CLINICAL PRACTICE GUIDELINES ON ADULT VACCINATION IN SINGAPORE

Society of Infectious Diseases Singapore
Institute of Infectious Diseases and Epidemiology
College of Family Physicians Singapore
Chapter of Infectious Disease Physicians

Under the auspices of

SOCIETY OF INFECTIOUS DISEASE (SINGAPORE)

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Introduction

The epidemiology of infectious disease globally and in Singapore has changed dramatically since the turn of the century. The mortality and impact of disease due to infectious diseases have significantly decreased. Infectious diseases now rank below cardiovascular diseases, 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 improved 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, there are emerging infectious diseases and bioterrorism which 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 protects 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 tuberculosis, 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 encompass all age groups from 18 years and beyond, which can span 6 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.

These clinical practice guidelines on adult vaccination in Singapore aim 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.

These guidelines are meant only to guide clinical practice, and are not intended to replace medical judgement when managing adult individuals.

References:

1. World Health Organization. Singapore: WHO statistical profile. Available at: www.who.int/gho/countries/sgp.pdf?ua=1. Accessed 15 August 2015.
2. Ministry of Health, Singapore. Principal causes of death. Available at: www.moh.gov.sg/content/moh_web/home/statistics/Health_Facts_Singapore/Principal_Causes_of_Death.html. Accessed 03 November 2015.
3. Ong A, Goh KT, eds. A Guide on Infectious Diseases of Public Health Importance In Singapore (7th Edition). Singapore: Ministry of Health; 2011.
4. World Health Organization. Vaccine-preventable diseases and vaccines. In: World Health Organization. International Travel and Health. Geneva: World Health Organization; 2012.
5. Ministry of Health, Singapore. Preventive Health Services. Available at: https://www.moh.gov.sg/content/moh_web/home/statistics/Health_Facts_Singapore/Preventive_Health_Services.html. Accessed 15 August 2015.

Chapter 1: Methodology of Guideline Development and Level of Evidence

This clinical practice guideline on adult vaccinations in Singapore was developed through a collaboration between the Society of Infectious Diseases (Singapore), the Institute of Infectious Diseases and Epidemiology, the College of Family Physicians Singapore, and the Chapter of Infectious Diseases. The collaboration convened a committee of eight experts tasked to review the literature on adult vaccinations and develop recommendations for Singapore. The process was aided by a medical writer but the sponsor had no input into the content of the guidelines.

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 develop 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 took into account 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

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

RCT, randomised controlled trial.

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.
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

Recommendations to Improve Vaccine Coverage and Administration

Adult immunization is a cost-effective way of preventing morbidity and mortality in at-risk individuals. While data on adult vaccination coverage in Singapore is lacking, literature from other developed countries have identified several barriers to adult vaccination. These include:[1]

- 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 these 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. Assessment 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.[2] 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 the 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.[3] 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.

Vaccine storage and administration

Proper vaccine storage minimises vaccine degradation, vaccine administration errors, and injuries due to accidents. Refer to the section on *Vaccine Storage and Handling* on page 13.

Safe vaccine administration entails the appropriate delivery, timing, spacing, deferral, or withholding (contraindications) of adult vaccines. Refer to the section on *General Rules of Vaccination* on page 16.

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.[2,3] A retrospective study on 67 adult anaphylaxis patients in Singapore found that none were due to vaccinations.[4] 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 (www.hsa.gov.sg/content/dam/HSA/HPRG/Safety_Alerts_Product_Recalls_Enforcement/HSA_VAEReportingForm.pdf).[5]

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.[1,6] 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.[5] 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 • Persistent (more than three hours) inconsolable screaming • Hypotonic-hyporesponsive episode • 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, including febrile seizures • Encephalopathy	Within 14 days of vaccination
• Acute flaccid paralysis • Brachial neuritis • Intussusception • Thrombocytopaenia	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

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

AEFIs should be reported to the Vigilance Branch of the Vigilance, Compliance and Enforcement Division, Health Products Regulation Group, Health Sciences Authority of Singapore, using the Vaccine Adverse Event (VAE) Report (http://www.hsa.gov.sg/content/dam/HSA/HPRG/Safety_Alerts_Product_Recalls_Enforcement/HSA_VAEReportingForm.pdf; accessed 09 August 2015) or the Suspected VAE Online Reporting Form (http://eservice.hsa.gov.sg/adr/adr/vaeOnline.do?action=load; accessed 09 August 2015).

Strong recommendation; low quality of evidence.

Vaccines Storage and Handling

Vaccines are biological materials that can denaturate and deteriorate, which leads 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.[2,6] 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.[2,6] Note that 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. 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.

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.[6] 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.[6] For multi-dose vials, 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.

References:

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. 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.
3. Bohlke K, Davis RL, Marcy SM, et al. Risk of anaphylaxis after vaccination of children and adolescents. *Pediatrics* 2003;112:815-820.
4. Thong BY, Cheng YK, Leong KP, Tang CY, Chng HH. Anaphylaxis in adults referred to a clinical immunology/allergy centre in Singapore. *Singapore Med J* 2005;46:529-534.
5. Health Sciences Agency. Report Adverse Events related to Health Products. Available at: www.hsa.gov.sg/content/hsa/en/Health_Products_Regulation/Safety_Information_and_Product_Recalls/Report_Adverse_Events_related_to_health_products.html#AE Online Database. Accessed 15 August 2015.
6. Public Health Agency of Canada. National Guidelines for Immunization Practices. Available at: http://www.phac-aspc.gc.ca/publicat/cig-gci/p01-03-eng.php. Accessed 15 August 2015.

Chapter 3: General Rules of Adult Vaccinations

Types of Vaccinations

These guidelines categorise 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 these guidelines.

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, live attenuated 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 lesser 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

Some bacterial infectious cause pathology 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 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 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.[3]

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

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		
< 3-month stay	0.02 mL/kg (3.3 mg IgG/kg) IM	3 months
≥ 3-month stay	0.06 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)	1 g/kg IV	10 months
Post-exposure varicella prophylaxis	400 mg/kg IV	8 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.

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.[3-5] 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 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 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.

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.[3,5] 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 (eg, 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.[3,5] 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 81.

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 far exceeds 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.**
- **Pregnant or immunosuppressed household member.** The only vaccine that should not be administered in this situation is oral polio vaccine (OPV) 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.
- **Breastfeeding** with the exception of yellow fever vaccine, unless there is unavoidable travel to an area endemic for yellow fever.
- **Family history of AEFI.**
- **Administration of tuberculin skin test.** However, a TST may be falsely negative when performed within 4 weeks of MMR vaccination.
- **Multiple vaccines**.

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 in the past 3 months?
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

References:

1. National Institute of Allergy and Infectious Diseases. Types of vaccines. Available at: www.niaid.nih.gov/topics/vaccines/understanding/pages/typesvaccines.aspx. Accessed 15 August 2015.
2. Dintzis RZ. Rational design of conjugate vaccines. *Pediatr Res.* 1992;32:376-385.
3. General recommendation on 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.
4. King GE, Hadler SC. Simultaneous administration of childhood vaccines: an important public health policy that is safe and efficacious. *Pediatr Infect Dis J* 1994;13:394–407.
5. Rendi-Wagner P, Kollaritsch H. Principles of Immunization. In: Keystone JS, Kozarsky P, Freedman DO, Nothdurft HD, Connor BA. Travel Medicine, 3rd ed. Toronto: Elsevier Canada; 2013.
6. Ljungman P, Cordonnier C, Einsele H, et al. Vaccination of hematopoietic cell transplant recipients. *Bone Marrow Transplant* 2009;44:521-526.

Chapter 4:
Specific Vaccines for Adults

Cholera Vaccine

Cholera is an acute diarrhoeal illness caused by *Vibrio cholerae* 01, biotypes El Tor and classical, serotypes Inaba and Ogawa; and *V. cholerae* synonym Bengal (South Asia).[1] It is a legally notifiable disease in Singapore, and official reporting has identified that it occurs sporadically in Singapore, with only two notified cases in 2014.[2] It is a water-borne disease, and primary prevention is mainly through proper disposal of human waste, adequate supply of clean drinking water, and good food-handling practices. At present, cholera has an oral and a parenteral vaccine (Table 4). These vaccines are useful during humanitarian crisis relief missions, especially in water-affecting crises such as tsunamis, typhoons or floods.

Table 4. Cholera vaccine for adults

	Oral	Parenteral
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 0.5 mL injection contains approximately $8x10^{11}$ killed *V. cholerae* cells (strains dependent on brand)[2]
Summary of evidence	• A meta-analysis on 23 randomised and quasi-randomised trials found that cholera vaccines in general have an efficacy of 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, unlike parenteral vaccines.	• The US Pharmacopoeia states that the efficacy is 50%, based on field trials.[3]
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 severe diarrhoea due to cholera. In adults, it is advised for those who will be visiting areas where the risk of cholera infection is high.

