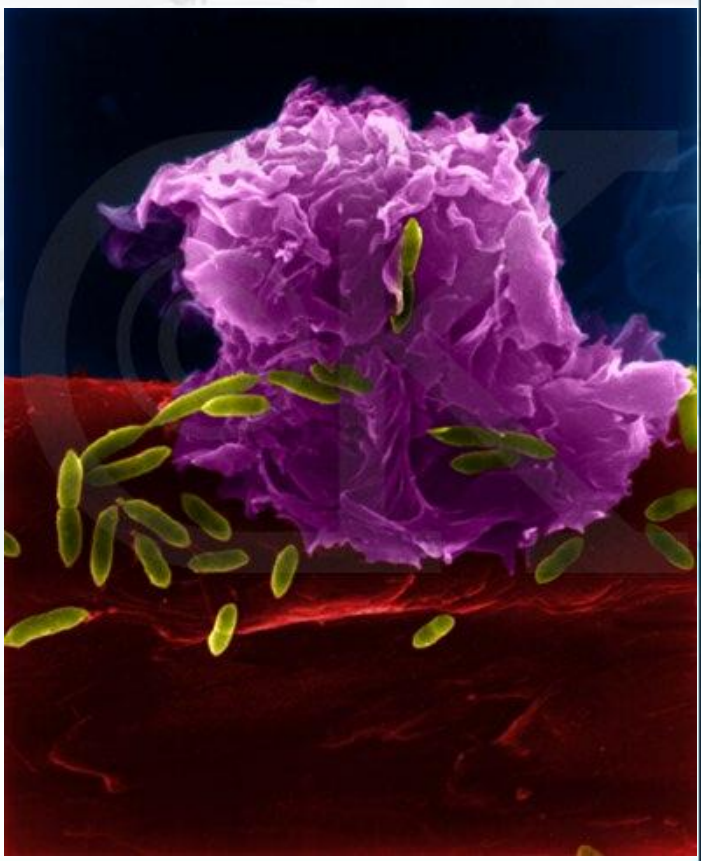
? What is Immunity ?

- Immunity = the protection against infectious disease conferred either by the immune response generated by immunization or previous infection or by other nonimmunologic factors…a.k.a. body's ability to resist infection

- 2 types of immunity
  - Non-specific (innate)
  - Specific (adaptive, acquired)

Innate Immunity

- Skin
  - What characteristics of the skin make it an effective mechanical barrier ?
- Mucous membranes (mechanical)
  - Cilia in respiratory tract
  - Lysozyomes, pH
- Iron-binding proteins
  - Some bacteria require iron for growth
  - Transferrin, lactoferrin
- Phagocytosis
  - PMNs, monocytes and macrophages
- Complement

