VACCINATION AGAINST INFECTIOUS DISEASES

Vaccination or immunisation may be defined as the artificial production of specific, active immunity to a microorganism by the administration of antigenic material from that organism to an individual. Although often used interchangeably, the term ‘vaccination’ more correctly refers to the administration of those antigens and all that entails, whereas ‘immunisation’ includes the processes by which a person develops immunity. As the latter is a process not routinely tested in everyday practice and includes passive induction of immunity by administration of pre-formed antibodies, in this chapter the term ‘vaccination’ will be used.

The most common way to induce active immunity to an infectious agent is following natural infection. The immune system, using both the T and B cells, produces immunological memory. Upon re-exposure to the same antigen, a rapid protective response is typically mounted. Immunological memory is durable and may, depending on the infecting agent, be lifelong. Vaccination seeks to replicate this process without causing disease by using live, attenuated microorganisms, antigenic components of organisms (such as capsular polysaccharides) or modified toxins/toxoids. Unlike natural infection, immunological protection may not be lifelong and depends on a number of factors: chemical and physical characteristics of the antigen and the manner of presentation to the immune system, characteristics of the individual both physiological, such as age and immune status, as well as genetic characteristics. All are taken into consideration in both the design of the vaccines as well as their dosing schedules.

The following information is not exhaustive and has been sourced from the following websites to which readers are referred for additional information and updates:

- www.cdc.gov/vaccines/pubs/pinkbook/index.html
- www.nicd.ac.za/assets/files/NICD%20Vaccine%20Booklet%20D132%20FINAL.pdf

ROUTINE VACCINATION SCHEDULES

The Expanded Programme of Immunisation (EPI) of the Department of Health prescribes the minimum vaccine requirements for all children in South Africa. It is based on a six, 10 and 14 weeks schedule. The schedule in private is also based on this timing and includes additional recommended vaccines.
<table>
<thead>
<tr>
<th>AGE OF CHILD</th>
<th>EPI SCHEDULE</th>
<th>PRIVATE SCHEDULE</th>
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</table>
| Birth       | BCG – TB vaccine  
              OPV (0) – Oral polio vaccine | BCG  
              OPV |
| 6 weeks     | OPV (1) – Oral polio vaccine  
              RV (1) – Rotavirus vaccine  
              DTaP-IPV-Hib-HBV (1) – Combined diphtheria, tetanus, acellular pertussis, inactivated polio vaccine and *Haemophilus influenzae* type B and hepatitis B  
              PCV (1) – pneumococcal conjugate vaccine | OPV (1)  
              RV (1)  
              DTaP-IPV-Hib-HBV (1)  
              PCV (1) |
| 10 weeks    | DTaP-IPV-Hib-HBV (2) – Combined diphtheria, tetanus, acellular pertussis, inactivated polio vaccine and *Haemophilus influenzae* type B and hepatitis B | DTaP-IPV-Hib-HBV (2)  
              RV (2)  
              PCV (2) |
| 14 weeks    | RV (2) - Rotavirus vaccine  
              DTaP-IPV-Hib-HBV (3) – Combined diphtheria, tetanus, acellular pertussis, inactivated polio vaccine and *Haemophilus influenzae* type B and hepatitis B  
              PCV (2) – pneumococcal conjugate vaccine | RV (2 or 3)  
              DTaP-IPV-Hib-HBV (3)  
              PCV (3) |
| 6 months    | Measles vaccine (NB: measles vaccine should not be administered with other vaccines) | |
| 9 months    | PCV (3) – pneumococcal conjugate vaccine | Measles (1) or MMR (1) – measles, mumps and rubella  
              MCV (1) – meningococcal (groups A, C, W and Y) conjugate vaccine |
| 12–15 months| Measles vaccine (2) – at 12 months. (NB: do not administer with other vaccines) | PCV (4)  
              MMR (1 or 2)  
              MCV (2)  
              Varicella (1)  
              Hepatitis A (repeat after 6 months) |
| 18 months   | DTaP-IPV-Hib-HBV (4) – Combined diphtheria, tetanus, acellular pertussis, inactivated polio vaccine and *Haemophilus influenzae* type B and hepatitis B | DTaP-IPV-Hib-HBV (4) |
| 5-6 years   | Td vaccine – Tetanus and reduced strength of diphtheria vaccine | DTaP or Tdap-IPV  
              MMR (2 or 3)  
              Varicella (2) |
<table>
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<tr>
<th>9 years</th>
<th>HPV – human papillomavirus vaccine, bivalent (girls only)</th>
<th>HPV – quadrivalent from 9 years (boys and girls)</th>
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<tbody>
<tr>
<td>12 years</td>
<td>Td vaccine</td>
<td>Tdap-IPV</td>
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NOTES ON SPECIFIC VACCINES

