About this module…

This module discusses target diseases for immunization programmes and describes the vaccines used to prevent them. The diseases are listed in alphabetical order. Where combination vaccines are recommended, their details are presented in summary tables within the relevant sections.

Each country determines its own immunization schedule and chooses vaccine presentations. Health workers should always refer to their national schedules and vaccine handling instructions when providing immunization services.

The vaccine summary tables provided in this module show schedule recommendations from WHO position paper summaries, which are available online at http://www.who.int/immunization/policy/immunization_tables/en/index.html.

Immunization programmes provide opportunities to promote integrated services and improve the overall health of recipients. Different sections of this module introduce some of these: human papillomavirus (HPV) vaccination as an opportunity to link to cervical cancer control and adolescent health services; Vitamin A supplementation as part of the Expanded Programme on Immunization (EPI) Plus; and pneumonia and diarrhoea control measures complementary to immunization as part of the 2013 integrated Global Action Plan for Pneumonia and Diarrhoea.
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1 Diphtheria

1.1 What is diphtheria?

Diphtheria is caused by the bacterium *Corynebacterium diphtheriae*. This bacterium produces a toxin that can harm or destroy human body tissues and organs. One type of diphtheria affects the throat and sometimes the tonsils. Another type, which is more common in the tropics, causes ulcers on the skin.

Diphtheria affects people of all ages, but most often it strikes unimmunized children. In temperate climates, diphtheria tends to occur during the colder months.

1.2 How is diphtheria spread?

Diphtheria is transmitted from person to person through close physical and respiratory contact.

1.3 What are the symptoms and signs of diphtheria?

When diphtheria affects the throat and tonsils, the early symptoms are sore throat, loss of appetite and slight fever. Within two to three days, a bluish-white or grey membrane forms in the throat and on the tonsils. This membrane sticks to the soft palate of the throat and can bleed. If there is bleeding, the membrane may become greyish-green or black. The patient may either recover at this point or develop severe weakness and die within six to 10 days. Patients with severe diphtheria do not develop a high fever but may develop a swollen neck and obstructed airway.

1.4 What are the complications of diphtheria?

The most severe complication of diphtheria is respiratory obstruction followed by death. During the early phase of the illness, or even weeks later, patients may develop abnormal heartbeats that can result in heart failure. Some patients with diphtheria experience inflammation of the heart muscle and valves, and this may lead to chronic heart disease and heart failure.

1.5 What is the treatment for diphtheria?

Children who develop diphtheria should be given diphtheria antitoxin and such antibiotics as erythromycin or penicillin. They should be isolated to avoid exposing others to the disease. About two days after starting antibiotic treatment, patients are no longer infectious.
To confirm the diagnosis, health workers should obtain throat cultures from suspected cases. However, treatment should begin urgently without waiting for culture results.

1.6 How is diphtheria prevented?

The most effective way to prevent diphtheria is to maintain a high level of immunization in the community. In most countries, diphtheria vaccine is given in combination with tetanus and pertussis vaccines (DTP). Some countries now use pentavalent vaccine that combines DTP with hepatitis B (HepB) and *Haemophilus influenzae* type b (Hib) vaccines. Pentavalent (DTP+HepB+Hib) vaccine reduces the number of injections needed for infant immunization. Sections 1.7–1.9 and Table 1.1 below describe diphtheria-containing vaccines.

1.7 What are diphtheria-containing vaccines?

Diphtheria-containing vaccines include: the combination with tetanus toxoid (DT/dT); the combination with tetanus and pertussis (DTP); and the combination with tetanus, pertussis, hepatitis B and *Haemophilus influenzae* type b (pentavalent). They are supplied in single- and multi-dose presentations. Pentavalent vaccine with a freeze-dried (also called lyophilized) Hib component requires reconstitution: see Module 5 (*Managing an immunization session*), Section 4.2 for details. They must be stored between +2 °C and +8 °C without being frozen. Pentavalent vaccine is freeze-sensitive. If freezing is suspected, the “Shake Test” should be performed to determine whether a vial is safe to use (see Module 2 (*The vaccine cold chain*), Section 7). Opened multi-dose vials must be handled according to national multi-dose vial policy (see Module 2, Section 5 for WHO policy).

Diphtheria-containing vaccines are administered as 0.5 ml doses given intramuscularly in the anterolateral (outer) thigh in infants and in the deltoid muscle (upper arm) of older children and adults.

1.8 How safe is diphtheria vaccine and what are the potential adverse events following immunization?

Diphtheria vaccine is usually used in combination with other vaccines, and severe adverse events due to it alone have not been reported. Mild events occur more frequently among people who have already received several booster doses, and usually improve without treatment. Among adults receiving boosters, local injection site reactions – redness and swelling in 38% and pain in 20% – have been reported.
WHO safety information summaries for DTP combination vaccines are on the website: http://www.who.int/vaccine_safety/initiative/tools/vaccinfosheets/en/.

1.9 When are diphtheria-containing vaccines administered?

Diphtheria-containing vaccine should be included in infant immunization programmes. A three-dose primary series starting as early as six weeks of age, with an interval of four to six weeks between doses, is generally recommended.

Unimmunized children aged one to seven years should receive three doses of DTP with an interval of two months between the first and second doses and an interval of six to 12 months between the second and third doses.

For all children over seven years of age and for all adults, including pregnant women, dT should be used since it has a lower concentration of diphtheria toxoid. For unimmunized individuals over seven years of age, two doses of dT one to two months apart followed by a third dose after six to 12 months is recommended.

When combined with tetanus vaccine, a total childhood schedule of five doses is required: three in infancy, another (DT) in early childhood (1–6 years) and another (dT) during adolescence (12–15 years). A further dose in adulthood is likely to provide lifelong protection.

Key points about diphtheria

- Diphtheria is spread from person to person in airborne droplets.
- Symptoms of the disease include sore throat, loss of appetite and mild fever.
- Patients with the disease can experience complications, such as abnormal heartbeat and inflammation of the heart muscle and valves, and this can lead to heart failure.
- Children with diphtheria should be treated with diphtheria antitoxin and antibiotics.
- The most effective way to prevent the disease is to maintain a high level of immunization within a community.
### Table 1.1 Diphtheria-containing vaccine summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Toxoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of doses</td>
<td>3–5 – see schedules</td>
</tr>
<tr>
<td><strong>Schedule – Pentavalent or DTP for infants</strong></td>
<td>For infant immunization doses:</td>
</tr>
<tr>
<td></td>
<td>• pentavalent1/DTP1 starting at age 6 weeks (minimum) with pentavalent2/DTP2 and pentavalent3/DTP3 at intervals of 4 weeks (minimum) to 8 weeks after the previous dose</td>
</tr>
<tr>
<td><strong>Schedule – DTP for unimmunized ages 1–7 years</strong></td>
<td>For children aged 1–7 years who have not previously been immunized:</td>
</tr>
<tr>
<td></td>
<td>• 3 doses of DTP with an interval of 2 months between the first and second doses and an interval of 6–12 months between the second and third doses</td>
</tr>
<tr>
<td><strong>Schedule – dT for unimmunized ages over 7 years</strong></td>
<td>For previously unimmunized individuals 7 years of age and older:</td>
</tr>
<tr>
<td></td>
<td>• dT1 and dT2 should be given 1–2 months apart, and dT3 given 6–12 months after dT2</td>
</tr>
<tr>
<td><strong>Booster</strong></td>
<td>When combined with tetanus vaccine, a total childhood schedule of 5 doses (3 in infancy), another (DT) in early childhood (1–6 years), and another (dT) during adolescence (12–15 years) is required. A further dose in adulthood is likely to provide lifelong protection.</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Anaphylaxis or hypersensitivity (allergy) after a previous dose</td>
</tr>
<tr>
<td><strong>Adverse events</strong></td>
<td>Severe adverse events due to diphtheria toxoid alone have not been reported</td>
</tr>
<tr>
<td></td>
<td>Mild: injection site reactions, fever</td>
</tr>
<tr>
<td><strong>Special precautions</strong></td>
<td>None</td>
</tr>
<tr>
<td><strong>Dosage</strong></td>
<td>0.5 ml</td>
</tr>
<tr>
<td><strong>Injection site</strong></td>
<td>Anterolateral (outer) thigh in infants</td>
</tr>
<tr>
<td></td>
<td>Deltoid muscle of upper arm in older children and adults</td>
</tr>
<tr>
<td><strong>Injection type</strong></td>
<td>Intramuscular</td>
</tr>
<tr>
<td><strong>Storage</strong></td>
<td>Between +2 °C and +8 °C</td>
</tr>
<tr>
<td></td>
<td>Do not freeze</td>
</tr>
</tbody>
</table>
Haemophilus influenzae type b disease

2.1 What is Haemophilus influenzae type b?

*Haemophilus influenzae* is a bacterium found commonly in the nose and throats of children. There are six types of *Haemophilus influenzae* that have an outer capsule. Of these six capsular types, type b is the largest public health concern. *Haemophilus influenzae* type b, or Hib, causes 90% of all serious *Haemophilus influenzae* infections.

Hib is responsible for severe pneumonia, meningitis and other invasive diseases, almost exclusively in children aged less than 5 years.

2.2 How is Hib spread?

Hib is spread from person to person in droplets released when sneezing and coughing. Children may carry Hib in their noses and throats without showing any symptoms or signs of illness (also known as healthy carriers), but they can still infect others.

2.3 What are the symptoms and signs of Hib disease?

The serious diseases caused most frequently by Hib are pneumonia and meningitis. While Hib is not the only cause of these diseases, it should be suspected in any child with relevant symptoms and signs. Children with pneumonia can have fever, chills, cough, rapid breathing and chest wall retractions. Children with meningitis can have fever, headache, sensitivity to light, neck stiffness and sometimes confusion or altered consciousness.

Hib can cause other diseases by infecting different parts of the body. Seen less frequently, but still serious, Hib disease includes epiglottitis (inflammation of the flap at the entrance to the larynx) resulting in stridor (noisy breathing) and breathing difficulty; and septicaemia (bloodstream infection) resulting in fever, shaking or chills, and further spread of the bacteria.

2.4 What are the complications of Hib disease?

Children who survive Hib meningitis may develop permanent neurological disability, including brain damage, hearing loss and mental retardation, in up to 40% of cases.
2.5 What is the treatment for Hib disease?

Hib disease can be treated with antibiotics, such as ampicillin, cotrimoxazole, cephalosporins and chloramphenicol. Hib that is resistant to some of the commonly used antibiotics is now being seen in many parts of the world.

2.6 How is Hib disease prevented?

Hib disease is best prevented by Hib-containing vaccine given in infancy or before 24 months of age. Vaccination is becoming increasingly important as Hib antibiotic resistance grows. Sections 2.8–2.10 and Table 1.2 below describe Hib-containing vaccines, including pentavalent vaccine.

2.7 What is needed for global Hib disease control?

The use of Hib vaccines should be part of a comprehensive strategy to control pneumonia including exclusive breastfeeding for six months, handwashing with soap, improved water supply and sanitation, reduction of household air pollution, and improved case management at community and health facility levels. Hib disease is included in the 2013 integrated Global Action Plan for Pneumonia and Diarrhoea, which outlines a “Prevent, Protect and Treat” framework (see Section 19 of this module).

2.8 What are Hib-containing vaccines?

Hib-containing vaccines prevent pneumonia, meningitis, epiglottitis, septicaemia and other Hib disease. They do not protect against other types of *Haemophilus influenzae* or other bacteria that cause similar diseases.

Hib-containing vaccines are available in stand-alone and combination forms. Hib combined with DTP and HepB vaccines, or pentavalent vaccine (DTP+HepB+Hib), reduces the number of injections an infant has to receive while completing the recommended immunization schedule.

Hib-containing vaccines are supplied in liquid or freeze-dried powder (also called lyophilized) formulations in single- and multi-dose presentations. Pentavalent vaccine is available in two- and 10-dose vials. Pentavalent vaccine with a freeze-dried Hib component requires reconstitution: see Module 5 (*Managing an immunization session*), Section 4.2 for details. The diluent for pentavalent vaccine is the DTP+HepB component. Hib-containing vaccines must be stored between +2 °C and +8 °C without being frozen. Freezing does not damage stand-alone freeze-dried Hib vaccine but does damage liquid Hib and pentavalent vaccines. If freezing is suspected, the Shake Test should be performed to determine whether a vial is safe to use (see Module 2 (*The vaccine cold chain*), Section 7). Opened multi-dose vials must be handled according to national multi-dose vial policy (see Module 2, Section 5 for WHO policy).
For infants, Hib-containing vaccines are administered as 0.5 ml doses in the anterolateral (outer) thigh. For older children (12–24 months of age), they may be given in the deltoid muscle (upper arm).

2.9 How safe is Hib vaccine and what are the potential adverse events following immunization?

Hib vaccine is one of the safest vaccines in current use. There are no known serious adverse events to date. Mild events include injection site pain, redness or swelling in approximately 10% of recipients and fever in 2%.

WHO safety information summaries for Hib and combination vaccines are on the website: http://www.who.int/vaccine_safety/initiative/tools/vaccinfosheets/en/.

2.10 When is Hib-containing vaccine administered?

Since serious Hib disease occurs mainly before 24 months of age, and infants are most at risk at between four and 18 months of age, Hib-containing vaccines should be included in all infant immunization schedules. Any of three schedules may be followed: three primary doses without a booster (3p+0), two primary doses plus a booster (2p+1), and three primary doses with a booster (3p+1). The series should start from six weeks of age, or as early as possible thereafter. The interval between doses should be at least four weeks if three primary doses are given, and at least eight weeks if two primary doses are given. When given, the booster dose should be given at least six months after completion of the primary series. Children who start vaccination late, but are aged less than 12 months, should complete the schedule. When a first dose is given to a child over 12 months of age, only one dose is recommended. Hib vaccine is not required for healthy children after five years of age.

Key points about Hib disease

- Hib disease primarily affects children under two years of age in developing countries.
- Healthy carriers as well as sick patients can spread Hib.
- Hib disease can affect different parts of the body. The most frequently seen serious diseases are pneumonia and meningitis.
- Hib conjugate vaccine protects only against the type b strain. The type b strain is found in 90% of serious *Haemophilus influenzae* cases.
- Hib vaccination should be given in infancy as part of a comprehensive package to reduce childhood pneumonia (see Section 19 of this module).
### Table 1.2 Hib-containing vaccines (Hib, pentavalent (DTP+HepB+Hib) summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Conjugate (capsular polysaccharide bound to a carrier protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of doses</td>
<td>3</td>
</tr>
</tbody>
</table>
| Schedules       | • Given as pentavalent, or as a separate injection at the same time as DTP from age 6 weeks  
                  • 3p+0: 3 primary doses given at minimum intervals of 4 weeks  
                  • 2p+1: 2 primary doses given at minimum intervals of 8 weeks and booster given at least 6 months after 2nd primary dose  
                  • 3p+1: 3 primary doses given at minimum intervals of 4 weeks and booster given at least 6 months after 3rd primary dose  
                  • Children >12 months of age without a primary series may be given a single dose |
| Booster         | As above                                                    |
| Contraindications| Anaphylaxis or hypersensitivity (allergy) after a previous dose |
| Adverse events  | • Severe: none reported to date  
                  • Mild: injection site reactions, fever |
| Special precautions | For pentavalent: do not use pentavalent vaccine to provide a birth dose of hepatitis B vaccine |
| Dosage          | 0.5 ml                                                      |
| Injection site  | • Anterolateral (outer) thigh in infants  
                  • Deltoid muscle of upper arm in older children and adults |
| Injection type  | Intramuscular                                               |
| Storage         | • Between +2 °C and +8 °C  
                  • Do not freeze   |
3.1 What is hepatitis B?

Hepatitis B is caused by a virus that infects the liver. Among adults who get hepatitis B, 90% recover completely. But among infants infected during birth or before one year of age, 90% develop chronic disease. Approximately 780,000 people die each year due to the consequences of hepatitis B such as cirrhosis or liver cancer.

3.2 How is hepatitis B spread?

The hepatitis B virus is spread by contact with infected blood and other body fluids in various situations: a) from mother to child during birth; b) during social interaction between children with cuts, scrapes, bites, and/or scratches; c) from person to person during sexual intercourse; and d) through unsafe injections and/or transfusions, or needle stick accidents with infected blood. Overall, hepatitis B is 50 to 100 times more infectious than HIV.

