Inflammation

Steps of the Inflammatory Response

The inflammatory response is a body's second line of defense against invasion by pathogens. Why is it important that clotting factors from the circulatory system have access to the injured area?

1. Damaged tissues release histamines, increasing blood flow to the area.

2. Histamines cause capillaries to leak, releasing phagocytes and clotting factors into the wound.

3. Phagocytes engulf bacteria, dead cells, and cellular debris.

4. Platelets move out of the capillary to seal the wounded area.
Inflammation

- Pulmonary diseases
- Neurological diseases
- Autoimmune diseases
- Cancer
- Cardiovascular diseases
- Alzheimer
- Diabetes II
- Arthritis
Inflammation: Tissue Response to Injury

- The inflammatory response is triggered whenever body tissues are injured
  - Prevents the spread of damaging agents to nearby tissues
  - Disposes of cell debris and pathogens
  - Sets the stage for repair processes
- The four cardinal signs of acute inflammation are redness, heat, swelling, and pain
Plasma cascade systems

- **The complement system**, when activated, results in the increased removal of pathogens via opsonisation and phagocytosis.

- **The kinin system** generates proteins capable of sustaining vasodilation and other physical inflammatory effects.

- **The coagulation system or clotting cascade** which forms a protective protein mesh over sites of injury.

- **The fibrinolysis system**, which acts in opposition to the *coagulation system*, to counterbalance clotting and generate several other inflammatory mediators.
Comparison between acute and chronic inflammation:

<table>
<thead>
<tr>
<th></th>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Causative agent</strong></td>
<td>Pathogens, injured tissues</td>
<td>Persistent acute inflammation due to non-degradable pathogens, persistent foreign bodies, or autoimmune reactions</td>
</tr>
<tr>
<td><strong>Major cells involved</strong></td>
<td>Neutrophils, mononuclear cells (monocytes, macrophages)</td>
<td>Mononuclear cells (monocytes, macrophages, lymphocytes, plasma cells), fibroblasts</td>
</tr>
<tr>
<td><strong>Primary mediators</strong></td>
<td>Vasoactive amines, eicosanoids</td>
<td>IFN-γ and other cytokines, growth factors, reactive oxygen species, hydrolytic enzymes</td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>Immediate</td>
<td>Delayed</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>Few days</td>
<td>Up to many months, or years</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Resolution, abscess formation, chronic inflammation</td>
<td>Tissue destruction, fibrosis</td>
</tr>
</tbody>
</table>
INFLAMMATION

HEAT
REDNESS
SWELLING
PAIN
LOSS OF FUNCTION
The classic signs and symptoms of acute inflammation:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Redness</strong></td>
<td><strong>Rubor</strong></td>
</tr>
<tr>
<td><strong>Swelling</strong></td>
<td><strong>Tumor/Turgor</strong></td>
</tr>
<tr>
<td><strong>Heat</strong></td>
<td><strong>Calor</strong></td>
</tr>
<tr>
<td><strong>Pain</strong></td>
<td><strong>Dolor</strong></td>
</tr>
<tr>
<td><strong>Loss of function</strong></td>
<td><strong>Functio laesa</strong></td>
</tr>
</tbody>
</table>
Figure. Pharmacology of Traditional NSAIDs and Selective COX-2 Inhibitors on Prostaglandin Synthesis

Membrane Phospholipids → Phospholipase A₂ → Arachidonic Acid

COX-1 ( Constitutive ) - Traditional NSAID → Prostaglandins associated with: GI mucosal integrity, Platelet function, Renal function

COX-2 ( Inducible ) - COX-2 inhibitor → Prostaglandins associated with: Pain, Fever, Inflammation
• **acute inflammation**: inflammation, usually of sudden onset, characterized by the classical signs in which the vascular and exudative processes predominate.

• **subacute inflammation**: a condition intermediate between chronic and acute inflammation, exhibiting some of the characteristics of each.

• **chronic inflammation**: inflammation of slow progress and marked chiefly by the formation of new connective tissue; it may be a continuation of an acute form or a prolonged low-grade form, and usually causes permanent tissue damage.

**granulomatous inflammation**: an inflammation, usually chronic, characterized by the formation of granulomas
Inflammation Response

• Begins with a flood of inflammatory chemicals released into the extracellular fluid

• Inflammatory mediators:
  • Kinins, prostaglandins (PGs), complement, and cytokines
  • Released by injured tissue, phagocytes, lymphocytes, and mast cells
  • Cause local small blood vessels to dilate, resulting in hyperemia
Toll-like Receptors (TLRs)

- Macrophages and cells lining the gastrointestinal and respiratory tracts bear TLRs
- TLRs recognize specific classes of infecting microbes
- Activated TLRs trigger the release of cytokines that promote inflammation
Inflammatory Response: **Vascular Permeability**

- Chemicals liberated by the inflammatory response increase the permeability of local capillaries

- **Exudate**—fluid containing proteins, clotting factors, and antibodies
  - Exudate seeps into tissue spaces causing local edema (swelling), which contributes to the sensation of pain
Inflammatory Response: **Edema**

- The surge of protein-rich fluids into tissue spaces (edema):
  - Helps dilute harmful substances
  - Brings in large quantities of oxygen and nutrients needed for repair
  - Allows entry of clotting proteins, which prevents the spread of bacteria
Inflammatory Response: **Phagocytic Mobilization**

- Four main phases:
  - **Leukocytosis** – neutrophils are released from the bone marrow in response to leukocytosis-inducing factors released by injured cells
  - **Margination** – neutrophils cling to the walls of capillaries in the injured area
  - **Diapedesis** – neutrophils squeeze through capillary walls and begin phagocytosis
  - **Chemotaxis** – inflammatory chemicals attract neutrophils to the injury site
**Figure 21.4**

Neutrophils enter blood from bone marrow

- **Inflammation**
  - Chemicals diffusing from the inflamed site act as chemotactic agents

1. Neutrophils enter blood from bone marrow
2. Margination
3. Diapedesis
4. Positive chemotaxis

Innate defenses → Internal defenses
• **Transudate** is extravascular fluid with

- low protein content
- a low specific gravity (< 1.012).
- low nucleated cell counts (less than 500 to 1000 /microlit) and the primary cell types are mononuclear cells: macrophages, lymphocytes and mesothelia cells.

