? 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)
    Our bodies are throwing everything at the organism.
  - Specific (adaptive, acquired)

Innate Immunity

- Skin
  - What characteristics of the skin make it an effective mechanical barrier ? It is impermeable, has an acid pH, skin is dry, has secretion glands, has its own microflora
- Mucous membranes (mechanical)
  - Cilia in respiratory tract
  - Lysozyomes, pH - around 1 or 2 in stomach
- Iron-binding proteins
  - Some bacteria require iron for growth
  - Transferrin, lactoferrin
- Phagocytosis
  - PMNs, monocytes and macrophages

Certain WBC that circulate inside the body and mop up certain things.

- Complement - A set of circulating proteins inside the blood —>Can recognize certain sugars on the cell wall of bacteria (called membrane attack complex)

—> also can bind to anti-bodies and make them more attractive to the immune system

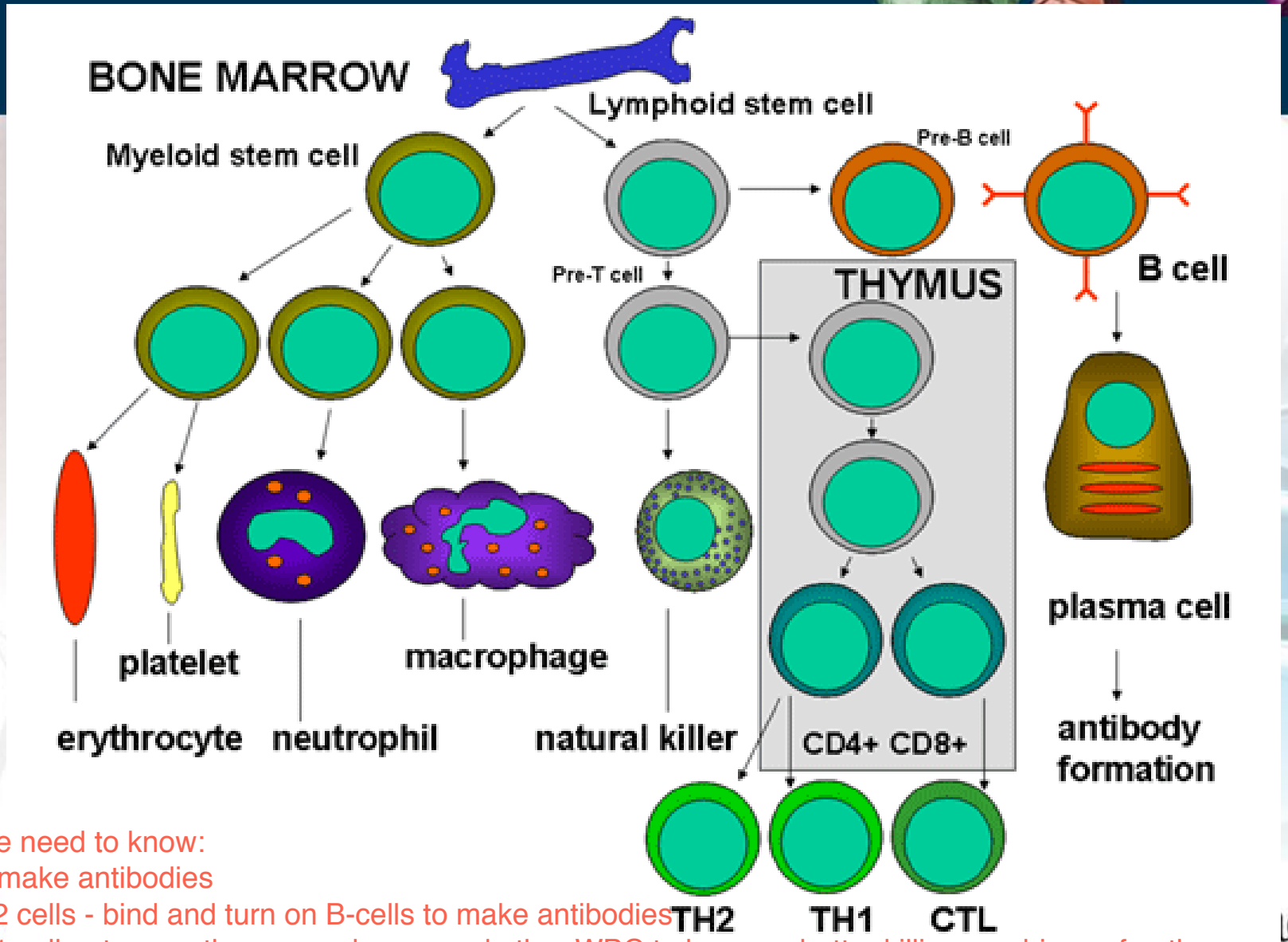
Specific Immunity

2 types of 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 Non-specific
  - ***Adaptive***: directed against one type of invader, dependant on past exposure Specific

Where do immune cells come from?



