only when benefit clearly outweighs risks.[1,2] Category C	

Strong recommendation; strong quality of evidence

References:

1. Tiwari TSP. Tetanus. In: Centers for Disease Prevention and Control. Manual for the Surveillance of Vaccine-Preventable Diseases. Available at: http://www.cdc.gov/vaccines/pubs/surv-manual/chpt16-tetanus.html. Accessed 10 June 2019.

2. Liang JL, Tiwari T, Moro P, et al. MMWR Recomm Rep 2018;67(No. RR-2):1–44.

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TUBERCULOSIS: BACILLUS-CALMETTE GUERIN VACCINE

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, in a chronic airborne-transmitted infection that commonly infects the lungs, but may disseminate to other lung lobes (miliary TB) or other body parts.[1,2] Common presentations of extra-pulmonary TB include TB meningitis, TB osteomyelitis, TB lymphadenitis or infections of the gastrointestinal tract. The Bacillus-Calmette-Guerin (BCG) vaccine **(Table 23)**, an attenuated vaccine from *M. bovis*, is intended to prevent the progression of TB to miliary TB or TB meningitis in childhood.[1]

Disease burden

In Singapore, the prevalence of TB is around 40 cases per 100,000 population.[1] In 2014, 1,454 new cases of TB were reported, for an incidence of 26 cases per 100,000.[3] The continued transmission of TB in the community necessitates decreasing morbidity through BCG vaccination. BCG vaccination is part of the National Childhood Immunisation Programme, and coverage has been at least 98% since 2008.[4]

Vaccination

BCG is currently the only available TB vaccine. Whilst BCG has demonstrated effectiveness in a few populations, protection has not been consistent against all forms of TB and in all age groups.

There is evidence from meta-analysis of RCTs that there is a role for the BCG vaccine during the neonatal period for reduction in severe TB (meningitis and military TB).[5]

BCG vaccination is recommended in countries or settings with high incidence of TB and/or high leprosy. A selective vaccination strategy according to risk profile is required for adults at risk, and may be recommended for uninfected, unvaccinated individuals who are at high risk of infection. These include those with an occupational risk of exposure, such as healthcare personnel, personnel of long-term care facilities, prison personnel, and workers with exposure to cattle or monkeys.

Weak recommendation, moderate quality of evidence

Tuberculin skin testing is recommended before vaccination to confirm lack of current or previous infection.[1]

Strong recommendation; low quality of evidence.

Table 23. BCG Vaccine for Adults

Description	Each dose contains $2x10^6$ to $8x10^6$ colony-forming units of an attenuated strain of M. bovis (BCG) Danish strain 1331.
Summary of evidence	A meta-analysis on 132 studies found that BCG vaccination reduced pulmonary TB by 13% and miliary TB by 46% in tropical populations.[5]
Indication/Target population	In adults, prevention of tuberculosis infection Adults at high risk include those with occupational exposure to TB
Schedule	Single dose. Booster is not recommended.
Administration	Intradermal injection.
Storage and handling	Keep refrigerated (between 2°C and 8°C). Do not freeze. Protect from light.

Common adverse events	Local reactions at the injection site.
Contraindications	• Anaphylaxis to any vaccine component • Immunocompromised patients
Precautions	• Administration should be postponed in individuals with acute severe illness. • BCG vaccination does not replace other preventive measures.
Pregnancy and breastfeeding	Pregnant women should not receive the vaccine. Vaccination should be avoided in breastfeeding women. Category C
Medisave	No

Strong recommendation; moderate quality of evidence.

References:

1. Tuberculosis. In: Ong A, Goh KT, eds. A Guide on Infectious Diseases of Public Health Importance In Singapore (7th Edition). Singapore: Ministry of Health; 2011.

2. 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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4. Ministry of Health, Singapore. Available at: https://www.moh.gov.sg/docs/librariesprovider5/resources-statistics/reports/childhood-immunisation.pdf. Accessed 08 June 2019.

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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, and milk and milk products.[1,2] Faecal–oral transmission may also occur.