	Oral	Parenteral
Schedule	• Two doses taken 1 week apart. If interval exceeds 6 weeks, restart with two doses. A booster dose may be given after 2 years. • The second dose should be given 7 days before travel.	• Two doses taken 1 week apart. If interval exceeds 6 weeks, restart with two doses. A booster dose may be given after 2 years
Administration	• Taken orally on an empty stomach. Avoid food or drinks 2 hours 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.	• Intramuscular, subcutaneous or intradermal injection
Storage and handling	• Keep refrigerated (between 2°C and 8°C). Do not freeze.	
Common adverse events	• Gastrointestinal symptoms including stomach pain and discomfort, diarrhoea, bloating, gas, nausea and vomiting • Headache	• Pain, erythema and induration at injection site • Fever, malaise and headache
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.	• Vaccination should be postponed during acute illness or pregnancy.[3] • During travel, exercise caution and hygienic practices with food and water intake. • Simultaneous administration with yellow fever vaccine can decrease antibody levels induced by either vaccines, although its true impact on efficacy is unclear. Thus, administration of yellow fever and cholera vaccines should have a 3-week interval, unless time constrains preclude this.[3] • Parenteral vaccine does not seem to interrupt *V. cholerae* transmission during outbreaks, and its widespread use during an outbreak may interfere with sanitary and therapeutic interventions.[3]

	Oral	Parenteral
Pregnancy and breastfeeding	May be given to pregnant and breastfeeding women	Vaccination should be postponed in pregnant women. There is no safety data on breastfeeding women.
Medisave	No	

Strong recommendation; moderate quality of evidence.

References:

1. Cholera. 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. Ministry of Health, Singapore. *Weekly Infect Dis Bull* 2014;11(53):1-8.
3. Ryan ET, Calderwood SB. Cholera vaccines. *Clin Infect Dis* 2000;31:561-565. Epub 2000 Sep 7.
4. Graves P, Deeks J, Demicheli V, Pratt M, Jefferson T. Vaccines for preventing cholera. *Cochrane Database Syst Rev*2000;(2):CD000974.

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 2014, there were only six reports of Hib infection.[3] Furthermore, Hib vaccination rates are increasing in Singapore. 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 5). Immunity is not lifelong, and boosters may be required for long-term protection.

Table 5. 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, IgG2 subclass immunodeficiency, or immunosuppression from cancer chemotherapy or HIV infection, and HSCT.[2]
Schedule	• At-risk adults require one dose of paediatric vaccine.
Administration	• Intramuscular injection • Subcutaneously for patients with thrombocytopaenia 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	• Up to S$400 per year per account

Strong recommendation; moderate quality of evidence.

References:

1. Haemophilus influenzae type B (Hib) disease. 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. Haemophilus influenzae type b. 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 Infect Dis Bull* 2014;11(53):1-8.
4. Decker MD, Edwards KM. Haemophilus influenzae type b vaccines: history, choice and comparisons. *Pediatr Infect Dis J* 1998;17:S113–S116.
5. Dockrell DH, Poland GA, Steckelberg JM, et al. Immunogenicity of three Haemophilus influenzae type b protein conjugate vaccines in HIV seropositive adults and analysis of predictors of vaccine response. *Vaccine* 1999;17:2779-2785.
6. Anderson P, Insel RA, Smith DH, et al. A polysaccharide-protein complex from Haemophilus influenzae type b. III. Vaccine trial in human adults. *J Infect Dis* 1981;144:530-538.
7. Barra A, Cordonnier C, Preziosi MP, et al. Immunogenicity of Haemophilus influenzae type b conjugate vaccine in allogeneic bone marrow recipients. *J Infect Dis* 1992;166:1021-1028.
8. Sever MS, Yildiz A, Eraksoy H, et al. Immune response to Haemophilus influenzae type B vaccination in renal transplant recipients with well-functioning allografts. *Nephron* 1999;81:55-59.

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 2014, there were 21 sporadic local cases and 71 sporadic imported cases of hepatitis A.[2] Outbreaks may occur, which are usually due to contaminated food. Nonetheless, contact tracing is recommended during potential outbreaks.

Strong recommendation; low quality of evidence

Vaccine description

The available adult hepatitis A vaccine contains formalin-inactivated hepatitis A whole-virus (Table 6). 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 6).

Table 6. 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%, although 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: • 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.
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 lost, irritability, headache. • Drowsiness, gastrointestinal symptoms (eg, 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

Strong recommendation; moderate quality of evidence.

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.

References:

1. Viral Hepatitis. 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. Ministry of Health, Singapore. *Weekly Infect Dis Bull* 2014;11(53):1-8.
3. Hepatitis A. 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.
4. Demicheli V, Tiberti D. The effectiveness and safety of hepatitis A vaccine: a systematic review. *Vaccine* 2003;21:2242-2245.

Hepatitis B Vaccine

Viral hepatitis B is the major cause of chronic viral hepatitis. It is caused by an orthohepadnavirus, which is transmitted through transfer of contaminated blood or serous fluids, sexual transmission, and vertical mother-to-child transmission.[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 2014, only 50 new cases of acute hepatitis B were reported.[5] Despite the low incidence and high immunity (since 2006, the childhood coverage of hepatitis B vaccine has ranged from 95% to 97% under the National Childhood Immunisation Programme[6]) in Singapore, 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

The available hepatitis B vaccine is a parenteral vaccine that contains 20 to 40 mcg of purified recombinant hepatitis B surface antigen (HbsAg) (Table 7).

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 7. Hepatitis B vaccine for adults

Description	• Each dose contains 20 to 40 mcg of purified recombinant HbsAg.
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, • Adults with diabetes, • International travellers to regions with high or intermediate hepatitis B prevalence, and, • People living with HIV.
Schedule	• 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.[2,3]
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] • Additional doses may also be given to patients undergoing haemodialysis, people living with HIV, or other immunocompromised patients.[2]
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$400 per year per account

Strong recommendation; moderate quality of evidence.

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 patients undergoing haemodialysis, people living with HIV or other immunocompromised patients, 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

Healthcare personnel who have contact with patients or blood have a risk of injuries, and should be tested for seroconversion after 1 to 2 months of the last vaccine dose or opportunistically at routine screenings by employee health.[2]

Strong recommendation; low quality of evidence

References:

1. Viral Hepatitis. 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. Hepatitis B. 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. World Health Organization. Vaccine-preventable diseases and vaccines. In: World Health Organization. International Travel and Health. Geneva: World Health Organization; 2012.
4. Ang LW, Cutter J, James L, Goh KT. Seroepidemiology of hepatitis B virus infection among adults in Singapore: a 12-year review. *Vaccine* 2013;32:103-110.
5. Ministry of Health, Singapore. *Weekly Infect Dis Bull* 2014;11(53):1-8.
6. Ministry of Health, Singapore. Preventive Health Services. Available at: https://www.moh.gov.sg/content/moh_web/home/statistics/Health_Facts_Singapore/Preventive_Health_Services.html. Accessed 15 August 2015.

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 two types of HPV vaccine, one protective against subtypes 16 and 18 (bivalent), and the other against subtypes 6, 11, 16 and 18 (tetravalent) (Table 8).[1,2] Both vaccines are inactivated subunit vaccines, and were intended to prevent HPV infection as well as premalignant cervical lesions and cervical cancer. Men should receive the tetravalent vaccine. The labelled indication for the HPV vaccine in Singapore is for individuals below the age of 25 as the goal is primary prevention of HPV infection.

Table 8. Human papillomavirus (HPV) vaccine for adults

	Bivalent vaccine	Tetravalent vaccine
Description	• Each dose contains HPV type 16 L1 protein (20 mcg) and type 18 L1 (20 mcg).	• Each dose contains HPV type 6 L1 protein (20 mcg), type 11 L1 (40 mcg), type 16 L1 (40 mcg) and type 18 L1 (20 mcg).
Summary of evidence	• Both vaccines were found to be highly immunogenic to 99% of vaccine recipients.	
Indication/Target population	• Prevention of HPV infection, precancerous lesion, and cervical cancer in women aged below 25.	• Prevention of HPV infection, precancerous lesion, and cervical cancer in women aged below 25. • Prevention of HPV infection and genital warts in men aged below 25.
Schedule	• Three doses, with the second and third dose given 2 and 6 months after the first dose, is recommended. However, delay in administration does not warrant restarting the dosing series.[1] • The vaccine is recommended to be administered starting 9 years of age. However, catch-up vaccination may be given until age 25 years, preferably until age 21 years. This also applies to men in the case of the tetravalent vaccine.	
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	
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$400 per year per account up to age 26 years	

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 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.
2. World Health Organization. Vaccine-preventable diseases and vaccines. In: World Health Organization. International Travel and Health. Geneva: World Health Organization; 2012.
3. Tay SK, Oon LL. Prevalence of cervical human papillomavirus infection in healthy women is related to sexual behaviours and educational level: a cross-sectional study. *Int J STD AIDS* 2014;25:1013-1021.

