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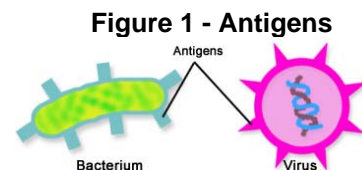
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1.0 THE IMMUNE SYSTEM

1.1 Introduction

The body is protected from infectious agents and other harmful substances by a variety of cells and molecules that make up the immune system. Immunity is the ability of the human body to tolerate the presence of material indigenous to the body (self), and to eliminate foreign (non-self) material.

Foreign substances such as viruses, bacteria, toxins, and parasites are surrounded by *antigens* that, when introduced into the body, are capable of inducing a response by the immune system. This discriminatory ability provides protection from infectious disease, since most agents or associated toxins are identified as foreign by the immune system.



1.2 Cells of the Immune System

The immune system depends upon the activities of three categories of white blood cells (WBCs) that are derived from bone marrow:

- Phagocytic cells:
Macrophages and dendritic cells are phagocytic cells that reside in the blood and tissues waiting to engulf foreign substances.
- T cells:
After leaving the bone marrow, some WBCs reach the thymus gland where they differentiate and become thymus-derived lymphocytes or T cells.
- B cells:
WBCs that do not reach the thymus gland become B lymphocytes or B cells

1.3 Lymphatic system

Some of the WBCs migrate to guard peripheral tissues, some reside within the tissues, and others circulate in the blood stream and in a specialized system of vessels and nodules in the lymphatic system.

The lymphatic system drains extracellular fluid and frees cells from tissues. The extracellular fluid and cells are transported through the body via the lymphatic vessels as lymph, and eventually emptied back into the blood system.

The lymphatic vessels closely parallel the body's veins and arteries. Lymph nodes are found throughout the lymphatic vessels and provide meeting areas for interaction between the immune system cells.

The lymphatic system contains the following:

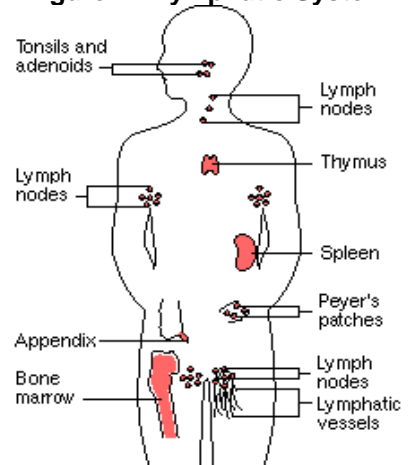
Primary lymphoid organs

- Bone marrow
- Thymus
- Lymphatic vessels

Secondary lymphoid organs

- Spleen
- Lymph nodes

Figure 2 - Lymphatic System



1.4 Types of Immunity (See Figure 3)

Passive Immunity:

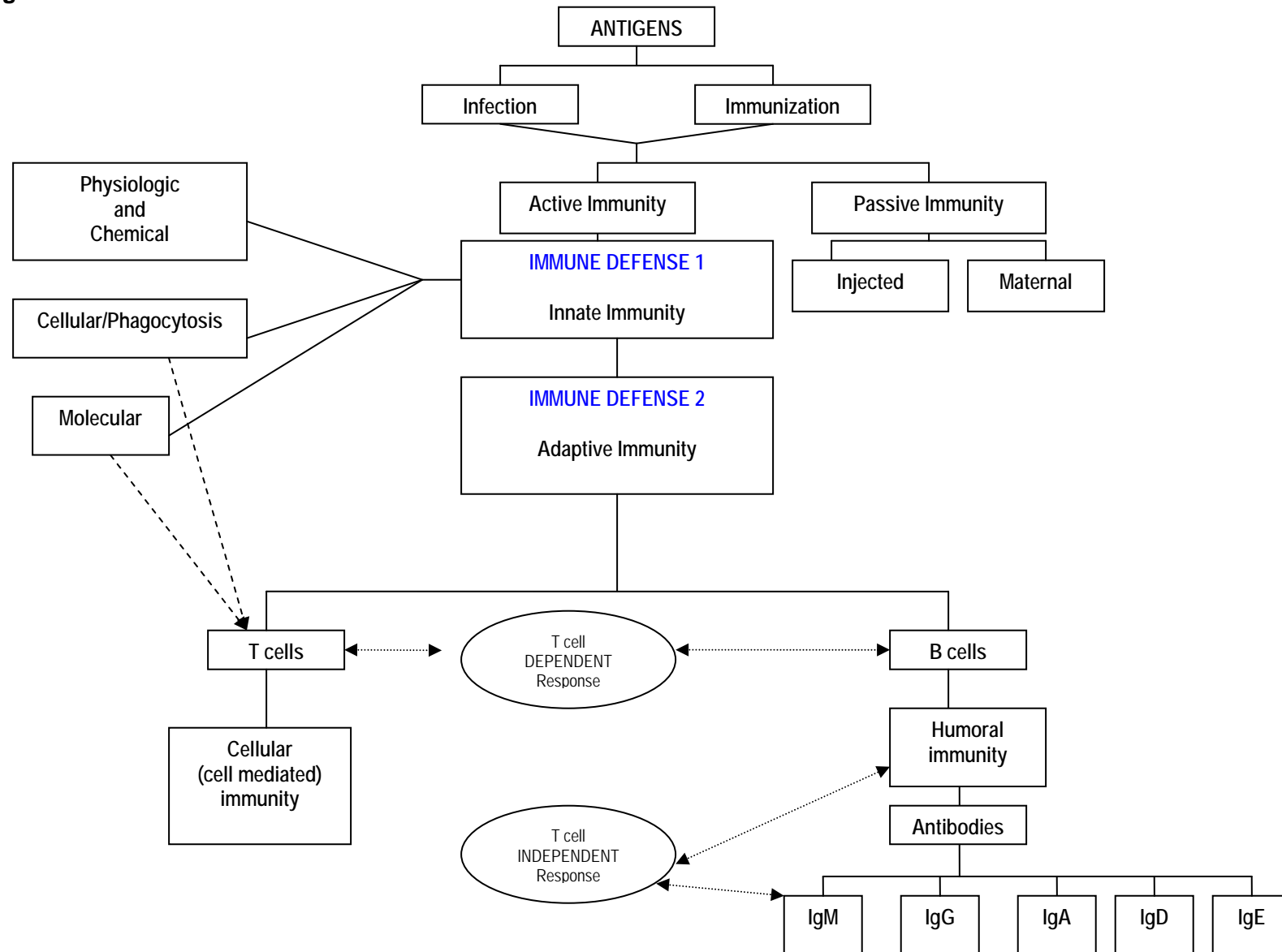
- Antibodies from another person or animal that can be injected or transfused.
- Called passive because the individual did not create the antibodies, but instead received pre-formed antibodies.
- Protection is effective, but duration is short lived and no memory is created.
- Examples of passive immunity are maternal antibodies (trans-placental and breast milk) and injected antibodies (e.g., rabies, varicella, and tetanus immune globulins).