In Singapore, 65 and 43 cases of typhoid fever were reported in 2017 and 2018, respectively.[3]

Vaccine description

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

Weak recommendation; moderate quality of evidence

The available typhoid vaccines in Singapore include the injectable polysaccharide vaccine and a live oral vaccine **(Table 24)**.

Table 24. Typhoid Vaccine for Adults

Vaccine type	Polysaccharide vaccine	Live 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)	Each oral dose consists of an enteric-coated oral capsule, containing contains *Salmonella enterica* serovar Typhi Ty21a (≥2 x 10^9 viable cells per capsule.
Summary of evidence	Vaccination confers protective efficacy of 55% (95% CI 30% to 70%) against typhoid fever.[4]	Vaccination confers protective efficacy of 48% (95% CI 34% to 58%)[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).	

Vaccine type	Polysaccharide vaccine	Live vaccine
Schedule	Single dose. Booster may be given every 3 years if risk persists.	One capsule taken on day 1. The second capsule should be taken on day 3 and the third capsule on day 5.* In the case of travel from a non-endemic area to an endemic area, an annual booster consisting of three doses is recommended.
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.	The blister containing the vaccine capsules should be inspected to ensure that the foil seal and capsules are intact. The capsule should be taken approximately one hour before a meal, with a cold or lukewarm (≤37°C) drink. The vaccine capsule should not be chewed and should be swallowed as soon as possible after placing in the mouth.
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	• Abdominal pain, nausea, diarrhoea, vomiting • Fever, influenza-like illness • Headache • Rash
Contraindications	Anaphylaxis to any vaccine component or a previous dose	• Anaphylaxis to any vaccine component or a previous dose • Congenital or acquired immune deficiency (including patients receiving immunosuppressive or antimitotic drugs). • Acute febrile illness or during an acute gastrointestinal illness. Vaccination should be postponed until after recovery.

**Unless the immunisation schedule of 3 vaccine capsules is completed, an optimal immune response may not be achieved. Even after three doses, not all recipients of the vaccine will be fully protected against typhoid fever. Travellers should take all necessary precautions to avoid contact with or ingestion of potentially contaminated food or water. Protection against typhoid fever commences approximately 7-10 days after ingesting the third dose of vaccine. Under conditions of repeated or continuous exposure to S. typhi, protection persists for at least 3 years.*

Vaccine type	Polysaccharide vaccine	Live vaccine
Precautions	• Administration should be postponed in individuals with acute severe illness. • Vaccination does not replace food and water hygiene practices.	• Vaccination should not commence within 3 days after completing treatment with any antibacterial agents. Antibacterial therapy should not commence within 3 days after the last dose of the vaccine. • If malaria prophylaxis is also required, the fixed combination of atovaquone and proguanil can be given concomitantly with the vaccine. Doses of mefloquine and the vaccine should be separated by at least 12 hours. For other antimalarials, there should be an interval of at least 3 days between the last dose of the vaccine and the first dose of malaria prophylaxis. • May be administered concomitantly with the live attenuated vaccines yellow fever vaccine and oral polio vaccine.
Pregnancy and breastfeeding	Pregnant women may receive the vaccine. Category C Vaccination should be given with caution in breastfeeding women.	Give to a pregnant woman only if clearly needed. There are no data regarding administration of the vaccine to nursing mothers.
Medisave	No	

Strong recommendation; moderate quality of evidence.

References:

1. Typhoid and paratyphoid fever. In: Ong A, Goh KT, eds. A Guide on Infectious Diseases of Public Health Importance In Singapore (7th Edition). Singapore: Ministry of Health; 2011.

2. 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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VARICELLA VACCINE AND POST-EXPOSURE PROPHYLAXIS

The *Varicella zoster* virus (VZV), a herpesvirus, 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 25)** intended for the prevention of varicella.[3] The vaccine is also found in combination preparations with MMR.

Table 25. Varicella Vaccine for Adults

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
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. • Should not be administered together with the MMR vaccine. • 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. Category C Caution should be exercised when administering to breastfeeding mothers, as VZV may be secreted in breast milk.
Medisave	No

Strong recommendation; moderate quality of evidence.