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.

The clinical picture of influenza includes fever, chills, headache, malaise, myalgia, anorexia, and respiratory symptoms such as sore throat, cough and nasal discharge.[1] Elderly patients may present with 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. More recent data showed that between 1,500 and 3,500 people in Singapore experience influenza-like illness every week.[3] In 2014, around a fifth of these patients had confirmed influenza. Furthermore, there seems to be little variation in the incidence of influenza-like illness throughout the year in Singapore.

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 to respiratory secretions.[1] Control measures include hygiene (eg, frequent hand washing) and vaccination.

Vaccine description

At present, the available influenza vaccines in Singapore are the parenteral trivalent vaccine and the parenteral quadrivalent vaccine (Table 9). The influenza virus undergoes 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 lack of efficacy of vaccines for one type of strain against other strains. Thus, the vaccine is updated annually according to the prevalent influenza strains at the time, and yearly vaccination is recommended. The live attenuated influenza vaccine is not yet available in Singapore.

Strong recommendation; moderate quality of evidence.

Table 9. Influenza vaccine for adults

Vaccine type	Parenteral trivalent vaccine	Parenteral quadrivalent vaccine
Description	• Each dose contains 15 mcg each of three influenza surface antigens. Covers against an influenza A H1N1 virus, an influenza A H3N2 virus, and one B virus (either Victoria or Yamagata according to the prevailing WHO recommendations).	• Each dose contains 15 mcg each of four influenza surface antigens covering for an influenza A H1N1 virus, an influenza A H3N2 virus, and both B viruses Victoria and Yamagata.
Summary of evidence	• A meta-analysis on 31 studies reported that trivalent inactivated vaccines had a 59% efficacy among adults aged 18 to 65 years.[4]	• The immunogenicity and safety of the quadrivalent vaccine is similar to that of the trivalent vaccines.[5]
Indication/ Target population	• Prevention of influenza A and B infection among all individuals aged 6 months and above, including adults. • Among adults, vaccination is strongly recommended in the following high-risk populations: • 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 updated vaccine	
Administration	• Intramuscular or deep subcutaneous injection	• Intramuscular

Vaccine type	Parenteral trivalent vaccine	Parenteral quadrivalent vaccine
Storage and handling	• Keep refrigerated (between 2°C and 8°C). Do not freeze. Protect from light. Discard after a year.	
Common adverse events	• Headache, sweating, myalgia, arthralgia, fever, malaise, shivering and/or fatigue • Redness, swelling, pain, ecchymosis or induration at the injection site	• Irritability, myalgia, fatigue, appetite loss, drowsiness, headaches, shivering, fever, sweating • Nausea, vomiting, diarrhoea, abdominal pain arthralgia • Injection site redness, swelling, induration
Contraindications	• Anaphylaxis to any vaccine component or a previous dose. The flu vaccine may contain egg/chicken protein and certain antibiotics (eg, 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	• May be used in pregnant and breastfeeding women • Category B	
Medisave	• Claimable (S$400 per year per account) for persons with higher risk of developing influenza-related complications and severe pneumococcal disease, respectively.	

Strong recommendation; moderate quality of evidence.

References:

1. Human and avian influenza. 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. 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 Infect Dis Bull* 2014;11(53):1-8.
4. Osterholm MT, Kelley NS, Sommer A, Belongia EA. *Lancet Infect Dis* 2012;12:36–44.
5. Graaf HD, Faust SN. *Expert Rev Vaccines* 2015;14:1055-1063.

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

Since the phase-out of pig farming in Singapore, JE has become rare.[3] It is endemic in some agricultural areas and countries.

Vaccine description

A live attenuated vaccine and an inactivated vaccine against JEV are available in Singapore (Table 10). However, due to the very low incidence of JE and the lack of the necessary swine host, routine vaccination against JEV is not recommended.

Strong recommendation; moderate quality of evidence

Table 10. JEV vaccine for adults

Vaccine type	Live attenuated	Inactivated
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%.[4-6]	• A meta-analysis of randomised controlled trials on the inactivated vaccine found a seroprotection rate of 95% after the 2-dose series.[7]
Indication/Target population	• Prevention of JE infection. Vaccination is strongly recommended for people traveling to and staying for 1 month or with extensive outdoor rural exposure in areas where JE is endemic, such as China, India, Bangladesh, Nepal, Sri Lanka and Southeast Asia (Cambodia, Indonesia, Laos, Myanmar, the Philippines, Thailand and Vietnam).[1,8]	
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.
Administration	• Subcutaneous injection • Do not administer intravenously.	• Intramuscular injection (deltoid) • 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	• Vaccination should be postponed in pregnant and breastfeeding women.	
Medisave	• No	

Strong recommendation; moderate quality of evidence.

References:

1. Japanese encephalitis. 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. Koh YL, Tan BH, Loh JJP, et al. Japanese Encephalitis, Singapore. *Emerg Infect Dis* 2006;12:525–526.
3. Ministry of Health, Singapore. Frequently Asked Questions On Japanese Encephalitis. Available at: https://www.moh.gov.sg/content/moh_web/home/pressRoom/pressRoomItemRelease/1999/Frequently_Asked_Questions_On_Japanese_Encephalitis.html. Accessed 15 August 2015.
4. Zhou B, Jia L, Xu X. A large-scale study on the safety and epidemiological efficacy of Japanese encephalitis (JE) live vaccine (SA14-14-2) in the JE endemic areas. *Zhonghua Liu Xing Bing Xue Za Zhi* 1999;20:38-41.
5. Tandan JB, Ohrr H, Sohn YM, et al. Single dose of SA 14-14-2 vaccine provides long-term protection against Japanese encephalitis: a case-control study in Nepalese children 5 years after immunization. *Vaccine* 2007;25:5041-5045.
6. Bista MB, Banerjee MK, Shin SH, et al. Efficacy of single-dose SA 14-14-2 vaccine against Japanese encephalitis: a case control study. *Lancet* 2001;358:791-795.
7. Schiøler KL, Samuel M, Wai KL. Vaccines for preventing Japanese encephalitis. *Cochrane Database Syst Rev* 2007;(3):CD004263.
8. World Health Organization. Vaccine-preventable diseases and vaccines. In: World Health Organization. International Travel and Health. Geneva: World Health Organization; 2012.

Measles-Mumps-Rubella Vaccine

The measles-mumps-rubella (MMR) vaccine (Table 11) 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 fevers, cough, nasal congestion and rashes, and may lead to bacterial middle-ear infection and pneumonia.[1,2] Mumps primarily infects the salivary glands, 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, 46 and 141 cases of measles have been reported in Singapore in 2013 and 2014, respectively.[4] The corresponding rates for mumps were 495 and 478 cases; and for rubella, 48 and 18 cases. It is unclear as to whether these individuals were vaccinated in childhood.

Table 11. 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 may be recommended to all adults who have not received complete vaccination for measles, mumps, or rubella during childhood. • Vaccination is recommended among adults who are at higher risk of infection. These 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. • 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.
Schedule	• One to two doses given at least 28 days apart.[7]
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 to eggs, or current thrombocytopaenia. • 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]

Pregnancy and breastfeeding	• Pregnant women should not receive the vaccine. • Category C • Vaccination should be avoided in breastfeeding women.
Medisave	• Up to S$400 per year per account

Strong recommendation; strong 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. Ministry of Health, Singapore. Preventive Health Services. Available at: https://www.moh.gov.sg/content/moh_web/home/statistics/Health_Facts_Singapore/Preventive_Health_Services.html. Accessed 15 August 2015.
4. Ministry of Health, Singapore. *Weekly Infect Dis Bull* 2014;11(53):1-8.
5. Ong G, Hoon HB, Ong A, et al. A 24-year review on the epidemiology and control of measles in Singapore, 1981-2004. *Southeast Asian J Trop Med Public Health* 2006;37:96-101.
6. 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.
7. 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 an 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, stiff neck 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 10 cases reported in 2014.[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 is increased.[3]

Vaccine description

The meningococcal vaccines available in Singapore are the quadrivalent polysaccharide and quadrivalent conjugate vaccine (Table 12), both being protective against meningococcal serogroups A, C, Y and W-135. 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. Other high-risk groups may also be vaccinated. Otherwise, routine vaccination is not recommended.[1,3]

Strong recommendation; moderate quality of evidence.