Active Immunity:

When the body is exposed to a foreign substance the cells of the immune system “actively” respond. Active immunity is further divided into categories:

- Innate Immunity - protective mechanisms we are born with
- Adaptive Immunity – cell mediated immunity and humoral immunity

Figure 3 - Immune Defenses





1.5 Active Immunity

The body's immune response can be understood by following the course of an infection as described below:

- Most pathogens are kept outside of the body by protective mechanisms such as tears or skin that act as barriers.
- When there is an injury to tissue, bacteria or viruses can enter the tissue and cause infection.
- Innate cells (macrophages, dendritic cells) respond by recognizing viruses and bacteria as foreign and specialize in engulfing these invaders (*phagocytosis*). These innate cells and protective barriers are part of innate immunity because they “innately” respond to foreign substances.
- In addition, dendritic cells display the antigens on their cell surface and travel to the lymph nodes.
- In the lymph nodes the dendritic cells present the antigen to the T cells. The T cells then activate the B cells to make antibodies. The T cells and B cells are part of the adaptive immunity because they are “adapting” to the foreign substance and creating memory against future infections.

1.6 Innate Immunity - “First” Immune Defense

Innate immunity consists of protective mechanisms we are born with, and are the first line of defense against anything recognized as non-self.

The produced immune response is not specific to the antigen and no memory of the antigen persists.

However, innate immunity is the crucial first step in most adaptive immune responses.

The following are the protective mechanisms of innate immunity (see Table 1):

- Physical and Chemical Mechanisms
- Phagocytosis
- Molecular Response
- Inflammatory Response

Table 1 - Innate Immunity

Physical and Chemical Mechanisms	Phagocytosis	Molecular Response	Inflammatory Response
<p>Physical barriers:</p> <ul style="list-style-type: none"> • intact skin • mucous membrane barrier (sneezing, coughing) • cilia <p>Chemical barriers:</p> <ul style="list-style-type: none"> • tears • acid (pH) • saliva • bile 	<p>Macrophages:</p> <ul style="list-style-type: none"> • engulf and kill invading organisms <p>Dendritic cells:</p> <ul style="list-style-type: none"> • engulf pathogen • display antigen on cell surface • travel to lymph node to present antigen to T cells • critical link between the innate and adaptive immune responses. 	<p>Cytokines: Cytokines are small proteins made by a cell that affect the behavior of other cells. Examples:</p> <ul style="list-style-type: none"> • Cytokines cause vasodilation (heat and redness) • Some types of <i>interferon</i> are antiviral cytokines which help healthy cells resist viral infection <p>Chemokines: Chemokines are proteins secreted by macrophages that attract cells out of the blood stream and into the infected tissues.</p> <p>Complement: The complement system is a group of approximately 20 proteins that coat bacterial surfaces and promote bacterial destruction by macrophages.</p>	<p>The accumulation of fluid and cells at the site of infection causes the redness, swelling, heat, and pain known as inflammation.</p> <p>Inflammation is beneficial because it:</p> <ul style="list-style-type: none"> • recruits cells out of the blood stream, • increases the flow of lymph to take away microbes and antigen-bearing cells to the lymphoid tissue which will lead to adaptive immunity, and • brings the T cells and B cells back to the site of infection.



