Module 5
Vaccine Immune Response

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1. Competency
Explain how vaccines work using basic knowledge of the immune system.

2. Learning Objectives
By the end of this module you will be able to:

- Differentiate between the primary and memory immune response to a vaccine.
- Explain why some vaccines induce a memory response while others do not.
- Name some host and vaccine-related factors that affect the immune response to vaccines.
- Respond to the concern that giving too many vaccines will overload the immune system.
- Discuss the pros and cons of immunity gained through immunization as opposed to wild type infection.
- Identify the key differences in the immune response to purified polysaccharide versus polysaccharide protein conjugate vaccines.

3. Introduction
Vaccines are highly regulated, complex biologic products designed to induce a protective immune response both effectively and safely.

4. Vaccine Immune Response
Vaccines interact with the immune system and produce an immune response similar to that produced by the natural infection, but they do not subject the recipient to the disease and its potential complications. Vaccines produce immunologic memory similar to that acquired by having the natural disease.

The antigen is the part of the vaccine that stimulates the immune response. Deciding on which antigens to include in the vaccine takes years of laboratory work. Antigens are also the basis for classification of vaccine type: Replicating Vaccines (live attenuated); Non-replicating Vaccines (inactivated/subunit); Conjugate and Polysaccharide Vaccines (See Table 1).

<table>
<thead>
<tr>
<th>Table 1: Active Immunizing Agents</th>
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<tbody>
<tr>
<td><strong>Type of Vaccine</strong></td>
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<tr>
<td>Replicating Vaccines</td>
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<tr>
<td>Non-Replicating Vaccines</td>
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<tr>
<td>Subunit</td>
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<td>Polysaccharide</td>
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<td>Conjugate</td>
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</table>
The immune or antibody response to replicating vaccines (live attenuated) is different than the response to non-replicating vaccines (inactivated/subunit).

4.1 Antibody Response to a REPLICATING Vaccine

Live attenuated vaccines (replicating vaccines) are produced by modifying a disease-producing “wild” virus or bacterium in a laboratory. The resulting vaccine organism retains the ability to replicate (grow) and produce immunity. The immune response to a live attenuated vaccine is virtually identical to that produced by a natural infection. Replicating vaccines will need fewer doses to create lasting memory.

Figure 1: Immune Response to Replicating Vaccines
4.2 Antibody Response to a NON-REPLICATING Vaccine

Inactivated/subunit vaccines (non-replicating vaccines) will need more doses to build an adequate and lasting immune response.

- Primary Immune Response
  - Antibody level following the first exposure to an antigen is primarily IgM
  - Response is of brief duration and low intensity

- Secondary/Memory Immune Response
  - Antibody level following the second and subsequent immunogenic challenges is primarily IgG
  - Memory cells (antigen sensitive cells) are already present at time of repeat exposure and carry the memory of how to make the specific antibodies.

**Figure 2: Immune Response to Non-Replicating Vaccines**

4.3 Antibody Response to Polysaccharide and Conjugate Vaccines

- Polysaccharide Vaccines: T-Cell Independent Antigens

T-cell independent antigens stimulate B cells without the help of T cells. The antibody made in response to these antigens is mostly of the IgM class and immunologic memory is not produced. Polysaccharide vaccines are composed of long chains of sugar molecules that make up the surface capsule of encapsulated bacteria. Polysaccharide vaccines produce T-Cell independent response, and are not immunogenic in young children (See Figure 3).
• Conjugate Vaccines: T-Cell Dependent Antigens
Conjugate vaccines link a protein to the polysaccharide antigens. Conjugate vaccines produce T-Cell dependent response providing protection in young children. T-Cell dependent antigens stimulate the interaction of T and B cells to generate the production of antibodies. The antibodies produced include IgG, providing longer protection and immunologic memory (See Figure 4).

5. Factors to Consider in the Vaccine Immune Response
The vaccine immune response is affected by vaccine related factors and host related factors.

5.1 Vaccine Related Factors
• Nature of the Antigen
  Live, inactivated/subunit, conjugate and polysaccharide vaccines each generate immune responses to a different degree and duration.

• Dose of the Antigen
  A certain threshold dose of antigen is required to elicit an immune response.

• Presence of Vaccine Adjuvants
  Live, inactivated, and subunit vaccines each generate immune responses to a different degree and duration.

5.2 Host Related Factors
• Circulating Antibodies
  Antibody from any source (e.g. maternal, transfusion) can interfere with the live vaccine replication. For example: Potential antibody interference is the reason
to defer MMR vaccine until maternal antibodies have declined. Immune globulins (Ig) may interfere with live vaccine replications.

- Age of the Client
  - Protection should proceed the age of greatest risk. For example: Human Papillomavirus vaccine is ideally given before an individual is sexually active.
  - Children <2 years do not create a protective immune response to T cell independent antigens such as polysaccharides. For example: Polysaccharide vaccines are not immunogenic in children <2 years of age. Conjugate vaccines will produce an immune response in young children.

6. Vaccine Antigen Load
This section reviews the capacity of the immune system, vaccine antigen load and evidenced based articles.