Table 12. Meningococcal vaccine for adults

Vaccine type	Polysaccharide vaccine	Conjugate vaccine
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.
Summary of evidence	• Vaccines are seroprotective in 90% of healthy recipients.[3]	• Vaccines are seroprotective in 98% of healthy recipients.[3]
Indication/Target population	• Prevention of invasive meningococcal disease among high-risk groups:[1-3] • 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; • Immunocompromised patients, including those with complement component deficiencies; • Personnel handling *N. meningitidis* isolates; • Close contacts of meningococcal disease patients; and, • 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] • Students living in dormitories, • Unvaccinated students, and, • Military personnel. *Weak recommendation; low quality of evidence*	
	• 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).[5]	• 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,[5] or human immunodeficiency virus infection. • Revaccination is recommended every 5 years for individuals as long as the risk remains increased.[3]	
Administration	• Subcutaneous injection	

Vaccine type	Polysaccharide vaccine	Conjugate vaccine
Storage and handling	• Keep refrigerated (between 2°C and 8°C). Do not freeze.	
Common adverse events	• Pain, induration, redness or swelling at the injection site • Headache, fatigue, irritability or drowsiness • Diarrhoea or anorexia	
Contraindications	• Anaphylaxis to any vaccine component or a previous dose.	
Precautions	• Vaccination should be postponed in individuals with acute severe illness. • Vaccination may not protect against all serotypes of *N. meningitidis*. • Response may be impaired in some immunocompromised individuals. • Administration of pneumococcal conjugate vaccine and Menactra brand meningococcal conjugate vaccine should be separated by a 4-week interval in patients with functional or anatomical asplenia.	
Pregnancy and breastfeeding	• Data on pregnant or breastfeeding women is lacking – administer only when benefit clearly outweighs risks. • Category C	
Medisave	• No	

Srong 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. Meningococcal disease. 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. Meningococcal disease. 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.
4. Ministry of Health, Singapore. *Weekly Infect Dis Bull* 2014;11(53):1-8.
5. Centers for Disease Control and Prevention. Recommended Adult Immunization Schedule—United States – 2015. Atlanta, GA: Centers for Disease Control and Prevention; 2015.

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 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 2014, the number of reported pneumococcal disease cases was 164.[3]

Despite this low number and a declining trend, prevention of IPD through vaccination is still a public health priority. Aside from the high morbidity and mortality associated with the disease, 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

The adult pneumococcal vaccines intended to prevent IPD and pneumonia that are available in Singapore are a 23-valent polysaccharide vaccine (PPSV23), and a 13-valent conjugate vaccine (PCV13) (Table 13). 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 9 months and older, compared with 2 years and older for the polysaccharide vaccine.

Table 13. 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 70%. Efficacy in adults with underlying illnesses may be reduced.	• Vaccine efficacy among adults ≥65 years old was around 75% against vaccine-type IPD.[4]
Indication/Target population	• Prevention of IPD and pneumonia • Among adults, vaccination is recommended in the following at-risk groups:[1,2,5] • Those aged 65 years and above. • Those aged 19 years or older with certain medical conditions: 1. Immunocompetent adults with chronic medical conditions, including: alcoholism; cigarette smoking; diabetes mellitus; chronic heart disease including congestive heart failure and cardiomyopathies; chronic liver disease; and chronic lung disease including chronic obstructive pulmonary disease, emphysema and asthma; 2. Immunocompetent adults with cochlear implants and cerebrospinal fluid leaks; 3. Those with functional or anatomical asplenia due to congenital or acquired asplenia, sickle cell disease or other hemoglobinopathies, or elective splenectomy; 4. Immunocompromised persons, including those with chronic renal failure or nephrotic syndrome; generalised malignancy including Hodgkin disease, leukaemia, lymphoma and multiple myeloma; Human Immunodeficiency Virus infection; or solid organ transplant recepients; 5. Those with congenital or acquired immunodeficiencies, such as B (humoral) or T-lymphocyte deficiency, complement deficiencies or phagocytic disorders; or, 6. Those with iatrogenic immunosuppression (eg, due to immunosuppressive drugs, long-term systemic corticosteroids or radiation therapy.	

Vaccine type	23-valent polysaccharide vaccine (PPSV23)	13-valent conjugate vaccine (PCV13)
Schedule	• See Table 14 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]	
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$400 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 14. Schedule of pneumococcal vaccine administration by subgroup and vaccination history[6]

Present age	History of PCV13 administration	History of PPSV23 administration	Schedule
Adults aged 65 years or older	None	None	Administer PCV13 followed by PPSV23 after 6 to 12 months.
	None	Given before age 65 years	Administer PCV13 at least 1 year after the most recent dose of PPSV23; administer a dose of PPSV23 6 to 12 months after PCV13, or as soon as possible if this time window has passed, and at least 5 years after the most recent dose of PPSV23.
	None	Given at age 65 years or older	Administer PCV13 at least 1 year after the last PPSV23 dose.
	Given before age 65 years	None	Administer PPSV23 6 to 12 months after PCV13 or as soon as possible if this time window has passed.
	Given before age 65 years	Given before age 65 years	Administer PPSV23 6 to 12 months after PCV13, or as soon as possible if this time window has passed, and at least 5 years after the most recent dose of PPSV23.
Adults aged 19 through 64 years with immunocompromising conditions, anatomical or functional asplenia, cerebrospinal fluid leaks or cochlear implants	None	None	Administer PCV13 followed by PPSV23 at least 8 weeks after PCV13; administer a second dose of PPSV23 at least 5 years after the first dose of PPSV23.
	None	One dose only	Administer PCV13 at least 1 year after the PPSV23; administer a second dose of PPSV23 at least 8 weeks after PCV13 and at least 5 years after the first dose of PPSV23.
	None	Two doses	Administer PCV13 at least 1 year after the most recent dose of PPSV23.
	Yes	None	Administer PPSV23 at least 8 weeks after PCV13; administer a second dose of PPSV23 at least 5 years after the first dose of PPSV23.
	Yes	One dose	Administer a second dose of PPSV23 at least 5 years after the first dose of PPSV23.

Present age	History of PCV13 administration	History of PPSV23 administration	Schedule
Adults aged 19 through 64 years with chronic conditions (Refer also to Table 32).	Any	Any	Administer one dose of PPSV23 only.

References:

1. Pneumococcal disease. In: Centers for Disease Control and Prevention. Epidemiology and Prevention of Vaccine-Preventable Diseases. Atkinson W, Hamborsky J, Wolfe S, eds. 12th ed. Washington DC: Public Health Foundation, 2012.
2. Invasive pneumococcal disease. 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. Ministry of Health, Singapore. *Weekly Infect Dis Bull* 2014;11(53):1-8.
4. Tomczyk S, et al. Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine Among Adults Aged ≥65 Years: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2014;63;822-825.
5. World Health Organization. Vaccine-preventable diseases and vaccines. In: World Health Organization. International Travel and Health. Geneva: World Health Organization; 2012.
6. Centers for Disease Control and Prevention. Recommended Adult Immunization Schedule—United States – 2015. Atlanta, GA: Centers for Disease Control and Prevention; 2015.

Polio Vaccine

Poliomyelitis (also known as infantile paralysis or polio) is a central nervous system disorder caused by infection with poliovirus types 1, 2 and 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]

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

In Singapore, both inactivated polio vaccine (IPV) and live oral polio vaccine (OPV) are available (Table 11). 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] This makes the IPV vaccine also 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

The WHO recommendation for the primary series is three doses of OPV and one dose of IPV given during childhood. However, unvaccinated adults and other adults at risk should receive vaccination as described in Table 15.

Strong recommendation; low quality of evidence

Table 15. Polio vaccine for adults

Vaccine type	Oral vaccine	Inactivated vaccine
Description	• Each dose (0.1 mL or two drops) contains at least 106 $CCID_{50}$ for type1, 105 $CCID_{50}$ for type 2 and 105.8 $CCID_{50}$ 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 (i.e., Afghanistan and Pakistan) or where polio transmission has been known to occur (eg, Somalia, Ethiopia, Kenya, Syria, Cameroun, Israel, Niger, Chad and Yemen). This should be updated in consultation with a travel medicine practitioner. • 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.
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	• Up to S$400 per year per account	

Strong recommendation; low quality of evidence.

References:

1. Poliomyelitis. 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. Poliomyelitis. 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. World Health Organization. Vaccine-preventable diseases and vaccines. In: World Health Organization. International Travel and Health. Geneva: World Health Organization; 2012.
4. Ministry of Health, Singapore. Preventive Health Services. Available at: https://www.moh.gov.sg/content/moh_web/home/statistics/Health_Facts_Singapore/Preventive_Health_Services.html. Accessed 15 August 2015.

