Lecture 26: Infectious Diseases
Suggested Reading: Chap. 12
Key Terms:
- Antigenic drift/shift
- Bacterial Evasion Mechanisms
- Viral evasion mechanisms
- Dengue Fever
- T-cell dependent responses

A. Summary of response to extracellular bacterial infections:

A1: Innate Response:
- Physical Barriers – Skin, mucus, biofilms of non-pathogenic commensal bacteria on mucosal membranes (e.g. vaginal).
- Physiological/Chemical Barriers:
- Cellular Barriers: Local tissue phagocytes clear up small infections. Activation via TLR-4.

A2: Humoral Response:
- Antibody binds to antigens on bacterial surface and opsonizes the organism; phagocytosis in tissue or spleen (blood) clears the bacteria.
- Antibody to bacterial toxins binds to the toxin molecule and antibody-toxin complex is cleared by phagocytes like other antigen-antibody complexes.

A3: Complement system
- Activated by binding of specific antibody to bacterium or by the alternative pathway.
- Direct lysis can occur.
- Opsonization by C3b followed by C3b receptor mediated phagocytosis via Mφ, neutrophil
- Release of split products like C3a and C5a that are anaphylatoxins, inducing mast cell degranulation releasing mediators that cause vasodilation and chemotactic factors that attract lymphocytes, macrophages and neutrophils thereby building up phagocytic cells at the site of infection.

Effectiveness of pathogen clearance:
- Uncoated (90%)
- Ab opsonized w/o C3b (1%)
- C3b opsonization + MAC (0.01%)
B. Mucosal Defense System:  
Pathogens on the outside of the body are constantly sampled by lymphocytes and dendritic cells in MALT (mucosal associated lymphoid tissue). IgA secreted by B-cells in the MALT tissue prevents entry of pathogen.

Transcytosis of Secretory IgA:  
1. IgA binds to poly-Ig receptor  
2. Endocytosis occurs  
3. Vesicle transported across cell  
4. Fusion and release of cargo, containing part of the poly-Ig receptor.

C. Key Concepts for Pathogen Evasion:  

C1. Antigenic Drift: Small changes in the structure of surface antigens lead to loss of recognition of antigen, e.g. capsid protein on HIV (human immunodeficiency virus).

C2. Antigenic Shift: Large changes in antigen. Some pathogens repeatedly change the antigenic composition of their surface. e.g: i) pili on Neisseria gonorrhoeae, ii) flu virus.

C3. Multiple Serotypes: Single protein has many different alleles each of which is antigenically different. No interconversion between serotypes.

D: Some Bacterial Evasion Mechanisms.

D1. Degradation of Secretory IgA. Secretion of a protease that cleaves IgA, rendering it ineffective e.g. Neisseria gonorrhoeae, Neisseria meningitidis, Hemophilus influenzae.

D2. Attachment to host cells - bacteria have specialized structures or molecules that enhance the ability to attach to host cells. For example, gram negative bacteria have pili, such as N. gonorrhoeae, that enable them to attach to the membrane in intestine and genitourinary tracts.

*Salmonella* – projection that binds MAC away from cell membrane.

*Staphylococcus* – C3 convertase (C3bBb) can’t bind.

D4. Bacteria possess surface structures that inhibit phagocytosis. For example, secretion of variant polysaccharide capsule e.g. *Streptococcus pneumoniae*

D5. Intracellular growth – Formation of granuloma (TB, leprosy)


E. Innate & Adaptive Immune Response to Viruses

- Type I IFNs (alpha, beta) cause neighboring cells to enter anti-viral state
- NK cells kill virally-infected cells.

- B-Cell produce Ab that neutralize virus particles
- CD8+ T<sub>CTL</sub> cells kill virally infected cells, requiring T<sub>H</sub> participation.
D3. Interfering with the complement system. 
*Haemophilus influenzae* – inactivates C5a
*N. gonorrhoeae* produces an outer-
membrane protein that inhibits the insertion
of C5b-C9. Also enhances degradation of
C3 convertase.
*Salmonella* – projecion that binds MAC
away from cell membrane.
*Staphylococcus* – C3 convertase (C3bBb)
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