ABSTRACT
A vaccine is a biological preparation that helps protect the body against a particular disease. Vaccines are intended to prime the body so that it will recognize a harmful virus or a bacterium. There are several different types of vaccines. Each type has been developed to combat specific challenges presented by the virus or bacteria it was designed to protect against. There are two types of developed vaccine polysaccharide and conjugate vaccines. Thus this review discusses advantages of conjugate vaccine over polysaccharide vaccine. As vaccine research and development has continued to advance, though, more conjugate vaccines have been developed.

KEYWORDS: Vaccine, Polysaccharide, Conjugate, Toxoids.

INTRODUCTION
Vaccines are biological preparations that improve immunity to particular diseases. A vaccine contains a disease-causing microorganism and is often made from weakened or killed forms of the microbe, its toxins or one of its surface proteins.

The disease-causing agent stimulates the body's immune system to recognize the agent as foreign, destroy it, and keep a record of it, so that the immune system can more easily recognize and destroy any of these microorganisms that it later encounters.

There are several types of vaccines as Killed, Attenuated, Toxoid, Subunit, and Conjugate. There are two basic types of vaccines: live attenuated and inactivated [1].
Live attenuated vaccines are produced by modifying a disease-producing virus or bacterium. These wild viruses or bacteria are attenuated, or weakened, usually by repeated culturing. Immune response achieved when, live attenuated virus or bacteria grows (replicate) in the vaccinated person. A very small dose of virus or bacteria is administered, which replicates in the body and creates enough of the organism to stimulate an immune response.

The majority of live attenuated vaccines available in the United States contain live viruses. These vaccine have severe adverse reactions possible. i.e Interference with circulating antibody, it must handled and stored carefully.

Inactivated vaccines are produced by growing the bacterium or virus in culture media, then inactivating it with heat or chemicals (usually formalin). Here, the main virulence part of bacteria or virus also used (fractions, toxoid, subunit) for vaccine production purpose. In the case of fractional vaccines, the organism is further treated to purify only those components to be included in the vaccine (e.g., the polysaccharide capsule of bacteria, Carrier proteins, DNA etc).

Inactivated vaccines are not alive and cannot replicate. The entire dose of antigen is administered in the injection. These vaccines cannot cause disease from infection, even in an immunodeficient person. Inactivated antigens are less affected by circulating antibody than are live agents, so they may be given when antibody is present in the blood. It requires multiple doses for better immune response[2].

**Table No.1. Types of Vaccines with examples**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Examples</th>
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<tbody>
<tr>
<td><strong>Immunoglobulin (IG)</strong></td>
<td>Varicella Zoster IG</td>
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<tr>
<td></td>
<td>Human Normal IG</td>
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<tr>
<td></td>
<td>Hep B IG, Tetanus IG</td>
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<tr>
<td><strong>Anti-toxins</strong></td>
<td>Diphtheria anti-toxin</td>
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<tr>
<td></td>
<td>Botulinum anti-toxin</td>
</tr>
<tr>
<td><strong>Inactivated/subunit vaccine</strong></td>
<td>Acellular pertussis, Diphtheria, tetanus, rabies, anthrax, <em>Haemophilus influenzae</em> b</td>
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<tr>
<td></td>
<td>Hepatitis A vaccine (HAV)</td>
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<tr>
<td></td>
<td>Hepatitis B vaccine (HBV), Meningococcal C</td>
</tr>
<tr>
<td><strong>Live attenuated</strong></td>
<td>Measles, mumps and rubella (MMR), Yellow fever, oral polio, BCG.</td>
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The effectiveness of these vaccines is increased by giving them in Adjuvant. Adjuvant slow antigen release for a more sustained immune stimulation. Inactivated Vaccine having drawbacks towards antigens and the immune system.

To overcome the specific challenges presented in the virus or bacteria there is need for development of vaccine process.