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.

The clinical presentation of rabies is 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 available in Singapore is cultured from purified chick embryo cells (Table 16). 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 17).[1,2] In addition, post-exposure prophylaxis may include administration of rabies immunoglobulin.

Table 16. Rabies vaccine for adults

Vaccine type	• Purified chick embryo cell (PCEC) vaccine
Description	• Each dose contains at least 2.5 IU of inactivated rabies virus (strain Fury LEP) cultured in PCEC.
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]
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 17).
Schedule	• **Pre-exposure prophylaxis:** • 3 doses given on days 0, 7, and 21 or 28. A booster injection is given 1 year later, and every 5 years thereafter. • **Post-exposure prophylaxis:**[5] • In previously unvaccinated adults: 4 doses, given on days 0, 3, 7 and 14. • For unvaccinated adults on immunosuppression: Add a fifth dose on Day 28. • In previously vaccinated adults: 2 doses, given on days 0 and 3. • For Category III exposure (Table 17): also administer a dose of rabies immunoglobulin if available.
Administration	• Intramuscular injection in the deltoid or anterolateral thigh. Do not inject intravascularly, as this could result in severe adverse reactions.
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. • Treatment of wounds with rabies risk includes immediate cleansing with soap and water; then treatment with 70% alcohol or iodine solution. Wounds should not be sutured. • Rabies immunoglobulin should also be given to Category III rabies exposure.
Pregnancy and breast-feeding	• There is limited data on the safety of rabies vaccine in breastfeeding women. Vaccinate with caution if benefits clearly outweighs risks.[6,7] • 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; moderate quality of evidence.

Rabies immunoglobulin is not widely available. Patients requiring rabies immunoglobulin treatment should be immediately referred to an animal bite referral centre, such as Tan Tock Seng Hospital (11 Jalan Tan Tock Seng, Singapore).[2]

Strong recommendation; low quality of evidence.

Table 17. Treatment of animal bite by category[1,2]

Category	Type of contact with a suspected or confirmed rabid domestic or wild animal* or animal of unverifiable rabies status	Recommended post-exposure prophylaxis
I. No exposure	• Touching or feeding of the animal • Licks on intact skin	• None, if history is reliable
II. Minor exposure	• Nibbling of uncovered skin • Minor scratches or abrasions without bleeding	• Administer vaccine immediately. • Stop treatment if animal remains healthy throughout an observation period of 10 days** or is proved to be negative for rabies by a reliable laboratory using appropriate diagnostic techniques. • If an apparently healthy-looking cat or dog from Singapore is placed under observation for 10 days, treatment delay is allowed.
III. Severe exposure	• Single or multiple transdermal bites or scratches, or licks on broken skin • Contamination of mucous membrane with saliva (i.e., licks) • Exposures to bats, especially following bites or scratches or exposure to mucous membranes.	• Administer rabies immunoglobulin and vaccine immediately. • Stop treatment if animal remains healthy throughout an observation period of 10 days** or is proved to be negative for rabies by a reliable laboratory using appropriate diagnostic techniques.

*Exposure to rodents, rabbits and hares seldom requires post-exposure prophylaxis.

**Only dogs and cats are allowed for observation. Other suspected domestic or wild animals, except threatened or endangered species, should be euthanized after laboratory confirmation of rabies.

Strong 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. Rabies. 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. Canadian Immunization Guide. Part 4. Active Vaccines: Rabies Vaccine. Available at: http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-rabi-rage-eng.php. Accessed 15 August 2015.
4. World Health Organization. WHO Guide to Rabies Pre and Post-exposure Prophylaxis in Humans (revised 15 June 2010). Available at: http://www.who.int/rabies/PEP_prophylaxis_guidelines_June10.pdf. Accessed 15 August 2015.
5. Rupprecht CE, Briggs D, Brown CM, et al. *MMWR Recomm Rep* 2010;59(RR-2):1-9.
6. World Health Organization. WHO Position Paper on Rabies Vaccine - 6 August 2010. Available at: http://www.who.int/immunization/rabies_grad_efficacy.pdf. Accessed 13 October 2015.
7. General Recommendations on Immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP). *MMWR* 2002; 51(RR-2):1-36.

Rotavirus Vaccine

Rotaviruses of the Reoviridae family cause an acute gastroenteritis characterised by profuse watery diarrhoea, vomiting and fever in infants and young children.[1] Rotaviruses are transmitted via the faecal–oral route, direct person-to-person route, and indirect transmission through contamination of fomites. In adults, rotavirus infection often has a subclinical presentation, except occasionally among elderly and immunocompromised adults.

Vaccination is recommended among children aged 5 years and below.[1,2] However, there is limited data on the efficacy and safety of routine rotavirus vaccination in adults. Furthermore, some studies have demonstrated that vaccination of children within the household provides sufficient indirect protection to adults, including the elderly and immunocompromised individuals.[3,4]

Thus, the use of rotavirus vaccine in adults is not recommended. To protect the elderly or immunocompromised adults, vaccination of children aged 5 years and below within the household is recommended. Likewise, despite the worldwide distribution of the virus, vaccination among adult travellers is not currently recommended.

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. Rotavirus. 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. Dorleans F, Falkenhorst G, Böttiger B, et al. A case-control study of risk factors for rotavirus infections in adults, Denmark, 2005-2009. *Epidemiol Infect* 2015;6:1-7.
4. Anderson EJ, Shippee DB, Weinrobe MH, et al. Indirect protection of adults from rotavirus by pediatric rotavirus vaccination. *Clin Infect Dis* 2013;56:755-760.

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. 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

References:

1. World Health Organization. Vaccine-preventable diseases and vaccines. In: World Health Organization. International Travel and Health. Geneva: World Health Organization; 2012.
2. Lim V, Chang KM, Cheong SK, et al. Clinical Practice Guidelines on Adult Vaccination. Putrajaya: Ministry of Health Malaysia; 2003.
3. Smallpox. In: Ong A, Goh KT, eds. A Guide on Infectious Diseases of Public Health Importance In Singapore (7th Edition). Singapore: Ministry of Health; 2011.

Tetanus, Diphtheria and Acellular 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] The vaccine is a combination vaccine that protects against tetanus, diphtheria pertussis.

Tetanus is a muscular spastic disease caused by the toxin of *Clostridium tetani*. *C. tetani* is 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 *Campylobacter 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

There is limited information about the incidence of tetanus in Singapore. There were no reports of diphtheria in Singapore in 2014 and 2013, but there were 17 reports of pertussis in 2013, and 21 reports in 2014.[5]

Vaccination

Vaccination against tetanus, diphtheria and pertussis, using the DPT vaccine, is part of the National Childhood Immunisation Programme.[2] Since 2008, childhood coverage rates have been at least 95%.[6] 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 18) boosts waning immunity to tetanus and diphtheria vaccines and reduces carriage of pertussis among adults.

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

Table 18. Tdap vaccine for adults

	Tdap	Td
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.[8] 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.[9]	
Indication/Target population	• Booster vaccination to reduce morbidity of tetanus, diphtheria and pertussis. • Tdap vaccination is recommended in the following groups:[1,2] • Adults aged 19 to 64 years if their last vaccination was at least 10 years ago, • Adults in close contact with an infant aged less than 12 months,[4] • Women of childbearing age before pregnancy or immediately after delivery (during the third trimester of every pregnancy, regardless of interval from the last Tdap/Td vaccination), and, • Healthcare personnel with direct patient contact.	• Booster vaccination to reduce morbidity of tetanus and diphtheria. • Td vaccination is recommended in the following groups:[1,2] • Adults aged 19 to 64 years if their last vaccination was at least 10 years ago, • Adults in close contact with an infant aged less than 12 months,[4] • Women of childbearing age before pregnancy or immediately after delivery (during the third trimester of every pregnancy, regardless of interval from the last Tdap/Td vaccination), and, • Healthcare personnel with direct patient contact.
Schedule	• Single dose. Tetanus vaccine may be given as booster every 10 years.	
Administration	• Intramuscular injection, preferably at the deltoid area	
Storage and handling	• Keep refrigerated (between 2°C and 8°C). Do not freeze.	