1.7 Adaptive Immunity - “Second” Immune Defense

Adaptive immunity is the second line of defense against anything recognized as non-self and it provides protection against re-exposure to the same pathogen.

Characteristics of adaptive immunity:

- Specificity: the immune response is specific to the antigen that produced it (e.g. antibody for measles antigen has no effect on rubella antigen)
- Tolerance: the immune response is able to differentiate between self and non-self so that body tissues are not destroyed
- Memory: with subsequent exposure to an antigen there is a rapid and strong immune response. This is called an anamnestic response.

Adaptive immunity is divided into two categories:

- Cell mediated immunity
- Humoral (antibody) immunity

1.8 Adaptive Immunity - Cell Mediated Immunity

Cell mediated immunity describes any immune response where T cells have the main role.

B cells are not activated by most antigens without “help” from helper T cells. The activation of T cells is an essential first stage in virtually all adaptive immune responses. This is called the “T cell-dependent immune response”.

T cells do not recognize microorganisms in the extracellular fluids. Instead, T cell receptors bind to fragments of antigens (*epitopes*) that are presented on the surface of antigen presenting cells (APC).

There are three main types of APC:

- Macrophages
- Dendritic cells
- Naïve B cells

When T cells recognize an antigen presented by the APC, they can differentiate into several different types of T cells:

- Cytotoxic T cells:
Kill cells infected with intracellular pathogens such as viruses

- Helper T cells:
 - Activate antigen and stimulate B cells to differentiate and produce antibodies
 - Activate macrophages to become more efficient at killing the pathogen
 - Control intracellular bacterial infections (e.g. tuberculosis) that grow in intracellular membrane-bound vesicles of macrophages. The macrophages can't kill the bacteria but instead display the bacterial antigen on the surface so that it can be recognized by T cells
- Regulatory T cells:
Suppress lymphocytes and control the immune response

1.9 Adaptive Immunity - Humoral Immunity

Humoral immunity is mediated by B cells. B cells react against foreign substances in the extracellular spaces of the body by producing and secreting antibodies (Abs). These Abs are present in the biological fluids of the body (the humours); hence the term humoral immunity.

Many microorganisms multiply in the extracellular spaces of the body, and most intracellular pathogens spread by moving from cell to cell through the extracellular fluids.

These extracellular spaces are protected by humoral immunity where antibodies either kill the extracellular organism and the intracellular organism as it is moving from cell to cell or bind the pathogen and present it to T cells.

B cells display immunoglobulin molecules (antibodies) on their surface membranes, which act as receptors for the antigens. B cell antibody receptors can either bind to helper T cells that have interacted with an APC or bind to extracellular microorganisms such as bacteria.

Once an antigen binds to an antibody with the best "fit", the B cell differentiates into plasma cells or B memory cells.

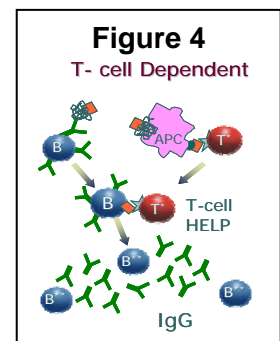
- Plasma cells:
These cells operate as factories to manufacture the chosen antibody and then secrete those antibodies.
- B memory cells:
These cells mediate immunological memory. They respond rapidly on re-exposure to the antigen that originally induced them.

Except for the phenomenon of cross-protective immunity, each antibody can recognize and bind to only one specific antigen and no other.

Seroconversion is the phase of an infection when antibodies against an infecting agent are first detectable in the blood. To test for immunity against a particular disease an antibody titre may be ordered to assess the amount of circulating antibody specific to that pathogen.

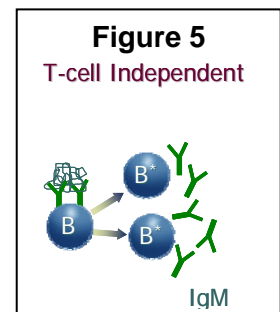
T cell-dependent antigens (Figure 4)

- Most antigens require the interaction of T cells and B cells to generate the production of antibodies. These antigens are referred to as T cell-dependent antigens.
- The antibodies produced in response to T cell-dependent antigens are primarily IgG and the response produces immunologic memory.



T cell-independent antigens (Figure 5)

- In some situations, B cells can create antibodies without the help of T cells.
- Many common extracellular bacteria (e.g. *Haemophilus influenzae* type b) are surrounded by a polysaccharide capsule that enables them to resist ingestion by phagocytes and therefore avoid stimulating the T cell response
- Antibodies produced are of the IgM class and immunologic memory is not created.



1.10 Antibodies

Classes of Antibodies

There are five classes of antibodies: IgM, IgG, IgA, IgD and IgE. Each class performs particular functions. The immune response to injected vaccines involves IgG and IgM. Antibodies as a class are known as immunoglobulins:

Immunoglobulin M (IgM):

- A valuable diagnostic marker for infectious disease because it is usually the first immunoglobulin made following Ag exposure and is relatively short-lived
- Effective in activating complement
- Participates in the lysis (bursting apart) of cells
- Generally remains in the blood; does not diffuse into the surrounding tissues due to its large size

Immunoglobulin G (IgG):

- The most abundant class of antibody, constituting approximately 80% of all antibodies in serum
- Produced slowly upon primary exposure to an antigen
- Produced rapidly during secondary or subsequent exposure, becoming the major antibody present
- The principal humoral component of immunological memory
- The only antibody that crosses the placenta. It helps protect the newborn from infection through passive immunity.

