Hemolytic disease of the newborn is caused primarily by clearance of fetal Rh+ red blood cells that have bound maternal Rh IgG. Cytotoxic clearance of the IgG bound fetal blood cells occurs primarily via destruction by macrophages in the fetal spleen. In contrast, RBCs bound by recipient IgM in transfusion reactions are agglutinated, then eliminated primarily by complement activation and hemolysis of the transfused RBCs.

Important terms:

- Hypersensitivity – immune responses that cause 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
      - abundant on leukocytes = HLAs
      - tissue typing minimizes incompatibility

Requires immunosuppression for successful transplants
- minor antigens cause rejection
- immunosuppressants may be needed indefinitely
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
- Specificity leads to fewer side effects than radiation and cytotoxicity inhibitors

The fetus as allograft (Perspective 18.1 – page 452)

- Half the fetus’ antigens are foreign (father’s)
- Fetus is thus an allograft, but is not rejected. Why?
- Mother makes anti-Rh, anti-MHC antibodies
- Mother in fact has small number of fetal cells in circulation
- Therefore not due to lack of exposure to fetal antigen
- Trophoblast forms barrier as outer layer of placenta
- No MHC molecules expressed
- NK cells suppressed
- “Immunologically privileged” sites; do not drain via lymph
- Avoid APCs and immune stimulation
- Also produce immunosuppressive cytokines
- Pregnancy also causes immunosuppression in mother

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 18.4 Characteristics of Some Autoimmune Diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Organ Specificity</th>
<th>Major Mechanism of Tissue Damage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graves’ disease</td>
<td>Thyroid</td>
<td>Autoantibodies to thyroid stimulating hormones, goiter formation.</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Pancreas</td>
<td>Autoantibodies to insulin receptor, diabetes mellitus.</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>Kidney</td>
<td>Autoantibodies to nuclear antigens, glomerulonephritis.</td>
</tr>
</tbody>
</table>

Treatment of autoimmune diseases

- Immunosuppressants (eg cyclosporins)
- Anti-inflammatory drugs (eg steroids)
- Replacement therapy (eg insulin, thyroid hormone)

*including transplantation of pancreatic insulin-producing cells for insulin-dependent diabetes*
Treatment of autoimmune diseases

- Immunosuppressants (e.g., cyclosporins)
- Anti-inflammatory drugs (e.g., steroids)
- Replacement therapy (e.g., 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>Disease/Condition</th>
<th>Disorder/Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe combined immunodeficiency (SCID)</td>
<td>no functional T, B cells</td>
</tr>
<tr>
<td>X-linked SCID</td>
<td>X-linked hyper-IgM syndrome</td>
</tr>
<tr>
<td>MHC class II deficiency</td>
<td>Wisott-Aldrich syndrome</td>
</tr>
<tr>
<td>CD3 deficiency</td>
<td>Ataxia telangiectasia</td>
</tr>
<tr>
<td>CD8 deficiency</td>
<td>Chronic granulomatous disease</td>
</tr>
<tr>
<td>X-linked agammaglobulinemia</td>
<td>Leukocyte adhesion deficiency</td>
</tr>
<tr>
<td></td>
<td>*Many complement deficiencies</td>
</tr>
</tbody>
</table>

**Treatments for primary immunodeficiencies**

- eg SCID children
  - bone marrow transplants
  - repair faulty genes
  - adenosine deaminase needed for B, T cell proliferation
  - replacement therapy with enzyme
  - collect T cells, introduce deaminase gene

**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