13.3B: Artificially Acquired Immunity

Skills to Develop

1. Define and give at least one example of each of the following types of immunity:
   a. artificially acquired active immunity
   b. artificially acquired passive immunity

2. List 3 different forms of antigen that may be used for artificially acquired active immunity and state 2 common examples of each.

3. State what DTaP stands for and what specifically is being injected with the DTaP vaccine.

4. Briefly compare active immunization with passive immunization in terms of tetanus prophylaxis.

5. Define adjuvant.

6. In artificially acquired immunity, active immunization is preferred over passive immunization. Explain why.

7. Describe what is meant by herd immunity (community immunity).

Active Artificially Acquired Immunity

Active artificially acquired immunity refers to any immunization with an antigen. By giving a safe form of the antigen artificially, the body will produce its own antibodies and, more importantly, develop circulating, long-lived B-memory cells with high affinity B-cell receptors on their surface. If at a later date the body is again exposed to that same antigen, the memory cells will cause immediate and rapid production of the appropriate antibodies for protection. With artificially acquired active immunity, one is immunized with one or more of the following:
Attenuated microbes

Attenuated microbes are living, non-virulent strains of a microbe. Viruses are attenuated by growing them in non-human cells until they mutate and adapt to the non-human host. In the process, they lose virulence for humans. Viruses can also be attenuated using recombinant DNA techniques to either mutate or delete virulence genes in the viral genome.

Attenuated viral vaccines tend to be immunologically quite effective since the viruses can multiply slowly in the body, thus increasing the amount and persistence of the antigen for a greater antibody response. In addition, attenuated viruses enter the cytosol of cells and peptides from viral antigens can be presented by MHC-I molecules to activate naive T8-lymphocytes and stimulate the production of cytotoxic T-lymphocytes (CTLs). Living attenuated microbes can, however, sometimes be potentially dangerous to highly immunosuppressed individuals in whom they may cause opportunistic infections.

Examples of vaccines that contain attenuated microbes include:

- The MMR vaccine containing attenuated measles, mumps, and rubella viruses;
- The MMRV vaccine containing attenuated measles, mumps, rubella viruses and varicella zoster (chickenpox) viruses;
- The TOPV or trivalent oral polio vaccine containing attenuated poliomyelitis viruses types 1, 2, and 3;
- The yellow fever vaccine containing attenuated yellow fever viruses;
- The Var or varicella zoster virus vaccine containing attenuated varicella zoster viruses.

The body responds by producing antibodies that block viral adsorption to host cells.

Killed organisms, fragmented microorganisms, or antigens produced by recombinant DNA technology

Examples of vaccines containing killed or inactivated microbes include:

- The IPV or inactivated poliomyelitis vaccine containing inactivated poliomyelitis viruses types 1, 2, and 3;
- The rabies vaccines containing whole, killed rabies viruses;
- The influenza vaccines consist of inactivated influenza viruses, either whole or broken down;
- The hepatitis A vaccine containing inactivated hepatitis A virus;
- RV1, an attenuated strain of a human rotavirus. Rotaviruses are the most common cause of gastroenteritis in children.

Examples of vaccines containing fragments of microorganisms include the immunizations for:

- Meningococcal meningitis; contains capsular polysaccharide from 4 strains of Neisseria meningitidis;
• Pneumococcal pneumonia; PCV13 containing capsular material from the 13 most serious strains of *Streptococcus pneumoniae* in children conjugated to diphtheria toxoid protein; PCV 23 containing capsular material from the 23 most serious strains of *S. pneumoniae* in adults conjugated to diphtheria toxoid protein;

• *Hemophilus influenzae* type b containing capsular polysaccharide from *H. influenzae* type B conjugated to protein (either diphtheria toxoid or an outer membrane protein from *Neisseria meningitidis*).

These vaccines contain polysaccharide capsular material from the bacteria, usually conjugated to protein for greater immunogenicity. The body responds by producing opsonizing antibodies against the capsule.

While the B-cell receptors of B-lymphocytes can recognize epitopes on polysaccharides, T4-lymphocytes can only recognize peptide epitopes bound to MHC-II molecules. The protein conjugate added to the polysaccharide in the vaccine is degraded into peptides and bound to MHC-II molecules by APCs. They then present the peptide to the TCRs on T4-lymphocytes for their activation. In this way the cytokines produced by the activated T4-lymphocytes become available for use by the B-lymphocytes sensitized to the polysaccharide component of the vaccine.

c. Examples of vaccines produced by recombinant DNA technology include:

• The hepatitis B vaccine, the first human vaccine produced by recombinant DNA technology, contains hepatitis B virus surface antigen (HBsAG);

• The acellular pertussis part of the diphtheria, tetanus, and acellular pertussis vaccine (DTaP) containing diphtheria toxoid, tetanus toxoid, and antigens from the whooping cough bacterium *Bordetella pertussis* (Acellular pertussis vaccines contain inactivated pertussis toxin (PT) and may contain one or more other bacterial components (e.g., filamentous hemagglutinin [FHA], an outer-membrane protein; pertactin [Pn], and fimbriae [Fim] types 2 and 3);

• The vaccine against Lyme disease;

• Gardasil, a vaccine against human papilloma virus (HPV) types 6, 11 that cause about 90% of genital warts, and types 16, and 18 responsible for around 70% of cervical cancer in the US; and Cervarix, a vaccine against HPV types 16 and 18. Both contain recombinant L1 capsid protein from the different strains of HPV;

• RV5, an oral vaccine against human rotavirus gastroenteritis. Capsid proteins from human rotaviruses have been expressed on the surface of harmless non-human rotavirus strains.