Immunoglobulin A (IgA):

- Represents approximately 10% to 20% of the immunoglobulins in serum
- Most abundant immunoglobulin in tissues
- Prevents or interferes with the attachment of viruses and bacteria to mucosa of respiratory and digestive systems
- Protects against enterotoxins released by certain bacteria; for example, forms an antibody-antigen complex with cholera toxin, preventing it from binding to specific receptors on the intestinal membrane
- Plays a role in eliminating food antigens from the circulatory system
- The main secretory immunoglobulin; found in exocrine secretions (e.g., breast milk, saliva, tears, respiratory and digestive secretions, urine).

Immunoglobulin D (IgD)

- Constitutes only a very small fraction (0.2%) of immunoglobulin in the body
- Acts as an antigen receptor on the surfaces of B cells
- Unknown activity.

Immunoglobulin E (IgE)

- Minute concentration in serum
- Involved in mediating allergic reactions
- Elevated in people with hypersensitivity to allergens, as well as those with eczema, asthma, or other respiratory problems
- Especially useful against parasitic infections (e.g., worms)

Antibody function

Antibodies have three main functions:

1) Neutralization:

Antibodies bind to pathogens (e.g., viruses, bacteria) and block their access to cells, then the antibody-antigen complex is engulfed by a macrophage.

- 2) **Opsonization:**
 Encapsulated bacteria (e.g., Hib, pneumococcal, and meningococcal) evade the innate immune system because they are not recognized by macrophages or dendritic cells. However, encapsulated bacteria can be recognized by antibodies. The antibody coats the bacteria to enable the ingestion by macrophages and dendritic cells through the process of opsonization.

- 3) **Complement Activation:**
 Antibodies bind to certain bacteria in the plasma. A region on the antibody is a receptor to complement proteins which will help lyse the bacteria or attract the macrophages to it.

Figure 6 - Antibody Function

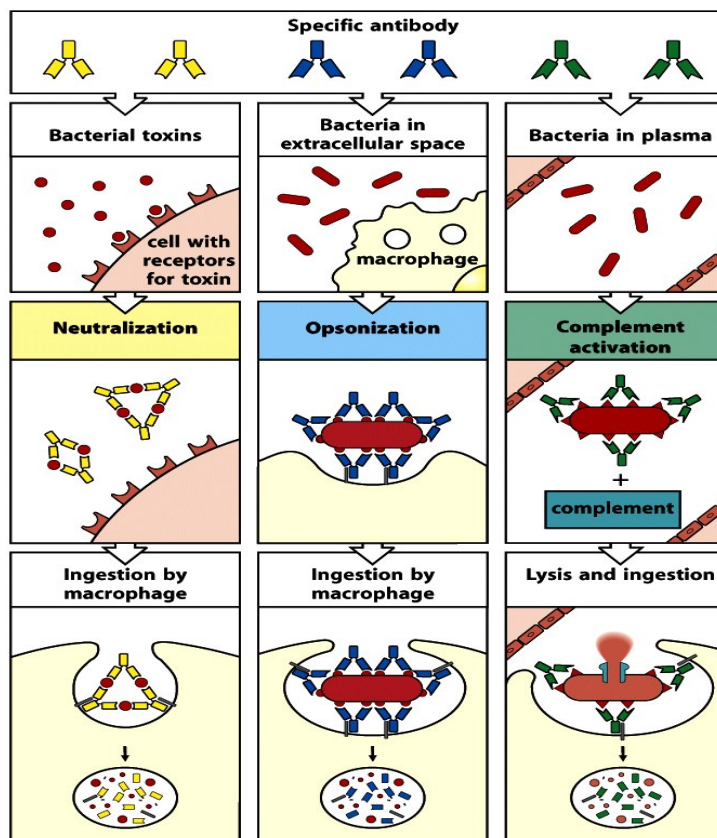


Figure 1-26 Immunobiology, 7ed. (© Garland Science 2008)

Figure 6: ©2007 From Janeway's Immunobiology, 6E by Murphy et al. Reproduced by permission of Garland Science/Taylor & Francis, LLC.

1.11 Fetal and Infant Immune System

The development of the immune system occurs early in fetal development.

Table 2 - Fetal Immunity	
Passive Immunity (passage of maternal antibody -IgG only)	Active Immunity
<ul style="list-style-type: none"> • Beginning at 8 weeks gestational age (GA) • IgG levels correlate with GA: <ul style="list-style-type: none"> • low until 20 weeks • by 40 weeks, it doubles that of 32 wks 	<ul style="list-style-type: none"> • B cells and T cells present by 14 weeks' GA • Relatively sterile environment in utero. There is an enormous unchallenged capacity

Newborns (even premature infants) can actively distinguish self from non-self.