Developed Vaccines to combat bacteria with polysaccharide capsules fall into two main types:
a) Plain polysaccharide Vaccine-
b) Conjugate polysaccharide Vaccine-

1.1. POLYSACCHARIDE VACCINE
Polysaccharide vaccines are composed of unique type of inactivated long chains of sugar molecules that make up the surface capsule of certain bacteria. Polysaccharide may used for vaccine in the form of capsular polysaccharide.

Pure polysaccharide vaccines are available for three diseases: pneumococcal disease, meningococcal disease, and Salmonella Typhi.

Polysaccharides in some bacteria help to dissemble the protein that would be detected by body and destroyed it, so plain polysaccharide vaccines are developed to increase immune response against the polysaccharide capsule.

The immune response to a pure polysaccharide vaccine is typically T-cell independent, which means that these vaccines are able to stimulate B cells without the assistance of T-helper cells. T-cell–independent antigens, including polysaccharide vaccines, are not consistently immunogenic in children younger than 2 years of age. Young children do not respond consistently to polysaccharide antigens, probably because of immaturity of the immune system.

Repeated doses of most inactivated protein vaccines cause the antibody titer to go progressively higher, or “boost.” This does not occur with polysaccharide antigens; repeat doses of polysaccharide vaccines usually do not cause a booster response. Antibody induced with polysaccharide vaccines has less functional activity than that induced by protein
antigens. This is because the predominant antibody produced in response to most polysaccharide vaccines is IgM, and little IgG is produced [5].

Plain polysaccharide vaccines have been effective in helping protect many adults against the invasive and potentially life-threatening illness, but they have some limitations, including:
- Little or only short-lived impact on carriage of a bacteria.
- People can carry bacteria for months or years without symptoms, but they can still spread it to others.
- Close contact with a carrier can increase the risk of acquiring the bacteria by 800 fold.
- Decreased immune response after repeated doses

- In the case of meningococcal disease, authorities recommend that people who have higher risks of infection receive a vaccination every few years
- People at increased risk include those who travel to areas known for meningococcal outbreaks

- Limited ability to protect children less than 2 years of age
- Infants and toddlers are particularly susceptible to contracting an illness because their immune systems are still developing

**1.2. CONJUGATE VACCINE**

In the late 1980s, it was discovered that the problems noted above could be overcome through a process called conjugation.

A **conjugate vaccine** is created by covalently attaching a polysaccharide (antigen) to a carrier protein (of same microorganism). This technique for the creation of an effective immunogen is most often applied to bacterial polysaccharides for the prevention of invasive bacterial disease. Conjugate vaccines based on proteins that are easily recognizable to the immune system are linked to the molecules that form the outer coat of disease-causing bacteria to promote an immune response. Conjugate vaccines are designed primarily for very young children because their immune systems cannot recognize the outer coats of certain bacteria.
Polysaccharide coatings disguise a bacterium’s antigens so that the immature immune systems of infants and younger children can’t recognize or respond to them. Conjugate vaccines, a special type of subunit vaccine, get around this problem. When making a conjugate vaccine, scientists link antigens or toxoids from a microbe that an infant’s immune system can recognize to the polysaccharides. The linkage helps the immature immune system react to polysaccharide coatings and defend against the disease-causing bacterium [6].

Conjugation is the process of attaching (linking) the polysaccharide antigen to a protein carrier (e.g. diphtheria or tetanus) that the infant’s immune system already recognises in order to provoke an immune response

![Fig no 1. Conjugation Process](image)

Conjugate vaccines may have several advantages, including:

1] Ongoing protection against a bacteria  
- Conjugate vaccines may provide longer-lasting protection than plain polysaccharide vaccines  
- Conjugate vaccines may be more likely to maintain a consistent level of protection from repeated doses

2] Reduction in carriage  
- May be able to reduce the number of people who carry the bacteria in their nose or throat can decrease the number of people who spread a disease
- By reducing the number of people carrying bacteria, fewer people will come in contact and potentially contract an illness, a concept known as herd immunity

3) May offer protective immune response in infants
- By protecting infants, conjugate vaccines may fill a significant unmet need when used to combat certain illnesses.