	Tdap	Td
Common adverse events	• Pain, redness, swelling, mass or sterile abscess at the injection site • Headache, malaise, dizziness, nausea and gastrointestinal disorders	
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 thrombocytopaenia 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	• May be given on the third trimester (preferred), or immediately after delivery.[3] • Category C • Breastfeeding is not a contraindication.[3]	
Medisave	• Up to S$400 per year per account	• 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 15 August 2015.
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.
5. Ministry of Health, Singapore. *Weekly Infect Dis Bull* 2014;11(53):1-8.
6. Ministry of Health, Singapore. Preventive Health Services. Available at: https://www.moh.gov.sg/content/moh_web/home/statistics/Health_Facts_Singapore/Preventive_Health_Services.html. Accessed 15 August 2015.
7. Ang LW, James L, Goh KT. Prevalence of diphtheria and tetanus antibodies among adults in Singapore: a national serological study to identify most susceptible population groups. *J Public Health (Oxf)* 2015. [Epub ahead of print].
8. Thierry-Carstensen B1, Dalby T, Stevner MA, et al. Experience with monocomponent acellular pertussis combination vaccines for infants, children, adolescents and adults--a review of safety, immunogenicity, efficacy and effectiveness studies and 15 years of field experience. *Vaccine* 2013;31:5178-5191.
9. Blatter M, Friedland LR, Weston WM, Li P, Howe B. Immunogenicity and safety of a tetanus toxoid, reduced diphtheria toxoid and three-component acellular pertussis vaccine in adults 19-64 years of age. *Vaccine* 2009;27:765-772.

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

Table 19. Tetanus post-exposure prophylaxis recommendations in adults[1,2]

Tetanus vaccination status	Clean, minor wound	Tetanus-prone wound*
• < 3 tetanus doses or unknown	• Tetanus toxoid only	• Tetanus toxoid and TIG
• 3 or more tetanus doses, ≥10 years since last dose	• Tetanus toxoid only	• Tetanus toxoid • TIG if contaminated by manure, with extensively devitalised tissue, or patient is immunocompromised
• 3 or more tetanus doses, <10 years since last dose	• No toxoid or TIG	• Tetanus toxoid • TIG if contaminated by manure, with extensively devitalised tissue, or patient is immunocompromised

TIG, tetanus immunoglobulin.
*Contaminated with dirt, faeces, soil, and saliva; puncture wounds; avulsions; and wounds resulting from missiles, crushing, burns and frostbite.

Table 20 outlines the recommendations for the storage, handling, and administration of tetanus toxoid and immunoglobulin for post-exposure prophylaxis.

Table 20. Tetanus post-exposure prophylaxis

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.	
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 to12 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

Vaccine type	Tetanus toxoid	Tetanus immunoglobulin
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 15 August 2015.
2. Royal College of Physicians of Ireland, National Immunisation Advisory Committee. Immunisation Guidelines for Ireland 2008 . Available from: www.immunisation.ie/en/ HealthcareProfessionals/ ImmunisationGuidelines2008/. Accessed 15 August 2015.
3. Tetanus. 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.

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 21), an attenuated vaccine from *M. bovis,* is intended to prevent the progression of TB to miliary TB or TB meningitis.[1]

Disease burden

In Singapore, the prevalence of TB is around 40 cases per 100,000 population.[1] In 2014, 1,353 new cases of TB were reported.[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

In adults, BCG is recommended for previously 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.[1]

Strong 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 21. Bacillus-Calmette-Guerin 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	• Up to S$400 per year per account

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.
3. Ministry of Health, Singapore. *Weekly Infect Dis Bull* 2014;11(53):1-8.
4. Ministry of Health, Singapore. Preventive Health Services. Available at: https://www.moh.gov.sg/content/moh_web/home/statistics/Health_Facts_Singapore/Preventive_Health_Services.html. Accessed 15 August 2015.
5. Abubakar I, Pimpin L, Ariti C, et al. Systematic review and meta-analysis of the current evidence on the duration of protection by bacillus Calmette-Guérin vaccination against tuberculosis. *Health Technol Assess* 2013;17:1-372, v-vi.

Typhoid Vaccine

Typhoid fever is caused by the typhoid bacillus, *Salmonella typhi*.[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 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 contaminated shellfish, fruits and vegetables, and milk and milk products.[1,2] Faecal–oral transmission may also occur.

In Singapore, 84 cases of typhoid fever were reported in 2013, and 54 cases were reported in 2014.[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 does not confer 100% protection, and adequate food and water hygiene is still required.

Weak recommendation; moderate quality of evidence

The available typhoid vaccine in Singapore is the Vi polysaccharide vaccine (Table 22).

Table 22. Typhoid vaccine for adults

Description	• Each dose contains 25 mcg of purified Vi capsular polysaccharides of *S. typhi* (Ty2 strain).
Summary of evidence	• Vaccination confers protective efficacy of around 72% during the first year, and wanes to around 50% on the third year.[1]
Indication/Target population	• Prevention of typhoid fever, especially for travellers to areas of high endemicity and poor hygiene standards
Schedule	• Single dose. Booster may be given every 3 years if risk persists.
Administration	• Intramuscular or subcutaneous injection. 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 or a previous dose
Precautions	• Administration should be postponed in individuals with acute severe illness. • Vaccination does not replace food and water hygiene practices.
Pregnancy and breastfeeding	• Pregnant women may receive the vaccine. • Category C • Vaccination should be given with caution in breastfeeding women.
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.
3. Ministry of Health, Singapore. *Weekly Infect Dis Bull* 2014;11:1-8.

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 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, 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 23) intended for the prevention of varicella.[3] The vaccine is also found in combination preparations with MMR.

Table 23. 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	• Anaphylaxis to any vaccine component or a previous dose, including neomycin • Immunocompromised state
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.
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, 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]

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. Fatha N, Ang LW, Goh KT. Changing seroprevalence of varicella zoster virus infection in a tropical city state, Singapore. *Int J Infect Dis* 2014;22:73-77.

Yellow Fever Vaccine

Yellow fever 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 egypti*) vector.[2] In rural areas, monkeys are reservoirs of infection.

There have been no reported cases of yellow fever in Singapore in recent years.[3] 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 24), a live attenuated vaccine, prior to departure.[1,2]

Table 24. 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 area.
Schedule	• Single dose. Boosters are not recommended, but may be required by some countries.
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-Barré syndrome. Adults older than 60 years are at higher risk. • Very rarely, yellow fever vaccine-associated viscerotropic disease (YEL-AVD) may occur. YEL-AVD resembles fulminant infection by wild-type yellow fever virus, presenting fever, fatigue, myalgia, headache and hypotension, progressing to metabolic acidosis, muscle and liver cytolysis, lymphocytopaenia and thrombocytopaenia, 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

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.
2. World Health Organization. Vaccine-preventable diseases and vaccines. In: World Health Organization. International Travel and Health. Geneva: World Health Organization; 2012.
3. Ministry of Health, Singapore. *Weekly Infect Dis Bull* 2014;11(53):1-8.

Zoster Vaccine

Reactivation of varicella zoster virus (VZV) results in zoster.[1,2] This reactivation is more common among immunocompromised and elderly individuals. Patients with zoster can transmit VZV to susceptible individuals.

Zoster is vaccine preventable via a live attenuated vaccine (Table 25), which is recommended for adults aged 60 years and older.

Table 25. Zoster vaccine for adults

Description	• Each dose contains at least 19,400 plaque-forming units of the attenuated VZV
Summary of evidence	• Clinical trials on elderly individuals without prior zoster reported a 50% to 70% reduction in the incidence of zoster.[3]
Indication/Target population	• Prevention of zoster in adults aged 60 years and older
Schedule	• Single dose. Booster is not recommended.
Administration	• Subcutaneous injection
Storage and handling	• Store below -15°C.
Common adverse events	• Redness, pain and swelling at the injection site • Fever, headache, body aches, malaise, nausea and itching
Contraindications	• Anaphylaxis to any vaccine component or a previous dose, including neomycin and gelatin • Immunocompromised state
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.
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.

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.

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.