3.3 What are the symptoms and signs of hepatitis B?

Acute hepatitis B does not often cause symptoms and signs, but when it does, patients can have fatigue, nausea, vomiting, abdominal pain and jaundice (yellowing of the skin and eyes). Chronic hepatitis B patients have signs related to liver failure (such as swelling of the abdomen, abnormal bleeding and changing mental status) as the disease progresses.

3.4 What are the complications of hepatitis B?

A small proportion of acute infections can be severe (fulminant hepatitis) and lead to death. Other serious complications that occur in people with chronic infection include cirrhosis and liver cancer.

3.5 What is the treatment for hepatitis B?

There is no specific treatment for acute hepatitis B. Chronic hepatitis B can be treated with interferon and antiviral agents in some cases.
3.6 How is hepatitis B prevented?

Hepatitis B can be prevented by immunization. Since perinatal (around the time of birth) or postnatal (during the early days of life) transmission is an important cause of chronic infections globally, all infants should receive their first dose of HepB as soon as possible (less than 24 hours) after birth even in low-endemicity countries. After the birth dose, HepB vaccine should be administered with DTP and Hib, preferably in the form of pentavalent (DTP+HepB+Hib) vaccine. Sections 3.7–3.9 and Table 1.3 below describe HepB-containing vaccines.

People who recover completely from acute hepatitis B are protected from becoming infected again throughout their lives.

3.7 What are hepatitis B-containing vaccines?

Hepatitis B (HepB)-containing vaccines are available in stand-alone or combination (pentavalent or quadrivalent DTP+HepB) formulations. Stand-alone HepB vaccine is a liquid supplied in single- or multi-dose vials, or in prefilled auto-disable injection devices. Pentavalent vaccine with a freeze-dried Hib component requires reconstitution: see Module 5 (Managing an immunization session), Section 4.2 for details. HepB-containing vaccines must be stored between +2 °C and +8 °C. They are freeze-sensitive. If freezing is suspected, the Shake Test should be performed to determine whether a vial is safe to use (see Module 2 (The vaccine cold chain), Section 7). Opened multi-dose vials must be handled according to national multi-dose vial policy (see Module 2, Section 5 for WHO policy).

HepB-containing vaccines are administered as 0.5 ml doses given intramuscularly in the anterolateral (outer) thigh in infants and in the deltoid muscle (upper arm) of older children and adults.

If HepB vaccine vials stand for a long time, the vaccine may separate from the liquid. When separated, the vaccine looks like fine sand at the bottom of the vial. Shake the vial to mix it before using.
3.8 How safe is HepB vaccine and what are the potential adverse events following immunization?

HepB vaccine has an excellent safety profile. Severe adverse events include anaphylaxis, which has been reported in about one per million vaccine doses administered. Mild events include injection site pain in 3–29% of those vaccinated, redness or swelling in about 3%, headache in about 3% and fever in 1–6%.


3.9 When are HepB-containing vaccines administered?

All infants should receive HepB vaccine at birth, preferably within the first 24 hours. Only stand-alone HepB vaccine can be used for the birth dose. It can be given with BCG vaccine. HepB combinations such as pentavalent vaccine are recommended for subsequent doses. Two additional doses can be given in the form of pentavalent1 and 3. Alternatively, three additional doses can be given in the form of pentavalent1, 2 and 3. There should be a minimum interval of four weeks between doses.

HepB vaccine may also be used for older age groups at risk of infection, including patients who require frequent transfusions, dialysis patients, injecting drug users, household members and sexual contacts of known chronic hepatitis B patients, and health care workers.

Key points about hepatitis B

- 90% of infants infected develop chronic disease while 90% of healthy adults infected recover completely. Early vaccination at birth is important.
- The hepatitis B virus is spread through contact with blood or other body fluids from an infected person. It is 50 to 100 times more infectious than HIV.
- Chronic hepatitis B infection leads to cirrhosis, liver cancer, liver failure and death.
- All children should receive stand-alone hepatitis B vaccine at birth followed by two to three doses given with the DTP and Hib schedule, preferably as pentavalent vaccine.
### Table 1.3 HepB-containing vaccine summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Recombinant DNA or plasma-derived</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of doses</td>
<td>3 or 4 (including birth dose)</td>
</tr>
<tr>
<td><strong>Schedule – HepB birth dose followed by pentavalent</strong></td>
<td></td>
</tr>
<tr>
<td>• 3-dose primary series: stand-alone HepB as soon as possible after birth (&lt;24h), pentavalent1, pentavalent3</td>
<td></td>
</tr>
<tr>
<td>• 4-dose primary series: stand-alone HepB as soon as possible after birth (&lt;24h), pentavalent1, pentavalent2, pentavalent3</td>
<td></td>
</tr>
<tr>
<td>• Minimum interval of 4 weeks between doses required for both series</td>
<td></td>
</tr>
<tr>
<td>• For the pentavalent schedule, see Table 1.2: starting at age 6 weeks (minimum) with second and third doses at 4–8 week intervals after the previous dose</td>
<td></td>
</tr>
<tr>
<td>Booster</td>
<td>None</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Anaphylaxis or hypersensitivity (allergy) after a previous dose</td>
</tr>
<tr>
<td>Adverse events</td>
<td>• Severe: rare anaphylaxis</td>
</tr>
<tr>
<td></td>
<td>• Mild: injection site reactions (pain, redness, swelling); headache; fever</td>
</tr>
<tr>
<td>Special precautions</td>
<td>Use only stand-alone HepB vaccine for the birth dose (do not use pentavalent vaccine for the birth dose)</td>
</tr>
<tr>
<td>Dosage</td>
<td>0.5 ml</td>
</tr>
<tr>
<td>Injection site</td>
<td>• Anterolateral (outer) thigh in infants</td>
</tr>
<tr>
<td></td>
<td>• Deltoid muscle of upper arm in older children and adults</td>
</tr>
<tr>
<td>Injection type</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>Storage</td>
<td>• Between +2 °C and +8 °C</td>
</tr>
<tr>
<td></td>
<td>• Do not freeze</td>
</tr>
</tbody>
</table>
Human papillomavirus infection and cervical cancer

4.1 What is human papillomavirus?

Human papillomavirus (HPV) is a common sexually transmitted virus that causes genital warts and various cancers. There are more than 100 types of HPV. Some types cause only genital warts, but at least 13 different types cause cancer. While HPV does cause cancer of the anus, external genitalia and oral cavity in both sexes, it is of particular concern in women since it is now known to be the cause of 99% of cervical cancers.

Cervical cancer is the leading cause of cancer death in adult women in the developing world and the second most common cancer among women worldwide. Approximately 85% of these deaths occur in developing countries.

4.2 How is HPV spread?

HPV spreads easily by skin-to-skin contact. Almost all sexually active individuals become infected with it at some point, usually early in their sexual lives.

4.3 What are the symptoms and signs of cervical cancer?

Most HPV infections do not cause symptoms or disease and usually clear within a few months. About 90% of infections clear within two years, but some infections continue. Infection that continues can progress to cervical cancer with specific types of HPV (particularly types 16 and 18). This progression takes 20 years on average and tends to cause symptoms only after the cancer has reached an advanced stage.

Symptoms and signs of cervical cancer include abnormal vaginal bleeding (after sexual intercourse and/or between menstrual periods); pelvic, back and/or leg pain; vaginal discharge; fatigue and weight loss. Anaemia, renal failure and fistulae can also occur in advanced stages of cervical cancer.

4.4 What is the treatment for cervical cancer?

A comprehensive approach should be taken to prevent cervical cancer as described in Section 4.5.

If cervical cancer is caught early by screening methods such as the Papanicolaou smear (Pap smear), HPV-DNA tests and/or visual inspection with acetic acid, then it can be
removed and cured effectively with localized treatment (e.g. cryotherapy). Treatment of advanced cancer is complicated and usually involves combinations of surgery, radiotherapy and chemotherapy.

4.5 What can be done to prevent and control cervical cancer?

Comprehensive cervical cancer prevention and control consists of: a) primary prevention by vaccination against HPV infection for girls nine to 13 years of age and, for both girls and boys, health education warning against tobacco use, sexuality education and promotion of condom use, and male circumcision; b) secondary prevention in women aged 30–49 years with a screen and treat approach, since vaccination does not protect against all cancer-causing HPV types; and c) tertiary prevention by treatment of invasive cancer at any age.

Currently available HPV vaccines can prevent infection with the two HPV types, 16 and 18, which are known to cause 70% of cervical cancers. This is important particularly in countries that lack resources for effective screening programmes. Screening by Pap smear, HPV-DNA or visual inspection with acetic acid is recommended at least once for women between 30 and 49 years of age even after vaccination, since cervical cancer related to other HPV types may still occur. Condom use can also reduce the risk of infection with HPV. For an HIV-positive woman, screening should start when the HIV diagnosis is confirmed, regardless of her age.

HPV vaccines should be introduced as part of a coordinated strategy to prevent cervical cancer.

HPV vaccination of males is not recommended as a priority, especially in resource-constrained settings. The available evidence indicates that the first priority should be for cervical cancer reduction by timely and high-coverage vaccination of young females.

Sections 4.6–4.8 and Table 1.4 describe available HPV vaccines.

4.6 What is HPV vaccine?

Two HPV vaccines are currently available worldwide: a bivalent vaccine, Cervarix®, which protects against HPV types 16 and 18, and a quadrivalent vaccine, Gardasil®, which protects against four HPV types (6 and 11 (which cause genital warts), and 16 and 18). Both are available in single-use vials or prefilled syringes. The bivalent HPV vaccine (Cervarix®) also comes in two-dose vials. These vaccines do not require reconstitution. They must be stored between +2 °C and +8 °C. Opened multi-dose vials must be handled according to national policy (see Module 2, Section 5 for WHO multi-dose vial policy).

Both vaccines are administered intramuscularly in two or three separate 0.5 ml doses.
4.7 How safe is HPV vaccine and what are the potential adverse events following immunization?

Both HPV vaccines are well tolerated and have excellent safety profiles. Serious events include rare anaphylaxis with quadrivalent vaccine (1.7–2.6 per million doses). Mild events include local injection site reactions (pain, redness and swelling). These usually resolve without treatment. Other mild events reported following HPV vaccination include fever, dizziness and nausea. Adolescents are known to sometimes faint after any injection and should be seated during vaccination and for at least 15 minutes afterwards.

WHO safety information summary for HPV vaccines is available on the website: http://www.who.int/vaccine_safety/initiative/tools/vaccinfosheets/en/.

4.8 When is HPV vaccine administered?

The recommended target population for the prevention of cervical cancer is females aged nine to 13 years, prior to becoming sexually active. For females younger than 15 years, a two-dose schedule with an interval of six months is recommended. Even those females who are over 15 years at the time of the second dose are adequately protected by two doses. There is no maximum recommended interval between doses. However, an interval of no greater than 12–15 months is suggested in order to complete the schedule promptly and before the start of sexual activity. If the interval between the two doses is less than five months, a third dose should be given at least six months after the first dose. For females over 15 years of age, or who are known to have a compromised immune system (that does not respond normally) and/or are HIV-infected, a three-dose schedule (at 0, 1 or 2 and 6 months) is recommended.

HPV vaccines can be delivered through a healthcare facility-based strategy, or a school- and/or other community-based outreach service. If a girl gets pregnant before she has been fully immunized, the remaining dose(s) should be postponed since it is not licensed for use in pregnancy. To date, no health problems for mother or child have been observed following vaccination during pregnancy.
Module 1: Target diseases and vaccines

Key points about HPV and cervical cancer

- Cervical cancer is the leading cause of cancer death among women in developing countries.
- Almost all cervical cancers are caused by HPV, a sexually transmitted virus. Two types of HPV (types 16 and 18) cause 70% of cervical cancer cases.
- Cervical cancer develops many years after initial HPV infection and does not usually show symptoms and signs until it is late stage and difficult to treat.
- HPV vaccination, condom use, prevention of tobacco use, and cervical cancer screening later in life are all needed to prevent cervical cancer.
- Screening to detect early changes that lead to cancer is needed at least once for all women aged 30–49 years, including those who were vaccinated, because the vaccine does not protect against all HPV types that cause cervical cancer.
- Two HPV vaccines, a bivalent and a quadrivalent, are currently available.

### Table 1.4 Summary of HPV vaccines for girls aged between 9 and 13 years

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Recombinant protein capsid, liquid vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of doses</td>
<td>2</td>
</tr>
<tr>
<td>Schedule –</td>
<td></td>
</tr>
<tr>
<td><strong>bivalent</strong> (HPV types 16 and 18; GSK Cervarix®) and <strong>quadrivalent</strong> (HPV types 6, 11, 16 and 18; Merck Gardasil®)</td>
<td>• 0 and 6 months</td>
</tr>
<tr>
<td></td>
<td>• There is no maximum interval between doses – as long as the girl is under 15 years of age at the time of the first dose, two doses are sufficient</td>
</tr>
<tr>
<td></td>
<td>• If the interval between doses is less than 5 months, a third dose should be given at least 6 months after the first dose.</td>
</tr>
<tr>
<td><strong>Note:</strong> For females ≥15 years of age, or who are known to have a compromised immune system and/or are HIV-infected, a 3-dose schedule (at 0, 1 or 2 and 6 months) is recommended</td>
<td></td>
</tr>
<tr>
<td>Contraindications</td>
<td>Anaphylaxis or hypersensitivity (allergy) after a previous dose</td>
</tr>
<tr>
<td>Adverse events</td>
<td>• Severe: rare anaphylaxis</td>
</tr>
<tr>
<td></td>
<td>• Mild: injection site reactions; fever, dizziness, nausea</td>
</tr>
<tr>
<td>Special precautions</td>
<td>• Postpone vaccination for pregnancy</td>
</tr>
<tr>
<td></td>
<td>• Adolescents should be seated during injections and for 15 minutes afterwards since they sometimes faint</td>
</tr>
<tr>
<td>Dosage</td>
<td>0.5 ml</td>
</tr>
<tr>
<td>Injection site</td>
<td>Deltoid muscle of upper arm</td>
</tr>
<tr>
<td>Injection type</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>Storage</td>
<td>Between +2 °C and +8 °C</td>
</tr>
<tr>
<td></td>
<td>Do not freeze</td>
</tr>
</tbody>
</table>
5.1 What is Japanese encephalitis?

Japanese encephalitis (JE) is an infection of the brain caused by a virus. It is found in nearly all Asian countries, some Pacific Islands and a small part of Northern Australia. Although traditionally considered a childhood disease, JE can occur in all ages, particularly when the virus is introduced into new areas where the population has no pre-existing immunity.

5.2 How is Japanese encephalitis spread?

The JE virus is spread by mosquitoes. It normally infects birds and domestic animals, especially wading birds and pigs, which serve as its reservoirs. Humans may contract the disease when a mosquito that has bitten an infected animal then bites a person.

In temperate climate zones, JE occurs more frequently during the warm season. In subtropical and tropical areas, the disease occurs at the highest rate during and shortly after the rainy season, although where irrigation permits mosquito breeding, transmission can occur all year. People living in rural areas, especially where rice is grown, are most at risk although patterns of the disease are changing.

5.3 What are the symptoms and signs of Japanese encephalitis?

The majority of infections result in mild symptoms or no symptoms at all. On average, only one of every 250 people infected with the virus develops symptoms. Symptoms, which usually appear four to 14 days after infection, are flu-like, with sudden onset of fever, chills, headache, tiredness, nausea and vomiting. In children, stomach or abdominal pain may be the most prominent symptom during the early stage of the illness. Signs of confusion or coma occur after three to four days. Children often have seizures.

5.4 What are the complications of Japanese encephalitis?

JE is fatal in about 20–30% of cases, with young children (less than 10 years of age) having a greater risk of severe disease and a higher case fatality rate. Of those who survive the disease, 30–50% will have brain damage and paralysis.
5.5 What is the treatment for Japanese encephalitis?

There is no specific treatment. Since JE is caused by a virus, antibiotics are not effective. Supportive treatment should be given to reduce symptoms.

5.6 How is Japanese encephalitis prevented?

Immunization is the single most important measure to control JE. No effective method of environmental control of JE transmission is known. Socioeconomic improvements and changes in agricultural practices may reduce viral transmission in some places, but large-scale vaccination of affected populations with effective and affordable vaccines appears to be the logical control measure, at least in the short term. Sections 5.7–5.9 and Table 1.5 describe JE vaccine.

