General Trends in Infectious Disease

Four phenomena underline the increase in ID problems:

– Aging population
– Increasing numbers of immunocompromised patients
– Increased mobility of the population
– Newly emerging infection
  • *Legionella* species
  • Fungi (*Ex*: *Scedosporium, Fusarium*)
  • Viruses (*Ex*: HHV-6, -7, -8; hemorrhagic fevers)
Paradigm: Tuberculosis

- AIDS promotes the spread of tuberculosis
- Because of the impaired inflammatory response, disease further advanced, with higher microbial burden at time of discovery. Facilitates spread from person-to-person
- Confluence of two processes in the same population (inner city minorities and developing countries)
  - Drug-resistant TB
  - HIV infection
- End result: Potential disaster
- Solution: Case finding and surveillance; directly observed therapy
Symptom
Severity

Time

- Normal host
- Immunocompromised host
Microbial load

Time

Normal host
Drug Resistance

• Bacteria produce enzymes that either destroy the antibiotic (beta-lactamases) or add bulky groups to structure, presenting penetration of bacterial cell wall (Ex: aminoglycosides)

• Alteration of target molecules
  – Penicillin binding proteins
  – Folic acid synthetic enzymes

• Change in porins that permit antimicrobial entry into bacterial cells

• Acquisition or expression of pumps that rid the cell of the antimicrobial drugs
Problem Organisms

• Multi drug-resistant *Mycobacterium tuberculosis*

• Beta-lactamase producing bacteria
  – *Staphylococcus aureus*
  – Gram negatives, particularly beta lactamase hyper-producing gram negative bacilli (e.g., *Serratia, Enterobacter*, etc.)

• Vancomycin-resistant enterococci
  – Vancomycin intermediate resistance in *S. Aureus*

• Penicillin-resistant *Streptococcus pneumoniae*

• Azole-resistant yeast
Special Problems of the Enterococci

- Naturally **tolerant** (bacteriostatic effect)
  - Conventional treatment: penicillin + gentamicin = synergistic killing (bactericidal effect)

- High level gentamicin resistance (= no bactericidal effect)

- Beta lactamase production--need vancomycin

- Vancomycin-resistant enterococci (change in penicillin binding proteins)

- Enterococci are “wimp organisms”. Big worry is if *Staphylococcus aureus*, a virulent species, becomes vancomycin resistant (as of today, only intermediately resistant *Staphylococcus aureus*)
What Has Been Done to Meet These Challenges?

• A dearth of new structures that are effective antimicrobial agents
  – Virtually all new antimicrobials represent old structures with new medicinal chemistry.

• Minimal efforts for new vaccines
  – Liability issues and tort law

• Need new technology for both discovery and development
Clinical Conditions Which Require Bactericidal Therapy

• Severe neutropenia
• Central Nervous System infection
• Staphylococcal (and presumably other forms) of osteomyelitis
• Cardiovascular infection
• Prosthesis-associated infections
  – Hip, knee, and other joint prostheses
  – Vascular access devices
  – Foreign body associated infection
The Second Law of Thermodynamics
According to an Infectious Disease Practitioner

• The world is constantly heading towards chaos and disaster.
  – The Post-antimicrobial Era (antimicrobial resistance)
  – Bio-terrorism
  – Newly Emerging Infections
1969 - Lhassa Fever

- index illness: a native nurse who had cared for a local person with a similar illness, dying with:
  - Encephalitis (seizures, focal neurologic disease)
  - Hepatic necrosis
  - DIC

- SPREAD:
  - American nurse → 5 caretakers at Presbyterian Hospital
The Paradigm of Patient Care

Algorithms vs. Anomalies
“... It is time to close the book on infectious diseases. The war against pestilence is over.”

William Stewart, Surgeon General in a message to Congress, 1969
“Our heads are round so that our thinking can change direction.”

- Francis Picaba
"No medicine in the world can do thee good ...."

Laertes to Hamlet

*Hamlet*, Act V, Scene 2

W. Shakespeare