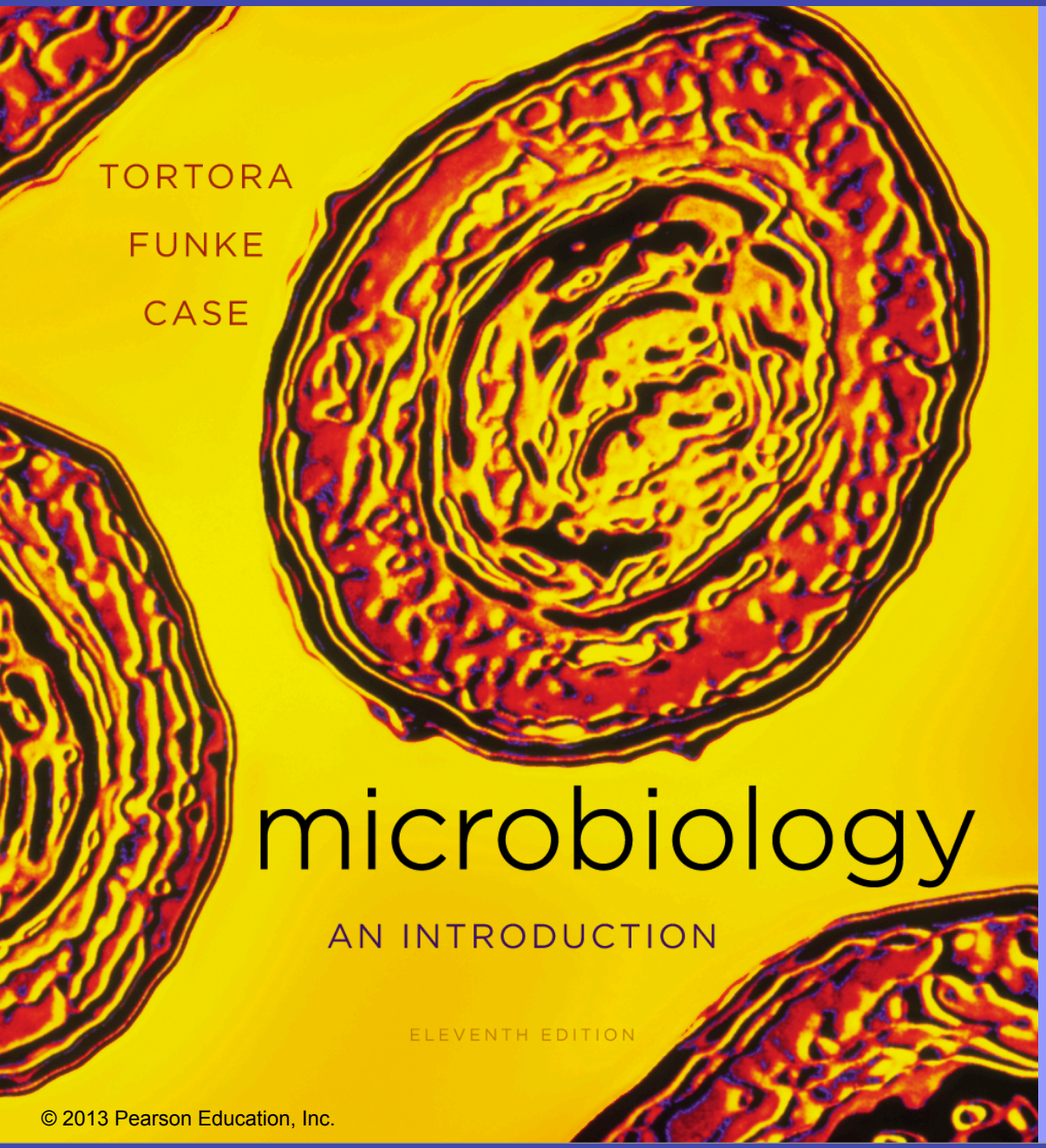
Module 12

Applications/Disorders of the Immune System



Chapter 18

Practical Applications of Immunology

Lectures prepared by Helmut Kae

Active vs Passive Vaccination

- **Active vaccination**: introduction of antigen to stimulate immune response
  - Long lasting protection
- **Passive vaccination**: introduction of protective or neutralizing antibodies
  - Short term protection

Vaccines

- **Vaccine**: suspension of organisms or fractions of organisms that induce immunity
  - Early 1700's, exposed smallpox scabs to veins
  - Edward Jenner developed smallpox vaccine in 1798
- Development of vaccines most important application of microbiology
  - Jenner's work won him Nobel Prize

Chapter 18, page 510, Reported numbers of measles cases in the United States, 1960–2010. (CDC, 2010)

