Vaccines and Immunological Products

Vaccines are one of medical science’s most widely used and effective products. During the 19th century it was discovered that particular microbes gave rise to specific diseases and this link led to the development of vaccines.

Immunisation

Artificial immunity is induced by immunisation. This is achieved by giving a vaccine (active immunisation) or immunoglobulin (passive immunisation). The term vaccination (which means ‘protection from smallpox’ - vaccinae meaning 'of the cow') references back to the work of Jenner. [1]

Active immunity

This is the stimulation of the immune mechanism to produce antibodies by giving an antigen as a vaccine. Such vaccines may be:

- Live attenuated viruses (rubella, measles, oral polio, mumps) or bacteria - bacillus Calmette-Guérin (BCG).
- Inactivated viruses (parenteral polio, hepatitis A) or parts of the virus (pneumococcal vaccine, influenza).
- Inactivated bacterial toxins (diphtheria and tetanus).
- Genetically engineered (hepatitis B vaccine).
### Bacterial Vaccines

- BCG vaccination.
- Typhoid vaccination (oral).
- Cholera vaccination (oral).

### Viral Vaccines

- Measles vaccination.
- Mumps vaccination.
- Rubella vaccination.
- Oral polio vaccination (Sabin).
- Yellow fever vaccination.
- Varicella (chickenpox) vaccination.
- Rotavirus vaccination.
- Japanese encephalitis vaccination.

#### Live attenuated vaccines

- Pertussis (whooping cough) vaccination.\(^2\)
- Cholera vaccination (oral, combined with recombinant B subunit).
- Anthrax vaccination.
- Plague vaccination.
- Meningitis B vaccine.\(^3\)

#### Inactivated vaccines

- Influenza vaccination.
- Hepatitis A vaccination.
- Injectable polio vaccination (Salk).
- Rabies vaccination.
- Tick-borne encephalitis vaccination.
- Japanese encephalitis vaccination.

#### Toxoids

- Diphtheria vaccination.
- Tetanus vaccination.

#### Polysaccharide extracts of virus

- *Haemophilus influenzae* type B (Hib) vaccination.
- Meningococcal A and C vaccination.
- Pneumococcal vaccination.
- Typhoid vaccination.

#### Genetically engineered

- Hepatitis B vaccination.

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The immune response may be humoral (as with most bacterial vaccines) or cell-mediated (as with live vaccines, including BCG).

**Live attenuated vaccines**

Produce longer-lasting immunity, similar but less than that produced by natural infection. Often one dose confers long-lasting immunity; however, they are inherently less stable than killed vaccines, with the possibility of reversion to wild strain, as in polio. Some may spread, enhancing herd immunity but putting at risk the immunocompromised.

**Inactivated vaccines**

Usually require a series of primary vaccinations followed by boosters. Some of these vaccines have adjuvants (for example, aluminium hydroxide, aluminium phosphate) to enhance the antibody response. There is no risk of person-to-person spread, and the vaccines are more stable.

**Humoral immunity**

Activation of B lymphocytes by an antigen produces millions of antibodies (immunoglobulins IgG, IgM, IgA, IgD, IgE), which bind to and neutralise the antigen. After recognising their particular antigen, they multiply and differentiate into plasma cells. Plasma cells produce large amounts of antibody in the form of large glycoproteins (immunoglobulins). Initially IgM is produced - the primary response. This is a slow response and two injections may be needed. Further injections of antigen will produce, after a few months, an accelerated or secondary response producing IgG. IgG antibodies are longer-lasting. When levels of IgG fall, a further dose of vaccine or booster will increase IgG levels again.
Cell-mediated immunity
The cell-mediated immune response does not involve major antibody production but does rely on antigen recognition (in association with self major histocompatibility complex (MHC) molecules) and lymphocyte responses to destroy infected cells and prevent organisms replicating within cells. Lymphocytes differentiating in the thymus and called T lymphocytes are mainly of two types (expressing two major forms of MHC):

- **CD4 or T-helper cells** - interact with class II MHC molecules, leading to stimulation of various immunological molecules - eg, B lymphocytes - to produce antibody. They also produce cytokines which activate macrophages. They are further classified according to the cytokines produced as T-helper 1 (activate macrophages - involved in cytotoxic and delayed hypersensitivity responses) and T-helper 2 (make interleukin-4 and -5 and stimulate B lymphocytes to support antibody production).

- **CD8 or T-suppressor/cytotoxic cells** - interact with class I MHC molecules, leading to a chain of events that destroys host cells infected by a virus.

Passive immunity
This is achieved by giving immunoglobulins and the protection is immediate but lasts only a few weeks. There are two types:

- Human normal immunoglobulin (HNIG) from pooled plasma. This contains antibodies to infections prevalent in the donor population. Some of these, such as that for hepatitis A, may be falling, ultimately affording less protection.

- Specific immunoglobulin for tetanus, varicella-zoster virus, rabies and hepatitis B. These are derived from pooled serum of convalescent patients.

A natural transfer of immunoglobulin occurs from mother to child by the placental route and from breast milk. This confers protection for a few months - hence:

- Infants can start vaccinations for diphtheria, tetanus, pertussis, polio, *H. influenzae* type B and meningococcal infection at 2 months.
- Measles vaccine is postponed until after 12 months because persisting passively acquired immunoglobulins may interfere with the immune response before 12 months.
- Sometimes a compromise is needed - pertussis would take from birth but passively acquired tetanus antibodies would interfere with the immune response to tetanus. Childhood immunisations could be started at 6 weeks but 8 weeks is recommended in the UK.