*For instance, an ultrafiltrate of blood plasma is transudate.*

*It results from increased fluid pressures or diminished colloidal oncotic forces in the plasma.*

In females, transudation is a method of lubrication during sexual arousal.
Exudate [pus like]

- **extravascular fluid** due to vessel alteration during inflammation (increased permeability, vascular constriction then dilation).

  - high protein content,
  - cell debris present
  - high specific gravity (>1.020).

This is in contrast to transudate where the extracellular fluid is an ultrafiltrate of blood plasma and thus larger molecules such as proteins and cell debris are absent.
Exudate Types

**Purulent** or **suppurative** exudate consists of plasma with both active and dead neutrophils, fibrinogen, and necrotic parenchymal cells. This kind of exudate is consistent with more severe infections, and is commonly referred to as pus.

**Fibrinous** exudate is composed mainly of fibrinogen and fibrin. It is characteristic of **rheumatic carditis**, but is seen in all severe injuries such as strep throat and bacterial pneumonia. Fibrinous inflammation is often difficult to resolve due to the fact that blood vessels grow into the exudate and fill the space that was occupied by fibrin. Often, large amounts of antibiotics are necessary for resolution.

**Catarrhal** exudate is seen in the nose and throat and is characterized by a high content of mucus.

**Serous** exudate (sometimes classified as serous transudate) is usually seen in mild inflammation, with little protein content. Its consistency resembles that of serum, and can usually be seen in certain disease states like tuberculosis. (See below for difference between transudate and exudate)

**Malignant** (or cancerous) pleural effusion is effusion where cancer cells are present. It is usually classified as exudate.
<table>
<thead>
<tr>
<th>Transudate vs. exudate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main causes</strong></td>
</tr>
<tr>
<td>Transudate</td>
</tr>
<tr>
<td>Increased hydrostatic pressure, Decreased colloid osmotic pressure</td>
</tr>
<tr>
<td>Exudate</td>
</tr>
<tr>
<td>Inflammation</td>
</tr>
<tr>
<td><strong>Appearance</strong></td>
</tr>
<tr>
<td>Transudate</td>
</tr>
<tr>
<td>Clear</td>
</tr>
<tr>
<td>Exudate</td>
</tr>
<tr>
<td>Cloudy (^{1})</td>
</tr>
<tr>
<td><strong>Specific gravity</strong></td>
</tr>
<tr>
<td>Transudate</td>
</tr>
<tr>
<td>&lt; 1.012</td>
</tr>
<tr>
<td>Exudate</td>
</tr>
<tr>
<td>&gt; 1.020</td>
</tr>
<tr>
<td><strong>Protein content</strong></td>
</tr>
<tr>
<td>Transudate</td>
</tr>
<tr>
<td>&lt; 2 g/dL</td>
</tr>
<tr>
<td>Exudate</td>
</tr>
<tr>
<td>&gt; 2.9 g/dL</td>
</tr>
<tr>
<td>(\text{fluid protein}) (\text{serum protein})</td>
</tr>
<tr>
<td>Transudate</td>
</tr>
<tr>
<td>&lt; 0.5</td>
</tr>
<tr>
<td>Exudate</td>
</tr>
<tr>
<td>&gt; 0.5</td>
</tr>
<tr>
<td><strong>Difference of albumin content with blood albumin</strong></td>
</tr>
<tr>
<td>Transudate</td>
</tr>
<tr>
<td>&gt; 1.2 g/dL</td>
</tr>
<tr>
<td>Exudate</td>
</tr>
<tr>
<td>&lt; 1.2 g/dL</td>
</tr>
<tr>
<td>(\text{fluid LDH}) (\text{upper limit for serum})</td>
</tr>
<tr>
<td>Transudate</td>
</tr>
<tr>
<td>&lt; 0.6 or &lt; (\frac{2}{3})</td>
</tr>
<tr>
<td>Exudate</td>
</tr>
<tr>
<td>&gt; 0.6 or &gt; (\frac{2}{3})</td>
</tr>
<tr>
<td>(\text{fluid glucose}) (\text{serum glucose})</td>
</tr>
<tr>
<td>Transudate</td>
</tr>
<tr>
<td>&lt; 0.8</td>
</tr>
<tr>
<td>Exudate</td>
</tr>
<tr>
<td>&gt; 0.8</td>
</tr>
<tr>
<td><strong>Cholesterol content</strong></td>
</tr>
<tr>
<td>Transudate</td>
</tr>
<tr>
<td>&lt; 45 mg/dL</td>
</tr>
<tr>
<td>Exudate</td>
</tr>
<tr>
<td>&gt; 45 mg/dL</td>
</tr>
</tbody>
</table>
4.56 Blood-stained pleural aspirate. This patient had pleural secondaries from carcinoma of the breast.

4.57 Chylous pleural effusion. This patient had bronchial carcinoma, which had invaded and obstructed the thoracic duct.

4.58 Pleural transudate. This pale effusion is typically found in patients with heart failure or other causes of generalized oedema.
**Rivalta test** is used in order to differentiate a transudate from an exudate\[1\]. A test tube is filled with distilled water and acetic acid is added. To this mixture one drop of the effusion to be tested is added. If the drop dissipates, the test is negative, indicating a transudate. If the drop precipitates, the test is positive, indicating an exudate\[2]\.

Using a pH 4.0 acetic acid solution, 8 types of proteins were identified in Rivalta reaction-positive turbid precipitates: C-reactive protein (CRP), Alpha 1-antitrypsin (alpha1-AT), Orosomucoid ((Alpha-1-acid glycoprotein or AGP)), haptoglobin (Hp), transferrin (Tf), ceruloplasmin (Cp), fibrinogen (Fg), and hemopexin (Hpx). Since those are Acute-phase proteins, a positive Rivalta's test may be suggestive of inflammation.