Bed nets may help prevent JE in small children since mosquitoes carrying JE tend to bite in the twilight hours.

5.7 What is Japanese encephalitis vaccine?

There are now four types of vaccines that protect against JE:

- Inactivated Vero cell-derived vaccine (so called since the virus is grown in Vero cells) – the vaccine with the brand name JEEV® has been WHO prequalified.

- Live attenuated (weakened) vaccine – single- and multi-dose vials of the vaccine are WHO prequalified.

- Live recombinant vaccine – this type of vaccine, which is also grown in Vero cells and is WHO prequalified, combines parts of an attenuated JE virus with an attenuated yellow fever vaccine virus (brand names include IMOJEV®, JE-CV® and ChimeriVax-JE®).

- Inactivated mouse brain-derived vaccine (so called because the virus is grown in mouse brains) – this is an older type of vaccine that is slowly being replaced with the newer ones above. No inactivated mouse brain-derived vaccines are WHO prequalified.

Summaries of these vaccines are in Tables 1.5–1.8.

WHO recommends the first three newer vaccine types over the older inactivated mouse brain-derived vaccines.
5.8 How safe is Japanese encephalitis vaccine and what are the potential adverse events following immunization?

JE vaccines have acceptable safety profiles. The tables in this section include adverse events noted for each type of JE vaccine.


5.9 When is Japanese encephalitis vaccine administered?

JE vaccine should be integrated into EPI programmes in all areas where JE constitutes a public health problem. The most effective immunization strategy in JE-endemic settings is one-time catch-up campaigns, including child health weeks or multi-antigen campaigns in the locally defined primary target population, followed by incorporation of the JE vaccine into the routine immunization programme.

Key points about Japanese encephalitis

- JE is found in nearly all Asian countries, some Pacific islands and a small part of northern Australia.
- The disease is spread by infected mosquitoes.
- In temperate zones, JE occurs more frequently during the warm season. In subtropical and tropical areas, the disease occurs with the rainy season, although transmission can occur all year.
- The illness can progress to encephalitis, a serious infection/inflammation of the brain that is fatal in 20–30% of cases. It can also cause paralysis and brain damage.
- There is no specific treatment for JE.
- Immunization with JE vaccine is the single most important control measure.
### Table 1.5 Inactivated Vero cell-derived Japanese encephalitis vaccine summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Inactivated Vero cell-derived</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of doses</td>
<td>Two doses at 4-week intervals, with the primary series starting at ( \geq 6 ) months of age in endemic settings</td>
</tr>
<tr>
<td>Schedule</td>
<td>As above</td>
</tr>
<tr>
<td>Booster</td>
<td>WHO position states that the need for a booster in endemic settings has not been clearly established</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Known allergy to the vaccine or its components</td>
</tr>
<tr>
<td>Adverse events</td>
<td>Injection site reactions: pain, redness, swelling (in 4% of cases); hives (6%); headache and dizziness (less than 1%); fever (12%)</td>
</tr>
<tr>
<td>Special precautions</td>
<td>Postpone vaccination in persons with acute severe febrile conditions</td>
</tr>
<tr>
<td>Dosage</td>
<td>0.25 ml for those aged &lt;3 years, 0.5 ml for those aged ( \geq 3 ) years</td>
</tr>
<tr>
<td>Injection site</td>
<td>Anterolateral (outer) thigh for children</td>
</tr>
<tr>
<td></td>
<td>Deltoid muscle of upper arm for adults</td>
</tr>
<tr>
<td>Injection type</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>Storage</td>
<td>Between +2 °C and +8 °C</td>
</tr>
</tbody>
</table>

### Table 1.6 Live attenuated Japanese encephalitis vaccine summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Live attenuated virus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of doses</td>
<td>1</td>
</tr>
<tr>
<td>Schedule</td>
<td>Single dose administered at ( \geq 8 ) months of age</td>
</tr>
<tr>
<td>Booster</td>
<td>WHO position states that the need for a booster in endemic settings has not been clearly established</td>
</tr>
</tbody>
</table>
| Contraindications       | - Known allergy to the vaccine or any of its components  
                          - Pregnancy  
                          - Any condition that results in a decreased or abnormal immune system response, including due to any infection (such as HIV), medication and/or congenital problems (since birth)  
                          - Acute diseases, severe chronic diseases, and chronic diseases with acute symptoms and/or fever  
                          - Encephalopathy (brain disease), uncontrolled epilepsy (seizures) or other diseases of the nervous system |
| Adverse events          | High fever (5–7% of those vaccinated); injection site reactions (redness, swelling: in less than 1% with some types of vaccine); low-grade fever, irritability, nausea and dizziness (rare) |
| Special precautions      | - Review medical history – caution needed for family or individual history of seizures or other chronic diseases, allergies and for women who are lactating  
                          - Postpone vaccination for at least 3 months if the person has been given immunoglobulin  
                          - There should be at least a 1 month interval (either before or after) between JE and other live vaccines  
                          - Women of childbearing age should avoid pregnancy for at least 3 months after immunization  
                          - Live attenuated JE vaccine is not meant to be given during JE epidemic seasons |
| Dosage                  | 0.5 ml |
| Injection site          | Upper arm |
| Injection type          | Subcutaneous |
| Storage                 | Between +2 °C and +8 °C |
### Table 1.7  Live recombinant Japanese encephalitis vaccine summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Live recombinant virus vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of doses</td>
<td>1</td>
</tr>
<tr>
<td>Schedule</td>
<td>Single dose at &gt;9 months of age</td>
</tr>
<tr>
<td>Booster</td>
<td>WHO position states that the need for a booster in endemic settings has not been clearly established</td>
</tr>
</tbody>
</table>
| Contraindications             | • Known allergy to the vaccine or any of its components  
|                               | • Pregnancy                                     |
|                               | • Lactation                                     |
|                               | • Any condition that results in a decreased or abnormal immune system response, including due to any infection (such as HIV), medication and/or congenital problems (since birth)  
|                               | • Symptomatic HIV infection                      |
| Adverse events                | Comparable to other vaccines; lower local reaction rates in adults (compared to mouse brain-derived JE vaccines); high fever, acute viral illness have been reported only twice |
| Special precautions            | Postpone vaccination for acute febrile illness |
| Dosage                        | Per manufacturer’s instructions                 |
| Injection site                | Upper arm                                       |
| Injection type                | Subcutaneous                                    |
| Storage                       | Between +2 °C and +8 °C                         |

### Table 1.8  Japanese encephalitis mouse brain-derived vaccine summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Live attenuated vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of doses</td>
<td>1 (primary immunization)</td>
</tr>
<tr>
<td>Schedule</td>
<td>First dose at 9–12 months of age</td>
</tr>
<tr>
<td>Booster</td>
<td>After 1 year</td>
</tr>
</tbody>
</table>
| Contraindications             | • Hypersensitivity (allergy) to gelatin, gentamycin, kanamycin  
|                               | • Pregnancy                                    |
|                               | • Any condition that results in a decreased or abnormal immune system response, including due to any infection (such as HIV), medication and/or congenital problems (since birth)  |
| Adverse events                | • Severe: anaphylaxis in 1–2% of those vaccinated; hypersensitivity (allergy) reactions, sometimes up to 9 days after vaccination in 17%; nervous system complications in 1–2.3%  
|                               | • Mild: fever, injection site swelling in about 20% of those vaccinated; headache, muscle aches, low-grade fever, nausea, vomiting, abdominal pain, rash, chills, dizziness in 5–30% |
| Special precautions            | Not usually given before 9 months of age       |
| Dosage                        | 0.5 ml                                         |
| Injection site                | Upper arm                                      |
| Injection type                | Subcutaneous                                   |
| Storage                       | Between +2 °C and +8 °C                        |
Measles

6.1 What is measles?

Measles is a highly infectious disease caused by a virus. It remains an important cause of death among young children globally, despite the availability of a safe and effective vaccine. More than 95% of measles deaths occur in countries with low incomes and weak health infrastructures.

Because the disease is so infectious, it tends to occur as an epidemic with high death rates in settings such as refugee camps. Severe measles is particularly likely to occur in poorly nourished children, especially those who do not receive sufficient vitamin A, who live in crowded conditions, and whose immune systems have been weakened by HIV/AIDS or other diseases.

6.2 How is measles spread?

Measles is spread through contact with nose and throat secretions of infected people and in airborne droplets released when an infected person sneezes or coughs.

People with measles can infect others for several days before and after they develop symptoms. The disease spreads easily in places where infants and children gather, such as health centres and schools.

6.3 What are the symptoms and signs of measles?

The first sign of infection is a high fever, which begins approximately 10 to 12 days after exposure to the measles virus and lasts several days. During this period, the patient may develop a runny nose, a cough, red and watery eyes, and small white spots (Koplik spots) inside their cheeks. About seven to 18 days after exposure, a slightly raised rash develops, usually on the face and upper neck. Over a period of about three days, the rash spreads to the body and then to the hands and feet. It lasts for five to six days and then fades.

6.4 What are the complications of measles?

Unimmunized children under five years of age and, especially, infants are at the highest risk of contracting measles and suffering from its complications, which can include death. Infected infants may suffer from dehydration due to severe diarrhoea. Children may also develop malnutrition, inflammation of the middle ear, pneumonia and encephalitis (brain infection). Measles is a major cause of blindness among children in Africa and other areas of the world where it is endemic.
Pneumonia is the most common cause of death associated with measles. The pneumonia may be caused by the measles virus itself or by a secondary bacterial infection.

6.5 What is the treatment for measles?

There is no specific antiviral treatment for measles. Antibiotics should be prescribed only for bacterial ear infections and pneumonia. General nutritional support and the treatment of dehydration with oral rehydration solution are important. Children with measles should therefore be encouraged to eat and drink.

All children in developing countries diagnosed with measles should receive two doses of vitamin A supplement given 24 hours apart to help prevent eye damage and blindness. Vitamin A supplementation reduces the number of deaths from measles by 50%.

6.6 How is measles prevented?

Measles is prevented by immunization with measles-containing vaccine (MCV). High coverage with a two-dose schedule is needed to prevent measles epidemics. Sections 6.8–6.10 and Table 1.9 below describe MCVs. Children who have recovered from measles are immune for the rest of their lives.

6.7 What is needed for global measles control?

The Global Measles and Rubella Strategic Plan (2012–2020) focuses on five core components: a) achieving and maintaining high levels of population immunity by providing high vaccination coverage with two doses of measles-containing vaccine; b) monitoring disease and evaluating programmatic efforts to ensure progress; c) developing and maintaining outbreak response and case management capacities; d) communicating to build public confidence and demand for immunization; and e) performing research and development to support cost-effective operations and to improve vaccination and diagnostic tools.

6.8 What are measles-containing vaccines?

Measles-containing vaccines (MCVs) include measles only (M) or a combination of measles with rubella (MR), mumps (MM, MMR) and varicella (MMRV) vaccines. MCVs can be used interchangeably in immunization programmes. MM and MMRV are not discussed in this module; national guidelines should be made available if either is used routinely in an immunization programme.

M, MR and MMR are supplied as freeze-dried (also called lyophilized) powders with diluents in separate vials. They must be reconstituted before use with only the diluent supplied: see Module 5 (Managing an immunization session), Section 4.2 for details. Measles-containing vaccines must be stored between +2 °C and +8 °C and protected
from sunlight since they are sensitive to both heat and light. Opened multi-dose vials must be handled according to national multi-dose vial policy (see Module 2, Section 5 for WHO policy).

MCVs are administered by subcutaneous injection.

In countries where vitamin A deficiency is common, vitamin A supplements are often given at the same time as the vaccine (see Section 18 of this module).

6.9 How safe is measles vaccine and what are the potential adverse events following immunization?

All MCVs approved for immunization programmes are safe and effective. Serious events are rare and include anaphylaxis in 1–3.5 per one million doses administered, severe allergic reaction in one per 100 000 doses, and thrombocytopenia (decreased platelet count) in one per 30 000 doses. Encephalitis (brain infection) has been reported rarely but there is no definite proof that the vaccine was the cause. Mild events are more common and include local injection site pain and tenderness, fever (in 5–15%) and rash (in about 5%), which can occur five to 12 days after vaccination.

A WHO safety information summary for MMR vaccine is available on the website: http://www.who.int/vaccine_safety/initiative/tools/vaccinfosheets/en/.

6.10 When are measles-containing vaccines administered?

All children should receive two doses of MCV. Very high (90–95%) coverage with both doses is required to prevent measles outbreaks. The first dose (MCV1) should be given at nine or 12 months of age. Because many cases of measles occur in children over 12 months of age who have not been vaccinated, routine delivery of MCV1 should not be limited to infants ages nine to 12 months. All unvaccinated children over 12 months should be offered MCV1 using every opportunity when the child comes in contact with health services.

MCV2 should be given between 15–18 months of age. Vaccinating in the second year of life reduces the number of unprotected children. This may be linked to the timing of other routine immunizations (for example, a DTP booster). Screening for measles vaccination at school entry helps to ensure that all children receive both doses.

In measles outbreaks or in areas where there is a high rate of both HIV infection and measles, the first dose of MCV1 may be offered as early as age six months. Two additional doses of measles vaccine should be administered to these children according to the national immunization schedule.
Key points about measles

- Measles is a highly infectious viral disease that is spread from person to person through sneezing, coughing and close personal contact.
- The first sign of infection is a high fever lasting one to seven days. A generalized rash develops seven to 18 days after exposure to the virus.
- Pneumonia is the most common cause of death associated with measles.
- Severe complications can be avoided through proper case management, including vitamin A supplementation.
- Measles can be prevented by immunization. All children should receive two doses of measles vaccine. Very high coverage (90–95%) is needed with both doses.

Table 1.9 Measles-containing vaccines summary (MCV = M, MR, or MMR)

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Live attenuated (weakened) viral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of doses</td>
<td>2</td>
</tr>
</tbody>
</table>
| Schedule | • MCV1: 9 or 12 months of age; minimum age 6 months (for infants at high risk, see text)  
• MCV2: at least 1 month after MCV1 |
| Contraindications | • Known allergy to vaccine components (including neomycin and gelatin)  
• Pregnancy  
• Severe congenital or acquired immune disorders, including advanced HIV infection/AIDS |
| Adverse events | • Serious: thrombocytopenia (decreased platelets), anaphylaxis, encephalitis (brain infection, though causal link not certain)  
• Mild: fever, rash 5–12 days following administration |
| Special precautions | None |
| Dosage | 0.5 ml |
| Injection site | Anterolateral thigh or upper arm depending on the child’s age |
| Injection type | Subcutaneous |
| Storage | • Between +2 °C and +8 °C  
• Keep all MCVs away from sunlight |
7.1 What is meningococcal disease?

Meningococcal meningitis is an infection of the meninges (membranes covering the brain and spinal cord) caused by the bacterium *Neisseria meningitidis* (also known as the meningococcus). Each *Neisseria meningitidis* bacterium has a capsule and, depending on the type of this capsule, it is put in a serogroup. *Neisseria meningitidis* serogroups A, B, C, X, W135 and Y cause most cases of meningococcal meningitis. It occurs globally, but in the sub-Saharan Africa meningitis belt, epidemics occur every two to three years. Since the 1980s, the intervals between major epidemics of meningococcal meningitis have become shorter and more irregular.

The meningococcus bacterium can also cause septicaemia (bloodstream infection), which is less common but more severe and often fatal.

7.2 How is meningococcal disease spread?

The meningococcus is spread from person to person via airborne droplets emitted from the nose and throat of infected people. Meningococcal disease is most common in young children, but older children and young adults living in crowded conditions can also be at high risk.

7.3 What are the symptoms and signs of meningococcal disease?

Meningococcal meningitis is marked by the sudden onset of intense headache, fever, nausea, vomiting, sensitivity to light and stiff neck. Other signs include lethargy, delirium, coma and convulsions. Infants may not have sudden-onset illness and a stiff neck; they may only appear to be slow, inactive, irritable or are feeding poorly and may be vomiting.

A petechial rash (petechiae are small spots of bleeding into the skin) is the key sign of meningococcal septicaemia, which can be followed by rapid shock and death.