Table 3 - Neonatal and Infant Immunity		
Birth	Passive Immunity (maternally acquired antibodies)	Active Immunity
<ul style="list-style-type: none"> • Instant challenge • Within hours, GI tract heavily colonized 	<ul style="list-style-type: none"> • Circulating placental IgG lasts 6 months or longer • Secretory IgA in breast milk and colostrum 	<ul style="list-style-type: none"> • B cell responses are good. Until two years of age, children do not respond well to T cell-independent antigens (i.e., polysaccharides) • Full T cell subsets. Infants respond well to T cell-dependent antigens (i.e., proteins)



2.0 IMMUNIZING AGENTS

Immunizing agents are classified as passive or active.

2.1 Passive Immunizing Agents

The prevention of illness through the transfer of pre-formed IgG antibodies is called immunoprophylaxis.

While the protection is immediate, it is temporary and it can only be offered if the exposure is recognized.

Protection is also time-sensitive. Post-exposure immunoprophylaxis must be initiated within a short time frame, usually within days of exposure to the infection.

Passive agents may not be completely free of blood borne pathogens despite all current safeguards and technology in place.

Types of Passive Immunizing Agents:

- Standard immune globulin – pooled antibody from thousands of donors. It is now primarily used for post-exposure prophylaxis against measles.
- Hyperimmune globulins – made from donated plasma of persons with high levels of a specific IG (e.g., Hepatitis B Immune Globulin).
- Hyperimmune serum – produced in animals (e.g., botulinum and diphtheria antitoxins).



Table 4 - Passive Immunizing Agents		
Agent		Indication/Action
Standard Immune Globulin	Immune globulin (human)	Exposure to measles for susceptible individuals who cannot receive live attenuated measles-containing vaccine; exposure to Hepatitis A for individuals who cannot receive Hepatitis A vaccine
Hyperimmune Globulins	Varicella-zoster immune globulin (Varlg)	Varlg is recommended for high risk susceptible people with significant exposure to varicella
	Rabies immune globulin (Rablg)	Post-exposure prophylaxis against rabies in susceptible exposed individuals
	Tetanus immune globulin (Tlg)	Tlg neutralizes tetanus toxin in the body fluids
	Hepatitis B immune globulin (HBlg)	Provides immediate and effective short-term passive immunity to hepatitis B
Hyperimmune Serum	Botulism antitoxin (equine)	Recommended for established or suspected botulism
	Diphtheria antitoxin (equine)	Neutralizes diphtheria toxin in the body fluids

2.2 Active Immunizing Agents

Protection acquired through active immunizing agents is produced by one's own immune response. Protection takes longer than with passive immunizing agents, but is stronger and may be permanent.

Table 5 – Active Immunizing Agents		
Replicating Vaccines	Virus	MMR, Varicella
	Bacteria	Typhoid (oral)
Non-Replicating Vaccines	Viral	Polio (inj), hepatitis A, rabies
	Bacteria	Typhoid (inj)
	Proteins (subunit)	Acellular pertussis, influenza
	Protein toxoid (subunit)	Diphtheria, tetanus
	Recombinant (subunit)	Hepatitis B, Human papillomavirus
	Polysaccharide (subunit)	Pneumococcal, Meningococcal, Typhoid (inj)
	Conjugate (subunit)	Act-HIB, Meningococcal, Pneumococcal

2.2.1 Replicating Vaccines - Live Attenuated Vaccines

These vaccines contain whole, living virus or bacteria that induce immunity by actively replicating within the host.

Attenuated means the vaccine strains are weakened so that infection is usually inapparent or very mild.

Because these vaccines replicate, the immune response is both cell mediated and humoral and therefore protection is long-lasting, probably life-long.

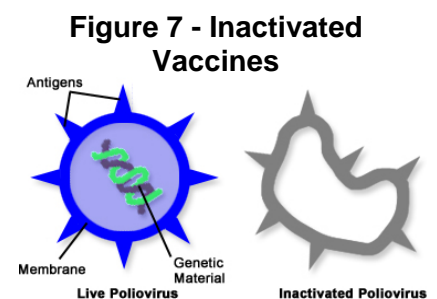
Limitations:

- Circulating antibodies can interfere with vaccine virus replication
- Sensitive to exposure to heat and light
- Use with caution/contraindicated in immunocompromised persons
- Live vaccines must be given on the same day or 28 days apart because circulating interferon may interfere with the replication of the second live vaccine.

2.2.2 Non-Replicating Vaccines

Because these vaccines do not replicate, protection takes longer to achieve as more vaccine doses are needed to create a protective immune response. After the scheduled numbers of vaccine doses are given, the immune response is strong and may be permanent. With some vaccines, antibody levels may fall over time and as a result booster doses may be needed.

- Inactivated Vaccines (Figure 7):
Inactivated vaccines contain killed bacteria or viruses.
- Subunit Vaccines
Subunit vaccines contain purified products that usually come from the bacteria or virus that causes natural infection, but may also be synthesized in the laboratory using recombinant technology.
 - Proteins
Purified, inactivated proteins from the outer coating of viruses or bacteria. Aluminum salt is added as an adjuvant to enhance the immune response.
 - Protein Toxoid
Vaccines made from inactivated bacterial toxins. Aluminum salt is added as an adjuvant to enhance the immune response.