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**Toxoid**

A toxoid is an exotoxin treated so as to be non-poisonous but still immunogenic. Examples of vaccines containing toxoids include the diphtheria and tetanus components of the DTaP and Td vaccines. The body responds by making antibodies capable of neutralizing the exotoxin. The antigen may be adsorbed to an adjuvant, a substance such as aluminum hydroxide or aluminum phosphate that is not immunogenic but enhances the immunogenicity of antigens.

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Updated: Thu, 17 Oct 2019 04:10:49 GMT

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Routine immunization practices protect more than just the individuals receiving the vaccine. When a critical portion of a community becomes immunized against a particular infectious disease, most members of the community - including those who were not immunized - are protected against that disease because there is little opportunity for an outbreak. This is known as herd immunity or community immunity.

Passive Artificially Acquired Immunity

Passive artificially acquired immunity refers to the injection of antibody-containing serum, or immune globulin (IG), from another person or animal. Since the body is not making its own antibodies and memory cells are not produced, passive artificially acquired immunity is short lived and offers only mediate, short term protection. Also, the injection of serum during passive immunization carries a greater risk of allergic reactions than the injection of antigens during active immunization. These allergic reactions are referred to as serum sickness and will be discussed later under hypersensitivities.

Examples include:

- The use of pooled adult human immune globulin (IG) to prevent hepatitis A and measles and to prevent infections in people with certain immunodeficiency diseases;
- Human HBIG to prevent hepatitis B in those not actively immunized with the HepB vaccine;
- Human TIG to prevent tetanus in those not actively immunized with the DTP, DTaP, or Td vaccines;
- RhOGAM to prevent Rh hemolytic disease of newborns;
- VZIG to prevent varicella;
- CMV-IGIV to prevent cytomegalovirus infections in highly immunosuppressed individuals;
- RIG to prevent rabies, given concurrently with active immunization with the rabies vaccine;
- The antisera used for botulism; and
- IVIG (intravenous immune globulin), now being used to reduce infections in people with certain immunosuppressive diseases such as primary immunodeficiency syndrome and chronic lymphocytic leukemia as well as to treat certain autoimmune diseases such as immune thrombocytopenia purpura (ITP) and Kawasaki disease.

Tetanus provides a nice example of how active immunization (DTaP) and passive immunization (TIG) may be used in preventing a disease (Table 13.3B.1).

Table 13.3B.1: Tetanus prophylaxis in Routine Wound Management

<table>
<thead>
<tr>
<th>History of tetanus toxoid doses</th>
<th>Clean, minor wound</th>
<th>All other wounds (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Td (2)</td>
<td>Td</td>
</tr>
<tr>
<td>Unknown or &lt; 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>TIG (3)</td>
<td>TIG</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Three or more</td>
<td>No (4)</td>
<td>No (5)</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
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(1) Such as, but not limited to, wounds contaminated with dirt, feces, soil, saliva, etc.: puncture wounds, avulsions, and wounds resulting from missles, crushing, burns, and frostbite.

(2) Tetanus toxoid, diphtheria toxoid (active immunization).

(3) Tetanus Immune Globulin (passive immunization).

(4) Yes, if more than 10 years since last dose.

(5) Yes, if more than 5 years since last dose. (More frequent boosters are not needed and can accentuate side effects.)

There is also some early evidence that immunization may be of value in the treatment of some infections as well as in their prevention, possibly by supercharging the immune system of those already infected. Vaccine therapies in various stages of testing include those against diseases such as herpes, leprosy, tuberculosis, and hepatitis B.

Exercise: Think-Pair-Share Questions

A patient with a deep puncture wound who has never received a DTaP vaccination is given both Td and TIG. Another patient with an identical wound and who had 4 DTaP vaccinations as a child and a Td booster 3 years ago is given nothing. Discuss the reasoning behind this.

Summary

Active artificially acquired immunity refers to any immunization with an antigen. During artificially acquired active immunity, one is immunized with one or more of the following: attenuated microbes, killed organisms, fragmented microorganisms, or antigens produced by recombinant DNA technology, or toxoids. Passive artificially acquired immunity refers to the injection of antibody-containing serum, or immune globulin (IG), from another person or animal. Since the body is not making its own antibodies and memory cells are not produced, passive artificially acquired immunity is short lived and offers only immediate, short term protection. When a critical portion of a community becomes immunized against a particular infectious disease, most members of the community - including those who were not immunized - are protected against that disease because there is little opportunity for an outbreak. This is known as herd immunity or community immunity.

Contributors

- Dr. Gary Kaiser (COMMUNITY COLLEGE OF BALTIMORE COUNTY, CATONSVILLE CAMPUS)