3 Cells we need to know:
B-Cells - make antibodies
T-helper 2 cells - bind and turn on B-cells to make antibodies
T-helper 1 cells - turn on the macrophages and other WBC to become better killing machines of pathogens

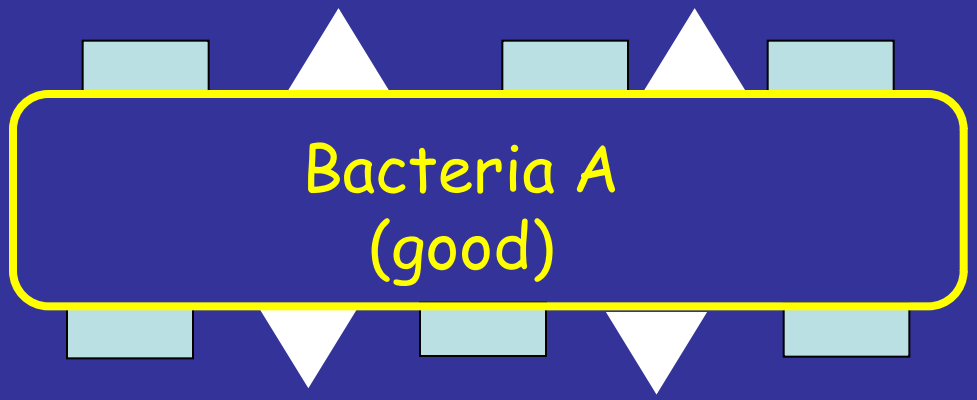
Humoral Immunity

- 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" - it doesn't recognize itself (so that it doesn't bind to and attack itself)
  - Protein, glycoprotein, lipoprotein, polysaccharide
  - What structures could be "antigenic" in a bacteria? Virus?
    - something about the cell wall or the outside of the cell wall

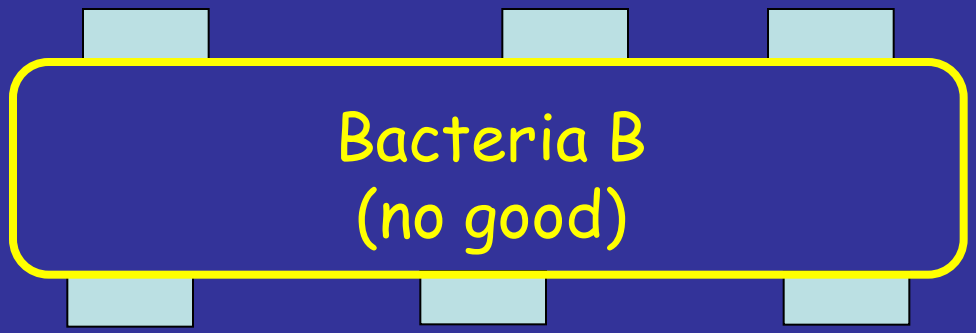
Antibody Binding: how does it occur?

Consider antibody as the shape of a “Y”. The bottom stick is the part we all have (the constant region) while the upper “v” is the specific binding part (variable region).