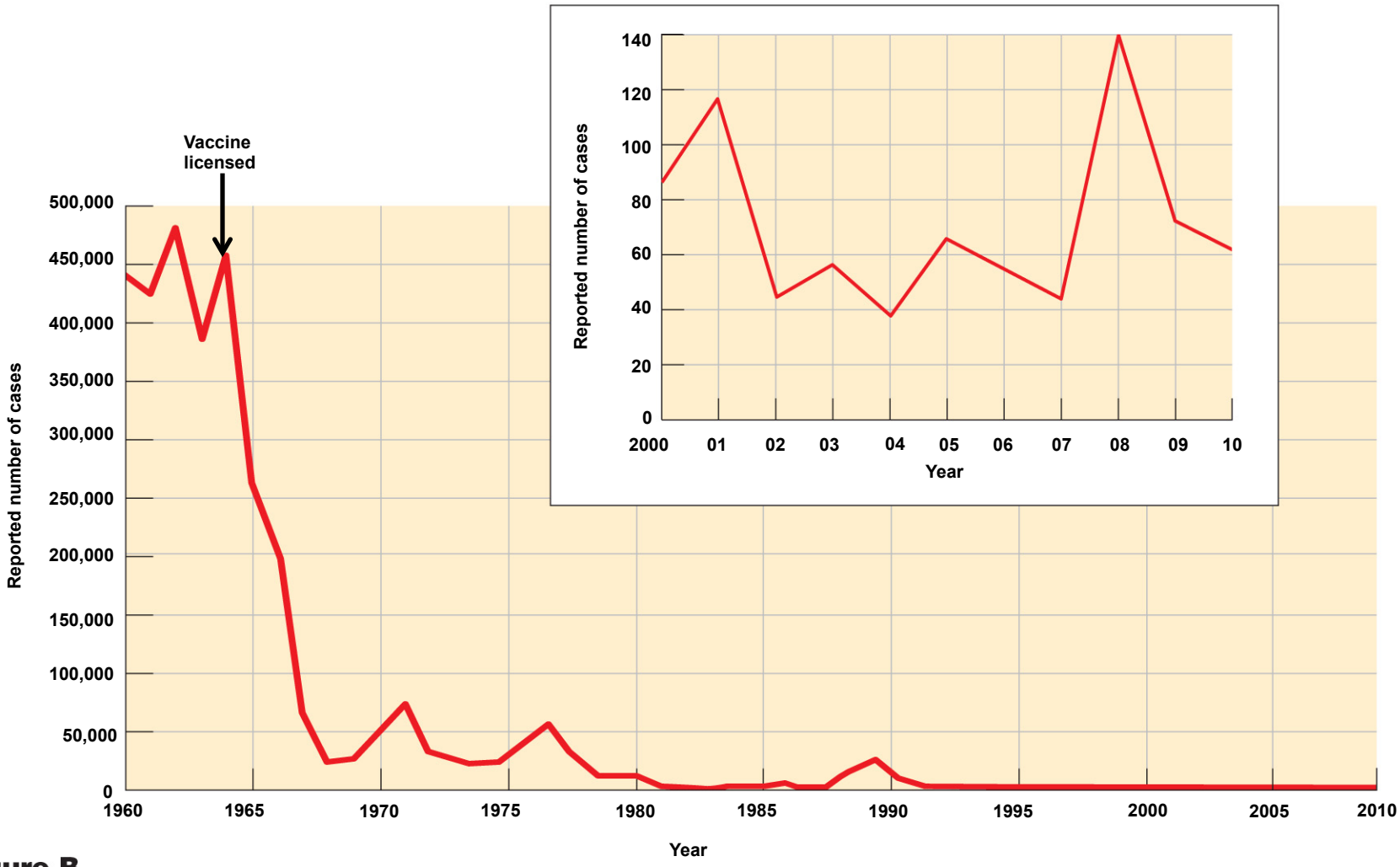


Figure B

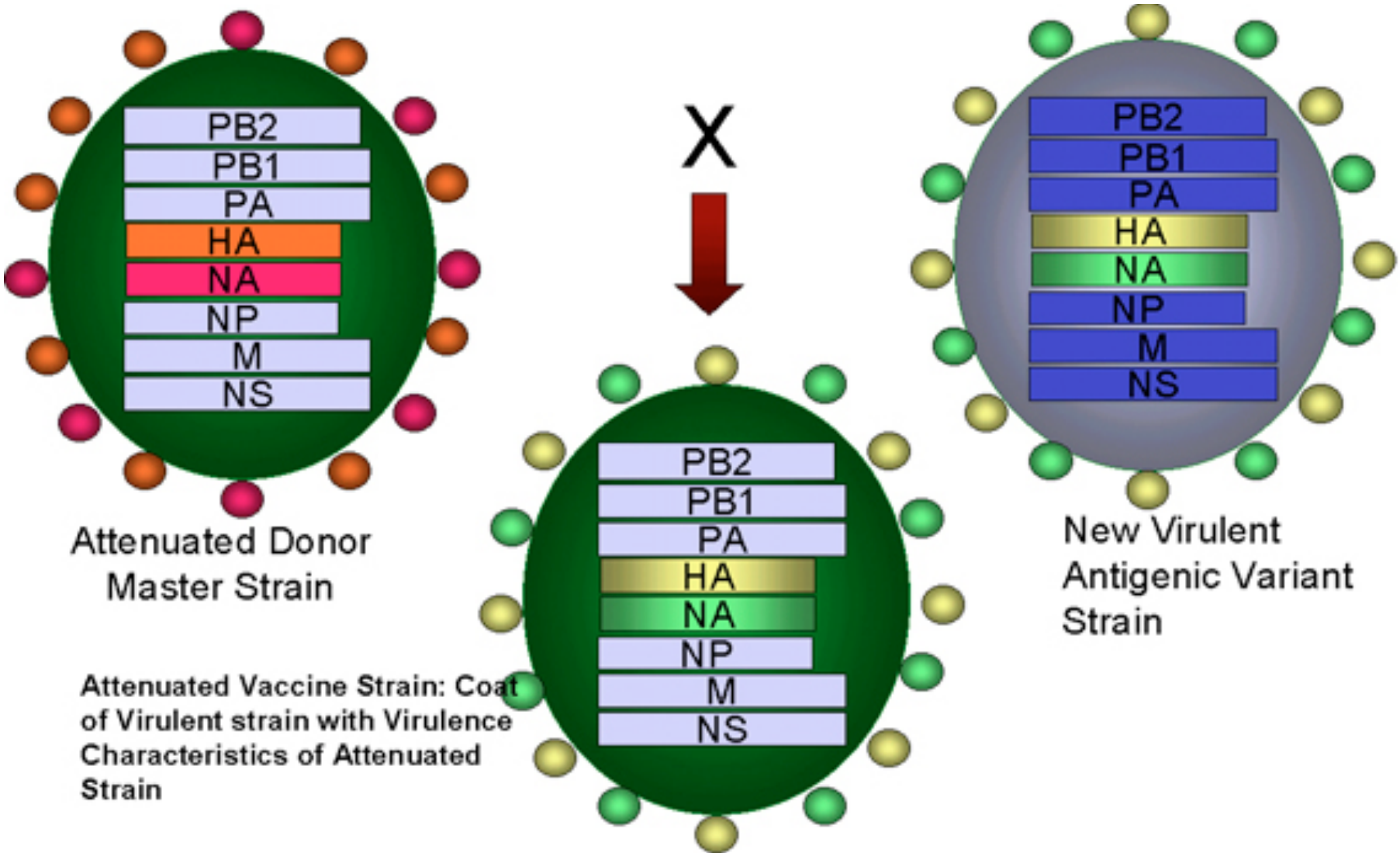
Principles and Effects of Vaccination

- Main purpose of active vaccination → stimulate memory cell production
  - "Vaccine" for small pox was infection with cowpox
  - Closely related to smallpox, milder symptoms
  - Stimulates memory cells against cow and smallpox
- Herd immunity works by immunizing most of a population
  - Protects susceptible people by limiting spread
- Several types of vaccines exist

Attenuated Whole-Agent Vaccines

- Living but attenuated (weak) microbes
- Live vaccine, mimics infection more effectively
- Can achieve lifelong immunity, especially against virus
- Attenuated microbe derived in lab from many mutations
- But, possibility of “back mutation” to virulent strain
  - Not used on people with weak immune systems

