NOVARTIS

Vaccine Development: Conjugate vs. Polysaccharide

Protecting the Body from Disease

Vaccines are one of the most significant public health interventions ever implemented, sparing millions of people from illness and death caused by infectious diseases. Use of currently available vaccines has been calculated to save more than 8 million lives annually, translating to one person saved every four seconds[1].

A vaccine is a biological preparation that helps protect the body against a particular disease. Vaccines are designed to prime the body so that it will recognize a harmful virus or a bacterium, destroy it and remember it, so that the body's immune system can more easily recognize and destroy the virus or bacteria if it encounters it again[2a].

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.

Vaccines developed to combat bacteria with polysaccharide capsules fall into two main categories:

- Plain polysaccharide
- Conjugate polysaccharide

Building Bacteria-Targeting Vaccines

Plain polysaccharide vaccines have been used for decades to help combat a number of diseases, including meningococcal disease, pneumococcal bacteria and Hib. Polysaccharides in some bacteria help cloak the protein that would normally help the body detect and destroy it, so plain polysaccharide vaccines were developed to train the immune system to build an immune response to the polysaccharide capsule.

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[3]

    - People can carry bacteria for months or years without symptoms, but they can still spread it to others[4, 5]
    - Close contact with a carrier can increase the risk of acquiring the bacteria by 800 fold[6a]

- Decreased immune response after repeated doses[7]
    - 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[8]

- Limited ability to protect children under 2 years of age
    - Infants and toddlers are particularly susceptible to contracting an illness because their immune systems are still developing[6b]

The Advantages of Conjugate Vaccines

Conjugate polysaccharide vaccines – or conjugate vaccines – are developed by attaching a polysaccharide antigen to a carrier protein, which helps the body recognize the antigen as a foreign substance that must be destroyed. This method enhances the body's immune response to a vaccine[9a].

Conjugate vaccines have several advantages, including:

- Ongoing protection against a bacteria
    - Conjugate vaccines provide longer-lasting protection than plain polysaccharide vaccines[9a]
    - Conjugate vaccines also are more likely to maintain a consistent level of protection from repeated doses[9b]

- Reduction in carriage
    - Reduction in the number of people who carry the bacteria in their nose or throat can decrease the number of people who spread a disease[9c]
    - 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[9c]

- Ability to offer protective immune response in infants[9a]
    - By protecting infants, conjugate vaccines may fill a significant unmet need when used to combat certain illnesses

- Lack of hyporesponsiveness
    - Conjugate vaccines are less likely to induce a diminished immune response when repeated doses are administered[9b]

Despite 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. As vaccine research and development has continued to advance, though, more conjugate vaccines have been developed.

# # #

References

1. Lattanzi M, Rappuoli R. The grand challenge for the future. Vaccines for poverty-related diseases from bench to field. In: Kaufmann SHE, Lambert P, eds. Basel: Birkhauser; 2005:77-98.
2. National Partnership for Immunization (NPI*).* Reference Guide on Vaccine and Vaccine Safety: Vaccines and How They Work. Available at: http://www2.cdc.gov/nip/isd/immtoolkit/content/products/NPIGuide.pdf. Accessed on January 26, 2010.
3. Trotter, C. and Maiden, M. (2009). Meningococcal vaccines and herd immunity: Lessons learned from serogroup C conjugate vaccination programs. *Expert Review of Vaccines* 2009:8(7), 851-861. Available at: http://www.medscape.com/viewarticle/706711_3. Accessed on January 26, 2010.
4. World Health Organization. Meningococcal Disease. Available at: http://www.who.int/csr/disease/meningococcal/en/index.html. Accessed on January 26, 2010.
5. Wilder-Smith, A. et al. (2009). Meningococcal vaccines: A neglected topic in travel medicine?, *Expert Review of Vaccines 2009: 8(*10), 1343-1350. Available at: http://www.medscape.com/viewarticle/710606. Accessed on January 26, 2010.
6. Schaffner, W. et al. The Changing Epidemiology of Meningococcal Disease Among US Children, Adolescents, and Young Adults. National Foundation for Infectious Diseases. November 2004.Available at: http://www.nfid.org/pdf/meningitis/FINALChanging_Epidemiology_of_Meningococcal_Disease.pdf. Accessed on January 26, 2010.
7. Centers for Disease Control and Prevention. Principles of Vaccination. (The Pink Book: Course Textbook). 10th Edition, 2nd printing. February 2008 update. Available at: http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/prinvac.pdf. Accessed on January 26, 2010.
8. World Health Organization. Meningococcal Meningitis Fact Sheet. Available at: http://www.who.int/mediacentre/factsheets/fs141/en/index.html. Accessed on January 26, 2010.
9. Centers for Disease Control and Prevention. Prevention and Control of Meningococcal Disease – Recommendations of the Advisory Committee on Immunization Practices. MMWR 2005; 54 (RR07): 1-21. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5407a1.htm. Accessed on January 26, 2010.