ROUTINE SA CHILDHOOD VACCINES

BACILLE CALMETTE-GUERIN (BCG)

- **Trade name:** BCG Vaccine SSI®
- **Antigen:** Live, attenuated Bacillus Calmette-Guerin mycobacterium, part of the *Mycobacterium* complex group.
- **Action:** Protects mostly against severe forms *M. tuberculosis* disease, especially TB meningitis, for up to 15 years. Protects variably against pulmonary TB.
- **Side effects:** Swelling and blistering at injection site which may last weeks to months, is normal. Ulceration or abscess at site or in arm-pit requires specialist consultation. Immunocompromised children may develop severe disseminated BCG disease.
- **Contraindications:** Should not be given to children with primary immune deficiencies, those with signs of HIV disease or known to be HIV-infected, severely ill children or those with allergies to any components. As this is given at birth, it is usually not possible to know whether a child is HIV-infected if born to an HIV-infected mother. HIV-infection in a mother is not a contraindication to BCG vaccination of her newborn.
- **Administration:** Single intradermal injection
- **What if a dose is missed?** Vaccine may be given up to one year, but specialist consultation is suggested.

POLIO VACCINE (OPV)

- **Trade names:** OPV-Merieux® or Polioral®
- **Antigens:** Live attenuated poliovirus type one and three (bivalent). Trivalent OPV was discontinued globally in April 2016.
- **Action:** Virus replicates in the GIT after administration, and after full course protects 95% of recipients against infection with wild type one and three poliovirus infection. Vaccine-derived virus is excreted and thus provides herd immunity. In South Africa a birth and six weeks dose of OPV is still recommended to provide some herd immunity while we transition to global polio eradication.
- **Side effects:** Very rarely, about one in 2.4 million doses, recipients develop a polio-like illness. If vaccine coverage is low, a vaccine-derived poliovirus circulates for a prolonged time and may accumulate mutations and revert to virulence. This may lead to vaccine-derived polio-virus disease. Therefore it is very important to vacinate with OPV.
- **Contraindications:** Children who are severely ill or who have primary immune deficiencies should not be vaccinated. Minor concurrent diarrhoea and illness is not a contraindication to receiving vaccine.
- **What if a dose is missed?** Polio vaccine can be caught up at any age, but injectable, inactivated vaccine is preferred in adults.
ROTAVIRUS VACCINE (RV)
- Trade names: Rotarix® and Rotateq®
- Antigens: Live attenuated rotavirus A. Rotavirus A causes more than 90% of rotavirus disease.
- Action: Vaccine stimulates gut immunity to rotavirus A, and a full course protects against the first, severe attack of rotavirus disease. Mild rotavirus disease may still occur subsequently.
- Side effects: Mild side effects of irritability, mild diarrhoea or vomiting may occur. Severe allergic reactions are rare, as is intussusception.
- Contraindications: Children with severe immunosuppression or who are severely ill. Children who have had intussusception or an allergic reaction to a previous dose or known allergy to any vaccine components.
- Administration: The entire dose in the syringe should be given orally inside the cheek.
- What if a dose is missed? If Rotarix® is used it can be given up to 24 weeks. The Rotateq® first dose must be given before 12 weeks and the last dose by 32 weeks. Doses beyond these cut-offs should not be administered.

PNEUMOCOCCUS, PURIFIED POLYSACCHARIDE ANTIGEN CONJUGATED VACCINE (PCV)
- Trade names: Prevenar-13® and Synflorix®
- Antigens: Capsular polysaccharide subunits of Streptococcus pneumoniae conjugated to a protein to increase antigenicity. 13 capsular types are included.
- Action: The complete course induces durable immunity, usually into late adulthood to 13 types of S. pneumoniae which cause most severe disease, such as pneumonia and meningitis.
- Side effects: Commonly mild swelling and pain at injection site as well as loss of appetite. Less commonly inconsolable crying, high fever and drowsiness may occur. Severe allergic reactions are rare.
- Contraindications: Children who are allergic to any vaccine component or who have had an allergic reaction to a previous dose. Any child who is severely ill.
- Administration: Given as a series of intramuscular injections.
- What if a dose is missed? May be caught up but the number of doses depends on the patient’s age.