7.4 What are the complications of meningococcal disease?

Death occurs in almost all untreated cases. Even with early treatment, up to 10% of patients die. About 10–20% of meningococcal meningitis survivors suffer from complications, such as mental retardation, deafness, paralysis and seizures.
7.5 What is the treatment for meningococcal disease?

Because the meningococcus is a bacterium, antibiotics such as ceftriaxone, chloramphenicol and penicillin G are effective. Each case should be considered as a medical emergency and referred to a hospital to reduce the risk of death from rapidly progressing disease.

7.6 How is meningococcal meningitis prevented?

Several vaccines are available to protect against meningococcal serogroups A, C, W135 and Y. No vaccine protects against serogroup X at this time. Countries must choose a vaccine based on the meningococcal serogroups most often identified locally. Sections 7.8–7.10 and Tables 1.10–1.12 describe meningococcal vaccines.

7.7 What is needed for meningococcal disease control?

Epidemic control relies on good surveillance with early detection and treatment of cases as well as immunization. A mass immunization campaign that reaches at least 80% of the entire population with vaccine against serogroups A and C can prevent an epidemic in areas where these serogroups are the cause of outbreaks.

7.8 What is meningococcal vaccine?

There are two categories of meningococcal vaccine, as shown in Table 1.10 below: polysaccharide vaccines with specific capsule serogroup antigens and polysaccharide-protein conjugate vaccines, which have serogroup antigens bound to a protein that helps increase the immune system response to the vaccine. Conjugate vaccines are preferred over polysaccharide vaccines due to their potential for herd protection and their increased ability to generate immunity, particularly in children under two years of age (this is similar for pneumococcal conjugate vaccines, see Section 10 of this module).

Meningococcal vaccines should be stored between +2 °C and +8 °C. Polysaccharide vaccines are generally given as a 0.5 ml dose subcutaneously. Conjugate vaccines are administered as a 0.5 ml dose intramuscularly.

Table 1.10 Meningococcal vaccines

<table>
<thead>
<tr>
<th>Meningococcal vaccine category</th>
<th>Serogroups (and other antigens)</th>
<th>How supplied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polysaccharide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>bivalent</td>
<td>A, C</td>
<td>Freeze-dried powder requiring reconstitution</td>
</tr>
<tr>
<td>trivalent</td>
<td>A, C, W135</td>
<td>Single- or multi-dose vials</td>
</tr>
<tr>
<td>quadrivalent</td>
<td>A, C, W135, Y</td>
<td></td>
</tr>
<tr>
<td>Conjugate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>monovalent</td>
<td>A or C</td>
<td></td>
</tr>
<tr>
<td>quadrivalent</td>
<td>A, C, W135, Y</td>
<td></td>
</tr>
<tr>
<td>combination</td>
<td>C, Hib</td>
<td></td>
</tr>
</tbody>
</table>
7.9 How safe are meningococcal vaccines and what are the potential adverse events following immunization?

Meningococcal vaccines have an excellent safety record. Severe adverse events with polysaccharide vaccines include rare anaphylaxis (one per one million doses of vaccine administered) and infrequent neurologic reactions, such as seizures. Mild events include local injection site reactions in up to 56% and fever in less than 5% (most commonly in infants).

Conjugate vaccines have excellent safety profiles. No severe adverse events have been associated with them. Mild events include local injection site reactions, and fever and irritability in children.

Both conjugate and polysaccharide vaccines are safe and effective when used in pregnant women.

7.10 When are meningococcal vaccines administered?

For MenA conjugate vaccine (5μg), a one-dose schedule is recommended at nine to 18 months of age based on local programme factors. The vaccine should be administered by deep intramuscular injection, preferably in the anterolateral (outer) aspect of the thigh. There is no reason to expect interference when co-administered with other vaccines. The need for a booster dose has not been established. If in a specific setting there is a strong reason to vaccinate infants younger than nine months, a two-dose schedule should be used starting at three months of age, with an interval of at least eight weeks between doses.

For monovalent MenC conjugate vaccine, a single intramuscular dose is recommended for children aged over 12 months, teenagers and adults. Children aged two to 11 months require two doses administered at an interval of at least two months and a booster about one year after. If the primary series is interrupted, vaccination should be resumed without repeating the previous dose.

Quadrivalent conjugate vaccines (A,C,W135,Y-D and A,C,W135,Y-CRM) should be administered as one single intramuscular dose to individuals aged over two years. A,C,W135,Y-D is also licensed for children nine to 23 months of age, and given as a two-dose series, three months apart beginning at age nine months. If the primary series is interrupted, vaccination should be resumed without repeating the previous dose.

Meningococcal polysaccharide vaccines can be used for those over two years of age to control outbreaks in countries where limited economic resources or insufficient supply restrict the use of meningococcal conjugate vaccines. Polysaccharide vaccines should be administered to individuals over two years of age as one single dose. One booster three to five years after the primary dose may be given to persons considered to be at continued high risk of exposure, including some health workers.
Key points about meningococcal disease

➢ Meningococcal disease is caused by a bacterium, *Neisseria meningitides*, and most commonly affects young children.

➢ The meningococcus is spread by contact with respiratory droplets from the nose and throat of the infected person.

➢ Meningococcal meningitis typically presents with sudden-onset intense headache, fever, nausea, vomiting, light sensitivity and stiff neck. Infants may only be slow, irritable and feeding poorly.

➢ A petechial rash is the key sign of meningococcal septicaemia.

➢ Meningococcal disease can be rapidly fatal and should always be treated as a medical emergency.

➢ Conjugate vaccines are the preferred choice due to their better protection of children under two years of age and herd immunity.

Table 1.11  Meningococcal polysaccharide vaccines summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Purified bacterial capsular polysaccharide; bivalent, trivalent or quadrivalent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of doses</td>
<td>1</td>
</tr>
<tr>
<td>Schedule</td>
<td>2 years of age and older</td>
</tr>
<tr>
<td>Booster</td>
<td>One dose after 3–5 years if still at risk</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Anaphylaxis or hypersensitivity (allergy) after a previous dose</td>
</tr>
<tr>
<td>Adverse events</td>
<td>• Severe: rare anaphylaxis</td>
</tr>
<tr>
<td></td>
<td>• Mild: injection site reaction, fever</td>
</tr>
<tr>
<td>Special precautions</td>
<td>Children under 2 years of age are not protected by the vaccine</td>
</tr>
<tr>
<td>Dosage</td>
<td>0.5 ml</td>
</tr>
<tr>
<td>Injection site</td>
<td>Upper arm</td>
</tr>
<tr>
<td>Injection type</td>
<td>Subcutaneous</td>
</tr>
<tr>
<td>Storage</td>
<td>Between +2 °C and +8 °C</td>
</tr>
</tbody>
</table>
### Module 1: Target diseases and vaccines

#### Table 1.12 Meningococcal conjugate vaccines summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purified bacterial capsular polysaccharide bound to protein; monovalent, quadrivalent</td>
<td></td>
</tr>
</tbody>
</table>

| Number of doses     | 1 or 2 – see schedules below |

<table>
<thead>
<tr>
<th>Schedule – monovalent MenA conjugate</th>
<th>Single dose 9–18 months (5 µg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schedule – monovalent MenC conjugate</td>
<td>Single dose 12 months and older</td>
</tr>
<tr>
<td></td>
<td>[A,C,W135,Y-D] vaccine only: 2 doses (at least 12 weeks apart) for 9–23 months of age</td>
</tr>
</tbody>
</table>

| Booster               | MenC after 1 year if given to infants 2–11 months |

| Contraindications     | Anaphylaxis or hypersensitivity (allergy) after a previous dose |

| Adverse events        | Serious: rare anaphylaxis |
|                       | Mild: injection site reactions, fever |

| Special precautions   | See schedules above for age restrictions |

| Dosage                | 0.5 ml |

| Injection site        | Anterolateral (outer) thigh in infants |
|                       | Deltoid muscle of upper arm in children and adults |

| Injection type        | Intramuscular |

| Storage               | Between +2 °C and +8 °C |
|                       | Do not freeze MenC |
8 Mumps

8.1 What is mumps?

Mumps is an infection caused by a virus that is present throughout the world. It is also known as infectious parotitis since it most often involves the salivary glands. When the mumps virus infects the testicles, the disease is called mumps orchitis.

Mumps most often affects children of between five and nine years of age. The mumps virus can also infect adults, in which case the complications are more likely to be serious.

8.2 How is mumps spread?

The mumps virus is spread by airborne droplets released when an infected person sneezes or coughs, and by direct contact with an infected person. A person who has mumps can infect others from about six days before to about nine days after salivary gland infection.

8.3 What are the symptoms and signs of mumps?

About 33% of individuals infected with the mumps virus have no symptoms or signs. If they do appear, they usually begin 14–21 days after infection. Symptoms include pain on chewing or swallowing. Fever and weakness can occur. Swelling of the salivary glands, just below and in front of the ears, is the most prominent sign and may occur on one or both sides of the neck.

If mumps orchitis develops, the testicles usually become tender and swollen.

8.4 What are the complications of mumps?

Complications from mumps are rare, but they can be serious. In men and teenage boys, mumps orchitis may cause sterility. Encephalitis (brain infection), meningitis (infection of the membranes covering the brain and spinal cord) and hearing loss are other rare complications that can occur with mumps at any age.

8.5 What is the treatment for mumps?

There is no specific treatment for mumps. Since it is caused by a virus, antibiotics are not effective. Supportive treatment should be given to relieve symptoms.
Module 1: Target diseases and vaccines

8.6 How is mumps prevented?

Mumps is prevented by immunization with mumps-containing vaccine. In countries implementing mumps vaccine, MMR, the combination measles-, mumps- and rubella-containing vaccine, is recommended. Sections 8.8–8.10 and Table 1.13 below describe mumps vaccine. Measles and rubella vaccines are described in Sections 6 and 13 of this module respectively.

People who recover from mumps are thought to have lifelong immunity against the virus.

8.7 What is needed for global mumps control?

Routine mumps vaccination is recommended in countries with well-established programmes that maintain measles and rubella coverage at over 80%. Measles and congenital rubella syndrome are considered priorities because of their higher mortality and disease burden. Like rubella, mumps may cause more serious disease burden in older age groups if childhood vaccination lapses. Two doses of mumps-containing vaccine are required to maintain the high level of immunization coverage needed for mumps control. Countries must decide on the addition of mumps-containing vaccine based on the burden of this disease and its public health priority.

8.8 What are mumps-containing vaccines?

Mumps-containing vaccines such as MMR are supplied as freeze-dried (also called lyophilized) powders. They must be reconstituted before use: see Module 5 (Managing an immunization session), Section 4.2 for details. They should be kept at a temperature of between +2 °C and +8 °C. They are sensitive to heat but are not damaged by freezing. Opened multi-dose vials must be handled according to national multi-dose vial policy (see Module 2, Section 5 for WHO policy).

Mumps-containing vaccines are administered by subcutaneous injection.

8.9 How safe is mumps vaccine and what are the potential adverse events following immunization?

Mumps vaccine is very safe to use. Infrequently, depending on the vaccine virus strain used, aseptic meningitis (inflammation of the membranes covering the brain and spinal cord) has been reported at different rates. Children recover from it without long-term problems, although some may need to be hospitalized. Mild events include pain at the injection site (in 17–30% of those vaccinated) and parotid swelling (in 1–2%). There is no evidence to support an association between MMR and autism.

A WHO safety information summary for MMR vaccine is available on the website: http://www.who.int/vaccine_safety/initiative/tools/vaccinfosheets/en/.
8.10 When are mumps-containing vaccines administered?

Two doses of mumps-containing vaccines are required for long-term protection. The first dose should be given at the age of 12–18 months. The second should be given at least one month before school entry; the age may range from the second year of life to about six years. Countries should decide on optimal timing to maximize programme coverage. The required minimum interval between doses is one month.

Key points about mumps

- Mumps is transmitted in airborne droplets emitted by infected individuals when they cough or sneeze.
- About one-third of individuals infected with mumps have no symptoms.
- The most prominent sign is swelling in the salivary glands.
- Complications from mumps are rare but can be serious.
- Mumps vaccine should be given in combination with measles and rubella vaccines (MMR) in high-performing immunization programmes with coverage over 80%.

Table 1.13 Mumps-containing vaccines summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Live attenuated (weakened) viral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of doses</td>
<td>2</td>
</tr>
<tr>
<td>Schedule</td>
<td>Mumps1: 12–18 months of age with MCV</td>
</tr>
<tr>
<td></td>
<td>Mumps2: in the second year of life to school entry with MCV</td>
</tr>
<tr>
<td></td>
<td>Minimum 1-month interval required between doses</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Known allergy to vaccine components (including neomycin and gelatin)</td>
</tr>
<tr>
<td></td>
<td>Pregnancy</td>
</tr>
<tr>
<td></td>
<td>Severe congenital or acquired immune disorders, including advanced HIV infection/AIDS</td>
</tr>
<tr>
<td>Adverse events</td>
<td>Serious: aseptic meningitis (with some strains); orchitis (inflammation of the testicles); sensorineural deafness; acute myositis (inflammation of the muscles)</td>
</tr>
<tr>
<td></td>
<td>Mild: injection site reactions; parotid swelling</td>
</tr>
<tr>
<td>Special precautions</td>
<td>None</td>
</tr>
<tr>
<td>Dosage</td>
<td>0.5 ml</td>
</tr>
<tr>
<td>Injection site</td>
<td>Anterolateral (outer) thigh or upper arm depending on the child’s age</td>
</tr>
<tr>
<td>Injection type</td>
<td>Subcutaneous</td>
</tr>
<tr>
<td>Storage</td>
<td>Between +2 °C and +8 °C</td>
</tr>
<tr>
<td></td>
<td>If using combination vaccines, keep all measles-containing vaccines away from sunlight</td>
</tr>
</tbody>
</table>
9 Pertussis

9.1 What is pertussis?

Pertussis, or whooping cough, is a disease of the respiratory tract caused by *Bordetella pertussis* bacteria that live in the mouth, nose and throat. Because it is highly communicable and affects unimmunized infants in particular, pertussis remains a public health concern globally, including in countries where vaccination coverage is high.

9.2 How is pertussis spread?

Pertussis spreads very easily from person to person in droplets produced by coughing or sneezing. Untreated patients may be infectious and spread pertussis for up to three weeks after the typical cough starts. In many countries, the disease occurs in regular epidemic cycles of three to five years.

9.3 What are the symptoms and signs of pertussis?

About 10 days after infection, symptoms similar to a common cold appear – runny nose, watery eyes, sneezing, fever and a mild cough. The cough worsens to many rapid bursts. At the end of these bursts, the typical patient takes in air with a high-pitched whoop. Children may turn blue because they do not get enough oxygen during a long burst of coughing. Vomiting and exhaustion often follow the coughing attacks, which are particularly frequent at night.

9.4 What are the complications of pertussis?

Pneumonia is the main complication of pertussis – it has been found to occur in about 6% of cases in industrialized countries. The risk of pneumonia in infants under six months of age can be up to four times higher than that in older children.

Children may experience complications, such as convulsions and seizures, due to fever or reduced oxygen supply to the brain during bursts of coughing.

9.5 What is the treatment for pertussis?

Treatment with an antibiotic, usually erythromycin, may reduce the severity of the illness. Because the medication kills bacteria in the nose and throat, antibiotics also reduce the ability of infected people to spread pertussis to others.
9.6 How is pertussis prevented?

Prevention involves immunization with pertussis vaccine, which has been given in combination with diphtheria and tetanus vaccines (as DTP) for many years, but is more recently being given in pentavalent vaccine that covers hepatitis B and *Haemophilus influenzae* type b as well as DTP. Pentavalent vaccine reduces the number of injections needed for infant immunization. DTP and pentavalent vaccines are described in the diphtheria and *Haemophilus influenzae* type b sections of this module. Sections 9.7–9.9 and Table 1.14 below describe pertussis-containing vaccines.

9.7 What are pertussis-containing vaccines?

Pertussis vaccine is most often given in DTP or pentavalent combination form. Pertussis-containing vaccines are supplied in single- and multi-dose presentations. Pentavalent vaccine with a freeze-dried Hib component requires reconstitution: see Module 5 (*Managing an immunization session*), Section 4.2 for details. Pertussis-containing vaccines must be stored between +2 °C and +8 °C without being frozen. They are freeze-sensitive: see Module 2 (*The vaccine cold chain*), Section 7 for instructions on the Shake Test that determines whether a vial is safe to use if freezing is suspected. Opened multi-dose vials must be handled according to national multi-dose vial policy (see Module 2, Section 5 for WHO policy).