Among the vaccines directed against infectious diseases, the vaccines in development in Table 26 are noteworthy for possibly addressing diseases with no available vaccine at present.[1]

Table 26. Selected novel vaccines for infectious diseases in mid- to late-stage development[1]

Vaccine	Indication	Development phase
Dengvaxia (quadrivalent dengue vaccine, live attenuated) *Sanofi Pasteur* This vaccine has a reported efficacy of around 60%.[2,3] It is administered via subcutaneous injection given on Months 0, 6 and 12. The vaccine is complimentary to, but not meant to replace other mosquito-bourne disease control measures, such as bite avoidance. As of December 2015, this vaccine has been approved in three endemic countries: Mexico, Philippines and Brazil.	Prevention of dengue fever	Phase III completed
Mosquirix™ malaria vaccine *GlaxoSmithKline* This is a recombinant protein-based vaccine reported to reduce malaria risk by around 40%.[4] It is administered by intramuscular injection given on Months 0, 1, 2 and 20. The vaccine is not meant to replace other mosquito-bourne disease control measures, such as bite avoidance.	Prevention of malaria (*Plasmodium falciparum*)	Phase III completed (approved in Europe)
ACAM-Cdiff (toxoid vaccine) *Sanofi Pasteur*	Prevention of *Clostridium difficil*e infection	Phase III
ASP-0113 (plasma DNA-based vaccine) *Astellas Pharma*	Prevention of CMV infection	Phase III
DermaVir™ Patch (DNA topical patch vaccine) *Genetic Immunity*	Treatment of HIV-1 infection	Phase II

GI-5005 (tarmogen T-cell immunity stimulator) *GlobeImmune*	HCV infection	Phase II
HerpV (herpes simplex vaccine) *Agenus*	Treatment of HSV-2 infection	Phase II
HIV vaccine *GeoVax Labs*	Prevention of HIV infection	Phase II
PF-06290510 (4-antigen *Staphylococcus aureus* vaccine, SA4Ag)	Staphylococcal infection	Phase II
Recombinant botulinum neurotoxin vaccine *DynPort Vaccine Company* *U.S. Department of Defense* *Washington, DC*	Prevention against botulinum neurotoxin types A and B	Phase II
TG-4040 (vector-based therapeutic vaccine) *Transgene*	HCV	Phase II

CMV, cytomegalovirus; HIV, human immunodeficiency virus; HCV, hepatitis C virus; HSV, herpes simplex virus.

References:

1. Pharmaceutical Research and Manufacturers of America. Vaccines: A Report on the Prevention and Treatment of Diseases Through Vaccines (2013 Report). Washington, DC: PhRMA; 2013.
2. Capeding MR, Tran NH, Hadinegoro SR, et al. *Lancet* 2014;384:1358–1365.
3. Villar L, Dayan GH, Arredondo-García JL, et al. *N Engl J Med* 2015;372:113–123.
4. RTS,S Clinical Trials Partnership. *Lancet* 2015;386:31–45.

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 (eg, urban or rural);

3) planned activities (eg, 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 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.

Table 27 summarizes the critical vaccines recommended for travel.

Table 27. 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, Senegal, Sierra, Leone, Sudan, Suriname, Togo, Trinidad & Tobago, Uganda, Venezuela

Strong recommendation; low quality of evidence

Table 28 shows other vaccines that may be given to unvaccinated travellers that have a high risk of exposure at their destination.

Table 28. Vaccine recommendation by country or region of travel[1-4]

Country/ region of travel or special circumstance	Vaccine								
	Cholera	Hepatitis A (<40 years old)	Hepatitis B	Japanese encephalitis*	Meningococcal disease*	Polio (IPV)	Rabies	Typhoid	Yellow fever*
Southeast Asia									
Brunei		+	+	+			+	++	
Cambodia		++	+	+			+	++	
Indonesia		++	+	+			+	++	
Laos		++	+	+		++	+	++	
Malaysia		++	+	+			+	++	
Myanmar		++	+	+		++	+	++	
Philippines		++	+	+			+	++	
Thailand		++	+	+			+	++	
Vietnam		++	+	+			+	++	
Other countries/ regions									
China		++	+	+		+	+	++	
India		++	+	+			+	++	
Other East Asian countries		++	+	+			+	++	
Other South Asian countries		++	+	+			+	++	
Northern Africa		++	+	+			+	++	
Central Africa		++	+	+	++	++	+	++	
Southern Africa		++	+	+			+	++	
North America			+						
Central America		++	+				+	++	++
South America		++	+				+	++	++

Country/ region of travel or special circumstance	Vaccine								
	Cholera	Hepatitis A (<40 years old)	Hepatitis B	Japanese encephalitis*	Meningococcal disease*	Polio (IPV)	Rabies	Typhoid	Yellow fever*
Europe			+						
Special circumstances									
War-torn areas	++	++	+				+	++	
Hajj or Umrah					++				
Pregnant traveller (delay travel unless necessary)	+	+	+				+		

* Use in conjunction with Table 27.
++ 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.*

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 Health Information for International Travel: The Yellow Book. Altanta, GA: Centers for Disease Control and Prevention; 2015.
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 29.[1,2] Furthermore, Singapore requires a yellow fever vaccination certificate prior to entry for travellers from high-risk countries.[3]

Table 29. 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: 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, Senegal, Sierra, Leone, Sudan, Suriname, Togo, Trinidad & 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 15 August 2015.
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 15 August 2015.
3. Immigration and Checkpoints Authority, Singapore. Entry Requirements. Available at: www.ica.gov.sg/page.aspx?pageid=95. Accessed 15 August 2015.

Vaccination in Pregnant and Pre-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 30 summarizes the general recommendations for vaccination in pregnant women.[4,5] In addition, Table 31 summarizes recommendations for vaccination in non-pregnant women who intend to get pregnant. In these women, 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 30. Vaccinations for pregnant women[4,5]

Indication	Vaccines recommended
Routine	• Influenza (inactivated) • Tdap
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 toxoid • Tetanus immunoglobulin
Not recommended	• Human papillomavirus vaccine
Contraindicated	• Varicella vaccine • Zoster vaccine
Insufficient data to make a recommendation. Delay if possible.	• Pneumococcal vaccines • 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

Table 31. Vaccinations for pre-pregnant women

Indication	Vaccines recommended
Routine	• Influenza (inactivated) • Tdap
Recommended; with guidance from available previous screening	• Rubella (part of measles-mumps-rubella vaccine*) if not immune • Hepatitis A vaccine • Hepatitis B vaccine
Recommended if previously unvaccinated or incompletely vaccinated	• Varicella vaccine* • Pneumococcal vaccines • *Haemophilus influenzae* B vaccine
May be given if indicated	• Meningococcal vaccine • Tetanus toxoid • Tetanus immunoglobulin if required

*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 Committeeon 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. Altanta, 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 32 summarizes the recommendations for vaccinations for these patients.

Table 32. 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.	• 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. Good 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).	

Condition	Prioritised vaccine	Routine vaccine
Chronic heart disease Chronic endocrine diseases including diabetes	• One dose 23-valent pneumococcal vaccine (13-valent pneumococcal vaccine only if >65 years).	• Annual influenza vaccine
Chronic liver disease	• 23-valent pneumococcal vaccine	• Annual influenza vaccine
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
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 and symptomatic human immunodeficiency virus infection	• Live vaccines are 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.	
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	

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.	

*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), chemotherapy, radiation therapy, post-organ-transplant therapy, certain anti-rheumatic drugs, and drugs used for the management of inflammatory bowel disease.

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 15 August 2015.

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 at constant exposure with 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 33 summarizes the vaccination recommendations for adults in the healthcare setting.

Table 33. Vaccination for adults in the healthcare setting[1,2]

At-risk group	Prioritised vaccines	Routine vaccines
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. Booster should be given if anti-Hbs titres are less than 10 IU/L. • 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 15 August 2015.

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)					
Influenza	Annually				Strongly recommended	
MMR (for those without two documented doses as children)	1 dose					
Pneumococcal						1 dose of PCV13 followed by PPSV23 in 6 to 12 months.
Tdap	1 dose					
Varicella	2 doses (0-1 mo schedule)					
Zoster					1 dose	
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	1 dose of PPSV23					

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

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Vaccine	Available Brands	Indication	Administration	Schedule (unvaccinated adults)
Cholera vaccine (oral)	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 (parenteral)	Cholera Vaccine Berna (Berna Biotech) Cholera Vaccine CSL (CSL Ltd)	Prevention of diarrhoea due to cholera especially during travel	IM/SQ/ID	
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, illegal drug use)	IM (deltoid)	2 doses 6-12 months apart

Vaccine	Available Brands	Indication	Administration	Schedule (unvaccinated adults)
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
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, 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		
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

Vaccine	Available Brands	Indication	Administration	Schedule (unvaccinated adults)
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)		IM	2 doses 1 month apart
Measles-mumps-rubella vaccine*	M-M-R II (MSD) Priorix (GlaxoSmithKline)	Prevention of measles, mumps and rubella in all unvaccinated individuals	SQ	1 to 2 doses given 1 month apart

Vaccine	Available Brands	Indication	Administration	Schedule (unvaccinated adults)
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	Refer to section on Pneumococcal vaccine on page 48.
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 or 28. Post-exposure: Days 0, 3, 7 14 and 28.

Vaccine	Available Brands	Indication	Administration	Schedule (unvaccinated adults)
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
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)	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

Vaccine	Available Brands	Indication	Administration	Schedule (unvaccinated adults)
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	IM/SQ	Single dose
Varicella vaccine	Okavax Live Attenuated Varicella Virus Vaccine – BIKEN (Sanofi Pasteur) Varilrix (GlaxoSmithKline)	Prevention of varicella in all adults without evidence of immunity, especially healthcare personnel with potential exposure to VZV.	SQ	2 doses 4 weeks apart
Yellow Fever	Stamaril (Sanofi Pasteur)	Prevention of yellow fever, particularly for travellers to endemic area.	IM	Single dose

Vaccine	Available Brands	Indication	Administration	Schedule (unvaccinated adults)
Zoster Vaccine	Zostavax (MSD)	Prevention of zoster in adults aged 60 years and older	SQ	Single dose

*Claimable to Medisave (S$400 per year per account). Indicates those claimable by adults.

