Important terms:

- **Hypersensitivity** – immune responses that causes tissue damage
- **Autoimmune disease** – immune responses to self-antigens
- **Immunodeficiency** – insufficient immune response

Topics

- Transplantation immunity
- Autoimmune diseases
- Immunodeficiency disorders
Transplantation immunity

- Allografts
- Xenografts
- Genetically non–identical grafts cause rejections
- Type IV reaction – delayed cell-mediated
  - Immunological rejection of transplant
    - Killing of graft by sensitized cytotoxic T cells
    - Natural killer cells (ADCC)
    - MHC antigens major cause of rejection
  - Requires immunosuppression for successful transplants
    - Cyclosporin A, tacrolimus
    - Interfere with cell signaling
    - Inhibit clonal expansion of T cells

Autoimmune disease

Negative selection eliminates self reactive lymphocytes
Autoimmune diseases caused by body responding to self antigens
MHC genes involved; genetically based
Autoimmune disease

- Spectrum of autoimmune reactions
- Treatment of autoimmune diseases

<table>
<thead>
<tr>
<th>Disease (Known MHC Relationship)</th>
<th>Organ Specificity</th>
<th>Major Mechanism of Tissue Damage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graves’ disease (DR3)</td>
<td>Thyroid</td>
<td>Autoantibodies bind thyroid-stimulating hormone receptor, causing overstimulation of thyroid.</td>
</tr>
<tr>
<td>Malignant granulomatosis (DR3)</td>
<td>Muscle</td>
<td>Autoantibodies bind to acetylcholine receptor on muscle, preventing muscle contraction.</td>
</tr>
<tr>
<td>Insulin-dependent diabetes mellitus (DR3/DR4)</td>
<td>Pancreas</td>
<td>γ-Cell destruction of pancreatic cells.</td>
</tr>
<tr>
<td>Autoimmune hemolytic anemia</td>
<td>Red blood cells</td>
<td>Antibody, complement, and phagocyte destruction of red cells.</td>
</tr>
<tr>
<td>Rheumatoid arthritis (DR4)</td>
<td>Widespread, especially joints</td>
<td>Lymphocytic destruction of joint tissues; immune complexes of IgG and anti-IgG. Type III Hypersensitivity.</td>
</tr>
<tr>
<td>Systemic lupus erythematosus (DR3)</td>
<td>Widespread (glomerulonephritis, vasculitis, arthritis)</td>
<td>Autoantibodies to DNA and other nuclear components form immune complexes in small blood vessels. Type III.</td>
</tr>
</tbody>
</table>
Treatment of autoimmune diseases

- Immunosuppressants (eg cyclosporins)
- Anti-inflammatory drugs (eg steroids)
- Replacement therapy (eg insulin, thyroid hormone)
- Feeding or oral tolerance (induce tolerance to antigen)
  - Feed insulin for diabetes
  - Collagen for rheumatoid arthritis
  - Cause local intestinal immune response, down regulation of antigen receptors deletion of immune cells

Immunodeficiency disorders

- Primary immunodeficiencies (genetic, inborn)
- Secondary immunodeficiencies (acquired, disease)
Primary immunodeficiencies

- Lack of B – cell function
- Lack of the different T – cell functions
- Lack of both T and B cell functions
- Defective phagocytes

Table 18.6 Some Primary Immunodeficiency Diseases for Which Genetic Defects Are Known

<table>
<thead>
<tr>
<th>Severe combined immunodeficiency (SCID)</th>
<th>no functional T, B cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-linked SCID</td>
<td></td>
</tr>
<tr>
<td>MHC class II deficiency</td>
<td>*</td>
</tr>
<tr>
<td>CD3 deficiency</td>
<td></td>
</tr>
<tr>
<td>CD8 deficiency</td>
<td></td>
</tr>
<tr>
<td>X-linked agammaglobulinemia</td>
<td>no Ig</td>
</tr>
</tbody>
</table>

X-linked hyper-IgM syndrome
Wiscott-Aldrich syndrome
Ataxia telangiectasia
* Chronic granulomatous disease
* Leukocyte adhesion deficiency
* Many complement deficiencies
Secondary immunodeficiencies

- Malnutrition
- Immunosuppressive agents
- Infections (measles, AIDS, SARS, promote secondary infections)
- Malignancies (multiple myeloma – from one B cell)
  - consumes immune resources
  - can’t mount normal responses