Attenuated Whole-Agent Vaccines

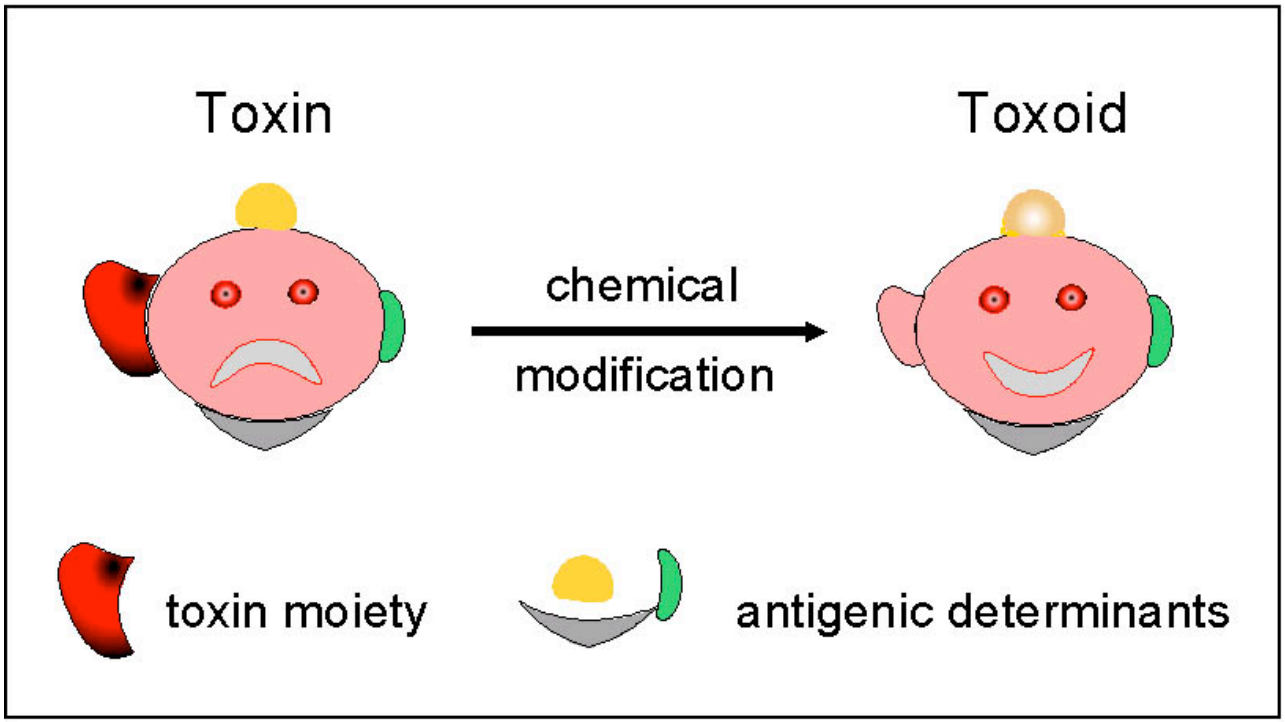


Inactivated Whole-Agent Vaccines

- Microbes that have been killed
- Usually killed by chemicals, formalin or phenol
- Often used in immune compromised people

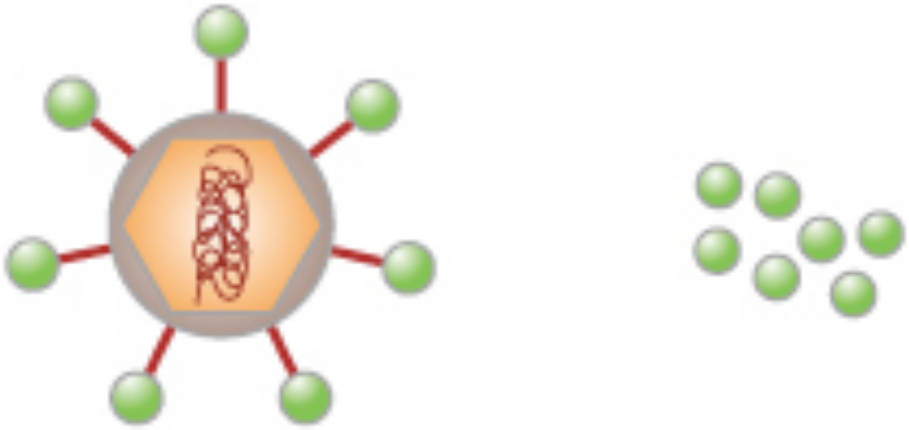
Toxoids

- Inactivated toxins
- Directed at toxins produced by pathogen
- Require occasional **boosters**: periodic shots given to maintain effectiveness of vaccine



Subunit Vaccines

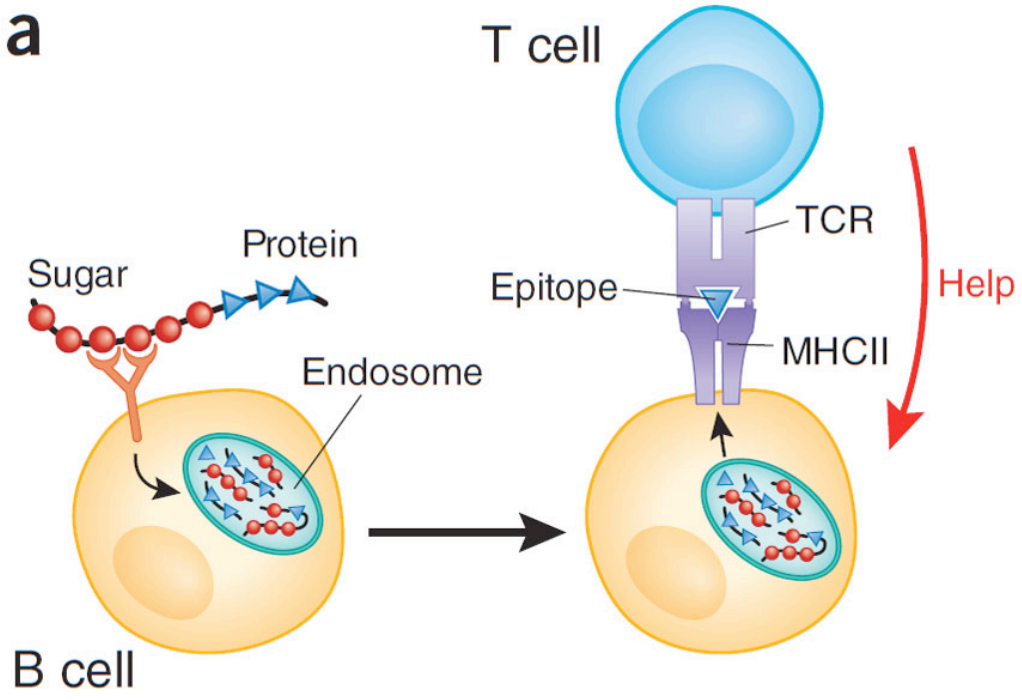
- Use only antigenic fragments of microbes
- Aka acellular or recombinant vaccines
- Choose antigen that best stimulates immune response
- Safer – cannot reproduce, fewer adverse effects



