Pathologic Immune Responses

- Hypersensitivity Reactions:
  - Allergic Responses - An over-response to an antigen
  - Autoimmunity - Body makes antibodies against its own tissues
  - Allelloimmunity - "Graft rejection" grafted tissue is recognized as foreign

- Immunodeficiencies
  Body is not able to produce an adequate immune response

Hypersensitivity Reactions:
Four types of mechanisms involved
- Ig E mediated Reactions (Type I)
- Tissue Specific Reactions (Type II)
- Immune Complex mediated Reactions (Type III)
- Cell mediated Reactions (Type IV)
Figure 7-1 Mechanism of type I, IgE-mediated reactions.
Initial (first exposure) sensitization to an allergen stimulates B lymphocytes, which differentiate into plasma cells. Upon subsequent exposure (second exposure), IgE antibodies bind to Fc receptors on mast cells, leading to degranulation and release of histamine. This produces an inflammatory response experienced as the allergic response to the antigen. Respiratory airways, GI tract, and skin are sites with abundant mast cells.
**Type I Rxns**
Result from production of IgE antibodies after exposure to an antigen.

**Type II Rxns**
Antibodies are produced against membrane proteins normally expressed on cell membranes.

*EX. Myasthenia Gravis*
Body produces antibodies that bind to acetylcholine receptors on muscle fibers, resulting in destruction of the receptors leading to muscle weakness.
Antibody opsonizes cell for phagocytosis

Complement-mediated lysis

Phagocytosis by extravascular macrophage

Complement system activated

Neutrophils attracted to site and release chemical agents that damage tissue

Neutrophil-mediated damage

Receptor may be activated or deactivated when antibody binds to it

Copyright © 2008 by Mosby, Inc., an affiliate of Elsevier Inc.
Type III \textit{Rxns}

Antigen - Antibody complexes forming in the circulation and then depositing in the walls of blood vessels or other tissues.
Antibody-Antigen complex forms in circulation

Ab-Antigen complex deposits in tissues

Neutrophils release chemical agents that damage tissue

Ex. Systemic Lupus Erythematosus
Type III Rxn

Results from activation of T cells + macrophages.

Sometimes referred to as a delayed hypersensitivity Rxn because the Rxn doesn't occur immediately upon exposure.
T Cytotoxic cell

T Helper cell

T Cell receptor

Apoptosis

Antigen

Lysosomal granules

Activated macrophage

Lysozymes

Free radicals released by macrophages that damage the tissue

Ex. Allergic reaction to poison ivy

Poison Ivy produces a chemical that combines with membrane protein on skin cells
Immunodeficiencies

Result from impaired function of one or more of the components of the immune and/or inflammatory systems.

Two categories:
- Congenital Immunodeficiencies
- Acquired Immunodeficiencies

Congenital immunodeficiencies result from genetic abnormalities (person is born with it).

Usually kill the person early in life

Ex DiGeorge Syndrome
Thymus is absent or underdeveloped.
So, there is a lack or absences of
T cells.

Acquired immunodeficiencies are result of an external factor:

- Poor nutrition:
  Affects both T and B cell number, as well as plasmatic protein production.

- Medical treatments:
  (Infectious immunodeficiency)
  Ex. Chemotherapeutic drugs can kill B and T cells.

- Burns:
  Severe burns depress normal immune responses, particularly neutrophil function, and level of plasmatic proteins in body.
Stress

Spleen + thymus are innervated by the autonomic nervous system, imbalance between sympathetic + parasympathetic activity can alter function of these lymphoid organs.

AIDS (Acquired Immunodeficiency Syndrome)

Caused by the HIV virus

Retrovirus—carry their genetic info in the form of RNA rather than DNA

When HIV infects a cell, it injects the cell with its RNA together with an enzyme called Reverse Transcriptase
Once inside the cell the reverse transcriptase converts the viral RNA into viral DNA, which subsequently is inserted into the DNA of the host cell.

CD4 acts as the primary receptor for the HIV virus.

Main cells expressing CD4 are Th cells.

Infection of Th cells results in a reduction in the # of Th cells in the infected person.

This severely compromises the person's immune system.
Treatment for AIDS involves the use of two antimicrobial agents:

- **AZT**—Azidothymidine—works by preventing the reverse transcriptase from converting viral RNA into viral DNA

- **Protease Inhibitors**—Inhibit viral enzymes from making viral proteins

- **Entrance inhibitors**—prevent virus from injecting its RNA into the cell

- **Integrate Inhibitors**—prevent viral DNA from integrating into host DNA
Endocrine System

Endocrine glands synthesize and secrete hormones distributed through circulation by the blood. Hormones help to coordinate physiologic functions of the cells and body.
Heart muscle cells produce a hormone Atrial Natriuretic Peptide (ANP) involved in salt and water balance in the body.