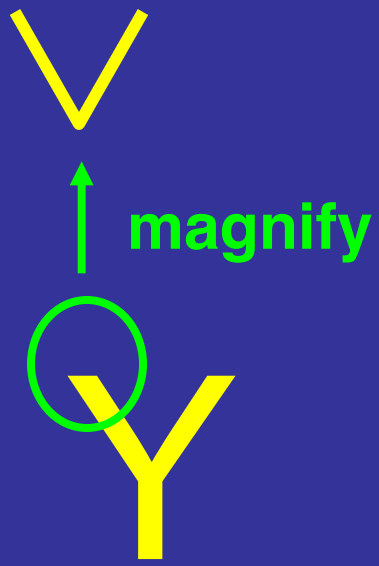


Antigen A

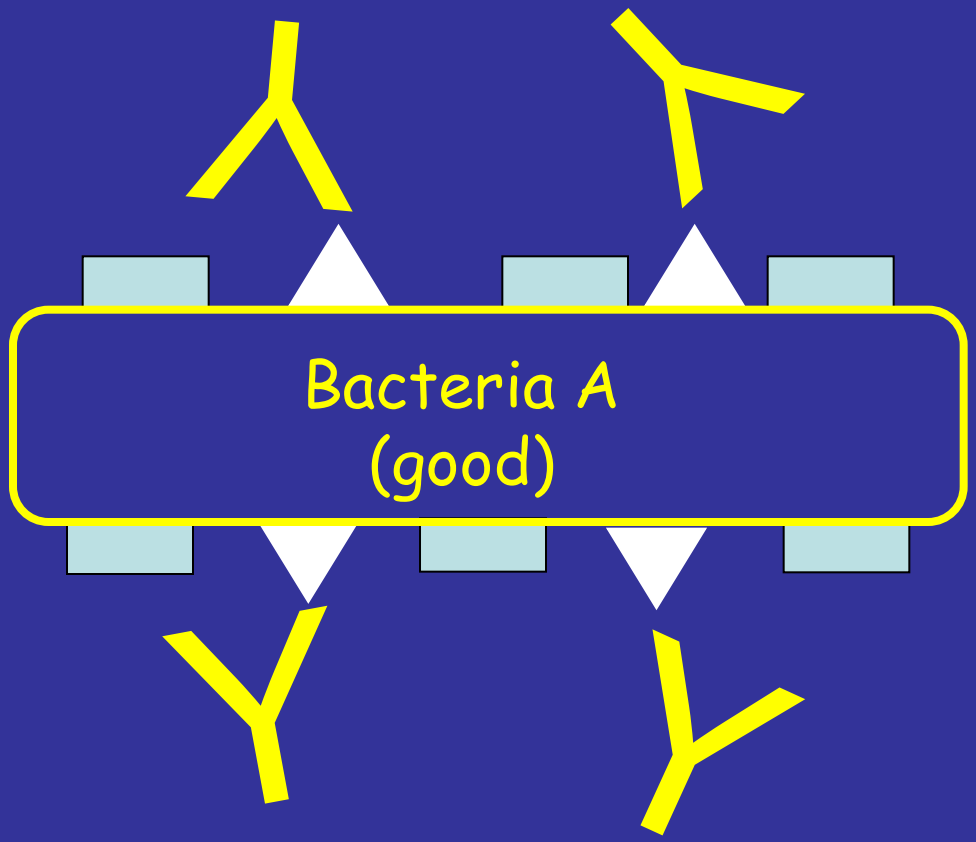
Antigen B



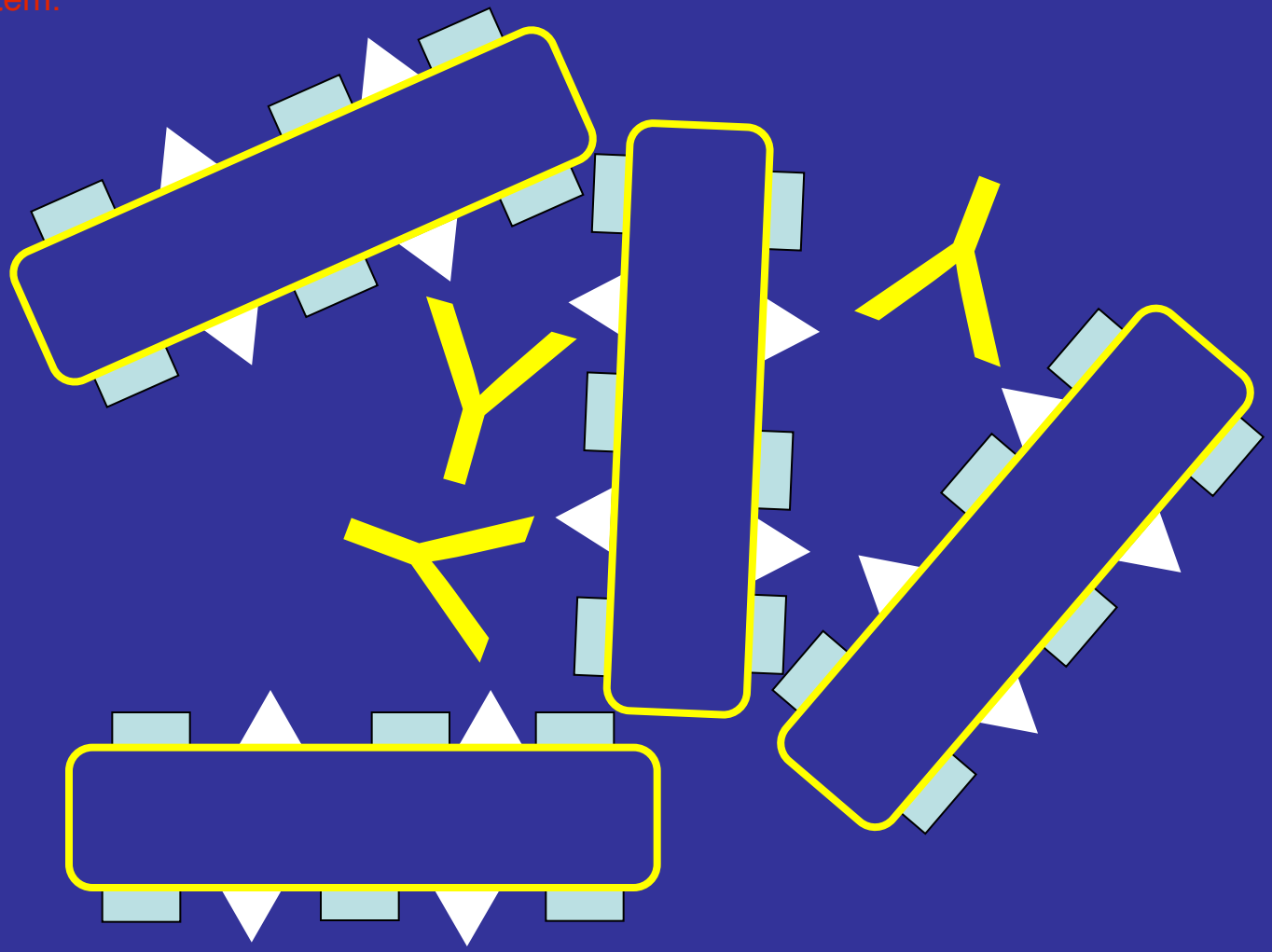
Antigen B



Antibody


Bacteria A
(good)

Agglutination is the binding and bringing together of pathogens by the antibodies which signals the immune system.