Viral Pathogen **Subunit Vaccine**

Conjugated Vaccine

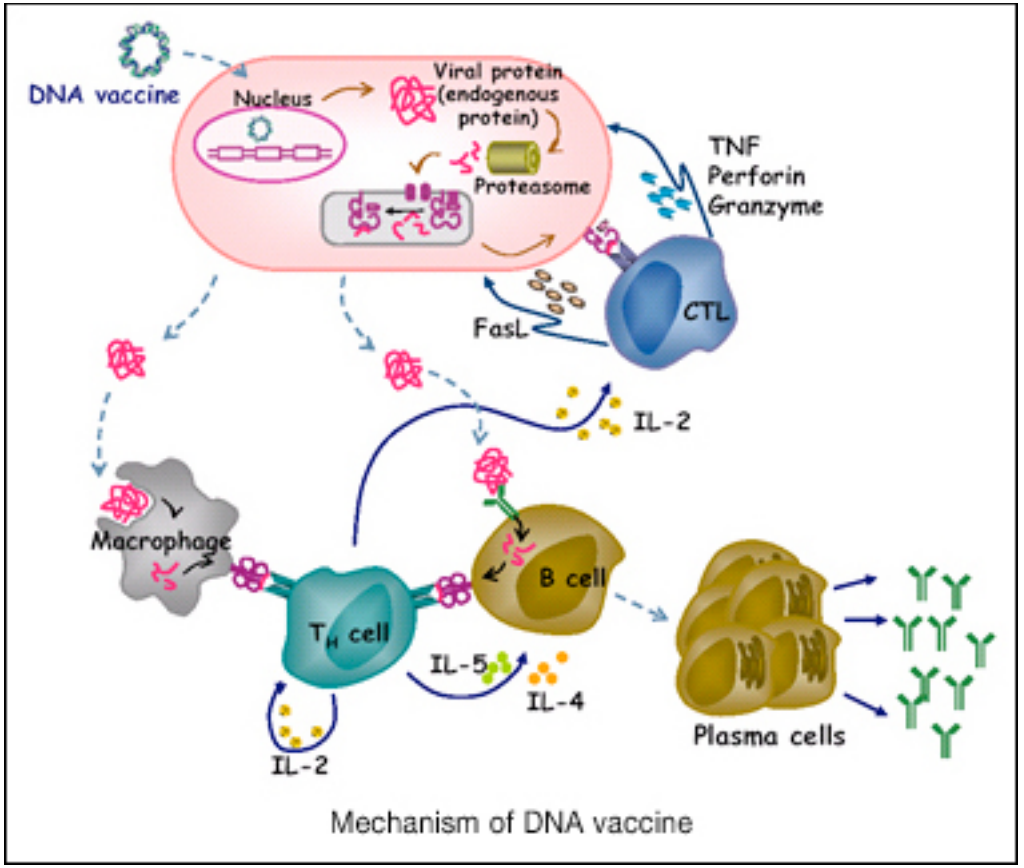
- Antigen attached to polysaccharide
- Polysaccharides help increase immune response



Nucleic Acid Vaccines

- DNA vaccines
- Newest, most promising
- No commercial vaccines yet
- Injection of “naked” DNA, often as plasmid, into muscle
  - Results in production of protein that stimulate immune response
- DNA can be easily degraded, so it may not have long lasting effectiveness

Nucleic Acid Vaccines



Mechanism of DNA vaccine

The Development of New Vaccines

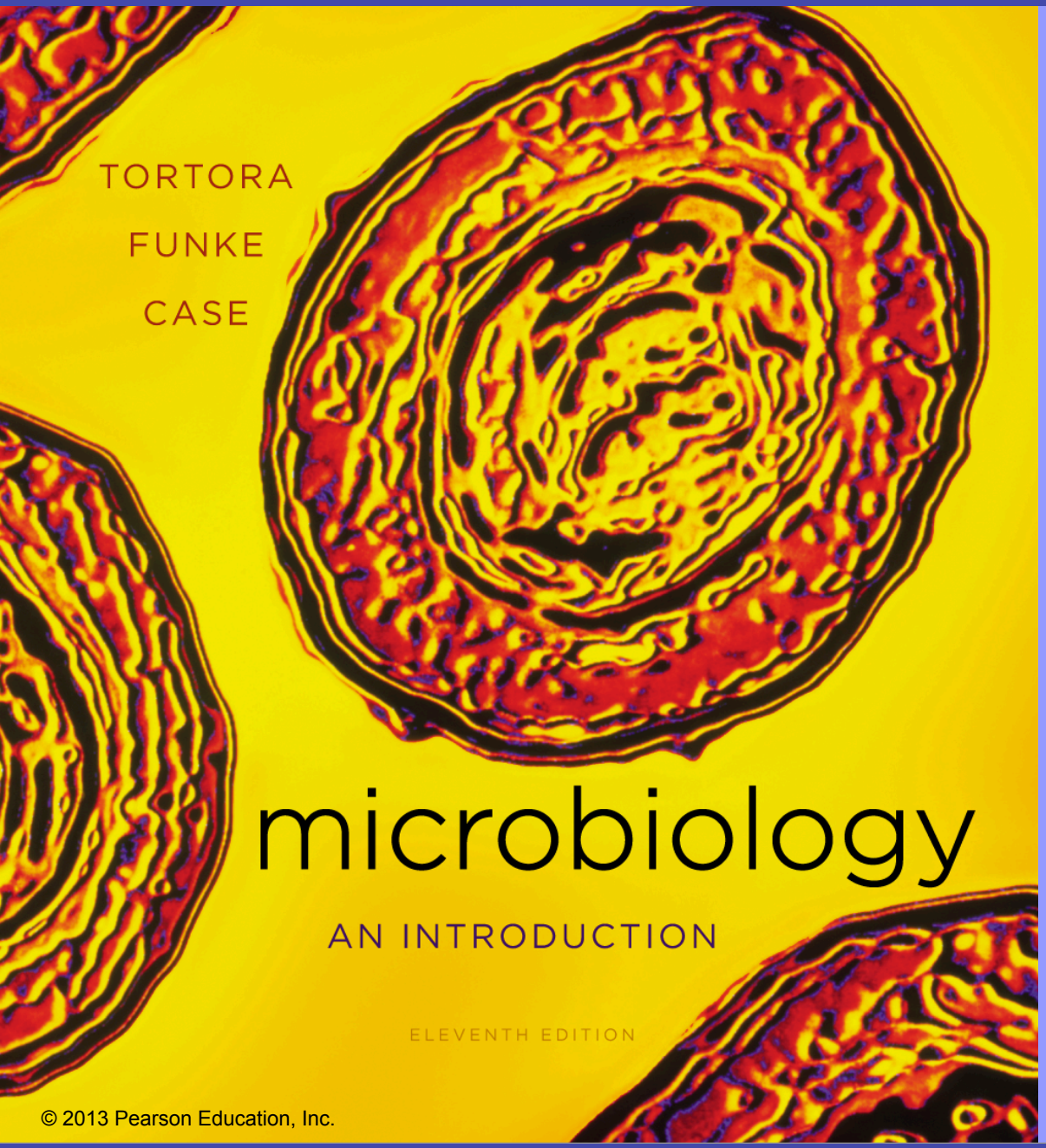
- Vaccine development decreased until recently
- Introduction of viral culture techniques has allowed growth of viral vaccines
- The ideal vaccine would include
  - Eating instead of injection
  - Lifelong immunity from one dose
  - Stable without refrigeration
  - Affordable