Pertussis-containing vaccines are administered as 0.5 ml doses given intramuscularly in the anterolateral (outer) thigh in infants and in the deltoid muscle (upper arm) of older children and adults.

9.8 How safe is pertussis vaccine and what are the potential adverse events following immunization?

Safety information on pertussis vaccine is from studies on combination vaccines. Severe events include rare anaphylaxis with some types of vaccine (1.3 per 1 million doses with whole cell pertussis vaccine). Prolonged crying and febrile seizures have been noted in less than one in 100 doses and hypotonic–hyporesponsive episodes (loss of muscle tone and awareness or consciousness) in less than one in 1000–2000 doses. Mild events are common and include pain, redness and swelling at the injection site and fever and agitation (in one in 2–10 doses).


9.9 When are pertussis-containing vaccines administered?

A three-dose primary series is recommended; it should be started at six weeks of age with subsequent doses given four to eight weeks apart. Ideally, all three doses of pertussis vaccine should be given by six months of age. A booster is recommended
at between one and six years of age, preferably between one to two years of age. The booster dose should be given at least six months after the last primary dose.

Schedules for combination vaccines are shown in the diphtheria and *Haemophilus influenzae* type b sections of this module.

### Key points about pertussis

- Pertussis, or whooping cough, is a disease of the respiratory tract.
- Pertussis is a bacterial infection spread from person to person by sneezing and coughing.
- Infants and young children are most likely to be infected, to have serious complications, and to die from the disease.
- The most effective way to prevent pertussis is to immunize all infants with pertussis-containing vaccine.

### Table 1.14 Pertussis-containing vaccine summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Killed whole cell or acellular (without intact cells)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of doses</td>
<td>3</td>
</tr>
<tr>
<td>Schedule</td>
<td>Pentavalent or DTP or pertussis vaccine 3-dose primary series starting at age 6 weeks (minimum) with second and third doses at intervals of 4–8 weeks after the previous dose</td>
</tr>
</tbody>
</table>
| Booster                                | • Children between 1 and 6 years: 1 booster dose at least 6 months after the 3-dose primary series, preferably in the second year of life  
• Each country should make its own decision on booster doses in adolescents and adults |
| Contraindications                      | Anaphylaxis or hypersensitivity (allergy) after a previous dose |
| Adverse events                         | • Severe: rare anaphylaxis, hypotonic–hyporesponsive episodes (loss of muscle tone and responsiveness/consciousness); febrile seizures; prolonged crying  
• Mild: injection site reactions (pain, redness, swelling); fever and agitation |
| Special precautions                    | None                                                |
| Dosage                                 | 0.5 ml                                              |
| Injection site                         | • Anterolateral (outer) mid-thigh in infants  
• Outer deltoid muscle of upper arm in children and adults |
| Injection type                         | Intramuscular                                       |
| Storage                                | • Between +2 °C and +8 °C  
• Do not freeze |
10 Pneumococcal disease

10.1 What is pneumococcal disease?

Pneumococcal disease is caused by infection with a bacterium called *Streptococcus pneumoniae* (also known as the pneumococcus) in different parts of the body. The pneumococcus is a common cause of serious diseases, such as pneumonia, meningitis (infection of the membranes covering the brain and spinal cord) and septicaemia (bloodstream infection) and milder ones, such as otitis media (middle ear infection) and sinusitis.

Pneumococcal diseases are a common cause of morbidity and mortality worldwide, although rates of disease and death are higher in developing countries, with the majority of deaths occurring in sub-Saharan Africa and Asia. It is most common in very young children and elderly people.

For infants, risk factors for pneumococcal disease include lack of breastfeeding and exposure to indoor smoke. HIV infection, sickle cell disease, asplenia (lack of a functioning spleen), chronic kidney disease and previous influenza virus infection are risk factors for all ages.

10.2 How is pneumococcal disease spread?

Pneumococcal disease is spread from person to person by coughing, sneezing or close contact. Pneumococcus is transmitted by direct contact with respiratory secretions from patients and from people who have pneumococcus in their noses and/or throats (healthy carriers). In some groups, up to 70% may be healthy carriers.

10.3 What are the symptoms and signs of pneumococcal disease?

Because the pneumococcus can affect many parts of the body, symptoms and signs vary, depending on the site of infection. Fever and shaking or chills can occur with all types of pneumococcal disease. Children with pneumonia can present with cough, rapid breathing and chest wall retractions; older patients may complain of shortness of breath and pain when breathing in and on coughing. Patients with meningitis can present with headaches, sensitivity to light, neck stiffness, convulsions and sometimes confusion or altered consciousness. Those with otitis or sinusitis may have pain, tenderness and/or discharge from the affected area.
10.4 What are the complications of pneumococcal disease?

Pneumonia can be complicated by septicaemia (bloodstream infection) and/or empyema (pus in the pleural space, which is the space between the lung and the membrane covering it) and/or lung abscesses. Meningitis survivors may suffer complications, including hearing loss, mental retardation, motor abnormalities and seizures.

10.5 What is the treatment for pneumococcal disease?

Pneumococcal disease can be treated with antibiotics, such as amoxicillin. Some of the commonly used antibiotics are no longer effective in some areas since the pneumococcus is developing resistance.

10.6 How is pneumococcal disease prevented?

Pneumococcal disease can be prevented by vaccination. While improved living conditions (e.g. reduced crowding and indoor air pollutants) and nutrition can reduce the risk of pneumococcal disease and death, they are less effective than vaccines for prevention. Sections 10.8–10.10 and Table 1.16 below describe pneumococcal conjugate vaccine.

10.7 What is needed for global pneumococcal disease control?

The use of pneumococcal vaccine should be seen as complementary to the use of other pneumonia control measures, such as appropriate case management, promotion of exclusive breastfeeding for first six months of life, and the reduction of known risk factors, such as indoor pollutants and tobacco smoke. The 2013 integrated Global Action Plan for Pneumonia and Diarrhoea outlines a “Prevent, Protect and Treat” framework, which is discussed in Section 19 of this module.

10.8 What is pneumococcal conjugate vaccine?

The pneumococcus is a bacterium with an outer polysaccharide (or sugar) capsule. Many different strains, or serotypes, of pneumococcus have been identified based on differences in this capsule. Pneumococcal vaccines have been developed based on the serotypes frequently found in severe pneumococcal disease patients.

There are two categories of pneumococcal vaccines. Pneumococcal polysaccharide vaccines were used for many years; they contain the purified capsule of up to 23 serotypes of pneumococcus but only produce short-term protection and are not effective in infants and young children. Pneumococcal conjugate vaccines (PCV) overcome the limitations of polysaccharide vaccines by conjugating, or binding, the capsule with a protein; this results in longer-lasting protection and makes the vaccine more effective in children.
Each pneumococcal vaccine protects against disease caused by the pneumococcal serotypes that it contains; it is unlikely to protect against serotypes that it does not contain. It does not protect against other bacteria that cause the same types of infections (pneumonia, meningitis, etc.) as the pneumococcus. The fact that the vaccine cannot protect against all causes of pneumonia should be emphasized in health education so that it is not misunderstood as a failure of the vaccine.

Available pneumococcal conjugate vaccines are listed in Table 1.15 below. The number indicates how many pneumococcal serotypes the vaccine contains (for example, PCV10 protects against 10 serotypes of pneumococcus).

PCVs in these presentations do not require reconstitution. They must be stored at a temperature of between +2 °C and +8 °C without being frozen. They are freeze-sensitive. If freezing is suspected, the Shake Test should be performed to determine whether a vial is safe to use (see Module 2 (The vaccine cold chain), Section 7). Opened multi-dose vials must be handled according to national multi-dose vial policy (see Module 2, Section 5 for WHO policy).

For infants and children, 0.5 ml of PCV is administered by intramuscular injection in the anterolateral thigh.

### Table 1.15  Pneumococcal vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Formulation</th>
<th>Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCV10</td>
<td>Liquid</td>
<td>Single-dose vial</td>
</tr>
</tbody>
</table>
| PCV10   | Liquid      | • 2-dose, preservative-free vial
|         |             | • Prefilled syringe          |
| PCV13   | Liquid      | • Single-dose vial           |
|         |             | • Prefilled syringe          |

10.9 How safe is pneumococcal conjugate vaccine and what are the potential adverse events following immunization?

Pneumococcal conjugate vaccine is safe and well tolerated in all target groups. No severe adverse events have been proven with use of these vaccines to date. Mild events include soreness at the injection site in about 10% of those vaccinated; fever has been reported in less than 1%.

10.10 When is pneumococcal conjugate vaccine administered?

PCVs should be given priority in childhood immunization programmes, particularly in countries with high mortality in children under five years of age (more than 50/1000 live births). Three doses are required and can be given as a three-primary (3p+0) or, as an alternative, two-primary-plus-one booster (2p+1) schedule. The 3p+0 schedule can be started as early as six weeks of age, with a minimum interval of four weeks between doses. The 2p+1 schedule is shown in Table 1.16 below. In choosing between schedules factors such as the epidemiology of the disease, likely coverage, and the timeliness of vaccination should be considered.

Once a series has been started, the same product should ideally be used for all three doses; for example, if PCV10 is used for the first dose, it should be used for the second and third doses also. If this is not possible, the schedule may be completed with the available PCV.

Previously unvaccinated or incompletely vaccinated children, including those who recover from pneumococcal disease, should be vaccinated according to their age. Children 12–24 months require only two doses, with an interval of at least eight weeks.

Key points about pneumococcal disease

- Pneumococcal disease is a leading cause of death in children under five years of age, especially in developing countries.
- The pneumococcus can cause infections in different parts of the body; the most common severe diseases are pneumonia, meningitis and septicaemia.
- Healthy carriers as well as patients can spread pneumococcus.
- Pneumococcal vaccination should be given as part of a comprehensive package to protect, prevent and treat and to reduce mortality and morbidity from childhood pneumonia.
- Each pneumococcal vaccine protects against disease caused only by the pneumococcal serotypes that it contains. It does not protect against other bacteria that cause the same types of infections (pneumonia, meningitis, etc.).
**Table 1.16  Pneumococcal conjugate vaccine summary**

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Conjugate (pneumococcal polysaccharide bound to a carrier protein; does not contain any live bacteria)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of doses</td>
<td>3</td>
</tr>
<tr>
<td>Schedule – 3p+0</td>
<td>First dose as early as 6 weeks of age with 4–8 weeks interval between doses</td>
</tr>
</tbody>
</table>
| Schedule – 2p+1 | • 2 primary doses ideally completed by six months of age, starting as early as 6 weeks of age with an interval of 8 weeks or more between doses  
• For infants ≥7 months who started vaccination late; a minimum interval of 4 weeks between doses is possible |
| Booster | • With 2p+1 schedule: one booster dose between 9–15 months of age  
• HIV+ infants and preterm neonates who receive 3p doses before 12 months of age may benefit from a booster dose during the second year of life |
| Contraindications | Anaphylaxis or hypersensitivity (allergy) after a previous dose |
| Adverse events | • Severe: none known  
• Mild: injection site reactions and fever |
| Special precautions | Postpone vaccination if the child has moderate to severe illness (with temperature ≥39 °C) |
| Dosage | 0.5 ml |
| Injection site | Anterolateral (outer) thigh in infants and children |
| Injection type | Intramuscular |
| Storage | • Between +2 °C and +8 °C  
• Do not freeze |
**11.1 What is poliomyelitis?**

Poliomyelitis, or polio, is a highly infectious disease caused by poliovirus types 1, 2 or 3. These are also called wild polioviruses (WPVs) since they are the naturally occurring types that circulate and infect people.

Polio mainly affects children of less than five years of age. One in 200 infections causes irreversible paralysis when the virus attacks the spinal cord nerve cells that control the muscles.

Due to the Global Polio Eradication Initiative, which was launched in 1988, the number of countries still reporting WPVs has been reduced from 125 to three in 2015.

**11.2 How is polio spread?**

Poliovirus spreads by the faecal-to-oral route. In areas with poor sanitation, it is thought to more commonly enter the body through the mouth when people eat food or drink water that is contaminated with faeces. The majority of infected people do not show symptoms but can still spread the disease.

**11.3 What are the symptoms and signs of polio?**

Following infection with poliovirus, approximately 25% of those infected develop a minor illness, usually with fever, headache and sore throat. Paralysis occurs in approximately 1% of those infected. Death occurs in approximately 5–10% of those paralysed.

**11.4 What is the treatment for polio?**

There is no cure for polio. Treatment consists of supportive, symptomatic care. A ventilator can help patients who have difficulty breathing. Orthopedic treatment, regular physiotherapy and the use of braces can help reduce the long-term crippling effects.

**11.5 How is polio prevented?**

Polio can be prevented through immunization with oral polio vaccine (OPV) and/or inactivated polio vaccine (IPV). WHO recommends that all countries using only OPV add at least one dose of IPV to the routine immunization schedule.
11.6 What is polio vaccine?

OPV is a live attenuated (weakened) poliovirus vaccine that contains types 1, 2 and 3 individually or in combination (types 1, 2 and 3, or 1 and 3). It is supplied in multi-dose vials. It is very heat-sensitive and must be kept frozen during long-term storage. After thawing, it can be kept at a temperature of between +2 °C and +8 °C for a maximum of six months or can be refrozen.

IPV is an inactivated poliovirus vaccine available as a stand-alone product or in combination with diphtheria, tetanus, pertussis, hepatitis B and/or Hib. It is stable outside the cold chain but should be stored between +2 °C and +8 °C. It must not be frozen. It is supplied in one-, five- or ten-dose vials.

OPV is given orally and IPV is injected intramuscularly as a 0.5 ml dose.

11.7 How safe is polio vaccine and what are the potential adverse events following immunization?

Both OPV and IPV are extremely safe. With OPV, vaccine-associated paralytic polio (VAPP) can occur in approximately 1 in 2.7 million doses. VAPP usually occurs with the first dose of OPV, and this small risk declines further with subsequent doses. On rare occasions, over time, in areas of low vaccination coverage, the live attenuated (weakened) viruses contained in OPV can begin to circulate and regain the ability to cause paralytic cases. This is known as circulating vaccine-derived poliovirus.

IPV is one of the safest vaccines in routine use. No serious adverse events have been linked to it. Mild events include injection site redness in less than 1% of those vaccinated, swelling in 3–11% and soreness in 14–29%.

A WHO safety information summary for polio vaccines is available on the website: http://www.who.int/vaccine_safety/initiative/tools/vaccinfosheets/en/.

11.8 When is polio vaccine administered?

Polio vaccine schedules for countries no longer infected are shown in Table 1.17. Countries reporting infections should refer to guidance available on the WHO website: http://www.who.int/immunization/documents/positionpapers/en/.
Key points about polio

- Polio is caused by wild type polioviruses 1, 2 and 3 and is easily spread by the faecal-to-oral and oral-to-oral routes.
- The majority of individuals infected do not have symptoms but can still spread the disease.
- Approximately 1% of infections result in paralytic poliomyelitis; when paralysis occurs, it will lead to death in approximately 5–10% of cases.
- For countries using OPV only, WHO recommends that they introduce at least one dose of IPV to the routine immunization schedule.

Table 1.17  Polio vaccination summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>OPV – Live attenuated (weakened) viral; IPV – Inactivated viral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of doses</td>
<td>3–4</td>
</tr>
</tbody>
</table>
| Schedule – OPV plus IPV          | • 3 OPV doses initiated from 6 weeks of age with minimum interval of 4 weeks; an IPV dose should be given from 14 weeks of age (with OPV dose).  
  • Note: In areas where polio is endemic or there is high-risk for importation, an OPV birth dose (a zero dose) should be given |
| Schedule – Sequential IPV-OPV    | 1–2 doses of IPV starting from 2 months of age, followed by at least 2 doses of OPV; an interval of 4–8 weeks is required between all doses |
| Schedule – IPV-only              | 3 doses beginning at 2 months of age, with an interval of 4–8 weeks between doses |
| Booster IPV-only schedule        | If the series begins before 2 months of age, then give booster ≥ 6 months after last dose |
| Contraindications                | Known hypersensitivity (allergy) or anaphylaxis to a previous dose |
| Adverse events                   | • OPV – Rare vaccine-associated paralytic polio (VAPP)  
  • IPV – No known serious reactions; mild injection site reactions do occur |
| Special precautions               | Postpone vaccination if the child has moderate to severe illness (with temperature ≥39 °C) |
| Dosage                           | • OPV – 2 drops into the mouth  
  • IPV – 0.5 ml injection |
| Route of administration          | • OPV – Oral only  
  • IPV – Intramuscular injection; anterolateral (outer) mid-thigh in infants and children |
| Storage                          | • OPV – Keep frozen; very heat sensitive; storage in temperatures of between +2 °C and +8 °C is possible for a maximum of 6 months  
  • IPV – between +2 °C and +8 °C; do not freeze |
12.1 What is rotavirus gastroenteritis?