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

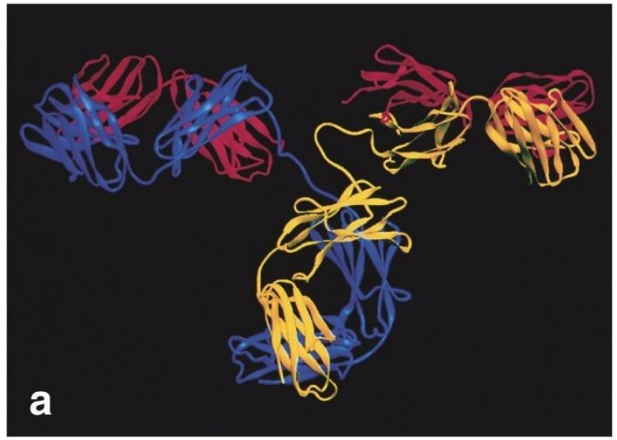


Figure 3-1 part 1 of 3 Immunobiology, 6/e. (© Garland Science 2005)

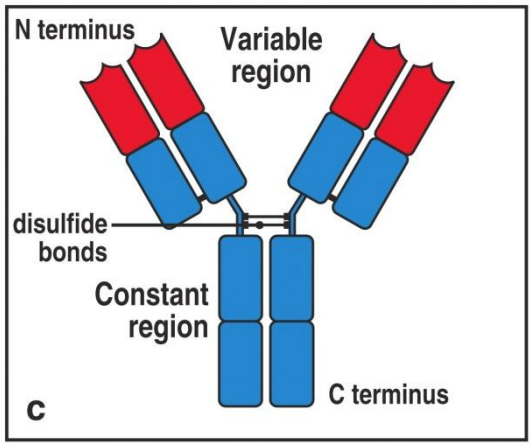
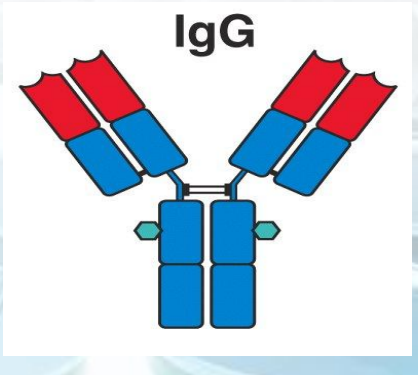