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. Post-exposure prophylaxis after 5 days of exposure is not recommended.[3]

People without evidence of immunity who have contraindications to vaccination and who are at risk for severe varicella and complications are recommended to receive postexposure 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. Varicella zoster immunoglobulin provides maximum benefit when administered as soon as possible after exposure but may 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 postexposure prophylaxis among immunocompromised people are limited.

The zoster vaccine has no role in post-exposure prophylaxis.[3]

Weak recommendation; moderate quality of evidence.

References:

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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6. Recommendations of the Immunization Practices Advisory Committee (ACIP) Varicella-Zoster Immune Globulin for the Prevention of Chickenpox. MMWR Morb Mortal Wkly Rep 1984;33(7);84-90,95-100.

7. Marin M, Lopez AS. Varicella (Chickenpox). Available at: https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-related-infectious-diseases/varicella-chickenpox. Accessed 05 December 2019.

YELLOW FEVER VACCINE

Yellow fever (YF) is caused by the yellow fever virus (genus Flavivirus).[1,2] Endemic in sub-Saharan Africa and north to central South America, infection is usually asymptomatic but can lead to an acute biphasic illness. The first is characterised by fever, muscle pain, headache, chills, anorexia, nausea, vomiting and bradycardia. Around 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. Fatality rate is 50% and death occurs within 10 to 14 days of the onset of illness.[2]

Epidemiology

Yellow fever is a mosquito-borne infection. In urban areas, transmission is from human to human via mosquito (*Aeges aegypti*) vector.[2] In rural areas, monkeys are reservoirs of infection.

There have been recent yellow fever outbreaks in Brazil, Angola, the Democratic Republic of Congo and Uganda in 2016-2017.[3,4] Of significance, 11 Chinese workers infected during the 2016 yellow fever Angola outbreak imported YF into China.[5] There have been no reported cases of yellow fever in Singapore in recent years.[6] Thus, the risk of transmission exists only for travellers to the aforementioned areas where yellow fever is endemic. These travellers should receive yellow fever vaccination **(Table 26)**, a live attenuated vaccine, at least 10 days prior to departure.[1,2]

Yellow fever vaccination requirements are regulated by the International Health Regulations.

Table 26. 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 (i.e., pregnant women, hematopoietic stem cell transplant recipients, and HIV-infected persons). Fractional-dose yellow fever vaccine used in recent outbreak control circumstances is not recommended for routine use.
Administration	Intramuscular injection (deltoid). Do not inject intravascularly.
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-Barre 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 incidence of YEL-AND and YEL-AVD in the USA is 0.8 and 0.3 per 100,000 doses administered, but may be higher (1.2 and 2.2 per 100,000 doses) in people aged ≥60 years.*

Strong recommendation; moderate quality of evidence.

References:

1. Yellow fever and other viral haemorrhagic fevers. In: Ong A, Goh KT, eds. A Guide on Infectious Diseases of Public Health Importance In Singapore (7th Edition). Singapore: Ministry of Health; 2011.

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ZOSTER VACCINE

Reactivation of 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 shingles vaccine, but generally should make sure the shingles rash has disappeared before getting vaccination.

Zoster is vaccine preventable via a live attenuated vaccine **(Table 27)**, which is recommended for adults aged 60 years and older. However, Zostavax is approved for use for those 50 years and older.

Table 27. Zoster Vaccine for Adults

	Live attenuated	Recombinant, adjuvanted
Description	Each dose contains at least 19,400 plaque-forming units of the attenuated VZV	Each dose contains lyophilized varicella zoster virus glycoprotein E (gE) antigen component, to be reconstituted with the accompanying vial of AS01B adjuvant suspension component.[6]
Summary of evidence	Clinical trials on elderly individuals without prior zoster reported a 50% to 70% reduction in the incidence of zoster.[3]	A randomized, 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 to 99.0; p<0.001) against zoster.[7]
Indication/Target population	Prevention of zoster in adults aged 50 years and older, even in the absence of a previous zoster episode.[4,5] Revaccination is not recommended.	Prevention of zoster in adults aged 50 years and older.
Schedule	Single dose. Booster is not recommended.	Administer 2 doses (0.5 mL each) at 0 and 2 to 6 months.
Administration	Subcutaneous injection	Intramuscular injection
Storage and handling	Store below -15°C.	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	• Redness, pain and swelling at the injection site • Fever, headache, body aches, malaise, nausea and itching	• Injection site pain, redness and swelling • Myalgia, fatigue, headache, shivering, fever and gastrointestinal symptoms

