Important terms:

Hypersensitivity – immune responses that causes tissue damage

Autoimmune disease – immune responses to self-antigens

Immunodeficiency – insufficient immune response

18-1

Topics

- **Transplantation immunity**
- **Autoimmune diseases**
- **Immunodeficiency disorders**

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**
  - **Requires immunosuppression for successful transplants**
    - **Cyclosporin A, tacrolimus**
    - **interfere with cell signaling**
    - **inhibit clonal expansion of T cells**

18-3

Autoimmune disease

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

18-4

Autoimmune disease

- **Spectrum of autoimmune reactions**
- **Treatment of autoimmune diseases**

18-5

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 *Type III Hypersensitivity*
Systemic lupus erythematosus (DR3)	Widespread (glomerulonephritis, vasculitis, arthritis)	Autoantibodies to DNA and other nuclear components form immune complexes in small blood vessels *Type III*

18-6

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

18-7

Immunodeficiency disorders

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

18-8

Primary immunodeficiencies

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

18-9

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

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

18-10

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**

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