Foundations of Public Health
Immunology

Humoral Immune Response

Objectives
• Identify and explain the clonal selection and expansion process
• Identify similarities and differences of the primary and secondary immune responses
• Describe the processes of isotype switching, affinity maturation, & memory
• Describe the relationship between humoral immune response and vaccines

Humoral Immunity
• Mediated by antibodies
• Principal defense against extracellular microbes & their toxins
  • Critical for defense against microbes with capsules rich in lipids or sugars
  • Improves during immune response

Immune System Fights Back!
• Humoral Immune Response: Outline
  • Clonal Selection & Expansion
  • Primary & secondary responses
  • Changing of the guard: Affinity maturation & isotype Switching
  • Memory & vaccine intro

Clonal Selection & Expansion Theory
• Immune system can distinguish between nearly a billion different antigens
• Every person has a vast pool of clonally derived lymphocytes (T & B) with different Ag receptors
• When an antigen enters, it selects a preexisting clone and activates it

Clonal Expansion
• Activated clone expands to make identical effector & memory cell clones
• Plasma cells produce antibodies to clear the antigen & some memory cells remain to prevent future antigen attacks
• Reason why VACCINES work!
  • Vaccinated (given an Ag) as a child so that you will activate the clone & produce antibodies, memory cells
  • If you are re-exposed later in life, your immune system already has clones ready to go!!
  • Some vaccines provide lifetime of immunity
Clonal Selection & Expansion

Phases of Humoral Immune Responses

Primary Immune Response
- It takes time to build an effective immune response after Ag recognition
- On first exposure to an antigen, clonal selection will take many days to expand & produce effector cells for antibody production
- Affinity maturation & class switching occur as the immune response progresses (IgM to IgG)

Secondary Immune Response
- On second exposure to the same antigen, memory cells will quickly respond to produce antibodies
- Decreased lag time & much stronger response

The Antibody Response Curve
Isotypes in Primary vs. Secondary

- Primary response
  - B cells produce IgM and low levels of IgG antibodies
- Secondary response
  - B cells produce some IgM at first
  - Quickly switch and produce high levels of IgG antibodies
- Note the different times and strengths of each response!

Note: Only have a strong secondary response to same Ag A, but normal primary response to Ag B when added at same time. Specificity!
**Isotype Switching**

- Progressive change in the relative quantities of Ab isotype with time
- Isotype & subclass depends upon stimulus and location
- For example, IgA & E – MALT
- Usually IgM to IgG
- Requires T cell help (CD4+ cells) & cytokines

---

**Affinity Maturation**

- Higher average affinity of Abs produced during a secondary response
- Associated with IgM to IgG isotype switch
- T-cell dependent Ags only
- Low Ag dose induces better affinity maturation than high Ag doses; only B cells with high affinity receptors can bind enough Ag, selective clonal expansion
- Somatic hypermutation can increase affinity with out changing Ag specificity

---

**Advantages of High Affinity Antibody**

- Hemagglutination
- Hemolysis
- Complement fixation
- Passive cutaneous anaphylaxis
- Bactericidal activity
- Toxin neutralization
- Opsonic activity
- Immune elimination of antigen
- Membrane damage
- Virus neutralization
- Protective capacity against bacteria and viruses
- Enzyme inactivation

---

**Memory**

- The capacity to mount a secondary response to the same Ag
- Larger numbers of antigen-specific T & B lymphocytes produced as a result of clonal expansion during the primary response
- Memory T cells have higher affinity TcR Ag receptors & IgG is made earlier by B cells
- Memory T cells respond to lower doses of Ag
- Memory CD4+ T cells produces cytokines more rapidly

---

**Anatomy & Humoral Immunity**
Memory & Vaccination
- The capacity of the immune system to remember a pathogen has practical applications – Memory is the key!!
- Vaccines are the most important application of the humoral immune response

Extremely Brief Intro to Vaccines
- Principle of vaccination: introduce harmless antigen(s) with epitopes also found on the pathogen
- The immune system develops its own immunity against the pathogen
- 5 types: live, killed/inactivated, subunit, toxoid, & recombinant vaccines

Vaccine Intro
- Most vaccines generate antibody response, not cell-mediated
- Vaccination stimulates clonal expansion of B cells to antigen(s) like those found on real pathogen
- Generates memory
  - If a person is re-exposed to the real agent, the immune system can quickly neutralize the agent (protective immunity) via humoral immunity

In Summary
- Clonal selection & expansion theory
- Differences between the primary & secondary immune response
- Understand processes of isotype switching and affinity maturation to improve immune response
- Describe how memory is generated, where memory cells reside

Self-Test Questions
- What is clonal selection? Are the B cells created after the antigen enters?
- What isotype is produced during the primary immune response? Secondary?
- What is needed to stimulate isotype switching?
- What is affinity maturation? How does this improve the immune response? Where does it occur in the lymph node?
- Why do vaccines generate protective immunity (in terms of the humoral immune response)?