Antimicrobial Proteins

• Enhance the innate defenses by:
  • Attacking microorganisms directly
  • Hindering microorganisms’ ability to reproduce

• The most important antimicrobial proteins are:
  • Interferon
  • Complement proteins
Interferon (IFN)

- **Genes that synthesize IFN are activated when a host cell is invaded by a virus**
- Interferon molecules leave the infected cell and enter neighboring cells
- Interferon stimulates genes for **PKR (an antiviral protein)**
- **PKR nonspecifically blocks viral reproduction in the neighboring cell**
Interferon Family

• Family of related proteins each with slightly different physiological effects

• Lymphocytes secrete gamma (\(\gamma\)) interferon, but most other WBCs secrete alpha (\(\alpha\)) interferon

• Fibroblasts secrete beta (\(\beta\)) interferon

• Interferons also activate macrophages and mobilize NKs

• FDA-approved alpha IFN is used:
  • As an antiviral drug against hepatitis C virus
  • To treat genital warts caused by the herpes virus
C-reactive Protein (CRP)

• CRP is produced by the liver in response to inflammatory molecules
• CRP is a clinical marker used to assess:
  • The presence of an acute infection
  • An inflammatory condition and its response to treatment
Functions of C-reactive Protein

- Binds to PC receptor of pathogens and exposed self-antigens
- Plays a surveillance role in targeting damaged cells for disposal
- **Activates complement**
<table>
<thead>
<tr>
<th>ELEMENT</th>
<th>FUNCTION IN IMMUNE RESPONSE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MOLECULES</strong></td>
<td></td>
</tr>
<tr>
<td>Antibody (immunoglobulin)</td>
<td>Protein produced by B cell or by plasma cell. Antibodies produced by plasma cells are released into body fluids (blood, lymph, saliva, mucus, etc.), where they attach to antigens, causing complement fixation, neutralization, precipitation, or agglutination, which “mark” the antigens for destruction by complement or phagocytes</td>
</tr>
<tr>
<td>Perforin, granzymes</td>
<td>Released by T&lt;sub&gt;C&lt;/sub&gt; cells. Perforin creates large pores in the target cell's membrane, allowing entry of apoptosis-inducing granzymes</td>
</tr>
<tr>
<td>Complement</td>
<td>Group of bloodborne proteins activated after binding to antibody-covered antigens or certain molecules on the surface of microorganisms; enhances inflammatory response and causes lysis of some microorganisms</td>
</tr>
<tr>
<td>Antigen</td>
<td>Substance capable of provoking an immune response. Typically a large complex molecule (e.g., protein or modified protein) not normally present in the body</td>
</tr>
<tr>
<td><strong>CYTOKINES</strong></td>
<td></td>
</tr>
<tr>
<td>Interferons (IFNs)</td>
<td>Secreted by leukocytes, fibroblasts, and other cells; antiviral effects; activate macrophages and NK cells</td>
</tr>
<tr>
<td>- Alpha (α) and beta (β)</td>
<td></td>
</tr>
<tr>
<td>- Gamma (γ)</td>
<td>Secreted by lymphocytes; activates macrophages; stimulates synthesis and expression of more class I and II MHC proteins; promotes differentiation of T&lt;sub&gt;H&lt;/sub&gt; cells into T&lt;sub&gt;H&lt;/sub&gt;1</td>
</tr>
<tr>
<td>Interleukins (ILs)</td>
<td>Secreted by activated macrophages; promotes inflammation and T cell activation; causes fever (a pyrogen that resets the thermostat of the hypothalamus)</td>
</tr>
<tr>
<td>- IL-1</td>
<td></td>
</tr>
<tr>
<td>- IL-2</td>
<td>Secreted by T cells; stimulates proliferation of T cells; activates NK cells</td>
</tr>
<tr>
<td>- IL-3</td>
<td>Stimulates production of leukocytes and mast cells</td>
</tr>
</tbody>
</table>
### Table 21.4: Cells and Molecules of the Adaptive Immune Response (continued)

<table>
<thead>
<tr>
<th>ELEMENT</th>
<th>FUNCTION IN IMMUNE RESPONSE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CYTOKINES</strong></td>
<td></td>
</tr>
<tr>
<td>Interleukins (ILs)</td>
<td></td>
</tr>
<tr>
<td>- IL-4</td>
<td>Secreted by T&lt;sub&gt;H&lt;/sub&gt; cells; promotes differentiation to T&lt;sub&gt;H&lt;/sub&gt;2; promotes B cell activation; switches antibody production to IgE</td>
</tr>
<tr>
<td>- IL-5</td>
<td>Secreted by some T&lt;sub&gt;H&lt;/sub&gt; cells and mast cells; attracts and activates eosinophils; causes plasma cells to secrete IgA antibodies</td>
</tr>
<tr>
<td>- IL-6</td>
<td>Induces lymphocyte activation and increases antibody production; stimulates liver to secret C-reactive protein, which binds certain bacteria, resulting in complement activation and opsonization</td>
</tr>
<tr>
<td>- IL-7</td>
<td>Induces lymphocyte proliferation and maturation</td>
</tr>
<tr>
<td>- IL-8 (also called CXCL8)</td>
<td>Stimulates chemotaxis of neutrophils, basophils, and T cells; promotes angiogenesis</td>
</tr>
<tr>
<td>- IL-10</td>
<td>Inhibits macrophages and dendritic cells; turns down cellular and innate immune response</td>
</tr>
<tr>
<td>- IL-12</td>
<td>Secreted by dendritic cells and macrophages; stimulates T&lt;sub&gt;C&lt;/sub&gt; and NK cell activity; promotes T&lt;sub&gt;H&lt;/sub&gt;1 differentiation</td>
</tr>
<tr>
<td>- IL-13</td>
<td>Secreted by T&lt;sub&gt;H&lt;/sub&gt; cells; switches antibody production to IgE</td>
</tr>
<tr>
<td>Migration inhibitory factor (MIF)</td>
<td>Inhibits macrophage migration and keeps them in the area of antigen deposition; a generic term for a number of cytokines</td>
</tr>
<tr>
<td>Suppressor factors</td>
<td>A generic term for a number of cytokines that suppress the immune system, for example TGF-β and IL-10</td>
</tr>
<tr>
<td>Transforming growth factor beta (TGF-β)</td>
<td>A suppressor factor similar to IL-10</td>
</tr>
<tr>
<td>Tumor necrosis factors (TNFs)</td>
<td>Produced by lymphocytes and in large amounts by macrophages. Enhance nonspecific killing; slow tumor growth by selectively damaging tumor blood vessels; enhance granulocyte chemotaxis; help activate T cells, phagocytes, and eosinophils; promote cell death by apoptosis</td>
</tr>
</tbody>
</table>