COMBINED DIPHTHERIA, TETANUS, ACELLULAR PERTUSSIS, INACTIVATED POLIO AND HAEMOPHILUS INFLUENZAE TYPE B AND HEPATITIS B VACCINE – DTAP-IPV-HIB-HBV
- Trade names: Hexaxim® and Infanrix Hexa®
- Hexavalent vaccine against diphtheria, tetanus, pertussis, polio, invasive Haemophilus influenzae type B disease and hepatitis B.
- Combined vaccine is recommended to reduce the number of injections, but separate vaccines may be given in certain situations.
- Antigens:
  - DTaP – diphtheria and tetanus toxoids, which are modified bacterial toxins. Acellular pertussis vaccine is purified, inactivated components of B. pertussis cells, including toxoids, namely pertussis toxin, filamentous haemagglutinin and pertactin.
  - IPV – killed (inactivated) whole cell vaccine, which contains all the serotypes of poliovirus.
  - Hib – subunit of the capsule of type B Haemophilus influenzae conjugated to protein to improve antigenicity.
  - HBV – subunit vaccine containing recombinant hepatitis B surface antigen (HBsAg).
• Action:
  This is the infant dosage formula. Reduced quantities of diphtheria toxoids are used in older children and adult formulations, noted by a lower case “d”.
  – DTaP – Diphtheria, tetanus and pertussis are toxin-mediated diseases. The diphtheria toxin and tetanus toxins are inactivated by formalin to create toxoids. Acellular pertussis vaccine is less effective than whole cell pertussis vaccine but has fewer adverse events. Immunity to DTaP is not long-lived and therefore booster doses are recommended in adolescents and certain adults.
  – IPV – more than 99% immunity after 3 doses
  – Hib – *Haemophilus influenzae* type B causes the most serious invasive disease such as meningitis. Efficacy is estimated at 95–100% against invasive disease, but the vaccine is less immunogenic in HIV-infected patients.
• HBV – overall about 95% effective in preventing infection or clinical hepatitis after a complete series.
• Side effects:
  – Local side effects include pain, redness and swelling at the injection site. Others include low grade fever, irritability, tiredness and occasionally mild vomiting
  – Rarely more serious side effects are usually due to the pertussis component and may include swelling of the limb into which the vaccine was given, prolonged crying, seizures and hypotonic hyporesponsive syndrome. In hypotonic hyporesponsive syndrome the child becomes unresponsive and hypotonic for a few hours followed by a full recovery. The risk is ~1 in 10 000.
  – Severe allergic reactions are rare
• Contraindications
  – Allergies to any of the vaccine components
  – Children who experienced the more serious side effects described above. The pertussis component should be omitted in follow-up doses.
  – Severely ill children
• What if a dose is missed? DTaP can be caught up at any age, but after the age of seven, reduced dose diphtheria (lower case “d”) should be used. The same applies for HBV and IPV. It is recommended that IPV, be given as the first dose in adults, catching up polio vaccination. Hib may be caught up until the age of five.

**MEASLES VACCINE**

• Trade names: Measbio® and Rouvax®
• Antigen: Live, attenuated virus vaccine. Measbio® which is the only single measles vaccine available in South Africa in 2017, must be given subcutaneously and not with any other vaccines. Other vaccines may be given a month later. More effective when given at 12 months or older, but due to circulating measles in South Africa and measles infections in younger infants, the EPI gives the first dose at six months followed by a second dose at 12–15 months.
• Action: two doses are required. 95% efficacy after two doses.
• Side effects: Pain and redness at site at injection with low grade fever are common. Also a transient measles-like rash and fever may present up to a few weeks after vaccination. Severe allergic reactions are rare.
• Contraindications: Should not be given to children who are severely immunosuppressed. HIV-infected children must, however, be immunised to protect these high risk patients. A severe allergic reaction to any of the ingredients is a contraindication.
• Administration: Rouvax®- intramuscular injection or deep subcutaneous injection; Measbio®- deep subcutaneous injection.
• What if a dose is missed? Measles vaccine can be caught up at any age.

MEASLES, MUMPS AND RUBELLA VACCINE (MMR)
• Trade names: Trimovax® and Priorix®
• Antigen: live, attenuated measles, mumps and rubella viruses.
• Action: two to five percent do not respond after the first dose but after second dose 98% efficacy after 15 months.
• Side effects: as for measles vaccine (above).
• Contraindications: as for measles vaccine above. Moderate to severe illness and severe immunosuppression is a contraindication. Of note, history of egg allergy is not a contraindication for MMR. Recent administration of blood products may interfere with response to vaccination.
• Administration: Intramuscular injection or deep subcutaneous injection.