	Live attenuated	Recombinant, adjuvanted
Contraindications	• Anaphylaxis to any vaccine component or a previous dose, including neomycin and gelatine • Immunocompromised state, except those with leukaemia in remission and who have not received chemotherapy or radiation for at least 3 months.[4]	Anaphylaxis to any component of the vaccine or a previous dose
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.	Review the immunization 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	Pregnant women should not receive the vaccine. Pregnancy should be avoided until 3 months after vaccination. Category C Caution should be exercised when administering to breastfeeding mothers, as VZV may be secreted in breast milk.	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.
Medisave	No	

Strong recommendation; moderate quality of evidence.

The zoster vaccine has no role in post-exposure prophylaxis.[3]

Weak recommendation; moderate quality of evidence.

References:

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

2. Chickenpox In: Ong A, Goh KT, eds. A Guide on Infectious Diseases of Public Health Importance In Singapore (7th Edition). Singapore: Ministry of Health; 2011.

3. Varicella. In: Centers for Disease Prevention and Control. Epidemiology and Prevention of Vaccine-Preventable Diseases. Atkinson W, Hamborsky J, Wolfe S, eds. 12th ed. Washington DC: Public Health Foundation, 2012.

4. Esposito S, Bonanni P, Maggi S, et al. Hum Vaccin Immunother. 2016 Jul 2;12(7):1777-94.

5. Dooling KL, Guo A, Patel M, et al. MMWR Morb Mortal Wkly Rep 2018;67:103–108.

6. Zoster Vaccine (Recombinant, Adjuvanted) suspension for intramuscular injection (Shingrix®) [prescribing information]. USA: GlaxoSmithKline Biologicals; 2017.

7. Lal H, Cunningham AL, Godeaux O, et al. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. N Engl J Med. 2015 May 28;372(22):2087-96.

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

Table 28. 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
Respiratory syncytial virus	RSV F Nanoparticle	Recombinant subunit (non VLP)	Novavax

Pathogen	Candidate vaccine	Immunogen platform	Sponsor
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

References:

1. World Health Organization Vaccine Pipeline Tracker. Available at: https://www.who.int/immunization/research/vaccine_pipeline_tracker_spreadsheet/en/. Accessed 09 September 2019.

Chapter 5:
Vaccination of Special Populations

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).

Table 29 summarizes the critical vaccines recommended for travel.

Table 30 shows other vaccines that may be given to unvaccinated travellers that have a high risk of exposure at their destination.

Table 29. 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, Cote 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, Cote d'Ivoire, Democratic Republic of Congo, Ecuador, Equatorial Guinea, Ethiopia, French, Guyana, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Guyana, Kenya, Liberia, Mali, Mauritania, Niger, Nigeria, Panama, Paraguay, Peru, Rwanda, South Africa, Senegal, Sierra, Leone, Sudan, Suriname, Togo, Trinidad & Tobago, Uganda, Venezuela

Strong recommendation; low quality of evidence

Table 30. Vaccine recommendation by destination[1,4]

Country/ region of travel or special circumstance	Cholera	Hepatitis A	Hepatitis B	Japanese encephalitis*	Meningococcal disease*	Rabies	Typhoid	Yellow fever*
Africa and Middle East								
East Africa	++							+
Saudi Africa (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 29**.

**Please refer also to the Saudi Arabian Ministry of Hajj website (http://haj.gov.sa/english/pages/default.aspx) 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.

Strong recommendation; low quality of evidence.

Last-Minute Travel

Vaccines typically take 2 weeks to elicit some 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.[3]

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.[3] 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.[3]

Strong recommendation; low quality of evidence.

References:

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

2. Ong A, Goh KT, eds. A Guide on Infectious Diseases of Public Health Importance In Singapore (7th Edition). Singapore: Ministry of Health; 2011.