*Copyright © 2006 Pearson Education, Inc., publishing as Benjamin Cummings.*

Table 21.4.3
COMPLEMENT
Complement

**Definition**: series of heat-labile serum proteins

**Site**: serum and all tissue fluids except urine and CSF

**Synthesis**: in liver – appear in fetal circulation during 1st 13 W

**Function**: Responsible for certain aspects of immune response and inflammatory response

**Activation**: antigen-antibody complex or endotoxin, capsule series of proteins activated sequentially

**Inactivation**: inhibitors in plasma (short lived)

**Biological effects**: either beneficial or harmful to host
Complement

• 20 or so proteins that circulate in the blood in an inactive form

• Proteins include C1 through C9, factors B, D, and P, and regulatory proteins

• Provides a major mechanism for destroying foreign substances in the body
Complement

• Amplifies all aspects of the inflammatory response

• Kills bacteria and certain other cell types (our cells are immune to complement)

• Enhances the effectiveness of both nonspecific and specific defenses
Complement Pathways

**Classical Pathway**
- Antigen-antibody complex
- C1
- C4
- C2

**Alternative Pathway**
- Microorganisms’ cell wall polysaccharides
- Factor B, Factor D, and Factor P (properdin)

**Opsonization**
- Coats bacterial surfaces, which enhances phagocytosis

**Causes Inflammation**
- Stimulates histamine release, increased blood vessel permeability, chemotactic attraction of phagocytes, etc.

**Insertion of MAC and Cell Lysis**
- Holes in target cell’s membrane

**Complement Proteins**
- C5b–C9

**Pore**
- Membrane of target cell
Figure 2-19 Immunobiology, 6/e. (© Garland Science 2005)
Part v : Fever
Fever = pyrexia \[\text{IL}_1\]

• A systematic, non specific defensive response caused by
  • infection from bacteria and virus,
  • indicated by abnormal high body temperature.

Beneficial effects of fever:
  • Helps set up specific defense (production of T HELPER cells)
  • Speed up metabolism for tissue repair
  • Increases the antiviral effect of interferons

- IFNs are a class of anti-viral proteins that disrupt viral multiplication
- Not very effective (short-lived and no effect for infected cells)
- Nonspecific to viral types
Fever can be classified as low (oral reading of 99° to 100.4° F [37.2° to 38° C]), moderate (100.5° to 104° F [38.1° to 40° C]), or high (above 104° F). Fever over 106° F (41.1° C) causes unconsciousness and, if sustained, leads to permanent brain damage, HEART BLOCK.

• The body’s thermostat is reset upwards in response to **pyrogens**, chemicals **secreted by leukocytes and macrophages exposed to bacteria** and other foreign substances.

• Fever can be classified as low (oral reading of 99° to 100.4° F [37.2° to 38° C]), moderate (100.5° to 104° F [38.1° to 40° C]), or high (above 104° F). Fever over 106° F (41.1° C) causes unconsciousness and, if sustained, leads to permanent brain damage, HEART BLOCK.
Fever: causes

• Infectious disease is the most common cause of fever in primary patient care.
• Other possible causes of fever are:
  • inflammatory intestinal,
  • joint and connective tissue diseases,
  • allergic reactions,
  • malignant tumours
  • hematological diseases.
Fever

• High fevers are dangerous because they can **denature enzymes**

• Moderate fever can be beneficial, as it causes:
  • The liver and spleen to sequester iron and zinc (needed by microorganisms)
  • An increase in the metabolic rate, which speeds up tissue repair
  • INCREASE IGA
LOW GRADE FEVER LET IT BE
SECRETION OF IGA, KEEP YOU HEALTHIER.
Disruption of hypothalamic thermostat by:
- central nervous system disease
- inherited malignant hyperthermia

Increased production of heat from:
- strenuous exercise or other stress
- chills (skeletal muscle response)
- thyrotoxicosis

Decreased loss of heat from:
- anhidrotic asthenia (heatstroke)
- heart failure
- skin conditions, such as ichthyosis and congenital absence of sweat glands
- drugs that impair sweating

Failure of the body's temperature-regulating mechanisms

FEVER

Elevation of hypothalamic set point

Production of endogenous pyrogens

Entrance of exogenous pyrogens, such as bacteria, viruses, or immune complexes, into the body
Immunoglobulins
Antibodies

• Also called immunoglobulins
  • Constitute the gamma globulin portion of blood proteins
  • Are soluble proteins secreted by activated B cells and plasma cells in response to an antigen
  • Are capable of binding specifically with that antigen

• There are five classes of antibodies: IgD, IgM, IgG, IgA, and IgE
Immunoglobulins (i.e., antibodies)

Antibodies with different specificities differ in the amino acid sequence of the variable regions of the heavy and light chains.

The two heavy chains are identical and the two light chains are identical so the two antigen binding sites are identical.
Two Forms of Immunoglobulin
Immunoglobulin Classes

I. IgG
   - **Structure:** Monomer
   - **Percentage serum antibodies:** 80%
   - **Location:** Blood, lymph, intestine
   - **Half-life in serum:** 23 days
   - **Complement Fixation:** Yes
   - **Placental Transfer:** Yes
   - **Known Functions:** Enhances phagocytosis, neutralizes toxins and viruses, protects fetus and newborn.
Immunoglobulin Classes

II. IgM

- **Structure**: Pentamer
- **Percentage serum antibodies**: 5-10%
- **Location**: Blood, lymph, B cell surface (monomer)
- **Half-life in serum**: 5 days
- **Complement Fixation**: Yes
- **Placental Transfer**: No
- **Known Functions**: First antibodies produced during an infection. Effective against microbes and agglutinating antigens.
Immunoglobulin Classes

III. IgA

- **Structure:** Dimer
- **Percentage serum antibodies:** 10-15%
- **Location:** Secretions (tears, saliva, intestine, milk), blood and lymph.
- **Half-life in serum:** 6 days
- **Complement Fixation:** No
- **Placental Transfer:** No
- **Known Functions:** Localized protection of *mucosal* surfaces. Provides immunity to infant digestive tract.
Immunoglobulin Classes