Precautions prior to vaccination[^4]

- Ask about allergies and previous reactions to vaccine (anaphylaxis to a preceding dose of vaccine or to vaccine components is a contra-indication to further doses). Anaphylactic hypersensitivity to eggs precludes those vaccines grown in chick embryos - current influenza vaccine, tick-borne encephalitis vaccine and yellow fever vaccine. Beware of patients who are extremely sensitive to any of the excipients in vaccines. Possible excipients include:
  - Informed consent should always be obtained, either verbal or written, before each immunisation.
  - Acute febrile illness - postpone (but not minor illness without fever).
  - Avoid local sepsis at the injection site.
  - Ensure vaccines are correctly stored (discard multi-dose vials after a vaccination session).
  - Add diluents slowly to avoid frothing.
  - The site of vaccination is important:
    - Adults and older children - use their right arm, deltoid.
    - Avoid pinching and going too low.
    - Anterolateral thigh in infants under 1 year (not too low).
  - Avoid alcohol swabs (or allow for evaporation before vaccinating).
  - Use of swabs is associated with higher incidence of local reactions and they may inactivate live vaccine.

Consider other factors affecting an immunisation course/schedule[^4]

- Premature babies should have vaccinations started two months from actual birth (not expected).
- Unknown immunisation history: should be fully immunised. Under 10 years this should be the full UK primary immunisation schedule.
• Interrupted courses: no need to recommence apart from rabies vaccination.

**Consider other conditions affecting immunisation**[^4]

- Patients on warfarin. Check that INR is within the therapeutic range and proceed, warning of slightly increased risk of haematoma. Use the subcutaneous route where possible.
- Bleeding disorders. Use the subcutaneous route.
- Asplenia. Additional vaccines are recommended because of the increased risk of bacterial infections after splenectomy (H. influenzae type b, meningococcal group C, pneumococcal, influenza).
- HIV-positive individuals can receive some vaccines (oral cholera, diphtheria, Hib, hepatitis A and B, influenza, meningococcal, pertussis, pneumococcal, injectable poliomyelitis, rabies, tetanus, injectable typhoid - all inactivated vaccines) but NOT BCG or yellow fever.[^5] Measles, mumps and rubella (MMR) and varicella-zoster vaccines should be avoided if immunity is significantly impaired (see 'Immunodeficiency and live vaccines', below).

Increasing age is associated with reduced response to vaccines but this should not hinder vaccination in older patients.[^6]

**Additional precautions prior to administration of live vaccines**[^4]

- Live virus vaccines can be inactivated by antibodies and therefore rendered ineffective if given within a few weeks of immunoglobulins or blood transfusions. A delay of three months is recommended for live virus vaccination after administration of HNIG (with the exception of yellow fever and possibly oral polio vaccine for immediate travellers).
- Maternal antibodies can inactivate live virus vaccines if given too soon after birth; MMR is given after the child is 1 year old.
- Live vaccines can be given simultaneously but must be given in different sites. If not given simultaneously, an interval of at least three weeks is recommended.
- BCG can be given simultaneously with live virus vaccines at different sites; otherwise, a three-week interval is recommended.
- A three-week interval is recommended between live virus vaccination and tuberculin testing (risk of false negatives).
- Live vaccines should not be given in pregnancy. However, if the risk of exposure to serious disease is very high, vaccination in the case of polio and yellow fever may be considered despite risk to the fetus.

**Immunodeficiency and live vaccines**

**Live vaccines should not be given to:**[^4]

- Patients actively being treated for malignancy (chemotherapy, generalised radiotherapy).
- Patients within six months of such treatment.
- Transplant patients on immunosuppressive drugs.
- Patients within six months of bone marrow transplant.
- Adults who are within three months of receiving 40 mg/day of prednisolone for more than a week.
- Children who are within three months of receiving certain doses of prednisolone (2 mg/kg/day for one week or 1 mg/kg/day for one month).
Patients being given a combination of steroids and immunosuppressive drugs (the specialist in charge should be consulted).
Patients with impaired cell-mediated immunity or immunodeficiency syndromes such as DiGeorge’s syndrome and severe combined immunodeficiency syndrome.

Side-effects and adverse reactions to vaccines
Vaccines vary in their profile of side-effects. Some are virtually free of side-effects whilst others commonly produce a mild reaction, which with some is a mild form of the disease itself. More serious reactions should be reported to the Commission on Human Medicines. Anaphylaxis can occur and treatment for this should be available wherever vaccinations are being given.

Fever after vaccinations in infants

Vaccine damage payment scheme
Any person over the age of 2 and immunised in the UK or in the Armed Forces before the age of 18, suffering 80% disability as a result of the immunisation, may apply for compensation (within six years of immunisation). [7] 1,430 claims were made between 1996 and 2004 and over 1,000 were successful.

Further reading & references
2. Whooping Cough Vaccination Programme for Pregnant Women; Dept of Health, 2012
4. Immunisation against infectious disease - the Green Book (latest edition); Public Health England
5. Guidelines for immunization of HIV-infected adults; British HIV Association (2008)
6. Vaccination Programmes in Older People - Good Practice Guide; British Geriatrics Society (2011)
7. Vaccine Damage Payment; GOV.UK

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