Rotavirus gastroenteritis is a highly infectious diarrhoeal disease caused by strains of rotavirus infecting the small intestine. Rotavirus gastroenteritis is the leading cause of severe diarrhoea in infants and young children worldwide. It occurs everywhere, including in countries where sanitation standards and access to safe water are good.

Deaths occur mainly in infants of between three and 12 months of age when they develop severe gastroenteritis following their first infection and are very vulnerable to the effects of dehydration.

12.2 How is rotavirus spread?

Rotavirus spreads by the faecal-to-oral route. Large quantities of virus can be shed in the faeces of an infected child. Shedding can occur from two days before to 10 days after the onset of symptoms. Rotavirus is stable in the environment and can spread via contaminated food, water and objects.

12.3 What are the symptoms and signs of rotavirus gastroenteritis?

Rotavirus gastroenteritis can range from mild loose stools to severe watery diarrhoea and vomiting leading to dehydration. Symptoms usually begin one to three days after infection. Fever and vomiting can occur before diarrhoea. The diarrhoea lasts for three to seven days on average.

12.4 What are the complications of rotavirus gastroenteritis?

Once vomiting and/or watery diarrhoea begins, infants can rapidly become severely dehydrated, leading to complications such as shock, kidney and liver failure, and death.

12.5 What is the treatment for rotavirus gastroenteritis?

There is no specific antiviral treatment for rotavirus gastroenteritis. As with other causes of diarrhoea, key supportive measures are fluid replacement with oral rehydration solution (ORS) and treatment with zinc supplementation. Severe dehydration may require intravenous infusion in addition to ORS for the urgent replacement of fluid and electrolytes.
12.6 How is rotavirus gastroenteritis prevented?

Over the past 20 years, global deaths due to diarrhoea from other causes have decreased significantly due to improved nutrition, hygiene and sanitation and the availability of ORS and zinc. Improvements in sanitation and access to safe water are less effective for reducing rotavirus infections, and vaccination has become important for prevention of severe rotavirus disease in particular. Sections 12.8–12.10 and Table 1.18 describe rotavirus vaccines.

The first infection will give some, but not complete, immunity. The severity of infection tends to become less with each repeat infection.

12.7 What is needed for global rotavirus gastroenteritis control?

The use of rotavirus vaccines should be part of a comprehensive strategy to control diarrhoeal diseases with the scaling up of both prevention (exclusive breastfeeding for six months, vitamin A supplementation, safe drinking water, hygiene/handwashing with soap, and sanitation) and treatment (low-osmolarity ORS, zinc and continued feeding). The 2013 integrated Global Action Plan for Pneumonia and Diarrhoea outlines a “Prevent, Protect and Treat” framework, which is discussed in Section 19 of this module.

12.8 What is rotavirus vaccine?

The currently available rotavirus vaccines (RV) contain one or more live attenuated (weakened) virus strains. They are given orally to protect against rotavirus gastroenteritis. They do not protect against other causes of diarrhoea, a fact that is important to emphasize in health education.

Two oral rotavirus vaccines are available: Rotarix® (RV1 or monovalent RV), which contains one strain; and RotaTeq® (RV5 or pentavalent RV), which contains five strains.

Rotarix® comes in single-dose freeze-dried (also called lyophilized) powder and in liquid forms. Freeze-dried RV1 must be reconstituted using diluent in a prefilled oral applicator. Liquid Rotarix® is ready to use in an oral applicator or a squeezable tube. All of these must be stored between +2 °C and +8 °C without being frozen. They should be used immediately after reconstitution or opening. If not used immediately, reconstituted freeze-dried vaccine can be stored between +2 °C and +8 °C or at ambient temperatures of less than 25 °C and used within 24 hours (see Table 1.18).

RotaTeq® is a ready-to-use liquid that should be stored at a temperature of between +2 °C and +8 °C without freezing. It should be used as soon as possible after being removed from the refrigerator.
12.9 How safe are rotavirus vaccines and what are the potential adverse reactions?

The available rotavirus vaccines are safe and well tolerated. There is a low risk of intussusception (about one to two per 100,000 infants vaccinated; see box on intussusception). Both are approved for administration with other vaccines in infant immunization programmes. Mild adverse reactions include irritability, runny nose, ear infection, vomiting and diarrhoea (in 5% or more of children vaccinated).

Rotavirus vaccines are generally not recommended for infants with a history of intussusception. Studies show a much smaller increase in risk (five to 10 times lower) of intussusception after the first dose of Rotarix® or RotaTeq® than with an earlier vaccine called RotaShield® that was withdrawn from the market. The benefits of the currently available rotavirus vaccines are far greater than the potential risks.


What is intussusception?

- Intussusception is a folding or telescoping of one segment of the intestine within another.
- Intussusception usually results in a blockage of the intestine (bowel obstruction).
- Intussusception occurs primarily in infants; peak incidence is between four and 10 months of age.
- Symptoms and signs of intussusception include abdominal pain sometimes accompanied by a lump that can be felt on examination, vomiting, stools with blood and mucus, and lethargy.
- These are not specific and may be caused by other bowel diseases, but intussusception should be considered as one of the possible diagnoses in relevant cases.
- Early diagnosis and treatment of intussusception are essential to save the intestine and the child.
- A child that has any of the above symptoms should be taken immediately to the nearest hospital for urgent evaluation and appropriate treatment.
12.10 When is rotavirus vaccine administered?

Rotarix® is given on a two-dose schedule along with pentavalent1 and 2 (the first two doses of DTP+HepB+Hib vaccine). RotaTeq® is given on a three-dose schedule along with pentavalent1, 2 and 3. For both vaccines, there should be a minimum interval of four weeks between doses.

WHO recommendations encourage early vaccination (first dose of RV to be given as soon as possible after six weeks of age), but allow infants to receive rotavirus vaccine together with pentavalent vaccine (DTP+HepB+Hib) regardless of the time of vaccination.

Because rotavirus disease mainly affects very young children, vaccination after 24 months of age is not recommended. The duration of protection of RV is not yet known, but boosters are also not recommended.

Key points about rotavirus gastroenteritis

- Rotavirus is a common cause of gastroenteritis in infants and young children.
- The disease spreads by the faecal-to-oral route and the virus is stable in the environment.
- Severe disease can lead to rapid dehydration resulting in shock and death if fluids are not replaced quickly by ORS and, if needed, intravenous infusion.
- Vaccination is the best prevention for rotavirus gastroenteritis since safe water and sanitation measures are less effective in preventing rotavirus infections than in preventing other causes of diarrhoea.
- Rotavirus vaccination prevents only rotavirus gastroenteritis and should be included as part of a comprehensive treatment and prevention strategy to control diarrhoea.
Table 1.18 Rotavirus vaccines summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Live attenuated (weakened) viral</th>
</tr>
</thead>
</table>
| Number of doses | • 2 for RV1 (monovalent RV, Rotarix®)  
• 3 for RV5 (pentavalent RV, RotaTeq®) |
| Schedule – Rotarix® | • First dose with pentavalent1; second dose with pentavalent2, with a minimum interval of 4 weeks.  
• Not recommended after 24 months of age |
| Schedule – RotaTeq® | • First dose with pentavalent1; second dose with pentavalent2; third dose with pentavalent3, with a minimum interval of 4 weeks.  
• Not recommended after 24 months of age |
| Booster | Not recommended at this time |
| Contraindications | • Severe allergic reaction to previous dose  
• Severe immunodeficiency (but not HIV infection) |
| Adverse events | • Severe: intussusception  
• Mild: irritability, runny nose, ear infection, diarrhoea, vomiting |
| Special precautions | • Should be postponed for acute gastroenteritis and/or fever with moderate to severe illness  
• Not routinely recommended for history of intussusception or intestinal malformations that possibly predispose to intussusception |
| Dosage | • Rotarix®: 1.5 ml of liquid  
• RotaTeq®: 2 ml |
| Route of administration | Oral only |
| Storage | • Between +2 °C and +8 °C  
• Do not freeze |
Rubella and congenital rubella syndrome

13.1 What are rubella and congenital rubella syndrome?

Rubella is an infection caused by a virus and is usually mild in children and adults. Congenital rubella syndrome (CRS) is a group of birth defects that occur when the rubella virus infects a fetus. A woman infected with the rubella virus early in pregnancy has a 90% chance of passing the virus on to her fetus and this can lead to death of the fetus or to CRS. The most common birth defect is deafness, but CRS can also cause defects in the eyes, heart and brain.

13.2 How is rubella virus spread?

Rubella is spread in airborne droplets released when infected people sneeze or cough. The virus spreads throughout the body and, in a pregnant woman, to the fetus, about five to seven days after infection.

Infected individuals are most likely to spread virus on days one to five of the rubella rash (see below), but they can spread it from seven days before to about 14 days after the rash appears. Infants with CRS can transmit the virus for a year or more.

13.3 What are the symptoms and signs of rubella and CRS?

About seven to 14 days after exposure to the virus, mild fever, conjunctivitis (more often in adults) and swollen neck lymph nodes may occur and then be followed by a rash five to 10 days later. The rash most often begins on the face and spreads towards the feet. It is an erythematous maculopapular rash, which means it is red and raised but usually fainter than a measles rash. The rash typically lasts for one to three days. Studies have shown that 20–50% of rubella infections occur without a rash. Up to 70% of adult women may have joint pain and stiffness.

Children with CRS usually show birth defects, such as cataracts and loss of hearing in infancy, but some do not show signs for two to four years. Mental retardation can occur.

13.4 What are the complications of rubella?

Complications of rubella tend to occur more often in adults than in children. Encephalitis occurs in about one in 6000 cases and is most common in adult women. Problems with bleeding occur in about one in 3000 cases, usually among children. Guillain-Barré syndrome has been reported rarely.
13.5 What is the treatment for rubella and CRS?

There is no specific antiviral medication for rubella or for CRS. Supportive measures should be taken to alleviate symptoms.

13.6 How are rubella and CRS prevented?

Rubella and CRS are prevented with safe, effective rubella vaccines. For infant immunization, rubella vaccine is usually given in combination with measles and mumps vaccine (MR or MMR). In some countries, mostly in the industrialized world, rubella has been nearly eliminated through childhood immunization programmes. It is important to ensure that coverage in infants is sustained at over 80% to avoid shifting rubella transmission to older age groups. For prevention of CRS, women of childbearing age are the primary target group for rubella immunization. Sections 13.8–13.10 and Table 1.19 describe the rubella vaccine. Measles and mumps vaccines are described in Sections 6 and 8 of this module respectively.

13.7 What is needed for global rubella and CRS disease control?

Although the global burden of rubella and CRS has decreased over time due to vaccination, the remaining burden can be readily addressed along with measles control efforts using combination vaccines (MR, MMR). Rubella and CRS are therefore part of the Global Measles and Rubella Strategic Plan described in Section 6.7. Because situations and approaches vary greatly, countries must decide on their use of rubella-containing vaccines based on the burden of this disease and its public health priority.

13.8 What are rubella-containing vaccines?

MR and MMR are supplied as freeze-dried (also called lyophilized) powders. They must be reconstituted before use: see Module 5 (Managing an immunization session), Section 4.2 for details. Rubella-containing vaccines must be stored between +2 °C and +8 °C. They are sensitive to heat but not damaged by freezing. Opened multi-dose vials must be handled according to national multi-dose vial policy: see Module 2 (The vaccine cold chain), Section 5 for WHO policy.

Rubella-containing vaccines are administered in 0.5 ml doses by subcutaneous injection.

13.9 How safe is rubella-containing vaccines and what are the potential adverse events?

Adverse events following immunization with rubella-containing vaccines are mild in children. Rubella vaccine may cause a temporary form of arthritis one to three weeks after vaccination in up to one in four postpubertal females (who have already reached
sexual maturity). This is very rare in young children. Long-term joint disease has not been associated with rubella-containing vaccines after reviewing the data from large studies.


### 13.10 When is rubella-containing vaccine administered?

Rubella-containing vaccine should be given at nine to 12 months of age. It can be introduced into childhood immunization programmes with the two-dose schedule for measles-containing vaccines. Countries should establish national schedules for older children, adolescents and adults as needed.

#### Key points about rubella and CRS

- Rubella and CRS are infections caused by a virus.
- Rubella is normally a mild childhood disease, but women who contract rubella early in pregnancy can pass the virus on to their fetuses and this can lead to fetal death or CRS.
- The rash associated with rubella infection may not occur in 20–50% of cases.
- CRS includes birth defects of the ears, eyes, heart and brain.
- WHO currently recommends that countries use rubella vaccine in conjunction with measles vaccine (MR or MMR) for the goal of rubella and CRS elimination.
Table 1.19 Rubella-containing vaccines summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Live attenuated (weakened) viral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of doses</td>
<td>1 (but when given in combination with measles/mumps, 2 doses are required for programmatic reasons)</td>
</tr>
</tbody>
</table>
| Schedule                | • Rubella1: 9 or 12 months of age with MCV  
                          | • Refer to national schedules for older children, adolescents and adults |
| Contraindications       | • Known allergy to vaccine components (including neomycin and gelatin)  
                          | • Pregnancy  
                          | • Severe congenital or acquired immune disorders, including advanced HIV infection/AIDS |
| Adverse events          | • In some adult women: serious arthritis (joint inflammation) and mild arthralgia (joint pain)  
                          | • Mild: injection site reactions |
| Special precautions     | None |
| Dosage                  | 0.5 ml |
| Injection site          | Anterolateral (outer) thigh or upper arm depending on the child’s age |
| Injection type          | Subcutaneous |
| Storage                 | • Between +2 °C and +8 °C  
                          | • If using combination vaccines, keep all measles-containing vaccines away from sunlight |
Seasonal influenza

14.1 What is seasonal influenza?

Seasonal influenza is a respiratory disease caused by influenza viruses A and B. In temperate climates, it can occur primarily in winter epidemics. In tropical climates, it can occur year-round with high attack rates and deaths. Globally, seasonal influenza can affect 5–10% of adults and 20–30% of children each year. Children under five years of age, pregnant women, the elderly (over 65 years of age) and people with HIV/AIDS, asthma, and other chronic heart or lung conditions are at greater risk.

14.2 How is seasonal influenza spread?

Influenza A and B viruses are spread mainly in droplets and aerosols released when an infected person coughs or sneezes.

14.3 What are the symptoms and signs of seasonal influenza?

Symptoms of influenza usually occur after a one- to four-day incubation period and include fever, cough, sore throat, runny nose, headache and muscle and joint aches. Signs of severe disease in children include difficulty breathing, increased respiratory rate, poor feeding, irritability, dehydration and decreased alertness.

14.4 What are the complications of seasonal influenza?

Bacterial pneumonia is a frequent complication in the elderly and people with certain chronic diseases. Two of the bacteria that are often found, *Streptococcus pneumoniae* and *Haemophilus influenzae*, are discussed in previous sections of this module.

Pregnant women are at increased risk of severe disease and death, and complications for their babies, such as stillbirth, preterm delivery, neonatal death and low birth weight. Elderly persons (age 65 years or over) have the highest risk of mortality from influenza.

14.5 What is the treatment for seasonal influenza?

Several antiviral drugs are available to treat influenza but these are most often used in high-income countries.
14.6 How is seasonal influenza prevented?

Annual vaccination is recommended to prevent seasonal influenza, particularly for high-risk groups. WHO recommends that pregnant women should be the first priority for influenza vaccine. Children aged six to 59 months, the elderly (over 65 years of age), people with chronic conditions and health care workers may also be vaccinated based on the local burden of disease, available resources and competing health priorities. Sections 14.7–14.9 and Table 1.20 describe influenza vaccines.