IV. IgD

- **Structure:** Monomer
- **Percentage serum antibodies:** 0.2%
- **Location:** B-cell surface, blood, and lymph
- **Half-life in serum:** 3 days
- **Complement Fixation:** No
- **Placental Transfer:** No
- **Known Functions:** In serum function is unknown. On B cell surface, initiate immune response.
Immunoglobulin Classes

V. IgE

- **Structure:** Monomer
- **Percentage serum antibodies:** 0.002%
- **Location:** Bound to mast cells and basophils throughout body. Blood.
- **Half-life in serum:** 2 days
- **Complement Fixation:** No
- **Placental Transfer:** No
- **Known Functions:** Allergic reactions. Possibly lysis of worms.
**Table 21.3** Immunoglobulin Classes

IgD is virtually always attached to the external surface of a B cell, where it functions as the antigen receptor of the B cell; important in B cell activation.

IgM exists in monomer and pentamer (five united monomers) forms. The monomer, which is attached to the B cell surface, serves as an antigen receptor. The pentamer (illustrated) circulates in blood plasma and is the first Ig class released by plasma cells during the primary response. (This fact is diagnostically useful because presence of IgM in plasma usually indicates current infection by the pathogen eliciting IgM’s formation.) Because of its numerous antigen-binding sites, IgM is a potent agglutinating agent and readily fixes and activates complement.
TABLE 21.3 Immunoglobulin Classes (continued)

<table>
<thead>
<tr>
<th>Immune Globulin</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IgG (monomer)</strong></td>
<td>IgG is the most abundant and diverse antibody in plasma, accounting for 75–85% of circulating antibodies. It protects against bacteria, viruses, and toxins circulating in blood and lymph, readily fixes complement, and is the main antibody of both secondary and late primary responses. It crosses the placenta and confers passive immunity from the mother to the fetus.</td>
</tr>
<tr>
<td><strong>IgA (dimer)</strong></td>
<td>IgA monomer exists in limited amounts in plasma. The dimer (illustrated), referred to as secretory IgA, is found in body secretions such as saliva, sweat, intestinal juice, and milk, and helps prevent attachment of pathogens to epithelial cell surfaces (including mucous membranes and the epidermis).</td>
</tr>
<tr>
<td><strong>IgE (monomer)</strong></td>
<td>IgE is slightly larger than the IgG antibody. It is secreted by plasma cells in skin, mucosae of the gastrointestinal and respiratory tracts, and tonsils. Its stem region becomes bound to mast cells and basophils, and when its receptor ends are triggered by an antigen, it causes the cells to release histamine and other chemicals that mediate inflammation and an allergic reaction. Typically only traces of IgE are found in plasma, but levels rise during severe allergic attacks or chronic parasitic infections of the gastrointestinal tract.</td>
</tr>
</tbody>
</table>

Copyright © 2006 Pearson Education, Inc., publishing as Benjamin Cummings.
Immunoglobulin, Ig

- Definition: Glycoprotein molecules that are produced by plasma cells in response to an immunogen and which function as antibodies.
- The immunoglobulins are a group of glycoproteins present in the serum and tissue fluids of all mammals.
Immune serum
Ag adsorbed serum
albumin
globulins

Amount of protein

Mobility

α₁ α₂ β γ

Immune serum
Ag adsorbed serum
albumin
globulins
ADAPTIVE IMMUNE SYSTEM

T-lymphocytes
- T-cytotoxic
- Cytoxic

B-lymphocytes
- Plasma cells
- Antibodies

Response takes 7 to 10 days
Adaptive Immune System

- T and B Lymphocytes
- Highly specific for pathogen
- Response improves with repeated exposure
- Memory
- Life-long immunity
T versus B cell Response

B cells recognise native antigen
T cells recognise processed antigen
Part VII: Antibodies - Antigens
Consequences of Antibody Binding

- **Agglutination**: Enhances phagocytosis and reduces number of infectious units to be dealt with.
- **Protector mechanism of binding antibodies to antigens**:
  - **Activation of complement**: Cell lysis
  - **Opsonization**: Coating antigen with antibody enhances phagocytosis
  - **Inflammation**: Disruption of cell by complement/reactive protein attracts phagocytic and other defensive immune system cells
  - **Neutralization**: Blocks adhesion of bacteria and viruses to mucosa
  - **Antibody-dependent cell-mediated cytotoxicity**: Antibodies attached to target cell cause destruction by non-specific immune system cells

© BENJAMIN/CUMMINGS
Consequences of Antigen-Antibody Binding

Antigen-Antibody Complex: Formed when an antibody binds to an antigen it recognizes.

Affinity: A measure of binding strength.

1. **Agglutination:** Antibodies cause antigens (microbes) to clump together.
   - IgM (decavalent) is more effective that IgG (bivalent).
   - **Hemagglutination:** Agglutination of red blood cells. Used to determine ABO blood types and to detect influenza and measles viruses.

2. **Opsonization:** Antigen (microbe) is covered with antibodies that enhances its ingestion and lysis by phagocytic cells.
Humoral Immunity (Continued)

3. **Neutralization:** IgG inactivates viruses by binding to their surface and neutralize toxins by blocking their active sites.

4. **Antibody-dependent cell-mediated cytotoxicity:** Used to destroy large organisms (e.g.: worms). Target organism is coated with antibodies and bombarded with chemicals from nonspecific immune cells.