Figure 3-1 part 3 of 3 Immunobiology, 6/e. (© Garland Science 2005)

Classes of Igs

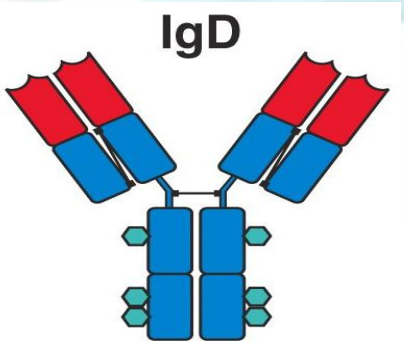
- 5 classes: IgG, IgA, IgM, IgE, IgD

- IgG
  - Host defense
  - Crosses placenta and protects newborn



- IgD
  - Role is unknown

We don't need to remember anything about this.
Its in such low levels in body



Classes of Igs

- IgA
  - Host defense
  - Found in secretions
    - Tears, saliva, milk, respiratory, GI and genito-urinary tract
  - Dimer
    - need two of them together to have a functional IgA molecule)
- IgM
  - Host defense
  - Early immune response
  - Pentamer
    First antibody produced
- IgE - bind to mast cells during allergic reaction to suppress the release of histamines
  - Hypersensitivity (allergies)
  - Defends against parasites

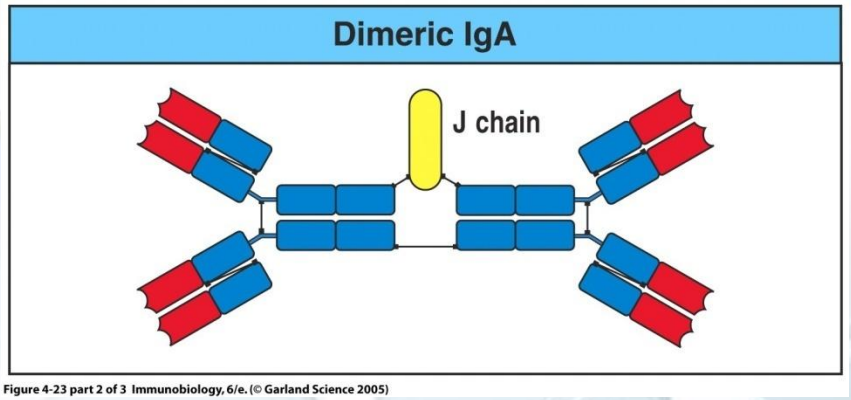


Figure 4-23 part 2 of 3 Immunobiology, 6/e. (© Garland Science 2005)

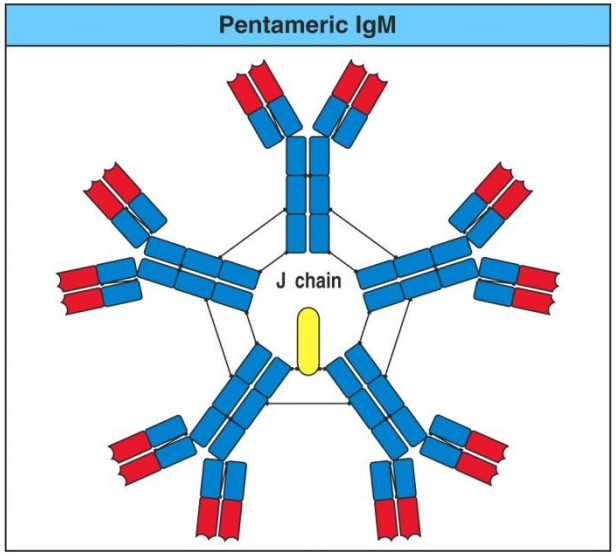


Figure 4-23 part 1 of 3 Immunobiology, 6/e. (© Garland Science 2005)