- **Recombinant Vaccines**
Vaccine antigens produced using genetic engineering technology.
- **Polysaccharide Vaccines**
Polysaccharide vaccines are composed of long chains of sugar molecules that make up the surface capsule of encapsulated bacteria. The immune response to a pure polysaccharide vaccine is typically T cell-independent.
- **Conjugate Vaccines**
By linking a polysaccharide to a protein (diphtheria toxoid protein is commonly used) the immune response becomes T cell-dependent and immunogenicity is improved in infants and young children < 2 years of age. This process is called conjugation; hence the term “conjugate vaccines.”

3.0 VACCINE IMMUNE RESPONSE

3.1 Introduction

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 immunological memory similar to that acquired by having the natural disease. The antigen is the part of the vaccine that stimulates the immune response.

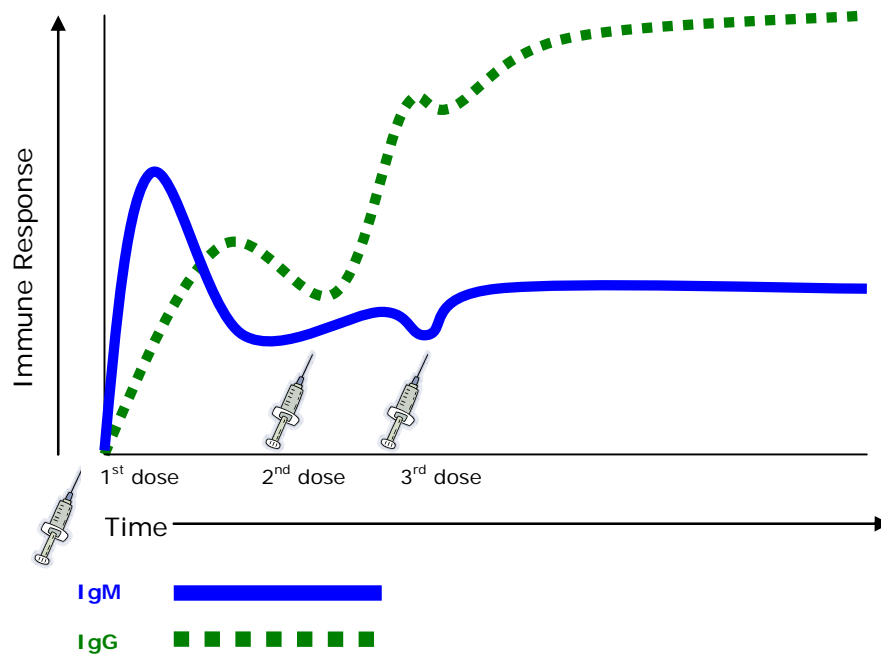
The immune or antibody response to non-replicating vaccines (inactivated/subunit) is different from the response to replicating vaccines (live attenuated).

3.2 Antibody response to a NON-REPLICATING Vaccine

Inactivated/subunit vaccines will need more doses to build an adequate and lasting immune response (Figure 8).

- **Primary immune response:**
Antibody following the first exposure to an antigen is primarily IgM. Response is of brief duration and low intensity.
- **Secondary immune response:**
Antibody following the second and subsequent immunogenic challenges is primarily IgG. Memory cells are already present at time of repeat exposure and make the specific antibodies more rapidly.

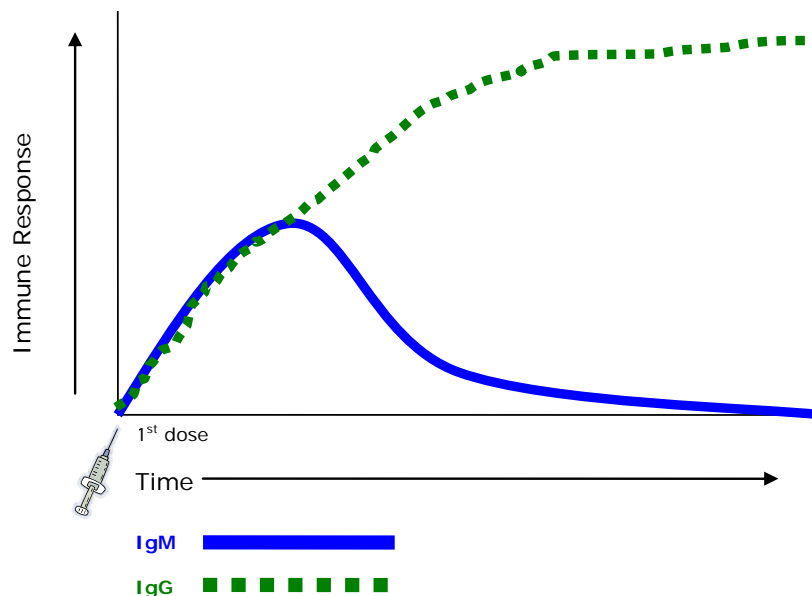
Figure 8 - Immune Response to Non-Replicating Vaccines



3.3 Antibody response to a REPLICATING Vaccine

The immune response to a live attenuated vaccine is virtually identical to that produced by a natural infection as cell-mediated and humoral immunity are fully activated. Replicating vaccines will need fewer doses to create lasting memory.