5. **Complement Activation:** Both IgG and IgM trigger the complement system which results in cell lysis and inflammation.
Consequences of Antibody Binding

- **Binding of antibodies to antigens inactivates antigens by**
  - **Neutralization** (blocks viral binding sites; coats bacteria and/or opsonization)
  - **Agglutination of antigen-bearing particles, such as microbes**
  - **Precipitation of soluble antigens**
  - **Complement fixation (activation of complement)**

- **Enhances**
  - **Phagocytosis**
  - **Macrophage**

- **Leads to**
  - **Cell lysis**

©1999 Addison Wesley Longman, Inc.
Vaccination

* Vaccination prevents and control such diseases as cholera, rabies, poliomyelitis, diphtheria, tetanus, measles, and typhoid fever

* Vaccines can be:

a- prophylactic (e.g. to prevent the effects of a future infection by any natural or "wild" pathogen

b- Therapeupic (e.g. vaccines against cancer are also being investigated)

Dr. Schreiber of San Augustine giving a typhoid inoculation at a rural school, San Augustine County, Texas. Transfer from U.S. Office of War Information, 1944.
Vaccination

Vaccination:
*Producing immunity against pathogens (viruses and bacteria) by the introduction of live, killed, or altered antigens that stimulate the body to produce antibodies against more dangerous forms

*Vaccines work with the immune system's ability to recognize and destroy foreign proteins (antigens)
Vaccination

Immunization of young children and adolescents:

- Hepatitis B (HepB) and Hepatitis A (HepA)

- Diphtheria, tetanus and pertussis (whooping cough) given together as DTaP (formerly DTP)

- *Haemophilus influenzae b* (Hib)

- Poliomyelitis (IPV)

- Measles, Mumps, and Rubella, given together as MMR

- Chicken pox (Var)

- *Neisseria meningitidis* (meningococcal meningitis)
<table>
<thead>
<tr>
<th>Dose one (minimum age)</th>
<th>Minimum interval between doses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dose one to dose two</td>
</tr>
<tr>
<td>DTaP (6 wks)</td>
<td>4 wks</td>
</tr>
<tr>
<td>IPV (6 wks)</td>
<td>4 wks</td>
</tr>
<tr>
<td>HepB&lt;sup&gt;3&lt;/sup&gt; (birth)</td>
<td>4 wks</td>
</tr>
<tr>
<td>MMR (12 mos)</td>
<td>4 wks</td>
</tr>
<tr>
<td>Varicella (12 mos)</td>
<td></td>
</tr>
<tr>
<td>Hib&lt;sup&gt;5&lt;/sup&gt; (6 wks)</td>
<td>4 wks&lt;sup&gt;1&lt;/sup&gt; if 1&lt;sup&gt;st&lt;/sup&gt; dose given at age &lt;12 mos</td>
</tr>
<tr>
<td></td>
<td>8 wks (as final dose): if 1&lt;sup&gt;st&lt;/sup&gt; dose given at age 12–24 mos</td>
</tr>
<tr>
<td></td>
<td>No further doses needed: if 1&lt;sup&gt;st&lt;/sup&gt; dose given at age ≥15 mos</td>
</tr>
<tr>
<td>PCV&lt;sup&gt;7&lt;/sup&gt; (6 wks)</td>
<td>4 wks&lt;sup&gt;1&lt;/sup&gt; if 1&lt;sup&gt;st&lt;/sup&gt; dose given at age &lt;12 mos and current age &lt;24 mos</td>
</tr>
<tr>
<td></td>
<td>8 wks (as final dose): if 1&lt;sup&gt;st&lt;/sup&gt; dose given at age ≥12 mos or current age 24–59 mos</td>
</tr>
<tr>
<td></td>
<td>No further doses needed: for healthy children if 1&lt;sup&gt;st&lt;/sup&gt; dose given at age ≥24 mos</td>
</tr>
</tbody>
</table>

1. Diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP): The fifth dose is not necessary if the fourth dose was given after the fourth birthday.
2. Inactivated Polio (IPV): For children who received an all-IPV or all-OPV series, a fourth dose is not necessary if third dose was given at age ≥4 years. If both OPV and IPV were given as part of a series, a total of 4 doses should be given, regardless of the child’s current age.
3. Hepatitis B vaccine (HepB): All children and adolescents who have not been vaccinated against hepatitis B should begin the hepatitis B vaccination series during any visit. Providers should make special efforts to immunize children who were born in, or whose parents were born in, areas of the world where hepatitis B virus infection is moderately or highly endemic.
4. Measles, mumps, and rubella vaccine (MMR): The second dose of MMR is recommended routinely at age 4–6 years, but may be given earlier if desired.
5. Haemophilus influenzae type b (Hib): Vaccine is not recommended generally for children aged ≥5 years.
6. Hib: If current age is <12 months and the first 2 doses were PRP-OMP (PedvaxHIB<sup>®</sup> or ComVax<sup>®</sup> Merck<sup>®</sup>), the third (and final) dose should be given at age 12–15 months and at least 8 weeks after the second dose.
7. Pneumococcal conjugate vaccine (PCV): Vaccine is not recommended generally for children aged ≥5 years.
### TABLE 2. Catch-up schedule for children aged 7–18 years

<table>
<thead>
<tr>
<th></th>
<th>Minimum interval between doses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dose one to dose two</td>
</tr>
</tbody>
</table>
| **Td:**                 | 4 wks                       | Td: 6 mos               | Td\(^1\): 6 mos: if 1\(^{st}\) dose given at age \(<12\) mos and current age \(<11\) yrs  
                           |                             |                         | 5 yrs: if 1\(^{st}\) dose given at age \(\geq12\) mos and 3\(^{rd}\) dose given at age \(<7\) yrs and current age \(\geq11\) yrs  
                           |                             |                         | 10 yrs: if 3\(^{rd}\) dose given at age \(\geq7\) yrs |
| **IPV\(^2\):**          | 4 wks                       | IPV\(^2\): 4 wks        | IPV\(^2\): 4 wks |
| **HepB:**               | 4 wks                       | HepB: 8 wks (and 16 wks after 1\(^{st}\) dose) | IPV\(^2\): 4 wks |
| **MMR:**                | 4 wks                       |                           | IPV\(^2\): 4 wks |
| **Varicella:**          | 4 wks                       |                           | IPV\(^2\): 4 wks |

1. **Tetanus toxoid**: For children aged 7–10 years, the interval between the third and booster dose is determined by the age when the first dose was given. For adolescents aged 11–18 years, the interval is determined by the age when the third dose was given.
2. **Inactivated Polio (IPV)**: Vaccine is not recommended generally for persons aged \(\geq18\) years.
3. **Varicella**: Give 2-dose series to all susceptible adolescents aged \(\geq13\) years.
FIGURE. Recommended childhood and adolescent immunization schedule¹ — United States, 2003