MENINGOCOCCAL QUADRIVALENT POLYSACCHARIDE VACCINE (MVC)
• Trade names: Menactra®
• Antigen: Capsular polysaccharides of *Neisseria meningitidis* serogroups A,C,W and Y conjugated to diphtheria toxoid protein to improve antigenicity.
• Action: T-cell dependant response to serogroups A, C W and Y. Of note in South Africa, serogroup B also circulates especially in the Western Cape and no protection is conferred by Menactra® to serogroup B. Antibody responses to Menactra® have been shown to wane with time (over three to five years) and booster doses may be considered in high risk adolescents.
• Side effects: Mild local reactions of pain and swelling at the site of injection. Fever, headache and syncopy are also reported. Serious adverse events are rare.
• Contraindications: Children and adults with severe allergic reactions to any of the vaccine components or who are severely ill.
• Administration: Intramuscular injection.
• What if a dose is missed? May be caught up at any age.

VARICELLA VACCINE (CHICKENPOX VACCINE)
• Trade name: Varilrix®
• Antigen: Live, attenuated viral vaccine.
• Action: 70–90% effective against any varicella disease. 90–100% effective against moderate to severe varicella disease. Should be given after 12 months of age. Breakthrough infection is encountered but disease is less severe, fewer lesions experienced and the rash is often maculopapular as opposed to vesicular.
• Side effects: Local reactions of pain and erythema at the injection site. Generalised rash is reported in three percent of vaccine recipients.
• Contraindications: Severe allergic reaction to any vaccine components or with a previous dose of vaccine. Moderate to severe illness and primary or severe acquired immunosuppression is a contraindication. Children with CD4 T-lymphocyte percentage of 15% or higher or older children with a CD4 count of 200 cells/µL or higher may be considered for vaccination with single-antigen varicella vaccine. Recent administration of blood products may interfere with response to vaccination.
• Administration: Subcutaneous injection only.
• What if a dose is missed? May be caught up at any time after 12 months.

HEPATITIS A VACCINE
• Trade names: Avaxim® (paediatric and adult formulations) and Havrix® (paediatric and adult formulations)
• Antigen: Inactivated whole-virus vaccine.
• Action: More than 97% IgG seropositivity after one dose and 100% after two.
• Side effects: Mild local reactions of pain and swelling at the site of injection. Fewer than 10% report fever, malaise and low grade fever. No serious adverse events reported.
• Contraindications: Severe allergic reactions to any component or to a previous dose. Also moderate to severe acute illness.
• Administration: Two doses 6–12 months apart by means of an intramuscular injection.
• What if a dose is missed? May be caught up at any time ensuring the correct formulation for age.

HUMAN PAPILLOMAVIRUS VACCINE (HPV)
• Trade names: Cervarix® and Gardasil®
• Indication for use: Used to prevent cervical cancer and genital warts and typically given to adolescent girls and boys before they become sexually active. It may also be given to men and women up to 26 years of age who have not received the vaccine as a teenager.
• Antigens: Subunit vaccine of L1 protein of HPV. Cervarix® is bivalent containing L1 protein from high risk HPV genotypes 16 and 18. Gardasil® is quadrivalent containing L1 antigen from HPV 16 and 18 as well as the low risk types six and 11 which cause genital warts.
• Action: Although there are no serological correlates for protection, vaccines are highly efficacious in preventing HPV vaccine type-related persistent infection, CIN 2 and 3, and adenocarcinoma in situ.
• Side effects: Local reaction of pain, redness and swelling at injection site. Also fever sometimes reported, including syncope. No serious adverse events are known.
• Contraindications: Severe allergies to any vaccine components and serious illness.
• Recommended number of doses: Adolescents < 15 years give two doses six months apart. Adolescents ≥ 15 years and adults should receive three doses at zero, one and six months.
• What if a dose is missed? May be caught up at any time depending on the patient’s age.

NON ROUTINE CHILDHOOD, ADOLESCENT AND ADULT VACCINES

RABIES VIRUS VACCINE
• Trade names: Rabipur® and Verorab®
• Indication for use: Rabies pre-exposure prophylaxis is recommended for persons at continual or frequent risk of exposure to rabies. This includes vets and their practice staff, animal welfare staff, wildlife workers and laboratory personnel who may be exposed. In addition, travellers to high-risk countries should be vaccinated against rabies.
• Antigen: Inactivated whole virus vaccine.
• Action: Pre-exposure vaccination does not eliminate the need for additional post-exposure prophylaxis, however makes it simpler as only two doses of vaccine are indicated post exposure without rabies immune globulin.
• Side effects: Modern rabies vaccines are well tolerated. Local reactions such as pain at the injection site, redness, swelling and induration may occur. Mild systemic reactions are also reported (e.g., fever, headache, dizziness, gastrointestinal symptoms).
• Contraindications: A known life-threatening systemic hypersensitivity reaction to any component of the vaccine.
• Recommended number of doses: three doses of vaccine by intramuscular injection (deltoid in adults, anterolateral thigh in children) on days zero, seven, and 21 or 28. Routine monitoring of rabies antibody levels is advised every six months (continuous exposure such as a research lab worker) or every two years (frequent exposure such as vets, animal welfare, wildlife workers). A single booster dose should be given if protective rabies virus antibodies fall below 0.5 IU/mL.