Figure 17-1 Principal endocrine glands. (From Thibodeau GA, Patton KT: Anatomy & physiology, ed 5, St Louis, 2003, Mosby.)
Endocrine System acts in coordination with the nervous system to maintain homeostasis in the body.

Disruption in the normal functioning of the endocrine system results in a disruption of homeostasis.

3 categories of endocrine dysfunctions

— Too little hormone in the blood.

Two common causes:
— Hyposecretion of the hormone, due to:
  - tumor in the endocrine gland producing the hormone
- Atrophy of the endocrine gland producing the hormone
  loss of hormone synthesizing cells

- Failure of normal feedback mechanisms that stimulate the synthesis and secretion of the hormone.

- Too much hormone in the blood.

3 common causes:

- Hypersecretion of the hormone by the endocrine cell. Due hyperplasia of the endocrine cells, or tumor in the endocrine gland.

- Failure of feedback mechanisms that normally serve to decrease synthesis and secretion of the hormone.
- Secretion of the hormone by ectopic tissues (don't normally synthesize & secrete the hormone).
  Ex. Lung tumors secrete hormones.

- Abnormal Target Cell responses

  - Receptor Associated Disorders
    - decrease in the # of receptors being expressed by the target cell.
    - Receptor structure is faulty so hormone can't bind and activate receptor normally

  - Abnormal intracellular response to hormone binding to receptor
Pituitary Gland

most important endocrine gland

- Synthesizes and secretes 9 hormones.
  Some are trophic hormones (ex. TSH, ACTH) that control
  the synthesis and secretion of other hormones.

- Synthesis and secretion of the pituitary hormones is
  under the influence of the nervous system. Specifically,
  the hypothalamus, which sets
  & regulates the daily rhythms
  of the body.
Figure 17-8 Hypophysial portal system. Neurons in the hypothalamus synthesize releasing hormones. These hormones are transported down to the hypophysial portal system. Released hormones stimulate the anterior hypophysial artery to secrete releasing hormones. Hypothalamic neurosecretory cells synthesize releasing hormones.
synthesize and secrete hormones into circulation in post. pit.
Endocrine Related Diseases

Diseases involving the pituitary:

- Syndrome of Inappropriate ADH secretion (SIADH)
- Diabetes Insipidus

SIADH

characterized by oversecretion of ADH leading to excess water retention in the body.

Most commonly caused by ectopic secretion of ADH by tumor cells. Ex: Adenocarcinomas of the lungs, carcinomas of the duodenum, carcinomas of the pancreas, and lymphomas.
Since these cancer cells are not sensitive to normal feedback mechanisms that regulate ADH levels in the blood, the synthesis and secretion of ADH by these cells result in increased levels of ADH in the blood.

ADH regulates water reabsorption by the kidneys.
280 mOsm

↑ decreased reabsorption of water increases body fluid conc.

↓ water reabsorption from filtrate by the kidneys

↑ ADH levels in the blood

↓ decrease synthesis and secretion of ADH

↑ ADH levels in the blood

↓ water reabsorption from filtrate by the kidneys

↑ water dilutes body fluids

↓ 280 mOsm

↑ sensed by neurosecretory cells of hypothalamus

↓ sensed by neurosecretory cells in hypothalamus

↑ increase synthesis and secretion of ADH
Too much ADH in the blood causes abnormal reabsorption of water from the filtrate in the kidneys.

It has 3 effects on the body:

- Expands the volume of the body fluids, particularly the blood volume → ↑ Blood pressure
  
  \[
  \text{ADH = Vasopressin} \text{ - causes contraction of blood vessel smooth muscle}
  \]

- Excess water in the body dilutes the normal ionic concentrations of the body fluids.

→ cause Hyponatremia - very low Na⁺ conc. in body fluids
APB inhibits the Renin-Angiotensin-Aldosterone system which regulates Na+ reabsorption by the kidneys → inhibition of this system results in loss of Na+ through the urine.

So, have increased loss of Na+ in urine, and dilution of Na+ remaining in the body fluids.

Maintaining normal Na+ levels in the body fluids is critical for normal functioning of the nervous system.

So, in SIADH you get:
- Dulling of the senses
- Muscle twitching
- Mental confusion
- Convulsions
- Coma & death if left untreated.

Treatment of SIADH:
- Removal of ectopic tissue secreting the excess ADH
- Na+ replacement
- Restriction of fluid intake
- Use of diuretic drugs to promote water loss through the urine to bring volume of body fluids down to normal.