3. CDC Yellow Book 2020: Health Information for International Travel. Atlanta, GA: Centers for Disease Control and Prevention; 2019.

4. Centers for Disease Control and Prevention. Pregnant Travellers. Available at: wwwnc.cdc.gov/travel/yellowbook/2016/advising-travelers-with-specific-needs/pregnant-travelers. Accessed 23 March 2016.

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 31**.[1,2] Furthermore, Singapore requires a yellow fever vaccination certificate prior to entry for travellers from high-risk countries.[3]

Table 31. 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, Cote 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

References:

1. Centers for Disease Prevention and Control. Health Information for Travelers to Singapore. Available at: http://wwwnc.cdc.gov/travel/destinations/traveler/none/singapore. Accessed 10 June 2019.

2. Public Health Agency of Canada. Singapore. Available at: http://www.phac-aspc.gc.ca/tmp-pmv/countries-pays/country-pays-eng.php?id=383. Accessed 10 June 2019.

3. Immigration and Checkpoints Authority, Singapore. Entry Requirements. Available at: www.ica.gov.sg/page.aspx?pageid=95. Accessed 10 June 2019.

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 immunization status and vaccinate, thus protecting mother and neonate. Although pregnancy is considered to be 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] Sufficiently high-quality data on vaccines in pregnancy that would enable a strong recommendation are often lacking (except for the growing body of evidence for the benefit of influenza vaccination in pregnant women in developing countries).[2] Hence, 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.[3]

Table 32 summarizes the general recommendations for vaccination in pregnant women.[4,5] In addition. For non-pregnant women who intend to get pregnant, 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, meningococcal disease or tetanus.

Table 32. Vaccinations for pregnant women[4,5]

Indication	Vaccines recommended
Routine	Influenza (inactivated) Tdap (preferably between 16-32 weeks, see Tdap section)
May be given if indicated after 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.
Not recommended	Human papillomavirus vaccine
Contraindicated	Varicella vaccine Zoster vaccine Measles-mumps-rubella vaccine Yellow Fever Vaccine
Insufficient data to make a recommendation. Delay if possible. Discuss risk and benefit.	Japanese encephalitis Haemophilus influenzae B vaccine

See Vaccination for Travellers for additional information about travel vaccinations for pregnant women.
Strong recommendation; moderate quality of data

Live vaccines may be given only until more than 1 month from the 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.[6]

Strong recommendation; low quality of data

References:

1. General recommendations for immunization. In: Centers for Disease Prevention and Control. Epidemiology and Prevention of Vaccine-Preventable Diseases. Atkinson W, Hamborsky J, Wolfe S, eds. 12th ed. Washington DC: Public Health Foundation, 2012.

2. Advisory Committee on Immunization Practices Workgroup on the Use of Vaccines during Pregnancy and Breastfeeding. Guiding Principles for Development of ACIP Recommendations for Vaccination during Pregnancy and Breastfeeding (April 2008). Atlanta, GA: Centers for Disease Prevention and Control; 2008.

3. CDC. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2011;60:26.

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. 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 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 similarly are at 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 33** summarizes the recommendations for vaccinations for these patients.

Table 33. Vaccination recommendations for adult patients with chronic medical conditions or immunocompromised states[1-3]

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
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

** 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.*

Condition	Prioritised vaccine	Routine vaccine
Chronic liver disease	• 23-valent pneumococcal vaccine	• Annual influenza vaccine • Hepatitis A and B vaccines, if unvaccinated
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
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
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	

***These include, but not limited to, the following: corticosteroids (oral prednisolone ≥ 2 mg/kg per day or ≥ 20 mg per day for more than 14 days duration, until >4 weeks after high dose steroid use), chemotherapy, radiation therapy, post-organ-transplant therapy, certain anti-rheumatic drugs, and drugs used for the management of inflammatory bowel disease. 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.*

Condition	Prioritised vaccine	Routine vaccine
Recipients of solid-organ transplant	Patients should be vaccinated with all indicated vaccines with the following schedule: • The vaccination of inactivated vaccines should be completed 2 weeks before transplantation. • The vaccination of live vaccines should be completed 4 weeks before transplantation. • After transplantation, live vaccines are generally contraindicated. Inactivated vaccines may be given if indicated.	