The Development of New Vaccines

- New vaccines for drug addictions, Alzheimer's disease, cancer
- Currently, 20 injections required for children
  - Additional combination vaccines would be beneficial
  - Routes other than injection
    - Intranasal spray, skin patches

Safety of Vaccines

- No vaccination is 100% safe
- Some risk involved in receiving vaccines
  - Sometimes they cause disease
    - Rota virus causes infant diarrhea
    - In some, vaccine caused intestinal blockage
- Some tried to link MMR to autism
  - Links unsubstantiated
- Overall, very low risk is worth the great gain of immunity



Chapter 19

Disorders of the Immune System

Lectures prepared by Helmut Kae

Hypersensitivity

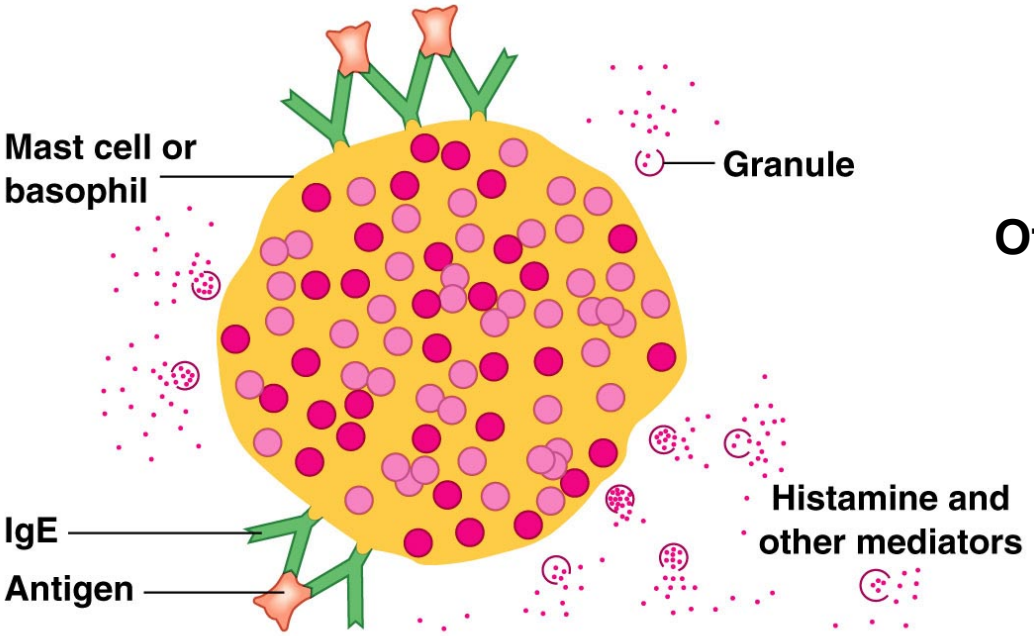
- Abnormal antigen induced response
  - An undesired reaction of the immune system
  - Aka **allergies**
  - Antigen is called **allergen**

Hypersensitivity

- Occurs when individual is **sensitized** by initial exposure to allergens
  - Generates memory cells against allergen
  - 2nd exposure stimulates immune response
- Reactions fall into 4 categories
  - Type I, II, III, IV

Type I (Anaphylactic) Reactions

- **Anaphylaxis**: “the opposite of protected”
- Occurs when allergens combine with IgE antibodies
  - IgE+allergen binds to mast cells, basophils
  - Binding triggers release of histamine



