

*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*

18-1

## Transplantation immunity

18-4

### Important terms:

**Hypersensitivity** – immune responses that causes tissue damage

**Autoimmune disease** – immune responses to self-antigens

**Immunodeficiency** – insufficient immune response

18-2

## 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*

18-5

## Topics

- Transplantation immunity
- Autoimmune diseases
- Immunodeficiency disorders

18-3

## 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**  
*minor antigens cause rejection*  
*immunosuppressants may be needed indefinitely*

18-6

## 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*

18-7

## Autoimmune disease

- Spectrum of autoimmune reactions
- Treatment of autoimmune diseases

18-10

### *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*

18-8

Table 18.4 Characteristics of Some Autoimmune Diseases

Disease (Known MHC Relationship)	Organ Specificity	Major Mechanism of Tissue Damage
Graves' disease (DR3)	Thyroid	Autoantibodies bind thyroid-stimulating hormone receptor, causing overstimulation of thyroid
Myasthenia gravis (DR3)	Muscle	Autoantibodies bind to acetylcholine receptor on muscle, preventing muscle contraction
Insulin-dependent diabetes mellitus (DR3/DR4)	Pancreas	T-cell destruction of pancreatic cells
Autoimmune hemolytic anemia	Red blood cells	Antibody, complement, and phagocyte destruction of red cells
Rheumatoid arthritis (DR4)	Widespread, especially joints	Lymphocyte destruction of joint tissues; immune complexes of IgG and anti-IgG, <i>Type III Hypersensitivity</i>
Systemic lupus erythematosus (DR3)	Widespread (glomerulonephritis, vasculitis, arthritis)	Autoantibodies to DNA and other nuclear components form immune complexes in small blood vessels, <i>Type III</i>

18-11

## Autoimmune disease

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

18-9

## 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*

18-12

## 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

18-13

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.  
**Table 18.6** Some Primary Immunodeficiency Diseases for Which Genetic Defects Are Known

Severe combined immunodeficiency (SCID) <i>no functional T, B cells</i>	X-linked hyper-IgM syndrome
X-linked SCID	Wiscott-Aldrich syndrome
MHC class II deficiency *	Ataxia telangiectasia
CD3 deficiency	* Chronic granulomatous disease
CD8 deficiency	* Leukocyte adhesion deficiency
X-linked agammaglobulinemia <i>no Ig</i>	* Many complement deficiencies

18-16

## Immunodeficiency disorders

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

18-14

## 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*

18-17

## Primary immunodeficiencies

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

18-15

## 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

18-18