Focus on bacterial and viral diseases

No attempt to comprehensive

Limited selection of illustrative organisms

The key roles of the immune system

Ability of bacteria and viruses to cause disease is largely dependent on their ability to resist elimination by immune responses.

Many bacterial and viral functions that are essential for virulence neutralize immune system functions

Immune responses are responsible for a substantial fraction of the pathogenesis during infection

Importance

Disease burden

As a probe of host system function

The need for new vaccines and anti-infectives

Comments on Evolution

Idiosyncratic nature

Limits the predictive power of general principals

Results in a very complex array of species and interactions

Requires detailed study of specific interactions for understanding

Infectious disease is among the most powerful forces driving evolution

Formal definition of evolution: change in allele frequency

Ability of infectious disease to produce rapid evolutionary change

The time scale is short enough to be of practical concern at several levels

New variants of important diseases arise frequently

Mutation routinely gives rise to variants of clinical importance in individual patients with particular infections

Development of drug resistance is a major problem
Is high virulence ever advantageous?

Patterns of disease

*Intimacy of interactions with cells*

Extracellular bacteria with no cell association

Extracellular bacteria that bind to cell surfaces

Usually involves delivery of effector proteins to host cell cytoplasm

Facultative intracellular bacteria

Retain the ability to grow in the absence of host cells

Some grow within modified vacuoles and manipulate vacuole trafficking

Others escape from vacuoles and grow free in cytoplasm

Obligate intracellular bacteria

Cannot grow outside of host cells

Highly degenerate bacteria with small genomes

Some species (all chlamydiae, one rickettsia) have a two-stage life cycle and produce a hardy metabolically inactive infectious form

Viruses

Mature infectious virion is metabolically inactive

Viral protein synthesis is entirely dependent on host cell machinery

Viral nucleic acid and protein synthesis do not occur in a membrane-bound compartment sequestered from the host cell as they do for intracellular bacteria

This allows host antiviral strategies (inhibition of protein synthesis, degradation of nRNA, detection dsRNA) that don’t work with bacteria.

*As use of intracellular lifestyle by bacteria increases, cell-mediated immunity becomes more important.*
For organisms that grow or survive in macrophages or dendritic cells, the potential for dissemination also increases.

Five major mechanisms of pathogenesis

- Tissue damage or alteration of tissue function mediated by specific toxins or cytopathic effects independent of immune responses
- Localized tissue damage due to inflammation
- Induction of global inflammatory response by systemic infection
- Autoimmune sequelae
- Genetic alteration of host cells: Cancer

*Note that immune response contribute to pathogenesis in three of these four mechanisms*

Degree of control by immune responses

- Complete control by innate immunity
  - Most bacterial infections
  - Escapes control by innate immunity, but adaptive response can eliminate pathogen
  - If pathogen grows rapidly and spreads, adaptive response may not result in survival
  - Escapes control by innate immunity, and persists in a chronic state in the face of adaptive immunity
  - The immune system has no role in determining the course of infection

Dissemination

- Remains localized to the site of infection
- Limited spread to adjacent tissue by non-hematogenous route
- Unlimited spread to adjacent tissues by non-hematogenous route
- Reaches bloodstream, but is effectively cleared
- Reaches bloodstream and establishes infection in specific organs
- Reaches bloodstream and establishes infection in many organs