Histamine triggers inflammation

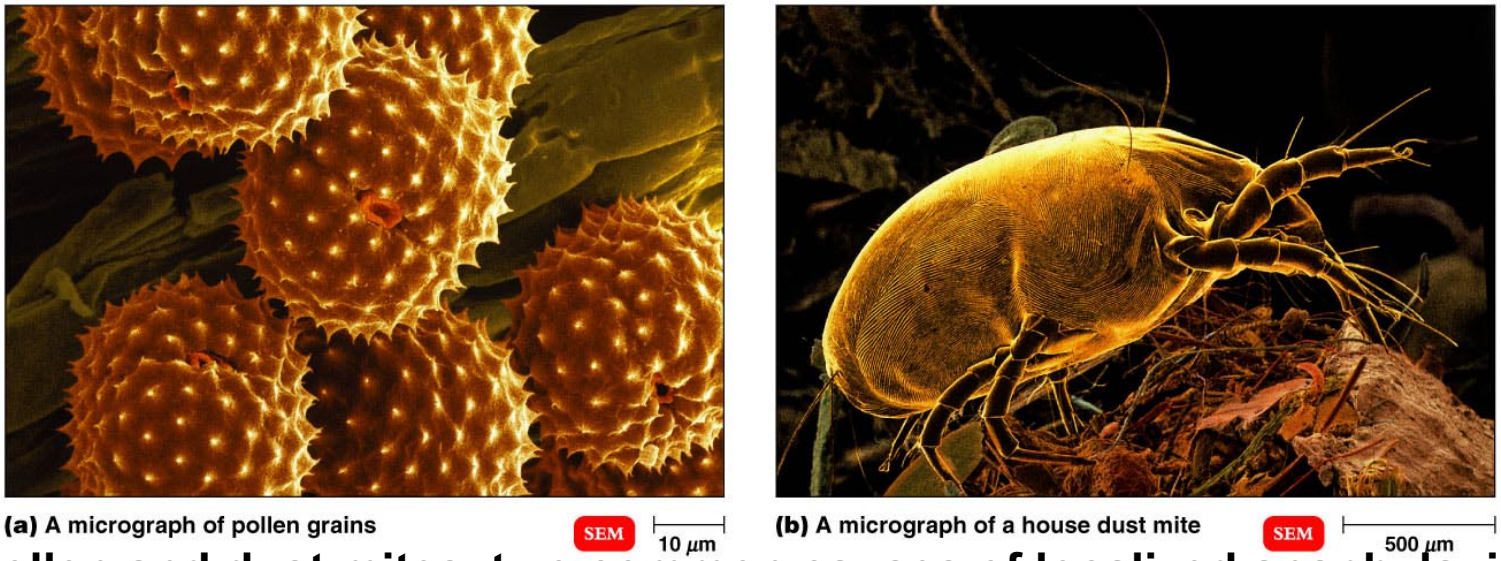
Other effects are mucus secretions in nose, difficulties breathing

Systemic anaphylaxis

- Aka **anaphylactic shock**
- Results upon second exposure to *injected* allergens
- Blood vessels enlargen → ↓ blood pressure → shock
- Reactions can be fatal in minutes
- Treated with epinephrine injection → constricts blood vessels
- Allergens include penicillin, insect stings, jellyfish stings

Localized Anaphylaxis

- Associated with inhaled or ingested allergens
- Inhaled allergens sensitize mast cells in resp. tract
  - Re-exposure → congested nasal passage, sneezing
  - Antihistamines neutralize effects of histamine



Pollen and dust mites, two common causes of localized anaphylaxis

Localized Anaphylaxis

- Ingested allergens into GI tract can sensitize individual
- Result in GI upset, hives
- May result in systemic anaphylaxis if serious
- Most common food allergens are eggs, peanuts, tree-grown nuts, milk, soy, seafood, wheat, and peas

Prevention of Anaphylactic Reactions

- Avoiding contact is best method
- **Desensitization**: series of gradually increasing dosage of allergen → IgG vs IgE
- IgG acts as neutralizing antibodies

- Skin tests used to diagnose sensitivities
- Scrape small amounts of allergen beneath skin
- A “wheal” → positive test

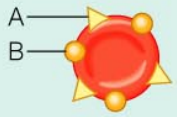
Type II (Cytotoxic) Reactions

- Involve activation of complement by IgG or IgM
  - Antigen is foreign cell, or antigen bound to host cell
- Activation of complement lyses cells
- Most common involves blood group system
  - ABO, Rh blood group systems
- Another type is drug-induced cytotoxic reactions

ABO Blood Group System

- A person's ABO blood type depends on RBC antigens
  - "A" or "B" antigens

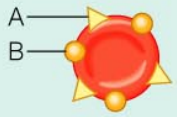
ABO Blood Group System

Illustration	Plasma Antibodies	Blood That Can Be Received	Fre... / Wh...
	Neither anti-A nor anti-B antibodies	A, B, AB, O (Universal recipient)	3
	Anti-A	B, O	9
	Anti-B	A, O	41
	Anti-A and Anti-B	O (Universal donor)	47

ABO Blood Group System

- A person has antibodies against other blood antigens
  - Recognized as “non-self”

ABO Blood Group System

Illustration	Plasma Antibodies	Blood That Can Be Received	Fre… / Wh…
	Neither anti-A nor anti-B antibodies	A, B, AB, O (Universal recipient)	3
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ABO Blood Group System

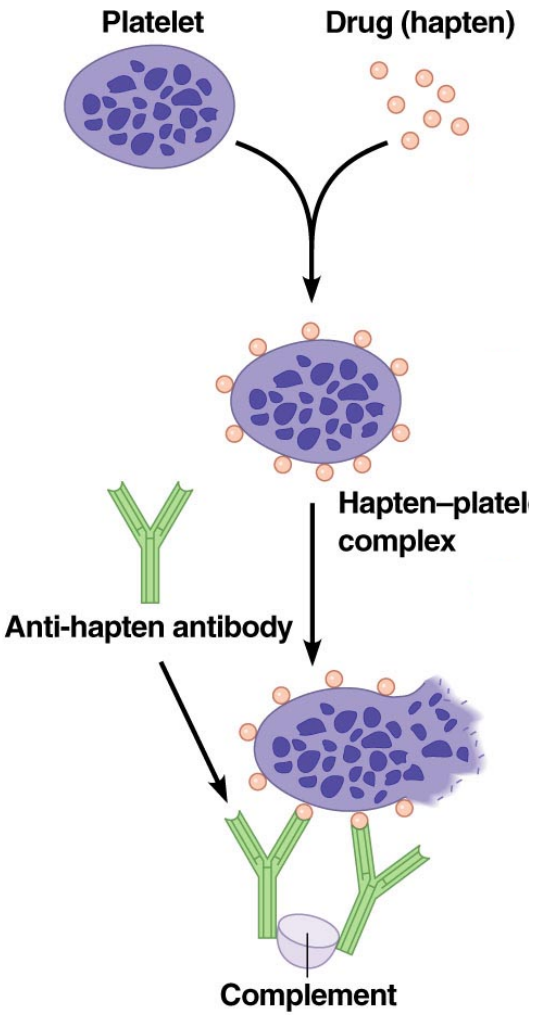
- When blood transfusion is incompatible, antigen-antibody complex activates complement → cells lyse
  - When Type A blood is transfused into person with Type B blood
  - Presence of anti-A antibodies react with A antigens on incoming Type A blood