ZOSTER VACCINE (SHINGLES VACCINE)
• Trade names: Zostavax®
• Indication for use: Herpes zoster vaccination can decrease the risk of developing herpes zoster (shingles) and post herpetic neuralgia among individuals ≥ 50 years of age. It is indicated in all adults ≥ 50 years of age, particularly in those receiving low dose immune suppression or expected to receive high dose immune suppression.
• Antigen: Live attenuated virus vaccine.
• Action: Boosts virus specific cell mediated immunity and significantly reduces the risk of developing shingles.
• Side effects: Zoster vaccine is generally well tolerated. The most common side effect after administration is pain at the injection site.
• Contraindications: Zoster vaccine is contraindicated in patients who are highly immunocompromised, have a history of an anaphylactic reaction to gelatin or neomycin, and pregnant women.
• Recommended number of doses: A single dose given by subcutaneous injection. It is not necessary to determine whether patients have a history of varicella or zoster prior to vaccination since waning antibodies in previously exposed patients (particularly older adults) may lead to negative results despite past infection.

INFLUENZA VIRUS VACCINE
• Trade names: Vaxigrip® and Influvac®
• Indication for use: Children and adults at high risk for influenza and its complications. This includes young children, adults ≥ 65 years; persons with chronic lung, heart, kidney and neurological disease, immune suppressed persons including HIV and pregnant women.
• Antigen: A trivalent subunit vaccine containing antigen from influenza A H1N1, H3N2 and influenza B. These antigens are changed on an annual basis as the virus changes from year to year.
• Action: Induces neutralising antibodies against the haemagglutinin antigen. Vaccine efficacy varies from year to year and in different patient groups. A mismatch between the vaccine and the circulating strain will significantly reduce vaccine efficacy.
• Side effects: Vaccines are generally well tolerated, with the most common side effect being pain at the injection site. Systemic symptoms such as fever, myalgia and headache are uncommon.
• Contraindications: A known systemic/anaphylactic reaction to egg protein.
• Recommended number of doses: Children and adults should be given a single dose by intramuscular injection. Children younger than nine years who have not been previously vaccinated should receive two doses one month apart.

**YELLOW FEVER VACCINE**

• Trade name: Stamaril®

• Indication for use: Yellow fever vaccine is recommended for people aged nine months and older that are travelling to, or living in, areas in South America and Africa where there is yellow fever virus transmission. In addition, some countries require proof of yellow fever vaccination for entry.

• Antigen: Live attenuated virus vaccine.

• Action: A single dose provides life-long protection in most immune-competent people. Booster doses is no longer a general requirement, but is recommended in certain populations.

• Side effects: Up to 30% of people report low-grade fever, myalgias and headache which may last up five days post vaccination. More serious, but rare adverse events include hypersensitivity reactions, yellow fever vaccine–associated neurologic disease (YEL-AND) and yellow fever vaccine-associated viscerotropic disease (YEL-AVD).

• Contraindications:
  - Children less than six months of age. Use with caution in children aged six to eight months.
  - HIV-infected persons with CD4 T cell counts < 200 cells/µL or < 15% of total lymphocytes for children younger than six years. CDC advises that vaccine should be used with caution asymptomatic HIV infection with CD4 T cell counts 200–499 cells/µL or 15–24% of total lymphocytes for children younger than six years.
  - Immunosuppressive and immunomodulatory therapies.
  - Other immunosuppressive conditions, such a primary immune deficiencies and thymus disorders such as myasthenia gravis.
  - Caution is also advised in pregnant and breast-feeding women and all adults > 60 years.
  - Administration: Intramuscular injection or subcutaneous injection.

For further information wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/yellow-fever

**VACCINATION IN TRAVELLERS**

Choice of vaccination in travellers includes many factors such as destination, season of travel, type of travel and accommodation, destination disease transmission epidemiology, regulatory requirements, health and immune status of the traveller. Also other measures of personal protection such as mosquito avoidance must be stressed.