Strong recommendation; moderate quality of evidence

References:

1. CDC. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2011;60:26.

2. Ong A, Goh KT, eds. A Guide on Infectious Diseases of Public Health Importance In Singapore (7th Edition). Singapore: Ministry of Health; 2011.

3. Public Health Agency of Canada. Vaccination of Specific Populations. Available at: http://www.phac-aspc.gc.ca/publicat/cig-gci/p03-07-eng.php#a3. Accessed 10 June 2019.

4. CDC. Immunocompromised travellers. Available at: https://wwwnc.cdc.gov/travel/yellowbook/2020/travelers-with-additional-considerations/immunocompromised-travelers. Accessed 26 November 2019.

VACCINATION OF ADULTS IN THE HEALTHCARE SETTING

There are many groups at risk 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 disease. 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, whichever is applicable.

Residents of long-term care and nursing homes are at significant risk because of the potentially rapid spread of infection 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 infection. 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 infection, but will also prevent transmission of these infections to patients.

Table 34 summarizes the vaccination recommendations for adults in the healthcare setting.

Table 34. 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 after 1 to 2 months of series completion or routinely. • Two doses of varicella vaccine spaced 4 to 8 weeks apart • At least 2 doses of measles-mumps-rubella vaccine spaced 28 days apart • Vaccines for meningococcal disease, typhoid and poliomyelitis should be given to laboratory staff handling infectious agents causing these diseases.	• Annual influenza vaccine • Single dose of Tdap

Strong recommendation; moderate quality of evidence

References:

1. CDC. Immunization of Health-Care Personnel: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2011;60(RR07):1-45.

2. Schaffner W, Rehm SJ. Nurses Urged to Take a Role in Vaccinating Older Adults. Available at: www.adultvaccination.org/professional-resources/nbna-geriatric-vaccination.pdf. Accessed 10 June 2019.

CHAPTER 6: APPENDICES

Quick Guide for Adult Vaccination

	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				Strongly recommended	
MMR	2 doses at least 28 days apart for those without two documented doses as children					
Pneumococcal	See Table 15					
Tdap	1 dose					
Varicella	2 doses (0-1 mo schedule)					
Zoster					1 dose for the live attenuated vaccine 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)		Screen first for circulating IgG levels 2 doses (0-6 mo schedule) for susceptible individuals			
Hepatitis B	3 doses (0-1-6 mo schedule)					
Meningococcal	1 dose every 5 years					
Pneumococcal	See Table 15					

**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.

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
Cholera vaccine (oral attenuated)	Vaxchora (PaxVax)	Protection against disease caused by *V. cholerae* serogroup O1 in adults 18 through 64 years of age traveling to cholera-affected areas		Single dose ≥10 days before potential exposure
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)

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
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

Vaccine	Available Brands	Indication	Administration	Schedule (unvaccinated adults)
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	
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	
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 immunocom-promised).
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

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
Tuberculosis (Bacillus-Calmette-Guerin) vaccine	BCG Danish Strain 1331 (Statens Serum Institute) BCG Vaccine Glaxo (GlaxoSmithKline) Euro BCG (BB-NCIPD) Euro Pharma BCG (Euro Pharma) Japan BCG Vaccine (Japan BCG Lab)	Prevention of tuberculosis infection in previously unvaccinated individuals, especially those at high risk (e.g., occupational exposure)	ID	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
Typhoid (oral attenuated)	Vivotif (PaxVax)		Oral	One dose on Days 1, 3 and 5. Booster after 3 years involving 3 doses.
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

Vaccine	Available Brands	Indication	Administration	Schedule (unvaccinated adults)
Yellow Fever	Stamaril (Sanofi Pasteur)	Prevention of yellow fever, particularly for travellers to endemic area.	IM/SQ	Single dose
Zoster vaccine, live attenuated	Zostavax (MSD)	Prevention of zoster in adults aged 50 years and older	SQ	Single dose
Zoster vaccine, recombinant, adjuvanted	Shingrix (GSK)		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.