+HPV claimable (S$400 per year per account) up to 26 years old.

**Influenza and pneumococcal vaccinations are claimable (S$400 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 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)	Orally on empty stomach	2 doses 1 week apart, and a booster after 2 years	✓	✓		After 2 years
Cholera (parenteral)	IM/SQ/ID		✓	✓		
Hepatitis A	IM (deltoid)	2 doses 6-12 months apart	✓		✓	
Hepatitis B	IM (SQ for those with thrombocytopaenia 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	✓	✓		

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	
Meningococcal (polysaccharide)	SQ	At least 1 dose	✓			
Meningococcal (conjugate)	IM					
Polio (oral)	Oral	3 doses (months 0, 1-2, and 6-12)	✓	✓	✓	Every 10 years for IPV
Polio (inactivated)	IM (preferred)/SQ					
Typhoid	IM/SQ	Single dose	✓			Every 3 years 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 thrombocytopaenia or bleeding)	3 doses (months 0, 1 and 6)	✓	✓	✓	
Influenza (trivalent)	IM/deep SQ	Single dose yearly	✓			
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 (trivalent)	IM/deep SQ	Single dose yearly	✓			
Influenza (quadrivalent)	IM	Single dose	✓			
Tdap	IM (deltoid)	Single dose	✓			

Pre-pregnant women

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 thrombocytopaenia or bleeding)	Single dose	✓			
Hepatitis A	IM (deltoid)	2 doses 6-12 months apart	✓		✓	
Hepatitis B	IM (SQ for those with thrombocytopaenia or bleeding)	3 doses (months 0, 1 and 6	✓	✓	✓	
Influenza (trivalent)	IM/deep SQ	Single dose yearly	✓			
Influenza (quadrivalent)	IM	Single dose	✓			
MMR	SQ	1 to 2 doses given 1 month apart	✓	✓		
PPSV23	SQ/IM	Refer to section on Pneumococcal vaccine on page 48.				
PCV13	IM					
Tdap	IM (deltoid)	Single dose	✓			
Varicella	SQ	2 doses 4 weeks apart	✓	✓		

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 thrombocytopaenia or bleeding)	Single dose	✓			
Hepatitis A	IM (deltoid)	2 doses 6-12 months apart	✓		✓	
Hepatitis B	IM (SQ for those with thrombocytopaenia or bleeding)	3 doses (months 0, 1 and 6	✓	✓	✓	
Influenza (trivalent)	IM/deep SQ	Single dose yearly	✓			
Influenza (quadrivalent)	IM	Single dose	✓			
Meningococcal (polysaccharide)	SQ	At least 1 dose	✓			
Meningococcal (conjugate)	IM					
PPSV23	SQ/IM	One PCV13 dose followed by PPSV23 after 2 months		✓		Single booster after 5 years
PCV13	IM		✓			

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 thrombocytopaenia or bleeding)	3 doses (months 0, 1 and 6)	✓	✓	✓	
Influenza (trivalent)	IM/deep SQ	Single dose yearly	✓			
Influenza (quadrivalent)	IM	Single dose	✓			
PPSV23	SQ/IM	One PCV13 dose followed by PPSV23 after 2 months		✓		Single booster after 5 years
PCV13	IM		✓			

Chronic lung disease patients

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	
Influenza (trivalent)	IM/deep SQ	Single dose yearly	✓			
Influenza (quadrivalent)	IM	Single dose	✓			
PPSV23	SQ/IM	Single dose (for patients 65 years and younger)	✓			
PCV13	IM	Single dose (for patients older than 65 years)	✓			

Chronic heart disease patients

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	
Influenza (trivalent)	IM/deep SQ	Single dose yearly	✓			
Influenza (quadrivalent)	IM	Single dose	✓			
PPSV23	SQ/IM	Single dose (for patients 65 years and younger)	✓			
PCV13	IM	Single dose (for patients older than 65 years)	✓			

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 (trivalent)	IM/deep SQ	Single dose yearly	✓			
Influenza (quadrivalent)	IM	Single dose	✓			
PPSV23	SQ/IM	Single dose (for patients 65 years and younger)	✓			
PCV13	IM	Single dose (for patients older than 65 years)	✓			

Chronic liver disease patients

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	
Influenza (trivalent)	IM/deep SQ	Single dose yearly	✓			
Influenza (quadrivalent)	IM	Single dose	✓			
PPSV23	SQ/IM	One 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 (trivalent)	IM/deep SQ	Single dose yearly	✓			
Influenza (quadrivalent)	IM	Single dose	✓			
PPSV23	SQ/IM	One PCV13 dose followed by PPSV23 after 2 months		✓		Single booster after 5 years
PCV13	IM		✓			

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 (trivalent)	IM/deep SQ	Single dose yearly	✓			
Influenza (quadrivalent)	IM	Single dose	✓			
PPSV23	SQ/IM	One PCV13 dose followed by PPSV23 after 2 months		✓		Single booster after 5 years
PCV13	IM		✓			

Patients with immunocompromised states due to medical conditions, including cancer and symptomatic human immunodeficiency syndrome

Vaccine	Administration	Schedule	Visit			Booster
			1	2 (1-2 months after visit 1)	3 (6 months after visit 2)	
PPSV23	SQ/IM	One PCV13 dose followed by PPSV23 after 2 months		✓		Single booster after 5 years
PCV13	IM		✓			
Meningococcal disease	SQ	Two doses given 2 months apart			✓	Revaccination every 5 years as long as risk remains increased

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 thrombocytopaenia or bleeding)	3 doses (months 0, 1 and 6)	✓	✓	✓	
Influenza (trivalent)	IM/deep SQ	Single dose yearly	✓			
Influenza (quadrivalent)	IM	Single dose	✓			
MMR	SQ	1 to 2 doses given 1 month apart	✓	✓		
Tdap	IM (deltoid)	Single dose	✓			
Varicella	SQ	2 doses 4 weeks apart	✓	✓		

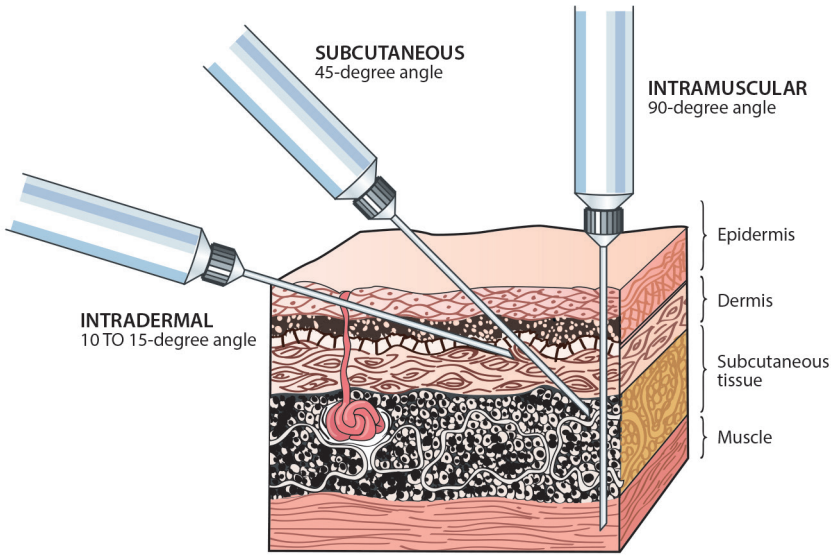
Sample Vaccine Record

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							
	3							
	4							
Tdap								
Varicella								
	1							
	2							

Zoster									
Haemophilus influenza B									
Hepatitis A									
	1								
	2								
Hepatitis B									
Meningococcal vaccine Indicate type (polysaccharide or conjugate)									
Others (indicate vaccine type)									

Vaccine Administration

Intradermal, 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

- **Travelers' 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/

Abbreviations

CCID50	50% Cell culture infectious dose
ACIP	Advisory Committee on Immunization Practices
BCG	Bacillus-Calmette-Guerin vaccine
BMI	Body mass index
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
IPV	Inactivated polio vaccine
IDU	Injecting drug use
IPD	Invasive pneumococcal disease
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
TIG	Tetanus immunoglobulin
Tdap	Tetanus-reduced diphtheria-acellular pertussis vaccine
TB	Tuberculosis
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

Notes page





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