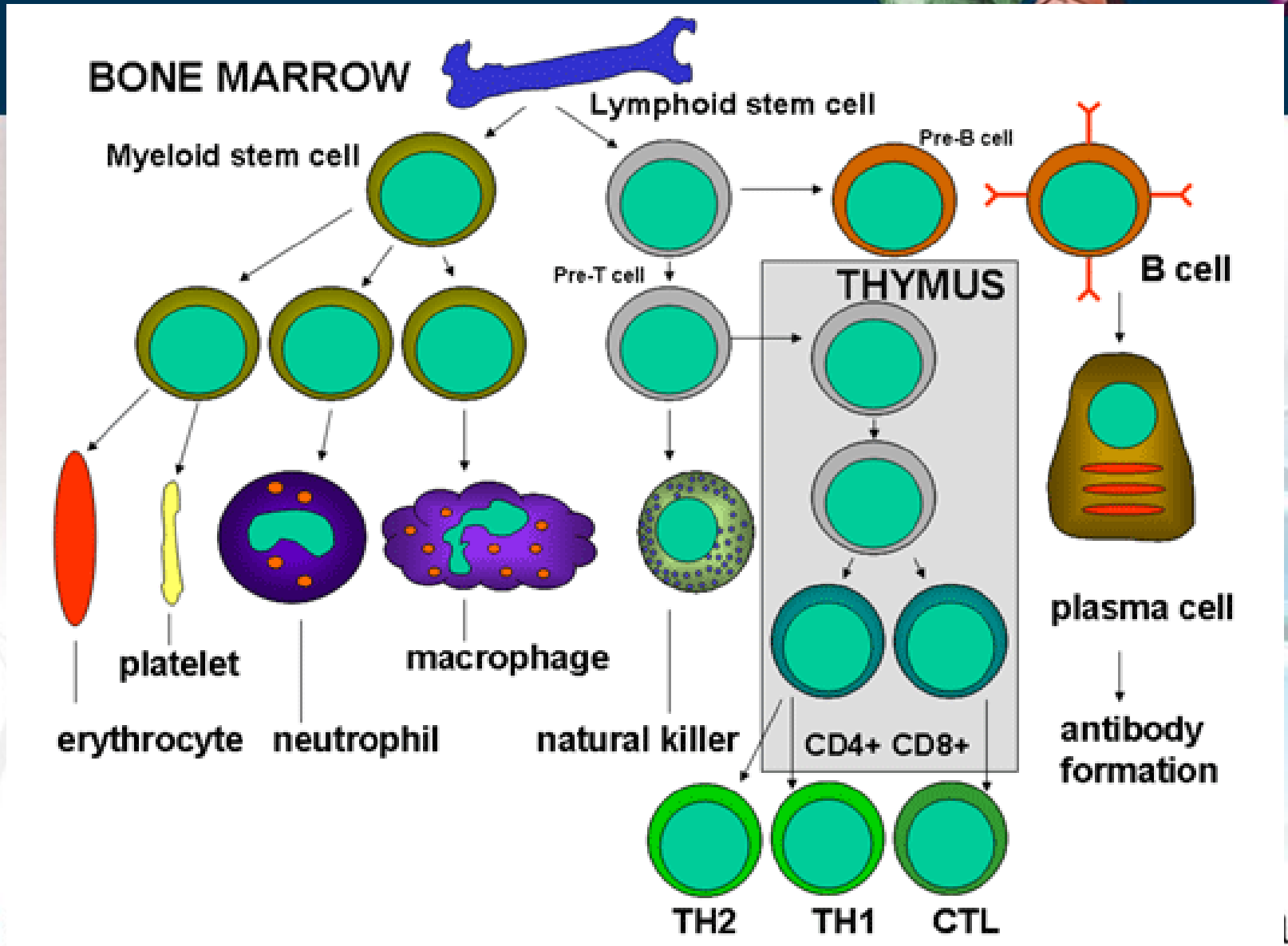


Specific Immunity

- Humoral and Cell-Mediated (CMI)

- What is the difference between innate immunity and adaptive immunity?
  - ***Innate***: protects against ANY invader, does not discriminate
  - ***Adaptive***: directed against one type of invader, dependant on past exposure

Where do immune cells come from?

