Microbiology

Applications of Immunology -
Vaccines
Diagnostic Immunology

Controlling infection in populations

• Breaking the chain of transmission
  – Maintain adequate water quality
  – Ensure food safety
  – Control vector populations
  – Provide reproductive health services
  – Screen critical personnel for exposure (e.g., TB tine testing)

• Vaccination
  – Potentially allows secondary immune response to primary pathogen exposure
  – Goal is herd immunity, where transmission cannot be maintained in a population

Edward Jenner

• First to demonstrate that immunity could be invoked by something other than the infectious agent
• The word vaccination refers to the cowpox virus, Vaccinia
• His enemies
  – Denied efficacy of vaccination relative to variolation
  – Then tried to deny priority!
Earl of Sandwich: “Upon my honor, Wilkes, I do not know whether you will die on the gallows or of the pox.”

John Wilkes: “That must depend, my Lord, upon whether I first embrace your Lordship’s principles or your Lordship’s mistresses.”

Products of the Jennerian revolution

- **Attenuated vaccines**
  - “Live” microorganism capable of limited reproduction in healthy hosts
  - Examples: measles, mumps, rubella, varicella, polio (Sabin), BCG
  - Advantages
    - Relatively inexpensive to produce
    - Invoke balanced immunity with T cell memory
    - May vaccinate people who haven’t been vaccinated!
  - Disadvantages
    - Relatively expensive to store and transport
    - Potential for reversion to virulence
    - Potential for virulent infection of immunocompromised hosts
**Attenuation**

- Basic idea is to select for mutants that have lost virulence
- Repeated subculture on nonhuman cell lines, growth at low temperature
- Genetic engineering offers great promise, but…

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**Inactivated vaccines**

- “Killed”, whole microorganisms
- Examples: Influenza, polio (Salk), pertussis, typhoid
- Advantages
  - Stable antigenic preparations
  - If properly prepared, no risk of reversion to virulence or infection of immunocompromised hosts
- Disadvantages
  - Relatively expensive to prepare
  - Inadequate inactivation could be disastrous
  - Memory weak compared to natural infection, attenuated vaccination
Other vaccines

- **Subunit** vaccines - Macromolecular components of microorganisms
  - Examples: hepatitis B, HIB, pneumovax, meningococcal meningitis, pertussis (acellular)
  - Bacterial polysaccharides are conjugated to proteins to provide T cell epitopes
  - Proteins may be produced in recombinant culture
- **Toxoids**
  - Exotoxins lightly denatured
  - Examples: tetanus, diphtheria
Other experimental vaccines

• Synthetic antigens
  – Proteins engineered to express particular combinations of T cell and B cell epitopes
  – Care must be taken to ensure effective presentation by multiple MHC haplotypes

• DNA vaccines
  – If foreign genes can be introduced into cells, their expression may invoke T cell responses
  – If they work, DNA vaccines would be the ultimate in stability and economy
Diagnostic Immunology - Precipitin

- **Antigen-antibody complexes** form visible precipitates.
- This allows clinical laboratory scientists to:
  - use specific antibody to identify antigen in a sample
  - use antigen to identify specific antibody in a sample

Ouchterlony Double Diffusion

Diagnostic Immunology - Agglutination
DIAGNOSTIC IMMUNOLOGY - FLUORESCENCE ANTIBODY TECHNIQUES

Fluorescence-Activated Cell Sorting (FACS)

ENZYMATIC LINKED IMMUNOSORBENT ASSAYS (ELISAs)
Indirect ELISA for detection of antibody

1. Antigen is adsorbed to well.
2. Patient antibodies are added; conjugated anti-antibody binds to bound antibody.
3. Enzyme-linked anti-antibody is added and binds to bound antibody.
4. Enzyme’s substrate is added, and reaction produces a visible color change.

A positive indirect ELISA to detect antibodies.