

isolated capsular polysaccharide or surface glycoproteins, and purified key recombinant protein antigens. Subunit vaccines are developed using recombinant DNA technology and high resolution biochemical methods. The safest way to produce sufficient quantities of the purified toxins that go into the generation of toxoid vaccines involves cloning the exotoxin genes from pathogenic organisms into easily cultured cells. A number of genes encoding surface antigens from viral, bacterial, and protozoan pathogens have also been successfully cloned into cellular expression systems for use in vaccine development. Advantages of subunit vaccines include; the ability to induce a well defined monofunctional immune response, biologically stable, no requirement to keep chilled and so they are cost effective in tropical countries, the fact that they can be synthesised with high reproducibility, purity and quantity, they prime the immune system to recognize bacterial toxins, and the ability to select specific antigens thus lowering the risk of adverse reactions. One limitation of some subunit vaccines, especially polysaccharide vaccines, is their inability to activate T helper cells. Instead they typically activate B cells in a thymus independent type 2 manner, resulting in immunoglobulin M production but little class switching, no affinity maturation, and little, if any, development of memory cells. This can be avoided in vaccines that conjugate a polysaccharide antigen to a protein carrier, which induces T helper cell responses against both the protein and polysaccharide. Additional disadvantages include difficulties in development. Some bacterial pathogens, including those that cause diphtheria and tetanus, produce exotoxins that account for all of the disease symptoms resulting from infection. Diphtheria and tetanus vaccines have been made by purifying the bacterial exotoxin and then deactivating it with formaldehyde to form a toxoid. Vaccination with the toxoid induces anti-toxoid antibodies capable of binding the toxin and neutralising its effects. Conditions for the production of toxoid vaccines must be carefully controlled to avoid excessive modification of the epitope structure while also accomplishing complete detoxification. Passive immunity can be used to provide temporary protection in unvaccinated individuals exposed to organisms that express these exotoxins. The virulence of some pathogenic bacteria depends on the antipathogenic properties of their hydrophilic polysaccharide capsule. Coating the capsule with antibodies and/or complement greatly increases the ability of macrophages and neutrophils of phagocytose such pathogens, thus providing the rationale for vaccines consisting of purified capsular polysaccharides. The current vaccine for streptococcus pneumoniae consists of 13 antigenically distinct capsular polysaccharides. The vaccine induces formation of opsonizing antibodies.

Recombinant vector vaccines

Recombinant vector vaccines prolong immunogen delivery and encourage cell-mediated responses, whilst avoiding reversion to pathogenic forms. Individual genes that encode key antigens of especially virulent pathogens can be introduced into safe attenuated viruses or bacteria that are used as live carriers. The attenuated organism serves as a vector, replicating within the vaccinated host and expressing the individual gene products it carried from the pathogen. Since most of the genome of the pathogen is missing, reversion potential is eliminated. Vaccinia virus, the attenuated vaccine used to eradicate smallpox has been widely employed as a vector for the design of new vaccines. This large complex virus, with a genome of about 200 genes can be engineered to carry several dozen foreign genes without impairing its capacity to infect host cells and replicate. The gene that encodes the desired antigen is inserted into a plasmid vector adjacent to a vaccinia promoter and flanked on