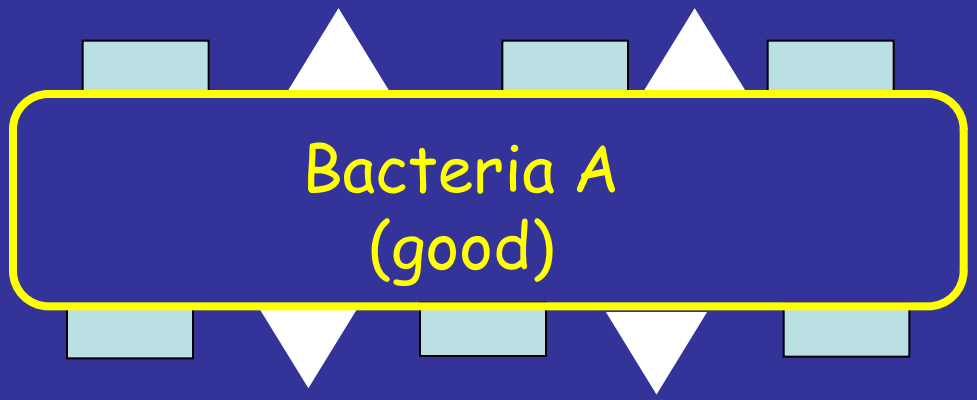


Humoral Immunity

- Circulating antibodies

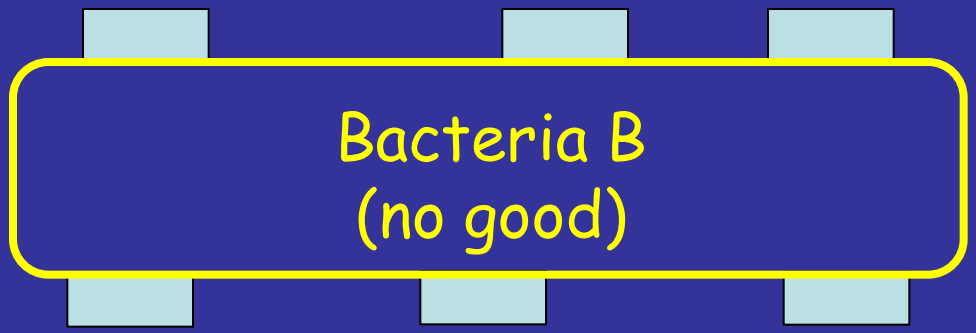
- Antibody: protein that binds specifically to a substance (its antigen)
  - Igs or immunoglobulins
  - Produced by B-lymphocytes upon stimulation from antigen presenting T-cells
  - Recognize toxins, capsules, some viral proteins
- Antigen
  - “non-self”
  - Protein, glycoprotein, lipoprotein, polysaccharide
  - What structures could be “antigenic” in a bacteria? Virus?

Antibody Binding: how does it occur?

