Immunization

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Abstract

Immunization has played a major role in protection against infectious disease, and indeed the development of vaccines has been classed as one of the greatest medical achievements. The introduction of vaccines has been so successful that we are on the verge of seeing the eradication of vaccine-preventable diseases. Moreover, the proportion of disease prevented by the routine childhood immunization schedule is higher than for any other routine public health intervention. To ensure the continued efforts of controlling, eliminating and eradicating infectious diseases, it is necessary to encourage the collaboration of health groups, organizations and the public to maintain adequate vaccine coverage and to persist with the development of effective and safe vaccines.

Keywords Immunization; infectious diseases; MRCP; vaccine

Key points

- Vaccination is an effective and safe method of preventing serious infectious diseases
- Maintaining high vaccine coverage is crucial in preventing the re-emergence of disease
- Live vaccines are contraindicated in those who are immunosuppressed
- Childhood vaccinations should be given in a timely manner to all infants, especially premature infants

Introduction

Immunization is the process whereby individuals are made immune to infectious diseases. This can be achieved through active immunity, where immunity is induced by vaccination, the delivery of antigens to the individual, or it can be achieved by passive immunity, the administration of antibodies to the individual.

Active immunity

Active immunity acquired through vaccination induces humoral and/or cell-mediated immune responses to provide protection similar to that of natural infection. Immunity generated by this mechanism is often long-lasting. There are various types of vaccine available: live attenuated, inactivated whole-cell (killed antigen), toxoid (inactivated toxins) and subunit (purified antigen).

Vaccination with live attenuated vaccines (e.g. measles/mumps/rubella (MMR), rotavirus, smallpox, varicella-zoster, yellow fever, influenza, typhoid, tuberculosis (TB; bacillus Calmette–Guerin (BCG)), oral polio vaccine (OPV)) involves the replication of the live organism in the host to give rise to an immune response that mimics that induced by natural infection. These vaccines confer long-lasting antibody responses after one or two doses and, because these vaccines are attenuated, they can cause subclinical infection, albeit with very low risk of disease.

Inactivated vaccines can be made of whole, inactivated microorganisms (e.g. hepatitis A, Japanese encephalitis, rabies, inactivated polio vaccine (IPV) or specific microbial components (toxoid and subunit vaccines)). These vaccines cannot cause the disease that they are designed to protect against; however, they often do not provide such long-term immunity as that of live attenuated vaccines.

Toxoid vaccines (e.g. diphtheria, tetanus) are protein toxins that have been modified to reduce pathogenicity but are immunogenic. Other component vaccines are made from purified subunits (e.g. acellular pertussis, pneumococcus, meningococcus), engineered subunits (e.g. *Haemophilus influenzae* type b (Hib), pneumococcal and meningococcal polysaccharide conjugate vaccines) or recombinant subunits (hepatitis B, human papillomavirus (HPV)) of microorganisms that can induce immunity.

Passive immunity

Passive immunization allows short-term protection from disease through the transfer of antibodies. This process occurs naturally during pregnancy, when immunoglobulin (Ig) G is transferred across the placenta to the fetus. Protection through passive immunization can also be conferred by the transfusion of blood or blood products including Ig (e.g. hepatitis B, tetanus, rabies, varicella-zoster Ig). This mechanism can provide immediate, albeit short-lived protection.

Vaccine failure

A small proportion of individuals are prone to infection despite vaccination. Vaccine failures can be categorized into primary and secondary. Individuals with primary vaccine failures do not have any immunological response to the vaccine. In those with secondary vaccine failure, there is an initial immunological response but this wanes over time. Booster doses are required with vaccine failure.

Herd immunity

Vaccines protect individuals directly and, by reducing the risk of transmission, can also lead to protection of unvaccinated

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individuals as they are no longer being exposed to the infection. Herd immunity refers to the fact that the susceptible unvaccinated population is being protected by the vaccinated population. It is, however, paramount that a high vaccine coverage is maintained to induce high levels of herd immunity and prevent the re-emergence of disease.

Vaccines

Diphtheria is caused by the action of diphtheria toxin, which is produced by *Corynebacterium diphtheriae* or *Corynebacterium ulcerans* and can result in paralysis and cardiac failure. The vaccine is made from a cell-free purified toxin treated with formaldehyde, converting it into diphtheria toxoid, and adsorbed onto an adjuvant. Diphtheria vaccines are produced in two strengths: high dose (D), used in the primary immunization of children <10 years of age, and low dose (d), used in those aged 10 years of age or over, as well as for boosting. The vaccine is administered in a combined vaccine, and a total of five doses of diphtheria vaccine are given in the recommended immunization schedule.