14.7 What is seasonal influenza vaccine?

Most seasonal influenza vaccines are trivalent, containing two strains of influenza A and one strain of influenza B, which are chosen based on known circulating strains. Both inactivated and live attenuated (weakened) trivalent vaccines are available. A quadrivalent live attenuated (weakened) vaccine was licensed in the USA in 2012.

Inactivated influenza vaccines are usually available in multi-dose vials that have preservative (thiomersal). Preservative-free, single-dose vials and prefilled syringes are in limited supply and more expensive. They do not require reconstitution and must be stored at a temperature of between +2°C and +8°C without freezing.

Inactivated influenza vaccines are administered intramuscularly in 0.5 ml doses.

Live attenuated (weakened) vaccines are administered as nasal sprays and are generally used for healthy individuals between two and 49 years of age.

The rest of this section focuses on inactivated influenza vaccines since they are recommended for pregnant women at any time, children six to 59 months of age and persons of 50 years of age and older.

14.8 How safe are inactivated influenza vaccines and what are the potential adverse events following immunization?

Inactivated influenza vaccines are considered safe. Severe adverse events have included anaphylaxis in 0.7 per million vaccinations, Guillain-Barré syndrome in one to two per million (in older adults) and oculo (eye)-respiratory syndrome in 76 per million. Mild events include local injection site reactions in 10–64%, fever in 12% of children aged one to five years and fever in 5% of children aged six to 15 years.

Inactivated influenza vaccines are contraindicated in cases of known allergic reaction to a previous dose or to a vaccine component, including egg protein.

14.9 When are inactivated influenza vaccines administered?

Annual vaccination for high-risk groups should be incorporated into immunization programmes following national policy. WHO recommends that pregnant women have the highest priority. Pregnant women can be vaccinated in any trimester. Ideally, influenza vaccine should be made available throughout the year and it may be given at the same time as tetanus vaccine. Immunizing pregnant women also benefits their babies after birth since the vaccine is not given to infants before six months of age.

A single dose is recommended for those over nine years of age, including pregnant women. Children aged six to 59 months are at high risk of severe disease and should be given two doses at least four weeks apart. Children aged six to 35 months should receive a pediatric dose. For elderly persons (over 65 years of age) vaccination is the most effective public health intervention to reduce their risk of death from influenza.

Health care workers are an important group to vaccinate to reduce the risk of transmission to patients.

Annual vaccination (or re-vaccination, if the vaccine strains are identical) is recommended. Previously vaccinated children aged six to 59 months require only one dose.

Key points about seasonal influenza

- Seasonal influenza due to influenza virus types A and B results in significant disease and economic burden each year.
- Pregnant women are the highest priority for vaccination in order to protect young infants (vaccine cannot be given to those under six months of age).
- Additional risk groups to be considered include children six to 59 months, as well as the elderly over age 65 years. The elderly are most at risk of death.
- The main complication is bacterial pneumonia, which can be fatal.
- Annual vaccination is recommended, particularly for high-risk groups.
### Table 1.20 Inactivated influenza vaccines summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Inactivated viral: tri- or quadrivalent for 2 strains of influenza A and 1–2 strains of influenza B</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total number of doses</strong></td>
<td>• 1 for ≥ 9 years of age, including pregnant women and adults</td>
</tr>
<tr>
<td></td>
<td>• 2 for children 6–59 months of age (children 6–35 months should receive a pediatric dose)</td>
</tr>
<tr>
<td><strong>Schedule</strong></td>
<td>• Annual</td>
</tr>
<tr>
<td></td>
<td>• For children 6–59 months of age, 2 doses with an interval of 4 weeks minimum.</td>
</tr>
<tr>
<td></td>
<td>Previously vaccinated children aged 6–59 months require only 1 dose</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Known hypersensitivity (allergy) or anaphylaxis to a previous dose or to a vaccine component such as egg protein</td>
</tr>
<tr>
<td><strong>Adverse events</strong></td>
<td>• Severe: rare anaphylaxis, Guillain-Barré syndrome, oculo-respiratory syndrome</td>
</tr>
<tr>
<td></td>
<td>• Mild: injection site reactions and fever</td>
</tr>
<tr>
<td><strong>Special precautions</strong></td>
<td>May postpone vaccination in case of moderate to severe illness (with temperature ≥39 °C)</td>
</tr>
<tr>
<td><strong>Dosage</strong></td>
<td>0.5 ml</td>
</tr>
<tr>
<td><strong>Injection site</strong></td>
<td>Outer (anterolateral) mid-thigh in infants and children; upper arm (deltoid) adults</td>
</tr>
<tr>
<td><strong>Injection type</strong></td>
<td>Intramuscular</td>
</tr>
<tr>
<td><strong>Storage</strong></td>
<td>• Between +2 °C and +8 °C</td>
</tr>
<tr>
<td></td>
<td>• Do not freeze</td>
</tr>
</tbody>
</table>
15.1 What is tetanus?

Tetanus is caused by the bacterium *Clostridium tetani*, which is present in soil everywhere. Infection with this bacterium occurs when soil enters a wound or cut. A toxin released by the bacterium causes severe, painful muscle spasms that can lead to death.

Neonatal tetanus (in newborns) and maternal tetanus (in mothers) is a serious problem in areas where home deliveries without sterile procedures are common.

15.2 How is tetanus spread?

Tetanus is not transmitted from person to person. In people of all ages, the bacterium can enter a wound or cut from items such as dirty nails, knives, tools, wood splinters, dirty tools used during childbirth, or deep puncture wounds from animal bites. It grows well in deep wounds, burns and crush injuries.

In newborn babies, infection can occur when delivery occurs on dirty mats or floors, a dirty tool is used to cut the umbilical cord, dirty material is used to dress the cord or when the hands of the person delivering the baby are not clean.

Infants and children may also contract tetanus when dirty tools are used for circumcision, scarification and skin piercing, and when dirt, charcoal or other unclean substances are rubbed into a wound.

15.3 What are the symptoms and signs of tetanus?

The incubation period (time between getting infected and showing symptoms) is usually three to 21 days, but can be as much as several months depending on the wound. The risk of death from the disease increases as the incubation period decreases.

In children and adults, muscular stiffness in the jaw (trismus or lock-jaw) is a common first sign of tetanus. This is followed by stiffness in the neck, abdomen and/or back, difficulty swallowing, muscle spasms, sweating and fever. Newborns with tetanus are normal at birth but stop feeding at three to 28 days of age. They then become stiff and severe muscle spasms occur.
15.4 What are the complications of tetanus?

When muscles used in breathing are affected, respiratory failure and death can occur. Neonates and elderly patients are at highest risk. Pneumonia is also common. Fractures of the spine or other bones may occur as a result of muscle spasms and convulsions. Long-term neurologic impairment has been described in survivors of neonatal tetanus.

15.5 What is the treatment for tetanus?

Tetanus at any age is a medical emergency best managed in a referral hospital. Antitetanus immunoglobulins, antibiotics, wound care and supportive measures are needed.

15.6 How is tetanus prevented?

Tetanus toxoid-containing (TTCV) vaccine protects against tetanus. Infants and children may receive combination vaccines, such as DTP, pentavalent (DTP+HepB+Hib) or DT. Anyone older than seven years of age should receive dT, which contains tetanus toxoid and lower levels of diphtheria antigen. Sections 15.8–15.10 and Tables 1.21–1.23 describe tetanus toxoid-containing vaccines.

Neonatal tetanus can be prevented by immunizing women of reproductive age with tetanus toxoid, either during or before pregnancy. Clean delivery procedures are needed even when the mother has been immunized. Clean umbilical cord care for the newborn is equally important.

People who recover from tetanus do not have natural immunity and can be infected again. WHO recommends completion of a six-dose schedule.

15.7 What is needed for global tetanus disease control?

WHO, the United Nations Children’s Fund (UNICEF) and the United Nations Population Fund (UNFPA) have set 2015 as the target date for the worldwide elimination of neonatal tetanus, which means less than one case per 1000 live births per year in every district. Because the tetanus bacterium survives in the environment, eradication of tetanus is not feasible and high levels of immunization need to be maintained even after elimination.

The strategies to achieve the maternal and neonatal tetanus (MNT) elimination goal are improved vaccination coverage of pregnant women with TT-containing vaccines, vaccination of all women of reproductive age in high-risk areas, promotion of clean delivery and cord care practices, and improved surveillance and reporting of neonatal tetanus cases.

After MNT elimination, countries must maintain high coverage of pregnant women with TTCV through routine immunization, use all opportunities such as mother-and-
child health days and periodic intensification of routine immunization to ensure high protection, promote school-based TTCV booster doses, promote clean delivery and cord care practices, and maintain surveillance of cases.

15.8 What are tetanus toxoid-containing vaccines?

Tetanus toxoid vaccine is available as TT, which protects only against tetanus and neonatal tetanus. It is also available in pentavalent, DTP and dT/DT combinations. TT vaccine is supplied as a liquid in single- and multi-dose vials and also in prefilled auto-disable syringes. Pentavalent vaccine with a freeze-dried Hib component requires reconstitution: see Module 5 (Managing an immunization session), Section 4.2 for details. Tetanus toxoid-containing vaccines must be stored between +2 °C and +8 °C without being frozen. They are freeze-sensitive. If freezing is suspected, the Shake Test should be performed to determine whether a vial is safe to use (see Module 2 (The vaccine cold chain), Section 7). Opened multi-dose vials must be handled according to national multi-dose vial policy (see Module 2, Section 5 for WHO policy).

Tetanus toxoid-containing vaccines are administered as 0.5 ml doses given intramuscularly in the anterolateral (outer) thigh in infants and in the deltoid muscle (upper arm) of older children and adults.

15.9 How safe is tetanus toxoid vaccine and what are the potential adverse events following immunization?

Tetanus toxoid is very safe. Severe events are rare and include anaphylaxis (1.6 per 1 million doses) and neurologic problems such as brachial neuritis (inflammation of arm nerves). Guillain-Barré syndrome has been reported but TTCV has not been established as the cause. Mild events include injection site pain, redness and/or swelling. These are more common after later doses than earlier ones, and may affect between 50% and 85% of people who receive TT booster doses. Fever may develop in 10% of those vaccinated.


15.10 When are tetanus toxoid-containing vaccines given?

For long-term immunity against tetanus in all individuals, five doses of TTCV are recommended in childhood: three doses in the primary series given in infancy by pentavalent vaccine, one booster dose between four and seven years of age using dT vaccine, and a second booster dose with dT between 12 and 15 years of age. For women, one additional dose of dT is recommended during pregnancy to ensure protection throughout reproductive age and probably for life.
Because increasing numbers of women have documentation of prior receipt of TT-containing vaccines when they are assessed for vaccination during childbearing years, three childhood doses are considered equivalent in protection to two doses of TT or Td given in adulthood (see Tables 1.21–1.23).

### Key points about tetanus

- Tetanus is caused by a bacterium found in the environment.
- Infection occurs during unclean delivery of babies, when contaminated objects are used to cut the umbilical cord, or whenever tetanus bacteria enter a wound or cut.
- Neonatal tetanus remains a serious problem in countries with poor immunization coverage and unsafe childbirth and cord care practices.
- Most newborns who contract tetanus will die.
- The best way to prevent maternal and neonatal tetanus is to give the WHO six-dose TTCV schedule of infant and booster doses, immunize pregnant women in all areas (and all women of reproductive age in high-risk areas), and ensure clean delivery and cord care practices.

### Table 1.21 Tetanus-toxoid vaccine summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Toxoid</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total number of doses</strong></td>
<td>5</td>
</tr>
</tbody>
</table>
| **Schedule** | • With pentavalent: starting at age 6 weeks (minimum) with second and third doses at 4–8 week intervals after the previous dose (see Table 1.2)  
• For women, see Tables 1.22 and 1.23 |
| **Booster** | • 4–7 years; and adolescence 12–15 years  
• For women, see Tables 1.22 and 1.23 |
| **Contraindications** | Known hypersensitivity (allergy) or anaphylaxis to a previous dose |
| **Adverse events** | • Severe: rare anaphylaxis, brachial neuritis  
• Mild: injection site reactions and fever |
| **Special precautions** | None |
| **Dosage** | 0.5 ml |
| **Injection site** | Anterolateral (outer) thigh in infants and children; upper arm (deltoid) in adults |
| **Injection type** | Intramuscular |
| **Storage** | • Between +2 °C and +8 °C  
• Do not freeze |
Table 1.22  Tetanus toxoid immunization schedule for routine immunization of pregnant women who were not previously vaccinated in childhood

<table>
<thead>
<tr>
<th>Dose of TT or Td</th>
<th>Schedule</th>
<th>Expected duration of protection*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>At first contact or as early as possible in pregnancy</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>At least 4 weeks after TT1</td>
<td>1–3 years</td>
</tr>
<tr>
<td>3</td>
<td>At least 6 months after TT2 or during subsequent pregnancy</td>
<td>At least 5 years</td>
</tr>
<tr>
<td>4</td>
<td>At least 1 year after TT3 or during subsequent pregnancy</td>
<td>At least 10 years</td>
</tr>
<tr>
<td>5</td>
<td>At least 1 year after TT4 or during subsequent pregnancy</td>
<td>For all reproductive years and possibly longer</td>
</tr>
</tbody>
</table>

*Recent studies suggest that the duration of protection may be longer than indicated in the table. This matter is currently under review.

Table 1.23  Guidelines for tetanus toxoid immunization of women who were immunized during infancy, childhood and adolescence

<table>
<thead>
<tr>
<th>Age at last vaccination</th>
<th>Previous immunizations (based on written records)</th>
<th>Recommended immunizations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>At present contact/pregnancy</td>
</tr>
<tr>
<td>Infancy</td>
<td>3 DTP</td>
<td>2 doses of TT/Td (min 4 weeks interval between doses)</td>
</tr>
<tr>
<td>Childhood</td>
<td>4 DTP</td>
<td>1 dose of TT/Td</td>
</tr>
<tr>
<td>School age</td>
<td>3 DTP + 1 DT/Td</td>
<td>1 dose of TT/Td</td>
</tr>
<tr>
<td>School age</td>
<td>4 DTP + 1 DT/Td</td>
<td>1 dose of TT/Td</td>
</tr>
</tbody>
</table>
16 Tuberculosis

16.1 What is tuberculosis?

Tuberculosis (TB) is caused by the bacterium *Mycobacterium tuberculosis*, which usually attacks the lungs, but can also affect other parts of the body, including the bones, joints and brain.

Not everyone who is infected with TB bacteria develops the disease. People who are infected may not feel ill and may have no symptoms. The infection can last for a lifetime, but the infected person may never develop the disease itself. People who are infected and who do not develop the disease do not spread the infection to others.

16.2 How is TB spread?

TB is spread from one person to another through the air, often when an infected person coughs or sneezes. TB spreads rapidly, especially in areas where people are living in crowded conditions, have poor access to health care, and/or are malnourished. A person can contract bovine tuberculosis, another variety of TB, by consuming raw milk from infected cattle.

People of all ages can develop TB, but the risk is highest in children younger than three years of age and in older people. People with TB infection who have weakened immune systems (for example, people with HIV/AIDS) are more likely to develop the disease.

16.3 What are the symptoms and signs of TB?

The period from infection to development of the first symptoms is usually four to 12 weeks, but the infection may persist for months or even years before the disease develops. A person with the disease can infect others for several weeks after he or she begins treatment.

The symptoms of TB include general weakness, weight loss, fever and night sweats. In TB of the lungs, which is called pulmonary tuberculosis, the symptoms include persistent cough, coughing up of blood and chest pain. In young children, however, the only sign of pulmonary TB may be stunted growth or failure to thrive. Other symptoms and signs depend on the part of the body that is affected. For example, in tuberculosis of the bones and joints, there may be swelling, pain and crippling effects on the hips, knees or spine.
16.4 What are the complications of TB?

TB can present in many ways and may be very difficult to diagnose. Untreated pulmonary TB results in debility and death. This may be more rapid in people infected with HIV/AIDS.

16.5 What is the treatment for TB?

People with TB must complete a course of therapy, which usually includes taking two or more antituberculosis drugs for at least six months. This therapy is called Directly Observed Treatment Schedule (DOTS). Unfortunately, some people fail to take the medication as prescribed or do not complete the course of therapy. Some may be given ineffective treatment. This can lead to multidrug-resistant TB that is even more difficult to treat and more dangerous if spread to other people. When people who have developed TB fail to complete standard treatment regimens or are given the wrong treatment regimen, they may remain infectious.