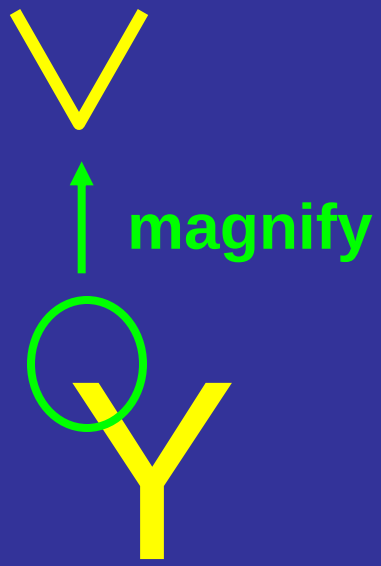


Antigen A

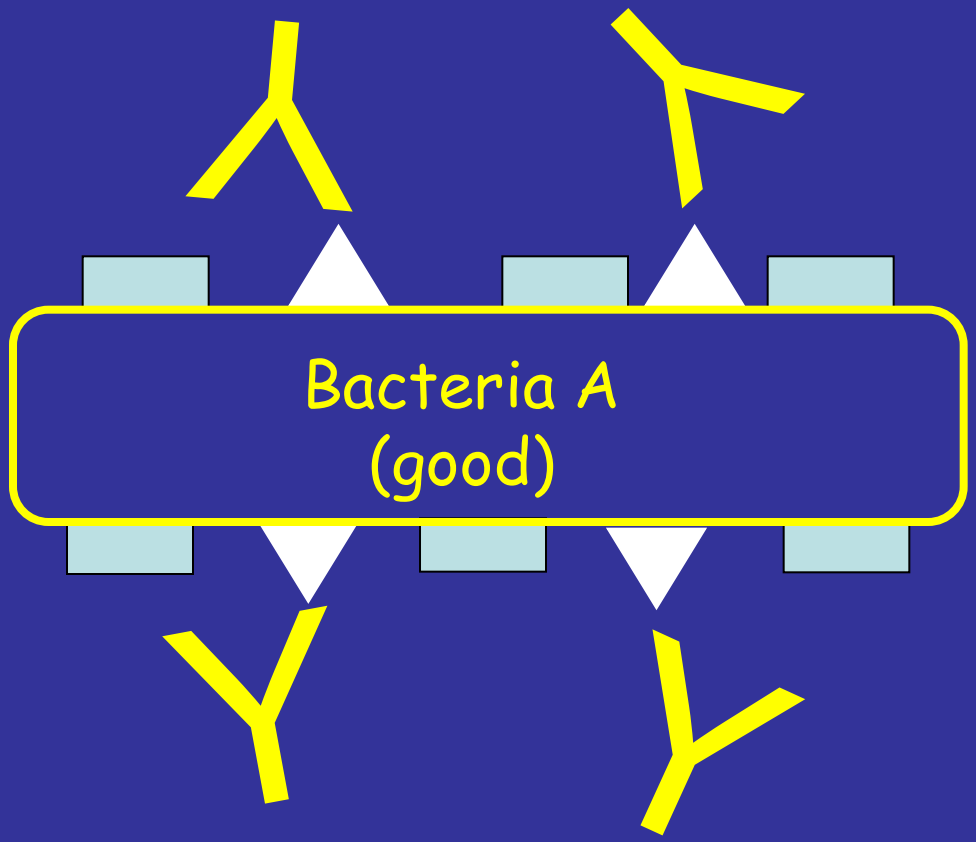
Antigen B

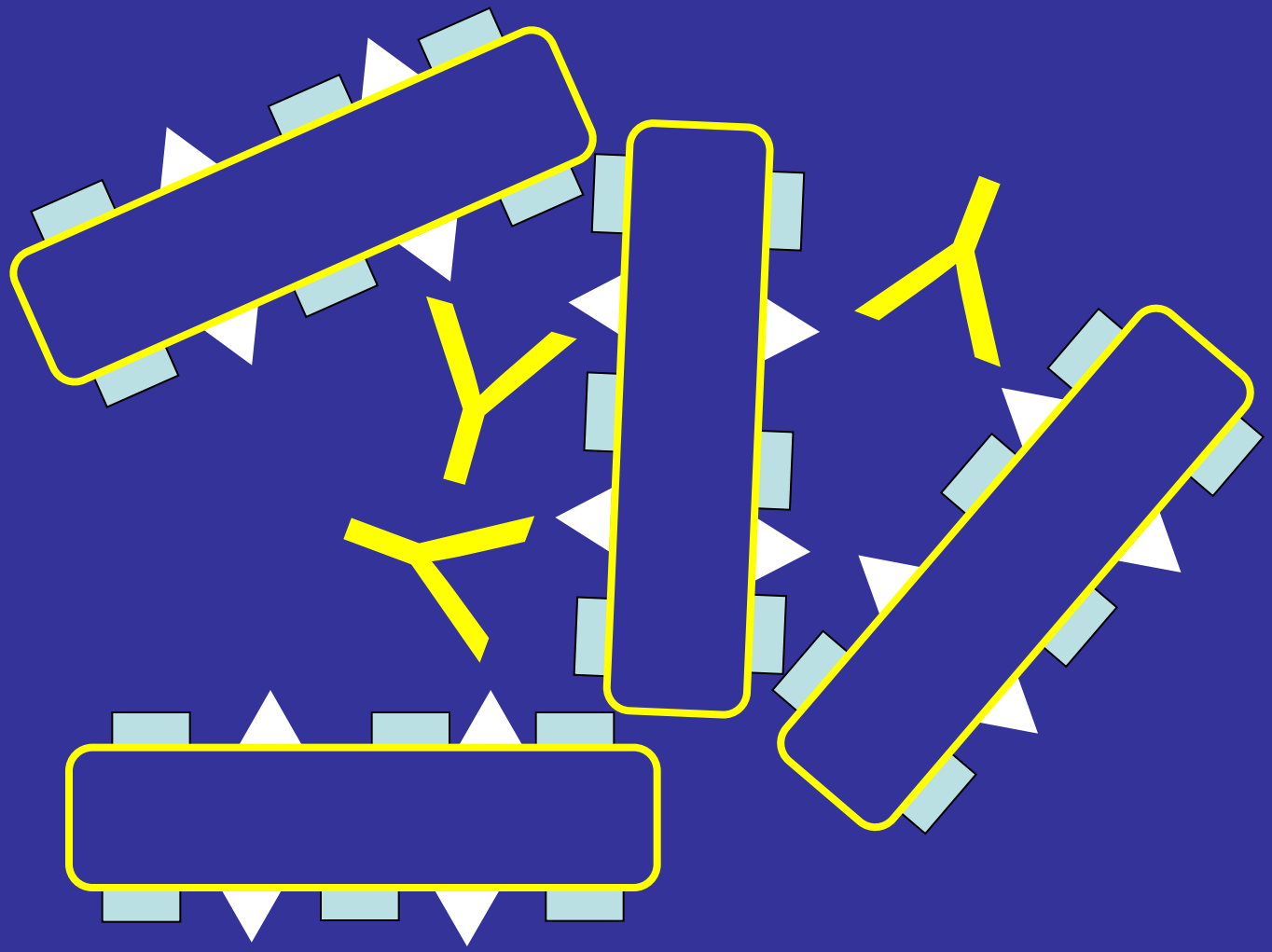


Antigen B



Antibody


Bacteria A
(good)



Immunoglobulins (Igs) a.k.a. Antibodies

- **Antibody:** Ig produced in response to stimulation by an antigen and reacting *specifically* with it.
- Distinguish “non-self” from “self”
- Constant and variable region
  - Variable region is responsible for antigen recognition