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Birth 1 mo</th>
<th>2 mos</th>
<th>4 mos</th>
<th>6 mos</th>
<th>12 mos</th>
<th>15 mos</th>
<th>18 mos</th>
<th>24 mos</th>
<th>4–6 yrs</th>
<th>11–12 yrs</th>
<th>13–18 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B² (HepB)</td>
<td>HepB #1</td>
<td></td>
<td></td>
<td></td>
<td>HepB #2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diphtheria, Tetanus, Pertussis (DTaP)</td>
<td>DIP</td>
<td>DIP</td>
<td>DIP</td>
<td></td>
<td></td>
<td>DIP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae Type b (Hib)</td>
<td>Hib</td>
<td>Hib</td>
<td>Hib</td>
<td>Hib</td>
<td></td>
<td>Hib</td>
<td>Hib</td>
<td>Hib</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inactivated Polio</td>
<td>IPV</td>
<td>IPV</td>
<td>IPV</td>
<td>IPV</td>
<td>IPV</td>
<td>IPV</td>
<td>IPV</td>
<td>IPV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles, Mumps, Rubella¹</td>
<td>MMR #1</td>
<td></td>
<td></td>
<td></td>
<td>MMR #2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella⁶</td>
<td>Varicella</td>
<td>Varicella</td>
<td>Varicella</td>
<td>Varicella</td>
<td>Varicella</td>
<td>Varicella</td>
<td>Varicella</td>
<td>Varicella</td>
<td>Varicella</td>
<td>Varicella</td>
<td></td>
</tr>
<tr>
<td>Pneumococcal⁷</td>
<td>PCV</td>
<td>PCV</td>
<td>PCV</td>
<td>PCV</td>
<td>PCV</td>
<td>PCV</td>
<td>PCV</td>
<td>PCV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis A⁸</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza⁹</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Vaccines below this line are for selected populations

1. Indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2002, for children through age 18 years. Any dose not given at the recommended age should be given at any subsequent visit when indicated and feasible. ²Indicates age groups that warrant special effort to administer those vaccines not given previously. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and the vaccine's other components are not contraindicated. Providers should consult the manufacturers' package inserts for detailed recommendations.

2. Hepatitis B vaccine (HepB). All infants should receive the first dose of HepB vaccine soon after birth and before hospital discharge; the first dose also may be given by age 2 months if the infant's mother is HBSAg-negative. Only monovalent HepB vaccine may be used for the birth dose. Monovalent or combination vaccine containing HepB may be used to complete the series; 4 doses of vaccine may be given when a combination vaccine is used. The second dose should be given at least 1 month after the first dose except for combination vaccines, which cannot be administered before age 6 weeks. The third dose should be given at least 1 month after the second dose. The last dose in the vaccination series (third or fourth dose) should be administered before age 6 months. Infants born to mothers whose HIV status is unknown should receive the first dose of the HepB vaccine series within 12 hours of birth. A maternal blood sample should be drawn as soon as possible to determine the mother's HIV status; if the HIV status is positive, the infant should receive HBIG as soon as possible (no later than age 1 week). The second dose is recommended at age 1–2 months. The last dose in the vaccination series should be administered before age 6 months. These infants should be tested for HBsAg and anti-HBs at ≥6–12 months of age. Infants born to mothers whose HIV status is known should receive the first dose of the HepB vaccine series within 12 hours of birth. The maternal blood sample should be drawn as soon as possible to determine the mother's HIV status; if the mother is positive, the infant should receive HBIG as soon as possible (no later than age 1 week). The second dose is recommended at age 1–2 months. The last dose in the vaccination series should be administered before age 6 months.

3. Diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP). The fourth dose of DTaP may be administered at age 12 months provided that 6 months have elapsed since the third dose and the child is unlikely to return at age 15–18 months. Diphtheria and tetanus toxoids (Td) is recommended at age 11–12 years if at least 5 years have elapsed since the last dose of Td-containing vaccine. Subsequent routine Td boosters are recommended every 10 years.

4. Haemophilus influenzae type b (Hib) conjugate vaccine. Three Hib conjugate vaccines are licensed for infant use. If PRP-OMP (PedvaxHIB® or Comvax [Merck]) is administered at age 2 months, 1 dose at age 4 months is not required. DTaP-Hib combination products should not be used for primary vaccination in infants age 2, 4, or 6 months but can be used as boosters following any Hib vaccine. The second dose of MMR vaccine administration should be given at age 11–12 years. MMR-containing vaccines are recommended routinely at age 4–6 years but may be administered during any visit provided that at least 4 weeks have elapsed since the first dose and that both doses are administered beginning at or after age 12 months. Those who have not received the second dose previously should complete the series by the visit at age 11–12 years.

5. Varicella vaccine. Varicella vaccine is recommended at any visit at or after age 12 months for susceptible children (i.e., those who lack a reliable history of chickenpox). Susceptible persons aged ≤13 years who should receive 2 doses given at least 4 weeks apart. The first dose should be administered at age 12 months or older. The second dose should be administered at age 4–6 years. Additional information about vaccines, including precautions and contraindications for vaccination and vaccine shortages, is available at http://www.cdc.gov/nip or at the National Immunization Information hotline, telephone 800–232–2322 (English) or 800–232–0333 (Spanish). Copies of the schedule can be obtained at http://www.cdc.gov/nip/recs/child-schedule.htm. Approved by the Advisory Committee on Immunization Practices (http://www.cdc.gov/nip/acip), the American Academy of Pediatrics (http://www.aap.org), and the American Academy of Family Physicians (http://www.aafp.org).
Hypersensitivity Reaction

Henoch-Schonlein purpura
Hypersensitivity Reaction

**Hypersensitivity or allergy**

* An immune response results in exaggerated reactions harmful to the host

* There **are four types** of hypersensitivity reactions:

  Type I, Type II, Type III, Type IV

* Types I, II and III are antibody mediated

* Type IV is cell mediated
Type I: Immediate hypersensitivity

* An antigen reacts with cell **fixed antibody (Ig E)**
  leading to release of soluble molecules
An antigen (allergen)
soluble molecules (mediators)

* Soluble molecules cause the manifestation of disease

* **Systemic life threatening; anaphylactic shock**

* Local atopic allergies; bronchial asthma, hay fever and food allergies
Pathogenic mechanisms

* Three classes of mediators derived from mast cells:

1) Preformed mediators stored in granules (histamine)