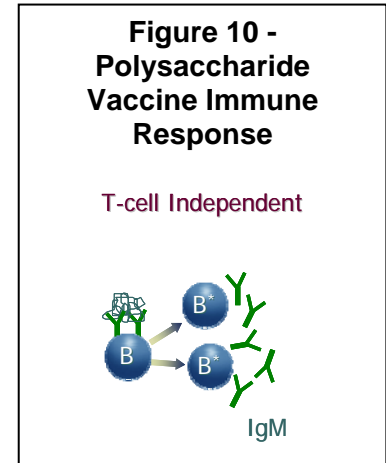
Figure 9 - Immune Response to Replicating Vaccines
Live Attenuated Vaccines



3.4 Antibody response to conjugate and polysaccharide vaccines

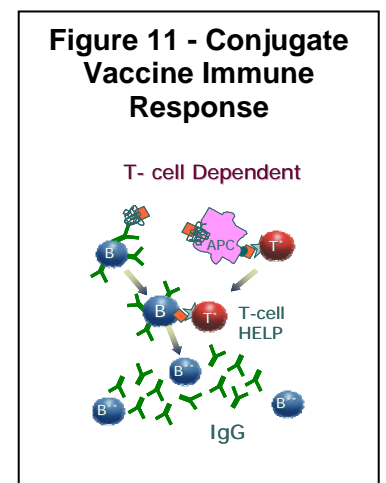
Polysaccharide Vaccine Immune Response (Figure 10)

- Polysaccharide vaccines stimulate B cells without the help of T cells, resulting in a T cell-independent immune response
- The antibody made in response to these vaccines is mostly of the IgM class and immunologic memory is not produced.
- Polysaccharide vaccines are not immunogenic in children < 2 years of age.



Conjugate Vaccine Immune Response (Figure 11)

- Conjugate vaccines stimulate T cells and B cells, resulting in a T cell-dependent immune response
- The antibodies produced include IgG, providing longer protection and immunologic memory.
- Conjugate vaccines are immunogenic in children < 2 years of age



3.5 Factors that influence the Vaccine Immune Response:

Vaccine-related factors:

- Nature of the antigen
 Live, inactivated/subunit, conjugate and polysaccharide vaccines each generates immune responses of a different intensity and duration.
- Dose of the antigen
 A certain threshold dose of antigen is required to elicit an immune response.
- Presence of vaccine adjuvants

Vaccine adjuvants are added to the inactivated and subunit vaccines to enhance the immune response through three mechanisms: the “depot effect” increases the immunologic half-life of the antigen at the injection site; adjuvants induce the production of cytokines to assist T cells; and adjuvants induce dendritic cell maturation.

Host-related factors:

- **Circulating antibodies:**
Antibody from any source (e.g., maternal, transfusion) can interfere with live vaccine replication. For example: potential antibody interference is the reason to defer MMR vaccine until 1 year of age when maternal antibodies have declined. Administration of immune globulins (Ig) may interfere with live vaccine replication.
- **Age of the client:**
Protection should precede the age of greatest risk (e.g., human papillomavirus vaccine is ideally given before an individual is sexually active). Children <2 years do not mount a protective immune response to T cell-independent antigens such as polysaccharides. Conjugate vaccines will produce an immune response in young children.
- **Genetics:**
Deficiencies in the terminal components of complement and properdin result in an impaired immune response.
- **Nutritional factors:**
Malnutrition results in reduction of cell-mediated immunity.
- **Co-existing disease:** e.g., immunodeficiency.
- **Previous exposure to antigen/vaccine (anamnestic response)**

3.6 Vaccine Antigen Load

3.6.1 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.

3.6.2 Vaccine Antigen Load: “Then and Now”

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;
- knowledge of antigens needed to induce protective immunity.



Figure 12 - Vaccine antigen load. Source: Offit, P.A., Quarles et al (2002). Addressing parents' concerns: Do multiple vaccines overwhelm or weaken the infants' immune system? Paediatrics. Vol 109, pages 124 - 129.

TABLE 2. Number of Immunogenic Proteins and Polysaccharides Contained in Vaccines Over the Past 100 Years

1900		1960		1980		2000	
Vaccine	Proteins	Vaccine	Proteins	Vaccine	Proteins	Vaccine	Proteins/ Polysaccharides
<u>Smallpox*</u>	<u>~200</u>	Smallpox	~200	Diphtheria	1	Diphtheria	1
Total	~200	Diphtheria†	1	Tetanus	1	Tetanus	1
		Tetanus‡	1	WC-Pertussis¶¶	~3000	AC-Pertussis¶¶¶	2-5
		WC-Pertussis§	~3000	Polio	15	Polio	15
		Polio	15	Measles¶¶	10	Measles	10
		Total	~3217	Mumps#	9	Mumps	9
				Rubella**	5	Rubella	5
				Total	~3041	Hib††	2
						Varicella‡‡	69
						Pneumococcus§§	8
						Hepatitis B	1
						Total	123-126