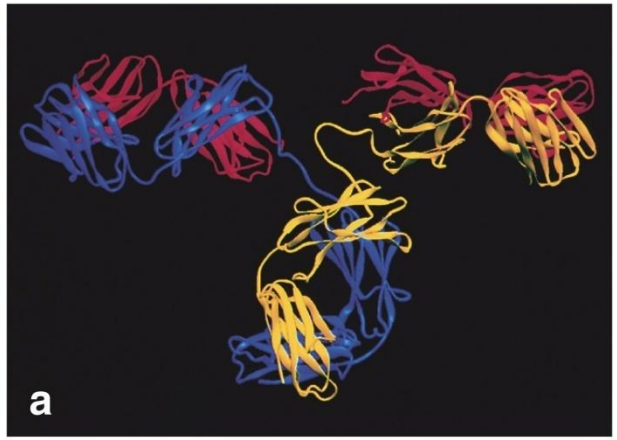


Figure 3-1 part 1 of 3 Immunobiology, 6/e. (© Garland Science 2005)

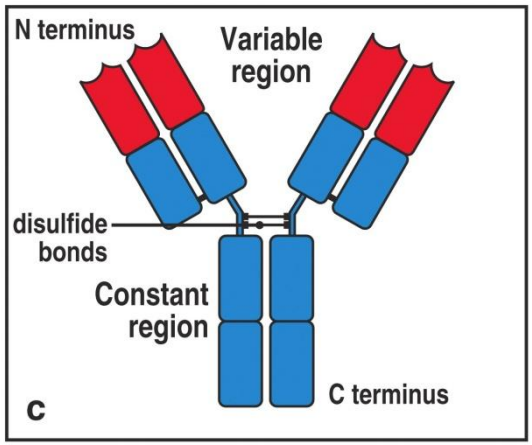
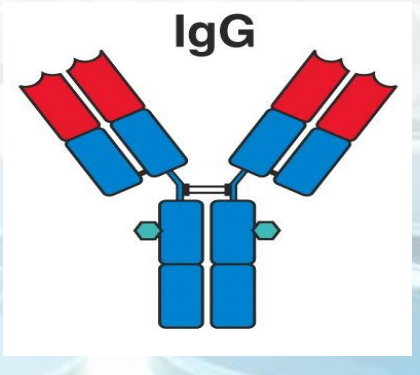


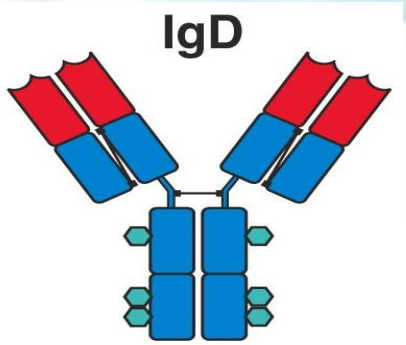
Figure 3-1 part 3 of 3 Immunobiology, 6/e. (© Garland Science 2005)

Classes of Igs

- 5 classes: IgG, IgA, IgM, IgE, IgD
- IgG
  - Host defense
  - Crosses placenta and protects newborn



- IgD
  - Role is unknown



Classes of Igs

- IgA
  - Host defense
  - Found in secretions
    - Tears, saliva, milk, respiratory, GI and genito-urinary tract
  - Dimer

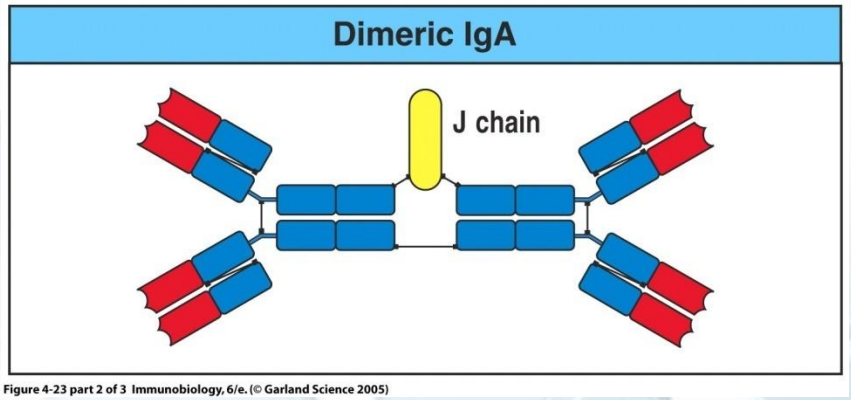


Figure 4-23 part 2 of 3 Immunobiology, 6/e. (© Garland Science 2005)