1º and 2º Immune Response

- 1º Response The first time a body encounters an antigen
  - 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 The second (or third or fourth) time a body encounters an antigen.
  - ★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

1°

2°

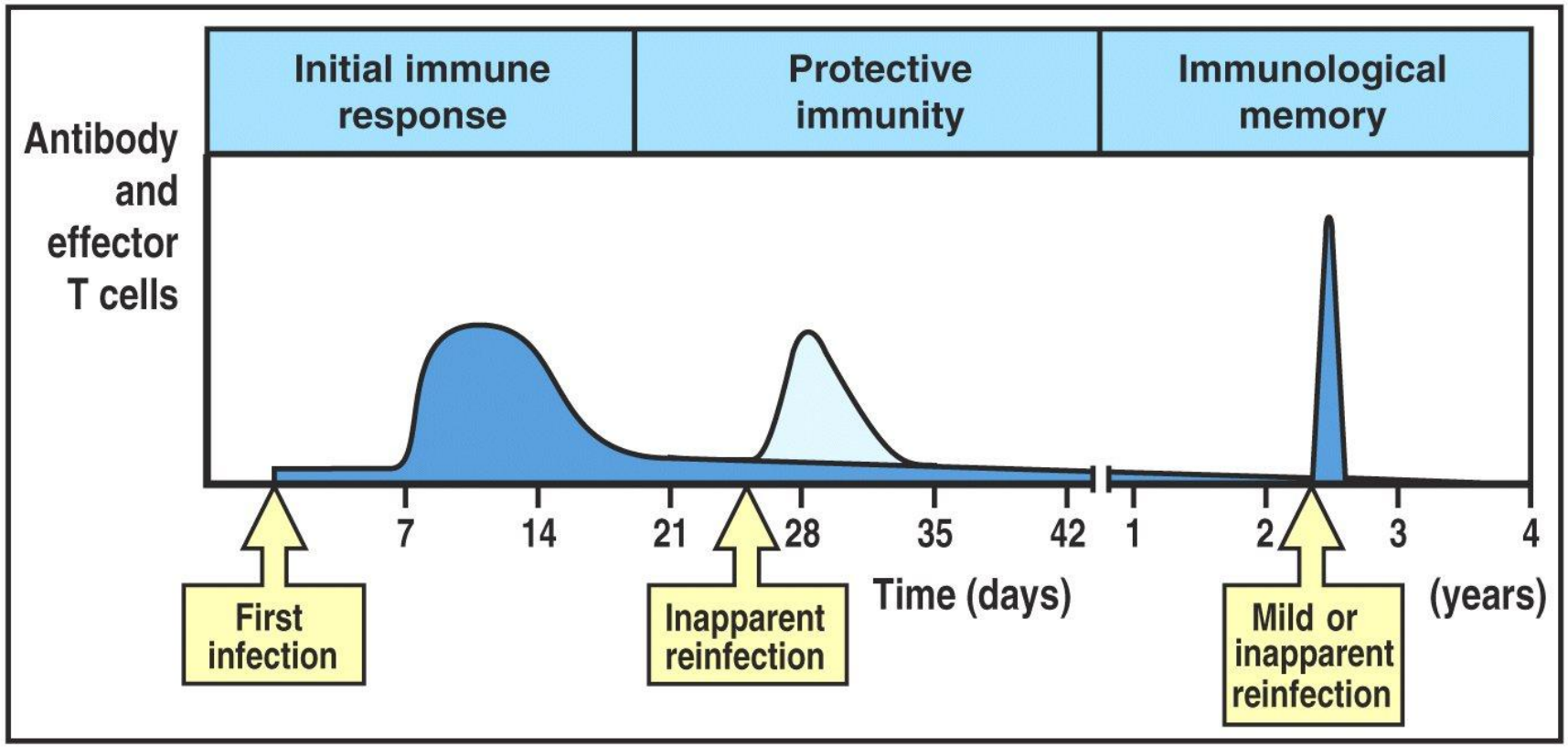


Figure 10-18 Immunobiology, 6/e. (© Garland Science 2005)

