A vaccine is a preparation of microorganisms (or some part of product of them) that will induce an immune response when injected into a host.

- The practice of vaccination (like many medical practices) predates our understanding of the process.
  - Many cultures afflicted with smallpox adopted the practice of intentionally exposing themselves to material from smallpox lesions.
    - If successful, this led to a mild infection followed by immunity.
    - If unsuccessful, it could lead to severe infection and even death.
  - In the 18th century, Edward Jenner established a safer method for vaccination against smallpox.
    - Jenner observed that persons that had been exposed to cowpox, which causes a mild infection in humans, exhibited immunity to smallpox.
    - Jenner began deliberately exposing patients to material from (what was thought to be) cowpox lesions in the first controlled vaccination trials.
    - Eventually, these efforts led to one of the greatest public health victories in history: complete elimination of smallpox from human populations.

- Vaccines are critically important for control of infectious diseases for which other preventative efforts and/or antimicrobial drugs are inadequate; this is especially the case for infectious diseases caused by viruses.

- The goal of vaccination efforts is to provide herd immunity to a population so that, if an outbreak should occur, an epidemic cannot develop because there are not enough susceptible hosts.

- Vaccines may be of several types, depending on the targeted pathogen.
  - **Inactivated** vaccines are preparations of killed microorganisms; the original Salk polio vaccine was an inactivated vaccine.
  - **Attenuated** vaccines (of which Jenner's vaccine was an example) are viable but so weakened as to be nonpathogenic.
    - An advantage of attenuated vaccines is that they may cause a limited infection that invokes a stronger immune response than an inactivated vaccine preparation.
    - Attenuated vaccines are currently used for polio, measles, rubella and mumps.
  - **Subunit** (component) vaccines employ part of a virus or bacterium.
    - The (highly recommended) vaccine for hepatitis B virus consists of one of the capsid proteins of the virus.
    - Capsular polysaccharides are used as vaccines against infection with Streptococcus pneumoniae (agent of bacterial pneumonia) and Haemophilus influenzae (agent of bacterial meningitis).
  - **Toxoids** are denatured bacterial toxins; toxoids are used in vaccination against tetanus and diphtheria.

- Vaccine administration does carry some degree of risk.
  - In very rare cases, an attenuated vaccine may mutate to a pathogenic form or cause a pathogenic infection in a severely immunocompromised host; this has been recorded for the Sabin polio vaccines.
  - There may be negative reactions in some individuals; this is at the root of concerns about liability for pertussis vaccine.

- Advances in molecular biology are contributing to vaccine development.
  - Attenuated vaccines can be analyzed and manipulated in efforts to avoid the possibility of "reversion" mutants arising.
  - Subunit vaccines can be prepared by genetic engineering; this is already the case for the hepatitis B vaccine, which is synthesized by yeast cells.
DNA vaccines are currently receiving a lot of attention

- The idea here is that the genes will be expressed in cells and invoke a cell-mediated immune response
- Compared with whole and protein vaccines, DNA offers tremendous advantages in cost and stability

- Principle vaccines available for bacterial and viral vaccines, along with recommended vaccination schedules, are outlined in Tortora et al., Tables 18.1, 18.2 and 18.3.

Diagnostic immunology employs the antigen-antibody interaction to identify the presence of antigen or antibody in test materials

- Serology, detection and measurement of specific antibodies in patient serum, is often important in identifying infectious agents, particularly (as in most viral infections) when isolation of the agent is difficult

- Precipitation reactions involve formation of large aggregates of antigen and antibody
  - Such aggregates form only when there is an optimal ratio of antigen:antibody (Tortora et al., Figure 18.2)
  - A variety of techniques, including diffusion of antigen and antibody through agar gels (Tortora et al., Figure 18.3), can be used to visualize the characteristic precipitin

  - Whereas precipitation reactions involve soluble antigen, agglutination reactions involve antigen bound to particles (Tortora et al., Figures 18.4-18.6)

  - Direct agglutination is very useful for detecting the presence of antibodies directed against antigens found on the surface of cells
    - ABO blood typing is a classic example of direct agglutination; in this case, it is the antigen (on erythrocytes) that is being detected
    - Direct agglutination is used to detect serum antibodies specific for bacterial cell surface antigens

  - Soluble antigens can be used in agglutination reactions if they are first bound to particles such as latex spheres or "tanned" erythrocytes

- Fluorescent antibody (FA) techniques use antibodies labeled with fluorescent dyes

  - When the labeled antibody binds to antigen, the fluorescence can be detected in a specially-equipped microscope

  - In direct FA tests, a specific antibody is labeled and used to identify cells exhibiting the antigen of interest (Tortora et al., Figure 18.10a)

  - In indirect FA tests, the fluorescent group is attached to an anti-immunoglobulin, which recognizes specific antibody bound to antigen (Tortora et al., Figure 18.10b)

  - Fluorescence-activated cell sorters (FACS) (Tortora et al. Figure 18.11) are extremely valuable in counting particular classes of cells on the basis of surface antigens

  - In FACS, a mixture of cells (such as total mononuclear cells from blood) is labeled with one or more fluorescent antibodies

  - The instrument detects the fluorescence and counts different cell populations accordingly

- Enzyme-linked immunosorbent assays (ELISA) have found wide applicability in diagnostic immunology

  - ELISAs depend on antibodies labeled with enzyme molecules that catalyze reactions which result in formation of a colored product

  - The basic rule for understanding ELISAs is, "if the labeled antibody is present at the end of the test, the color change is seen and the test is positive"

  - The double antibody sandwich method (Tortora et al., Figure 18.12a) is used for detection of antigen

    - Specific antibody, immobilized to the bottom of a well, binds to the antigen

    - If the antigen is present, a second, enzyme-labeled antibody will bind to it, leading to a positive reaction
The *indirect ELISA* (Tortora et al., Figure 18.12b) is used to detect the presence of specific antibody in test serum.

- In these tests, it is antigen that is bound to the well.
- The presence of antibody bound to the antigen is detected with enzyme-labeled anti-immunoglobulin.
- An indirect ELISA is used to screen donor blood for the presence of antibodies specific for HIV.