- IgM
  - Host defense
  - Early immune response
  - Pentamer

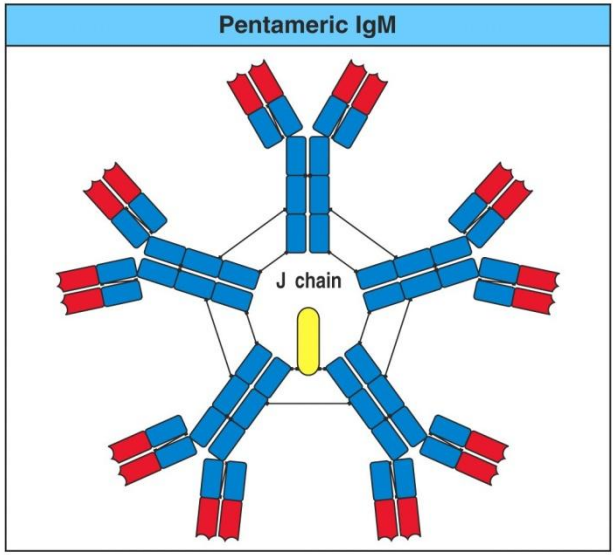


Figure 4-23 part 1 of 3 Immunobiology, 6/e. (© Garland Science 2005)

- IgE
  - Hypersensitivity (allergies)
  - Defends against parasites

1º and 2º Immune Response

- 1º Response
  - Ab production triggered on first antigen introduction
  - Latent period of several days
  - Circulating antibody detectable after 5-10 days
  - Antibody in serum is maximum at ~21 days, then drops to low levels
- 2º Response
  - ★Basis for Immunizations★
  - Occurs when Ab is introduced $2^{nd,}$ 3^{rd},4^{th} …time
  - Lag, rapid Ab increase (2-3 days), slow decrease
  - Booster injections to maximize Ab levels