* *Vaccinia vaccine*: Goebel SJ, Johnson GP, Perkus ME, et al. *Virology*. 1990;179:247-266.
 † *Diphtheria toxoid*: MMWR Morb Mortal Wkly Rep. 1991 (August);40:1-28.
 ‡ *Tetanus toxoid*: MMWR Morb Mortal Wkly Rep. 1991 (August);40:1-28.
 § *Whole cell pertussis vaccine*: Number estimated from genome size. The sequence of Bordetella pertussis Tohama I strain will soon be completed at the Sanger Center in Great Britain.
 || *Polio vaccine*: Wimmer E, Nomoto A. *Biologicals*. 1993;21:349-356; Kitamura N, Semler BL, Rothberg PG, et al. *Nature*. 1981;291:547-553; Five proteins per poliovirus virion and 3 poliovirus strains in the inactivated poliovirus vaccine (IPV).
 ¶ *Measles vaccine*: Griffen D, Bellini WL. Measles virus. In: Fields BN, ed. Knipe DM, Howley PM, et al, eds. Philadelphia, PA: Lipincott-Raven Publishers; 1996.
 # *Mumps vaccine*: Elango N, Varsanyi TM, Kovamees J, Norrby E. *J Gen Virol*. 1988;69:2893-2900.
 ** *Rubella vaccine*. Hofmann J, Gerstenberger S, Lachmann I, et al. *Virus Res*. 2000;68:155-160.
 †† *Conjugate Haemophilus influenzae type b vaccine*: MMWR Morb Mortal Wkly Rep. 1991 (January);40:1-7.
 ‡‡ *Varicella vaccine*: Cohen JL. *Infect Dis Clin North Am*. 1996;10:457-468.
 §§ *Streptococcus pneumoniae vaccine*: MMWR Morb Mortal Wkly Rep. 2000;49:1-29.
 ||| *Hepatitis B vaccine*: MMWR Morb Mortal Wkly Rep. 1991 (November);40:1-25.
 ¶¶ *Acellular pertussis vaccine*: MMWR Morb Mortal Wkly Rep. 1997 (March);46:1-25.



4.0 GLOSSARY

Active immunity

When the body is exposed to a foreign substance the cells of the immune system “actively” respond

Adaptive immunity

The cells of the immune system “adapt” to the foreign substance and create memory against future infections.

Adjuvant

A substance added to a vaccine to enhance the immune response by intensity and/or duration.

Anamnestic response

A renewed rapid production of an antibody on the second (or subsequent) encounter with the same antigen

Antigen

A foreign substance which, when introduced into the body is capable of inducing an immune response.

APC (antigen presenting cell)

Highly specialized cells that process antigens and display their peptide fragments on their surface

Cytotoxic T cells

Kill intracellular pathogens like viruses

Dendritic cells

Phagocytic cells found in most tissues. They act as antigen presenting cells (APC), travel to lymph nodes and present antigens to T cells

Epitope

The site on an antigen that is recognized by an antibody or an antigen receptor

Helper T cells

T cells that stimulate B cells to differentiate and produce antibodies

Immunoglobulin

A class of antibodies



Immunoprophylaxis

Disease prevention by immunologic means. Active immunoprophylaxis involves the administration of vaccines to stimulate the host's own immune system. Passive immunoprophylaxis involves the administration of immune globulins from an immune donor.

Innate immunity

Protective mechanisms we are born with e.g., cilia, skin, mucosal membranes

Interferon

Antiviral cytokines which help healthy cells resist viral infection

Lymph

Extracellular fluid that accumulates in tissues and is carried through the lymphatic system by the lymphatic vessels

Lysis

Process of disintegration or dissolution of cells

Macrophage

Large phagocytic cell; creates inflammation cytokines; acts as an antigen presenting cell (APC)

Memory cell

Lymphocytes that mediate immunological memory

Passive immunity

Antibodies from another person or animal are injected or transfused into an individual who receives "passive" immunity

Phagocytosis

The process by which a cell engulfs and digests solid substances

Plasma Cell

Specialized B cells that create antibodies

Regulatory T cells

Suppress lymphocytes and control the immune response

Seroconversion

The phase of an infection when antibodies against a pathogen are detected in the blood



5.0 REFERENCES

Centers for Disease Control and Prevention (2009). Principles of vaccination. *Epidemiology and Prevention of Vaccine -Preventable Diseases* (11th ed.). <http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/prinvac.pdf>.

Murphy, K., Travers, P., Walport, M., (2008). *Janeway's immunobiology* (7th ed.). Garland Science.

Offit, P.A., Quarles et al (2002). Addressing parents' concerns: Do multiple vaccines overwhelm or weaken the infants' immune system? *Paediatrics*. Vol 109, pages 124 - 129.

Public Health Agency of Canada (2006). *Canadian immunization guide* (7th ed.). <http://www.phac-aspc.gc.ca/publicat/cig-gci/index-eng.php>.

6.0 RESOURCES

The following documents are available on line, as well as in print, free of charge:

National Institutes of Health (2007). *Understanding the immune system. How it works*. U.S. Department of Health and Human Services. <http://www3.niaid.nih.gov/topics/immuneSystem/PDF/theImmuneSystem.pdf>

National Institutes of Health (2007). *Understanding vaccines. What they are and how they work*. U.S. Department of Health and Human Services. <http://www3.niaid.nih.gov/topics/vaccines/PDF/undvacc.pdf>