

General Trends in Infectious Disease

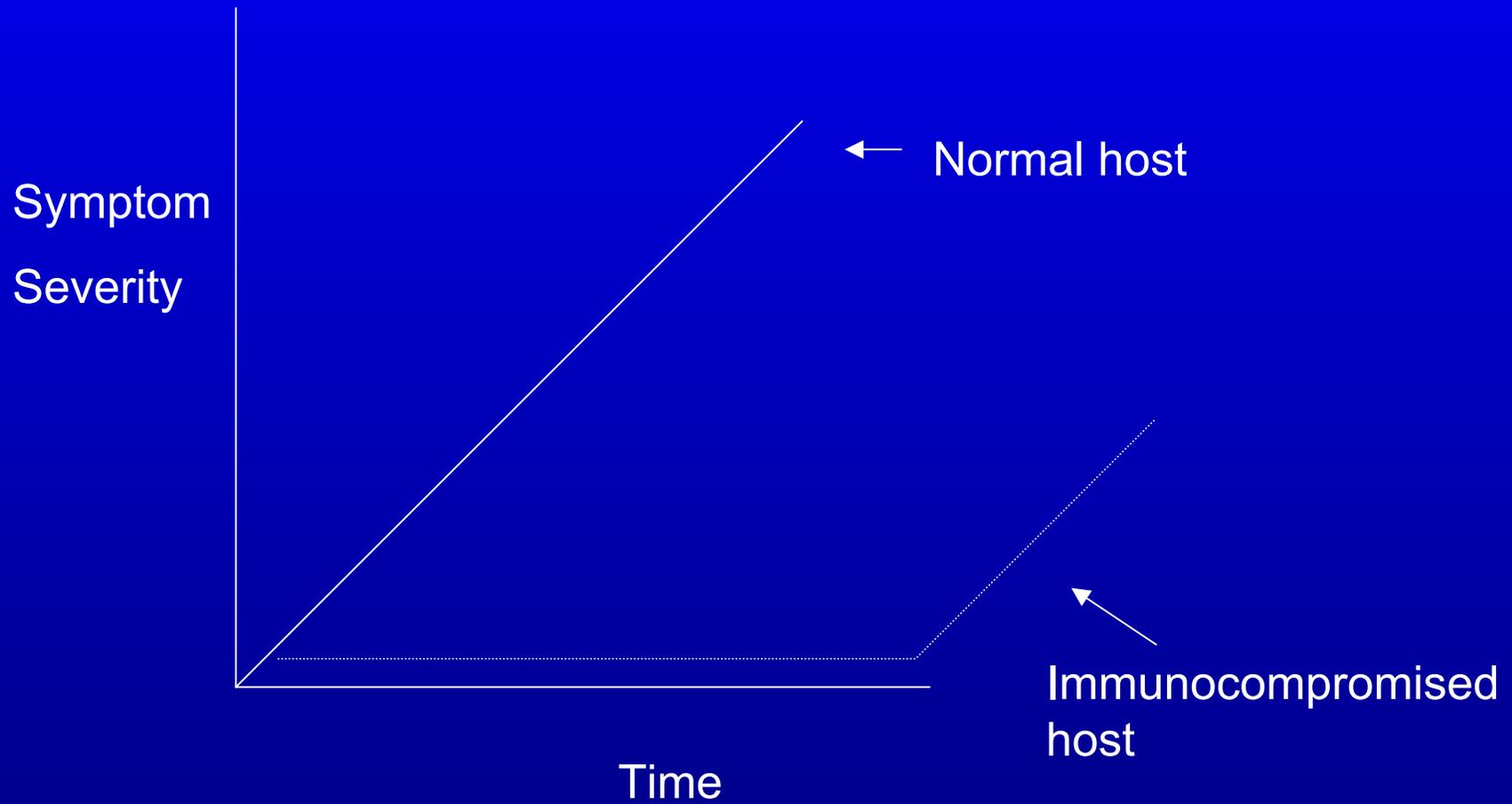
Four phenomena underline the increase in ID problems:

- 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)

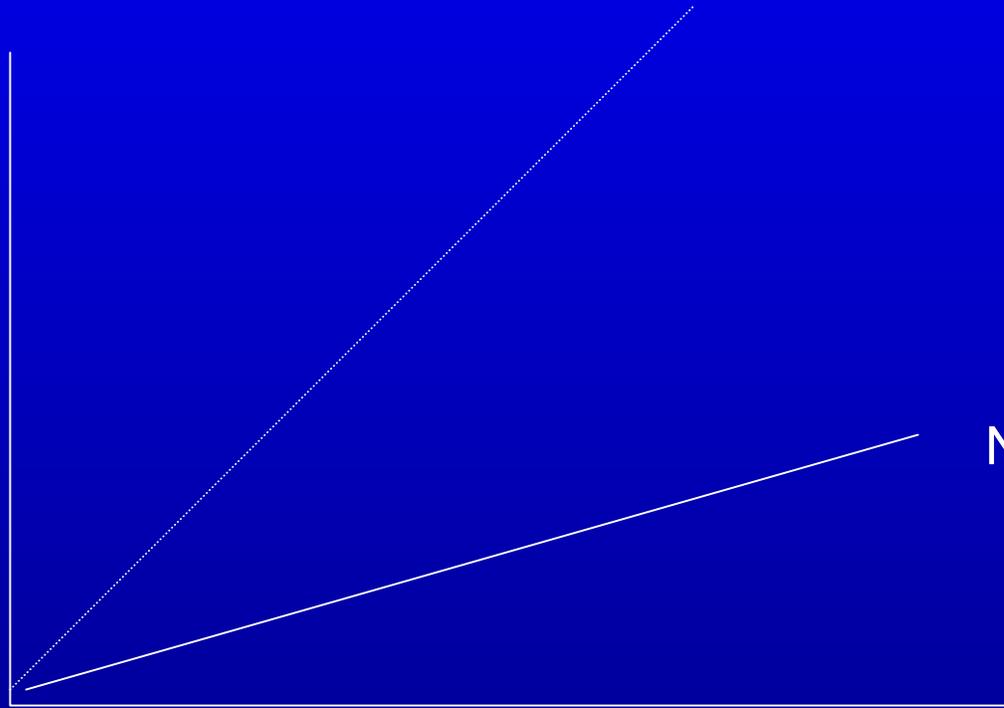
AIDS and Other Infections

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



Microbial
load



Normal host

Time

Drug Resistance

- Bacteria produce enzymes that either destroy the antibiotic (beta-lactamases) or add bulky groups to structure, preventing 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 - Lhasa 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