1º

2º

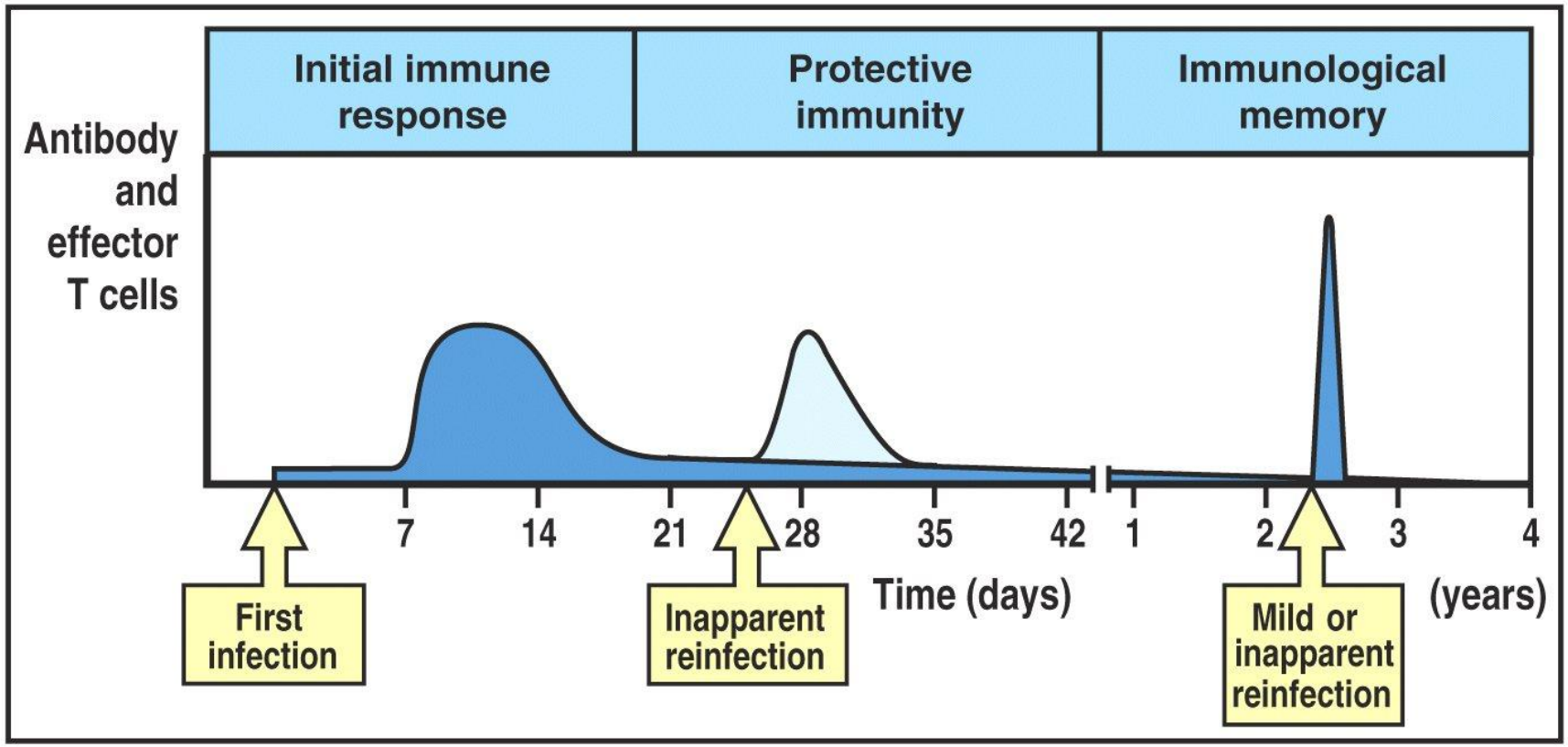
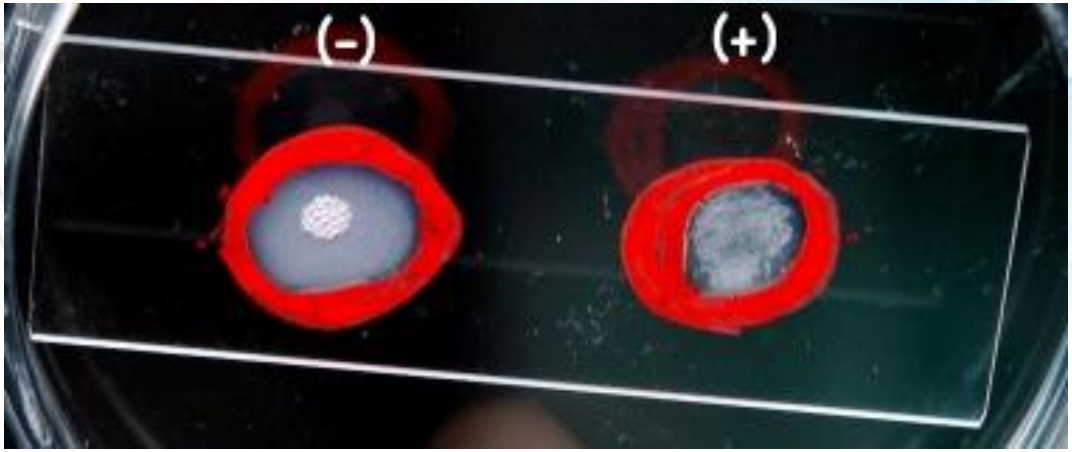


Figure 10-18 Immunobiology, 6/e. (© Garland Science 2005)

Antibody Detection

- Serological Reaction
  - Detects presence of antibodies in serum sample
  - Antigen and antibody interact; agglutination
  - Antibody titration
  - Detect unknown microorganisms using known antisera



Cell-Mediated Immunity (CMI)

- T-cells NOT antibodies!
  - Helper, suppressive, cytotoxic (killer) generated from memory T-cells
- Exposure to antigen induces response from trained T-cells
- Essential for defense against intracellular organisms, parasites, tumors and other foreign cells (i.e., transplants, grafts)
- Immune-suppressive medication for transplant recipients

Disorders of Immunity

1 Allergy and Hypersensitivity
- OVER-reaction to antigens in absence of true infection
- Can be fatal…..ANAPHYLAXIS

2 Auto-immune diseases
- Immune system reacts to its own “self” antigens
- “auto-antibodies”
- Type I diabetes, MS, rheumatoid arthritis, lupus

3 Immunodeficiency states
- Inability to produce antibodies and/or disfunctional CMI
- Congenital, disease, AIDS

4 Graft rejection
- NORMAL immune reaction to “non-self”
- Control by immune-suppressive medication

Immunization

- Passive Immunization
  - administration of pre-formed antibody against a *specific* microbial agent
  - IgG animal origin: short lived, risk of hypersensitivity reaction
  - IgG human origin: short lived, no risk of reaction
  - Gamma globulin (IgG): pooled from large grouped of blood donors and has antibodies to many common infections
  - Hyperimmune globulins (IgG): specific for a particular microbe