Rh Blood Group System

- Another blood antigen is Rh factor
- Those that have Rh factor are called Rh^+, vs Rh^-
- Rh^- individuals do not have antibodies to Rh factor
- Exposure to Rh^+ blood can sensitize individuals
  - Produce anti-Rh antibodies
- Second exposure to Rh^+ blood causes reaction with Rh factor
  - Serious hemolytic reaction develops

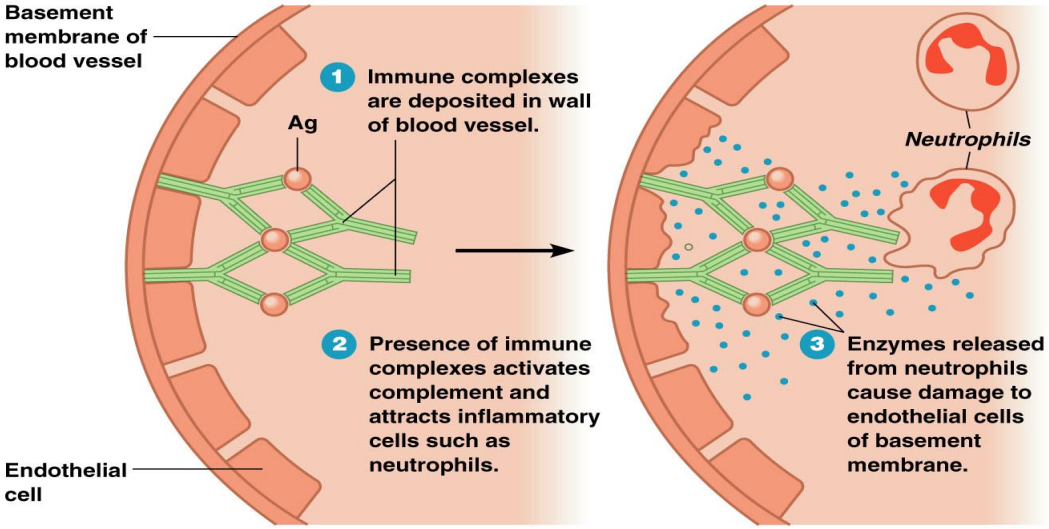
Drug-induced Cytotoxic Reactions

- Cytotoxic reactions caused by drugs
- Drugs bound to blood cells cause complement induced lysis
- Thrombocytopenic purpura: drug coats platelets → destroyed
  - Loss results in purple spots
- Hemolytic anemia: drug coats RBC
- Agranulocytosis: drug coats WBC



Type III (Immune Complex) Reactions

- Involve antibodies against soluble antigens
- **Immune complex**: complex of antigen and antibodies
  - Form only under certain conditions
- Can activate complement, cause inflammatory damage



Immune complex becomes trapped against tissue membranes → inflammation damages tissue

Glomerulonephritis: inflammatory damage of kidneys due to infection

Type IV (Delayed Cell-Mediated) Reactions

- Type IV is cell-mediated, mainly T cells
- After sensitization, reaction is unapparent for days
  - Time required for T cells to accumulate
- Common mechanism involved in tissue transplant rejection
  - Mediated by CTLs

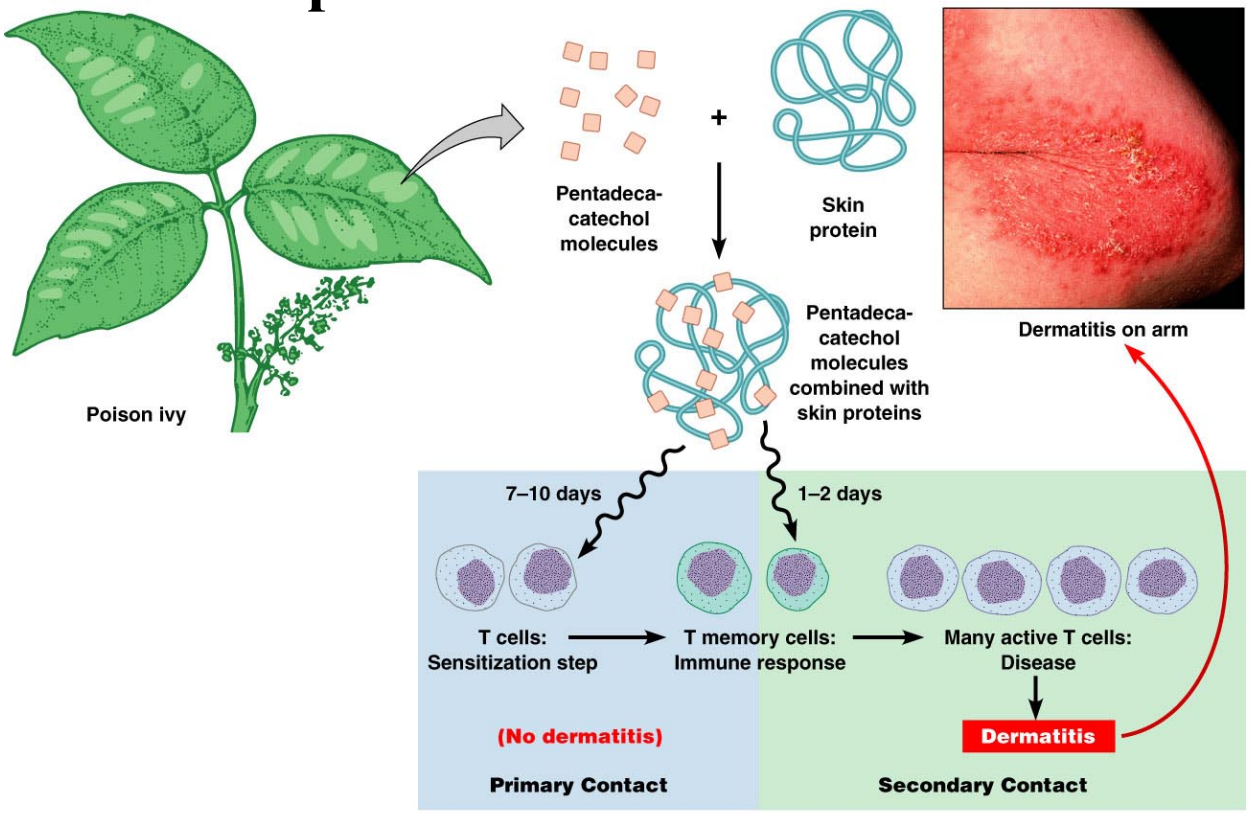
Type IV (Delayed Cell-Mediated) Reactions