4) Potential lack of hypo responsiveness
- Conjugate vaccines are less likely to induce a diminished immune response when repeated doses are administered

Although the advantages of conjugate vaccines, the complex process involved in conjugation of polysaccharides has limited the number of commercially available vaccines that employ conjugate technology.

The steps in the production of conjugate vaccines can be summarized as follows:
- Protein production: fermentation of host organism, collect, wash, homogenize, recover and purify protein
- Polysaccharide production: fermentation of donor organism, disrupt cells, purify Polysaccharide, trim by hydrolysis (acid)
- Derivativization: make both components reactive
- Conjugation: React components together
- Purification: Remove unwanted compounds
- Finish and fill: Concentrate to final strength, dialyze into appropriate solute, sterile fill as liquid or lyophilize

Each of these simple activities does require a number of very precise intermediate steps [8].

The first conjugated polysaccharide vaccine was for Hib. A conjugate vaccine for pneumococcal disease was licensed in 2000. A meningococcal conjugate vaccine was licensed in 2005. There are a limited number of polysaccharide protein conjugate vaccines currently in use. Examples of successful polysaccharide protein conjugate vaccines are listed here.
### Table No 2. Examples of Polysaccharide Conjugate Vaccine

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Description</th>
<th>Impact</th>
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<tbody>
<tr>
<td><em>Haemophilus influenzae</em> B (Hib; bacterial meningitis and pneumonia)</td>
<td>Hib is a major cause of meningitis in children &lt;5 years old as well as a cause of pneumonia. The vaccines consist of polysaccharide linked to the tetanus or diphtheria toxoid proteins as carriers. The first Hib vaccine was approved by the FDA in 1985.</td>
<td>As of 2009, the World Health Organization (WHO) estimates that global vaccination of children under 5 for Hib is 38%. Widespread use of the vaccine in the U.S. and western Europe has nearly eliminated Hib as a public health problem in infants.</td>
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<tr>
<td><em>Neissera meningitides</em> (bacterial meningitis)</td>
<td>Two vaccines are currently available for the prevention of meningitis caused by <em>N. meningitides</em>; MPSV4 has been available in the U.S. since the 1970s and MCV4 was FDA approved in 2005. The polysaccharides in MCV4 are conjugated to the diphtheria toxoid protein.</td>
<td>The <em>N. meningitides</em> vaccines are primarily used in high risk populations in the developed world. A new meningitis vaccine developed jointly by WHO and PATH that is specifically designed to target meningitis in the 25 countries of the epidemic “Meningitis Belt” of sub-Saharan Africa was rolled out in 2010. The potential for impact of an <em>N. meningitides</em> vaccine in the developing world will largely be determined by the outcomes of this rollout.</td>
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<tr>
<td><em>Streptococcus pneumoniae</em> (bacterial pneumonia)</td>
<td>There are current three vaccines in use for the prevention of <em>S. pneumoniae</em>, consisting of 10 and 23 polysaccharides conjugated to <em>H. influenzae</em> or diphtheria carrier proteins.</td>
<td><em>S. pneumoniae</em> vaccines are primarily used in high risk groups in developed countries such as the elderly. Because so many polysaccharides must be included to achieve immunity, these vaccines are too expensive for use in the developing world. The introduction of a US$1.5 billion Advance Market Commitment in 2009 aims to bring down the cost of pneumonia vaccines for use in the developing world which is likely to drive impact of these vaccines.</td>
</tr>
</tbody>
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### REFERENCES


8. Carla C. A. M. Peeters¹, Patrick R. Lagerman¹, Odo de Weers¹, Lukas A. Oomen¹ Preparation of Polysaccharide-Conjugate Vaccines.