Active Immunization

- Stimulates immune system by administration of antigen
- LONGER LASTING
- Live-attenuated vaccine
  - Sub-clinical or mild illness mimicking the disease
  - Local (IgA) and humoral (IgG) immunity
  - Rapid immunity development
  - Serious illness in immuno-compromised individuals

Active Immunization (con't)

- Killed vaccines, sub-unit vaccines and toxoids
  - Antigens without infectivity
  - May require boosters
  - Adjuvant with toxoids
  - Polysaccharide vaccines can be conjugated to protein (see conjugate vaccines)
- Recombinant vaccines
  - DNA recombinant technology
  - Attenuates microorganism
  - Hep B vaccine
- Adsorbed vaccines
  - Vaccine mixed with inorganic salt for slower adsorption and longer-lasting immunity
  - Tetanus, diptheria

Active Immunization (con't)

- Conjugate vaccines
  - Designed for poorly antigenic microorganisms
  - Conjugate antigen of interest to immunogenic, non-toxic protein
  - *Haemophilus influenzae* type b
- Combined vaccines
  - For ease of administration
- Combined Active-Passive Immunization
  - Immediate protection after possible exposure to microbe
  - Hyperimmune Igs and vaccine injected at DIFFERENT sites
  - Tetanus, Rabies, Hep B

Canada's Immunization Guide:

http://www.phac-aspc.gc.ca/publicat/cig-gci/index.html

Canadian Immunization Guide

Health Canada Santé Canada

Canada

Antibiotic Resistance

Introduction

- The first antibiotic (?)
  - discovered in 1929 by Sir Alexander Fleming
- World War II
  - penicillin used to treat staphylococci and streptococci (1946)
- How effective was penicillin?

Introduction

- Resistance to penicillin recognized almost immediately
  - 80% of all strains of *Staphylococcus aureus*
  - *Streptococcus pyogenes* (Group A strep) still treated with penicillin
  - Interestingly, penicillin has never been effective against Gm-negatives (*Salmonella*, *Shigella*, *Bordetella pertussis*, *Yersinia pestis*, *Pseudomonas*) – why? ☺
- Late 1940s and early 1950s?

Antibiotic therapy

- Effective chemotherapy depends on selective toxicity
  - good against pathogen, does not affect host… ☺
- Exploit pathogen processes not seen in humans
  - cell wall, metabolism, etc.
- Knowledge of likely microorganism is crucial…
  - site
  - organism
  - allergy to host?

Antibiotic therapy

- Other considerations…
  - route of administration
- Monitoring therapy
- Adverse effects
  - GI-tract, skin, haemopoietic system, renal system, liver

Acquired resistance

- Three major mechanisms of resistance
  - Alteration in drug target
  - Production of inactivating enzymes
  - Decreased uptake of antibiotic

Antibiotic resistance

- Resistance occurs when a susceptible microorganism is no longer inhibited by an antibiotic agent
- Many reasons why this can happen
  - intrinsic - characteristics of microorganism vis-à-vis antibiotic's mecanism of action (inherent or "natural"
  - acquired - new or added (driven by two genetic processes in bacteria…mutation and selection (vertical evolution); and exchange of genetic material (horizontal evolution)

The chromosome: role in antibiotic resistance…

- Mutations lead to
  - Change it site of antibiotic target (but protein for bacterial still works fine!)
  - Regulatory genes
    - turn on alternative path
    - turn on efflux mechanisms
  - Change cell permeability

Post-antibiotic era: is it possible?

- With current overuse of antibiotics, we are *forcing* bacteria to change (evolve) in order to survive

- How is this achieved/helped by us?

Decreasing antimicrobial resistance?

- Withhold antibiotics
  - self-limited viral infections (i.e., the “common cold”)
- Use narrowest spectrum antimicrobial agents
- Base decision about broadness of empiric antibiotic coverage on severity of illness
  - clinically stable and not at risk for significant morbidity…may be appropriate to wait culture results and MIC testing

Decreasing antimicrobial resistance?

- Prevention of infection
  - hygiene, handwashing
- Education
  - helps to achieve therapeutic and preventative goals
  - when are antibiotics needed?
  - how to take them?
  - proper duration!!
- Earlier detection of therapeutic failure
  - good for patients with antibiotic-resistant pathogens