2) Newly sensitized mediators:
leukotrienes, prostaglandins, platelets activating factor

3) Cytokines produced by activated mast cells, basophils
e.g. TNF, IL3, IL-4, IL-5 IL-13, chemokines

* These mediators cause: smooth muscle contraction,
mucous secretion and bronchial spasm, vasodilatation,
vascular permeability and edema
Anaphylaxis

* Systemic form of Type I hypersensitivity

* Exposure to allergen to which a person is previously sensitized

* Allergens:
  Drugs: penicillin
  Serum injection: anti-diphtheritic or ant-tetanic serum
  anesthesia or insect venom

* Clinical picture:
  Shock due to sudden decrease of blood pressure, respiratory distress due to bronhospasm, cyanosis, edema, urticaria

* Treatment: corticosteroids injection, epinephrine, antihistamines
Atopy

* Local form of type I hypersensitivity

* Exposure to certain allergens that induce production of specific Ig E

* Allergens:
  Inhalants: dust mite feces, tree or pollens, mould spor.
  Ingestants: milk, egg, fish, chocolate
  Contactants: wool, nylon, animal fur
  Drugs: penicillin, salicylates, anesthesia insect venom

* There is a strong familial predisposition to atopic allergy

* The predisposition is genetically determined
Type II: Cytotoxic or Cytolytic Reactions

* An antibody (Ig G or Ig M) reacts with antigen on the cell surface

* This antigen may be part of cell membrane or circulating antigen (or hapten) that attaches to cell membrane
Clinical Conditions

1) Transfusion reaction due to ABO incompatibility

2) Rh-incompatability (Haemolytic disease of the newborn)

3) Autoimmune diseases
   The mechanism of tissue damage is cytotoxic reactions
   e.g. SLE, autoimmune haemolytic anaemia, idiopathic thrombocytopenic purpura, myasthenia gravis, nephrotoxic nephritis, Hashimoto’s thyroiditis

4) A non-cytotoxic Type II hypersensitivity is Graves’s disease
   It is a form of thyroditits in which antibodies are produced against TSH surface receptor
   This lead to mimic the effect of TSH and stimulate cells to over-produce thyroid hormones
Clinical Conditions

5- Graft rejection cytotoxic reactions:
   In hyperacute rejection the recipient already has performed antibody against the graft

6- Drug reaction:
   Penicillin may attach as haptens to RBCs and induce antibodies which are cytotoxic for the cell-drug complex leading to haemolysis

   Quinine may attach to platelets and the antibodies cause platelets destruction and thrombocytopenic purpura
Penicillin Allergy

Emory U./Dr. Sellers
Type III Hypersensitivity

Immune Complex Mediated Reaction
Type III: Immune Complex Mediated Reaction

* When antibodies (Ig G or Ig M) and antigen coexist immune complexes are formed

* Immune complexes are removed by reticuloendoth. syst.

* Some immune complexes escape phagocytosis

* Immune complexes deposited in tissues on the basement membrane of blood vessels and cause tissue injury
Mechanism Of Tissue Injury

Immune complexes trigger inflammatory processes:

1) Immune complexes activate the complement, releasing anaphylatoxins C3a, C5a.

   stimulate release
   degranulation of basophiles and mast cells histamine

   Histamine stimulates vascular permeability and helps deposition of immune complexes.

2) Neutrophils are attracted to the site by immune complexes and release lysosomal enzymes which damage tissues and intensify the inflammatory process.

3) Platelets are aggregated with two consequences:
   a- release of histamine
   b- formation of microthrombi which lead to ischemia.
Clinical conditions of Type III Hypersensitivity

Diseases produced by immune complexes are those in which antigens persists without being eliminated as:

a- Repeated exposure to extrinsic antigen

b- Injection of large amounts of antigens

c- Persistent infections

d- Autoimmunity to self components
1- Arthus Reaction

* This is a local immune complex deposition phenomenon e.g. diabetic patients receiving insulin subcutaneously

* Local reactions in the form of edema, erythema, necrosis

* Immune complexes deposited in small blood vessels leading to vasculitis, microthrombi formation, vascular occlusion, necrosis.
2- Serum Sickness

* A systemic immune complex phenomenon
* Injection of large doses of foreign serum
* Antigen is slowly cleared from circulation
* Immune complexes are deposited in various sites

* 10 days after injection

  - fever
  - urticaria
  - arthralgia
  - lymphadenopathy
  - splenomegaly
  - glomerulonephritis
  - antidiphtheritic serum
  - penicillin
  - sulphonamides

* e.g. treatment with
Type IV
Cell Mediated
Delayed Type Hypersensitivity
Type IV: Cell Mediated Delayed Type Hypersensitivity

triggering DTH reactions by TH1

* T-cells cause tissue injury by or
directly killing target cells by CD8

* TH1 and CD8 T cells secrete cytokines (IFN-γ and TNF)

* Cytokines
  - attract lymphocytes
  - activate macrophages
  - induce inflammation

* Tissue damage results from products of activated macrophages
Tuberculin – Type Hypersensitivity

* When PPD is injected intradermally in sensitized person

* Local indurated area appears injection site (48-72 hs)

* Indurations due to accumulation of:
  macrophages and lymphocytes

* Similar reactions observed in diseases
  e.g. brucellosis, lepromin test in leprosy, Frei’s test in lymphogranuloma venereum

THERE IS MORE TO IT
NOT REQUIRED TO KNOW UNLESS MEDSCHOOLER
T CELLS IMMUNODEFICIENCY = DIE FROM VIRAL INFECTION = CMV

- DIGEORGE SYNDROME [THE ONLY IMMUNODEFICIENCY WITH HYPOCALCEMIA]
- CHRONIC MUCOCUTANEOUS CANDIDIASIS
- STEROIDS
- CYCLOSPORINE
- HAIRY CELL LEUKEMIA
- SCID
- WISKOTT-ALDRIDGE SYNDROME
- HIV
Steroids

• Anti-inflammatory action:
  • Kills T cells and eosinophils
  • Inhibit macrophages migration
  • Stabilizes mast cells membranes
  • Stabilizes endothelium
  • Inhibits phospholipase a
The end

- Stop complaining, it has been resumed

It can be worst