16.6 How is TB prevented?

Vaccination before 12 months of age with bacille Calmette-Guérin vaccine (BCG) can protect against TB meningitis and other severe forms of TB in children of less than five years of age. Sections 16.7–16.9 and Table 1.24 describe BCG vaccine.

16.7 What is BCG vaccine?

BCG vaccine protects infants against tuberculosis. The letters B, C, G stand for bacillus Calmette-Guérin. Bacillus describes the rod shape of the bacterium. Calmette and Guérin are the names of the people who developed the vaccine.

BCG vaccine is supplied in freeze-dried powder (also called lyophilized) form. It must be reconstituted with a diluent before use: see Module 5 (Managing an immunization session), Section 4.2 for details. BCG vaccine must be stored between +2 °C and +8 °C after reconstitution. Opened multi-dose vials must be handled according to national multi-dose vial policy: see Module 2 (The vaccine cold chain), Section 5 for WHO policy.

16.8 How safe is BCG vaccine and what are the potential adverse events following immunization?

Severe events following immunization with BCG include generalized infection in about one per 230 000–640 000 doses of vaccine given, primarily in HIV-infected persons or those with severe immune deficiencies. Known HIV infection or other immune deficiency is a contraindication for BCG (refer to Module 5, Section 3.1). Other severe events include swelling and abscesses in about one per 1000–10 000 doses. Swollen glands (in the armpit or near the elbow) and/or abscesses sometimes
occur because an unsterile needle or syringe was used, too much vaccine was injected or, most commonly, the vaccine was injected incorrectly under the skin instead of into the top layer (refer to Module 5, Section 4.7 for injection technique).

A mild reaction at the site of injection occurs in almost all children. When BCG vaccine is injected, a small raised lump usually appears at the injection site and then disappears within 30 minutes. After about two weeks, a red sore (about the size of the end of an unsharpened pencil) forms. This sore usually lasts for another two weeks and then heals, leaving a small scar about 5 mm across – the scar is a sign that the child has been effectively immunized.


16.9 When is BCG vaccine administered?

BCG is recommended for infants living in countries with a high TB disease burden and high-risk children living in countries with a low disease burden. It should be given routinely at, or as soon as possible after, birth to all infants except those known to have HIV or any condition that results in a decreased or abnormal immune system response.

In areas where TB is highly endemic but services are limited, BCG should be given at birth to all infants regardless of HIV exposure. Infants with known HIV-positive mothers should be followed closely to monitor for any BCG-related complications. If services are available, BCG should be postponed until HIV-exposed infants (born to known HIV-positive mothers) can be confirmed to be HIV negative.

BCG vaccine is not recommended after 12 months of age because the protection provided is less certain.

Key points about TB

- TB usually affects the lungs but can affect other parts of the body, including the bones, joints and brain.
- TB is spread through the air.
- The symptoms of TB disease include general weakness, weight loss, fever and night sweats.
- People who develop TB disease must complete a course of drug therapy to cure it and to avoid spreading it to others.
- The recommended method of TB prevention for children is BCG vaccine given at, or as soon as possible after, birth and before 12 months of age.
### Table 1.24 BCG vaccine summary

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Live bacterial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of doses</td>
<td>1</td>
</tr>
<tr>
<td>Schedule</td>
<td>At or as soon as possible after birth</td>
</tr>
<tr>
<td>Booster</td>
<td>None</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Known HIV infection or other immune deficiency</td>
</tr>
</tbody>
</table>
| Adverse events  | • Severe: generalized disease or infections such as osteomyelitis (bone infection); abscess; regional lymphadenitis (lymph node inflammation)  
• Mild: injection site reactions |
| Special precautions | Correct intradermal administration is essential – a specific syringe and needle are used for BCG (see Module 5, Section 4.8) |
| Dosage          | 0.05 ml        |
| Injection site  | Outer upper left arm or shoulder |
| Injection type  | Intradermal    |
| Storage         | • Between +2 °C and +8 °C  
• Do not freeze |
17 Yellow fever

17.1 What is yellow fever?

Yellow fever (YF) is a mosquito-borne viral disease of humans and other primates that is currently endemic (occurring regularly) in 44 tropical zone African and South American countries.

17.2 How is yellow fever spread?

YF is spread by several species of *Haemagogus* and *Aedes* mosquitoes. In forest areas and humid regions of Africa, people become infected by the bites of mosquitoes that have previously fed on infected nonhuman primates. During large epidemics in crowded urban areas, mosquitoes can spread the disease from person to person.

17.3 What are the symptoms and signs of yellow fever?

Infection with YF virus can cause no symptoms or signs in some cases. In other cases, signs usually appear three to six days after the infected mosquito bite and include fever, muscle pain, shivering, loss of appetite, nausea and vomiting, congestion of the conjunctivae and face and a relatively slow heart rate during fever. Approximately 15% of infections are associated with more severe symptoms, such as jaundice (yellowing of the conjunctivae and skin), bleeding and liver and kidney failure that can lead to death. Severe YF can be confused with malaria, leptospirosis, viral hepatitis, other types of haemorrhagic fevers and poisoning.

17.4 What are the complications of yellow fever?

About 20–50% of patients who develop liver and kidney failure die, usually seven to 10 days after the onset of the disease. Survivors may experience prolonged weakness and fatigue, but the liver and kidneys usually heal completely.

17.5 What is the treatment for yellow fever?

There is no WHO recommendation for antiviral medication in YF treatment. Supportive measures should be taken to alleviate symptoms. Severe cases usually require hospital care. Paracetamol is used in mild cases that can be managed at home. Aspirin and similar medications should be avoided since they may cause bleeding, particularly in the stomach and intestines.
17.6 How is yellow fever prevented?

YF is prevented by immunization, which is recommended to protect people living in endemic and epidemic disease areas and travellers visiting these areas, and to prevent international spread by infected travellers. Large-scale YF vaccination has been very effective in endemic areas, but major outbreaks have occurred where coverage has decreased after the discontinuation of immunization campaigns.

Measures to control mosquito populations in urban areas have also been part of prevention strategies.

17.7 What is yellow fever vaccine?

Live attenuated (weakened) virus vaccines for preventing YF are currently in use. They are supplied in freeze-dried (also called lyophilized) form and must be reconstituted with the diluent supplied by the manufacturer before use: see Module 5 (Managing an immunization session), Section 4.2 for details. YF vaccine must be stored between +2 °C and +8 °C. It is not damaged if accidentally frozen. Opened multi-dose vials must be handled according to national multi-dose vial policy: see Module 2 (The vaccine cold chain), Section 5 for WHO policy.

It is administered as a single 0.5 ml dose either subcutaneously in the upper arm or intramuscularly in the anterolateral thigh.

17.8 How safe is yellow fever vaccine and what are the potential adverse events following immunization?

Severe adverse events include hypersensitivity (allergy) or anaphylaxis (0.8 per 100,000 vaccinations) occurring most commonly in people with allergies to eggs or gelatin. YF vaccine-associated neurologic disease (inflammation of different parts of the nervous system, including the brain) and viscerotropic disease (affecting internal organs) have been reported; overall rates are low but older patients (over 60 years of age) receiving primary YF vaccine doses seem to be at higher risk. YF vaccine-associated viscerotropic disease (affecting internal organs with symptoms and signs similar to infection with YF) has been fatal in over 60% of cases.

Mild adverse events, such as injection site pain, headache, muscle ache, low-grade fever, itching, hives and other rashes are reported in up to 25% of those vaccinated.
17.9 When is yellow fever vaccine administered?

A single dose of YF vaccine is sufficient for life-long protection and, in endemic countries, should be integrated into routine immunization programmes, with children aged 9–12 months receiving the vaccine at the same time as measles-containing vaccine. Preventive mass immunization campaigns are recommended in endemic countries where YF vaccine coverage is low. It should be provided to everyone aged nine months or more in areas with reported cases. Unvaccinated travellers aged nine months or more going to and from high-risk areas should receive YF vaccine unless otherwise contraindicated.

YF vaccine is contraindicated in children aged under six months and not recommended for children aged six to eight months, except during epidemics. It is contraindicated in anyone with allergies to egg antigens and in HIV-infected individuals with CD4 T-cell values of under 200 per mm$^3$.

See Table 1.25 for YF vaccination summary.

Key points about yellow fever

- Yellow fever is a viral disease spread by infected mosquitoes primarily in tropical zones of Africa and South America.
- YF symptoms and signs can range from none to liver and kidney failure that leads to death; they can be easily confused with other diseases.
- No specific antiviral treatment is recommended at this time.
- YF vaccine is effective as a single dose and, if not contraindicated, should be given to all people aged nine months or more living in or travelling to high-risk areas.
### Table 1.25  Yellow fever vaccine summary

| Type of vaccine | Live attenuated (weakened) viral |
| Number of doses | 1 |
| **Schedule**          | • In endemic areas: 9–12 months of age with MCV1  
                         • In areas with reported cases: all persons aged ≥9 months  
                         • For travellers to high-risk areas: all persons aged ≥9 months |
| **Booster**            | None |
| **Contraindications** | • Age <6 months; age 6–8 months except during epidemics  
                            • Known allergy to egg antigens or to a previous dose  
                            • HIV infection with CD4 T-cell values <200 per mm$^3$ |
| **Adverse events**    | • Severe: anaphylaxis; YF vaccine-associated neurologic (nerve) disease and viscerotropic (affecting internal organs) disease; encephalitis in infants aged <6 months  
                            • Mild: headache, muscle pain, fever |
| **Special precautions**| Carry out a risk–benefit assessment before administering to pregnant women or people aged >60 years |
| **Dosage**            | 0.05 ml |
| **Injection site**    | Outer upper left arm or shoulder (for subcutaneous); or anterolateral (outer) thigh in infants and children (for intramuscular) |
| **Injection type**    | Subcutaneous or intramuscular |
| **Storage**           | Between +2 °C and +8 °C |
18 Opportunities for integration of services: EPI Plus and vitamin A deficiency

Immunization programmes provide an opportunity to deliver other essential health services such as vitamin A supplementation, de-worming, malaria prevention with insecticide-treated nets and Integrated Management of Childhood Illness. These additional services are part of EPI Plus programmes. Vitamin A deficiency is discussed further here.

18.1 Vitamin A deficiency

Any immunization contact is an opportunity to screen infants and young children for eligibility to receive vitamin A, particularly if vaccinations have been delayed and the child is six months or older.

18.2 What is vitamin A?

Vitamin A is a substance that is required by the human body. It strengthens resistance to infection, increases a child’s chances of surviving an infection, promotes growth and protects the cornea (the transparent part of the eye). Lack of vitamin A, or vitamin A deficiency, can result in poor vision in dim light.

The human body cannot make vitamin A. So all the vitamin A it needs must come from food intake. Vitamin A is present in the following foods:

- breast milk
- liver, eggs, meat, fish liver oil
- milk, cheese and other dairy products
- yellow and orange fruits, such as mangoes and papayas
- yellow and orange vegetables, such as pumpkins and carrots
- dark green, leafy vegetables
- red palm oil.

Vitamin A can be added to such foods as sugar, vegetable oil and wheat flour during processing. This is called food fortification.
18.3 When does vitamin A deficiency occur?

Vitamin A deficiency occurs when a person does not eat enough food containing vitamin A or when the body uses it up too fast. This often happens during illness, during pregnancy and lactation, and when children’s growth is most rapid – from six months to five years of age.

18.4 What are symptoms and signs of vitamin A deficiency?

Vitamin A deficiency (VAD) reduces resistance to infections, leading to more severe and prolonged illnesses and increasing the risk of death. It can cause eye damage, such as corneal lesions and, when severe, can cause blindness. Generally, the first clinical sign of vitamin A deficiency is night blindness (impared vision in dim light). Because vitamin A deficiency reduces the body’s resistance to infection, it is a threat even before any direct signs become apparent.

Children suffering from vitamin A deficiency are more likely to get infections, such as measles, as well as diarrhoea and fevers. These infections are more likely to be severe, sometimes resulting in death.

18.5 What is vitamin A supplementation?

When diets do not contain food with enough vitamin A, it is possible to increase vitamin A levels in the body by periodically taking a concentrated dose in the form of a capsule. This is called supplementation. When given to children, vitamin A capsules are cut open and the drops of liquid inside are squeezed into the mouth.

Vitamin A supplementation can be combined with immunization services for children when health officials know or suspect that vitamin A deficiency is present in an area or among a certain population.

In addition, vitamin A supplements are also given for the treatment of measles and xerophthalmia (dryness of the eyes that can lead to corneal damage and blindness).

18.6 Are there any side effects of vitamin A supplements?

There are usually no side effects. On rare occasions, a child may experience headache, loss of appetite or vomiting. These symptoms pass in time, and no treatment is necessary. Parents should be advised that this is normal.
18.7 What are the opportunities to link vitamin A and routine immunization?

Table 1.26 shows how vitamin A supplementation can be linked with routine immunization.

<table>
<thead>
<tr>
<th>Target for vitamin A</th>
<th>Immunization contact</th>
<th>Vitamin A dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants 6–11 months</td>
<td>• Measles/yellow fever&lt;br&gt;• Polio NIDs</td>
<td>100 000 IU</td>
</tr>
<tr>
<td>Children 12 months and older</td>
<td>• Other EPI campaigns&lt;br&gt;• Boosters</td>
<td>200 000 IU</td>
</tr>
<tr>
<td>Children 12–59 months</td>
<td>• Booster doses&lt;br&gt;• Delayed primary immunization</td>
<td>200 000 IU</td>
</tr>
</tbody>
</table>

The optimal interval between doses of vitamin A is four to six months. The minimum recommended safe interval between doses is one month. The interval between doses can be reduced to treat clinical vitamin A deficiency and measles cases. Follow national guidelines for the appropriate measles treatment schedule.
Pneumonia and diarrhoea remain two of the leading killers of young children globally. Together, these diseases account for 24% of all deaths of children under five years of age, and the concentration of these deaths among the poorest countries is the starkest example of the child survival gap. Tackling these two leading killers of children together will have the single greatest impact on improving child survival.

As both illnesses have multiple causes, no single intervention can prevent and control either condition, and although low-cost and effective interventions have been well established, they are not always promoted or implemented together to achieve maximum benefit. Coverage of core interventions remains low, services are too often provided piecemeal, and those most at risk are still not being reached. However, as many of the risk factors and underlying causes of disease, as well as the preventive strategies and available delivery platforms, are nearly identical, it is now clear that pneumonia and diarrhoea can and should be addressed in an integrated and coordinated manner.

Ending Preventable Child Deaths from Pneumonia and Diarrhoea by 2025 – the integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD; available at http://www.who.int/maternal_child_adolescent/documents/global_action_plan_pneumonia_diarrhoea/en/) was launched in 2013 by WHO and UNICEF with contributions from a wide group of partners and stakeholders. The GAPPD outlines an integrated framework of key interventions proven to effectively protect, prevent and treat pneumonia and diarrhoea and provides a range of supporting activities to improve and accelerate the implementation of these interventions, which, when delivered together, can save countless children from avoidable deaths due to both diseases.

As shown in Figure 1.1, GAPPD emphasizes a “Protect, Prevent and Treat” framework to achieve pneumonia and diarrhoea control: protecting children by establishing and promoting good health practices; preventing children from becoming ill from pneumonia and diarrhoea by ensuring universal coverage of immunization, HIV prevention and healthy environments; and treating children who are ill from pneumonia and diarrhoea with appropriate treatment.

Protection measures include:

- exclusive breastfeeding for the first six months of life
- adequate complementary feeding
- vitamin A supplementation.
Prevention measures include:

- vaccines (measles, pertussis, H. influenzae type b, pneumococcus and rotavirus)
- handwashing with soap
- safe drinking water and sanitation
- reduced indoor air pollution
- HIV prevention
- cotrimoxazole prophylaxis for HIV-infected children as indicated.

Treatment measures include:

- improved care seeking and referral
- case management at health facility and community level
- supplies (ORS, zinc, antibiotics and oxygen)
- continued feeding (including breastfeeding).

**Figure 1.1** GAPPD “Protect, Prevent and Treat” framework