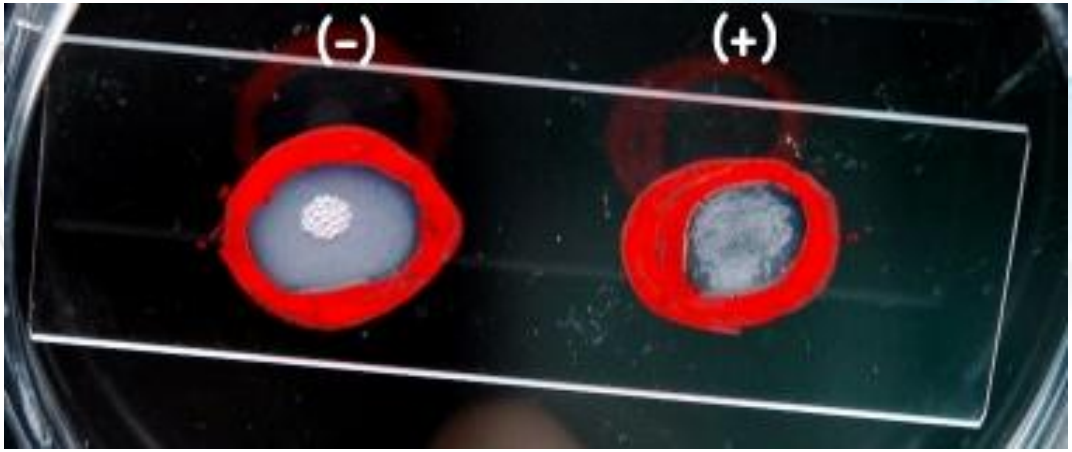
Antibody Detection

- Serological Reaction
  - Detects presence of antibodies in serum sample
  - Antigen and antibody interact; agglutination
  - Antibody titration

Measure how much antibodies you have circulating (to see if you have fought, are fighting or about to fight an infection).

  - Detect unknown microorganisms using known antisera

Where the antigens react to the antibodies, it results in a positive test.



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

Very strong immune system response

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

Demyelination of the myeline sheath is the immune system attacking the myeline sheath (causing MS)

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

Paralyzes immune response

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

During organ transplant try to find the “right match”. Have an organ with very similar antigens as your own body (reason for necessity of immune-suppressive medication).

Immunization

- Passive Immunization DO NOT WRITE TETNIS OR MEASLES ON THE EXAM (he does not want to know the names, you can use them as examples though)!
  - administration of pre-formed antibody against a *specific* microbial agent
  - IgG animal origin: short lived, risk of hypersensitivity reaction Bottom part of Y more different
  - IgG human origin: short lived, no risk of reaction Less chance of allergic 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

Only lasts for a short time (around a month) because it is a primary response (used when you do not have much time to be immunized)

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

- some antigens need to be in a live organism in order to work (the antigen must be extremely beat up in the lab so that they do not end up infecting you

Active Immunization (con't)

- Killed vaccines, sub-unit vaccines and toxoids
  - Antigens without infectivity
  - May require boosters because memory cells are dying or the immune response goes down
  - 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 So that the antigens hangs around for a longer time
  - 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

So that you can be protected for long periods of time

Canada's Immunization Guide:

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

Health Canada Santé Canada

Canada

Antibiotic Resistance

Introduction

- The first antibiotic (?)
  - discovered in 1929 by Sir Alexander Fleming
    He discovered penicillin
- World War II
  - penicillin used to treat staphylococci and streptococci (1946)
- How effective was penicillin?
  Very good for some, ineffective for others.

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? ☺ Figure out for next class
- Late 1940s and early 1950s?

Other antibiotics were also found

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 (Remember there's certain places in the body that shouldn't have things in it)
  - organism
  - allergy to host?

Antibiotic therapy

- Other considerations…
  - route of administration
    IV, orally, topical (skin)
- Monitoring therapy
- Adverse effects
  - GI-tract, skin, haemopoietic system, renal system, liver

Acquired resistance

WE WILL BE ASKED THESE ON THE EXAM

- Three major mechanisms of resistance
  - Alteration in drug target
  - Production of inactivating enzymes
    Ex. staph picked up a piece of DNA that encodes an enzyme that inactivates penicillin
  - Decreased uptake of antibiotic
    Physically change the porosity of the cell membrane so the antibiotic cannot get in or
    Antibiotic gets into the cell but then is pumped out just as fast

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?

  - Overprescribing antibiotics (especially the wrong antibiotic) (good bacteria inside body can become resistant to the antibiotic and they can then pass this resistance on to invading bacteria when they enter the body).
  - Not using the whole script
  - antibiotic use in healthy animals to promote growth

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