6.1 Capacity of the Immune System
The immune system has the capacity to respond to extremely large numbers of antigens: There are \(10^9\) to \(10^{11}\) different antibody specificities 2 billion T helper cells are replenished each day. Each infant has the theoretical capacity to respond to about 10,000 vaccines at any one time. Using this estimate, if 11 vaccines were given to an infant at one time, then about 0.1% of the immune system is needed to respond.

6.2 Vaccine Antigen Load
Even though the number of vaccines given to a child has increased over the past 45 years, the number of antigens has decreased. There are fewer antigens per vaccine because of improved purification processes and knowledge of antigens needed to induce protective immunity (See Table 2).

| Table 2: Vaccine Antigen Load |
|-------------------------------|----------|---------|---------|
| Vaccines                      | 1960’s   | 1980’s  | 2005    |
| Small Pox                     | ~ 200    | n/a     | n/a     |
| Diphtheria                    | 1        | 1       | 1       |
| Tetanus toxoid                | 1        | 1       | 1       |
| Polio                         | 15       | 15      | 15      |
| Measles                       | 10       | 10      |         |
| Mumps                         | 9        | 9       |         |
| Rubella                       | 5        | 5       |         |
| Varicella                     |          |         |         |
| Hepatitis B                   |          |         |         |
| Pertussis                     | ~3000(whole) | ~3000(whole) | 5 (acell.) |
| Pneumococcus (conj.)          | 8        | 8       |         |
| H. Influenzae (Hib)           | 2        | 2       |         |
| TOTALS                        | ~3217    | ~3041   | 126     |
6.3 Evidence Based Articles
http://pediatrics.aappublications.org/cgi/reprint/109/1/124

7. Immunity: Vaccine versus Disease
Natural immunity, both innate and adaptive, are good shields but vaccines tip the scales further by priming the immune system for a much more rapid response, thus preventing a great deal of damage and destruction. The following compares and contrasts the benefits of natural immunity versus vaccine immunity.

7.1 Natural Immunity
- Natural immunity resulting from disease is not always life long. Example: Hib disease (In infancy T-Cell independent response = no immune memory).
- It can take days to weeks to create immunity which is too late to prevent disease complications.
- Being ill from a vaccine preventable disease may make a person more susceptible to other infections. Examples:
  - Influenza disease may result in the person being more susceptible to pneumonia.
  - Varicella (chicken pox) disease increases the risk of severe invasive group A streptococcal infections.

7.2 Vaccine Immunity
- Vaccine immunity may be better after vaccine than with natural infection. Example: Hib vaccine (T cell dependent response = immune memory)
- Vaccine immunity offers protection without the risk of complications from the disease.
- One study found that children who received immunizations in the first three months of life had fewer infections from vaccine-related and from unrelated pathogens than did the non-vaccinated group.

8. Summary
Vaccines interact with the immune system and produce an immune response similar to that produced by the natural infection, but they do not subject the recipient to the disease and its potential complications.

9. Required Reading
N.S. Department of Health and Wellness Chapter 2 – General Principles of Immunology and Immunization, N.S. Immunization Manual
http://www.gov.ns.ca/hpp/cdpc/info-for-professionals.asp
http://pediatrics.aappublications.org/cgi/reprint/109/1/124

10. References


Centers for Disease Control and Prevention (2007) Principles of vaccination Epidemiology and Prevention of Vaccine-Preventable Diseases (10th ed.).


11. Quiz

Question #1
The IgG antibodies created by a MMR vaccine rise slowly, do not wane and remain high for a long period of time?

A. True
B. False

Question #2
An adult tetanus booster vaccination is an example of a primary immune response?

A. True
B. False

Question #3
Conjugate vaccines fool the immune system in creating a T-Cell dependent immune response therefore longer immunity?
A. True
B. False

**Question #4**
Which one of the following is NOT a Vaccine Related Factor that affects the immune response to vaccines?

A. Nature of antigen
B. Circulating antibodies
C. Presence of adjuvants
D. Dose of antigen

**Question #5**
Because there are more vaccines given to children now than 45 years ago, the number of antigens a child receives in childhood is greater?

A. True
B. False

**Question #6**
Being ill from a vaccine-preventable disease makes one more susceptible to other diseases?

A. True
B. False
12. Quiz Answers

Question #1
Answer: True
IgG antibodies created after a live vaccine do not decrease and remain high in the bloodstream for a long time.

Question #2
Answer: False
A vaccine booster dose is an example of a secondary/memory immune response.

Question #3
Answer: True
By linking (conjugating) a polysaccharide antigen to a protein, the immune response changes from a T-Cell independent (primarily IgM) to a longer lasting T-Cell dependent immune response (primarily IgG).

Question #4
Answer: B
Circulating antibodies is a Host Related Factor that affects the immune response to vaccines.

Question #5
Answer: False
The number of vaccines given today is greater but the number of antigens is less. There are fewer antigens per vaccine because of the improved purification process and the increased scientific knowledge of the number of antigens needed to induce protective immunity.

Question #6
Answer: True
Being ill from a vaccine-preventable disease makes one more susceptible to other diseases. For example, Influenza disease may result in the person being more susceptible to pneumonia.