Tetanus is caused by the action of tetanus toxin, produced by the bacterium *Clostridium tetani* and resulting in generalized rigidity. The vaccine is made from a cell-free purified toxin treated with formaldehyde, converting it into tetanus toxoid, and is adsorbed onto an adjuvant. The tetanus vaccine (T) is administered as part of a combined vaccine and is given as a five-dose regimen, as well as given to those individuals with tetanus-prone wounds.

Pertussis is a highly infectious disease caused by *Bordetella pertussis*. The vaccines are made from purified components of the *B. pertussis* organism and then adsorbed onto adjuvants. The acellular pertussis vaccine is currently used in the UK primary immunization schedule and is given as part of a combined vaccine that is administered three times during the primary immunizations with a booster dose at 3 years of age. The incidence of local and systemic reactions is lower with the acellular pertussis vaccine (aP) compared with the previously used whole-cell pertussis vaccine.

In response to the pertussis outbreak in 2012, the Department of Health introduced a temporary programme offering pertussis vaccination to pregnant women between 28 and 32 weeks of pregnancy. This was put in place to protect infants from birth by passive immunity until they were old enough to be protected through routine immunization. The Joint Committee on Vaccination and Immunisation (JCVI) advised that this programme continue for at least a further 5 years. The minimum gestational age for vaccination was subsequently reduced to 16 weeks.

Poliomyelitis is caused by one of three serotypes of poliovirus (serotypes 1, 2 and 3). Until 2004, the live attenuated OPV (Sabin) was used for routine immunization in the UK. Because of the risk of vaccine-associated paralytic polio with OPV, it was replaced by IPV as part of a combined vaccine. A regimen of five doses of IPV provides long-term protection.

***H. influenzae* type b** can cause serious invasive disease. The Hib vaccine is a protein–polysaccharide conjugate vaccine. It is available as part of a combined vaccine given in three doses followed by a booster dose at 12 months with a Hib vaccine combined with the meningococcal group C (MenC vaccine).

Hepatitis B vaccine is produced using recombinant DNA technology and adsorbed onto an adjuvant. The regimen involves a minimum of three doses of hepatitis B vaccine (at 0, 1 and 6 months) for individuals at high risk of exposure (Table 2). A specific hepatitis B Ig is also available to provide passive and temporary immunity in those exposed to the virus. There are plans to introduce the vaccine Infanrix hexa® (DTaP/IPV/Hib/hepatitis B) in late 2017. This vaccine will replace the current 5-in-1 vaccine (DTaP/IPV+Hib) for primary immunizations, adding protection against hepatitis B.

Hepatitis A vaccines can be given to high-risk individuals as a monovalent vaccine (whole, inactivated virus) or combined with either typhoid or hepatitis B vaccines. Human normal Ig can be used to provide immediate but temporary immunity.

Pneumococcal vaccines are available as pneumococcal polysaccharide vaccine (PPV) and pneumococcal conjugate vaccine (PCV). PPV contains purified capsular polysaccharide from 23 capsular types of pneumococcus that account for about 96% of the pneumococcal isolates causing serious infection in the UK. PPV is used in individuals aged 65 years or over and in at-risk patients aged 2 years or over. PCV contains polysaccharide from 13 common capsular types and is conjugated to proteins, which improves its immunogenicity. Unlike PPV, this conjugate vaccine confers immunity in infants from 2 months of age and is given as a three-dose regime.

Rotavirus vaccine was introduced into the UK immunization schedule in 2013 to protect babies and infants from this cause of diarrhoea and vomiting. It is a live attenuated vaccine given orally at 2 months and 3 months of age.

Meningococcal disease is caused by *Neisseria meningitidis*. There are currently 13 capsular groups identified of which groups B, C, W and Y are the most common. There have been a number of changes to the meningococcal vaccination schedule. The infant doses of MenC vaccines were removed in 2016 in recognition of the rarity of MenC disease in infants. Because of an increase in numbers of meningococcal capsular group W (MenW) disease, the JCVI has advised a change of the adolescent MenC vaccine to the quadrivalent ACWY conjugate vaccine. In 2015, a meningococcal group B (MenB) vaccine was added to the routine UK immunization schedule to provide protection against infection caused by meningococcal group B strains. The current schedule consists of three doses of MenB as well as one dose of MenC followed by the MenACWY conjugate vaccine in 14-year-olds.

MMR vaccines consist of live attenuated strains of measles, mumps and rubella viruses. This vaccine is given to children aged 12–13 months of age with a booster at 3 years of age, and is offered to school leavers if they have not already been given these full two doses.

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