- Sensitization occurs when foreign antigens are phagocytized, presented to T cells
  - T cells mature into memory cells
- Re-exposure results in “delayed hypersensitivity reactions”
  - Memory T cells activate CTLs → destroy antigens
- TB skin test is delayed hypersensitivity
  - *M. tuberculosis* in macrophage sensitizes individual
  - Injection of antigen results in delayed reaction

Type IV (Delayed Cell-Mediated) Reactions

Allergic Contact Dermatitis

Caused by small molecules that combine with skin proteins



Reactions to Transplantation

- Foreign tissue transplants are “rejected”
  - Attack by T cells, macrophages, antibodies
- **Immunosuppression**: suppression of immune system
  - Often to prevent rejection of transplant
- Favorable to suppress cell-mediated immunity
  - If humoral immunity not suppressed, can still resist many microbes
- **Cyclosporine**: drug that suppresses activation of CTLs
  - No effect on humoral immunity

Autoimmune Diseases

- **Autoimmune disease**: immune system responds against “self” antigens
  - Cause damage to own tissues, organs
- Occur when there is a loss of self-tolerance
  - Immune’s ability to discriminate self from non-self

Cell-mediated Autoimmune Diseases

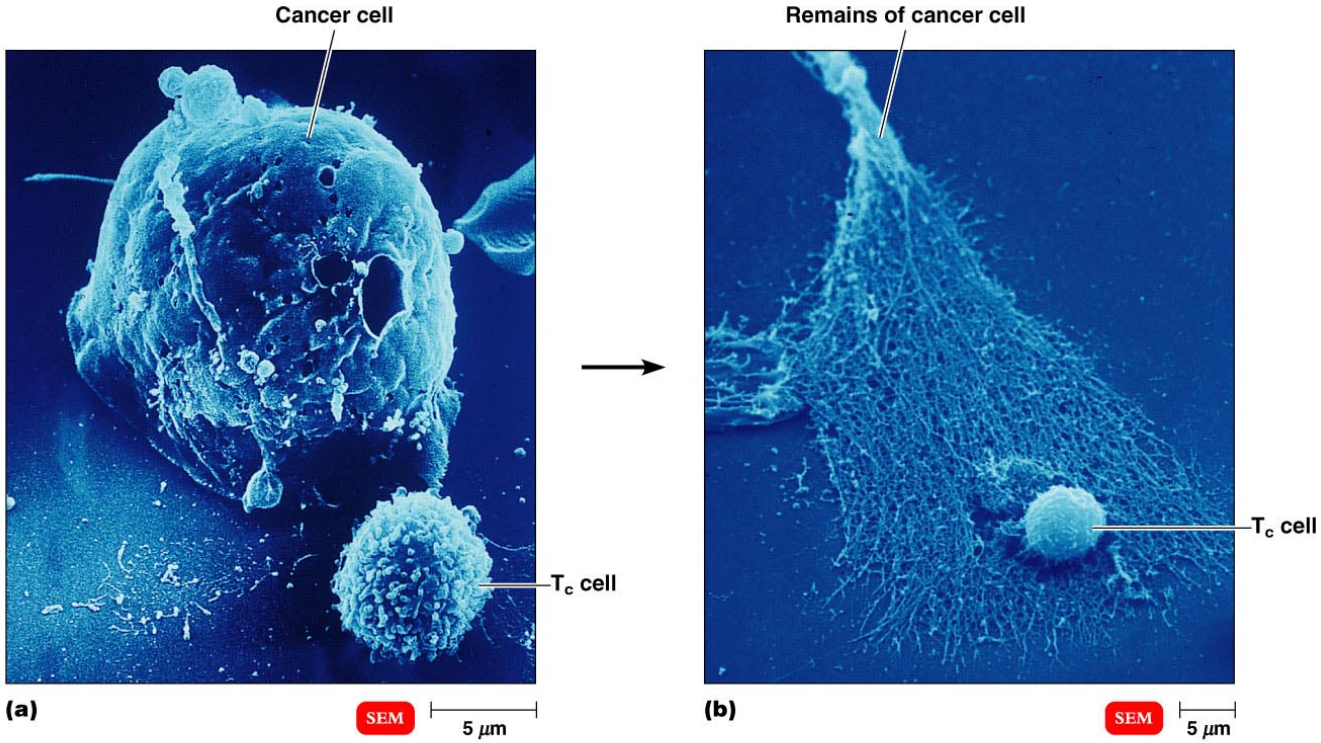
- Attack of own tissues by T cells and macrophages
- **Multiple sclerosis**: autoimmune attack of motor nerve cells
  - Progressive loss of muscle function
- **Insulin-dependent diabetes mellitus**: destruction of insulin-secreting cells in pancreas

The Immune System and Cancer

- **Immune surveillance**: cancer cells develop frequently, but are removed by immune system
- Surface of tumor cells develop "tumor-associated antigens" → recognized as non-self
  - Can be destroyed by CTLs, NK cells, macrophages
- Tumors can evade immune system if:
  - Tumor antigen fails to stimulate immune system
  - Tumor cells grow too rapidly
  - Tumor cells grow in tissue and move to bloodstream

Immunotherapy for Cancer

- Use of immune system to prevent or cure cancer
  - Stimulate immune response against tumor cells
- Attractive therapeutic → avoids damage to healthy cells



Immunotherapy for Cancer

- One approach is to mix dendritic cells with genetic material from a tumor
  - Dendritic cells are APC that activate CTLs
- Another is the use of **immunotoxins**: combo of toxin and antibody
  - Could be used to specifically kill tumor cells
  - Requires that antibodies can reach tumor cells – difficult with large tumor masses

Cancer Vaccines

Therapeutic vaccine: used to treat existing cancer

- Therapeutic vaccine follow two approaches
- Whole-cell vaccines – prepared from cancer cells
- Antigen-type vaccines – antigens found on cancer cells

Prophylactic vaccines: used to prevent development of cancer

- Hepatitis B (liver), HPV (cervical) are viruses that can cause cancer
- Vaccine against virus is indirect prophylactic vaccine

Immunodeficiencies

- Absence of a sufficient immune response
- Can be either congenital or acquired

Congenital Immunodeficiencies

- Determined by inherited genes
- **DiGeorge's syndrome**: lack of thymus gland
- **Agammaglobulinanemia**: growth of B cells is blocked

Acquired Immunodeficiencies

- Acquired via cancers, drugs, infectious agents
- Many viruses can infect and kill lymphocytes
  - HIV infects Helper T cells