VACCINATION GUIDE FOR SPECIAL POPULATIONS

Travellers

Recommended vaccination may vary according to the travel destination. Please refer to **Tables 27** and **28**.

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	
Cholera (oral inactivated)	Orally on empty stomach	2 doses 1 week apart, and a booster after 2 years	✓	✓		After 2 years
Cholera (oral attenuated)	Orally on empty stomach	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)	✓	✓	✓	
JE (attenuated)	SQ	Single dose	✓			After 1-2 years if risk persists
JE (inactivated)	IM	2 doses 1 month apart	✓	✓		
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	✓			

Immigrants to Singapore

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

Pregnant women

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	
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)	
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)	✓	✓	✓	
Influenza (quadrivalent)	IM	Single dose	✓			
Meningococcal (polysaccharide)	SQ	At least 1 dose	✓			
Meningococcal (conjugate)	IM		✓			
PCV13	IM	One PCV13 dose followed by PPSV23 after 2 months	✓			
PPSV23	SQ/IM			✓ (8 weeks after visit 1)		Single booster after 5 years

Chronic kidney disease patients

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

Chronic heart disease patients

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

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)	
Influenza (quadrivalent)	IM	Single dose	✓			
PCV13/PPSV23	See **Table 14** and **15**					

Chronic liver disease patients

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	
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	✓			

Non-malignant haematological disease patients

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

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)	
Influenza	IM	Yearly	✓			
PCV13/PPSV23	See **Table 14** and **15**					
Meningococcal disease	SQ	Two doses given 2 months apart	✓	✓		Every 5 years if needed
MMR	SQ	Two doses given 1 month apart	✓	✓		
Haemophilus influenzae B	IM (SQ for those with thrombocy-topaenia or bleeding)	3 doses given 1 month apart	✓	✓	✓	
Meningococcal	See **Table 13**					
Hepatitis A	IM	Two doses given 6 to 12 months apart	✓		✓	
Hepatitis B	See **Table 8**					

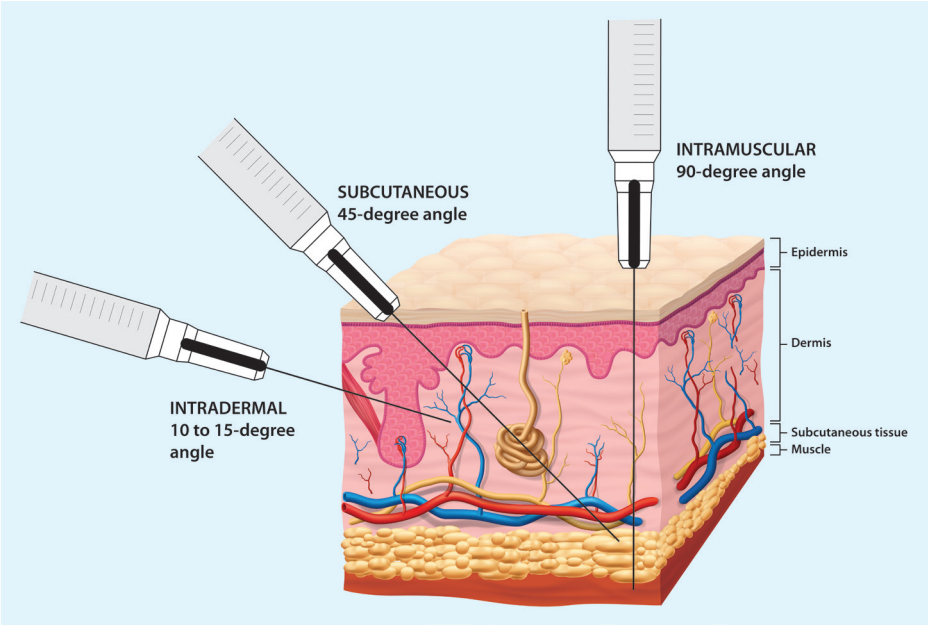
Adults in the healthcare setting

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	
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 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)								

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/